Enantioselective addition-alkylation reactions via bisguanidinium silicate ion pair catalysis

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**Enantioselective Addition-Alkylation Reactions via
Bisguanidinium Silicate Ion Pair Catalysis**

CHEN WENCHAO

SCHOOL OF PHYSICAL AND MATHEMATICAL SCIENCES

2020

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SCHOOL OF PHYSICAL AND MATHEMATICAL SCIENCES

A thesis submitted to the Nanyang Technological
University in partial fulfilment of the requirement for the
degree of Doctor of Philosophy

2020

Statement of Originality

I hereby certify that the work embodied in this thesis is the result of original research done by me except where otherwise stated in this thesis. The thesis work has not been submitted for a degree or professional qualification to any other university or institution. I declare that this thesis is written by myself and is free of plagiarism and of sufficient grammatical clarity to be examined. I confirm that the investigations were conducted in accord with the ethics policies and integrity standards of Nanyang Technological University and that the research data are presented honestly and without prejudice.

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Tan Choon-Hong

Authorship Attribution Statement

This thesis contains material from one paper manuscript where I was the first author.

Chapter 2 and chapter 3 are manuscript as Wenchao Chen, Zhijie Chua, Siu-Min Tan, Jingyun Ren, Ziqi Yang, Esther Cai Xia Ang, Bo Teng, Richmond Lee, Haihua Lu, and Choon-Hong Tan. Enantioselective Reduction-Addition of Chromones and Coumarins via Bisguanidinium Silicate Ion Pair Catalysis. (First author)

The contributions of the co-authors are as follows:

- Prof. Choon-Hong Tan suggested the materials area and edited the manuscript drafts.
- I wrote the drafts of the manuscript. The manuscript was revised by every author.
- I performed all the materials synthesis, HPLC analysis, NMR spectra, and conducted data evaluation.
- Dr Richmond Lee and Su-Min Tan performed the computational calculation part.
- Dr. Yongxin Li conducted the X-ray diffraction data and single crystal structure determinations.

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Abstract

The aim of this research work is to further develop the application of hypervalent silicates in highly enantioselective reactions via asymmetric ion-pairing catalysis. In this thesis, the project revealed the novel enantioselective reduction-addition strategy as an excellent synthetic methodology, and the essence of chemistry was studied mechanistically.

The first chapter (Chapter 1) introduced the background from two aspects, including the introduction of asymmetric ion-pairing catalysis and the application of hypervalent silicon species in stereoselective synthesis. The following chapter presented the research project utilizing our designed enantioselective reduction-addition strategy.

Since the last few years, our group has developed a series of chiral quaternary ammonium phase-transfer catalysts, which were successfully applied in asymmetric phase-transfer catalysis. Meanwhile, asymmetric ion pair catalysis was put forward as a branched subject in this field. Motivated by the concept of ion-pairing, the work described in this thesis proved the potential application of the bisguanidinium silicate ion pair in asymmetric catalysis.

In Chapter 2, the high enantioselective reduction-alkylation and reduction-addition of chromones and coumarins was realized through bisguanidinium silicate ion-pairing catalysis. The active hypervalent silicate intermediates were characterized by NMR spectroscopy, control experiments and supported by computational data.

Chapter 3 is the detailed mechanistic study.

Chapter 4 is the experimental procedures and characterization data of the chiral products.

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Chapter 1

Introduction

1.1 Chiral cation-directed ion-pairing catalysis

1.1.1 Introduction to asymmetric ion-pairing catalysis

The concept of ion pairs was presented for the first time in 1926 by Bjerrum.¹ It was defined officially in textbook by Anslyn and Dougherty in 2006.² It said, ion pair is defined to exist when a cation and an anion are close enough, and the required dissociation energy is higher than the thermal energy (at room temperature) available for separating them. From the other perspective, the lifetime of ion pair is longer than the time required for forming non-interacting ions caused by *Brownian motion*.

Asymmetric ion-pairing catalysis was then developed as a kind of asymmetric catalysis taking place specifically with charged reagents or charged intermediates. It is distinct from other covalent types of asymmetric catalysis such as chiral Lewis acid catalysis³ and other chiral organocatalysis⁴. While covalent catalysts have achieved great success in enantioselective synthesis, however, their application in reactions involving charged intermediates is often not straightforward. Asymmetric ion-pairing catalysis emerges as a more attractive approach for enantioselective reactions of charged reagents or intermediates as the enantioselectivity can be induced through electrostatic or other noncovalent interactions between the charged intermediates and charged chiral catalysts.⁵

Two general approaches that have emerged for asymmetric catalysis of reactions proceeding via charged reagents or intermediates. One is ion-pairing with a charged catalyst and the other is noncovalent binding to the intermediate ion pair with a neutral catalyst (Figure 1.1)⁵. Chiral cation-directed ion-pairing catalysis contains a chiral catalyst with cationic charge. As for cationic phase-transfer catalysis, most reactions are Brønsted base reactions, in which the functional anion is usually either hydroxide or carbonate. Occasionally, other functional anions such as cyanide (CN^-) and hypochlorite (ClO^-) are used in phase-transfer Strecker or oxidation reactions, respectively. An innovative example is the use of (hypo)iodite (IO^-), generated *in*

situ from iodide, by Ishihara for a phase-transfer oxidative cycloetherification.⁶ However, these reactions are but a subset of a more general strategy of chiral cationic ion-pairing catalysis, which is defined as reactions using a catalyst composed of an organic chiral cation and an inorganic anionic salt. Ion-pairing catalysis by anionic catalysts is also called asymmetric counter anion-directed catalysis. In the other variation of asymmetric ion-pairing catalysis called cation or anion binding catalysis, the chiral catalyst is neutral but binds to an intermediate ion pair in a noncovalent way.

Figure 1.1 Types of asymmetric ion-pairing catalysis

1.1.2 Chiral quaternary ammonium cation-directed catalysis

The history of ion-pairing catalysis as an important approach in asymmetric synthesis can be traced to the 1984 in which the first example of chiral cation-directed catalysis was reported by Dolling, Davis & Grabowski using a chiral cinchonidine based phase transfer catalyst in the synthesis of indacrinone (Figure 1.2)⁷.

Figure 1.2 First reported chiral quaternary ammonium catalyzed alkylation reaction

This result revealed for the first time that high enantioselectivity can be achieved solely through noncovalent interactions of a charged intermediate with a chiral ionic catalyst. Since that seminal discovery, chiral quaternary ammonium cation-directed catalysis was well developed. A remarkable number of chiral quaternary ammonium salts have been synthesized and become the largest class of chiral phase-transfer catalysts.⁸ Representative examples are shown in Figure 1.3. New generations of chiral quaternary ammonium catalysts can be classified into two groups: one possesses sp^3 -nitrogen center, and another possesses sp^2 -nitrogen center. Maruoka and co-workers developed C_2 -symmetric bis-binaphthyl based sp^3 -nitrogen centered chiral spiro ammonium salts.⁸ Shibasaki and co-workers developed two sp^3 -nitrogen centered TADDOL derived ammonium catalysts.¹⁰

Figure 1.3 Representative examples of chiral quaternary ammonium catalysts

In recent decades, our group has developed a series of guanidine-based chiral pentanidium and bisguanidinium salts as sp^2 -nitrogen centered chiral ammonium catalysts (Figure 1.4) which were successfully utilized in asymmetric phase-transfer catalysis.¹¹⁻¹²

Figure 1.4 Pentanidium and bisguanidinium salts developed by our group

The pentanidium salt (**PN**) was first demonstrated and successfully applied to asymmetric Michael addition of glycine derived Schiff base to α,β -unsaturated acceptor in 2011.¹³ The single diastereomer product was obtained in high yield and enantioselectivity (Figure 1.5).

Figure 1.5 Pentanidium-catalyzed Michael addition of Schiff base

On the basis of preliminary models of catalysts, a new generation of guanidinium-based chiral ammonium catalyst was synthesized, which was first reported and described as bisguanidinium (**BG**) in 2015.¹⁴ A strategy of changing the linker between the two guanidinium units was attempted in our group. In a series of catalyst derivatives, piperazine-linked **BG** was found to be the best catalyst for the application in asymmetric dihydroxylation and oxohydroxylation oxidation with potassium permanganate as oxidant. (Figure 1.6) Owing to the ion-pairing between chiral bisguanidinium cation and permanganate anion, the dihydroxylation and oxohydroxylation products were obtained with high enantioselectivities.

Figure 1.6 Bisguanidinium-catalyzed dihydroxylation and oxohydroxylation

After that, **BG** was also successfully utilized in asymmetric sulfoxidation with changing metallic anion from permanganate to tungstate¹⁵ anion or molybdate.¹⁶ (Figure 1.7a). Direct hydrogen peroxide transfer was proved not efficient, while catalytic amount of metal oxide made the reaction proceed much faster. Highly enantioselective epoxidation was also achieved under the same catalytic system as shown in Figure 1.7b.

Figure 1.7 Bisguanidinium catalyzed sulfoxidation and epoxidation reactions

On the other hand, **BG** showed ability to form chiral ion pair with hypervalent silicate intermediates. In 2016, an asymmetric alkylation using silylamide as probase was successfully achieved with **BG** as catalyst.¹⁷ (Figure 1.8)

Figure 1.8 Bisguanidinium catalyzed enantioselective alkylations

The bisguanidinium silicate ion pairing catalysis was also applied to enantioselective 1,2-anionotropic rearrangement of acylsilane to furnish chiral secondary alcohol with high yield and excellent enantioselectivity. The intramolecular 1,2-Brook rearrangement occurred in the presence of CsF which worked as an activator of acylsilane to generate reactive hypervalent silicate intermediate. A bisguanidinium hypervalent silicate ion pair was proposed to be the key intermediate for the stereo determining step. (Figure 1.9).¹⁸

Figure 1.9 Enantioselective 1, 2-anionotropic rearrangement of acylsilane

1.2 Hypervalent silicates in stereoselective synthesis

Silicon comes directly below carbon in the periodic table. Silicon does not form very stable multiple bonds, because the large 3p orbital on Si cannot overlap well with the 2p orbital of C, O or N. As a result, $\text{Si}=\text{C}$, $\text{Si}=\text{O}$ and $\text{Si}=\text{N}$ are generally not found. However, silicon forms very strong bonds to oxygen and fluorine. Much of organosilicon chemistry is driven by the formation of Si-O (108 kcal/mol) or Si-F (135 kcal/mol) bond at the expense of weaker bonds. Silicon is able to access hypervalent complexes, it can adopt 4-, 5- and 6-coordinated complexes. Electron density at silicon will decrease with the increasing of coordination, causing the Lewis acidity of the silicon center to be increased (Figure 1. 10).

Figure 1.10 Coordination of silicon

Silicon compounds with a coordination number higher than four have been known since the adduct $\text{SiF}_4 \cdot 2\text{NH}_3$ was reported by Gay-Lussac in 1809.¹⁹ Since the last decades of 20th century, there is an increasing interest in the distinctive reactivity displayed by penta- and hexa-

coordinated hypervalent silicon compounds in organic synthesis.²⁰⁻²¹ After that, asymmetric versions of several reactions promoted by silicon-based catalysts have been developed²² specially promoted by hypervalent silicate intermediates used as chiral Lewis bases²³.

Figure 1.11 Bond Order and charge distribution of silicon compounds

Consider bond order and charge distribution^{20,24}, silicon is capable to form more bonds than the four needed for fulfilling the octet rule. In the presence of Lewis base, it is likely to form five-, six- and even seven- coordinated hypervalent silicate species (Figure 1.11). Some of them have been isolated and/or characterized²⁰⁻²¹. The “hypervalent bonding” theory²⁵ rules out the participation of the 3d orbitals in the bonding process and hypothesizes a so-called “hypervalent bonding”: the generation of a penta- or hexa-coordinated hypervalent silicon species would involve one or two 3-center-4-electron molecular bonds separately, each formed by a p-orbital of silicon and two p-orbitals of electronegative ligands featuring a relative *trans*-disposition. It’s helpful in explanation of the increased Lewis acidity of the silicon atom and the electronic density transfer to the ligands, which confer to silicon-bound R groups (*cf.* Figure 1.10) nucleophilic properties.

Hypervalent silicate is usually generated *in situ* by the reaction between a four-coordinated silane and a Lewis base in the “activation step” (*cf.* Figure 1.12). The so-formed penta- or hexa-coordinated hypervalent silicon species is able to promote the reaction in a catalytic process if

the Lewis base can dissociate from silicon after the formation of the desired product. Generally, three kinds of reaction mechanism can be classified according to the role played by the hypervalent silicates (Figure 1.12): (i) the hypervalent silicate acts as a Lewis acid coordinating to the substrate and activating it towards the attack of another nucleophile (Figure 1.12, pathway a); (ii) a nucleophilic silicon ligand is transferred to the substrate which is not coordinated by silicon (Figure 1.12, pathway b); (iii) the hypervalent silicate coordinates to the substrate, meanwhile, one of the ligands is transferred (Figure 1.12, pathway c). The mechanism operating through pathway a was explored by Denmark, where a basic ligand is employed to increase the activity of the Lewis acid. In the pathway c, both of the particular properties of hypervalent silicates are so exploited and the cyclic transition state allows an efficient stereoselectivity control of the product.

Figure 1.12. Reaction mechanism involving hypervalent silicon species

1.2.1 Stereoselective C-H bond formation

Stereoselective reduction of ketones

Various kinds of catalytic methods have been employed for stereoselective reduction of ketones and ketimines: hydrogenation, hydrosilylation and hydroboration. Among others, trialkoxysilanes activated by coordination with different bases have been developed in the reduction of carbonyl compounds. In early 1980s, Corriu reported the fluoride activated silicon hydride reduction of ketones in nonchiral version (Figure 1.13a).²⁶⁻²⁷ Both penta-coordinated and hexa-coordinated silicates were involved in the proposed mechanism (Figure 1.13b).

a) fluoride promoted hydrosilylation

b) proposed mechanism

Figure 1.13 Fluoride activated silicon hydride reduction of ketones

In 1988, Hosomi discovered that lithium alkoxides can act as reversible binding Lewis bases to activate trimethoxysilane for the reduction of ketones. The reaction underwent a highly catalytic processes with only 0.4 mol% catalyst loading (Figure 1.14a).²⁸ In 1997, Kagan reported the use of a chiral monolithium salt of (*R*)-binaphthol as an activator of trimethoxysilane for the enantioselective reduction of ketones (Figure 1.14b).²⁹ Dilithium salt of histidine were reported as promoters as well (Figure 1.14c).³⁰ However, for most of the

products, only moderate enantioselectivities were obtained. The major problem is that the product alkoxide can also act as a Lewis base catalyst leading to the low enantioselectivity.

Figure 1.14 Chiral Lewis base activation of trialkoxysilanes for the reduction of ketones

Asymmetric silicon hydride reduction with metal-free systems were also developed. In particular, trichlorosilane is an attractive reducing agent due to its low price and easy for preparation. A series of Lewis bases, such as *N,N'*-dimethylformamide, trialkylamines, acetonitrile, can be used for the activation of trichlorosilane to generate hexa-coordinated hydrosilicate, which is the real active reducing agent. In 1999, it was reported that *N*-formylproline derivatives can work as organic catalysts for the reduction of aromatic ketones with trichlorosilane (Figure 1.15)³¹ The reaction proceeded at room temperature in dichloromethane, however, only modest yields and enantioselectivities were obtained.

Figure 1.15 Trichlorosilane as reducing agent for stereoselective reduction of ketones

Stereoselective reduction of imines

Later the methodology was extended to the reduction of imines derived from aromatic carbonyl derivatives (Figure 1.16a).³²

Figure 1.16 Representative examples of stereoselective reduction of imines

In 2003, Hosomi reported chiral lithium-alkoxide catalyzed enantioselective reduction of imines with trimethoxyhydrosilane (Figure 1.16b).³³ In 2004, Malkov et al. developed a more successful methodology using amino acid-derived chiral formamides as catalysts for the stereoselective reduction of imines (Figure 1.16c).³⁴ A new family of organocatalysts able to activate trichlorosilane were developed by Sun group in 2006 (Figure 1.16d).³⁵ The

enantioselective reduction of a broad range of N-aryl ketimines was achieved in the presence of a chiral sulfinamide catalyst. In 2007, Tsogoeva et al. reported the enantioselective reduction of imines with new N-formylproline derivatives (Figure 1.16e).³⁶ The yields and enantioselectivities can be improved by employing HMPA or *p*-nitro benzoic acid as additives.

Stereoselective conjugate reduction of α , β -unsaturated system

Stereoselective conjugate reduction of α , β -unsaturated carbonyl compounds is an attractive and challenging approach for the construction of chiral ketones. During the past few decades, considerable efforts have been devoted to this area and great improvement was made in transition metal catalyzed asymmetric hydrogenation. However, only a few examples about chiral Lewis base catalyzed conjugate hydrosilylation of α , β -unsaturated carbonyl compounds have been reported.

Figure 1.17 Enantioselective conjugate reduction of α , β -unsaturated ketones

In 2008, Nakajima and co-workers³⁷ reported a Lewis base-catalyzed 1,4-reduction of α , β -unsaturated ketones with trichlorosilane (Figure 1.17a). Since the 1,2-reduction of aldehydes

scarcely proceeded under the reaction conditions, one-pot reductive aldol reaction was also successfully achieved. In 2015 Han developed a general, efficient, and highly enantioselective method for the synthesis of structurally diverse chiral P-stereogenic phosphinamides, which were utilized as Lewis base organocatalysts and successfully applied in the highly enantioselective reduction of α,β -unsaturated carbonyl compounds (Figure 1.17b)³⁸. In 2019, Wang reported the enantioselective conjugate reduction of β,β -disubstituted α,β -unsaturated ketones with trichlorosilane in the presence of a chiral picolinamide–sulfonate Lewis base catalyst, affording various chiral ketones bearing a chiral center at the β -position in high yields and moderate enantioselectivities (Figure 1.17c)³⁹. Very recently, Kotani's group reported a chiral bisphosphine dioxide-catalyzed asymmetric conjugate reduction of acyclic β,β -disubstituted α,β -unsaturated ketones with trichlorosilane affording saturated ketones bearing a chiral carbon center at the carbonyl β -position with high enantioselectivities (up to 98% ee).⁴⁰

Figure 1.18 Enantioselective conjugate reduction of α,β -unsaturated esters

Enantioselective conjugate reduction of β -enamino esters were also reported. In 2011 Zhang et al. reported the catalytic asymmetric hydrosilylation of α -acetoxy β -enamino esters in the presence of a chiral Lewis base catalyst (Figure 1.18a).⁴¹ The conjugate reduction proceeded smoothly providing a broad range of chiral α -acetoxy β -amino acid derivatives with good

enantioselectivities and diastereoselectivities (up to 96% *ee*, 99:1 *dr*). In 2016 Sun's group reported a chiral Lewis base-catalyzed enantioselective reduction of unprotected β -enamino esters (Figure 1.18b).⁴² The supposedly moisture sensitive reduction system with trichlorosilane was found to be highly efficient and stereoselective when using one equivalent water as an additive. This method enables the conjugate reduction of a wide range of *N*-alkyl β -enamino esters to afford *N*-alkyl β -amino esters in good yields and excellent enantioselectivities.

1.2.2 Allylation of C=O and C=N group

The coordination of a Lewis base to the silicon atom of silane leads to hypervalent silicon species of increased Lewis acidity at silicon center. As consequence, such hypervalent silicates become very reactive carbon nucleophiles with a strong electrophilicity at silicon and an enhanced capability to transfer a formally electronegative group to an acceptor. Based on this, several asymmetric catalysis systems involving hypervalent silicate intermediates have been explored for stereoselective carbon–carbon bond construction.

Allylation of C=O group

In 1987, Sakurai et al. reported racemic Lewis Base promoted allylation using fluorides and alkoxides to activate tetravalent silanes.⁴³ In 1994, Denmark's group reported the first enantioselective, noncatalytic, chiral phosphotriamide promoted allylation of allyltrichlorosilane to aldehydes (Figure 1.19a).⁴⁴ In 2006, the same group reported the enantioselective allylation of benzaldehyde in the presence of a chiral bidentate phosphoroamide catalyst, affording the product in high yield and up to 72% *ee*. (Figure 1.19b).⁴⁵ Based on these results, new bidentate catalysts derived from 2,2'-bispyrrolidine and 2,2'-bispiperidine units were investigated and promoted the allylation reaction in high yields and enantioselectivities.⁴⁶ Various γ -substituted allyltrichlorosilanes were employed affording the allylation products in high yields and enantioselectivities, showing a good correlation

between the configuration of the C=C bond in the reagent and the *syn/anti* diastereoisomeric ratio of the products (Figure 1.19c)⁴⁵

Figure 1.19 Phosphoroamides promoted addition of allyltrichlorosilane to aldehydes

Other organocatalysts were also investigated with less success in the asymmetric allylation of carbonyl compounds, such as sulfoxides that however were used in non-catalytic amounts. phosphine oxides. In 2005 Hashimoto's group reported chiral phosphine oxides promoted enantioselective addition of several β -substituted allyltrichlorosilanes to aldehydes in the presence of tetrabutylammonium iodide as an additive providing the products with moderate enantioselectivities.⁴⁷

Allylation of C=N group

Compared to enantioselective allyl addition to carbonyl compounds, the analogous reaction with imines and imino esters is less developed. In 2003 Kobayashi's group reported the first example of enantioselective allylation of allyltrichlorosilane to *N*-acylhydrazones promoted by stoichiometric amount of a chiral sulfoxide providing the products with high enantioselectivities (up to 96% *ee*).⁴⁸ In this case the use of *E*-crotylsilanes afforded the *syn* products, while the use of *Z*-crotylsilanes afforded the *anti* adducts, as shown in Figure 1.20a.

Kobayashi also developed a zinc fluoride catalyzed enantioselective allylation of allyltrimethoxy silane to acylhydrazono esters in the presence of a chiral diamine ligand (Figure 1.20b).⁴⁹ In this reaction water played an important role in generating the products. In 2004 Fernandes and Yamamoto reported the asymmetric addition of allyltrimethoxysilane to simple imines promoted by a dual activation process involving the use of TBAF and a chiral palladium complex, affording the products in good enantioselectivities (up to 84% *ee*), but very low yields (Figure 1.20c).⁵⁰

Figure 1.20 Enantioselective allylation of imines and imino esters

Finally, it was reported that stoichiometric amount of chiral phosphine oxide may also be employed to achieve high yields and enantioselectivities in the enantioselective allyltrimethylsilane addition to acylhydrazono esters as shown in Figure 1.20d.⁵¹ An efficient catalytic enantioselective organocatalyzed version of this reaction is still in highly desirable.

