TECHNISCHE UNIVERSITÄT MÜNCHEN

DEPARTMENT CHEMIE

LEHRSTUHL FÜR ORGANISCHE CHEMIE I

Enantioselective Lewis Acid Catalyzed Photochemical Rearrangement Reactions of Cyclohexadienones

Malte Christian Leverenz

Vollständiger Abdruck der von der Fakultät für Chemie der Technischen Universität zur Erlangung des akademischen Grades eines Doktors der Naturwissenschaften genehmigten Dissertation.

Vorsitzender: Hon.-Prof. Dr. Richard W. Fischer

Prüfer der Dissertation:
1. Prof. Dr. Thorsten Bach
2. Prof. Dr. Ulrich K. Heiz

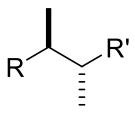
Die Dissertation wurde am 09.03.2020 bei der Technischen Universität München eingereicht und durch die Fakultät für Chemie am 13.04.2020 angenommen.

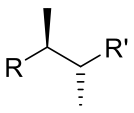
This thesis was prepared at Chair of Organic Chemistry I at Technische Universität München under the supervision of Prof. Dr. Thorsten Bach between June 2016 and February 2020.

Parts of this thesis were published:

M. Leverenz, C. Merten, A. Dreuw, T. Bach, *J. Am. Chem. Soc.* **2019**, *141*, 20053-20057.

In this thesis the relative configuration of racemates is represented with straight bonds (bold or hashed). The absolute configuration of enantiomerically pure or enriched compounds is illustrated with wedged bonds (bold or hashed).

racemic 

enantiomerically pure
enantiomerically enriched 

Beginnen möchte ich damit, meinem Doktorvater Prof. Dr. Thorsten Bach für die herzliche Aufnahme in seinen Arbeitskreis und die Betreuung während meiner Promotion zu danken. Die faszinierende und anspruchsvolle Themenstellung konnte ich dank der gewissenhaften Betreuung mit vielen aufschlussreichen Gesprächen erfolgreich meistern. Gleichzeitig bin ich dankbar für die Freiheiten, die ich im Rahmen meiner Forschung erhalten und denen ich wichtige Erfahrungen zu verdanken habe. Ebenso weiß ich den Aufwand der fachlichen Weiterbildung außerhalb meines Promotionsthemas sehr zu schätzen.

Bei Prof. Dr. Richard Fischer und Prof. Dr. Ulrich Heiz bedanke ich mich herzlich für die Übernahme des Prüfungsvorsitzes und des Koreferats.

Bei Dr. Andreas Bauer möchte ich mich, vor allem als Photochemiker, für die immense Unterstützung bei praktischen Problemen im Photolabor bedanken. Die große Leidenschaft für das Equipment und dessen stetige Erweiterung haben sehr zum Gelingen meiner Arbeit beigetragen. Bei Dr. Stefan Breitenlechner bedanke ich mich für die Unterstützung im Laboralltag und das offene Ohr für allerlei Probleme. Auch werden mir die zahlreichen Beisitze bei Kolloquien in guter Erinnerung bleiben. Beiden möchte ich außerdem für ihre Unterstützung während der Praktikumsbetreuung, ihre gute Laune und die daraus resultierende angenehme Arbeitsatmosphäre meinen Dank aussprechen.

Ein besonderer Dank gilt Kerstin Voigt, der ich es zu verdanken habe mehr Zeit mit meiner Forschung anstatt mit Bürokratie zu verbringen. Ihre kompetente und schnelle Hilfe in so vielen Belangen, sowie die vielen netten Gespräche haben meine Promotion sehr erleichtert.

Olaf Ackermann möchte ich für den verlässlichen Einsatz rund um die Laborausrüstung, sowie die gewissenhafte Messung meiner HPLC-Proben danken. Jürgen Kudermann möchte ich für die enthusiastische Hilfe und fruchtbaren Diskussionen über Gaschromatographie, die mir ein hohes Maß an Unabhängigkeit für meine Messungen verschafften, meinen Dank aussprechen.

Dr. Christian Merten danke ich für seine VCD-Messungen zur Aufklärung der Absolutkonfiguration meiner Photoprodukte. Prof. Dr. Andreas Dreuw gebührt mein Dank für seine DFT- und TDDFT-Berechnungen zur Aufklärung des Reaktionsmechanismus.

Ein besonderer Dank gilt allen ehemaligen und aktuellen Mitgliedern des AK Bach mit denen ich gemeinsame Zeit verbracht habe, sei es im Labor, im Seminar, in der Kaffeeküche oder auch außerhalb der Universität. Die außerordentlich angenehme Arbeitsatmosphäre und die großartige Hilfsbereitschaft meiner Kollegen haben meine Promotion zu einer unvergesslichen Zeit gemacht, an die ich mich gerne erinnern werde.

Meinen Labornachbarinnen und -nachbarn in Box 2, Simone Stegbauer, Julia Dürner, Alexander Böhm, Raja Sekarreddy Annapuredy und Johanna Löhr danke ich für ein kollegiales und hilfreiches Miteinander. Meinen Subgroup-Mitstreitern, Verena Edtmüller, Saner Poplata, Simone Stegbauer, Sachinkumar Modha, Noah Jeremias und Johanna Löhr gebührt mein Dank für ihre qualitativ hochwertigen Diskussionen, insbesondere dabei Saner und Simone für den regelmäßigen Austausch über die Oxazaborolidinchemie auch außerhalb der Meetings.

Meine Forschungspraktikanten Markus Weber, Matthias Nobis, Lilla Koser, Daniel Schwinger, Christian Gawanda, Simon Bodesheim, Niklas Pflaum, Anton Maier und meinem Bacherlorstudenten Dennis Huber möchte ich herzlich für ihren Einsatz im Labor und ihren Beitrag zu meinem Forschungserfolg danken.

Desweiteren bedanke ich mich bei Simone Stegbauer, Hanusch Grab, Raphaela Graßl, Lukas Fritz, Franziska Pecho, Manuel Plaza Martinez, Lilla Koser, Golo Storch, Yeshua Sempere Molina und Johannes Großkopf für ihre akribischen Korrekturen und hilfreichen Anmerkungen, die maßgeblich Anteil an der Qualität dieser Arbeit besitzen.

Außerdem möchte ich mich von ganzem Herzen bei meinem Freundeskreis bedanken. Ob in München, Köln oder Irland (thanks lads), ich konnte mich immer darauf verlassen etwas Besonderes zu erleben.

Zu guter Letzt gebührt mein großer Dank meiner Familie, allen voran meinen Eltern und meinen Brüder Nils und Jan, die mich in all der Zeit bedingungslos unterstützt und mir die Ausdauer für dieses Projekt gegeben haben. Den größten Rückenhalt habe ich jedoch Maximiliane zu verdanken. Seit fast zehn Jahren finde ich bei ihr immer ein geduldiges, offenes Ohr und uneingeschränkt die Unterstützung, die mich vor allem nach Rückschlägen immer wieder neu motiviert. Danke, dass ich dich habe!

Für meine Familie

Umlagerungen sind eine nützliche Methode um bestimmte Kohlenstoffgerüste herzustellen, die anderweitig einen großen synthetischen Aufwand erfordern. Photochemische Umlagerungen sind dabei ein besonders faszinierendes Werkzeug um komplexe Grundstrukturen aufzubauen und haben zahlreiche Anwendungen in dem Bereich der Naturstoffsynthese gefunden. Die enantioselektiven Varianten dieser Photoumlagerungen haben trotz Fortschritten eine weniger erfolgreiche Geschichte. Die Stereokontrolle von angeregten Intermediaten stellt eine bedeutende Hürde für dieser Art von Photoreaktionen dar. Die vorliegende Arbeit beschäftigt sich mit enantioselektiven Lewis-Säure-katalysierten photochemischen Umlagerungen von 2,4-Cyclohexadienonen. Untersuchungen ergaben, dass chirale Oxazaborolidinium-Komplexe während der Reaktion eine Enantioselektivität hervorrufen konnten. In einer umfassenden Studie mit einer Vielzahl von Oxazaborolidinium-Komplexen wurde ein neuer Katalysator entwickelt, welcher die photochemische Umlagerung von 2,4-Cyclohexadienonen bei sichtbarem Licht und niedrigen Katalysatorbeladungen mit guten Ausbeuten und exzellenten Enantioselektivitäten katalysieren konnte. Durch eine große Substratbreite konnte die Toleranz des Katalysators gegenüber sterischen Substituenten und funktionellen Gruppen untersucht werden. Die Anwendbarkeit der Methodik wurde mit Hilfe einer Totalsynthese des Naturstoffs Chrysanthemumsäure gezeigt. Triplett-Löschungsexperimente und DFT-Berechungen offenbarten einen Reaktionspfad auf der Singlett-Hyperfläche.

Rearrangement reaction bear a suitable method to access desired carbon skeletons, that otherwise would require a huge synthetic effort. Photochemical rearrangements are a particularly fascinating tool to construct complex core structures and have been applied in various total syntheses of natural products. The enantioselective version of such photorearrangements has a less successful history, even though attempts and progress have been made. The stereocontrol of excited intermediates proves to be a considerable obstacle in this class of photoreactions. This work deals with the enantioselective Lewis acid catalyzed photochemical rearrangements of 2,4-cyclohexadienones. It was found that chiral oxazaborolidinium complexes were able to achieve an asymmetric induction during the photoreaction. An intensive screening of several oxazaborolidinium complexes led to the development of a new catalyst, which was capable to catalyze the photochemical rearrangement of 2,4-cyclohexadienones at visible light and low catalyst loading in good yields and excellent enantioselectivity. A broad substrate scope was used to evaluate the tolerance of the catalyst towards steric substituents and functional groups. Applicability of the developed method was shown by the total synthesis of natural product chrysanthemic acid without loss of from one of the photoproducts. Triplet quenching experiments and DFT calculations revealed a reaction mechanism on the singlet hypersurface.

1. Introduction

'*Der Weg ist das Ziel*' - *Confucius*

This ancient saying can be loosely translated to 'The journey is the reward' and highlights the focus on the journey itself as well as the experiences gained underway in contrast to a fixation solely on the destination. Striving to transfer this understanding to chemistry, catalysis comes to mind. Its research focusses in many cases on the energetic pathways and their alteration to make reactions more efficient and selective rather to concentrate solely on the actual or new products. The importance of catalysis is highlighted by various *Nobel* prizes awarded in chemistry associated with this topic.[1] Amongst others, *Ostwald* received the prize in 1909 for his research on catalysis. The unchallenged industrial synthesis of ammonia from its elements, derived from the *Haber-Bosch* process, extremely depends on the catalyst. Due to its novelty and importance *Haber* became a *Nobel* laureate in 1918. Over the last decade, the work on palladium catalyzed cross-coupling reactions by *Heck*, *Negishi* and *Suzuki* was honored with the *Nobel* prize 2010 and in the modern age, most industrial relevant processes are catalyzed.[2] Catalytic cycles in which catalysts are regenerated enabling them to take action more than once bear a high economic and ecologic advantage of catalysts to stoichiometric reagents. Another asset is the transfer of asymmetry of a chiral catalyst to multiple prochiral substrates to generate enantiomerically pure compounds without high cost of separation and loss of material, i.e. the undesired enantiomer. Major accomplishments in the field of asymmetric catalysis were made by *Knowles*, *Noyori* and *Sharpless* and were rewarded with the *Nobel* prize in 2001.[1]

1.1. Enantioselective Catalysis in Photochemistry

Photochemical reactions have attracted awareness due to the possibility of creating complex molecular structures via high-energy intermediates that are not accessible with thermal energy.[3-6] Nonetheless, participation of these intermediates leads to the necessity to find different approaches to apply catalysts in photoreactions compared to their thermal counterpart. The mode of action of a catalyst in a thermal reaction simply relies on the ability of lowering the activation energy (E_a) (Figure 1). For example, the catalyst interacts with the substrate to form an energetically low-lying intermediate. Therefore, less energy ($E_{a\ catalyzed} < E_{a\ uncatalyzed}$) is needed to convert the substrate (sub) to the product (prod). The higher this energy difference, the greater will be the ratio of catalyzed to uncatalyzed reaction. A suitable chiral catalyst creates an asymmetric environment for an achiral substrate and is therefore capable of inducing

the formation of only one of two enantiomers, if a chiral product is generated. The enantiodifferentiation itself is subject to different activation energies towards each chiral product or intermediate, but will not further be discussed. The situation changes dramatically, when activation barriers become irrelevant. When a substrate absorbs a photon with a suitable energy (hν) to reach its excited state (sub*) from which the reaction occurs, catalysis seems to lose significance at first (Figure 1).[7]

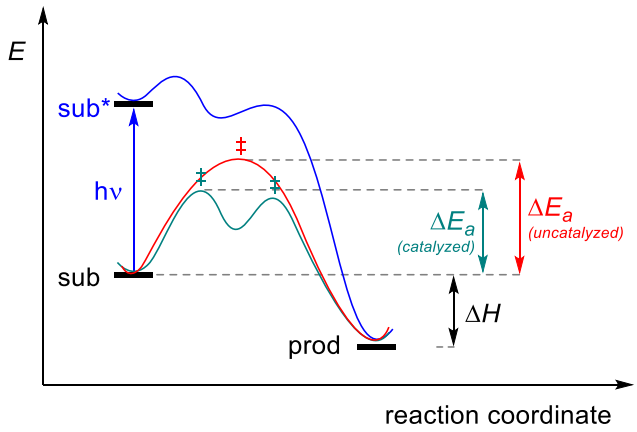


Figure 1. Reaction energy diagram of an uncatalyzed thermal reaction (*red*), a catalyzed thermal reaction (*green*) and a photoreaction (*blue*).[7-8]

However, there are different modes of actions for catalysts in photochemical reactions, that can also be used when asymmetric induction is desired (Figure 2). Substrate-catalyst complexes (sub·cat, *blue*) may have lower lying excited energy levels and need less energy to get excited. Considering the spectroscopic properties, this can be seen by a bathochromic shift of the absorbance maximum to a longer wavelength (Figure 2a). By choosing a suitable irradiation source, a selective excitation of the substrate-catalyst complex can be achieved. In addition, with longer wavelengths the reaction becomes less power-consuming. The shift away from short wavelengths with energies in the range of C-C bond dissociation, also results in less decomposition of substrate and product in many cases. Secondly, a substrate-catalyst complex may have a considerably higher extinction coefficient resulting in an exceptionally higher absorption compared to the non-complexed substrate (Figure 2b). This often occur when the absorption of a quantum mechanically allowed ππ* transition is shifted and obscures the forbidden nπ* transition band. This enables a selective excitation of the complex as it will ideally absorb all emitted photons before the uncomplexed substrate can be excited. Catalysts

with a very efficient intersystem crossing (ISC) from their first excited singlet (S_1) to the first excited triplet state (T_1) can act as triplet sensitizer (sens). Prerequisite is a triplet energy that lies close to the triplet energy of the substrate to allow a triplet energy transfer (Figure 2c).[9] This may enable a reaction from the triplet state of a substrate with an insufficient intersystem crossing and therefore prevents a reaction from the singlet state or deactivation to the ground state (S_0) by fluorescence. When a difference in singlet energy, corresponding to a different excitation wavelength exists, the sensitizer can be selectively excited and no racemic background pathway via intersystem crossing from the substrate's singlet state is possible. Asymmetric induction is feasible in this situation as the energy transfer is distance dependent, thus a chiral sensitizer is capable of creating an asymmetric environment for the substrate prior to transferring its energy. Sensitization bears also the opportunity to be combined with a second catalyst that lowers the first triplet energy of the substrate. By selecting a sensitizer with a triplet energy in between the triplet energies of uncomplex and complexed substrate, exclusive excitation of the complex can be achieved. In this case, an achiral sensitizer may be applied, when the complexing catalyst is chiral. A fourth example of catalysis is the alteration of the reaction course on the different energy hypersurfaces (Figure 2d). An example may be the change of hypersurfaces to inhibit the deactivation pathway or to lead the reaction course onto a different hypersurface to uncover a new pathway in an enantioselective environment.[7]

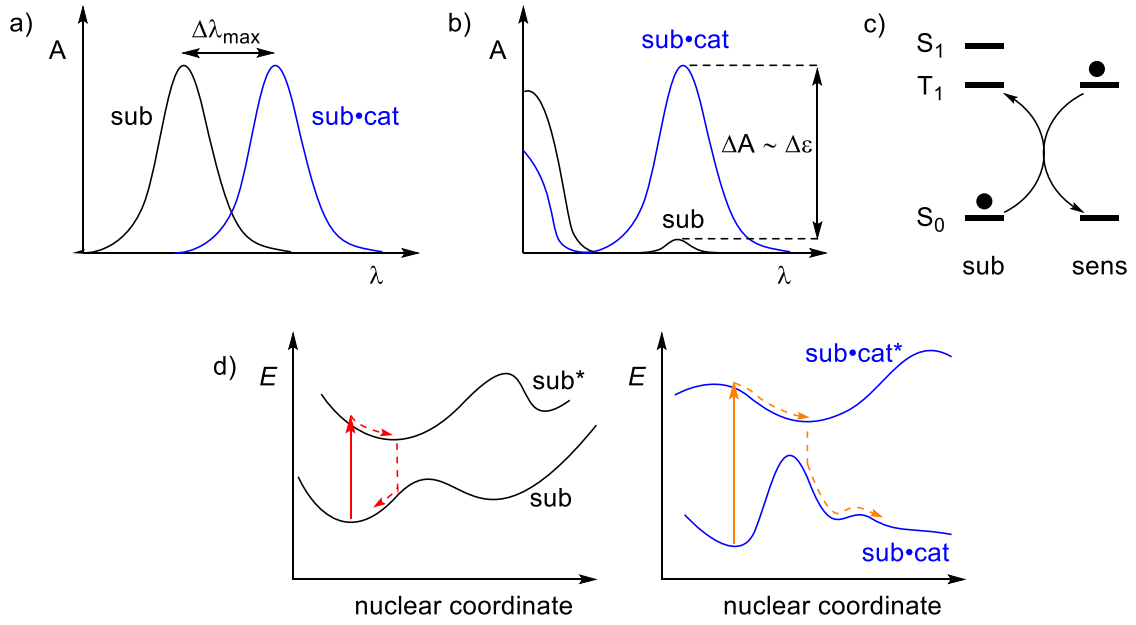


Figure 2. Different modes of action for catalysts in photochemistry: a) bathochromic shift of absorption maximum, b) difference of extinction coefficients, c) selective sensitization to the triplet state, d) alteration of reaction pathway.[7]

1.2. Enantioselective Lewis Acid Catalysis in Photochemistry

With the rise of photochemistry in the last century and new challenges to penetrate the field in catalytic and asymmetric fashion, various approaches can be mentioned. A large impact has certainly been made by photocatalysts in photoredox chemistry. These molecules can be highly conjugated organic molecules, for example organic dyes. In other cases, transition metal complexes or even inorganic clusters were used. Several enantioselective reactions have been published, combining photoredox processes with chiral catalysts, such as metal complexes, organocatalysts, Brønsted acids or Lewis acids.[10-15]

However, in the case of photoredox chemistry only the photocatalyst gets excited. The reaction mechanism proceeds from substrate to product via ground state radicals. A likewise greater challenge is to control enantioselectivity when the substrate itself is excited. The successful application of chiral crystalline matrices, chiral auxiliaries and non-covalent bound templates needs to be mentioned.[15] Chiral hydrogen-bonding triplet sensitizers successfully catalyzed a variety of reactions.[16-22] The use of chiral Lewis acids has also been of major interest. Especially carbonyl containing chromophores can be readily activated by Lewis acids.[23] Upon

coordination of the Lewis acid to the carbonyl-oxygen lone pair, the C-O π* orbital, the lowest unoccupied molecular orbital (LUMO) is energetically lowered. This results in a higher eletrophilicity of carbonyl compounds and altered photophysical properties.

1.2.1. Oxazaborolidinium Catalysts as Chiral Lewis Acids in Photochemical Reactions

Pioneering studies of our group in the field of Lewis acid catalysis in photochemistry commenced in 2010 when oxazaborolidines, more specifically oxazaborolidinium complexes, were found be suitable Lewis acids in photochemical reactions.[24] This class of chiral Lewis acids was already connected to a successful history of enantioselective thermal reactions. The most commonly used oxazaborolidine is the oxazaborolidnium-borane complex **1**, known as *Corey-Bakshi-Shibata* (CBS) catalyst.[25] Catalyst **1** was effectively applied in the enantioselective reduction of prochiral ketones over decades. it was found to be of vital importance that coordination of borane took place, as otherwise donation of the nitrogen lone pair into the nitrogen-boron bond and loss of the boron atom's Lewis acidity occurred. The previously empeded coordination to the oxygen atom of carbonyl compounds, was therefore more stable for oxazaborolidinium complexes. Further research compiles numerous examples of highly enantioselective *Diels-Alder* reactions with α,β-unsaturated carbonyl compounds as dienophiles.[26] Examples of the applied catalysts are shown in Figure 3 (structures **1**-**4**). Activation by Brønsted, e.g. trifluoromethanesulfonic acid (TfOH) or bis(trifluoromethane)sulfonimide (Tf_2NH) and Lewis acids, e.g. aluminum bromide ($AlBr_3$) yielded highly potent oxazaborolidinium complexes for *Diels-Alder* reactions.[26-29] Application also proved fruitful in the catalysis of Baylis-Hillman reactions.[30] or thermal [2+2] cycloadditions.[31-33]

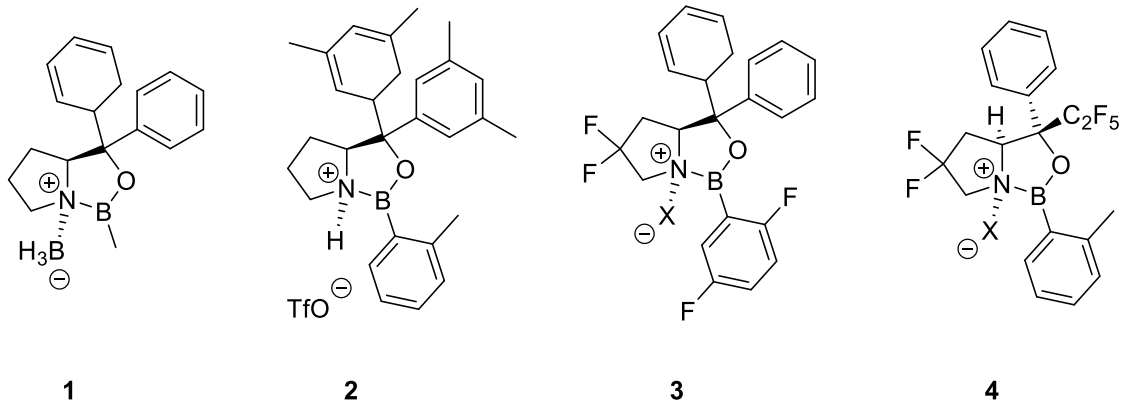


Figure 3. Different oxazaborolidinium catalysts published by *Corey* (X = $AlBr_3$, HOTf, $HNTf_2$). [25, 27-29]

The mode of action of oxazaborolidinium catalysts can be explained by models of the intermediary substrate-catalyst complexes in Figure 4. As depicted, oxazaborolidinium catalysts interact with α,β-unsaturated carbonyl compounds to form a bidentate complex, where the carbonyl compound is fixated throughout the reaction. In addition to the boron-carbonyl oxygen coordination (*blue*) a non-classical hydrogen bond exists between the oxazaborolidine oxygen and the hydrogen in α-position to the carbonyl group (α-CH−O interaction, *red*) in the case of α,β-unsaturated ketones or esters (Figure 4a). α,β-unsaturated aldehydes form a non-classical hydrogen bond with their formyl hydrogen (formyl CH−O, *orange*) to the oxazaborolidine oxygen (Figure 4b). With the aryl groups shielding the one side of the reacting double bond, the reaction can only occur on one side. Hence one enantiomer is formed preferentially.[26, 34]

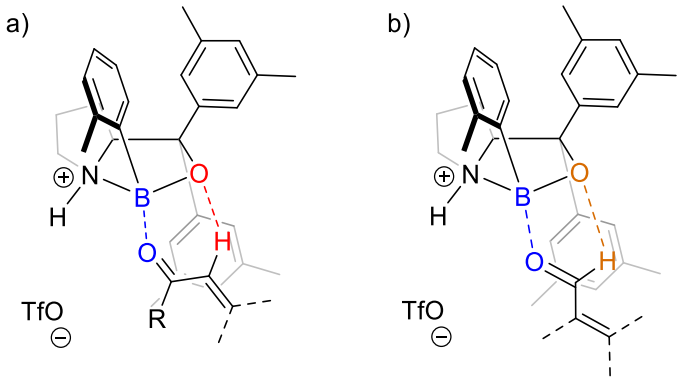
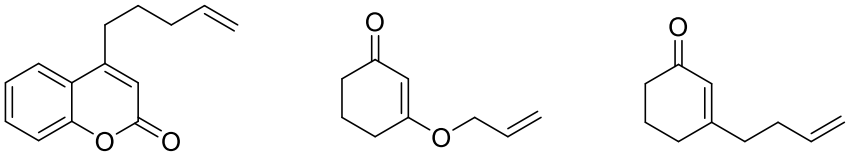


Figure 4. Model of oxazaborolidinium coordination to α,β-unsaturated carbonyl compounds that explains the observed enantioselectivity. a) α-CH−O interaction (*red*) exists for α,β-unsaturated ketones (R = Alkyl) and esters (R = OAlkyl), b) formyl CH−O interaction (*orange*) for α,β-unsaturated aldehydes.[26, 34]

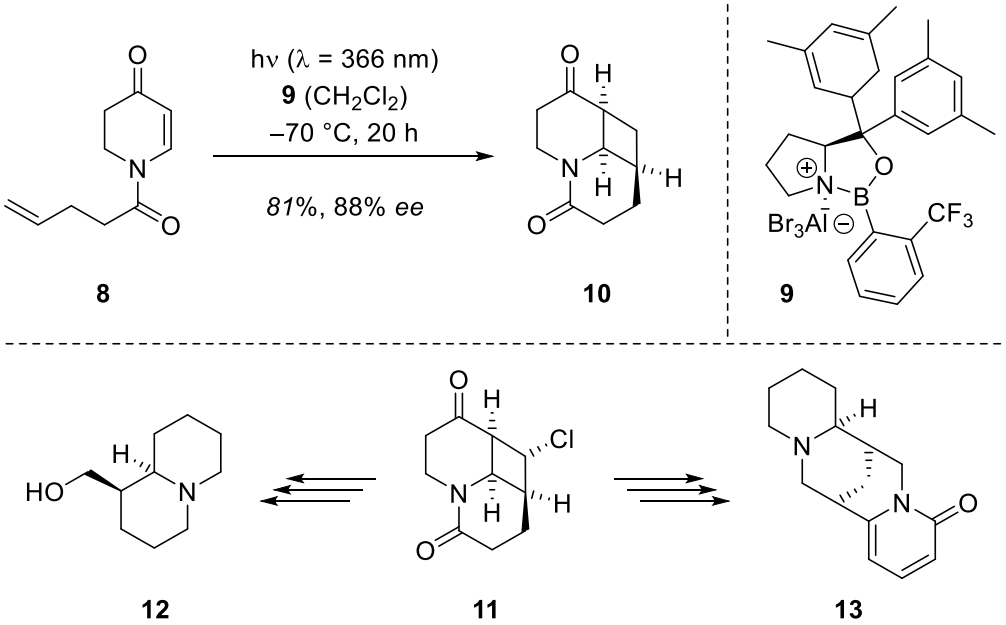
The potential of oxazaborolidines in photochemistry was discovered in our group by *Guo*, who found their aluminum bromide complexes to be the superior Lewis acids for an enantioselective intramolecular [2+2] photocycloaddition of coumarin **5** (Figure 5).[24, 35] Upon Lewis acid complexation a bathochromic shift of the ππ* absorption band occurred that partially obscured the nπ* absorption of the uncomplexed coumarin, associated to modes of action a) and b) in Figure 2. In addition, *Brimioulle* determined that the Lewis acid catalyzed reaction proceeded on the triplet hypersurface and showed higher reaction rates. This was explained by an enhanced stabilization of the first singlet state (S_1) by the Lewis acid. The uncomplexed coumarin would rapidly suffer deactivation to the ground state, whereas the coumarin-Lewis acid complex could undergo intersystem crossing (ISC) to the triplet state more easily due to the longer lifetime of the S_1-state.[36] Irradiation at λ = 366 nm at −70 °C gave the [2+2] photoproduct in high yield (84%) and enantioselectivity (82% *ee*), however due to a racemic background reaction a high catalyst loading of 50 mol% was necessary.[24, 35] High enantioselectivities were also achieved by *Brimioulle* in the [2+2] photocycloaddition of alkenoxycyclohexenone **6** (Figure 5). Irradiation had to be conducted at a shorter wavelength (λ = 300 nm). Without Lewis acid, a background reaction was observed due to a weak nπ* transition. However, when a Lewis acid was present, the large difference of extinction coefficients of the ππ* transition of the substrate-Lewis acid complex and the nπ* transition of the uncomplexed substrate led to an exclusive excitation of the complex. The mode of action therefore correlates to Figure 2b. At a catalyst loading of 50 mol%, a background reaction was only observed when the photon flux was increased. A catalyst loading of 40 mol% did not result in decreased enantioselectivity, however, catalyst loadings of 50 mol% were used to achieve complete conversion in reasonable reaction times. The photocycloaddition of **6** proceeded with high efficiency (90%, 80% *ee*).[37] In the case of alkenylcyclohexenone **7** irradiation was possible at λ = 366 nm (Figure 5). Unfortunately, it again needed an extensive catalyst screening by *Poplata* and 50 mol% of catalyst to form the desired photoproduct in 80% yield and 83% *ee*.[38]



5 **6** **7**

Figure 5. Suitable substrates for oxazaborolidinium catalyzed enantioselective intramolecular [2+2] photocycloaddition reactions.[24, 37-38]

Brimioulle also looked into the [2+2] photocycloaddition of dihydropyridone **8**.[36, 39] Application of 50 mol% catalyst **9** led to formation of cyclobutane **10** in 81% yield and 88% *ee* (Scheme 1). Successful enantioselective catalysis was achieved by an extensive bathochromic shift of the ππ* absorption. The quantum mechanically forbidden nπ* absorption of the uncomplexed substrate **8** was located in the same region, however the large difference of extinction coefficients resulting from the difference of allowed and forbidden transitions made a selective excitation of the strongly absorbing substrate-Lewis acid complex possible. Interestingly, the racemic reaction was evaluated to be fast with efficient intersystem crossing to the triplet hypersurface from which the reaction occurred. The catalyzed reaction, however, proceeded at a lower rate in this case.[39] The method was utilized to synthesize chlorocyclobutane **11**. This was a useful precursor to conclude an enantioselective total synthesis of (+)-lupinine (**12**) and an enantioselective formal synthesis of (+)-thermopsine (**13**) (Scheme 1).[39]



Scheme 1. Enantioselective intramolecular [2+2] photocycloaddition of dihydropyridone **8** catalyzed by oxazaborolidinium catalyst **9**. Photoproduct **11** could be converted to (+)-lupinine (**12**) in a total synthesis and to (+)-thermopsine (**13**) in a formal synthesis.[39]

In order to explain the enantioseletivity in the mentioned [2+2] photocycloaddition reactions, substrate-Lewis acid complex **8·9** can be used as example (Figure 6). Coordination via a boron-oxygen bond and a non-classical hydrogen bond leads to the *si* face being shielded by one aryl group of the catalyst. The alkenyl linker is therefore forced to approach the chromophore from the *re* face and leads to the previously depicted configuration of **10**.[39]

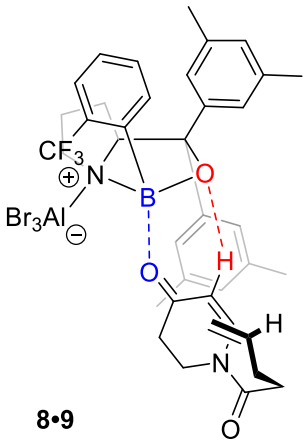
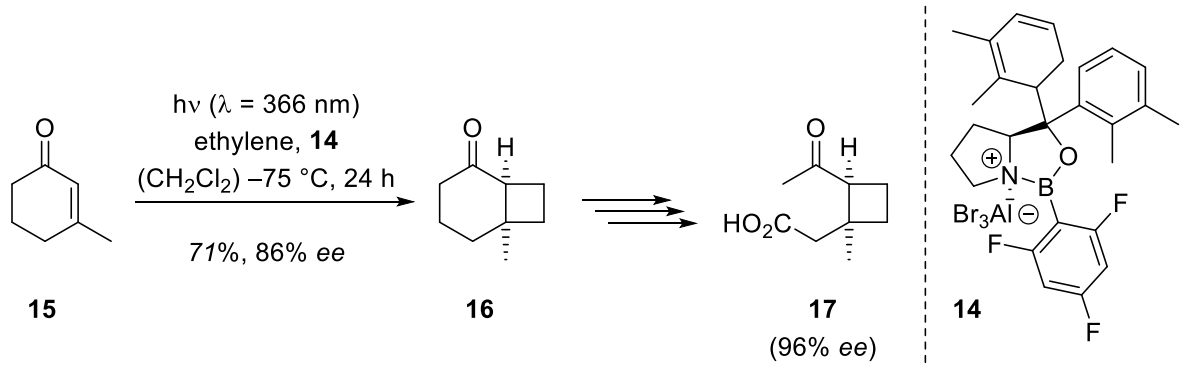


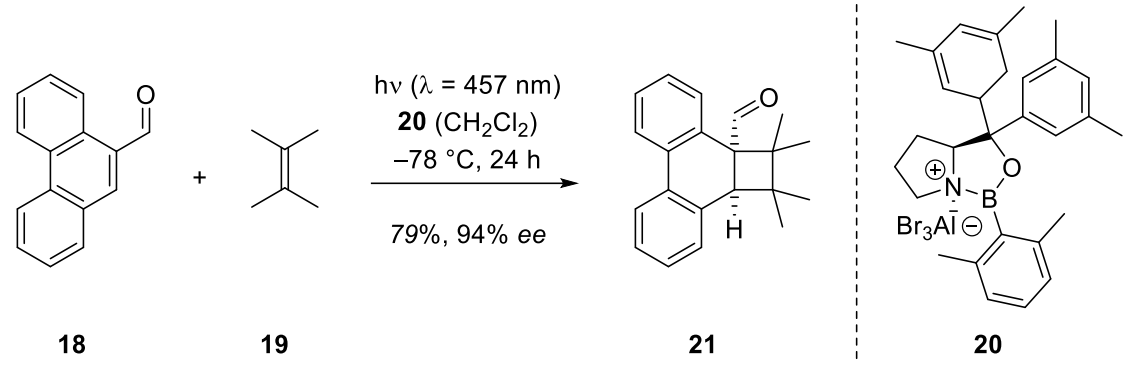
Figure 6. Model of substrate-Lewis acid complex to explain the enantioselectivity of the[2+2] photocycloaddition.[39]

Recently, *Poplata* developed the oxazaborolidinium catalyst **14**, which was capable of efficiently converting cyclohexenone **15** with ethylene in an intermolecular [2+2] photocycloaddition to bicyclooctanone **16**. Further transformations of **16** enabled the first enantioselective total synthesis of (−)-grandisol (**17**). Alteration of the oxazaborolidine aryl group's substitution pattern was fundamental to prevent hydrogen abstraction from the methyl groups by the long-living radical intermediates of the intermolecular photocycloaddition.[40]



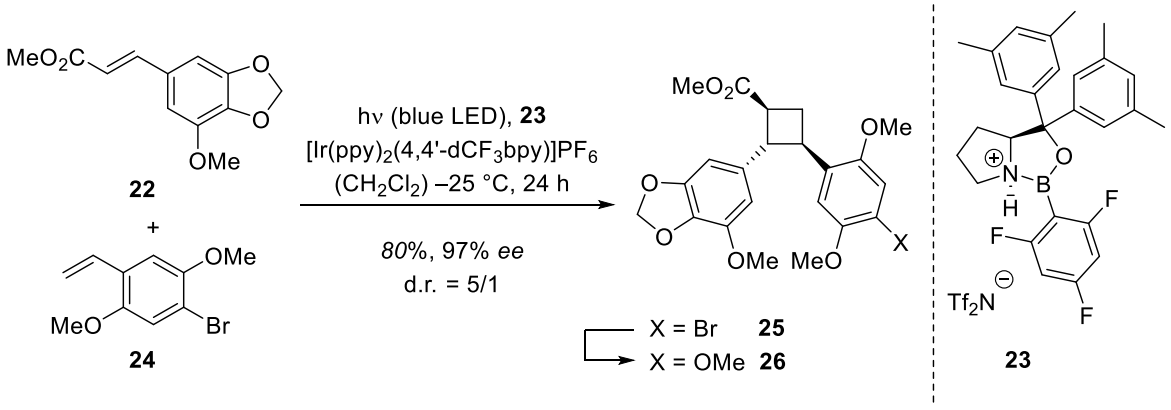
Scheme 2. Enantioselective intermolecular [2+2] photocycloaddition of **14** and ethylene catalyzed by oxazaborolidinium catalyst **14**. Bicyclooctanone**16** was transformed into the natural product (−)-grandisol (**17**).[40]

Our group further extended substrate classes, *Stegbauer* showed that phenanthrene carboxaldehde **18** reacted enantioselectively with dimethylbutene **19** in presence of the chiral Lewis acid **20** in an *ortho*-photocycloaddition. Reaction conditions using visible light and 20 mol% catalyst at low temperatures made it possible to isolate cyclobutane carboxaldehyde **21** in good yield (79%) and excellent enantioselectivity (94% *ee*) (Scheme 3). The bathochromic shift of the Lewis acid was sufficient to shift the ππ* absorption band to a longer wavelength than the nπ* absorption, inhibiting a racemic background reaction.[41] This result also proved the viability of using *Corey*'s binding model for α,β-unsaturated aldehydes (Figure 4) in photochemical reactions.



Scheme 3. Enantioselective intermolecular [2+2] photocycloaddition of phenanthrene carboxaldehyde **18** and dimethylbutene **19** catalyzed by oxazaborolidinium catalyst **20**.[41]

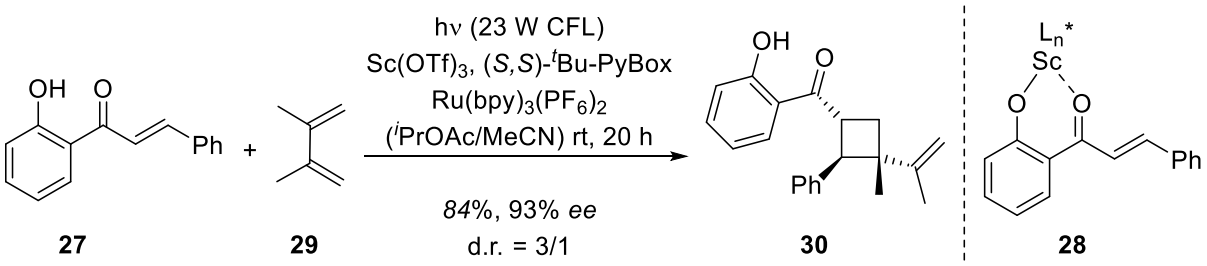
Oxazaborolidinium catalysts have also attracted interest in dual catalysis. The group of *Yoon* showed that a complex of cinnamic ester **22** and Brønsted activated catalyst **23** could be selectively sensitized by an iridium(III)-catalyst.[42-43] In this case, the catalysis plays a role by sensitization (Figure 2c), but by forming a substrate-Lewis acid complex with a lower triplet energy than the uncomplexed substrate. This enables selective sensitization of the complex and avoids a racemic background reaction when a sensitizer with a suitable triplet energy is employed. The enantioselective [2+2] photocycloaddition with styrene **24** provided cyclobutane **25** that was converted to the norlignan natural product **26** in one step. High yields and excellent enantioselectivities were achieved with only 25 mol% of catalyst **23** and 1 mol% of sensitizer.[42]



Scheme 4. Enantioselective [2+2] photocycloaddition of cinnamic ester **22** and styrene **24** catalyzed by triplet sensitization in combination with Lewis acid **23**. Cyclobutane **25** was transformed to the norlignan natural product **26**.[42]

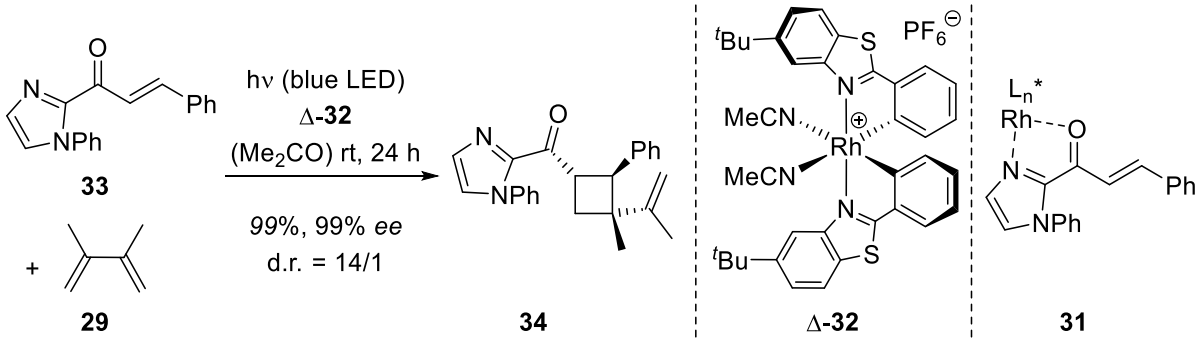
1.2.2. Photocatalysis with Metal Complexes as Chiral Lewis Acids

Preceding their work on dual catalysis with oxazaborolidines, *Yoon* and coworkers published an enantioselective triplet-sensitized [2+2] photocycloaddition of 2-hydroxychalcones and olefins with a C_2-symmetric Scandium(III) complex as Lewis acid in 2017.[44] Mode of action in this case again refers to Figure 2c. Upon bidentate coordination of chalcone **27** with the chiral Lewis acid, the configuration of complex **28** is fixed and diene **29** can only attack from one side as the chiral pyridine-bis(oxazoline) ligands (PyBox) occupy one side of the chromophore. Upon complexation the first triplet energy of **27** is lowered by over 80 kJ/mol. Irradiation conditions were chosen to prevent direct excitation of **27** and complex **28**. The triplet energy of the applied sensitizer $[Ru(bpy)_3](PF_6)_2$ was only sufficient to transfer its triplet energy to the low-lying triplet state of **28** and no racemic background reaction from the energetically higher triplet state of **27** could occur, which yielded in a high enantioselectivity of 93% for cyclobutane **30** with 2.5 mol% of sensitizer and 10 mol% of Lewis acid (Scheme 5).



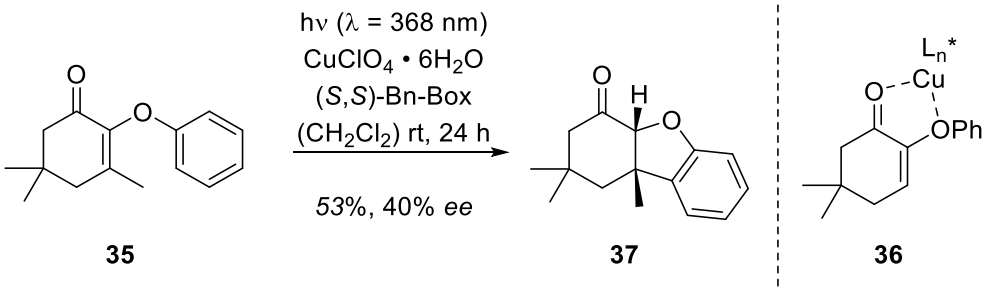
Scheme 5. Enantioselective [2+2] photocycloaddition of 2-hydroxychalcone **27** with diene **29**. Chiral chelate complex **28** was selectively sensitized by $Ru(bpy)_3(PF_6)_2$.[44]

The group of *Meggers* applied a chiral-at-metal catalyst as chiral Lewis acid in a [2+2] photocycloaddition of α,β-unsaturated acylimidazoles.[45] In this case, the imidazole was vital to achieve a chelating complex **31** of chiral Lewis acid Δ-**32** with the α,β-unsaturated carbonyl group of **33**. Complex **31** could be selectively excited by irradiation with visible light to undergo a reaction with diene **29**. The mode of action can hence be linked to Figure 2a, because absence of catalyst delivered only minimal amounts of racemic product. 2 mol% of Lewis acid proved to be sufficient as catalyst loading and delivered the product **34** in excellent yield, diastereoselectivity and enantioselectivity (Scheme 6).



Scheme 6. Enantioselective [2+2] photocycloaddition of α,β-unsaturated acyl imidazole **33** with diene **29** catalyzed by chiral-at-metal Lewis acid Δ-**32**. Δ-**32** activates the chromophore and transfers its chirality by forming the *N,O*-chelate **31**.[45]

An example from our group features an enantioselective 6π-photocyclization of aryloxycylohexenone **35** catalyzed by a chiral copper(I) bisoxazoline complex.[46] Unfortunately, the bathochromic shift upon Lewis acid coordination was insufficient to enable a selective excitation of the chiral substrate-Lew is acid complex **36**. With 50 mol% catalyst loading dihydrofuran **37** could only be isolated in 53% yield and moderate enantioselectivity of 40% *ee*. The enantioselectivity could be further improved by using a dual catalysis concept. Addition of thioxanthone enabled visible light irradiation and thioxanthone turned out to have a suitable triplet energy to sensitize complex **36**. However, enantioselectivity could not be improved and substrates bearing electron-deficient groups appeared to have unsuitable triplet energies, as full conversion was not achieved in these cases (Scheme 7).



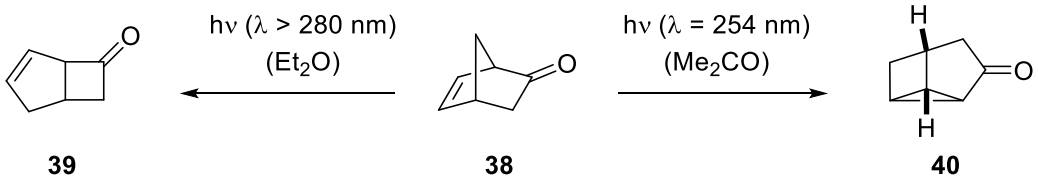
Scheme 7. Enantioselective 6π-photocyclization of **35** catalyzed by a chiral copper(II) catalyst. Selective excitation of Lewis acid complex **36** preferentially formed enantiomer **37**.[46]

1.3. Photochemical Rearrangement Reactions

The [2+2] photocycloaddition is one of the most important photochemical transformation. However, addition reactions are only part of the picture that photochemistry paints. The focus of this work lies on photorearrangement reactions of cyclohexadienones. Therefore, a brief look into rearrangement reactions from excited states is done.

As rearrangement is a broadly applicable term, it covers also isomerization reactions, e.g. *E*/*Z*-isomerization reactions of olefins. This area has had a huge impact on research, also towards enantioselective methods and has aroused a lot of interest especially with the *Nobel* prize in 2017 for molecular machines. Photodeconjugation reactions of α,β-unsaturated carbonyl compounds provide another example to mention, which has also been achieved in an enantioselective manner.[47-48] However, isomerizations of double bonds will not be discussed further.

An interesting class of molecules for photochemical rearrangement reactions are β,γ-unsaturated carbonyl compounds. The different reactivity of these compounds was amongst others observed by *Ipaktshi*, when irradiation of dehydronorcamphor (**38**) in acetone led to formation of a different reaction product[49-50] than the previously isolated bicyclo[3.2.0]heptenone **39**.[51] After investigation of its structure to be confirmed as **40**, mechanistic studies uncovered that the excited states were in fact different. **39** was proposed to be formed by an 1,3-acyl shift in a singlet reaction, that was not affected by a triplet quencher. Rearrangement to **40** was quenched and thought to be formed by a 1,2-acyl shift, also known as oxadi-π-methane rearrangement. In this case, acetone acted as efficient triplet sensitizer to populate the T_1 state of **38**, circumventing the reaction pathway via the S_1 hypersurface.



Scheme 8. Photochemistry of dehydronorcamhor (**38**): direct excitation leads to **39** via 1,3-acyl shift, sensitization leads to **40** via oxadi-π-methane rearrangement.[49, 51]

Looking closely into the energy levels of this compound class (Figure 7), it is vital to know that reactions mainly occur from the first singlet state (S_1) and the first triplet state (T_1), which is

accessible by intersystem crossing (*blue*). Although some reactions are postulated to arise from the S_2 or T_2 excited state, these are rare exceptions to *Kasha*'s rule, stating that reactions always occur from the lowest excited state due to rapid internal conversion (IC, *magenta*). Also, intersystem crossing from S_1 to T_2, is forbidden according to *El Sayed*'s rule. Generally, the two separate pathways via S_1 or T_1 lead to two different rearrangements, 1,3-acyl shift [1,3] and 1,2-acyl shift [1,2], and hence to two different products (Figure 7).

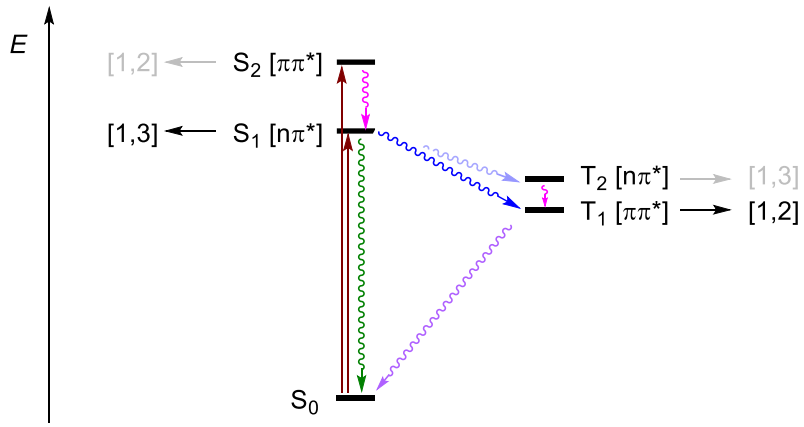
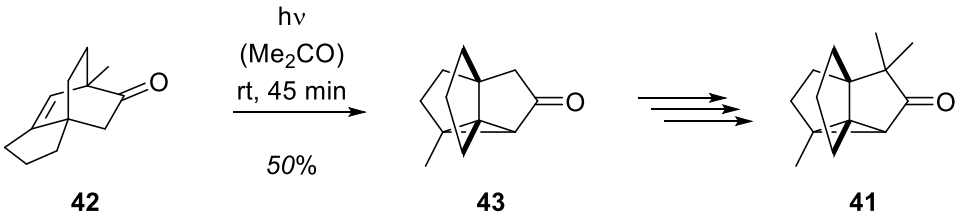


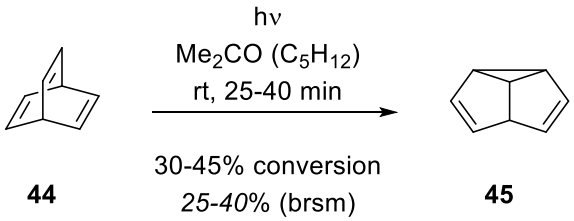
Figure 7. Excited states of β,γ-unsaturated carbonyl compounds and their corresponding electronic processes [excitation (*brown*), fluorescence (*green*), phosphorescence (*violet*), internal conversion (IC, *magenta*), intersystem crossing (ISC, *blue*)]. Reactions occurring from the excited states are the oxadi-π-methane rearrangement [1,2] and the 1,3-acyl shift [1,3].[48]

Both rearrangements can bring a higher level of complexity into a system and have therefore been used synthetically to construct challenging molecules. *Metha* successfully incorporated the oxadi-π-methane rearrangement as key step into the total synthesis of tetracyclic natural product (±)-modhephene (**41**). **42** was readily sensitized by acetone and delivered the highly complex molecule **43** in moderate yield (Scheme 9). As a great part of the carbon skeleton had been successfully built up, only minor transformations were needed to yield **41**.[52]



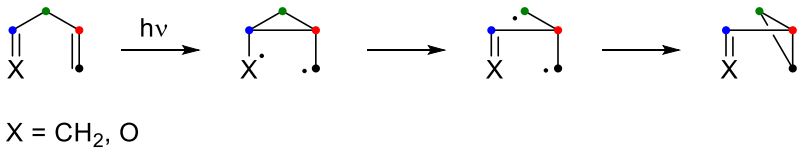
Scheme 9. Oxadi-π-methane rearrangement as key step in the total synthesis of (±)-modhephene (**41**).[52]

An almost identical rearrangement can be observed with 1,4-dienes. Featuring a methylene group instead of the carbonyl moiety, the reaction is called di-π-methane rearrangement and leads to molecules with equally challenging carbon skeletons. *Zimmerman* and *Grunewald* observed the formation of semibullvalene (**44**) after irradiation of barrelene (**45**) in acetone (Scheme 10). Comparing structures of substrate and product of both rearrangements, the same mechanism may be suitable to explain the formation of the rearranged products. However, in contrast to the oxadi-π-methane rearrangement, the di-π-methane rearrangement often proceeds by direct irradiation and is accessible from the singlet as well as from the triplet hypersurface.[53-54]



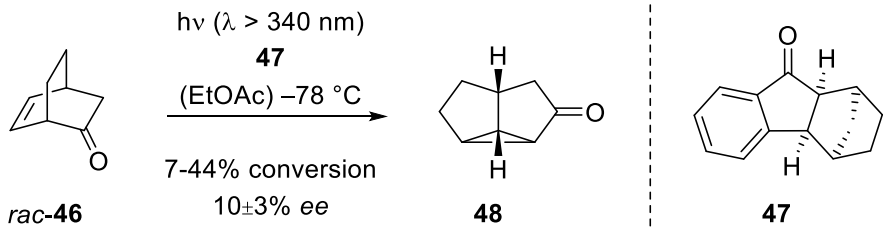
Scheme 10. Di-π-methane rearrangement of barrelene (**44**) to semibullvalene (**45**).

Labelling experiments gave insights into the rearrangement mechanism of both reactions.[54-55] Mechanistic explanations involve the initial formation of a cyclopropane ring, that is cleaved to regenerate either the carbonyl or one of the olefinic double bonds. Recombination of the two radicals yields the observed cyclopropyl ketone or vinylcyclopropane.



Scheme 11. Mechanism of di-π-methane rearrangement (X = CH_2) and oxadi-π-methane rearrangement (X = O).[48, 55]

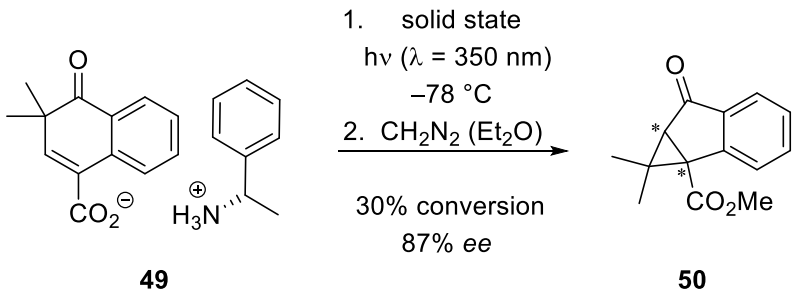
Although there are a range of examples for the mentioned examples in literature, the catalysis of such reactions in an enantioselective fashion remains a great challenge. In 1980, *Demuth* published an attempt of catalyzing the oxadi-π-methane rearrangement of a racemic mixture *rac*-**46** with a chiral triplet sensitizer **47**.[56] However, tricyclo[3.3.0.0]octanone **48** was only isolated with 10±3% *ee* at best. Conversions were also kept below 50% as this was an attempt of a kinetic resolution, where only one enantiomer should be sensitized by **47**. Due to the fact that triplet sensitization is a distance dependent process, there was a degree of differenciation between both enantiomers of *rac*-**46** at low temperatures. This was however very inefficient, as stated before.



Scheme 12. Enantioselective oxa-di-π-methane rearrangement of bicyclooctenone *rac*-**46** sensitized by chiral triplet sensitizer **47**.[56]

A different approach was chosen by *Scheffer* and coworkers, who investigated the photochemical rearrangement of naphtalenones.[57] By using chiral ionic auxiliaries, enantioselectivity was observed when irradiating the ionic crystal lattice. Ammonium carboxylate salt **49** could be rearranged and converted to the corresponding methyl ester **50** in two steps with a high degree of selectivity at −78 °C. A disadvantage of this method was the inability to reach high enantioselectivities at high conversions. Due to product formation, the crystal lattice was altered and lost its ability to induce an efficient asymmetric photochemical rearrangement of **49**. When conducted in chloroform, the ion pairs were separated and the

reaction occurred racemically. This oxadi-π-methane rearrangement was proposed to originate from the singlet hypersurface, because attempts of a triplet quenching failed.



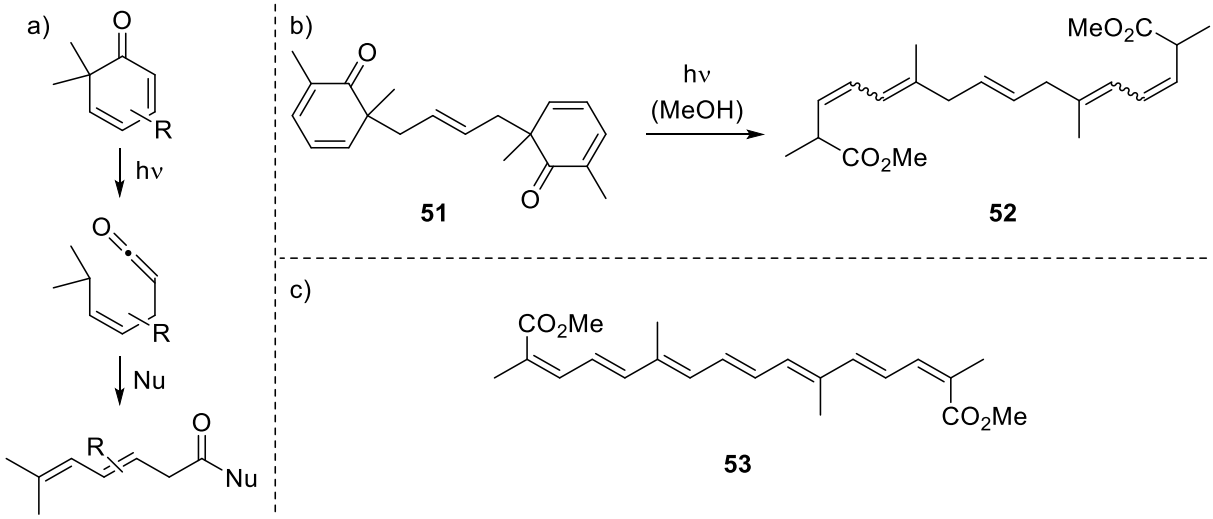
49 **50**

Scheme 13. Ionic chiral auxiliary approach. Ammonium carboxylate salt **49** was converted enantioselectively to **50** in two steps.[57]

2. Photochemical Reactions of 2,4-Cyclohexadienones

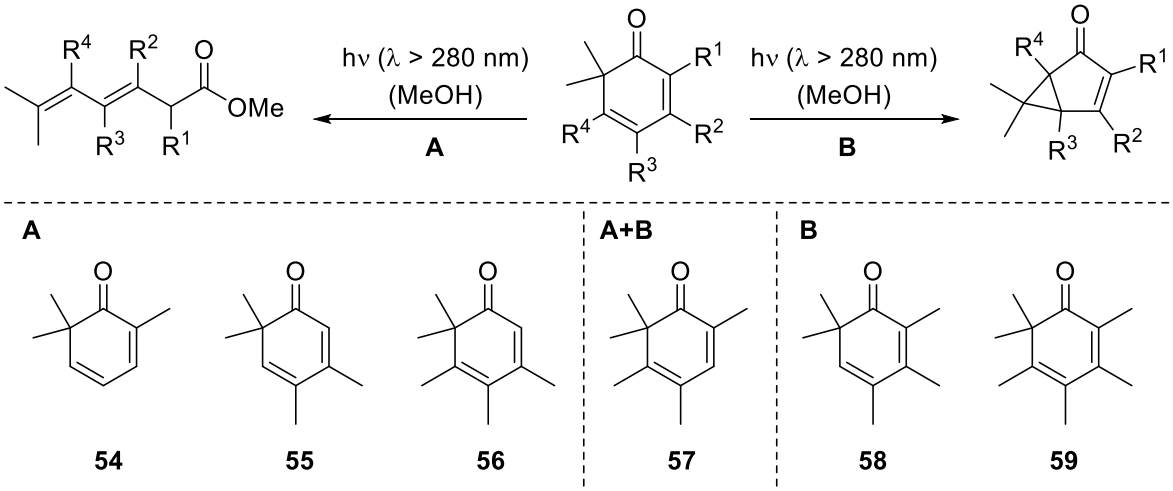
2.1. Literature Background and Previous Work

2,4-Cyclohexadienones have been subject to photochemical research since the last century. They were mostly known for their capability to form open-chained ketenes resulting from an α-cleavage. Trapping of the ketenes with nucleophiles such as water or alcohols, usually used as solvents, or amines in unpolar solvents yielded the corresponding carboxylic acid derivatives (Scheme 14a). Hence, the process was known as photoacidification and found a number of applications. For example, **51**, containing two cyclohexadienone chromophores, could be irradiated in methanol to form dimethylester **52** (Scheme 14b), a direct precursor to the food colorant crocetin (**53**) (Scheme 14c).[58-59]



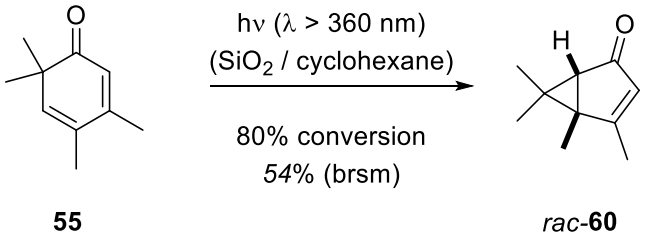
Scheme 14. Photoacidification of cyclohexadienones: a) Mechanistic process. b) Irradiation of **51** in methanol forms methylester **52**, direct precursor to c) food colorant dimethyl crocetin (**53**).[59]

Investigations on alkyl substituted cyclohexadienones revealed a second product. With increasing substitution, bicyclohexenones could be formed, however, these were also formed by the intermediary ketene. For example, cyclohexadienones **54**-**56** gave the expected linear methylesters when irradiated in methanol (Scheme 15, path **A**). Cyclohexadienone **57** gave a mixture and **58** and **59** cyclized from the ketene to the bicyclohexenone (Scheme 15, path **B**). The higher the substitution, the less likely was the ketene to change its conformation and make a nucleophilic attack possible.[60-61]



Scheme 15. Photochemistry of 2,4-Cyclohexadienonesand the effect of substitution on the reaction outcome.[60-61]

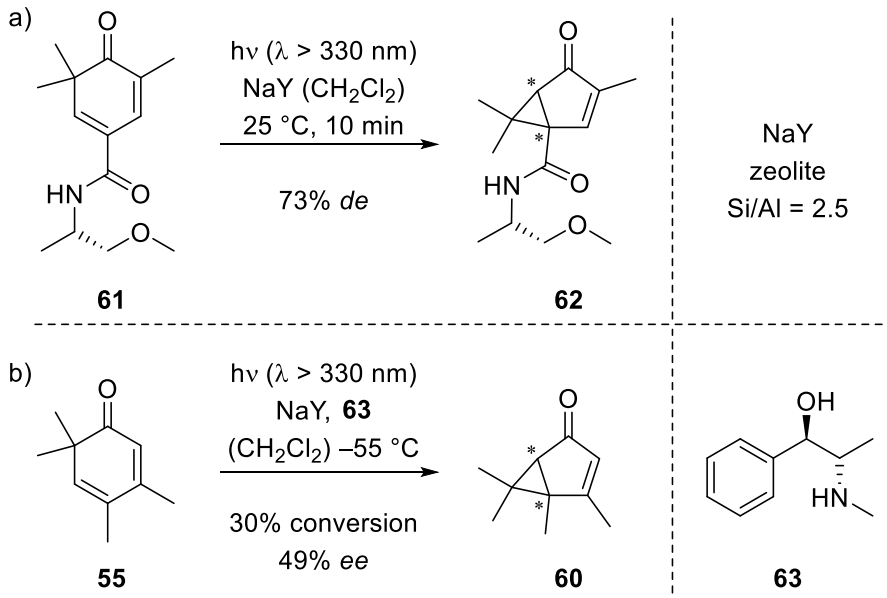
However, as *Griffiths* and *Hart* found out, the reaction medium played a vital role in the reactivity of cyclohexadienones. In protic environments, such as trifluoroethanol as well as a silica gel slurry in cyclohexane, they observed a bathochromic shift of the ππ* absorption and the nπ* absorption vanished or was obscured. Irradiation in these media resulted in the formation of bicyclohexenone *rac*-**60** from cyclohexadienone **55**, which previously gave exclusively the ring-opened acid derivatives (Scheme 16). Thus, the substitution pattern did not appear to be the key for the chemoselectivity but instead a new reaction path. A ketene intermediate was not observed and attempted triplet quenching with piperylene failed. Consequently, it was proposed that the reaction occurred from the ππ* singlet state.[62]



Scheme 16. Photochemical rearrangement of cyclohexadienone **55** to bicyclohexenone *rac*-**60**.[62]

The bathochromic shift upon adsorption on a protic surface as in the case of silica gel was used in more recent studies to induce selectivity to this photochemical rearrangement. *Ramamurthy*

and coworkers showed that in zeolites, cyclohexadieones could photochemically rearrange diastereoselectively when an auxiliary was attached. In a zeolite cage with the right size, the auxiliary of **61** was able to induce an asymmetric environment to yield **62** with high diastereoselectivity (Scheme 17a).[63-64] In an enantioselective version, the group achieved moderate enantioselectivity by applying chiral inductors, such as (−)-ephedrine (**63**) (Scheme 17b).[64] When in the same cage, the inductor molecule acts in the same way as an auxiliary. To ensure a high ratio of **55** being in the same zeolite cages as inductors, ten equivalents of inductor were used. In both studies no yields and absolute configurations were given and samples were only irradiated to a certain conversion to neglect secondary reaction and focus solely lied on selectivity.



Scheme 17. Auxiliary (a) and inductor (b) approaches towards diastereoselective and enantioselective photochemical rearrangements of cyclohexadienones in zeolites. (−)-ephedrine (**63**) was used as inductor.[63-64]

Results we obtained, preceeding to this work, had shown that it was possible to enable the photochemical rearrangement of **55** by addition of Lewis acid.[8] At λ = 366 nm, the reaction proceeded with low yields due to large amounts of secondary products formed by thermal and photochemical reactions. UV-Vis spectra revealed the possibility of irradiation in the visible light range.

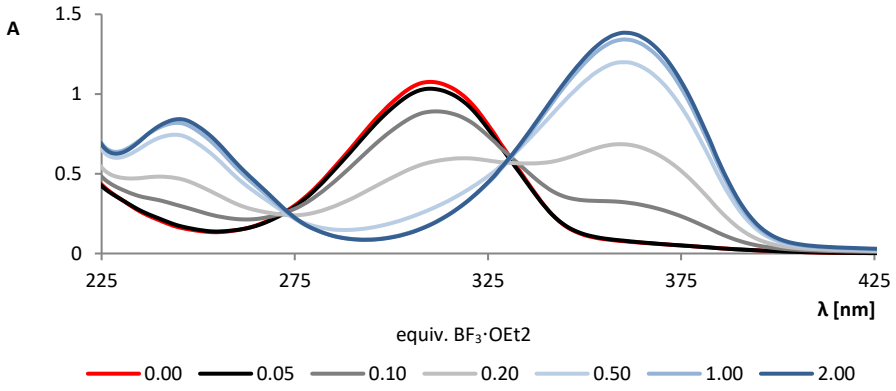
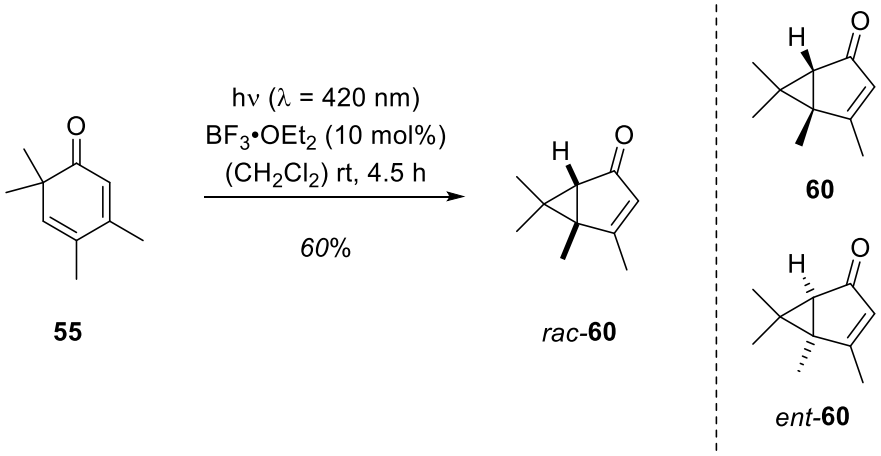


Figure 8. UV/Vis spectra of cyclohexadienone **55** with different equivalents of Lewis acid.

This gave access to much higher yields up to 78% and also showed that catalytic amounts of Lewis acid were able to achieve complete conversion and a good yield of 60% at λ = 420 nm (Scheme 18). Boron trifluoride evolved as the best choice of racemic Lewis acids. In addition, evidence of a background reaction was not found as 2,4-cyclohexadienone **55** did not show any reactivity when the Lewis acid was omitted.[8]



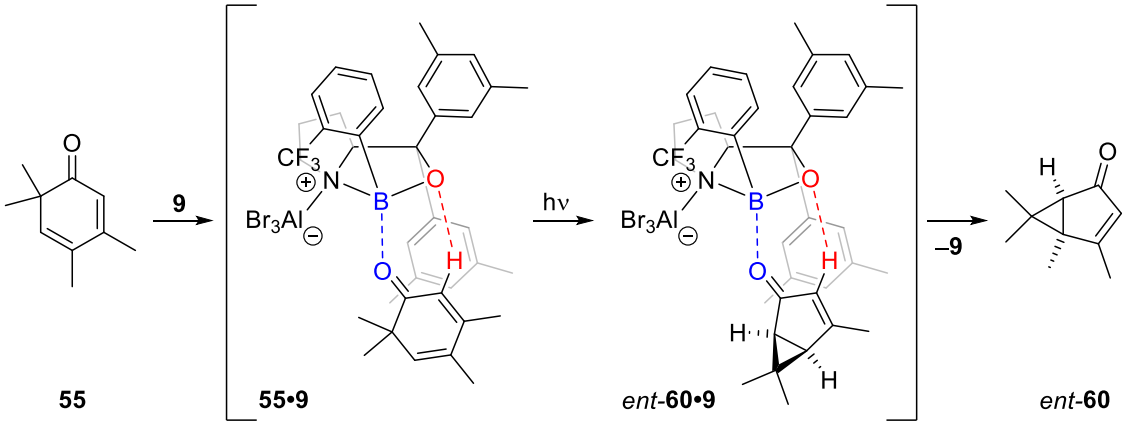
Scheme 18. Racemic Lewis acid catalyzed photochemical rearrangement of cyclohexadienone **55**. The racemic mixture of photoproduct *rac*-**60** consists of enantiomers **60** and *ent*-**60**.[8]

2.2. Project Aims

Evaluation of racemic reaction conditions, demonstrated the possibility of a Lewis acid catalyzed photorearrangement at visible light. The previously mentioned findings were promising for the development of an enantioselective approach. An efficient reaction with a low Lewis acid loading and the absence of a background reaction at visible light, encouraged us to a transition to chiral Lewis acids. The low presence of enantioselective examples of photochemical rearrangements in literature motivated us greatly to investigate the optimal reaction conditions and catalysts for a photorearrangement reaction with high enantioselectivity. In addition, the structure of the obtained photoproducts appeared to interesting chiral building blocks.

As a result of several successful applications of chiral oxazaborolidinium complexes in enantioselective photoreactions, they were unarguably our preferred choice to evaluate the possibility of an enantioselective version of the previously established catalyzed photorearrangement reaction .[37, 39-41] Besides obvious differences of reaction outcome and mechanisms between [2+2] photocycloaddition and photochemical rearrangement, we were more interested in the similarities of our substrates concerning binding to the catalyst. The efficient chirality transfer from catalyst to substrate greatly depended on the successful formation of a configurational stable substrate-catalyst complex.

The prerequisite of the chelating binding motif of the oxazaborolidinium catalyst to the substrate was met by 2,4-cyclohexadienones with a hydrogen in 2-position, e.g. **55**. Therefore, the coordination between boron atom of the catalyst and carbonyl oxygen atom of the substrate (*blue*) would be accompanied by the second coordination between the catalyst's oxygen atom and the hydrogen atom in 2-position of the substrate (*red*). Hence, once bound to the catalyst, e.g. Lewis acid **9**, 2,4-cyclohexadienone **55** would not have the freedom to rotate and would therefore react enantioselectively, if chirality was efficiently transferred from the catalyst to the coordinated 2,4-cyclohexadienone in complex **55·9** (Scheme 19). Our hypothesis was that the quaternary carbon with its *gem*-dimethyl groups try to evade the catalyst's 3,5-dimethylphenyl group (*grey*) during the rearrangement, hence we expected enantiomer *ent*-**60** to be formed in excess (Scheme 19).



Scheme 19. Envisioned enantioselective photochemical rearrangement of **55** to *ent*-**60** via hypothesized substrate-Lewis acid complex **55**·**9**.

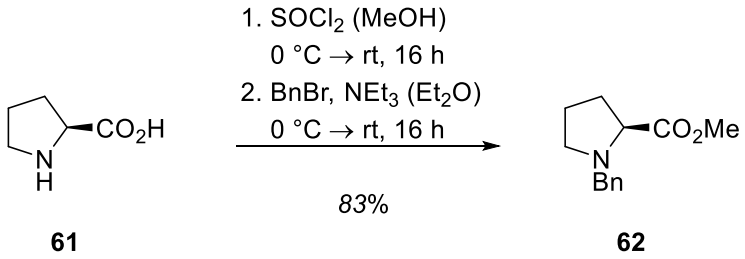
However, in comparison to substrates used in [2+2] photocycloaddition reactions, there is no approach of an alkenyl linker or olefin and in this case the reaction center is located on the opposite site of the carbonyl group. This led to the application of several, including new, oxazaborolidinium catalysts.

2.3. Synthesis of Chiral Oxazaborolidinium Complexes

Literature of oxazaborolidinium catalysts shows that even though this class of chiral Lewis acids proves to be very effective in a variety of reactions featuring α,β-unsaturated carbonyl compounds, there is often demand for some fine tuning of the catalyst's electronic and steric properties in order to achieve the best outcome for a certain reaction. Oxazaborolidinium catalysts have the potential of derivatization in different positions.[27-28, 38] This work will almost exclusively deal with oxazaborolidines prepared from *L*-proline, however other amino acids can serve as chiral building blocks. Additionally, activation of oxazaborolidines to form the Lewis acidic oxazaborolidinium complexes, is done using aluminum tribromide throughout this work. It needs to be mentioned, that other Lewis acids or Brønsted acids can act in an equal fashion and have been used in literature.[27-29] In addition, a broad library of oxazaborolidines can be synthesized by condensing a given prolinol with different boronic acids, thus creating a quick access to variation of the substituent at the boron atom. Last but not least, the two substituents creating the oxazaborolidines backbone can be varied. Per contra, in contrast to boronic acids only few prolinols are commercially available and therefore need to be synthesized.

