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ARTICLE

Novel Binaphthyl and Biphenyl α- and β-Amino Acids and Esters: Organocatalysis of Asymmetric Diels Alder Reactions. A Combined Synthetic and Computational Study.

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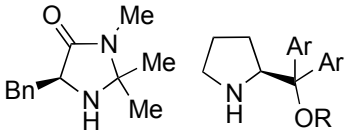
Asymmetric catalysis of the Diels-Alder reaction between cyclopentadiene and cinnamaldehydes has been studied using as catalysts a range of novel α- and β- aminoacids and aminoesters with binaphthyl and biphenyl backbones, providing enantioselectivities of up to 62% ee. B3LYP/6-31G* calculations, including free energy corrections, have been carried out on a binaphthyl catalyst example to identify transition state structures and to aid in the identification of major enantiomers. The calculated product ratios agree well with the experimental data; the transition states identified involve preferential approach of cyclopentene along a trajectory adjacent to the acid/ester group. The four lowest energy transition states display a stabilizing dipolar interaction between the carbonyl group oxygen atom and a terminal proton of the diene unit.

Introduction

The main text of the article should appear here with headings as appropriate.

Since the first report of the Diels–Alder reaction in 1928,[1] the potential of the process to create up to four contiguous stereocentres in a controlled manner has been used to synthesise numerous natural products and drugs.[2] Koga reported the first metal-catalysed asymmetric Diels-Alder reaction using chiral alkoxyaluminium dichloride,[3] and the first asymmetric organocatalysed Diels-Alder reaction was reported by Kagan using a number of amino alcohols as catalysts in up to 61% ee.[4] Inspired by the report by Baum and Jung on dienophile activation using iminium moieties,[5] MacMillan proposed that the LUMO energy-lowering activation observed with Lewis acid catalysts would also occur if α,β-unsaturated aldehydes were converted into the corresponding iminium species *in situ*. The imidazolidinone catalyst **1** mediated such enantioselective Diels-Alder reactions in up to 96% ee.[6] Asymmetric organocatalytic LUMO energy-lowering activation has since also been achieved using a number of other amine-based catalysts *via* iminium species,[7] and Lewis[8] or Brønsted[9] acid activation. HOMO energy-raising activation has been employed in organocatalysed asymmetric Diels Alder reactions through the formation of enamines, with Jørgensen's diarylprolinols **2** being among the most successful catalysts.[10] Bifunctional catalysts have also been designed to affect both LUMO and HOMO energy levels.[11] The use of amino acids as organocatalysts in asymmetric catalysis has grown since the first report of proline-catalysed aldol reactions in 2000,[12] and many other transformations have been studied using proline or other amino acids as catalysts.[13] One such catalyst, binaphthyl species **3**, designed by Maruoka,[14] led to high enantioselectivities in aldol reactions. The Diels-Alder reaction and its variants are no exception, and several asymmetric amino acid-catalysed examples have been reported.[15]

We reasoned that binaphthyl and biphenyl α- and β-aminoacids, such as **4** and **5**, might prove useful as organocatalysts.



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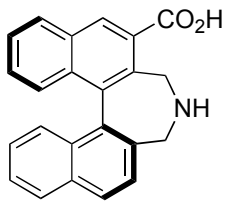

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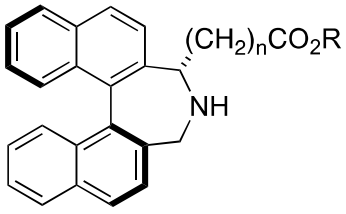
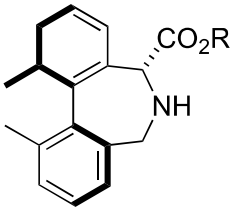


4 (n=0,1)



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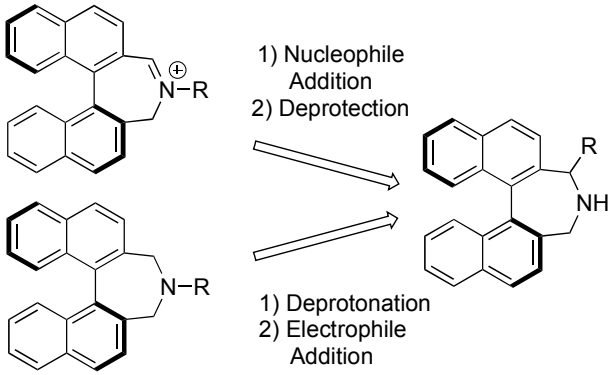
We identified two general routes towards our target catalysts: stereocontrolled attack of a nucleophile at an iminium moiety to generate a new chiral centre and the desired functionality,[16] and protection of the nitrogen with an electron-withdrawing group to increase the acidity of the protons on C2,[17] which would allow for deprotonation followed by reaction with a suitable electrophile (Scheme 1).[18]



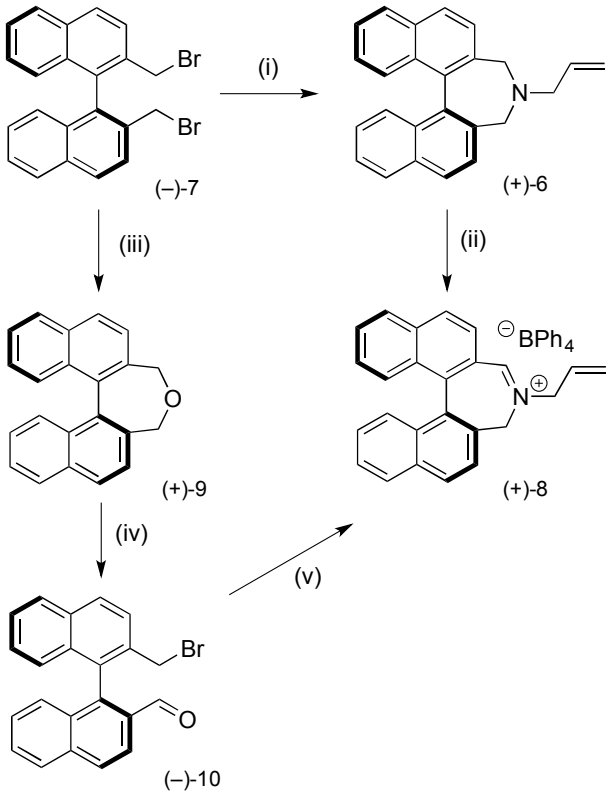
Scheme 1: Approaches towards target structures

Results and discussion

Catalyst synthesis

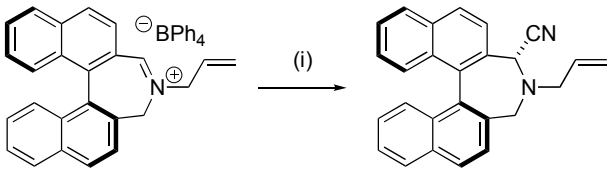
We first investigated synthesis of the α-aminoacid catalysts using the iminium route. Selecting suitable nitrogen protecting groups was key in both routes. The allyl group was chosen because it is widely used for the protection of alcohol and amine moieties, and its removal is easily achieved. Furthermore, *N*-allyl azepine **6** had been previously reported.[19] Azepine **6** was prepared in high yield *via* the known dibromo compound **7**;[20] oxidation using NBS and counter-ion exchange to provide crystallinity led to the corresponding iminium species **8** in 81% yield (Scheme 2). Alternatively, compound **7** could be converted into oxepine **9**, followed by treatment with bromine to provide bromoaldehyde **10**.[21] Condensation of allylamine with **10** and anion exchange afforded iminium species **8**.

Preparation of the desired α-amino acid was initially approached by stereoselective addition and hydrolysis of a nitrile group. We have previously shown that addition of Grignard reagents to biphenyl and binaphthyl azepinium species takes place to give the pseudo-axial orientation.[16] Addition of methyl Grignard reagent to **8** and subsequent removal of the N-allyl group using palladium(0) catalysis was successful. We were then pleased to find that addition of sodium cyanide to iminium species **8** in a dichloromethane/water biphasic mixture with vigorous stirring afforded the desired α-cyano *N*-allyl amine **11** as a single diastereoisomer in high yield and purity after aqueous work-up (Scheme 3).



Reagents and conditions: (i) allylamine (1.1 equiv.), K_2CO_3 (3 equiv.), MeCN, reflux, 16 h, 84%; (ii) 1) NBS (1.05 equiv.), CH_2Cl_2, 0 °C; then 2) $NaBPh_4$ (1.1 equiv.), EtOH, MeCN, 10 min, 81%; (iii) Saturated sodium carbonate, 1,4 dioxane (1:1), reflux, 12 h, 87%; (iv) Br_2 (1.125 equiv.), cyclohexane, 0 °C→reflux, 1 h, 50%; (v) allylamine (1 equiv.), EtOH, 40 °C, 12 h, $NaBPh_4$ (1.1 equiv.), MeCN, 65%

Scheme 2: Synthesis of binaphthyl azepinium salt **8**



Reagents and conditions: (i) NaCN (5 equiv.), CH_2Cl_2/H_2O, r.t., 2 h, >95%

Scheme 3. Synthesis of α-cyano *N*-allyl amine derivative **11**

Scheme 3: Synthesis of α-cyano *N*-allyl amine derivative **11**

Crystals suitable for single crystal X-ray crystallography were obtained and confirmed the expected pseudo-axial orientation of the nitrile residue (Figure 1).[22]

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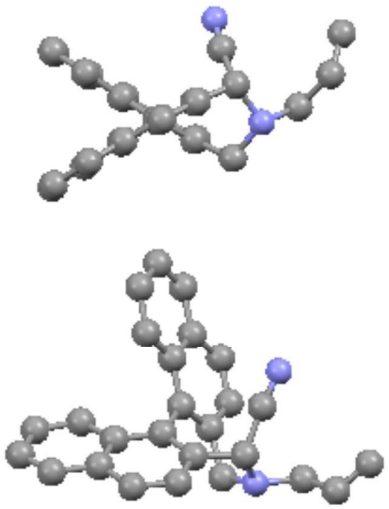
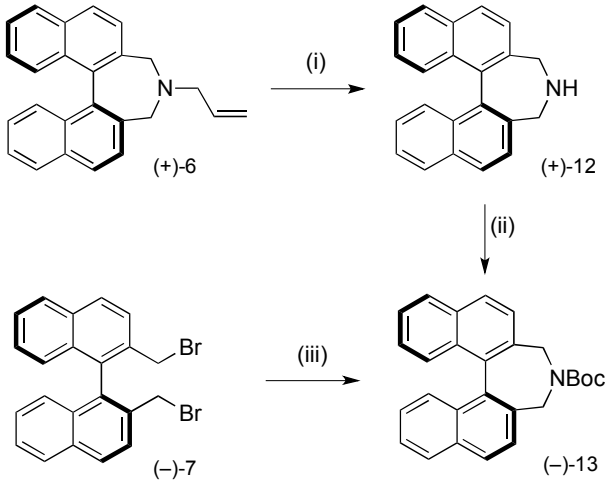


Figure 1: Crystal structure of α-cyano *N*-allyl amine **11**

Attempted purification using silica gel column chromatography, however, led to complete decomposition of **11**. Perhaps unsurprisingly, attempted hydrolysis of the nitrile group under acidic conditions also led to decomposition. Attempts to form the tetrazole from **11** were unsuccessful, and also led to decomposition.[20] When reduction of the nitrile group was attempted using $LiAlH_4$, decomposition of the starting material was observed, whereas when DIBAL was used, allyl azepine (+)-**6** was obtained in quantitative yield, presumably through regeneration and reduction of iminium species (+)-**8**.

Our ultimately successful strategy for synthesis of the target catalysts, achieved after a number of unsuccessful routes were tested, involved deprotonation of suitably protected azepines at the α-position. Binaphthyl azepines have been methylated at the α-position using formamidine N-protection,[18a] and the *N*-nitroso protected azepine has been used previously to prepare binaphthyl ligands for dialkylzinc addition to aldehydes.[18c] To avoid the difficult formamidine synthesis and the potentially problematic Raney nickel hydrogenation step, we chose the Boc-protected azepine analogue. Allyl azepine (+)-**6** was deprotected using palladium(0) catalysis to give *N-H* azepine (+)-**12** in 80% yield. Addition of Boc anhydride to a solution of (+)-**12** in *tert*-BuOH led smoothly to formation of the desired Boc-protected azepine (−)-**13** (Scheme 4).

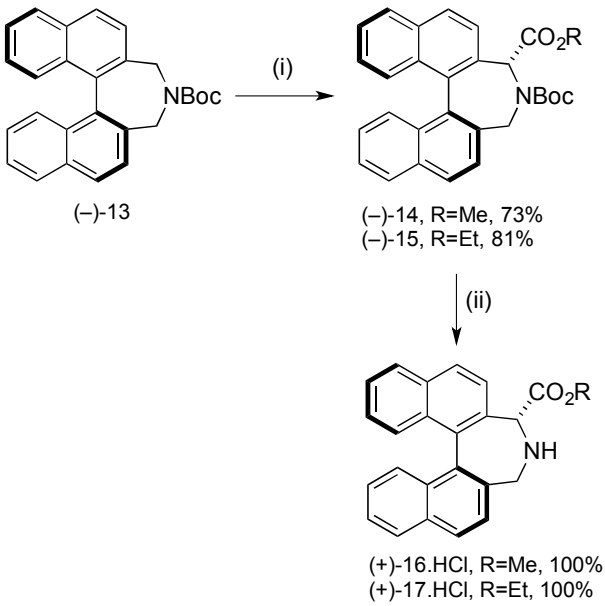
A direct synthesis of N-Boc azepine (−)-**13** from the dibromo compound (–)-**7** was also achieved by treatment with *t*-butyl carbamate and sodium hydride,[23] providing a shorter and more practical route. One drawback of this more direct route is the potential formation in the presence of water of oxepine (+)-**9**, which co-elutes on column chromatography with N-Boc azepine (−)-**13** (Scheme 4).



Reagents and conditions: (i) 1) $Pd(PPh_3)_4$ (2 mol %), *N*,*N*-dimethylbarbituric acid (3 equiv.), CH_2Cl_2, 50 °C, 16 h; 2) CH_2Cl_2, HCl, 5 min; 3) saturated $NaHCO_3$, CH_2Cl_2, 30 min, 80% over the three steps; (ii) di-*tert*-butyl dicarbonate (1.05 equiv.), *t*BuOH, r.t., 16 h, 92%; (iii) NaH (4 equiv.), *t*-$BuOCONH_2$ (1 equiv.), DMF, 0 °C→r.t., 4 d, 86%.

Scheme 4: Synthesis of *N*-Boc azepine (−)-**13**

Deprotonation of Boc-azepine (−)-**13** was accomplished at –78 °C using *sec*-BuLi in diethyl ether, and was followed by the addition of alkyl chloroformates.[24] These conditions afforded the methyl and ethyl esters (−)-**14** and (−)-**15** as single diastereoisomers in 73% and 81% yields, respectively. When *tert*-butyl anhydride was used as the electrophile, starting material was recovered. Deprotection of Boc-azepine esters (−)-**14** and (−)-**15** by heating in acetone in the presence of hydrochloric acid led to the formation of (+)-**16.HCl** and (+)-**17.HCl** in quantitative yields as the corresponding hydrochloride salts (Scheme 5).[25]



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Reagents and conditions: (i) *s*-BuLi (1.3 equiv.), Et_2O, −78 °C, 1 h, ClC(O)OR (3 equiv.), −78 °C→ r.t., 16 h; (ii) HCl (6M), acetone, 70 °C, 16 h.

Scheme 5: Synthesis of α-amino esters (+)-**16** and (+)-**17**

At room temperature, both the methyl and ethyl esters are observed as mixtures of rotamers by ^{1}H NMR spectroscopy due to conformational restrictions around the bulky Boc protecting group. Variable temperature ^{1}H experiments verified this; coalescence of the duplicate peaks were seen when the temperature was increased to 380 K for both (+)-**16** and (+)-**17**. Single crystal X-ray crystallography of (+)-**16** confirmed that the ester group adopts a pseudo-axial orientation (Figure 2).[26]

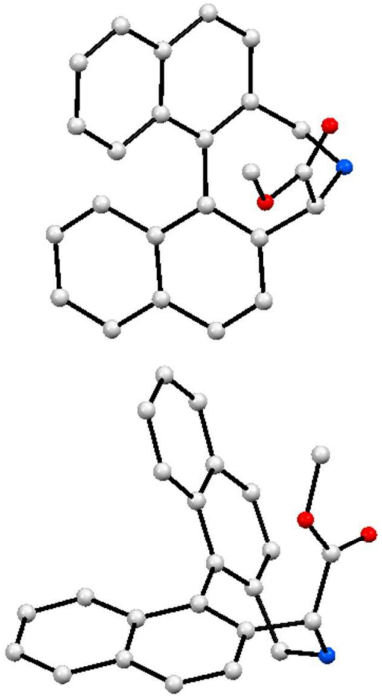
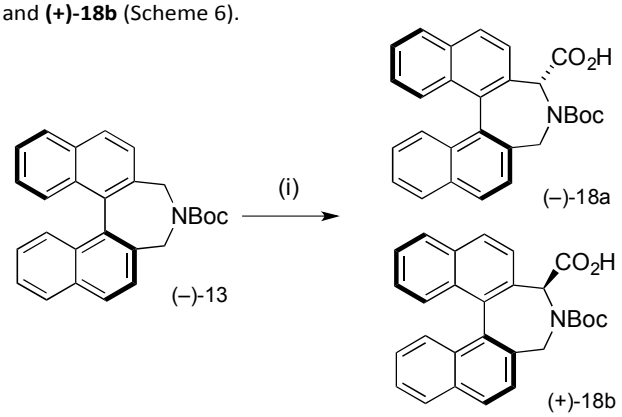


Figure 2: Pseudoaxial orientation of the ester group in (+)-**16**

Surprisingly, all attempts to saponify the methyl and ethyl esters failed, both in the case of the N-Boc and N-H azepines. The esters were subjected to strongly basic conditions and high temperature for prolonged periods of time, yet no hydrolysed material was detected. Lithium aluminium hydride reductions of both N-Boc and N-H azepine were also attempted to prepare the corresponding alcohol, but only starting materials were isolated.

The α-aminoacids were finally accessed directly by use of carbon dioxide as the electrophile. Following deprotonation of **(–)-13** as described above, carbon dioxide was bubbled through the solution. α-Aminoacid diastereoisomers **(–)-18a** and **(+)-18b** were isolated in 34% and 31% yields, respectively. Increasing the reaction time to 16 h did not greatly affect the yield; increasing the quantity of *sec*-butyllithium and the reaction time resulted in a significant reduction in the yield. Addition of carbon dioxide in the form of dry ice pellets resulted in a slight decrease in the yield of products **(–)-18a** and **(+)-18b** (Scheme 6).



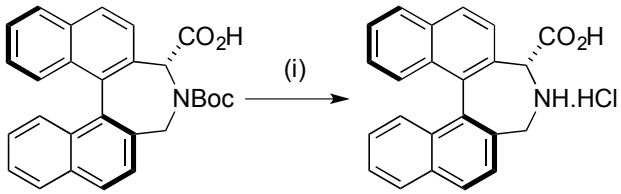
Reagents and conditions: (i) *s*-BuLi, Et_2O, −78 °C, 1 h, then CO_2, −78 °C→ r.t.

Scheme 6: CO_2 addition

The assignment of stereochemistry of **(–)-18a** and **(+)-18b** was based on the ^{1}H NMR chemical shifts of the pseudoaxial and pseudoequatorial protons adjacent to the acid group:[18,27] the chemical shifts for the methine protons of **(–)-14**, **(–)-15** and **(–)-18a** are similar for each compound (5.85, 5.82 and 5.71 ppm, respectively).

Variable temperature ^{1}H NMR experiments (up to 360 K) were performed in order to increase the resolution to identify the coupling patterns and to define the chemical shifts of those protons for each diastereoisomer. In **(+)-**(S_{ax},*S*)-**18b**, the pseudoaxial proton experiences less deshielding from the proximal naphthalene group and therefore the signal appears further upfield (δ_H 4.36 ppm) compared to the pseudoequatorial proton in **(–)-**(S_{ax},*R*)-**18a** (δ_H 5.71 ppm).[27c]

N-Deprotection of both **(–)-18a** and **(+)-18b** was achieved in quantitative yields through heating under reflux in a mixture of acetone and aqueous hydrochloric acid overnight, giving the α-aminoacids **(+)-19a** and **(+)-19b** as the hydrochloride salts (Scheme 7).



(–)-18a **(+)-19a.HCl**

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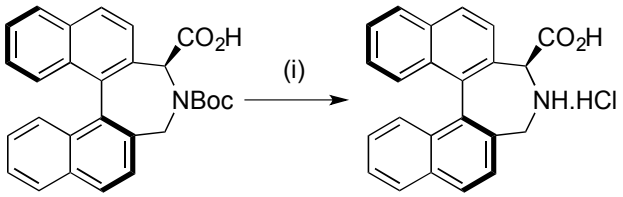
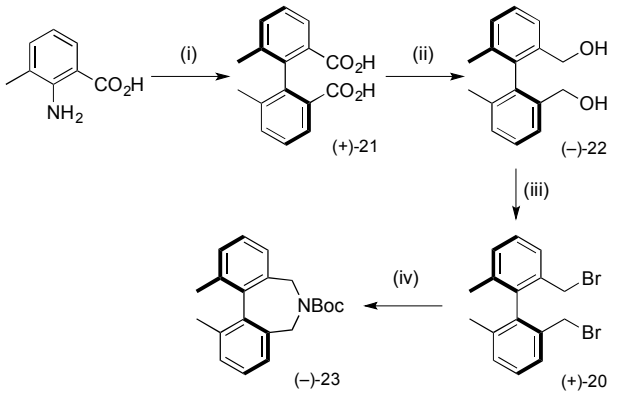


(+)-18b **(+)-19b.HCl**

Scheme 7: Deprotection of **(–)-18a** and **(+)-18b**

Maruoka has reported that the biphenyl analogue of his binaphthyl catalyst **3** is more reactive and required much lower catalyst loadings in asymmetric aldol reactions.[28] He observed similar effects in asymmetric Diels-Alder reactions, although the binaphthyl analogue led to higher exo-endo selectivity than the biphenyl.[29] We therefore turned our attention to the 3,3'-dimethylbiphenyl analogues of **(+)-16**, **(+)-19a** and **(+)-19b**.

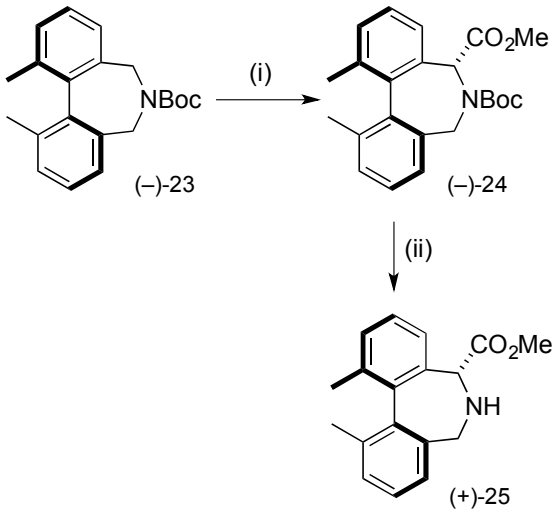
The synthesis of the dibromo compound (+)-**20** was carried out using literature procedures (Scheme 8).[30] Thus, 3-methyl-2-aminobenzoic acid was converted into *bis*-acid (±)-**21** in 41% yield. Resolution of the enantiomers using quinine led to the isolation of *bis*-acid (+)-**21** (The quinine complex crystallizes from ethanol). Reduction of both acid moieties using $LiAlH_4$ afforded *bis*-alcohol (−)-**22** in quantitative yield. An Appel reaction employing phosphorus tribromide and pyridine gave dibromo compound (+)-**20** in 88% yield. Boc-protected azepine (−)-**23** was then isolated in high yield following the procedure used for the binaphthyl analogues (Scheme 8).



Reagents and conditions: (i) 1) NaOH (1.3 equiv.), $NaNO_2$ (1 equiv.), H_2O, 0 °C, 4M HCl, $CuSO_4.5H_2O$ (1.7 equiv.), 30 % NH_4OH, NH_2OH (prepared from $(NH_2OH)_2.H_2SO_4$ (1.9 equiv.), 3M NaOH, 0 °C), 110 °C, 1 h, then conc. HCl, r.t., 12 h, 54%; 2) Quinine (1 equiv.), 90% EtOH, 70 °C→ r.t., EtOAc, 3M HCl, 16 h, 33%; (ii) Et_2O, $LiAlH_4$, 0 °C, *quant*.; (iii) pyridine (0.1 equiv.), toluene, PBr_3 (3 equiv.), 60 °C, 3 h, 88%; (iv) NaH (2.05 equiv.), DMF, 0 °C, *t*-$BuOCONH_2$ (1 equiv.), 88%.

Scheme 8: Synthesis of 3,3'-dimethylbiphenyl *N*-Boc azepine

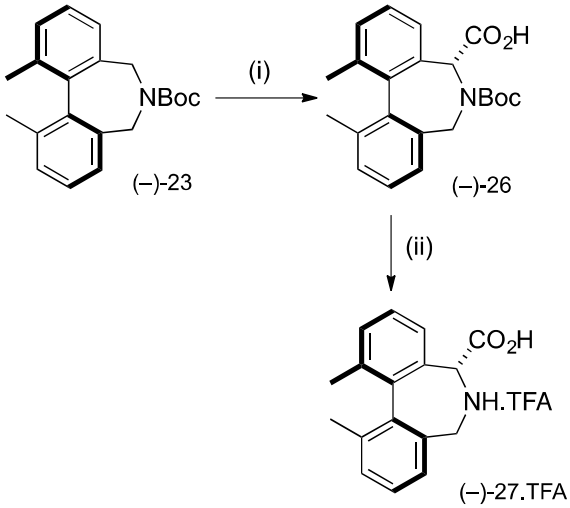
Azepine (−)-**23** was lithiated using *sec*-butyl lithium, and the resulting anion treated with methyl chloroformate to form **(–)-24** in 79% yield. TFA-mediated Boc group deprotection afforded (+)-**25** in 75% yield (Scheme 9).