1.2.3 Aldol reaction

Compared with the corresponding allylsilanes, silyl enol ethers have a higher reactivity. The aldol reaction of trichlorosilyl enol ethers with aldehydes proceeds readily at room temperature even without a catalyst. Nevertheless, the reaction can be substantially accelerated by Lewis bases setting the scene for the development of an asymmetric version. Denmark et al. developed a range of efficient chiral phosphoramides as nucleophilic activators for enantioselective aldol reactions of silyl enol ethers with aldehydes. Meanwhile, a detailed mechanistic investigation was also carried out.⁵²

Figure 1.21 Enantioselective aldol reaction of trichlorosilyl enol ethers

In 1996 Denmark reported the first example of enantioselective chiral phosphoroamide catalyzed aldol condensation of trichlorosilyl enol ethers affording the products in 95% yield, 65:1 syn/anti ratio and 93% *ee* (Figure 1.21a).⁵³ It was demonstrated that the diastereoselectivities were largely dependent on the structure of the chiral catalyst. Denmark was able to show that also pyridine *N*-oxides can promote the aldol reaction. In 2002 Denmark's group reported a chiral bis-*N*-oxide catalyzed enantioselective aldol reaction, affording the products in good yields and enantioselectivities (Figure 1.21b).⁵⁴ Other chiral *N*-

oxides were also employed, but with less success. Also phosphine oxide, already employed in allylation reaction, was shown to be able to catalyze the enantioselective aldol reaction of trichlorosilyl enol ethers with activated aromatic aldehydes in high stereoselectivity. (Figure 1.21c).⁵⁵ Denmark explored the possibility to develop chiral hypervalent silicates to be used as Lewis acid. A highly efficient enantioselective aldol reaction of silyl enol ethers catalyzed by a Lewis base activated with tetrachlorosilane was reported.⁵⁶ Catalytic amounts of phosphoramidate (1 mol%) in the presence of stoichiometric amount of tetrachlorosilane promoted the addition of silyl ketene acetals to aromatic aldehydes in high yields and stereoselectivities (Figure 1.22a). The enantioselective vinylogous aldol addition of conjugated N, O-silyl ketene acetals to aldehydes was also described (Figure 1.22b)⁵⁷

Figure 1.22 Chiral phosphoroamide catalyzed aldol reaction of silyl ketene acetals

1.2.4 Allenylation and propargylation reactions

Allenyl trichlorosilane and propargyl trichlorosilane were shown to react with aromatic aldehydes under Lewis base activation, similarly to the addition of allyltrichlorosilane to carbonyl compounds.⁵⁸ The addition of propargyl trichlorosilane to aldehydes generates allenyl alcohols, while the addition of allenyl trichlorosilane to aldehydes leads to the corresponding propargyl alcohol products. Nakajima reported the asymmetric version.⁵⁹ The chiral

biquinoline bis-*N*-oxide was employed as catalyst, however, the only moderate enantioselectivities were observed (Figure 1.23).

Figure 1.23 Biquinoline bis-*N*-oxide catalyzed allenylation and propargylation reactions

1.2.5 Trimethylsilyl cyanide addition

Reactions involving trimethylsilyl derivative (including trimethylsilyl enol ether) and catalyzed by chiral Lewis bases have been well established.⁶⁰ Among these reactions, the enantioselective addition of trimethylsilyl cyanide to carbonyl or imine derivatives has been studied in more detail.

Figure 1.24 *N, N'*-dioxides catalyzed enantioselective cyanosilation

In 2003 Feng and co-workers reported the enantioselective Strecker reaction of trimethylsilyl cyanide and aldimines in the presence of chiral *N,N'*-dioxides.⁶¹ However, stoichiometric

amount of chiral Lewis base promoters was needed in this case. With the most efficient *N,N'*-dioxide, the reaction proceeded under mild conditions with a broad range of aromatic *N*-benzhydrylimines affording the products in high yields and moderate to excellent enantioselectivities (up to 95% ee) (Figure 1.24a). In 2005 Feng's group developed a new class of proline-based *N, N'*-dioxides which were employed in the enantioselective cyanosilylation of aldehydes with a catalyst loading as low as 2.5 mol% (Figure 1.24b).⁶²

In 2007 Feng and co-workers⁶³ further extended the reaction to dialkoxy ketones by using bifunctional *N,N'*-dioxide catalyst (Figure 1.24c). The mechanistic study indicated that the *N, N'*-dioxide performed as a bifunctional catalyst where the *N*-oxide moiety acted as a Lewis base to activate the trimethylsilyl cyanide and the amide hydrogen worked as a Brønsted acid for the activation of the carbonyl group of the substrate. A hexa-coordinated hypervalent silicate was involved in the proposed transition state as shown in Figure 1.25.

Figure 1.25 Proposed transition state

In 2003 Deng's group reported the first example of highly enantioselective cyanosilylation of acetal ketones using a modified cinchona alkaloid catalyst.⁶⁴ Only 2.0 mol % catalyst loading was required for achieving high enantioselectivity, up to 98% ee was obtained (Figure 1.26).

Figure 1.26 Cinchona alkaloid catalyzed cyanosilylation of acetal ketones

Asymmetric cyanosilylation can also be promoted by chiral metal complexes. In 2000 Shibasaki and co-workers⁶⁵ reported a chiral titanium complex promoted enantioselective cyanosilylation of ketones affording the products in good enantioselectivities.

a) titanium complex catalyzed enantioselective cyanosilylation

b) proposed transition state (involving penta-coordinated hypervalent silicate)

c) aluminum complex catalyzed enantioselective cyanosilylation

Figure 1.27 Asymmetric cyanosilylation catalyzed by chiral metal complexes

In 2001 Shibasaki's group⁶⁶ further modified the chiral ligand making the catalyst more efficient by the introduction of a benzoyl group at the catechol moiety (Figure 1.27a). The products of cyanosilylation of ketones are obtained with high yields and enantioselectivities. The authors also proposed the transition state showed in Figure 1.27b: the titanium atom acts as a Lewis acid to activate ketone, while the phosphine-oxide oxygen coordinates to the silicon atom of trimethylsilyl cyanide generating a penta-coordinated hypervalent silicon species and thus enhancing the nucleophilicity of the cyanide group. Shibasaki's group also reported a new bifunctional chiral aluminum complex (Figure 1.27c) with one Lewis-acidic site (the aluminum atom) and two Lewis-basic sites (the phosphine-oxide oxygen atoms).⁶⁷ In this case the enantioselective cyanosilylation of aldehydes is promoted via a dual activation: the aldehyde is activated by coordination with aluminum, while trimethylsilyl cyanide is activated by the phosphine oxides in this process.

1.2.6 Ring opening reaction of epoxides

Epoxides play an important role in organic synthesis as a variety of nucleophiles can be employed in the ring opening reactions. Denmark et al.⁶⁸ reported the first chiral phosphoramidate catalyzed enantioselective ring opening reaction of mesoepoxides with tetrachlorosilane (Figure 1.28). A penta-coordinated hypervalent silicate intermediate, generated by the reaction of Lewis base and tetrachlorosilane, was proposed in the mechanistic studies. The substrate was activated by coordinating of the oxygen atom to the silicate intermediate, which made the epoxide more electrophilic. Followed by chloride attacking which proceeded in an S_N2 fashion.

Figure 1.28 Chiral phosphoramidate catalyzed ring opening reaction of *meso*-epoxides

In 2001, Fu and co-workers⁶⁹ reported a new family of chiral catalysts promoting the ring opening reaction of *meso*-epoxides with tetrachlorosilane, affording the desired products in high enantioselectivity (up to 98% *ee*) (Figure 1.29). A hexa-coordinated silicate intermediate was proposed. The authors showed that the stereoselectivity was increased with the increasing of the steric hindrance of the catalyst.

Figure1.29 Chiral pyridine *N*-oxide catalyzed ring opening reaction

Nakajima et al. showed that chiral bipyridine *N,N'*-dioxide can be utilized in the enantioselective ring opening of *meso*-epoxides with tetrachlorosilane (Figure 1.30a).

a) chiral bipyridine *N,N'*-dioxide catalyzed ring opening reaction

b) chiral phosphine oxide catalyzed ring opening reaction

Figure1.30 Bipyridine *N, N'*-dioxide and phosphine oxide catalyzed opening reaction

The catalyst acts as a bidentate ligand coordinating to the silicon atom of tetrachlorosilane to form a hexa-coordinated silicate to increase the nucleophilicity of the chloride. In 2005 Nakajima's group reported that also chiral phosphine oxide (S)-BINAPO⁷¹ can catalyze the

enantioselective ring opening of *meso*-epoxides in the presence of tetrachlorosilane, affording the corresponding chlorohydrins in high enantioselectivities (up to 90% *ee*) (Figure 1.30b).

1.3 Summary

Over the past decades the power of hypervalent silicates has begun to be harnessed. In particular, Denmark et al. had made a great contribution to the development of this area both in terms of reaction development and mechanistic rationale. As hypervalent silicate species may work through different activation mechanisms, they have recently attracted much attention for their diversity and for the possibility to develop more catalytic processes. However, it's difficult to accurately assess the accurate nature, coordination and conformation of the active hypervalent silicate intermediate and transition state orientation. The use of substoichiometric amounts of an organic compound of relatively low molecular weight and simple structure capable to promote reactions under transition metal free conditions is very attractive. The developing of new enantioselective reactions in the presence of cheap, low toxic and environmentally- friendly silicon-based reagents is still highly desirable.

Compared to covalent catalysis, asymmetric ion-pairing catalysis is a more attractive approach for enantioselective reactions of charged intermediates as the enantioselectivity can be induced through electrostatic or other noncovalent interactions between the charged intermediates and charged chiral catalysts. Since hypervalent silicon compounds always contain negative charge, the chiral cation-directed catalysis will have potential application in enantioselective reactions involving hypervalent silicate intermediates.

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Chapter 2

Enantioselective Addition-Alkylation of Chromones and Coumarins via Bisguanidinium Silicate Ion Pair Catalysis

2.1 Introduction

Penta- and hexa-coordinated hypervalent silicates are known to be crucial intermediates in chiral Lewis base-catalyzed stereoselective reactions (Figure 2.1a).¹⁻³ Neutral organosilanes are also able to be activated by fluoride for the reduction of carbonyl compounds.⁴⁻⁶ In addition, chiral phosphine-catalyzed enantioselective conjugate reduction of α,β -unsaturated ketones using trichlorosilane as hydride source were also reported (Figure 2.1b).⁷⁻¹² As silyl enol ethers were formed during the reduction of α,β -unsaturated ketones, enantioselective tandem reduction-aldol reaction have been developed (Figure 2.1b).^{7,13-14}

a) Silicate-mediated stereoselective reactions catalyzed by chiral Lewis bases (ref. 1-3)

R = - H, - CN, - alkyl, - allyl, enolate ect.

LB = Lewis base

HS = hypervalent silicate

b) Enantioselective reduction and reductive-aldol reaction of α,β -unsaturated carbonyls with silane catalyzed by chiral Lewis bases (ref. 7-9; 13-14)

Figure 2.1 Silicate-mediated stereoselective reactions catalyzed by chiral Lewis bases

Despite such advances and tremendous chemistry of silyl enol ether available, the trapping

of this useful *in situ* generated intermediates by hydride transfer reduction to provide synthetically interesting building blocks have not fully been achieved, and current enantioselective systems are limited to chiral phosphine promoters.

Asymmetric phase transfer and ion-pairing catalysis, which chiral cation work synergistically with anions, were reported for many enantioselective transformations.¹⁵⁻¹⁸ In particular, we have previously reported enantioselective reactions using dicationic bisguanidinium to direct various kinds of metal-centered anions.¹⁹ Preliminary research on hypervalent silicate centered anionic complexes have been carried out. We have also proposed bisguanidinium hypervalent silicates as key intermediates in enantioselective alkylations using silylamide²⁰ (Figure 2.2a) and enantioselective 1,2-anionotropic rearrangement of acylsilane²¹ (Figure 2.1b).

Figure 2.2 Stereoselective reactions via bisguanidinium silicates ion pair catalysis

In this work, we demonstrate that silicon hydride can be activated with fluoride in the presence of bisguanidinium **BG** catalyst to form hypervalent hydridosilicate ion pair (Figure 2.2c). This is followed by conjugate reduction of α,β -unsaturated ketones, to generate a hypervalent enolsilicate intermediate, followed by an enantioselective alkylation reaction.

Similarly, alkynylsilanes and alkoxy silanes can also lead to the formation of hypervalent alkynylsilicate and alkoxy silicate ion pairs. The addition-alkylation with alkynylsilanes and alkoxy silanes resulted in the construction of two vicinal chiral carbon centers with excellent enantioselectivities and diastereoselectivities.

2.2 Enantioselective reduction-alkylation of chromones

Asymmetric phase transfer alkylation of β -keto esters is an attractive approach to obtain chiral quaternary carbon centers. Due to its low pKa, it is difficult to avoid background reactions.²² A tandem reduction-alkylation is a useful strategy to circumvent this difficulty. Conjugate reduction-alkylation of α,β -unsaturated aldehydes with alcohols was reported using chiral secondary amines through enamine, iminium and acid pathways.²³ Another reduction-alkylation route through Cu-catalyzed conjugate reduction and Pd-catalyzed arylation led to β -arylated cycloalkanones.²⁴ The chromone or xanthone skeletons exist in a wide variety of natural products.²⁵⁻²⁷ Introduction of substituents into the chromone (4H-1-benzopyran-4-one) ring has been studied from the standpoint of developing synthetic methodology and investigating the reaction mechanism of such heterocycles.²⁸⁻³⁴ Chromones can be regarded as α,β -unsaturated ketones, however, there are limited synthetic methods for the construction of chiral quaternary carbon center at α position of the heterocycle ring without ring opening or transformation of the heterocycle.^{28,35} In this regard, we chose 4-oxochroman-3-carbonitrile as a model compound to investigate our approach.

Firstly, we screened the phase-transfer catalysts (PTC). Different chiral cationic pentanidium (**PN**) and dicationic bisguanidinium (**BG**) chlorides were synthesized and applied to the reaction (Figure 2.3). With various kinds of phase-transfer catalysts in hand, we started systematically optimization for the enantioselective reduction-alkylation of 4-oxochroman-3-carbonitrile **1a** with benzyl bromide **2a** as electrophile and polymethylhydrosiloxane (PMHS), which is an attractive reagent due to its low price, stability against air and moisture, and easy

handling,⁶ as the silicon hydride source (Table 2.1).

Figure 2.3 PN and BG applied to the reduction-alkylation of chromones

When pentanidium **PN1** bearing 3,5-di-tert-butylbenzyl group was used, we isolated the product **3a** in 42% yield and 36% *ee* (entry 1). We modified the 3,5-di-tert-butylbenzyl group with halide atoms, but both the yields and *ee* values decreased (entries 2-4). Then we tried different bisguanidinium **BG**. When **BG1** bearing 3,5-di-tert-butylbenzyl group was used, the reaction proceeded well affording the product in 82% yield and 81% *ee* (entry 5). After the 3,5-di-tert-butylbenzyl group was modified with chloro or bromo substitution, we got **BG2** and **BG3**, but the yields and enantioselectivities couldn't be increased (entries 6-7). Then we changed the 3,5-di-tert-butylbenzyl group to 3,5-di-trifluoromethylbenzyl group and got **BG4**,

we also have tried changing half of the 3,5-di-tert-butylbenzyl group to 3,5-difluoromethylbenzyl group and got **BG5**. However, **BG4** and **BG5** cannot further improve the results (entries 8-9). So **BG1** (bisguanidinium salt with 3,5-diterbutyl substitution) is the best catalyst for the reduction-alkylation reaction.

Table 2.1 Catalyst screening

Entry	PTC	yield (%)	ee (%)
1	PN1	42	36
2	PN2	36	15
3	PN3	38	28
4	PN4	37	27
5	BG1	82	91
6	BG2	36	33
7	BG3	42	25
8	BG4	46	63
9	BG5	37	27

Based on our previous hypothesis, the silanes used in the reaction will have a big influence on the profile of the reaction. As a result, in our preliminary studies, various kinds of silyl compounds were evaluated in our designed reaction condition. Using **BG1** as the catalyst, we investigated our approach with a variety of silanes (Table 2.2, entries 1-10). When we tuned the substituents on silanes, both the yields and enantioselectivities were influenced. We found that silanes with larger proportion hydrides led the decreasing of yields (entries 1-3). When we increase the proportion of alkyl substituents, the enantioselectivities were increased, however

the yields were decreased a lot (entries 4-6). Trialkyloxyl substituents on silanes furnished good yield and enantioselectivity (entry 7). Changing the alkyloxyl substituent to more bulky one, both the enantioselectivity and yield were decreased (entry 8). Decreasing the number of alkyloxyl substituents, the yields were decreased (entries 9-10). PMHS as silicon hydride source can provide the reduced chromone **3a** with excellent result, further low down the temperature could not improve the enantioselectivity with slightly decreasing of the yield (entries 11-12). We prefer to use PMHS, due to its low price, stability and easy handling, as hydride source to further investigate the reaction conditions.

Table 2.2 Silicon hydride source screening

entry	[SiH]	yield (%)	ee (%)
1	PhSiH ₃	24	75
2	PhMeSiH ₂	30	78
3	Ph ₃ SiH	75	76
4	Ph ₂ MeSiH	68	90
5	PhMe ₂ SiH	41	96
6	Et ₃ SiH	10	97
7	(MeO) ₃ SiH	77	89
8	(EtO) ₃ SiH	60	60
9	(EtO) ₂ MeSiH	50	67
10	(EtO)Me ₂ SiH	trace	--
11	PMHS	82	91
12*	PMHS	76	91

*Reaction temperature is -10 °C.

As solvent is one of the most important factors to produce enantioselectivity, we started

investigating the effect of solvent (Table 2.3). For aromatic solvents, mono-substituted aromatic solvents usually afforded products in good yields and enantioselectivities (entries 1-4). With the increasing of substituents on the aromatic ring, both the yields and enantioselectivities were decreased (entries 5-7). THF was not good solvent for this reaction resulting in low yield and enantioselectivity (entry 8). Ether type solvents afforded the products in excellent enantioselectivities (entries 9-12). Both 1-butoxybutane and diisopropyl ether furnished the products in 99% *ee*, however, the yields were not satisfactory (entries 10-11). CPME was the best ether solvent affording product in 84% yield and 98% *ee* (entry 12).

Table 2.3 Solvent screening

Entry	Solvent	yield (%)	ee (%)
1	Tol	81	86
2	ethylbenzene	82	85
3	4-(tert-butyl)-tolene	78	85
4	Sec-Butyl benzene	71	83
5	o-xylene	66	82
6	m-xylene	51	76
7	mesitylene	49	77
8	THF	18	61
9	Et ₂ O	53	91
10	1-butoxybutane	58	99
11	diisopropyl ether	69	99
12	CPME	84	98

With suitable conditions in hand, we next investigated the substrate scope of the reduction

alkylation using different chromones **1b-v** (Figure 2.4).

Figure 2.4 Substrates scope of reduction-alkylation of chromones

The transformation of the reduction-alkylation reaction is rather general in standard reaction conditions. Benzyl bromides **2b-2h**, bearing both electron-withdrawing and electron-donating

groups, delivered the desired products in good yields and excellent enantioselectivities regardless of the substitution at para-, meta-, or ortho- positions (**3b-3h**). Besides, we further examined different electrophiles **2i-2s** and found that different activated bromides, including allylic, propargylic, ester substituted ones gave good results (**3i-3o**). Allylic bromides gave the corresponding products with good yields and enantioselectivities (**3i-3l**). To our delight, the long chain allylic substituted substrate **3m** also showed satisfactory result (85% yield, 95% *ee*). Different chromones **1t-u** were also investigated and good yields and excellent enantioselectivities were obtained (**3t-3u**). Changing the aryl group to naphthalene ring also provided reduced chromone **3v** with satisfactory result.

2.3 Enantioselective Reduction-Alkylation of Coumarins

With the optimized best condition of model reaction in hand, we tried to apply it in other substrates. Dihydrocoumarin compounds have attracted much attentions due to their desirable biological activities.³⁶⁻³⁹ Generation of an α -quaternary carbon center of hydrocoumarins is non-trivial and there are few known examples of catalytic enantioselective synthesis.^{20,40-44} Direct alkylation is an attractive strategy but the difficulty lies in overcoming the labile lactone, which does not survive most basic conditions.⁴⁴ So we chose coumarins further expand our substrate scope.

Figure 2.5 Enantioselective reduction-alkylation of coumarin with bromides

Using similar conditions developed previously (*cf.* Figure 2.4), it was found that coumarin **4a** underwent the reduction-alkylation smoothly with benzyl bromide **2a** to give the corresponding product **5a** with good yield, however, only moderate enantioselectivity was obtained (Figure 2.5a). To our delight, when we changed the benzyl bromide to allylic bromide **6a**, enantioselectivity was improved a lot affording the desired product **7a** in 76% yield and 84% *ee* (Figure 2.5b). With allylic bromide as the electrophile, then we further optimized the reaction conditions for the enantioselectivities to be satisfactory.

AS **BG** showed better results than **PN**, so we focused on the investigation of **BG** catalysts. The enantioselectivity of this reduction-alkylation reaction was significantly improved when we used **BG1** as the catalyst (Table 2.1). This encouraged us to synthesize more catalysts with similar structure of **BG1** for better enantioselectivity (Figure 2.6).

Figure 2.6 **BG** utilized in the reduction-alkylation of coumarins

Then we started investigating the catalysts (Table 2.4). We used **BG2** and **BG3** in which the 3,5-di-tert-butylbenzyl groups were modified with chloro or bromo substitution, the yields and

enantioselectivities couldn't be improved (entries 2-3). We also have tried **BG4** (bisguanidinium salt with 3,5-di-trifluoromethylbenzyl substitution) and **BG5** (changing half of the 3,5-di-tert-butylbenzyl groups to 3,5-di-trifluoromethylbenzyl groups), however, the enantioselectivities were not increased and the yields dropped a lot (entries 4-5). When the 3,5-di-tert-butylbenzyl groups were changed to 3,5-di-methoxybenzyl group, we got **BG6** which catalyzed the reaction affording the product in low yield and enantioselectivity (entry 6). When the 3,5-di-tert-butylbenzyl groups were changed to 3,5-di-(trimethylsilyl)benzyl groups, this bisguanidinium **BG7** provided the product with 82% *ee*, but only in 58% yield (entry 7). As a result, **BG1** (bisguanidinium salt with 3,5-diterbutyl substitution) was still the best catalyst for the reduction-alkylation of coumarins.

Table 2.4 Catalyst screening for reduction-alkylation of coumarins

Entry	PTC	yield (%)	ee (%)
1	BG1	76	84
2	BG2	43	26
3	BG3	57	44
4	BG4	69	35
5	BG5	41	70
6	BG6	48	60
7	BG7	58	82

With **BG1** as catalyst, we optimized the solvents using **4a** as the model substrate (Table 2.5). Different ether solvents were then tested as they showed better results compared with other kinds of solvents (*cf.* Table 2.3). TBME is the best solvent affording the product **7a** in 78% yield and 87% *ee* (entry 5).

Table 2.5 Solvent screening for reduction-alkylation of coumarins

Entry	Solvent	yield (%)	ee (%)
1	Et ₂ O	49	79
2	1-butoxybutane	42	71
3	diisopropyl ether	26	72
4	hexyl ether	trace	–
5	TBME	78	87
6	THF	48	62
7	tert-butylethyl ether	messy	–

We also investigated the equivalent of CsF and PMHS effect on the reduction-alkylation reaction (Table 2.6). Adjustment of the equivalent of CsF and PMHS showed that 4.0 equivalent of CsF and 4.0 equivalent of PMHS afforded the product with the best yield and enantioselectivity (entry 4).

Table 2.6 CsF and PMHS loading effect on reduction-alkylation of coumarins

Entry	CsF (equiv.)	PMHS (equiv.)	yield (%)	ee (%)
1	3	2	58	74
2	3	3	62	78
3	3	4	65	84
4	4	4	78	87
5	4	5	77	85

We further screened fluoride source (Table 2.7). The fluoride source had an effect on both the reactivity and enantioselectivity (entries 1-4). **KF** as fluoride source gave the best result with 80% yield and 92% *ee* (entry 2).