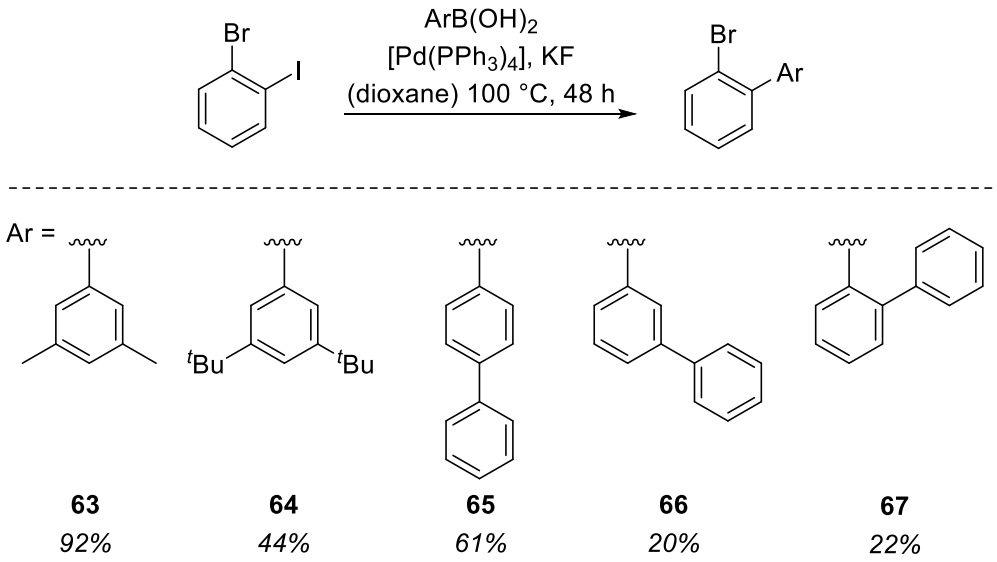
2.3.1. Synthesis of Prolinols

In this work, *L*-Proline (**61**) served as chiral building block for enantiomerically pure oxazaborolidines. Converting this amino acid to the *N*-benzyl protected proline methyl ester **62** using a literature-known procedure[65] that was further optimized in our group,[66] leads to a common intermediate for different prolinols that can be further converted to oxazaborolidines. A twofold *Grignard* addition to this intermediate introduces the catalyst's aryl groups and for this reason substitution can be easily varied by reacting **62** with different aryl *Grignard* reagents. Due to the broad commercial availability of aryl bromides, a large variety of substituted prolinols is available and was already subject to studies in our group.[38]



Scheme 20. Synthesis of benzyl proline methyl ester **62** from *L* -proline (**61**).

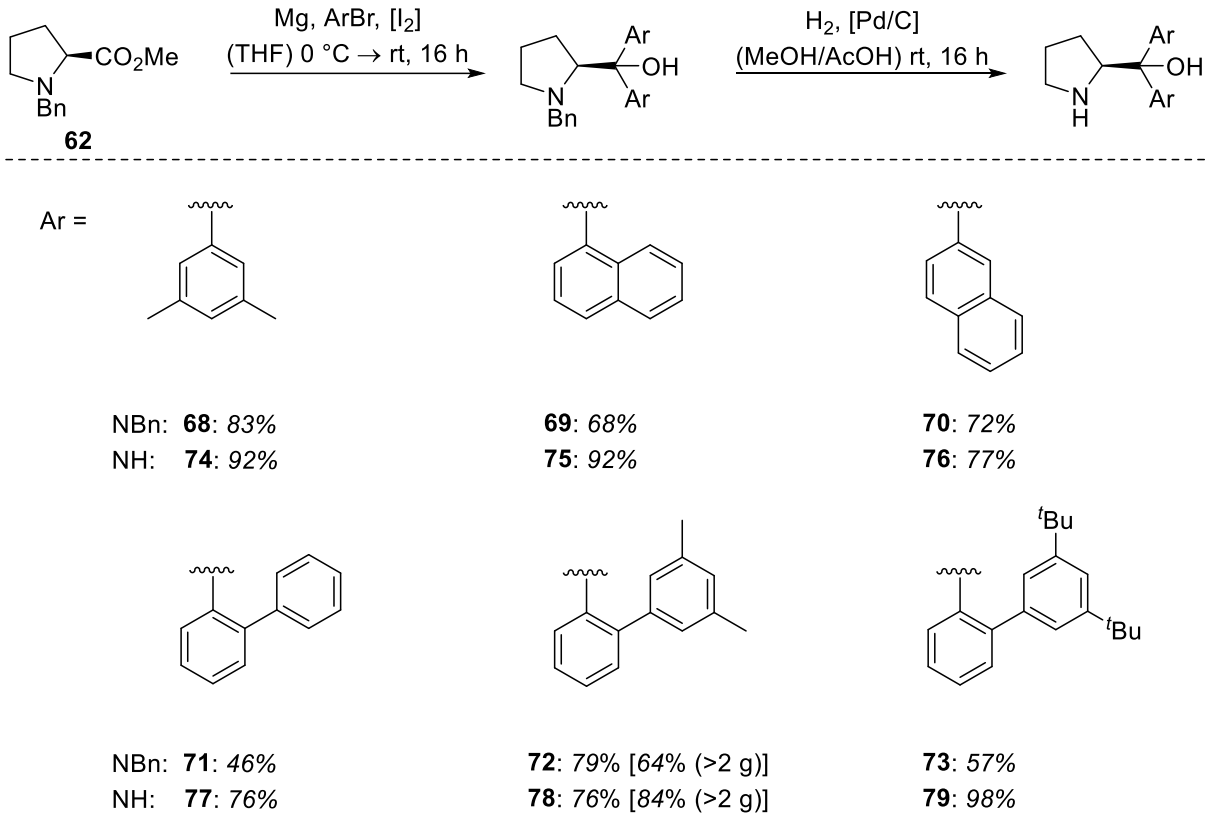
In order to extend our prolinol library, we also evaluated biphenyl groups. However, substituted 2-biphenyl bromides were not commercially available. Their preparation was achieved by *Suzuki* coupling of 2-bromoiodobenzene with the respective aryl boronic acid (Scheme 21). Following a protocol by *Zhang* et al.[67], yields varied from 44-92% for 3'5'-substituted biphenyl bromides **63** and **64** and 20-61% for terphenyl bromides **65-67**.



Scheme 21. Synthesis of aryl bromides **63-67** via *Suzuki* coupling of 2-bromoiodobenzene with arylboronic acids.

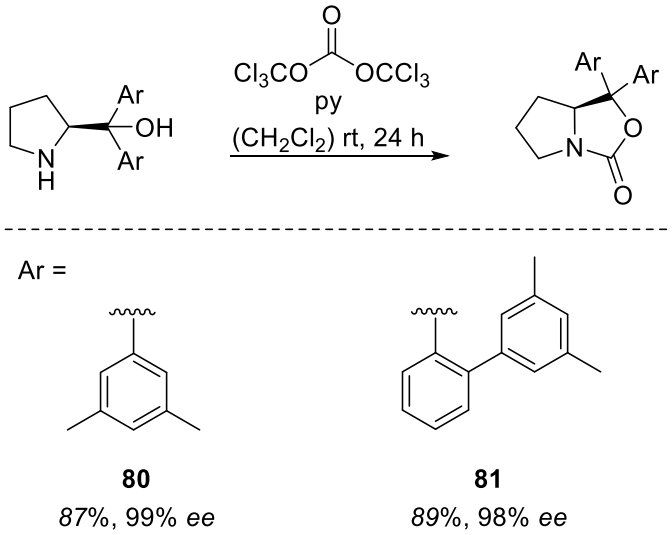
Grignard reagent preparation and addition to ester **62** proceeded in good yields with 1-bromo-3,5-dimethyl benzene to **68** (83%), 1-bromonaphtalene to **69** (83%) and 2-bromonaphtalene to **70** (83%), as well as with the prepared 2-bromo-3',5'-dimethyl biphenyl to **71** (79%). Preparation of **71** on a larger scale was not as successful as on small scale, the yield remained satisfactory, however. Biphenyl prolinols **72** and **73** could be synthesized in moderate yields

(46% and 57%). Removal of the benzyl group using hydrogenolysis proceeded in good to excellent yields in all cases (**74**-**78**,76-98%), including hydrogenolysis on larger scale (**77**, 84%) (Scheme 22).



Scheme 22. Synthesis of diaryl prolinols via twofold *Grignard* addition and removal of the benzyl group.

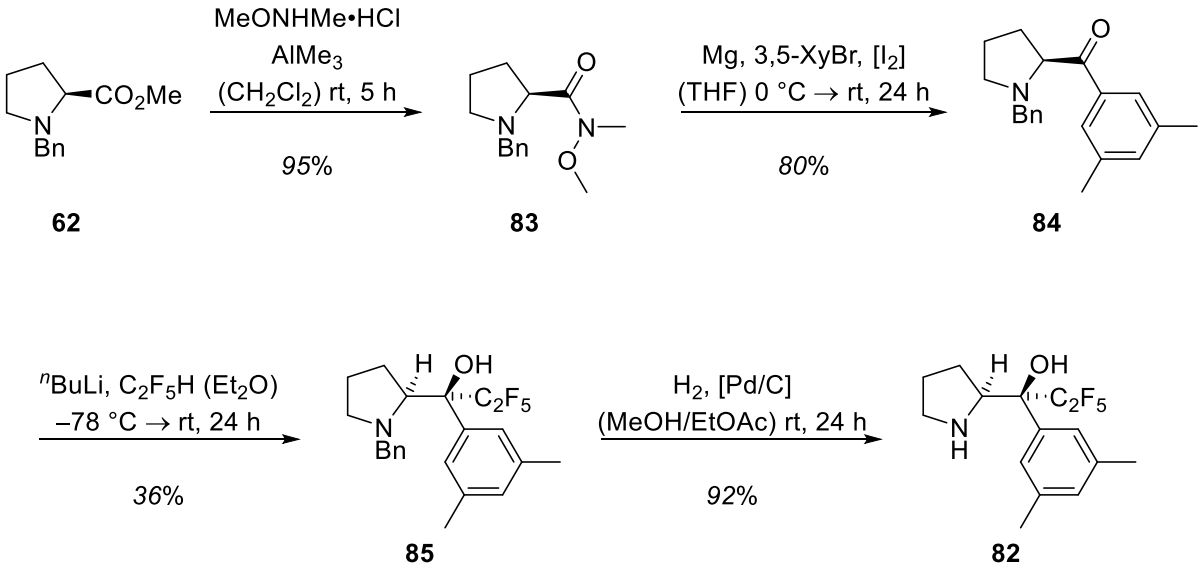
The enantiopurity of the synthesized prolinols were determined via chiral HPLC analyses of their cyclized derivatives, due to the fact that the free amino alcohols proved to be not separable. For this purpose, prolinols **74** and **78** were cyclized to oxazolones **80** (87%) and **81** (89%) in high yields according to a procedure by *Palomo* et al. using triphosgene.[68] Enantiopurity in both cases was very high (**80**: 99% *ee*, **81**: 98% *ee*), indicating that almost no racemization took place during the course of preparation (Scheme 23).



Scheme 23. Synthesis of Oxazolidinones **80** and **81** for chiral HPLC analyses.

In addition to new diaryl substituted prolinols, a pentafluoroethyl substitution was incorporated in our prolinol library. Considering *Corey*'s second-generation oxazaborolidines, we prepared pentafluoroethyl prolinol **82**. Modification of the synthetic route as well as the aryl substitution led us to the following approach.

Weinreb amide **83** was successfully prepared from our common intermediary ester **62**. After *Grignard* addition, aryl ketone **84** could be isolated. Due to its lability, this was promptly converted with pentafluoroethyllithium, which was *in situ* prepared from *n*-butylllithium and pentafluoroethane. After some alterations concerning the procedure, we found out that pentafluoroethyllithium was most reliably formed when a degassed *n*-butyllithium solution was stirred under a pentafluoroethane atmosphere at −78 °C. The yield was modest at best, but it gave enough material of **85** as single diastereomer for the benzyl group removal, which again worked very well (Scheme 24).



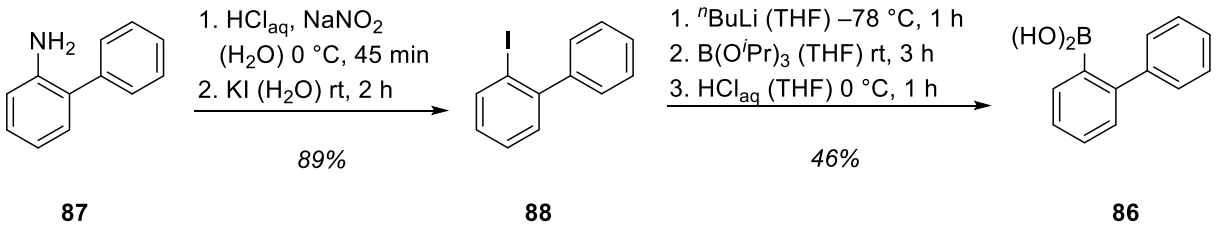
62 **83** **84** **85** **82**

Scheme 24. Synthesis of pentafluoroethyl substituted prolinol **82**.

2.3.2. Synthesis of Biphenyl Boronic Acids

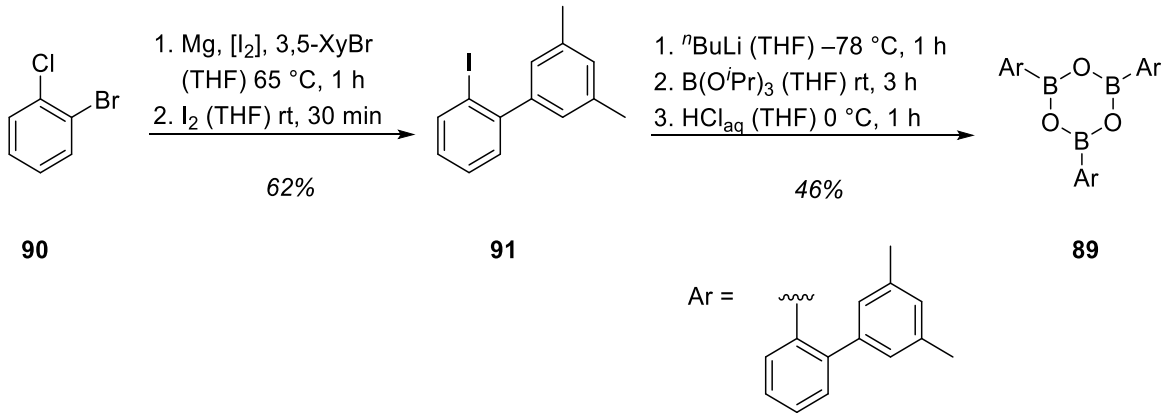
Having extended our prolinol library, the synthesis of two biphenyl boronic acids was approached. Oxazaborolidinium catalysts incorporating 2-biphenyl boronic acid or its 3',5'-dimethyl substituted derivative had previously been successfully applied in an intramolecular chirality transfer [2+2] cycloaddition and had attracted our interest.[69]

2-Biphenyl boronic acid **86** is accessible by converting 2-aminobiphenyl (**87**) to 2-iodobiphenyl (**88**) in a *Sandmeyer*-type reaction. Following a protocol reported by *Porriel* using potassium iodide.[70] **88** could be isolated as colorless oil in 89%. Due to its instability to light, a pink color developed when light was not completely excluded upon storage. Boronic acid **86** was subsequently synthesized from iodide **88** by employing a procedure used by *Li* et al.[71] After halogen-metal exchange with *n*-butyllithium, the corresponding diisopropyl boronic ester was formed, which yielded the boronic acid after hydrolysis. In order to achieve the desired purity, column chromatography needed to be followed by recrystallization to give pure boronic acid **86** in 46% yield.



Scheme 25. Synthesis of biphenylboronic acid **86**.

Boroxin **89** was synthesized according to a protocol applied by *Xu* et al.[69] 2-Bromochlorobenzene (**90**) was converted with freshly prepared 3,5-dimethyl-phenylmagnesium bromide in a *Wurtz*-type coupling and subsequently treated with iodine to give iodobiphenyl **91** in 62% yield. This compound showed a similar instability to light as **88** and was therefore stored under exclusion of light or directly transformed to **89**. Employing the same reaction conditions as in the synthesis of **86**, albeit with different recrystallization conditions, boroxine **89** was isolated in 46% yield. It is possible that after recrystallization, amounts of boronic acid are still present, which can be condensed to the trimer by heating under reflux in toluene in a *Dean-Stark* apparatus.

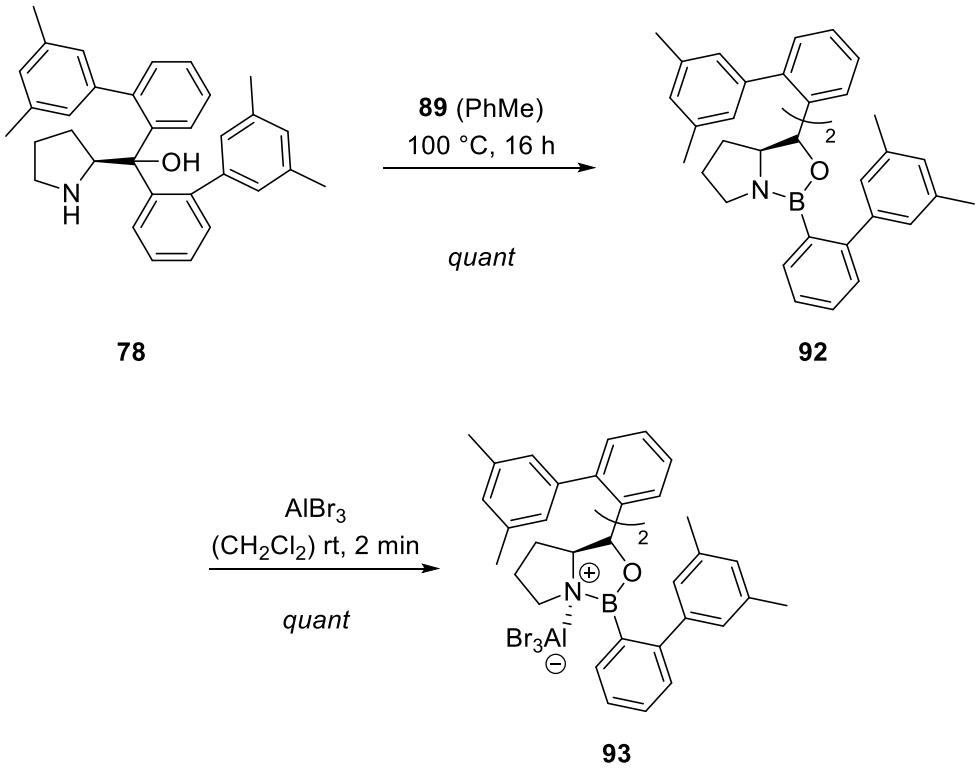


Scheme 26. Synthesis of biphenylboroxin **89.**

2.3.3. Synthesis of Oxazaborolidines and Oxazaborolidinium Complexes

Condensation of prolinols with boronic acids, represented by the synthesis of **92** in Scheme 27, was performed by applying a literature-known procedure,[27] which had been further modified

in our group.[35, 40] Due to high instability of oxazaborolidinium aluminum bromide complexes such as **93** towards hydrolysis, it is crucial to obtain oxazaborolidines under complete exclusion of moisture. Consequently, in order to eliminate even last traces of water the majoritiy of toluene is distilled off and replaced with fresh anhydrous toluene repeatedly during preparation. More importantly, fresh oxazaborolidines were synthesized immediately before each photochemical reaction. Even though oxazaborolidines are stable in storage, complete exclusion of moisture proved to be difficult and led to decrease in performance and lack of reproducibility in earlier studies by *Brimioulle*.[72] In order to ensure a successful synthesis of **92**, a sample synthesized under representative conditions was fully characterized. Nonetheless, it was fundamental to record NMR spectra of **92** in thoroughly dried and degassed benzene-d_6 stored in a glovebox to obtain spectra that showed pure compound **92**. Activation of oxazaborolidines using aluminum tribromide was conducted immediately prior to the application in photochemical reactions. Due to the mentioned high instability towards moisture, as well as temperatures above −20 °C, aluminum tribromide complex **93** is not suitable for storage and analytical data were not recorded. It was determined that formation of complex **93** could be conducted at room temperature and cooled almost immediately, as it was completed instantaneously after addition of aluminum tribromide to a solution of oxazaborolidine **92** (Scheme 27). This procedure gave the same reproducible results as to when complex **93** was formed at low temperature.

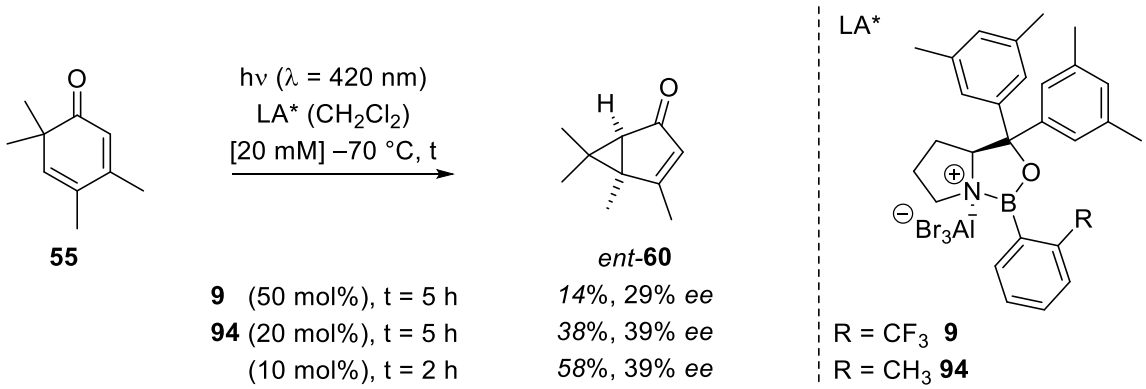


Scheme 27. Synthesis of oxazaborolidine **92** and aluminum bromide oxazaborolidinium complex **93**.

2.4. Enantioselective Photochemical Rearrangement Reactions

2.4.1. Optimization of Reaction Conditions

Previous studies[8] had shown that at −40 °C, 50 mol% of catalyst **9** were in fact able to catalyze the photochemical rearrangement of **55** enantioselectively to *ent*-**60**, though enantioselectivity was < 30% *ee*. It was observed that lowering the catalyst loading to 20 mol% left the enantioselectivity unchanged as no background reaction occurred. Irradiation at room temperature showed rapid catalyst decomposition with atrocious yield and enantiomeric excess. At −70 °C, the reaction gave a higher yield and a slightly higher enantiomeric excess. This was the best result obtained so far, represented in Scheme 28.

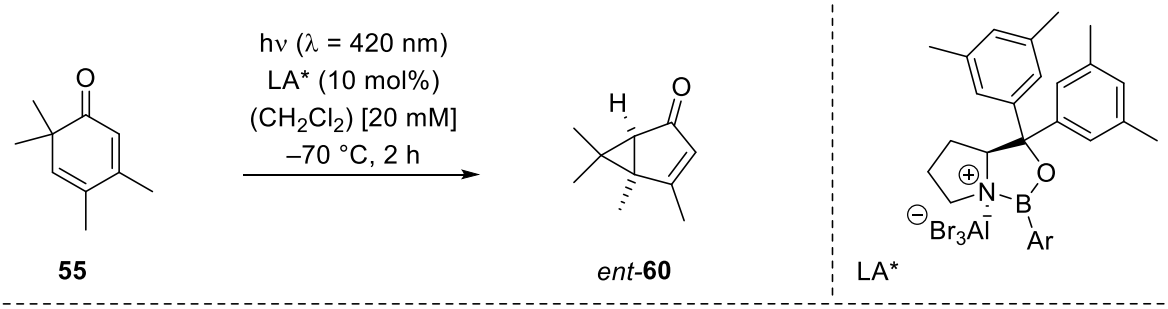


Scheme 28. Enantioselective photochemical rearrangement of **55** with catalysts **20** and **94**.

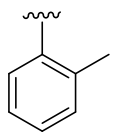
Based on this state of knowledge, it was further discovered that the enantioselectivity could be increased by using catalyst **94**, differing by the absence of fluorination, obtaining *ent*-**60** in 38% yield and 39% *ee* (Scheme 28). In a series of experiments, monitoring conversion, yield and enantiomeric excess by GC chromatography, it was found that the reaction in fact proceeded much faster than expected and previously concluded from TLC reaction monitoring. This is due to the fact that due some degree of photoproduct degradation, the optimal yield of *ent*-**60** could be achieved when the reaction was terminated before complete conversion was reached. Taking this into consideration, we decreased catalyst loading and reaction time which led to an increased yield of 58% with an unchanged enantiomeric excess of 39% (Scheme 28). Applied reaction conditions were set as standard conditions for further catalyst screenings.

2.4.2. Screening of Boronic Acids

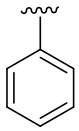
Once a moderate yield was achieved, we focused on the enantioselectivity in the photochemical rearrangement of **55**, which so far had not met our standards. Firstly, further evaluation of substitution changes at the oxazaborolidine's boron atom was conducted (Scheme 29). Unfortunately, it seemed that we already had reached our limit with the previously shown catalyst **94** with a 2-methylphenyl group at the boron atom. Other aryl substitution did not lead to a decrease of enantiomeric excess, but additionally to lower yields, in most cases <40%, and significant amounts of recovered starting material (15-46%) indicating a slower rate of conversion, As previously mentioned, the photoreaction of **55** was stopped before full conversion was reached. However, according to GC the amounts of residual **55** were at a very low level (5%). Substitution featuring a phenyl group (**95**) led to a decrease in enantiomeric excess to 22% *ee* and applying standard conditions to the previously used catalyst (**9**) showed a similar result. Changing electronic properties more drastically failed, as fluorine atoms at the phenyl ring (**96**) or a methoxy substituent (**97**) led to an almost racemic reaction outcome (3% and 6% *ee*). Different substitution patterns with alkyl groups (**20**, **98**-**104**) did not lead to any improvements either, with results of 23-57% yield and 21-31% *ee*. Interestingly, having a methyl group in *ortho*-position of the phenyl ring appeared to be slightly better than their competitors lacking it. The low enantioselectivity (21% *ee*) in the case of **105** with an isopropyl group was therefore very disappointing. In addition, substitution with 1-naphtyl (**106**) and 2-naphtyl groups (**107**) was tested resulting in low yields (35% and 30%) and low enantioselectivity (21% and 18% *ee*). Solely catalysts **108** and **109** possessing *ortho*-biphenyl substituents were able to perform equally to **94** and *ent*-**60** could be isolated in 57% and 52% yield with 41% and 42% *ee*.



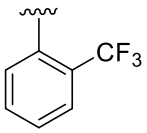
55 *ent*-**60** LA*



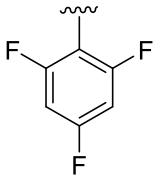
94
58%, 39% *ee*



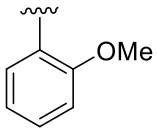
95
32%, 22% *ee*
26% rsm



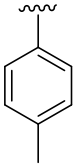
9
35%, 23% *ee*
45% rsm



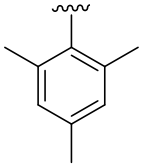
96
24%, 3% *ee*
37% rsm



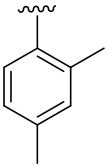
97
19%, 6% *ee*
46% rsm



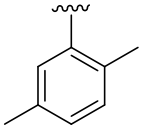
98
32%, 22% *ee*
26% rsm



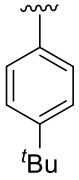
99
23%, 31% *ee*
36% rsm



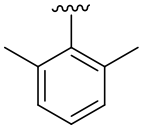
100
54%, 30% *ee*
19% rsm



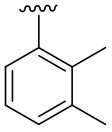
101
46%, 27% *ee*
15% rsm



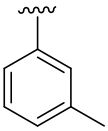
102
33%, 26% *ee*
15% rsm



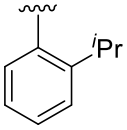
20
23%, 31% *ee*
36% rsm



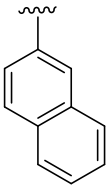
103
30%, 26% *ee*
30% rsm



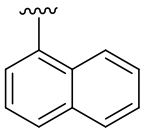
104
36%, 20% *ee*
14% rsm



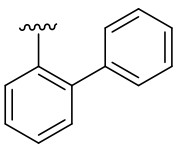
105
57%, 21% ee
12% rsm



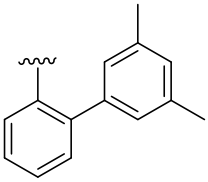
106
35%, 21% *ee*
34% rsm



107
30%, 18% *ee*
44% rsm



108
57%, 41% *ee*
24% rsm



109
52%, 42% *ee*
24% rsm

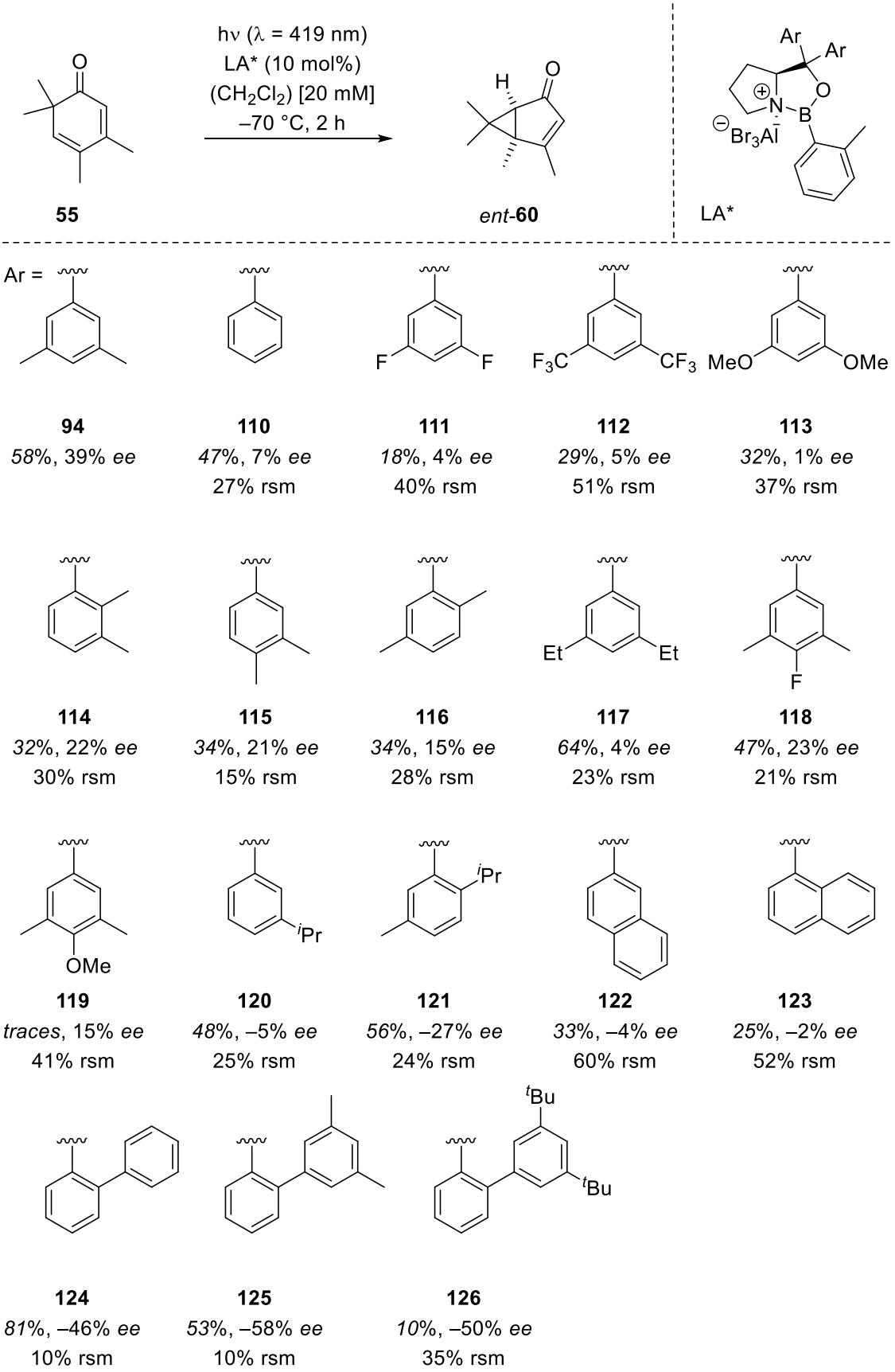
Scheme 29: Screening of chiral Lewis acids **9**, **20** and **94 - 109** in the enantioselective photorearrangement reaction of cyclohexadienone **55.**

Since the variation of the boronic acids in the syntheses of oxazaborolidines was deficient in increasing yield and especially enantioselectivity in the photochemical rearrangement of **55**, we realigned our focus on the catalyst's backbone substitutions. Oxazaborolidinium catalysts (**93, 110**-**121**) prepared from prolinols recently developed in our group[38, 40] with 2-methylphenyl boronic acid were tested and our screening was completed with the evaluation of oxazaborolidinium complexes (**122**-**126**) derived from literature-known naphthyl prolinols and our new biphenyl substituted prolinols.

2.4.3. Screening of Prolinols

For reasons of overlapping screening series, our bench mark for the screening was again catalyst **94**, with the additional advantage that 2-methylphenyl boronic acid is commercially available in contrast to dimethylbiphenylboroxin **89**. Similar variations of the aryl groups were tested as in the previous screening of the boron-attached substituents. However, results appeared to be even more discouraging as in our first screening. No substitution (**110**, 7% *ee*), electronic deficient (**111**, 4% *ee*; **112**, 5% *ee*) and electron donating substituents (**113**, 1% *ee*) proved to obliterate all selectivity in the photochemical rearrangement. Especially alteration of electronic properties led additionally to a substantial decrease in conversion and consequently in yield. 2,3-Dimethyl, 3,4-dimethyl and 2,5-dimethyl substitution (**114**-**116**) led to a decrease in enantiomeric excess (15-22% *ee*) in slower reactions. Changing the 3,5-dimethyl substitution to 3,5-diethyl (**117**) was also disastrous for enantioselectivity (7% *ee*), in spite of a better yield of 64%. Returning to the 3,5-dimethyl motif with an additional substituent in 4-position, catalysts **118** and **119** were investigated. Fluorine in 4-position gave the photoproduct in 47% yield and 23% *ee*, whereas a methoxy group shut down the reaction almost completely with low selectivity (15% *ee*). Nonetheless, photoreactions with catalysts **120** and **121** featuring an isopropyl group aroused our interest. 3-Isopropylphenyl substituted catalyst **120** gave a moderate yield of 48% with a very low enantioselectivity, however preferring the other enantiomer **121**. Almost racemic, it seemed negligible at first, still the observed effect of enantiodivergence (indicated by a 'minus') was a lot more distinct with the isopropyl group in 2-position of the phenyl ring (**121**), when enantiomer **60** was isolated in 56% yield and 27% *ee*. Comparing catalysts **94** and **121**, we observed a difference of 66% in enantiomeric excess and thus we investigated the possibility increasing the selectivity for **60** even further. Investigating an effect of annulated rings, naphthyl substituted catalysts **122** and **123** fell short of our expectations, with almost racemic reaction outcomes. Biphenyl catalyst **124** showed that an aryl

substitution in 2-position was much more effective, giving **60** in an excellent yield of 81% and 46% *ee* and 3',5'-dimethyl-2-biphenyl catalyst **125** exceeded **124** in enantioselectivity (58% *ee*). *tert*-Butyl groups in 3',5'-position of catalyst **126** presumably caused a steric bulk that affected the binding of cyclohexadienone **55** to the catalyst as the low yield indicates.

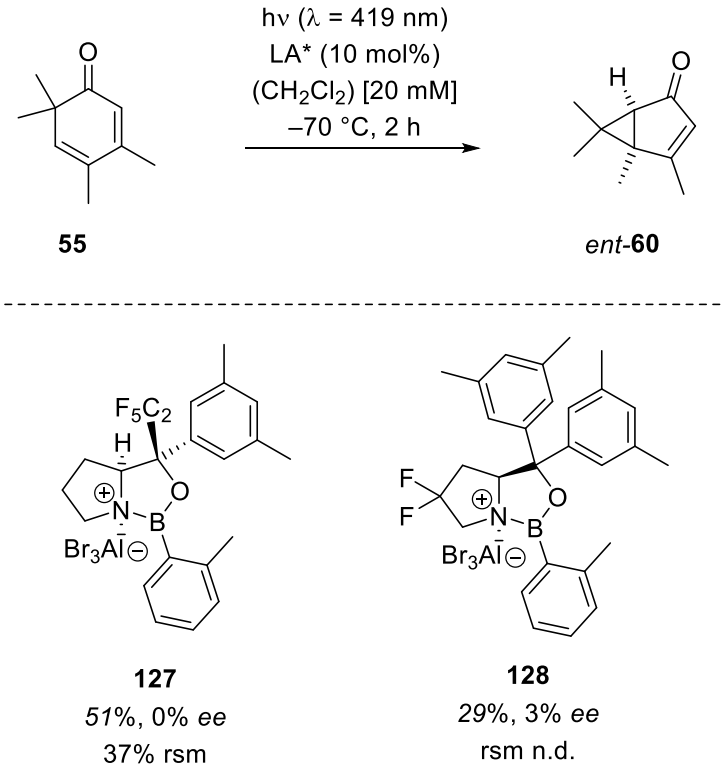


Scheme 30. Screening of chiral Lewis acids **94** and **110** - **126** in the enantioselective photorearrangement reaction of cyclohexadienone **55**.

2.4.4. Oxazaborolidines Derived from Fluorinated Prolinols

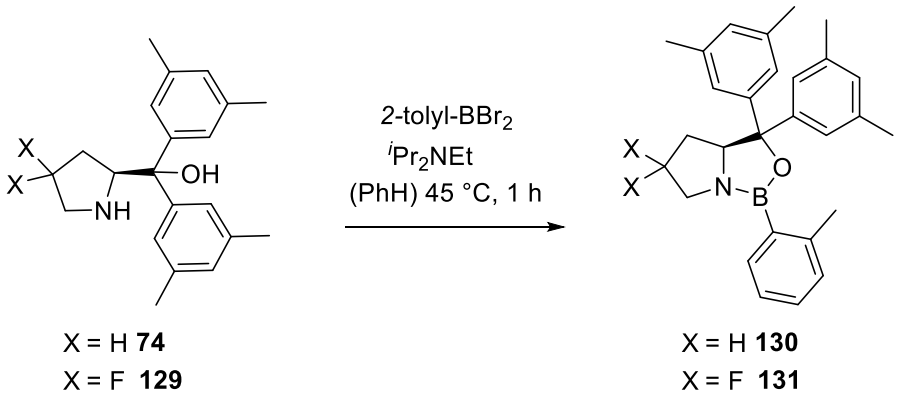
In addition to the mentioned variations of substituents at the oxazaborolidine's aryl groups, two catalysts were tested that were modified structures of *Corey*'s second-generation oxazaborolidines.[28-29] Synthesis of the precursor to **127** has been described previously, the precursor to **128** had been synthesized in our group.[73]

The observation that these second-generation catalysts, were more potent in cycloaddition reactions than the unfluorinated first generation[28], offered hope for a potential improvement in our photochemical rearrangements. Unfortunately, the negative effect of electron deficient substituents at the aryl groups also held true for fluorine substitution at the pyrrolidine ring and exchange of one aryl ring with the certainly electronegative pentafluoroethyl group. *ent*-**60** could only be isolated 51% and 29% yield as racemic mixture of both enantiomers (0% and 3% *ee*) (Scheme 31).



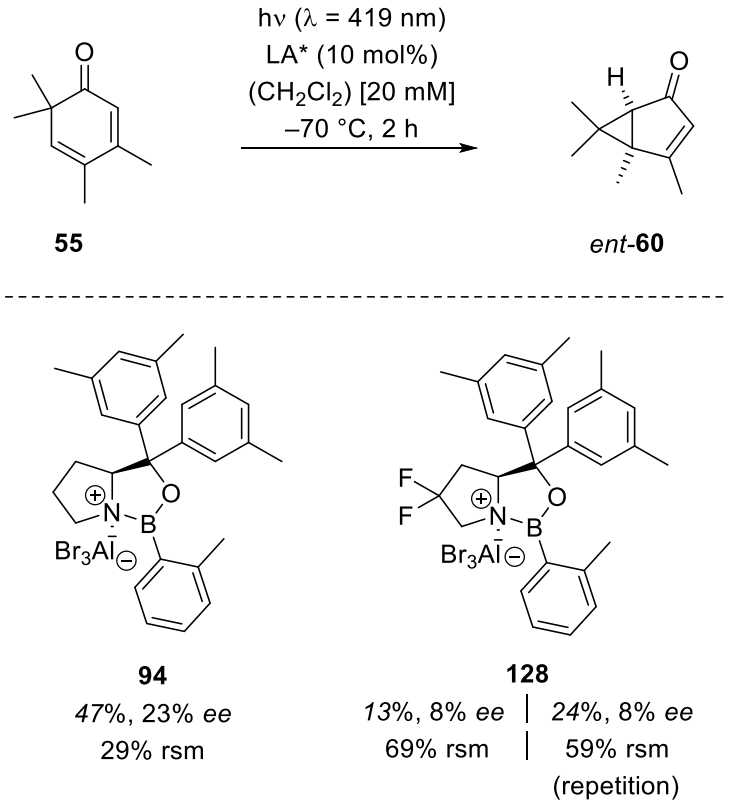
Scheme 31. Screening of chiral Lewis acids **127** and **128** in the enantioselective photorearrangement reaction of cyclohexadienone **55**.

In order to rule out decomposition of our catalyst previous to the reaction, we changed the condensation protocol. Following a protocol published by *Reddy* et al.[28], 2-methylphenylboron dibromide was prepared from 2-bromotoluene via the corresponding trimethyl silane in two steps[28] and condensed with prolinols **74** and **129** in the presence of diisopropylethylamine (Scheme 32). Synthesis of **130** was performed and it was used in a control experiment to compare the new procedure with standard condensation conditions using a boronic acid. After removal from the precipitated ammonium salts oxazaborolidines **130** and **131** were obtained and were directly activated to catalysts **94** and **128** according to the standard activation procedure.The catalysts were directly applied in the photoreaction.



Scheme 32. Alternative synthesis of oxazaborolidines **94** and **129**.[28]

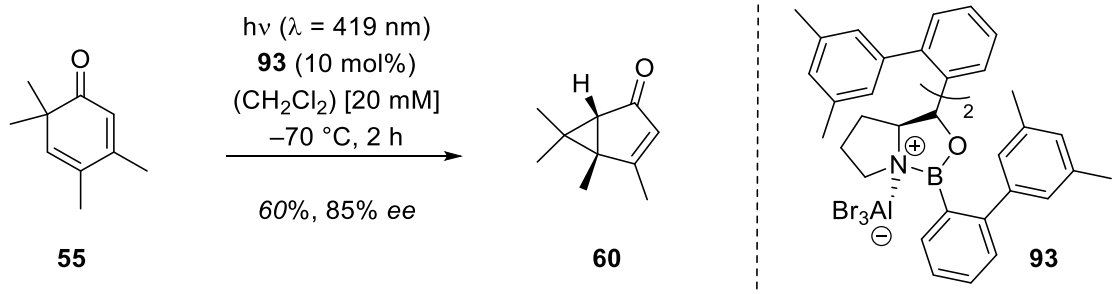
In the control experiment, rearranged photoproduct *ent*-**60** was obtained in 47% and 23% *ee* with catalyst **94**, compared to 58% yield and 39% *ee*, indicating that the catalyst was less effective but not completely inoperative when prepared by the new procedure. Presumably, traces of diisopropylethylamine inhibit catalyst activation or impair it. Catalyst **128** gave a low yield of 13% and minimally higher enantiomeric excess (8%) than when prepared from the boronic acid. Repetition afforded 24% of *ent*-**60** with 8% *ee*, giving evidence to the fact that catalyst **55** was not suitable for the investigated photochemical rearrangement.



Scheme 33. Screening of chiral Lewis acids **94** and **128**, synthesized by condensation with 2-tolylboron dibromide, in the enantioselective photorearrangement reaction of cyclohexadienone **55**.

2.4.5. Final Optimization of Reaction Conditions

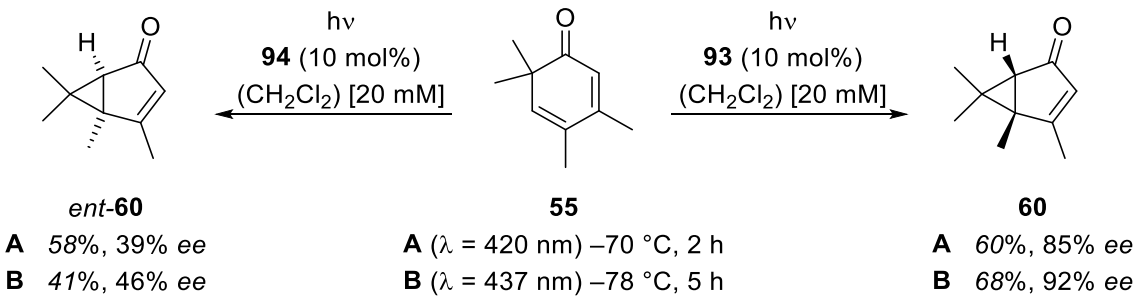
Returning to the most promising prolinol **78**, condensation with the most promising boroxin **89** gave catalyst **93** after activation, featuring three dimethylbiphenyl groups. To our delight, this combination proved to be extremely fruitful. Photochemical rearrangement of **55** proceeded with good yield (60%) and very high enantioselectivity (85% *ee*) (Scheme 34). Doubts, that catalyst **93** would be too sterically demanding or having a mismatching impact of the biphenyl groups, did not hold true.



Scheme 34. Enantioselective photochemical rearrangement of cyclohexadienone **55** catalyzed by catalyst **93**.

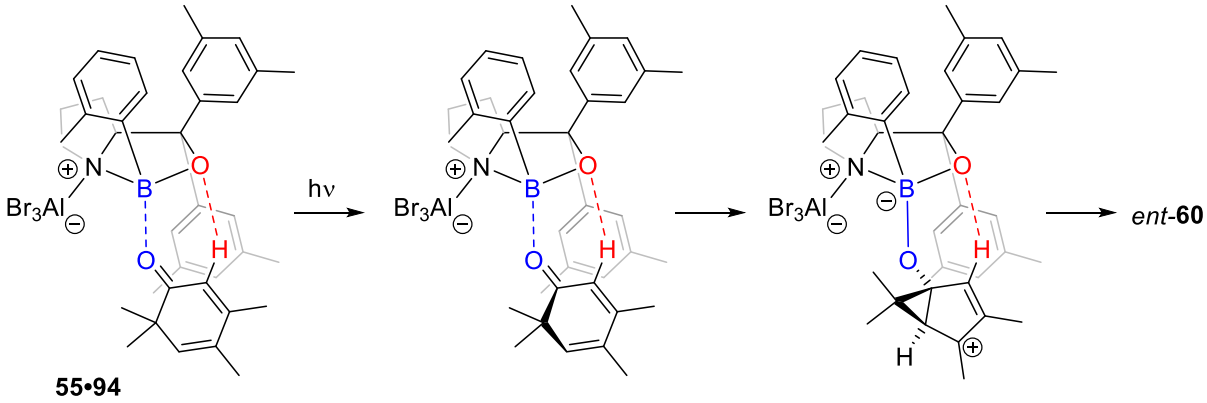
Having finally achieved a high level of enantioselectivity combined with a satisfying yield, a last fine-tuning was attempted. A small change of wavelength from λ = 420 nm to λ = 437 nm led to further improvement. Yet, this small alteration came with a change in equipment. Irradiations at λ = 420 nm are conducted in a phototube, immersed in a cooling finger within a reactor with 16 fluorescent light tubes. The employed light source at λ = 437 nm is a light emitting diode (LED) connected to a glassrod with a sandblown end submerged in the reaction solution. This negative geometry leads to a high efficiency, because almost all photons emitted pass through the reaction solution. Nonetheless, reactor power (16 × 8 W) is much greater than the 10 W of the LED. Hence, rate of the reaction was decreased and duration of irradiation had to be reevaluated.

Irradiation in the presence of catalyst **94** at λ = 437 nm gave a lower yield, compared to λ = 420 nm, but an improved enantioselectivity. Light sources were also compared when catalyst **93** was applied and at λ = 437 nm the yield increased by 8% in comparison and enantioselectivity improved additionally, producing **60** in excellent enantioselectivity (Scheme 35). At this stage, the developed reaction conditions were put on trial with different 2,4-cyclohexadienones.



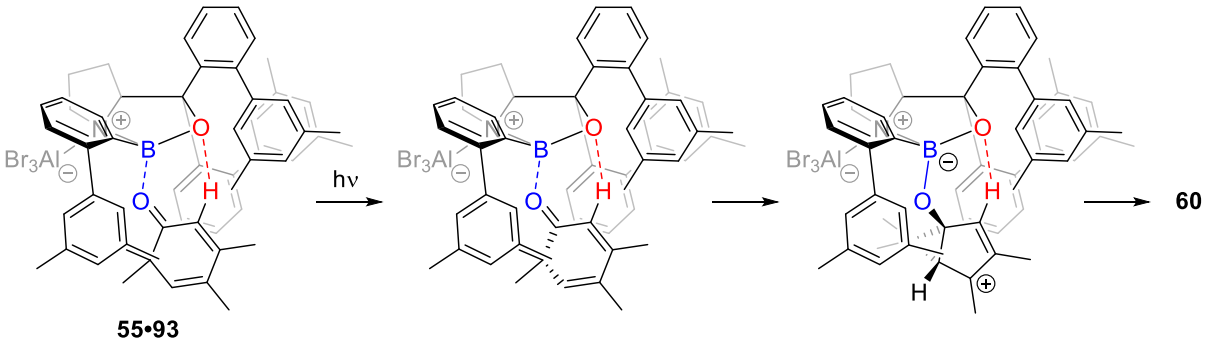
Scheme 35. Comparison of the influence of catalysts **94** to **93** and photoreactor (**A**) to LED setup (**B**) in the photochemical rearrangement of cyclohexadienone **55**.

The observed enantiodivergence in the photorearrangment reaction can be explained by using proposed structures of the substrate-Lewis acid complexes (Scheme 36). In the case of catalyst **55·94** we expected one of the dimethylaryl groups to induce a steric effect from the *si* face of the carbonyl oxygen atom. Upon excitation to the singlet state, the sterically demanding *gem*-dimethyl carbon atom (C-6) bends out of plane and tries to evade the dimethylaryl group. Bond formation between C-1 and C-5 carbon atoms leads to a zwitterionic intermediate with two defined stereocenters and the cyclopropane ring pointing away from the aryl group of the catalyst as result of the previous bend. A 1,4-migration then leads to the observed enantiomer *ent*-**60** (Scheme 36). Considering the low enantioselectivity (<50% *ee*) for the rearrangement when catalyst **94** is applied, the position of the relevant dimethylphenyl group is not optimal to largely affect the out-of-plane bend of C-6.



Scheme 36. Mechanistic model for the formation of bicyclohexenone *ent*-**60** from substrate-Lewis acid complex **55·94**.

In complex **55·93** we propose the steric influence of the dimethylbiphenyl groups to play a vital role. The two dimethylbiphenyl groups at the carbon atom push the dimethylbiphenyl group at the boron atom to the *re* face of the carbonyl oxygen atom. Thus, steric bulk of the dimethylbiphenyl group at the boron atom leads to a bend of the C-6 carbon atom in the opposite direction as with catalyst **94** and induces the formation of enantiomer **60** during the photochemical rearrangement (Scheme 37).



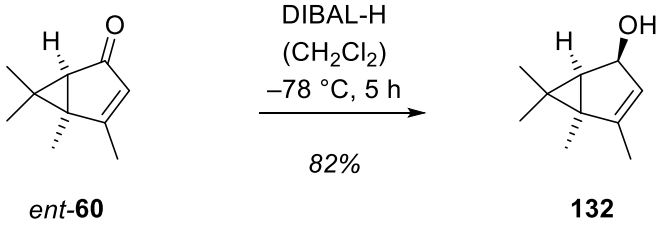
Scheme 37. Mechanistic model for the formation of bicyclohexenone **60** from substrate-Lewis acid complex **55·93**.

2.5. Determination of the Absolute Configurations

2.5.1. Derivatization of Bicyclohexenones

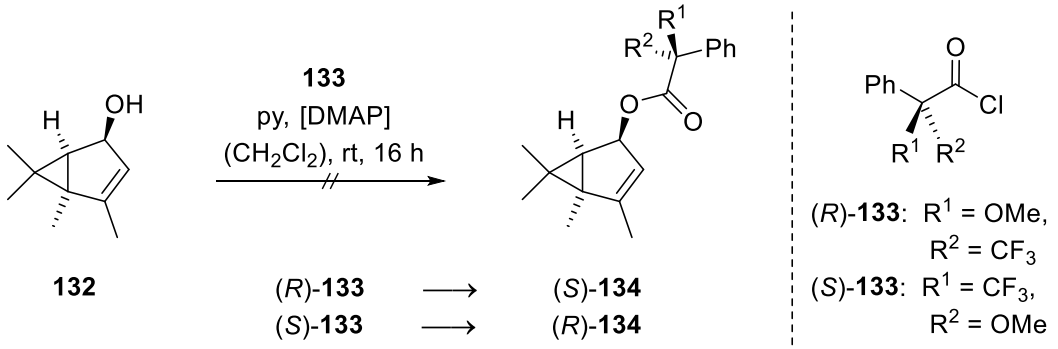
In order to obtain proof for the proposed absolute configuration of the photoproducts, standard photoproduct *ent*-**60** was derivatized. As the experiments were conducted simultaneously to the catalyst screening, enantiomeric excess of the material was low (<40% *ee*). Therefore, analysis of the respective *Mosher* esters was considered.

Diisobutylaluminum hydride was determined to be the best reducing reagent and after reduction at −78 °C alcohol **132** could be obtained as a single diastereomer.



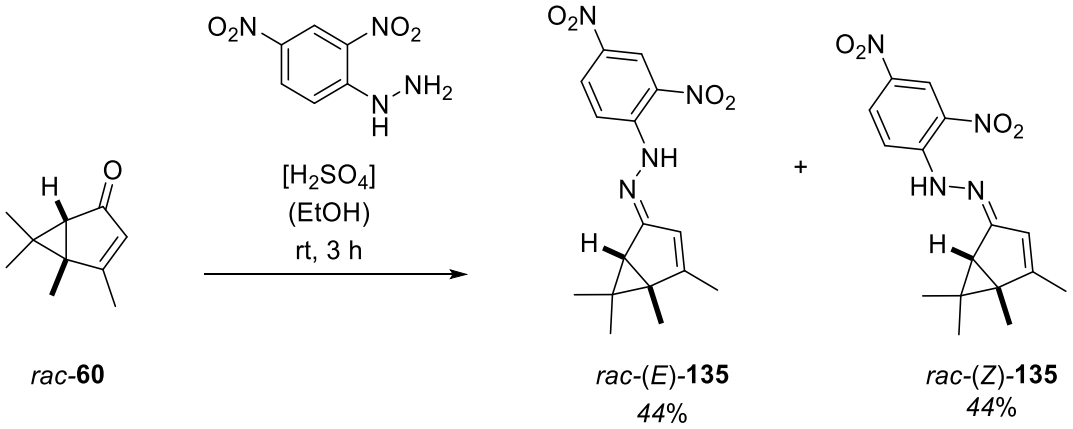
Scheme 38. Reduction of bicyclohexenone *ent*-**60** to bicyclohexenol **132**.

Esterification with the respective *Mosher*-acid chlorides (*R*)-**133** and (*S*)-**133** under the given reaction conditions, gave (*S*)-**134** and (*R*)-**134** in low yields (<40%) (Scheme 39). However, the compounds seemed to be instable and could not be purified to enable sufficient analysis. ^{1}H-NMR spectra showed the formation of diastereomeric mixtures. Use of opposite enantiomers of the acid chloride showed the reversed ratio of diastereomers in NMR. However, due to the low purity a sufficient assignment of the signals turned out to be impossible and after several trials, a change of strategy was contemplated. Also, attempts to alter stability of **132** by removal of the double bond, e.g. by hydrogenation of allyl alcohol **132** using Wilkinson's catalyst or cuprate addition to *ent*-**60**, failed.



Scheme 39. Attempted synthesis of Mosher esters **134** from alcohol **132**.

Aiming at a determination of configuration by X-ray crystallography, conversion of the photoproduct to the respective dinitrophenyl hydrazone was conducted. Racemic material *rac*-**60** was readily transformed to the desired hydrazone *rac*-**135** as a separable *E*/*Z*-mixture of 1/1 in an overall yield of 88%.



Scheme 40. Derivatization of bicyclohexenone *rac*-**60** to the corresponding hydrazones *rac*-(*E*)-**135** and *rac*-(*Z*)-**135**.

The obtained hydrazones were crystalline, but their enantiomers could not be separated by preparative HPLC. With low enantioselectivities in photoreaction at the time, X-ray crystallography was neglected.

2.5.2. VCD Spectroscopy

Instead, absolute configuration of *ent*-**60** and **60** was determined by vibrational circular dichroism (VCD) spectroscopy conducted by *Merten* at the Ruhr-Universität Bochum (Figure 9). Comparison of measured and *Gaussian*-calculated VCD spectra of enantiomer **60** matched (Figure 9), giving proof to our proposed (1*R*,5*S*)-configuration of **60** (Figure 9).

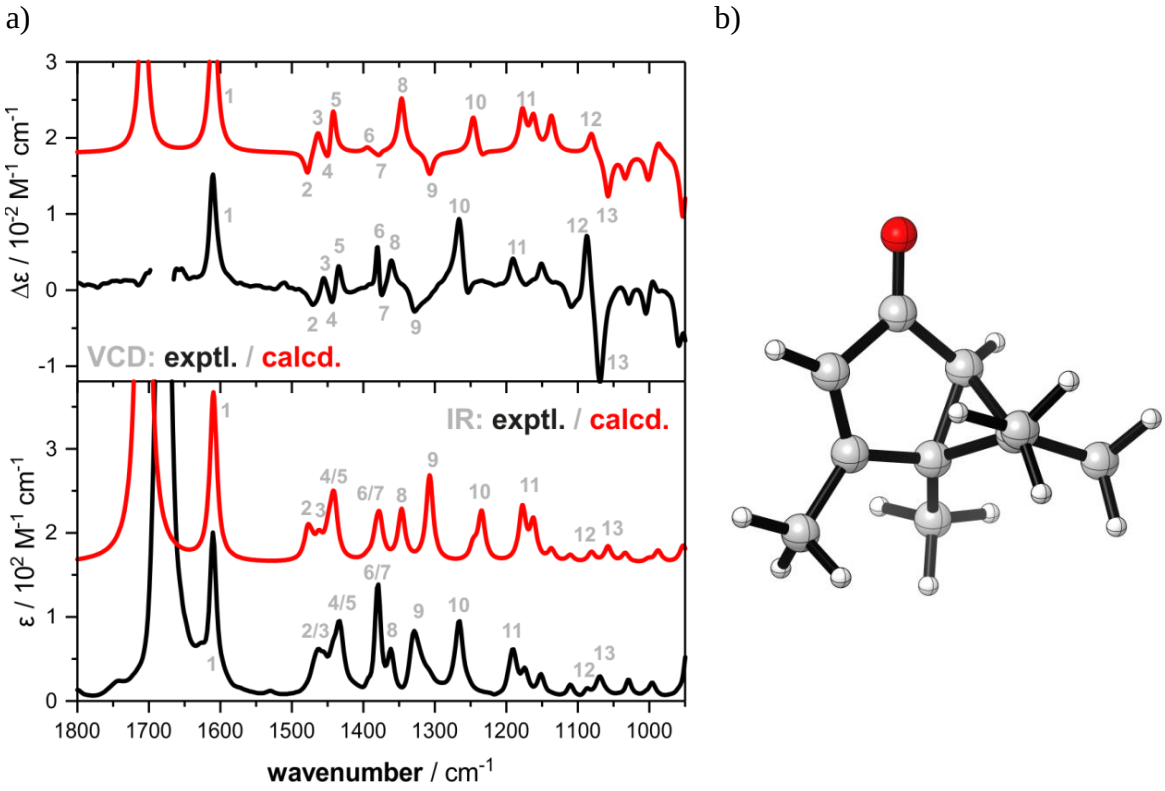


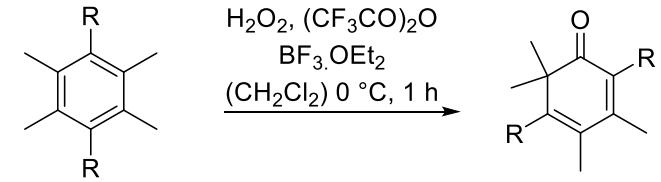
Figure 9. a) Comparison of experimental IR and VCD spectra recorded in chloroform (0.6 M, 100 µm path length) with the calculated spectra of (1*R*,5*S*)-tetramethylbicyclo[3.1.0]hex-3-en-2-one (**60**) (B3LYP/6-311++G(2d,p)/IEFPCM)[74]. The numbers indicate band assignments used to determine the absolute configuration of **60**. b) Structure of (1*R*,5*S*)-**t**etramethylbicyclo[3.1.0]hex-3-en-2-one (**60**).[75] Reprinted (https://pubs.acs.org/doi/abs/10.1021/jacs.9b12068) with permission from the ACS. Further permission to reuse should be directed to the ACS.

2.6. Substrate Synthesis

2.6.1. Synthesis from Alkylbenzenes

2,4-Cyclohexadienones are in some cases referred to as ‘blocked phenols’ or ‘blocked aromatic molecules.[76] The acid-catalyzed dienone-phenol rearrangement of 2,4- or 2,5-cyclohexadienones to phenols is one example of the synthetic proximity to aromatic molecules.[77-78] In fact, literature-known protocols to synthesize 2,4-cyclohexadienones often employ strategies to convert aromatic molecules to the desired dearomatized compounds.[61, 79-80]

Standard substrate **55** and hexamethyl cyclohexadienone **59** were synthesized by an oxidative dearomatizing protocol by *Hart* et al.[60-61] Treatment of durene (**136**) and mellitene (**137**) with boron trifluoride and trifluoroperacetic acid, *in situ* prepared from hydrogen peroxide and trifluoroacetic anhydride, led to hydroxylation of the aromatic ring and a subsequent semipinacol rearrangement yielded the desired product. Yields depended highly on substitution and symmetry of the starting material. In the case of **59** no benzochinones or phenols could be formed as side products, which explains the greater yield of 75% compared to 32% of **55**, where side reactions due to reasons of regioselectivity and overoxidation played a bigger role (Scheme 41).

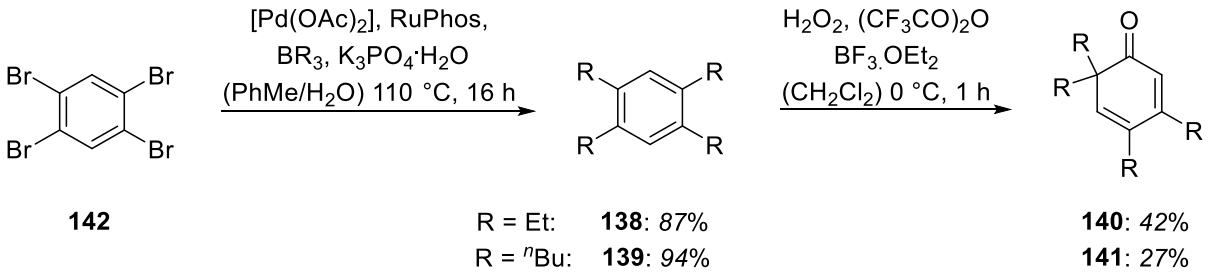


R = H: **136**
R = Me: **137**

55: *32%*
59: *75%*

Scheme 41. Oxidation of alkylbenzenes **136** and **137** to 2,4-cyclohexadienones **55** and **59**.

Application of the oxidative dearomatizing protocol to tetraethyl- and tetrabutyl-substituted benzenes **138** and **139** gave the respective 2,4-cyclohexadienones **140** and **141** in 42% and 27% yield. **138** and **139** could be easily prepared from tetrabromobenzene **142** and the respective trialkyl boranes by a *Suzuki*-coupling in high yields (87%, 94%) (Scheme 42). Unfortunately, the oxidative dearomatizing protocol proved to be not successful when 1,2,3,4,5,6,7,8-octahydroanthracene was used.

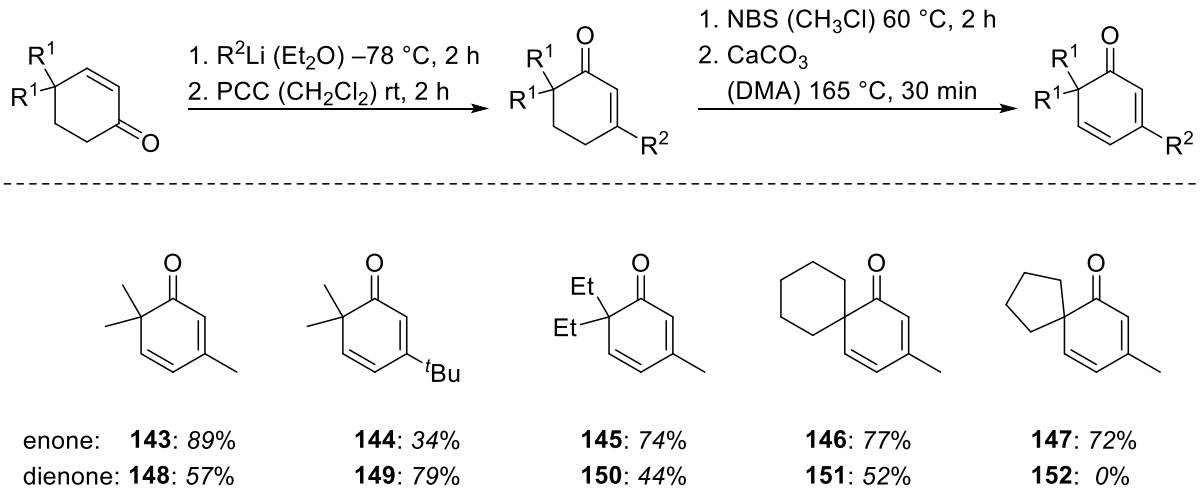


Scheme 42. Synthesis of tetraalkylbenzenes **138** and **139** and oxidation to tetraalkyl cyclohexadienones **140** and **141**.

2.6.2. Synthesis from Cyclohexenones

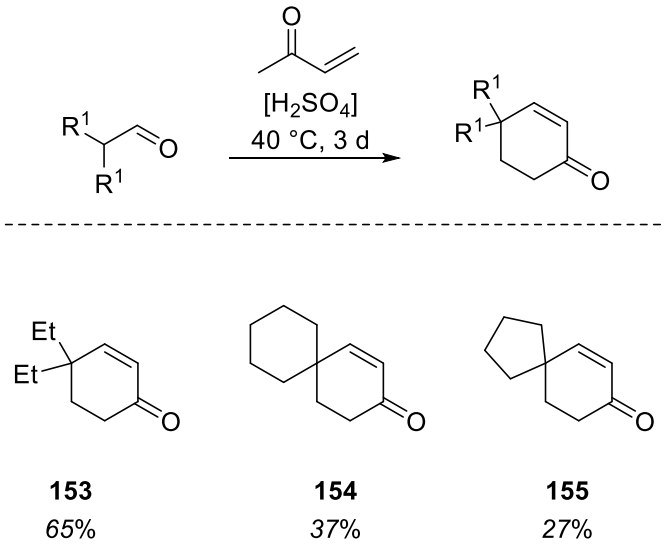
Employing a protocol published by *Dauben* and *Michno*[81] 4,4-dialkylcyclohexenones were converted to cyclohexenones **143**-**147**. The reaction sequence consisted of a 1,2-addition of the respective organolithium reagent to a tertiary allylic alcohol, which was then transformed in a *Dauben* rearrangement using pyridinium chlorochromate. *Wenkert* et al. used a two-step sequence to acquire trimethylcyclohexadienone **148** from trimethylcyclohexenone **143** by allylic bromination and elimination of hydrogen bromide.[82]

2,4-Cyclohexadienone **149** was prepared according to the mentioned literature in two two-step procedures with yields similar to the ones in literature. The same sequence further worked with *tert*-butyllithium to introduce a butyl group at the 3-position. However, the yield of cyclohexenone **144** was disappointing but still gave enough material for a successful synthesis of **149**. The strategy also enabled a variation of substituents in 6-position depending on the cyclohexenone employed. Yields were very good (72-77%) for the synthesis of diethyl substituted cyclohexenone **145** and spiro compounds **146** and **147**. The bromination-elimination sequence worked with lower yields for **150** and **151**, unfortunately in the case of **152** no product could be isolated in multiple reactions (Scheme 43). A draw-back of the sequence was the limitation to methyl or *tert*-butyl groups in 3-position due to problems of regioselectivity during bromination with substrates featuring a secondary or tertiary carbon in 3-position. The presence of an isopropyl group even shut down any reactivity towards bromination at all.



Scheme 43. Synthesis of 6,6-dialkyl-2,4-cyclohexadienones starting from 4,4-dialkylcyclohexenones.

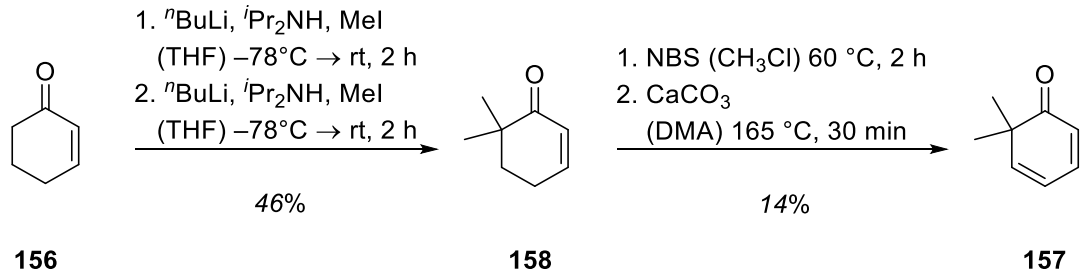
Commercially unavailable 4,4-dialkylcyclohexenones were synthesized by annulation reactions of dialkyl carbaldehydes with methyl vinyl ketone.[83-84] The reaction proceeded well with ethyl butyraldehyde to provide **153** in 65% yield. Cyclohexane carbaldehyde and cyclopentane carbaldehyde were transformed less efficiently to cyclohexenones **154** and **155** (Scheme 44).



Scheme 44. Synthesis of 4,4-dialkylcyclohexenones **153**-**155**.

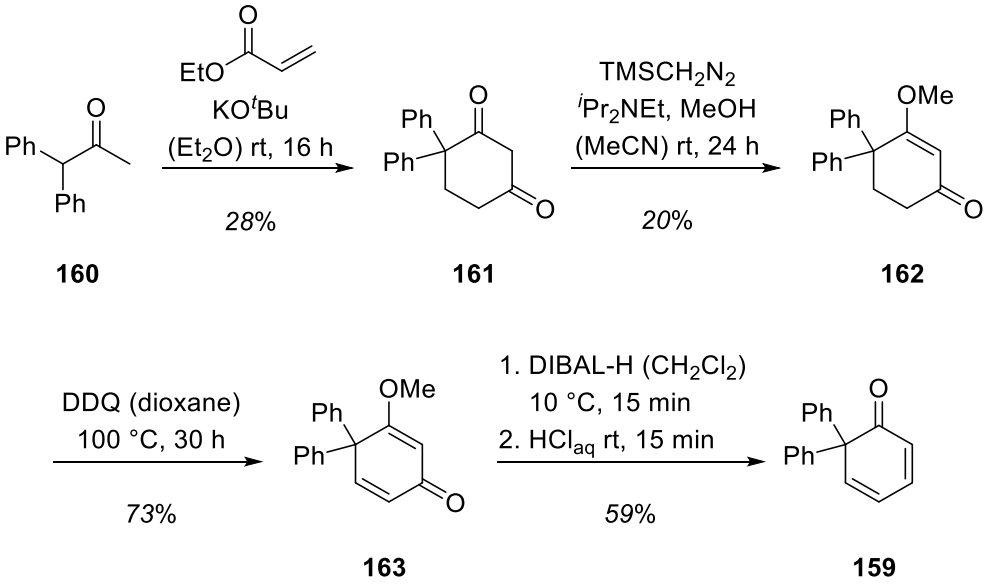
To access substrates without substituents in 2-,3-,4- and 5-position, cyclohexenone **156** was methylated twice in 46% overall yield. Using *Wenkert*'s strategy to oxidize 2-cyclohexenones to 2,4-cyclohexadienones, 2,4-cyclohexenone **157** was synthesized from **158** in low yield

(Scheme 45). Presumably, volatility and side reactions are heavily impacting the reaction's outcome. **157** proved to be unstable upon storage at −20 °C over longer periods of time. Probably formation of a *Diels-Alder* adduct plays a role in depletion of **157**.[79, 85]



Scheme 45. Synthesis of 6,6-dimethyl-2,4-cyclohexadienone (**157**).

Diphenyl-2,4-cyclohexadienone **159** was prepared using a sequence published by *Zimmerman* et al. starting from 1,1-diphenylacetone (**160**).[86-87] Annulation with ethyl acrylate generated diketone **161** in 28%. Methylation using trimethylsilyl diazomethane gave two regioisomers, the desired isomer **162** was isolated in 20% yield. Dehydrogenation with dichlorodicyano benzoquinone (DDQ) gave **163** in 73% yield, which was reduced with diisobutylaluminum hydride (DIBAL-H) and hydrolyzed by hydrochloric acid to provide 59% of 2,4-cyclohexadienone **159**.

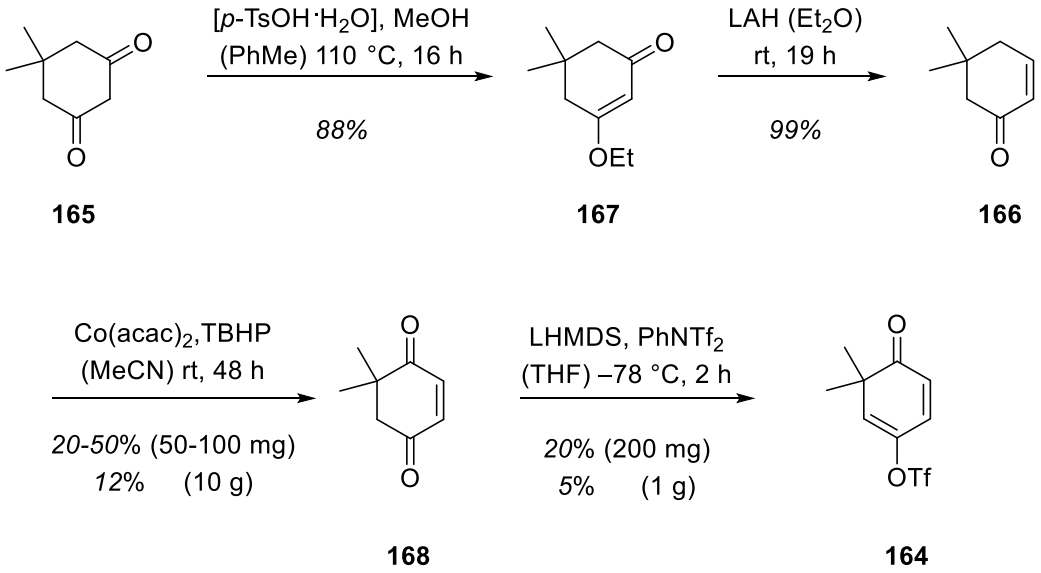


Scheme 46. Synthesis of 6,6-diphenyl-2,4-cyclohexadienone (**159**) from 1,1-diphenylacetone (**160**).

2.6.3. Synthesis of Cross-Coupling Precursors

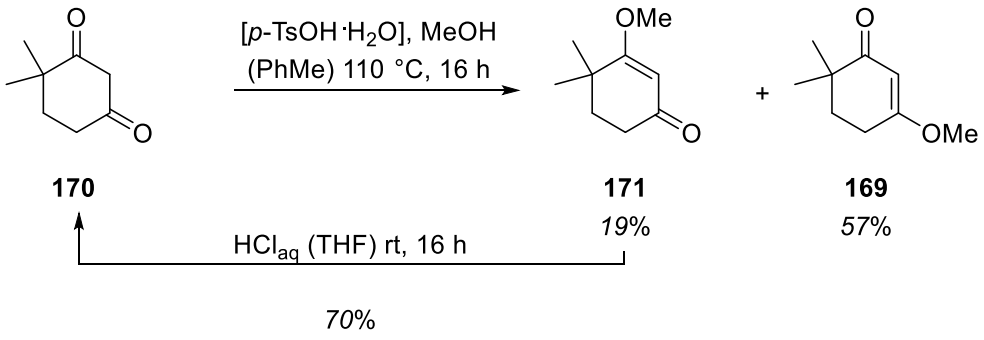
Already, several strategies to synthesize different 2,4-cyclohexadienones have been mentioned. Thus, a strategy was searched for precursors, which enabled a late stage derivatization to produce a broad substrate scope with less synthetic effort. Hence, synthesis of cyclohexadienone **164** was pursued. The trifluoromethanesulfonyl group in 4-position had the potential to be substituted in cross-coupling reactions by suitable organometallic reagents, thus enabling derivatization in just one step from **164**.