Reagents and conditions: (i) Et_2O, −78 °C, *s*-BuLi (2 equiv.), 1 h, $ClCO_2Me$ (1.5 equiv.), 1 h, −78 °C, 79%; (ii) 1) TFA (14 equiv.), CH_2Cl_2, r.t., 1 h; 2) saturated $NaHCO_3$, 75%.

Scheme 9: Synthesis of methyl α-amino ester (+)-**25**

Use of CO_2 gas as the electrophile under the conditions evolved for the BINAP series afforded α-amino acid **(–)-26** in 45% isolated yield as a single isomer, in contrast to the stereochemical outcome in preparing **(–)-18a** and **(+)-18b**. Removal of the Boc protecting group afforded the desired amino acid **(–)-27** as the hydrochloride salt in quantitative yield. Trifluoroacetic acid was also used to remove the Boc group, leading to the formation of (−)-**27.TFA** in 50% yield (Scheme 10).



Reagents and conditions: (i) Et_2O, −78 °C, *s*-BuLi (2 equiv.), 1 h, CO_2 gas, 1 h, −78 °C→ r.t., 45 %; (ii) TFA (14 equiv.), CH_2Cl_2, 0.5 h, 50%.

Scheme 10: Synthesis of α-amino acid (−)-**27.TFA**

The stereochemistry of the acid group of (−)-**27.TFA** was confirmed by single crystal X-ray crystallography to adopt a pseudoaxial conformation (Figure 3).

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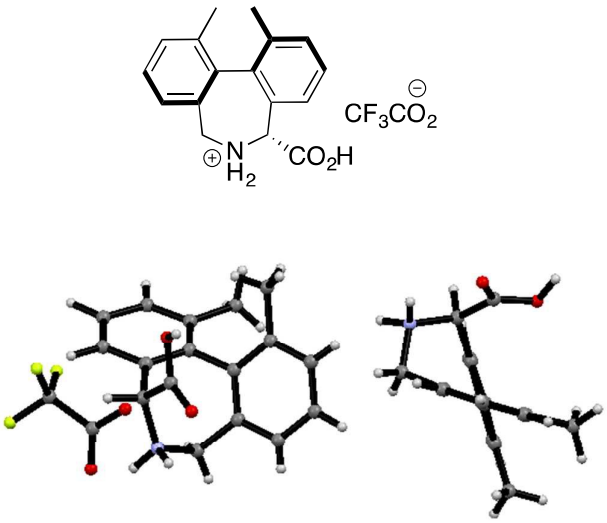
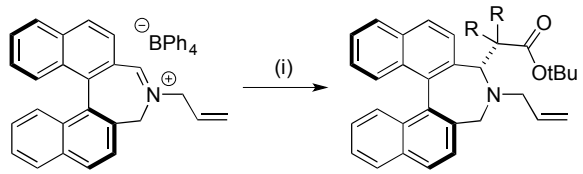


Figure 3: Crystal structure of **(–)-27.CF_3COOH**

That the configuration of **26/27** is the same as that of **24/25** is supported by inspection of proton NMR spectra. For example, in the BOC-protected series, the chemical shifts for the methine proton adjacent to the acid/ester group in **26** is 5.52 ppm, and that of **24** is 5.61 ppm. Similar figures are seen the binaphthyl series: the chemical shifts for the corresponding methine proton in **18a** is 5.71 ppm, and that of **14** is 5.85 ppm. It is noteworthy that in the proton NMR spectrum of **18b**, which has the opposite relative configuration and presumably an axial methane proton, the chemical shift is a very different 4.36 ppm. Similar differences have been previously observed in similar systems.[27]

The β-amino acids and esters were targeted using nucleophilic addition to iminium species. Attempted addition of malonates to iminium species led to recovery of starting material, as did Lewis acid-mediated addition of silyl enol ethers. Use of zinc-mediated Reformatsky reaction conditions,[31,32] however, did prove successful. *tert*-Butyl bromoacetate was chosen as the haloester as we expected that the hydrolysis of the *tert*-butyl ester would require mild conditions. Zinc activation was achieved by heating a zinc suspension in tetrahydrofuran under reflux in the presence of *tert*-butyl bromoacetate and additives 1,2-dibromoethane and/or chlorotrimethylsilane,[33] or DIBAL.[34] A solution of the iminium species **(+)-8** in tetrahydrofuran was then added to the mixture. After work-up, β-amino ester **(+)-28** was isolated as a single diastereoisomer, as we have observed in other addition reactions (Scheme 11).[16]

When increased quantities of activating agents 1,2-dibromoethane and chlorotrimethylsilane were used in combination with an increase in temperature to 65 °C, no product was observed. We concluded that iminium salt **(+)-8** decomposes at higher temperatures. Indeed, upon reducing the addition temperature to 25 °C, ester **(+)-28** was isolated in 19% yield. When DIBAL was used to activate the zinc dust and the substrate added at low temperature, ester **(+)-28** was obtained in 28% yield. As the addition temperature was lowered, yields increased, affording ester **(+)-28** in 71% yield under optimum conditions when the reaction as carried out at −78 °C using TMSCl as the activating agent.



(+)-8 **(+)-28, R=H, 71%**
(+)-29, R=Me,76%

Reagents and conditions: (i) Zn dust, Me_3SiCl, THF, reflux, 30 min; *tert*-butylbromoacetate, reflux, 30 min; **8**, THF, −78 °C; *tert*-butylbromoacetate, −78 °C → r.t.

Scheme 11: Addition of Reformastky reagents to iminium species **(+)-8**

Crystals of **(+)-28** suitable for single crystal X-ray crystallography were obtained, and the orientation of the ester group was confirmed as pseudoaxial (Figure 4).

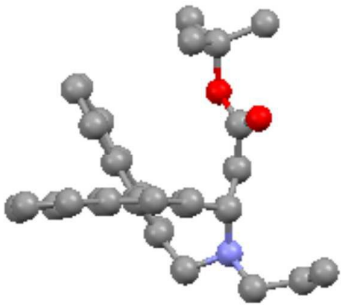


Figure 4: Crystal structure of β-amino ester **(+)-28**

Reasoning that a more sterically congested β-amino acid might induce improved selectivity in any catalysed reaction by increasing crowding nearer to the site of catalysis, we generated β-amino acid **(+)-29** by use of *tert*-butyl bromo isobutyrate under optimized conditions in 76% yield (Scheme 11).

Deallylation of **(+)-28** and **(+)-29** was accomplished following a literature procedure,[35] affording *N-H* azepines **(+)-30** and **(+)-31**. The *tert*-butyl esters underwent acid-catalysed ester hydrolysis using trifluoroacetic acid, followed by washing with aqueous sodium hydrogen carbonate solution to afford the β-amino acids **(+)-32** and **(+)-33** in 94% and 61% yield, respectively, over the two steps (Scheme 12). Nucleophilic additions to the corresponding N-PMB iminium species were

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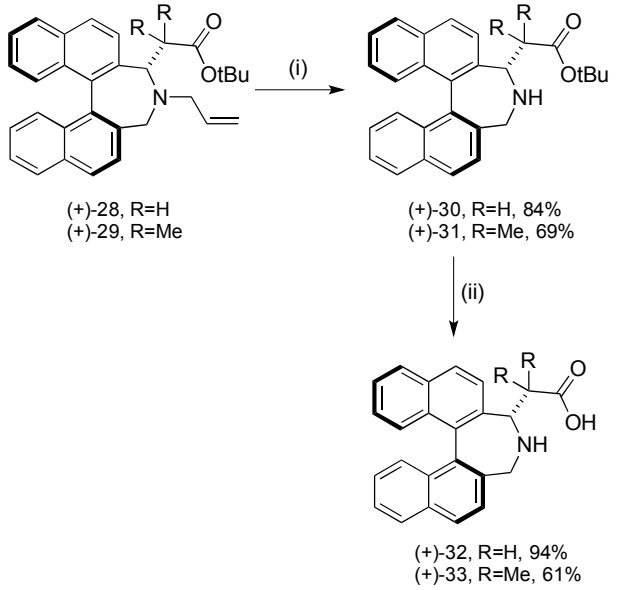
also successful, but we were unable subsequently to remove the PMB group.



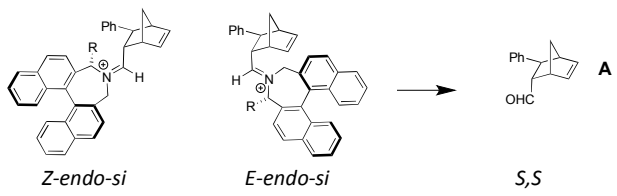
Reagents and conditions: i) $Pd(PPh_3)_4$ (2 mol%), *N,N*-dimethylbarbituric acid (3 equiv.), CH_2Cl_2, 50 °C, 24 h; ii) 1) TFA (12 equiv.), CH_2Cl_2, r.t., 16 h; 2) saturated $NaHCO_3$.

Scheme 12: Protecting group removal

Calculations

Initial testing of the new catalysts suggested that, while aldol and Mannich reactions could be catalysed, enantioselectivities were poor, and the Diels-Alder reaction between cinnamaldehyde and cyclopentadiene appeared to be more promising. Thus, concurrently with the synthetic work, B3LYP/6-31g* calculations were carried out to locate the possible transition states for the Diels-Alder reaction between cyclopentadiene and the simplest BINAP-based iminium salt, that derived from **16** by reaction with *E*-cinnamaldehyde. Eight configurations were identified, based on a *Z* or *E* geometry around the iminium bond, an *endo* or *exo* Diels-Alder transition state, and the diastereofacial approach of the cyclopentadiene to the *si-si* or *re-re* face of the E-cinnamaldehyde double bond. Two conformational minima were identified for each, denoted a and b, corresponding to two rotational isomers of the substituent methyl ester unit R

Four different transition states thus contributed to each of the four possible products. Figure 5 shows the products of this Diels-Alder reaction, and the four aldehyde products resulting from *in-situ* hydrolysis of each under the reaction conditions.



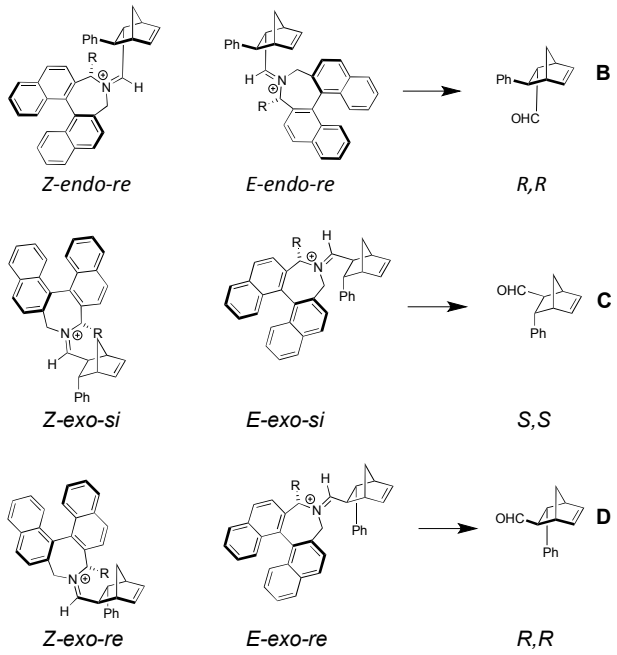


Figure 5: Diels-Alder Reaction Products

Optimizations of each of the 16 transition states were performed at the B3LYP/6-31G* level of theory, using Gaussian09.[36] All transition states possessed one imaginary frequency along the reactive mode. An IRC calculation was performed on the E-Exo-si-b transition state, to show that it did indeed form the product. All other transition states were similar with respect to the forming bond lengths and the magnitude of the imaginary frequency, indicating that the correct saddle-point has been found for all transition structures. The electronic energy and Gibbs free energy correction were used to calculate a Boltzmann distribution at 298.15 K. This was then used to calculate the product ratios, which is a methodology that has previously been successfully applied to predicting stereoselectivity in Diels-Alder reactions.[37,38] The contributions of each transition state to the Boltzmann distribution are given in Table 3. The Cartesian coordinates for all transition structures can be found in the SI.

Table 1. Relative Energies and Boltzmann Distribution of Calculated Transition States

Transition State	Relative Free Energy/kJ/mol^{-1}	Boltzmann Ratio
Z-Endo-si-a	22.22	0.000
Z-Endo-si-b	11.17	0.006
Z-Endo-re-a	22.31	0.000
Z-Endo-re-b	4.88	0.076
E-Endo-si-a	23.61	0.000
E-Endo-si-b	2.99	0.163
E-Endo-re-a	22.54	0.000
E-Endo-re-b	19.99	0.000
Z-Exo-si-a	17.37	0.000

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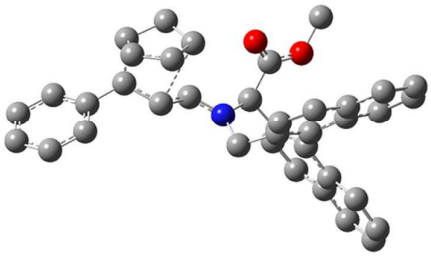
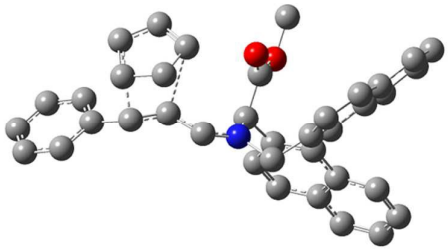
Z-Exo-si-b	11.17	0.006
Z-Exo-re-a	20.82	0.000
Z-Exo-re-b	2.57	0.193
E-Exo-si-a	18.28	0.000
E-Exo-si-b	0.00	0.545
E-Exo-re-a	18.19	0.000
E-Exo-re-b	9.95	0.010

The product ratios for **A**:**B**:**C**:**D** are 0.169 : 0.076 : 0.551: 0.203. **A** and **B** are the two enantiomers of the *endo* product; **C** and **D** are the two enantiomers of the *exo* product. The calculated ratios would therefore suggest enantiomeric excesses of 37.8% ee for the *endo* **A/B** pair in favour of the *S,S* enantiomer **A**, and 46.2% ee for the *exo* **C/D** pair in favour of the *S,S* enantiomer **C**.

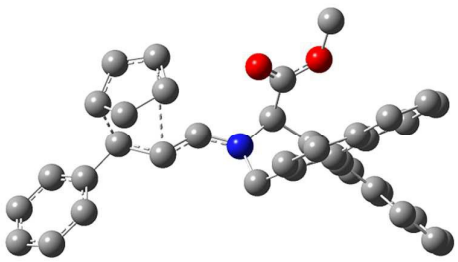
The transition states identified all appear to involve preferential approach of cyclopentene along a trajectory adjacent to the acid/ester group. The optimized transition structures of the four lowest energy transition states are shown below (Figure 6).



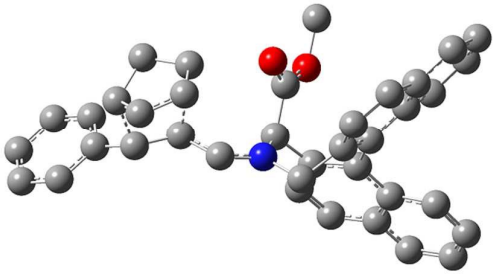
E-exo-si-b (relative energy: 0.00)



Z-exo-re-b (relative energy: 2.57 kJ mol^{-1})



E-Endo-si-b (relative energy: 2.99 kJ mol^{-1})



Z-Endo-re-b (relative energy: 4.88 kJ mol^{-1})

Figure 6: Four Lowest Energy Transition States.

The four lowest energy transition states display a stabilizing dipolar interaction between the carbonyl group oxygen atom and a terminal proton of the diene unit. The O—H distance is between 2.3 and 2.6 Å in these cases. Figure 7 highlights the stabilizing interaction for the lowest energy transition state.

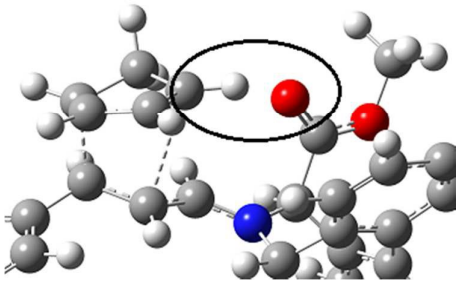


Figure 7: Zoom-in of the lowest energy transition state (E-*exo-si*-b) highlighting the stabilizing interaction.

This interaction is absent from all of the higher energy transition states: For eight of the higher energy transition structures, the cyclopentadiene approaches from the underside of the iminium salt with respect to the carbonyl group and for the other four cases the carbonyl group is facing away from the cyclopentadiene.

Diels-Alder Reactions

With our targeted catalysts in hand, we first investigated the Diels-Alder reaction between cyclopentadiene and cinnamaldehyde at room temperature in a methanol-water (95:5 *v/v*) mixture in the presence of catalyst (10 mol%) (Table 1). (*S*)-Proline and MacMillan's imidazolidinone catalyst **1** were also evaluated under these conditions.

Table 2: Asymmetric Diels-Alder reaction catalyst evaluation

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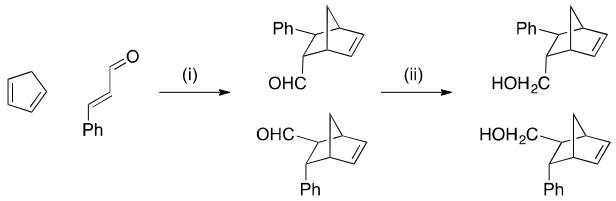

Catalyst	Time/d	Conv/% [b]	*exo:endo* [c]	*endo* ee/% [d,e]	*exo* ee/% [d,e]
Pyrrolidine [f]	5	73	1:1	—	—
(*S*)-proline	5	74	1:0.6	21 (2*R*, 3*R*)	43 (2*R*, 3*R*)
(*S*)-proline methyl ester	7	100	1:0.4	43 (2*R*, 3*R*)	47 (2*R*, 3*R*)
1	2	100	1:1.1	95 (2*S*, 3*S*)	89 (2*S*, 3*S*)
30	5	44	1:0.8	13 (2*S*, 3*S*)	27 (2*S*, 3*S*)
31	5	<10	—		
32	5	<10	—		
33	5	<10	—		
32.HCl	7	44	1:0.5	14 (2*S*, 3*S*)	26 (2*S*, 3*S*)
33.HCl	7	68	1:0.5	13 (2*S*, 3*S*)	30 (2*S*, 3*S*)
16	5	26	1:0.7	17 (2*S*, 3*S*)	43 (2*S*, 3*S*)
16.HCl	5	100	1:0.5	34 (2*S*, 3*S*)	56 (2*S*, 3*S*)
16.HCl [g]	5	77	1:0.5	31 (2*S*, 3*S*)	56 (2*S*, 3*S*)
16.HCl [h]	2	96	1:0.5	36 (2*S*, 3*S*)	58 (2*S*, 3*S*)
16.HCl [i]	7	77	1:0.4	39 (2*S*, 3*S*)	62 (2*S*, 3*S*)
16.HCl [j]	3	98	1:0.4	33 (2*S*, 3*S*)	57 (2*S*, 3*S*)
17	4	36	1:0.4	31 (2*S*, 3*S*)	57 (2*S*, 3*S*)
17.HCl	5	92	1:0.4	34 (2*S*, 3*S*)	58 (2*S*, 3*S*)
19a	7	23	1:1.2	<5	<5
19a.HCl	7	12	1:1.4	<5	11 (2*S*, 3*S*)
19b	5	21	1:1.6	<5	<5
19b.HCl	7	<10	—	—	—
25	5	70	1:0.7	21 (2*S*, 3*S*)	51 (2*S*, 3*S*)
27.TFA	5	14	1:0.8	9 (2*S*, 3*S*)	43 (2*S*, 3*S*)

[a] *Reagents and conditions:* i) cyclopentadiene (3 equiv.), cinnamaldehyde (1 equiv.), catalyst (10 mol%), MeOH:H_2O (95:5 *v/v*), r.t.; ii) $LiAlH_4$, Et_2O, 0 °C, 2 h; [b] Conversions determined from ^1H NMR spectra of the reaction mixture; [c] Ratios determined from ^1H NMR spectra of the reaction mixture; [d] Enantiomeric excesses were determined following reduction to the corresponding alcohols by HPLC using a Chiralcel® OJ column (hexane:iPrOH=90:10, λ=222 nm), 1.0 mL; *endo* isomer (t_R 15 min, 35 min) *exo* isomer (t_R 47 min, 65 min)); [e] Absolute configuration of the major enantiomer was determined by comparison with literature reports[6a] and by DFT calculation (*vide infra*); [f] reaction performed in toluene; [g] Catalyst loading 5 mol%; [h] Catalyst loading 20 mol%; [i] reaction conducted at −3 °C; [j] 10 mol% of CH_3COOH added.

(*S*)-Proline provided modest *exo* selectivity and delivered the *exo* adduct in 43% ee. (*S*)-Proline methyl ester hydrochloride led to higher diastereo- and enantioselectivity. Imidazolidinone catalyst **1** provided a fast reaction time and excellent enantioselectivity, although poor diastereoselectivity was observed.

Most of our aminoacid and aminoester catalysts favoured the formation of the *exo* isomer. Dimethyl-substituted binaphthyl β-aminoacid salt **33.HCl** out-performed the unsubstituted **32.HCl** in terms of reactivity, perhaps surprisingly due to its crowded structure, as well as enantioselectivity. α-Aminoesters **16** and **17** led to modest enantioselectivity but also poor conversion. Use of the hydrochloride salt **16.HCl** led to an improvement in diastereoselectivity, enantioselectivity and reaction rate, whereas use of **17.HCl** only improved the reaction rate. When the reaction was carried out using **16.HCl** at a lower temperature, the *exo* selectivity and ee (62% and 39% ee for the *exo* and *endo* diastereoisomers, respectively) were improved. Interestingly, the corresponding aminoacid catalysts **19a** and **19b** and their respective hydrochloride salts showed slight *endo* selectivity. Both salts **19a.HCl** and **19b.HCl** showed reduced activity compared to the free amine forms, alongside lower enantioselectivities. Biphenyl α-aminoester **25** and the binaphthyl analogue **16** gave the same diastereoselectivity, but the enantioselectivity obtained was higher when using the biphenyl catalyst. Similarly, biphenyl α-aminoacid **27** gave reduced *exo*:*endo* selectivity compared to the corresponding binaphthyl analogue **19a**. However, **27** imparted higher levels of enantioselectivity, affording the *exo* adduct in 43% ee

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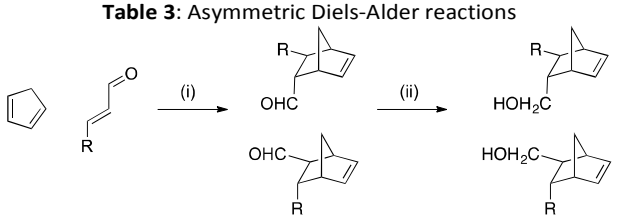
The addition of acids to reactions using catalysis by α-aminoester **16.HCl** catalysis was also investigated: acetic acid, benzoic acid, trifluoroacetic acid and triflic acid all led to an increase in the reaction rate, leading to full conversion within three days (cf five days without) and negligible changes in the diastereo- and enantioselectivity. Increase and decrease in the catalyst loading did not lead to changes in the reaction outcome. Overall, α-aminoester catalyst **16.HCl** appears to provide the optimum balance of conversion and selectivities.

A number of solvents were also tested, but no improvement was detected. When dichloromethane was used, a reduction in the activity of the catalyst and lower ees were observed. The highest enantioselectivities were observed when the reaction was conducted in polar solvents, with water and alcoholic mixtures showing a marginal improvement over all others. The optimum solvent mixture proved to be methanol/water (95:5). Water was found to be essential in providing diastereoselectivity: when the reaction was conducted in methanol, the diastereoisomeric ratio was reduced to 1:1, although the reaction time was reduced.

Catalyst **16-HCl** was next tested in the Diels-Alder reaction between cyclopentadiene and *o*- and *p*-substituted cinnamaldehyde derivatives with electron-withdrawing nitro and electron-donating methoxy substituents (Table 2).[39,40] Catalyst **1** was also tested.