Table 2.7 Fluoride source screening for reduction-alkylation of coumarins

Entry	Fluoride source	yield (%)	ee (%)
1	CsF	78	87
2	KF	80	92
3	AgF	36	65
4	NH ₄ F	80	83

With optimized reaction conditions in hand, we next investigated the substrate scope of the

reduction-alkylation using different coumarins **4b-j** (Figure 2.4). The transformation of the reduction-alkylation of coumarins is general in standard reaction conditions. The allylic bromides **5b-5d**, bearing electron-withdrawing groups delivered the desired products **7b-7d** in good yields and enantioselectivities. Increasing the length of alkyl chain of ketone substitution also afforded the products **7e-7j** in good results.

Figure 2.7 Substrates scope of reduction-alkylation of coumarins

2.4 Enantioselective addition-alkylation of chromones using alkynylsilanes

With the success of reduction-alkylation, we then investigated if other functional groups can be added in place of hydride. In the following investigations, we used the general reaction conditions (*cf.* Figure 2.4) for different types of silyl compounds in initial attempt. Then we adjusted the conditions for each substrate to achieve the best yield and enantioselectivity as sho

-wn in Figure 2.8.

Figure 2.8 Enantioselective addition-alkylation of chromones using alkynylsilanes

We tested alkynylsilanes and found that the addition-alkylation proceeded well for a variety of chromones **8a-8f** and following alkylation, two vicinal chiral carbon centers were constructed with excellent enantioselectivities and diastereoselectivities (up to 99% *ee*, > 99:1 *dr* was achieved). However, due to the low reactivity of alkynylsilanes, only moderate yields were obtained. To our delight, terminal alkynylsilane also worked well with satisfactory result for alkynylchromone **9f** (73% yield, 95% *ee*, > 99:1 *dr*). For different substituents in aromatic ring of alkynylsilanes, regardless of the substituents in different position of aromatic ring, both the electron-donating and electron-withdrawing groups, delivered the desired products **9g-9h** in moderate yields excellent enantioselectivities and diastereoselectivities. Changing the aryl group to thiophene ring also provided alkynyl-chromone **9i** with satisfactory result.

2.5 Enantioselective addition-alkylation of chromones using alkyloxysilanes

To the best of our knowledge, up to now, there is no available example on the transfer of alkyloxyl group from corresponding silanes via fluoride activation. Next, we applied the addition-alkylation strategy to alkyloxysilanes for the transfer of alkyloxyl groups for the construction of two vicinal chiral carbon centers which would be more challenging.

Figure 2.9 Enantioselective addition-alkylation of chromones using alkyloxysilanes

Alkyloxysilanes, on the other hand, reacted smoothly with high reactivities and high yields were achieved (Figure 2.9). The transfer of the alkyoxyl group from alkoxy silanes also resulted in the construction of two vicinal chiral carbon centers with high yields, good enantioselectivities and excellent diastereoselectivities for a variety of chromones **10a-f**. Changing trimethoxysilane to triethoxysilane did not affect the profile of the alkoxyated chromones **11a** and **11b** significantly.

2.6 Determination of the Absolute Configuration by X-ray Crystallography

The absolute configurations of **3d**, **7h**, and **11c** are determined by X-ray crystallography. For other products, the absolute configurations are determined by analogy.

The supplementary crystallographic data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

(A) Single-crystal structure of **3d**

Figure 2.10 Single-crystal structure of **3d** (CCDC 1965062)

(B) Single-crystal structure of **7h**

Figure 2.11 Single-crystal structure of **7i** (CCDC 1965064)

(C) Single-crystal structure of **11c**

Figure 2.12 Single-crystal structure of **11c** (CCDC 1965063)

2.7 Summary

We have developed a bisguanidinium catalyzed enantioselective addition-alkylation strategy. Silicon hydrides, alkynylsilanes and alkoxy silanes were activated with fluoride in the presence of bisguanidinium catalyst to form hypervalent silicate ion pairs. These activated silicates then undergo 1,4-additions to chromones and coumarins, generating enolsilicate intermediates,

followed by stereoselective alkylation. For the reductive-alkylation reaction, it proceeded under mild condition using PMHS, a cheap and environmentally-friendly hydride source. The addition-alkylation reactions with alkynylsilanes and alkoxy silanes resulted in the construction of two vicinal chiral carbon centers with excellent enantioselectivities and diastereoselectivities.

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Chapter 3

Mechanistic Study

3.1 Control experiment of chromone substrate

After demonstrating the wide scope of this reductive alkylation strategy through two type of substrates, we turned our attention to investigating the mechanism. Upon our previous work, we have kept on evidencing the hypervalent silicate intermediates. The best identical way is growing a single crystal to collect X-ray data. In 2007, McGrady and Steed reported the [K ([18] crown-6)]⁺ salt of [Ph₃SiF₂]⁻ and [(p-FC₆H₄)₃Si(F)H]⁻, which were characterized them by NMR spectroscopy and X-ray diffraction.¹ In our case, the hypervalent silicate intermediates are rather unstable. We tried different methods to grow the crystal. We mixed the **BG**, silanes and CsF in static solvents. However, we cannot get the crystal at last. At the same time, we have tried some other techniques. For example, CSI-HRMS (cold spray ionizing-high resolution mass spectra) is now available in our division. It is an efficient method to measure the molecular weight of ionic species under both positive and negative mode. We hoped to detect hypervalent silicate species of the reaction. However, the hypervalent silicate intermediates are so reactive that they decomposed during the injection of the reaction mixture. As a result, we turned our attention to using NMR technique, especially ¹⁹F NMR, to detect the hypervalent silicate species as all the hypervalent silicate intermediates contain fluorine. Density functional theory calculations using the gauge independent atomic orbital method were performed to predict the ¹⁹F NMR shifts of possible intermediates produced for comparison with the experimental data.

3.1.1 ¹⁹F NMR studies of hypervalent silicate intermediates

As we can see from the data (Table 3.1)^{2, 3}, the counter ion changing doesn't have much influence on the ¹⁹F NMR chemical shifts of the hypervalent silicates. As a result, the ¹⁹F NMR chemical shifts of tetrabutylammonium hypervalent silicates can help us predict the chemical shifts of the bisguanidinium hypervalent silicate intermediates

Table 3.1 Known data for hypervalent silicates

Structure	^{19}F NMR (ppm)	Solvent
$\text{Bu}_4\text{N}^+ [\text{Ph}_3\text{SiF}_2]^-$	-96.0	DMSO (d_6)
$\text{K}^+ [\text{Ph}_3\text{SiF}_2]^-$	-98.2	DMSO (d_6)
$\text{Bu}_4\text{N}^+ [(4\text{-Cl-Ph})_3\text{SiF}_2]^-$	-97.6	DMSO (d_6)
$\text{K}^+ [(4\text{-Cl-Ph})_3\text{SiF}_2]^-$	-97.6	DMSO (d_6)

Because the hypervalent silicates intermediates are very reactive species, considering the stability of the intermediates and simplicity of the spectral, we first studied hypervalent silicates generated using tetrabutylammonium fluoride (TBAF) as the fluoride source with ^{19}F NMR due to it more stable and much easier for calculation. Using the data of TBAF, we can match with the hypervalent silicates obtained using bisguanidinium fluoride.

The general approach involved reaction of TBAF with a neutral silane precursor in the presence of NMR solvent to generate hypervalent silicates. Although no products were isolated, the details of the proving of hypervalent silicate intermediates are based on ^{19}F NMR spectroscopic evidence.

1) TBAF (1 M in THF) ^{19}F NMR (CDCl_3 ; $-20\text{ }^\circ\text{C}$)

As TBAF is not stable at room temperature (TBAF decomposes slowly in THF by E2 elimination if warmed above 0 °C)⁴, the ^{19}F NMR was performed at low temperature (-20 °C). The ^{19}F NMR spectrum of TBAF showed a peak at -120.3 ppm.

2) Ph_3SiF ^{19}F NMR (CDCl_3 ; -20 °C)

Since Ph_3SiF is a possible byproduct of the reaction, we also measured its chemical shift of ^{19}F NMR, which is -169.8 ppm.

2) TBAF (1 M in THF) + Ph_3SiH ^{19}F NMR (CDCl_3 ; -20 °C)

The ^{19}F NMR spectrum of a mixture of TBAF and Ph_3SiH showed a new peaks at -98.3 ppm which should be the ^{19}F NMR shift of silicate ion pair $\text{TBA}^+ [\text{Ph}_3\text{SiFH}]^-$ as it's close to our calculated data which is -95.5 ppm.

3) TBAF (1 M in THF) + $\text{PhSi}(\text{OMe})_3$ ^{19}F NMR (CDCl_3 ; -20 °C)

The mixture of TBAF and alkynylsilanes showed messy signals in the ^{19}F NMR spectrum hence calculation was not done. The mixture of TBAF (1 M in THF) and $\text{PhSi}(\text{OMe})_3$ showed two new peaks in the ^{19}F NMR spectrum at -115.7 ppm and -145.0 ppm . The peak at -145.0 ppm should be the ^{19}F NMR shift of $\text{PhSi}(\text{OMe})_2\text{F}$ as it's very close to the reported data (-145.58 ppm)⁵. The peak at -115.7 ppm should be the ^{19}F NMR shift of silicate ion pair $\text{TBA}^+ [\text{PhSi}(\text{OMe})_3\text{F}]^-$ as it's close to our calculated data which is -113.1 ppm.

5) $[\text{BG}][\text{F}][\text{X}]$ ^{19}F NMR (CDCl_3 ; -20 °C)

The mixture of **BG** and AgF in acetonitrile at room temperature can generate bisguanidinium fluoride $[\text{BG}][\text{F}][\text{X}]$ which is detected by ^{19}F NMR (chemical shift is -157.5 ppm). However,

up to now, we cannot confirm the exact structure bisguanidinium fluoride whether the X is fluoride or chloride.

6) $[\text{BG}][\text{F}][\text{X}]$ in CDCl_3 at 0°C for 2h ^{19}F NMR

However, **[BG][F][X]** is not stable in CDCl_3 even at 0 °C, a new peak at -129.3 ppm was appeared after staying in CDCl_3 at 0 °C for 2 hours. According to literature report⁶, fluoride forms extremely strong bonds to protons (H-F 136 kcal/mol, HF_2^- 46 kcal/mol), fluoride is expected to be an aggressive Brønsted base and Christe et al. have shown that TBAF can deprotonate CD_3CN , consuming F^- to form more stable DF_2^- . A similar process was observed with **[BG][F][X]** in CDCl_3 , **[BG][F][X]** can react with CDCl_3 to form **[BG][X][DF₂]**. So we supposed the new ^{19}F NMR signal at -129.3 ppm belongs to **[BG][X][DF₂]**.

7) **[BG][F][X]** + Ph_3SiH ^{19}F NMR (CDCl_3 ; -20 °C)

The ^{19}F NMR (performed at -20 °C) spectrum of a mixture of **[BG][F][X]** and Ph_3SiH showed two new peaks at -97.0 ppm and -169.8 ppm. The peak at -169.8 ppm is consistent with ^{19}F NMR data for Ph_3SiF , while the peak at -97.0 ppm should be the ^{19}F NMR chemical shift of bisguanidinium silicate ion pair $[\text{Ph}_3\text{SiFH}]^- \text{BG}^{2+} [\text{X}]^-$ as it's close to experimental data of $\text{TBA}^+[\text{Ph}_3\text{SiFH}]^-$ (-98.3 ppm).

8) **[BG][F][X]** + $\text{PhSi}(\text{OMe})_3$ ^{19}F NMR (CDCl_3 ; -20 °C)

The mixture of **[BG][F][X]** and PhSi(OMe)_3 showed two new peaks in the ^{19}F NMR spectrum at -120.1 ppm and -145.0 ppm, The peak at -145.0 ppm should be the signal of $\text{PhSi(OMe)}_2\text{F}$ as we have mentioned before. The peak at -120.1 ppm should be the ^{19}F NMR shift of bisguanidinium silicate ion pair $[\text{PhSi(OMe)}_3\text{F}]^- \text{BG}^{2+} [\text{X}]^-$ as it's close to both the calculated and experimental data of $\text{TBA}^+ [\text{PhSi(OMe)}_3\text{F}]^-$ (-115.7 ppm).

3.1.2 ^1H NMR studies of hypervalent silicate intermediate

1) Ph_3SiH ^1H NMR (CDCl_3 ; -20 °C)

2) TBAF (1 M in THF) + Ph₃SiH ¹H NMR (CDCl₃, -20 °C)

In addition, the ¹H NMR (performed at -20 °C) spectrum of the mixture of TBAF (1 M in THF) and Ph₃SiH in CDCl₃ showed a new peak at 5.57 ppm, which is consistent with our calculated ¹H NMR shift for Si-H in TBA⁺ [Ph₃SiFH]⁻ (5.90 ppm).

Using these data, we managed to match the hypervalent silicates obtained using bisguanidinium fluoride. We proposed that the crucial intermediates in this methodology are penta-coordinated hypervalent silicate ion pairs with bisguanidinium.

3.1.3 Identification of hypervalent silicate intermediates

We wanted to ‘catch’ the bisguanidinium hypervalent silicate intermediates in action. First, we changed the sequence of addition to generate hypervalent silicate through the addition of the fluoride source to Ph₃SiH or PhSi(OMe)₃ at the beginning (Figure 3.1) to generate hypervalent silicate intermediates which were detected using ¹⁹F NMR, followed by chromone **1a** and lastly, benzyl bromide.

Figure 3.1. Identification of hypervalent silicate intermediates

The reduced chromone **3a** or **9a** was obtained in moderate yields when both TBAF (Scheme 3.1a and 3.1c) and bisguanidinium fluoride **[BG][F][X]** (Scheme 3.1b and 3.1d) were used, enantioselectivity was observed only in the reaction using **[BG][F][X]**. The geometries of structures for configurational isomers of hypervalent silicate intermediates were also taken

into consideration. Compared with DFT calculation results, we can see the most possible configurational isomers of the two kinds of hypervalent silicates are the same. This would be a further evidence to support our calculation and prove the existence of penta-coordinated hypervalent silicate intermediates.

3.2 Computational studies for identification of reaction intermediates

3.2.1 Computational methods

Density functional theory studies were carried out with Gaussian 16⁷ computational chemistry suite. Geometries of gas phase minimum electronic structures were optimized using the B3LYP functional⁸⁻⁹ with Pople's basis set 6-31+G(d,p).¹⁰ Frequency calculations were carried out at that level to ensure convergence, i.e. all positive eigenvalues for minima. NMR shielding tensors were calculated with the Gauge-Independent Atomic Orbital (GIAO)¹¹⁻¹⁵ method using the B3LYP functional and 6-311+(2d, p)¹⁶⁻¹⁷ basis set.

3.2.2 DFT calculations

¹⁹F NMR

A training set consisting of 10 fluorinated molecules, TM-1 to TM-10, were used to determine the linear regression scaling factor (Table 3.2). Geometries of electronic structures were optimized in gas-phase with B3LYP/6-31+G (d, p) and isotropic shielding shifts were calculated in gas-phase with single point B3LYP/6-311+(2d, p). Scaled ¹⁹F NMR chemical shifts were obtained by where is the scaled NMR shift and is the calculated isotropic value.¹⁸ The correlation coefficient (R^2), slope and intercept were found to be 0.9705, -1.1656 and 160.34 respectively (Figure 3.2).

Table 3.2: Experimental ¹⁹F NMR chemical shifts, calculated isotropic values and scaled NMR chemical shifts of training set molecules

Molecule	Experimental NMR Shift	Calculated Isotropic Values	Scaled NMR Shift	Diff. ^c
TM-1	0.65 ^a	186.55	3.99	3.34
TM-2	-112.96 ^a	307.94	-110.90	2.06
TM-3	-161.64 ^a	356.48 ^b	-156.84	4.80
TM-4	-62.61 ^a	256.53 ^b	-62.24	0.37
TM-5	-75.39 ^a	270.52 ^b	-75.48	-0.09
TM-6	-98.2	303.00 ^b	-106.23	-8.03
TM-7	-97.6	292.33 ^b	-96.13	1.47
TM-8	-95.2	295.70 ^b	-99.31	-1.71
TM-9	-97.7	294.21 ^b	-97.90	-0.20
TM-10	-97.6	293.49 ^b	-97.22	-2.02
Linear regression				
Correlation coefficient (R^2): 0.9926				
Slope: -1.0565				
Intercept: 190.7725				

^a literature values¹⁹

^b average of isotropic values

^c Scaled NMR Shift Value - Exp. Shift

Figure 3.2: Graph of calculated isotropic values versus experimental NMR shifts

Target molecules

The geometries of electronic structures for configurational isomers of each compound (see Table 3.3) were optimized with M062X/6-31+G(d) and SMD implicit solvation (chloroform parameters). In some cases, isomerization to an existing structure occurred during the optimization process (marked by * and isomerization product in brackets). Isotropic shielding shifts were calculated with single point M062X/6-31+G(d) and SMD implicit solvation (chloroform parameters). Scaled ^{19}F NMR chemical shifts were obtained in the same manner as with the training set. The configurational isomer with the smallest difference between the scaled NMR shift and the experimental shift is predicted to be the observed isomer and is highlighted in gray.

Table 3.3: Experimental ^{19}F NMR chemical shifts, calculated isotropic values and scaled ^{19}F NMR chemical shifts of target molecules

Molecule	Exp. NMR Shift	Calculated Isotropic Values	Scaled NMR Shift	Diff.
A-ax-1	-98.3	291.72	-95.54	2.76
A-ax-2	-98.3	249.10	-55.21	43.09
B-ax-1	-115.7	310.24	-113.08	2.62
B-ax-2	-115.7	298.27	-101.75	13.95
B-eq-1	-115.7	296.70	-100.26	15.44
B-eq-2	-115.7	309.80	-112.65	3.05

¹H NMR

The gas-phase geometries of electronic structures for configurational isomers A-ax-1 and A-ax-2 (see Table 3.3) were optimized with B3LYP/6-31+G (d). (Table 3.4) Isotropic shielding shifts were calculated in gas-phase with single point B3LYP/6-311+ G (2d, p). Scaled ¹H NMR chemical shifts were obtained by where is the scaled NMR shift and is the calculated isotropic

value. The intercept and slope values were obtained from existing scaling factors in CHESHIRE Chemical Shift Repository (<http://www.cheshirenmr.info/ScalingFactors.htm>).

The configurational isomer with the smallest difference between the scaled NMR shift and the experimental shift is predicted to be the observed isomer and is highlighted in gray.

Table 3.4: Experimental ^1H NMR chemical shifts, calculated isotropic values and scaled NMR chemical shifts of A-ax-1 and A-ax-2.

	Exp.	Calculated	Scaled	
	NMR	Isotropic	NMR	
Molecule	Shift	Values	Shift	Diff.
A-ax-1	5.57	25.72	5.90	0.33
A-ax-2	5.57	25.63	5.98	0.41

3.3 Control experiment of dihydrocoumarin substrate

We speculated that reduced coumarin **12a** is an intermediate for the reduction-alkylation of coumarin **4a** to alkylated coumarin **5a**. We found that reduced coumarin **12a** underwent alkylation more efficient in the presence of PMHS (Figure 3.3, Eqn. 1 and 2) than in its absence. The results suggested that the reductive alkylation may go through an enolsilicate intermediate (Figure 3.3, Eqn. 3). In our previous work, we have used silylamide BSA as a probase which was converted to a strong base in the presence of fluoride. It is also a silylating reagent and transfer TMS to generate silyl enol ether. In the presence of BSA, similar enantioselectivity was obtained as the experiment using PHMS (Figure 3.3, Eqn. 3, 81% *ee*).

Figure 3.3 Control experiment of dihydrocumarin substrate

3.4 Proposed catalytic cycle

Based on the above control experiments, we proposed the catalytic cycle of the cascade addition and alkylation strategy (Figure 3.4). After anion exchange, chiral bisguanidinium fluoride **[BG][F][X]** was generated. It can activate silicon compounds to form penta-coordinated hypervalent silicates **I** which will react with α,β -unsaturated ketones to *in situ* generate silyl enolate intermediate **II**. Then chiral bisguanidinium silicate ion pair **II** reacts with bromide electrophile to afford the desired product and regenerate the catalyst.

We thus propose a working model that includes these two key roles. The neutral silane is activated with fluoride to provide a hypervalent silicate intermediate, which is an ion-pair between chiral bisguanidinium cation and penta-coordinated hypervalent silicate anion. As for the reduction-alkylation reaction, no chiral center is generated in the reduction step. So the followed enantioselective alkylation is the enantio-determining step, which is controlled by the ion-pairing between the *in situ* generated silyl enolate and the chiral bisguanidinium cation. As

for the addition-alkylation reaction, chiral center is generated in both the addition step and alkylation step. Two bisguanidinium silicate ion-pairs are formed and both of them determine the selective enantiofacial approach of the electrophiles.

Figure 3.4 Proposed catalytic cycle of cascade reductive alkylation strategy

3.5 Summary

In summary, we have conducted a series of mechanistic studies for this bisguanidinium **BG**-catalyzed enantioselective addition-alkylation reaction. Silicon hydride and alkoxy silane were activated with fluoride sources, TBAF and bisguanidinium fluoride, to form hypervalent silicate ion pairs which were detected by NMR. DFT calculations revealed that penta-coordinated hypervalent silicates are the crucial intermediates. These silicate intermediates then undergo 1,4-addition to α,β -unsaturated ketones, generating enolsilicate intermediates,

followed by stereoselective alkylation to afford the products with excellent enantioselectivities and diastereoselectivities.

3.6 References

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Chapter 4

Experimental Procedures

4.1 General information

General procedures and methods

Commercially available materials purchased from Alfa Aesar or Aldrich was used as received. HPLC grade solvents (toluene and methanol) were used without further purification. Experiments involving moisture and/or air sensitive components were performed under a positive pressure of nitrogen in oven-dried glassware equipped with a rubber septum inlet. Dried solvents and liquid reagents were transferred by oven-dried syringes or hypodermic syringe cooled to ambient temperature in a desiccator. Reaction mixtures were stirred in 4 mL sample vial with Teflon-coated magnetic stirring bars unless otherwise stated. Moisture in non-volatile reagents/compounds was removed in high *vacuo* by means of an oil pump and subsequent purging with nitrogen. Solvents were removed in *vacuo* under ~30 mmHg and heated with a water bath at 40–45 °C using rotary evaporator with aspirator. The condenser was cooled with running water at 0 °C.

All experiments were monitored by analytical thin layer chromatography (TLC). TLC was performed on pre-coated plates, Qingdao Yu Min Yuan Chemicals (P. R. China) 60 F₂₅₄. After elution, plate was visualized under UV illumination at 254 nm for UV active material. Further visualization was achieved by staining KMnO₄, or anisaldehyde solution. For those using the aqueous stains, the TLC plates were heated on a hot plate.

Columns for flash chromatography (FC) contained silica gel 200–300 mesh. Columns were packed as slurry of silica gel in hexane and equilibrated solution using the appropriate solvent system. The elution was assisted by applying pressure of about 2 atm with an air pump.