Starting from dimedone (**165**), dimethylcyclohexenone **166** was synthesized in two steps via vinylogous ester **167** with yields of 88% and 99%. Oxidation using a modified procedure published by *Han* et al.[88] produced diketone **168** in varying yields between 20 and 52% on a 50-100 mg scale. Attempts on a larger scale (10 g) led to a discouraging yield of 12%. Alternative oxidation procedures using phosphomolybdic acid and oxygen[89], palladium or manganese catalysts in combination with *tert*-butyl hydroperoxide[90-92] were less effective, if successful. Triflate **164** was prepared by reacting **168** with lithium bis(trimethylsilyl)amide and *N*-Phenyl-bis(trifluoromethansulfonimide), in analogy to a literature-known procedure by *Lin* et al.[93] Sadly, yields did not exceed 20% and were frustratingly even lower on larger scale. Alternatively, converting **167** with trifluoromethanesulfonic anhydride and pyridine only led to decomposition. Even though preliminary results showed that **164** was a suitable precursor for cross-coupling reactions, the inability of synthesizing **164** in larger amounts made this strategy ineffective.



Scheme 47. Synthesis of cross-coupling precursor **164** starting from dimedone (**165**).

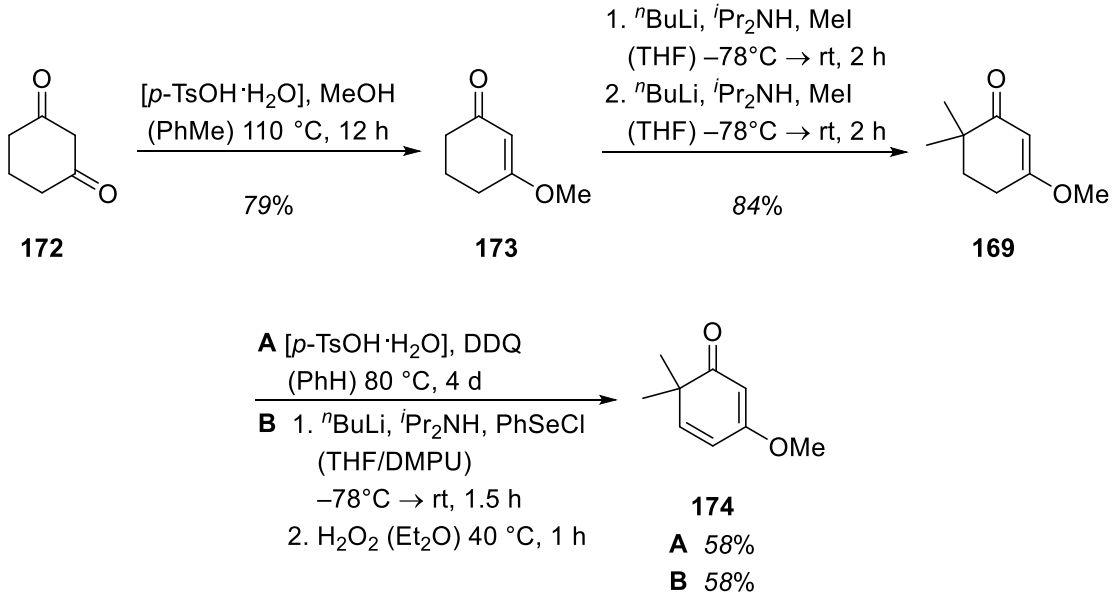
Our next attempt, was a cross-coupling precursor with a trifluoromethanesulfonyl group in 3-position. Vinylogous ester **169** could be prepared from **170**, but unfortunately separation from regioisomer **171** was necessary. Regenerating starting material **170** from the minor regioisomer **171** was possible with a moderate yield, however separation of regioisomers led to extensive efforts on large scale (Scheme 48).



Scheme 48. Synthesis of vinylogous esters **169** and **171** and hydrolysis of **171** to regenerate starting material **170**.

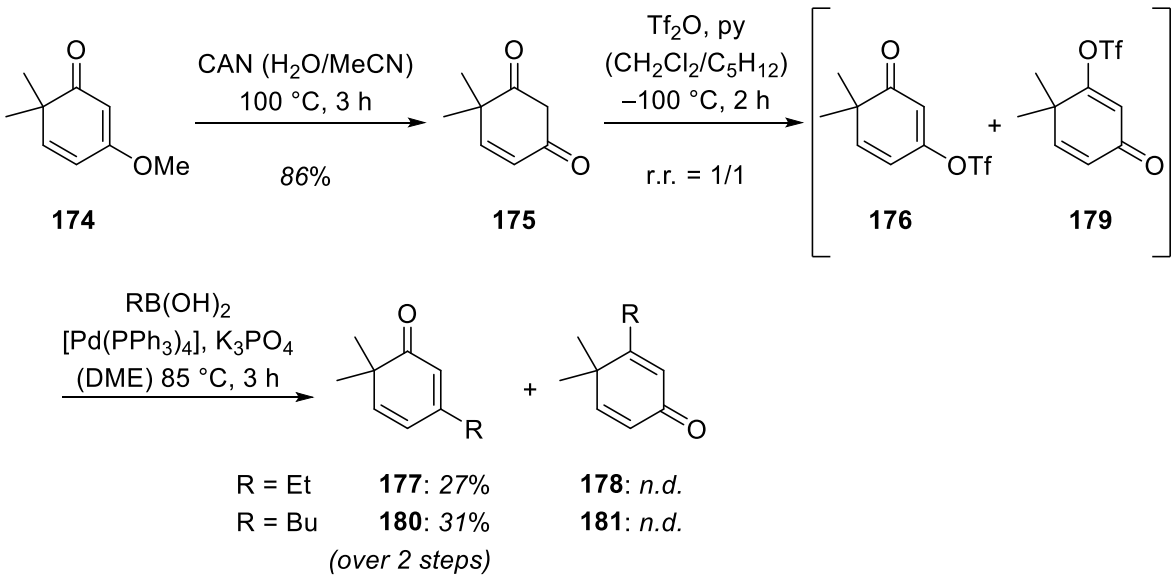
Starting from 1,3-cyclohexanedione (**172**), vinylogous ester **169** was prepared via vinylogous ester **173** in three steps and an overall yield of 66%. Dehydrogenation was possible with DDQ as well as by selenoxide elimination, both reactions gave **174** in 58% yield (Scheme 49). To our dissatisfaction, at larger scale, reactions were incomplete, even with increased equivalents

of reagents. Starting material and product were almost inseparable and provided another obstacle in producing large amounts of **174**.



Scheme 49. Synthesis of 2,4-cyclohexadieone **174** starting from 1,3-cyclohexanedione (**172**).

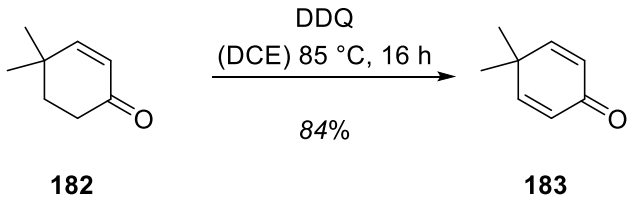
In order to convert 2,4-cyclohexadienone **174** to a cross-coupling precursor, the next step proceeded well with conversion to the diketone **175** in 84% and further to a mixture of triflate **176**, which was then directly used in the *Suzuki* cross-coupling to give 2,4-cyclohexadienone **177** and 2,5-cyclohexadienone **178**. The latter was formed because triflation gave a mixture of regioisomers that was unfortunately not higher than 1/1 under optimized conditions and given the instability of triflate, the regioisomers **176** and **179** were not separated. This also explains the low yields of the two-step reaction sequence of 27% and 31% for the synthesis of 2,4-cyclohexadienone **180** (Scheme 50). After cross-coupling of the regioisomeric mixture with the respective boronic acid, the undesired 2,5-cyclohexadienones **178** and **181** were neglected and not isolated or quantified. Unfortunately, further attempts with different boronic acids did not gave the desired results. Both attempts to create a broad substrate scope by late stage cross-coupling reactions were therefore not effective.



Scheme 50. Synthesis of 2,4-cyclohexadienones **177** and **178** from 2,4-cyclohexadienone **174** via a *Suzuki* cross-coupling strategy.

2.6.4. Synthesis from 2,5-Cyclohexadienones

Returning to the approach of preparing 3,6,6-trisubstituted cyclohexenones by *Dauben* rearrangement, the new strategy circumvented the necessity of subsequent bromination. Oxidation of the C-4, C-5 carbon-carbon bond was done first by dehydrogenation of dimethylcyclohexenone **182** to 2,5-cyclohexadieone **183**.

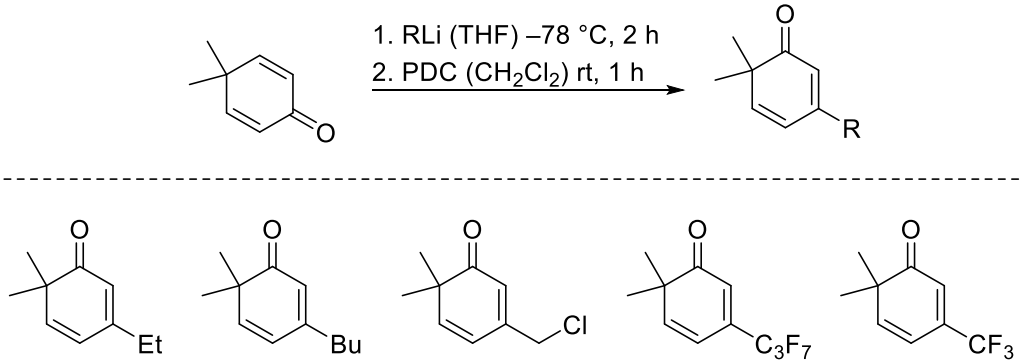


Scheme 51. Dehydrogenation of cyclohexenone **182** to 2,5-cyclohexadienone **183** with DDQ.

This could be easily achieved with DDQ and dichloroethane (DCE) proved to be suitable solvent in this reaction (Scheme 51). The same approach of 1,2-addition and *Dauben*

rearrangement was conducted. Small modifications were implemented in the rearrangement step by changing the oxidation reagent and shortening reaction time to produce higher yields.

The approach was successful, enabling preparation of various 2,4-cyclohexadienones in three steps overall from commercially available cyclohexenone **182**. Ethyl, butyl, chloromethyl and perfluoropropyl substitution (**177**, **180**, **184** and **185**) was achieved in moderate to good yields using the respective organolithium reagents (Scheme 52). In case of **184** and **185** the reagents were produced *in situ* from the respective iodine compounds by halogen-metal exchange with methyllithium. Trifluoromethyl-2,4-cyclohexadienone **186** was synthesized in moderate yield of 57% by a modified literature-known procedure of *Prakash* et al. [94] (Scheme 52), where the trifluoro carbanion nucleophile is *in situ* generated by catalytic addition of tetrabutylammonium fluoride to trifluoromethyltrimethylsilane, known as *Ruppert-Prakash* reagent.[94]



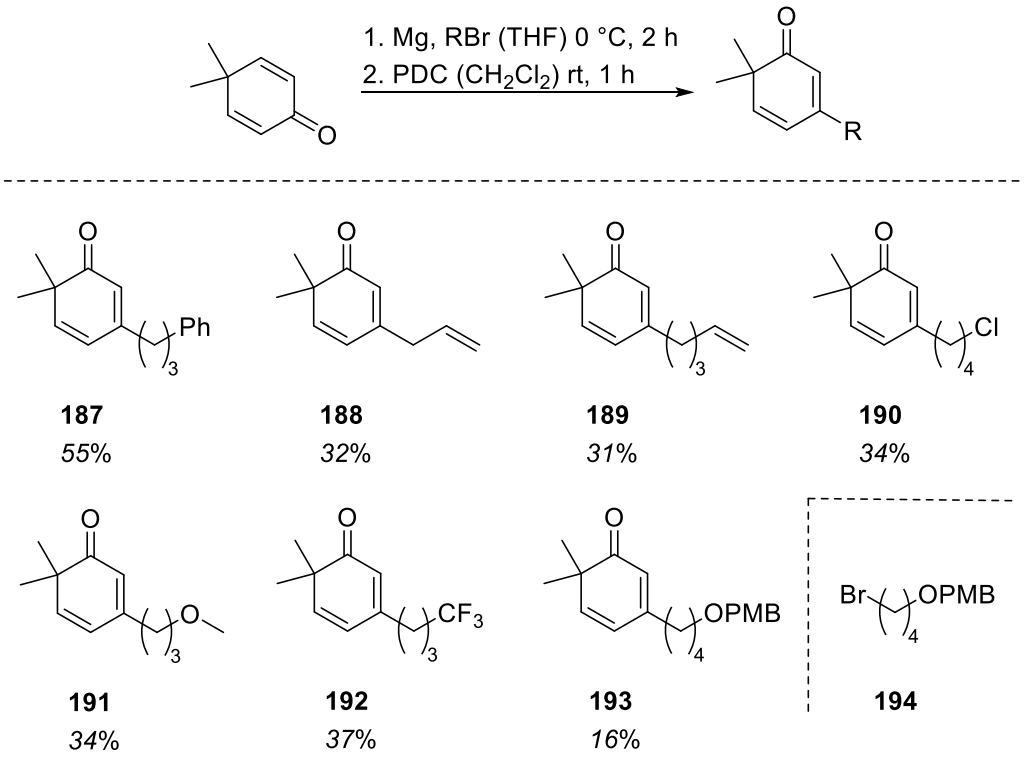
177	**180**	**184**	**185**	**186**
29%	*71%*	*46%*	*49%*	*57%*[a]

[a] $TMSCF_3$, [TBAF] was used instead of an organolithium reagent

Scheme 52. Synthesis of 2,4-cyclohexadinones **177**, **180**, **184**-**186**.

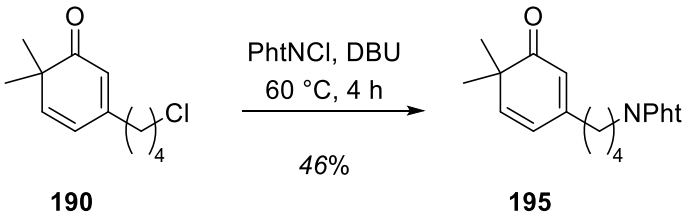
The reaction sequence worked as well when 1,2-addition reactions where performed with the respective *Grignard* reagents. In most cases, some amounts of 1,4-adducts were observed, however, application of the respective cerium reagents led to low conversion and consequently low yield. With moderate yields for the two-step sequence, further reaction optimization with cerium reagents was neglected. For the syntheses of 2,4-cyclohexadienones **187**-**192**, *Grignard* reagents were freshly prepared from commercially available bromides and the desired products were obtained in 31-55% yield. In order to synthesize 2,4-cyclohexadienone **193** with a *para*-methoxybenzyl ether side chain the respective bromide **194** needed to be prepared from

3-bromopropanol in 49% yield and the desired product of the corresponding *Grignard* addition was obtained in only 16% yield (Scheme 53). Presumably, the *para*-methoxybenzyl ether was less stable under the given reaction conditions, as various side products were formed - judged from thin layer chromatography.



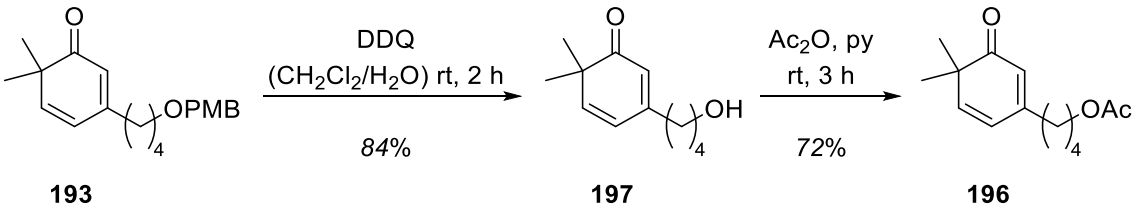
Scheme 53. Synthesis of 2,4-cyclohexadinones **187**-**193** and structure of synthesized bromide **194**.

The successful synthesis of functionalized 2,4-cyclohexadienones enabled access to additional functional groups by functional group interconversion. Substitution of the chloride of **190** with a phthaloyl group yielded 46% of 2,4-cyclohexadienone **195**.



Scheme 54. Conversion of 2,4-cyclohexadienone **190** to cyclohexadienone **195** by nucleophilic substitution.

An ester functionality could be incorporated by converting the *para*-methoxybenzyl ether **193** to acetate **195** in two steps. The attempt to cleave methyl ether **191** with boron tribromide resulted in dissatisfying yields as alcohol **196** was instable towards the cleaving conditions. Removal of the *para*-methoxybenzyl group with DDQ readily produced alcohol **197** in 84% yield and esterification with acetic anhydride in pyridine gave 72% of acetate **196**.

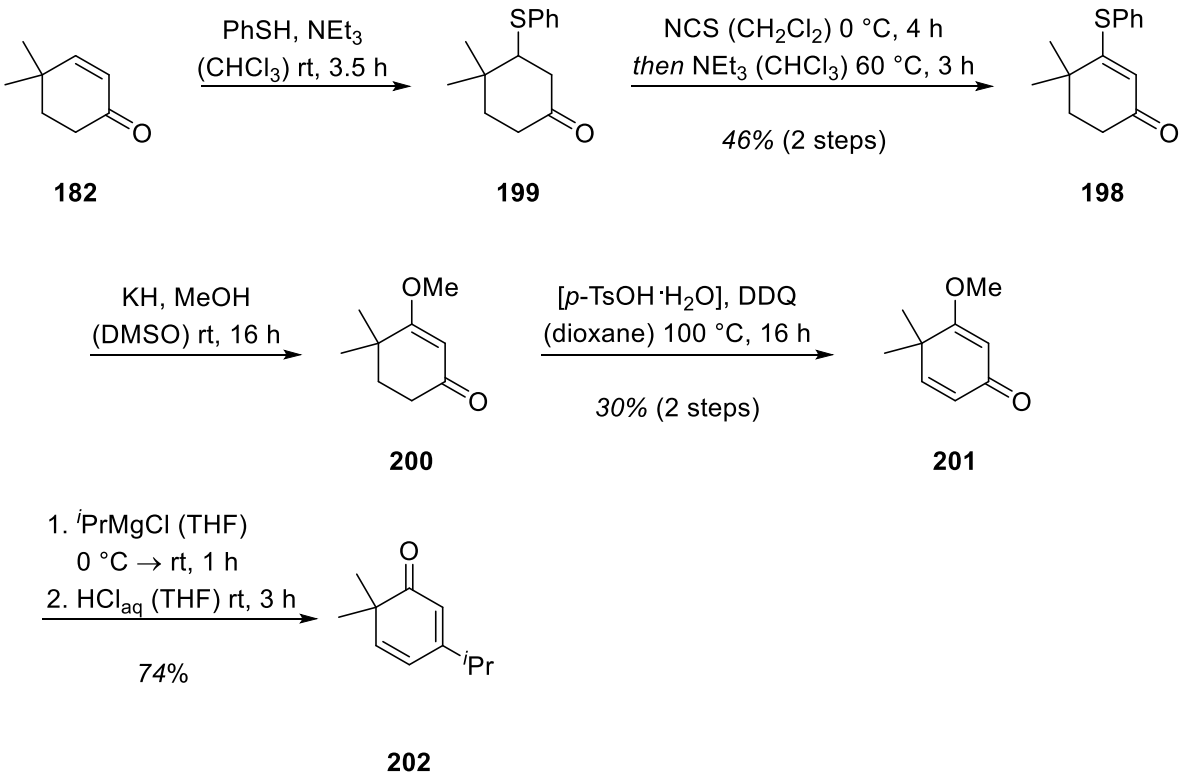


193 **197** **196**

Scheme 55. Synthesis of Acetate **196** from methoxybenzyl ether **193**.

A major drawback of the modified two-step sequence a 2,5-cyclohexadienone appeared to be the convergence of electronic structures towards aromatic compounds, as previously described. When secondary *Grignard* or organolithium reagents, e.g. isopropylmagnesium chloride or *tert*-butyllithium, were used, *Dauben* rearrangement of the desired intermediary alcohol did not take place. Instead, only aromatic compounds were found. This indicates that for sterically more demanding groups, the hydroxy group of the formed allylic tertiary alcohol is particularly prone to elimination as soon as it forms the chromate ester. The resulting carbenium ion can readily aromatize by migration of a methyl group and successive deprotonation.

In order to get hands on the isopropyl substituted substrate **199**, a synthetic route was envisioned with the first three steps based on a sequence published by *Maeda*.[95]



Scheme 56. Route towards sterically more demanding groups in 3-position, e.g. isopropyl substituted cyclohexadienone **202**.

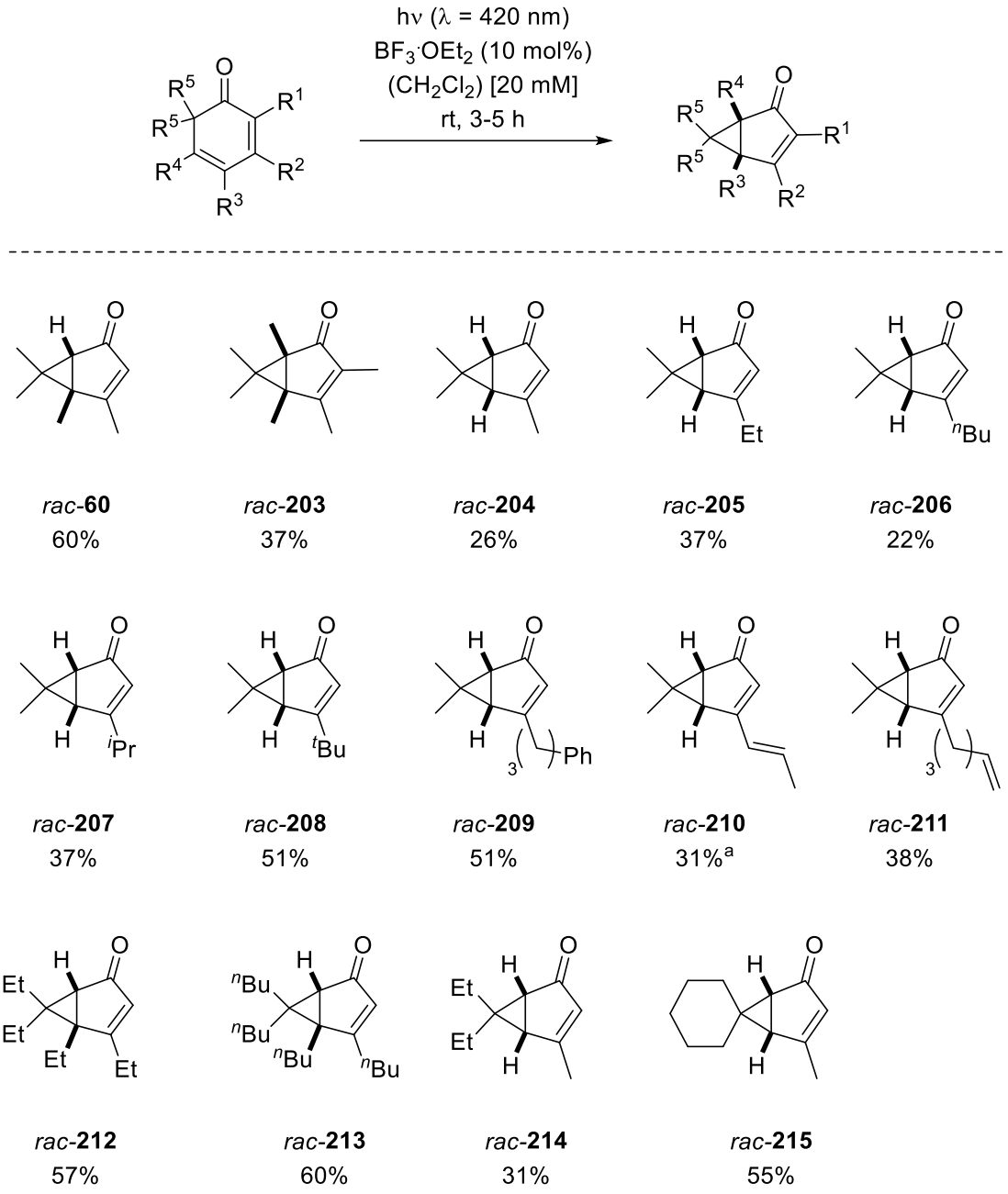
Cyclohexenone **182** was converted to vinylogous thioester **198** over via thioester **199** two steps in a yield of 46%. Conversion to the vinylogous methyl ester **200** and dehydrogenation to 2,5-cyclohexadienone **201** was achieved in 30% yield. *Grignard* addition and successive hydrolysis gave isopropyl-2,4-cyclohexadienone **202** in 74%, representing a viable route towards sterically more hindered substitutions.

2.7. Photochemical Rearrangement Reactions

2.7.1. Racemic Lewis Acid Catalyzed Photochemical Rearrangement Reactions

The prepared library of 2,4-cyclohexadienones was tested in photochemical rearrangement reactions under the optimized racemic reaction conditions.

Besides standard substrate **55**, forming bicyclohexenone *rac*-**60** in 60% yield, 6,6-dimethyl-2,4-cyclohexadienones with alkyl substituents were readily converted to the desired bicyclohexenones *rac*-**203**-**208** in low to moderate yields (22-51%). 2,4-Cyclohexadienones *rac*-**209**-**211** with an aryl group or an olefinic functionality worked as well in moderate yields (31-51%). Interestingly, in the case of *rac*-**210**, the terminal double bond had isomerized, no photoproduct with a terminal double bond could be isolated. Substrates with different alkyl substitution at C-6 also converted smoothly to the respective bicyclic hexenones *rac*-**212**-**215** in 31-60% yield.

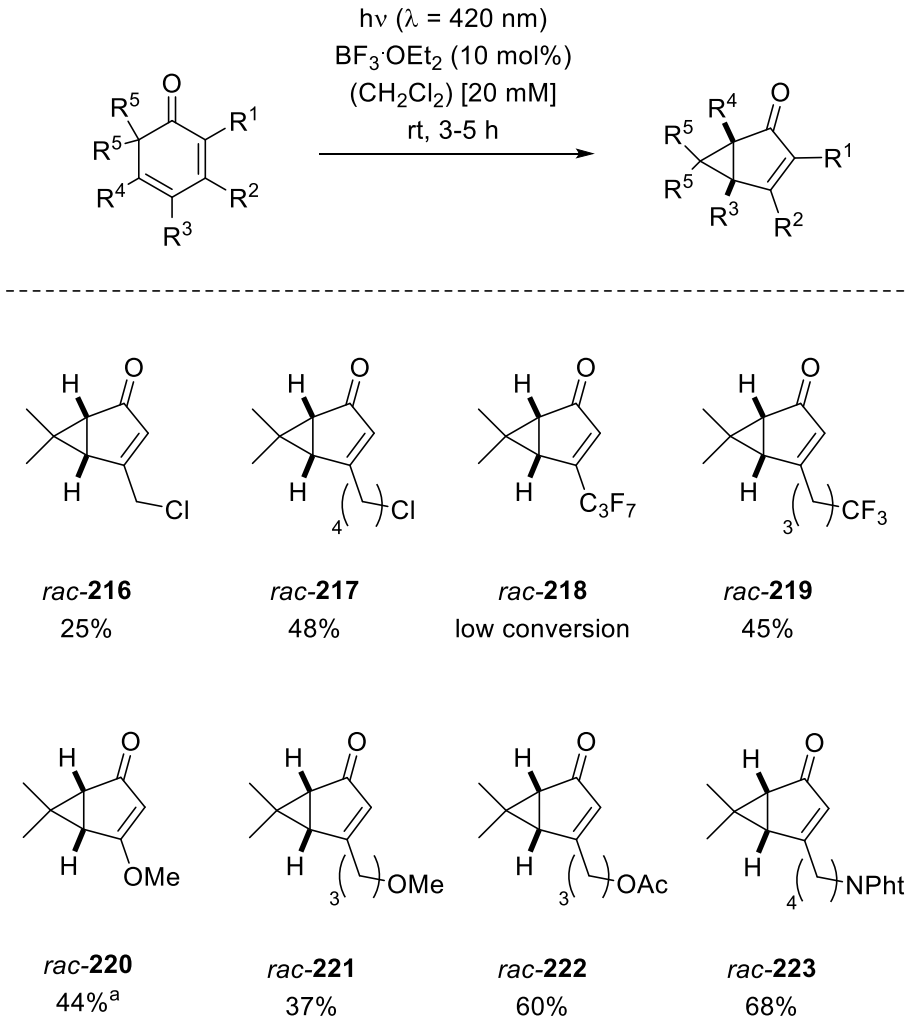


[a] Irradiation product of **188**; Isomerization of the terminal double bond to the internal double bond occured under reaction conditions

Scheme 57. Racemic Lewis acid catalyzed photorearrangement reactions of cyclohexadienones **60** and **203**-**215**.

To our delight, the developed racemic conditions tolerated functional groups as well. Chloromethyl and chlorobutyl substrates were converted to **216** and **217** in 25% and 48% yield. The perfluoropropyl group prevented a photochemical rearrangement towards **218**, possibly the electronic withdrawing effect was too excessive for an adequate coordination of the Lewis acid. A trifluorobutyl group was tolerated and **219** could be isolated in 45% yield. Methoxy

substitution altered the chromophore as well and irradiation at a shorter wavelength of λ = 398 nm for 24 hours were necessary to produce 44% of **220**. Methyl ether, acetate and phthalimide groups were tolerated well and bicyclohexenones **221**-**223** were obtained in moderate to good yields (37-68%).

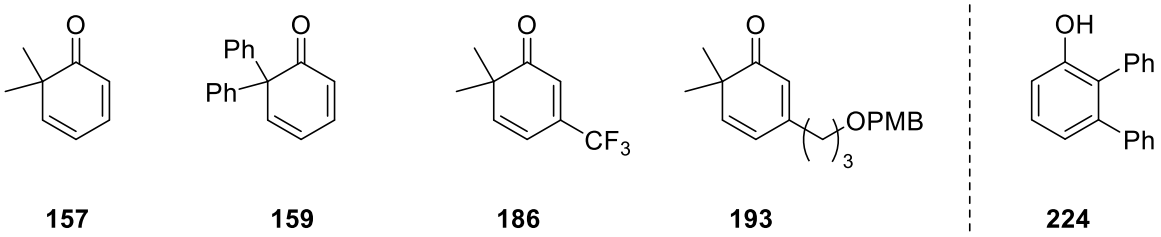


[a] Irradiation at λ = 398 nm for 24 h

Scheme 58. Racemic Lewis acid catalyzed photorearrangement reactions of functionalized cyclohexadienones **216**-**223**.

Fortunately, the majority of synthesized 2,4-cyclohexadienones were suitable substrates for photochemical rearrangement reactions. Only four substrates did not convert to the desired products.

In the photoreaction of 2,4-cyclohexadienone **157** no desired product could be isolated. Probably due to lack of steric hinderance *Diels-Alder* adducts form, which was not further investigated. Diphenyl substrate **159** directly rearranged thermally to 2,3-diphenylphenol (**224**) quantitatively and was therefore not suitable for Lewis acid catalysis. Trifluoromethyl substrate **186** reacted sluggishly and the respective photoproduct could not be isolated. Substrate **193** reacted upon irradiation but gave a complex mixture of innumerable products that did not contain the desired bicyclohexenone.



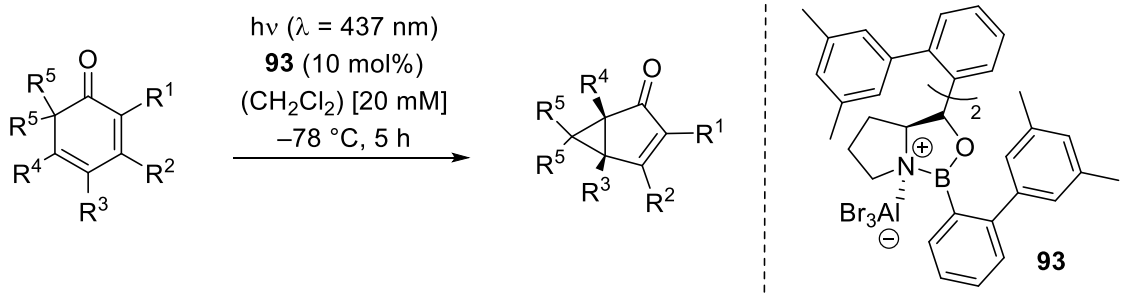
157 **159** **186** **193** **224**

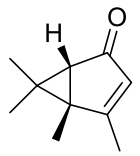
Scheme 59. Cyclohexadienones unsuitable for Lewis acid catalyzed photorearrangement reactions and thermal rearrangement product **224**.

2.7.2. Enantioselective Lewis Acid Photochemical Rearrangement Reactions

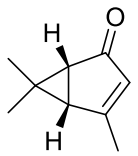
After a successful substrate screening under racemic reaction conditions, the next step was to apply the developed enantioselective reaction conditions with the new chiral Lewis acid **93**.

Gratifyingly, the high enantioselectivity that was observed in the case of photoproduct **60**, could be reproduced by all other alkyl substituted 6,6-dimethylbicyclohexenones (**204**-**208**) with 93-95% *ee* and good yields of 52-70%. Greater steric bulk at the 3-position did not show a negative effect on the reaction outcome. Volatility of **201** resulted in some loss and a lower yield in comparison. **209** was formed in 67% yield and 93% *ee* and showed toleration of an aryl group. Unfortunately, no formation of **210** was observed, but a longer alkenyl chain was suitable. Photoproduct **211** was isolated in good yield and with excellent enantiomeric excess (56, 93% *ee*). Formation of tetraethylbicyclohexenone **212** proceeded with good yield (52%), but very low enantioselectivity (25% *ee*). Tetrabutylcyclohexadienone **141** was therefore not tested. Diethylbicyclohexenone **214** was produced in higher enantioselectivity, but very inefficiently (15%, 75% rsm). Spirocyclic compound **215** was formed very efficiently (80%) and with high enantiopurity of 95% *ee*. Chlormethylbicyclohexenone **216** was very unstable under the reaction conditions, which prevented a complete isolation and resulted in a low yield (<20%) and unsatisfying enantiomeric excess (67% *ee*). Chlorobutyl compound **217** gave again a high yield of 66% with 93% *ee*. **218** was not formed, even at shorter wavelengths of $\lambda = 425$ nm and $\lambda = 398$ nm. Other functional groups, more specifically trifluorobutyl, methoxy, methyl ether and phthalimide groups were tolerated and photoproducts **219**-**223** were isolated in good yields (50-78%) and with excellent enantioselectivites (92-97% *ee*). Only in the case of **220** the reaction was incomplete, even under altered reaction conditions.

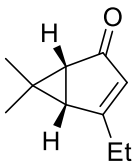




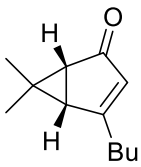
60
68%, 92% *ee*



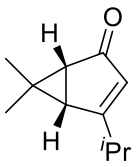
204
52%, 93% *ee*



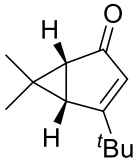
205
65%, 95% *ee*



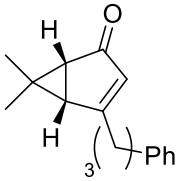
206
63%, 93% *ee*



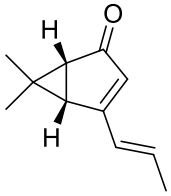
207
70%, 93% *ee*



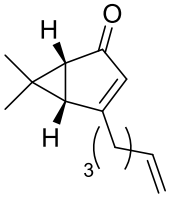
208
75%, 93% *ee*



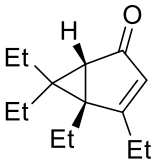
209
67%, 93% *ee*



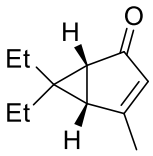
210
0%



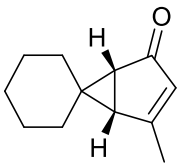
211
56%, 93% *ee*



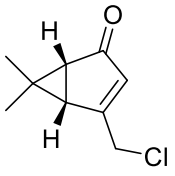
212
52%, 25% *ee*



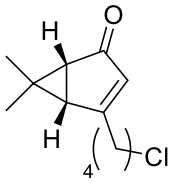
214
15%[a], 47% *ee*
75% rsm[a]



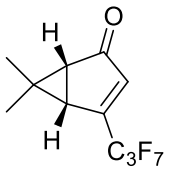
215
80%, 95% *ee*



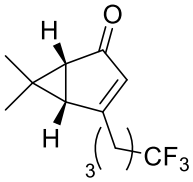
216
<20%, 67% *ee*



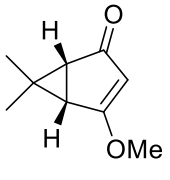
217
66%, 93% *ee*



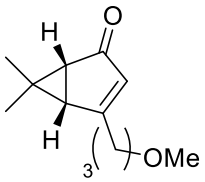
218
no conversion[b]



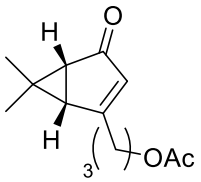
219
54%, 93% *ee*



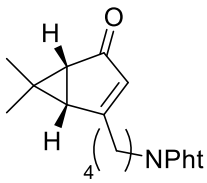
220
50%, 93% *ee*
41% rsm[c]



221
78%, 93% *ee*



222
57%, 92% *ee*



223
60%, 97% *ee*

[a] NMR-yield (calculated from crude NMR; internal standard: 1,3,5-trimethoxybenzene)

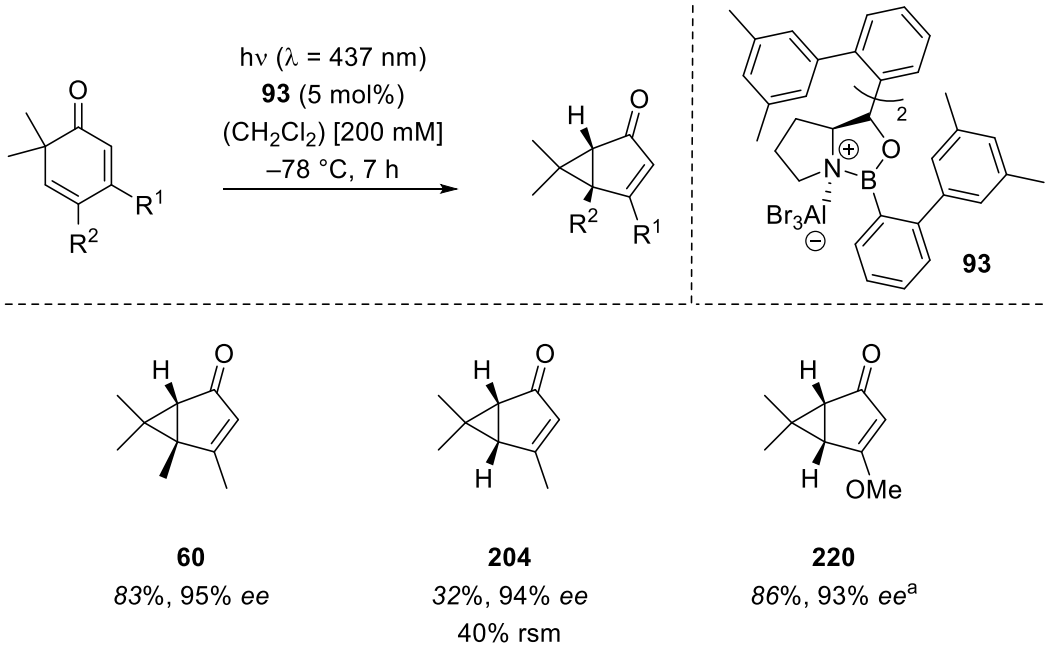
[b] Irradiation at λ = 437 nm, 425 nm and 398 nm

[c] Irradiation at λ = 425 nm for 24 h

Scheme 60. Enantioselective Lewis acid catalyzed photorearrangement reactions.

In order to evaluate the possibility of preparing greater amounts of the respective photoproducts, enantioselective photoreactions were conducted on larger scale.

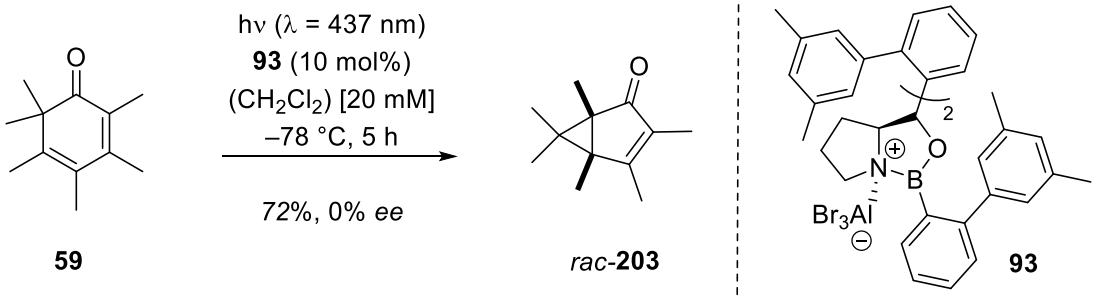
Standard substrate **55** was irradiated at a concentration of 200 mM, while the catalyst loading was reduced to 5 mol%. The reaction time was therefore prolonged to seven hours. **60** was isolated in very good yield (83%) and excellent enantiomeric excess (95% *ee*). The same conditions also gave **204** with 94% *ee*, but conversion was incomplete resulting in a lower yield of 32%. Also 2,4-cyclohexadienone **174** could be converted efficiently at higher concentration of 100 mM to give **220** in 86% yield and 93% *ee* (Scheme 61).



[a] Irradiation at [100 mM], λ = 425 nm with 10 mol% **93** for 24 h

Scheme 61. Enantioselective Lewis acid catalyzed photorearrangement reactions at higher concentrations with 5-10 mol% **93**.

Hexamethyl-2,4-cyclohexadienone (**59**) was irradiated under the same conditions to evaluate the importance of a hydrogen in 2-position for a chelating catalyst binding. Bearing a methyl group, no non-classical hydrogen bond exists and a racemic product is expected. Hexamethylbicyclohexenone (*rac*-**203**) was formed in 72% yield and determined to be completely racemic, supplying proof for the necessity of a non-classical hydrogen bond between catalyst and substrate for an enantioselective reaction (Scheme 62).

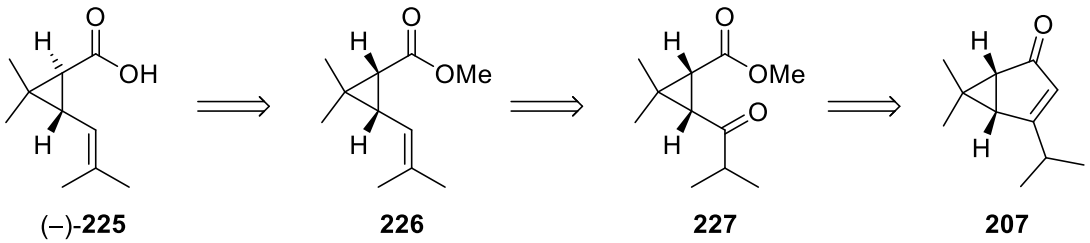


Scheme 62. Control experiment for the proposed binding motif: Enantioselective Lewis acid catalyzed photorearrangement reaction of **59**.

2.8. Total Synthesis of Chrysanthemic Acid

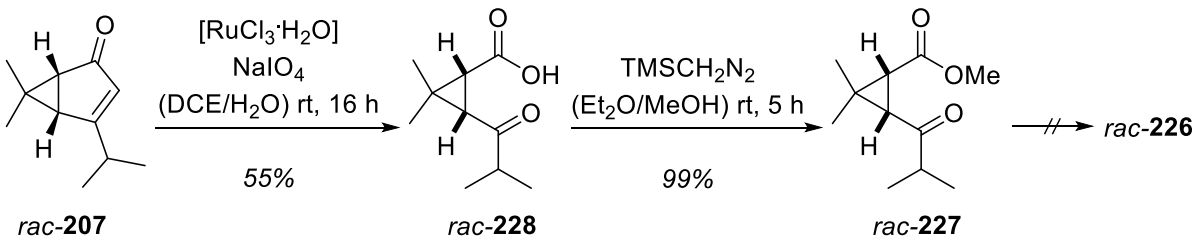
In order to prove the utility of the developed methodology, an application was searched for. Natural product chrysanthemic acid (**225**) was found to be an appropriate target as it contains the *gem*-dimethyl cyclopropane element, which was also part of most of the synthesized bicyclohexenones.

Retrosynthetic analysis of (−)-chrysanthemic acid [(−)-**225**] involved transformation to *cis*-configured ester **226**, which could be further converted to ketoester **227**. Retrosynthetic ring closure then led to isopropylbicyclohexenone **207** (Scheme 63).



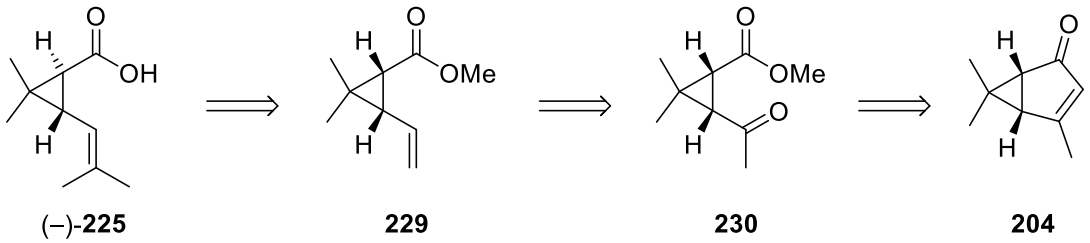
Scheme 63. Retrosynthetic approach to **(−)**-chrysanthemic acid [(−)-**225]** starting from bicyclohexenone **204**.

Studies commenced on racemic photoproduct *rac*-**207**. A literature-known ruthenium(III)-catalyzed oxidative cleavage of the double bond[96] evolved to be the best option and after optimization of work-up conditions keto acid *rac*-**228** was isolated in 55% yield. Methylation with trimethylsilyl diazomethane proceeded with excellent yield to give the desired methyl ester *rac*-**227** (Scheme 64)**.** The strategy in mind to convert the isopropyl keto group involved transformation to the corresponding vinyl triflate. This could further be defunctionalized into the desired isopropylidene group. Unfortunately, the desired vinyl triflate could not be isolated after screening different conditions. Other methods, e.g. reduction, to convert the keto group into *rac*-**226** failed too**.**



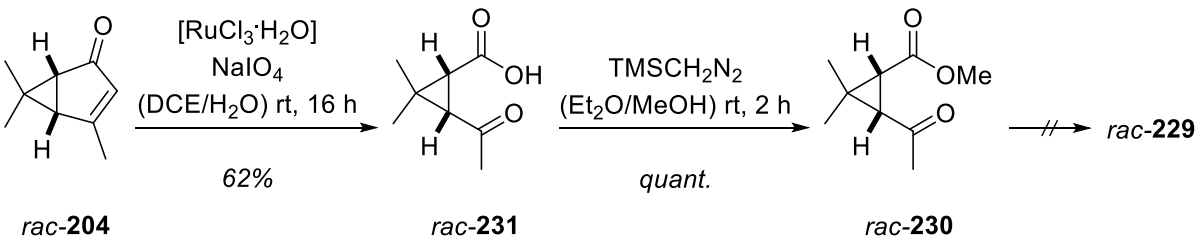
Scheme 64. Oxidative cleavage of *rac*-**207** and methylation of the resulting carboxylic acid *rac*-**228** to methyl ester *rac*-**227**.

To prevent intervention of the isopropyl group on the ketone's reactivity, the approach was changed to a different photoproduct. In close analogy to the previous retrosynthetic approach, (−)-chrysanthemic acid [(−)-**225**] was transformed to ester **229**, that could be converted by ozonolysis, *Wittig* reaction and successive epimerization to the *trans*-isomer. The olefin seemed less sterically hindered and easier to prepare from ketone **230**, which would be prepared from bicyclohexenone **204** by the previously established oxidative ring-opening reaction (Scheme 65).



Scheme 65. Retrosynthetic approach to **(−)**-chrysanthemic acid [(−)-**225**] starting from bicyclohexenone **204**.

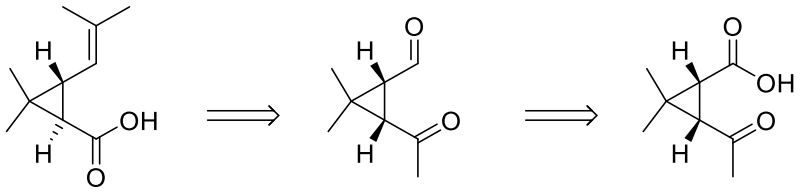
Oxidative cleavage of the double bond to open the bicyclic system worked also well for bicyclohexenone *rac*-**204**. Same held true for methylation of acid *rac*-**231** to methyl ester *rac*-**230** (Scheme 66). Unfortunately, also the methyl ketone could not be converted into the desired olefin *rac*-**229**. Attempts to reduce the keto group to the corresponding alcohol did not succeed. Instead ^{1}H-NMR and GC analysis hinted towards lactone formation during reduction reactions. Because the aimed for isopropylidene group could not be synthesized from the keto group, it was tried to access it from the ester group.



rac-**204** *rac*-**231** *rac*-**230**

Scheme 66. Oxidative cleavage of *rac*-**204** and methylation of the resulting carboxylic acid *rac*-**231** to methyl ester *rac*-**230**.

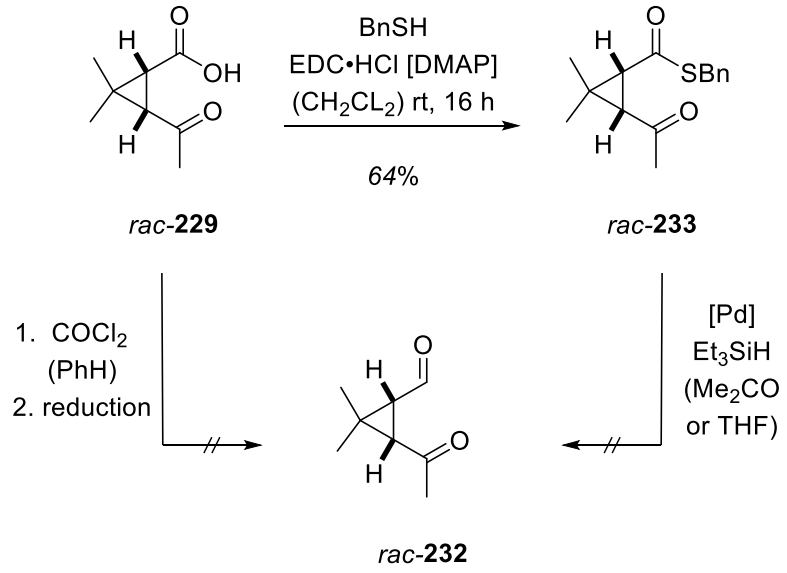
Retrosynthetic fragmentation of the (+)-enantiomer of chrysanthemic acid [(+)-**225**] led to ketoaldehyde **232** that would be accessible by the same enantiomer of the previously synthesized ketoester **230** (Scheme 67). Unfortunately, the ester group could not be selectively reduced to the desired aldehyde or the corresponding alcohol.



(+)-**225** **232** **231**

Scheme 67. Second retrosynthetic approach from carboxylic acid **231** to (+)-chrysanthemic acid [(+)-**225**].

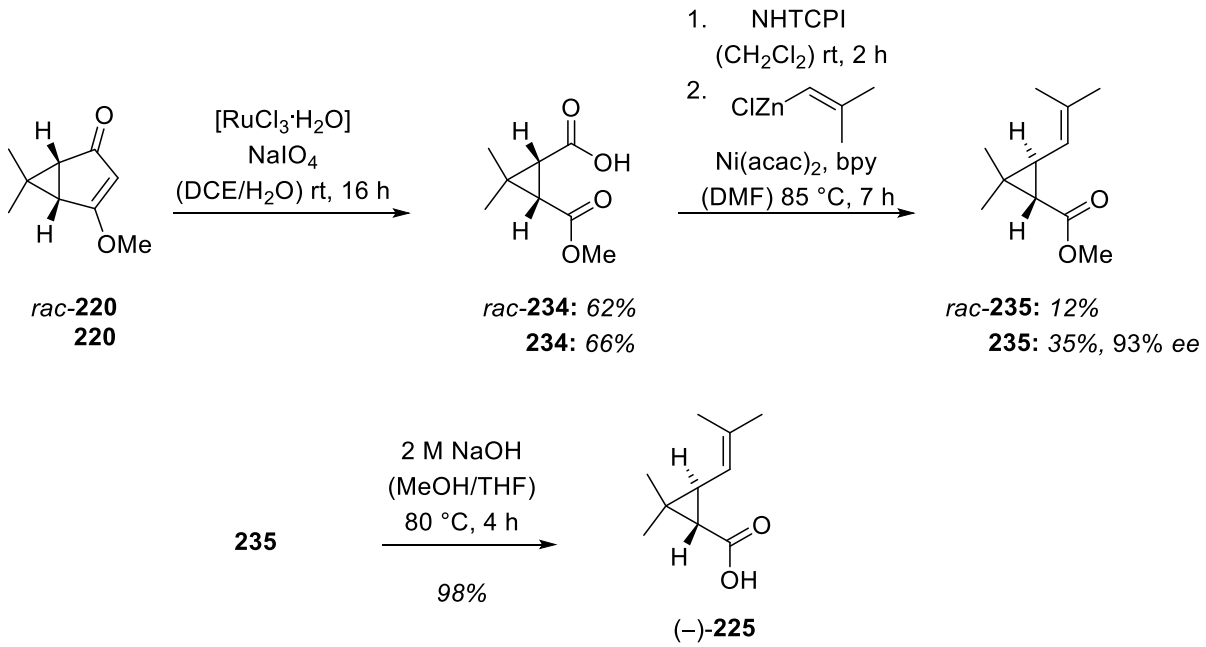
Carboxylic acid *rac*-**231** was successfully converted to benzyl thioester *rac*-**233** (Scheme 68) in order to employ a reduction protocol published by *Fukuyama*[97]. Applying literature-known reaction conditions with different palladium catalysts and catalyst loadings led only to decomposition and no formation of the corresponding aldehyde could be observed. Reduction of the corresponding acid chloride was also attempted. Different conditions [(a) $^{t}Bu_3AlH$; Pd/C, lutidine, H_2; (b) Pd-$BaSO_4$, quinoline; (c) $Pd(PPh_3)_4$, $HSnBu_3$] were applied. Aldehyde **232** remained not accessible, at best lactone formation could be observed.



Scheme 68. Different attempts to synthesize aldehyde *rac*-**232**.

A suitable route was finally found by oxidative ring opening of bicyclohexenone **220**. The resulting hemi-ester *rac*-**234** had been used racemically by *Edwards* et al. in a synthesis of racemic *trans*-chrysanthemic acid. The key step involved a nickel-catalyzed decarboxylative alkenylation that was published with an acceptable yield of 29%.[98]

Oxidative ring-opening worked in 62% for the racemic and in 66% for the enantioenriched material. The product needed a more careful work-up procedure than the other ring opening products to eliminate any isomerization to the *trans*-isomer. Decarboxylative alkenylation of *rac*-**234** via the corresponding tetrachlorophtalimide carboxylate, which was not isolated, produced methyl chrysanthemate (*rac*-**235**) in low yield. Using enantioenriched material the yield was 35% and the enantiomeric excess of 93% showed no racemization during the synthesis. Hydrolysis of **235** yielded (−)-chrysanthemic acid [(−)-**225**] in 98% yield to conclude a successful total synthesis (Scheme 69). The specific optical rotation of the synthesized natural confirmed the absolute configuration of photoproduct **220**.



Scheme 69. Total synthesis of (−)-chrysanthemic acid [(−)-**225**].

2.9. Mechanistic Studies

Griffiths and *Hart* had postulated that the photochemical rearrangement of 2,4-cyclohexadienone **55** occurred on the singlet hypersurface. Their conclusion was drawn from quenching experiments in their silica-gel slurry, where no triplet quenching occured with piperylene.[62]

2.9.1. Triplet Quenching

In order to investigate the nature of our Lewis acid-substrate complexes, the photochemical rearrangement of **55** was conducted under racemic as well as enantioselective reaction conditions in the presence of piperylene. Different amounts of piperylene were chosen and the conversion and product formation closely monitored by GC. In addition, it was ruled out that **55** reacted with piperylene in thermal or photochemical side reactions.

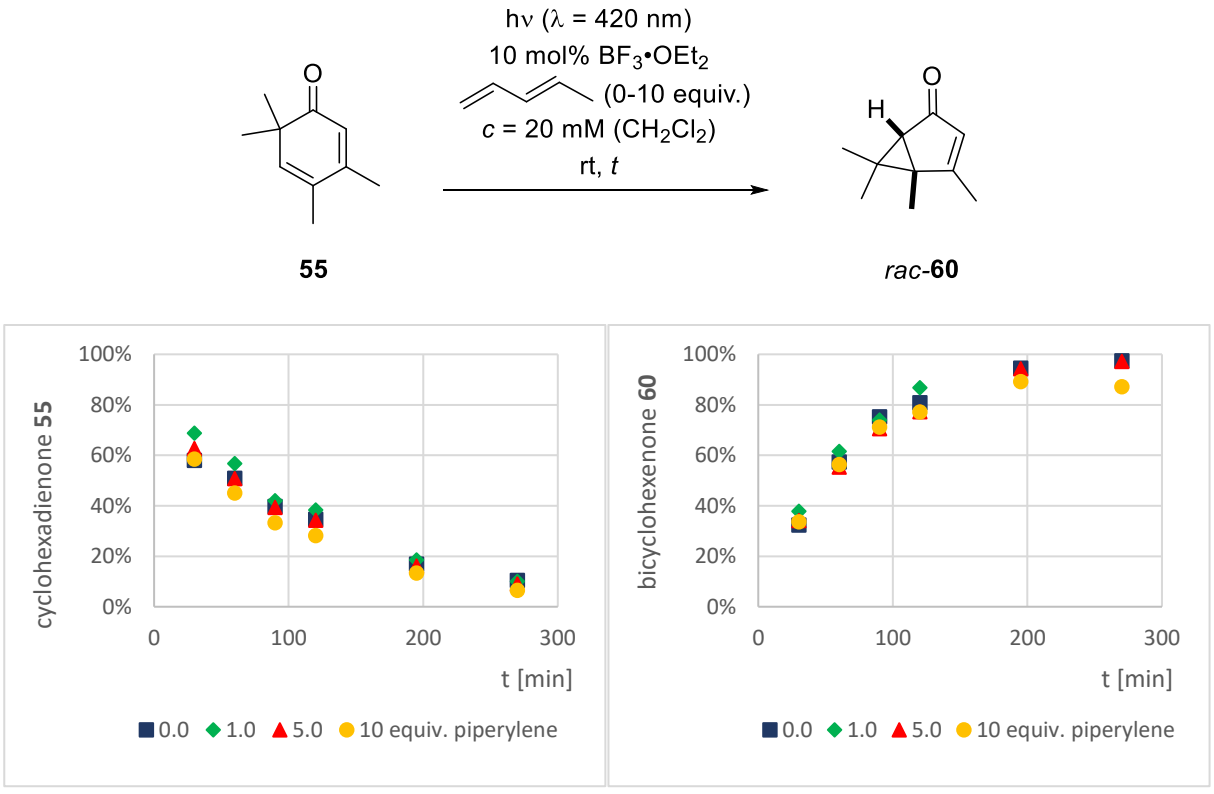


Figure 10. Consumption of **55** and formation of *rac*-**60** in the racemic photorearrangement reaction monitored on GC. Different equivalents of piperylene were used as triplet quencher.

The experiments delivered the expected result. Neither in the case of boron trifluoride as achiral catalyst (Figure 10), nor in the case of the chiral catalyst **93** (Figure 11), conversion of **55** or formation of the racemic photoproduct *rac*-**60** or enantioenriched photoproduct **60** deviated when piperylene was present in solution. Different piperylene concentrations were tested and no difference was observed. We therefore concluded that the photochemical rearrangement reaction must take place on the singlet hypersurface.

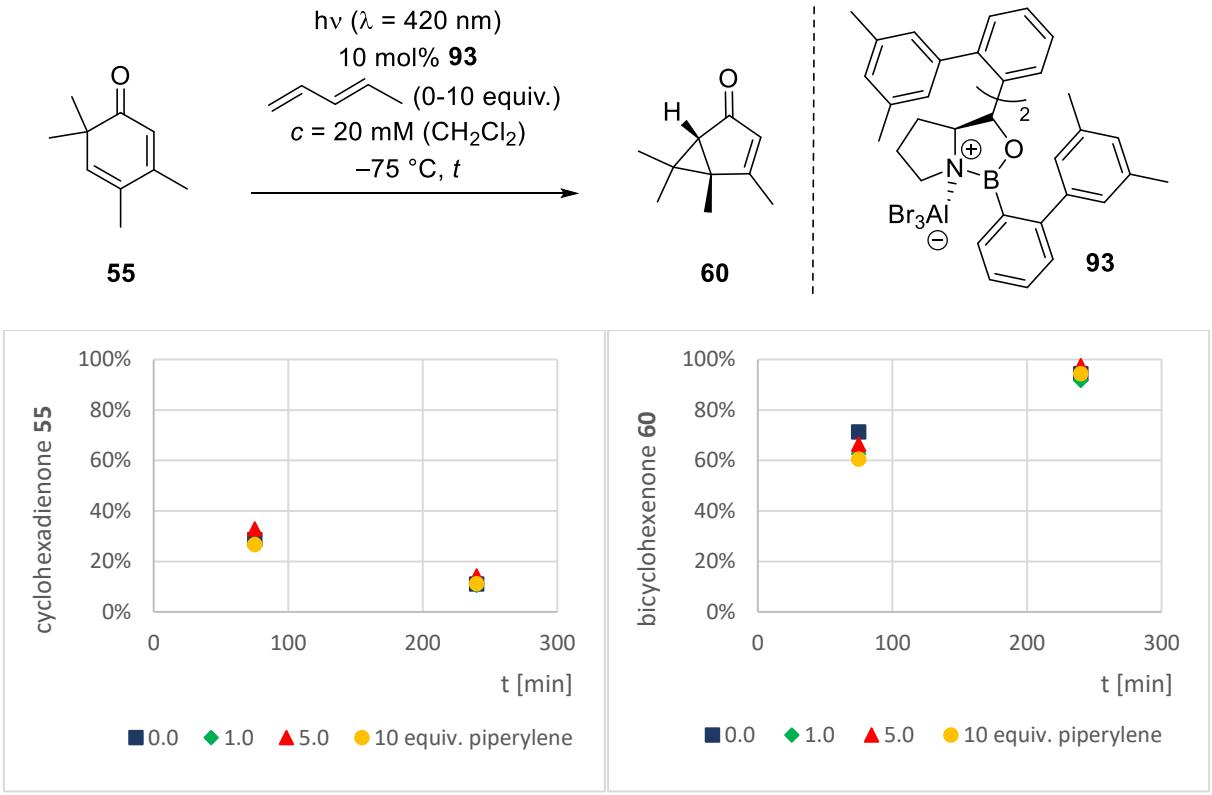


Figure 11. Consumption of **55** and formation of *rac*-**60** in the enantioselective photorearrangement reaction monitored on GC. Different equivalents of piperylene were used as triplet quencher.

2.9.2. DFT Calculations

Additionally, densitiy functional theory (DFT) and spin-flip linear-response time-dependent DFT (TDDFT) calculations were conducted for the boron trifluoride catalyzed reaction by *Dreuw* at the Ruprecht-Karls Universität in Heidelberg. These calculations served to elucidate the reaction pathway further. When boron trifluoride-**55** complex is excited to the first accessible singlet state S_1, intersystem crossing to the triplet state does not occur. However,

instead of relaxation to the ground state S_0, the excited complex can react to a zwitterionic species. This is possible due to a conical intersection, which is energetically easily accessible. Interestingly, the excited complex loses its symmetry due to a out-of-plane bending by the C-6 carbon with its *gem*-dimethyl group. Presumably, this distortion is influenced by chiral catalysts and is the origin of the observed enantioselectivity. The calculations further showed the bond-length between C-1 and C-5 to decrease from 218 ppm to 193 ppm at the conical intersection. This results in the formation of a zwitterionic species, where the resulting bond measures 150 ppm. The zwitterion rearranges via 1,4-shift to the boron trifluoride-*rac*-**60** complex and catalyst dissociation yields photoproduct *rac*-**60** (Figure 12).

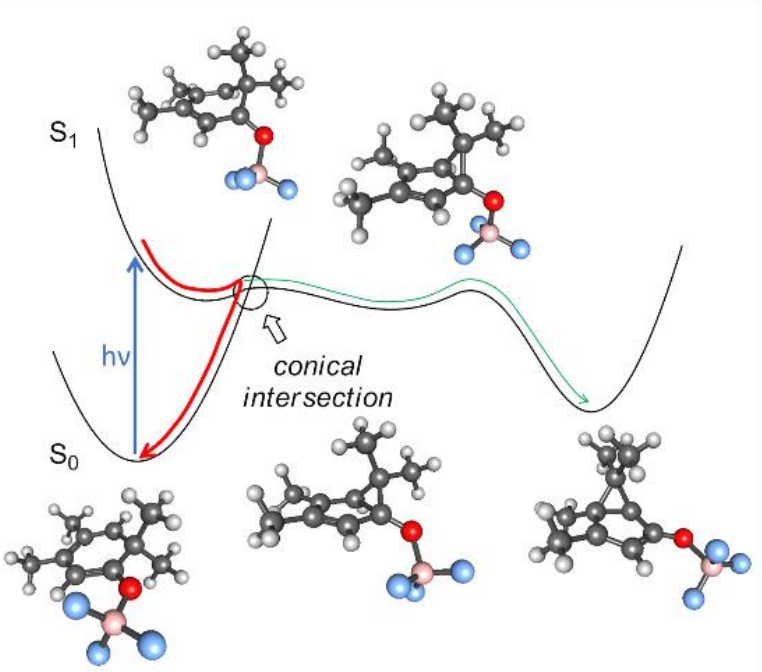
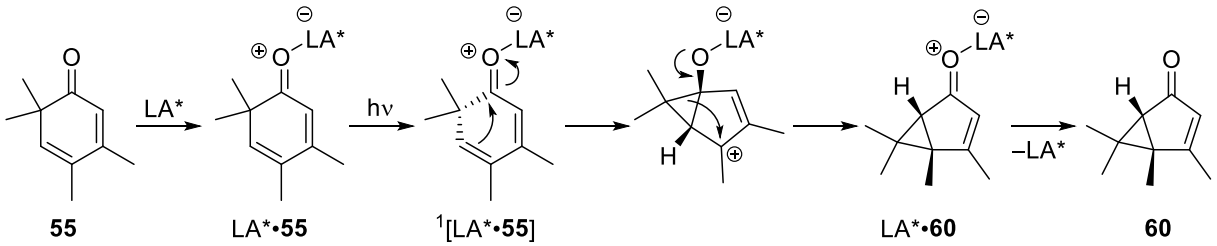


Figure 12. Calculated reaction mechanism of the photorearrangement of Lewis acid complex BF_3·*rac*-**55**.[75] Reprinted (https://pubs.acs.org/doi/abs/10.1021/jacs.9b12068) with permission from the ACS. Further permission to reuse should be directed to the ACS.

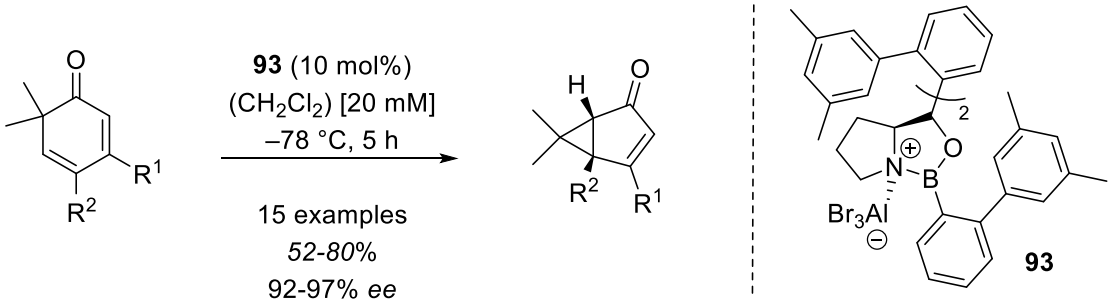
Depicting the reaction mechanism in the case of a chiral Lewis acid LA*, e.g. **93**, singlet intermediate ^{1}LA*-**55**, will be selectively deformed, which leads to the preferred formation of only one enantiomer of a zwitterion. (Scheme 70). Stereoconfiguration at C-5 is fixed during 1,4-migration and determines the final configuration of **60** (see also Scheme 37 in chapter 2.4.5).



Scheme 70. Reaction mechanism of **55** to **60** in presence of a chiral Lewis acid (LA*) via C-1-C-5 bond formation and 1,4-migration.

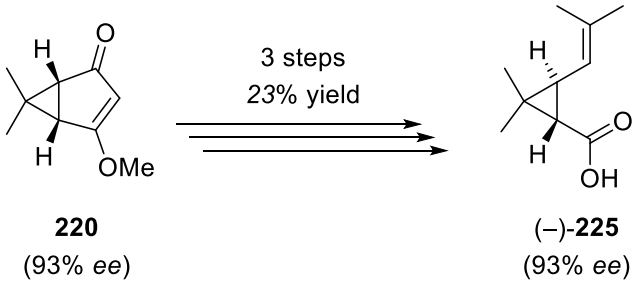
2.10. Summary

Photorearrangement reactions are a powerful tool to transform simple molecules into complex frameworks. However, so far enantioselective approaches have not met with great success. In this work the enantioselective catalysis of photochemical rearrangements of 2,4-cyclohexadienones was investigated. Based on studies by *Griffiths* and *Hart*[62], the aim was to find a suitable chiral Lewis acid for high yields and high enantioselecitivites. Due to a previously observed bathochromic shift, photoreactions could be performed by visible light (λ = 437 nm) and enantioselectivity could be attained by use of chiral oxazaborolidinium complexes as Lewis acids. After screening of various oxazaborolidine-aluminum bromide complexes, Lewis acid **93** was found to deliver the desired bicyclohexenones in good yields (52-80%) and excellent enantioselectivites (92-97% *ee*) (Scheme 71). Due to the enhanced bathochromic shift, no background reaction was observed and catalyst loadings could be kept low (5-10 mol%). Sterically demanding substituents and different functional groups were shown to be tolerated by the catalyst.



Scheme 71. Enantioselective Lewis acid catalyzed photorearrangement reactions of 2,4-cyclohexadienones.

The methodology was applied to a total synthesis of (−)-chrysanthemic acid [(−)-**225**] from photoproduct **220** in three steps and without loss of enantioselectivity (Scheme 72). The absolute configuration of the obtained photoproducts was proven by VCD measurements and the configuration of the synthesized natural product.



220
(93% *ee*)

(–)-**225**
(93% *ee*)

Scheme 72. Total synthesis of (−)-chrysanthemic acid [(−)-**225**] from bicyclohexenone **220** in three steps.

In addition, triplet quenching experiments and DFT/TDDFT calculations revealed a reaction mechanism that proceed via a singlet intermediate and a zwitterionic ground state intermediate.

3. Experimental Part

3.1. General Information

All air and moisture sensitive reactions were carried out in flame-dried glassware under an argon atmosphere using standard *Schlenk* techniques. Commercially available chemicals were used without further purification unless otherwise mentioned. For moisture sensitive reactions, tetrahydrofuran (THF), diethylether (Et_2O) and dichloromethane (CH_2Cl_2) were dried using a MBSPS 800 *MBraun* solvent purification system. The following columns were used:

THF:	2 × MB-KOL-M type 2 (3 Å molecular sieve)
Et_2O:	1 × MB-KOL-A type 2 (aluminum oxide),
	1 × MB-KOL-M type 2 (3 Å molecular sieve)
CH_2Cl_2:	2 × MB-KOL-A type 2 (aluminum oxide)

The following dry solvents are commercially available and were used without further purification:

Chloroform:	*Acros Organics*, 99.9% extra dry, over molecular sieves
N,*N*-Dimethylacetamide:	*Acros Organics*, 99.5% extra dry, over molecular sieves
Methanol:	*Acros Organics*, 99.9% extra dry, over molecular sieves
Pyridine:	*Acros Organics*, 99.5% extra dry, over molecular sieves
Toluene:	*Acros Organics*, 99.8% extra dry, over molecular sieves

For photochemical reactions, dry dichloromethane was degassed by three freeze-pump-thaw cycles and stored over 4 Å molecular sieves. Technical solvents (pentane, diethyl ether, dichloromethane, methanol, *n*-hexane, ethyl acetate, cyclohexane) were distilled prior to column chromatography. Diisopropylamine was distilled over calcium hydride under argon atmosphere prior to use. Flash column chromatography was performed on silica 60 (*Merck*, 230-400 mesh) with the indicated eluent mixtures. Cooling baths used were ice/water (0 °C) and dry ice/ethanol (−78 °C).

Photochemical experiments at λ = 366 nm or λ = 420 nm were carried out in heat gun-dried *Duran* tubes in a positive geometry setup (cylindrical array of 16 *Philips* Black Light Blue fluorescent light tubes, 8 W nominal power, λ_{max} = 366 nm or *Luzchem* LZC-420 fluorescent light tubes, 8 W nominal power, λ_{max} = 420 nm) with the sample placed in the center of the illumination chamber. Photochemical experiments at λ = 398 nm, λ = 425 nm or λ = 437 nm were carried out in a Schlenk tube (diameter = 1 cm) with a polished quartz rod as an optical fiber, which was roughened by sandblasting at one end and the other end attached to the LED. The roughed end (length = 5 cm) has to be completely submerged in the solvent during the reaction, in order to guarantee optimal and reproducible irradiation conditions. The Schlenk tube was cooled using an ethanol bath cooled by a cryostat (*Huber* TC100E).

3.2. Analytical Methods

Thin Layer Chromatography (TLC) was performed on silica coated glass plates (*Merck*, silica 60 F254) with detection by UV-light (λ = 254 nm) and/or by staining with a potassium permanganate solution [$KMnO_4$] or with a cerium ammonium molybdate solution [CAM] followed by heat treatment.

$KMnO_4$-staining solution: potassium permanganate (3.00 g), potassium carbonate (20.0 g) and 5% aqueous sodium hydroxide solution (5.00 mL) in water (300 mL). CAM-staining solution: cerium sulfate tetrahydrate (1.00g), ammonium molybdate (25.0 g) and concentrated sulfuric acid (25.0 mL) in water (250 mL).

Infrared Spectra (IR) were recorded on a *Perkin Elmer* Frontier IR-FTR spectrometer by ATR technique. The signal intensity is assigned using the following abbreviations: *br* (broad), vs (very strong), s (strong), m (medium), w (weak).

Nuclear Magnetic Resonance-Spectra were recorded at room temperature either on a *Bruker* AVHD-300, AVHD-400, AVHD-500 or an AV-500 cryo. ^{1}H NMR spectra were referenced to the residual proton signal of chloroform-d_1 (δ = 7.26 ppm), benzene-d_6 (δ = 7.16 ppm) or methanol-d_4 (δ = 3.31 ppm). ^{13}C NMR spectra were referenced to the ^{13}C-D triplet of $CDCl_3$ (δ = 77.16 ppm), the ^{13}C-D triplet of C_6D_6 (δ = 128.06 ppm) or to the ^{13}C-D septet of CD_3OD (δ = 49.00 ppm). ^{19}F NMR spectra were referenced to the ^{19}F signal of CCl_3F (δ = 0.0 ppm). Apparent multiplets which occur as a result of coupling constant equality between magnetically non-equivalent protons are marked as virtual (*virt*.). The following abbreviations for single multiplicities were used: *br*-broad, s-singlet, d-doublet, t-triplet, q-quartet, quin-quintet, sex-sextet, sept-septet. Assignment and multiplicity of the ^{13}C NMR signals were determined by two-dimensional NMR experiments (COSY, HSQC, HMBC).