Table 3: Asymmetric Diels-Alder reactions



Catalyst	Dienophile R	Conv /% [b]	exo:endo [c]	endo ee/%	exo ee/%
1 [d]	4-C_6H_5OMe	62	1:0.8	90	76
16.HCl [d]	4-C_6H_5OMe	20	1:0.6	54	30
1 [e]	2-C_6H_5OMe	100	1:0.7	93	90
16.HCl [e]	2-C_6H_5OMe	78	1:0.6	46	29
16.HCl [f]	4-$C_6H_5NO_2$	90	1:0.5	53	30
16.HCl [g]	2-$C_6H_5NO_2$	57	1:0.8	54	51

[a] *Reagents and conditions:* i) Cyclopentadiene (3 equiv.), dienophile (1 equiv.), Catalyst (10 mol%), MeOH:H2O (95:5 *v/v*), r.t., 4 days.; ii) $LiAlH_4$, Et_2O, 0 °C, 2 h; [b] Conversions were determined from 1H NMR spectra of the reaction mixture [c] Ratios were determined from 1H NMR spectra of the reaction mixture [d] Enantiomeric excesses were determined following reduction to the corresponding alcohols by HPLC using a Chiralcel® AS-3 column (hexane/iPrOH=95:5, λ=222 nm), 0.5 mL; *endo* isomer (t_R 35 min, 59 min) *exo* isomer (t_R 39 min, 56 min)) [e] Enantiomeric excesses were determined following reduction to the corresponding alcohols by HPLC using a Chiralcel® AD-H column (hexane/iPrOH=98:2, λ=222 nm), 0.5 mL; *endo* isomer (t_R 74 min, 90 min) *exo* isomer (t_R 64 min, 77 min)); [f] Enantiomeric excesses were determined following reduction to the corresponding alcohols by HPLC using a Chiralcel® AD-H column (hexane/iPrOH=90:10, λ=254 nm), 0.5 mL; *endo* isomer (t_R 49 min, 57 min) *exo* isomer (t_R 43 min, 53 min)) [g] Enantiomeric excesses were determined following reduction to the corresponding alcohols by HPLC using a Chiralcel® AD-H column (hexane/iPrOH=95:5, λ=254 nm), 0.5 mL; *endo* isomer (t_R 37 min, 39 min) *exo* isomer (t_R 41 min, 50 min)).

The electronic nature of the aromatic ring had little impact on the outcome of the reaction: dienophiles with electron-donating and -withdrawing substituents were well tolerated and gave comparable ees. Favourably, catalyst **16.HCl** provided marginally greater diastereoselectivity than did **1** in the reactions screened. We also noted an increased *endo* enantioselectivity in all cases, compared with cinnamaldehyde as dienophile. Electron-withdrawing *p*-nitro-cinnamaldehyde gave the best conversion, perhaps because of the increased reactivity of the Diels-Alder substrate, while also providing the greatest *exo*/*endo* selectivity.

The calculated figures for the Diels-Alder reaction between cyclopentadiene and *E*-cinnamaldehyde catalysed by **16** are an excellent match with the observed ee for the *endo* product of around 33% ee, and a very good match for the observed ee for the *exo* product of around 57% ee.

Conclusions

A number of α- and β- aminoacids and aminoesters with binaphthyl and biphenyl backbones have been shown to be effective asymmetric catalysts in the enantioselective Diels-Alder reaction between cyclopentadiene and cinnamaldehydes. Enantioselectivities of up to 62% ee were observed. α-Aminoester **16.HCl** appears to offer the optimum balance of conversion and selectivity. Density function theory was used to identify 16 transition states, and the calculated product ratios matched well with the experimental results. Theoretical analysis of the transition structures has identified a key stabilizing interaction which may offer insights for future catalyst development.

Experimental Detail

Melting points were recorded using a Büchi B-545 Melting Point apparatus. Optical rotations were obtained using a Bellingham and Stanley Ltd ADP440 polarimeter and the solvents used for these measurements were of HPLC-grade quality. IR spectra were recorded on a Perkin-Elmer 100 FT-IR spectrophotometer; samples were used as thin films on KBr plates. NMR spectra were recorded on a Bruker 500 MHz Spectrometer. Chemical shifts were recorded in parts per

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million (ppm), *J* values are given in Hertz (Hz) and are referenced against tetramethylsilane or the residual deuteriated solvents peak. High-resolution mass spectra were obtained from the EPSRC Mass Spectrometry Unit at the University of Swansea. Enantiomeric excesses were determined by chiral high performance liquid chromatography using a Hitachi Elite LaChrom HPLC system using an L-2200 autosampler, L-2130 pump and L-2400 UV detector. All HPLC samples were run against racemic mixture as a standard and using a hexane-isopropanol mixture; conditions varied and are provided in detail below. Unless otherwise stated, all starting materials were sourced from commercial suppliers and were used without any purification. THF and Et_2O were distilled from the sodium-benzophenone ketyl radical. Toluene, CH_2Cl_2 and CH_3CN were distilled over CaH_2; DMF was distilled over $MgSO_4$. Needles and glassware were oven-dried and allowed to cool under a positive pressure of nitrogen gas prior to use. Light petroleum ether was distilled at 40-60 °C to remove impurities. Dicyclopentadiene was cracked on the day of use to produce cyclopentadiene.

_(S)_-(+)-Allyl-4,5-dihydro-3H-4-aza-cyclohepta-[2,1-a;3,4-a']-dinaphthalene (+)-6 [19a]

(S)-2,2'-Bis-(bromomethyl)-[1-1']-binaphthalene (2.50 g, 5.7 mmol) and allylamine (0.5 mL, 6.25 mmol, 1.1 equiv.) were dissolved in acetonitrile (25 mL). Anhydrous potassium carbonate (2.36 g, 17.1 mmol, 3.0 equiv.) was added and the reaction mixture heated at reflux overnight or until completion was observed using TLC. The reaction mixture was cooled to room temperature, diluted with dichloromethane (40 mL) and filtered to remove potassium carbonate. The filtrate was washed with H_2O (3 x 10 mL) and saturated brine (2 x 20 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure yielding an orange solid. Recrystallization (hot acetone) yielded the title compound as a pale yellow solid (1.60 g, 84%).

m.p. 167-169 °C (Lit [19a] 148-149 °C); $[\alpha]_D^{23}$ +396.2 ° (*c* 1.80, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3944, 3054, 2987, 2829, 2685, 2410, 2305, 1508, 1421, 1263, 1156, 896, 820; ^{1}H NMR (500 MHz, $CDCl_3$) 7.96 (4H, d, *J*= 8.3 Hz), 7.56 (2H, d, *J*= 8.2 Hz), 7.49-7.45 (4H, m), 7.31 (2H, ddd, *J*= 8.3, 6.8, 1.1 Hz), 6.07-5.95 (1H, m), 5.29 (1H, dd, *J*= 17.1, 1.3 Hz), 5.24 (1H, d, *J*= 10.0 Hz), 3.76 (2H, d, *J*= 12.5 Hz), 3.17 (2H, d, *J*= 12.5 Hz), 3.16-3.12 (2H, m); ^{13}C NMR (126 MHz, $CDCl_3$) 136.3, 135.1, 133.4, 133.2, 131.4, 128.4, 128.3, 127.8, 127.5, 125.8, 125.5, 118.1, 58.5, 54.8.

_(S)_-(+)-4-Allyl-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-4-ium tetraphenylborate (+)-8

Method A: (*S*)-Allyl-4,5-dihydro-3H-4-aza-cyclohepta-[2,1-a;3,4-a']-dinaphthalene (1.00 g, 3.0 mmol) was dissolved in dichloromethane (50 mL). The solution was cooled to 0 °C, and *N*-bromosuccimide (0.56 g, 3.13 mmol, 1.05 equiv.) added. The mixture was stirred for 1 h or until completion was observed using TLC. The solvent was removed under reduced pressure to yield the crude bromide salt as an orange foamy solid (3.83 g crude mass, not routinely isolated). The crude *(S)*-4-allyl-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-4-ium bromide was dissolved in a minimum volume of ethanol, and a solution of sodium tetraphenylborate (1.13 g, 3.3 mmol, 1.1 equiv.) in the minimum volume of acetonitrile added. The solution was stirred for 10 min. The bright yellow precipitate was collected by filtration and washed with cold ethanol to yield the title compound as a yellow solid, which was dried at 70 °C overnight (1.55 g, 80%).

Method B: (*S*)-Allyl-4,5-dihydro-3H-4-aza-cyclohepta-[2,1-a;3,4-a']-dinaphthalene (2.12 g, 6.3 mmol) was dissolved in anhydrous dichloromethane (100 mL). Dried crushed 4Å molecular sieve and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (2.87 g, 12.6 mmol, 2 equiv.) were added. The mixture was stirred at ambient temperature for 2 h or until completion was observed using TLC. A solution of sodium tetraphenylborate (2.37 g, 6.93 mmol, 1.1 equiv.), in the minimum volume of acetonitrile was added, and the reaction stirred for a further 10 min. The solvent was removed under reduced pressure and the orange residue triturated in hot EtOH to yield the title compound as a bright yellow solid (1.9 g, 46%).

Method C: (*S*)-2'-Bromomethyl-[1,1']-binaphthalene-2-carboxaldehyde (1.41 g, 3.76 mmol) was dissolved in EtOH (15 mL), and a solution of allylamine (0.3 mL, 3.76 mmol, 1 equiv.) in ethanol (0.5 mL) added dropwise. The mixture was warmed to 35 °C and stirred for 4 h or until consumption of starting material was observed by TLC. The mixture was allowed to reach room temperature, and a solution of sodium tetraphenylborate (1.42 g, 4.14 mmol, 1.10 equiv.) in the minimum volume of acetonitrile added. The solution was stirred for 10 min, the solvents were removed under reduced pressure, and the crude residue triturated in hot EtOH to yield the title compound as a bright yellow solid (1.59 g, 65%).

m.p.* 160 °C (**decomp.*); $[\alpha]_D^{23}$ +410.5 ° (*c* 1.00, MeCN); ν_{max} (CH_2Cl_2)/cm^{-1} 3054, 2987, 2685, 2410, 2305, 1521, 1263, 1156, 896; ^{1}H NMR (500 MHz, d6-DMSO) δ 9.55 (1H, s), 8.38 (1H, d, *J*= 8.6 Hz), 8.25 (2H, t, *J*= 8.8 Hz), 8.08 (2H, dd, *J*= 14.3, 8.3 Hz), 7.85 (1H, d, *J*= 8.5 Hz), 7.79 (1H, t, *J*= 7.4 Hz), 7.55 (1H, t, *J*= 7.5 Hz), 7.49 (1H, t, *J*= 7.6 Hz), 7.44 (1H, d, *J*= 8.5 Hz), 7.29 (1H, t, *J*= 7.7 Hz), 7.18 (8H, s), 6.99 (1H, d, *J*= 8.7 Hz), 6.92 (8H, t, *J*= 7.3 Hz), 6.78 (4H, t, *J*= 7.1 Hz), 6.03–5.89 (1H, m), 5.65 (1H, d, *J*= 17.5 Hz), 5.53 (1H, d, *J*= 10.1 Hz), 5.14 (1H, d, *J*= 13.5 Hz), 4.84 (2H, d, *J*= 5.5 Hz), 4.69 (1H, d, *J*= 13.6 Hz); ^{13}C NMR (126 MHz, d6-DMSO) δ 169.6, 164.4, 141.0, 136.6, 136.0, 135.2, 133.8, 131.31, 131.24, 130.5, 129.8, 129.6, 129.5, 129.2, 128.1, 127.51, 127.46, 127.2, 126.8, 126.7, 125.80, 125.78, 125.76, 125.74, 124.3, 122.0, 64.1, 62.0 56.3; HRMS (NSI-FTMS) *m/z*: $[M\text{-}BPh_4]^+$ Calcd for $[C_{25}H_{20}N]^+$ 334.1596; Found 334.1595.

(3S,11cS)-(+)-4-Allyl-3-methyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine

(*S*)-4-Allyl-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-4-ium tetraphenylborate (843 mg, 1.29 mmol) was dissolved in anhydrous THF (20 mL). The solution was cooled to –78 °C, and a solution of methyl magnesium bromide (3M in Et_2O, 2.2 mL, 6.45 mmol, 5 equiv.) was added slowly. The mixture was allowed to reach room temperature overnight. The excess Grignard reagent was quenched with H_2O (5 mL), and the reaction mixture diluted with Et_2O (30 mL). The organic layer was washed with H_2O (20 mL) and saturated brine (10 mL), and dried over anhydrous $MgSO_4$. The solvents were removed under reduced pressure and the residue was purified using column chromatography on silica gel (7:3 light

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petroleum/EtOAc 3% TEA) to yield the title compound as a colourless oil (388 mg, 86%).

$[\alpha]_D^{25}$ +317 ° (*c* 1.00, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3048, 3005, 2959, 2928, 2904, 2805, 2866, 1506, 1366, 1264, 1112, 819, 750, 738; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95-7.87 (4H, m), 7.65 (1H, d, *J*= 8.3 Hz), 7.48 (1H, dd, *J*= 8.6, 0.7 Hz), 7.44–7.38 (3H, m), 7.33 (1H, d, *J*= 8.3 Hz), 7.21 (2H, dddd, *J*= 8.1, 7.0, 5.7, 1.3 Hz), 6.00 (1H, dddd, *J*= 17.6, 10.1, 7.6, 5.5 Hz), 5.25 (1H, dd, *J*= 17.0, 1.5 Hz), 5.19 (1H, dd, *J*= 11.0, 1.0 Hz), 4.04 (1H, q, *J*= 7.3 Hz), 3.72 (1H, d, *J*= 11.0 Hz), 3.26 (1H, ddt, *J*= 13.6, 5.4, 1.4 Hz), 3.15 (1H, dd, *J*= 13.7, 7.6 Hz), 3.10 (1H, d, *J*= 11.0 Hz), 0.54 (3H, d, *J*= 7.4 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.4, 136.6, 135.8, 135.1, 133.3, 133.2, 132.9, 132.1, 132.0, 129.2, 128.8, 128.4, 128.1, 128.0, 127.42, 127.40, 125.9, 125.7, 125.5, 117.9, 61.9, 61.0, 56.8, 22.2; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{26}H_{24}N]^+$ 350.1909; Found 350.1902.

(3*S*,11cS)-(+)-3-Methyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine

(3*S*,11cS)-4-Allyl-3-methyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine (700 mg, 2.00 mmol) was dissolved in anhydrous dichloromethane (20 mL). $Pd(PPh_3)_4$ (92 mg, 0.08 mmol, 0.04 equiv.) and 1,3-dimethylbarbituric acid (937 mg, 6.00 mmol, 3 equiv.) were added, and the reaction mixture was heated at reflux overnight or until TLC showed complete consumption of the starting material. The reaction was allowed to cool to room temperature, and washed with 1 M NaOH (2 x 15 mL), H_2O (2 x 10 mL), and saturated brine (2 x 10 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue purified using column chromatography on silica gel (10% MeOH in CH_2Cl_2) to yield the title compound as a yellow foam (341 mg, 55%).

m.p. 110-112 °C, $[\alpha]_D^{23}$ +498.0 ° (*c* 1.00, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3049, 2951, 2923, 2864, 1673, 1594, 1075, 819, 750; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99–7.89 (4H, m), 7.61 (1H, d, *J*= 8.3 Hz), 7.50–7.45 (3H, m), 7.41 (1H, d, *J*= 8.2 Hz), 7.37 (1H, d, *J*= 8.3 Hz) 7.29–7.21 (2H, m), 4.41 (1H, q, *J*= 7.3 Hz), 3.86 (1H, d, *J*= 12.4 Hz), 3.78 (1H, d, *J*= 12.3 Hz), 2.31 (1H, s), 0.72 (3H, d, *J*= 7.2 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.5, 135.4, 133.5, 133.3, 133.2, 132.20, 132.17, 129.2, 129.1, 128.4, 128.2, 127.3, 127.2, 127.0, 126.1, 125.8, 125.7, 125.7, 57.3, 48.4, 22.5; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{23}H_{20}N]^+$ 310.1596; Found 310.1589.

(+)-*tert*-Butyl 2-((3S,11cS)-4-allyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl) acetate (+)-28

A mixture of zinc dust (1.90 g, 29.1 mmol, 10 equiv.), anhydrous THF (40 mL) and TMSCl (0.37 mL, 2.9 mmol, 1 equiv.) was heated at reflux for 30 min. tert-Butyl bromoacetate (0.43 mL, 2.9 mmol) was added, and the mixture heated at reflux for a further 30 min. The mixture was cooled to –78 °C. (*S*)-4-Allyl-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-4-ium tetraphenylborate (1.90 g, 2.9 mmol) was dissolved in anhydrous THF (40 mL), and the solution transferred into the zinc slurry at –78 °C using a cannula. The mixture was stirred at –78 °C for 1 h, and t-butyl bromoacetate (4.3 mL, 29.1 mmol, 10 equiv.) added in small portions over 20 min, while maintaining the temperature. The mixture was allowed to reach room temperature and reaction progress monitored by TLC. Saturated aqueous ammonium chloride (5 mL) was added. Et_2O (50 mL) was added, and the mixture filtered through a pad of celite. The filtrate was washed with H_2O (3 x 20 mL) and saturated brine (3 x 20 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to give a yellow oil. The product was purified using column chromatography on silica gel (9:1 light petroleum ether/ EtOAc) to yield the title compound as a colourless oil (932 mg, 71%).

$[\alpha]_D^{22}$ +158 ° (*c* 1.00, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3052, 2978, 1724, 1507, 1367, 1264, 1150, 820; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98-7.90 (4H, m), 7.62 (1H, d, *J*= 8.3 Hz), 7.48-7.41 (4H, m), 7.36 (1H, d, *J*= 8.1 Hz), 7.27-7.19 (2H, m), 5.97 (1H, m), 5.25 (1H, dd, *J*= 17.1, 1.5 Hz) 5.19 (1H, *appt* d, *J*= 10.2 Hz) 4.41 (1H, t, *J*= 7.8 Hz), 3.71 (1H, d, *J*= 10.9 Hz), 3.35–3.20 (2H, m), 3.08 (1H, d, *J*= 10.9 Hz), 1.73 (1H, dd, *J*= 15.1, 7.0 Hz), 1.51 (1H, dd, *J*= 15.1, 8.4 Hz), 1.15 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 136.1, 135.5, 135.2, 135.0, 133.5, 133.3, 133.0, 131.9, 131.8, 129.9, 129.0, 128.4, 128.3, 128.1, 128.0, 127.6, 127.4, 125.9, 125.7, 125.6, 125.6, 118.0, 79.9, 64.1, 61.4, 56.1, 42.6, 27.9; HRMS (Cl^+) *m/z*: $[M+H]^+$ Calcd for $[C_{31}H_{32}NO_2]^+$ 450.2433; Found for: 450.2424.

(+)-*tert*-Butyl 2-((3S,11cS)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)acetate (+)-30

tert-Butyl 2-((3S,11cS)-4-allyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)-acetate (1.20 g, 2.67 mmol) was dissolved in anhydrous dichloromethane (60 mL). 1,3-Dimethylbarbituric acid (1.25 g, 8.00 mmol, 3 equiv.) and $Pd(PPh_3)_4$ (0.06 g, 0.05 mmol, 0.02 equiv.) were added, and the mixture heated at reflux overnight or until full consumption of the starting material was observed by TLC. The mixture was allowed to reach room temperature, and the solvent removed under reduced pressure. The residue was redissolved in Et_2O (50 mL) and the solution washed with 1 M NaOH solution (2 x 10 mL), H_2O (2 x 10 mL), and saturated brine (10 mL), and dried over anhydrous $MgSO_4$. The solvents were removed under reduced pressure, and the residue was purified using column chromatography on silica gel (6:4 light petroleum ether/EtOAc) to yield the title compound as a fluffy pale yellow foam (0.92 g, 84%).

m.p. 78-79 °C; $[\alpha]_D^{22}$ +206° (*c* 1.00, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3052, 2976, 1719, 1507, 1437, 1366, 1293, 1219, 1148, 1118; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02-7.91 (4H, m), 7.60 (1H, d, *J*= 8.3 Hz), 7.54 (1H, d, *J*= 8.4 Hz), 7.48-7.44 (2H, m), 7.40 (1H, d, *J*= 8.6 Hz), 7.34 (1H, d, *J*= 8.3 Hz), 7.26–7.22 (2H, m), 4.67 (1H, t, *J*= 7.6 Hz), 3.84 (1H, d, *J*= 12.2 Hz), 3.74 (1H, d, *J*= 12.2 Hz), 1.82 (1H, dd, *J*= 15.3, 7.6 Hz), 1.72 (1H, dd, *J*= 15.2, 7.7 Hz), 1.18 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.4, 137.5, 136.7, 135.0, 133.8, 133.2, 133.1, 132.1, 129.3, 129.1, 128.8, 128.5, 128.4, 128.1, 127.5, 127.4, 127.0, 125.9, 125.7, 125.6, 125.5, 80.2, 59.1, 48.8, 43.0, 27.9; HRMS (CI+) *m/z*: $[M+H]^+$ Calcd for $[C_{28}H_{28}NO_2]^+$ 410.2120; Found 410.2114.

(+)-2-((3S,11cS)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)acetic acid (+)-32

tert-Butyl 2-((3S,11cS)-4-allyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)acetate (660 mg, 1.6 mmol) was dissolved in dichloromethane (30 mL), and trifluoroacetic acid (1.5 mL, 19.3 mmol, 12 equiv.) added. The mixture was stirred until consumption of the starting material was observed by TLC. Saturated aqueous sodium hydrogen carbonate was added to bring the solution to neutral pH. The mixture was washed using H_2O (15 mL)and

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saturated brine (2 x 10 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue recrystallized (CH_2Cl_2 and light petroleum ether) to yield the title compound as a colourless solid (535 mg, 94%).

m.p. 228–230 °C; $[\alpha]_D^{22}$ +264 ° (*c* 1.00, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3345, 3072, 2971, 1719, 1597, 1507, 1375, 1204, 1152; ^{1}H NMR (400 MHz, *d6*-DMSO) δ 8.10 (2H, d, *J* = 8.3 Hz), 8.07 (2H, d, *J* = 8.3 Hz), 7.73 (1H, d, *J* = 8.3 Hz), 7.62 (1H, d, *J* = 8.4 Hz), 7.57-7.48 (2H, m), 7.37-7.28 (2H, m), 7.24 (1H, d, *J* = 8.5 Hz), 7.16 (1H, d, *J* = 8.4 Hz), 4.66 (1H, dd, *J* = 10.5, 5.8 Hz), 3.97 (1H, d, *J* = 12.0 Hz), 3.52 (1H, d, *J* = 11.9 Hz), 1.73 (1H, dd, *J* = 16.2, 5.8 Hz), 1.30 (1H, dd, *J* = 16.2, 5.8 Hz); ^{13}C NMR (101 MHz, *d6*-DMSO) δ 176.4, 136.5, 135.2, 133.4, 133.3, 133.2, 131.8, 131.7, 131.59, 129.67, 129.52, 129.28, 129.02, 128.77, 128.02, 126.90, 126.85, 126.81, 126.59, 126.43, 126.42, 57.12, 46.75, 38.32; HRMS (Cl^+) *m/z*: $[M+H]^+$ Calcd for $[C_{24}H_{20}NO_2]^+$ 354.1494; Found 354.1487.

(–)-(*S*)-*tert*-Butyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-4(5H)-carboxylate (–)-13

Method A: (*S*)-4,5-Dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine (1.32 g, 4.5 mmol) was dissolved in warmed *t*-BuOH (30 mL). A solution of di-*tert*-butyl dicarbonate (1.02 g, 4.7 mmol, 1.05 equiv.) in *t*-BuOH (10 mL) was added, and the mixture stirred at room temperature for 3 h. A further portion of di-*tert*-butyl dicarbonate (0.12 equiv.) was added, and the mixture stirred until full consumption of the starting material was observed by TLC. EtOAc (50 mL) was added, and the solution washed with H_2O (2 x 20 mL) and saturated brine (20 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to yield the product as a pale yellow solid (1.65 g, 92%).

Method B: (*S*)-2,2'-Bis-bromomethyl-[1,1']binaphthalene (600 mg, 1.36 mmol) was dissolved in anhydrous DMF (30 mL). The pale yellow solution was cooled to 0 °C, and NaH (130 mg, 5.45 mmol, 4 equiv.) added in one portion. *t*-Butyl carbamate (160 mg, 1.36 mmol, 1 equiv.) was added slowly in small portions. The mixture was stirred for 4 days or until full consumption of the starting material was observed by TLC. The mixture was cooled to 0 °C, and saturated aqueous ammonium chloride (10 mL) added. The majority of the solvent was removed under reduced pressure. Et_2O (100 mL) was added, and the mixture washed with H_2O (5 x 20 mL) and saturated brine (3 x 20 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue purified by recrystallization (acetone) to yield the title compound as a colourless solid (469 mg, 87%).

m.p. 219- 221 °C; $[\alpha]_D^{23}$ −7.0° (*c* 1.00, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3057, 2979, 2933, 2253, 1819, 1682, 1508, 1464, 1405, 1367, 1275, 1252, 1219, 1163, 1106, 908, 867, 819;^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99-7.91 (4H, m), 7.60 (2H, d, *J*= 8.0 Hz), 7.47 (2H, ddd, *J*= 8.0, 7.0, 1.0 Hz), 7.43 (2H, d, *J*= 8.5 Hz), 7.26 (2H, ddd, *J*= 8.5, 7.0, 1.0 Hz), 4.93 (2H, br s), 3.65 (2H, d, *J*= 13.0 Hz), 1.51 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.4, 135.0, 133.33, 133.28, 131.5, 129.2, 128.3, 127.51, 127.47, 126.0, 125.8, 85.2, 80.0, 28.6, 27.4; ; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{27}H_{26}NO_2]^+$ 396.1964; Found 396.1955.