Instrumentation

Proton nuclear magnetic resonance (¹H NMR), carbon NMR (¹³C NMR), and fluorine (¹⁹F NMR) spectra were recorded in CDCl₃ otherwise stated. ¹H (300 MHz), ¹³C (75 MHz) and ¹⁹F

NMR (282 MHz) were performed on a Bruker AV300 spectrometer. The low temperature NMR was performed on ECA AV400 spectrometer. ^1H (500 MHz) and ^{13}C (126 MHz) were performed on a Bruker AV500 spectrometer. Chemical shifts are reported in parts per million (ppm), using the residual solvent signal as an internal standard: CDCl_3 (^1H NMR: δ 7.26, singlet; ^{13}C NMR: δ 77.0, triplet). Multiplicities were given as: *s* (singlet), *d* (doublet), *t* (triplet), *q* (quartet), *quintet*, *m* (multiplets), *dd* (doublet of doublets), *dt* (doublet of triplets), and *br* (broad). Coupling constants (*J*) were recorded in Hertz (Hz). The number of proton atoms (*n*) for a given resonance was indicated by *n*H. The number of carbon atoms (*n*) for a given resonance was indicated by *n*C. Flash chromatography was performed using Merck silica gel 60 with distilled solvents. Analytical thin-layer chromatography (TLC) was carried out on Merck 60 F254 pre-coated silica gel plate (0.2 mm thickness). Visualization was performed using a UV lamp. High resolution mass spectral analysis (HRMS) was performed on Waters Q-TOF Premier mass spectrometer. MS and HRMS were reported in units of mass of charge ratio (*m/z*). Mass samples were dissolved in CH_3CN (HPLC Grade) unless otherwise stated. Optical rotations were recorded on a Jasco P1030 polarimeter with a sodium lamp of wavelength 589 nm and reported as follows; $[\alpha]_{\lambda}^{T^\circ\text{C}}$ (*c* = g/100 mL, solvent). Melting points were determined on a X-6 microscopic melting point apparatus.

Enantiomeric excesses were determined by chiral High Performance Liquid Chromatography (HPLC) analysis. UV detection was monitored at 254 nm, 230 nm and 210 nm at the same time. HPLC samples were dissolved in HPLC grade isopropanol (IPA) unless otherwise stated.

Materials

All commercial reagents were purchased from Sigma-Aldrich, J&K, Alfa-Aesar, TCL and Aladdin of the highest purity grade. They were used without further purification unless specified. All solvents used, mainly hexane and ethyl acetate (EtOAc), were distilled. Anhydrous DCM and MeCN were freshly distilled from CaH_2 and stored under N_2 atmosphere.

TBME, CPME, THF, Et₂O and toluene were freshly distilled from sodium/benzophenone before use. Anhydrous methanol was distilled from Mg. All compounds synthesized were stored in a -20 °C freezer and light-sensitive compounds were protected with aluminium foil.

4.2 Procedure for reduction-alkylation of chromones

Reaction was conducted with of **1a** (0.1 mmol, 1.0 equiv.), CsF (0.4 mmol, 4.0 equiv.) in 0.5 mL CPME in the presence of 10 mol% **BG1** at 0 °C. The reaction mixture was stirred at 0°C for 1 min, then **2a** (0.4 mmol, 4.0 equiv.), PMHS (0.4 mmol, 4.0 equiv.) was added sequentially. The reaction mixture was stirred at 0°C for 48h. Upon complete consumption of **1a**, the reaction mixture was directly loaded onto a short silica gel column, followed by gradient elution with hexane/EA mixture (50/1–20/1 ratio). Removing the solvent in vacuo, afforded product **3a-v**.

4.3 Procedure for reduction-alkylation of coumarins

Reaction was conducted with of **4a** (0.1 mmol, 1.0 equiv.), KF (0.4 mmol, 4.0 equiv.) in 0.5 mL TBME in the presence of 10 mol% **BG1** at 0 °C. The reaction mixture was stirred at 0 °C for 1 min, then bromide (0.4 mmol, 4.0 equiv.), PMHS (0.4 mmol, 4.0 equiv.) was added sequentially. The reaction mixture was stirred at 0 °C for 48h. Upon complete consumption of

4a, the reaction mixture was directly loaded onto a short silica gel column, followed by gradient elution with hexane/EA mixture (50/1–20/1 ratio). Removing the solvent in vacuo, afforded products **7a-i**.

4.4 Procedure for addition-alkylation of chromones using alkynylsilanes

Reaction was conducted with of **8a** (0.1 mmol, 1.0 equiv.), CsF (0.4 mmol, 4.0 equiv.) in 0.5 mL Et_2O in the presence of 10 mol% **BG1** at $0\text{ }^\circ\text{C}$. The reaction mixture was stirred at $0\text{ }^\circ\text{C}$ for 1 min, then bromide (0.4 mmol, 4.0 equiv.), silane (0.4 mmol, 4.0 equiv.) was added sequentially. The reaction mixture was stirred at $0\text{ }^\circ\text{C}$ for 72h. Upon complete consumption of **8a**, the reaction mixture was directly loaded onto a short silica gel column, followed by gradient elution with hexane/EA mixture (100/1–50/1 ratio). Removing the solvent in vacuo, afforded products **9a-i**.

4.5 Procedure for addition-alkylation of chromones using alkyloxysilanes

Reaction was conducted with of **10a** (0.1 mmol, 1.0 equiv.), CsF (0.4 mmol, 4.0 equiv.) in 0.5 mL CPME in the presence of 10 mol% **BG1** at $0\text{ }^\circ\text{C}$. The reaction mixture was stirred at $0\text{ }^\circ\text{C}$ for 1 min, then bromide (0.4 mmol, 4.0 equiv.), silane (0.4 mmol, 4.0 equiv.) was added sequentially. The reaction mixture was stirred at $0\text{ }^\circ\text{C}$ for 48h. Upon complete consumption of **10a**, the reaction mixture was directly loaded onto a short silica gel column, followed by

gradient elution with hexane/EA mixture (50/1–20/1 ratio). Removing the solvent in vacuo, afforded products **11a-f**.

4.6 Procedure for identification of reaction intermediates

4.6.1 Procedure for control experiment of chromone substrate

To a solution of Ph_3SiH (52mg, 0.2 mmol, 4.0 equiv.) in TBME (0.5 mL) was added TBAF (1 M in THF, 200 μL , 0.2 mmol, 4.0 equiv.) at 0 °C. The resulting mixture was stirred at 0 °C for 2 hours. The hypervalent silicate intermediates were generated and detected by ^{19}F NMR (The ^{19}F NMR was performed on ECA AV400 spectrometer at -20 °C). Then **1a** (0.05 mmol, 1.0 equiv.), benzyl bromide (0.2 mmol, 1.0 equiv.) was added sequentially. The reaction mixture was stirred at 0 °C for 48h. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane/EA = 50/1-20/1) to afford **3a** as a white solid in 45% yield and 0% *ee*.

To a solution of Ph_3SiH (52 mg, 0.2 mmol, 4.0 equiv.) in TBME (0.5 mL) was added $[\text{BG}][\text{F}][\text{X}]$ (0.2 mmol, 4.0 equiv.) at 0 °C. The resulting mixture was stirred at 0 °C for 2 hours. The hypervalent silicate intermediates were generated and detected by ^{19}F NMR (The ^{19}F NMR was performed on ECA AV400 spectrometer at -20 °C). Then **1a** (0.05 mmol, 1.0 equiv.),

benzyl bromide (0.2 mmol, 1.0 equiv.) was added sequentially. The reaction mixture was stirred at 0 °C for 48h. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane/EA = 50/1-20/1) to afford **3a** as a white solid in 60% yield and 72% *ee*.

To a solution of PhSi(OMe)_3 (40 μL , 0.2 mmol, 4.0 equiv.) in TBME (0.5 mL) was added TBAF (1 M in THF, 200 μL , 0.2 mmol, 4.0 equiv.) at 0 °C. The resulting mixture was stirred at 0 °C for 0.5 hour. The hypervalent silicate intermediates were generated and detected by ^{19}F NMR (The ^{19}F NMR was performed on ECA AV400 spectrometer at -20 °C). Then **1a** (0.05 mmol, 1.0 equiv.), benzyl bromide (0.2 mmol, 4.0 equiv.) was added sequentially. The reaction mixture was stirred at 0 °C for 48h. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane/EA = 50/1-20/1) to afford **11a** as a white solid in 41% yield and 0% *ee*.

To a solution of PhSi(OMe)_3 (40 μL , 0.2 mmol, 4.0 equiv.) in TBME (0.5 mL) was added $[\text{BG}][\text{F}][\text{X}]$ (0.2 mmol, 4.0 equiv.) at 0 °C. The resulting mixture was stirred at 0 °C for 0.5 hour. The hypervalent silicate intermediates were generated and detected by ^{19}F NMR (The ^{19}F NMR was performed on ECA AV400 spectrometer at -20 °C). Then **1a** (0.05 mmol, 1.0

equiv.), benzyl bromide (0.2 mmol, 4.0 equiv.) was added sequentially. The reaction mixture was stirred at 0 °C for 48h. The solvent was removed under reduced pressure, and the residue was purified by flash chromatography on silica gel (hexane/EA = 50/1-20/1) to afford **11a** as a white solid in 95% yield and 81% *ee*.

Procedure for the preparation of [BG][F][X]: To a solution of **BG** (140.0 mg, 0.1 mmol) in CH₃CN (1 mL) at room temperature, AgF (50.8. mg, 0.4mmol) was added under Argon atmosphere. The resulting mixture was stirred at room temperature for 24h. After filtration, concentration, product [BG][F][X] was obtained as a brown oil. The ¹⁹F NMR signal didn't change even increased the loading of AgF to 10 equiv. However, up to now, we cannot confirm the exact structure bisguanidinium fluoride [BG][F][X]. We are not sure whether the X is fluoride or chloride.

4.6.2 Procedure for control experiment of dihydrocumarin substrate

(1) Reaction was conducted with of **12a** (0.1 mmol, 1.0 equiv.), CsF (0.4 mmol, 4.0 equiv.) in 0.5 mL TBME in the presence of 10 mol% **BG1** at 0 °C. The reaction mixture was stirred at 0 °C for 1 min, then bromide (0.4 mmol, 4.0 equiv.) was added. The reaction mixture was stirred at 0 °C for 48h. Upon complete consumption of **12a**, the reaction mixture was directly loaded

onto a short silica gel column, followed by gradient elution with hexane/EA mixture (50/1–20/1 ratio). Removing the solvent in vacuo, afforded product **7a** in 57% yield and 54% *ee*.

(2) Reaction was conducted with of **12a** (0.1 mmol, 1.0 equiv.), CsF (0.4 mmol, 4.0 equiv.) in 0.5 mL TBME in the presence of 10 mol% **BG1** at 0 °C. The reaction mixture was stirred at 0 °C for 1 min, then bromide (0.4 mmol, 4.0 equiv.), PMHS (0.4 mmol, 4.0 equiv.) was added sequentially. The reaction mixture was stirred at 0 °C for 48h. Upon complete consumption of **12a**, the reaction mixture was directly loaded onto a short silica gel column, followed by gradient elution with hexane/EA mixture (50/1–20/1 ratio). Removing the solvent in vacuo, afforded product **7a** in 77% yield and 73% *ee*.

(3) Reaction was conducted with of **12a** (0.1 mmol, 1.0 equiv.), CsF (0.4 mmol, 4.0 equiv.) in 0.5 mL TBME in the presence of 10% mol **BG1** at 0 °C. The reaction mixture was stirred at 0 °C for 1 min, then bromide (0.4 mmol, 4.0 equiv.), bis(trimethylsilyl)acetamide (BSA) (0.2 mmol, 2.0 equiv.) was added sequentially. The reaction mixture was stirred at 0 °C for 48h. Upon complete consumption of **12a**, the reaction mixture was directly loaded onto a short silica gel column, followed by gradient elution with hexane/EA mixture (50/1–20/1 ratio). Removing the solvent in vacuo, afforded product **7a** in 61% yield and 81% *ee*.

4.7. Characterization of products

White solid, Mp 135.4 – 135.8 °C; 84% yield; 98% *ee*; $[\alpha]_D^{26}$ -2.10 (*c* 1.47, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.00 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.62 – 7.58 (m, 1H), 7.41 – 7.34 (m, 5H), 7.16 (t, *J* = 8.0 Hz, 1H), 7.08 (d, *J* = 8.3 Hz, 1H), 4.47 – 4.35 (m, 2H), 3.28 – 3.13 (m, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 185.1, 160.6, 137.3, 132.7, 130.3, 128.9, 128.6, 128.2, 122.9, 118.2, 118.1, 116.0, 69.3, 49.3, 36.7.

HRMS (ESI) *m/z* 264.1035 [M+H]⁺, calc. for C₁₇H₁₄NO₂ 264.1025.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 13.3 min (major) and 16.3 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	13.357	3178585	95219	50.772
2	16.359	3081933	76168	49.228

Peak#	Ret. Time	Area	Height	Area%
1	13.345	2304293	74844	99.104
2	16.339	20835	807	0.896

White solid, Mp 95.6 – 96.8 °C; 80% yield; 96% *ee*; $[\alpha]_D^{26}$ -1.89 (*c* 1.35, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.99 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.63 – 7.59 (m, 1H), 7.35 – 7.33 (m, 2H), 7.18 – 7.15 (m, 1H), 7.10 – 7.07 (m, 3H), 4.49 – 4.34 (m, 2H), 3.25 – 3.11 (m, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 184.9, 163.7, 160.5, 137.3, 132.0, 132.0, 128.4, 128.4, 123.0, 118.1,

116.0, 115.8, 69.2, 49.4, 36.0. ¹⁹F NMR (282 MHz, CDCl₃) δ -113.7.

HRMS (ESI) *m/z* 282.0911 [M+H]⁺, calc. for C₁₇H₁₃FNO₂ 282.0930.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 8.4 min (major) and 14.2 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	8.346	10609660	505262	50.473
2	14.117	10410899	284724	49.527

Peak#	Ret. Time	Area	Height	Area%
1	8.360	5825462	291832	97.811
2	14.192	130392	4142	2.189

White solid, Mp 101.3 – 101.7 °C; 72% yield; 95% *ee*; $[\alpha]_D^{26}$ -2.33 (*c* 1.60, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.99 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.63 – 7.59 (m, 1H), 7.38 – 7.25 (m, 4H), 7.18 – 7.15 (m, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 4.41 (dd, *J* = 68.0, 11.7 Hz, 2H), 3.24 – 3.11 (m, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 184.8, 160.5, 137.4, 134.4, 131.6, 131.2,

129.2, 128.6, 123.1, 118.1, 115.8, 69.3, 49.2, 36.1.

HRMS (ESI) *m/z* 298.0611 [M+H]⁺, calc. for C₁₇H₁₃NCIO₂ 298.0635.

The *ee* was determined by HPLC analysis. CHIRALPAK IE (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 15.5 min (major) and 22.6 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	15.411	6103954	294118	50.389
2	22.255	6009748	204879	49.611

Peak#	Ret. Time	Area	Height	Area%
1	15.529	2806035	151855	97.590
2	22.658	69302	2829	2.410

White solid, Mp 108.8 – 109.3 °C; 83% yield; 98% *ee*; $[\alpha]_D^{26}$ -1.39 (*c* 3.38, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.99 (dd, *J* = 8.0, 1.8 Hz, 1H), 7.64 – 7.60 (m, 1H), 7.53 (d, *J* = 8.3 Hz, 2H), 7.24 (d, *J* = 8.5 Hz, 2H), 7.14 – 7.19 (m, 1H), 7.08 (dd, *J* = 8.4, 1.0 Hz, 1H), 4.50 – 4.32 (m, 2H), 3.24 – 3.08 (m, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 184.8, 160.5, 137.4,

132.1, 132.0, 131.7, 128.6, 123.1, 122.5, 118.2, 118.1, 115.8, 69.3, 49.2, 36.2.

HRMS (ESI) *m/z* 341.9597 [M+H]⁺, calc. for C₁₇H₁₃NBrO₂ 342.0130.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 9.0 min (major) and 15.1 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	9.043	5919379	270662	50.648
2	15.101	5767943	153185	49.352

Peak#	Ret. Time	Area	Height	Area%
1	9.035	1895091	83770	98.901
2	15.117	21050	819	1.099

Colorless oil; 74% yield; 98% *ee*; $[\alpha]_D^{26}$ -0.90 (*c* 1.29, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.00 (dd, *J* = 8.0, 1.9 Hz, 1H), 7.66 (d, *J* = 7.8 Hz, 2H), 7.64 – 7.60 (m, 1H), 7.50 (d, *J* = 7.9 Hz, 2H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.10 (d, *J* = 8.4 Hz, 1H), 4.51 – 4.33 (m, 2H), 3.24 – 3.18 (m, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 184.6, 160.5, 137.5, 136.8, 130.8, 128.6,

125.9, 125.9, 123.2, 118.2, 118.1, 115.6, 69.4, 49.1, 36.5, 31.5. ¹⁹F NMR (282 MHz, CDCl₃) δ -62.7.

HRMS (ESI) *m/z* 332.0927 [M+H]⁺, calc. for C₁₈H₁₃NF₃O₂ 332.0898.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 10.8 min (major) and 21.2 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	10.869	10267118	319981	50.626
2	21.155	10013184	158727	49.374

Peak#	Ret. Time	Area	Height	Area%
1	10.830	3292449	132516	98.709
2	21.218	43075	1342	1.291

White solid, Mp 117.5 – 118.2 °C; 76% yield; 95% *ee*; $[\alpha]_D^{26}$ -3.38 (*c* 1.20, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.99 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.61 – 7.58 (m, 1H), 7.29 (d, *J* = 8.7 Hz, 2H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 6.92 (d, *J* = 8.6 Hz, 2H), 4.47 – 4.35 (m, 2H), 3.82 (s, 3H), 3.22 – 3.08 (m, 2H). ¹³C NMR (126 MHz, CDCl₃) δ

185.2, 160.6, 159.5, 137.2, 131.4, 128.5, 124.5, 122.9, 118.2, 118.1, 116.1, 114.3, 69.3, 55.3, 49.6, 36.1. HRMS (ESI) *m/z* 294.1137 [M+H]⁺, calc. for C₁₈H₁₆NO₃ 294.1130.

The *ee* was determined by HPLC analysis. CHIRALPAK IE1010 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 90/10; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 18.2 min (major) and 25.5 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	18.201	4736816	189136	50.490
2	25.333	4644848	130388	49.510

Peak#	Ret. Time	Area	Height	Area%
1	18.233	4555407	192102	97.403
2	25.504	121469	4103	2.597

White solid, Mp 86.1 – 86.5 °C; 63% yield; 90% *ee*; $[\alpha]_D^{26}$ -1.37 (*c* 1.81, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.98 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.62 – 7.57 (m, 2H), 7.54 – 7.52 (m, 1H), 7.36 – 7.33 (m, 1H), 7.21 – 7.18 (m, 1H), 7.16 – 7.13 (m, 1H), 7.06 (dd, *J* = 8.5, 1.0 Hz, 1H), 4.60 – 4.50 (m, 2H), 3.53 (dd, *J* = 127.7, 14.4 Hz, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 184.3, 160.8,

137.4, 133.5, 133.1, 132.3, 129.8, 128.6, 128.0, 125.7, 122.8, 118.4, 118.2, 116.1, 70.5, 48.7, 35.4.

HRMS (ESI) *m/z* 342.0143 [M+H]⁺, calc. for C₁₇H₁₃NBrO₂ 342.0130.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 10.5 min (major) and 11.9 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	10.595	2391758	92174	48.133
2	11.997	2577331	84215	51.867

Peak#	Ret. Time	Area	Height	Area%
1	10.522	87360	4685	5.075
2	11.900	1634080	55806	94.925

Colorless oil; 65% yield; 93% *ee*; $[\alpha]_D^{26} -2.50$ (*c* 1.13, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.01 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.62 – 7.59 (m, 1H), 7.35 (d, *J* = 5.4 Hz, 1H), 7.25 – 7.21 (m, 3H), 7.18 – 7.15 (m, 1H), 7.08 (dd, *J* = 8.4, 1.0 Hz, 1H), 4.53 – 4.45 (m, 2H), 3.42 – 3.11 (m, 2H), 2.42 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 185.2, 160.5, 137.7, 137.3, 131.3, 131.2, 131.1, 128.6, 128.2, 126.3, 123.0, 118.2, 118.1, 116.2, 69.6, 49.2, 33.0, 19.8. HRMS (ESI) *m/z* 278.1188 [M+H]⁺, calc. for C₁₈H₁₅NO₂ 278.1181.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 9.8 min (major) and 11.4 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	9.760	11237076	453657	49.214
2	11.380	11596117	400744	50.786

Peak#	Ret. Time	Area	Height	Area%
1	9.834	106172	6227	3.435
2	11.451	2984471	115923	96.565

White solid, Mp 67.5 – 67.9 °C; 80% yield; 96% *ee*; $[\alpha]_D^{26}$ -3.56 (*c* 1.05, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.95 (d, *J* = 7.9 Hz, 1H), 7.58 (t, *J* = 7.8 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 1H), 5.95 – 5.87 (m, 1H), 5.37 – 5.30 (m, 2H), 4.53 (dd, *J* = 61.3, 11.6 Hz, 2H), 2.81 – 2.59 (m, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 184.7, 160.6, 137.3, 129.7, 128.5, 122.9, 122.1, 118.3, 118.1,

116.0, 70.1, 47.5, 35.1.

HRMS (ESI) *m/z* 214.0896 [M+H]⁺, calc. for C₁₃H₁₂NO₂ 214.0868.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 13.5 min (major) and 15.8 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	13.600	5880061	323263	50.083
2	16.032	5860512	269663	49.917

Peak#	Ret. Time	Area	Height	Area%
1	13.495	2640183	174276	98.095
2	15.853	51273	2403	1.905

Colorless oil; 87% yield; 95% *ee*; $[\alpha]_D^{26} +6.73$ (*c* 1.26, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.95 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.58 – 7.55 (m, 1H), 7.13 – 7.10 (m, 1H), 7.03 (d, *J* = 8.5 Hz, 1H), 5.30 – 5.26 (m, 1H), 4.57 – 4.44 (m, 2H), 2.72 – 2.60 (m, 2H), 1.79 (s, 3H), 1.65 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 185.2, 160.6, 139.5, 137.1, 128.4, 122.7, 118.3, 118.0, 116.4, 115.2, 70.0, 48.3, 29.7, 26.0, 18.1.

HRMS (ESI) *m/z* 242.1162 $[\text{M}+\text{H}]^+$, calc. for $\text{C}_{15}\text{H}_{16}\text{NO}_2$ 242.1181.

The *ee* was determined by HPLC analysis. CHIRALPAK IE (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 90/10; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 12.0 min (major) and 14.7 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	11.772	10795938	684242	51.632
2	13.976	10113309	535927	48.368

Peak#	Ret. Time	Area	Height	Area%
1	12.053	8818054	542969	97.359
2	14.367	239163	14071	2.641

Colorless oil; 65% yield; 92% *ee*; E/Z = 3:1; $[\alpha]_D^{26} +12.00$ (*c* 0.89, CHCl₃); ¹H NMR (500 MHz, CDCl₃) E (major) δ 7.96 – 7.93 (m, 1H), 7.59 – 7.55 (m, 1H), 7.14 – 7.10 (m, 1H), 7.04 – 7.02 (m, 1H), 5.77 – 5.70 (m, 2H), 5.56 – 5.50 (m, 2H), 4.58 – 4.46 (dd, *J* = 11.6, 48.0 Hz, 2H), 2.72 – 2.68 (m, 1H), 2.57 – 2.53 (m, 1H), 1.75 (d, *J* = 6.4 Hz, 3H), 1.65 (d, *J* = 7.5 Hz, 1H). ¹³C NMR

(126 MHz, CDCl₃) E (major) δ 185.0, 160.6, 137.2, 133.2, 131.2, 128.4, 122.7, 122.0, 118.0, 116.2, 70.0, 48.0, 34.1, 18.1.