Melting Points were determined using a *Kofler* („Thermopan“, Fa. *Reichert*) melting point apparatus and were not corrected.

Mass Spectroscopy (MS) and High Resolution Mass Spectroscopy (HRMS) was measured on a *Thermo Scientific* LTQ-FT Ultra (ESI) or a *Thermo Scientific* DFS-HRMS spectrometer (EI).

UV/Vis Spectra were measured on a *Perkin Elmer* Lambda 35 UV/Vis spectrometer. Spectra were recorded using a *Hellma* precision cell made of quartz SUPRASIL® with a pathway of 1 mm. Solvents and concentrations are given for each spectrum.

Chiral Gas Chromatography (GC) was measured on an *Agilent* 7890 B gas chromatograph using an *Agilent* CycloSil-B column (30 m x 0.25 mm x 0.25 μm, SN: USF620714H) or a *Macherey-Nagel* Lipodex E column (25 m x 0.25 mm, SN: 23393-92) with a flame ionization detector. The temperature method is given for the corresponding compounds.

Analytical High Performance Liquid Chromatography (HPLC) was measured using a chiral stationary layer and UV-detection. Column, eluent and method details are given for the corresponding compounds.

Specific Rotation was determined using a Bellingham+Stanley ADP440+ polarimeter and is reported as follows: $[\alpha]_D^T$ (c in g per 100 mL solvent).

3.3. Synthetic Procedures and Analytical Data

General Procedure 1: Oxidation of Alkylbenzenes with Perfluoroacetic Acid

In analogy to a modified literature procedure[60]: Trifluoroacetic anhydride (3.50 - 5.40 equiv.) was added dropwise to a solution of hydrogen peroxide (35 - 50 wt% in water, 1.20 equiv.) in dichloromethane [3 M] over 30 minutes at 0 °C. The solution was transferred dropwise to a solution of the respective alkylbenzene (1.00 equiv.) in dichloromethane [400 mM] over 15 minutes at 0 °C. Simultaneously, boron trifluoride diethyl etherate (1.20 equiv.) was added dropwise to the alkylbenzene solution. The resulting deep red solution was stirred for one hour at 0 °C before water was added and the mixture saturated with sodium chloride. The organic layer was washed with water (2×), saturated sodium bicarbonate solution (2×), Claisen alkali solution (10 g potassium hydroxide in 10 mL water and 30 mL methanol) (3×), water (2×), saturated sodium thiosulfate solution, brine and dried over sodium sulfate. The solvent was removed in vacuo and the product purified by column chromatography.

General Procedure 2: Addition of Organolithium Reagents to Enones and Dienones

In analogy to a modified literature procedure[81]: A solution of organolithium reagent (1.10 equiv.) was added dropwise to a solution of the respective enone (1.00 equiv.) in diethyl ether [750 mM] at – 78 °C. The reaction mixture was stirred at – 78 °C until complete conversion of starting material was indicated by TLC. After excess of alkyl lithium reagent was quenched by the addition of water, the mixture was warmed to room temperature and was extracted with diethyl ether (3×). The combined organic layers were washed with brine, dried over sodium sulfate and the solvent was removed in vacuo. The crude tertiary allylic alcohol was submitted to oxidation without further purification.

General Procedure 3: Addition of Grignard reagents to Dienones

In analogy to a modified literature procedure[99]: The respective bromide (0.10 equiv.) was added to a suspension of activated magnesium (2.00 equiv.) and iodine (0.01 equiv.) in tetrahydrofuran [2.5 M] and the resulting yellow reaction mixture was stirred at room temperature until the formation of the Grignard reagent initiated, indicated by a change to a brownish or greyish color. Immediately, the remaining bromide (1.90 equiv.) was added dropwise and afterwards the reaction mixture was stirred at room temperature for 30 minutes.

The reaction mixture was cooled to 0 °C and a solution of cyclohexa-2,5-dienone (1.00 equiv.) in tetrahydrofuran [1.0 M] was added dropwise and the reaction mixture warmed to room temperature until complete conversion of starting material was indicated by TLC. The reaction mixture was cooled to 0 °C and excess of Grignard reagent was quenched by the addition of saturated ammonium chloride solution. The mixture was extracted with diethyl ether (3 ×) and the combined organic layers were washed with brine, dried over sodium sulfate and the solvent was removed in vacuo. The crude tertiary allylic alcohol was submitted to oxidation without further purification.

General Procedure 4: Oxidation of Tertiary Allylic Alcohols with Pyridinium Chlorochromate

In analogy to a modified literature procedure[81]: Pyridinium chlorochromate (2.00 equiv.) was added to a solution of crude tertiary allylic alcohol (1.00 equiv.) in dichloromethane [250 mM] and the reaction mixture was stirred vigorously until complete conversion of starting material was indicated by TLC. The reaction mixture was decanted and the residual black resin was washed with diethyl ether (3×). The combined organic layers were washed with 1 M aqueous sodium hydroxide solution (1×), 1 M aqueous hydrochloric acid solution (1×), saturated sodium bicarbonate solution (2×), brine and dried over sodium sulfate. The solvent was removed in vacuo and the product purified by column chromatography.

General Procedure 5: Oxidation of Tertiary Allylic Alcohols with Pyridinium Dichromate

Pyridinium dichromate (1.10 equiv.) was added to a solution of crude tertiary allylic alcohol (1.00 equiv.) in dichloromethane [250 mM] and the reaction mixture was stirred vigorously until complete conversion of starting material was indicated by TLC. Diethyl ether was added and the mixture filtered through a pad of silica gel. The solvent was removed in vacuo and the product purified by column chromatography.

General Procedure 6: Oxidation of Cyclohexenones to 2,4-Cyclohexadienones

In analogy to a modified literature procedure[82]: *N*-Bromosuccinimide (1.00 equiv.) was added to a solution of the respective 2-cyclohexenone (1.00 equiv.) in chloroform [250 mM] and the reaction mixture was heated under reflux until complete conversion of starting material was

indicated by TLC. The mixture was filtered and the solvent removed in vacuo. The crude 4-bromo-2-cyclohexenone was taken up in *N*,*N*-dimethylacetamide [350 mM], calcium carbonate (4.35 equiv.) was added and the mixture heated under reflux for 30 minutes. The reaction mixture was cooled to room temperature, filtered and water was added to the filtrate. The mixture was extracted with diethyl ether (3 ×), the combined organic layers were washed with brine and dried over sodium sulfate. The solvent was removed in vacuo and the product purified by column chromatography.

General Procedure 7: Suzuki Coupling of 2-Bromoiodobenzene and Aryl Boronic Acids

In analogy to a modified literature procedure[67]: The respective aryl boronic acid (1.31 equiv.), potassium fluoride (4.17 equiv.) and tetrakis(triphenylphosphine) palladium(0) (1.50 mol%) were added to a solution of 2-bromoiodobenzene (1.00 equiv.) in 20 mL 1,4-dioxane [275 mM] and the reaction mixture heated under reflux for 48 hours. The reaction mixture was cooled to room temperature, the solvent was removed in vacuo, and the residue taken up in dichloromethane and 1 M hydrochloric acid (v/v = 1/1). The suspension was stirred for ten minutes and the layers were separated. The aqueous layer was extracted with dichloromethane (2×). The combined organic layers were washed with brine, dried over sodium sulfate, filtered, and the solvent was removed in vacuo and the product purified by column chromatography.

General Procedure 8: Grignard Addition to Methyl Benzylpyrroldine Carboxylate

In analogy to a modified literature procedure : A small amount of the respective aryl bromide (0.10 equiv.) was added dropwise to a suspension of activated magnesium (2.50 equiv.) and iodine (0.01 equiv.) in tetrahydrofuran [2.0 M] and the resulting yellow reaction mixture was stirred at 40 °C until the formation of the Grignard reagent initiated, indicated by a change to a brownish or greyish color. Immediately, the remainder of the respective aryl bromide (3.00 equiv.) was added dropwise and the reaction mixture was heated under reflux for one hour. The mixture was cooled 0 °C and a solution (*S*)-methyl-1-benzylpyrroldine-2-carboxylate (1.00 equiv.) in tetrahydrofuran [500 mM] added dropwise. The reaction mixture was warmed to room temperature over 16 hours and quenched with saturated ammonium chloride solution. The aqueous layer was extracted with ethyl acetate (3×). The combined organic layers were

washed with brine, dried over sodium sulfate, filtered, and the solvent was removed in vacuo and the product purified by column chromatography.

General Procedure 9: Hydrogenolysis of Benzyl Diaryl Prolinols

In analogy to a modified literature procedure: Palladium on charcoal (10 wt%) and acetic acid (6 vol%) were added to a solution of the respective benzyl diaryl prolinol (1.00 equiv.) in methanol [125 mM]. The flask was evacuated and filled with hydrogen three times and the reaction mixture was stirred for 24 hours at room temperature. The suspension was filtered over celite and the filter cake was washed with methanol (5×). The filtrate was concentrated in vacuo and suspended in ethyl acetate and water (v/v = 1/1). Sodium hydroxide was added until a homogenous solution was obtained. The layers were separated and the aqueous layer was extracted with ethyl acetate (2×). The combined organic layers were washed with brine, dried over sodium sulfate, filtered, and the solvent was removed in vacuo and the product purified by column chromatography.

General Procedure 10: Racemic Lewis Acid Catalyzed Photorearrangement Reactions

A solution of the respective cyclohexadienone (200 µmol, 1.00 equiv.) in 3 mL degassed dichloromethane was transferred to a flame-dried Duran phototube. To the phototube were added 49.4 µL (203 mM in dichloromethane, 2.84 mg, 20.0 µmol, 0.10 equiv.) of a freshly prepared boron trifluoride diethyl etherate solution. [In a flame-dried Schlenk flask 50 µL (57.5 mg, 40.5 µmol) boron trifluoride diethyl etherate was diluted with degassed dichloromethane to a volume of 2.0 mL]. Degassed dichloromethane was added to the phototube until a concentration of 20 mM (relative to the substrate) was reached. The reaction mixture was irradiated at $\lambda = 420$ nm at ambient temperature for the appropriate time. The Lewis acid was quenched by addition of 100 µL triethylamine and the phototube was shaken vigorously to ensure homogeneity of the solution. The solution was carefully concentrated at room temperature to less than 500 µL and directly subjected to column chromatography.

General Procedure 11: Enantioselective Lewis Acid Catalyzed Photorearrangement Reactions at 437 nm (150 µmol scale)

A solution of the respective cyclohexadienone (150 µmol, 1.00 equiv.) in 3 mL degassed dichloromethane was transferred to a flame-dried 10 mL Schlenk tube equipped with a sand-blown glass rod. 750 µL of the freshly prepared solution of activated catalyst (see chapter 0, 15.0 µmol, 0.10 equiv.) were added to the reaction mixture. Degassed dichloromethane was added to the Schlenk tube until a concentration of 20 mM (relative to the substrate) was reached. The reaction mixture was cooled to –78 °C for 20 minutes and irradiated at λ = 437 nm for five hours. The reaction was quenched by addition of 150 µL triethylamine, the reaction mixture stirred for 15 minutes at –78 °C and then warmed to room temperature. The solution was carefully concentrated at room temperature to less than 500 µL and directly subjected to column chromatography.

General Procedure 12: Enantioselective Lewis Acid Catalyzed Photorearrangement Reactions at 437 nm (1.50 mmol scale)

A solution of the respective cyclohexadienone (1.50 mmol, 1.00 equiv.) in 3 mL degassed dichloromethane was transferred to a flame-dried 10 mL Schlenk tube equipped with a sand-blown glass rod. 750 µL of the freshly prepared solution of activated catalyst (see Synthesis of Chiral Catalysts, 75.0 µmol, 0.05 equiv.) were added to the reaction mixture. Degassed dichloromethane was added to the phototube until a concentration of 200 mM (relative to the substrate) was reached. The reaction mixture was cooled to –78 °C for 20 minutes and irradiated at λ = 437 nm for seven hours. The reaction was quenched by addition of 500 µL triethylamine, the reaction mixture stirred for 15 minutes at –78 °C and then warmed to room temperature. The solution was carefully concentrated at room temperature to less than 1 mL and directly subjected to column chromatography.

General Procedure 13: Oxidative Ring Opening of Bicyclohexenones

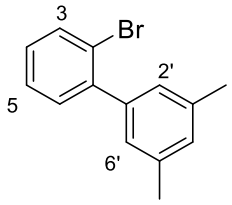
In analogy to a modified literature procedure[96]: Sodium periodate (3.00 equiv.) was added in portions to a solution of the respective bicyclohexenone (1.00 equiv.) and ruthenium(III) chloride hydrate (3.50 mol%) in a mixture of dichloroethane and water (v/v = 5/4) [40 mM] over 15 minutes. The mixture was vigorously stirred at room temperature

until all starting material was consumed. The reaction was quenched with sodium sulfite and then directly acidified to a pH = 1-2. The mixture was extracted with dichloromethane (3×) and the combined organic layers were washed with brine, dried over sodium sulfate and the solvent was removed in vacuo. The respective carboxylic acid was used without further purification.

3.3.1. Synthesis of Chiral Catalysts

Synthesis of Arylbromides

2-Bromo-3',5'-dimethyl-1,1'-biphenyl (63)



$C_{14}H_{13}Br$
MW = 261.16 g/mol

Following GP7, 1.56 g 2-bromoiodobenzene (5.51 mmol, 1.00 equiv.) and 1.09 g 3,5-dimethylphenylboronic acid (7.23 mmol, 1.31 equiv.) were coupled in the presence of 93.7 mg tetrakis(triphenylphosphine) palladium(0) (81.1 µmol, 1.50 mol%) and 1.33 g potassium fluoride (23.0 mmol, 4.17 equiv.) in 48 hours. After purification by column chromatography (silica, P = 100%) 1.33 g bromobiphenyl **63** (5.08 mmol, 92%) were obtained as a colourless oil.

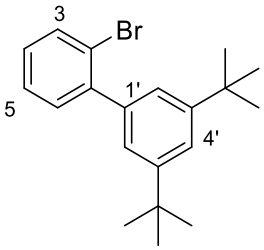
TLC: R_f = 0.33 (P = 100%) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ [ppm] = 2.38 (s, 6 H, 2 × CH_3), 7.01 - 7.01 (m, 3 H, H-2'. H-4', H-6'), 7.18 (ddd, ^3J = 8.0 Hz, ^3J = 6.9 Hz, ^4J = 2.1 Hz, 2 H, H-4), 7.29 - 7.36 (m, 2 H, H-5, H-6), 7.65 (dd, ^3J = 8.0 Hz, ^4J = 1.1 Hz, 1 H, H-3).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 21.5 (q, 2 × CH_3), 122.7 (s, C-2), 127.3 (d, C-2', C-6'), 127.4 (d, C-5), 128.7 (d, C-4), 129.4 (d, C-4'), 131.4 (d, C-6), 133.1 (d, C-3), 137.6 (s, C-3', C-5'), 141.1 (s, C-1'), 142.9 (s, C-1).

The analytical data obtained matched those reported in the literature.[67]

2-Bromo-1,1':4'1''-terphenyl (64)



$C_{20}H_{25}Br$
MW = 345.32 g/mol

Following GP7, 1.19 g 2-bromoiodobenzene (4.21 mmol, 1.00 equiv.) and 985 mg 3,5-*tert*-butylphenylboronic acid (4.21 mmol, 1.00 equiv.) were coupled in the presence of 73.0 mg tetrakis(triphenylphosphine) palladium(0) (63.1 µmol, 1.50 mol%) and 1.02 g potassium fluoride (17.5 mmol, 4.17 equiv.) in 48 hours. After purification by column chromatography (silica, P = 100%) 632 mg bromobiphenyl **64** (1.83 mmol, 44%) were obtained as a colourless oil.

TLC: R_f = 0.34 (P = 100%) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3029 (w, $C_{sp2}H$), 1465(s, C=C), 1004 (w), 1027 (w), 839 (w), 752 (vs, $C_{sp3}H$), 696 (m).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.37 [s, 18 H, 2 × $C(CH_3)_3$], 7.19 (ddd, ^3J = 8.0 Hz, ^3J = 6.8 Hz, ^4J = 2.3 Hz, 1 H, H-5), 7.27 (d, ^4J = 1.8 Hz, 2 H, H-2', H-6'), 7.34 - 7.40 (m, 2 H, H-3, H-4), 7.43 (t, ^4J = 1.8 Hz, 1 H, H-4'), 7.68 (dd, ^3J = 8.1 Hz, ^4J = 1.1 Hz, 1 H, H-6).

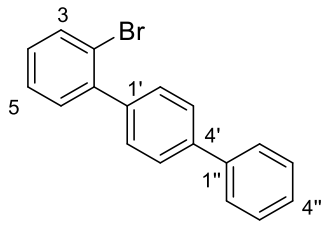
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 31.6 [q, 2 × $C(CH_3)_3$], 35.1 [s, 2 × $C(CH_3)_3$], 121.4 (d, C-4'), 122.9 (s, C-2), 124.1 (d, C-2', C-6'), 127.5 (d, C-3), 128.5 (d, C-5), 131.6 (C-4), 133.3 (d, C-6), 140.1 (s), 143.6, (s) 150.3 (s, C-3', C-5').

MS (EI, 70 eV): *m/z* (%) = 344 (21) $[M]^+$, 329 (100) $[M–CH_3]^+$, 193 (5), 179 (5), 165 (4), 57 (55) $[C_4H_79]^+$.

HRMS (EI, 70 eV): calc. for $C_{20}H_{25}{}^{79}Br$ $[M]^+$: 344.1134; found: 344.1131;

calc. for $C_{19}{}^{13}CH_{25}{}^{79}Br$ $[M]^+$: 345.1168; found: 345.1169.

2-Bromo-1,1':4'1''-terphenyl (65)



$C_{18}H_{13}Br$
MW = 309.21 g/mol

Following GP7, 1.20 g 2-bromoiodobenzene (4.24 mmol, 1.00 equiv.) and 1.09 g 4-biphenylboronic acid (5.51 mmol, 1.30 equiv.) were coupled in the presence of 73.5 mg tetrakis(triphenylphosphine) palladium(0) (63.6 µmol, 1.50 mol%) and 1.03 g potassium fluoride (17.7 mmol, 4.17 equiv.) in 48 hours. After purification by column chromatography (silica, P = 100%) 804 mg bromoterphenyl **65** (2.60 mmol, 61%) were obtained as a colourless solid.

Mp: 82 - 84 °C.

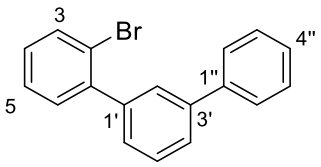
TLC: R_f = 0.24 (P = 100%) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 7.22 (*virt.* dt, ^3J = 8.6 Hz, $^4J \cong {}^4J$ = 4.6 Hz, 1 H, H-5), 7.35 - 7.41 (m, 3 H, H_{Ar}), 7.47 (*virt.* t, $^3J \cong {}^3J$ = 7.6 Hz, 2 H, H_{Ar}), 7.51 (d, ^3J = 8.1 Hz, 2 H, H_{Ar}), 7.65 - 7.71 (m, 5 H, H_{Ar}).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 122.8 (s, C-2), 126.9 (d, 2 × C_{Ar}), 127.3 (d, 2 × C_{Ar}), 127.5 (d, C_{Ar}), 127.6 (d, 2 × C_{Ar}), 128.9 (d, 2 × C_{Ar}), 129.0 (d, C_{Ar}), 130.0 (d, C_{Ar}), 131.5 (d, C_{Ar}), 133.4 (d, C-6), 140.1 (s, C_{Ar}), 140.6 (s, C_{Ar}), 140.8 (s, C_{Ar}), 142.3 (s, C_{Ar}).

The analytical data obtained matched those reported in the literature.[100]

2-Bromo-1,1':3'1''-terphenyl (66)



$C_{18}H_{13}Br$
MW = 309.21 g/mol

Following GP7, 1.20 g 2-bromoiodobenzene (4.24 mmol, 1.00 equiv.) and 1.09 g 3-biphenylboronic acid (5.51 mmol, 1.30 equiv.) were coupled in the presence of 73.5 mg tetrakis(triphenylphosphine) palladium(0) (63.6 µmol, 1.50 mol%) and 1.03 g potassium fluoride (17.7 mmol, 4.17 equiv.) in 48 hours. After purification by column chromatography (silica, P = 100%) 266 mg bromoterphenyl **66** (860 µmol, 20%) were obtained as a colourless oil.

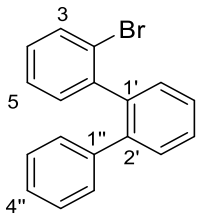
TLC: R_f = 0.16 (P = 100%) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ [ppm] = 7.23 (ddd, ^3J = 8.1 Hz, ^3J = 6.4 Hz, ^4J = 2.8 Hz, 1 H, H_{Ar}), 7.34 - 7.42 (m, 4 H, H_{Ar}), 7.45 (dd, ^3J = 8.3 Hz, ^3J = 7.0 Hz, 2 H, H_{Ar}), 7.51 (t, ^3J = 7.6 Hz, 1 H, H_{Ar}), 7.60 - 7.67 (m, 4 H, H_{Ar}), 7.68 - 7.72 (m, 1 H, H_{Ar}).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 122.8 (s, C-2), 126.5 (d, C_{Ar}), 127.4 (d, C-2'', C-6''), 127.4 (d, C_{Ar}), 127.6 (d, C_{Ar}), 127.6 (d, C_{Ar}), 128.4 (d, C_{Ar}), 128.5 (d, C_{Ar}), 128.6 (d, C_{Ar}), 128.9 (d, C-3'', C-5''), 129.0 (d, C_{Ar}), 131.5 (d, C_{Ar}), 133.3 (d, C_{Ar}), 141.0 (s, 2 × C_{Ar}), 141.7 (s, C_{Ar}), 142.6 (s, C_{Ar}).

The analytical data obtained matched those reported in the literature.[101]

2-Bromo-1,1':2'1''-terphenyl (67)



$C_{18}H_{13}Br$
MW = 309.21 g/mol

Following GP7, 1.20 g 2-bromoiodobenzene (4.24 mmol, 1.00 equiv.) and 1.09 g 2-biphenylboronic acid (5.51 mmol, 1.30 equiv.) were coupled in the presence of 73.5 mg tetrakis(triphenylphosphine) palladium(0) (63.6 µmol, 1.50 mol%) and 1.03 g potassium fluoride (17.7 mmol, 4.17 equiv.) in 48 hours. After purification by column chromatography (silica, P = 100%) 289 mg bromoterphenyl **67** (936 µmol, 22%) were obtained as a colourless oil.

TLC: R_f = 0.38 (P/Cl_2Cl_2 = 19/1) [UV, $KMnO_4$].

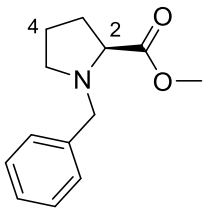
^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 7.05 - 7.10 (m, 2 H, H_{Ar}), 7.12 - 7.20 (m, 6 H, H_{Ar}), 7.31 - 7.36 (m, 1 H, H_{Ar}), 7.39 - 7.44 (m, 1 H, H_{Ar}), 7.44 - 7.49 (m, 2 H, H_{Ar}), 7.50 (m, 1 H, H_{Ar}).

^{13}C NMR (101 MHz, $CDCl_3$, 300 K): δ [ppm] = 124.0 (s, C-2), 126.7 (d, C_{Ar}), 126.9 (d, C_{Ar}), 127.0 (d, C_{Ar}), 127.8 (d, C-2'', C-6''), 128.3 (d, C_{Ar}), 128.6 (d, C_{Ar}), 129.6 (d, C-3'', C-5''), 130.2 (d), 130.9 (d, C_{Ar}), 132.3 (d, C_{Ar}), 132.7 (d, C_{Ar}), 139.8 (s, C_{Ar}), 141.2 (s, C_{Ar}), 141.3 (s, C_{Ar}), 142.5 (s, C_{Ar}).

The analytical data obtained matched those reported in the literature.[100]

Synthesis of Prolinols

(*S*)-Methyl-1-benzylpyrroldine-2-carboxylate (62)



$C_{13}H_{17}NO_2$
MW = 219.28 g/mol

4.40 mL Thionyl chloride (7.22 g, 60.0 mmol, 1.20 equiv.) were added dropwise to a solution of 5.76 g *L*-proline (50.0 mmol, 1.00 equiv.) in 100 mL methanol at 0 °C, the reaction mixture was warmed to room temperature and stirred for 24 hours. The solvent was removed in vacuo and 50 mL toluene was added and removed under reduced pressure three times. The residue was dissolved in 50 mL dichloromethane and 30.1 mL triethylamine (5.88 g, 61.9 mmol, 2.50 equiv.) were added. After 15 minutes, the formed precipitate was filtered and washed with dichloromethane (3× 30 mL). The solvent was removed in vacuo and the residue was suspended in 50 mL diethyl ether, filtered, and washed with diethyl ether (3× 30 mL). The solvent was removed in vacuo and the residue was dissolved in 60 mL diethyl ether and after addition of 7.60 mL triethylamine (5.55 g, 55.0 mmol, 1.10 equiv.) cooled to 0°C and 6.60 mL benzyl bromide (9.50 g, 55.0 mmol, 1.10 equiv.) was slowly added dropwise. After stirring for 24 hours at room temperature the reaction mixture was filtered, washed with diethyl ether (3 × 30 mL) and the solvent was removed in vacuo. After purification by column chromatography (silica, P/Et_2O = 9/1) 9.07 g benzylprolin ester **S18** (41.4 mmol, 83%) was obtained as a pale yellow oil.

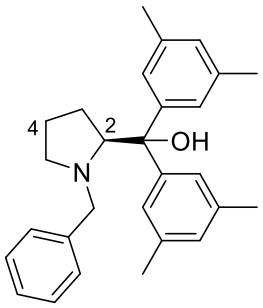
TLC: R_f = 0.30 (P/EtOAc = 9/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ [ppm] = 1.81 - 1.74 (m, 1 H, H-4), 1.85 - 2.00 (m, 2 H, H-3, H-4), 2.09 - 2.17 (m, 1 H, H-3), 2.38 - 2.45 (m, H-5), 3.03 - 3.06 (m, 1 H, H-5), 3.25 (dd, ^3J = 9.0 Hz, ^3J = 6.4 Hz, H-2), 3.57 (d, ^3J = 12.8 Hz, C*H*HAr), 3.64 (s, 3 H, OCH_3), 3.88 (d, ^3J = 12.8 Hz, CH*H*Ar), 7.22 - 7.33 (m, 5 H, H_{Ar}).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 23.1 (t, C-4), 29.5 (t, C-3), 51.9 (q, $COOCH_3$), 53.5 (t, C-5), 59.0 (t, CH_2Ph), 65.5 (d, C-2), 128.3 (d, 2 × $C_{p\text{-Ar}}$), 129.4 (d, 2 × $C_{o\text{-Ar}}$), 127.3 (d, $C_{p\text{-Ar}}$), 138.4 (s, $C_{i\text{-Ar}}$), 174.8 (s, $COOCH_3$).

The analytical data obtained matched those reported in the literature.[40]

(*S*)-(1-benzylpyrrolidin-2-yl)bis(3,5-dimethylphenyl)methanol (68)



$C_{28}H_{33}NO$
MW = 399.58 g/mol

Following GP8, 500 mg methyl benzylpyrrolidine carboxylate **62** (2.28 mmol, 1.00 equiv.) were converted with 166 mg magnesium (6.84 mmol, 3.00 equiv.), 929 µL 1-bromo-3,5-dimethylbenzene (1.27 g, 6.84 mmol, 3.00 equiv.) and 5.79 mg iodine (22.8 µmol, 0.01 equiv.) in 16 hours. After purification by column chromatography (silica, P/EtOAc = 1/0 → 19/1 → 9/1) 848 mg diarylprolinol **68** (2.12 mmol, 93%) were obtained as a colourless foam.

Mp: 97 °C.

TLC: R_f = 0.52 (P/EtOAc = X/X) [UV, $KMnO_4$].

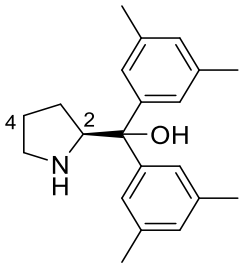
^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.58 - 1.67 (m, 2 H, H-4), 1.76 (*virt.* ddt, ^2J = 12.8 Hz, ^3J = 8.1 Hz, $^3J \approx {}^3J$ = 4.7 Hz, 1 H H-3), 1.96 (*virt.* dq, ^2J = 12.8 Hz, $^3J \approx {}^3J \approx {}^3J$ = 9.1 Hz, 1 H, H-3), 2.24 (s, 6 H, 2 × CH_3), 2.30 (s, 6 H, 2 × CH_3), 2.31 - 2.38 (m,

1 H, H-5), 2.88 - 2.94 (m, 1 H, H-5), 2.99 (d, ^{2}J = 12.6 Hz, 1 H, C*H*HPh), 3.15 (d, ^{2}J = 12.6 Hz, 1 H, CH*H*Ph), 3.89 (dd, ^{3}J = 9.5 Hz, ^{3}J = 4.5 Hz, 1 H, H-2), 4.77 (*br* s, 1 H, OH), 6.69 - 6.73 (m, 1 H, $H_{p\text{-Ar}}$), 6.79 - 6.83 (m, 1 H, $H_{p\text{-Ar}}$), 7.03 - 7.07 (m, 2 H, 2 × $H_{o\text{-Ph}}$), 7.16 - 7.21 (m, 3 H, 2 × $H_{o\text{-Ar}}$, $H_{p\text{-Ph}}$), 7.21 - 7.25 (m, 2 H, 2 × $H_{m\text{-Ph}}$), 7.29 (*br* s, 2 H, 2 × $H_{o\text{-Ar}}$).

^{13}C NMR (100 MHz, $CDCl_3$, 300 K): δ [ppm] = 21.7 (q, 2 × CH_3), 21.8 (q, 2 × CH_3), 24.5 (t, C-4), 30.0 (t, C-3), 55.8 (t, C-5), 60.8 (t, *C*H_2Ph), 71.0 (d, C-2), 78.2 (s, COH), 123.6 (d, 2 × $C_{o\text{-Ar}}$), 123.7 (d, 2 × $C_{o\text{-Ar}}$), 126.9 (d, $C_{p\text{-Ph}}$), 128.0 (d, $C_{p\text{-Ar}}$), 128.2 (d, $C_{p\text{-Ar}}$), 128.2 (d, 2 × $C_{o\text{-Ph}}$), 128.8 (d, 2 × $C_{m\text{-Ph}}$), 137.4 (s, 2 × $C_{m\text{-Ar}}$), 137.5 (s, 2 × $C_{m\text{-Ar}}$), 140.1 (s, $C_{i\text{-Ph}}$), 146.6 (s, $C_{i\text{-Ar}}$), 148.0 (s, $C_{i\text{-Ar}}$).

The analytical data obtained matched those reported in the literature.[102]

(*S*)-bis(3,5-dimethylphenyl)(pyrrolidin-2-yl)methanol (74)



$C_{21}H_{27}NO$
MW = 309.45 g/mol

Following GP9, 820 mg diarylprolinol **68** (2.41 mmol, 1.00 equiv.) were hydrogenolysed in the presence of 82.0 mg palladium on charcoal (10 wt% palladium) under hydrogen atmosphere (1 atm) in 24 hours. After purification by column chromatography (silica, CH_2Cl_2/CH_3OH = 9/1) 637 mg diarylprolinol **74** (2.06 mmol, 93%) were obtained as a colorless solid.

Mp: 92 °C.

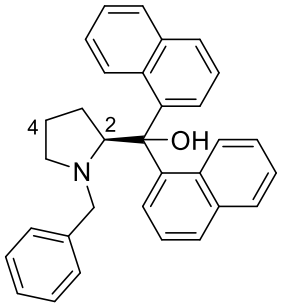
TLC: R_f = 0.18 (CH_2Cl_2/CH_3OH = 9/1) [UV, $KMnO_4$].

^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.52 - 1.81 (m, 4 H, H-3, H-4), 2.27 (s, 6 H, 2 × CH_3), 2.29 (s, 6 H, 2 × CH_3), 2.87 - 3.02 (m, 2 H, H-5), 4.25 (*virt.* t, $^3J \approx {}^3J$ = 7.6 Hz, 1 H, H-2), 6.78 - 6.82 (m, 2 H, 2 × $H_{p\text{-Ar}}$), 7.05 (*br* s, 2 H, 2 × $H_{o\text{-Ar}}$), 7.16 (*br* s, 2 H, 2 × $H_{o\text{-Ar}}$).

^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ [ppm] = 21.7 (q, 2 × CH_3), 21.7 (q, 2 × CH_3), 25.5 (t, C-4), 26.5 (t, C-3), 46.9 (t, C-5), 64.8 (d, C-2), 79.1 (s, COH), 123.3 (d, 2 × $C_{o\text{-Ar}}$), 123.8 (d, 2 × $C_{o\text{-Ar}}$), 128.2 (d, $C_{p\text{-Ar}}$), 128.6 (d, $C_{p\text{-Ar}}$), 137.4 (s, 2 × $C_{m\text{-Ar}}$), 137.8 (s, 2 × $C_{m\text{-Ar}}$), 147.9 (s, $C_{i\text{-Ar}}$), 148.1 (s, $C_{i\text{-Ar}}$).

The analytical data obtained matched those reported in the literature.[103]

(*S*)-(1-Benzylpyrrolidin-2-yl)di(naphthalen-1-yl)methanol (69)



$C_{32}H_{29}NO$
MW = 443.59 g/mol

Following GP8, 500 mg methyl benzylpyrrolidine carboxylate **62** (2.28 mmol, 1.00 equiv.) were converted with 166 mg magnesium (6.84 mmol, 3.00 equiv.), 1.42 g 1-bromonaphtalene (6.84 mmol, 3.00 equiv.) and 5.79 mg iodine (22.8 µmol, 0.01 equiv.) in 24 hours. After purification by column chromatography (silica, P/EtOAc = 9/1) 690 mg diarylprolinol **69** (1.55 mmol, 68%) were obtained as a brownish foam.

Mp: 164 °C.

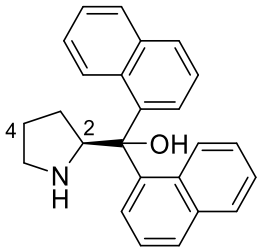
TLC: R_f = 0.51 (P/EtOAc = 9/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.73 (*br* s, 2 H, H-4), 2.17 - 2.79 (m, 5 H, H-3, H-5, C*H*HPh), 2.86 - 2.99 (m, 1 H, CH*H*Ph), 4.43 (*br* s, 1 H, H-2), 4.98 (*br* s, 1 H, OH), 6.93 (*br* s, 2 H, H_{Ar}), 7.11 - 7.33 (m, 2 H, H_{Ar}), 7.52 - 7.79 (m, 6 H, H_{Ar}), 8.05 (*br* s, 1 H, H_{Ar}), 8.44 (*br* s, 1 H, H_{Ar}), 8.68 (*br* s, 2 H, H_{Ar}).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.0 (t, C-4), 31.7 (t, C-3), 55.9 (t, *C*H_2Ph), 60.5 (t, C-5). 69.4 (d, C-2), 82.0 (s, COH), 123.6 (d, C_{Ar}), 124.8 (d, C_{Ar}), 125.1 (d, C_{Ar}), 125.4 (d, C_{Ar}), 126.0 (d, C_{Ar}), 126.9 (d, C_{Ar}), 127.7 (d, C_{Ar}), 128.1 (d, C_{Ar}), 128.7 (d, C_{Ar}), 128.7 (d, C_{Ar}), 128.7 (d, C_{Ar}), 129.1 (d, C_{Ar}), 129.3 (d, C_{Ar}), 131.1 (s, C_{Ar}), 132.6 (s, C_{Ar}), 134.6 (s, C_{Ar}), 135.0 (s, C_{Ar}), 139.4 (s, C_{Ar}), 141.7 (s, C_{Ar}).

The analytical data obtained matched those reported in the literature.[104-105]

(*S*)-Di(naphthalen-1-yl)(pyrrolidin-2-yl)methanol (75)



$C_{25}H_{23}NO$
MW = 353.47 g/mol

Following GP9, 598 mg diarylprolinol **69** (1.35 mmol, 1.00 equiv.) were hydrogenolysed in the presence of 60.0 mg palladium on charcoal (10 wt% palladium) under hydrogen atmosphere (1 atm) in 24 hours. After purification by column chromatography (silica, CH_2Cl_2/CH_3OH = 9/1) 440 mg diarylprolinol **75** (1.24 mmol, 92%) were obtained as a colorless solid.

Mp: 94 - 97 °C.

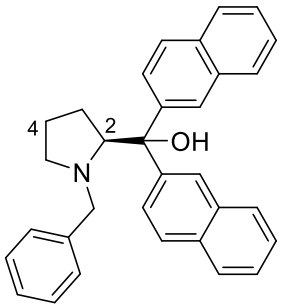
TLC: R_f = 0.16 (CH_2Cl_2/MeOH = 9/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ [ppm] = 1.56 - 1.96 (m, 4 H, H-3, H-4), 3.04 - 3.20 (m, 2 H, H-5), 4.80 (*br* s, 1 H, H-2), 6.90-7.25 (m, 10 H, H_{Ar}), 7.30 - 8.16 (m, 10 H, H_{Ar}), 8.49 (*br* s, 1 H, H_{Ar}).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.5 (t, C-3), 27.8 (t, C-4), 46.5 (t, C-5), 63.3 (s, C-2), 78.4 (s, COH), 123.7 (d. C_{Ar}), 124.2 (d, C_{Ar}), 124.8 (d, C_{Ar}), 125.1 (d, C_{Ar}), 127.3 (d, C_{Ar}), 128.2 (d, C_{Ar}), 128.6 (d, C_{Ar}), 128.7 (d, C_{Ar}), 128.8 (d, C_{Ar}), 134.5 (s, C_{Ar}), 135.1 (s, C_{Ar}), 141.1 (s, C_{Ar}), 142.8 (s, C_{Ar}).

The analytical data obtained matched those reported in the literature.[105]

(*S*)-(1-Benzylpyrrolidin-2-yl)di(naphthalen-2-yl)methanol (70)



$C_{32}H_{29}NO$
MW = 443.59 g/mol

Following GP8, 500 mg methyl benzylpyrrolidine carboxylate **62** (2.28 mmol, 1.00 equiv.) were converted with 166 mg magnesium (6.84 mmol, 3.00 equiv.), 1.42 g 2-bromonaphtalene (6.84 mmol, 3.00 equiv.) and 5.79 mg iodine (22.8 µmol, 0.01 equiv.) in 24 hours. After purification by column chromatography (silica, P/EtOAc = 19/1) 764 mg diarylprolinol **70** (1.72 mmol, 76%) were obtained as a colorless foam.

Mp: 81 °C.

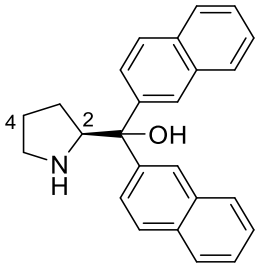
TLC: R_f = 0.29 (P/EtOAc = 19/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.64 - 1.75 (m, 2 H, H-4), 1.83 - 1.93 (m, 1 H, H-3), 2.00 - 2.13 (m, 1 H, H-3), 2.39 - 2.47 (m, 1 H, H-5), 2.97 (ddd, ^3J = 9.4 Hz, ^3J = 6.2 Hz, ^4J = 2.8 Hz, 1 H, H-5), 3.07 (d, ^2J = 12.6 Hz, C*H*HPh), 3.30 (d, ^2J = 12.6 Hz, 1 H, CH*H*Ph), 4.24 (dd, ^3J = 9.4 Hz, ^3J = 4.8 Hz, 1 H, H-2), 5.24 (s, 1 H, OH), 6.97 - 7.03 (m, 2 H, $H_{o\text{-Ph}}$), 7.11 - 7.20 (m, 3 H, $H_{m\text{-Ph}}$, $H_{p\text{-Ph}}$), 7.33 - 7.48 (m, 4 H, H_{Ar}), 7.67 - 7.87 (m, 8 H, H_{Ar}), 8.11 (d, ^4J = 1.3 Hz, 1 H, H_{Ar}), 8.35 (d, ^4J = 1.8 Hz, 1 H, H_{Ar}).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 24.4 (t, C-4), 30.1 (t, C-3), 55.7 (t, C-5), 60.7 (t, *C*H_2Ph), 70.2 (d, C-2), 78.5 (s, COH), 124.1 (d, C_{Ar}), 124.2 (d, C_{Ar}), 124.5 (d, C_{Ar}),124.6 (d, C_{Ar}),125.8 (d, C_{Ar}),125.8 (d, C_{Ar}),126.0 (d, C_{Ar}), 127.0 (d, $C_{p\text{-Ph}}$), 127.6 (d, C_{Ar}), 127.6 (d, C_{Ar}), 127.6 (d, C_{Ar}), 127.9 (d, C_{Ar}), 128.1 (d, C_{Ar}),.128.2 (d, 2 × $C_{m\text{-Ph}}$), 128.3 (d, C_{Ar}), 128.4 (d, C_{Ar}), 128.7 (d, 2 × $C_{o\text{-Ph}}$), 132.2 (s, C_{Ar}), 133.3 (s, C_{Ar}), 133.4 (s, C_{Ar}), 139.6 (s, C_{Ar}), 144.0 (s, C_{Ar}), 145.4 (s, C_{Ar}).

The analytical data obtained matched those reported in the literature.[104]

(*S*)-Di(naphthalen-2-yl)(pyrrolidin-2-yl)methanol (76)



$C_{25}H_{23}NO$
MW = 353.47 g/mol

Following GP9, 471 mg diarylprolinol **70** (1.06 mmol, 1.00 equiv.) were hydrogenolysed in the presence of 50.0 mg palladium on charcoal (10 wt% palladium) under hydrogen atmosphere (1 atm) in 24 hours. After purification by column chromatography (silica,

CH_2Cl_2/CH_3OH = 9/1) 288 mg diarylprolinol **76** (815 µmol, 77%) were obtained as a colorless solid.

Mp: 125 - 126 °C.

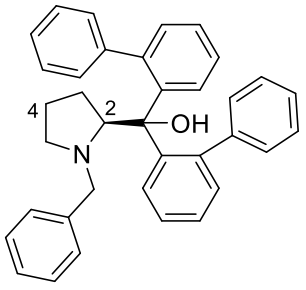
TLC: R_f = 0.08 (CH_2Cl_2/MeOH = 9/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.58 - 1.85 (m, 4 H, H-3, H-4), 2.94 - 3.14 (m, 2 H, H-5), 4.52 (t, ^3J = 7.3 Hz, 1 H, H-2), 7.38 - 7.51 (m, 4 H, H_{Ar}), 7.58 (dd, ^3J = 8.6 Hz, ^4J = 1.8 Hz, 1 H, H_{Ar}), 7.65 - 7.78 (m, 5 H, H_{Ar}), 7.82 - 7.90 (m, 2 H, H_{Ar}), 8.08 - 8.10 (m, 2 H, H_{Ar}).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.7 (t, C-4), 26.6 (t, C-3), 47.0 (t, C-5), 64.1 (d, C-2), 77.7 (s, COH), 123.9 (d, C_{Ar}), 124.1 (d, C_{Ar}), 124.5 (d, C_{Ar}), 125.4 (d, C_{Ar}), 125.8 (d, C_{Ar}), 125.9 (d, C_{Ar}), 126.0 (d, C_{Ar}), 126.2 (d, C_{Ar}), 127.6 (d, C_{Ar}), 127.8 (d, C_{Ar}), 128.2 (d, C_{Ar}), 128.3 (d, C_{Ar}), 128.4 (d, C_{Ar}), 132.3 (s, C_{Ar}), 132.4 (s, C_{Ar}), 133.2 (s, C_{Ar}), 133.3 (s, C_{Ar}), 142.7 (s, C_{Ar}), 145.4 (s, C_{Ar}).

The analytical data obtained matched those reported in the literature.[106]

(*S*)-Di([1,1'-biphenyl]-2-yl)(1-benzylpyrrolidin-2-yl)methanol (71)



$C_{36}H_{33}NO$
MW = 495.67 g/mol

Following GP8, 250 mg methyl benzylpyrrolidine carboxylate **62** (1.14 mmol, 1.00 equiv.) were converted with 166 mg magnesium (6.84 mmol, 6.00 equiv.), 1.42 g 2-bromobiphenyl (6.84 mmol, 6.00 equiv.) and 5.79 mg iodine (22.8 µmol, 0.02 equiv.) in 24 hours. After

purification by column chromatography (silica, P/EtOAc = 19/1) 262 mg diarylprolinol **71** (528 µmol, 46%) were obtained as a colorless foam.

Mp: 69 °C.

TLC: R_f = 0.29 (P/EtOAc = 9/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3405 (br w, NH, OH), 3057 (w, $C_{sp2}H$), 2962 (w, $C_{sp3}H$), 1596 (m, C=C), 1495 (m, C=C), 1470 (m, $C_{sp3}H$), 1437 (w), 1074 (w), 910 (m, $C_{sp2}H$), 753 (s, $C_{sp2}H$), 733 (m, $C_{sp3}H$), 699 (s, $C_{sp2}H$).

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ [ppm] = 1.50 - 1.62 (m, 2 H, H-4), 1.90 - 2.10 (m, 1 H, H-3), 2.18 - 2.26 (m, 1 H, H-5), 2.77 - 2.83 (m, 1 H, H-5), 3.10 (d, ^2J = 12.1 Hz, 1 H, C*H*HPh), 3.20 (*br* s, 1 H, CH*H*Ph), 3.85 (dd, ^3J = 9.5 Hz, ^4J = 3.5 Hz, 1 H, H-2), 6.29 (*br* s, 1 H, H_{Ar}), 6.48 (*br* s, 1 H, H_{Ar}), 6.74 (t, ^3J = 7.7 Hz, 1 H, H_{Ar}), 6.80 (dd, ^3J = 7.3 Hz, ^4J = 1.6 Hz, 1 H, H_{Ar}), 6.86 - 6.94 (m, 3 H, H_{Ar}), 6.98 - 7.03 (m, 2 H, H_{Ar}), 7.03 - 7.09 (m, 4 H, H_{Ar}), 7.11 - 7.20 (m, 7 H, H_{Ar}), 7.21 - 7.25 (m, 2 H, H_{Ar}), 7.46 - 7.52 (m, 1 H, H_{Ar}).

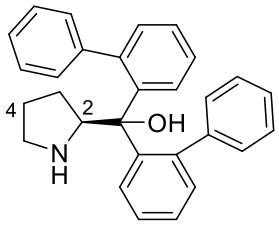
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 24.7 (t, C-4), 31.2 (t, C-3), 55.7 (t, C-5), 61.1 (t, *C*H_2Ph), 69.9 (d, C-2), 80.3 (s, COH), 125.4 (d, C_{Ar}), 125.7 (d, C_{Ar}), 125.8 (d, C_{Ar}), 125.9 (d, C_{Ar}), 126.1 (d, C_{Ar}), 126.3 (d, C_{Ar}), 126.4 (d, C_{Ar}), 126.7 (d, C_{Ar}), 126.8 (d, C_{Ar}), 127.5 (d, C_{Ar}), 128.0 (d, C_{Ar}), 128.4 (d, C_{Ar}), 128.6 (d, C_{Ar}), 129.0 (d, C_{Ar}), 129.2 (d, C_{Ar}), 129.3 (d, C_{Ar}), 129.4 (d, C_{Ar}), 129.9 (d, C_{Ar}), 130.4 (d, C_{Ar}), 131.7 (d, C_{Ar}), 132.1 (d, C_{Ar}), 140.6 (s, C_{Ar}), 142.1 (s, C_{Ar}), 143.3 (s, C_{Ar}), 143.5 (s, C_{Ar}), 143.5 (s, C_{Ar}), 144.2 (s, C_{Ar}).

MS (EI, 70 eV): *m/z* (%) = 181 (3), 170 (100) $[M-C_{26}H_{27}N]^+$, 141 (33) , 115 (24) $[C_9H_7]^+$, 91 (5) $[C_7H_7]^+$, 77 (10) $[C_6H_5]^+$.

HRMS (ESI): calc. for $C_{36}H_{34}NO$ $[M+H]^+$: 496.2635; found: 496.2634.

Specific Rotation: $[\alpha]_D^{25}$ = 296 (c = 0.11, $CHCl_3$).

(*S*)-Di([1,1'-biphenyl]-2-yl)(pyrrolidin-2-yl)methanol (77)



$C_{29}H_{27}NO$
MW = 405.54 g/mol

Following GP9, 202 mg diarylprolinol **71** (408 µmol, 1.00 equiv.) were hydrogenolysed in the presence of 20.4 mg palladium on charcoal (10 wt% palladium) under hydrogen atmosphere (1 atm) in 24 hours. After purification by column chromatography (silica, CH_2Cl_2/CH_3OH = 9/1) 125 mg diarylprolinol **77** (308 µmol, 76%) were obtained as a colorless solid.

Mp: >230 °C (decomp.).

TLC: R_f = 0.18 (CH_2Cl_2/MeOH = 9/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3312 (br w, NH, OH), 3055 (m, $C_{sp2}H$), 2962 (w, $C_{sp3}H$), 1594 (w, C=C), 1472 (m, C=C), 1441 (m, $C_{sp3}H$), 1437 (w), 1074 (w), 908 (w, $C_{sp2}H$), 756 (s, $C_{sp2}H$), 700 (s, $C_{sp2}H$).

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ [ppm] = 1.21 - 1.49 (m, 1 H, H-3), 1.56 - 1.81 (m, 3 H, H-3, H-4), 2.85 - 3.02 (m, 1 H, H-5), 3.15 (*br* s, 1 H, H-5), 4.33 (*br* s, 1 H, H-2), 6.20 (*br* s, 2 H, H_{Ar}), 6.57 (*br* s, 1 H, H_{Ar}), 6.73 - 6.92 (m, 5 H, H_{Ar}), 6.94 (dd, ^3J = 7.5 Hz, ^4J = 1.5 Hz, 1 H, H_{Ar}), 6.98 - 7.10 (m, 3 H, H_{Ar}), 7.10 - 7.19 (m, 3 H, H_{Ar}), 7.19 - 7.35 (m, 3 H, H_{Ar}).

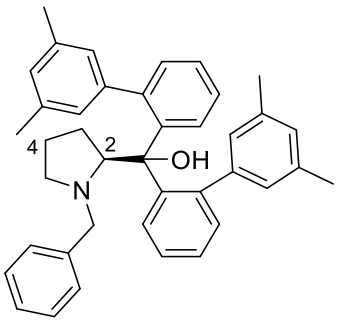
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.6 (t, C-4), 27.8 (t, C-3), 47.2 (t, C-5), 63.7 (d, C-2), 78.2 (s, COH), 126.0 (d, C_{Ar}), 126.0 (d, C_{Ar}), 126.1 (d, C_{Ar}), 126.4 (d, C_{Ar}), 126.5 (d, C_{Ar}), 126.6 (d, C_{Ar}), 126.7 (d, C_{Ar}), 126.9 (d, C_{Ar}), 127.1 (d, C_{Ar}), 127.3 (d, C_{Ar}), 128.7 (d, C_{Ar}), 129.2 (d, C_{Ar}), 131.2 (d, C_{Ar}), 132.7 (d, C_{Ar}), 142.2 (s, C_{Ar}), 142.7 (s, C_{Ar}), 142.7 (s, C_{Ar}), 143.1 (s, C_{Ar}).

MS (EI, 70 eV): *m/z* (%) = 387 (12) $[M–H_2O]^+$, 334 (11) $[M– C_4H_9N]^+$, 318 (18) $[M– C_5H_{11}O]^+$, 153 (12) $[C_{12}H_9]^+$, 91 (10) $[C_7H_7]^+$, 70 (100) $[C_4H_8N]^+$.

HRMS (ESI): calc. for $C_{29}H_{28}NO$ $[M+H]^+$: 406.2166; found: 406.2168.

Specific Rotation: $[\alpha]_D^{25} = -49.0$ (c = 1.35, $CHCl_3$).

(*S*)-(1-Benzylpyrrolidin-2-yl)bis(3',5'-dimethyl-[1,1'-biphenyl]-2-yl)methanol (72)



$C_{40}H_{41}NO$
MW = 551.77 g/mol

Following GP8, 250 mg methyl benzylpyrrolidine carboxylate **62** (1.14 mmol, 1.00 equiv.) were converted with 83.1 mg activated magnesium (3.42 mmol, 3.00 equiv.), 893 mg bromobiphenyl **63** (3.42 mmol 3.00 equiv.) and 5.79 mg iodine 1.45 mg iodine (11.4 µmol, 0.01 equiv.) in 24 hours. After purification by column chromatography (silica, P/EtOAc = 19/1) 498 mg diarylprolinol **72** (903 µmol, 79%) were obtained as a colourless foam.

Mp: 75 °C.

TLC: R_f = 0.40 (P/EtOAc = 19/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3402 (s, OH), 3027 (m, $C_{sp2}H$), 2946 (m, $C_{sp3}H$), 2916 (m, $C_{sp3}H$), 2794 (w), 1602 (m, C=C), 1495 (w, $C_{sp3}H$), 1453 (m, $C_{sp3}H$), 1374 (m, $C_{sp3}H$), 1295 (w), 1209 (w), 1097 (w), 1076 (w), 1030 (w), 909 (m, $C_{sp2}H$), 849 (m, $C_{sp3}H$), 758 (s, $C_{sp3}H$), 733 (s, $C_{sp3}H$).

^{1}H NMR (400 MHz, CD_3OD, 328 K): δ [ppm] = 1.80 - 1.97 (m, 2 H, H-4), 2.25 - 2.32 (m, 2 H, H-3), 2.32-2.60 (m, 12 H, 2 × CH_3), 2.60 - 2.66 (m, 1 H, H-5), 3.06 - 3.20 (m, 1 H, H-5), 3.36 - 3.49 (m, 1 H, C*H*HPh), 3.56 - 3.59 (m, 1 H, CH*H*Ph), 4.17 - 4.29 (m, 1 H, H-2), 6.18 - 6.66 (m, 1 H, H_{Ar}), 6.70 - 6.92 (m, 1 H, H_{Ar}), 6.95 - 7.03 (m, 1 H, H_{Ar}), 7.06 - 7.17 (m, 5 H, H_{Ar}), 7.24 - 7.66 (m, 11 H, H_{Ar}).

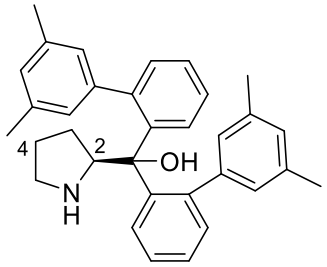
13C NMR (100 MHz, CD_3OD, 328 K): δ [ppm] = 21.4 (q, 4 × CH_3), 25.5 (t, C-3), 31.7 (t, C-4), 56.4 (t, C-5), 62.6 (t, *C*H_2Ar), 73.8 (d, C-2), 82.8 (s, COH), 125.9 (d, C_{Ar}), 126.3 (d, C_{Ar}), 126.8 (d, C_{Ar}), 127.6 (d, C_{Ar}),128.5 (d, C_{Ar}), 128.7 (d, C_{Ar}), 128.8 (d, C_{Ar}), 128.9 (d, C_{Ar}), 129.7 (d, C_{Ar}), 129.8 (d, C_{Ar}), 132.7 (d, C_{Ar}), 133.2 (d, C_{Ar}), 136.7 (s, C_{Ar}), 136.7 (s, C_{Ar}), 138.7 (s, C_{Ar}), 142.5 (s, C_{Ar}),144.5 (s, C_{Ar}),144.7 (s, C_{Ar}).

MS (EI, 70 eV): *m/z* (%) = 362 (85) $[M-C_{12}H_{15}NO]^+$, 286 (78) $[M-C_{18}H_{19}NO]^+$, 256 (52) $[M-C_{20}H_{25}NO]$, 198 (100) $[M-C_{26}H_{27}N]^+$, 183 (93) $[C_2H_5N]^+$, 169 (43) $[C_7H_9]^+$, 105 (34) $[C_8H_9]^+$, 91 (73) $[C_7H_7]^+$, 77 (44) $[C_6H_5]^+$, 57 (41) $[C_2H_5O]^+$, 43 (62) $[C_2H_5N]^+$.

HRMS (ESI): calc. for $C_{40}H_{42}NO$ $[M+H]^+$: 552.3261; found: 552.3259.

Specific Rotation: $[\alpha]_D^{25}$ = +64.2 (c = 1.06, $CHCl_3$) [98.5% *ee*].

(*S*)-Bis(3',5'-dimethyl-[1,1'-biphenyl]-2-yl)(pyrrolidin-2-yl)methanol (78)



$C_{33}H_{35}NO$
MW = 461.65 g/mol

Following GP9, 250 mg diarylprolinol **72** (634 µmol, 1.00 equiv.) were hydrogenolysed in the presence of 35.0 mg palladium on charcoal (10 wt% palladium) under hydrogen atmosphere (1 atm) in 24 hours. After purification by column chromatography (silica, CH_2Cl_2/CH_3OH = 19/1) 223 mg diarylprolinol **78** (48.3 µmol, 79%) were obtained as a colorless solid.

Mp: 88 °C.

TLC: R_f = 0.19 (CH_2Cl_2/CH_3OH = 19/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3315 (*br*, OH), 2915 (m, $C_{sp3}H$), 2865 (m, $C_{sp3}H$), 1602 (m, $C_{=}C$), 1468 (m, $C_{sp3}H$), 1440 (m, $C_{sp3}H$), 1400 (w, $C_{sp3}H$), 1376 (w), 1266 (w), 1165 (w), 980 (w), 849 (s, $C_{sp2}H$), 758 (s, $C_{sp2}H$), 737 (s, $C_{sp3}H$), 710 (s, $C_{sp2}H$), 657 (m).

^{1}H NMR (500 MHz, CDCl3, 300 K): δ [ppm] = 1.30 - 1.55 (m, 1 H, H-3), 1.62 - 1.82 (m, 3 H, H-3, H-4, H-4), 1.98 (*br* s, 6 H, 2 × CH_3), 2.19 - 2.42 (m, 6 H, 2 × CH_3), 2.87 - 2.97 (m, 1 H, H-5), 3.08 (*br* s, 1 H, H-5), 4.32 (*virt.* dd, $^{3}J \cong {}^{3}J$ = 7.9 Hz, 1 H, H-2), 5.71 (*br* s, 1 H, H_{Ar}), 6.74 - 6.76 (m, 2 H, H_{Ar}), 6.76 - 6.84 (m, 3 H, H_{Ar}), 6.84 - 6.89 (m, 2 H, H_{Ar}), 6.89 - 7.00 (m, 3 H, H_{Ar}), 7.05 - 7.16 (3 H, H_{Ar}).

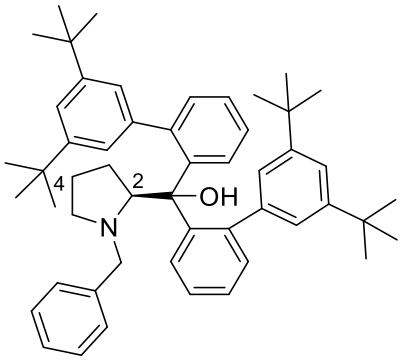
^{13}C NMR (126 MHz, CDCl3, 300 K): δ [ppm] = 21.3 (q, CH_3), 21.4 (q, CH_3), 21.4 (q, CH_3), 21.6 (q, CH_3), 25.7 (t, C-4), 27.8 (t, C-3), 47.3 (t, C-5), 63.7 (d, C-2), 78.6 (s, COH), 126.0 (d, C_{Ar}), 126.0 (d, C_{Ar}), 126.1 (d, C_{Ar}), 126.2 (d, C_{Ar}),126.7 (d, C_{Ar}), 126.8 (d, C_{Ar}), 127.0 (d, C_{Ar}), 127.2 (d, C_{Ar}), 127.5 (d, C_{Ar}), 127.8 (d, C_{Ar}), 128.1 (d, C_{Ar}), 128.4 (d, C_{Ar}), 131.2 (d, C_{Ar}), 132.4 (d, C_{Ar}), 136.3 (s, C_{Ar}), 136.5 (s, C_{Ar}),136.7 (s, C_{Ar}),142.3 (s, C_{Ar}),142.7 (s, C_{Ar}).

MS (EI, 70 eV): *m/z* (%) = 461 (86) $[M]^+$, 443 (36) $[M-H_2O]^+$, 390 (25) $[M-C_4H_9N]^+$, 375 (38) $[M-C_4H_8NO]^+$, 209 (100) $[C_{16}H_{17}]^+$, 193 (31) $[C_{15}H_{13}]^+$, 181 (26) $[C_{14}H_{13}]^+$, 166 (57) $[C_{13}H_{10}]^+$.

HRMS (ESI): calc. for $C_{40}H_{42}NO$ $[M+H]^+$: 552.3261; found: 552.3259.

Specific Rotation: $[\alpha]_D^{25}$ = −49.4 (c = 1.21, $CHCl_3$) [98.5% *ee*].

(*S*)-(1-benzylpyrrolidin-2-yl)bis(3',5'-di-tert-butyl-[1,1'-biphenyl]-2-yl)methanol (73)



$C_{52}H_{65}NO$
MW = 720.10 g/mol

Following GP8, 130 mg methyl benzylpyrrolidine carboxylate **62** (593 µmol, 1.00 equiv.) were converted with 36.0 mg magnesium (1.48 mmol, 2.50 equiv.), 512 mg bromobiphenyl **64** (1.48 mmol, 2.50 equiv.) and 1.50 mg iodine (5.93 µmol, 0.01 equiv.) in 16 hours. After purification by column chromatography (silica, P/EtOAc = 49/1 → 29/1) 243 mg diarylprolinol **73** (337 µmol, 57%) were obtained as a colorless oil.

Mp: 94 - 95 °C.

TLC: R_f = 0.49 (P/EtOAc = 19/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2962 (vs, $C_{sp3}H$), 1593 (m, C=C), 1478 (w, $C_{sp3}H$), 1362 (m, $C_{sp3}H$), 1248 (w), 875 (m, $C_{sp3}H$), 754 (s, $C_{sp3}H$).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.06 - 1.07 [m, 18 H, 2 × $C(CH_3)_3$], 1.33 - 1.44 [*br* s, 18 H, 2 × $C(CH_3)_3$], 1.63 (*virt.* td, $^3J \approx {}^3J$ = 6.4 Hz, ^3J = 4.2 Hz, 2 H, H-4), 1.80 - 2.40 (m, 3 H, H-3, H-5), 2.87 (t, ^3J = 7.3 Hz, H-5), 3.10 (*br* s, 2 H, CH_2Ph), 3.88 (*br* s, 0.49 H, CH_2Ph), 4.08 (d, 9.4 Hz, 1 H, H-2), 5.85 - 6.58 (m, 3 H, H_{Ar}), 6.62 (*br* s, 2 H, H_{Ar}), 6.89 - 6.94 (m, 2 H, H_{Ar}), 6.94 - 6.93 (m, 1 H, H_{Ar}), 6.94 - 7.02 (m, 2 H, H_{Ar}), 7.03 - 7.11 (m, 3 H, H_{Ar}), 7.12 - 7.24 (m, 7 H, H_{Ar}).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 24.8 (t, C-3), 31.7 (t, C-4), 31.5 [q, C(*C*H_3)$_3$], 31.6 [q, C(*C*H_3)$_3$], 31.8 [q, C(*C*H_3)$_3$], 31.8 [q, C(*C*H_3)$_3$], 34.5 [q, *C*$(CH_3)_3$], 34.6 [q, *C*$(CH_3)_3$], 34.9 [q, *C*$(CH_3)_3$], 35.0 [q, *C*$(CH_3)_3$], 56.6 (t, C-5), 62.4 (t, *C*H_2Ar), 70.9 (d, C-2), 80.8 (s, COH), 120.3 (d, C_{Ar}), 120.5 (d, C_{Ar}), 120.8 (d, C_{Ar}), 122.2 (d, C_{Ar}), 123.0 (d, C_{Ar}), 123.2 (d,

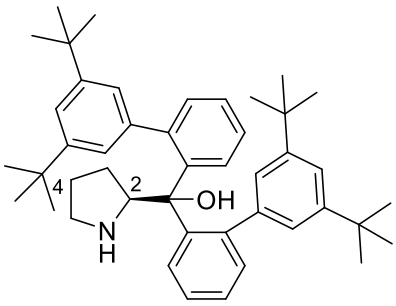
C_{Ar}), 123.4 (d, C_{Ar}), 123.4 (d, C_{Ar}), 124.2 (d, C_{Ar}), 124.8 (d, C_{Ar}), 126.0 (d, C_{Ar}), 126.1 (d, C_{Ar}), 126.9 (d, C_{Ar}), 127.1 (d, C_{Ar}), 128.1 (d, C_{Ar}), 129.0 (d, C_{Ar}), 129.1 (d, C_{Ar}), 129.2 (d, C_{Ar}), 130.3 (d, C_{Ar}), 131.8 (s, C_{Ar}), 132.2 (s, C_{Ar}), 134.4 (s, C_{Ar}), 136.2 (s, C_{Ar}), 140.6 (s, C_{Ar}), 142.0 (s, C_{Ar}), 142.5 (s, C_{Ar}), 143.6 (s, C_{Ar}), 148.2 (s, C_{Ar}), 151.7 (s, C_{Ar}), 152.7 (s, C_{Ar}).

MS (EI, 70 eV): *m/z* (%) = 702 (2) $[M-H_2O]^+$, 558 (11) $[M-C_{12}H_{20}O]^+$, 501 (13), 282 (35) $[C_{20}H_{24}N]^+$, 267 (100) $[C_{19}H_{21}N]^+$, 160 (46), 105 (19) $[C_6H_5]^+$, 83 (38) $[C_5H_9N]^+$, 57 (82) $[C_4H_9]^+$.

HRMS (ESI): calc. for $C_{52}H_{66}NO$ $[M+H]^+$: 720.5139; found: 720.5140.

Specific Rotation: $[\alpha]_D^{25}$ = 10.1 (c = 0.99, $CHCl_3$).

(*S*)-bis(3',5'-di-tert-butyl-[1,1'-biphenyl]-2-yl)(pyrrolidin-2-yl)methanol (79)



$C_{45}H_{59}NO$
MW = 629.97 g/mol

Following GP9, 215 mg diarylprolinol **73** (299 µmol, 1.00 equiv.) were hydrogenolysed in the presence of 21.5 mg palladium on charcoal (10 wt% palladium) under hydrogen atmosphere (1 atm) in 24 hours. After purification by column chromatography (silica, CH_2Cl_2/CH_3OH = 19/1) 186 mg diarylprolinol **79** (295 µmol, 98%) were obtained as a colorless solid.

Mp: 102 - 104 °C.

TLC: R_f = 0.16 (CH_2Cl_2/MeOH = 19/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2963 (vs, $C_{sp3}H$), 1593 (m, C=C), 1478 (w, $C_{sp3}H$), 1362 (m, $C_{sp3}H$), 1248 (w), 875 (m, $C_{sp3}H$), 754 (s, $C_{sp3}H$).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.04 - 1.18 [m, 18 H, 2 × $C(CH_3)_3$], 1.28 - 1.42 [m, 20 H, , H-4, 2 × $C(CH_3)_3$], 1.65 (*br* s, 1 H, H-3), 1.65 (*br* s, 1 H, H-3), 3.01 (*virt.* dt, ^3J = 8.5 Hz, $^3J \approx {}^3J$ = 7.9 Hz), 4.32 - 4.39 (m, 1 H, H-2), 6.21 (s, 1 H, H_{Ar}), 6.28 (s, 1 H, H_{Ar}), 6.45 (s, 1 H, H_{Ar}), 6.69 - 6.78 (m, 3 H, H_{Ar}), 6.87 - 7.04 (m, 4 H, H_{Ar}), 7.15 (s, 1 H, H_{Ar}), 7.19 (t, ^3J = 1.8 Hz, 1 H, H_{Ar}), 7.21 - 7.25 (m, 1 H, H_{Ar}), 7.50 (*br* s, 1 H, H_{Ar}).

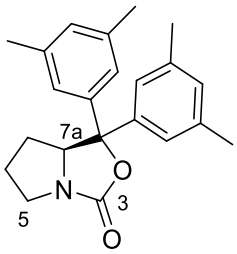
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.7 (t, C-4), 28.3 (t, C-3), 31.7 (t, C-4), 31.5 [q, 2 × C(*C*H_3)$_3$], 31.6 [q, C(*C*H_3)$_3$], 31.7 [q, C(*C*H_3)$_3$], 34.5 [q, *C*$(CH_3)_3$], 34.6 [q, *C*$(CH_3)_3$], 34.8 [q, *C*$(CH_3)_3$], 34.9 [q, *C*$(CH_3)_3$], 46.9 (t, C-5), 64.0 (d, C-2), 77.4 (s, COH), 120.3 (d, C_{Ar}), 120.8 (d, C_{Ar}), 122.9 (d, C_{Ar}), 123.2 (d, 2 × C_{Ar}), 125.2 (d, C_{Ar}), 125.7 (d, 2 × C_{Ar}), 126.0 (d, C_{Ar}), 126.2 (d, C_{Ar}), 126.4 (d, C_{Ar}), 126.9 (d, C_{Ar}), 130.9 (d, C_{Ar}), 133.7 (d, C_{Ar}), 140.0 (s, C_{Ar}), 141.8 (s, C_{Ar}), 142.0 (s, C_{Ar}), 142.5 (s, C_{Ar}), 143.8 (s, C_{Ar}), 144.5 (s, C_{Ar}), 147.9 (s, C_{Ar}), 148.4 (s, C_{Ar}), 149.2 (s, C_{Ar}).

MS (EI, 70 eV): *m/z* (%) = 629 (23) $[M]^+$, 611 (78) $[M-C_2H_4]^+$, 559 (82) $[M-C_5H_{10}]^+$, 501 (79) $[M-C_5H_{10}]^+$, 447 (25), 317 (33), 237 (60), 221 (49), 181 (100) $[C_{14}H_{13}]^+$.

HRMS (ESI): calc. for $C_{45}H_{60}NO$ $[M+H]^+$: 630.4670; found: 630.4667.

Specific Rotation: $[\alpha]_D^{25}$ = 26.0 (c = 1.00, $CHCl_3$).

(*S*)-1,1-bis(3,5-dimethylphenyl)tetrahydro-1H,3H-pyrrolo[1,2-c]oxazol-3-one (80)



$C_{22}H_{25}NO_2$
MW =335.45 g/mol

A solution of 28.8 mg triphosgene (97.0 μmol, 1.00 equiv) in 1.5 mL dichloromethane was added to a solution of 30.0 mg diarylprolinol **74** (97.0 μmol, 1.00 equiv.) and 15.6 μL pyridine (15.3 mg, 2.00 equiv) in 1.0 mL dichloromethane at 0 °C. After stirring for 24 hours at room temperature, the excess of triphosgene was quenched with brine (5 mL) and subsequently extracted with dichloromethane (2 × 5 mL). The combined organic layers were dried over sodium sulfate, filtered, and the solvent was removed in vacuo. After column chromatography (silica, P/EtOAc = 9/1 → 4/1) 28.4 mg oxazolone **80** (84.7 μmol, 87%, 99% *ee*) were obtained as a colorless solid.

Mp: 141 - 142 °C.

TLC: R_f = 0.50 (P/EtOAc = 4/1) [UV, $KMnO_4$].

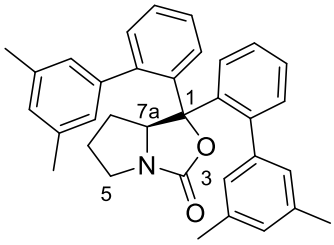
^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.03 - 1.20 (m, 1 H, H-7), 1.64 - 1.76 (m, 1 H, H-7), 1.78 - 1.91 (m, 1 H, H-6), 1.92 - 2.02 (m, 1 H, H-6), 2.29 (s, 6 H, 2 × CH_3), 2.30 (s, 6 H, 2 × CH_3), 3.23 (ddd, ^2J = 11.4 Hz, ^3J = 9.4 Hz, ^3J = 3.7 Hz, 1 H, H-5), 3.72 (*virt.* dt, ^2J = 11.4 Hz, $^3J \approx {}^3J$ = 8.1 Hz, 1 H, H-5), 4.50 (dd, ^2J = 10.6 Hz, ^3J = 5.4 Hz, 1 H, H-7a), 6.87 - 6.90 (m, 1 H, $H_{p\text{-Ar}}$), 6.92 - 6.95 (m, 1 H, $H_{p\text{-Ar}}$), 6.98 (*br* s, 2 H, 2 × $H_{o\text{-Ar}}$), 7.13 (*br* s, 2 H, 2 × $H_{o\text{-Ar}}$).

^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ [ppm] = 21.6 (q, 2 × CH_3), 21.6 (q, 2 × CH_3), 25.0 (t, C-6), 29.2 (t, C-7), 46.2 (t, C-5), 69.3 (d, C-7a), 86.0 (s, C-1), 123.3 (d, 2 × $C_{o\text{-Ar}}$), 123.8 (d,

2 × $C_{o\text{-Ar}}$), 129.4 (d, $C_{p\text{-Ar}}$), 130.0 (d, $C_{p\text{-Ar}}$), 138.0 (s, 2 × $C_{m\text{-Ar}}$), 138.2 (s, 2 × $C_{m\text{-Ar}}$), 140.5 (s, $C_{i\text{-Ar}}$), 143.6 (s, $C_{i\text{-Ar}}$), 160.7 (s, C-3).

The analytical data obtained matched those reported in the literature.[107]

(S)-1,1-Bis(3',5'-dimethyl-[1,1'-biphenyl]-2-yl)tetrahydro-1H,3H-pyrrolo[1,2-c]oxazol-3-one (81)



$C_{34}H_{33}NO_2$
MW = 487.64 g/mol

A solution of triphosgene (19.3 mg, 65.0 μmol, 1.00 equiv) in 1.0 mL dichloromethane was added to a solution of prolinol **78** (30.0 mg, 65.0 μmol, 1.00 equiv.) and pyridine (10.5 μL, 10.3 mg, 2.00 equiv) in 1.0 mL dichloromethane at 0 °C. After stirring for 24 hours at room temperature, the excess triphosgene was quenched with brine (5 mL) and subsequently extracted with dichloromethane (2 × 5 mL). The combined organic layers were dried over sodium sulfate, filtered, and the solvent was removed in vacuo. After column chromatography (silica, P/Et2O = 9/1), 28.2 mg oxazolone **81** (75.8 μmol, 89%, 98% *ee*) were obtained as a colorless solid.

Mp: 168 °C.

TLC: R_f = 0.24 (P/EtOAc = 4/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2916 (w, $C_{sp3}H$), 1759 (vs, C=O), 1602 (w, C=C), 1444 (w, $C_{sp3}H$), 1352 (m, $C_{sp3}H$), 1223 (s, COC), 1055 (w), 984 (w), 850 (m, $C_{sp2}H$), 755 (s, $C_{sp2}H$), 707 (w).

^{1}H NMR (500 MHz, CDCl3, 298 K): δ [ppm] = 1.01 (*virt.* dddd, $^{2}J \cong {}^{3}J \cong {}^{3}J$ = 11.5 Hz, ^{3}J = 9.1 Hz, 1 H, H-7), 1.44 (*virt*. ddd, ^{2}J = 12.5 Hz, $^{3}J \cong {}^{3}J$ = 6.0 Hz, 1 H, H-7), 1.61 - 1.74 (m, 1 H, H-6), 1.85 - 1.94 (m, 1 H, H-6), (1 H, H-6), 1.96 (s, 3 H, CH_3), 2.11 (*br* s, 6 H, 2 × CH_3), 2.34 (s, 3 H, CH_3) 3.10 - 3.25 (m, 1 H, H-5), 3.75 (ddd, ^{3}J = 12.6 Hz, ^{3}J = 10.6 Hz, ^{3}J = 7.5 Hz, 1 H, H-5), 3.95 (dd, ^{3}J = 10.6 Hz, ^{3}J = 5.1 Hz, 1 H, H-7), 5.96 (s, 1 H, H_{Ar}), 6.66 - 6.92 (m, 6 H, H_{Ar}), 6.94 - 7.12 (m, 6 H, H_{Ar}), 7.24 (td, ^{3}J = 7.3 Hz, ^{4}J = 1.3 Hz, 1 H, H_{Ar}).