(–)-(3R,11cS)-4-tert-Butyl 3-methyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3,4(5H)-dicarboxylate (–)-14

(*S*)-*tert*-Butyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-4(5H)-carboxylate (900 mg, 2.3 mmol) was dissolved in anhydrous Et_2O (50 mL). The solution was cooled to −78 °C, and *sec*-BuLi (1.3 M in cyclohexane, 2.3 mL, 3.0 mmol, 1.3 equiv.) added dropwise, causing the pale yellow solution to turn black. The mixture was stirred at −78 °C for 1 h. Methyl chloroformate (0.53 mL, 6.8 mmol, 3 equiv.) was added, causing the solution to turn bright yellow. The mixture was allowed to reach room temperature over 12 h, or until complete consumption of the starting material was observed by TLC. The mixture was cooled to 0 °C, and saturated aqueous ammonium chloride (5 mL) added. The mixture was washed with H_2O (2 x 20 mL) and saturated brine (2 x 10 mL), dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (9:1 light petroleum ether/EtOAc) to yield title compound as a colourless fluffy solid (845 mg, 81%).

m.p. 124-126 °C; $[\alpha]_D^{23}$ −20.8° (*c* 0.5, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3053, 2975, 2946, 2884, 1751, 1696, 1508, 1456, 1392, 1366, 1296, 1164, 960, 823; ^{1}H NMR (500 MHz, *d6*-DMSO at 380 K) δ 8.13 (1H, d, *J*= 8.3 Hz), 8.08 (1H, d, *J*= 8.2 Hz), 8.04 (1H, d, *J*= 8.3 Hz), 8.01 (1H, d, *J*= 8.2 Hz), 7.76 (1H, d, *J*= 8.3 Hz), 7.60 (1H, d, *J*= 8.3 Hz), 7.56 (1H, ddd, *J*= 8.1, 6.6, 1.3 Hz), 7.51 (1H, ddd, *J*= 8.1, 6.8, 1.1 Hz), 7.37-7.32 (1H, m), 7.32–7.28 (2H, m), 7.19 (1H, d, *J*= 8.5 Hz), 5.85 (1H, s), 5.10 (1H, d, *J*= 13.3 Hz), 3.61 (1H, d, *J*= 13.4 Hz), 2.54 (3H, s), 1.50 (9H, s); ^{13}C NMR (126 MHz, *d6*-DMSO at 380 K) δ 169.9, 153.9, 134.5, 134.3, 134.2, 133.7, 133.6, 133.5, 131.63, 131.58, 129.8, 129.7, 128.9, 128.7, 128.6, 128.3, 127.1, 126.9, 126.73, 126.67, 126.4, 126.2, 80.5, 79.6, 51.2, 28.7, 28.6; HRMS (ESI-FTMS) *m/z*: $[M+Na]^+$ Calcd for $[C_{29}H_{27}NNaO_4]^+$ 476.1838; Found 476.1832.

(+)-(3R,11cS)-Methyl 4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylate hydrochloride (+)-16.HCl

(3R,11cS)-4-*tert*-Butyl 3-methyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3,4(5H)-dicarboxylate (258 mg, 0.57 mmol) was dissolved in acetone (30 mL), concentrated aqueous HCl (3 drops) added, and the mixture heated at reflux overnight. The mixture was allowed to cool to room temperature, and the solvent removed under reduced pressure. The residue was purified by recrystallization (MeOH and Et_2O) to yield the title compound as a beige solid (222 mg, 100%).

m.p. 220-230 °C; $[\alpha]_D^{21}$ + 296.0 ° (*c* 1.00, $CHCl_3$); ν_{max} (solid)/cm^{-1} 3406, 3053, 2950, 2673, 1746, 1596, 1508, 1439, 1371, 1248, 1212, 1058, 864, 822; ^{1}H NMR (500 MHz, *d6*-DMSO) δ 9.67 (1H, s), 8.26 (1H, d, *J*= 8.0 Hz), 8.17-8.15 (2H, m), 8.12 (1H, d, *J*= 8.5 Hz), 7.81 (1H, d, *J*= 8.5 Hz), 7.71 (1H, d, *J*= 8.3 Hz), 7.65 (1H, ddd, *J*= 8.0, 6.6, 1.0 Hz), 7.61 (1H, ddd, *J*= 8.1, 6.8, 1.0 Hz), 7.42-7.37 (2H, m), 7.27 (1H, d, *J*= 8.4 Hz), 7.16 (1H, d, *J*= 8.5 Hz), 5.86 (1H, s), 4.36 (1H, d, *J*= 13.2 Hz), 3.70 (1H, d, *J*= 13.2 Hz), 2.45 (3H, s); ^{13}C NMR (126 MHz, *d6*-DMSO) δ 167.8, 134.2, 134.1, 133.6, 133.4, 130.74, 130.66, 130.5, 130.0, 129.9, 129.5, 129.2, 128.8, 128.5, 127.9, 127.1, 126.9, 126.8, 126.5, 126.3 58.6, 52.0, 45.4; HRMS (NSI-FTMS) *m/z*: $[M-Cl]^+$ Calcd for $[C_{24}H_{20}NO_2]^+$ 354.1494; Found 354.1488.

(–)-(3R,11cS)-4-(*tert*-Butoxycarbonyl)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid (–)-18a and (+)-(3S,11cS)-4-(*tert*-butoxycarbonyl)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-

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azepine-3-carboxylic acid (+)-18b

(*S*)-*tert*-Butyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-4(5H)-carboxylate (500 mg, 1.26 mmol) was dissolved in anhydrous Et_2O (30 mL) under a positive pressure of argon, and the mixture was cooled to −78 °C. *sec*-BuLi (1.4 M solution in cyclohexane, 1.2 mL, 1.6 mmol, 1.3 equiv.) was added, causing the solution to turn from a pale yellow to a black colour. The mixture was stirred at −78 °C for 1 h. CO_2 gas was bubbled directly into the solution *via* a drying tube filled with $CaCl_2$. The mixture was stirred overnight at −78 °C under an atmosphere of argon. Saturated aqueous ammonium chloride (10 mL) and EtOAc (20 mL) were added. The organic layer was washed with H_2O (2 x 20 mL) and saturated brine (2 x 20 mL), dried over anhydrous Na_2SO_4, and the solvent removed under reduced pressure. The residue was purified by column chromatography on silica gel (4:1 light petroleum ether/EtOAc).

For the first eluting diastereoisomer **18a**: isolated as a colourless solid (188 mg, 34%), m.p. 164-167 °C; $[\alpha]_D^{24}$ −47.2 ° (*c* 1.00, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3056, 2976, 2937, 1754, 1694, 1393, 1367, 1303, 1245, 1156, 912, 819, 749; ^{1}H NMR (500 MHz, *d6*-DMSO, 363 K) δ 8.07 (1H, d, *J*= 8.7 Hz), 8.02 (1H, d, *J*= 8.7 Hz), 7.98–7.94 (2H, m), 7.70 (1H, d, *J*= 8.6 Hz), 7.57 (1H, d, *J*= 8.2 Hz), 7.49 (1H, ddd, *J*= 8.1, 6.8, 1.5 Hz), 7.44 (1H, ddd, *J*= 8.1, 6.8, 1.5 Hz), 7.25 (2H, m), 7.20-7.15 (2H, m), 5.72 (1H, s), 5.07 (1H, d, *J*= 15.5 Hz), 3.56 (1H, d, *J*= 15.5 Hz), 1.45 (9H, s); ^{13}C NMR (126 MHz, *d6*-DMSO, 363 K) δ 170.5, 154.0, 134.3, 133.5, 131.8, 131.7, 129.5, 129.4, 128.7, 128.6, 128.4, 127.4, 127.2, 126.5, 126.2, 126.0, 80.2, 62.1, 47.4, 28.7; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{28}H_{26}NO_4]^+$ 440.1862; Found 440.1854.

For the first eluting diastereoisomer **18b**: isolated as a colourless solid (170 mg, 31%), m.p. 255-257 °C; $[\alpha]_D^{24}$ +58.4 ° (*c* 1.00, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3052, 3006, 2976, 2927, 1751, 1725, 1696, 1395, 1367, 1251, 1219, 1151, 820, 772, 759, 677; ^{1}H NMR (500 MHz, *d6*-DMSO, 353 K) δ 8.07 (2H, d, *J*= 8.3 Hz), 8.02 (2H, dd, *J*= 11.6, 8.3 Hz), 7.66 (1H, d, *J*= 9.0 Hz), 7.58 (1H, d, *J*= 9.0 Hz), 7.52-7.48 (2H, m), 7.35-7.31 (2H, m), 7.27-7.24 (1H, m), 7.16 (1H, d, *J*= 8.7 Hz), 4.95 (1H, d, *J* =15.0 Hz), 4.36 (1H, s), 3.55 (1H, d, *J* =15.0 Hz), 1.40 (9H, s); ^{13}C NMR (126 MHz, *d6*-DMSO, 353 K) δ 171.4, 155.75, 136.3, 135.1, 133.5, 133.4, 132.6, 132.3, 131.7, 131.5, 129.8, 129.2, 128.9, 128.7, 127.21, 127.16, 126.8, 126.8, 126.7, 126.3, 126.1, 125.2, 81.1, 62.7, 48.7, 28.4; ; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{28}H_{26}NO_4]^+$ 440.1862; Found 440.1852.

(+)-(3R,11cS)-4,5-Dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid hydrochloride (+)-19a.HCl

3R,11cS)-4-(*tert*-Butoxycarbonyl)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid (230 mg, 0.52 mmol) was dissolved in acetone (20 mL), concentrated aqueous HCl (3 drops) added, and the mixture heated at reflux overnight. The mixture was allowed to cool to room temperature and the solvent removed under reduced pressure. The residue was purified by recrystalization (MeOH and light petroleum ether) to yoeld the title compound as a pale yellow solid (197 mg, 100%).

m.p. 265-267 °C; $[\alpha]_D^{22}$ +294 ° (*c* 1.00, MeOH); ν_{max} $(CH_2Cl_2)/cm^{-1}$ 3019, 2400, 1741, 1528, 1425, 1215, 928, 757, 669, 625; ^{1}H NMR (500 MHz, *d6*-DMSO) δ 13.26 (1H, s), 11.10 (1H, s), 9.43 (1H, s), 8.23 (1H, d, *J*= 8.4 Hz), 8.15 (2H, dd, *J*= 8.3, 3.7 Hz), 8.09 (1H, d, *J*= 8.2 Hz), 7.80 (1H, d, *J*= 8.4 Hz), 7.71 (1H, d, *J*= 8.4 Hz), 7.66-7.54 (2H, m), 7.43-7.34 (2H, m), 7.18 (2H, t, *J*= 8.0 Hz), 5.71 (1H, s), 4.34 (1H, d, *J*= 13.1 Hz), 3.67 (1H, d, *J*= 13.1 Hz); ^{13}C NMR (126 MHz, *d6*-DMSO) δ 168.9, 134.7, 134.6, 134.1, 134.0, 131.34, 131.25, 130.2, 129.9, 129.8, 129.68, 129.65, 129.6, 129.0, 128.9, 128.4, 127.4, 127.3, 127.2, 127.1, 127.0, 59.4, 46.0; HRMS (NSI-FTMS) *m/z*: $[M-Cl]^+$ Calcd for $[C_{23}H_{18}NO_2]^+$ 340.1338; Found 340.1333.

(+)-2,2'-bis(Bromomethyl)-6,6'-dimethyl-1,1'-biphenyl (+)-20

(6,6'-Dimethyl-[1,1'-biphenyl]-2,2'-diyl)dimethanol (500 mg, 2.1 mmol) and pyridine (19 µL, 0.23 mmol, 0.11 equiv.) were dissolved in anhydrous toluene (50 mL). Phosphorus tribromide (0.6 mL, 6.3 mmol, 3 equiv.) was added dropwise. The mixture was heated at 60 °C for 3 h. H_2O (50 mL) was added, and the mixture washed with saturated aqueous sodium hydrogen carbonate (20 mL). The organic layer was dried over anhydrous $MgSO_4$, decolourized with carbon black, filtered, and the solvent removed under reduced pressure to yield the title compound as an orange solid (677 mg, 88%), used without further purification.

m.p. 45-47 °C; $[\alpha]_D^{19.4}$ +35.2 ° (*c* 1.00, $CHCl_3$); ν_{max} $(CH_2Cl_2)/cm^{-1}$ 3064, 3018, 2970, 2918, 2856, 1593, 1459, 1437, 1381, 1246, 1210, 1166, 1005, 935, 788, 755, 735, 626, 613;^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (2H, d, *J*= 7.6 Hz), 7.32 (2H, t, *J*= 7.6 Hz), 7.26 (2H, d, *J*= 7.6 Hz), 4.15 (4H, q, *J*= 10.1 Hz), 1.98 (6H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.7, 136.7, 135.4, 130.5, 128.6, 128.4, 32.4, 20.2.

(–)-(*S*)-*tert*-Butyl 1,11-dimethyl-5H-dibenzo[c,e]azepine-6(7H)-carboxylate (–)-23

2,2'-bis(Bromomethyl)-6,6'-dimethyl-1,1'-biphenyl (500 mg, 1.36 mmol) was dissolved in anhydrous DMF (30 mL), and NaH (67 mg, 2.78 mmol, 2.05 equiv.) added. The mixture was cooled to 0 °C, and *tert*-butyl carbamate (159 mg, 1.36 mmol, 1 equiv.) added in one portion. On completion of the reaction (TLC), DMF was removed under reduced pressure and the residue redissolved in EtOAc (60 mL). The solution was washed with H_2O (5 x 10 mL) and saturated brine (2 x 20 mL), dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The residue was purified by column chromatography (9:1 light petroleum ether/EtOAc) to yield the product as a colourless oil (385 mg, 88%).

$[\alpha]_D^{22}$ −238 ° (*c* 1.50, $CHCl_3$); ν_{max} $(CH_2Cl_2)/cm^{-1}$ 3063, 2974, 2927, 2866, 1691, 1459, 1400, 1364, 1036, 1247, 1216, 1158, 1100, 869; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42-7.10 (6H, m), 4.71 (2H, d, *J*= 9.7 Hz), 3.45 (2H, d, *J*= 13.1 Hz), 2.18 (6H, s), 1.48 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.3, 138.2, 136.1, 134.9, 130.0, 127.9, 126.5, 79.7, 47.8, 28.6, 19.7; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{21}H_{26}NO_2]^+$ 324.1964; Found 324.1960.

(–)-(5R,11bS)-6-tert-Butyl 5-methyl 1,11-dimethyl-5H-dibenzo[c,e]azepine-5,6(7H)-dicarboxylate (–)-24

tert-Butyl 1,11-dimethyl-5H-dibenzo[c,e]azepine-6(7H)-carboxylate (645 mg, 1.99 mmol) was dissolved in anhydrous Et_2O (60 mL), and the solution cooled to −78 °C. *s*-BuLi (1.4 M in cyclohexane, 2.85 mL, 3.99 mmol, 2 equiv.) was added, and the mixture stirred for 1 h. Methyl chloroformate (0.23 mL, 2.99 mmol, 1.5 equiv.) was added, and the mixture stirred for 1 h at −78 °C. Saturated aqueous ammonium chloride was added. The mixture was washed with H_2O (2 x 30 mL) and saturated brine (2 x 10 mL), dried over anhydrous $MgSO_4$, and the solvents removed under reduced pressure. The

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residue was purified by column chromatography (9:1 light petroleum ether/EtOAc) to yield the product as a colourless fluffy solid (600 mg, 79%).

m.p. 74-76 °C; $[\alpha]_D^{23}$ −248 ° (*c* 1.00, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3065, 3002, 2975, 2948, 2930, 2872, 2250, 1752, 1686, 1600, 1474, 1458, 1433, 1392, 1366, 1355, 1308, 1255, 1221, 1206, 1161, 1105, 1004, 912, 875; ^{1}H NMR (500 MHz, *d6*-DMSO, 373 K) δ 7.42-7.16 (6H, m), 5.61 (1H, s), 4.85 (1H, d, *J*= 13.3 Hz), 3.38 (1H, d, *J*= 13.1 Hz), 3.10 (3H, s), 2.13 (3H s), 2.07 (3H, s), 1.47 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ ^{3}C NMR (126 MHz, $CDCl_3$) δ 170.8, 170.5, 154.3, 153.9, 137.5, 137.5, 137.3, 137.2, 136.9, 136.7, 136.6, 136.4, 135.2, 134.9, 134.7, 134.6, 130.6, 130.4, 129.8, 129.7, 128.50, 128.47, 128.2, 128.1, 128.04, 128.01, 127.3, 127.1, 80.5, 80.4, 62.1, 60.8, 51.7, 47.7, 46.4, 28.5, 28.4, 19.52, 19.46; ^{1}HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{23}H_{28}NO_4]^+$ 382.2018; Found 382.2013.

(+)-(5R,11bS)-Methyl 1,11-dimethyl-6,7-dihydro-5H-dibenzo[c,e]azepine-5-carboxylate (+)-25

(5R,11bS)-6-tert-Butyl 5-methyl 1,11-dimethyl-5H-dibenzo[c,e]azepine-5,6(7H)-dicarboxylate (100 mg, 0.26 mmol) was dissolved in dichloromethane (8 mL), trifluoroacetic acid (0.28 mL, 3.64 mmol, 14 equiv.) added in one portion, and the solution stirred for 30 minutes. Saturated aqueous sodium hydrogen carbonate was added to bring the pH to neutral. The solvent was removed under reduced pressure, and the residue redissolved in EtOAc (10 mL). The solution was washed with H_2O (3 x 10 mL) and saturated brine (3 x 5 mL), and dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The residue was purified by recrystallization ($CHCl_3$) to yield the title compound as a colourless solid (55 mg, 75%).

$[\alpha]_D^{26}$ +37.7 ° (*c* 0.70, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3316, 3062, 3017, 2948, 2926, 2867, 1732, 1493, 1432, 1378, 1302, 1265, 1228, 1211, 1122, 1099, 994, 785, 770, 741, 680; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.29 (2H, m), 7.29-7.22 (2H, m), 7.18 (1H, d, *J*= 7.4 Hz), 7.11 (1H, d, *J*= 7.3 Hz), 4.44 (1H, s), 3.64 (1H, d, *J*= 13.6 Hz), 3.35 (1H, d, *J*= 13.6 Hz), 3.22 (3H, s), 2.64 (1H, s), 2.15 (3H, s), 2.12 (3H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 138.3, 137.9, 136.9, 136.6, 136.3, 135.1, 130.3, 129.2, 128.5, 128.0, 127.9, 125.6, 62.4, 51.9, 48.3, 19.5, 19.4; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{18}H_{20}NO_2]^+$ 282.1494; Found 282.1489.

(–)-(5R,11bS)-6-(*tert*-Butoxycarbonyl)-1,11-dimethyl-6,7-dihydro-5Hdibenzo[c,e]azepine-5-carboxylic acid (–)-26

tert-Butyl 1,11-dimethyl-5H-dibenzo[c,e]azepine-6(7H)-carboxylate (645 mg, 1.99 mmol) was dissolved in anhydrous Et_2O (60 mL), and the solution cooled to −78 °C. *s*-BuLi (1.4 M in cyclohexane, 2.85 mL, 4.00 mmol, 2 equiv.) was added. After stirring for 1 h at −78 °C, CO_2 gas was bubbled into the mixture through a drying tube of $CaCl_2$ over 1 h. The mixture was allowed to reach ambient temperature overnight. Saturated aqueous ammonium chloride was added at 0 °C. The mixture was washed with H_2O (2 x 20 mL) and saturated brine (2 x 10 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography (4:1 light petroleum ether/EtOAc) to yield the title compound as a colourless solid (330 mg, 45%).

m.p. 117-119 °C; $[\alpha]_D^{24}$ −250 ° (*c* 1.00, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3066, 3009, 2976, 2928, 2782, 1751, 1717, 1601, 1456, 1394, 1367, 1310, 1254, 1219, 1160, 883, 760, 744; ^{1}H NMR (500 MHz, *d6*-DMSO, 380 K) δ 11.35 (1H, s), 7.37-7.32 (2H, m), 7.29-7.21 (3H, m), 7.17 (1H dd, *J*= 6.7, 2.0 Hz), 5.52 (1H, s), 4.84 (1H, d, *J*= 13.1 Hz), 3.39 (1H, d, *J*= 13.2 Hz), 2.13 (3H, s), 2.08 (3H, s), 1.47 (9H, s); ^{13}C NMR (126 MHz, *d6*-DMSO, 380 K) δ 170.7, 153.9, 137.8, 137.7, 136.9, 136.3, 135.7, 135.2, 130.5, 130.0, 128.6, 128.4, 128.3, 127.4, 80.0, 63.4, 28.7, 28.7, 19.7, 19.5; HRMS (NSI-FTMS) *m/z*: $[M-H]^-$ Calcd for $[C_{22}H_{24}NO_4]^-$ 366.1705; Found 366.1702.

(–)-(5R,11bS)-1,11-Dimethyl-6,7-dihydro-5H-dibenzo[c,e]azepine-5-carboxylic acid trifluoroacetic acid (–)-27.TFA

(5R,11bS)-6-(*tert*-Butoxycarbonyl)-1,11-dimethyl-6,7-dihydro-5H dibenzo[c,e]azepine-5-carboxylic acid (250 mg, 0.68 mmol) was dissolved in dichloromethane (10 mL), trifluoroacetic acid (0.71 mL, 9.53 mmol, 14 equiv.) added in one portion, and the solution stirred for 30 minutes. The solvent was removed under reduced pressure, and the residue redissolved in EtOAc (10 mL). The solution was washed with H_2O (3 x 10 mL) and saturated brine (3 x 5 mL), dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The residue was purified by recrystallization ($CHCl_3$) to yield the title compound as a colourless solid (128 mg, 50%).

m.p. 250-252 °C; $[\alpha]_D^{24}$ −34.8 ° (*c* 1.02, MeOH); ν_{max} (solid)/cm^{-1} 3169, 2800, 1729, 1643, 1566, 1433, 1379, 1348, 1285, 1249, 1150, 1136, 1059, 839, 786, 725, 675; ^{1}H NMR (500 MHz, *d6*-DMSO) δ 13.49 (1H, s), 10.10 (1H, s), 9.13 (1H, s), 7.52-7.28 (6H, m), 5.43 (1H, s), 4.09 (1H, d, *J* = 12.9 Hz), 3.43 (1H, d, *J* = 12.9 Hz), 2.11 (3H, s), 2.08 (3H, s); ^{13}C NMR (126 MHz, *d6*-DMSO) δ ^{13}C NMR (126 MHz, DMSO) δ 168.7, 137.2, 136.9, 136.7, 136.4, 131.8, 131.48, 130.45, 130.0, 129.3, 128.5, 128.2, 128.0, 59.0, 45.6, 19.2, 19.0; HRMS (NSI-FTMS) *m/z*: $[M-CF_3CO_2H_2]^-$ Calcd for $[C_{17}H_{16}NO_2]^-$ 266.1181; Found 266.1187.

General procedure for the organocatalytic Diels-Alder reaction

The catalyst (10 mol%) was dissolved in MeOH:H_2O (95:5, 1 mL), and an α-β unsaturated aldehyde (1.0 mmol) was added. After 5 minutes the diene was added (3 mmol, 3 equiv.). The reaction was monitored by TLC, and upon complete consumption of cinnamaldehyde the mixture was diluted with Et_2O (5 mL), washed with H_2O (3 x 5 mL) and saturated brine (2 x 5 mL), and concentrated under reduced pressure. Hydrolysis of the dimethyl acetal adduct was performed by stirring in TFA:H_2O:$CHCl_3$ (1:1:2) for 2 h. The mixture was neutralized with aqueous sodium hydrogen carbonate, and extracted with Et_2O (2 x 10 mL). The combined organic layers were washed with saturated brine (2 x 5 mL), dried over anhydrous $MgSO_4$, and the solvents were removed under reduced pressure. The residue was purified by column chromatography. Reduction to the corresponding alcohol was performed using $LiAlH_4$ in anhydrous Et_2O to allow separation on HPLC media.

Conflicts of interest

There are no conflicts to declare.

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A Combined Synthetic and Computational Study of Novel Binaphthyl and Biphenyl α- and β-Amino Acids and Esters: Organocatalysis of Asymmetric Diels Alder Reactions

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Supporting information

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General Experimental Detail

Melting points were recorded using a Büchi B-545 Melting Point apparatus. Optical rotations were obtained using a Bellingham and Stanley Ltd ADP440 polarimeter and the solvents used for these measurements were of HPLC-grade quality. IR spectra were recorded on a Perkin-Elmer 100 FT-IR spectrophotometer and samples were used as thin film DCM solutions on KBr plates. NMR spectra were recorded on a Bruker 500 MHz Spectrometer. Chemical shifts were recorded in parts per million (ppm), *J* values are given in Hertz (Hz) and are referenced against tetramethylsilane or the residual deuterated solvents peak. High-resolution mass spectra were obtained from the EPSRC Mass Spectrometry Unit at the University of Swansea. Enantiomeric excesses were determined by chiral high performance liquid chromatography using a Hitachi Elite LaChrom HPLC system using an L-2200 autosampler, L-2130 pump and L-2400 UV detector. All HPLC samples were run against racemate as a standard and using a hexane-isopropanol mixture. Conditions varied and are provided in detail below. Unless otherwise stated, all starting materials were sourced from commercial suppliers and were used without any purification. Reactions which required the use of anhydrous solvents were, in the case of THF and Et_2O, dried and distilled over sodium and benzophenone. Toluene, DCM and CH_3CN were distilled over CaH_2 and DMF was distilled over $MgSO_4$. Needles and glassware were oven-dried were and allowed to cool under a positive pressure of nitrogen gas prior to use. Light petroleum ether was distilled at 40-60 °C to remove impurities. Dicyclopentadiene was cracked on the day of use to distil cyclopentadiene.