HRMS (ESI) *m/z* 228.1071 [M+H]⁺, calc. for C₁₄H₁₃NO₂ 228.1024.

The *ee* was determined by HPLC analysis. CHIRALPAK IE (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 90/10; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 12.3 min (major) and 14.7 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	12.315	4098985	253303	36.438
2	13.027	1565664	91995	13.918
3	14.778	4103689	212787	36.480
4	15.373	1480752	78169	13.163

Peak#	Ret. Time	Area	Height	Area%
1	12.270	1926743	142922	96.270
2	14.701	74654	5500	3.730

White solid, Mp 53.6 – 54.1 °C; 84% yield; 96% *ee*; $[\alpha]_D^{26}$ -5.28 (*c* 2.20, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.95 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.59 – 7.56 (m, 1H), 7.14 – 7.11 (m, 1H), 7.04 (d, *J* = 8.4 Hz, 1H), 5.10 – 5.08 (m, 1H), 4.93 (d, *J* = 1.0 Hz, 1H), 4.61 – 4.50 (m, 2H), 2.76 – 2.58 (m, 2H), 1.94 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 185.0, 160.5, 138.1, 137.2, 128.5, 122.8, 118.1, 118.0,

116.7, 70.2, 46.9, 38.5, 23.4.

HRMS (ESI) *m/z* 228.1041 [M+H]⁺, calc. for C₁₄H₁₄NO₂ 228.1025.

The *ee* was determined by HPLC analysis. CHIRALPAK IE (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 14.8 min (major) and 18.3 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	14.961	7221420	202886	50.141
2	18.283	7180905	274401	49.859

Peak#	Ret. Time	Area	Height	Area%
1	14.791	2592817	62664	98.048
2	18.343	51623	2055	1.952

Colorless oil; 85% yield; 94% *ee*; $[\alpha]_D^{26} +20.38$ (*c* 1.31, CHCl₃); ¹H

NMR (500 MHz, CDCl₃) δ 7.95 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.58 – 7.55 (m, 1H), 7.13 – 7.10 (m, 1H), 7.03 (dd, *J* = 8.4, 1.0 Hz, 1H), 5.29 – 5.25 (m, 1H), 5.06 – 5.08 (m, 1H), 4.55 – 4.43 (m, 2H), 2.72 – 2.52 (m, 2H), 2.14 – 2.08 (m, 4H), 1.68 – 1.61 (m, 9H). ¹³C NMR (126 MHz, CDCl₃) δ 185.2, 160.6, 142.9, 137.1, 132.0, 128.4, 123.8, 122.7, 118.3, 118.0, 116.4, 115.3, 69.9, 48.2, 39.8, 29.6, 26.3, 25.7, 17.8, 16.4.

HRMS (ESI) *m/z* 310.1828 [M+H]⁺, calc. for C₂₀H₂₄NO₂ 310.1807.

The *ee* was determined by HPLC analysis. CHIRALPAK IE (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 8.8 min (major) and 9.98 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	8.563	2588837	238219	50.608
2	9.556	2526648	199527	49.392

Peak#	Ret. Time	Area	Height	Area%
1	8.833	10589622	793311	96.950
2	9.980	333112	26997	3.050

White solid, Mp 129.5 – 130.1 °C; 84% yield; 96% *ee*; $[\alpha]_D^{26}$ -1.97 (*c* 1.42, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.98 – 7.96 (m, 1H), 7.62 – 7.56 (m, 1H), 7.41 – 7.27 (m, 5H), 7.17 – 7.11 (m, 1H), 7.06 (dd, *J* = 8.4, 1.0 Hz, 1H), 6.63 (d, = 15.7 Hz, 1H), 6.31 – 6.21 (m, 1H), 4.64 – 4.50 (m, 2H), 2.93 – 2.75 (m, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 184.8, 160.6, 137.3, 136.8, 136.1, 128.7, 128.5, 128.2, 126.6, 122.9, 120.5, 118.3,

118.1, 116.1, 70.1, 47.9, 34.5.

HRMS (ESI) *m/z* 290.1195 [M+H]⁺, calc. for C₁₉H₁₆NO₂ 289.1181.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 14.2 min (major) and 17.3 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	13.773	13869900	395583	51.457
2	17.316	13084697	287458	48.543

Peak#	Ret. Time	Area	Height	Area%
1	14.183	2582990	74426	97.996
2	17.344	52810	2004	2.004

White solid, Mp 79.7 – 81.5 °C; 63% yield; 93% *ee*; $[\alpha]_D^{26}$ -2.32 (*c* 1.66, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.97 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.61 – 7.57 (m, 1H), 7.38 – 7.35 (m, 2H), 7.14 (t, *J* = 7.6 Hz, 1H), 7.07 – 7.00 (m, 3H), 6.58 (d, *J* = 15.7 Hz, 1H), 6.20 – 6.14 (m, 1H), 4.63 – 4.51 (m, 2H), 2.95 – 2.75 (m, 2H). ¹³C NMR

(75 MHz, CDCl₃) δ 184.7, 162.7 (d, *J*_{CF} = 246.8), 160.6, 137.4, 135.6, 132.3 (d, *J*_{CF} = 3.0), 128.5, 128.2 (d, *J*_{CF} = 8.2), 122.9, 120.3 (d, *J*_{CF} = 2.2), 118.1, 117.2 (d, *J*_{CF} = 169.5), 115.8, 115.5, 70.2, 48.0, 34.5. ¹⁹F NMR (282 MHz, CDCl₃) δ -109.7.

HRMS (ESI) *m/z* 308.1127 [M+H]⁺, calc. for C₁₉H₁₅NFO₂ 308.1087.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 90/10; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 17.6 min (major) and 20.2 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	17.541	11208299	257034	49.616
2	20.130	11381604	221323	50.384

Peak#	Ret. Time	Area	Height	Area%
1	17.630	4432944	112518	96.497
2	20.188	160925	4821	3.503

White solid, Mp 105.8–106.1 °C; 77% yield; 94% *ee*; $[\alpha]_D^{26}$ -1.05 (*c* 1.74, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.97 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.61 – 7.57 (m, 1H), 7.33 – 7.29 (m, 4H), 7.15 – 7.13 (m, 1H), 7.06 (dd, *J* = 8.4, 1.0 Hz, 1H), 6.57 (d, *J* = 15.7 Hz, 1H), 6.25 – 6.20 (m, 1H), 4.63 – 4.50 (m, 2H), 2.95 – 2.76 (m, 2H). ¹³C NMR

(126 MHz, CDCl₃) δ 184.6, 160.6, 137.4, 135.5, 134.6, 133.9, 128.8, 128.5, 127.8, 122.9, 121.3, 118.2, 118.1, 116.0, 70.1, 47.9, 34.5.

HRMS (ESI) *m/z* 324.0640 [M+H]⁺, calc. for C₁₉H₁₅NCIO₂ 324.0636.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 19.2 min (major) and 22.2 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	19.061	8820358	188186	50.617
2	22.156	8605331	155441	49.383

Peak#	Ret. Time	Area	Height	Area%
1	19.188	14963845	339177	97.107
2	22.239	445733	14602	2.893

Colorless oil; 80% yield; 91% *ee*; $[\alpha]_D^{26} +37.93$ (*c* 0.79, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.95 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.61 – 7.58 (m, 1H), 7.15 (t, *J* = 7.6 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 1H), 6.98 – 6.91 (m, 1H), 6.05 (d, *J* = 15.5 Hz, 1H), 4.52 (dd, *J* = 89.6, 11.7 Hz, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 2.95 – 2.74 (m, 2H), 1.31 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 183.9, 165.1, 160.6, 138.4, 137.5, 128.6, 127.8, 123.0, 118.2, 118.1, 115.5, 70.2, 60.8, 46.9, 33.3, 14.2.

HRMS (ESI) *m/z* 286.1103 [M+H]⁺, calc. for C₁₆H₁₆NO₄ 286.1079.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 80/20; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 9.6 min (major) and 14.2 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	9.556	1183859	49200	51.936
2	14.118	1095617	30213	48.064

Peak#	Ret. Time	Area	Height	Area%
1	9.631	4377583	179640	95.307
2	14.244	215567	7932	4.693

White solid, Mp 58.8 – 60.1 °C; 88% yield; 81% *ee*; $[\alpha]_D^{26} +3.02$ (c 1.09, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.94 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.60 – 7.57 (m, 1H), 7.15 – 7.12 (m, 1H), 7.07 (dd, *J* = 8.5, 1.0 Hz, 1H), 4.80 – 4.74 (m, 2H), 4.25 – 4.18 (m, 2H), 3.05 – 2.95 (m, 2H), 1.30 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 183.4, 168.1, 161.0, 137.5, 128.6, 122.9, 118.2, 115.7, 70.6, 61.8, 44.4, 34.3, 14.1. HRMS (ESI) *m/z* 260.0947 [M+H]⁺, calc. for C₁₄H₁₃NO₄ 260.0923.

The *ee* was determined by HPLC analysis. CHIRALPAK IE (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 90/10; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 18.4 min (major) and 21.3 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	18.139	1347460	67858	49.375
2	20.701	1381591	45581	50.625

Peak#	Ret. Time	Area	Height	Area%
1	18.450	13467016	552485	90.439
2	21.302	1423645	55944	9.561

Colorless oil; 90% yield; 92% *ee*; $[\alpha]_D^{26} -16.6$ (*c* 1.02, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.94 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.62 – 7.57 (m, 1H), 7.16 – 7.05 (m, 2H), 4.80 – 4.58 (m, 2H), 3.06 – 2.77 (m, 2H), 2.28 (t, *J* = 2.7 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃) δ 183.3, 160.9, 137.6, 137.5, 129.6, 123.0, 118.3, 118.1, 115.5, 74.0, 70.6, 46.3, 21.4. HRMS (ESI) *m/z* 212.0744 [M+H]⁺, calc.

for C₁₃H₁₀NO₂ 212.0712.

The *ee* was determined by HPLC analysis. CHIRALPAK IE (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 90/10; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 12.8 min (major) and 14.7 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	12.825	4728712	291259	50.209
2	14.704	4689417	247602	49.791

Peak#	Ret. Time	Area	Height	Area%
1	12.812	11720941	717399	95.844
2	14.718	508233	32005	4.156

Colorless oil; 80% yield; 95% *ee*; $[\alpha]_D^{26}$ -1.40 (*c* 2.60, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.78 (d, *J* = 1.5 Hz, 1H), 7.42 – 7.35 (m, 6H), 6.98 (d, *J* = 8.4 Hz, 1H), 4.44 – 4.31 (m, 2H), 3.25 – 3.11 (m, 2H), 2.36 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 185.3, 158.7, 138.5, 132.8, 132.6, 130.4, 128.9, 128.2, 128.0, 117.9, 117.8, 116.1, 69.4, 49.4, 36.8, 20.5.

HRMS (ESI) *m/z* 278.1217 [M+H]⁺, calc. for C₁₈H₁₆NO₂ 278.1181.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 90/10; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 8.8 min (major) and 14.0 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	8.857	2972205	156091	50.678
2	13.954	2892633	82649	49.322

Peak#	Ret. Time	Area	Height	Area%
1	8.787	3657191	184728	97.409
2	14.011	97267	4917	2.591

White solid, Mp 114.8 – 115.3 °C; 88% yield; 94% *ee*; $[\alpha]_D^{26}$ -3.10 (*c* 1.26, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.88 (d, *J* = 8.1 Hz, 1H), 7.41 – 7.31 (m, 5H), 6.96 (d, *J* = 7.2 Hz, 1H), 6.88 (s, 1H), 4.44 – 4.31 (m, 2H), 3.27 – 3.10 (m, 2H), 2.41 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 184.7, 160.6, 149.3, 132.8, 130.3, 128.9, 128.4, 128.1, 124.3, 118.0,

116.2, 115.9, 69.3, 49.2, 36.8, 22.1.

HRMS (ESI) *m/z* 294.1209 [M+H]⁺, calc. for C₁₈H₁₆NO₃ 294.1130.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 19.2 min (major) and 22.2 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	19.061	8820358	188186	50.617
2	22.156	8605331	155441	49.383

Peak#	Ret. Time	Area	Height	Area%
1	19.188	14963845	339177	97.107
2	22.239	445733	14602	2.893

Colorless oil; 60% yield; 95% *ee*; $[\alpha]_D^{26}$ -1.74 (*c* 1.47, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.34 (d, *J* = 8.4 Hz, 1H), 7.92 (d, *J* = 8.7 Hz, 1H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.72 – 7.70 (m, 1H), 7.63 – 7.60 (m, 1H), 7.53 (d, *J* = 8.7 Hz, 1H), 7.43 – 7.35 (m, 5H), 4.69 – 4.58 (m, 2H), 3.27 (dd, *J* = 84.6, 13.9 Hz, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 184.7, 159.4, 137.8, 132.8, 130.6, 130.4, 129.0, 128.2, 128.1, 126.9, 124.2, 123.5, 122.7, 122.2,

116.2, 112.9, 70.2, 48.7, 37.0.

HRMS (ESI) *m/z* 314.1237 [M+H]⁺, calc. for C₂₁H₁₆NO₂ 314.1181.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 17.5 min (minor) and 26.3 min (major).

Peak#	Ret. Time	Area	Height	Area%
1	17.488	6084146	138514	50.371
2	26.362	5994520	92202	49.629

Peak#	Ret. Time	Area	Height	Area%
1	17.513	271352	7737	2.515
2	26.312	10517413	160343	97.485

White solid, Mp 145.8 – 146.7 °C; 80% yield; 92% *ee*; $[\alpha]_D^{26} +1.54$ (*c* 1.11, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.38 – 7.30 (m, 4H), 7.23 – 7.18 (m, 3H), 7.12 – 7.02 (m, 2H), 6.48 (d, *J* = 15.8 Hz, 1H), 6.23 – 6.12 (m, 1H), 3.37 – 3.01 (m, 2H), 2.98 – 2.72 (m, 2H), 2.21 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 202.6, 168.5, 150.7, 136.6, 135.3, 128.6, 128.5, 127.8, 126.4, 125.0, 122.7, 121.4, 116.5, 59.4, 37.7, 31.0, 26.6.

HRMS (ESI) *m/z* 307.1152 [M+H]⁺, calc. for C₂₀H₁₉O₃ 307.1334.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 12.8 min (major) and 14.2 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	12.953	1194651	55640	49.962
2	14.331	1196472	45815	50.038

Peak#	Ret. Time	Area	Height	Area%
1	12.760	8401576	626637	95.914
2	14.204	357903	24130	4.086

White solid, Mp 122.3 – 123.8 °C; 81% yield; 92% *ee*; $[\alpha]_D^{26} +4.07$ (*c* 1.97, CHCl₃); ¹H NMR (500 MHz, CDCl₃) 7.31 – 7.29 (m, 2H), 7.24 – 7.18 (m, 2H), 7.11 – 7.08 (m, 1H), 7.04 – 6.97 (m, 3H), 6.45 – 6.41 (m, 1H), 6.12 – 6.06 (m, 1H), 3.18 (dd, *J* = 157.4, 16.1 Hz, 2H), 2.95 – 2.71 (m, 2H), 2.20 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 202.6,

168.5, 162.4 (d, *J*_{CF} = 247.0), 150.7, 134.0, 132.7 (d, *J*_{CF} = 3.8), 128.6, 128.4, 127.9 (d, *J*_{CF} = 8.8), 125.0, 122.5 (d, *J*_{CF} = 2.5), 121.3, 116.5, 115.5 (d, *J*_{CF} = 21.4), 59.3, 37.6, 31.0, 26.6. ¹⁹F NMR (282 MHz, CDCl₃) δ -114.1.

HRMS (ESI) *m/z* 325.1162 [M+H]⁺, calc. for C₂₀H₁₈FO₃ 325.1240.

The *ee* was determined by HPLC analysis. CHIRALPAK ODH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 11.8 min (major) and 12.5 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	11.871	9579625	481783	50.935
2	12.871	9227990	367669	49.065

Peak#	Ret. Time	Area	Height	Area%
1	11.837	34538995	1730556	96.320
2	12.520	1319746	102196	3.680

White solid, Mp 130.7 – 131.6 °C; 69% yield; 90% *ee*; $[\alpha]_D^{26} +1.83$ (*c* 1.06, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.26 – 7.17 (m, 6H), 7.12 – 7.02 (m, 2H), 6.48 (d, *J* = 15.8 Hz, 1H), 6.21 – 6.11 (m, 1H), 3.37 – 2.99 (m, 2H), 2.96 – 2.69 (m, 2H), 2.20 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 202.6, 168.5, 150.7, 135.0, 134.0, 133.5, 128.8,

128.7, 128.5, 127.6, 125.0, 123.6, 121.3, 116.5, 59.3, 37.7, 31.1, 26.7.

HRMS (ESI) *m/z* 341.0943 [M+H]⁺, calc. for C₂₀H₁₈ClO₃ 341.0944.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 16.8 min (minor) and 23.9 min (major).

Peak#	Ret. Time	Area	Height	Area%
1	16.798	2146495	45745	49.130
2	23.914	2222507	36747	50.870

Peak#	Ret. Time	Area	Height	Area%
1	16.794	1005222	32563	5.263
2	23.913	18094811	289078	94.737

White solid, Mp 140.2 – 140.8 °C; 76% yield; 86% *ee*; $[\alpha]_D^{26} +2.00$ (*c* 1.17, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.42 (d, *J* = 8.4 Hz, 2H), 7.24 – 7.18 (m, 4H), 7.10 (t, *J* = 7.4 Hz, 1H), 7.03 (d, *J* = 8.1 Hz, 1H), 6.41 (d, *J* = 15.7 Hz, 1H), 6.21 – 6.15 (m, 1H), 3.18 (dd, *J* = 161.9, 16.0 Hz, 2H), 2.94 – 2.71 (m, 2H), 2.20 (s, 3H). ¹³C NMR

(126 MHz, CDCl₃) δ 202.6, 168.4, 150.7, 135.4, 134.0, 131.7, 128.7, 128.4, 127.9, 125.0, 123.7, 121.6, 121.3, 116.5, 59.3, 37.6, 31.1, 26.6.

HRMS (ESI) *m/z* 385.0409 [M+H]⁺, calc. for C₂₀H₁₈BrO₃ 385.0439.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 90/10; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 10.5 min (minor) and 13.6 min (major).

Peak#	Ret. Time	Area	Height	Area%
1	10.610	2990538	106477	48.658
2	13.924	3155511	84888	51.342

Peak#	Ret. Time	Area	Height	Area%
1	10.500	2179957	79265	6.728
2	13.617	30223139	803250	93.272

White solid, Mp 87.5 – 88.8 °C; 85% yield; 90% *ee*; $[\alpha]_D^{26} +0.93$ (*c* 2.17, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.35 – 7.29 (m, 4H), 7.25 – 7.21 (m, 2H), 7.19 – 7.17 (m, 1H), 7.10 – 7.07 (m, 1H), 7.02 (dd, *J* = 8.1, 1.1 Hz, 1H), 6.49 – 6.45 (m, 1H), 6.22 – 6.16 (m, 1H), 3.21 (dd, *J* = 175.6, 16.0 Hz, 2H), 2.95 – 2.91 (m, 1H), 2.76 – 2.64 (m, 2H), 2.42 – 2.34 (m, 1H), 0.93 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 205.4, 168.8, 150.7, 136.6, 135.2, 128.6, 128.5, 128.4, 127.7, 126.3, 124.9, 123.0, 121.6, 116.4, 59.1, 38.2, 32.4, 31.1, 7.5.

HRMS (ESI) *m/z* 321.1630 [M+H]⁺, calc. for C₂₁H₂₁O₃ 321.1491.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 10.5 min (minor) and 13.6 min (major).

Peak#	Ret. Time	Area	Height	Area%
1	10.610	2990538	106477	48.658
2	13.924	3155511	84888	51.342

Peak#	Ret. Time	Area	Height	Area%
1	10.500	2179957	79265	4.728
2	13.617	30223139	803250	95.272

White solid, Mp 102.4–103.6 °C; 66% yield; 90% *ee*; $[\alpha]_D^{26} +2.48$ (*c* 1.18, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.30 (dd, *J* = 8.5, 5.5 Hz, 2H), 7.23 (t, *J* = 7.8 Hz, 1H), 7.18 (d, *J* = 7.5 Hz, 1H), 7.09 (t, *J* = 7.4 Hz, 1H), 7.03 – 6.97 (m, 3H), 6.42 (d, *J* = 15.8 Hz, 1H), 6.14 – 6.08 (m, 1H), 3.20 (dd, *J* = 178.2, 16.0 Hz, 2H), 2.92 – 2.89 (m, 1H), 2.73 – 2.63 (m, 2H), 2.41 – 2.33 (m, 1H), 0.92 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 205.3, 168.8, 162.4 (d, *J*_{CF} = 248.2), 150.7, 133.9, 132.8, 128.6, 128.4, 127.8 (d, *J*_{CF} = 7.6), 125.0, 122.8, (d, *J*_{CF} = 2.5) 121.5, 116.4, 115.5, (d, *J*_{CF} = 21.4), 59.1, 38.1, 32.5, 31.2, 7.5. ¹⁹F NMR (282 MHz, CDCl₃) δ -114.2.

HRMS (ESI) *m/z* 339.1375 [M+H]⁺, calc. for C₂₁H₁₉FO₃ 339.1396.

The *ee* was determined by HPLC analysis. CHIRALPAK IA3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 12.8 min (major) and 14.8 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	12.715	2724328	147321	49.647
2	14.526	2763081	146264	50.353

Peak#	Ret. Time	Area	Height	Area%
1	12.775	9244710	527445	95.136
2	14.778	472689	33007	4.864

White solid, Mp 131.2 – 132.6 °C; 71% yield; 92% *ee*; $[\alpha]_D^{26} +0.75$ (*c* 1.49, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.26 – 7.17 (m, 6H), 7.10 – 7.07 (m, 1H), 7.02 (dd, *J* = 8.1, 1.1 Hz, 1H), 6.43 – 6.40 (m, 1H), 6.20 – 6.14 (m, 1H), 3.19 (dd, *J* = 181.2, 16.0 Hz, 2H), 2.93 – 2.69 (m, 2H), 2.68 – 2.32 (m, 2H), 0.92 (t, *J* = 7.2 Hz, 3H). ¹³C NMR

(75 MHz, CDCl₃) δ 205.3, 168.7, 150.7, 135.1, 133.9, 133.4, 128.8, 128.6, 128.5, 127.6, 125.0, 123.8, 121.5, 116.5, 59.1, 38.1, 32.5, 31.3, 7.5.

HRMS (ESI) *m/z* 355.1201 [M+H]⁺, calc. for C₂₁H₁₉ClO₃ 355.1101.

The *ee* was determined by HPLC analysis. CHIRALPAK IE (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 13.8 min (minor) and 15.2 min (major).

Peak#	Ret. Time	Area	Height	Area%
1	13.503	2310268	85342	49.588
2	15.349	2348622	155513	50.412

Peak#	Ret. Time	Area	Height	Area%
1	13.755	1149702	33966	4.133
2	15.232	26668117	1746977	95.867

White solid, Mp 94.7 – 95.7 °C; 81% yield; 85% *ee*; $[\alpha]_D^{26} +8.78$ (*c* 3.25, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.31 – 7.30 (m, 4H), 7.25 – 7.14 (m, 6H), 7.10 – 7.07 (m, 1H), 7.03 – 6.99 (m, 3H), 6.43 – 6.39 (m, 1H), 6.10 – 6.04 (m, 7.5 Hz, 1H), 3.34 (d, *J* = 16.0 Hz, 1H), 3.00 – 2.94 (m, 2H), 2.88 – 2.83 (m, 1H), 2.77 – 2.66 (m, 4H). ¹³C NMR (126 MHz,

CDCl₃) δ 203.7, 168.5, 150.5, 140.2, 135.5, 135.2, 128.6, 128.5, 128.4, 128.3, 127.8, 126.4, 126.2, 125.0, 122.7, 121.5, 116.4, 59.2, 40.7, 37.9, 30.9, 29.2.