^{13}C NMR (126 MHz, CDCl3, 300 K): δ [ppm] = 21.1 (q, CH_3), 21.4 (q, 2 × CH_3), 21.5 (q, CH_3), 24.0 (t, C-6), 28.2 (t, C-7), 47.0 (t, C-5), 66.5 (d, C-7a), 85.2 (s, C-1), 125.5 (d, 2 × C_{Ar}), 125.8 (d, C_{Ar}), 126.1 (d, C_{Ar}), 126.5 (d, C_{Ar}), 127.3 (d, C_{Ar}), 127.8 (d, C_{Ar}), 127.9 (d, 2 × C_{Ar}), 128.5 (d, 2 × C_{Ar}), 129.2 (d, C_{Ar}), 130.8 (d, C_{Ar}), 132.5 (d, C_{Ar}), 135.8 (s, C_{Ar}), 136.1 (s, C_{Ar}), 136.5 (s, C_{Ar}), 138.1 (s, C_{Ar}), 138.1 (s, C_{Ar}), 139.8 (s, C_{Ar}), 141.2 (s, 2 × C_{Ar}), 142.0 (s, 2 × C_{Ar}), 161.6 (s, NCOO).

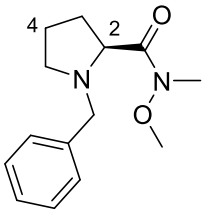
MS (EI, 70 eV): *m/z* (%) = 487 (36) $[M]^+$, 443 (45) $[M-CO_2]^+$, 375 (50) $[M-C_5H_6NO_2]^+$, 359 (20) $[M-C_5H_{11}NO_2]^+$, 338 (9), 292 (5) $[M-C_{15}H_{15}]^+$, 248 (7) $[C_{18}H_{18}N]^+$, 209 (14) $[C_{16}H_{17}]^+$, 180 $[C_{14}H_{12}]^+$, 151 $[C_{12}H_7]^+$, 123 (55), 104 (100) $[C_8H_8]^+$.

HRMS (ESI): calc. for $C_{40}H_{42}NO$ $[M+H]^+$: 552.3261; found: 552.3259.

Chiral HPLC: t_{R1} = 3.7 min, t_{R2} = 15.1 min, [Daicel, Chiralpak AS-RH, 150 x 4,6 mm, 5 µm, 80% MeCN/H_2O (0 min) → 100% MeCN (30min), 1 mL/min, 215 nm].

Specific Rotation: $[\alpha]_D^{25}$ = −218 (c = 1.05, $CHCl_3$) [98.5% *ee*].

(*S*)-1-Benzyl-N-methoxy-N-methylpyrrolidine-2-carboxamide (83)



$C_{14}H_{20}N_2O_2$
MW = 248.33 g/mol

6.84 mL Trimethylaluminum (5.13 g, 13.7 mmol, 3.00 equiv.) were added dropwise to a solution of 1.33 g *N*-*O*-dimethylhydroxylamine hydrochloride (13.7 mmol, 3.00 equiv.) in 35 mL dichloromethane at 0 °C. The solution was stirred for ten minutes and warmed to room temperature over 20 minutes. 1.00 g Methyl benzylpyrrolidin carboxylate **62** (4.56 mmol, 1.00 equiv.) were added and the reaction mixture was stirred for five hours. Diethyl ether (30 mL) and saturated potassium sodium tartrate solution (40 mL) were added and the mixture was stirred for two hours and left standing for 24 hours. The aqueous layer was extracted with ethyl acetate (3 × 30 mL) and the combined organic layers were washed with brine, dried over sodium sulfate, filtered, and the solvent was removed in vacuo. After column chromatography (silica, EtOAc/CH_3OH = 19/1) 1.07 g weinreb amide **83** (4.31 mmol, 95%) were obtained as a yellow oil.

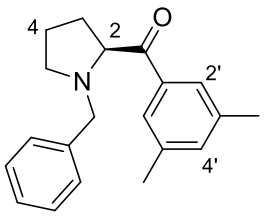
TLC: R_f = 0.40 (EtOAc/CH_3OH = 9/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ [ppm] = 1.74 - 1.98 (m, 3 H, H-3, H-4), 2.14 (dddd, ^2J = 11.7 Hz, ^3J = 8.9 Hz, ^3J = 8.4 Hz, ^3J = 5.58 Hz, 1 H, H-3), 2.44 (*virt.* q, $^2J \approx {}^3J \approx {}^3J$ = 8.5 Hz, 1 H, H-5), 2.3.09 (*virt.* td, $^2J \approx {}^3J$ = 8.3 Hz, ^3J = 3.2 Hz, 1 H, H-5), 3.16 (s, 3 H, NCH_3), 3.56 (d, 2.44 (d, ^2J = 12.8 Hz, 1 H, C*H*HPh), 3.56 - 3.57 (m, 3 H, OCH_3), 3.93 (d, 1 H, ^2J = 12.8 Hz, 1 H, CH*H*Ph), 7.20 - 7.25 (m, 1 H, $H_{p\text{-Ph}}$), 7.27 - 7.37 (m, 4 H, H_{Ph}).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 23.1 (t, C-4), 29.2 (t, C-3), 53.0 (t, C-5), 58.1 (t, *C*H_2Ph), 61.3 (q, OCH_3), 62.1 (d, C-2), 127.1 (d, $C_{p\text{-Ph}}$), 128.2 (d, 2 × $C_{m\text{-Ph}}$), 129.5 (d, 2 × $C_{o\text{-Ph}}$), 138.7 (s, $C_{i\text{-Ph}}$), 175.2 (s, NCO).

The analytical data obtained matched those reported in the literature.[108]

(*S*)-(1-Benzylpyrrolidin-2-yl)(3,5-dimethylphenyl)methanone (84)



$C_{20}H_{23}NO$
MW = 293.41 g/mol

Following GP8, 500 mg methyl benzylpyrrolidine carboxamide **83** (2.01 mmol, 1.00 equiv.) were converted with 70.0 mg magnesium (2.85 mmol, 1.40 equiv.), 387 µL 1-bromo-3,5-dimethylbenzene (527 mg, 2.85 mmol, 1.40 equiv.) and 2.55 mg iodine (20.1 µmol, 0.01 equiv.) in 24 hours. After purification by column chromatography (silica, CH_2Cl_2/CH_3OH = 49/1) 470 mg ketone **84** (1.60 µmol, 80%) were obtained as an orange oil.

TLC: R_f = 0.22 (CH_2Cl_2/CH_3OH = 19/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3029 (w, $C_{sp2}H$), 2920 (w, $C_{sp3}H$), 1684 (m, C=O), 1602 (m, C=C), 1495 (m, C=C), 1454 (m, $C_{sp3}H$), 1292 (m), 1160 (m), 1129 (m), 1067 (m), 857 (m, $C_{sp2}H$), 749 (s, $C_{sp2}H$), 698 (s, $C_{sp2}H$).

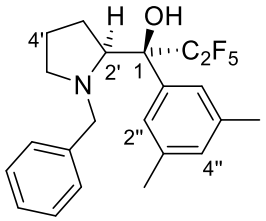
^{1}H NMR (400 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.78 - 1.99 (m, 3 H, H-3, H-4), 2.20 - 2.31 (m, 1 H, H-3), 2.36 [d, ^4J = 0.6 Hz, 6 H, (C-3')CH_3, (C-5')CH_3], 2.41 - 2.49 (m, 1 H, H-5), 3.09 - 3.18 (m, 1 H, H-5), 3.45 (d ^2J = 12.7 Hz, 1 H, C*H*HPh), 3.97 (d, ^2J = 12.7 Hz, 1 H, CH*H*Ph), 4.00 - 4.05 (m, 1 H, H-2), 7.18 - 7.20 (m, 1 H, H-4'), 7.19 - 7.31 (m, 5 H, H_{Ph}), 7.58 - 7.61 (m, 2 H, H-2', H-6').

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 21.4 (t, C-4), 30.1 (t, C-3), 53.2 (C-5), 58.5 (t, *C*H_2Ph), 68.5 (d, C-2), 126.4 (d, C-C-2', C-3'), 127.2 (d, $C_{p\text{-Ph}}$), 128.3 (d, 2 × $C_{m\text{-Ph}}$), 129.6 (d, 2 × $C_{o\text{-Ph}}$), 134.8 (d, C-4'), 136.5 (s, C-1'), 138.2 (s, C-C-3', C-5'), 138.4 (s, $C_{i\text{-Ph}}$), 200.9 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 175 (23) $[M-C_8H_6O]^+$, 160 (15) $[M-C_9H_9O]^+$, 150 (29) $[M-C_{10}H_7O]^+$, 133 (33) $[M-C_{11}H_{15}N]^+$, 105 (100) $[C_8H_9]^+$, 91 (45) $[C7H_7]^+$, 77 (65) $[C_6H_5]^+$, 51 (20) $[C_4H_4]^+$.

HRMS (EI, 70 eV): calc. for $C_{20}H_{24}NO$ $[M+H]^+$: 294.1852; found: 294.1852.

1-((S)-1-Benzylpyrrolidin-2-yl)-1-(3,5-dimethylphenyl)-2,2,3,3,3-pentafluoropropan-1-ol (85)



$C_{22}H_{24}F_5NO$
MW = 413.43 g/mol

200 µL *n*-Butyllithium (2.5 M in hexane, 562 mmol, 1.10 equiv.) in 1.0 mL diethyl ether were degassed by argon bubbling over the course of ten minutes at −78 °C. The argon atmosphere was substituted by a pentafluoroethane atmosphere (1 atm.) and the solution was stirred for one hour. A solution of 150 mg ketone **84** (511 µmol, 1.00 equiv.) in 1.0 mL diethyl ether was added dropwise and the reaction mixture was slowly warmed to room temperature over the course of 24 hours. Saturated ammonium chloride solution (10 mL) was added and the aqueous layer was extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with brine, dried over sodium sulfate, filtered, and the solvent was removed in vacuo. After column chromatography (silica, P/EtOAc = 49/1) 77.6 mg prolinol **85** (185 µmol, 36%) were obtained as a yellow oil.

TLC: R_f = 0.86 (P/EtOAc = 49/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2963 (w, $C_{sp3}H$), 1684 (m, C=C), 1607 (m, C=C), 1454 (m, $C_{sp3}H$), 1335 (m), 1215 (s, CF), 1183 (s, CF), 1125 (s, CF), 1069 (m), 817 (m, $C_{sp2}H$), 730 (s, $C_{sp3}H$).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.22 - 1.32 (m, 1 H, H-4), 1.50 - 1.58 (m, 3 H, H-3, H-4), 1.60 - 1.70 (m, 1 H, H-3), 2.35 (s, 6 H, 2 × CH_3), 2.65 (dt, ^2J = 10.9 Hz, ^3J = 6.3 Hz, 1 H, H-5), 2.85 (dt, ^2J = 10.9 Hz, ^3J = 6.3 Hz, 1 H, H-5), 3.68 (d, ^2J = 13.3 Hz, 1 H, HC*H*HPh), 3.93 (ddd, ^3J = 8.1 Hz, ^3J = 5.9 Hz, ^4J = 1.7 Hz, 1 H, H-2), 4.30 (d, ^2J = 13.3 Hz, 1 H, HC*H*HPh), 6.98 (d, ^4J = 1.8 Hz, 1 H, H-4'), 7.15 (s, 2 H, H-2'. H-6'), 7.29 - 7.33 (m, 1 H, $H_{p\text{-}Ph}$), 7.35 - 7.43 (m, 4 H, H_{Ph}).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 21.5 (q, 2 × CH_3), 24.3 (t, C-4), 30.8 (t, C-3), 55.3 (t, C-5), 60.8 (d, $^3J_{CF}$ = 6.0 Hz, C-2), 68.0 (t, *C*H_2Ph), 76.1 (d, $^2J_{CF}$ = 21.3 Hz, COH), 115.8

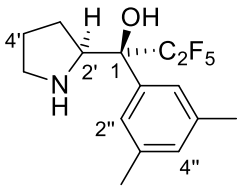
(tq, $^{1}J_{CF}$ = 267.1 Hz, $^{2}J_{CF}$ = 33.4 Hz, C*F*$_2$CF$_3$), 120.3 (qt, $^{1}J_{CF}$ = 289.8 Hz, $^{2}J_{CF}$ = 36.9 Hz, CF$_2$C*F*$_3$), 124.1 (d, C-6'), 124.1 (d, C-2'), 127.3 (d, C$_{p\text{-Ph}}$), 128.6 (d, C$_{o\text{-Ph}}$), 128.6 (d, C$_{m\text{-Ph}}$), 129.7 (d, C-4'), 136.8 (s, C-5'), 136.8 (s, C-3'), 137.5 (s, C-1'), 139.7 (s, C$_{i\text{-Ph}}$).

^{19}F NMR (376 MHz, $CDCl_3$, 300 K): δ [ppm] = −78.7 (s, CF$_2$C*F*$_3$), −118.7 (d, ^{2}J = 269.4 Hz, 1 F, C*F*FCF$_3$), −120.8 (d, ^{2}J = 269.4 Hz, 1 F, CF*F*CF$_3$).

MS (EI, 70 eV): *m/z* (%) = 321 (23) [M−C$_7$H$_8$]$^+$, 202 (33) [M−C$_9$H$_8$F$_5$]$^+$, 160 (100) [M−C$_{11}$H$_{10}$F$_5$O]$^+$, 105 (88) [C$_8$H$_9$]$^+$, 91 (73) [C$_7$H$_7$]$^+$, 77 (44) [C$_6$H$_5$]$^+$, 51 (10) [M−C$_4$H$_4$]$^+$.

HRMS (EI, 70 eV): calc. for C$_{15}$H$_{16}$NOF$_5$ [M−C$_7$H$_8$]$^+$: 321.1147; found: 321.1148.

1-(3,5-Dimethylphenyl)-2,2,3,3,3-pentafluoro-1-((S)-pyrrolidin-2-yl)propan-1-ol (82)



C$_{15}$H$_{18}$F$_5$NO
MW = 323.31 g/mol

Following GP9, 40.0 mg diarylprolinol **85** (95.4 µmol, 1.00 equiv.) were hydrogenolysed in the presence of 4.0 mg palladium on charcoal (10 wt% palladium) under hydrogen atmosphere (1 atm) in methanol and ethyl acetate (v/v = 1/1) in 24 hours. After purification by column chromatography (silica, P/EtOAc = 9/1) 28.4 mg prolinol **82** (87.8 µmol, 92%) were obtained as a colorless solid.

Mp: 49 - 52 °C.

TLC: R_f = 0.11 (P/EtOAc = 9/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3379 (w, NH), 2952 (m, C$_{sp3}$H), 1607 (m, C=C), 1449 (m, C$_{sp3}$H), 1338 (m), 1215 (vs, CF), 1168 (vs, CF), 1127 (vs, CF), 1070 (s), 848 (m, C$_{sp2}$H), 800 (m), 733 (vs, C$_{sp3}$H).

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ [ppm] = 1.05 - 1.15 (m, 1 H, H-3), 1.38 - 1.47 (m, 1 H, H-3), 1.51 - 1.67 (m, 2 H, H-4), 3.00 - 3.15 (m, 2 H, H-5), 4.09 (ddd, ^{3}J = 8.8 Hz, ^{3}J = 7.3 Hz, ^{4}J = 1.5 Hz, 1 H, H-2), 6.90 - 6.96 (s, 1H, H-4'), 7.11 (*br* s, 2 H, H-2', H-6').

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 21.6 (q, 2 × CH_3), 25.0 (t, C-4), 28.6 (t, C-3), 472. (t, C-5), 60.7 (d, C-2), 74.9 (t, COH), 76.1 (d, $^{2}J_{CF}$ = 21.3 Hz, COH), 115.9 (tq, $^{1}J_{CF}$ = 264.7 Hz, $^{2}J_{CF}$ = 34.3 Hz, C*F*$_2$CF$_3$), 119.0 (qt, $^{1}J_{CF}$ = 288.6 Hz, $^{2}J_{CF}$ = 36.2 Hz, CF$_2$C*F*$_3$), 124.2 (d, C-4'), 129.7 (d, C-2'. C-6'), 137.1 (d, $^{3}J_{CF}$ = 5.5 Hz, C-1'), 137.3 (s, C-3', C-5').

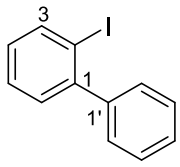
^{19}F NMR (376 MHz, $CDCl_3$, 300 K): δ [ppm] = −78.7 (s, CF$_2$C*F*$_3$), −118.9 (d, ^{2}J = 271.8 Hz, 1 F, C*F*FCF$_3$), −120.8 (d, ^{2}J = 271.8 Hz, 1 F, CF*F*CF$_3$).

HRMS (ESI): calc. for $C_{15}H_{19}F_5NO$ $[M+H]^+$: 324.1382; found: 324.1381.

Specific Rotation: $[\alpha]_D^{25}$ = 2.77 (c = 2.17, $CHCl_3$).

Synthesis of Boronic Acids and Boroxins

2-Iodo-1,1'-biphenyl (88)



$C_{12}H_9I$
MW = 280.11 g/mol

2.00 g 2-Aminobiphenyl (**87**, 11.8 mmol, 1.00 equiv.) were suspended in 14.4 mL hydrochloric acid (2.0 M, 28.0 mmol, 2.37 equiv.) and cooled to 0 °C. A solution of 978 mg sodium nitrite (14.2 mmol, 1.20 equiv.) in 3 mL water was added and the reaction mixture was stirred for 45 minutes. A solution of 3.90 g potassium iodide (23.6 mmol, 2.00 equiv.) in 3 mL water was added and the reaction mixture was stirred over night at room temperature. The mixture was extracted with diethyl ether (4 × 20 mL) and the combined organic layers were washed with 3 M hydrochloric acid (20 mL), saturated sodium bicarbonate solution (20 mL), brine, dried over magnesium sulfate, filtered, and the solvent was removed in vacuo. After purification by column chromatography (silica, P = 100%) 2.95 g iodobiphenyl **88** (10.5 mmol, 89%) were obtained as a pale purple oil.

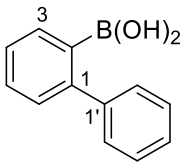
TLC: R_f = 0.77 (P = 100%) [UV].

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ [ppm] = 7.01 - (m, 1 H, H-4), 7.28 - 7.36 (m, 3 H, H-6, H-2', H-6'), 7.37 - 7.47 (m, 4 H, H-5, H-3', H-4', H-5'), 7.96 (dd, ^3J = 7.9 Hz, ^4J = 1.2 Hz, 1 H, H-3).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 98.8 (s, C-2), 127.8 (d, C-4'), 128.1 (d, C-3', C-5'), 128.3 (d, C-5), 128.9 (d, C-4), 129.4 (d, C-2', C-6'), 130.2 (d, C-6), 139.6 (d, C-3), 144.3 (s, C-1'), 146.7 (s, C-1).

The analytical data obtained matched those reported in the literature.[70]

[1,1'-biphenyl]-2-ylboronic acid (86)



$C_{12}H_{11}BO_2$
MW = 198.03 g/mol

According to a modified literature procedure[69, 109][69, 109][69, 106][69, 106][69, 106][69, 105][67, 103][67, 103][69, 109]: 3.34 mL *n*-Butyllithium solution (2.5 M in hexane, 8.57 mmol, 1.50 equiv.) were added dropwise to a solution of 1.60 g iodobiphenyl **88** (5.71 mmol, 1.00 equiv.) in 20 mL tetrahydrofuran at −78 °C and the reaction mixture was stirred for one hour. 2.65 mL triisopropyl borate (2.16 g, 11.4 mmol, 2.00 equiv.) were added, the reaction was mixture warmed to room temperature and stirred for three hours. After cooling to 0 °C, 1 M hydrochloric acid (30 mL) was added and stirring was continued for two hours. Diethyl ether (30 mL) was added and the aqueous layer extracted with diethyl ether (3 × 30 mL). The combined organic layers were washed with brine, dried over sodium sulfate, filtered, and the solvent was removed in vacuo. After column chromatography (silica, P/EtOAc = 4/1) and recrystallization from water/acetonitrile (v/v = 1/1) 470 mg boronic acid **86** (2.37 mmol, 42%) were obtained as a colorless solid.

Mp: 165 °C.

TLC: R_f = 0.02 (P/EtOAc = 9/1) [UV, $KMnO_4$].

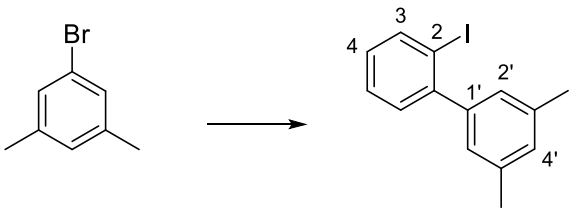
^{1}H NMR (500 MHz, DMSO-d_6, 298 K): δ [ppm] = 7.29 - 7.34 (m, 2 H, H_{Ar}), 7.36 (dd, ^3J = 7.8 Hz, ^4J = 1.5 Hz, 1 H, H_{Ar}), 7.37 - 7.43 (m, 3 H, H_{Ar}), 7.43 - 7.47 (m, 3 H, H_{Ar}), 7.96 [s, 2 H, $B(OH)_2$].

^{13}C NMR (126 MHz, DMSO-d_6, 300 K): δ [ppm] = 126.0 (d, C-4), 126.8 (d, C-3), 128.2 (d, C-6), 128.2 (d, C-2', C-6'), 128.2 (d, C-3', C-5'), 128.3 (d, C-5), 132.2 (d, C-3), 137.6 (s, C-2), 143.2 (s, C-1), 144.1 (s, C1').

^{11}B NMR (300 MHz, $CDCl_3$, 300 K): δ [ppm] = 30.0 [s, $B(OH)_2$].

The analytical data obtained matched those reported in the literature.[110]

2-Iodo-3',5'-dimethyl-1,1'-biphenyl (91)



$C_{14}H_{13}I$
MW = 308.16 g/mol

According to a modified literature procedure[69]: To a suspension of 1.06 g activated magnesium (44.2 mmol, 4.20 equiv.) and 46.7 mg iodine (184 µmol, 0.01 equiv.) in 20 mL tetrahydrofuran was added dropwise a small amount of 1-bromo-3,5-dimethylbenzene (0.05 equiv.) at 40 °C and the resulting yellow reaction mixture was stirred at until the formation of the Grignard reagent initiated, indicated by a change to a brownish or greyish color. Immediately, the remainder of 2.50 mL 1-bromo-3,5-dimethylbenzene (3.40 g, 18.4 mmol 1.00 equiv.) in 20 mL tetrahydrofuran was added dropwise and the reaction mixture was heated under reflux for one hour. 2.40 mL 2-bromochlorobenzene (**90**, 3.94 g, 20.2 mmol, 1.10 equiv.) were added dropwise over a course of 40 minutes and the mixture was subsequently heated under reflux for one hour. The mixture was cooled to room temperature and 5.11 g iodine (20.2 mmol, 1.10 equiv.) in 15 mL tetrahydrofuran were added dropwise and the reaction mixture stirred for 15 minutes at room temperature. The reaction was terminated by the addition of methanol until no further formation of precipitate was observed, the suspension was filtered and 50 mL diethyl ether added. The solution was washed with saturated sodium thiosulfate solution (100 mL) and the aqueous phase extracted with diethyl ether (2 × 50 mL). The combined organic layers were washed with brine and the aqueous phase was back-extracted with diethyl ether (70 mL). The combined organic layers were dried over

sodium sulfate, filtered, and the solvent was removed in vacuo. After column chromatography (silica, P = 100%) 3.50 g iodobiphenyl **91** (41.4 mmol, 62%) were obtained as a colourless oil.

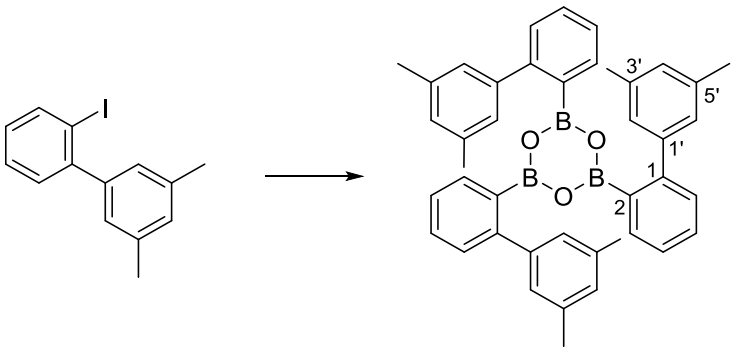
TLC: R_f = 0.40 (P = 100%) [UV, CAM].

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ [ppm] = 2.38 (s, 2 × CH_3), 6.96 (s, 2 H, H-2', H-6'), 7.05 - 6.98 (m, 2 H, H-4, H-5), 7.29 (dd, ^3J = 7.5 Hz, ^4J = 1.2 Hz, 1 H, H-4'), 7.37 (td, ^3J = 7.5 Hz, ^4J = 1.2 Hz, 1 H, H-6), 7.94 (dd, ^3J = 7.9 Hz, ^4J = 1.2 Hz, 1 H, H-3).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 21.5 (q, 2 × CH_3), 98.8 (s, C-2), 127.2 (d, C-2', C-6'), 128.2 (d, C-5), 128.7 (d, C-6), 129.3 (d, C-4), 130.2 (d, C-4'), 137.5 (s, C-3', C-5'), 139.5 (d, C-3), 144.2 (s, C-1'), 147.0 (s, C-1).

The analytical data obtained matched those reported in the literature. [69]

2,4,6-Tris(3',5'-dimethyl-[1,1'-biphenyl]-2-yl)-1,3,5,2,4,6-trioxatriborinane (89)



According to a modified literature procedure[69]: To a solution of 1.51 g iodobiphenyl **91** (4.88 mmol, 1.00 equiv.) in 20 mL tetrahydrofuran were added dropwise 2.34 mL *n*-butyllithium solution (2.5 M in hexane, 5.68 mmol, 1.20 equiv.) at −78 °C and the reaction mixture was stirred for one hour. 2.25 mL triisopropyl borate (1.83 g, 9.77 mmol, 2.00 equiv.)

were added, the reaction was mixture warmed to room temperature and stirred for three hours. After cooling to 0 °C, 30 mL 1 M hydrochloric acid were added and stirring was continued for two hours. 30 mL Diethyl ether were added and the aqueous phase extracted with diethyl ether (3 × 30 mL). The combined organic layers were washed with brine, dried over sodium sulfate, filtered, and the solvent was removed in vacuo. After column chromatography (silica, P/EtOAc = 9/1) and recrystallization from *n*-hexane 470 mg trioxatriborinane **89** (753 μmol, 46%) were obtained as a colorless solid.

Mp: 138 °C.

TLC: R_f = 0.10 (P/EtOAc = 9/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ [ppm] = 2.33 (s, 6 × CH_3), 6.78 (dd, ^3J = 7.5 Hz, ^4J = 1.5 Hz, 1 H, H-6), 6.96 (s, 2 H, H-2', H-6'), 7.06 (s, 1 H, H-4'), 7.12 (td, ^3J = 7.5 Hz, ^4J = 1.2 Hz, 1 H, H-5), 7.26 [m (*overlaps with peak of NMR solvent*), 1 H, H-3], 7.43 (td, ^3J = 7.5 Hz, ^4J = 1.5 Hz, 1 H, H-4).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 21.5 (q, 6 × CH_3), 125.9 (d, C-5), 127.1 (d, C-2', C-6'), 128.4 (d, C-4'), 129.8 (d, C-3), 131.4 (d, C-4), 137.4 (s, C-3', C-5'), 137.4 (d, C-6), 144.3 (s, C-1'), 150.4 (s, C-1).

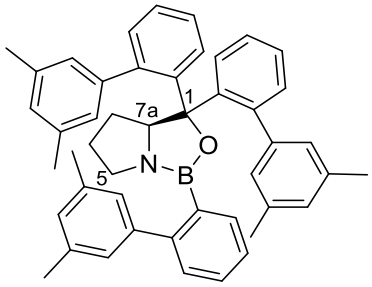
(The C-2 carbon signal is not visible due to its low intensity resulting from C-B coupling.)

^{11}B NMR (128 MHz, $CDCl_3$, 300 K): δ [ppm] = 29.7 [s, OBO].

The analytical data obtained matched those reported in the literature.[69]

Synthesis of Activated Oxazaborolidinium Complexes

(*S*)-1,3,3-Tris(3',5'-dimethyl-[1,1'-biphenyl]-2-yl)tetrahydro-1*H*,3*H*-pyrrolo[1,2-*c*][1,3,2]oxazaborole (92)



$C_{47}H_{46}BNO$
MW = 651.70 g/mol

According to a modified literature procedure (17):In a 25 mL Schlenk flask equipped with a *Dean-Stark* apparatus 11.5 mg of prolinol **78** (25.0 µmol, 1.00 equiv.) and 5.2 mg trioxatriborinane **89** (8.33 µmol, 0.33 equiv.) were dissolved in toluene and heated under reflux. After four and eight hours, the majority of toluene was carefully distilled off and fresh toluene was added. After 16 hours toluene was distilled off under an argon flow and the remainder of toluene removed in vacuo over night.

The oxazaborolidine should be freshly prepared for every enantioselective reaction to ensure reproducibility of the results.

Mp: 112 °C.

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2917 (w, $C_{sp3}H$), 1601 (m, C=C), 1441 (m, $C_{sp3}H$), 1376 (m, $C_{sp3}H$), 1092 (w), 1036 (w), 850 (m, $C_{sp2}H$), 756 (vs, $C_{sp2}H$), 710 (m).

^{1}H NMR (500 MHz, C_6D_6, 300 K): δ [ppm] = 0.96 - 1.06 (m, 1 H, H-7), 1.36 - 1.48 (m, 3 H, H-6, H-6, H-7), 2.61 - 2.69 (m, 1 H, H-5), 3.19 - 3.26 (m, 1 H, H-5), 4.01 (dd, ^3J = 10.4 Hz, ^3J = 4.6 Hz, 1 H, H-7a), 6.36 - 6.42 (m, 1 H, H_{Ar}), 6.81 (s, 1 H, H_{Ar}), 6.84 (s, 1 H, H_{Ar}), 6.89 - 6.92 (m, 1 H, 1 H, H_{Ar}), 6.96 (d, ^3J = 2.2 Hz, 1 H, H_{Ar}), 7.02 - 7.07 (m, 2 H, H_{Ar}), 7.12 (d, ^3J = 2.2 Hz, 2 H, H_{Ar}), 7.14 (d, ^3J = 2.2 Hz, 2 H, H_{Ar}), 7.22 - 7.25 (m, 3 H, H_{Ar}), 7.26 - 7.28 (m, 3 H, H_{Ar}), 7.38 (*virt.* td, $^3J \cong {}^3J$ = 7.6 Hz, ^4J = 1.5 Hz, 1 H, H_{Ar}), 7.44 (dd, ^3J = 8.1 Hz, ^3J = 1.3 Hz, 1 H, H_{Ar}), 7.54 (dd, ^3J = 7.7 Hz, ^4J = 1.2 Hz, 1 H, H_{Ar}), 7.84 (dd, ^3J = 7.4 Hz, ^4J = 1.4 Hz, 1 H, H_{Ar}).

^{13}C NMR (126 MHz, C_6D_6, 300 K): δ [ppm] = 21.4 (q, 2 × CH_3), 21.5 (q, 4 × CH_3), 24.5 (t, C-6), 30.0 (t, C-7), 44.1 (t, C-5), 69.5 (d, C-7a), 87.2 (s, C-1), 125.4 (d, C_{Ar}), 125.6 (d, C_{Ar}), 125.7 (d, C_{Ar}), 216.5 (d, C_{Ar}), 126.6 (d, C_{Ar}), 126.8 (d, C_{Ar}), 127.1 (d, C_{Ar}), 127.5 (d, C_{Ar}), 127.6 (d, C_{Ar}), 128.4 (d, C_{Ar}), 128.5 (d, C_{Ar}), 128.6 (d, C_{Ar}), 129.2 (d, C_{Ar}), 129.3 (d, C_{Ar}), 129.5 (d, C_{Ar}), 130.8 (d, C_{Ar}), 132.7 (d, C_{Ar}), 134.9 (d, C_{Ar}), 136.1 (s, C_{Ar}), 137.6 (s, C_{Ar}), 137.9 (s, C_{Ar}), 138.8 (s, C_{Ar}), 142.9 (s, C_{Ar}), 143.4 (s, C_{Ar}), 144.3 (s, C_{Ar}), 144.8 (s, C_{Ar}), 148.0 (s, C_{Ar}).

^{11}B NMR (128 MHz, C_6D_6, 300 K): δ [ppm] = 35.3 (s, NBO).

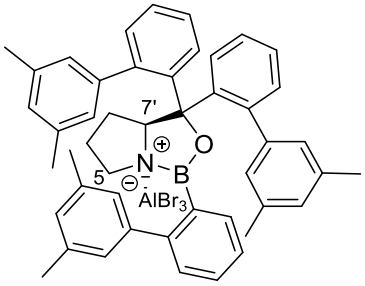
MS (EI, 70 eV): *m/z* (%) = 651 (52) $[M]^+$, 470 (3) $[M-C_{14}H_{13}]^+$, 443 (6) $[M-C_{16}H_{16}]^+$, 374 (100) $[M-C_{18}H_{20}NBO]^+$, 359 (29) $[M-C_{19}H_{23}NBO]^+$, 278 (14) $[C_{18}H_{21}NBO]^+$, 193 (27) $[C_{15}H_{13}]^+$, 179 (13) $[C_{14}H_{11}]^+$, 165 (9) $[C_{13}H_9]^+$.

HRMS (ESI): calc. for $C_{47}H_{47}BNO$ $[M+H]^+$: 652.3745; found: 652.3745.

Specific Rotation: $[\alpha]_D^{25} = -62.8$ (c = 1.50, $CHCl_3$) [98.5% *ee*].

(Note: The sample was measured in an J. Young valve NMR tube under inert gas using dry benzene-d_6.)

Tribromo{(*S*)-1,3,3-tris(3',5'-dimethyl-[1,1'-biphenyl]-2-yl)tetrahydro-1*H*,3*H*-7λ^4-pyrrolo[1,2-*c*][1,3,2]oxazaborol-7-yl}aluminate (93)



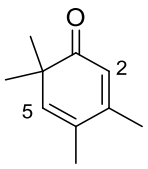
$C_{47}H_{46}AlBBr_3NO$
MW = 918.39 g/mol

To a solution of 16.3 mg oxazaborole **92** (25 µmol, 1.25 equiv.) in 800 µL degassed dichloromethane was added 200 µL of freshly prepared aluminum bromide solution (100 µm in dichloromethane, 4.00 mg, 20.0 µmol, 1.00 equiv.) at room temperature. The solution

[20 mm] was stirred for two minutes and the respective amount needed directly transferred to the vessel of the photoreaction.

3.3.2. Synthesis of Cyclohexadienones

3,4,6,6-Tetramethylcyclohexa-2,4-dien-1-one (55)



$C_{10}H_{14}O$
MW = 150.22 g/mol

Following GP1, 3.34 g 1,2,4,5-tetramethylbenzene (25.0 mmol, 1.00 equiv.) were converted with 2.58 mL hydrogen peroxide (35 wt% in water, 2.92 g, 30.0 mmol, 1.20 equiv.), 18.8 mL trifluoroacetic anhydride (28.4 g, 135 mmol, 5.40 equiv.) and 3.70 mL boron trifluoride diethyl etherate (4.26 g, 30.0 mmol, 1.20 equiv.). After purification by column chromatography (1. silica, P = 100% → Et2O = 100%, 2. silica, P/CH_2Cl_2 = 1/1 → P/Et_2O = 2/1) 1.19 g cyclohexadienone **55** (7.92 mmol, 32%)were obtained as a yellow oil.

TLC: R_f = 0.61 (P/Et_2O = 4/1) [UV, CAM].

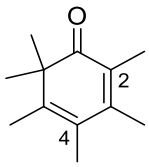
^{1}H NMR (300 MHz, $CDCl_3$, 298 K): δ [ppm] = 1.15 [s, 6 H, C-6(CH_3)$_2$], 1.93 [d, ^4J = 1.4 Hz, 3 H, (C-4)CH_3],], 2.06 [d, ^4J = 1.3 Hz, 3 H, (C-3)CH_3], 5.89 - 5.92 (m, 1 H, H-2), 5.95 - 5.99 (m, 1 H, H-5).

^{13}C NMR (75 MHz, $CDCl_3$, 298 K): δ [ppm] = 19.1 [q, (C-4)CH_3], 21.3 [q, (C-3)CH_3], 25.8 [q, C-6(CH_3)$_2$], 46.5 (s, C-6), 123.7 (d, C-2), 123.7 (d, C-4), 144.3 (d, C-5), 155.6 (s, C-3), 206.1 (s, CO).

UV-Vis (Cyclohexane, c = 2.0 mM): λ = 356 (ε = 48.7 cm^{-1} M^{-1}), 302 (ε = 4464 cm^{-1} M^{-1}); (Dichloromethane, c = 2.0 mM): 310 (ε = 5380 cm^{-1} M^{-1}).

The analytical data obtained matched those reported in the literature.[62, 64]

2,3,4,5,6,6-Hexamethylcyclohexa-2,4-dien-1-one (59)



$C_{12}H_{18}O$
MW = 178.28 g/mol

Following GP1, 1.00 g hexamethylbenzene (6.17 mmol, 1.00 equiv.) were converted with 427 µL hydrogen peroxide (50 wt% in water, 252 mg, 7.40 mmol, 1.20 equiv.), 3.01 mL trifluoroacetic anhydride (4.54 g, 21.6 mmol, 3.50 equiv.) and 913 µL boron trifluoride diethyl etherate (1.05 g, 7.40 mmol, 1.20 equiv.). After purification by column chromatography (silica, P $\rightarrow$ Et_2O = 19/1 $\rightarrow$ 9/1) 830 mg cyclohexadienone **59** (466 mmol, 75%) were obtained as a yellow oil.

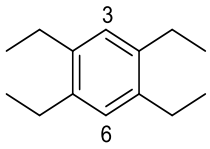
TLC: R_f = 0.17 (P/Et_2O = 19/1) [UV, CAM].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.18 [s, 6 H, C-6(CH_3)$_2$], 1.87 [s, 3 H, (C-4)CH_3], 1.90 [s, 6 H, C-3(CH_3), C-5(CH_3)], 2.06 [s, 3 H, (C-3)CH_3].

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 11.7 [q, (C-2)*C*H_3], 15.8 [q, (C-5)*C*H_3], 18.4 [q, (C-3)*C*H_3], 25.2 [q, C-6(*C*H_3)$_2$], 46.0 (s, C-6), 124.4 (s, C-2), 126.6 (s, C-4), 145.6 (s, C-5), 150.4 (s, C-3), 205.4 (s, CO).

The analytical data obtained matched those reported in the literature.[61, 111]

1,2,4,5-Tetraethylbenzol (138)



$C_{14}H_{22}$
MW = 190.33 g/mol

4.00 g 1,2,4,5-Tetrabromobenzene (10.2 mmol, 1.00 equiv.) were added to a suspension of 114 mg palladium(II) acetate (508 µmol, 5.00 mol%), 318 mg 2-dicyclohexylphophino-2',6'-diisopropoxybiphenyl (681 µmol, 6.68 mol%) and 18.7 g tripotassium phosphate hydrate (81.3 mmol, 8.00 equiv.) in 80 mL degassed toluene and 8.0 mL degassed water. After the dropwise addition of 20.3 mL triethylborane (1.0 M in hexane, 20.3 mmol, 2.00 equiv.) the reaction mixture was heated at 100 °C for 48 hours. The mixture was cooled to room temperature and water (50 mL) was added. The aqueous layer was extracted with ethyl acetate (3 × 50 mL) and the combined organic layers were washed with brine, dried over sodium sulfate and the solvent was removed in vacuo. After purification by column chromatography (silica, P = 100%) 1.88 g tetraethylbenzene **138** (9.87 mmol, 97%) were obtained as a colourless oil.

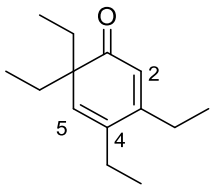
TLC: R_f = 0.67 (P = 100%) [UV].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.22 (td, ^3J = 7.6 Hz, ^5J = 1.5 Hz, 12 H, 4 × CH_2CH_3), 2.62 (qd, ^3J = 7.6 Hz, ^4J = 1.4 Hz, 8 H, 4 × CH_2CH_3), 6.97 (*br* s, 2 H, H-3, H-6).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 15.6 (q, 4 × CH_2CH_3), 25.3 (t, 4 × CH_2CH_3), 128.5 (s, C-1, C-2, C-4, C-5), 139.2 (d, C-3, C-6).

The analytical data obtained matched those reported in the literature.[112-113]

3,4,6,6-Tetraethylcyclohexa-2,4-dien-1-one (140)



$C_{14}H_{22}O$
MW = 206.33 g/mol

Following GP1, 300 mg tetraethylbenzene **138** (1.58 mmol, 1.00 equiv.) were converted with 110 µL hydrogen peroxide (50 wt% in water, 66.0 mg, 1.94 mmol, 1.23 equiv.), 803 µL trifluoroacetic anhydride (1.21 g, 5.77 mmol, 3.65 equiv.) and 234 µL boron trifluoride diethyl etherate (270 mg, 1.30 mmol, 1.20 equiv.). After purification by column chromatography (silica, P/Et2O = 19/1) 140 mg cyclohexadienone **140** (679 µmol, 43%) were obtained as a yellow oil.

TLC: R_f = 0.38 (P/Et_2O = 9/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2965 (s, $C_{sp3}H$), 2935 (m, $C_{sp3}H$), 2877 (m, $C_{sp3}H$), 1659 (s, C=O), 1637 (s, C=C), 1566 (m), 1378 (w, $C_{sp3}H$), 1249 (m), 1037 (m), 872 (s, $C_{sp2}H$).

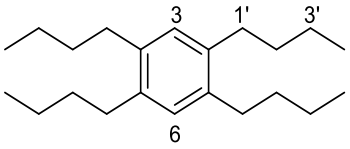
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.64 [t, ^3J = 7.4 Hz, 6 H, C-6(CH_2CH_3)$_2$], 1.15 (t, ^3J = 7.4 Hz, 6 H. (C-3)CH_2CH_3, (C-4)CH_2CH_3], 1.39 - 1.51 [m, 2 H, (C-6)CH_2CH_3], 1.84 - 1.94 (, 2 H, (C-6)CH_2CH_3], 2.34 [qd, ^3J = 7.4 Hz, ^4J = 1.4 Hz, 2 H, (C-3)CH_2CH_3], 2.42 [qd, ^3J = 7.4 Hz, ^4J = 1.4 Hz, 2 H, (C-4)CH_2CH_3], 5.88 - 5.89 (m, 1 H, H-2), 5.91 (m, 1 H, H-5).

^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ [ppm] = 9.1 [q, C-6(CH_2CH_3)$_2$], 12.6 [q, (C-4)CH_2CH_3], 14.2 [q, (C-3)CH_2CH_3], 25.1 [t, (C-3)CH_2CH_3], 27.1 [t, (C-4)CH_2CH_3], 33.9 [t, C-6(CH_2CH_3)$_2$], 56.3 (s, C-6), 123.8 (d, C-5), 137.9 (s, C-4), 140.7 (d, C-2), 161.1 (s, C-3), 206.5 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 206 (100) $[M]^+$, 191 (86) $[M–CH_3]^+$, 177 (77) $[M–C_2H_5]^+$, 149 (50) $[M–C_4H_9]^+$, 135 (57) $[M–C_5H_{11}]^+$, 121 (57) $[M–C_6H_{13}]^+$.

HRMS (EI, 70 eV): calc. for $C_{14}H_{22}O$ $[M]^+$: 206.1665; found: 206.1652.

1,2,4,5-Tetrabutylbenzol (139)



$C_{22}H_{38}$
MW = 302.55 g/mol

1.00 g 1,2,4,5-Tetrabromobenzene (2.54 mmol, 1.00 equiv.) were added to a suspension of 37.3 mg palladium(II) acetate (166 µmol, 6.54 mol%), 120 mg 2-dicyclohexylphophino-2',6'-diisopropoxybiphenyl (681 µmol, 6.68 mol%) and 4.71 g tripotassium phosphate hydrate (20.5 mmol, 8.07 equiv.) in 20 mL degassed toluene and 2.0 mL degassed water. After the dropwise addition of 5.00 mL tributylborane (1.0 M in tetrahydrofuran, 5.00 mmol, 1.97 equiv.) the reaction mixture was heated at 100 °C for 16 hours. The mixture was cooled to room temperature and water (25 mL) was added. The aqueous layer was extracted with ethyl acetate (3 × 50 mL) and the combined organic layers were washed with brine, dried over sodium sulfate and the solvent was removed in vacuo. After purification by column chromatography (silica, P = 100%) 767 mg of a mixture of tetrabutylbenzene **139** and 1,2,4-tributylbenzene (tetra/tri = 94/6, 2.54 mmol, *quant.*) were obtained as a colourless oil.

TLC: R_f = 0.71 (P = 100%) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2955 (s, $C_{sp3}H$), 2928 (s, $C_{sp3}H$), 2860 (m, $C_{sp3}H$), 1465 (m, C=C), 1378 (m), 1340 (w), 1249 (w), 1104 (w), 963 (w), 905 (w), 728 (w).

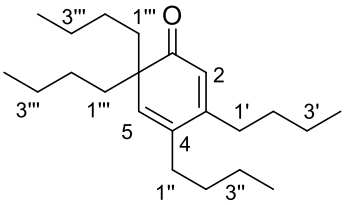
^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.95 (t, ^3J = 7.2 Hz, 12 H, H-4'), 1.34 - 1.47 (m, 8 H, H-3'), 1.50 - 1.61 (m, 8 H, H-2'), 2.50 - 2.64 (m, 8 H, H-1'), 6.90 (s, 2 H, H-3, H-6)..

^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ [ppm] =14.2 (q, C-4'), 23.1 (t, C-3'), 32.2 (t, C-1'), 33.8 (t, C-2'), 130.0 (d, C-3, C-6), 137.8 (s, C-1, C-2, C-4, C-5).

MS (EI, 70 eV): *m/z* (%) = 302 (27) $[M]^+$, 246 (22) $[M–C_4H_8]^+$, 217 (100) $[M–C_6H_{13}]^+$, 203 (31) $[M–C_7H_{15}]^+$, 161 (95) $[M–C_{10}H_{21}]^+$, 105 (23) $[M–C_{14}H_{29}]^+$.

HRMS (EI, 70 eV): calc. for $C_{22}H_{38}$ $[M]^+$: 302.2968; found: 302.2964.

3,4,6,6-Tetrabutylcyclohexa-2,4-dien-1-one (141)



$C_{22}H_{38}O$
MW = 318.55 g/mol

Following GP1, 500 mg tetrabutylbenzene **138** (1.65 mmol, 1.00 equiv.) were converted with 113 µL hydrogen peroxide (50 wt% in water, 67.6 mg, 1.98 mmol, 1.20 equiv.), 804 µL trifluoroacetic anhydride (1.21 g, 5.78 mmol, 3.50 equiv.) and 234 µL boron trifluoride diethyl etherate (270 mg, 1.30 mmol, 1.20 equiv.). After purification by column chromatography (silica, P/Et2O = 19/1) 141 mg cyclohexadienone **140** (443 µmol, 27%) were obtained as a yellow oil.

TLC: R_f = 0.22 (P/Et_2O = 19/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2956 (s, $C_{sp3}H$), 2931 (s, $C_{sp3}H$), 2860 (m, $C_{sp3}H$), 1657 (s, C=O), 1639 (s, C=C), 1561 (m, C=C), 1466 (m), 1379 (m), 1223 (m), 860 (w).

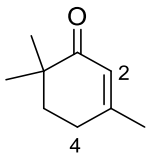
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.79 (t, ^3J = 7.3 Hz, 6 H, H-4’’’), 0.87 - 1.07 (m, 10 H, H-4’, H-4’’, H-2’’’), 1.10–1.22 (m, 4 H, H-3’’’), 1.30 - 1.55 (m, 10 H, H-2’, H-3’, H-2’’, H-3’’, H-1’’’), 1.84 (ddd, ^2J = 12.8 Hz, ^3J = 11.6 Hz, ^3J = 5.4 Hz, 2 H, H-1’’’), 2.24 - 2.31 (m, 2 H, H-1’’), 2.35 (td, ^3J = 7.6 Hz, 1.2 Hz, 2 H, H-1’), 5.89 (s, 1 H, H-2), 5.91 (s, 1 H, H-5).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.0 (q, C-4’’’), 14.1 (q, C-4’’), 14.1 (q, C-4’), 22.6 (t, C-3’’), 22.7 (t, C-3’), 23.3 (t, C-3’’’), 26.8 (t, C-2’’’), 30.9 (t, C-2’), 31.5 (t, C-1’’), 32.2 (t, C-2’’), 33.0 (t, C-1’), 41.3 (t, C-1‘‘‘), 54.9 (s, C-4), 124.7 (s, C-2), 135.3 (s, C-3), 142.6 (s, C-5), 159.9 (s, C-6), 206.7 (s, C-1).

MS (EI, 70 eV): *m/z* (%) =318 (86) $[M]^+$, 275 (90) $[M–C_3H_7]^+$, 261 (62) $[M–C_4H_9]^+$, 219 (99) $[M–C_7H_{15}]^+$, 191 (86) $[M–C_9H_{19}]^+$, 177 (100) $[M–C_{10}H_{21}]^+$, 163 (63) $[M–C_{11}H_{23}]^+$, 149 (69) $[M–C_{12}H_{25}]^+$.

HRMS (EI, 70 eV): calc. for $C_{22}H_{38}O$ $[M]^+$: 318.2917; found: 318.2912.

3,6,6-Trimethylcyclohex-2-en-1-one (143)



$C_9H_{14}O$
MW = 138.21 g/mol

Following GP 2, 2.00 g 4,4-dimethylcyclohex-2-en-1-one (16.1 mmol, 1.00 equiv.) were converted with 11.1 mL methyllithium solution (1.6 M in diethyl ether, 389 mg, 17.7 mmol, 1.10 equiv.) in two hours.

Following GP 4, the resulting tertiary allylic alcohol was converted with 6.70 g pyridinium chlorochromate (31.1 mmol, 1.10 equiv.) in two hours. After work-up 1.91 g cyclohexenone **143** (13.8 mmol, 89%) were obtained as a colourless oil.

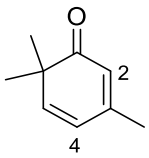
TLC: R_f = 0.42 (P/Et_2O = 4/1) [UV, CAM].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.09 [s, 6 H, C-6(CH_3)$_2$], 1.80 (d, ^3J = 6.1 Hz, 2 H, H-5), 1.93 [d, ^4J = 1.0 Hz, 3 H, (C-3)CH_3], 2.29 (tdd, ^3J = 6.1 Hz, ^4J = 1.6 Hz, ^4J = 1.6 Hz, 2 H, H-4), 5.77 (*virt.* sex, $^4J \cong {}^4J$ = 1.4 Hz, 1 H, H-2).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 24.2 [q, (C-3)*C*H_3], 24.4 [q, C-6(*C*H_3)$_2$], 28.6 (d, C-4), 36.5 (d, C-5), 40.3 (s, C-6), 125.3 (d, C-2), 160.4 (s, C-3), 204.6 (s, CO).

The analytical data obtained matched those reported in the literature.[81]

3,6,6-Trimethylcyclohexa-2,4-dien-1-one (148)



$C_9H_{12}O$
MW = 136.19 g/mol

Following GP 6, 1.91 g cyclohexenone **143** (13.8 mmol, 1.00 equiv.) were converted with 2.46 g *N*-bromosuccinimide (13.8 mmol, 1.00 equiv.) in two hours and the resulting bromide treated with 3.02 g calcium carbonate (60.1 mmol, 4.35 equiv.) for 30 minutes. After purification by column chromatography (silica, $P/Et_2O = 9/1 \rightarrow 4/1$) 1.08 g cyclohexadienone **148** (7.93 mmol, 57%) were obtained as a pale yellow oil.

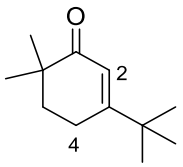
TLC: R_f = 0.34 (P/Et_2O = 4/1) [UV, CAM].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.18 [s, 6 H, C-6(CH_3)$_2$], 2.06 [d, ^4J = 1.4 Hz, 3 H, (C-3)CH_3], 5.87 - 5.90 (m, 1 H, H-2), 6.06 (dd, ^3J = 9.5 Hz, ^4J = 1.4 Hz, 1 H, H-4), 6.27 (d, ^3J = 9.5 Hz, 1 H, H-5).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 22.9 [q, (C-3)*C*H_3], 25.6 [q, C-6(*C*H_3)$_2$], 46.0 (s, C-6), 123.0 (d, C-2), 123.2 (d, C-4), 148.2 (d, C-5), 153.9 (s, C-3), 205.6 (s, CO).

The analytical data obtained matched those reported in the literature.[114]

3-(*tert*-Butyl)-6,6-dimethylcyclohex-2-en-1-one (144)



$C_{12}H_{20}O$
MW = 180.29 g/mol

Following GP 2, 1.00 g 4,4-dimethylcyclohex-2-en-1-one (8.05 mmol, 1.00 equiv.) were converted with 6.36 mL *tert*-butyllithium solution (1.9 M in pentane, 774 mg, 12.1 mmol, 1.50 equiv.) in three hours.

Following GP 4, the resulting tertiary allylic alcohol was converted with 6.94 g pyridinium chlorochromate (32.2 mmol, 4.00 equiv.) in 24 hours. After purification by column chromatography (silica, P/Et_2O = 19/1) 494 mg cyclohexenone **144** (2.74 mmol, 34%) were obtained as a colourless solid.

Mp: 28-29 °C.

TLC: R_f = 0.48 (P/Et_2O = 4/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2966 (s, $C_{sp3}H$), 1669 (vs, C=O), 1621 (s, C=C), 1565 (m), 1472 (m, $C_{sp3}H$), 1364 (m, $C_{sp3}H$), 1222 (m), 1159 (s, $C_{sp3}H$), 883 (w, $C_{sp2}H$).

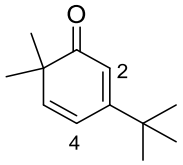
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.09 [s, 6 H, C-6(CH_3)$_2$], 1.12 [s, 9 H, C(CH_3)$_3$], 1.79 (t, ^3J = 6.1 Hz, 2 H, H-5), 2.37 (td, ^3J = 6.1 Hz, ^4J = 1.4 Hz, 2 H, H-4), 5.85 (t, ^2J = 1.4 Hz, 1 H, H-2).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 23.1 (t, C-4), 24.3 [q, C-6(*C*H_3)$_2$], 28.6 [q, C(*C*H_3)$_3$], 36.7 [s, *C*(CH_3)$_3$], 37.0 (t, C-5), 40.4 (s, C-6), 121.7 (d, C-2), 171.6 (s, C-3), 205.7 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 180 (29) $[M]^+$, 152 (3) $[M–C_2H_4]^+$, 137 (5) $[M–C_3H_7]^+$, 124 (100) $[C_8H_{12}O]^+$, 109 (86) $[C_7H_9O]^+$, 95 (54) $[C_6H_7O]^+$, 81 (21) $[C_6H_9]^+$, 67 (12) $[C_5H_7]^+$.

HRMS (EI, 70 eV): calc. for $C_{12}H_{20}O$ $[M]^+$: 180.1509; found: 180.1508.

3-(*tert*-Butyl)-6,6-dimethylcyclohexa-2,4-dien-1-one (149)



$C_{12}H_{18}O$
MW = 178.28 g/mol

Following GP 6, 400 mg cyclohexenone **144** (2.22 mmol, 1.00 equiv.) were converted with 434 mg *N*-bromosuccinimide (2.44 mmol, 1.10 equiv.) in three hours and the resulting bromide treated with 978 mg calcium carbonate (9.77 mmol, 4.40 equiv.) for 30 minutes. After purification by column chromatography (silica, $P/Et_2O = 19/1 \rightarrow 9/1$) 311 mg cyclohexadienone **149** (1.74 mmol, 79%) were obtained as a pale yellow solid.

Mp: 44 °C.

TLC: R_f = 0.21 (P/Et_2O = 9/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2967 (s, $C_{sp3}H$), 1659 (vs, C=O), 1640 (s, C=C), 1565 (m), 1468 (s, $C_{sp3}H$), 1371 (m, $C_{sp3}H$), 1190 (m, $C_{sp3}H$), 873 (m, $C_{sp2}H$), 782 (m).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.18 [s, 9 H, $C(CH_3)_3$], 1.19 [s, 6 H, C-6$(CH_3)_2$], 5.93 - 5.95 (m, 1 H, H-2), 6.25 - 6.31 (m, 2 H, H-4, H-5).

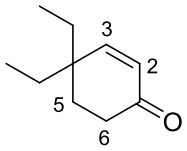
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.7 [q, C-6(CH_3)$_2$], 28.5 [q, C(CH_3)$_3$], 35.5 [s, C(CH_3)$_3$], 45.8 (s, C-6), 119.0 (d, C-2), 119.7 (d, C-4), 147.7 (d, C-5), 164.8 (s, C-3), 206.9 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 178 (79) $[M]^+$, 163 (100) $[M–CH_3]^+$, 135 (83) $[M–C_3H_7]^+$, 119 (32) $[C_8H_7O]^+$, 105 (23) $[C_8H_9]^+$, 91 (37) $[C_7H_7]^+$, 77 (25) $[C_6H_5]^+$.

HRMS (EI, 70 eV): calc. for $C_{12}H_{18}O$ $[M]^+$: 178.1352; found: 178.1352.

calc. for $C_{11}{}^{13}CH_{18}O$ $[M]^+$: 179.1386; found: 179.1390.

4,4-Diethylcyclohex-2-en-1-one (153)



$C_{10}H_{16}O$
MW = 152.24 g/mol

In analogy to a modified literature procedure[115]: 69.3 µL concentrated sulfuric acid (127 mg, 1.30 µmol, 1.30 mol%) were added to 10.0 g 2-ethylbutyraldehyde (100 mmol, 1.00 equiv.) and 5.61 mL methyl vinyl ketone (4.72 g, 67.3 mmol, 0.68 equiv.) and the reaction mixture was heated to 40 °C. After 24 hours, the same amount of methyl vinyl ketone (0.68 equiv.) and concentrated sulfuric acid (1.30 mol%) were added and the reaction mixture was heated for additional 48 hours. The mixture was cooled to room temperature, chloroform (100 mL) was added and the solvent removed in vacuo. After purification by vacuum distillation (11.0 mbar, 110 °C oil bath temperature) 9.93 g cyclohexenone **153** (65.2 mmol, 65%) were obtained as a colourless oil.

Bp: 88 °C (11.0 mbar).

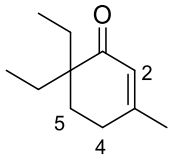
TLC: R_f = 0.38 (P/Et_2O = 4/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.88 (t, ^3J = 7.5 Hz, 2 × CH_2CH_3), 1.43 - 1.58 (m, 4 H, 2 × CH_2CH_3), 1.84 (ddd, ^3J = 7.6 Hz, ^3J = 6.5 Hz, ^4J = 1.0 Hz, 2 H, H-5), 2.43 (dd, ^3J = 7.6 Hz, ^3J = 6.5 Hz, 2 H, H-6), 5.92 (d, ^3J = 10.3 Hz, 1 H, H-2), 6.71 (dd, ^3J = 10.3 Hz, ^4J = 1.0 Hz, 2 H. H-3).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 8.3 (q, 2 × CH_2CH_3), 29.6 (t, 2 × CH_2CH_3), 30.1 (t, C-5), 34.0 (t, C-6), 38.4 (s, C-4), 128.1 (d, C-2), 159.0 (d, C-3), 200.0 (s, C-1).

The analytical data obtained matched those reported in the literature.[84]

6,6-Diethyl-3-methylcyclohex-2-en-1-one (145)



$C_{11}H_{18}O$
MW = 166.26 g/mol

Following GP 2, 2.00 g cyclohexenone **153** (13.1 mmol, 1.00 equiv.) were converted with 6.57 mL methyllithium lithium bromide complex solution (2.2 M in diethyl ether, 1.57 g, 14.5 mmol, 1.10 equiv.) in two hours.

Following GP 4, the resulting tertiary allylic alcohol was converted with 5.66 g pyridinium chlorochromate (26.3 mmol, 2.00 equiv.) in one hour. After purification by column chromatography (silica, P/Et_2O = 9/1) 1.62 g cyclohexenone **145** (9.74 mmol, 74%) were obtained as a colourless oil.

TLC: R_f = 0.37 (P/Et_2O = 4/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2969 (m, $C_{sp3}H$), 2935 (m, $C_{sp3}H$), 1662 (vs, C=O), 1639 (vs, C=C), 1437 (m, $C_{sp3}H$), 1380 (m, $C_{sp3}H$), 1211 (s, $C_{sp3}H$).

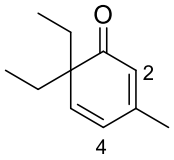
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.79 (t, ^3J = 7.5 Hz, 6 H, 2 × CH_2CH_3), 1.45 - 1.61 (m, 4 H, 2 × CH_2CH_3), 1.84 (t, ^3J = 6.3 Hz, 2 H, H-5), 1.90 [q, ^4J = 1.3 Hz, 3 H, (C-3)CH_3], 2.28 (td, ^3J = 6.3 Hz, ^4J = 1.7 Hz, 2 H, H-4), 5.74 (q, ^4J = 1.3 Hz, 1 H, H-2).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 8.3 (q, 2 × CH_2CH_3), 24.1 [q, (C-3)CH_3], 26.5 (t, 2 × CH_2CH_3), 28.1 (t, C-4), 30.1 (t, C-5), 46.6 (s, C-6), 126.0 (d, C-2), 159.8 (s, C-3), 203.9 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 166 (12) $[M]^+$, 138 (75) $[M–C_2H_4]^+$, 123 (20) $[C_8H_{11}O]^+$, 109 (17) $[C_7H_9O]^+$, 82 (100) $[C_6H_{10}]^+$, 54 (15).

HRMS (EI, 70 eV): calc. for $C_{11}H_{18}O$ $[M]^+$: 166.1352; found: 166.1346.

6,6-Diethyl-3-methylcyclohexa-2,4-dien-1-one (150)



$C_{11}H_{16}O$
MW = 164.25 g/mol

Following GP 6, 500 mg cyclohexenone **145** (3.01 mmol, 1.00 equiv.) were converted with 589 mg *N*-bromosuccinimide (3.31 mmol, 1.10 equiv.) in three hours and the resulting bromide treated with 1.33 g calcium carbonate (13.2 mmol, 4.40 equiv.) for 30 minutes. After purification by column chromatography (silica, $P/Et_2O = 9/1 \rightarrow 4/1$) 216 mg cyclohexadienone **150** (1.32 mmol, 44%) were obtained as a pale yellow oil.

TLC: R_f = 0.67 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2967 (s, $C_{sp3}H$), 1658 (vs, C=O), 1459 (m, $C_{sp3}H$), 1380 (m, $C_{sp3}H$), 1228 (m, $C_{sp3}H$).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.65 (t, ^3J = 7.5 Hz, 6 H, 2 × CH_2CH_3). 1.45 (dq, ^2J = 13.1 Hz, ^3J = 7.5 Hz, 2 H, 2 × $CHHCH_3$), 1.90 (dq, ^2J = 13.1 Hz, ^3J = 7.5 Hz, 2 H, 2 × $CHHCH_3$), 2.07 [d, ^4J = 1.4 Hz, 3 H, (C-3)CH_3], 5.88-5.91 (m, 1 H, H-3), 6.19 (d, ^3J = 9.6 Hz, 1 H, H-5), 6.26 (dd, ^3J = 9.6 Hz, ^4J = 1.4 Hz, 1 H, H-4).

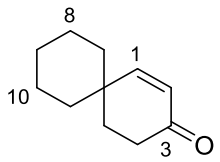
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 9.1 (q, 2 × CH_2CH_3), 23.0 [q, (C-3)CH_3], 33.8 (t, 2 × CH_2CH_3), 55.9 (s, C-6), 125.1 (d, C-2), 126.7 (d, C-5), 146.2 (d, C-4), 154.4 (s, C-3), 206.0 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 164 (100) $[M]^+$, 149 (42) $[M–CH_3]^+$, 135 (89) $[M–C_2H_5]^+$, 121 (91) $[C_8H_9O]^+$, 107 (63) $[C_7H_7O]^+$, 91 (90) $[C_7H_7]^+$, 77 (37) $[C_6H_5]^+$.

HRMS (EI, 70 eV): calc. for $C_{11}H_{16}O$ $[M]^+$: 164.1196; found: 164.1190.

calc. for $C_{10}{}^{13}CH_{16}O$ $[M]^+$: 165.1229; found: 165.1229.

Spiro[5.5]undec-2-en-1-one (154)



$C_{11}H_{16}O$
MW = 164.25 g/mol

According to a modified literature procedure (47): To 5.40 mL cyclohexane carbaldehyde (5.00 g, 44.6 mmol, 1.00 equiv.) and 2.50 mL methyl vinyl ketone (2.10 g, 30.0 mmol, 0.68 equiv.) were added 30.9 µL concentrated sulfuric acid (56.8 mg, 580 µmol, 1.50 mol%) and the reaction mixture was heated to 40 °C. After 24 hours, the same amount of methyl vinyl ketone (0.68 equiv.) and concentrated sulfuric acid (1.50 mol%) were added and the reaction mixture was heated for additional 48 hours. The mixture was cooled to room temperature, chloroform (50 mL) was added and the solvent removed in vacuo. After purification by vacuum distillation (2.0 mbar, 100 °C oil bath temperature) 2.70 g cyclohexenone **154** (16.4 mmol, 37%) were obtained as a colourless oil.

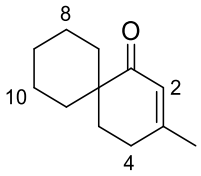
TLC: R_f = 0.38 (P/Et_2O = 4/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.47 - 1.59 (m, 10 H, H-7, H-8, H-9, H-10, H-11), 1.91 (*virt.* t, $^3J \cong {}^3J$ = 6.8 Hz, 2 H, H-5), 2.43 (dd, ^3J = 7.4 Hz, ^3J = 6.2 Hz, 2 H, H-4), 5.88 (d, ^3J = 10.2 Hz, 2 H, H-2), 6.84 (d, ^3J = 10.2 Hz, 2 H, H-1).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 21.8 (t, C-8, C-10), 26.1 (t, C-9), 33.0 (t, C-5), 33.9 (t, C-4), 35.7 (s, C-6), 36.1 (t, C-7, C-11), 127.5 (d, C-2), 159.3 (d, C-1), 200.3 (s, CO).

The analytical data obtained matched those reported in the literature.[116-117]

3-Methylspiro[5.5]undec-2-en-1-one (146)



$C_{12}H_{18}O$
MW = 178.28 g/mol

Following GP 2, 1.00 g spiroundecenone **154** (6.09 mmol, 1.00 equiv.) were converted with 3.04 mL methyllithium lithium bromide complex solution (2.2 M in diethyl ether, 729 mg, 6.70 mmol, 1.10 equiv.) in three hours.

Following GP 4, the resulting tertiary allylic alcohol was converted with 2.63 g pyridinium chlorochromate (12.2 mmol, 2.00 equiv.) in two hours. After purification by column chromatography (silica, P/Et_2O = 9/1) 836 mg cyclohexenone **146** (4.69 mmol, 77%) were obtained as a colourless oil.

TLC: R_f = 0.43 (P/Et_2O = 4/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2921 (s, $C_{sp3}H$), 2857 (m, $C_{sp3}H$), 1654 (vs, C=O), 1445 (m, $C_{sp3}H$), 1380 (m, $C_{sp3}H$), 1211 (m), 1194 (m, $C_{sp3}H$), 855 (w, $C_{sp2}H$).

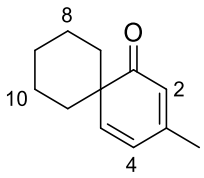
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.27 - 1.36 (m, 1 H, H-9), 1.36 - 1.47 (m, 4 H, H-7, H-8, H-10, H-11), 1.51 - 1.58 (m, 1 H, H-9), 1.58 - 1.64 (m, 2 H, H-8, H-10), 1.69 (ddd, ^2J = 12.8 Hz, ^3J = 11.3 Hz, ^3J = 3.8 Hz, 2 H, H-7, H-11), 1.90 (t, $^3J \cong {}^3J$ = 6.2 Hz, 2 H, H-5), 1.91 (d, ^4J = 1.0 Hz, 3 H, CH_3), 2.26 (td, ^3J = 6.2 Hz, ^4J = 1.7 Hz, 2 H, H-4), 5.75 (*virt.* sex, $^4J \cong {}^4J$ = 1.4 Hz, 1 H, H-2).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 21.8 (t, C-8, C-10), 24.0 (q, CH_3), 26.2 (t, C-9), 28.0 (t, C-4), 30.5 (t, C-5), 31.6 (t, C-7, C-11), 43.3 (s, C-6), 125.7 (d, C-2), 159.6 (s, C-3), 205.0 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 178 (33) $[M]^+$, 163 (4) $[M–CH_3]^+$, 150 (33) $[M–C_2H_4]^+$, 136 (9) $[M–C_3H_6]^+$, 123 (80) $[C_8H_{11}O]^+$, 110 (15) $[C_7H_{10}O]^+$, 95 (10) $[C_6H_7O]^+$, 82 (100) $[C_6H_{10}]^+$.

HRMS (EI, 70 eV): calc. for $C_{12}H_{18}O$ $[M]^+$: 178.1352; found: 178.1353.

3-Methylspiro[5.5]undeca-2,4-dien-1-one (151)



$C_{12}H_{16}O$
MW = 176.26 g/mol

Following GP 6, 500 mg spiroundecenone **146** (2.80 mmol, 1.00 equiv.) were converted with 549 mg *N*-bromosuccinimide (3.09 mmol, 1.10 equiv.) in three hours and the resulting bromide treated with 1.23 g calcium carbonate (12.3 mmol, 4.40 equiv.) for 30 minutes. After purification by column chromatography (silica, $P/Et_2O = 19/1 \rightarrow 9/1$) 255 mg cyclohexadienone **151** (1.45 mmol, 52%) were obtained as a pale yellow solid.

Mp: 57-58 °C.

TLC: R_f = 0.56 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2926 (s, $C_{sp3}H$), 2859 (m, $C_{sp3}H$), 1654 (vs, C=O), 1639 (vs, C=C), 1575 (w), 1452 (m, $C_{sp3}H$), 1322 (m, $C_{sp3}H$), 1194 (m, $C_{sp3}H$), 853 (w, $C_{sp2}H$), 765 (m).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.38 - 1.47 (m, 3 H, H-7, H-9, H-11), 1.49 - 1.60 (m, 2 H, H-8, H-10), 1.67 - 1.83 (m, 5 H, H-7, H-8, H-9, H-10, H-11), 2.06 (d, ^4J = 1.4 Hz, 3 H, CH_3), 5.87 - 5.90 (m, 1 H, H-2), 6.13 (dd, ^3J = 9.8 Hz, ^4J = 1.5 Hz, 1 H, H-4), 6.80 (d, ^3J = 9.8 Hz, 1 H, H-5).

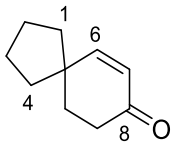
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 21.6 (t, C-8, C-10), 22.7 (q, CH_3), 25.6 (t, C-9), 34.4 (t, C-7, C-11), 49.9 (s, C-6), 123.6 (d, C-2), 123.9 (d, C-4), 144.7 (d, C-5), 152.3 (s, C-3), 205.9 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 176 (100) $[M]^+$, 161 (50) $[M–CH_3]^+$, 147 (37) $[M–C_2H_5]^+$, 134 (70) $[M–C_3H_6]^+$, 121 (82) $[C_8H_9O]^+$, 105 (58) $[C_8H_9]^+$, 91 (82) $[C_7H_7]^+$, 77 (37) $[C_6H_5]^+$.

HRMS (EI, 70 eV): calc. for $C_{12}H_{16}O$ $[M]^+$: 176.1196; found: 176.1194.

calc. for $C_{11}{}^{13}CH_{16}O$ $[M]^+$: 177.1229; found: 177.1235.

Spiro[4.5]dec-6-en-8-one (155)



$C_{10}H_{14}O$
MW = 150.22 g/mol

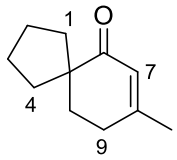
30.7 µL concentrated sulfuric acid (56.5 mg, 0.575 µmol, 1.30 mol%) were added to 4.73 mL cyclopentanecarboxaldehyde (4.35 g, 44.3 mmol, 1.00 equiv.) and 2.49 mL methyl vinyl ketone (2.09 g, 29.8 mmol, 0.68 equiv.) and the reaction mixture was heated to 40 °C. After 24 hours, the same amount of methyl vinyl ketone (0.68 equiv.) and concentrated sulfuric acid (1.30 mol%) were added and the reaction mixture was heated for additional 48 hours. The mixture was cooled to room temperature, chloroform (50 mL) was added and the solvent removed in vacuo. After purification by vacuum distillation (3.4 mbar, 120 °C oil bath temperature) 3.15 g cyclohexenone **155** (21.0 mmol, 47%) were obtained as a colourless oil.**Bp**: 98 °C (3.4 mbar).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.61 - 1.78 (m, 8 H, H-1, H-2, H-3, H-4), 1.90 (virt. t, $^{3}J \cong {}^{3}J$ = 6.7 Hz, 2 H, H-10), 2.43 (dd, ^{3}J = 7.3 Hz, ^{3}J = 6.1 Hz, 2 H, H-9), 5.84 (d, ^{3}J = 10.1 Hz, 1 H, H-7), 6.73 (d, ^{3}J = 10.1 Hz, 1 H, H-6).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 24.7 (t, C-2, C-3), 34.1 (t, C-10), 35.6 (t, C-9), 38.3 (t, C-1, C-4), 44.3 (s, C-5), 126.7 (d, C-7), 159.9 (d, C-6), 200.4 (s, C-8).

The analytical data obtained matched those reported in the literature.[118]

8-Methylspiro[4.5]dec-7-en-6-one (147)



$C_{11}H_{16}O$
MW = 164.25 g/mol

Following GP 2, 2.00 g cyclohexenone **155** (13.3 mmol, 1.00 equiv.) were converted with 6.66 mL methyllithium lithium bromide complex solution (2.2 M in diethyl ether, 1.59 g, 14.7 mmol, 1.10 equiv.) in one hour.

Following GP 4, the resulting tertiary allylic alcohol was converted with 5.74 g pyridinium chlorochromate (26.6 mmol, 2.00 equiv.) in two hours. After purification by column chromatography (silica, P/Et_2O = 9/1) 1.58 g cyclohexenone **147** (9.62 mmol, 72%) were obtained as a colourless oil.

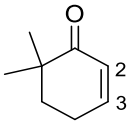
TLC: R_f = 0.40 (P/Et_2O = 4/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.41 (dddd, ^2J = 12.8 Hz, ^3J = 8.4 Hz, ^3J = 5.7 Hz, ^4J = 1.4 Hz, 2 H, H-1, H-4), 1.58 - 1.66 (m, 2 H, H-2, H-3), 1.70 (dddd, ^3J = 8.4 Hz, ^3J = 5.7 Hz, ^4J = 3.2 Hz, ^4J = 1.4 Hz, 2 H, H-2, H-3), 1.87 (t, ^3J = 6.1 Hz, 2 H, H-10), 1.91 (*virt.* q, $^4J \approx {}^4J$ = 1.0 Hz, 3 H, CH_3), 1.94 - 2.00 (m, 2 H, H-1, H-4), 2.26 - 2.30 (m, 2 H, H-9), 5.79 (q, ^3J = 1.4 Hz, 1 H, H-7).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 24.2 (q, CH_3), 25.7 (t, C-2, C-3), 29.3 (t, C-9), 34.8 (t, C-10), 35.0 (t, C-1, C-4), 51.6 (s, C-5), 125.7 (d, C-7), 160.5 (s, C-8), 204.1 (C-6).

HRMS (EI, 70 eV): calc. for $C_{11}H_{16}O$ $[M]^+$: 164.1196; found: 164.1190.