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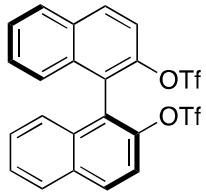
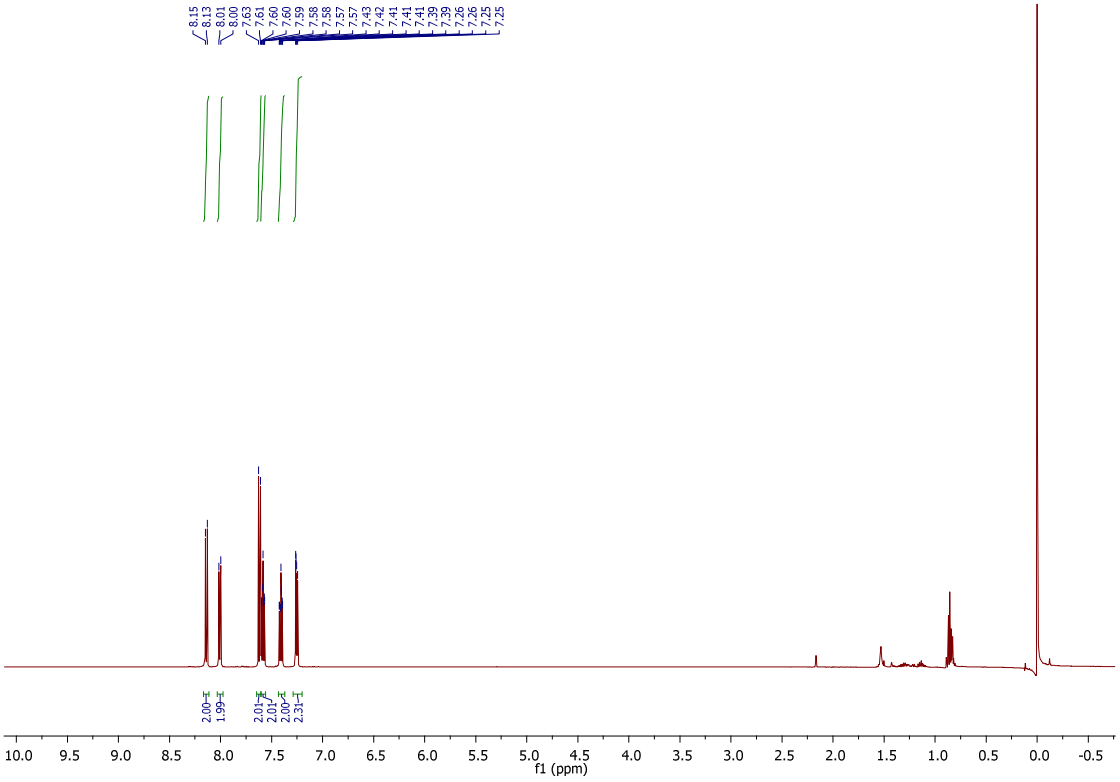
_(S)_-(+)-[1,1']-Binaphthalene-2,2'-diol bis-trifluoromethanesulfonate





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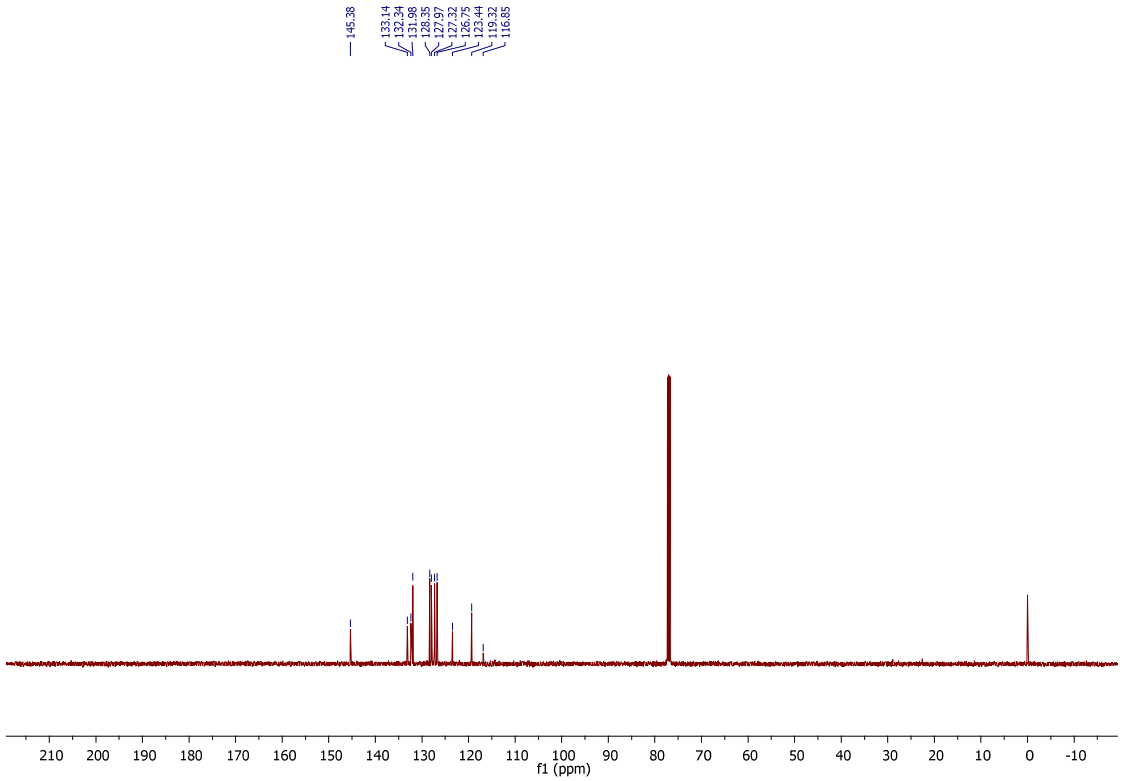
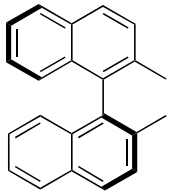


_(S)_-(+)-2,2'-Dimethyl-[1,1']binaphthalene



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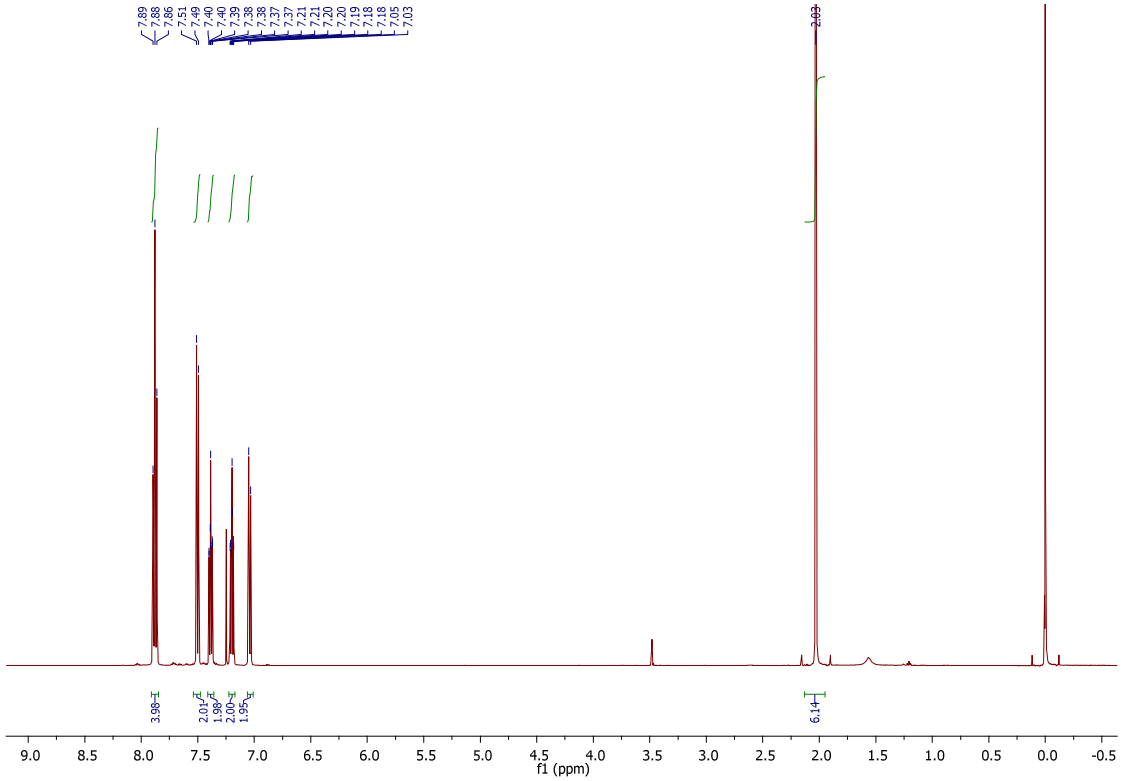

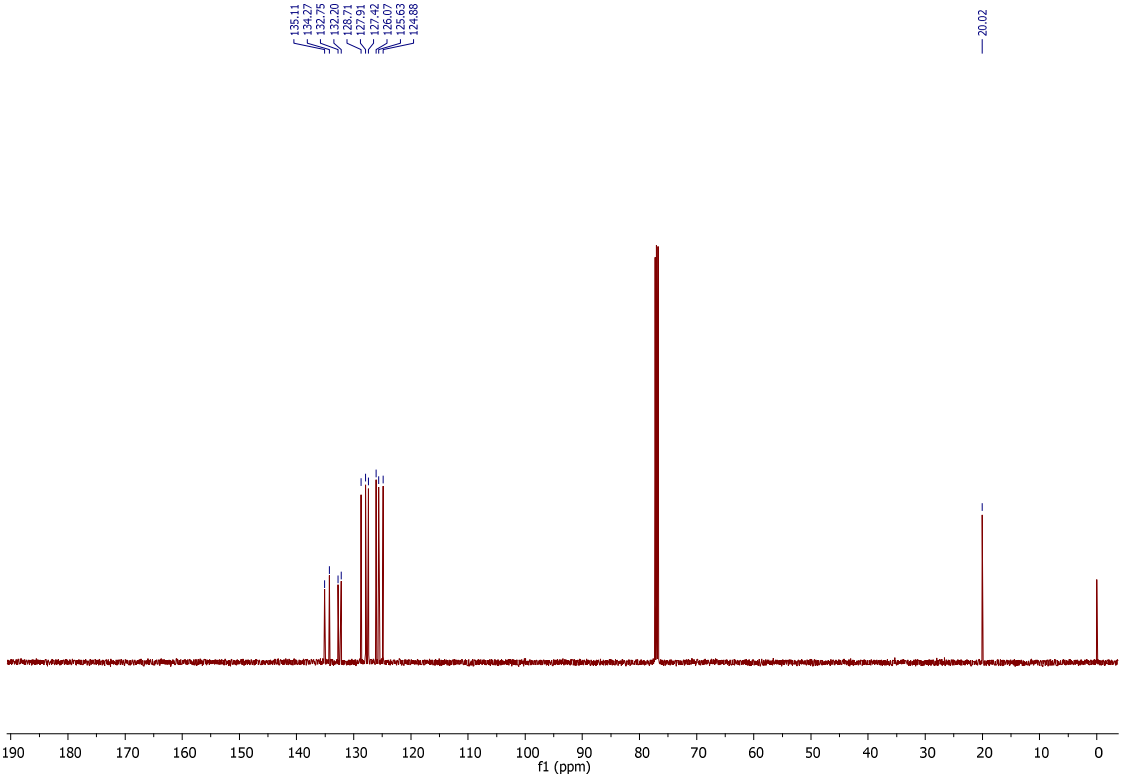

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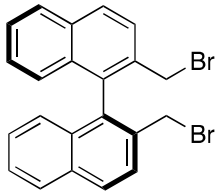
(*S*)-2,2'-*Bis*-bromomethyl-[1,1']binaphthalene (–)-7



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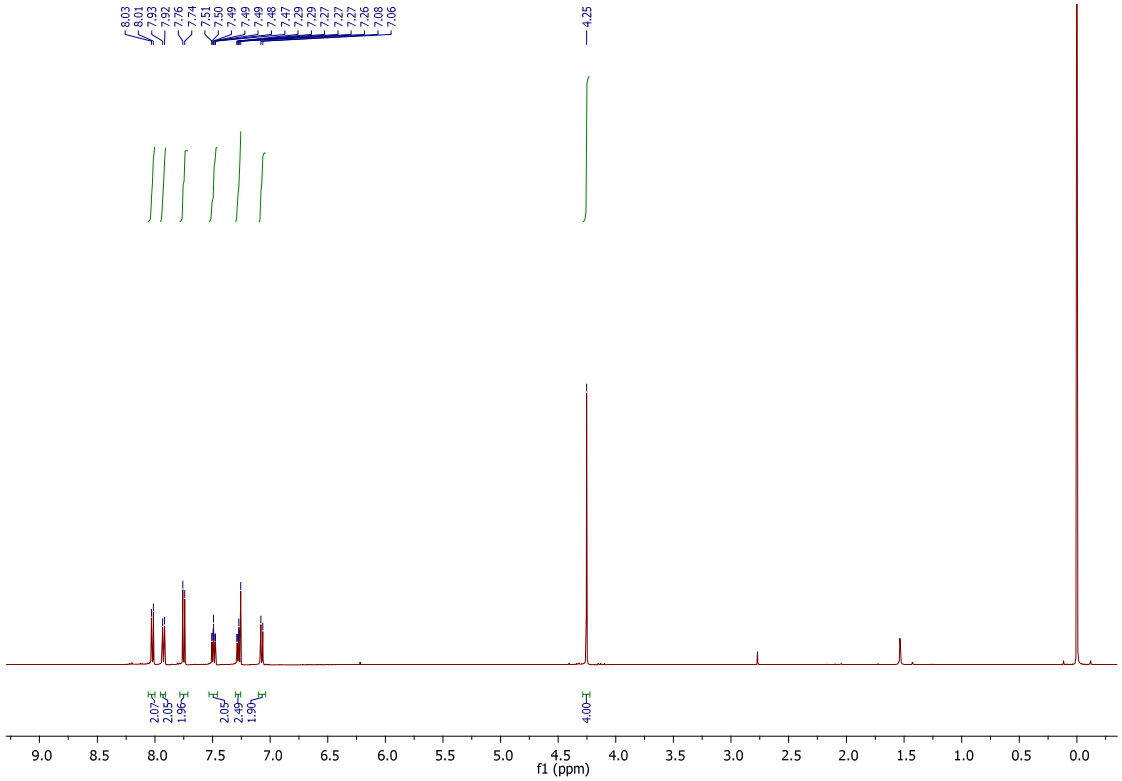

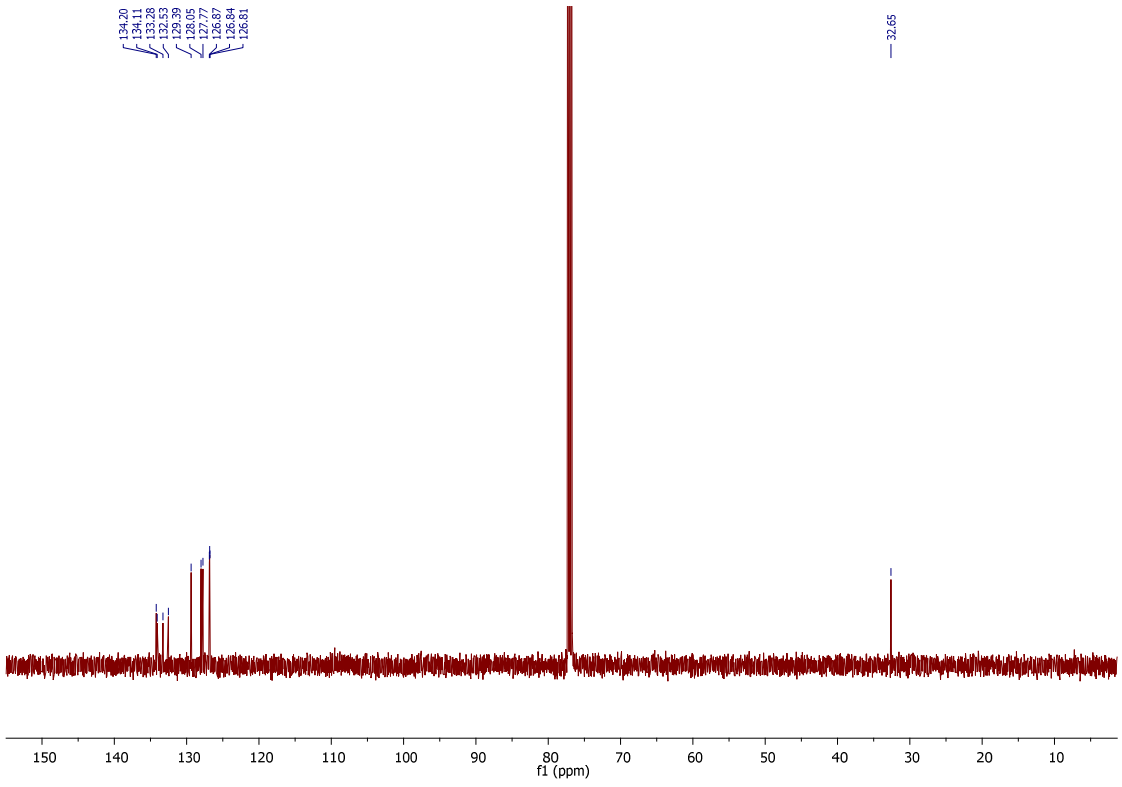

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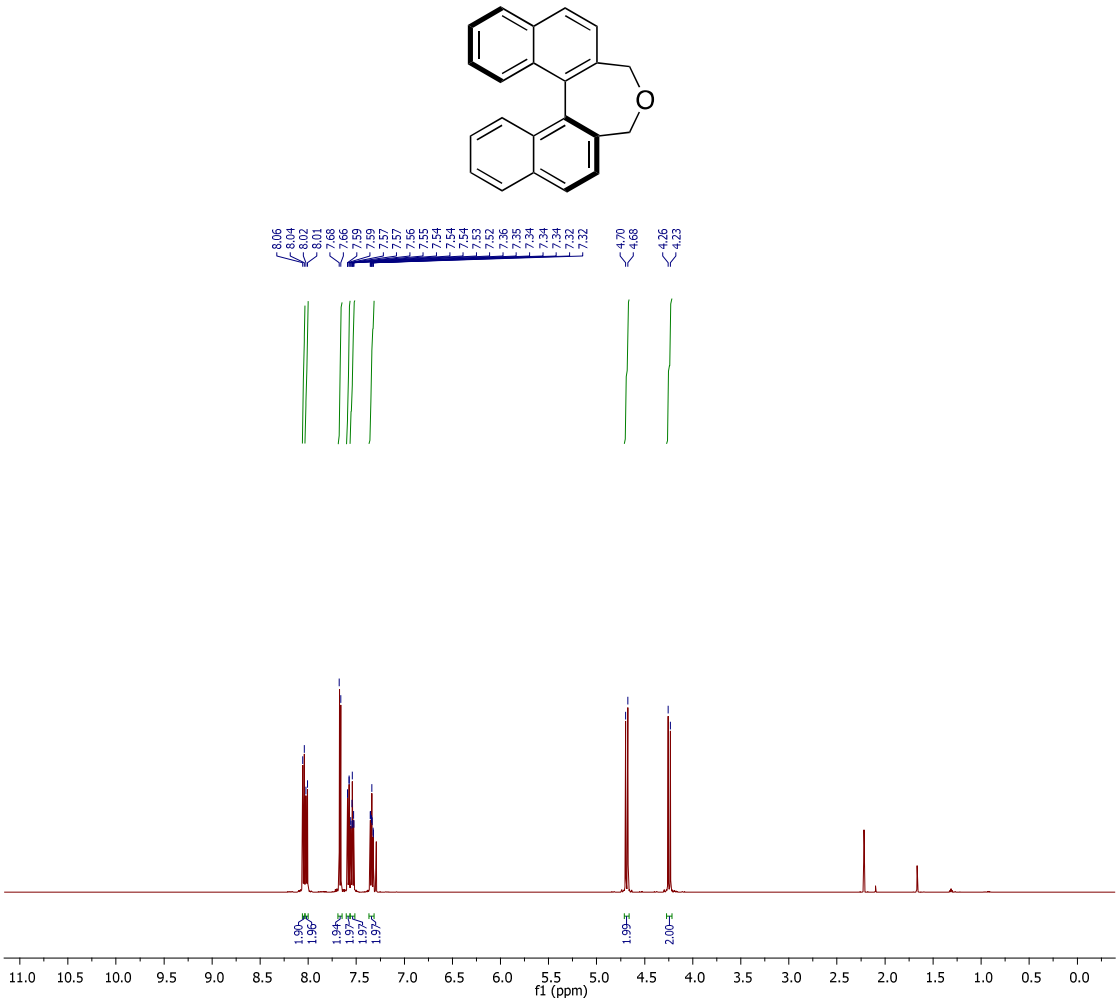

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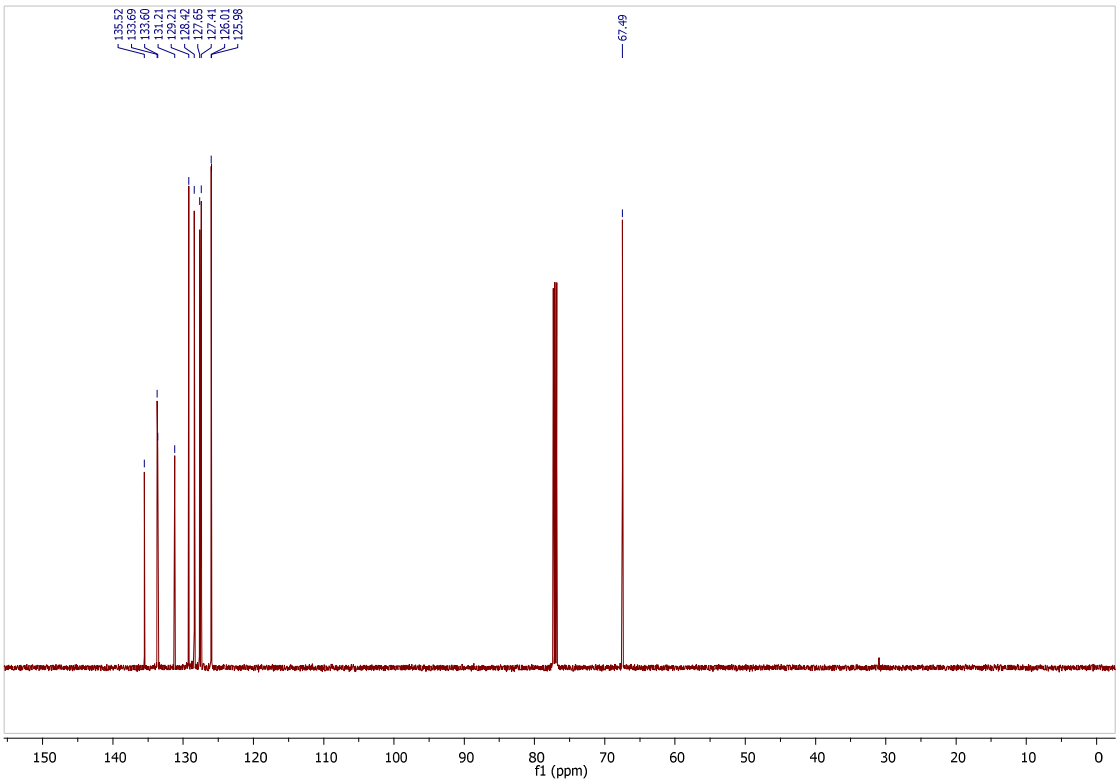
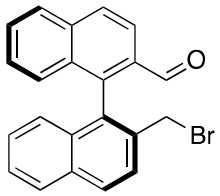


(*S*)-2'-Bromomethyl-[1,1']binaphthalene-2-carboxaldehyde (–)-10



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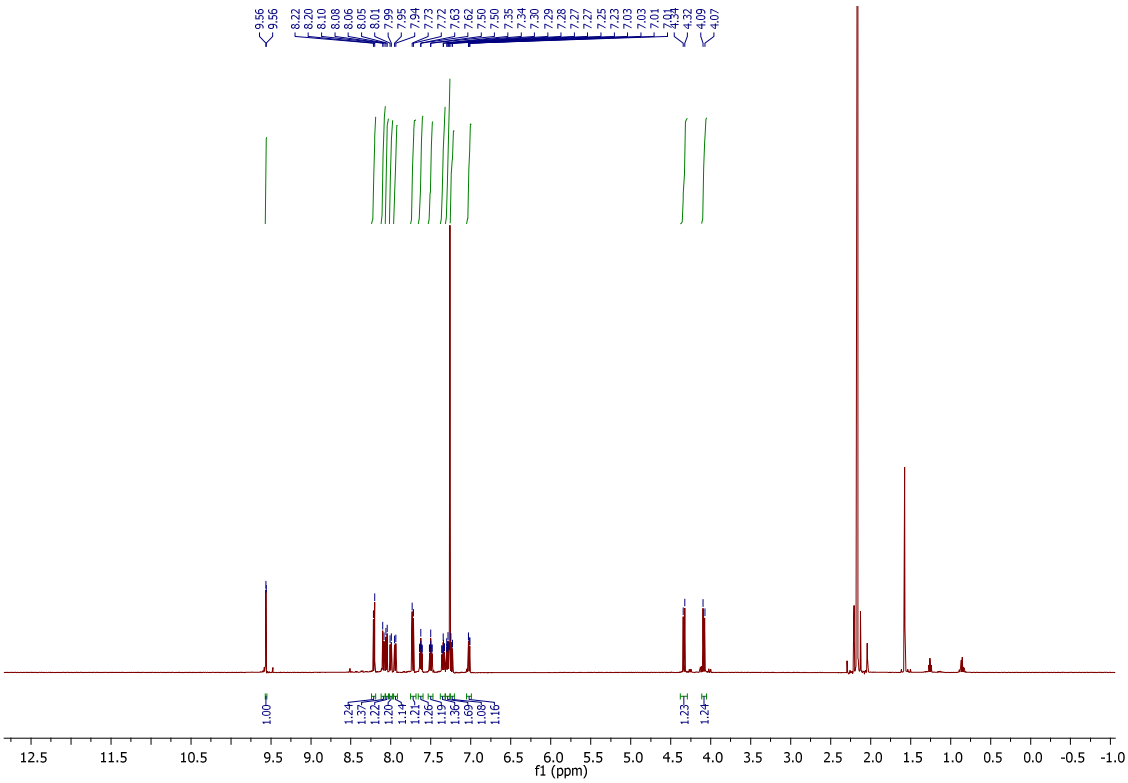