HRMS (ESI) *m/z* 397.1853 [M+H]⁺, calc. for C₂₇H₂₄O₃ 397.1854.

The *ee* was determined by HPLC analysis. CHIRALPAK IA3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 98/2; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 16.1 min (minor) and 17.7 min (major).

Peak#	Ret. Time	Area	Height	Area%
1	16.171	483158	14290	48.230
2	18.110	518628	16991	51.770

Peak#	Ret. Time	Area	Height	Area%
1	16.073	295468	11702	2.896
2	17.667	9907021	361811	97.104

Colorless oil; 65% yield; 88% *ee*; $[\alpha]_D^{26} +7.61$ (*c* 1.06, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.34 – 7.29 (m, 4H), 7.25 – 7.14 (m, 6H), 7.08 – 7.05 (m, 1H), 6.97 – 6.95 (m, 2H), 6.88 (d, *J* = 8.1 Hz, 1H), 6.46 (d, *J* = 15.7 Hz, 1H), 6.21 – 6.15 (m, 1H), 3.90 – 3.77 (m, 2H), 3.41 (d, *J* = 16.0 Hz, 1H), 3.03 – 2.97 (m, 2H), 2.82 (dd, *J* = 14.0, 7.7 Hz, 1H). ¹³C

NMR (126 MHz, CDCl₃) δ 201.8, 168.7, 150.6, 140.2, 136.6, 135.4, 132.2, 129.5, 128.6, 128.5, 128.4, 127.8, 127.2, 126.4, 125.0, 122.7, 121.5, 116.4, 59.4, 45.6, 38.1, 31.1.

HRMS (ESI) *m/z* 383.1636 [M+H]⁺, calc. for C₂₆H₂₂O₃ 383.1647.

The *ee* was determined by HPLC analysis. CHIRALPAK IB (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 97/3; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 10.8 min (minor) and 11.3 min (major).

Peak#	Ret. Time	Area	Height	Area%
1	10.900	11424674	925653	48.071
2	11.393	12341467	1037499	51.929

Peak#	Ret. Time	Area	Height	Area%
1	10.816	917997	85617	6.181
2	11.260	13933950	1062766	93.819

Colorless oil; 44% yield; 98% *ee*; > 99:1 dr; $[\alpha]_{\text{D}}^{26} +1.22$ (*c* 1.29, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.03 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.65 – 7.62 (m, 1H), 7.45 – 7.30 (m, 8H), 7.27 – 7.24 (m, 2H), 7.21 – 7.13 (m, 2H), 5.32 (s, 1H), 3.38 – 3.23 (m, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 184.2, 157.9, 137.4, 132.4, 132.1, 130.5, 129.5, 129.0, 128.4, 128.3, 123.3, 120.6, 118.6, 118.5, 115.6, 90.2, 81.0, 70.3, 55.5, 38.0.

HRMS (ESI) *m/z* 364.1357 [M+H]⁺, calc. for C₂₅H₁₈NO₂ 364.1338.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 17.3 min (major) and 29.0 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	17.138	7038198	147958	50.531
2	28.708	6890297	92338	49.469

Peak#	Ret. Time	Area	Height	Area%
1	17.299	6732279	140349	99.044
2	28.952	65011	1137	0.956

Colorless oil; 65% yield; 95% *ee*; > 99:1 dr; $[\alpha]_D^{26} +0.81$ (*c* 1.32, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.02 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.66 – 7.62 (m, 1H), 7.37 – 7.27 (m, 9H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.14 (d, *J* = 8.3 Hz, 1H), 5.29 (s, 1H), 3.37 – 3.21 (m, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 183.9, 157.9, 137.5, 134.6, 132.2, 131.8, 130.9, 129.6, 129.2, 128.3, 128.3, 123.4, 120.5, 118.6, 118.4, 115.5, 90.5, 80.8, 70.4, 55.3, 37.2.

HRMS (ESI) *m/z* 398.0962 [M+H]⁺, calc. for C₂₅H₁₇NCIO₂ 398.0948.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 22.4 min (major) and 32.8 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	14.134	830538	19174	3.257
2	16.644	867150	15734	3.400
3	22.218	11944863	176948	46.841
4	32.423	11858400	121237	46.502

Peak#	Ret. Time	Area	Height	Area%
1	22.411	745448	13511	97.451
2	32.790	19500	435	2.549

Colorless oil; 70% yield; 96% *ee*; > 99:1 dr; $[\alpha]_{\text{D}}^{26} +0.11$ (*c* 1.75, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.02 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.66 – 7.61 (m, 1H), 7.52 (d, *J* = 8.4 Hz, 2H), 7.35 – 7.29 (m, 6H), 7.24 – 7.12 (m, 3H), 5.28 (s, 1H), 3.37 – 3.19 (m, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 183.9, 157.9, 137.5, 132.2, 132.18, 131.5, 129.6, 128.4, 123.4, 122.7, 120.6, 118.6, 118.5, 115.5, 90.5, 80.8, 70.5, 55.2, 37.3.

HRMS (ESI) *m/z* 442.0422 [M+H]⁺, calc. for C₂₅H₁₇NBrO₂ 442.0443.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 19.4 min (major) and 28.6 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	12.529	1874419	64717	2.832
2	14.241	1552765	77105	2.346
3	19.386	31516377	391712	47.610
4	28.130	31254101	310725	47.213

Peak#	Ret. Time	Area	Height	Area%
1	19.435	10167321	189754	97.761
2	28.593	232807	4197	2.239

Colorless oil; 55% yield; 99% *ee*; >99:1 dr; $[\alpha]_D^{26} +1.92$ (*c* 1.53, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.91 (d, *J* = 8.0 Hz, 1H), 7.44 – 7.30 (m, 8H), 7.27 – 7.24 (m, 2H), 7.00 – 6.94 (m, 2H), 5.29 (s, 1H), 3.36 – 3.22 (m, 2H), 2.43 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 183.9, 157.9, 149.3, 132.6, 132.2, 130.5, 129.4, 128.9, 128.3, 128.3, 128.2, 124.6, 120.7, 118.6, 116.2, 115.8, 90.0, 81.2, 70.3, 55.4, 38.0, 22.1.

HRMS (ESI) *m/z* 378.1490 [M+H]⁺, calc. for C₂₅H₂₀NO₂ 378.1494.

The *ee* was determined by HPLC analysis. CHIRALPAK IA3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 12.0 min (major) and 18.9 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	12.044	5368753	326054	50.628
2	18.890	5030211	199556	49.372

Peak#	Ret. Time	Area	Height	Area%
1	12.001	18919065	1150608	99.234
2	18.920	146098	6250	0.766

Colorless oil; 62% yield; 95% *ee*; 94:6 dr; $[\alpha]_D^{26} +3.99$ (*c* 1.09, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.00 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.64 – 7.60 (m, 1H), 7.41 – 7.27 (m, 12H), 7.19 – 7.16 (m, 1H), 7.12 (dd, *J* = 8.3, 0.9 Hz, 1H), 6.68 (d, *J* = 15.7 Hz, 1H), 6.30 – 6.24 (m, 1H), 5.53 (s, 1H), 3.10 – 2.91 (m, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 183.9, 158.3, 137.4, 137.2, 136.0, 132.2, 129.6, 128.7, 128.4, 128.3, 128.2, 126.6, 123.2,

120.7, 120.2, 118.6, 118.5, 115.6, 90.4, 80.9, 71.2, 53.8, 35.7.

HRMS (ESI) *m/z* 390.1510 [M+H]⁺, calc. for C₂₇H₁₉NO₂ 390.1494 .

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 12.6 min (major) and 23.7min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	9.852	1102387	40775	5.921
2	10.728	965550	35940	5.186
3	12.527	8318642	266436	44.683
4	23.517	8230545	108800	44.210

Peak#	Ret. Time	Area	Height	Area%
1	12.559	3134404	94445	97.513
2	23.722	75607	1603	2.487

Colorless oil; 73% yield; 96% *ee*; >99:1 dr; $[\alpha]_{\text{D}}^{26} +2.74$ (*c* 1.02, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.02 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.66 – 7.63 (m, 1H), 7.41 – 7.34 (m, 5H), 7.21 (d, *J* = 7.8 Hz, 1H), 7.14 – 7.12 (m, 1H), 5.10 (d, *J* = 2.4 Hz, 1H), 3.32 – 3.19 (m, 2H), 2.58 (d, *J* = 2.3 Hz, 1H). ¹³C NMR (126 MHz, CDCl₃) δ 183.9, 157.7, 137.5, 132.2, 130.5, 129.0, 128.5, 128.4,

123.5, 118.6, 118.4, 115.4, 80.4, (t, *J*_{CF} = 31.5), 78.6, 69.6, 55.2, 37.9.

HRMS (ESI) *m/z* 288.1047 [M+H]⁺, calc. for C₁₉H₁₃NO₂ 288.1024.

The *ee* was determined by HPLC analysis. CHIRALPAK IE (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 20.5 min (major) and 55.8 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	20.515	1489438	48173	44.350
2	35.487	206959	3742	6.162
3	37.886	208402	3478	6.205
4	53.943	1453580	11588	43.282

Peak#	Ret. Time	Area	Height	Area%
1	20.500	7506541	241169	98.668
2	55.764	101345	949	1.332

Colorless oil; 63% yield; 92% *ee*; >99:1 dr; $[\alpha]_D^{26} +0.71$ (*c* 1.44, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.03 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.63 – 7.60 (m, 1H), 7.48 – 7.46 (m, 2H), 7.40 – 7.34 (m, 3H), 7.30 – 7.27 (m, 2H), 7.19 – 7.13 (m, 2H), 6.85 – 6.79 (m, 2H), 5.32 (s, 1H), 3.77 (s, 3H), 3.44 – 3.26 (m, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 184.2, 161.0, 158.2, 137.2, 133.8, 132.7, 131.0, 130.6, 128.9, 128.3, 128.2, 123.1, 120.3, 118.8, 118.7, 115.7, 110.8, 110.2, 87.1, 85.0, 70.7, 55.7, 55.4, 37.9.

HRMS (ESI) *m/z* 394.1461 [M+H]⁺, calc. for C₂₆H₁₉NO₃ 394.1443.

The *ee* was determined by HPLC analysis. CHIRALPAK IA3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 15.0 min (major) and 17.5 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	15.000	4261964	252415	50.490
2	17.722	4179323	197667	49.510

Peak#	Ret. Time	Area	Height	Area%
1	14.957	5679117	400741	96.074
2	17.504	232082	14901	3.926

Colorless oil; 44% yield; 99% *ee*; >99:1 dr; $[\alpha]_D^{26} +1.92$ (*c* 0.11, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.02 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.65 – 7.61 (m, 1H), 7.44 – 7.36 (m, 6H), 7.21 – 7.19 (m, 2H), 7.14 (dd, *J* = 8.4, 1.0 Hz, 1H), 7.00 (dd, *J* = 5.0, 1.2 Hz, 1H), 5.31 (s, 1H), 3.37 – 3.22 (m, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 183.5, 157.6, 137.7, 132.2, 132.12, 131.96, 130.48, 129.10, 128.58, 128.44, 123.69, 122.9, 121.5, 118.6, 118.3, 115.4, 86.6, 84.5, 69.9, 55.2, 38.0. ¹⁹F NMR (282 MHz, CDCl₃) δ -59.3.
HRMS (ESI) *m/z* 500.1096 [M+H]⁺, calc. for C₂₇H₁₅NF₆O₂

500.1085.

The *ee* was determined by HPLC analysis. CHIRALPAK IB3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 98/2; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 5.8 min (major) and 6.3 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	5.810	7183166	549280	46.958
2	6.351	7791320	549671	46.765
3	7.251	483334	30253	3.025
4	8.017	519615	35793	3.252

Peak#	Ret. Time	Area	Height	Area%
1	5.825	3765175	406026	99.330
2	6.306	25408	4848	0.670

Colorless oil; 50% yield; 96% *ee*; >99:1 dr; $[\alpha]_D^{26} +0.85$ (*c* 1.26, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.02 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.65 – 7.61 (m, 1H), 7.44 – 7.36 (m, 6H), 7.21 – 7.17 (m, 2H), 7.14 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.00 (dd, *J* = 5.0, 1.2 Hz, 1H), 5.31 (s, 1H), 3.37 – 3.22 (m, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 184.2, 157.9, 137.4, 132.4, 131.2, 130.5, 129.9, 129.0, 128.4, 128.3, 125.6, 123.3, 119.7, 118.6, 118.5, 115.6, 85.4, 80.8, 70.4, 55.4, 38.0.

HRMS (ESI) *m/z* 370.0930 [M+H]⁺, calc. for C₂₃H₁₅NSO₂ 370.0902.

The *ee* was determined by HPLC analysis. CHIRALPAK IA3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 15.3 min (major) and 16.2 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	15.551	4912104	281431	49.547
2	16.454	5001915	259544	50.453

Peak#	Ret. Time	Area	Height	Area%
1	15.337	16703687	1123984	97.913
2	16.153	356046	19323	2.087

Colorless oil; 92% yield; 87% *ee*; >99:1 dr; $[\alpha]_D^{26} +3.23$ (*c* 1.29, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.98 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.64 (dd, *J* = 1.8, 1.0 Hz, 1H), 7.39 – 7.36 (m, 5H), 7.21 – 7.10 (m, 2H), 5.14 (s, 1H), 3.44 (s, 3H), 3.25 – 3.13 (m, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 184.4, 155.3, 137.3, 132.6, 130.4, 128.9, 128.3, 127.9, 123.3, 118.8, 118.3, 115.8, 102.1, 57.1, 55.8, 38.7.

HRMS (ESI) *m/z* 294.1138 [M+H]⁺, calc. for C₁₈H₁₆NO₃ 294.1130.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 98/2; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 17.2 min (major) and 20.7 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	17.281	6959525	157022	50.168
2	21.167	6912839	121932	49.832

Peak#	Ret. Time	Area	Height	Area%
1	17.244	6447203	137658	93.327
2	20.739	460981	10898	6.673

Colorless oil; 90% yield; 85% *ee*; >99:1 dr; $[\alpha]_D^{26} +0.53$ (*c* 2.65, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 7.98 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.65 – 7.61 (m, 1H), 7.41 – 7.34 (m, 5H), 7.20 – 7.15 (m, 1H), 7.08 (dd, *J* = 8.3, 1.0 Hz, 1H), 5.23 (s, 1H), 3.82 – 3.57 (m, 2H), 3.24 – 3.12 (m, 2H), 1.10 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 184.6, 155.5, 137.3, 132.7, 130.3, 128.9, 128.2, 127.9, 123.1, 118.7, 118.3, 115.9, 101.0, 66.0, 56.0, 38.6, 14.6.

HRMS (ESI) *m/z* 308.1295 [M+H]⁺, calc. for C₁₉H₁₈NO₃ 308.1287.

The *ee* was determined by HPLC analysis. CHIRALPAK IG3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 15.8 min (major) and 20.2 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	16.297	1102711	40732	50.585
2	20.433	1077213	63524	49.415

Peak#	Ret. Time	Area	Height	Area%
1	15.810	558276	27506	93.210
2	20.215	40671	2145	6.790

White solid, Mp 124.4 – 128.8 °C; 95% yield; 85% *ee*; >99:1 dr; $[\alpha]_D^{26} +2.27$ (*c* 3.92, CHCl₃); ¹H NMR (300 MHz, CDCl₃) δ 8.00 (d, *J* = 7.8 Hz, 1H), 7.71 – 7.65 (m, 1H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.29 – 7.26 (m, 2H), 7.25 – 7.13 (m, 2H), 5.15 (s, 1H), 3.49 (s, 3H), 3.25 – 3.12 (m, 2H). ¹³C NMR (75 MHz, CDCl₃) δ 184.1, 155.2, 137.4, 132.1, 132.0, 131.6, 127.9,

123.4, 122.6, 118.7, 118.3, 116.0, 102.0, 57.1, 55.5, 38.0.

HRMS (ESI) *m/z* 372.0272 [M+H]⁺, calc. for C₁₈H₁₅NBrO₃ 372.0235.

The *ee* was determined by HPLC analysis. CHIRALPAK ADH (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 13.5 min (major) and 14.8 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	13.173	14770656	976193	49.992
2	14.335	14775159	905096	50.008

Peak#	Ret. Time	Area	Height	Area%
1	13.473	11141168	771647	92.585
2	14.754	892247	63175	7.415

Colorless oil; 85% yield; 83% *ee*; > 99:1 dr; $[\alpha]_D^{26} +9.60$ (*c* 0.86, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.98 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.65 – 7.62 (m, 1H), 7.36 (d, *J* = 6.7 Hz, 1H), 7.24 – 7.17 (m, 4H), 7.11 (d, *J* = 8.2 Hz, 1H), 5.27 (s, 1H), 3.46 (s, 3H), 3.29 – 3.22 (m, 2H), 2.38 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 184.5, 155.2, 137.7, 137.3, 131.3, 131.0, 130.9, 128.2, 127.9, 126.2, 123.3, 118.8, 118.2, 116.0, 102.2, 57.1, 55.6, 34.9 19.8.

HRMS (ESI) *m/z* 308.1201 [M+H]⁺, calc. for C₁₉H₁₈NO₄ 308.1236.

The *ee* was determined by HPLC analysis. CHIRALPAK IA3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 13.1 min (major) and 14.2 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	12.996	1025523	66650	49.910
2	14.182	1029242	55980	50.090

Peak#	Ret. Time	Area	Height	Area%
1	13.073	2489748	164536	91.232
2	14.232	239276	16592	8.768

Colorless oil; 84% yield; 90% *ee*; >99:1 dr; $[\alpha]_D^{26} +4.22$ (*c* 2.14, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.86 (d, *J* = 8.0 Hz, 1H), 7.38 – 7.34 (m, 5H), 7.00 – 6.92 (m, 2H), 5.10 (s, 1H), 3.43 (s, 3H), 3.21 – 3.13 (m, 2H), 2.43 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 184.0, 155.4, 149.2, 132.8, 130.3, 128.9, 128.2, 127.8, 124.5, 118.4, 116.4, 115.9, 102.0, 57.0, 55.7, 38.8,

22.1.

HRMS (ESI) *m/z* 308.1307 [M+H]⁺, calc. for C₁₉H₁₈NO₃ 308.1287.

The *ee* was determined by HPLC analysis. CHIRALPAK IA3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 10.6 min (major) and 12.9 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	10.444	3760255	316185	49.791
2	12.587	3791818	253520	50.209

Peak#	Ret. Time	Area	Height	Area%
1	10.630	14428542	1122111	94.851
2	12.913	783178	55242	5.149

Colorless oil; 85% yield; 80% *ee*; > 99:1 dr; $[\alpha]_D^{26} +7.35$ (*c* 1.21, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.41 (d, *J* = 8.4 Hz, 1H), 7.90 (dd, *J* = 20.7, 8.4 Hz, 2H), 7.73 – 7.69 (m, 2H), 7.58 (d, *J* = 8.7 Hz, 1H), 7.41 – 7.36 (m, 5H), 5.37 (d, *J* = 1.5 Hz, 1H), 3.50 (s, 3H), 3.33 – 3.23 (m, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 184.2, 153.6, 138.2, 132.7, 130.4, 130.3, 128.9, 128.3, 127.0, 124.5, 122.9, 121.9, 115.8, 113.4, 102.7, 57.5, 55.4, 38.9.

HRMS (ESI) *m/z* 344.1298 [M+H]⁺, calc. for C₂₂H₁₈NO₃ 344.1287.

The *ee* was determined by HPLC analysis. CHIRALPAK IA3 (4.6 mm i.d. x 250 mm); Hexane/2-propanol = 95/5; flow rate 1.0 ml/min; 25 °C; 254 nm; retention time: 14.1 min (major) and 17.2 min (minor).