6,6-Dimethylcyclohex-2-en-1-one (158)



$C_8H_{12}O$
MW = 124.18 g/mol

5.41 mL *n*-butyllithium solution (2.50 M in hexane, 865 mg, 13.5 mmol, 1.30 equiv.) were added to a solution of 20.5 mL diisopropylamine (2.95 g, 14.6 mmol, 1.40 equiv.) in 70 mL tetrahydrofuran at 0 °C. The mixture was stirred for 15 minutes and subsequently cooled to – 78 °C. 1.00 g cyclohex-2-ene-1-one (**150)** (10.4 mmol, 1.00 equiv.) were added to the solution over 15 minutes and the resulting orange mixture stirred for 15 minutes at – 78 °C, before 1.26 mL *N,N*-dimethylpropyleneurea (835 mg, 10.4 mmol, 1.00 equiv.) were added. The reaction was stirred for 15 minutes and 1.30 mL iodomethane (2.96 g, 20.8 mmol, 2.00 equiv.) were added and the resulting yellow reaction mixture stirred for 30 minutes at – 78 °C and warmed to room temperature. When full conversion was reached, the reaction mixture was cooled to –78 °C and in a separate flask, the same amount of lithium diisopropylamide (13.5 mmol) in 70 mL tetrahydrofuran was prepared by the same procedure and added to the reaction mixture. After stirring at –78 °C for 30 minutes, additional 1.30 mL iodomethane (2.96 g, 20.8 mmol, 2.00 equiv.) were added and the reaction mixture stirred for one hour at – 78 °C and warmed to room temperature. Saturated ammonium chloride solution (100 mL) was added and the mixture was extracted with diethyl ether (3 × 100 mL) and the combined organic layers were washed with brine, dried over sodium sulfate and the solvent was removed in vacuo. After purification by column chromatography (silica, P/Et_2O = 9/1) 591 mg dimethylcyclohexenone **158** (4.76 mmol, 46%) were obtained as a colourless oil.

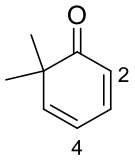
TLC: R_f = 0.41 (P/Et_2O = 4/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.11 (s, 6 H. 2 × CH_3), 1.82 (t, ^3J = 6.1 Hz, 2 H, H-5), 2.37 (tdd, ^3J = 6.1 Hz, ^3J = 4.0 Hz, ^4J = 2.1 Hz, 2 H, H-4), 5.91 (dt, ^3J = 10.1 Hz, ^4J = 2.1 Hz, 1 H, H-2), 6.86 (dt, ^3J = 10.1 Hz, ^3J = 4.0 Hz, 1 H, H-3).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 23.6 (t, C-4), 24.2 (q, 2 × CH_3), 36.3 (t, C-5), 41.6 (s, C-6), 128.4 (d, C-2), 148.8 (d, C-3), 204.9 (s, C-1).

The analytical data obtained matched those reported in the literature.

6,6-Dimethylcyclohexa-2,4-dien-1-one (157)



$C_8H_{10}O$
MW = 122.17 g/mol

Following GP 6, 280 mg cyclohexenone **158** (2.25 mmol, 1.00 equiv.) were converted with 482 mg *N*-bromosuccinimide (2.71 mmol, 1.20 equiv.) in three hours and the resulting bromide treated with 1.13 g calcium carbonate (11.3 mmol, 5.00 equiv.) for 30 minutes. After purification by column chromatography (silica, P/Et_2O = 9/1 → 4/1) 39.0 mg cyclohexadienone **157** (319 µmol, 14%) were obtained as a pale yellow oil.

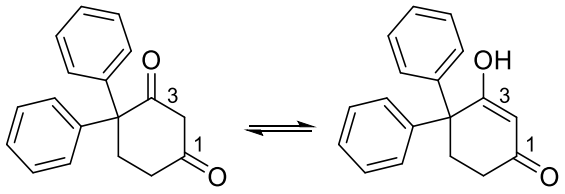
TLC: R_f = 0.30 (P/Et_2O = 4/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.21 (s, 6 H. 2 × CH_3), 6.04 (*virt.* dt, ^3J = 6.1 Hz, $^4J \approx {}^5J$ = 0.9 Hz, 1 H, H-2), 6.16 (ddd, ^3J = 9.4 Hz, ^3J = 5.7 Hz, ^4J = 0.9 Hz, 1 H, H-4), 6.30 (ddd, ^3J = 9.4 Hz, ^3J = 1.9 Hz, ^4J = 0.9 Hz, 1 H, H-5), 7.02 (ddd, ^3J = 9.4 Hz, ^3J = 5.7 Hz, ^4J = 1.9 Hz, 1 H, H-3).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.6 (q, 2 × CH_3), 47.6 (s, C-6), 119.2 (d, C-4), 125.7 (d, C-2), 141.7 (d, C-3), 149.1 (d, C-5), 206.3 (s, C-1)

The analytical data obtained matched those reported in the literature.[119]

4,4-Diphenylcyclohexane-1,3-dione (161)



$C_{18}H_{16}O_2$
MW = 264.32 g/mol

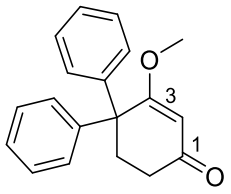
A solution of 2.70 mL Ethyl acrylate (2.48 g, 24.8 mmol, 1.00 equiv.) in 25 mL diethyl ether was added to a solution of 2.82 g potassium *tert*-butoxide (25.1 mmol, 1.01 equiv.) and 5.28 g 1,1-diphenylacetone (**159**, 25.1 mmol, 1.01 equiv.) in 75 mL diethyl ether. The reaction mixture was stirred at room temperature for 22 hours and the formed precipitate was filtered and washed with diethyl ether (5 × 10 mL). The precipitate was further dissolved in water and acidified with 1 M hydrochloric acid to pH = 7. The solution was extracted with chloroform (3 × 100 mL). The combined organic layers were washed with brine, dried over sodium sulfate, filtered and the solvent removed in vacuo. After recrystallization in 8.0 mL 1,4-dioxane 1.79 g cyclohexadione **161** (6.77 mmol, 27%) were obtained as a colourless solid (present as enol in NMR solvent).

^{1}H NMR (300 MHz, DMSO-d_6, 300 K): δ [ppm] = 2.26 - 2.31 (m, 2 H, H-5), 2.60 - 2.71 (m, 2 H, H-6) 5.30–5.48 (m, 1 H, H-2), 7.01–7.14 (m, 3 H, H_{Ar}), 7-19 - 7.45 (m, 7 H, H_{Ar}), 11.09 (*br* s, 1 H, OH).

^{13}C NMR (126 MHz, DMSO-d_6, 300 K): δ [ppm] = 26.7 (t, C-5), 40.0 (t, C-6), 57.4 (s, C-4), 104.5 (d, C-2), 126.3 (d, 2 × $C_{p\text{-Ar}}$), 127.7 (d, 4 × $C_{o\text{-Ar}}$), 128.4 (d, 4 × $C_{m\text{-Ar}}$), 142.7 (s, 2 × $C_{i\text{-Ar}}$), 178.0 (s, C-3), 200.5 (s, C-1).

The analytical data obtained matched those reported in the literature.[86, 120]

3-Methoxy-4,4-diphenylcyclohex-2-en-1-one (162)



$C_{19}H_{18}O_2$
278.35 g/mol

1.61 mL *N*,*N*-Diisopropylethylamine (9.48 mmol, 1.40 equiv.) and 7.0 mL tetrahydrofuran were added to a solution of 1.79 g cyclohexadione **161** (6.77 mmol, 1.00 equiv.) in 35 mL acetonitrile. After addition of 4.25 mL methanol (167 mmol, 24.8 equiv.), 5.00 mL trimethylsilyl diazomethane (2.0 M in hexane, 10.0 mmol, 1.48 equiv.) were added dropwise and the reaction mixture was stirred for 24 hours. Saturated sodium bicarbonate solution (20 mL) and water (10 mL) were added and the aqueous layer was extracted with diethyl ether (2 × 20 mL). The combined organic layers were washed with brine, dried over sodium sulfate, filtered and the solvent removed in vacuo. After purification by column chromatography (silica, P/Et_2O = 9/1) 380 mg vinylogous ester **162** (1.37 mmol, 20%) were obtained as a colourless solid.

Mp: 127 °C.

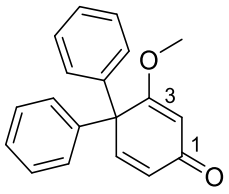
TLC: R_f = 0.04 (P/Et_2O = 1/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 2.24 - 2.32 (m, 2 H, H-6), 2.66 - 2.77 (m, 2 H, H-5), 3.72 (s, 3 H, OCH_3), 5.64 (s, 1 H, H-2), 7.15 - 7.19 (m, 4 H, H_{Ar}), 7.27 - 7.35 (m, 6 H, H_{Ar}).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 34.7 (t, C-6), 37.2 (t, C-5), 54.4 (s, C-4), 56.3 (q, OCH_3), 104.8 (s, C-2), 127.3 (d, 2 × $C_{p\text{-}Ar}$), 128.3 (d, 4 × $C_{o\text{-}Ar}$), 128.7 (d, 4 × $C_{m\text{-}Ar}$), 142.9 (s, 2 × $C_{i\text{-}Ar}$), 180.1 (s, C-3), 199.1 (s, C-1).

The analytical data obtained matched those reported in the literature.[86]

3-Methoxy-4,4-diphenylcyclohexa-2,5-dien-1-one (163)



$C_{19}H_{16}O_2$
276.34 g/mol

298 mg 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (1.31 mmol, 1.81 equiv.) were added to a solution of 202 mg vinylogous ester **162** (720 mmol, 1.00 equiv.) in 6.0 mL 1,4-dioxane. The reaction mixture was heated under reflux for 30 hours. After cooling to room temperature the solvent was removed in vacuo. Diethylether (10 mL) were added and the solution washed with 1 M sodium hydroxide solution (10 mL). The organic layer was washed with brine, dried over sodium sulfate and the solvent was removed in vacuo. After purification by column chromatography (silica, Et_2O = 100%) 145 mg cyclohexadienone **163** (525 mmol, 73%) were obtained as a brownish solid.

Mp: 145 °C.

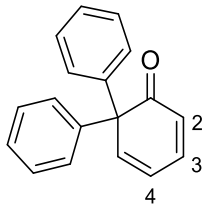
TLC: R_f = 0.40 (Et_2O = 100%) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 3.71 (s, 3 H, OCH_3), 5.77 (d, ^3J = 1.5 Hz, 1 H, H-2), 6.25 (dd, ^3J = 9.9 Hz, ^3J = 1.5 Hz, 1 H, H-6), 6.90 (d, ^3J = 9.9 Hz, 1 H, H-5), 7.20 - 7.24 (m, 4 H, H_{Ar}), 7.28 - 7.38 (m, 6 H, H_{Ar}).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 56.1 (q, OCH$_3$), 57.3 (s, C-4), 103.7 (d, C-2), 125.4 (d, C-6), 127.8 (d, 2 × $C_{p\text{-Ar}}$), 128.6 (d, 4 × $C_{o\text{-Ar}}$), 129.0 (d, 4 × $C_{m\text{-Ar}}$), 141.0 (s, 2 × $C_{i\text{-Ar}}$), 150.2 (d, C-5), 176.2 (s, C-3), 188.3 (s, C-1).

The analytical data obtained matched those reported in the literature.[86]

4,4-Diphenylcyclohexa-2,4-dien-1-one (159)



$C_{18}H_{14}O$
246.31 g/mol

110 µL Diisobutylaluminum hydride (1.0 M in dichloromethane, 110 µmol, 1.28 equiv.) were added dropwise to a solution of 23.8 mg cyclohexadienone **163** (86.1 µmol, 1.00 equiv.) in 2.0 mL dichloromethane at 8 °C. The reaction n mixture was stirred at 10 °C for 15 minutes. Water (7.5 mL) and 1.2 M hydrochloric acid (330 µL) were added and the mixture was stirred for 15 minutes at room temperature. The mixture was extracted with diethyl ether (2 × 10 mL) and the combined organic layers were washed with water (5 mL, back extracted with diethyl ether), saturated sodium bicarbonate solution (5 mL), brine, dried over sodium sulfate, filtered and the solvent removed in vacuo. After purification by column chromatography (silica, P/Et_2O = 19/1) 12.6 mg cyclohexadienone **159** (47.7 mmol, 55%) were obtained as a colourless solid.

Mp: 92 °C.

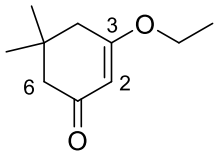
TLC: R_f = 0.09 (P/Et_2O = 19/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] =6.09 (ddd, ^3J = 9.8 Hz, ^4J = 0.9 Hz, ^5J = 0.5 Hz, 1 H, H-2), 6.39 (ddd, ^3J = 9.5 Hz, ^3J = 5.9 Hz, ^4J = 0.9 Hz, 1 H, H-4), 6.75 (ddd, ^3J = 9.5 Hz, ^4J = 1.8 Hz, ^5J = 0.9 Hz, 1 H, H-5), 7.10 (ddd, ^3J = 9.8 Hz, ^3J = 5.9 Hz, ^4J = 1.8 Hz, 1 H, H-3), 7.16 - 7.22 (m, 4 H, $H_{o\text{-Ar}}$), 7.25 - 7.33 (m, 6 H, H_{Ar}).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 65.0 (s, C-6), 119.8 (d, C-2), 125.8 (d, C-4), 127.6 (d, 2 × $C_{p\text{-Ar}}$), 128.7 (d, 4 × $C_{o\text{-Ar}}$), 129.0 (d, 4 × $C_{m\text{-Ar}}$), 141.3 (d, C-3), 142.0 (s, 2 × $C_{i\text{-Ar}}$), 146.5 (d, C-5), 202.0 (s, C-1).

The analytical data obtained matched those reported in the literature.[87, 121]

3-Ethoxy-5,5-dimethylcyclohex-2-en-1-one (167)



$C_{10}H_{16}O_2$
MW = 168.24 g/mol

60.0 mL Ethanol (47.4 g, 1.03 mmol, 5.80 equiv.) were added to a solution of 25.0 g 5,5-dimethylcyclohexane-1,3-dione (178 mmol, 1.00 equiv.), and 678 mg *para*-toluenesulfonic acid (3.57 mmol, 2.00 mol%) in 300 mL toluene. The reaction mixture was heated under reflux for 42 hours. The solvent was removed in vacuo and after purification by vacuum distillation (2.3 mbar, 110 °C oil bath temperature) 27.5 g vinylogous ester **167** (163 mmol, 92%) were obtained as a colourless oil.

Bp: 92 °C (2.3 mbar).

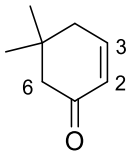
TLC: R_f = 0.18 (P/Et_2O = 2/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.07 [s, 6 H, C-5(CH_3)$_2$], 1.36 (t, ^3J = 7.1 Hz, 3 H, CH_2CH_3), 2.21 (s, 2 H, H-6), 2.27 (s, 2 H, H-4), 3.90 (q, ^3J = 7.1 Hz, 2 H, CH_2CH_3), 5.34 (s, 1 H, H-2).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.3 (q, CH_2CH_3), 28.4 [q, C-5(CH_3)$_2$], 32.6 (s, C-5), 43.1 (t, C-4), 50.9 (t, C-6), 64.4 (t, CH_2CH_3), 101.7 (d, C-2), 176.4 (s, C-3), 199.8 (s, C-1).

The analytical data obtained matched those reported in the literature.[122-123]

5,5-Dimethylcyclohex-2-en-1-one (166)



$C_8H_{12}O$
MW = 124.18 g/mol

A suspension of 2.48 g lithium aluminum hydride (65.3 mmol, 0.40 equiv.) in 50 mL diethyl ether was added in small portions to a solution of 27.5 g vinylogous ester **167** (163 mmol, 1.00 equiv.) in 100 mL diethyl ether at 0 °C and the reaction mixture was stirred at room temperature for 20 hours. Methanol (20 mL) and 1 M hydrochloric acid (150 mL) were added dropwise at 0 °C and the mixture was stirred at room temperature for 90 minutes. The aqueous layer was extracted with diethyl ether (2 × 100 mL) and the combined organic layers were washed with brine, dried over sodium sulfate and the solvent was removed in vacuo. After purification by vacuum distillation (20 mbar, 80 °C oil bath temperature) 20.1 g cyclohexenone **166** (162 mmol, 99%) were obtained as a colourless oil.

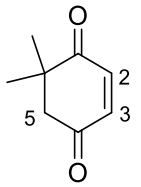
Bp: 59 °C (20 mbar).

^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.04 (s, 6 H, 2 × CH_3), 2.02–2.35 (m, 4 H, H-6, H-4), 6.02 (dt, ^3J = 10.1 Hz, ^3J = 2.1 Hz, 1 H, H-2), 6.85 (dt, ^3J = 10.1 Hz, ^3J = 4.1 Hz, 1 H, H-3).

^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ [ppm] = 28.0 (q, 2 × CH_3), 33.6 (t, C-4), 39.6 (s, C-5), 51.5 (t, C-6), 128.7 (d, C-2), 148.1 (d, C-3), 199.6 (s, C-1).

The analytical data obtained matched those reported in the literature.[122, 124]

5,5-Dimethylcyclohex-2-ene-1,4-dione (168)



$C_8H_{10}O_2$
MW = 138.17 g/mol

1.18 mL *tert*-Butylhydroperoxide (5.5 M in decane over 4Å molecular sieves, 6.44 mmol, 8.00 equiv.) were added dropwise to a solution of 100 mg cyclohexenone **166** (805 µmol, 1.00 equiv.) and 41.4 mg cobalt(II) acetylacetonate (161 mmol, 0.80 equiv.) in 2.0 mL acetone at room temperature and the reaction mixture was stirred for four days. Brine (30 mL) was added and the aqueous layer was extracted with diethyl ether (2 × 50 mL) and the combined organic layers were washed with brine, dried over sodium sulfate and the solvent was removed in vacuo. After purification by column chromatography (silica, P/Et2O = 1/1) 57.4 mg cyclohexenedione **168** (415 µmol, 52%) were obtained as a yellow oil.

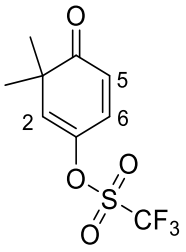
TLC: R_f = 0.60 (P/Et_2O = 1/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.25 (s, 6 H, 2 × CH_3), 2.75 (s, 2 H, H-6), 6.64 (d, ^3J = 10.3 Hz, 1 H. H-3), 6.69 (d, ^3J = 10.3 Hz,1 H, H-2).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 26.1 (q, 2 × CH_3), 45.5 (s, C-5), 51.8 (t, C-6), 139.5 (d, C-3), 198.2 (s, C-1), 203.3 (s, C-4).

The analytical data obtained matched those reported in the literature.[125]

3,3-Dimethyl-4-oxocyclohexa-1,5-dien-1-yl trifluormethanesulfonate (164)



$C_9H_9F_3O_4S$
MW = 270.22 g/mol

1.51 mL lithium bis(trimethylsilyl)amide (1.0 M in tetrahydrofuran, 1.51 mmol, 1.04 equiv.) were added dropwise to a solution of 200 mg cyclohexenedione **168** (1.45 mmol, 1.00 equiv.) in 1.6 mL tetrahydrofuran at −78 °C and the mixture was stirred for 15 minutes. After dropwise addition of a solution of 539 mg *N*-phenyl bis(trifluoromethanesulfonimide) (1.51 mmol, 1.04 equiv.) in 2.6 mL tetrahydrofuran the reaction mixture was stirred for two hours. After warming to room temperature, hydrochloric acid (3 mL) was added and the aqueous layer was extracted with diethyl ether (3 × 3 mL) and the combined organic layers were washed with brine, dried over sodium sulfate and the solvent was removed in vacuo. After purification by column chromatography (silica, P/Et2O = 9/1 → 4/1 → 2/1) 77.3 mg cyclohexenedione **164** (286 µmol, 20%) were obtained as a yellow oil.

TLC: R_f = 0.33 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2978 (w, $C_{sp3}H$), 1680 (m, C=O), 1646 (s, C=C), 1425 (m, $C_{sp3}H$), 1364 (m, $C_{sp3}H$), 1211 (vs, SO), 1141 (s, CF), 883 (m, $C_{sp2}H$).

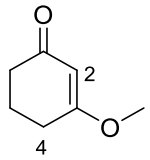
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.31 (s, 6 H, 2 × CH_3), 6.17 (d, ^3J = 10.3 Hz, 1 H, H-5), 6.25 (d, ^4J = 3.1 Hz, 1 H, H-2), 6.93 (dd, ^3J = 10.3 Hz, ^4J = 3.1 Hz, 1 H, H-6).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.8 (q, 2 × CH_3), 47.3 (s, C-3), 118.7 (q, $^1J_{CF}$ = 320.9 Hz, CF_3), 128.3 (d, C-5), 135.7 (d, C-2), 137.3 (s, C-3), 142.0 (s, C-1), 202.4 (s, C-4).

MS (EI, 70 eV): *m/z* (%) = 270 (11) $[M]^+$, 137 (86) $[M–SO_2CF_3]^+$, 109 (51) $[C_7H_9O]^+$, 81 (100).

For reasons of time high-resolution mass spectrometry was not conducted.

3-Methoxycyclohex-2-en-1-one (173)



$C_7H_{10}O_2$
MW = 126.16 g/mol

72.4 mL Methanol (57.2 g, 1.78 mol, 20.0 equiv.) were added to a solution of 10.0 g cyclohexane-1,3-dione (89.2 mmol, 1.00 equiv.) and 307 mg *para*-toluenesulfonic acid (1.78 mmol, 0.02 equiv.) in 100 mL toluene and after attaching a *Dean-Stark* apparatus the reaction mixture was heated under reflux for twelve hours. After cooling to room temperature, the volatile compounds were removed in vacuo. After purification by vacuum distillation (24 mbar, 150 °C oil bath temperature) 8.89 g vinylogous ester **173** (70.5 mmol, 79%) were obtained as a colourless solid.

Mp: 43 °C.

Bp: 123-124 °C (24 mbar).

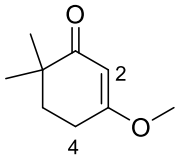
TLC: R_f = 0.28 (Et2O = 100%) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ [ppm] = 1.97 (*virt.* quin, $^3J \cong {}^3J$ = 6.4 Hz, 2 H, H-5), 2.34 (dd, ^3J = 7.2 Hz, ^3J = 6.1 Hz, 2 H, H-6), 2.40 (t, ^3J = 6.3 Hz, 2 H, H-4), 3.68 (s, 3 H, OCH_3), 5.36 (s, 1 H, H-2).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 21.4 (t, C-5), 28.9 (t, C-4), 36.9 (t, C-6), 55.7 (q, OCH_3), 102.5 (d, C-2), 178.9 (s, C-3), 199.9 (s, CO).

The analytical data obtained matched those reported in the literature.[126]

3-Methoxy-6,6-dimethylcyclohex-2-en-1-one (169)



$C_9H_{14}O_2$
MW = 154.21 g/mol

29.8 mL *n*-Butyllithium solution (2.50 M in hexane, 4.77 g, 74.5 mmol, 1.30 equiv.) were added to a solution of 11.3 mL diisopropylamine (8.12 g, 80.2 mmol, 1.40 equiv.) in 200 mL tetrahydrofuran at 0 °C. The mixture was stirred for 20 minutes and subsequently cooled to – 78 °C. To this solution of lithium diisopropylamide was added vinylogous ester **173** over 15 minutes and the resulting orange mixture stirred for 30 minutes at –78 °C, before 7.14 mL iodomethane (16.3 g, 115 mmol, 2.00 equiv.) were added and the resulting yellow reaction mixture stirred for one hour at –78 °C and warmed to room temperature. When full conversion was reached, the reaction mixture was cooled to –78 °C and in a separate flask, the same amount of lithium diisopropylamide (74.5 mmol) in 200 mL tetrahydrofuran was prepared by the same procedure and added to the reaction mixture. After stirring at –78 °C for 30 minutes, additional 7.14 mL iodomethane (16.3 g, 115 mmol, 2.00 equiv.) were added and the reaction mixture stirred for one hour at –78 °C and warmed to room temperature. Saturated ammonium chloride solution (500 mL) was added and the mixture was extracted with diethyl ether (3 × 500 mL) and the combined organic layers were washed with brine, dried over sodium sulfate and the solvent was removed in vacuo. After purification by column chromatography (silica, P/Et_2O = 2/1) 6.97 g vinylogous ester **169** (45.2 mmol, 79%) were obtained as a colourless oil.

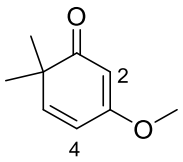
TLC: R_f = 0.28 (Et2O = 100%) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.11 [s, 6 H, C-6(CH_3)$_2$], 1.80 (t, ^3J = 6.4 Hz, 2 H, H-5), 2.42 (t, ^3J = 6.4 Hz, 2 H, H-4), 3.67 (s, 3 H, OCH_3), 5.26 (s, 1 H, H-2).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 24.7 [q, C-6(CH_3)$_2$], 26.2 (t, C-4), 35.2 (t, C-5), 40.4 (s, C-6), 55.8 (q, OCH_3), 100.8 (d, C-2), 176.7 (s, C-3), 204.6 (s, CO).

The analytical data obtained matched those reported in the literature.[127]

3-Methoxy-6,6-dimethylcyclohexa-2,4-dien-1-one (174)



$C_9H_{12}O_2$
MW = 152.19 g/mol

5.19 mL *n*-Butyllithium solution (2.50 M in hexane, 831 mg, 13.0 mmol, 2.00 equiv.) were added to a solution of 2.73 mL diisopropylamine (1.97 g, 19.5 mmol, 3.00 equiv.) in 45 mL tetrahydrofuran at 0 °C. The mixture was stirred for 20 minutes and subsequently cooled to – 78 °C. To this solution of lithium diisopropylamide was added a solution of 1.00 g vinylogous ester **169** (6.48 mmol, 1.00 equiv.) in 45 mL tetrahydrofuran and *N*,*N*-dimethylpropyleneurea (v/v = 25:1) over 15 minutes and the resulting orange mixture was stirred for two hours at – 78 °C, before a solution of 1.86 mg phenylselenyl bromide (9.73 mmol, 1.50 equiv.) in 6 mL tetrahydrofuran was added. The reaction mixture was warmed to room temperature over the course of one hour, before diethyl ether (100 mL) and saturated ammonium chloride solution (50 mL) were added. The aqueous phase was extracted with diethyl ether (100 mL) and the combined organic layers were washed with brine. 2.94 mL hydrogen peroxide solution (50 wt% in water, 1.75 g, 51.9 mmol, 8.00 equiv.) were added and the mixture heated under reflux for one hour. The organic layer was washed with water (50 mL), brine, dried over sodium sulfate, and the solvent was removed in vacuo. After purification by column chromatography (silica, CH_2Cl_2/Et_2O = 9/1) 570 mg cyclohexadienone **174** (3.75 mmol, 58%) were obtained as a pale yellow oil.

TLC: R_f = 0.42 (P/Et_2O = 1/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3494 (w, $C_{sp2}H$), 2967 (m, $C_{sp3}H$), 1652 (vs, C=O), 1575 (vs, C=C), 1413 (s, $C_{sp3}H$), 1373 (s), 1326 (s), 1249 (s, COC), 1213 (s, COC), 1174 (vs, COC), 1007 (m), 831 (m, $C_{sp2}H$), 783 (m), 668 (w).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.21 [s, 6 H, C-6(CH_3)$_2$], 3.76 (s, 3 H, OCH_3), 5.43 (d, ^4J = 2.2 Hz, 1 H, H-2), 6.04 (dd, ^3J = 9.9 Hz, ^4J = 2.2 Hz, 1 H, H-4), 6.33 (d, ^3J = 9.9 Hz, 1 H, H-5).

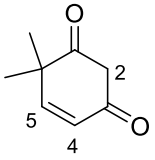
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.8 [q, C-6(CH_3)$_2$], 45.8 (s, C-6), 55.9 (q, OCH_3), 99.2 (d, C-2), 119.0 (d, C-4), 149.7 (d, C-5), 171.3 (s, C-3), 204.4 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 152 (100) $[M]^+$, 137 (24) $[M–CH_3]^+$, 124 (12) $[M–C_2H_4]^+$, 109 (72) $[M–C_3H_7]^+$, 91 (18) $[C_7H_7]^+$, 81 (30).

HRMS (EI, 70 eV): calc. for $C_9H_{12}O_2$ $[M]^+$: 152.0832; found: 152.0837.

calc. for $C_8{}^{13}CH_{12}O_2$ $[M]^+$: 153.0865; found: 153.0873.

6,6-Dimethylcyclohex-2-ene-1,3-dione (175)



$C_8H_{10}O_2$
MW = 138.17 g/mol

584 mg ammonium cerium(IV) nitrate (1.06 µmol, 0.10 equiv.) were added to a solution of 1.62 g cyclohexadienone **174** (10.6 mmol, 1.00 equiv.) in a degassed mixture of 50 mL water and 50 mL acetonitrile. The reaction mixture was heated under reflux for three hours. After cooling to room temperature brine (100 mL) was added and the mixture extracted with diethyl ether (3 × 100 mL). The combined organic layers were dried over sodium sulfate, filtered, and the solvent was removed in vacuo. After purification by column chromatography (silica, Et_2O = 100%) 1.26 g cyclohexenedione **175** (keto/enol = 73/27, 9.12 mmol, 86%) were obtained as a pale yellow solid.

Mp: 121 - 124 °C.

TLC: R_f = 0.46 (Et_2O = 100%) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2973 (w, $C_{sp3}H$), 1648 (vs, C=O), 1543 (vs, C=C), 1479 (m, $C_{sp3}H$), 1315 (w), 1230 (vs), 860 (w, $C_{sp2}H$).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.30 (s, 2 × CH_{3E}), 1.35 (s, 2 × CH_{3K}), 3.55 (s, 2 H, H-2_K), 5.60 (d, ^4J = 1.8 Hz, 1 H, H-2_E), 6.10 (dd, ^3J = 9.8 Hz, ^4J = 1.8 Hz, 1 H, H-4_E), 6.17 (d, ^3J = 10.2 Hz, H-4_K), 6.57 (d, ^3J = 9.8 Hz, H-5_E), 6.88 (d, ^3J = 10.2 Hz, H-5_K).

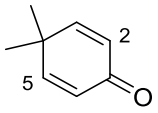
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.0 (q, 2 × CH_{3K}), 25.2 (q, 2 × CH_{3E}), 41.1 (s, C-6_E), 46.7 (s, C-6_K), 52.5 (t, C-2_E), 102.3 (d, C-2_E), 124.3 (d, C-4_E), 127.2 (d, C-5_K), 153.5 (d, C-5_E), 156.4 (d, C-5_K), 186.7 (s, C-3_E), 188.1 (s, C-1_E), 194.6 (s, C-3_K), 206.0 (s, C-1_K).

MS (EI, 70 eV): *m/z* (%) = 138 (5) $[M]^+$, 96 (100) $[C_6H_8O]^+$, 105 (28) $[C_7H_5O]^+$, 81 (45) $[C_6H_9]^+$, 67 (32) $[C_5H_7]^+$.

HRMS (EI, 70 eV): calc. for $C_8H_{10}O_2$ $[M]^+$: 138.0675; found: 138.0676;

calc. for $C_7{}^{13}CH_{10}O_2$ $[M]^+$: 139.0709; found: 139.0718.

4,4-Dimethylcyclohexa-2,5-dien-1-one (183)



$C_8H_{10}O$
MW = 122.17 g/mol

5.30 mL Dimethylcyclohexenone **182** (5.00 g, 40.3 mmol, 1.00 equiv.) were added to a suspension of 11.0 g 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (48.3 mmol, 1.20 equiv.) in 250 mL dichloroethane and the reaction mixture was heated under reflux for 72 hours. After cooling to room temperature, the volatile compounds were removed in vacuo. The residue was taken up in diethyl ether (250 mL), washed with a 1 M aqueous sodium hydroxide solution (3 × 100 mL) and brine, dried over sodium sulfate, filtered, and the solvent was removed in vacuo. After purification by column chromatography (silica, P/Et_2O = 4/1 → 2/1) 4.14 g cyclohexadienone **183** (33.9 mmol, 84%) were obtained as a colourless oil.

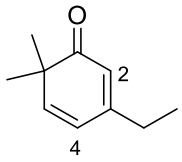
TLC: R_f = 0.20 (P/Et_2O = 4/1) [UV, $KMnO_4$].

^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.26 (s, 6 H, 2 × CH_3), 6.16 - 6.22 (m, 2 H, H-2, H-6), 6.79 - 6.86 (m, 2 H, H-3, H-5).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 26.9 (q, 2 × CH_3), 38.1 (s, C-4), 127.5 (d, C-2, C-6), 156.9 (d, C-3, C-5), 186.1 (s, CO).

The analytical data obtained matched those reported in the literature.[117, 128]

3-Ethyl-6,6-dimethylcyclohexa-2,4-dien-1-one (177)



$C_{10}H_{14}O$
MW = 150.22 g/mol

Following GP2, 300 mg cyclohexadienone **183** (2.46 mmol, 1.00 equiv.) were converted with 6.38 mL ethyllithium solution (0.5 M in benzene: cyclohexane, 115 mg, 3.20 mmol, 1.30 equiv.) in three hours.

Following GP5, the resulting tertiary allylic alcohol was converted with 1.02 g pyridinium dichromate (2.71 mmol, 1.10 equiv.) in one hour. After purification by column chromatography (silica, P/Et_2O = 19/1) 106 mg cyclohexadienone **177** (706 mmol, 29%) were obtained as a pale yellow oil.

TLC: R_f = 0.38 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2970 (s, $C_{sp3}H$), 1686 (vs, C=O), 1640 (m, C=C), 1464 (w, $C_{sp3}H$), 1372 (w, $C_{sp3}H$), 1182 (m, $C_{sp3}H$), 870 (w, $C_{sp2}H$).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.15 (t, ^{3}J = 7.5 Hz, 3 H, CH_2CH_3), 1.19 [s, 6 H, C-6$(CH_3)_2$], 2.35 (qd, ^{3}J = 7.5 Hz, ^{4}J = 1.4 Hz, 1 H, CH_2CH_3), 5.88 (*virt.* qd,

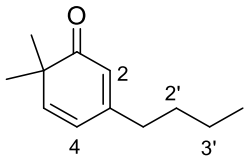
$^{4}J \cong {}^{4}J$ = 1.4 Hz, ^{5}J = 0.7 Hz, 1 H, H-2), 6.06 (dd, ^{3}J = 9.5 Hz, ^{4}J = 1.4 Hz, 1 H, H-4), 6.28 (d, ^{3}J = 9.5 Hz, ^{5}J = 0.7 Hz, 1 H, H-5).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 12.0 (q, $CH_2\mathit{C}H_3$), 25.7 [q, C-6($\mathit{C}H_3$)$_2$], 29.5 (t, $\mathit{C}H_2CH_3$), 46.2 (s, C-6), 121.2 (d, C-2), 122.3 (d, C-4), 148.2 (d, C-5), 159.2 (s, C-3), 206.0 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 150 (64) $[M]^+$, 135 (27) $[M–CH_3]^+$, 121 (11) $[C_8H_9O]^+$, 107 (100) $[C_7H_7O]^+$, 91 (44) $[C_7H_7]^+$, 79 (23) $[C_6H_7]^+$, 65 (7) $[C_5H_5]^+$.

HRMS (EI, 70 eV): calc. for $C_{10}H_{14}O$ $[M]^+$: 150.1039; found: 150.1042.

3-Butyl-6,6-dimethylcyclohexa-2,4-dien-1-one (180)



$C_{12}H_{18}O$
MW = 178.28 g/mol

Following GP2, 300 mg cyclohexadienone **183** (2.46 mmol, 1.00 equiv.) were converted with 1.28 mL butyllithium solution (2.5 M in hexanes, 205 mg, 3.20 mmol, 1.30 equiv.) in three hours.

Following GP5, the resulting tertiary allylic alcohol was converted with 1.02 g pyridinium dichromate (2.71 mmol, 1.10 equiv.) in one hour. After purification by column chromatography (silica, P/Et_2O = 19/1 → 9/1) 309 mg cyclohexadienone **180** (1.73 mmol, 71%) were obtained as a pale yellow oil.

TLC: R_f = 0.41 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2962 (s, $C_{sp3}H$), 2930 (s, $C_{sp3}H$), 2863 (m, $C_{sp3}H$), 1659 (vs, C=O), 1640 (m, C=C), 1467 (m, $C_{sp3}H$), 1372 (m, $C_{sp3}H$), 1181 (m, $C_{sp3}H$), 776 (w, $C_{sp3}H$).

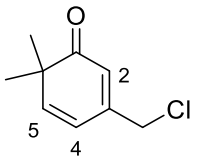
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.93 (t, ^{3}J = 7.3 Hz, 3 H, C-4'), 1.19 [s, 6 H, C-6(CH_3)$_2$], 1.36 (*virt.* sex, $^{3}J \cong {}^{3}J$ = 7.3 Hz, 2 H, C-3'), 1.53 (dddd, ^{3}J = 8.8 Hz, ^{3}J = 7.6 Hz, ^{3}J = 6.8 Hz, ^{3}J = 5.8 Hz, 2 H, C-2'), 2.29 - 2.34 (m, 2 H, C-1'), 5.85 - 5.88 (m, 1 H, H-2), 6.06 (dd, ^{3}J = 9.5 Hz, ^{4}J = 1.4 Hz, 1 H, H-4), 6.27 (d, ^{3}J = 9.5 Hz, ^{5}J = 0.7 Hz, 1 H, H-5).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.0 (q, C-4'), 22.4 (t, C-3'), 25.7 [q, C-6(CH$_3$)$_2$], 29.8 (t, C-2'), 36.3 (t, C-1'), 46.2 (s, C-6), 122.1 (d, C-2), 122.4 (d, C-4), 148.3 (d, C-5), 158.0 (s, C-3), 205.9 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 178 (100) $[M]^+$, 163 (16) $[M–CH_3]^+$, 149 (54) $[M–C_2H_5]^+$, 135 (57) $[M–C_3H_7]^+$, 121 (39) $[C_8H_9O]^+$, 107 (87) $[C_7H_7O]^+$, 91 (69) $[C_7H_7]^+$, 79 (34) $[C_6H_7]^+$, 65 (13) $[C_5H_5]^+$.

HRMS (EI, 70 eV): calc. for $C_{12}H_{18}O$ $[M]^+$: 178.1355; found: 178.1352.

3-(Chloromethyl)-6,6-dimethylcyclohexa-2,4-dien-1-one (184)



$C_9H_{11}ClO$
MW = 170.64 g/mol

In analogy to a modified literature procedure[129]: 402 mL Chloroiodomethane (975 mg, 5.53 mmol, 4.50 equiv.) were added to a solution of 150 mg cyclohexadienone **183** (1.23 mmol, 1.00 equiv.) in 2.5 mL THF and diethyl ether (v/v = 1/1) at −78 °C. 2.23 mL Methyllithium lithium bromide complex (2.2 M in diethyl ether, 4.91 mmol, 4.00 equiv.) were added dropwise and the reaction mixture was stirred for 90 minutes at −78 °C. The reaction was quenched by the addition of saturated ammonium chloride solution (5 mL). The mixture was extracted with diethyl ether (3 × 10 mL) and the combined organic layers were washed with brine, dried over sodium sulfate, filtered and the solvent was removed in vacuo. The crude tertiary allylic alcohol was submitted to oxidation without further purification.

Following GP4, the resulting tertiary allylic alcohol was converted with 522 mg pyridinium chlorochromate (2.42 mmol, 2.00 equiv.) in two hours. After purification by column chromatography (silica, P/Et_2O = 4/1) 95.1 mg cyclohexadienone **184** (55.7 µmol, 46%) were obtained as a pale yellow oil.

TLC: R_f = 0.42 (P/Et_2O = 2/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2969 (s, $C_{sp3}H$), 1661 (vs, C=O), 1642 (m, C=C), 1464 (w, $C_{sp3}H$), 1373 (w, $C_{sp3}H$), 1181 (w, $C_{sp3}H$), 701 (s, CCl).

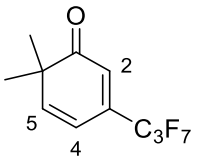
^{1}H NMR (400 MHz, $CDCl_3$, 298 K): δ [ppm] = 1.22 (s, 6 H, 2 × CH_3), 4.23 (^4J = 1.1 Hz, 2 H, CH_2Cl), 6.05 - 6.08 (m, 1 H, H-2), 6.20 (^3J = 9.6 Hz, ^4J = 1.5 Hz, 1 H, H-4), 6.37 (d, ^3J = 9.6 Hz, 1 H, H-5).

^{13}C NMR (101 MHz, $CDCl_3$, 298 K): δ [ppm] = 25.6 (q, 2 × CH_3), 45.5 (t, CH_2Cl), 46.9 (s, C-6), 119.6 (d, C-4), 123.1 (d, C-2), 149.2 (d, C-5), 150.6 (s, C-3), 204.2 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 170 (56) $[M]^+$, 135 (49) $[M–Cl]^+$, 107 (100) $[C_7H_7O]^+$, 91 (72) $[C_7H_7]^+$, 79 (23) $[C_6H_7]^+$.

HRMS (EI, 70 eV): calc. for $C_9H_{11}{}^{35}ClO$ $[M]^+$: 170.0493; found: 170.0494.

6,6-dimethyl-3-perfluoropropylcyclohexa-2,4-dien-1-one (185)



$C_{11}H_9F_7O$
MW = 290.18 g/mol

1.30 mL 1-Iodoperfluoropropane (2.66 g, 9.00 mmol, 2.20 equiv.) were added to a solution of cyclohexadienone **183** (4.09 mmol, 1.00 equiv.) in 30 mL diethyl ether at −78 °C. 3.35 mL

methyl lithium lithium bromide complex solution (2.2 M in diethyl ether, 802 mg, 7.37 mmol, 1.80 equiv.) were added dropwise and the reaction mixture was stirred for six hours at −78 °C and then warmed to room temperature over the course of two hours. The reaction was quenched with saturated ammonium chloride solution (25 mL). The aqueous layer was extracted with diethyl ether (3 × 30 mL). The combined organic layers were washed with brine, dried over sodium sulfate, filtered, and the solvent was removed in vacuo. The crude tertiary allylic alcohol was submitted to oxidation without further purification.

Following GP 4, the resulting tertiary allylic alcohol was converted with 1.76 g pyridinium chlorochromate (8.18 mmol, 2.00 equiv.) in four hours. After purification by column chromatography (silica, $P/Et_2O = 39/1 \rightarrow 19/1 \rightarrow 9/1$) 579 mg cyclohexenone **185** (2.00 mmol, 49%) were obtained as a pale yellow oil.

TLC: R_f = 0.62 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2977 (w, $C_{sp2}H$), 1753 (w, C=O), 1677 (m, C=C), 1389 (m), 1230 (vs, CF), 1180(s, CF), 1116 (vs, CF), 905 (w), 830 (w).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.27 (s, 6 H, 2 × CH_3), 6.22 - 6.27 (m, 1 H, H-4), 6.34 - 6.36 (m, 1 H, H-3), 6.46 (d, ^3J = 9.9 Hz, 1 H, H-5).

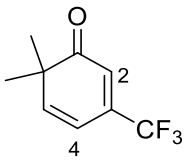
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.4 (q, 2 × CH_3), 47.8 (s, C-6), 115.2 (tt, $^3J_{CF}$ = 4.7 Hz, $^4J_{CF}$ = 2.1 Hz, C-4), 108.8 (tq, $^1J_{CF}$ = 265.7 Hz, $^2J_{CF}$ = 37.2 Hz, $CF_2CF_2CF_3$), 113.7 (tt, $^1J_{CF}$ = 256.8 Hz, $^2J_{CF}$ = 31.2 Hz, $CF_2CF_2CF_3$), 117.8 (qt, $^1J_{CF}$ = 287.6 Hz, $^2J_{CF}$ = 33.8 Hz, $CF_2CF_2CF_3$), 125.5 (t, $^3J_{CF}$ = 7.4 Hz, C-2), 141.5 (t, $^2J_{CF}$ = 22.9 Hz, C-3), 150.2 (s, C-5), 204.2 (s, C-1).

^{19}F NMR (471 MHz, $CDCl_3$, 300 K): δ [ppm] = −126.6 (s), −117.1 (q, $^3J_{FF}$ = 9.5 Hz), −80.2 (t, $^3J_{FF}$ = 9.5 Hz).

MS (EI, 70 eV): *m/z* (%) = 290 (42) $[M]^+$, 263 (20), 171 (13) $[M–C_2F_5]^+$, 143 (100), 127 (17), 91 (12) $[C_7H_7]^+$.

HRMS (EI, 70 eV): calc. for $C_{11}H_9F_7O$ $[M]^+$: 290.0536; found: 290.0536.

6,6-Dimethyl-3-(trifluoromethyl)cyclohexa-2,4-dien-1-one (186)



$C_9H_9F_3O$
MW = 190.17 g/mol

In analogy to a modified literature procedure[94] 2.46 mL Trifluoromethyltrimethylsilane (2.0 M, 4.91 mmol, 1.20 equiv.) were added to a solution of 500 mg cyclohexadienone **183** (4.09 mmol, 1.00 equiv.) in 8 mL tetrahydrofuran at room temperature. A catalytic amount of tetrabutylammonium fluoride solution (1.0 M in tetrahydrofuran) were added dropwise until an elevation in temperature and a change to an orange or brownish color occurred. The reaction was stirred at room temperature for two hours before 4.09 mL tetrabutylammonium fluoride (1.0 M in tetrahydrofuran, 4.09 mmol, 1.00 equiv.) were added in one portion. The reaction mixture was concentrated in vacuo, filtered over silica. The silica was washed with diethyl ether and the solvent evaporated in vacuo. The crude tertiary allylic alcohol was submitted to oxidation without further purification.

A solution of tertiary alcohol in 4 mL dichloromethane was added to a suspension of 2.64 g pyridinium chlorochromate (12.3 mmol, 3.00 equiv.) in 18 mL dichloromethane at room temperature. A catalytic amount of concentrated sulfuric acid was added dropwise and the reaction mixture was stirred for 24 hours. The mixture was diluted with diethyl ether (20 mL) and saturated sodium bicarbonate solution was added carefully. (*Vigorous formation of carbon dioxide!*) The aqueous layer was extracted with diethyl ether (3 × 30 mL), and the combined organic layers were washed with saturated sodium bicarbonate solution (20 mL), brine, dried over sodium sulfate, filtered, and the solvent was removed in vacuo. After purification by column chromatography (silica, P/Et_2O = 19/1) 444 mg cyclohexadienone **186** (2.33 mmol, 57%) were obtained as a pale yellow oil.

TLC: R_f = 0.58 (P/Et_2O = 4/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2981 (w, $C_{sp3}H$), 1731 (m, C=O), 1700 (m, C=C), 1267 (m, CF), 1170 (s, CF), 1124 (vs, CF).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.26 (s, 2 × CH_3), 6.23 - 6.27 (m, 1 H, H-4), 6.25 (dd, ^{3}J = 9.8 Hz, ^{4}J = 1.5 Hz, 1 H, H-2), 6.45 - 6.50 (m, 1 H, H-5).

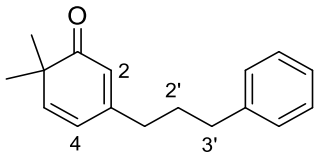
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.4 (q, 2 × CH_3), 47.8 (s, C-6), 114.6 (q, $^{3}J_{CF}$ = 2.4 Hz, C-4), 122.5 (q, $^{1}J_{CF}$ = 274 Hz, CF_3), 122.7 (q, $^{3}J_{CF}$ = 5.0 Hz, C-2), 141.8 (q, $^{2}J_{CF}$ = 32.3 Hz, C-3), 150.8 (d, C-5), 204.7 (s, C-1).

^{19}F NMR (376 MHz, $CDCl_3$, 300 K): δ [ppm] = −69.4 (s, CF_3).

MS (EI, 70 eV): *m/z* (%) = 190 (100) $[M]^+$, 175 (15) $[M–CH_3]^+$, 162 (18) $[M–C_2H_4]^+$, 147 (55) $[C_7H_6F_3]^+$, 127 (91), 93 (96) $[C_7H_9]^+$, 77 (37) $[C_6H_5]^+$.

HRMS (EI, 70 eV): calc. for $C_9H_9F_3O$ $[M]^+$: 190.0600; found: 190.0601.

6,6-Dimethyl-3-(3-phenylpropyl)cyclohexa-2,4-dien-1-one (187)



$C_{17}H_{20}O$
MW = 240.35 g/mol

Following GP3, 300 mg cyclohexadienone **183** (2.46 mmol, 1.00 equiv.) were converted with 119 mg magnesium (4.91 mmol, 2.00 equiv.) and 746 µL 1-bromo-3-phenylpropane (978 mg, 4.91 mmol, 2.00 equiv.) in one hour.

Following GP5, the resulting tertiary allylic alcohol was converted with 1.02 g pyridinium dichromate (2.71 mmol, 1.10 equiv.) in one hour. After purification by column chromatography (silica, P/Et_2O = 19/1) 321 mg cyclohexadienone **187** (1.34 mmol, 55%) were obtained as a pale yellow oil.

TLC: R_f = 0.34 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3423 (w, $C_{sp2}H$), 2974 (s, $C_{sp3}H$), 2932 (s, $C_{sp3}H$), 1718 (vs, C=O), 1673 (vs, C=C), 1453 (m, $C_{sp3}H$), 1385 (m), 1154 (s, $C_{sp3}H$), 749 (s, $C_{sp2}H$), 700 (vs, $C_{sp2}H$).

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ [ppm] = 1.19 (s, 6 H, 2 × CH_3), 1.85 - 1.93 (m, 2 H, H-2'), 2.34 (ddd, ^{3}J = 7.9 Hz, ^{3}J = 6.9 Hz, ^{4}J = 1.2 Hz, 2 H, H-1'), 2.66 (t, ^{3}J = 7.6 Hz, 2 H, H-3'), 5.89 (dd, ^{4}J = 1.4 Hz, ^{5}J = 0.7 Hz, 1 H, H-2), 6.04 (dd, ^{3}J = 9.5 Hz, ^{4}J = 1.4 Hz, 1 H, H-4), 6.27 (dd, ^{3}J = 9.5 Hz, ^{5}J = 0.7 Hz, 2 H, H-5), 7.16 - 7.19 (m, 2 H, $H_{p\text{-Ar}}$), 7.19 - 7.22 (m, 1 H, $H_{m\text{-Ar}}$), 7.27 - 7.32 (m, 2 H, $H_{o\text{-Ar}}$).

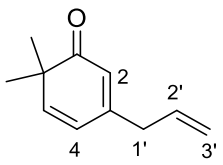
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.7 (q, 2 × CH_3), 29.3 (t, C-2'), 35.4 (t, C-3'), 35.9 (t, C-1'), 46.3 (s, C-6), 122.2 (d, C-4), 122.4 (d, C-2), 126.2 (s, $C_{p\text{-Ar}}$), 128.6 (d, 2 × $C_{o\text{-Ar}}$), 128.6 (d, 2 × $C_{m\text{-Ar}}$), 141.7 (s, $C_{i\text{-Ar}}$), 148.4 (d, C-5), 157.4 (s, C-3), 205.8 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 240 (9) $[M]^+$, 136 (12) $[M–C_8H_8]^+$, 105 (40) $[C_8H_9]^+$, 91 (43) $[C_7H_7]^+$, 77 (34) $[C_6H_5]^+$, 56 (32) $[M–CH_3]^+$, 42 (100) $[C_3H_6]^+$.

HRMS (EI, 70 eV): calc. for $C_{17}H_{20}O$ $[M]^+$: 240.1509; found: 240.1507.

calc. for $C_{16}{}^{13}CH_{20}O$ $[M]^+$: 241.1542; found: 241.1543.

3-Allyl-6,6-dimethylcyclohexa-2,4-dien-1-one (188)



$C_{11}H_{14}O$
MW = 162.23 g/mol

Following GP3, 500 mg cyclohexadienone **183** (4.09 mmol, 1.00 equiv.) were converted with 4.91 mL (1.0 M in diethyl ether, 4.91 mmol, 1.20 equiv.) in one hour.

Following GP5, the resulting tertiary allylic alcohol was converted with 1.69 g pyridinium dichromate (4.50 mmol, 1.10 equiv.) in one hour. After purification by column chromatography (silica, P/Et_2O = 95/5 → 94/6 → 92/8) 210 mg cyclohexadienone **188** (1.29 mmol, 32%) were obtained as a pale yellow oil.

TLC: R_f = 0.40 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2967 (w, $C_{sp3}H$), 1660 (vs, C=O), 1642 (vs, C=C), 1571 (w, $C_{sp3}H$), 1372 (w), 1180 (w, $C_{sp3}H$), 920 (w, $C_{sp2}H$).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.19 (s, 6 H, 2 × CH_3), 3.07 (dq, ^3J = 6.8 Hz, ^4J = 1.4 Hz, 2 H, H-1'), 5.12 - 5.20 (m, 2 H, H-3'), 5.83 (ddt, ^3J = 17.0 Hz, ^3J = 10.2 Hz, ^3J = 6.8 Hz, 1 H, H-2'), 5.88 - 5.91 (m, 1 H, H-2), 6.05 (dd, ^3J = 9.5 Hz, ^4J = 1.4 Hz, 1 H, H-4), 6.28 (dd, ^3J = 9.5 Hz, 1 H, H-5).

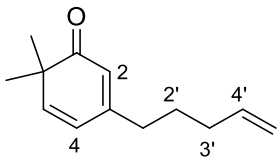
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.6 (q, 2 × CH_3), 40.6 (t, C-1'), 46.3 (s, C-6), 118.5 (t, C-3'), 122.0 (d, C-4), 122.7 (d, C-2), 133.4 (d, C-2'), 148.4 (d, C-5), 155.3 (s, C-3), 205.8 (s, C-1).

MS (EI, 70 eV): *m/z* (%) = 164 (100) $[M]^+$, 147 (53) $[M–CH_3]^+$, 121 (82) $[C_8H_7O]^+$, 105 (28) $[C_7H_5O]^+$, 91 (84) $[C_7H_7]^+$, 77 (31) $[C_6H_5]^+$.

HRMS (EI, 70 eV): calc. for $C_{11}H_{14}O$ $[M]^+$: 162.1039; found: 162.1033;

calc. for $C_{10}{}^{13}CH_{14}O$ $[M]^+$: 163.1073; found: 163.1071.

6,6-Dimethyl-3-(pent-4-en-1-yl)cyclohexa-2,4-dien-1-one (189)



$C_{13}H_{18}O$
MW = 190.29 g/mol

Following GP3, 300 mg cyclohexadienone **183** (2.46 mmol, 1.00 equiv.) were converted with 119 mg magnesium (4.91 mmol, 2.00 equiv.) and 582 µL 5-bromo-1-pentene (732 mg, 4.91 mmol, 2.00 equiv.) in 75 minutes.

Following GP5, the resulting tertiary allylic alcohol was converted with 1.02 g pyridinium dichromate (2.71 mmol, 1.10 equiv.) in one hour. After purification by column chromatography

(silica, P/Et_2O = 19/1) 147 mg cyclohexadienone **189** (773 µmol, 31%) were obtained as a pale yellow oil.

TLC: R_f = 0.42 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3422 (w, $C_{sp2}H$), 2974 (s, $C_{sp3}H$), 2930 (s, $C_{sp3}H$), 1675 (vs, C=O), 1459 (m, $C_{sp3}H$), 1385 (m), 1154 (m, $C_{sp3}H$), 994 (m, $C_{sp2}H$), 913 (s, $C_{sp2}H$).

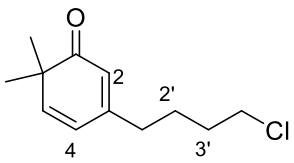
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.19 (s, 6 H, 2 × CH_3), 1.65 (tt, ^3J = 8.8 Hz, ^3J = 6.9 Hz, 2 H, H-2'), 2.10 (tdt, ^3J = 7.8 Hz, ^3J = 6.6 Hz, ^4J = 1.4 Hz, 2 H, H-3'), 2.32 (td, ^3J = 7.7 Hz, ^4J = 1.0 Hz, 2 H, H-1'), 4.97 - 5.07 (m, 2 H, H-5'), 5.80 (ddt, ^3J = 17.0 Hz, ^3J = 10.2 Hz, ^3J = 6.7 Hz, 1 H, H-4'), 5.87 (dt, ^4J = 1.7 Hz, ^4J = 1.0 Hz, 1 H, H-2), 6.05 (dd, ^3J = 9.5 Hz, ^4J = 1.7 Hz, 1 H, H-4), 6.27 (d, ^3J = 9.5 Hz, 1 H, H-5).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.7 (q, 2 × CH_3), 26.8 (t, C-2'), 33.2 (t, C-3'), 35.8 (t, C-1'), 46.3 (s, C-6), 115.5 (t, C-5'), 122.3 (d, C-4), 122.4 (d, C-2), 138.0 (d, C-4'), 148.4 (d, C-5), 157.5 (s, C-3), 205.8 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 190 (36) $[M]^+$, 175 (81) $[M–CH_3]^+$, 147 (56) $[M–C_3H_7]^+$, 136 (50) $[M–C_4H_7]^+$, 121 (56) $[C_8H_9O]^+$, 108 (62) $[C_7H_8O]^+$, 91 (100) $[C_7H_7]^+$, 77 (42) $[C_6H_5]^+$.

HRMS (EI, 70 eV): calc. for $C_{13}H_{18}O$ $[M]^+$: 190.1352; found: 190.1349.

6,6-Dimethyl-3-(4-chlorobutyl)cyclohexa-2,4-dien-1-one (190)



$C_{12}H_{17}ClO$
MW = 212.72 g/mol

Following GP3, 500 mg cyclohexadienone **183** (4.09 mmol, 1.00 equiv.) were converted with 199 mg magnesium (8.19 mmol, 2.00 equiv.) and 944 µL 1-bromo-4-chlorobutane (1.40 g, 8.19 mmol, 2.00 equiv.) in one hour.

Following GP5, the resulting tertiary allylic alcohol was converted with 1.69 g pyridinium dichromate (4.50 mmol, 1.10 equiv.) in one hour. After purification by column chromatography (silica, P/Et_2O = 19/1 → 9/1) 189 mg cyclohexadienone **190** (1.36 mmol, 34%) were obtained as a pale yellow oil.

TLC: R_f = 0.36 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2964 (m, $C_{sp3}H$), 2867 (m, $C_{sp3}H$), 1659 (vs, C=O), 1640 (s, C=C), 1570 (m), 1458 (s, $C_{sp3}H$), 1372 (m, $C_{sp3}H$), 1182 (m, $C_{sp3}H$), 1007 (m), 933 (w), 869 (w, $C_{sp2}H$), 775 (m, CCl).

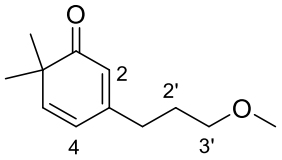
^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ [ppm] = 1.19 (s, 6 H, 2 × CH_3), 1.69 - 1.76 (m, 2 H, H-2'), 1.78 - 1.85 (m, 2 H, H-3'), 2.35 (td, ^3J = 7.5 Hz, ^3J = 1.3 Hz, 2H, H-1'), 3.56 (t, ^3J = 6.4 Hz, 2 H, H-4'), 5.86 - 5.88 (m, 1 H, H-2), 6.06 (dd, ^3J = 9.5 Hz, ^3J = 1.5 Hz, 1 H, H-4), 6.29 (dd, ^3J = 9.5 Hz, ^4J = 0.6 Hz, 1 H, H-5).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 24.9 (t, C-2'), 25.6 (q, 2 × CH_3), 32.0 (t, C-3'), 35.6 (C-1'), 44.7 (t, C-4'), 46.3 (s, C-6), 122.0 (d, C-4), 122.4 (d, C-2), 148.6 (d, C-5), 156.8 (s, C-4), 205.7 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 212 (64) $[M]^+$, 177 (21) $[M–Cl]^+$, 149 (57) $[M–C_{11}H_{10}NO_2]^+$, 135 (54) $[C_9H_{10}O]^+$, 121 (33) $[C_8H_9O]^+$, 107 (100) $[C_8H_{11}]^+$, 91 (67) $[C_7H_7]^+$, 77 (29) $[C_6H_5]^+$, 65 (13) $[C_5H_5]^+$.

HRMS (EI, 70 eV): calc. for $C_{12}H_{17}{}^{35}ClO$ $[M]^+$: 212.0962; found: 212.0957.

3-(3-Methoxybutyl)-6,6-dimethylcyclohexa-2,4-dien-1-one (191)



$C_{12}H_{18}O_2$
MW = 194.27 g/mol

Following GP3, 500 mg cyclohexadienone **183** (4.09 mmol, 1.00 equiv.) were converted with 199 mg magnesium (8.19 mmol, 2.00 equiv.) and 919 µL 1-bromo-3-methoxypropane (1.25 g, 8.19 mmol, 2.00 equiv.) in one hour.

Following GP5, the resulting tertiary allylic alcohol was converted with 1.69 g pyridinium dichromate (4.50 mmol, 1.10 equiv.) in 45 minutes. After purification by column chromatography (silica, P/Et_2O = 4/1 → 2/1) 270 mg cyclohexadienone **191** (1.39 mmol, 34%) were obtained as a pale yellow oil.

TLC: R_f = 0.36 (P/Et_2O = 1/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2926 (s, $C_{sp3}H$), 2870 (s, $C_{sp3}H$), 1659 (vs, C=O), 1640 (s, C=C), 1570 (m), 1372 (m, $C_{sp3}H$), 1182 (m, COC), 1118 (s, COC), 893 (w, $C_{sp2}H$), 778 (w).

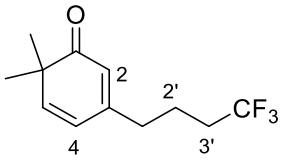
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.19 [s, 6 H, C-6(CH_3)$_2$], 1.78 - 1.85 (m, 2 H, H-2‘), 2.40 (td, ^3J = 7.6 Hz, ^4J = 1.2 Hz, 2 H, H-1‘), 3.34 (s, 3 H, OCH_3), 3.40 (t, ^3J = 6.3 Hz, 2 H, H-3‘), 5.88 (dt, ^4J = 1.4 Hz, ^4J = 1.2 Hz, 1 H, H-2), 6.07 (dd, ^3J = 9.5 Hz, ^4J = 1.4 Hz, 1 H, H-4), 6.28 (d, ^3J = 9.5 Hz, 1 H, H-5).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.7 [q, C-6(CH_3)$_2$], 27.7 (t, C-2’), 33.1 (t, C-1’), 46.3 (s, C-6), 58.8 (q, OCH_3), 71.7 (t, C-3’), 122.2 (d, C-4), 122.3 (d, C-2), 148.4 (d, C-5), 157.2 (s, C-3), 205.8 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 194 (93) $[M]^+$, 149 (44) $[M–C_2H_5O]^+$, 136 (78) $[M– C_3H_6O]^+$, 121 (60) $[C_8H_9O]^+$, 108 (45) $[C_7H_8O]^+$, 91 (100) $[C_7H_7]^+$, 77 (39) $[C_6H_5]^+$.

HRMS (EI, 70 eV): calc. for $C_{12}H_{18}O$ $[M]^+$: 194.1301; found: 194.1301.

6,6-Dimethyl-3-(4,4,4-trifluorbutyl)cyclohexa-2,4-dien-1-one (192)



$C_{12}H_{15}F_3O$
MW = 232.25 g/mol

Following GP3, 300 mg cyclohexadienone **183** (2.46 mmol, 1.00 equiv.) were converted with 119 mg magnesium (4.91 mmol, 2.00 equiv.) and 603 µL 1-bromo-4,4,4-trifluorobutane (938 mg, 4.91 mmol, 2.00 equiv.) in one hour.

Following GP5, the resulting tertiary allylic alcohol was converted with 1.02 g pyridinium dichromate (2.71 mmol, 1.10 equiv.) in one hour. After purification by column chromatography (silica, P/Et_2O = 9/1 → 6/1 → 4/1) 209 mg cyclohexadienone **192** (89.8 µmol, 37%) were obtained as a pale yellow oil.

TLC: R_f = 0.13 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3422 (w, $C_{sp2}H$), 2976 (s, $C_{sp3}H$), 1720 (vs, C=O), 1677 (vs, C=C), 1389 (m), 1253 (s), 1133(s, $C_{sp3}H$), 1016 (m).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.20 (s, 6 H, 2 × CH_3), 1.80 - 1.88 (m, 1 H, H-2'), 2.06 - 2.18 (m, H-3'), 2.40 (d, ^3J = 7.7 Hz, H-1'), 5.86 - 5.88 (m, 1 H, H-2), 6.05 (dd, ^3J = 9.5 Hz, ^4J = 1.5 Hz, H-4), 6.31 (d, ^3J = 9.5 Hz, 1 H, H-5).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 20.1 (q, $^3J_{CF}$ = 3.0 Hz, C-2'), 25.6 (q, 2 × CH_3), 33.2 (q, $^2J_{CF}$ = 28.7 Hz, C-3'), 35.1 (t, C-1'), 46.4 (s, C-6), 121.6 (d, C-4), 122.7 (d, C-2), 127.0 (q, $^1J_{CF}$ = 276 Hz, CF_3), 149.0 (d, C-5), 155.5 (C-3), 205.6 (s, CO).

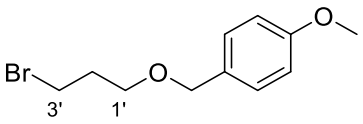
^{19}F NMR (376 MHz, $CDCl_3$, 300 K): δ [ppm] = –66.8 (t, $^3J_{HF}$ = 10.6 Hz, CF_3)

MS (EI, 70 eV): *m/z* (%) = 232 (74) $[M]^+$, 217 (14) $[M–CH_3]^+$, 149 (16) $[M–C_2H_2F_3]^+$, 135 (36) $[C_9H_{11}O]^+$, 121 (16) $[C_8H_9O]^+$, 107 (100) $[C_8H_{11}]^+$, 91 (51) $[C_7H_7]^+$, 79 (25) $[C_6H_7]^+$, 65 (10) $[C_5H_5]^+$, 51 (8) $[CHF_2]^+$.

HRMS (EI, 70 eV): calc. for $C_{12}H_{15}FO_3$ $[M]^+$: 232.1070; found: 232.1069.

calc. for $C_{11}{}^{13}CH_{15}FO_3$ $[M]^+$: 233.1103; found: 233.1106.

1-[(3-Bromopropoxy)methyl]-4-methoxybenzene (194)



$C_{11}H_{15}BrO_2$
MW = 259.14 g/mol

To a solution of 1.60 mL 3-bromopropanol (2.46 g, 17.7 mmol, 1.00 equiv.) and 3.67 mL 4-methoxybenzyl-2,2,2-trichloroacetimidate (5.00 g, 17.7 mmol, 1.00 equiv.) in 60 mL dichloromethane were added 411 mg camphorsulfonic acid (1.77 mmol, 0.10 equiv.) and the reaction mixture was stirred at room temperature for 24 hours. Saturated sodium bicarbonate solution (30 mL) was added and the mixture extracted with dichloromethane (3 × 30 mL). The combined organic layers were washed with brine, dried over sodium sulfate and the solvent was removed in vacuo. After purification by column chromatography (silica, P/Et_2O = 39/1 → 19/1) 2.25 g methoxybenzyl ether **194** (8.68 mmol, 49%) were obtained as a colourless oil.

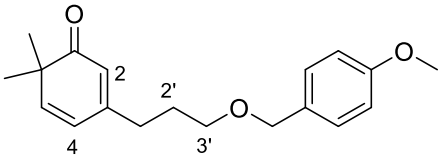
TLC: R_f = 0.32 (P/Et_2O = 19/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 2.08 - 2.16 (m, 2 H, H-2'), 3.53 (t, ^3J = 6.6 Hz, 2 H, H-1'), 3.58 (t, ^3J = 5.9 Hz, 2 H, H-3'), 3.81 (s, 3 H, OCH_3), 4.45 [s, 2 H, $C_{Ar}(CH_2)O$], 6.86 - 6.91 (m, 2 H, $H_{m\text{-}Ar}$), 7.23 - 7.29 (m, 2 H, $H_{o\text{-}Ar}$).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 30.9 (t, C-1'), 33.0 (t, C-2'), 55.4 (q, OCH_3), 67.5 (t, C-3'), 73.0 [t, $C_{Ar}(CH_2)O$], 113.9 (d, 2 × $C_{m\text{-}Ar}$), 129.4 (d, 2 × $C_{o\text{-}Ar}$), 130.4 (s, $C_{i\text{-}Ar}$), 159.4 (s, $C_{p\text{-}Ar}$).

The analytical data obtained matched those reported in the literature. [130]

3-{3-[(4-Methoxybenzyl)oxy]propyl}-6,6-dimethylcyclohexa-2,4-dien-1-one (193)



$C_{19}H_{24}O_3$
MW = 300.40 g/mol

Following GP3, 500 mg cyclohexadienone **183** (4.09 mmol, 1.00 equiv.) were converted with 199 mg magnesium (8.19 mmol, 2.00 equiv.) and 2.12 g methoxybenzyl ether **194** (8.19 mmol, 2.00 equiv.) in three hours.

Following GP5, the resulting tertiary allylic alcohol was converted with 1.69 g pyridinium dichromate (4.50 mmol, 1.10 equiv.) in 45 minutes. After purification by column chromatography (silica, P/Et_2O = 4/1) 688 mg cyclohexadienone **193** (2.29 mmol, 56%) were obtained as a pale yellow oil.

TLC: R_f = 0.40 (P/Et_2O = 1/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3420 (w, $C_{sp2}H$), 2927 (m, $C_{sp3}H$), 2866 (m, $C_{sp3}H$), 1715 (s, C=O), 1673 (s, C=C), 1605 (s, C=C), 1511 (s, C=C), 1372 (m, $C_{sp3}H$), 1246 (vs, COC), 1098 (s), 1031 (s), 820 (w, $C_{sp2}H$), 772 (w).

^{1}HNMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.18 (s, 6 H, 2 × CH_3), 1.84 (ddt, ^3J = 9.0 Hz, ^3J = 7.6 Hz, ^3J = 6.2 Hz, 2 H, H-2'), 2.41 (*virt.* td, $^3J \cong {}^3J$ = 7.6 Hz, ^4J = 1.2 Hz, H-1'), 3.46 (t, ^3J = 6.2 Hz, 2 H, H-3'), 3.81 (s, 3 H, OCH_3), 4.43 [s, 2 H, $C_{Ar}(CH_2)O$], 5.86 - 5.88 (m, 1 H, H-2), 6.05 (dd, ^3J = 9.5 Hz, ^4J = 1.5 Hz, 1 H, H-4), 6.26 (dd, ^3J = 9.5 Hz, ^5J = 0.6 Hz, 1 H, H-5), 6.86 - 6.90 (m, 2 H, $H_{m\text{-}Ar}$), 7.23 - 7.27 (m, 2 H, $H_{o\text{-}Ar}$).

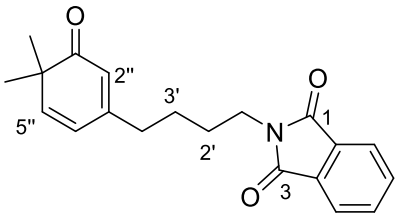
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.6 (q, 2 × CH_3), 27.8 (t, C-2'), 33.2 (t, C-1'), 46.2 (s, C-6), 55.4 (q, OCH_3), 68.9 (t, C-3'), 72.8 [t, $C_{Ar}(CH_2)O$], 113.9 (d, 2 × $C_{m\text{-}Ar}$), 122.2 (d, C-4), 122.3 (d, C-2), 129.5 (d, 2 × $C_{o\text{-}Ar}$), 130.5 (s, $C_{i\text{-}Ar}$), 148.4 (d, C-5), 157.3 (s, C-3), 159.3 (s, $C_{p\text{-}Ar}$), 205.8 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 300 (5) $[M]^+$, 285 (4) $[M–CH_3]^+$, 136 (7) $[C_9H_{11}O]^+$, 121 (100) $[C_8H_9O]^+$, 91 (8) $[C_7H_7]^+$, 77 (7) $[C_6H_5]^+$.

HRMS (EI, 70 eV): calc. for $C_{19}H_{24}O_3$ $[M]^+$: 300.1720; found: 300.1720.

calc. for $C_{18}{}^{13}CH_{24}O_3$ $[M]^+$: 301.1754 found: 301.1572.

2-[4-(4,4-dimethyl-3-oxocyclohexa-1,5-dien-1-yl)butyl]isoindoline-1,3-dione (195)



$C_{20}H_{21}NO_3$
MW = 323.39 g/mol

To a solution of 102 mg *N*-Chlorophthalimide (102 mg, 1.20 equiv.) in 1.0 mL dimethyl sulfoxide were added 84.4 µL 1,8-diazabicyclo[5.4.0]-7-undecene (85.9 mg, 564 µmol, 1.20 equiv.) and 100 mg chlorobutylcyclohexadienone **190** (470 µmol, 1.00 equiv.). The reaction mixture was stirred at room temperature for 15 minutes and subsequently heated to 60 °C for four hours. After cooling to room temperature, water (10 mL) was added and the mixture extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed with brine, dried over sodium sulfate and the solvent was removed in vacuo. After purification by column chromatography (silica, P/Et_2O = 4/1 → 3/1) 69.3 mg cyclohexadienone **195** (214 µmol, 46%) were obtained as a colourless solid.

Mp: 82 °C.

TLC: R_f = 0.09 (P/Et_2O = 2:1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2930 (m, $C_{sp3}H$), 1770 (w, C=O), 1707 (vs, C=O), 1675 (vs, C=C), 1396 (s, $C_{sp3}H$), 1037 (w), 720 (s, $C_{sp2}H$).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.18 (s, 6 H, 2 × CH_3), 1.57 - 1.64 (m, 2 H, H-3'), 1.69 - 1.78 (m, 2 H, H-2'), 2.36 (td, ^3J = 7.7 Hz, ^4J = 1.2 Hz, 2 H, H-4'), 3.72 (t, ^3J = 7.1 Hz, 2 H, H-1'), 5.85 (*virt.* qd, $^4J \cong {}^4J$ = 1.6 Hz, ^5J = 0.8 Hz, 1 H, H-2''), 6.05 (dd,

^{3}J = 9.5 Hz, ^{4}J = 1.5 Hz, 1 H, H-6''), 6.27 (dd, ^{3}J = 9.5 Hz, ^{5}J = 0.8 Hz, 1 H, H-5''), 7.72 (dd, ^{3}J = 5.4 Hz, ^{3}J = 3.0 Hz, 2 H, H_{Ar}), 7.85 (dd, ^{3}J = 5.4 Hz, ^{3}J = 3.0 Hz, 2 H, H_{Ar}).

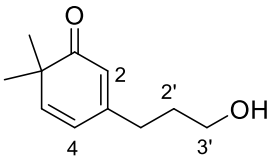
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.0 (t, C-3'), 25.7 (q, 2 × CH_3), 28.3 (t, C-2'), 36.0 (t, C-4'), 37.6 (t, C-1'), 46.3 (s, C-4''), 122.1 (d, C-6''), 122.4 (d, C-2''), 123.4 (d, 2 × C_{Ar}), 132.2 (s, 2 × C_{Ar}), 134.1 (d, 2 × C_{Ar}), 148.6 (d, C-5''), 157.0 (C-1''), 168.6 [$N(CO)_2$], 205.8 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 323 (72) $[M]^+$, 160 (73) $[C_9H_6NO_2]^+$, 149 (88) $[M–C_{11}H_{10}NO_2]^+$, 136 (100) $[C_9H_{11}O]^+$, 121 (16) $[C_8H_9O]^+$, 105 (37) $[C_8H_9]^+$, 91 (54) $[C_7H_7]^+$, 77 (39) $[C_6H_5]^+$.

HRMS (EI, 70 eV): calc. for $C_{20}H_{21}NO_3$ $[M]^+$: 323.1516; found: 323.1516.

calc. for $C_{19}{}^{13}CH_{21}NO_3$ $[M]^+$: 324.1550; found: 324.1553.