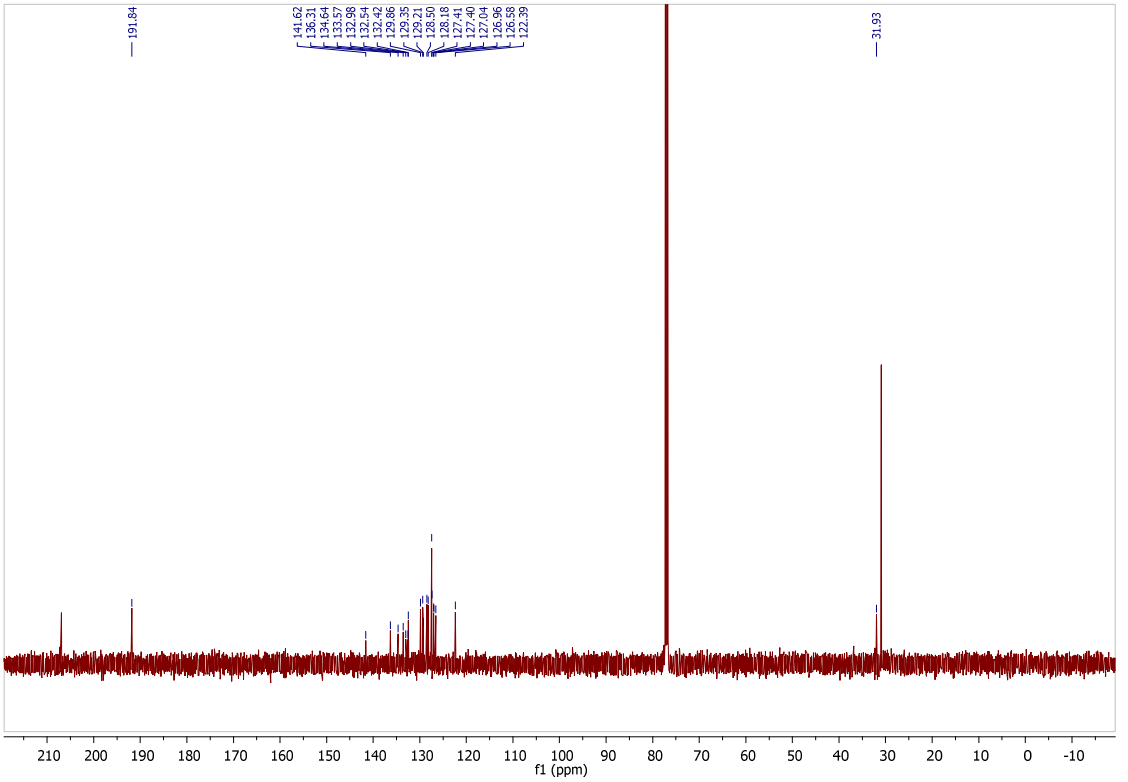

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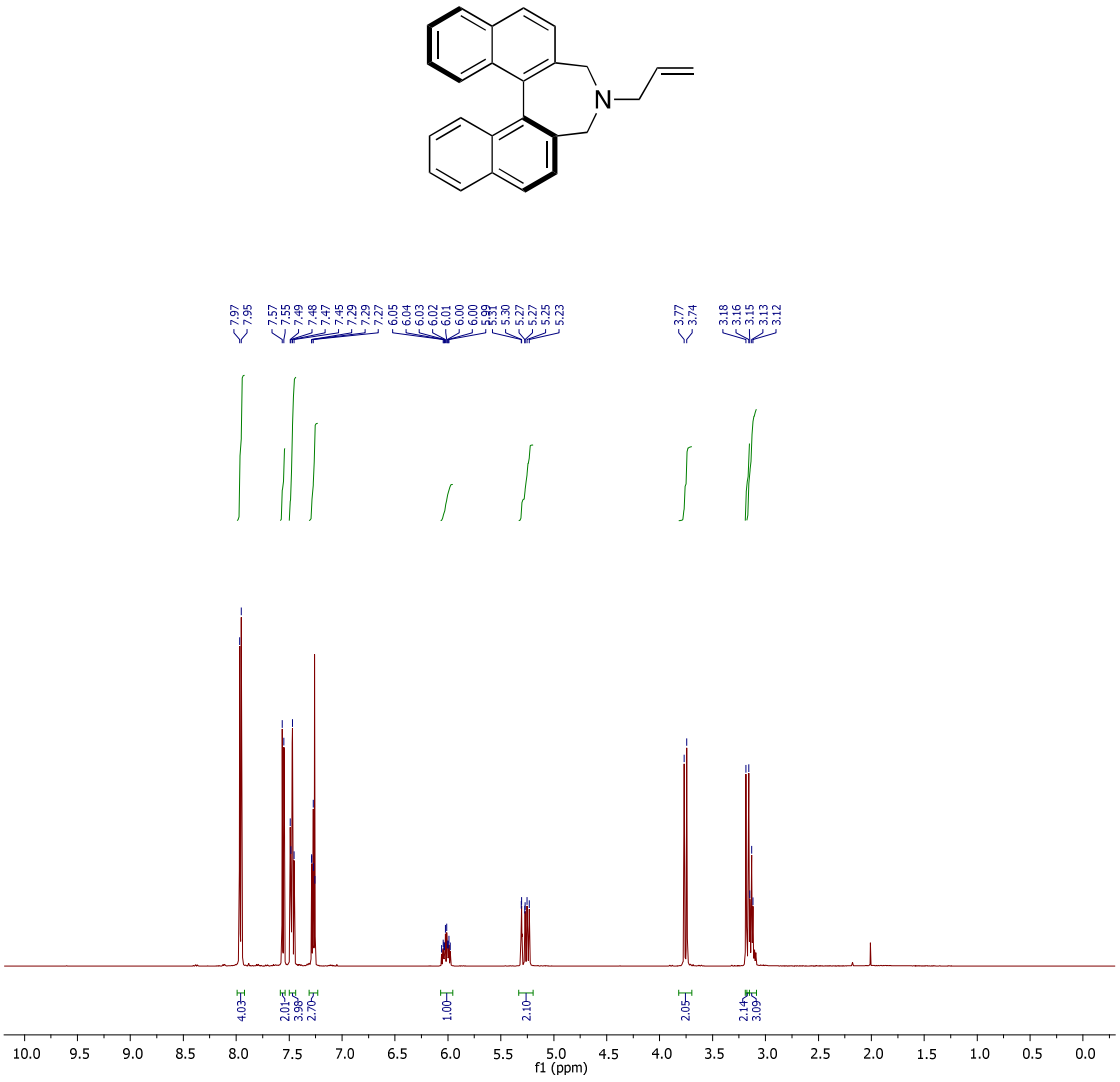
_(S)_-Allyl-4,5-dihydro-3H-4-aza-cyclohepta[2,1-a;3,4-a']dinaphthalene (+)-6



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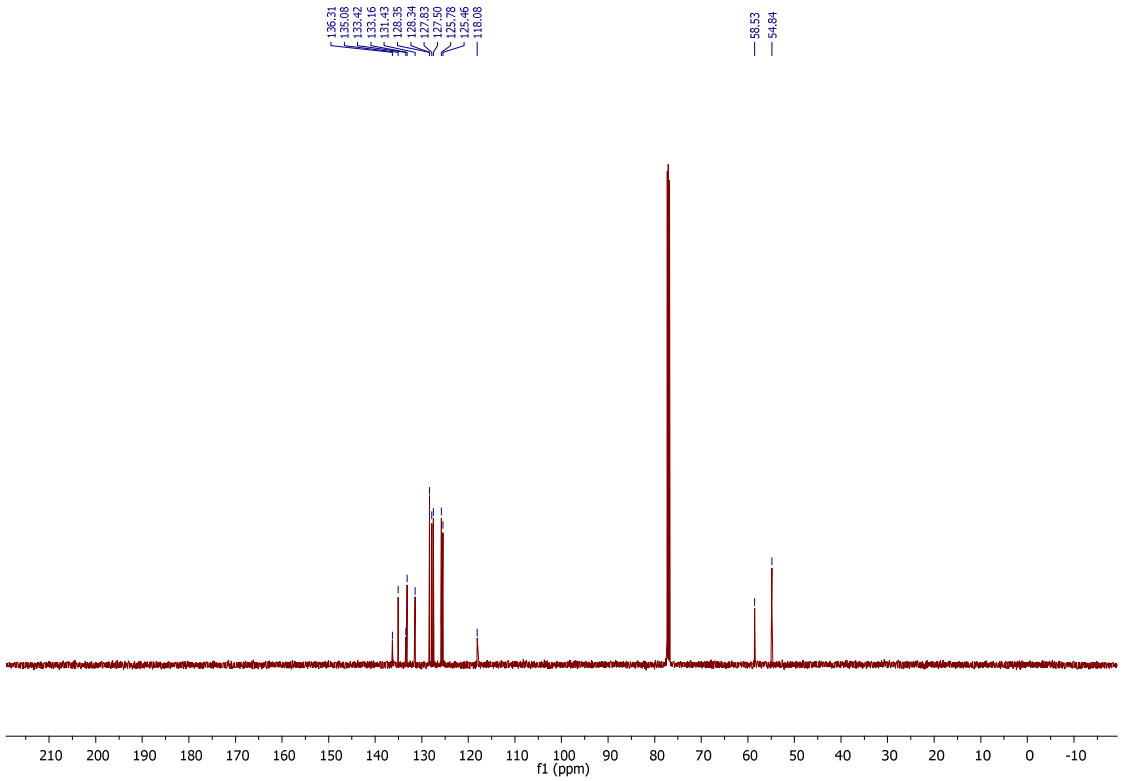

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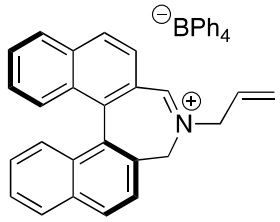

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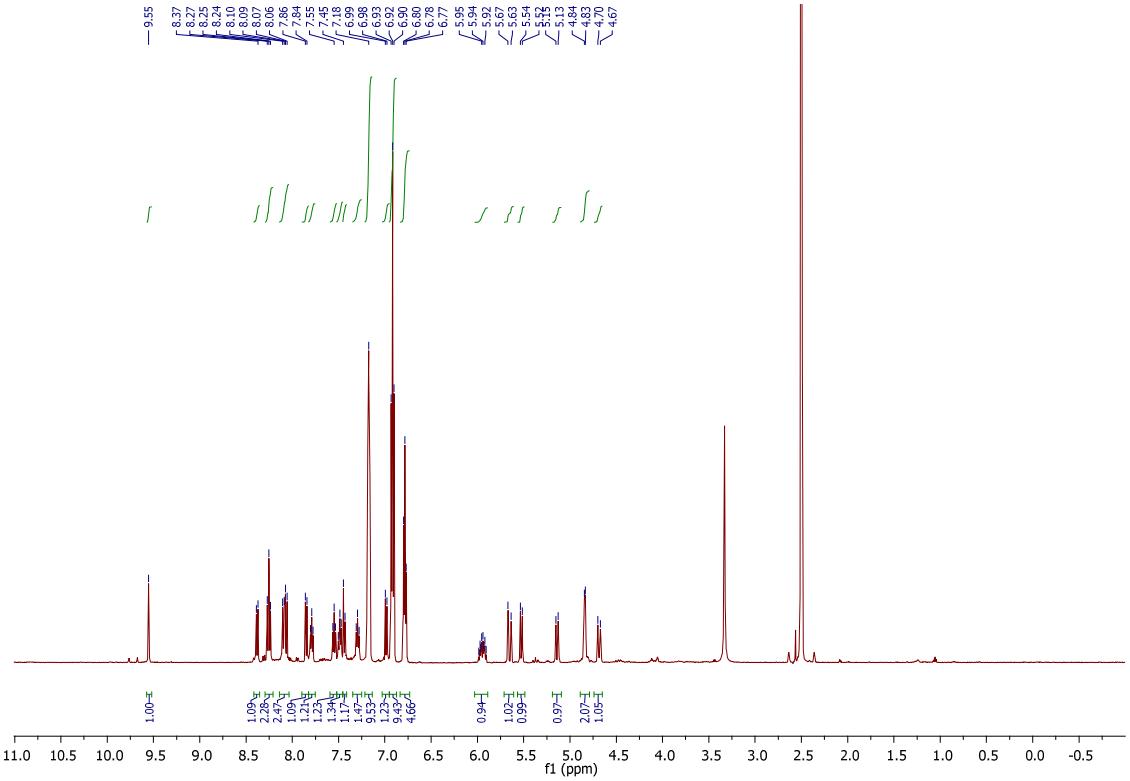

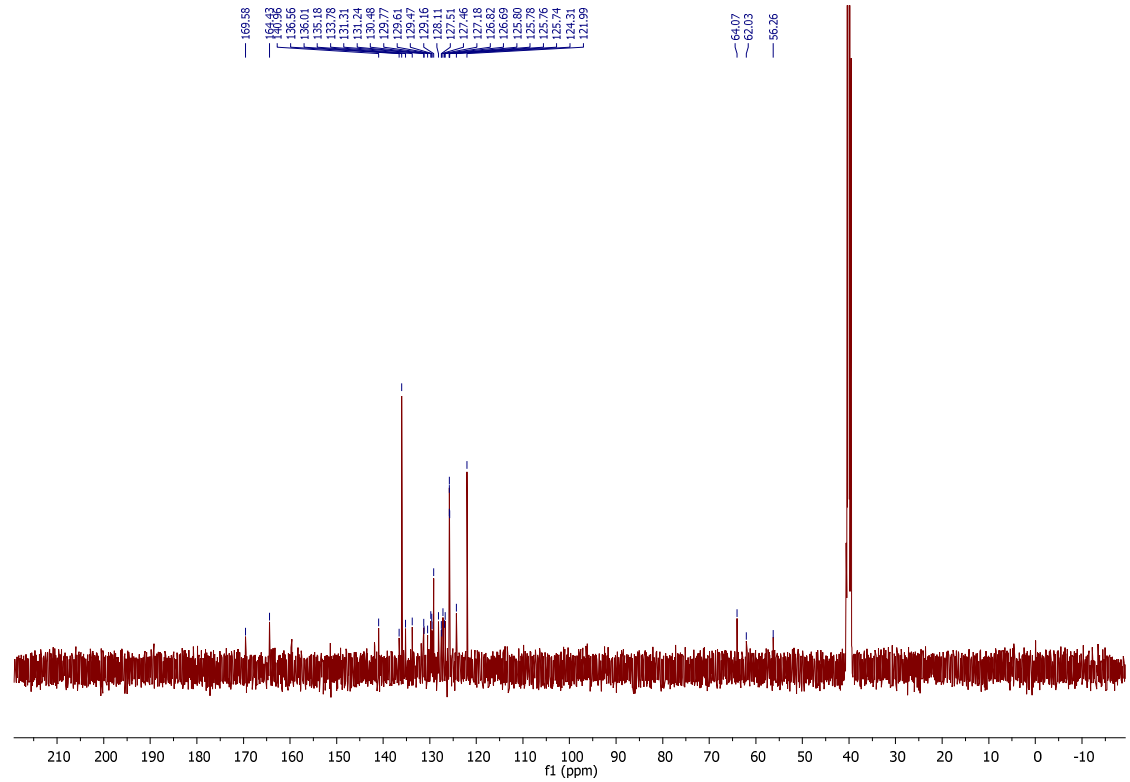

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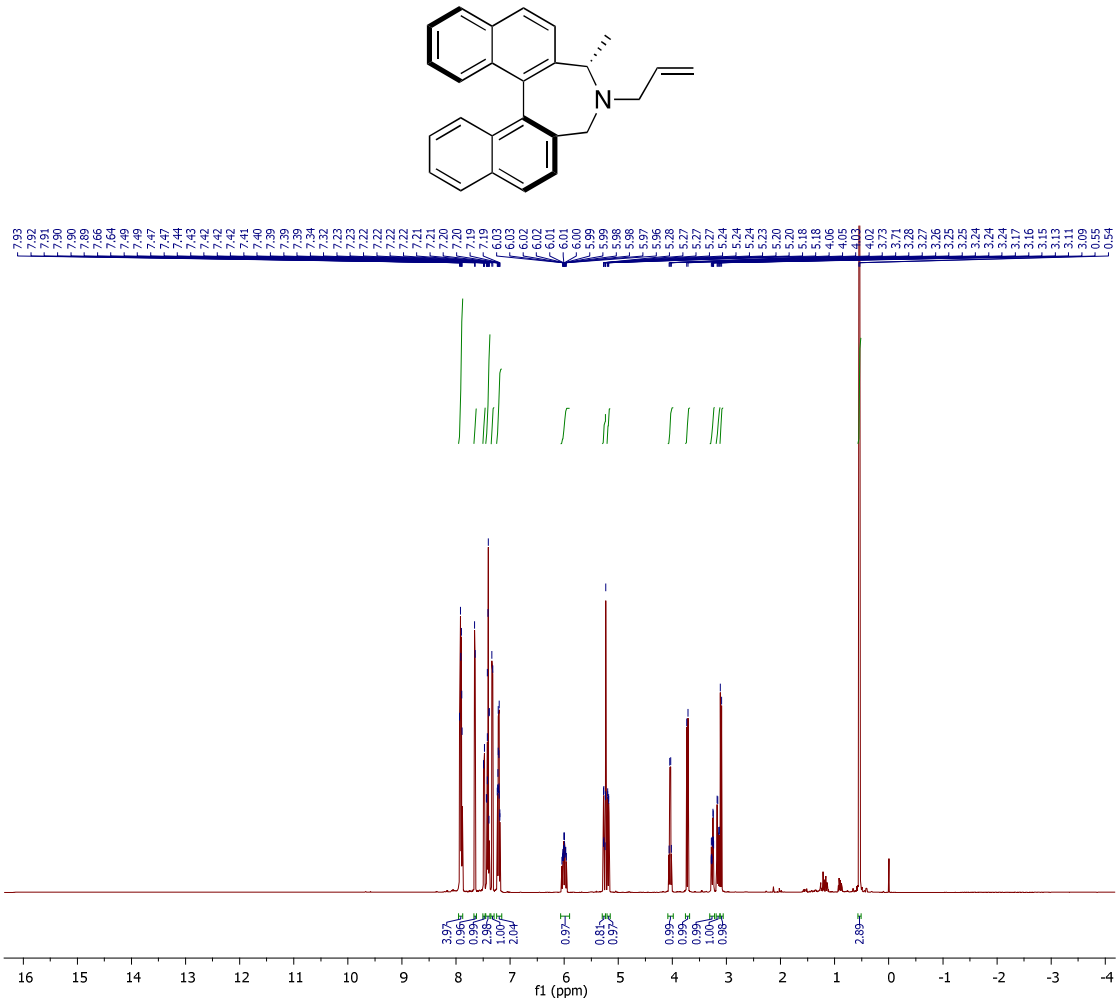

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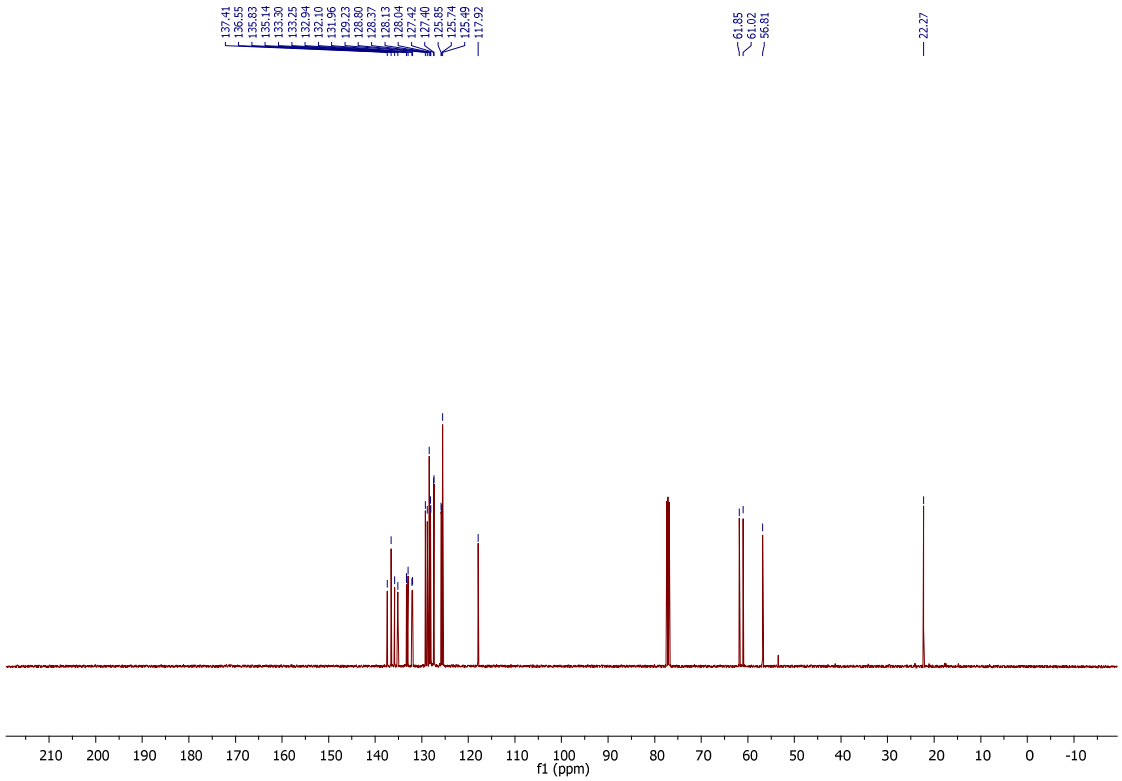
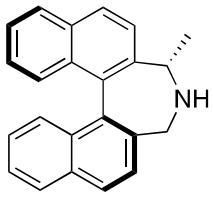


(+)-(3*S*,11cS)-3-Methyl-4,5-dihydro-3H-dinaphtho[2,1-c:1',2'-e]azepine



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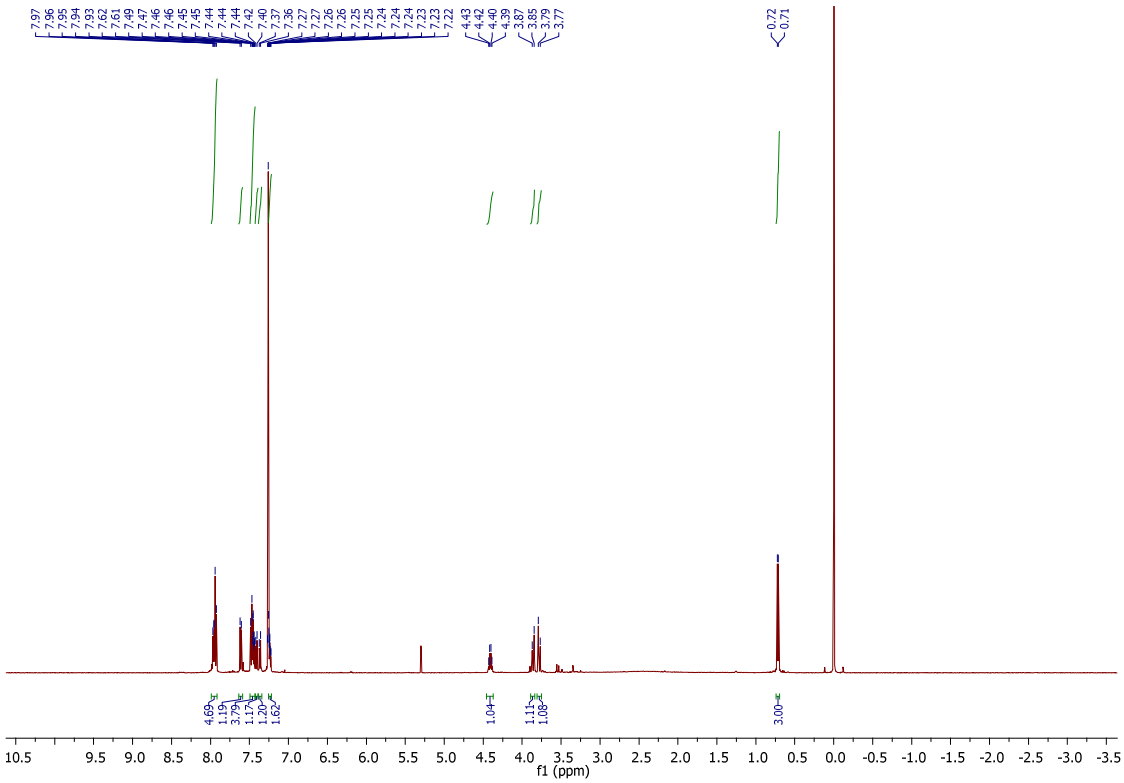