Peak#	Ret. Time	Area	Height	Area%
1	13.773	13869900	395583	50.585
2	17.316	13084697	287458	49.415

Peak#	Ret. Time	Area	Height	Area%
1	14.109	10847864	334973	90.239
2	17.271	912699	22492	9.761

Appendix

Copies of NMR spectra

3q

¹⁹ F NMR XYZ coordinates							
¹⁹ F NMR TM-1							
5							
C	0.00002	0.00001	0.24157	H	2.68341	-2.15254	0.00733
F	-0.00001	0.00013	1.59254	H	3.92827	-0.00059	0.02812
Cl	1.52676	-0.74196	-0.30943	H	2.68451	2.15199	0.00732
Cl	-1.40593	-0.95124	-0.30943	H	0.20326	2.15199	-0.03356
Cl	-0.12083	1.69312	-0.30951	C	-1.45234	0.00021	-0.00393
				F	-1.97994	-1.08721	-0.62073
				F	-1.93569	-0.00836	1.26970
				F	-1.98037	1.09525	-0.60649
				TM-5			
				8			
				C	-0.96555	0.16967	-0.00022
				O	-1.62474	-1.00088	0.00002
C	1.83760	0.00000	-0.00000	H	-1.02695	-1.76569	-0.00018
C	1.13690	1.21017	0.00002	O	-1.51005	1.23595	-0.00003
C	-0.26116	1.21998	-0.00001	C	0.58298	0.02581	-0.00002
C	-0.92691	-0.00001	0.00005	F	0.98235	-0.67569	-1.09082
C	-0.26116	-1.21999	0.00004	F	0.98225	-0.67343	1.09223
C	1.13692	-1.21016	-0.00003	F	1.19104	1.20604	-0.00122
H	2.92300	0.00002	-0.00002				
H	1.67627	2.15262	-0.00000	TM-6			
H	-0.82873	2.14419	-0.00004	37			
H	-0.82869	-2.14423	0.00003	Si	0.38528	0.00003	0.29491
H	1.67627	-2.15262	-0.00006	C	2.27953	0.00008	0.07597
F	-2.28791	0.00000	-0.00003	C	5.10783	0.00014	-0.17613
				C	3.11939	0.00013	1.20863
				C	2.90552	0.00006	-1.18691
				C	4.29778	0.00008	-1.31453
				C	4.51209	0.00016	1.08763
				H	2.67027	0.00015	2.19549
				H	2.29061	0.00002	-2.07968
				H	4.74934	0.00006	-2.30376
				H	5.13107	0.00021	1.98144
				H	6.19062	0.00016	-0.27293
				C	-0.64706	-1.64375	0.30030
				C	-2.22363	-4.01697	0.31898
				C	-1.49920	-1.95936	1.37897
				C	-0.60082	-2.57428	-0.76153
				C	-1.36566	-3.74712	-0.75245
				C	-2.28703	-3.11697	1.38634
				H	-1.52732	-1.29490	2.23661
				H	0.06001	-2.38041	-1.60177
				H	-1.28298	-4.45413	-1.57466
				H	-2.93595	-3.32368	2.23381
				H	-2.82139	-4.92454	0.32897
				C	-0.60111	2.57420	-0.76163
				C	-2.28718	3.11691	1.38633
				C	-0.64719	1.64373	0.30026
				C	-1.36602	3.74700	-0.75257
				C	-2.22393	4.01686	0.31891
TM-2							
12							
C	1.83760	0.00000	-0.00000				
C	1.13690	1.21017	0.00002				
C	-0.26116	1.21998	-0.00001				
C	-0.92691	-0.00001	0.00005				
C	-0.26116	-1.21999	0.00004				
C	1.13692	-1.21016	-0.00003				
H	2.92300	0.00002	-0.00002				
H	1.67627	2.15262	-0.00000				
H	-0.82873	2.14419	-0.00004				
H	-0.82869	-2.14423	0.00003				
H	1.67627	-2.15262	-0.00006				
F	-2.28791	0.00000	-0.00003				
TM-3							
12							
C	-0.54297	-1.28415	0.00006				
C	-1.38360	-0.17180	0.00016				
C	-0.84064	1.11230	-0.00000				
C	0.54302	1.28413	0.00007				
C	1.38359	0.17186	0.00011				
C	0.84059	-1.11233	-0.00004				
F	2.71158	0.33669	0.00005				
F	1.06408	2.51668	-0.00006				
F	-1.64737	2.17995	-0.00008				
F	-2.71156	-0.33683	-0.00002				
F	-1.06421	-2.51663	-0.00001				
F	1.64748	-2.17986	-0.00012				
TM-4							
15							
C	0.05300	0.00045	-0.03242				
C	0.74790	-1.21389	-0.01996				
C	2.14351	-1.21059	0.00178				
C	2.84236	-0.00029	0.01303				
C	2.14416	1.21031	0.00178				
C	0.74847	1.21436	-0.01994				
H	0.20218	-2.15125	-0.03361				

C	-1.49928	1.95936	1.37897			TM-8	
H	-1.28344	4.45396	-1.57482			89	
H	-2.82174	4.92439	0.32889	N	2.69296	0.34504	-0.29366
H	-1.52729	1.29494	2.23666	C	2.71998	1.17921	-1.57707
H	-2.93605	3.32363	2.23384	H	3.07029	0.50298	-2.35934
F	0.15099	-0.00000	-1.54869	H	3.48943	1.94190	-1.43114
H	0.05967	2.38032	-1.60191	C	1.40474	1.82876	-2.00561
F	0.44572	0.00006	2.01674	H	0.58367	1.10865	-1.98951
K	-2.34863	-0.00014	-1.66951	H	1.12503	2.62257	-1.30529
				C	1.54924	2.42884	-3.41501
		TM-7		H	1.77624	1.62567	-4.12924
		37		H	2.40695	3.11637	-3.44078
Si	0.32255	0.00001	0.28092	C	0.28722	3.17229	-3.86713
C	2.22208	-0.00005	0.13836	H	-0.58431	2.50965	-3.87064
C	5.03959	-0.00013	0.00118	H	0.41003	3.57285	-4.87839
C	3.01702	-0.00005	1.30189	H	0.06108	4.01153	-3.20007
C	2.89979	-0.00009	-1.09636	C	1.90672	-0.95046	-0.57388
C	4.29481	-0.00013	-1.17674	H	2.33321	-1.35835	-1.49294
C	4.41313	-0.00009	1.24595	H	0.87932	-0.63736	-0.76762
H	2.53340	-0.00002	2.27218	C	1.91764	-2.00406	0.53429
H	2.32627	-0.00009	-2.01608	H	1.33051	-1.66194	1.39253
H	4.79635	-0.00016	-2.13897	H	2.93498	-2.21309	0.88764
H	5.00513	-0.00009	2.15520	C	1.30584	-3.31626	0.00842
C	-0.69855	-1.64777	0.24887	H	0.28762	-3.12489	-0.34679
C	-2.23353	-4.02778	0.22197	H	1.88032	-3.66133	-0.86287
C	-1.56725	-1.98380	1.30699	C	1.28289	-4.41543	1.07538
C	-0.61697	-2.57380	-0.81334	H	0.84346	-5.33478	0.67541
C	-1.36289	-3.75787	-0.83472	H	0.68691	-4.10777	1.94061
C	-2.34168	-3.14933	1.29938	H	2.29424	-4.65444	1.42766
H	-1.62565	-1.32840	2.16980	C	1.98665	1.09666	0.84208
H	0.06049	-2.37389	-1.63861	H	2.01243	0.42348	1.70052
H	-1.26184	-4.46532	-1.65172	H	0.94170	1.17799	0.53517
H	-3.00748	-3.37942	2.12485	C	2.58271	2.45347	1.22112
C	-0.61710	2.57367	-0.81359	H	3.59665	2.34336	1.62447
C	-2.34114	3.14976	1.29952	H	2.65648	3.11148	0.34726
C	-0.69844	1.64786	0.24883	C	1.70697	3.14471	2.28213
C	-1.36296	3.75778	-0.83500	H	1.60955	2.48835	3.15575
C	-2.23326	4.02796	0.22189	H	0.69372	3.27743	1.88460
C	-1.56680	1.98417	1.30714	C	2.27320	4.50033	2.71754
H	-1.26210	4.46506	-1.65218	H	3.27291	4.39460	3.15531
H	-1.62498	1.32895	2.17009	H	1.62968	4.96917	3.46827
H	-3.00668	3.38006	2.12514	H	2.35060	5.19096	1.86965
F	0.16354	-0.00004	-1.56636	H	4.60949	1.02531	0.23369
H	0.06013	2.37356	-1.63901	C	4.12971	0.05296	0.12298
F	0.31633	0.00001	2.00250	H	4.07389	-0.40195	1.11414
K	-2.32633	-0.00016	-1.84390	C	4.94665	-0.83629	-0.81694
Cl	-3.19795	-5.50114	0.19796	H	5.02112	-0.38453	-1.81275
Cl	-3.19760	5.50138	0.19786	H	4.45565	-1.80619	-0.93986
Cl	6.80129	-0.00017	-0.08627	C	6.37086	-1.07471	-0.27372
				H	6.83987	-1.83960	-0.90315

H	6.30847	-1.50955	0.73289	H	-0.86320	-1.97291	-2.47657
C	7.27010	0.16845	-0.24820	C	-1.14844	-0.87128	-4.31276
H	7.34288	0.62439	-1.24271	H	-1.41775	0.14968	-4.61579
H	8.28386	-0.09639	0.06783	H	-1.90970	-1.53388	-4.74938
H	6.90824	0.93448	0.44631	C	0.22722	-1.22803	-4.88729
Si	-2.45991	-0.46533	0.22451	H	1.00728	-0.57383	-4.48462
C	-3.48753	1.14351	0.01632	H	0.23375	-1.12935	-5.97747
C	-5.07024	3.49164	-0.27018	H	0.50322	-2.25990	-4.64316
C	-4.87728	1.13247	0.25462	C	-2.16483	0.84936	-0.37054
C	-2.92229	2.37492	-0.37144	H	-2.59176	1.57186	-1.06944
C	-3.69508	3.53208	-0.51435	H	-1.09395	0.76054	-0.56166
C	-5.65819	2.28418	0.11555	C	-2.38932	1.30391	1.07211
H	-5.34661	0.20164	0.55323	H	-1.80520	0.68658	1.76206
H	-1.85611	2.42211	-0.56514	H	-3.44388	1.22586	1.36440
H	-3.22403	4.46517	-0.81670	C	-1.94870	2.77158	1.22849
H	-6.72742	2.23732	0.30837	H	-0.89702	2.86766	0.93830
H	-5.67513	4.38848	-0.37984	H	-2.52314	3.39926	0.53247
C	-1.67891	-0.84270	1.94792	C	-2.13921	3.28539	2.65917
C	-0.59111	-1.39412	4.52121	H	-1.81851	4.32873	2.74252
C	-1.79930	-2.11204	2.54529	H	-1.54850	2.69557	3.36749
C	-1.01027	0.14493	2.69579	H	-3.19094	3.23349	2.96799
C	-0.48382	-0.11490	3.96617	C	-2.03445	-1.60653	0.01854
C	-1.25207	-2.39416	3.80212	H	-2.20064	-1.38010	1.07298
H	-2.35099	-2.88978	2.02589	H	-0.97292	-1.43967	-0.17653
H	-0.92134	1.14623	2.28335	C	-2.45744	-3.04535	-0.28267
H	-0.00309	0.68224	4.53012	H	-3.49422	-3.22697	0.02564
H	-1.36126	-3.38841	4.22942	H	-2.40223	-3.25766	-1.35688
H	-0.18357	-1.60268	5.50727	C	-1.54519	-4.03811	0.46063
C	-1.55478	-1.09689	-2.49813	H	-1.57468	-3.82284	1.53593
C	-2.30895	-3.77049	-2.42654	H	-0.50670	-3.88072	0.14582
C	-2.14181	-1.58681	-1.31524	C	-1.94413	-5.49729	0.21657
C	-1.35339	-1.90748	-3.62052	H	-2.96724	-5.69504	0.55779
C	-1.71898	-3.25645	-3.58445	H	-1.27737	-6.17932	0.75306
C	-2.52959	-2.94151	-1.32095	H	-1.89169	-5.75214	-0.84844
H	-0.92130	-1.48570	-4.52583	H	-4.60036	-1.54816	-0.79799
H	-1.56178	-3.89289	-4.45174	C	-4.25882	-0.58126	-0.42867
H	-3.03289	-3.34657	-0.44898	H	-4.32743	-0.60154	0.66098
H	-2.61485	-4.81353	-2.38955	C	-5.13702	0.53976	-0.98874
F	-0.91565	0.44121	-0.19341	H	-5.08756	0.56212	-2.08345
H	-1.27030	-0.05003	-2.54716	H	-4.78218	1.51087	-0.63108
F	-3.84242	-1.42377	0.64849	C	-6.61012	0.37086	-0.56264
TM-9				H	-7.14488	1.28120	-0.85685
98				H	-6.66925	0.32752	0.53320
N	-2.77333	-0.51175	-0.76139	C	-7.32437	-0.84385	-1.17017
C	-2.60399	-0.69760	-2.27183	H	-7.27385	-0.82534	-2.26532
H	-2.98784	0.21872	-2.72464	H	-8.38209	-0.84868	-0.88914
H	-3.27368	-1.51282	-2.55829	H	-6.89860	-1.79448	-0.83087
C	-1.18798	-0.97145	-2.77799	Si	2.16128	0.54376	0.62493
H	-0.46818	-0.27661	-2.33946	C	3.43179	-0.67592	-0.13554
				C	5.38680	-2.47005	-1.23060

C	4.79321	-0.60686	0.22692	H	-0.40263	0.71547	-2.39562
C	3.08788	-1.67643	-1.06362	H	-0.56421	-0.83831	-3.18050
C	4.03846	-2.55271	-1.59857	C	-0.82607	0.83687	-4.51951
C	5.74483	-1.47972	-0.30433	H	-1.20187	1.86784	-4.47048
H	5.10426	0.14730	0.94149	H	-1.45118	0.31551	-5.25833
H	2.05231	-1.77091	-1.37237	C	0.62938	0.84601	-5.00044
H	3.72625	-3.31346	-2.31286	H	1.27790	1.37735	-4.29615
H	6.78438	-1.39036	0.00733	H	0.71648	1.33855	-5.97388
C	1.24195	0.03421	2.24130	H	1.01896	-0.17261	-5.10558
C	-0.05255	-0.73791	4.68643	C	-2.35998	0.78263	-0.35697
C	1.14563	0.90719	3.34163	H	-2.78076	1.70524	-0.76256
C	0.67950	-1.24277	2.41540	H	-1.27192	0.82996	-0.42494
C	0.05671	-1.62723	3.60833	C	-2.77330	0.60513	1.10463
C	0.49965	0.54119	4.52649	H	-2.22328	-0.22458	1.56009
H	1.60158	1.89072	3.27778	H	-3.84363	0.38625	1.19998
H	0.74852	-1.96380	1.60536	C	-2.46805	1.89276	1.89302
H	-0.33806	-2.63775	3.70963	H	-1.40064	2.12410	1.81095
H	0.44338	1.25343	5.34840	H	-3.00540	2.73501	1.43537
C	1.28812	2.21624	-1.63101	C	-2.86008	1.77679	3.36959
C	1.67155	4.64059	-0.35069	H	-2.63319	2.70418	3.90473
C	1.75543	2.18584	-0.30440	H	-2.31203	0.96496	3.85881
C	1.02853	3.41431	-2.30542	H	-3.93269	1.57856	3.48578
C	1.20740	4.65227	-1.67376	C	-2.02523	-1.60862	-0.96098
C	1.95434	3.43989	0.30684	H	-2.32023	-1.84276	0.06316
H	0.69034	3.38754	-3.34066	H	-0.97222	-1.32113	-0.93150
H	2.35654	3.47469	1.31420	C	-2.26275	-2.82010	-1.86412
H	1.83117	5.58491	0.16759	H	-3.30572	-3.15443	-1.81286
F	0.79965	-0.26049	-0.31717	H	-2.05580	-2.57785	-2.91302
H	1.14258	1.27831	-2.15867	C	-1.35408	-3.98920	-1.44194
F	3.35939	1.36721	1.57426	H	-1.54218	-4.23263	-0.38876
C	0.95730	5.95285	-2.40355	H	-0.30551	-3.67347	-1.50237
H	1.89481	6.38441	-2.77749	C	-1.56707	-5.23853	-2.30322
H	0.29806	5.80854	-3.26594	H	-2.59924	-5.60119	-2.23308
H	0.49797	6.70049	-1.74740	H	-0.90734	-6.05044	-1.98263
C	6.42443	-3.39891	-1.81942	H	-1.35413	-5.03567	-3.35922
H	7.06834	-2.87387	-2.53678	H	-4.49674	-1.35989	-2.00172
H	7.07863	-3.81269	-1.04343	C	-4.28898	-0.60765	-1.24103
H	5.95723	-4.23636	-2.34761	H	-4.45748	-1.06927	-0.26588
C	-0.69172	-1.15688	5.99147	C	-5.21649	0.59613	-1.42048
H	-1.37551	-2.00077	5.85109	H	-5.07077	1.05576	-2.40467
H	0.06600	-1.46960	6.72161	H	-4.99199	1.36153	-0.67162
H	-1.25649	-0.33520	6.44556	C	-6.69894	0.19281	-1.27739
TM-10				H	-7.29020	1.11534	-1.25862
89				H	-6.85383	-0.28438	-0.30046
N	-2.79133	-0.33194	-1.32934	C	-7.23208	-0.71764	-2.39158
C	-2.46429	0.11717	-2.75607	H	-7.08220	-0.26438	-3.37864
H	-2.91037	1.10788	-2.86180	H	-8.30580	-0.88855	-2.26733
H	-3.00428	-0.56085	-3.42200	H	-6.75037	-1.70156	-2.39713
C	-0.98642	0.17114	-3.14136	Si	1.91159	0.34377	0.99915
				C	3.36269	-0.39115	-0.01791

C	5.54093	-1.46475	-1.46274	H	1.40069	-6.12522	-1.12226
C	4.66569	-0.41816	0.51797	H	1.27747	-5.58101	0.55738
C	3.20327	-0.92552	-1.31091	C	1.60583	-0.38185	1.79340
C	4.27182	-1.45945	-2.03749	H	1.47745	0.65595	2.10739
C	5.75115	-0.94721	-0.18648	H	0.60901	-0.82695	1.72002
H	4.83204	-0.01451	1.51046	C	2.46445	-1.09737	2.83009
H	2.21729	-0.92334	-1.76225	H	3.37795	-0.52367	3.02714
H	4.12347	-1.86480	-3.03347	H	2.77270	-2.09260	2.49491
H	6.74479	-0.95668	0.24959	C	1.66586	-1.22998	4.12999
C	0.90794	-0.82971	2.15360	H	1.30826	-0.23944	4.44191
C	-0.52504	-2.56284	3.86768	H	0.77267	-1.83954	3.94272
C	0.63755	-0.49061	3.49203	C	2.49414	-1.85470	5.24906
C	0.45074	-2.08773	1.72149	H	3.37397	-1.24206	5.47681
C	-0.24795	-2.96202	2.56083	H	2.84481	-2.85399	4.96621
C	-0.08597	-1.33011	4.34652	H	1.90711	-1.95320	6.16758
H	1.01461	0.44667	3.88907	C	1.48798	0.88160	-0.30645
H	0.66231	-2.40708	0.70518	H	0.42622	0.81791	-0.05005
H	-0.56309	-3.94119	2.21321	H	1.57539	0.73014	-1.38638
H	-0.28857	-1.04002	5.37259	C	2.06610	2.23105	0.09207
C	1.07452	2.72971	-0.49435	H	3.09547	2.34072	-0.27274
C	1.12068	4.45331	1.69012	H	2.09440	2.34434	1.18333
C	1.43628	2.19870	0.75770	C	1.20047	3.35076	-0.49190
C	0.74750	4.07729	-0.67519	H	0.16571	3.21544	-0.15496
C	0.75832	4.92589	0.43061	H	1.18908	3.26915	-1.58692
C	1.46963	3.10610	1.83408	C	1.69803	4.73222	-0.07784
H	0.49493	4.46577	-1.65703	H	1.05474	5.51961	-0.48415
H	1.79376	2.75628	2.80853	H	2.71909	4.91249	-0.43532
H	1.14455	5.12800	2.53988	H	1.69972	4.83404	1.01393
F	0.73219	-0.07741	-0.33536	H	4.00388	-1.13130	0.86194
H	1.06571	2.07640	-1.36101	C	3.62469	-0.25609	0.33237
F	2.92999	0.77228	2.33608	H	3.89369	0.62622	0.92040
Cl	6.90112	-2.13787	-2.36764	C	4.24124	-0.19151	-1.05862
Cl	-1.43133	-3.64313	4.93307	H	3.76078	0.57929	-1.67298
Cl	0.32140	6.62555	0.22634	H	4.10897	-1.14879	-1.57704
A-ax-1				C	5.73716	0.11503	-0.94990
89				H	5.87156	1.08732	-0.45820
F	-1.41437	-0.58266	0.40087	H	6.21714	-0.63286	-0.30515
N	2.12115	-0.33514	0.36092	C	6.41802	0.13006	-2.31546
C	1.59519	-1.52727	-0.41417	H	7.48519	0.35538	-2.22334
H	1.94381	-1.39787	-1.44198	H	5.96969	0.88732	-2.96869
H	0.50902	-1.40041	-0.41143	H	6.32127	-0.84138	-2.81340
C	1.96659	-2.90627	0.10584	Si	-2.60549	0.46752	-0.44257
H	3.05245	-3.01250	0.22765	C	-2.11650	1.92297	0.73339
H	1.50050	-3.08609	1.08157	C	-1.28666	4.15377	2.28704
C	1.46591	-3.96382	-0.88288	C	-2.50936	3.23370	0.41558
H	1.93387	-3.79560	-1.86184	C	-1.31651	1.76883	1.88027
H	0.38455	-3.84015	-1.02523	C	-0.90603	2.85987	2.64907
C	1.76300	-5.38219	-0.40477	C	-2.09730	4.33724	1.16749
H	2.84064	-5.53684	-0.27604	H	-1.00816	0.76954	2.17305
				H	-0.29149	2.70180	3.53358

H	-2.41004	5.33847	0.88016	C	1.22374	2.09641	-2.58581
H	-0.96229	5.00766	2.87689	H	0.55059	1.38241	-3.07932
C	-3.98364	-0.82708	-0.06986	H	0.62477	2.60185	-1.81803
C	-6.07895	-2.68756	0.39536	C	1.72960	3.11775	-3.59937
C	-5.29511	-0.59031	-0.51397	H	2.29814	2.63392	-4.40229
C	-3.76020	-2.03421	0.61813	H	2.38469	3.85503	-3.12028
C	-4.78653	-2.95205	0.84982	H	0.89562	3.65973	-4.05744
C	-6.33122	-1.49951	-0.28964	C	2.08538	-1.78029	0.31199
H	-5.51041	0.33118	-1.05079	H	1.03473	-1.57346	0.53560
H	-2.76070	-2.25689	0.97917	H	2.56224	-2.13195	1.23036
H	-4.57773	-3.87534	1.38569	C	2.21831	-2.83227	-0.77997
H	-7.33386	-1.28017	-0.64920	H	3.26632	-3.13106	-0.91036
H	-6.88067	-3.39992	0.57390	H	1.86592	-2.45334	-1.74710
C	-1.54080	0.29053	-2.03279	C	1.39021	-4.06412	-0.40174
C	0.09400	0.10233	-4.34056	H	0.33978	-3.76903	-0.28841
C	-1.18588	1.42769	-2.77440	H	1.72015	-4.43817	0.57632
C	-1.06954	-0.94656	-2.49769	C	1.50767	-5.17248	-1.44386
C	-0.27418	-1.04902	-3.64182	H	0.90693	-6.04339	-1.16328
C	-0.36473	1.34630	-3.90109	H	2.54720	-5.50288	-1.55427
H	-1.55543	2.40449	-2.45998	H	1.15866	-4.82680	-2.42373
H	-1.32634	-1.85309	-1.95058	H	4.42591	0.45733	-0.80135
H	0.06289	-2.02535	-3.98488	C	4.07608	-0.54914	-0.56882
H	-0.09184	2.24923	-4.44308	H	3.96251	-1.08559	-1.51474
H	0.72071	0.03059	-5.22607	C	5.08922	-1.24569	0.33057
H	-3.62086	1.39309	-1.17917	H	4.69339	-2.19141	0.71933
H	-3.14778	3.39595	-0.45082	H	5.32955	-0.61368	1.19398
A-ax-2				C	6.37342	-1.52476	-0.45447
89				H	6.14355	-2.18786	-1.29860
				H	6.74862	-0.58671	-0.88421
F	-0.44832	-0.10836	1.33807	C	7.45210	-2.15765	0.41982
N	2.68883	-0.41625	0.00324	H	8.36116	-2.35800	-0.15596
C	2.68505	0.33011	1.32455	H	7.10658	-3.10780	0.84301
H	3.34852	-0.22542	1.99187	H	7.72029	-1.49744	1.25241
H	1.66099	0.23114	1.69509	Si	-1.87338	-0.28903	0.23100
C	3.08206	1.79673	1.27455	C	-3.34673	-0.67999	-1.04534
H	4.06519	1.93360	0.80582	C	-5.41496	-1.22164	-2.92464
H	2.35063	2.36714	0.68924	C	-3.13831	-1.50098	-2.16136
C	3.12236	2.36284	2.69694	C	-4.64094	-0.14353	-0.90315
H	3.86852	1.81413	3.28642	C	-5.66034	-0.40056	-1.81864
H	2.15157	2.19379	3.18034	C	-4.14772	-1.77442	-3.09386
C	3.44996	3.85332	2.70737	H	-2.15347	-1.94705	-2.31350
H	4.42537	4.04537	2.24535	H	-4.85869	0.49988	-0.04878
H	3.47940	4.24524	3.72900	H	-6.64710	0.03442	-1.67410
H	2.69691	4.42285	2.15068	H	-3.94454	-2.41861	-3.94702
C	1.75717	0.28358	-0.98239	H	-6.20630	-1.42824	-3.64106
H	1.31071	-0.49957	-1.59762	C	-1.70010	1.58302	-0.23270
H	0.95664	0.70408	-0.36738	C	-1.42194	4.34093	-0.88569
C	2.36395	1.33792	-1.90221	C	-1.02537	2.48469	0.61456
H	2.99843	0.86361	-2.66102	C	-2.22249	2.12149	-1.42187
H	2.98874	2.05336	-1.35807	C	-2.08233	3.47191	-1.75267