3-(3-Hydroxypropyl)-6,6-dimethylcyclohexa-2,4-dien-1-one (197)



$C_{11}H_{16}O_2$
MW = 180.25 g/mol

To a solution of 200 mg cyclohexadienone **193** (666 µmol, 1.00 equiv.) in 2.0 mL dichloromethane and 0.1 mL water were added 453 mg 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (2.00 mmol, 3.00 equiv.) and the reaction mixture was stirred at room temperature for two hours. Saturated sodium bicarbonate solution (5 mL) was added, the mixture filtered through celite and extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine, dried over sodium sulfate and the solvent was removed in vacuo. After purification by column chromatography (silica, Et_2O/P = 2/1) 101 mg alcohol **197** (560 µmol, 84%) was obtained as a pale yellow oil.

TLC: R_f = 0.25 (Et_2O) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3420 (*br*, OH), 2977 (m, $C_{sp3}H$), 2970 (m, $C_{sp3}H$), 1717 (vs, C=O), 1678 (vs, C=C), 1386 (w), 1057 (s, C-O), 749 (s, $C_{sp2}H$), 733 (vs, $C_{sp2}H$).

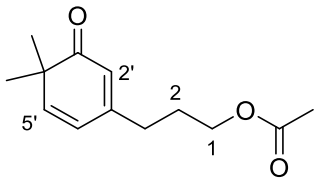
^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ [ppm] = 1.19 (s, 6 H, 2 × CH_3), 1.35 (t, ^3J = 5.0 Hz, 1 H, OH), 1.82 (ddt, ^3J = 9.1 Hz, ^3J = 7.6 Hz, ^3J = 6.3 Hz, 2 H, H-2'), 2.40 - 2.46 (2 H, H-1'), 3.70 (td, ^3J = 6.3 Hz, ^3J = 5.0 Hz, 2 H, H-3'), 5.90 (1 H-2), 6.08 (1 H, H-4), 6.29 (1 H, H-5).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.7 (q, 2 × CH_3), 30.5 (t, C-2'), 32.8 (t, C-1'), 46.3 (s, C-6), 62.1 (t, C-3'), 122.2 (d, C-4), 122.3 (d, C-2), 148.5 (s, C-3), 157.1 (d, C-5), 205.8 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 222 (42) $[M]^+$, 180 (100) $[M–C_2H_2O_2]^+$, 162 (19) $[]^+$, 147 (42) $[]^+$, 137 (25) $[]^+$, 119 (63) $[]^+$, 107 (34) $[C_8H_9O]^+$, 91 (77) $[C_7H_7]^+$, 77 (26) $[C_6H_5]^+$, 65 (11) $[C_5H_5]^+$, 53 (8).

HRMS (ESI): calc. for $C_{11}H_{16}O_2$ $[M+H]^+$: 181.1223; found: 181.1224.

3-(4,4-Dimethyl-3-oxocyclohexa-1,5-dien-1-yl)propyl acetate (196)



$C_{13}H_{18}O_3$
MW = 222.28 g/mol

To a solution of 90.0 mg alcohol **197** (499 µmol, 1.00 equiv.) in 161 µL pyridine (158 mg, 2.00 mmol, 4.00 equiv.) were added 142 µL acetic anhydride (153 mg, 1.50 mmol, 3.00 equiv.) and the reaction mixture was stirred at room temperature for three hours. Saturated ammonium chloride solution (2 mL) was added and the mixture extracted with diethyl ether (3 × 5 mL). The combined organic layers were washed with saturated copper(II) sulfate solution (2 mL), brine, dried over sodium sulfate and the solvent was removed in vacuo. After purification by column chromatography (silica, P/Et_2O = 2/1) 87.3 mg acetate **196** (392 µmol, 79%) was obtained as a pale yellow oil.

TLC: R_f = 0.33 (P/Et_2O = 1/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3489 (w, $C_{sp2}H$), 2943 (s, $C_{sp3}H$), 2868 (m, $C_{sp3}H$), 1663 (vs, C=C), 1447 (m, $C_{sp3}H$), 1436 (m), 1385 (w), 1211 (m, C-O), 869 (s, $C_{sp2}H$).

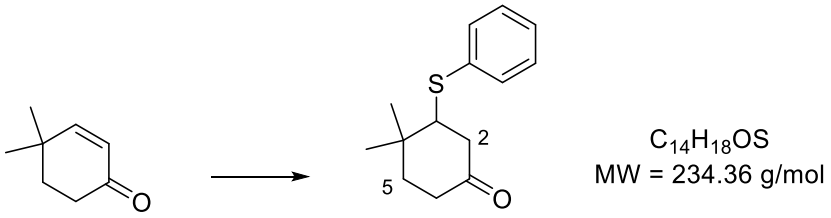
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.19 [s, 6 H, C-6(CH_3)$_2$], 1.86 - 1.93 (m, 2 H, H-2'), 2.06 (s, 3 H, $COOCH_3$), 2.40 (td, ^3J = 7.4 Hz, ^4J = 1.2 Hz, 2 H, H-1'), 4.10 (t, ^3J = 6.5 Hz, 2 H, H-3'), 5.87 - 5.90 (m, 1 H, H-2), 6.05 (dd, ^3J = 9.5 Hz, ^4J = 1.5 Hz, 1 H, H-4), 6.29 (d, ^3J = 9.5 Hz, 1 H, H-5).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 21.1 (OCO*C*H_3), 25.6 [q, C-6(*C*H_3)$_2$], 26.7 (t, C-2'), 32.9 (t, C-1'), 46.3 (C-6), 63.6 (t, C-3'), 122.0 (d, C-4), 122.4 (d, C-2), 148.7 (d, C-5), 156.2 (s, C-3), 171.2 (s, O*C*OCH_3), 205.6 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 222 (36) $[M]^+$, 180 (100) $[M–C_2H_2O]^+$, 162 (18) $[M–C_2H_4O_2]^+$, 147 (34) $[M–C3H_7O_2]^+$, 136 (26) $[M–C_4H_6O_2]^+$, 119 (39) $[C_8H_7O]^+$, 107 (40) $[C_8H_7O]^+$, 91 (43) $[C_7H_7]^+$, 79 (20) $[C_6H_7]^+$, 55 (15), 43 (84) $[C_2H_3O]^+$.

HRMS (EI, 70 eV): calc. for CHO $[M]^+$: 222.1250; found: 222.1253.

4,4-Dimethyl-3-(phenylthio)cyclohexan-1-one (199)



$C_{14}H_{18}OS$
MW = 234.36 g/mol

According to a modified literature procedure[131]: To a solution of 10.6 mL 4,4-dimethylcyclohex-2-en-1-one (10.0 g, 80.5 mmol, 1.00 equiv.) in 130 mL chloroform were added 2.24 mL triethylamine (1.63 g, 16.1 mmol, 0.20 equiv.) and 9.04 mL thiophenol (9.76 g, 88.6 mmol, 1.10 equiv.). The mixture was stirred at room temperature for 3.5 hours and

subsequently filtered through a silica plug. The solvent was evaporated in vacuo and the solid washed with hexane (15 mL). The crude thioether **199** was directly used without further purification.

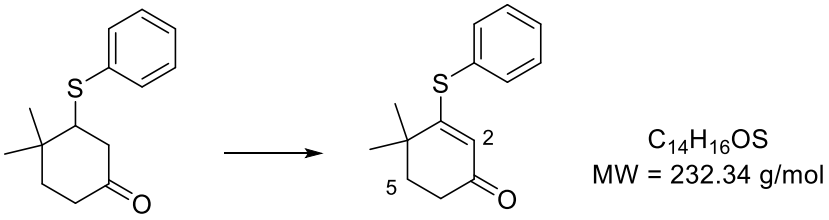
TLC: R_f = 0.22 (P/Et_2O = 4/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ [ppm] = 1.22 (s, 3 H, CH_3), 1.28 (s, 3 H, CH_3), 1.65 (ddd, ^2J = 13.9 Hz, ^3J = 12.3 Hz, ^3J = 5.1 Hz, 1 H, H-5), 1.90 (ddd, ^2J = 13.9 Hz, ^3J = 6.1 Hz, ^3J = 4.3 Hz, 1 H, H-5), 2.31 (dddd, ^2J = 15.3 Hz, ^3J = 5.1 Hz, ^3J = 4.3 Hz, ^4J = 2.0 Hz, 1 H, H-6), 2.46 (dddd, ^2J = 15.3 Hz, ^3J = 12.3 Hz, ^3J = 6.1 Hz, ^4J = 1.0 Hz, 1 H, H-6), 2.56 (ddd, ^2J = 15.2 Hz, ^3J = 11.1 Hz, ^4J = 1.0 Hz, 1 H, H-2), 2.63 (ddd, ^2J = 15.2 Hz, ^3J = 4.9 Hz, ^4J = 2.0 Hz, 1 H, H-2), 3.18 (dd, ^3J = 11.1 Hz, ^3J = 4.9 Hz, 1 H, H-3), 7.22 - 7.26 (m, 1 H, $H_{p\text{-Ar}}$), 7.27 - 7.32 (m, 2 H, $H_{m\text{-Ar}}$), 7.38 - 7.43 (m, 2 H, $H_{o\text{-Ar}}$).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 21.1 (q, CH_3), 29.2 (q, CH_3), 34.8 (s, C-4), 38.0 (t, C-6), 38.8 (t, C-5), 45.6 (t, C-2), 57.8 (d, C-3), 127.6 (d, $C_{p\text{-Ar}}$), 129.3 (d, 2 × $C_{o\text{-Ar}}$), 132.9 (d, 2 × $C_{m\text{-Ar}}$), 134.7 (s, C_{Ar}), 209.3 (s, CO).

The analytical data obtained matched those reported in the literature.[131]

4,4-Dimethyl-3-(phenylthio)cyclohex-2-en-1-one (198)



According to a modified literature procedure[131]: To a solution of crude thioether **199** in 160 mL dichloromethane were added 11.2 g *N*-chlorosuccinimide (83.8 mmol, 1.04 equiv.) at

0 °C and the reaction mixture was stirred at unchanged temperature for 4 hours. The formed precipitate was filtered off and the solvent evaporated before 12.8 mL triethylamine (9.37 g, 92.6 mmol, 1.15 equiv.) and 160 mL chloroform were added and the reaction mixture heated under reflux for three hours. The mixture was cooled to room temperature and stirred for 16 hours. 1 M aqueous sodium hydroxide solution (100 mL) was added and the aqueous phase extracted with dichloromethane (2 × 100 mL). The combined organic layers were washed with brine, dried over sodium sulfate, and the solvent was removed in vacuo. After purification by column chromatography (silica, Hex/EtOAc = 9/1) 8.66 g vinylogous thioester **198** (37.3 mmol, 46% over two steps) was obtained as a colourless oil.

Mp: 98 °C.

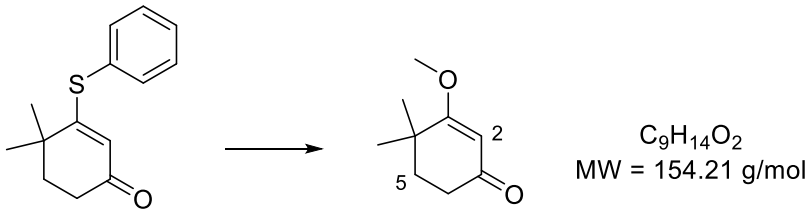
TLC: R_f = 0.10 (Hex/EtOAc = 9/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ [ppm] = 1.42 (s, 2 × CH_3), 1.93 (t, ^3J = 6.8 Hz, 2 H. H-5), 2.42 (t, ^3J = 6.8 Hz, 2 H, H-6), 5.29 (s, 1 H, H-2), 7.40 - 7.47 (m, 5 H, H_{Ar}).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 27.8 (q, 2 × CH_3), 34.2 (t, C-6), 37.5 (s, C-4), 37.9 (t, C-5), 120.6 (d, C-2), 128.6 (s, C_{Ar}), 130.1 (d, 2 × $C_{o\text{-}Ar}$), 130.2 (d, $C_{p\text{-}Ar}$), 136.0 (d, 2 × $C_{m\text{-}Ar}$), 177.2 (s, C-3), 195.8 (s, CO).

The analytical data obtained matched those reported in the literature.[131]

3-Methoxy-4,4-dimethylcyclohex-2-en-1-one (200)



$C_9H_{14}O_2$
MW = 154.21 g/mol

In a 250 mL flask, 18 mL dimethylsulfoxide were added to 3.81 g potassium hydride in mineral oil (25 wt%, 23.7 mmol, 1.5 equiv.) and the mixture stirred until gas evolution ceased (two hours). 963 µL methanol in 36 mL dimethyl sulfoxide were added and the mixture was stirred for 30 minutes before 3.68 g vinologous thioester **198** (15.8 mmol, 1.00 equiv.) in 108 mL dimethyl sulfoxide were added and the reaction mixture was stirred for 16 hours at room temperature. Water was added and the aqueous phase extracted with diethyl ether (3 × 110 mL). The combined organic layers were washed with brine, dried over sodium sulfate and the solvent was removed in vacuo. The crude vinylogous ester **200** was directly used without further purification.

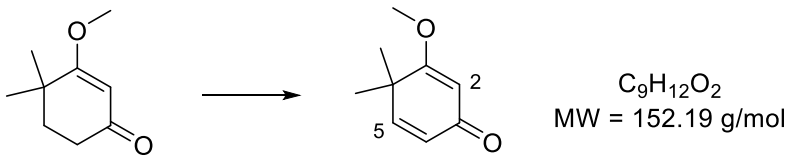
TLC: R_f = 0.44 (Et2O = 100%) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.20 [s, 6 H, C-4(CH_3)$_2$], 1.82 (dd, ^3J = 7.2 Hz, ^3J = 6.3 Hz, 1 H, H-5), 2.38 - 2.43 (m, 2 H, H-6), 3.67 (s, 3 H, OCH_3), 5.26 (s, 1 H, H-2).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.8 [q, C-4(CH_3)$_2$], 34.0 (t, C-6), 35.9 (s, C-4), 36.5 (t, C-5), 56.0 (q, OCH_3), 101.0 (d, C-2), 184.0 (s, C-3), 199.8 (s, CO).

The analytical data obtained matched those reported in the literature.[127]

3-Methoxy-4,4-dimethylcyclohexa-2,5-dien-1-one (201)



To crude vinologous ester **200** in 58 mL 1,4-dioxane were added 5.39 g 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (23.7 mmol, 1.5 equiv.) and 571 mg *para*-toluenesulfonic acid hydrate (3.00 mmol, 0.19 equiv.) and the reaction mixture was heated under reflux for 16 hours. The solvent was removed in vacuo and the residue dissolved in diethyl ether (500 mL). The resulting solution was washed with 1 M aqueous sodium hydroxide solution (450 mL), 1 M aqueous hydrochloric acid solution (300 mL), 1 M aqueous sodium hydroxide solution (2 × 300 mL) and brine, dried over sodium sulfate and the solvent was removed in vacuo. After purification by vacuum distillation (2.1 mbar, 100 °C oil bath temperature) 732 mg cyclohexadienone **201** (4.81 mmol, 30% over two steps) were obtained as a colourless oil.

Bp: 80 °C (2.1 mbar).

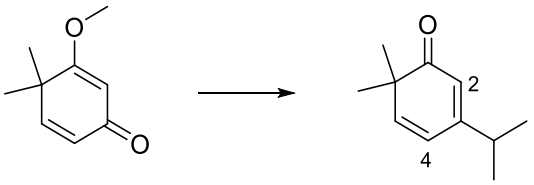
TLC: R_f = 0.15 (P/Et_2O = 1/1) [UV, $KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ [ppm] = 1.28 [s, 6 H, C-4(CH_3)$_2$], 3.74 (s, 3 H, OCH_3), 5.52 (d, ^4J = 1.6 Hz, 1 H, H-2), 6.11 (dd, ^3J = 9.8 Hz, ^4J = 1.6 Hz, 1 H, H-6), 6.55 (d, ^3J = 9.8 Hz, H-5).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 25.7 [q, C-4(CH_3)$_2$], 39.9 (s, C-4), 55.8 (q, OCH_3), 101.0 (d, C-2), 126.2 (d, C-6), 152.8 (d, C-5), 180.5 (s, C-3), 188.6 (s, CO).

The analytical data obtained matched those reported in the literature.[127]

3-Isopropyl-6,6-dimethylcyclohexa-2,4-dien-1-one (202)



$C_{11}H_{16}O$
MW = 164.25 g/mol

To 3.12 mL isopropylmagnesium chloride solution (2 M in diethyl ether, 641 mg, 6.24 mmol, 1.30 equiv.) in 3 mL tetrahydrofuran were added 731 mg cyclohexadienone **201** (4.80 mmol, 1.00 equiv.) in 8 mL tetrahdydrofuran and the reaction mixture was stirred at 0 °C for three hours. 1 M aqueous hydrochloric acid solution (20 mL) was added and the mixture stirred for 16 hours at room temperature. The aqueous phase was extracted with diethyl ether (3 × 30 mL) and the combined organic layers were washed with saturated sodium bicarbonate solution (30 mL), brine, dried over sodium sulfate, and the solvent was removed in vacuo. After purification by column chromatography (silica, P/Et_2O = 9/1) 581 mg cyclohexadienone **202** (5.34 mmol, 74%) was obtained as a pale yellow oil.

TLC: R_f = 0.40 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3425 (w, $C_{sp2}H$), 2966 (s, $C_{sp3}H$), 1659 (vs, C=O), 1639 (s, C=C) 1569 (w, C=C), 1467 (m, $C_{sp3}H$), 1385 (m, $C_{sp3}H$), 1185 (m), 867 (m, $C_{sp2}H$), 782 (w).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.15 [d, ^3J = 6.8 Hz, 6 H, CH(CH_3)$_2$], 1.19 [s, 6 H, C-6(CH_3)$_2$], 2.53 [septd, ^3J = 6.8 Hz, ^4J = 1.1 Hz, 1 H, CH(CH_3)$_2$], 5.86 - 5.88 (m, H-2), 6.11 (dd, ^3J = 9.6 Hz, ^4J = 1.5 Hz, H-4), 6.28 (d, ^3J = 9.6 Hz, ^5J = 0.7 Hz, H-5).

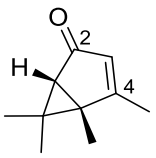
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 21.0 [q, CH(*C*H_3)$_2$], 25.7 [q, C-6(*C*H_3)$_2$], 34.4 [d, *C*H(CH_3)$_2$], 46.4 (s, C-6), 119.9 (d, C-2), 121.2 (d, C-4), 148.3 (d, C-5), 163.1 (s, C-3), 206.4 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 164 (63) $[M]^+$, 149 (57) $[M–CH_3]^+$, 121 (100) $[C_8H_9O]^+$, 105 (27) $[C_8H_9]^+$, 91 (27) $[C_7H_7]^+$, 79 (18) $[C_6H_7]^+$.

HRMS (EI, 70 eV): calc. for $C_{11}H_{16}O$ $[M]^+$: 164.1196; found: 164.1189.

3.3.3. Photorearrangement Reactions

(1*R*,5*S*)-4,5,6,6-Tetramethylbicyclo[3.1.0]hex-3-en-2-one (60)



$C_{10}H_{14}O$
MW = 150.22 g/mol

Racemic Photorearrangement:

Following GP10, 30.0 mg cyclohexadienone **55** (200 µmol, 1.00 equiv.) were irradiated in the presence of 2.47 µL boron trifluoride diethyl etherate (20.0 µmol, 0.10 equiv.) for 4.5 hours. After purification by column chromatography (silica, P/Et_2O = 4/1) 18.1 mg bicyclohexenone *rac*-**60** (120 µmol, 60%) were obtained as a colourless oil.

Enantioselective Photorearrangement:

Following GP11, 30.0 mg cyclohexadienone **55** (200 µmol, 1.00 equiv.) were irradiated in the presence of 18.4 mg oxazaborolidine-aluminum bromide complex (**93**, 20.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 19/1 → 9/1) 20.5 mg bicyclohexenone **60** (136 µmol, 68%, 92% *ee*) were obtained as a colourless oil.

Enantioselective Photorearrangement (1.50 mmol scale):

Following GP12, 225 mg cyclohexadienone **55** (1.50 mmol, 1.00 equiv.) were irradiated in the presence of 68.9 mg oxazaborolidine-aluminum bromide complex (**93**, 75.0 µmol, 0.05 equiv.) for seven hours. After purification by column chromatography (silica, P/Et_2O = 19/1 → 9/1) 186 mg bicyclohexenone **60** (1.24 µmol, 83%, 95% *ee*) were obtained as a colourless oil.

TLC: R_f = 0.21 (P/Et_2O = 4/1) [UV, CAM].

^{1}H NMR (500 MHz, CDCl3, 298 K): δ [ppm] = 1.16 [s, 3 H, (C-6)CH_3], 1.22 [s, 3 H, (C-6)CH_3], 1.41 [s, 3 H, (C-5)CH_3], 1.65 (s, 1 H, H-1), 1.98 [d, ^4J = 1.4 Hz, 3 H, (C-4)CH_3], 5.57 - 5.59 (m, 1 H, H-3).

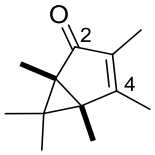
13C NMR (126 MHz, CDCl3, 298 K): δ [ppm] = 11.7 [q, (C-5)*C*H$_3$], 16.0 [q, (C-6)*C*H$_3$], 17.0 [q, (C-4)*C*H$_3$], 23.8 [q, (C-6)*C*H$_3$], 41.9 (s, C-5), 44.5 (d, C-1), 49.5 (s, C-6), 128.3 (d, C-3), 176.7 (s, C-4), 205.2 (s, CO).

Chiral GC: t_{R1} = 13.8 min, t_{R2} = 14.1 min, [60 °C (0 min), 120 °C (30 °C/min), 120 °C (10 min), 240 °C (30 °C/min), 240 °C (2 min)], CycloSil-B.

Specific Rotation: $[\alpha]_D^{25}$ = +428 (c = 1.00, $CHCl_3$) [95% *ee*].

The analytical data obtained matched those reported in the literature.[62, 132]

1,3,4,5,6,6-Hexamethylbicyclo[3.1.0]hex-3-en-2-one (203)



$C_{12}H_{18}O$
MW = 178.28 g/mol

Racemic Photorearrangement:

Following GP10, 35.7 mg cyclohexadienone **59** (200 µmol, 1.00 equiv.) were irradiated in the presence of 2.47 µL boron trifluoride diethyl etherate (20.0 µmol, 0.10 equiv.) for three hours. After purification by column chromatography (silica, P/Et_2O = 19/1) 20.4 mg bicyclohexenone *rac*-**203** (59.5 µmol, 50%) were obtained as a colourless oil.

Enantioselective Photorearrangement:

Following GP11, 26.7 mg cyclohexadienone **59** (150 µmol, 1.00 equiv.) were irradiated in the presence of 13.8 mg oxazaborolidine-aluminum bromide complex (**93**, 15.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 19/1) 19.1 mg bicyclohexenone *rac*-**200** (107 µmol, 72%, 0% *ee*) were obtained as a colourless oil.

TLC: R_f = 0.40 (P/Et_2O = 4/1) [UV, CAM].

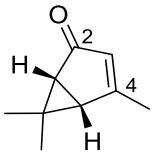
^{1}H NMR (500 MHz, CDCl3, 300 K): δ [ppm] = 0.95 [s, 3 H, (C-6)CH_3], 1.09 [s, 3 H, (C-6)CH_3], 1.17 [s, 3 H, (C-1)CH_3], 1.24 [s, 3 H, (C-5)CH_3], 1.62 [d, ^4J = 1.2 Hz, 3 H, (C-3)CH_3], 1.91 [d, ^4J = 1.2 Hz, 3 H, (C-4)CH_3].

13C NMR (126 MHz, CDCl3, 300 K): δ [ppm] = 7.5 [q, (C-3)*C*H_3], 7.7 [q, (C-1)*C*H_3], 8.8 [q, (C-5)*C*H_3], 14.8 [q, (C-4)*C*H_3], 17.3 [q, (C-6)*C*H_3], 19.9 [q, (C-6)*C*H_3], 40.1 (s, C-1), 40.1 (s, C-5), 50.5 (s, C-6), 133.2 (s, C-3), 168.2 (s, C-4), 208.5 (s, CO).

Chiral GC: t_{R1} = 27.3 min, t_{R2} = 28.2 min, [60 °C (0.5 min), 95 °C (5 °C/min), 95 °C (20 min), 120 °C (5 °C/min), 180 °C (20 °C/min), 180 °C (3 min)], Lipodex E.

The analytical data obtained matched those reported in the literature.[61, 133]

(1*R*,5*S*)-4,6,6-Trimethylbicyclo[3.1.0]hex-3-en-2-one (204)



$C_9H_{12}O$
MW = 136.19 g/mol

Racemic Photorearrangement:

Following GP10, 27.2 mg cyclohexadienone **148** (200 µmol, 1.00 equiv.) were irradiated in the presence of 2.47 µL boron trifluoride diethyl etherate (20.0 µmol, 0.10 equiv.) for six hours. After purification by column chromatography (silica, P/Et_2O = 19/1 → 9/1) 7.0 mg bicyclohexenone *rac*-**204** (51.4 µmol, 26%) were obtained as a colourless oil.

Enantioselective Photorearrangement:

Following GP11, 20.4 mg cyclohexadienone **148** (150 µmol, 1.00 equiv.) were irradiated in the presence of 13.8 mg oxazaborolidine-aluminum bromide complex (**93**, 15.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 19/1 → 9/1) 10.6 mg bicyclohexenone **204** (77.8 µmol, 52%, 93% *ee*) were obtained as a colourless oil.

Enantioselective Photorearrangement (1.50 mmol scale):

Following GP12, 204 mg cyclohexadienone **148** (1.50 mmol, 1.00 equiv.) were irradiated in the presence of 68.9 mg oxazaborolidine-aluminum bromide complex (**93**, 75.0 µmol, 0.05 equiv.) for seven hours. After purification by column chromatography (silica, P/Et_2O = 19/1 → 9/1) 81.5 mg of cyclohexadienone **147** (59.8 µmol, 40%) were recovered and 65.2 mg bicyclohexenone **204** [47.9 µmol, 32%, (53% brsm), 94% *ee*] were obtained as a colourless oil.

TLC: R_f = 0.10 (P/Et_2O = 4/1) [UV, CAM].

^{1}H NMR (500 MHz, $CDCl_3$, 298 K): δ [ppm] = 1.16 [s, 3 H, (C-6)CH_3], 1.21 [s, 3 H, (C-6)CH_3], 1.98 (dd, ^3J = 4.3 Hz, ^4J = 1.2 Hz, 1 H, H-5), 1.21 [d, ^3J = 1.4 Hz, 3 H, (C-4)CH_3], 2.25 (d, ^3J = 4.3 Hz, 1 H, H-1), 5.61 - 5.63 (m, 1 H, H-3).

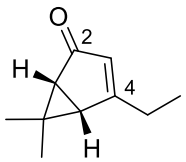
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.1 [q, (C-6)*C*H_3], 19.7 [q, (C-4)*C*H_3], 27.4 [q, (C-6)*C*H_3], 39.8 (d, C-1), 40.1 (d, C-5), 47.4 (s, C-6), 128.4 (d, C-3), 174.0 (s, C-4), 205.2 (s, CO).

Chiral GC: t_{R1} = 12.3 min, t_{R2} = 12.7 min, [60 °C (0 min), 120 °C (30 °C/min), 120 °C (10 min), 240 °C (30 °C/min), 240 °C (2 min)], CycloSil-B.

Specific Rotation: $[\alpha]_D^{25}$ = +317 (c = 1.06, $CHCl_3$) [94% *ee*].

The analytical data obtained matched those reported in the literature.[114]

(1*R*,5*S*)-4-Ethyl-6,6-dimethylbicyclo[3.1.0]hex-3-en-2-one (205)



$C_{10}H_{14}O$
MW = 150.22 g/mol

Racemic Photorearrangement:

Following GP10, 30.0 mg cyclohexadienone **177** (200 µmol, 1.00 equiv.) were irradiated in the presence of 2.47 µL boron trifluoride diethyl etherate (20.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 19/1 → 9/1) 11.1 mg bicyclohexenone *rac*-**205** (73.9 µmol, 37%) were obtained as a colourless oil.

Enantioselective Photorearrangement:

Following GP11, 22.5 mg cyclohexadienone **177** (150 µmol, 1.00 equiv.) were irradiated in the presence of 13.8 mg oxazaborolidine-aluminum bromide complex (**93**, 15.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 19/1 → 9/1) 14.7 mg bicyclohexenone **205** (97.9 µmol, 65%, 95% *ee*) were obtained as a colourless oil.

TLC: R_f = 0.17 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2969 (m, $C_{sp3}H$), 1687 (vs, C=O), 1601 (s, C=C), 1459 (w, $C_{sp3}H$), 1376 (m, $C_{sp3}H$), 1279 (m), 1175 (w, $C_{sp3}H$), 867 (m, $C_{sp2}H$).

^{1}H NMR (500 MHz, CDCl3, 300 K): δ [ppm] = 1.14 (t, ^3J = 7.5 Hz, 3 H, CH_2CH_3), 1.15 [s, 3 H, (C-6)CH_3], 1.21 [s, 3 H, (C-6)CH_3], 1.98 (dd, ^3J = 4.4 Hz, ^4J = 1.2 Hz, 1 H, H-5), 2.29 (d, ^3J = 4.4 Hz, 1 H, H-1), 2.32 (dqd, ^2J = 16.8 Hz, ^3J = 7.5 Hz, ^4J = 1.5 Hz, 1 H, $CHHCH_3$), 2.43 (dqd, ^2J = 16.8 Hz, ^3J = 7.5 Hz, ^4J = 1.5 Hz, 1 H, $CHHCH_3$), 5.61 - 5.63 (m, 1 H, H-3).

^{13}C NMR (126 MHz, CDCl3, 300 K): δ [ppm] = 11.3 (q, CH_2CH_3), 14.5 [q, (C-6)CH_3], 26.9 (t, CH_2CH_3), 27.4 [q, (C-6)CH_3], 38.9 (d, C-1), 39.4 (d, C-5), 47.3 (s, C-6), 126.4 (d, C-3), 179.4 (s, C-4), 205.3 (s, CO).

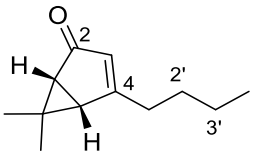
MS (EI, 70 eV): *m/z* (%) = 150 (55) $[M]^+$, 135 (21) $[M–CH_3]^+$, 121 (10) $[M–C_2H_5]^+$, 107 (100) $[C_7H_7O]^+$, 91 (55) $[C_7H_7]^+$, 79 (34) $[C_6H_7]^+$.

HRMS (EI, 70 eV): calc. for $C_{10}H_{14}O$ $[M]^+$: 150.1039; found: 150.1048.

Chiral GC: t_{R1} = 14.3 min, t_{R2} = 14.4 min, [60 °C (0 min), 120 °C (30 °C/min), 120 °C (10 min), 240 °C (30 °C/min), 240 °C (2 min)], CycloSil-B.

Specific Rotation: $[\alpha]_D^{25}$ = +359 (c = 1.21, $CHCl_3$) [95% *ee*].

(1*R*,5*S*)-4-Butyl-6,6-dimethylbicyclo[3.1.0]hex-3-en-2-one (206)



$C_{12}H_{18}O$
MW = 178.28 g/mol

Racemic Photorearrangement:

Following GP10, 35.7 mg cyclohexadienone **180** (200 µmol, 1.00 equiv.) were irradiated in the presence of 2.47 µL boron trifluoride diethyl etherate (20.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 39/1 → 19/1) 7.7 mg bicyclohexenone *rac*-**206** (43.2 µmol, 22%) were obtained as a colourless oil.

Enantioselective Photorearrangement:

Following GP11, 26.7 mg cyclohexadienone **180** (150 µmol, 1.00 equiv.) were irradiated in the presence of 13.8 mg oxazaborolidine-aluminum bromide complex (**93**, 15.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 39/1 → 29/1→ 19/1) 16.8 mg bicyclohexenone **206** (94.2 µmol, 63%, 93% *ee*) were obtained as a colourless oil.

TLC: R_f = 0.18 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2957 (s, $C_{sp3}H$), 2930 (s, $C_{sp3}H$), 1692 (vs, C=O), 1601 (m, C=C), 1458 (m, $C_{sp3}H$), 1377 (m, $C_{sp3}H$), 1175 (w, $C_{sp3}H$), 966 (w, $C_{sp2}H$), 865 (m, $C_{sp2}H$).

^{1}H NMR (500 MHz, CDCl3, 298 K): δ [ppm] = 0.94 (t, ^3J = 7.3 Hz, 3 H, H-4'), 1.15 [s, 3 H, (C-6)CH_3], 1.21 [s, 3 H, (C-6)CH_3], 1.35 - 1.43 (m, 2 H, H-3'), 1.47 - 1.59 (m, 2 H, H-2'), 1.97 (dd, ^3J = 4.4 Hz, ^4J = 1.2 Hz, 1 H, H-5), 2.26 (d, ^3J = 4.4 Hz, 1 H, H-1), 2.30 - 2.40 (m, 2 H, H-1'), 5.60 - 5.62 (m, 1 H, H-3).

^{13}C NMR (126 MHz, CDCl3, 300 K): δ [ppm] = 14.0 (q, C-4'), 14.5 [q, (C-6)*C*H_3], 22.8 (t, C-3'), 27.4 [q, (C-6)*C*H_3], 29.0 (t, C-2'), 33.5 (t, C-1'), 39.0 (d, C-1), 39.4 (d, C-5), 47.4 (s, C-6), 127.0 (d, C-3), 178.3 (s, C-4), 205.3 (s, CO).

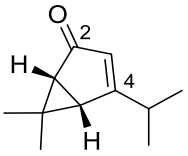
MS (EI, 70 eV): *m/z* (%) = 178 (72) $[M]^+$, 163 (13) $[M–CH_3]^+$, 149 (42) $[M–C_2H_5]^+$, 135 (52) $[M–C_3H_7]^+$, 121 (39) $[C_8H_9O]^+$, 107 (100) $[C_7H_7O]^+$, 91 (77) $[C_7H_7]^+$, 79 (44) $[C_6H_7]^+$.

HRMS (ESI): calc. for $C_{12}H_{18}O$ $[M+H]^+$: 179.1431; found: 179.1431.

Chiral GC: t_{R1} = 16.2 min, t_{R2} = 16.5 min, [60 °C (0 min), 150 °C (30 °C/min), 150 °C (15 min), 240 °C (30 °C/min), 240 °C (2 min)], CycloSil-B.

Specific Rotation: $[\alpha]_D^{25}$ = +309 (c = 0.11, $CHCl_3$) [93% *ee*].

(1*R*,5*S*)-4-Isopropyl-6,6-dimethylbicyclo[3.1.0]hex-3-en-2-one (207)



$C_{11}H_{16}O$
MW = 164,25 g/mol

Racemic Photorearrangement:

Following GP10, 32.9 mg cyclohexadienone **202** (200 µmol, 1.00 equiv.) were irradiated in the presence of 2.47 µL boron trifluoride diethyl etherate (20.0 µmol, 0.10 equiv.) for five hours.

After purification by column chromatography (silica, P/Et_2O = 9/1) 12.0 mg bicyclohexenone *rac*-**204** (73.1 µmol, 37%) were obtained as a colourless oil.

Enantioselective Photorearrangement:

Following GP11, 24.6 mg cyclohexadienone **202** (150 µmol, 1.00 equiv.) were irradiated in the presence of 13.8 mg oxazaborolidine-aluminum bromide complex (**93**, 15.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 9/1) 17.2 mg bicyclohexenone **207** (105 µmol, 70%, 93% *ee*) were obtained as a colourless oil.

TLC: R_f = 0.17 (P/Et_2O = 4:1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3267 (w, $C_{sp2}H$), 2964 (s, $C_{sp3}H$), 2929 (s, $C_{sp3}H$), 1691 (vs, C=O), 1597 (s, C=C), 1463 (m, $C_{sp3}H$), 1254 (m), 1174 (m, $C_{sp3}H$), 869 (m, $C_{sp2}H$).

^{1}H NMR (500 MHz, CDCl3, 300 K): δ [ppm] = 1.12 - 1.16 [m, 9 H, (C-6)CH_3, CH(CH_3)$_2$), 1.22 [s, 3 H, (C-6)CH_3], 1.98 (dd, ^3J = 4.4 Hz, ^4J = 1.2 Hz, 1 H, H-5), 2.29 (d, ^3J = 4.4 Hz, 1 H, H-1), 2.62 (septd, ^3J = 6.9 Hz, ^4J = 1.3 Hz, CH(CH_3)$_2$), 5.58 - 5.60 (m, 1 H, H-3).

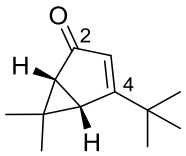
^{13}C NMR (126 MHz, CDCl3, 300 K): δ [ppm] = 14.8 [q, (C-6)CH$_3$], 20.2 [q, CH(CH$_3$)], 20.5 [q, CH(CH$_3$)], 27.4 [q, (C-6)CH$_3$], 32.1 [d, CH(CH_3)$_2$], 37.6 (d, C-1), 39.2 (d, C-5), 47.4 (s, C-6), 125.3 (d, C-3), 183.1 (s, C-4), 205.4 (s, CO).

Chiral GC: t_{R1} = 14.9 min, t_{R2} = 15.0 min, [60 °C (0 min), 120 °C (30 °C/min), 120 °C (10 min), 240 °C (30 °C/min), 240 °C (2 min)], CycloSil-B.

Specific Rotation: $[\alpha]_D^{25}$ = +390 (c = 1.42, $CHCl_3$) [93% *ee*].

The analytical data obtained matched those reported in the literature.[134]

(1*R*,5*S*)-4-(*tert*-Butyl)-6,6-dimethylbicyclo[3.1.0]hex-3-en-2-one (208)



$C_{12}H_{18}O$
MW = 178,28 g/mol

Racemic Photorearrangement:

Following GP10, 35.7 mg cyclohexadienone **149** (200 µmol, 1.00 equiv.) were irradiated in the presence of 2.47 µL boron trifluoride diethyl etherate (20.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 9/1) 18.3 mg bicyclohexenone *rac*-**208** (103 µmol, 51%) were obtained as a colourless oil.

Enantioselective Photorearrangement:

Following GP11, 24.6 mg cyclohexadienone **149** (150 µmol, 1.00 equiv.) were irradiated in the presence of 13.8 mg oxazaborolidine-aluminum bromide complex (**93**, 15.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 9/1 → 4/1) 20.1 mg bicyclohexenone **208** (113 µmol, 75%, 93% *ee*) were obtained as a colourless oil.

TLC: R_f = 0.19 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2965 (s, $C_{sp3}H$), 2871 (w, $C_{sp3}H$), 1693 (vs, C=O), 1592 (m), 1452 (m, $C_{sp3}H$), 1351 (m, $C_{sp3}H$), 1248 (m), 1175 (w, $C_{sp3}H$), 870 (m, $C_{sp2}H$).

^{1}H NMR (500 MHz, CDCl3, 300 K): δ [ppm] = 1.13 [s, 3 H, (C-6)CH_3], 1.16 [s, 9 H, C(CH_3)$_3$], 1.22 [s, 3 H, (C-6)CH_3], 1.99 (dd, ^3J = 4.5 Hz, ^4J = 1.1 Hz, 1 H, H-5), 2.36 (d, ^3J = 4.5 Hz, 1 H, H-1), 5.59 (d, ^4J = 1.1 Hz, 1 H, H-3).

^{13}C NMR (126 MHz, CDCl3, 300 K): δ [ppm] = 14.9 [q, (C-6)*C*H_3], 27.4 [q, (C-6)*C*H_3], 28.3 [q, C(*C*H_3)$_3$], 35.0 [s, *C*(CH_3)$_3$], 36.5 (d, C-1), 39.3 (d, C-5), 47.3 (s, C-6), 124.5 (d, C-3), 185.7 (s, C-4), 205.6 (s, CO).

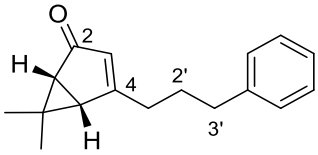
MS (EI, 70 eV): *m/z* (%) = 178 (82) $[M]^+$, 163 (100) $[M–CH_3]^+$, 135 (94) $[M–C_3H_7]^+$, 119 (44) $[C_9H_{11}]^+$, 105 (29) $[C_8H_9]^+$, 91 (48) $[C_7H_7]^+$, 79 (32) $[C_6H_7]^+$, 65 (11) $[C_5H_5]^+$, 57 (24) $[C_4H_9]^+$.

HRMS (EI, 70 eV): calc. for $C_{12}H_{18}O$ $[M]^+$: 178.1352; found: 178.1352.

Chiral GC: t_{R1} = 15.2 min, t_{R2} = 15.3 min, [60 °C (0 min), 120 °C (30 °C/min), 120 °C (10 min), 240 °C (30 °C/min), 240 °C (2 min)], CycloSil-B.

Specific Rotation: $[\alpha]_D^{25}$ = +314 (c = 1.06, $CHCl_3$) [93% *ee*].

(1*R*,5*S*)-6,6-Dimethyl-4-(3-phenylpropyl)bicyclo[3.1.0]hex-3-en-2-one (209)



$C_{17}H_{20}O$
MW = 240.35 g/mol

Racemic Photorearrangement:

Following GP10, 48.1 mg cyclohexadienone **187** (200 µmol, 1.00 equiv.) were irradiated in the presence of 2.47 µL boron trifluoride diethyl etherate (20.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 4/1) 24.4 mg bicyclohexenone *rac*-**209** (102 µmol, 51%) were obtained as a colourless oil.

Enantioselective Photorearrangement:

Following GP11, 36.1 mg cyclohexadienone **187** (150 µmol, 1.00 equiv.) were irradiated in the presence of 13.8 mg oxazaborolidine-aluminum bromide complex (**93**, 15.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 4/1) 24.2 mg bicyclohexenone **209** (101 µmol, 67%, 93% *ee*) were obtained as a colourless oil.

TLC: R_f = 0.12 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2929 (m, $C_{sp3}H$), 2865 (w, $C_{sp3}H$), 1688 (vs, C=O), 1600 (m), 1453 (m, $C_{sp3}H$), 1278 (m, $C_{sp3}H$), 750 (w), 700 (m).

^{1}H NMR (500 MHz, CDCl3, 298 K): δ [ppm] = 1.15 (s, 3 H, CH_3), 1.20 (s, 3 H, CH_3), 1.82 - 1.94 (m, 2 H, H-2'), 1.98 (dd, ^{3}J = 4.4 Hz, ^{4}J = 1.2 Hz, 1 H, H-5), 2.25 (d, ^{3}J = 4.4 Hz, 1 H, H-1), 2.31 - 2.44 (m, 2 H, H-1'), 2.68 (td, ^{3}J = 7.8 Hz, ^{4}J = 1.9 Hz, 2 H, H-3'), 5.63 - 5.65 (m, 1 H, H-3), 7.17 - 7.20 (m, 1 H, $H_{p\text{-Ar}}$), 7.20 - 7.24 (m, 2 H, $H_{m\text{-Ar}}$), 7.28 - 7.33 (m, 2 H, $H_{o\text{-Ar}}$).

^{13}C NMR (126 MHz, CDCl3, 300 K): δ [ppm] = 14.5 (q, CH_3), 27.4 (q, CH_3), 28.5 (t, C-2'), 33.2 (t, C-1'), 35.7 (t, C-3'), 39.0 (d, C-1), 39.4 (d, C-5), 47.4 (s, C-6), 126.2 (d, $C_{p\text{-Ar}}$), 127.2 (d, C-3), 128.6 (d, 2 × $C_{o\text{-Ar}}$), 128.6 (d, 2 × $C_{m\text{-Ar}}$), 141.5 (s, $C_{i\text{-Ar}}$), 177.6 (s, C-4), 205.1 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 240 (42) $[M]^+$, 225 (16) $[M–CH_3]^+$, 149 (24) $[M–C_7H_7]^+$, 136 (100) $[C_9H_{12}O]^+$, 121 (49) $[C_8H_9O]^+$, 107 (30) $[C_7H_7O]^+$, 91 (94) $[C_7H_7]^+$, 77 (38) $[C_6H_5]^+$, 65 (22) $[C_5H_5]^+$.

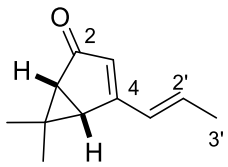
HRMS (EI, 70 eV): calc. for $C_{17}H_{20}O$ $[M]^+$: 240.1509; found: 240.1512.

calc. for $C_{16}{}^{13}CH_{20}O$ $[M]^+$: 241.1542; found: 241.1551.

Chiral GC: t_{R1} = 114.7 min, t_{R2} = 114.9 min, [Flow reduced from 0.9 mL/min (default) to 0.7 mL/min; 60 °C (0 min), 168 °C (30 °C/min), 168 °C (109.4 min), 240 °C (30 °C/min), 240 °C (2 min)], CycloSil-B.

Specific Rotation: $[\alpha]_D^{25}$ = +223 (c = 1.09, $CHCl_3$) [93% *ee*].

6,6-Dimethyl-4-((*E*)-prop-1-en-1-yl)bicyclo[3.1.0]hex-3-en-2-one (*rac*-210)



$C_{11}H_{14}O$
162.23 g/mol

Racemic Photorearrangement:

Following GP7, 32.4 mg cyclohexadienone **188** (200 µmol, 1.00 equiv.) were irradiated in the presence of 2.47 µL boron trifluoride diethyl etherate (20.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 9/1) 9.9 mg bicyclohexenone *rac*-**210** (61.0 µmol, 31%) were obtained as a colourless oil.

TLC: R_f = 0.19 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2929 (m, $C_{sp3}H$), 1678 (vs, C=O), 1637 (s, C=C), 1451 (w, $C_{sp3}H$), 1377 (m, $C_{sp3}H$), 1282 (m), 966 (m, $C_{sp2}H$).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.12 [s, 3 H, (C-6)CH_3], 1.21 [s, 3 H, (C-6)CH_3], 1.92 (ddd, ^3J = 6.4 Hz, ^4J = 1.2 Hz, ^4J = 0.6 Hz, 3 H, H-3'), 1.97 (dd, ^3J = 4.6 Hz, ^4J = 1.3 Hz, 1 H, H-5), 1.97 (d, ^3J = 4.6 Hz, 1 H, H-1), 5.59 - 5.63 (m, 1 H, H-3) , 6.29 - 6.52 (m, 2 H, H-1', H-2').

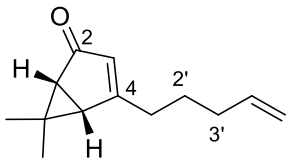
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.3 [q, (C-6)*C*H_3], 19.0 (q, C-3'), 27.4 [q, (C-6)*C*H_3], 35.6 (d, C-1), 38.9 (d, C-5), 45.3 (s, C-6), 126.4 (d, C-3), 128.3 (d, C-1'), 136.1 (d, C-2'), 169.0 (s, C-4), 204.8 (s, C-2).

MS (EI, 70 eV): *m/z* (%) = 162 (71) $[M]^+$, 147 (72) $[M–CH_3]^+$, 119 (100) $[C_8H_7O]^+$, 105 (34) $[C_7H_5O]^+$, 91 (83) $[C_7H_7]^+$, 77 (24) $[C_6H_5]^+$.

HRMS (ESI): calc. for $C_{11}H_{15}O$ $[M+H]^+$: 163.1118; found: 163.1118.

Chiral GC: t_{R1} = 14.3 min, t_{R2} = 14.4 min, [60 °C (0 min), 120 °C (30 °C/min), 120 °C (10 min), 240 °C (30 °C/min), 240 °C (2 min)], CycloSil-B.

(1*R*,5*S*)-6,6-Dimethyl-4-(pent-4-en-1-yl)bicyclo[3.1.0]hex-3-en-2-one (211)



$C_{13}H_{18}O$
MW = 190,29 g/mol

Racemic Photorearrangement:

Following GP10, 19.0 mg cyclohexadienone **189** (100 µmol, 1.00 equiv.) were irradiated in the presence of 1.23 µL boron trifluoride diethyl etherate (10.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 9/1) 7.2 mg bicyclohexenone *rac*-**211** (37.8 µmol, 38%) were obtained as a colourless oil.

Enantioselective Photorearrangement:

Following GP11, 28.5 mg cyclohexadienone **189** (150 µmol, 1.00 equiv.) were irradiated in the presence of 13.8 mg oxazaborolidine-aluminum bromide complex (**93**, 15.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 9/1) 16.0 mg bicyclohexenone **211** (84.1 µmol, 56%, 93% *ee*) were obtained as a colourless oil.

TLC: R_f = 0.24 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3325 (w, $C_{sp2}H$), 2930 (s, $C_{sp3}H$), 1673 (vs, C=O), 1599 (m), 1455 (m, $C_{sp3}H$), 1282 (m, $C_{sp3}H$), 992 (w, $C_{sp2}H$), 911 (m, $C_{sp2}H$).

^{1}H NMR (500 MHz, CDCl3, 300 K): δ [ppm] = 1.15 (s, 3 H, CH_3), 1.21 (s, 3 H, CH_3), 1.58 - 1.72 (m, 2 H, H-2'), 1.98 (dd, ^3J = 4.4 Hz, ^4J = 1.2 Hz, 1 H, H-5), 2.26 (d, ^4J = 1.2 Hz, 1 H, H-1), 2.29 - 2.42 (m, 2 H, H-1'), 2.08 - 2.17 (m, 2 H, H-3'), 4.99 - 5.07 (m, 2 H, H-5'), 5.62 (*virt.* quin, $^4J \cong {}^4J$ = 1.2 Hz, 1 H, H-3), 5.80 (ddt, ^3J = 17.0 Hz, ^3J = 10.2 Hz, ^3J = 6.7 Hz, 1 H, H-4').

^{13}C NMR (126 MHz, CDCl3, 300 K): δ [ppm] = 14.5 (q, CH_3), 26.1 (t, C-2'), 27.4 (q, CH_3), 33.1 (t, C-1'), 33.6 (t, C-3'), 39.0 (d, C-1), 39.4 (d, C-5), 47.4 (s, C-6), 115.6 (t, C-5'), 127.2 (d, C-3), 137.9 (d, C-4'), 177.8 (s, C-4), 205.4 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 190 (7) $[M]^+$, 175 (56) $[M–CH_3]^+$, 162 (14) $[M–C_2H_4]^+$, 147 (45) $[M–C_3H_7]^+$, 136 (49) $[M–C_4H_6]^+$, 121 (52) $[C_8H_9O]^+$, 105 (56) $[C_8H_9]^+$, 93 (100) $[C_7H_9]^+$, 79 (44) $[C_6H_7]^+$, 65 (13) $[C_5H_5]^+$.

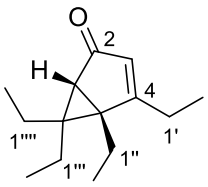
HRMS (EI, 70 eV): calc. for $C_{13}H_{18}O$ $[M]^+$: 190.1352; found: 190.1352.

calc. for $C_{12}{}^{13}CH_{18}O$ $[M]^+$: 191.1386 found: 191.1393.

Chiral GC: t_{R1} = 23.7 min, t_{R2} = 23.9 min, [60 °C (0 min), 150 °C (30 °C/min), 150 °C (20 min), 240 °C (30 °C/min), 240 °C (2 min)], CycloSil-B.

Specific Rotation: $[\alpha]_D^{25}$ = +352 (c = 0.58, $CHCl_3$) [93% *ee*].

(1*R*,5*S*)-4,5,6,6-Tetraethylbicyclo[3.1.0]hex-3-en-2-one (212)



$C_{14}H_{22}O$
MW = 206.33 g/mol

Racemic Photorearrangement:

Following GP10, 41.3 mg cyclohexadienone **140** (200 µmol, 1.00 equiv.) were irradiated in the presence of 2.47 µL boron trifluoride diethyl etherate (20.0 µmol, 0.10 equiv.) for three hours. After purification by column chromatography (silica, P/Et_2O = 9/1) 23.7 mg bicyclohexenone *rac*-**212** (115 µmol, 57%) were obtained as a colourless oil.

Enantioselective Photorearrangement:

Following GP11, 31.0 mg cyclohexadienone **140** (150 µmol, 1.00 equiv.) were irradiated in the presence of 13.8 mg oxazaborolidine-aluminum bromide complex (**93**, 15.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 9/1) 16.2 mg bicyclohexenone **212** (78.5 µmol, 52%, 25% *ee*) were obtained as a colourless oil.

TLC: R_f = 0.23 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2968 (m, $C_{sp3}H$), 2877 (m, $C_{sp3}H$), 1689 (s, C=O), 1604 (m, C=C), 1461 (m), 1379 (m, $C_{sp3}H$), 1256 (m), 1172 (m, $C_{sp3}H$), 890 (m), 846 (m), 796 (m).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.85 (t, ^3J = 7.4 Hz, 3 H, H-2’’), 0.90 (td, ^3J = 7.4, 1.2 Hz, 6 H, H-2’’’, H-2’’’’), 1.14 (t, ^3J = 7.4 Hz, 3 H, H-2’), 1.34 (dd, ^3J = 14.5, 7.3 Hz, 1 H, H-1’’’), 1.49 - 1.58 (m, 2 H, H-1’’), 1.60–1.63 (m, 1 H, H-1), 1.64 - 1.69 (m, 1 H, H-1’’’’), 1.70 - 1.75 (m, 1 H, H-1′′), 2.01 - 2.09 (m, 1 H, H-1′′′), 2.11 - 2.22 (m, 1 H, H-1’), 2.38 - 2.50 (m, 1 H, H-1’), 5.69 - 5.74 (m, 1 H, H-3).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 10.4 (q, C-2’’’), 11.2 (q, C-2’), 11.2 (q, C-2’’), 11.8 (q, C-2’’’’), 18.1 (t, C-1’’), 19.0 (t, C-1‘‘‘), 24.2 (t, C-1‘), 26.2 (t, C-1‘‘), 41.6 (d, C-1), 49.5 (s, C-6), 60.9 (s, C-5), 128.2 (d, C-3), 180.7 (s, C-4), 205.6 (s, C-2).

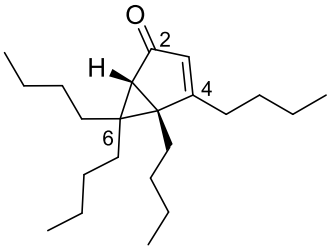
MS (EI, 70 eV): *m/z* (%) = 206 (70) $[M]^+$, 177 (76) $[M–C_2H5]^+$, 149 (64) $[M–C_4H_9]^+$, 135 (70) $[M–C_5H_{11}]^+$, 121 (100) $[M–C_6H_{13}]^+$, 93 (53) $[C_6H_5O]^+$.

HRMS (EI, 70 eV): calc. for $C_{16}H_{26}O$ $[M]^+$: 206.1650; found: 206.1665.

Chiral GC: t_{R1} = 14.3 min, t_{R2} = 14.4 min, [60 °C (0 min), 120 °C (30 °C/min), 120 °C (10 min), 240 °C (30 °C/min), 240 °C (2 min)], CycloSil-B.

Specific Rotation: $[\alpha]_D^{25}$ = +94.7 (c = 1.73, $CHCl_3$) [25% *ee*].

4,5,6,6-Tetrabutylbicyclo[3.1.0]hex-3-en-2-one (*rac*-213)



$C_{22}H_{38}O$
MW = 318.55 g/mol

Racemic Photorearrangement:

Following GP10, 31.9 mg cyclohexadienone **141** (100 µmol, 1.00 equiv.) were irradiated in the presence of 1.23 µL boron trifluoride diethyl etherate (10.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 19/1) 19.2 mg bicyclohexenone *rac*-**213** (60.3 µmol, 60%) were obtained as a colourless oil.

TLC: R_f = 0.79 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2957 (s, $C_{sp3}H$), 2930 (s, $C_{sp3}H$), 2872 (m, $C_{sp3}H$), 1694 (vs, C=O), 1604 (m, C=C), 1466 (m, $C_{sp3}H$).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.82 - 0.86 (m, 3 H, CH_3), 0.89* (t, ^3J = 7.3 Hz, 3 H, CH_3), 0.91* (t, ^3J = 7.3 Hz, 3 H, CH_3), 0.95 (t, ^3J = 7.3 Hz, 3 H, CH_3), 1.16 - 1.61 (m, 21 H, (C-6)C*H*H, 10 × CH_2], 1.63 (s, 1 H, H-1), 1.99 [ddd, ^2J = 14.8 Hz, ^3J = 9.5 Hz, ^3J = 5.6 Hz, 1 H, (C-6)CH*H*], 2.06 - 2.16 [m, 1 H, (C-4)C*H*H], 2.32 - 2.41 [m, 1 H, (C-4)CH*H*], 5.68 (t, ^4J = 1.4 Hz, 1 H, H-3).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.0 (q, CH_3), 14.1 (q, CH_3), 14.2 (q, CH_3), 14.2 (q, CH_3), 22.9 (t, CH_2), 23.0 (t, CH_2), 25.5 (t, CH_2), 25.7 [t, (C-6)*C*H_2], 28.3 (t, CH_2), 28.8 (t, CH_2), 29.2 (t, CH_2), 30.0 (t, CH_2), 30.9 [t, (C-4)*C*H_2], 34.0 (t, CH_2), 42.2 (d, C-1), 48.3 (s, C-6), 58.8 (s, C-5), 128.2 (d, C-3), 180.0 (s, C-4), 205.6 (s, C-2).

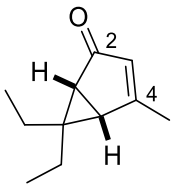
**signals overlap*

MS (EI, 70 eV): *m/z* (%) = 318 (73) $[M]^+$, 289 (65) $[M–C_2H_5]^+$, 275 (79) $[M–C_3H_7]^+$, 261 (27) $[M–C_4H_9]^+$, 233 (51) $[M–C_6H_{13}]^+$, 219 (57) $[M–C_7H_{15}]^+$, 205 (33) $[M–C_8H_{17}]^+$, 191 (100) $[M–C_9H_{19}]^+$, 177 (60) $[M–C_{10}H_{21}]^+$, 163 (43) $[M–C_{11}H_{23}]^+$, 149 (47) $[M–C_{12}H_{25}]^+$, 57 (41) $[C_4H_9]^+$.

HRMS (EI, 70 eV): calc. for $C_{22}H_{38}O$ $[M]^+$: 318.2917; found: 318.2911;

calc. for $C_{21}C^{13}H_{38}O$ $[M]^+$: 319.2951; found: 319.2949.

6,6-Diethyl-4-methylbicyclo[3.1.0]hex-3-en-2-one (*rac*-214)



$C_{11}H_{16}O$
MW = 164.25 g/mol

Racemic Photorearrangement:

Following GP10, 32.9 mg cyclohexadienone **150** (200 µmol, 1.00 equiv.) were irradiated in the presence of 2.47 µL boron trifluoride diethyl etherate (20.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 4/1) 10.2 mg bicyclohexenone *rac*-**214** (62.1 µmol, 31%) were obtained as a colourless oil.

TLC: R_f = 0.11 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2967 (s, $C_{sp3}H$), 1672 (vs, C=O), 1607 (s, C=C), 1460 (m, $C_{sp3}H$), 1381 (m, $C_{sp3}H$), 1140 (w, $C_{sp3}H$), 870 (w, $C_{sp2}H$).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 0.88 (t, ^3J = 7.4 Hz, 3 H, CH_2CH_3), 0.88 (t, ^3J = 7.4 Hz, 3 H, CH_2CH_3), 1.38 (dq, ^2J = 14.5 Hz, ^3J = 7.4 Hz, 1 H, $CHHCH_3$), 1.42 - 1.56 (m, 3 H, $CHHCH_3$, CH_2CH_3), 1.98 (dd, ^3J = 4.3 Hz, ^4J = 1.2 Hz, 1 H, H-5), 2.08 [d, ^4J = 1.5 Hz, 3 H, (C-4)CH_3], 2.26 (d, ^3J = 4.3 Hz, 1 H, H-1), 5.63 - 5.65 (m, 1 H, H-3).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 10.5 (q, CH_2CH_3), 11.1 (q, CH_2CH_3), 16.6 (t, CH_2CH_3), 19.7 [q, (C-4)CH_3], 29.9 (t, CH_2CH_3), 39.1 (d, C-5), 39.6 (d, C-1), 57.8 (s, C-6), 128.9 (d, C-3), 173.2 (s, C-4), 205.2 (s, C-2).

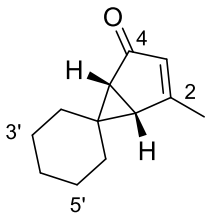
MS (EI, 70 eV): *m/z* (%) = 164 (88) $[M]^+$, 135 (79) $[M–C_2H_5]^+$, 121 (82) $[C_8H_9O]^+$, 107 (70) $[C_7H_7O]^+$, 91 (100) $[C_7H_7]^+$, 79 (44) $[C_6H_7]^+$.

HRMS (EI, 70 eV): calc. for $C_{11}H_{16}O$ $[M]^+$: 164.1196; found: 164.1188;

calc. for $C_{10}{}^{13}CH_{16}O$ $[M]^+$: 165.1229; found: 165.1226.

Chiral GC: t_{R1} = 14.3 min, t_{R2} = 14.4 min, [60 °C (0 min), 120 °C (30 °C/min), 120 °C (10 min), 240 °C (30 °C/min), 240 °C (2 min)], CycloSil-B.

(1*R*,5*R*)-2-Methylspiro(bicyclo[3.1.0]hexane-6,1‘-cyclohexan)-2-en-4-one (215)



$C_{12}H_{16}O$
MW = 176.26 g/mol

Racemic Photorearrangement:

Following GP10, 35.3 mg cyclohexadienone **151** (200 µmol, 1.00 equiv.) were irradiated in the presence of 2.47 µL boron trifluoride diethyl etherate (20.0 µmol, 0.10 equiv.) for three hours. After purification by column chromatography (silica, P/Et_2O = 19/1 → 9/1) 19.4 mg bicyclohexenone *rac*-**215** (110 µmol, 55%) were obtained as a colourless oil.

Enantioselective Photorearrangement:

Following GP11, 26.4 mg cyclohexadienone **151** (150 µmol, 1.00 equiv.) were irradiated in the presence of 13.8 mg oxazaborolidine-aluminum bromide complex (**93**, 15.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 19/1 → 9/1) 21.1 mg bicyclohexenone **215** (120 µmol, 80%, 95% *ee*) were obtained as a colourless oil.

TLC: R_f = 0.22 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2926 (s, $C_{sp3}H$), 2852 (m, $C_{sp3}H$), 1687 (vs, C=O), 1607 (m, C=C), 1444 (m, $C_{sp3}H$), 1351 (m, $C_{sp3}H$), 1271 (w), 1176 (w, $C_{sp3}H$), 874 (w, $C_{sp2}H$).

^{1}H NMR (500 MHz, CDCl3, 300 K): δ [ppm] = 1.37 - 1.45 (m, 2 H, H-2', H-3'*), 1.47 - 1.51 (m, 1 H, H-2'), 1.51 - 1.56 (m, 4 H, H-3'*, H-4'*, H-5'*), 1.56 - 1.59 (m, 2 H, H-4'*, H-6'*), 1.60 - 1.65 (m, 1 H, H-6'*), 2.00 (dd, ^3J = 4.3 Hz, ^4J = 1.3 Hz, 1 H, H-1), 2.11 (d, ^4J = 1.3 Hz, 3 H, CH_3), 2.29 (d, ^3J = 4.3 Hz, 1 H, H-5), 5.64 - 5.67 (m, 1 H, H-3).

^{13}C NMR (126 MHz, CDCl3, 300 K): δ [ppm] = 19.7 (q, CH_3), 24.6 (t, C-6'*), 25.7 (t, C-5'*), 25.9 (t, C-3'*), 26.5 (t, C-4'*), 38.1 (t, C-2'), 39.3 (d, C-1), 39.6 (d, C-5), 55.3 (s, C-6), 128.5 (d, C-3), 173.0 (s, C-2), 204.9 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 176 (100) $[M]^+$, 161 (53) $[M–CH_3]^+$, 147 (40) $[M–C_2H_5]^+$, 133 (61) $[M–C_3H_7]^+$, 121 (58) $[C_8H_9O]^+$, 105 (81) $[C_8H_9]^+$, 96 (43) $[C_7H_{12}]^+$, 91 (99) $[C_7H_7]^+$, 79 (41) $[C_6H_7]^+$, 65 (20) $[C_5H_5]^+$, 53 (13) $[C_4H_5]^+$.

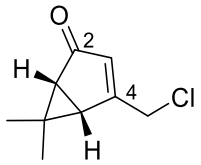
HRMS (EI, 70 eV): calc. for $C_{12}H_{16}O$ $[M]^+$: 176.1196; found: 176.1195.

calc. for $C_{11}{}^{13}CH_{16}O$ $[M]^+$: 177.1229; found: 177.1233.

Chiral GC: t_{R1} = 22.3 min, t_{R2} = 23.0 min, [60 °C (0 min), 150 °C (30 °C/min), 150 °C (20 min), 240 °C (30 °C/min), 240 °C (2 min)], CycloSil-B.

Specific Rotation: $[\alpha]_D^{25}$ = +367 (c = 0.95, $CHCl_3$) [95% *ee*].

(1*R*,5*S*)-4-(Chloromethyl)-6,6-dimethylbicyclo[3.1.0]hex-3-en-2-one (216)



$C_9H_{11}ClO$
MW = 170.64 g/mol

Racemic Photorearrangement:

Following GP10, 34.1 mg cyclohexadienone **184** (200 µmol, 1.00 equiv.) were irradiated in the presence of 2.47 µL boron trifluoride diethyl etherate (20.0 µmol, 0.10 equiv.) for three hours. After purification by column chromatography (silica, P/Et_2O = 4/1) 8.6 mg bicyclohexenone *rac*-**216** (50.4 µmol, 25%) were obtained as a colourless oil.

Enantioselective Photorearrangement:

Following GP11, 25.6 mg cyclohexadienone **184** (150 µmol, 1.00 equiv.) were irradiated in the presence of 13.8 mg oxazaborolidine-aluminum bromide complex (**93**, 15.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 4/1) 5.0 mg bicyclohexenone **216** (29.3 µmol, 20%, 67% *ee*) were obtained as a colourless oil.

TLC: R_f = 0.13 (P/Et_2O = 4/1) [UV, CAM].

^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.18 (s, 3 H, CH_3), 1.24 (s, 3 H, CH_3), 2.09 (dd, ^3J = 4.4 Hz, ^4J = 1.3 Hz, 1 H, H-5), 2.42 (d, ^3J = 4.4 Hz, 1 H, H-1), 4.18 - 4.36 (m 2 H, CH_2Cl), 5.87 (*virt.* qd, $^4J \approx {}^4J$ = 1.3 Hz, ^4J = 0.7 Hz, 1 H, H-3).

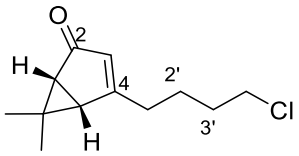
^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ [ppm] = 14.5 (q, CH_3), 27.3 (q, CH_3), 37.4 (d, C-1), 39.9 (d, C-5), 42.1 (t, CH_2Cl), 47.6 (s, C-6), 129.4 (d, C-3), 169.1 (s, C-4), 203.7 (s, C-2).

MS (EI, 70 eV): *m/z* (%) = 170 (24) $[M]^+$, 135 (40) $[M–Cl]^+$, 107 (100) $[C_7H_7O]^+$, 91 (79) $[C_7H_7]^+$, 79 (28) $[C_6H_7]^+$.

Chiral GC: t_{R1} = 14.3 min, t_{R2} = 14.4 min, [60 °C (0 min), 120 °C (30 °C/min), 120 °C (10 min), 240 °C (30 °C/min), 240 °C (2 min)], CycloSil-B.

Due to instability of the compound, full characterization of the compound was not conducted.

(1*R*,5*S*)- 4-(4-Chlorobutyl)-6,6-dimethylbicyclo[3.1.0]hex-3-en-2-one (217)



$C_{12}H_{17}ClO$
MW = 212.72 g/mol

Racemic Photorearrangement:

Following GP10, 42.5 mg cyclohexadienone **190** (200 µmol, 1.00 equiv.) were irradiated in the presence of 2.47 µL boron trifluoride diethyl etherate (20.0 µmol, 0.10 equiv.) for six hours. After purification by column chromatography (silica, P/Et_2O = 4/1 → 2/1) 20.3 mg bicyclohexenone *rac*-**217** (95.4 µmol, 48%) were obtained as a colourless oil.

Enantioselective Photorearrangement:

Following GP11, 31.9 mg cyclohexadienone **190** (150 µmol, 1.00 equiv.) were irradiated in the presence of 13.8 mg oxazaborolidine-aluminum bromide complex (**93**, 15.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 4/1 → 2/1) 21.0 mg bicyclohexenone **217** (98.7 µmol, 66%, 93% *ee*) were obtained as a colourless oil.

TLC: R_f = 0.17 (P/Et_2O = 2:1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3349 (w, $C_{sp2}H$), 2938 (s, $C_{sp3}H$), 2868 (m, $C_{sp3}H$), 1687 (vs, C=O), 1599 (s, C=C), 1453 (m, $C_{sp3}H$), 1282 (m), 865 (w, $C_{sp2}H$).

^{1}H NMR (500 MHz, CDCl3, 298 K): δ [ppm] = 1.16 (s, 3 H, CH_3), 1.22 (s, 3 H, CH_3), 1.68 - 1.78 (m, 2 H, H-2'), 1.85 (ddt, ^3J = 8.7 Hz, ^3J = 6.7 Hz, ^3J = 6.5 Hz, 2 H, H-3'), 1.99 (dd, ^3J = 4.4 Hz, ^4J = 1.2 Hz, 1 H, H-5), 2.27 (d, ^3J = 4.4 Hz, 1 H, H-1), 2.39 (dddd, ^2J = 10.1 Hz, ^3J = 8.2 Hz, ^3J = 6.5 Hz, ^4J = 1.3 Hz, 2 H, H-1'), 3.57 (t, ^3J = 6.5 Hz, 2 H, H-4'), 5.64 (t, ^4J = 1.3 Hz, 1 H, H-3).

^{13}C NMR (126 MHz, CDCl3, 300 K): δ [ppm] = 14.5 (q, CH_3), 24.2 (t, C-2'), 27.4 (q, CH_3), 32.3 (t, C-3'), 32.9 (t, C-1'), 38.9 (d, C-1), 39.4 (d, C-5), 44.7 (t, C-4'), 47.4 (C-6), 127.4 (d, C-3), 177.0 (s, C-4), 204.9 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 212 (44) $[M]^+$, 197 (8) $[M–CH_3]^+$, 177 (14) $[M–Cl]^+$, 149 (44) $[M–C_2H_4Cl]^+$, 135 (52) $[M–C_3H_6Cl]^+$, 121 (32) $[C_8H_9O]^+$, 107 (100) $[C_7H_7O]^+$, 91 (65) $[C_7H_7]^+$, 79 (34) $[C_6H_7]^+$, 65 (12) $[C_5H_5]^+$.

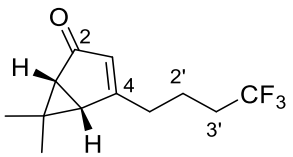
HRMS (EI, 70 eV): calc. for $C_{12}H_{17}{}^{35}ClO$ $[M]^+$: 212.0962; found: 212.0957.

calc. for $C_{11}{}^{13}CH_{17}{}^{35}ClO$ $[M]^+$: 213.0996; found: 213.0995.

Chiral GC: t_{R1} = 54.4 min, t_{R2} = 54.7 min, [60 °C (0 min), 155 °C (30 °C/min), 155 °C (50 min), 240 °C (30 °C/min), 240 °C (2 min)], CycloSil-B.

Specific Rotation: $[\alpha]_D^{25}$ = +239 (c = 1.27, $CHCl_3$) [93% *ee*].

(1*R*,5*S*)-6,6-Dimethyl-4-(4,4,4-trifluorobutyl)bicyclo[3.1.0]hex-3-en-2-one (219)



$C_{12}H_{15}F_3O$
MW = 232.25 g/mol

Racemic Photorearrangement:

Following GP10, 46.5 mg cyclohexadienone **192** (200 µmol, 1.00 equiv.) were irradiated in the presence of 2.47 µL boron trifluoride diethyl etherate (20.0 µmol, 0.10 equiv.) for five hours.

After purification by column chromatography (silica, P/Et_2O = 4/1) 20.9 mg bicyclohexenone *rac*-**219** (90.0 µmol, 45%) were obtained as a colourless oil.

Enantioselective Photorearrangement:

Following GP11, 34.8 mg cyclohexadienone **192** (150 µmol, 1.00 equiv.) were irradiated in the presence of 13.8 mg oxazaborolidine-aluminum bromide complex (**93**, 15.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 9/1 → 4/1) 18.8 mg bicyclohexenone **219** (80.9 µmol, 54%, 93% *ee*) were obtained as a colourless oil.

TLC: R_f = 0.06 (P/Et_2O = 4/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2957 (w, $C_{sp3}H$), 1688 (vs, C=O), 1600 (m), 1453 (m, $C_{sp3}H$), 1254 (s), 1135 (s, C-F), 015 (m), 871 (w).

^{1}H NMR (500 MHz, CDCl3, 300 K): δ [ppm] = 1.16 (s, 3 H, CH_3), 1.23 (s, 3 H, CH_3), 1.79 - 1.91 (m, 2 H, H-2'), 2.02 (dd, ^3J = 4.4 Hz, ^4J = 1.2 Hz, H-5), 2.10 - 2.21 (m, H-3'), 2.27 (d, ^3J = 4.4 Hz, H-1), 2.37 - 2.51 (m, H-1'), 5.64 - 5.67 (m, 1 H, H-3).

^{13}C NMR (126 MHz, CDCl3, 300 K): δ [ppm] = 14.3 (q, CH_3), 19.3 (q, $^3J_{CF}$ = 3.0 Hz, C-2'), 27.2 (q, CH_3), 32.2 (t, C-1'), 33.4 (q, $^2J_{CF}$ = 29.0 Hz, C-3'), 36.6 (d, C-1), 39.3 (d, C-5), 47.3 (s, C-6), 126.8 (q, $^1J_{CF}$ = 276 Hz, CF_3), 127.5 (d, C-3), 175.3 (s, C-4), 204.5 (s, CO).

^{19}F NMR (376 MHz, CDCl3, 300 K): δ [ppm] = –66.7 (t, $^3J_{HF}$ = 10.8 Hz, CF_3)

MS (EI, 70 eV): *m/z* (%) = 232 (63) $[M]^+$, 135 (29) $[C_9H_{11}O]^+$, 121 (14) $[C_8H_9O]^+$, 107 (100) $[C_7H_7O]^+$, 91 (54) $[C_7H_7]^+$, 77 (25) $[C_6H_5]^+$.

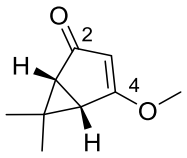
HRMS (EI, 70 eV): calc. for $C_{12}H_{15}FO_3$ $[M]^+$: 232.1070; found: 232.1069.

calc. for $C_{11}{}^{13}CH_{15}FO_3$ $[M]^+$: 233.1103; found: 233.1106.

Chiral GC: t_{R1} = 16.5 min, t_{R2} = 17.0 min, [60 °C (0 min), 150 °C (30 °C/min), 150 °C (15 min), 240 °C (30 °C/min), 240 °C (2 min)], CycloSil-B.

Specific Rotation: $[\alpha]_D^{25}$ = +215 (c = 1.19, $CHCl_3$) [93% *ee*].

(1*R*,5*S*)-4-Methoxy-6,6-dimethylbicyclo[3.1.0]hex-3-en-2-one (220)



$C_9H_{12}O_2$
MW = 152.19 g/mol

Racemic Photorearrangement:

Following GP10, 45.7 mg cyclohexadienone **174** (300 µmol, 1.00 equiv.) were irradiated in the presence of 7.40 µL boron trifluoride diethyl etherate (60.0 µmol, 0.20 equiv.) for 24 hours at λ = 398 nm. After purification by column chromatography (silica, Et_2O = 100%) 20.0 mg bicyclohexenone *rac*-**220** (131 µmol, 44%) were obtained as a colourless oil.