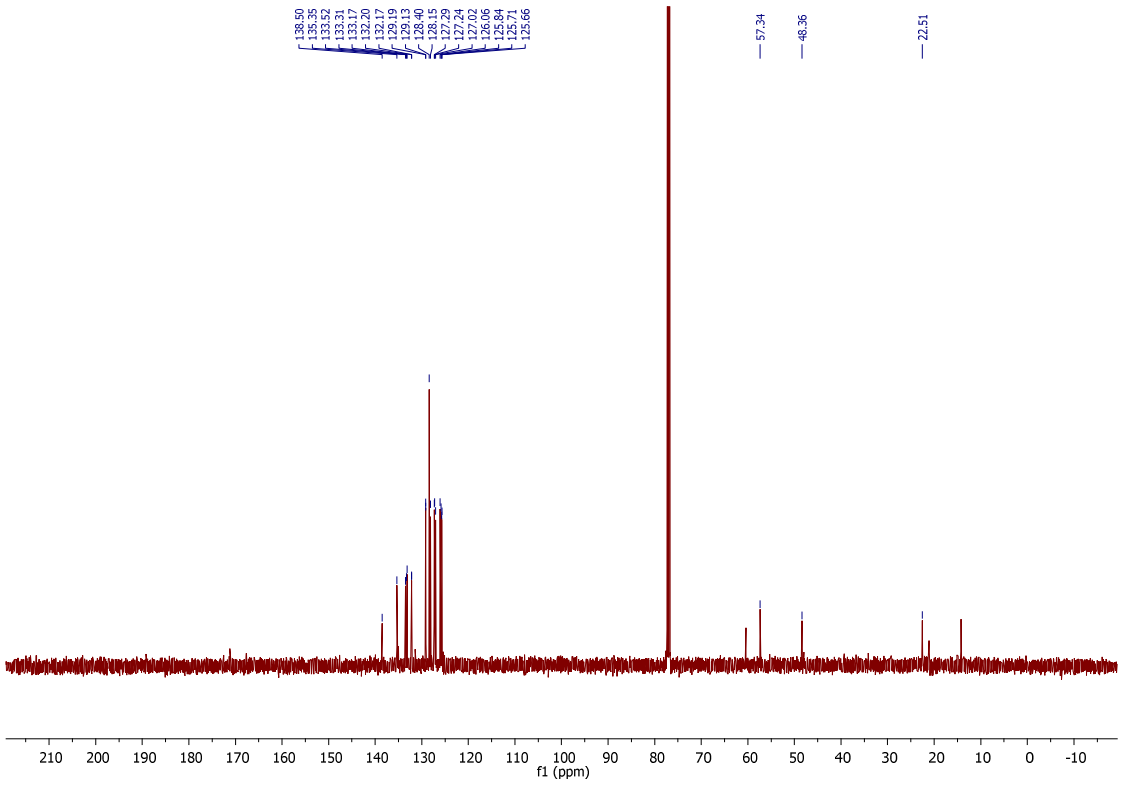

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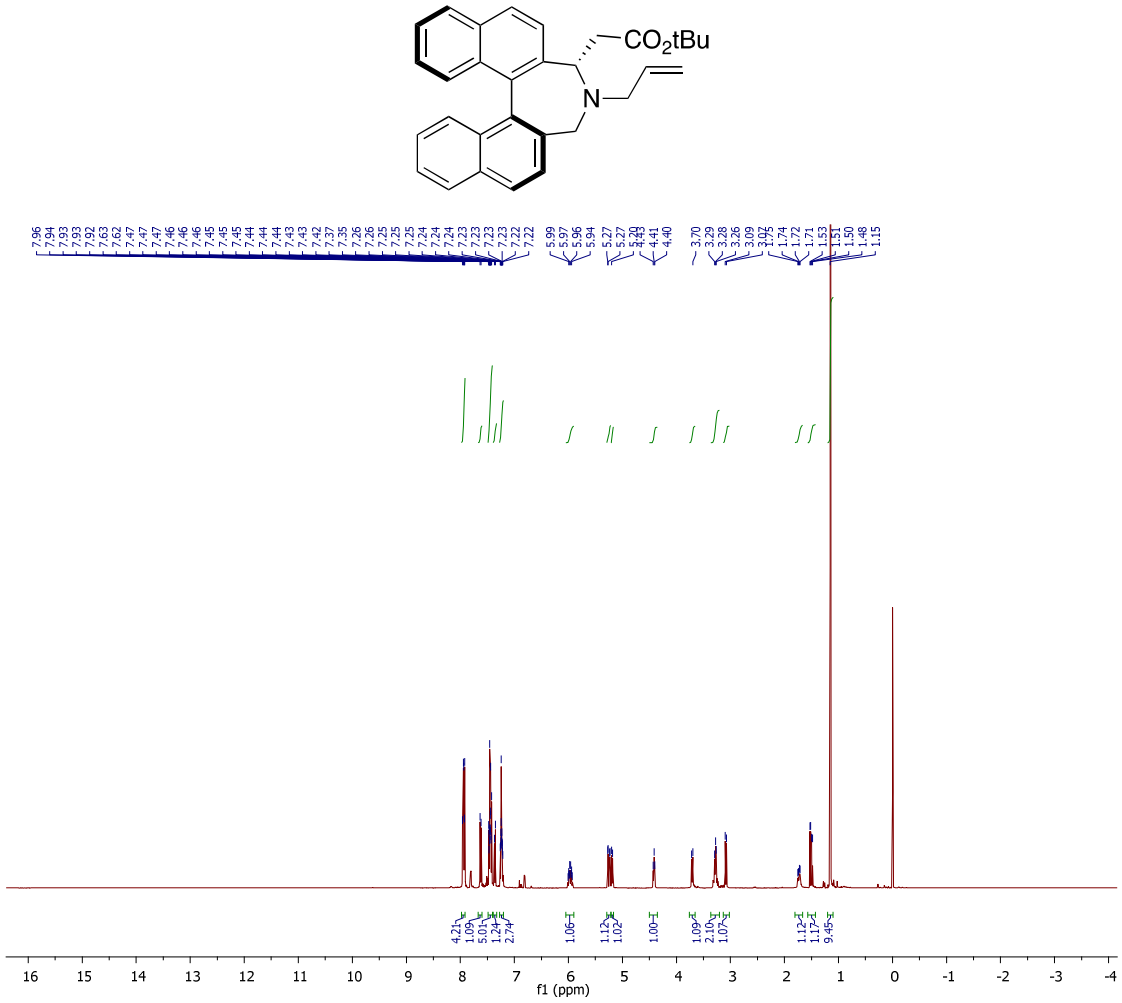
tert-Butyl 2-((3S,11cS)-4-allyl-4,5-dihydro-3H-dinaphtho[2,1-c:1',2'-e] azepin-3-yl) acetate (+)-28



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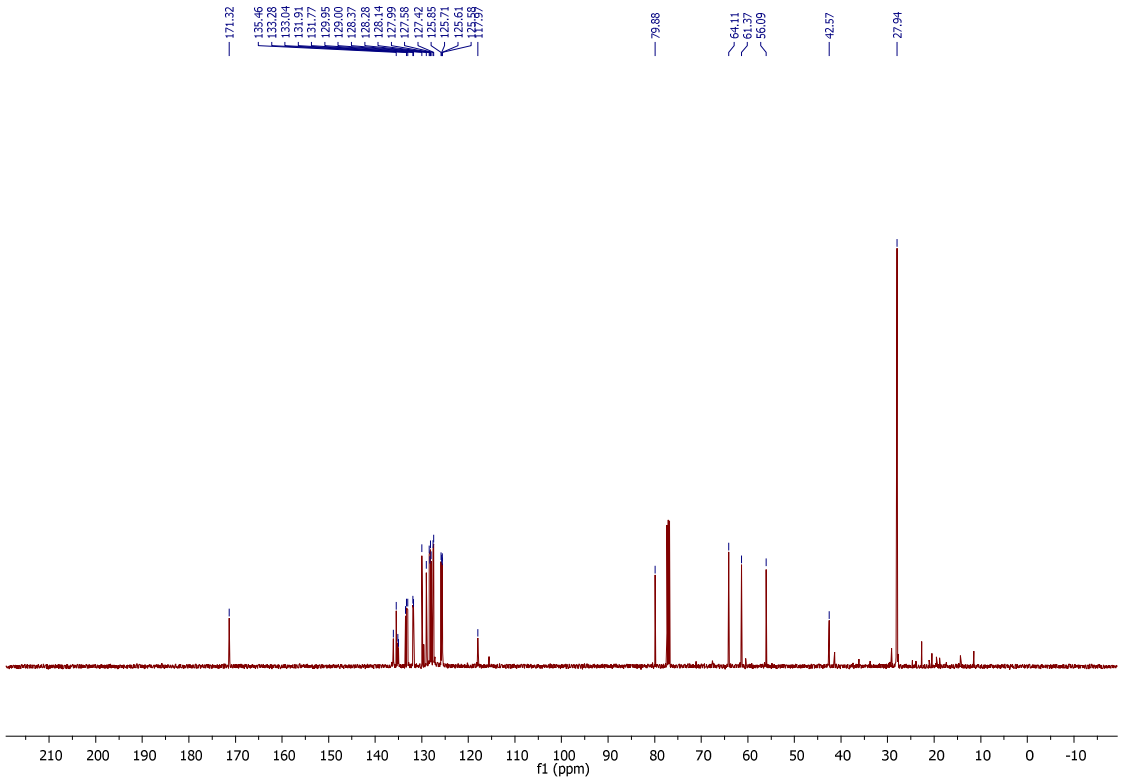
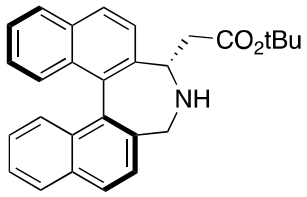


***tert*-Butyl 2-((3S,11cS)-4,5-dihydro-3H-dinaphtho[2,1-c:1',2'-e]azepin-3-yl) acetate (+)-30**



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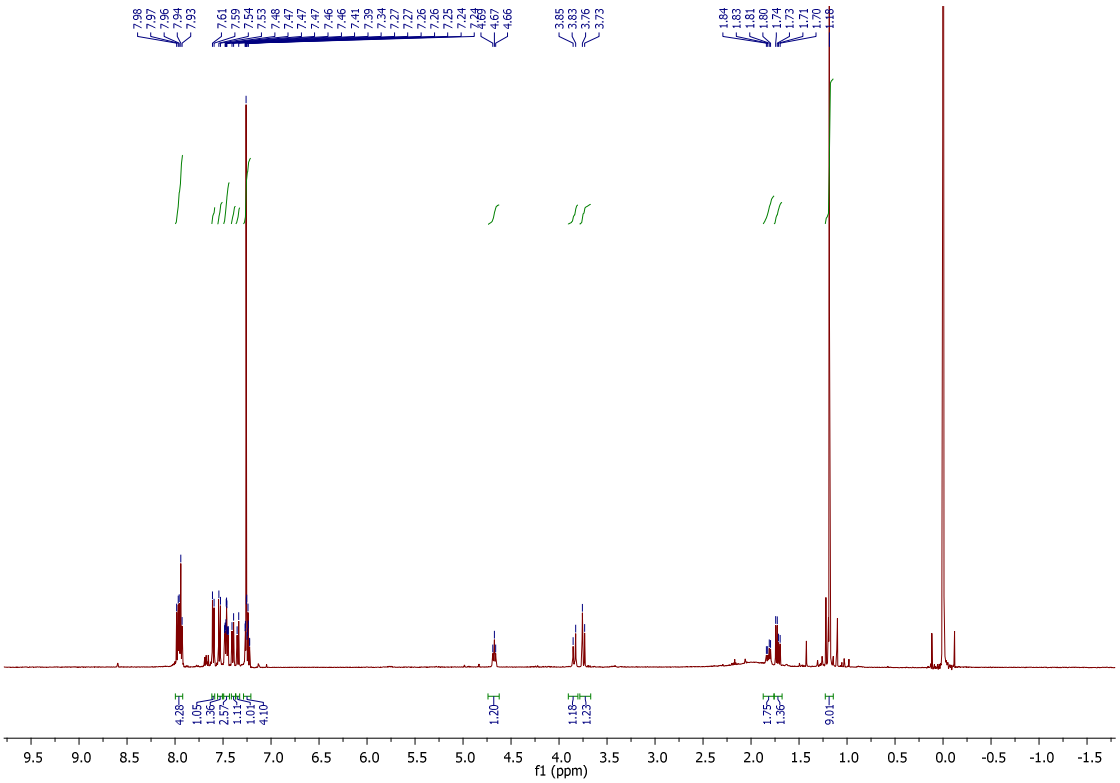

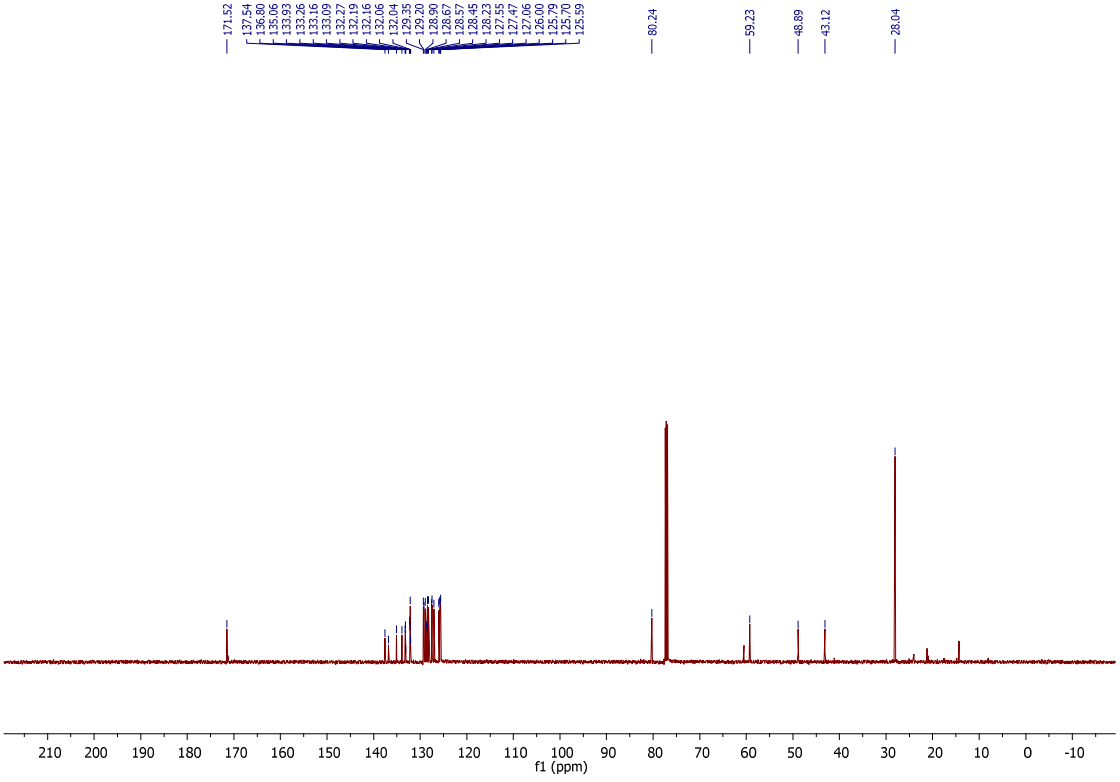

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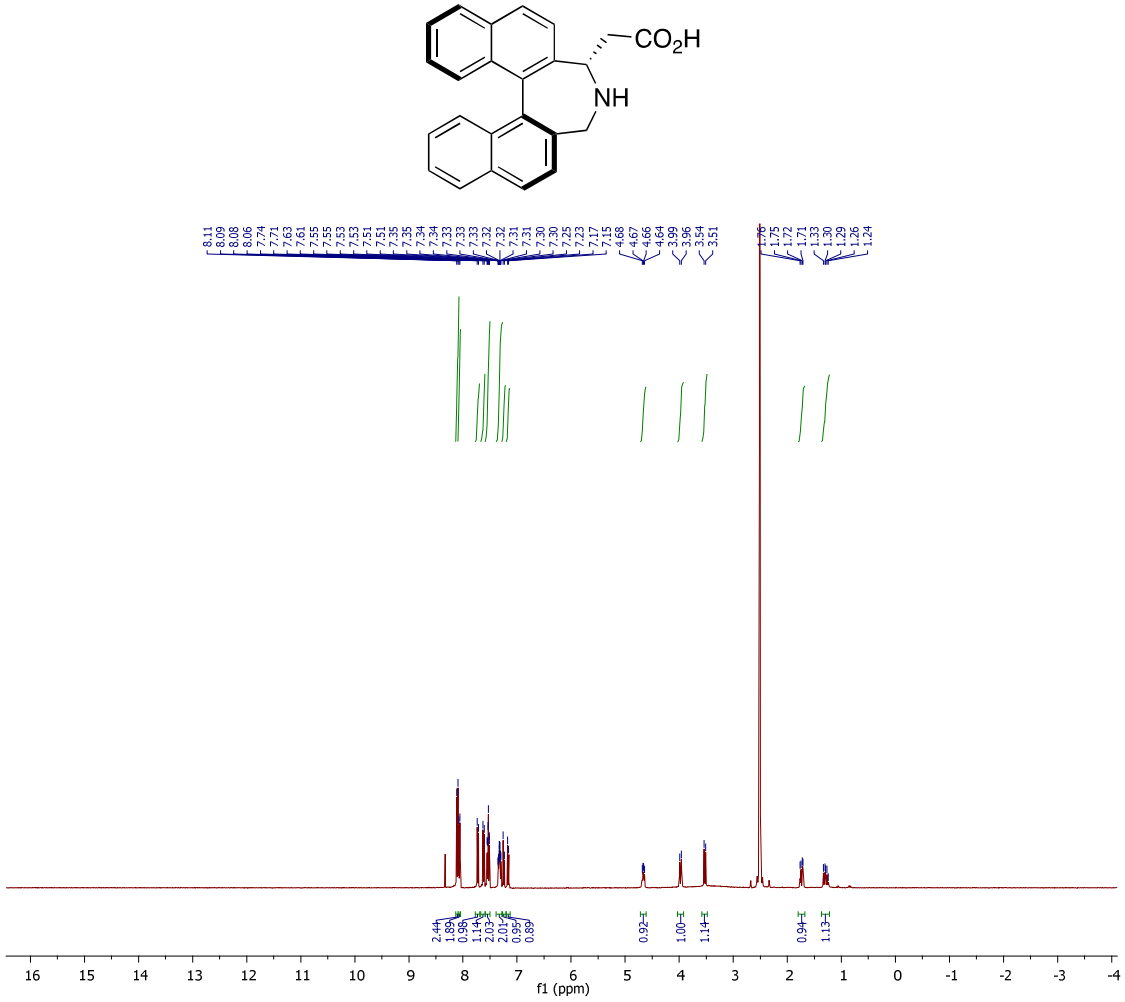
2-((3S,11cS)-4,5-dihydro-3H-dinaphtho[2,1-c:1',2'-e]azepin-3-yl)acetic acid (+)-32



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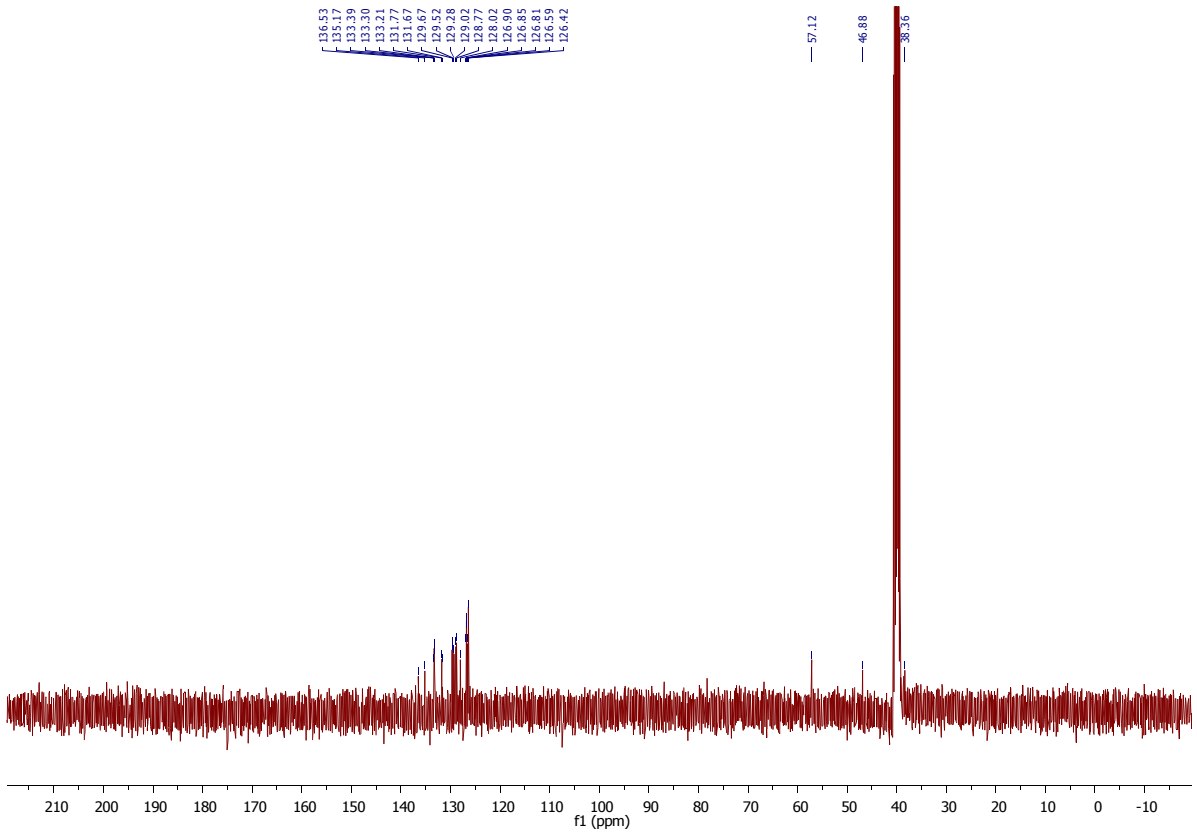
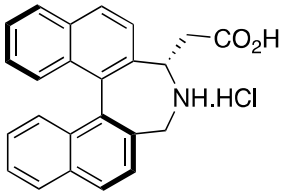


2-((3S,11cS)-4,5-Dihydro-3H-dinaphtho[2,1-c:1',2'-e]azepin-3-yl)acetic acid (+)-32.HCl



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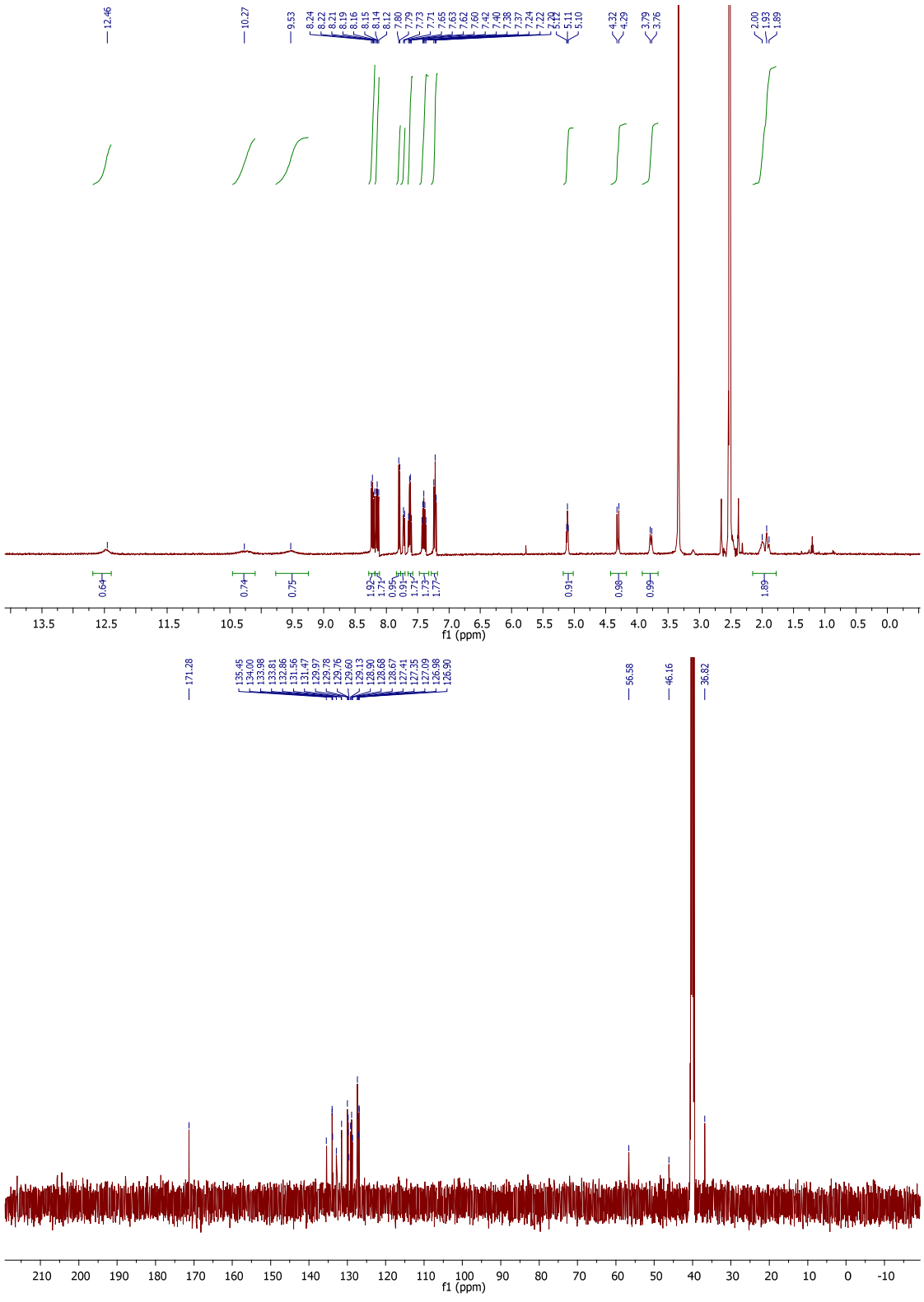