C	-0.89463	3.84027	0.30558	H	0.73456	1.31243	0.83612
H	-2.75078	1.47518	-2.11775	H	1.21820	1.82474	-0.77137
H	-2.49329	3.84339	-2.68856	C	2.56014	2.50940	0.76753
H	-0.37919	4.50539	0.99526	H	3.33263	2.77465	0.03459
H	-1.31848	5.39430	-1.13422	H	3.07700	2.13022	1.65776
C	-2.91837	-0.70912	1.78930	C	1.77662	3.76987	1.14545
C	-4.45066	-1.30427	4.09919	H	1.02671	3.51330	1.90408
C	-3.77715	-1.81844	1.83465	H	1.22317	4.12983	0.26813
C	-2.85035	0.08998	2.94224	C	2.68847	4.87547	1.66896
C	-3.61439	-0.18735	4.07727	H	2.11373	5.76664	1.94088
C	-4.52218	-2.12706	2.97502	H	3.42548	5.16907	0.91245
H	-3.87530	-2.45634	0.95749	H	3.23513	4.54433	2.55957
H	-2.18566	0.95163	2.95455	H	3.88733	-0.85746	-0.83636
H	-3.55316	0.46377	4.94630	C	3.51966	0.16475	-0.73677
H	-5.16712	-3.00270	2.98103	H	4.18758	0.68926	-0.04740
H	-5.04075	-1.53089	4.98368	C	3.50745	0.83892	-2.10208
H	-1.01050	-1.30647	-0.48190	H	2.99430	1.80700	-2.06423
H	-0.58812	2.11362	1.53767	H	2.97204	0.21485	-2.82806
B-ax-1				C	4.94306	1.05242	-2.58758
81				H	5.47004	1.70354	-1.87797
Si	-2.35561	0.00765	0.82064	H	5.47455	0.09174	-2.58863
F	-0.88412	-0.09868	1.77525	C	4.98868	1.66754	-3.98319
N	2.18115	0.09041	-0.05060	H	6.02050	1.82485	-4.31322
C	1.14643	-0.62466	-0.89829	H	4.47835	2.63741	-4.00070
H	1.05327	-0.04218	-1.81896	H	4.49704	1.01666	-4.71514
H	0.20826	-0.51404	-0.34700	C	-4.00474	0.12872	-0.23198
C	1.41028	-2.08396	-1.22644	C	-6.34322	0.46349	-1.83236
H	2.36257	-2.21286	-1.75703	C	-4.87004	1.22748	-0.07224
H	1.45531	-2.68593	-0.31194	C	-4.36878	-0.79853	-1.22339
C	0.26310	-2.60487	-2.09794	C	-5.51231	-0.64201	-2.01408
H	0.23989	-2.04297	-3.04111	C	-6.01638	1.40148	-0.85083
H	-0.69036	-2.40676	-1.58948	H	-4.63930	1.96866	0.69109
C	0.39622	-4.09716	-2.38585	H	-3.73894	-1.67219	-1.37757
H	1.33613	-4.31704	-2.90585	H	-5.75678	-1.38619	-2.76965
H	-0.42659	-4.45436	-3.01342	H	-6.65765	2.26605	-0.69094
H	0.38414	-4.67679	-1.45532	H	-7.23493	0.59008	-2.44176
C	2.30204	-0.58959	1.30802	O	-2.23259	-1.65108	0.46395
H	2.52792	0.19948	2.02770	O	-3.18418	0.59114	2.17944
H	1.29579	-0.95481	1.53259	O	-1.47121	1.11122	-0.14448
C	3.34830	-1.68965	1.45439	C	-1.39169	-2.58681	1.08752
H	4.35567	-1.25683	1.43902	H	-0.32768	-2.35636	0.94959
H	3.29834	-2.41959	0.64052	H	-1.59163	-3.57185	0.64688
C	3.13117	-2.41182	2.78664	H	-1.58098	-2.65166	2.16752
H	3.12641	-1.67876	3.60391	C	-2.61965	0.94865	3.41712
H	2.13924	-2.88230	2.78267	H	-2.19603	0.08383	3.94284
C	4.20300	-3.46647	3.04607	H	-3.41716	1.37267	4.03942
H	5.19965	-3.01213	3.08764	H	-1.82951	1.70296	3.30961
H	4.21096	-4.22116	2.25113	C	-1.72537	1.42099	-1.48926
H	4.02928	-3.98187	3.99611	H	-1.78528	0.52134	-2.12012
C	1.60191	1.47819	0.19083	H	-0.89683	2.04017	-1.85908

H	-2.65611	1.98713	-1.62448	H	-3.75160	-1.24729	-1.50037
		B-ax-2		H	-4.21335	0.45737	-1.48955
		81		C	-5.53151	-0.82285	-0.36601
Si	2.63166	0.50686	-0.93751	H	-5.46207	-1.74029	0.23278
F	1.67532	1.72123	-0.10577	H	-5.90757	-0.03756	0.30271
N	-1.76359	0.02191	-0.01177	C	-6.51151	-1.03183	-1.51686
C	-1.55266	1.19891	-0.94917	H	-7.50268	-1.31308	-1.14696
H	-2.15562	0.98827	-1.83638	H	-6.16496	-1.82671	-2.18729
H	-0.49645	1.15024	-1.23571	H	-6.62101	-0.11668	-2.10985
C	-1.88276	2.57638	-0.39900	C	2.46980	-0.62136	0.60487
H	-2.90754	2.62360	-0.00827	C	2.10214	-2.33177	2.84085
H	-1.19854	2.83295	0.41799	C	2.50025	-0.12970	1.91995
C	-1.72200	3.61304	-1.51460	C	2.26733	-2.00321	0.45183
H	-2.40835	3.37253	-2.33718	C	2.06047	-2.84884	1.54462
H	-0.70439	3.54727	-1.92037	C	2.34034	-0.96846	3.02546
C	-1.98785	5.03135	-1.01844	H	2.64348	0.93642	2.08611
H	-3.00613	5.12580	-0.62304	H	2.27939	-2.42346	-0.55250
H	-1.87209	5.76188	-1.82566	H	1.88507	-3.91127	1.38673
H	-1.28972	5.30203	-0.21820	H	2.38832	-0.55749	4.03157
C	-0.93444	0.21910	1.25532	H	1.96028	-2.98532	3.69812
H	-0.61921	-0.77585	1.58139	O	3.50855	-0.68647	-1.86321
H	-0.03932	0.75846	0.92940	O	3.94019	1.57765	-1.03275
C	-1.62019	0.92376	2.42261	O	1.35068	0.47661	-2.05758
H	-2.39738	0.28049	2.85212	C	1.23275	-0.37538	-3.16892
H	-2.10631	1.85295	2.10999	H	2.04218	-0.22505	-3.89147
C	-0.58780	1.24476	3.50523	H	0.27720	-0.15045	-3.66216
H	-0.09521	0.31770	3.82378	H	1.23605	-1.43593	-2.88148
H	0.19594	1.88495	3.07906	C	4.02348	2.85130	-0.44408
C	-1.22375	1.93272	4.71007	H	3.27765	3.54464	-0.85193
H	-1.99180	1.29694	5.16584	H	5.02101	3.25444	-0.65727
H	-1.69919	2.87624	4.41780	H	3.89548	2.81564	0.64565
H	-0.47630	2.15787	5.47772	C	4.80765	-1.05179	-1.50551
C	-1.19647	-1.17961	-0.75235	H	4.94291	-1.13512	-0.41363
H	-0.11618	-1.00724	-0.78479	H	5.54854	-0.32695	-1.87262
H	-1.57099	-1.11572	-1.77780	H	5.04100	-2.03360	-1.94213
C	-1.51403	-2.54683	-0.16532			B-eq-1	
H	-2.59545	-2.72980	-0.15346			81	
H	-1.15616	-2.62859	0.86850	F	-1.35612	0.04080	-1.92646
C	-0.84450	-3.63276	-1.01227	N	1.78690	-0.17521	-0.05754
H	0.23777	-3.45658	-1.04028	C	1.37335	-1.40480	-0.84627
H	-1.20296	-3.55723	-2.04746	H	2.06494	-1.47293	-1.68966
C	-1.12494	-5.03071	-0.46873	H	0.38244	-1.16742	-1.24494
H	-0.63810	-5.79801	-1.07916	C	1.32405	-2.72001	-0.08863
H	-2.20083	-5.24087	-0.45927	H	2.28926	-2.95416	0.37903
H	-0.75452	-5.13270	0.55795	H	0.57056	-2.66993	0.70428
H	-3.55170	0.71747	0.84696	C	0.94173	-3.84643	-1.05328
C	-3.21919	-0.17923	0.32320	H	1.71526	-3.94543	-1.82597
H	-3.25859	-1.00879	1.03500	H	0.01202	-3.57651	-1.57078
C	-4.13584	-0.44056	-0.86494	C	0.75998	-5.17625	-0.32732

H	1.68104	-5.47489	0.18718	H	-0.99426	4.52527	-0.53211
H	0.49095	-5.97523	-1.02548	H	-2.18763	2.79047	3.21576
H	-0.03576	-5.10578	0.42378	H	-1.30356	4.73461	1.93176
C	0.83986	0.03134	1.12169	H	-2.71602	0.67942	2.06357
H	0.75171	1.11091	1.26381	O	-2.81378	-1.76859	-1.82073
H	-0.13677	-0.33443	0.78945	O	-4.22636	0.09805	-1.16720
C	1.22776	-0.60811	2.45138	O	-2.19377	-1.17843	0.57317
H	2.11294	-0.11859	2.87506	C	-2.19553	-2.56818	0.78987
H	1.46884	-1.67054	2.34073	H	-3.18998	-2.92229	1.09404
C	0.05858	-0.46113	3.42997	H	-1.50182	-2.79144	1.61258
H	-0.16974	0.60421	3.56351	H	-1.88612	-3.12775	-0.10065
H	-0.83874	-0.91474	2.98909	C	-4.97816	1.13859	-0.59188
C	0.36310	-1.10064	4.78169	H	-5.04352	1.04710	0.50041
H	1.24568	-0.64391	5.24494	H	-5.99374	1.08094	-1.00099
H	0.55917	-2.17388	4.67318	H	-4.56761	2.12893	-0.82549
H	-0.47689	-0.98269	5.47373	C	-3.97779	-2.54113	-1.76565
C	1.59211	0.98914	-1.01811	H	-3.72691	-3.58902	-1.98923
H	0.51085	1.05426	-1.16857	H	-4.71863	-2.20367	-2.50537
H	2.04249	0.68348	-1.96608	H	-4.47309	-2.51827	-0.78301
C	2.15433	2.33228	-0.57918				
H	3.23502	2.27562	-0.39994			B-eq-2	
H	1.68402	2.67299	0.35113			81	
C	1.88984	3.37067	-1.67400	F	-1.25574	0.42252	-1.64900
H	0.82047	3.37351	-1.91881	N	2.22886	-0.01552	-0.10839
H	2.42159	3.07736	-2.58857	C	2.44427	-0.66960	-1.45672
C	2.32466	4.76933	-1.24675	H	3.13458	-0.02367	-2.00471
H	2.13219	5.50282	-2.03627	H	1.47266	-0.62115	-1.95726
H	3.39645	4.79645	-1.01717	C	2.95663	-2.10047	-1.44116
H	1.78215	5.08964	-0.34950	H	3.87480	-2.18442	-0.84618
H	3.27741	-1.11657	1.08752	H	2.20926	-2.76865	-0.99830
C	3.21440	-0.25884	0.41595	C	3.24490	-2.55688	-2.87391
H	3.38688	0.63985	1.01484	H	4.00664	-1.90225	-3.31670
C	4.26430	-0.38351	-0.68001	H	2.33744	-2.44099	-3.48017
H	4.15044	0.40659	-1.43178	C	3.71717	-4.00692	-2.92613
H	4.16539	-1.34452	-1.19880	H	4.63589	-4.14197	-2.34353
C	5.66478	-0.28973	-0.06808	H	3.92317	-4.31917	-3.95493
H	5.77688	0.68180	0.43077	H	2.95709	-4.68169	-2.51620
H	5.77560	-1.05722	0.70899	C	1.22164	-0.82056	0.71146
C	6.75948	-0.45835	-1.11783	H	0.63438	-0.09524	1.27616
H	7.75444	-0.38282	-0.66789	H	0.53909	-1.26004	-0.02254
H	6.68195	0.31282	-1.89280	C	1.77900	-1.88103	1.65445
H	6.68573	-1.43534	-1.60878	H	2.33444	-1.40733	2.47230
Si	-2.60963	-0.32789	-0.85282	H	2.46826	-2.56411	1.14730
C	-2.17597	1.35611	0.09227	C	0.62075	-2.68794	2.24724
C	-1.54594	3.80412	1.42382	H	-0.07696	-2.00601	2.75145
C	-2.34792	1.52039	1.47874	H	0.05893	-3.16737	1.43478
C	-1.68672	2.48040	-0.59751	C	1.10736	-3.74578	3.23374
C	-1.37235	3.68275	0.04481	H	1.64538	-3.28500	4.07022
C	-2.04231	2.71274	2.13979	H	1.78715	-4.45436	2.74651
H	-1.53866	2.41779	-1.67491	H	0.26898	-4.31561	3.64743

C	1.59226	1.33642	-0.41107	H	-1.61796	2.55048	1.93521
H	0.57386	1.10446	-0.73180	H	-0.95941	1.03810	2.61667
H	2.14771	1.75963	-1.25183	H	-2.67756	1.15317	2.19138
C	1.55449	2.32217	0.74499				
H	2.56525	2.65589	1.01478				
H	1.10988	1.86232	1.63630				
C	0.71086	3.53602	0.34648				
H	-0.30596	3.19293	0.12007	F	-1.18160	-0.32096	0.36743
H	1.11844	3.97699	-0.57357	N	2.16032	-0.23161	0.46849
C	0.68087	4.59183	1.44833	C	1.59987	-1.39494	-0.36652
H	0.04160	5.43635	1.17052	H	2.01443	-1.26556	-1.36772
H	1.68531	4.98281	1.65117	H	0.52548	-1.20240	-0.41672
H	0.29113	4.17136	2.38308	C	1.86941	-2.81131	0.13672
H	3.89969	-0.84940	0.86556	H	2.93471	-2.97693	0.34421
C	3.52443	0.15001	0.64330	H	1.32350	-2.99462	1.06760
H	3.26420	0.62539	1.59293	C	1.40464	-3.84005	-0.91005
C	4.59700	0.94766	-0.08596	H	1.95294	-3.67890	-1.84756
H	4.19541	1.88782	-0.48201	H	0.34734	-3.66592	-1.13996
H	4.98347	0.37352	-0.93689	C	1.60104	-5.28528	-0.44016
C	5.75030	1.25904	0.87076	H	2.65569	-5.49777	-0.22705
H	5.37309	1.86624	1.70388	H	1.26701	-5.99443	-1.20407
H	6.12477	0.32357	1.30683	H	1.02796	-5.48735	0.47195
C	6.89032	1.99392	0.17191	C	1.51672	-0.21807	1.86932
H	7.70418	2.21709	0.86916	H	1.50324	0.82794	2.17720
H	6.54237	2.94235	-0.25328	H	0.47931	-0.51336	1.69419
H	7.30341	1.39148	-0.64516	C	2.17975	-1.03853	2.97847
Si	-2.55228	0.88530	-0.66380	H	3.16566	-0.62917	3.22989
C	-3.46238	-0.60163	0.13886	H	2.33279	-2.08001	2.68226
C	-4.80302	-2.79741	1.33929	C	1.29912	-1.00560	4.24110
C	-4.81337	-0.87755	-0.13237	H	1.11816	0.03737	4.53274
C	-2.80907	-1.46767	1.03144	H	0.31592	-1.43253	4.00796
C	-3.45696	-2.55646	1.61832	C	1.92589	-1.76346	5.41641
C	-5.48254	-1.94926	0.46355	H	2.89453	-1.33390	5.69779
H	-5.34762	-0.24061	-0.83479	H	2.08786	-2.81884	5.16830
H	-1.76605	-1.27258	1.27217	H	1.27725	-1.72582	6.29712
H	-2.91597	-3.21257	2.29759	C	1.67157	1.04210	-0.25314
H	-6.53182	-2.12780	0.23977	H	0.58937	1.03508	-0.10877
H	-5.31742	-3.63759	1.79922	H	1.85959	0.88187	-1.31597
O	-1.33015	0.98470	0.60521	C	2.28994	2.36381	0.19929
O	-3.57368	0.92783	-2.08644	H	3.36414	2.39427	-0.02224
O	-3.04833	2.45574	-0.25017	H	2.18284	2.50666	1.28110
C	-4.14627	3.15233	-0.78619	C	1.60221	3.54217	-0.51519
H	-3.99992	3.39693	-1.84408	H	0.53563	3.54250	-0.26556
H	-4.25703	4.08564	-0.21957	H	1.66949	3.39678	-1.60131
H	-5.07974	2.58150	-0.69926	C	2.22145	4.89214	-0.13891
C	-3.53698	-0.09957	-3.03193	H	1.71355	5.71110	-0.65754
H	-2.74928	0.06495	-3.78261	H	3.28467	4.93624	-0.40530
H	-4.50082	-0.14262	-3.55924	H	2.13587	5.08046	0.93744
H	-3.36211	-1.09163	-2.58338	H	3.92726	-1.17928	1.11647
C	-1.66455	1.45241	1.87628	C	3.67133	-0.27350	0.56698

¹H NMR

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H	3.96184	0.57630	1.18901	N	2.71223	-0.36490	-0.20731
C	4.43271	-0.24803	-0.75920	C	2.69835	0.10470	1.25535
H	4.13490	0.61353	-1.36639	H	3.22343	-0.67121	1.81690
H	4.20534	-1.14403	-1.34712	H	1.64043	0.08354	1.53279
C	5.94944	-0.18750	-0.51005	C	3.30316	1.47129	1.56668
H	6.18787	0.71533	0.06812	H	4.32215	1.56908	1.17039
H	6.25167	-1.04049	0.11258	H	2.69869	2.26489	1.11756
C	6.76183	-0.19134	-1.80964	C	3.34007	1.68814	3.09042
H	7.83534	-0.14499	-1.60178	H	3.95470	0.90580	3.55630
H	6.50683	0.66805	-2.43994	H	2.32745	1.56742	3.49462
H	6.57402	-1.09978	-2.39304	C	3.88653	3.06669	3.47701
Si	-2.59448	0.45761	-0.62826	H	4.91015	3.20807	3.11018
C	-2.27042	2.09769	0.35215	H	3.90279	3.19145	4.56431
C	-1.91786	4.57049	1.72201	H	3.26788	3.86903	3.05966
C	-2.66606	3.32405	-0.21631	C	1.88304	0.59752	-1.08906
C	-1.70739	2.15569	1.64332	H	1.47975	-0.01659	-1.89435
C	-1.54306	3.36591	2.32635	H	1.03973	0.88765	-0.45905
C	-2.47860	4.54499	0.44210	C	2.59560	1.80233	-1.70731
H	-1.41090	1.22890	2.12392	H	3.35803	1.48084	-2.42758
H	-1.13191	3.37037	3.33404	H	3.10523	2.40816	-0.95230
H	-2.78839	5.47203	-0.03487	C	1.56828	2.68456	-2.44121
H	-1.78941	5.51328	2.24791	H	1.04612	2.08248	-3.19615
C	-3.78235	-0.90617	0.02972	H	0.79883	3.01802	-1.73586
C	-5.65037	-2.86273	0.91151	C	2.21679	3.89850	-3.11476
C	-5.11169	-0.92366	-0.43578	H	2.96438	3.59530	-3.85785
C	-3.42324	-1.90608	0.95641	H	2.71673	4.54109	-2.38037
C	-4.33833	-2.86879	1.39435	H	1.46480	4.50627	-3.62729
C	-6.03473	-1.88405	-0.00851	C	1.96521	-1.71366	-0.18293
H	-5.42563	-0.16522	-1.14829	H	0.94263	-1.44848	0.09883
H	-2.40759	-1.92028	1.33642	H	2.40495	-2.28380	0.63839
H	-4.02845	-3.62423	2.11351	C	1.99486	-2.54515	-1.46357
H	-7.05231	-1.86629	-0.39174	H	3.01635	-2.85495	-1.71820
H	-6.36395	-3.61007	1.24982	H	1.61017	-1.97518	-2.31673
C	-1.53537	0.06566	-2.19513	C	1.12190	-3.80164	-1.28682
C	-0.06520	-0.50159	-4.56781	H	0.09867	-3.49211	-1.04511
C	-0.97367	1.09097	-2.98016	H	1.48477	-4.37960	-0.42611
C	-1.34545	-1.25371	-2.64928	C	1.11462	-4.69154	-2.53409
C	-0.63206	-1.53831	-3.81970	H	0.48691	-5.57470	-2.37984
C	-0.23978	0.81912	-4.14049	H	2.12387	-5.03938	-2.78561
H	-1.12180	2.12962	-2.68953	H	0.71954	-4.15260	-3.40278
H	-1.77569	-2.07775	-2.08342	H	4.56322	0.48166	-0.74793
H	-0.52488	-2.56885	-4.15205	C	4.11816	-0.51321	-0.75103
H	0.17875	1.63808	-4.72202	H	4.01068	-0.81634	-1.79511
H	0.48657	-0.71736	-5.47930	C	5.03472	-1.48644	-0.00824
H	-3.69295	1.13454	-1.47273	H	4.58492	-2.48367	0.04914
H	-3.14826	3.31679	-1.19105	H	5.19717	-1.15038	1.02203
				C	6.39669	-1.59195	-0.71592
				H	6.24514	-1.93714	-1.74737
				H	6.84836	-0.59349	-0.78886
				C	7.36414	-2.53865	0.00281
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F	-0.29093	0.03937	0.98947				

H	8.32200	-2.59497	-0.52351
H	6.95634	-3.55416	0.06167
H	7.56547	-2.20016	1.02553
Si	-1.99612	-0.20316	0.14068
C	-3.63478	-0.55955	-0.91638
C	-5.95709	-1.10278	-2.48045
C	-3.59947	-1.41979	-2.02715
C	-4.88573	0.02107	-0.61950
C	-6.02827	-0.23952	-1.37992
C	-4.73469	-1.69465	-2.80341
H	-2.65515	-1.89307	-2.29690
H	-4.97221	0.69597	0.23082
H	-6.97478	0.22792	-1.11704
H	-4.66385	-2.36817	-3.65518
H	-6.84347	-1.30920	-3.07515
C	-1.97146	1.71199	-0.14626
C	-1.91984	4.52372	-0.60616
C	-1.49995	2.61501	0.82854
C	-2.41471	2.27341	-1.35964
C	-2.37852	3.65264	-1.59734
C	-1.48580	3.99712	0.61482
H	-2.80887	1.62266	-2.13507
H	-2.72477	4.04531	-2.55063
H	-1.13790	4.66327	1.40144
H	-1.90833	5.59718	-0.77805
C	-2.62239	-0.91605	1.82189
C	-3.54702	-2.00442	4.28630
C	-3.59436	-1.93469	1.86443
C	-2.12593	-0.46901	3.06342
C	-2.58726	-0.98795	4.27657
C	-4.04251	-2.48290	3.07161
H	-4.01736	-2.30862	0.93711
H	-1.35201	0.29047	3.07757
H	-2.19189	-0.60411	5.21452
H	-4.78667	-3.27578	3.06022
H	-3.90273	-2.41693	5.22722
H	-1.18296	-1.08286	-0.78099
H	-1.13495	2.22746	1.77405