Enantioselective Photorearrangement:

Following GP11, 22.8 mg cyclohexadienone **174** (150 µmol, 1.00 equiv.) were irradiated in the presence of 13.8 mg oxazaborolidine-aluminum bromide complex (**93**, 15.0 µmol, 0.10 equiv.) for 24 hours at λ = 425 nm. After purification by column chromatography (silica, Et_2O = 100%) 9.4 mg cyclohexadienone **174** (61.8 µmol, 41%) were recovered and 11.5 mg bicyclohexenone **220** [75.6 µmol, 50% (80% brsm) 94% *ee*] were obtained as a colourless oil.

Enantioselective Photorearrangement (750 µmol scale):

Following GP12, 114 mg cyclohexadienone **174** (750 µmol, 1.00 equiv.) were irradiated in the presence of 68.9 mg oxazaborolidine-aluminum bromide complex (**93**, 75.0 µmol, 0.10 equiv.) at a concentration of 100 mm for 24 hours at λ = 425 nm. After purification by column chromatography (silica, Et_2O = 100%) 98.0 mg bicyclohexenone **220** (644 µmol, 86%, 93% *ee*) were obtained as a colourless oil.

TLC: R_f = 0.34 (P/Et_2O = 100%) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2955 (m, $C_{sp3}H$), 1682 (s, C=O), 1581 (vs, C=C), 1372 (s, $C_{sp3}H$), 1236 (m), 980 (m, $C_{sp2}H$).

^{1}H NMR (500 MHz, CDCl3, 298 K): δ [ppm] = 1.19 [s, 3 H, (C-6)CH_3], 1.25 [s, 3 H, (C-6)CH_3], 2.01 (dd, ^{3}J = 5.0 Hz, ^{4}J = 1.2 Hz, 1 H, H-5), 2.17 (d, ^{3}J = 5.0 Hz, 1 H, H-1), 3.78 (s, 3 H, OCH_3), 4.94 - 4.96 (m, 1 H, H-3).

^{13}C NMR (126 MHz, CDCl3, 300 K): δ [ppm] = 14.6 [q, (C-6)*C*H_3], 26.8 [q, (C-6)*C*H_3], 34.2 (d, C-1), 38.5 (d, C-5), 44.2 (s, C-6), 58.8 (OCH_3), 101.3 (d, C-3), 187.0 (C-4), 201.4 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 152 (100) $[M]^+$, 137 (19) $[M–CH_3]^+$, 109 (60) $[M–C_3H_7]^+$, 91 (21) $[C_7H_7]^+$, 81 (40), 69 (23), 53 (126) $[C_4H_5]^+$.

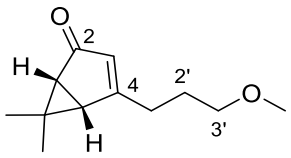
HRMS (EI, 70 eV): calc. for $C_9H_{12}O_2$ $[M]^+$: 152.0832; found: 152.0835.

calc. for $C_8{}^{13}CH_{12}O_2$ $[M]^+$: 153.0865; found: 153.0872.

Chiral GC: t_{R1} = 15.3 min, t_{R2} = 15.6 min, [60 °C (0 min), 120 °C (30 °C/min), 120 °C (10 min), 240 °C (30 °C/min), 240 °C (2 min)], CycloSil-B.

Specific Rotation: $[\alpha]_D^{25}$ = +205 (c = 0.73, $CHCl_3$) [94% *ee*].

(1*R*,5*S*)-4-(3-Methoxypropyl)-6,6-dimethylbicyclo[3.1.0]hex-3-en-2-one (221)



$C_{12}H_{18}O_2$
MW = 194.27 g/mol

Racemic Photorearrangement:

Following GP10, 38.9 mg cyclohexadienone **191** (200 µmol, 1.00 equiv.) were irradiated in the presence of 2.47 µL boron trifluoride diethyl etherate (20.0 µmol, 0.10 equiv.) for three hours. After purification by column chromatography (silica, P/Et_2O = 2/1) 14.4 mg bicyclohexenone *rac*-**221** (74.1 µmol, 37%) were obtained as a colourless oil.

Enantioselective Photorearrangement:

Following GP11, 29.1 mg cyclohexadienone **191** (150 µmol, 1.00 equiv.) were irradiated in the presence of 13.8 mg oxazaborolidine-aluminum bromide complex (**93**, 15.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 3/1 → 2/1) 22.6 mg bicyclohexenone **221** (116 µmol, 78%, 94% *ee*) were obtained as a colourless oil.

TLC: R_f = 0.16 (P/Et_2O = 1/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2967 (s, $C_{sp3}H$), 2872 (s, $C_{sp3}H$), 1689 (vs, C=O), 1602 (s, C=C), 1352 (w, $C_{sp3}H$), 1280 (m), 1117 (s, $C_{sp3}H$), 891 (m, $C_{sp2}H$).

^{1}H NMR (500 MHz, CDCl3, 298 K): δ [ppm] = 1.15 [s, 3 H, (C-6)CH_3], 1.21 [s, 3 H, (C-6)CH_3], 1.74 - 1.89 (m, 2 H, H-2'), 1.98 (dd, ^3J = 4.3 Hz, ^4J = 1.1 Hz, 1 H, H-5), 2.27 (d, ^3J = 4.3 Hz, 1 H, H-1), 2.37 - 2.50 (m, 2 H, H-1'), 3.35 (s, 3 H, OCH_3), 3.42 (t, ^3J = 6.2 Hz, 2 H, H-3'), 5.62 - 5.64 (m, 1 H, H-3).

^{13}C NMR (126 MHz, CDCl3, 300 K): δ [ppm] = 14.5 [q, (C-6)*C*H_3], 27.1 (t, C-2'), 27.4 [q, (C-6)*C*H_3], 30.4 (t, C-1'), 39.0 (d, C-1), 39.4 (d, C-5), 47.3 (C-6), 58.9 (q, OCH_3), 72.0 (t, C-3'), 127.2 (d, C-3), 177.4 (d, C-4), 205.1 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 194 (13) $[M]^+$, 162 (14) $[M–CH_4O]^+$, 149 (36) $[M–C_2H_5O]^+$, 136 (84) $[M–C_3H_6O]^+$, 119 (61) $[C_9H_{11}]^+$, 105 (37) $[C_8H_9]^+$, 93 (100) $[C_7H_9]^+$, 77 (34) $[C_6H_5]^+$, 65 (9) $[C_5H_5]^+$.

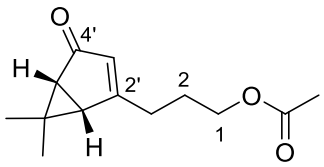
HRMS (EI, 70 eV): calc. for $C_{12}H_{18}O_2$ $[M]^+$: 194.1301; found: 194.1303.

calc. for $C_{11}{}^{13}CH_{18}O_2$ $[M]^+$: 195.1335; found: 195.1344.

Chiral GC: t_{R1} = 24.7 min, t_{R2} = 24.9 min, [60 °C (0 min), 150 °C (30 °C/min), 150 °C (20 min), 240 °C (30 °C/min), 240 °C (2 min)], CycloSil-B.

Specific Rotation: $[\alpha]_D^{25}$ = +262 (c = 1.54, $CHCl_3$) [94% *ee*].

3-((1*R*,5*S*)-6,6-Dimethyl-4-oxobicyclo[3.1.0]hex-2-en-2-yl)propyl acetate (222)



$C_{13}H_{18}O_3$
MW = 222.28 g/mol

Racemic Photorearrangement:

Following GP10, 11.1 cyclohexadienone **196** (50 µmol, 1.00 equiv.) were irradiated in the presence of 0.617 µL boron trifluoride diethyl etherate (5.00 µmol, 0.10 equiv.) for three hours. After purification by column chromatography (silica, P/Et_2O = 4/1) 6.7 mg bicyclohexenone *rac*-**222** (30.1 µmol, 60%) were obtained as a colourless oil.

Enantioselective Photorearrangement:

Following GP11, 33.3 mg cyclohexadienone **196** (150 µmol, 1.00 equiv.) were irradiated in the presence of 13.8 mg oxazaborolidine-aluminum bromide complex (**93**, 15.0 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 4/1) 19.0 mg bicyclohexenone **222** (85.5 µmol, 57%, 92% *ee*) were obtained as a colourless oil.

TLC: R_f = 0.12 (P/Et_2O = 1/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3376 (w, $C_{sp2}H$), 2957 (s, $C_{sp3}H$), 1739 (vs, OC=O), 1690 (vs, C=O), 1602 (m, C=C), 1452 (m, $C_{sp3}H$), 1366 (m, $C_{sp3}H$), 1240 (s, COC), 1041 (m), 965 (w), 884 (w, $C_{sp2}H$).

^{1}H NMR (500 MHz, CDCl3, 300 K): δ [ppm] = 1.15 [s, 3 H, (C-6')CH_3], 1.22 [s, 3 H, (C-6')CH_3], 1.84 - 1.94 (m, 2 H, H-2), 2.00 (dd, ^3J = 4.4 Hz, ^4J = 1.2 Hz, 1 H, H-1'), 2.07 (s, 3 H, OCH_3), 2.27 (d, ^3J = 4.4 Hz, 1 H, H-5'), 2.35 - 2.50 (m, 2 H, H-3), 4.12 (t, ^3J = 6.5 Hz, 2 H, H-1), 5.65 (*virt.* td, ^4J = 2.3 Hz, $^4J \cong {}^4J$ = 1.3 Hz, 1 H, H-3') .

^{13}C NMR (126 MHz, CDCl3, 300 K): δ [ppm] = 14.4 [q, (C-6')*C*H_3], 21.1 (q, OCO*C*H_3), 26.1 (t, C-22), 27.4 [q, (C-6')*C*H_3], 30.2 (t, C-3), 38.9 (d, C-5'), 39.4 (d, C-1'), 47.4 (s, C-6'), 63.8 (t, C-1), 127.4 (d, C-3'), 171.2 (s, O*C*OCH_3), 176.3 (s, C-2'), 204.8 (s, C-4).

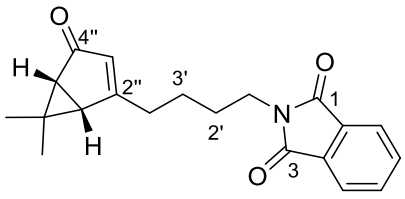
MS (EI, 70 eV): *m/z* (%) = 222 (42) $[M]^+$, 180 (100) $[M–C_2H_2O]^+$, 162 (19) $[M–C_2H_4O_2]^+$, 147 (42), 137 (25) $[M–C_3H_7O_2]^+$, 119 (63) $[C_9H_{11}]^+$, 107 (34) $[C_8H_9O]^+$, 91 (77) $[C_7H_7]^+$, 77 (26) $[C_6H_5]^+$, 65 (11) $[C_5H_5]^+$, 53 (8) $[C_4H_5]$.

HRMS (EI, 70 eV): calc. for $C_{13}H_{18}O_3$ $[M]^+$: 222.1250; found: 222.1266.

Chiral GC: t_{R1} = 48.7 min, t_{R2} = 49.4 min, [60 °C (0 min), 160 °C (30 °C/min), 160 °C (44 min), 200 °C (10 °C/min), 240 °C (20 °C/min), 240 °C (2 min)], CycloSil-B.

Specific Rotation: $[\alpha]_D^{25}$ = +227 (c = 1.00, $CHCl_3$) [92% *ee*].

2-(4-((1*R*,5*S*)-6,6-Dimethyl-4-oxobicyclo[3.1.0]hex-2-en-2-yl)butyl)isoindoline-1,3-dione (223)



$C_{20}H_{21}NO_3$
MW = 323.39 g/mol

Racemic Photorearrangement:

Following GP10, 6.5 mg cyclohexadienone **195** (20 µmol, 1.00 equiv.) were irradiated in the presence of 0.247 µL boron trifluoride diethyl etherate (2.00 µmol, 0.10 equiv.) for four hours. After purification by column chromatography (silica, P/Et_2O = 1/1) 4.4 mg bicyclohexenone *rac*-**223** (13.6 µmol, 68%) were obtained as a colourless oil.

Enantioselective Photorearrangement:

Following GP11, 43.7 mg cyclohexadienone **195** (135 µmol, 1.00 equiv.) were irradiated in the presence of 12.4 mg oxazaborolidine-aluminum bromide complex (**93**, 13.5 µmol, 0.10 equiv.) for five hours. After purification by column chromatography (silica, P/Et_2O = 1/1) 26.2 mg bicyclohexenone **223** (81.0 µmol, 60%, 97% *ee*) were obtained as a colourless oil.

TLC: R_f = 0.10 (P/Et_2O = 1/1) [UV, CAM].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2948 (w, $C_{sp3}H$), 1771 (w, C=O), 1712 (vs, C=O), 1688 (s, C=C), 1602 (w, C=C), 1397 (m, $C_{sp3}H$), 1035 (w), 721 (m, $C_{sp2}H$).

^{1}H NMR (500 MHz, CDCl3, 298 K): δ [ppm] = 1.13 (s, 3 H, CH_3), 1.20 (s, 3 H, CH_3), 1.54 - 1.66 (m, 1 H, H-3'), 1.76 (*virt.* quin, $^3J \cong {}^3J$ = 7.3 Hz, H-2'), 1.97 (d, ^3J = 4.5 Hz, 1 H, H-1''), 2.25 (d, ^3J = 4.5 Hz, 1 H, H-5''), 2.35 - 2.46 (m, 1 H, H-4'), 3.73 (t, ^3J = 7.1 Hz, H-1'), 5.61 (s, 1 H, H-3''), 7.73 (dd, ^3J = 5.5 Hz, ^3J = 3.0 Hz, 2 H, H_{Ar}), 7.85 (dd, ^3J = 5.5 Hz, ^3J = 3.0 Hz, 2 H, H_{Ar}).

^{13}C NMR (126 MHz, CDCl3, 300 K): δ [ppm] = 14.3 (q, CH_3), 24.1 (t, C-3'), 27.2 (q, CH_3), 28.4 (t, C-2'), 33.0 (t, C-4'), 37.5 (t, C-1'), 38.8 (d, C-5''), 39.3 (d, C-1''), 47.4 (C-6''), 123.3 (d, 2 × C_{Ar}), 127.2 (d, C-3''), 132.1 (s, 2 × C_{Ar}), 134.0 (d, 2 × C_{Ar}), 168.4 [s, $N(CO)_2$], 177.0 (s, C-2''), 204.9 (s, CO).

MS (EI, 70 eV): *m/z* (%) = 323 (7) $[M]^+$, 258 (11) $[M–C_5H_5]^+$, 214 (33) $[M–C_7H_9O]^+$, 184 (28) $[M–C_5H_5]^+$, 156 (90), 145 (65) $[C_8H_3NO_2]^+$, 127 (78), 121 (100) $[M–C_8H_9O]^+$, 115 (42), 91 (16) $[C_7H_7]^+$, 77 (20) $[C_6H_5]^+$, 55 (17) $[C_4H_7]^+$, 41 (25) $[C_3H_5]^+$.

HRMS (EI, 70 eV): calc. for $C_{20}H_{21}NO_3$ $[M]^+$: 323.1516; found: 323.1516.

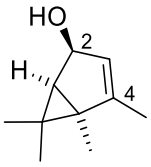
calc. for $C_{19}{}^{13}CH_{21}NO_3$ $[M]^+$: 324.1550; found: 324.1551.

Chiral HPLC: t_{R1} = 22.6 min, t_{R2} = 24.5 min, [Daicel, Chiralpak AD-H, 250 x 4,6 mm, 5 µm, 20% *i*-PrOH/*n*-heptane (50 min), 1 mL/min, 210 nm].

Specific Rotation: $[\alpha]_D^{25}$ = +462 (c = 0.126, $CHCl_3$) [97% *ee*].

3.3.4. Transformations of Bicyclohexenones and Total Synthesis of Chrysanthemic Acid

(1*R*,2*S*,5*S*)-4,5,6,6-Tetramethylbicyclo[3.1.0]hex-3-en-2-ol (132)

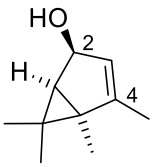


$C_{10}H_{16}O$
MW = 152.24 g/mol

599 µL Diisobutylaluminum hydride solution (1.0 M in dichloromethane, 599 µmol, 3.00 equiv.) were added dropwise to a solution of 30.0 mg bicyclohexenone *ent*-**60** (200 µmol, 1.00 equiv.) in 5.0 mL dichloromethane at −78 °C. The reaction mixture was stirred for five hours and subsequently warmed to room temperature. Saturated potassium sodium tartrate solution (5 mL) was added and the mixture was stirred for one hour at room temperature. The aqueous layer was extracted with diethyl ether (3 × 10 mL) and the combined organic layers were washed with brine, dried over sodium sulfate, filtered, and the solvent was removed in vacuo to give a crude diastereomeric mixture (d.r. = 96/4). After column chromatography (silica, P/Et_2O = 9/1) 25.0 mg bicyclohexenol **132** (164 µmol, 82%) were obtained as a single diastereomer and a colorless oil.

Note: Reduction using lithium aluminum hydride gave a significantly lower d.r., enabling isolation of the minor diastereomer and the corresponding NOESY experiment in order to confirm the relative configuration of both diastereomers.

major Diastereomer



TLC: R_f = 0.44 (P/Et_2O = 4/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3346 (*br* m, OH), 3346 (s, $C_{sp3}H$), 2870 (s, $C_{sp3}H$), 2872 (m, $C_{sp3}H$), 1650 (w, C=C), 1375 (m, $C_{sp3}H$), 1033 (vs, $C_{sp3}H$), 992 (m).

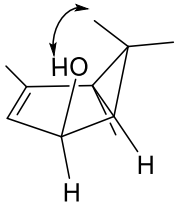
^{1}H NMR (500 MHz, DMSO-d_6, 300 K): δ [ppm] = 0.90 (dd, ^{3}J = 6.4 Hz, ^{4}J = 1.2 Hz, 1 H, H-1), 1.03 [s, 3 H, C-5)CH_3], 1.14 [s, 3 H, C-6)CH_3], 1.15 [s, 3 H, C-6)CH_3], 1.57 [*virt.* t, $^{4}J \approx {}^{5}J$ = 1.8 Hz, 3 H, C-4)CH_3], 4.30 (d, ^{3}J = 4.0 Hz, 1 H, OH), 4.97 (*virt.* ddq, ^{3}J = 6.4 Hz, ^{3}J = 4.0 Hz, $^{4}J \approx {}^{5}J$ = 2.0 Hz, 1 H, H-2), 5.04 (q, ^{4}J = 1.6 Hz, 1 H, H-3).

^{13}C NMR (126 MHz, DMSO-d_6, 300 K): δ [ppm] = 12.6 [q, (C-6)*C*H_3], 14.3 [q, (C-4)*C*H_3], 17.6 [q, (C-6)*C*H_3], 23.3 [q, (C-5)*C*H_3], 26.7 (s, C-6), 35.3 (d, C-1), 39.5* (s, C-5), 75.4 (d, C-2), 127.7 (d, C-3), 143.1 (s, C-4).

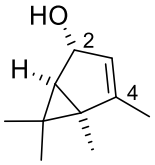
**obscured by residual proton signal of NMR solvent, assigned by HMBC.*

HRMS (ESI): calc. for $C_{10}H_{74}O$ $[M+H]^+$: 153.1274; found: 153.1274.

Important NOE contacts:



minor Diastereomer



TLC: R_f = 0.44 (P/Et_2O = 4/1) [UV, $KMnO_4$].

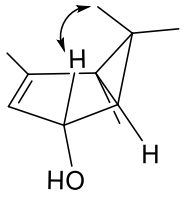
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 3346 (*br* m, OH), 3346 (s, $C_{sp3}H$), 2870 (s, $C_{sp3}H$), 2872 (m, $C_{sp3}H$), 1650 (w, C=C), 1375 (m, $C_{sp3}H$), 1033 (vs, $C_{sp3}H$), 992 (m).

^{1}H NMR (500 MHz, DMSO-d_6, 300 K): δ [ppm] = 0.74 [s, 3 H, C-5)CH_3], 0.97 (d, ^{4}J = 1.6 Hz, 1 H, H-1), 1.08 [s, 3 H, C-6)CH_3], 1.23 [s, 3 H, C-6)CH_3], 1.63 [*virt.* t, $^{4}J \approx {}^{5}J$ = 1.5 Hz, 3 H, C-4)CH_3], 3.90 (*virt.* dquin, ^{3}J = 6.6 Hz, $^{4}J \approx {}^{5}J$ = 1.8 Hz, 1 H, H-2), 4.52 (d, ^{3}J = 6.6 Hz, 1 H, OH), 5.22 (*virt.* sex, $^{3}J \approx {}^{4}J \approx {}^{4}J$ = 1.6 Hz, 1 H, H-3).

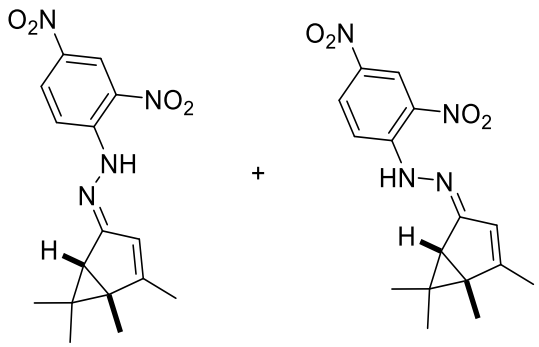
^{13}C NMR (126 MHz, DMSO-d_6, 300 K): δ [ppm] = 13.1 [q, (C-5)*C*H$_3$], 14.6 [q, (C-4)*C*H$_3$], 14.6 [q, (C-6)*C*H$_3$], 22.8 [q, (C-6)*C*H$_3$], 28.3 (s, C-6), 38.6 (s, C-5), 43.4 (d, C-1), 72.7 (d, C-2), 127.0 (d, C-3), 145.3 (s, C-4).

HRMS (ESI): calc. for $C_{10}H_{74}O$ $[M+H]^+$: 153.1274; found: 153.1274.

Important NOE contacts:



1-(2,4-dinitrophenyl)-2-(-4,5,6,6-tetramethylbicyclo[3.1.0]hex-3-en-2-ylidene)hydrazine (*rac*-135)

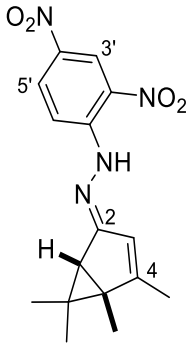


$C_{16}H_{18}N_4O_4$
MW = 330.34 g/mol

26.4 mg 2,4-Dinitrophenylhydrazine (67 wt% in water, 133 µmol, 1.00 equiv.) were added to a solution of 20.0 mg bicyclohexenone *rac*-**60** (133 mmol, 1.00 equiv.) in 1.0 mL ethanol at room temperature. A catalytic amount of an ethanolic sulfuric acid solution was added and the reaction mixture was stirred for three hours. The solvent was removed in vacuo and after column chromatography (silica, P/Et$_2$O = 49/1 → 19/1 → 9/1) 39.3 mg hydrazone *rac*-**135** (*E*/*Z* = 1/1, 119 µmol, 89%) were obtained as a bright red solid. After column chromatography

(P/Et_2O = 199/1 → 99/1 → 49/1) 19.5 mg hydrazone *rac*-(*E*)-**135** (59.0 µmol, 44%) and 19.2 mg hydrazone *rac*-(*Z*)-**135** (58.1 µmol, 44%) were obtained as bright red solids.

rac-(*E*)-**135**



Mp: 161 - 166 °C.

TLC: R_f = 0.21 (P/Et_2O = 9/1) [UV, $KMnO_4$].

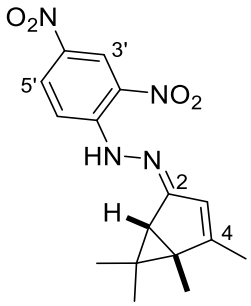
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2924 (vs, $C_{sp2}H$), 2855 (m, $C_{sp3}H$), 1618 (s, C=C), 1519 (w), 1333 (vs, NO), 1134 (m).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.03 [s, (C-6)CH_3], 1.40 [s, (C-6)CH_3], 1.44 [s, (C-5)CH_3], 1.94 - 1.96 (m, 1 H, H-1), 2.00 [d, ^4J = 1.4 Hz, 3 H, (C-4)CH_3], 5.86 - 5.88 (m, 1 H, H-3), 7.88 (d, ^3J = 9.7 Hz, 1 H, H-6'), 8.27 (dd, ^3J = 9.7 Hz, ^4J = 2.6 Hz, 1 H, H-5'), 9.14 (d, ^4J = 2.6 Hz, 1 H, H-3'), 11.23 (s, 1 H, NH).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 12.5 [q, (C-5)CH_3], 16.2 [q, (C-6)CH_3], 16.3 [q, (C-4)CH_3], 23.3 [q, (C-6)CH_3], 35.8 (d, C-1), 43.1 (s, C-6), 44.4 (s, C-5), 116.5 (d, C-6'), 123.9 (C-3'), 125.4 (d, C-1), 128.8 (s, C-2'), 130.0 (d, C-5'), 137.4 (s, C-4'), 144.9 (s, C-1'), 162.9 (s, C-2), 165.4 (s, C-4).

HRMS (ESI): calc. for $C_{10}H_{19}N_4O_4$ $[M+H]^+$: 331.1401; found: 331.1401.

rac-(*Z*)-**135**



Mp: 127 °C.

TLC: R_f = 0.21 (P/Et_2O = 9/1) [UV, $KMnO_4$].

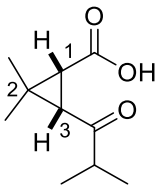
IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2924 (vs, $C_{sp2}H$), 2855 (m, $C_{sp3}H$), 1618 (s, C=C), 1519 (w), 1333 (vs, NO), 1134 (m).

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.05 [s, (C-6)CH_3], 1.28 [s, (C-6)CH_3], 1.43 [s, (C-5)CH_3], 1.89 - 1.92 (m, 1 H, H-1), 1.95 [d, ^4J = 1.5 Hz, 3 H, (C-4)CH_3], 6.12 - 6.14 (m, 1 H, H-3), 7.93 (d, ^3J = 9.6 Hz, 1 H, H-6'), 8.26 (dd, ^3J = 9.6 Hz, ^4J = 2.6 Hz, 1 H, H-5'), 9.12 (d, ^4J = 2.6 Hz, 1 H, H-3'), 11.25 (s, 1 H, NH).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 12.2 [q, (C-5)CH_3], 15.6 [q, (C-6)CH_3], 17.0 [q, (C-4)CH_3], 23.5 [q, (C-6)CH_3], 40.7 (d, C-1), 42.1 (s, C-6), 42.2 (s, C-5), 116.1 (d, C-3), 116.3 (d, C-6'), 124.0 (C-3'), 128.5 (s, C-2'), 130.0 (d, C-5'), 137.2 (s, C-4'), 144.6 (s, C-1'), 163.7 (s, C-2), 168.3 (s, C-4).

HRMS (ESI): calc. for $C_{10}H_{19}N_4O_4$ $[M+H]^+$: 331.1401; found: 331.1401.

3-Isobutyryl-2,2-dimethylcyclopropane-1-carboxylic acid (*rac*-228)



$C_{10}H_{16}O_3$
MW = 184.24 g/mol

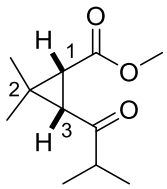
Following GP13, 100 mg bicyclohexenone *rac*-**207** (609 mmol, 1.00 equiv.) was converted with 4.80 mg ruthenium(III) chloride hydrate (21.3 µmol, 3.50 mol%) and 391 mg sodium periodate (1.83 mmol, 3.00 equiv.) over the course of 18 hours. 61.8 mg of the resulting crude keto acid *rac*-**228** (331 µmol, 55%) were directly used in the subsequent reaction without further purification.

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.17 [d, ^{3}J = 6.9 Hz, 3 H, CH(C*H*$_3$)CH$_3$], 1.20 [d, ^{3}J = 6.9 Hz, 3 H, CH(CH$_3$)C*H*$_3$], 1.25 [s, 3 H, (C-2)CH$_3$], 1.45 [s, 3 H, (C-2)CH$_3$], 2.23-2.39 (m, 2 H, H-1, H-3), 2.86 [sept, ^{3}J = 6.9 Hz, 1 H, C*H*(CH$_3$)$_2$], 12.2 (*br* s, 3 H, COOH).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 15.3 [q, (C-2)*C*H$_3$], 17.6 [q, CH(*C*H$_3$)$_2$], 28.2 [q, (C-2)*C*H$_3$], 28.9 (d, C-1), 32.5 (s, C-2), 39.3 (d, C-3), 40.2 [d, *C*H(CH$_3$)$_2$], 43.0 (q, COO*C*H$_3$), 170.3 (s, *C*OOCH$_3$), 219.3 [s, *C*OCH(CH$_3$)$_2$].

Due to time constraints, further analytical data were not obtained.

Methyl 3-isobutyryl-2,2-dimethylcyclopropane-1-carboxylate (*rac*-227)



$C_{11}H_{18}O_3$
MW = 198.26 g/mol

166 µL Trimethylsilyl diazomethane (2.0 M, 331 µmol, 1.00 equiv.) were added dropwise to a solution of 61.8 mg keto acid *rac*-**228** (331 µmol, 1.00 equiv.) in 900 µL diethyl ether and 450 µL methanol until a bright yellow color maintained. The reaction mixture was stirred for five hours and acetic acid was added dropwise until the solution was colorless and the solvent was removed in vacuo. After purification by column chromatography (silica, Et_2O = 100%) 65.0 mg methyl ester *rac*-**227** (328 µmol, 99%) were obtained as a colorless oil.

TLC: R_f = 0.42 (P/Et_2O = 4/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2967 (m, $C_{sp3}H$), 1736 (vs, C=O), 1698 (s, C=C), 1437 (m, $C_{sp3}H$), 1191 (m, CO), 1047 (m), 1020 (w), 832 (w).

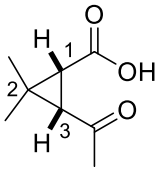
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.09 [d, ^3J = 7.0 Hz, 3 H, CH(CH_3)CH_3], 1.12 [d, ^3J = 7.0 Hz, 3 H, CH(CH_3)CH_3], 1.25 [s, 3 H, (C-2)CH_3], 1.28 [s, 3 H, (C-2)CH_3], 1.89 (d, ^3J = 9.0 Hz, 1 H, H-1), 2.15 (d, ^3J = 9.0 Hz, 1 H, H-3), 2.67 [sept, ^3J = 7.0 Hz, 1 H, CH(CH_3)$_2$], 3.70 (s, 3 H, $COOCH_3$).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 15.6 [q, (C-2)CH_3], 17.6 [q, CH(CH_3)CH_3], 18.2 [q, CH(CH_3)CH_3], 28.3 [q, (C-2)CH_3], 28.4 (s, C-2), 33.9 (d, C-1), 37.5 (d, C-3), 42.1 [d, CH(CH_3)$_2$], 51.8 (q, COOCH_3), 170.0 (s, COOCH_3), 209.5 [s, COCH(CH_3)$_2$].

MS (EI, 70 eV): *m/z* (%) = 198 (2) $[M]^+$, 155 (77) $[M–C_3H_7]^+$, 139 (100) $[M–C_3H_7O]^+$, 127 (78) $[M–C_4H_7O]^+$, 95 (80) $[C_6H_7O]^+$, 85 (37), 67 (41) $[C_5H_7]^+$.

HRMS (ESI): calc. for $C_{11}H_{19}O_3$ $[M+H]^+$: 199.1329; found: 199.1329.

3-Acetyl-2,2-dimethylcyclopropane-1-carboxylic acid (*rac*-231)



$C_8H_{12}O_3$
MW = 156.18 g/mol

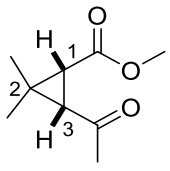
Following GP13, 160 mg bicyclohexenone *rac*-**204** (1.17 mmol, 1.00 equiv.) was converted with 9.27 mg ruthenium(III) chloride hydrate (41.1 µmol, 3.50 mol%) and 754 mg sodium periodate (3.52 mmol, 3.00 equiv.) over the course of 16 hours. 114 mg of the resulting crude keto acid *rac*-**231** (727 µmol, 62%) were directly used in the subsequent reaction without further purification.

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.30 [s, 3 H, (C-2)CH_3], 1.43 [s, 3 H, (C-2)CH_3], 2.19 - 2.27 (m, 2 H, H-1, H-3), 2.42 (s, 3 H, $COCH_3$).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 15.0 [q, (C-2)*C*H_3], 29.1 [q, (C-2)*C*H_3], 32.2 (s, C-2), 32.7 (d, C-1), 39.8 (d, C-3), 40.8 (q, CO*C*H_3), 170.3 (s, *C*OOH), 212.6 (*C*OCH_3).

Due to time constraints, further analytical data were not obtained.

Methyl 3-acetyl-2,2-dimethylcyclopropane-1-carboxylate (*rac*-230)



$C_9H_{14}O_3$
MW = 170.21 g/mol

352 µL Trimethylsilyl diazomethane (2.0 M, 704 µmol, 1.00 equiv.) were added dropwise to a solution of 110 mg keto acid *rac*-**231** (727 µmol, 1.00 equiv.) in 900 µL diethyl ether and

450 µL methanol until a bright yellow color maintained. The reaction mixture was stirred for two hours and acetic acid was added dropwise until the solution was colorless and the solvent was removed in vacuo. After purification by column chromatography (silica, Et_2O = 100%) 120 mg methyl ester *rac*-**230** (707 µmol, *quant.*) were obtained as a colorless oil.

TLC: R_f = 0.27 (P/Et_2O = 4/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ [cm^{-1}] = 2956 (w, $C_{sp3}H$), 1727 (s, C=O), 1700 (s, C=O), 1365 (m, $C_{sp3}H$), 1233 (m, CO), 1162 (vs, $C_{sp3}H$), 1120 (m), 833 (w, $C_{sp2}H$).

1464 (w, $C_{sp3}H$), 1372 (w, $C_{sp3}H$), 1182 (m, $C_{sp3}H$), 870 (w, $C_{sp2}H$).

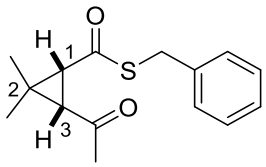
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.24 [s, 3 H, (C-2)CH_3], 1.33 [s, 3 H, (C-2)CH_3], 1.90 (d, ^3J = 9.1 Hz, 1 H, H-1), 2.06 (d, ^3J = 9.1 Hz, 1 H, H-3), 2.22 (s, 3 H, $COCH_3$), 3.70 (s, 3 H, $COOCH_3$).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 15.4 [q, (C-2)*C*H_3], 28.2 (s, C-2), 28.3 [q, (C-2)*C*H_3], 31.9 (s, CO*C*H_3), 33.6 (d, C-1), 39.5 (d, C-3), 51.8 (q, COO*C*H_3), 170.0 (s, *C*$OOCH_3$), 203.8 (s, *C*OCH_3).

MS (EI, 70 eV): *m/z* (%) = 170 (1) $[M]^+$, 155 (2) $[M–CH_3]^+$, 139 (72) $[M–CH_3O]^+$, 127 (47) $[M–C_2H_3O]^+$, 111 (100) $[M–C_2H_3O_2]^+$, 95 (60) $[C_6H_7O]^+$, 83 (48) $[C_6H_{11}]^+$.

HRMS (EI, 70 eV): calc. for $C_9H_{14}O_3$ $[M]^+$: 170.0726; found: 170.0728.

_S_-Benzyl 3-acetyl-2,2-dimethylcyclopropane-1-carbothioate (*rac*-233)



$C_{15}H_{18}O_2S$
MW = 262.37 g/mol

34.2 mg 1-(3-Dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (178 µmol, 1.05 equiv.) and 2.1 mg 4-(Dimethylamino)-pyridin (17.0 µmol, 0.10 equiv.) were added to a solution of 26.5 mg keto acid *rac*-**231** (170 µmol, 1.00 equiv.) in 1.1 mL dichloromethane. 19.9 µL Benzyl mercatptan (21.1 mg, 170 µmol, 1.00 equiv.) were added and the reaction mixture was stirred for 16 hours at room temperature. Diethyl ether (2 mL) and 1 M hydrochloric acid (2 mL) were added and the aqueous layer was extracted with diethyl ether (3 × 2 mL). The combined organic layers were washed with brine, dried over sodium sulfate, filtered, and the solvent was removed in vacuo. After purification by column chromatography (silica, P/Et_2O = 9/1 → 4/1) 28.5 mg thioester *rac*-**233** (109 µmol, 64%) were obtained as a colorless oil.

TLC: R_f = 0.38 (P/Et_2O = 4/1) [UV, $KMnO_4$].

IR (ATR): $\tilde{\nu}$ = 2941 (m, $C_{sp3}H$), 1711 (s, C=O), 1675 (s, C=O), 1406 (vs, C=C), 1358 (m, $C_{sp3}H$), 1103 (s, $C_{sp3}H$), 1007 (s), 980 (m, $C_{sp2}H$), 810 (m, $C_{sp2}H$), 703 (s, CSC).

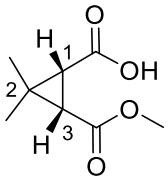
^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.23 [s, 3 H, C-2(CH_3)], 1.36 [s, 3 H, C-2(CH_3)], 2.06 (d, ^3J = 9.1 Hz, 1 H, H-1), 2.20 (d, ^3J = 9.1 Hz, 1 H, H-3), 4.10 - 4.19 (m, 2 H, $C_{Ar}CH_2$), 7.23 (ddd, ^3J = 9.0 Hz, ^3J = 5.4 Hz, ^4J = 3.6 Hz, 1 H, $H_{m\text{-}Ar}$), 7.27 - 7.30 (m, 4 H, H_{Ar}).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 15.4 [q, C-2(CH_3)], 28.3 [q, C-2(CH_3)], 30.2 (s, C-2), 31.5, (CO*C*H_3) 33.6 (C_{Ar}*C*H_2), 41.0 (d, C-3), 42.1 (d, C-1), 127.4 (s, C_{Ar}), 128.8 (d, $C_{o\text{-}Ar}$), 129.0 (d, $C_{m\text{-}Ar}$), 137.9 (d, $C_{p\text{-}Ar}$), 193.6 (s, *C*OSCH_2), 203.0 (s, *C*OCH_3).

MS (EI, 70 eV): *m/z* (%) = 262 (1) $[M]^+$, 139 (100) $[M–C_7H_7S]^+$, 124 (9) $[M–C_8H_{10}S]^+$, 111 (35) $[M–C_8H_7OS]^+$, 95 (26) $[C_6H_7O]^+$, 91 (88) $[C_7H_7]^+$, 77 (11) $[C_6H_5]^+$, 67 (21) $[C_5H_7]^+$.

HRMS (ESI): calc. for $C_{15}H_{19}O_2S$ $[M+H]^+$: 263.1101; found: 263.1098.

(1*R*,3*S*)-3-(Methoxycarbonyl)-2,2-dimethylcyclopropane-1-carboxylic acid (234)



$C_8H_{12}O_4$
MW = 172.18 g/mol

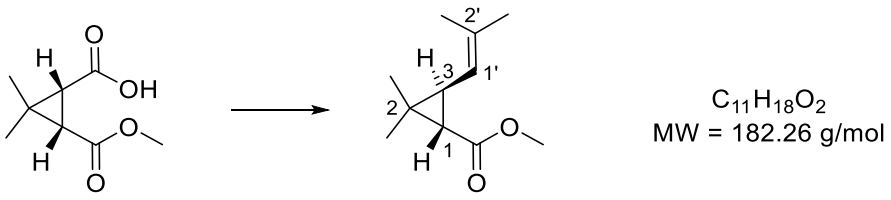
Following GP13, 98.0 mg bicyclohexenone **220** (644 µmol, 1.00 equiv.) was converted with 5.08 mg ruthenium(III) chloride hydrate (22.5 µmol, 3.50 mol%) and 413 mg sodium periodate (1.93 mmol, 3.00 equiv.) over the course of ten hours. 72.8 mg of carboxylic acid **234** (423 µmol, 66%) were obtained and used in the subsequent reaction without further purification. (*Note: Epimerization to the trans-isomer is observed when acidification during work-up is postponed.)*

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.33 [s, 3 H, (C-2)CH_3], 1.37 [s, 3 H, (C-2)CH_3], 1.95 (d, ^3J = 8.4 Hz, 1 H, H-3), 2.07 (d, ^3J = 8.4 Hz, 1 H, H-1), 3.78 (s, 3 H, $COOCH_3$).

^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 15.4 [q, (C-2)*C*H_3], 28.4 (s, C-2), 28.6 [q, (C-2)*C*H_3], 32.7 (d, C-1), 35.4 (d, C-3), 53.3 (q, COO*C*H_3), 170.4 (s, *C*$OOCH_3$), 174.5 (s, *C*OOH).

The analytical data obtained matched those reported in the literature [135].

Methyl (1*S*,3*S*)-2,2-dimethyl-3-(2-methylprop-1-en-1-yl)cyclopropane-1-carboxylate (235)



According to a literature procedure [98]:

Grignard reaction:

265 mg, Lithium chloride (6.25 mmol, 1.25 equiv.) were flame-dried under vacuum. After cooling to room temperatur, 304 mg magnesium turning (12.5 mmol, 2.50 equiv.) were added and suspended in 1.0 mL tetrahydrofuran. 61.0 µL 1,2-dibromoethane (93.9 µg, 500 µmol, 0.10 equiv.) were added dropwise and vigorous bubbling was observed. A freshly prepared solution of 511 µL 1-bromo-2-methyl-1-propene (675 mg, 5.00 mmol, 1.00 equiv.) in 4.0 mL tetrahydrofuran was added dropwise over 15 minutes. The mixture was heated under reflux for one hour, cooled to room temperature and directly used in the transmetalation.

Transmetalation:

681 mg Anhydrous zinc(II) chloride (5.00 mmol, 1.00 equiv.) were completely dissolved in 5.0 mL tetrahydrofuran and the prepared *Grignard* solution (5.00 mmol, 1.00 equiv.) was added dropwise over 15 minutes. The reaction mixture was stirred for 30 minutes, the solvent was carefully removed in vacuo and the residue taken up in 5.0 mL *N*,*N*-dimethylformamide to obtain a 1.0 M alkenyl zinc(II) chloride solution (based on the assumption of a quantitative yield).

Decarboxylative Alkenylation:

To a solution of 24.5 mg carboxylic acid **234** (142 µmol, 1.00 equiv.) and 51.4 mg *N*-hydroxytetrachlorophtalimide (171 µmol, 1.20 equiv.) in 1.0 mL dichloromethane were added dropwise 26.4 µL diisopropylcarbondiimide (171 µmol, 1.20 equiv.) and the mixture

was stirred for two hours at room temperature. The solvent was removed in vacuo and a solution of 18.5 mg nickel(II) acetylacetonate (72.1 µmol, 0.50 equiv.) and 11.3 mg, 2,2'-bpyridine (72.1 µmol, 0.50 equiv.) in 1.5 mL *N*,*N*-dimethylformamide were added. After addition of 871 µL alkenyl zinc(II) chloride solution (1.0 M in N,N-dimethylformamide, 871 µmol, 5.0 equiv.) the reaction was heated to 85 °C four seven hours. The mixture was cooled to room temperature and diethyl ether (2 mL) and 1 M hydrochloric acid (1 mL) was added. The aqueous phase was extracted with diethyl ether (3 × 3 mL) and the combined organic layers were washed with brine, dried over sodium sulfate and the solvent was removed in vacuo. After purification by column chromatography (silica, $P/Et_2O = 1/0 \rightarrow 19/1$) 9.1 mg methyl chrysanthemate (**235**, 50.0 µmol, 35%, d.r. > 95/5, 93% *ee*) were obtained as pale yellow oil.

TLC: R_f = 0.48 (P/Et_2O = 9/1) [$KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.13 [s, 3 H, (C-2)CH_3], 1.26 [s, 3 H, (C-2)CH_3], 1.39 (d, ^3J = 5.4 Hz, 1 H, H-1), 1.69 - 1.72 [m, 6 H, (C-2')CH_3], 2.05 (dd, ^3J = 8.6 Hz, ^3J = 5.4 Hz, 1 H, H-3), 3.67 (s, 3 H, $COOCH_3$), 4.88 (dsept, ^3J = 8.6 Hz, ^4J = 1.3 Hz,1 H, H-1').

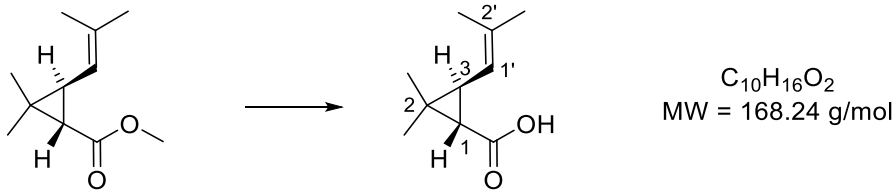
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 18.4 [q, (C-2')*C*H_3], 20.6 [q, (C-2)*C*H_3], 22.3 [q, (C-2)*C*H_3], 25.7 [q, (C-2')*C*H_3], 28.8 (C-2), 32.9 (d, C-3), 34.8 (d, C-1), 51.6 (q, COO*C*H_3), 121.2 (d, C-1'), 135.6 (s, C-2'), 173.2 (s, *C*$OOCH_3$).

Chiral HPLC: t_{R1} = 8.8 min, t_{R2} = 11.0 min, [Daicel, Chiralpak OD-H, 250 x 4,6 mm, 5 µm, 0.15% *i*-PrOH/*n*-heptane (30 min), 0.8 mL/min, 210 nm].

Specific Rotation: $[\alpha]_D^{25} = -16.6$ (c = 0.96, $CHCl_3$) [93% *ee*].

The analytical data obtained matched those reported in the literature [98].

(−)-*trans*-Chrysanthemic Acid [(−)-225]



According to a literature procedure [136]: To a solution of 5.0 mg methyl chrysanthemate (**235**, 27.4 µmol, 1.00 equiv.) in 1.5 mL tetrahydrofuran and methanol (v/v = 1/2) were added 100 µL 2 M sodium hydroxide solution (219 µmol, 8.00 equiv.) and the mixture was heated to 80 °C for four hours. After cooling to room temperature, the solvents were removed in vacuo. The residue was taken up in water (1 mL) and extracted with diethyl ether (3 × 2 mL). The aqueous phase was acidified with 6 M hydrochloric acid to pH = 1 and extracted with diethyl ether (3 × 2 mL). The combined organic layers were washed with brine, dried over sodium sulfate and the solvent was removed in vacuo to obtain 4.5 mg (−)-*trans*-chrysanthemic acid [(−)-**225**, 26.8 µmol, 98%, d.r. > 95/5] as colourless wax.

TLC: R_f = 0.62 (CH_2Cl_2/CH_3OH = 9/1) [$KMnO_4$].

^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ [ppm] = 1.15 [s, 3 H, (C-2)CH_3], 1.30 [s, 3 H, (C-2)CH_3], 1.40 (d, ^3J = 5.4 Hz, 1 H, H-1), 1.69 - 1.73 [m, 6 H, (C-2')CH_3], 2.09 (dd, ^3J = 8.6 Hz, ^3J = 5.4 Hz, 1 H, H-3), 4.90 (dsept, ^3J = 8.6 Hz, ^4J = 1.3 Hz,1 H, H-1'), 11.3 (*br* s, 1 H, COOH).

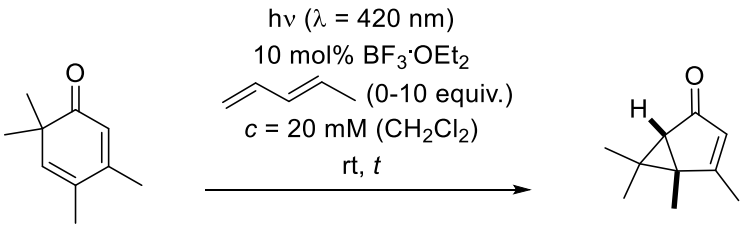
^{13}C NMR (126 MHz, $CDCl_3$, 300 K): δ [ppm] = 18.7 [q, (C-2')*C*H_3], 20.6 [q, (C-2)*C*H_3], 22.4 [q, (C-2)*C*H_3], 25.7 [q, (C-2')*C*H_3], 29.9 (C-2), 33.7 (d, C-3), 34.5 (d, C-1), 120.9 (d, C-1'), 136.0 (s, C-2'), 177.8 (COOH).

Specific Rotation: $[\alpha]_D^{25}$ = −17.1 (c = 1.06, $CHCl_3$) [93% *ee*].

The analytical data obtained matched those reported in the literature [137].

3.3.5. Triplet Quenching Experiments

Racemic Photorearrangement:



55 *rac*-**60**

Procedure:

Stock solution **A**:

In close analogy to GP7 (see chapter 0), 150 mg 3,4,6,6-tetramethylcyclhexa-2,4-dien-1-one (**55**) (100µmol, 1.00 equiv.), 12.3 µL boron trifluoride diethyletherate (14.2 mg, 100 µmol, 0.10 equiv.) and 75.0 mg dodecane (internal GC-standard) were dissolved in 10.0 mL degassed dichloromethane [100 mM referred to **55**].

Stock solution **B**:

341 mg piperylene (new commercial ampule from Sigma Aldrich, 5.00 mmol) were dissolved in 5.00 mL degassed dichloromethane [1.0 M].

Four flame-dried phototubes were filled with the respective volumina of stock solutions A and B and additional degassed dichloromethane (to obtain a concentration of [20 mM] referred to **55**).

Sample **1** (0.0 equiv. piperylene): 2.00 mL stock **A**; 8.00 mL CH_2Cl_2

Sample **2** (1.0 equiv. piperylene): 2.00 mL stock **A**; 0.20 mL stock **B**; 7.80 mL CH_2Cl_2

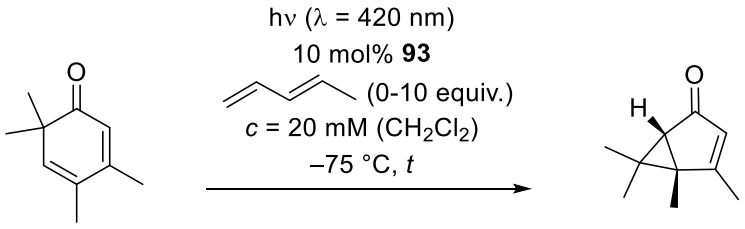
Sample **3** (5.0 equiv. piperylene): 2.00 mL stock **A**; 1.00 mL stock **B**; 7.00 mL CH_2Cl_2

Sample **4** (10 equiv. piperylene): 2.00 mL stock **A**; 2.00 mL stock **B**; 6.00 mL CH_2Cl_2

All samples were irradiated simultaneously at λ = 420 nm. Samples (100 µL) were taken from each phototube after each time interval and directly filtered over a short silica plug to quench the reaction. The plug was washed with 1 mL dry diethyl ether and the filtrates analyzed by GC.

Chiral GC: $t_{dodecane}$ = 13.8 min, $t_{\mathbf{1a}}$ = 13.8 min, $t_{\mathbf{2a}}$ = 13.8 min, $t_{\mathbf{ent\text{-}2a}}$ = 14.1 min, [60 °C (0 min), 120 °C (30 °C/min), 120 °C (10 min), 240 °C (30 °C/min), 240 °C (2 min)], CycloSil-B.

Enantioselective Photorearrangement:



55 **60**

Procedure:

Stock solution A:

In close analogy to GP8 (see chapter 0), 60.1 mg 3,4,6,6-tetramethylcyclohexa-2,4-dien-1-one (**55**) (400 µmol, 1.00 equiv.), 36.8 mg oxazaborolidine-aluminum bromide complex (**93**, 40.0 µmol, 0.10 equiv.) and 30.0 mg dodecane (internal GC-standard) were dissolved in 18.0 mL degassed dichloromethane [22.2 mM referred to **55**] in a round-bottom flask.

Stock solution **B**:

341 mg piperylene (new commercial ampule from Sigma Aldrich, 5.00 mmol) were dissolved in 2.50 mL degassed dichloromethane [2.0 M].

Four flame-dried phototubes were filled with the respective amounts of stock solutions A and B and additional degassed dichloromethane (to obtain a concentration of [20 mM] referred to **55**).

Sample **1** (0.0 equiv. piperylene): 4.50 mL stock **A**; 0.50 mL CH_2Cl_2

Sample **2** (1.0 equiv. piperylene): 4.50 mL stock **A**; 0.05 mL stock **B**; 0.45 mL CH_2Cl_2

Sample **3** (5.0 equiv. piperylene): 4.50 mL stock **A**; 0.25 mL stock **B**; 0.25 mL CH_2Cl_2

Sample **4** (10 equiv. piperylene): 4.50 mL stock **A**; 0.50 mL stock **B**

All samples were cooled and irradiated simultaneously at λ = 420 nm at −75 °C (*Note:* In order to irradiate all four samples simultaneously, the photoreaction was conducted in the 420 nm reactor instead of using the 437 nm LED set-up.) Cooling of the samples was achieved by using a transparent *Dewar* vessel inside the reactor, filled with ethanol and cooled by a *Huber* TC100E cryostat). Samples (100 µL) were taken from each phototube after each time interval and directly filtered over a short silica plug to quench the reaction. (*Note:* less data points were collected under enantioselective conditions to reduce the quenching of catalyst due to traces of moisture brought when taking samples) The plug was washed with 1 mL dry diethyl ether and the filtrates analyzed by GC (*Note:* Enantiomeric excess values were stationary between 70 - 75% *ee* for all samples).

Chiral GC: t_{dodecane} = 13.8 min, $t_{\mathbf{1a}}$ = 13.8 min, $t_{\mathbf{2a}}$ = 13.8 min, $t_{\mathbf{ent\text{-}2a}}$ = 14.1 min, [60 °C (0 min), 120 °C (30 °C/min), 120 °C (10 min), 240 °C (30 °C/min), 240 °C (2 min)], CycloSil-B.

(*Note:* A reaction of **55** with piperylene was not observed under racemic or enantioselective reaction conditions.)

Comparison of concentrations of **55** and **60** in all four reactions did not show a quenching effect of piperylene on the investigated photochemical rearrangement reaction under both racemic and enantioselective reaction conditions.

4. List of Abbreviations

A	absorbance
Å	Ångström
Ac	acetate
acac	acetylacetonate
aq	aqueous
Ar	aryl
Bn	benzyl
Box	bisoxazoline
bpy	bipyridyl
brsm	based on recovered starting material
Bu	butyl
c	concentration
CAN	ceric ammonium nitrate
cat	catalyst
CFL	compact fluorescent lamp
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	dichloroethane
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DFT	density functional theory
DIBAL-H	diisobutylaluminum hydride
DMA	*N*,*N*-dimethylacetamide
DMAP	*N*,*N*-dimethylaminopyridine
DME	dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DMPU	*N*,*N*-dimethylpropyleneurea

DMSO	dimethyl sulfoxide
d	days
de	diastereomeric excess
d.r.	diastereomeric ratio
E (E_a)	energy (activation energy)
EDC	1-ethyl-3-(3-dimethylaminopropyl)carbodiimid
ee	enantiomeric excess
EI	electron ionization
ent	enantio
equiv	equivalents
ESI	electron spray ionization
Et	ethyl
et al.	*et alii* (*lat.*) ‘and others’
GC	gas chromatography
gem	geminal
GP	general procedure
h	hour
HPLC	high performance liquid chromatography
HRMS	high resolution mass spectrometry
Hz	Hertz
IC	internal conversion
IR	infrared spectroscopy
ISC	intersystem crossing
J	Joule
k	kilo
K	Kelvin

λ	wavelength
LA	Lewis acid
LAH	lithium aluminum hydride
LED	light emitting diode
LHMDS	lithium hexamethyldisilazide
L	liter
LUMO	lowest unoccupied molecular orbital
m	milli
m	meter
M	mega
M	molar
µ	mikro
Me	methyl
min	min
MS	mass spectrometry
MW	molecular weight
n	nano
NBS	*N*-bromosuccinimide
NCS	*N*-chlorosuccinimide
n.d.	not determined
NMR	nuclear magnetic resonance
NHTCPI	*N*-hydroxytetrachlorophtalimide
Nu	nucleophile
PCC	pyridinium chlorochromate
PDC	pyridinium dichromate
Ph	phenyl

Pht	phthaloyl
PMB	*para*-methoxybenzyl
ppm	parts per million
ppy	phenylpyridyl
Pr	propyl
prod	product
Py	pyridyl
quant	quantitative
rac	racemic
R_f	retention factor
rt	room temperature
sens	sensitizer
sub	substrate
t	time
TBAF	tetrabutylammonium fluoride
TBHP	*tert*-butyl hydroperoxide
TDDFT	time-dependent density functional theory
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl
Tf	trifluoromethanesulfonyl
Ts	*para*-toluenesulfonyl
UV	ultraviolet
v	volume
VCD	vibrational circular dichroism
Vis	visible

W	Watt
wt	weight
Xy	xylyl

5. References

[1] All Nobel Prizes in Chemistry, https://www.nobelprize.org/prizes/lists/all-nobel-prizes-in-chemistry/, (accessed on 31.01.2020).

[2] K. P. de Jong, *Synthesis of Solid Catalysts*, Wiley-VCH, Weinheim, **2009**.

[3] P. Klán, J. Wirz, Wiley, Chichester, U.K, **2009**.

[4] N. Hoffmann, *Chem. Rev.* **2008**, *108*, 1052-1103.

[5] T. Bach, J. P. Hehn, *Angew. Chem. Int. Ed.* **2011**, *50*, 1000-1045.

[6] M. D. Kärkäs, J. A. Porco, C. R. J. Stephenson, *Chem. Rev.* **2016**, *116*, 9683-9747.

[7] R. Brimioulle, D. Lenhart, M. M. Maturi, T. Bach, *Angew. Chem. Int. Ed.* **2015**, *54*, 3872-3890.

[8] M. Leverenz, *Master's Thesis*, Technische Universität München **2016**.

[9] D. L. Dexter, *J. Chem. Phys.* **1953**, *21*, 836-850.

[10] C. Stephenson, T. Yoon, D. W. C. MacMillan, *Visible Light Photocatalysis in Organic Chemistry*, Wiley-VCH, Weinheim, **2018**.

[11] M. Silvi, P. Melchiorre, *Nature* **2018**, *554*, 41-49.

[12] H. Huo, X. Shen, C. Wang, L. Zhang, P. Röse, L.-A. Chen, K. Harms, M. Marsch, G. Hilt, E. Meggers, *Nature* **2014**, *515*, 100-103.

[13] K. L. Skubi, T. R. Blum, T. P. Yoon, *Chem. Rev.* **2016**, *116*, 10035-10074.

[14] D. M. Arias-Rotondo, J. K. McCusker, *Chem. Soc. Rev.* **2016**, *45*, 5803-5820.

[15] T. P. Yoon, *Acc. Chem. Res.* **2016**, *49*, 2307-2315.

[16] A. Bauer, F. Westkämper, S. Grimme, T. Bach, *Nature* **2005**, *436*, 1139-1140.

[17] R. Alonso, T. Bach, *Angew. Chem.* **2014**, *126*, 4457-4460.

[18] M. M. Maturi, T. Bach, *Angew. Chem. Int. Ed.* **2014**, *53*, 7661-7664.

[19] K. L. Skubi, J. B. Kidd, H. Jung, I. A. Guzei, M.-H. Baik, T. P. Yoon, *J. Am. Chem. Soc.* **2017**, *139*, 17186-17192.

[20] A. Tröster, R. Alonso, A. Bauer, T. Bach, *J. Am. Chem. Soc.* **2016**, *138*, 7808-7811.

[21] A. Hölzl-Hobmeier, A. Bauer, A. V. Silva, S. M. Huber, C. Bannwarth, T. Bach, *Nature* **2018**, *564*, 240-243.

[22] A. Tröster, A. Bauer, C. Jandl, T. Bach, *Angew. Chem. Int. Ed.* **2019**, *58*, 3538-3541.

[23] C. Brenninger, J. D. Jolliffe, T. Bach, *Angew. Chem. Int. Ed.* **2018**, *57*, 14338-14349.

[24] H. Guo, E. Herdtweck, T. Bach, *Angew. Chem. Int. Ed.* **2010**, *49*, 7782-7785.

[25] E. J. Corey, R. K. Bakshi, S. Shibata, *J. Am. Chem. Soc.* **1987**, *109*, 5551-5553.

[26] E. J. Corey, *Angew. Chem. Int. Ed.* **2009**, *48*, 2100-2117.

[27] E. J. Corey, T. Shibata, T. W. Lee, *J. Am. Chem. Soc.* **2002**, *124*, 3808-3809.

[28] K. Mahender Reddy, E. Bhimireddy, B. Thirupathi, S. Breitler, S. Yu, E. J. Corey, *J. Am. Chem. Soc.* **2016**, *138*, 2443-2453.

[29] B. Thirupathi, S. Breitler, K. Mahender Reddy, E. J. Corey, *J. Am. Chem. Soc.* **2016**, *138*, 10842-10845.

[30] B. K. Senapati, G.-S. Hwang, S. Lee, D. H. Ryu, *Angew. Chem. Int. Ed.* **2009**, *48*, 4398-4401.

[31] D. Liu, E. Canales, E. J. Corey, *J. Am. Chem. Soc.* **2007**, *129*, 1498-1499.

[32] J. M. Wiest, M. L. Conner, M. K. Brown, *Angew. Chem. Int. Ed.* **2018**, *57*, 4647-4651.

[33] J. M. Wiest, M. L. Conner, M. K. Brown, *J. Am. Chem. Soc.* **2018**, *140*, 15943-15949.

[34] D. H. Ryu, G. Zhou, E. J. Corey, *Org. Lett.* **2005**, *7*, 1633-1636.

[35] R. Brimioulle, H. Guo, T. Bach, *Chem. Eur. J.* **2012**, *18*, 7552-7560.

[36] R. Brimioulle, A. Bauer, T. Bach, *J. Am. Chem. Soc.* **2015**, *137*, 5170-5176.

[37] R. Brimioulle, T. Bach, *Angew. Chem. Int. Ed.* **2014**, *53*, 12921-12924.

[38] S. Poplata, A. Bauer, G. Storch, T. Bach, *Chem. Eur. J.* **2019**, *25*, 8135-8148.

[39] R. Brimioulle, T. Bach, *Science* **2013**, *342*, 840.

[40] S. Poplata, T. Bach, *J. Am. Chem. Soc.* **2018**, *140*, 3228-3231.

[41] S. Stegbauer, C. Jandl, T. Bach, *Angew. Chem. Int. Ed.* **2018**, *57*, 14593-14596.

[42] M. E. Daub, H. Jung, B. J. Lee, J. Won, M.-H. Baik, T. P. Yoon, *J. Am. Chem. Soc.* **2019**, *141*, 9543-9547.

[43] Z. D. Miller, B. J. Lee, T. P. Yoon, *Angew. Chem. Int. Ed.* **2017**, *56*, 11891-11895.

[44] T. R. Blum, Z. D. Miller, D. M. Bates, I. A. Guzei, T. P. Yoon, *Science* **2016**, *354*, 1391.

[45] X. Huang, T. R. Quinn, K. Harms, R. D. Webster, L. Zhang, O. Wiest, E. Meggers, *J. Am. Chem. Soc.* **2017**, *139*, 9120-9123.

[46] V. Edtmüller, A. Pöthig, T. Bach, *Tetrahedron* **2017**, *73*, 5038-5047.

[47] Y. Inoue, *Chem. Rev.* **1992**, *92*, 741-770.

[48] P. d. Mayo, *Rearrangements from Ground and Excited States, Vol. 42*, Academic Press, Inc., New York, **1980**.

[49] J. Ipaktschi, *Tetrahedron Lett.* **1969**, *10*, 2153-2156.

[50] J. Ipaktschi, *Chem. Ber.* **1972**, *105*, 1840-1853.

[51] D. I. Schuster, M. Amelrod, J. Auerbach, *Tetrahedron Lett.* **1963**, *4*, 1911-1916.

[52] G. Mehta, D. Subrahmanyam, *J. Chem. Soc., Chem. Commun.* **1985**, 768-769.

[53] H. E. Zimmerman, G. L. Grunewald, *J. Am. Chem. Soc.* **1966**, *88*, 183-184.

[54] H. E. Zimmerman, R. W. Binkley, R. S. Givens, M. A. Sherwin, *J. Am. Chem. Soc.* **1967**, *89*, 3932-3933.

[55] K. N. Houk, *Chem. Rev.* **1976**, *76*, 1-74.

[56] M. Demuth, P. R. Raghavan, C. Carter, K. Nakano, K. Schaffner, *Helv. Chim. Acta* **1980**, *63*, 2434-2439.

[57] E. Cheung, M. R. Netherton, J. R. Scheffer, J. Trotter, *Tetrahedron Lett.* **1999**, *40*, 8737-8740.

[58] D. H. R. Barton, G. Quinkert, *J. Chem. Soc.* **1960**, 1-9.

[59] G. Quinkert, *Angew. Chem. Int. Ed.* **1975**, *14*, 790-800.

[60] H. Hart, R. M. Lange, *J. Org. Chem.* **1966**, *31*, 3776-3779.

[61] H. Hart, P. M. Collins, A. J. Waring, *J. Am. Chem. Soc.* **1966**, *88*, 1005-1013.

[62] J. Griffiths, H. Hart, *J. Am. Chem. Soc.* **1968**, *90*, 5296-5298.

[63] S. Uppili, V. Ramamurthy, *Org. Lett.* **2002**, *4*, 87-90.

[64] K. Sivasubramanian, L. S. Kaanumalle, S. Uppili, V. Ramamurthy, *Org. Biomol. Chem.* **2007**, *5*, 1569-1576.

[65] C. Sparr, E.-M. Tanzer, J. Bachmann, R. Gilmour, *Synthesis* **2010**, *2010*, 1394-1397.

[66] S. Poplata, *Ph.D. Thesis*, Technische Universität München **2019**.

[67] B. Zhang, G. P. Manning, M. A. Dobrowolski, M. K. Cyrański, G. J. Bodwell, *Org. Lett.* **2008**, *10*, 273-276.

[68] C. Palomo, S. Vera, A. Mielgo, E. Gómez-Bengoa, *Angew. Chem. Int. Ed.* **2006**, *45*, 5984-5987.

[69] Y. Xu, Y. J. Hong, D. J. Tantillo, M. K. Brown, *Org. Lett.* **2017**, *19*, 3703-3706.

[70] C. Poriel, Y. Ferrand, S. Juillard, P. Le Maux, G. Simonneaux, *Tetrahedron* **2004**, *60*, 145-158.

[71] Z. Li, R. J. Twieg, *Chem. Eur. J.* **2015**, *21*, 15534-15539.

[72] R. Brimioulle, *Ph.D. Thesis*, Technische Universität München **2014**.

[73] S. Stegbauer, *unpublished results.*

[74] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T.

Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyey, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, Wallingford, CT, **2013**.

[75] M. Leverenz, C. Merten, A. Dreuw, T. Bach, *J. Am. Chem. Soc.* **2019**, *141*, 20053-20057.

[76] B. Miller, in *Mechanisms of Molecular Migrations*

(Ed.: B. S. Thyagarajan), New York, **1968**.

[77] G. R. Clemo, R. D. Haworth, E. Walton, *J. Chem. Soc.* **1930**, 1110-1115.

[78] S. Selman, J. F. Eastham, *Quarterly Reviews, Chemical Society* **1960**, *14*, 221-235.

[79] D. Y. Curtin, R. R. Fraser, *J. Am. Chem. Soc.* **1958**, *80*, 6016-6020.

[80] F. Wessely, G. Lauterbach-Keil, F. Sinwel, *Monatshefte für Chemie und verwandte Teile anderer Wissenschaften* **1950**, *81*, 811-818.

[81] W. G. Dauben, D. M. Michno, *J. Org. Chem.* **1977**, *42*, 682-685.

[82] E. Wenkert, N. F. Golob, R. A. J. Smith, *J. Org. Chem.* **1973**, *38*, 4068-4070.

[83] M. E. Flaugh, T. A. Crowell, D. S. Farlow, *J. Org. Chem.* **1980**, *45*, 5399-5400.

[84] M. H. Bolli, J. Velker, C. Müller, B. Mathys, M. Birker, R. Bravo, D. Bur, R. de Kanter, P. Hess, C. Kohl, D. Lehmann, S. Meyer, O. Nayler, M. Rey, M. Scherz, B. Steiner, *J. Med. Chem.* **2014**, *57*, 78-97.

[85] K. Alder, F. H. Flock, H. Lessenich, *Chem. Ber.* **1957**, *90*, 1709-1720.

[86] H. E. Zimmerman, R. J. Pasteris, *J. Org. Chem.* **1980**, *45*, 4876-4891.

[87] H. E. Zimmerman, P. Sebek, *J. Am. Chem. Soc.* **1997**, *119*, 3677-3690.

[88] X. Han, Z. Zhou, C. Wan, Y. Xiao, Z. Qin, *Synthesis* **2013**, *45*, 615-620.

[89] E. F. Murphy, M. Schneider, T. Mallat, A. Baiker, *Synthesis* **2001**, *2001*, 0547-0549.

[90] J.-Q. Yu, E. J. Corey, *J. Am. Chem. Soc.* **2003**, *125*, 3232-3233.

[91] T. K. M. Shing, Yeung, P. L. Su, *Org. Lett.* **2006**, *8*, 3149-3151.

[92] T. Hosokawa, S. Inui, S.-I. Murahashi, *Chem. Lett.* **1983**, *12*, 1081-1082.

[93] Y.-S. Lin, S.-Y. Chang, M.-S. Yang, C. P. Rao, R. K. Peddinti, Y.-F. Tsai, C.-C. Liao, *J. Org. Chem.* **2004**, *69*, 447-458.

[94] G. K. S. Prakash, E. C. Tongco, T. Mathew, Y. D. Vankar, G. A. Olah, *J. Fluor. Chem.* **2000**, *101*, 199-202.

[95] K. Maeda, Y. Inouye, *Bull. Chem. Soc. Jpn.* **1994**, *67*, 2880-2882.

[96] D. Yang, C. Zhang, *J. Org. Chem.* **2001**, *66*, 4814-4818.

[97] H. Tokuyama, S. Yokoshima, T. Yamashita, L. Shao-Cheng, L. Leping, T. Fukuyama, *J. Braz. Chem. Soc.* **1998**, *9*, 381-387.

[98] J. T. Edwards, R. R. Merchant, K. S. McClymont, K. W. Knouse, T. Qin, L. R. Malins, B. Vokits, S. A. Shaw, D.-H. Bao, F.-L. Wei, T. Zhou, M. D. Eastgate, P. S. Baran, *Nature* **2017**, *545*, 213.

[99] B. Oliver-Tomas, M. Renz, A. Corma, *Chem. Eur. J.* **2017**, *23*, 12900-12908.

[100] M. Iwasaki, Y. Araki, S. Iino, Y. Nishihara, *J. Org. Chem.* **2015**, *80*, 9247-9263.

[101] M. Navarro, D. Vidal, P. Clavero, A. Grabulosa, G. Muller, *Organometallics* **2015**, *34*, 973-994.

[102] K. Nakano, K. Nozaki, T. Hiyama, *J. Am. Chem. Soc.* **2003**, *125*, 5501-5510.

[103] D. J. Mathre, T. K. Jones, L. C. Xavier, T. J. Blacklock, R. A. Reamer, J. J. Mohan, E. T. T. Jones, K. Hoogsteen, M. W. Baum, E. J. J. Grabowski, *J. Org. Chem.* **1991**, *56*, 751-762.

[104] B. M. Trost, M.-Y. Ngai, G. Dong, *Org. Lett.* **2011**, *13*, 1900-1903.

[105] P.-A. Wang, W.-M. Liu, X.-L. Sun, *Org. Prep. Proc. Int.* **2011**, *43*, 477-483.

[106] J. Novacek, L. Roiser, K. Zielke, R. Robiette, M. Waser, *Chem. Eur. J.* **2016**, *22*, 11422-11428.

[107] R. Manzano, S. Datta, R. S. Paton, D. J. Dixon, *Angew. Chem. Int. Ed.* **2017**, *56*, 5834-5838.

[108] M.-H. Yang, S. S. Matikonda, R. A. Altman, *Org. Lett.* **2013**, *15*, 3894-3897.

[109] Z. Li, R. J. Twieg, *Chem. Eur. J.* **2015**, *21*, 15534-15539.

[110] T. Leermann, F. R. Leroux, F. Colobert, *Org. Lett.* **2011**, *13*, 4479-4481.

[111] R. Hollenstein, W. von Philipsborn, *Helv. Chim. Acta* **1972**, *55*, 2030-2044.

[112] K. V. Kilway, J. S. Siegel, *J. Am. Chem. Soc.* **1992**, *114*, 255-261.

[113] O. Sudmeijer, A. E. Wilson, G. R. Hays, *Org. Magn. Res.* **1984**, *22*, 459-463.

[114] O. L. Chapman, J. C. Clardy, T. L. McDowell, H. E. Wright, *J. Am. Chem. Soc.* **1973**, *95*, 5086-5087.

[115] M. H. Bolli, J. Velker, C. Müller, B. Mathys, M. Birker, R. Bravo, D. Bur, R. de Kanter, P. Hess, C. Kohl, D. Lehmann, S. Meyer, O. Nayler, M. Rey, M. Scherz, B. Steiner, *J. Med. Chem.* **2014**, *57*, 78-97.

[116] S. F. Martin, G. W. Phillips, T. A. Puckette, J. A. Colapret, *J. Am. Chem. Soc.* **1980**, *102*, 5866-5872.

[117] W. Gramlich, *Liebigs Ann. Chem.* **1979**, *1979*, 121-132.

[118] Y. Landais, F. Robert, E. Godineau, L. Huet, N. Likhite, *Tetrahedron* **2013**, *69*, 10073-10080.

[119] C. J. C. Whitehouse, N. H. Rees, S. G. Bell, L.-L. Wong, *Chem. Eur. J.* **2011**, *17*, 6862-6868.

[120] S. Nagasawa, Y. Sasano, Y. Iwabuchi, *Angew. Chem. Int. Ed.* **2016**, *55*, 13189-13194.

[121] A. A. Frimer, P. Gilinsky-Sharon, G. Aljadeff, H. E. Gottlieb, J. Hameiri-Buch, V. Marks, R. Philosof, Z. Rosental, *J. Org. Chem.* **1989**, *54*, 4853-4866.

[122] K. Wińska, A. Grudniewska, A. Chojnacka, A. Białońska, C. Wawrzeńczyk, *Tetrahedron: Asymm.* **2010**, *21*, 670-678.

[123] E. G. Meek, J. H. Turnbull, W. Wilson, *J. Chem. Soc.* **1953**, 811-815.

[124] H. Kotsuki, P. K. Datta, H. Hayakawa, H. Suenaga, *Synthesis* **1995**, *1995*, 1348-1350.

[125] P. Yates, D. J. Burnell, V. J. Freer, J. F. Sawyer, *Can. J. Chem.* **1987**, *65*, 69-77.

[126] A. J. Pearson, I. C. Richards, D. V. Gardner, *J. Org. Chem.* **1984**, *49*, 3887-3891.

[127] H. E. Zimmerman, P. A. Wang, *J. Am. Chem. Soc.* **1993**, *115*, 2205-2216.

[128] F. G. Bordwell, K. M. Wellman, *J. Org. Chem.* **1963**, *28*, 2544-2550.

[129] V. Pace, L. Castoldi, W. Holzer, *Adv. Synth. Catal.* **2014**, *356*, 1761-1766.

[130] A. Dahan, M. Portnoy, *J. Org. Chem.* **2001**, *66*, 6480-6482.

[131] Y. Inouye, M. Shirai, T. Michino, H. Kakisawa, *Bull. Chem. Soc. Jpn.* **1993**, *66*, 324-326.

[132] K. L. Cook, M. J. Hughes, A. J. Waring, *J. Chem. Soc., Perkin Trans. 2* **1972**, 1506-1508.

[133] D. W. Swatton, H. Hart, *J. Am. Chem. Soc.* **1967**, *89*, 5075-5076.

[134] P. Binger, A. Brinkmann, *Chem. Ber.* **1978**, *111*, 2689-2695.

[135] C. Bolm, I. Schiffers, C. L. Dinter, A. Gerlach, *J. Org. Chem.* **2000**, *65*, 6984-6991.

[136] L. Pohjala, S. Alakurtti, T. Ahola, J. Yli-Kauhaluoma, P. Tammela, *J. Nat. Prod.* **2009**, *72*, 1917-1926.

[137] A. F. Bramwell, L. Crombie, P. Hemesley, G. Pattenden, M. Elliott, N. F. Janes, *Tetrahedron* **1969**, *25*, 1727-1741.