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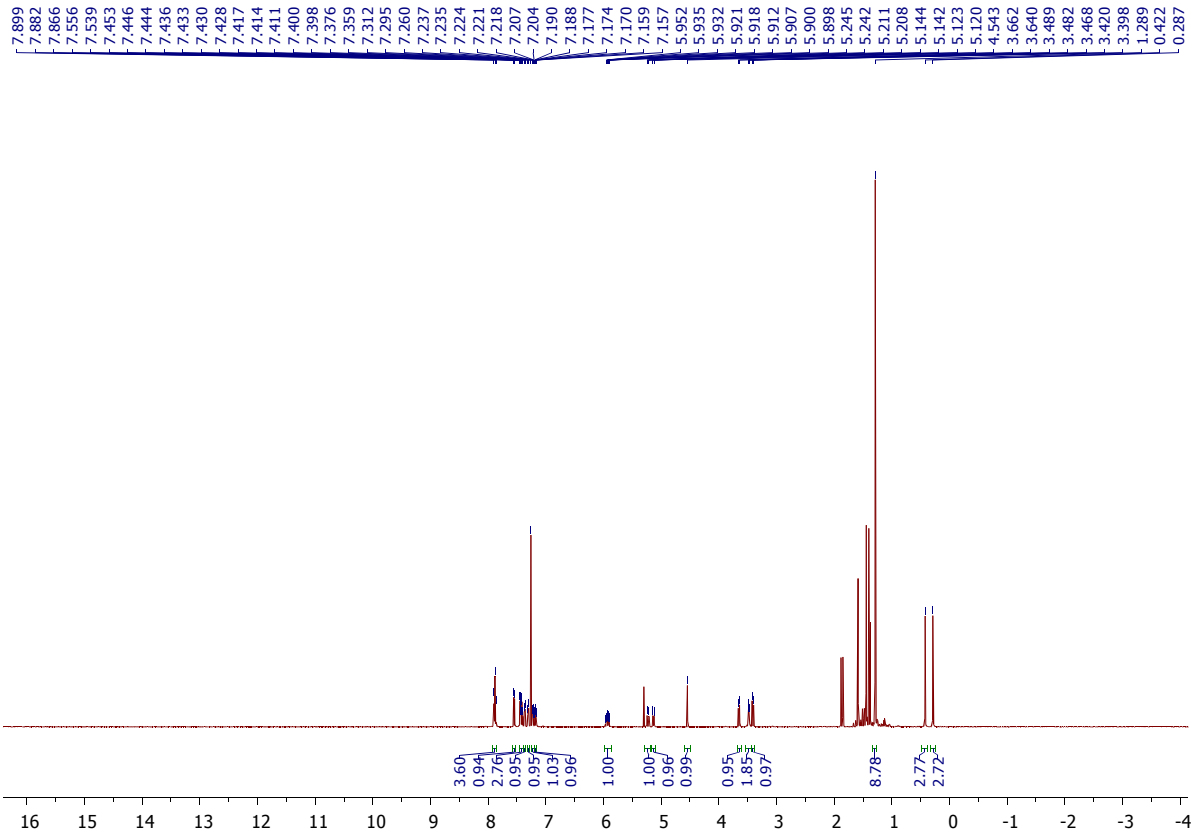
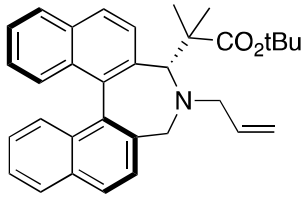
tert-Butyl 2-((3R,11cS)-4-allyl-4,5-dihydro-3H-dinaphtho[2,1-c:1',2'-e]azepin-3-yl)-2-methylpropanoate (+)-29





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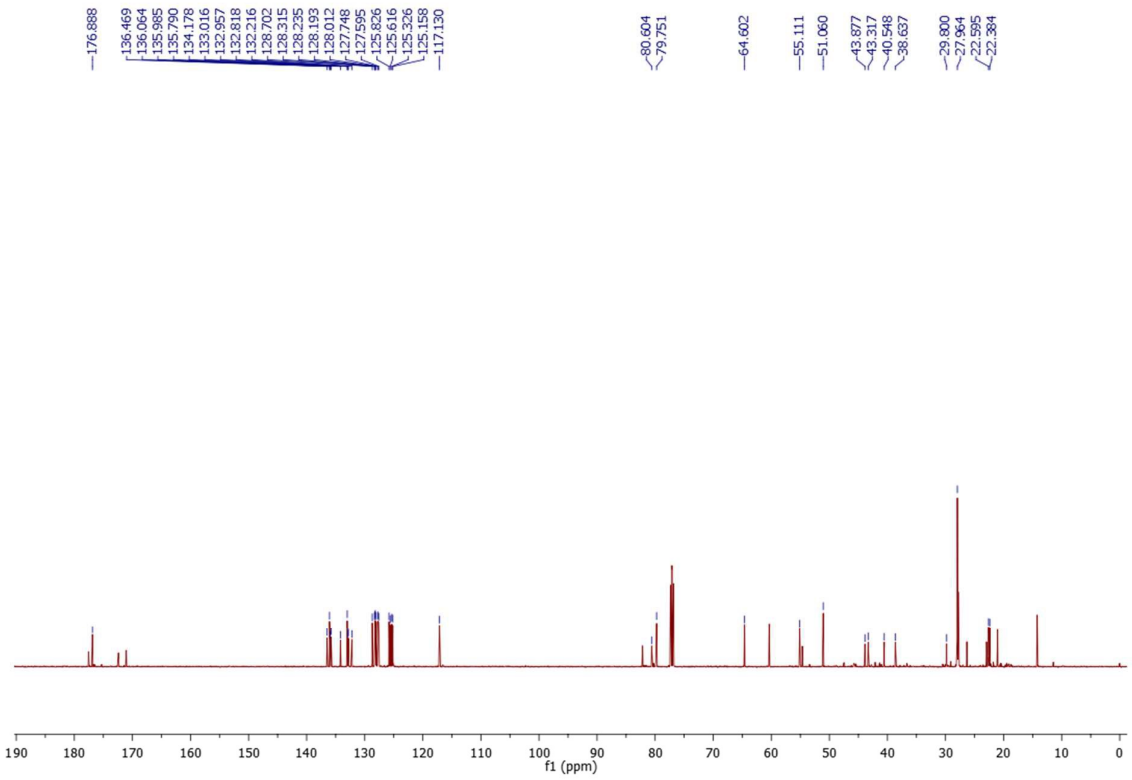
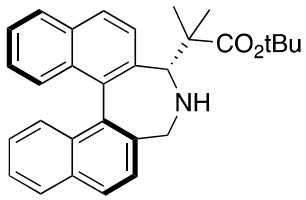


tert-Butyl 2-((3R,11cS)-4,5-dihydro-3H-dinaphtho[2,1-c:1',2'-e]azepin-3-yl)-2-methylpropanoate (+)-31



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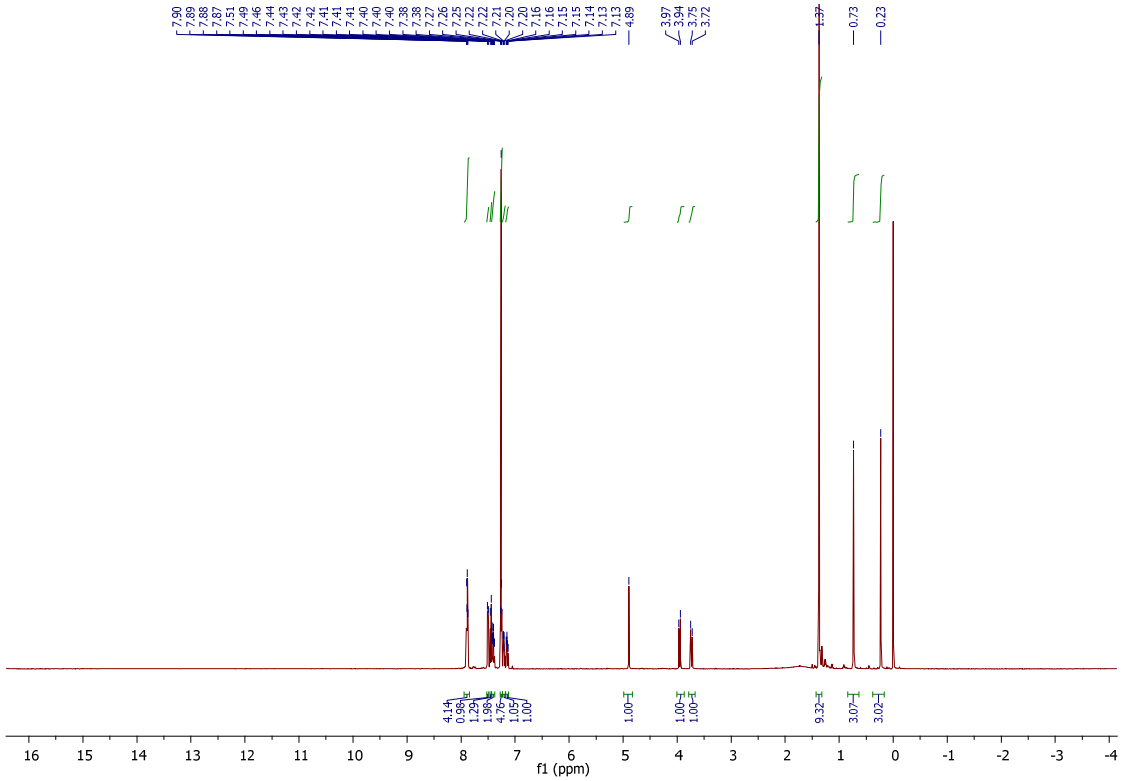

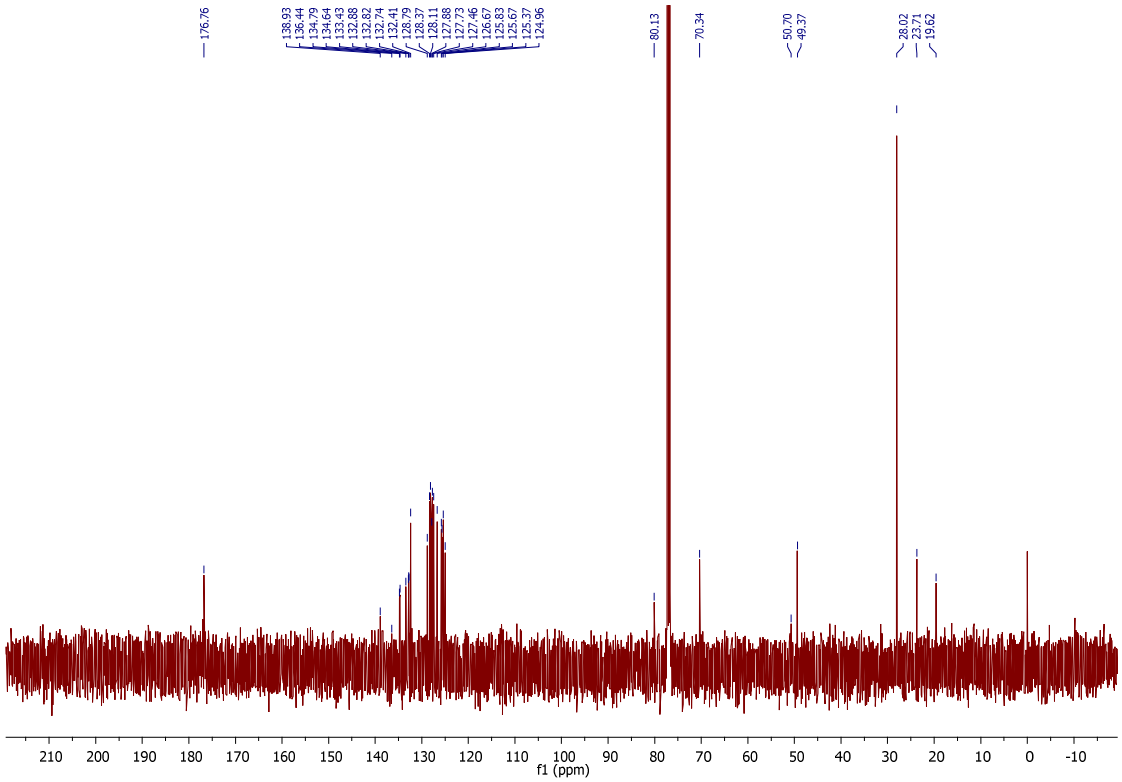

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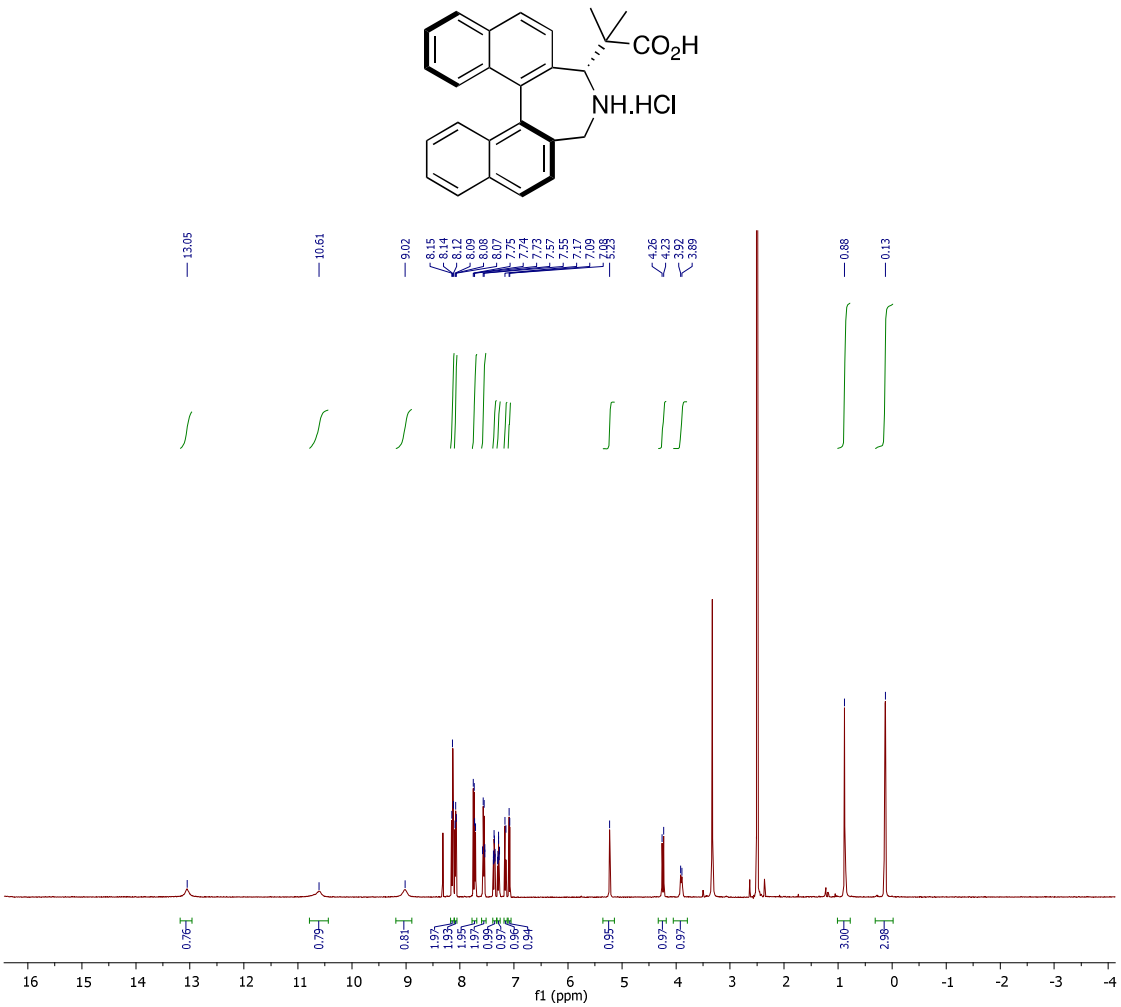
2-((3R,11cS)-4,5-Dihydro-3H-dinaphtho[2,1-c:1',2'-e]azepin-3-yl)-2-methylpropanoic acid hydrochloride (+)-33.HCl



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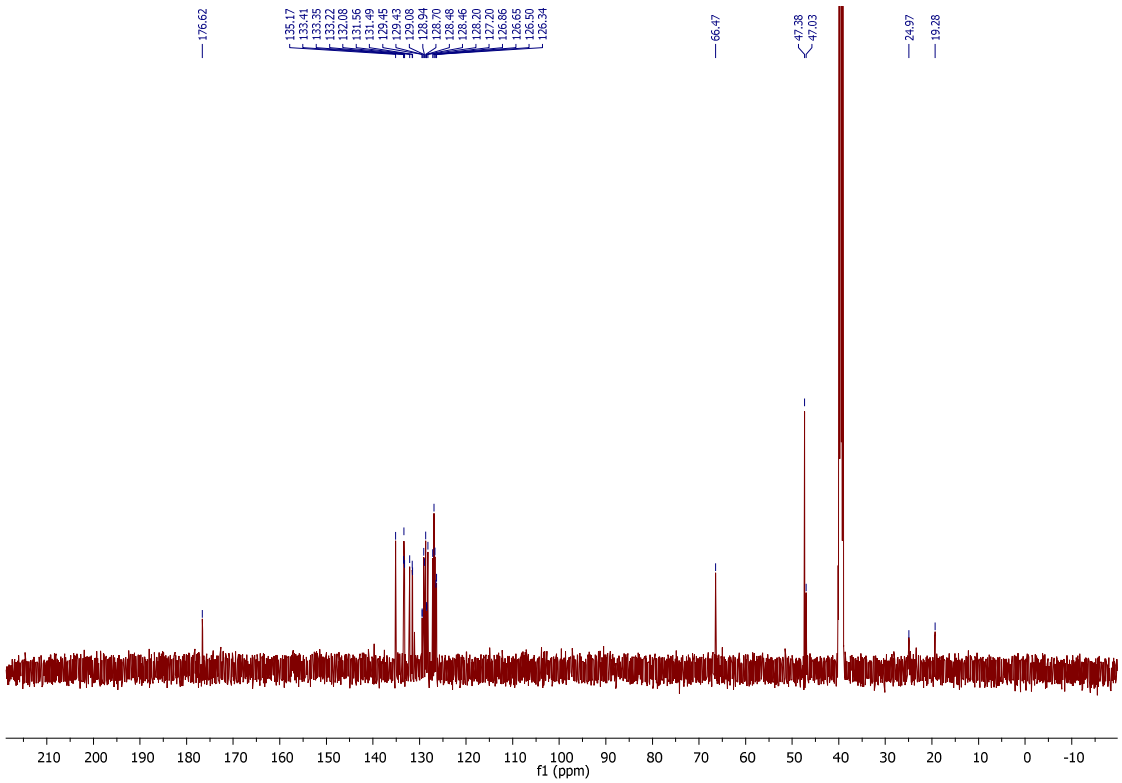
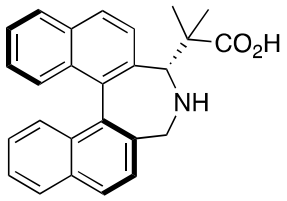


2-((3S,11cS)-4,5-dihydro-3H-dinaphtho[2,1-c:1',2'-e]azepin-3-yl)-2- methylpropanoic acid (+)-33



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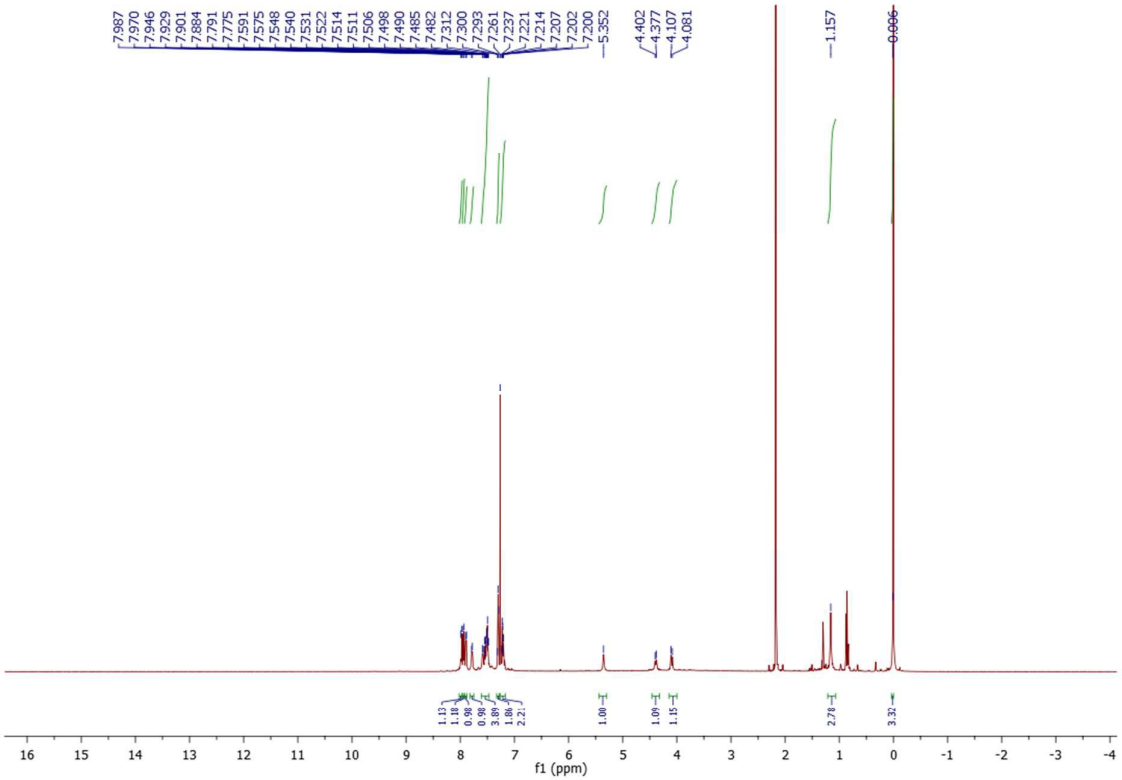

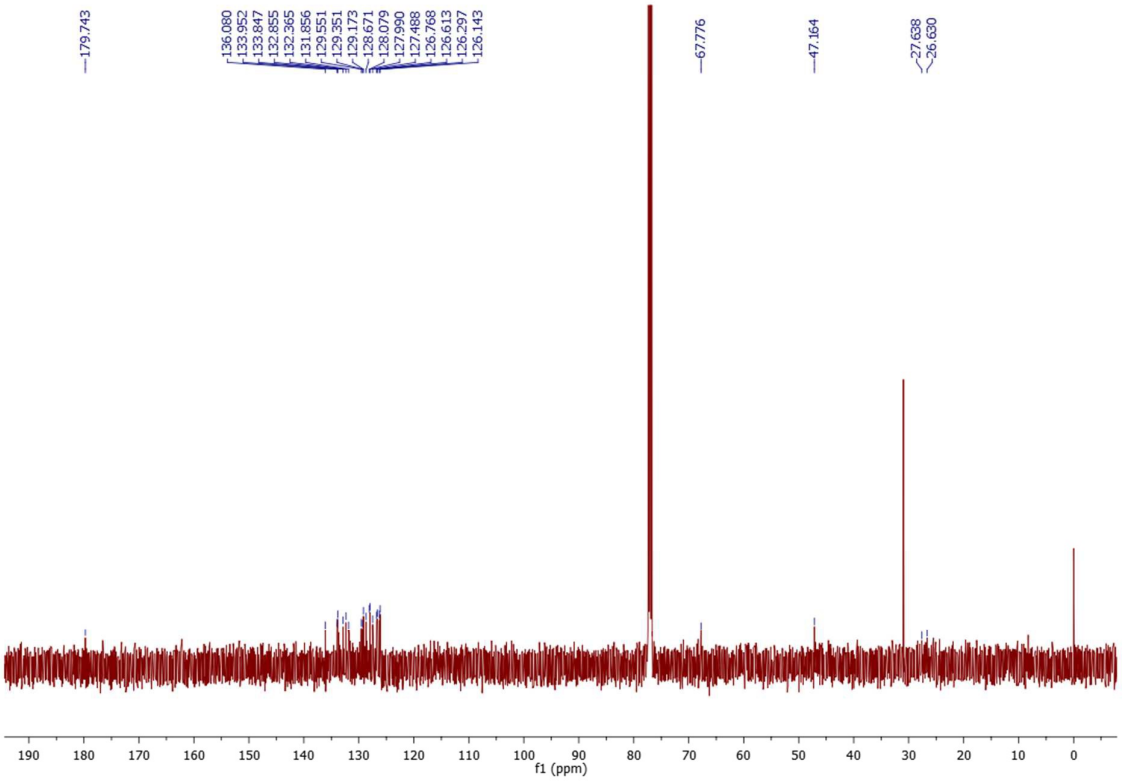

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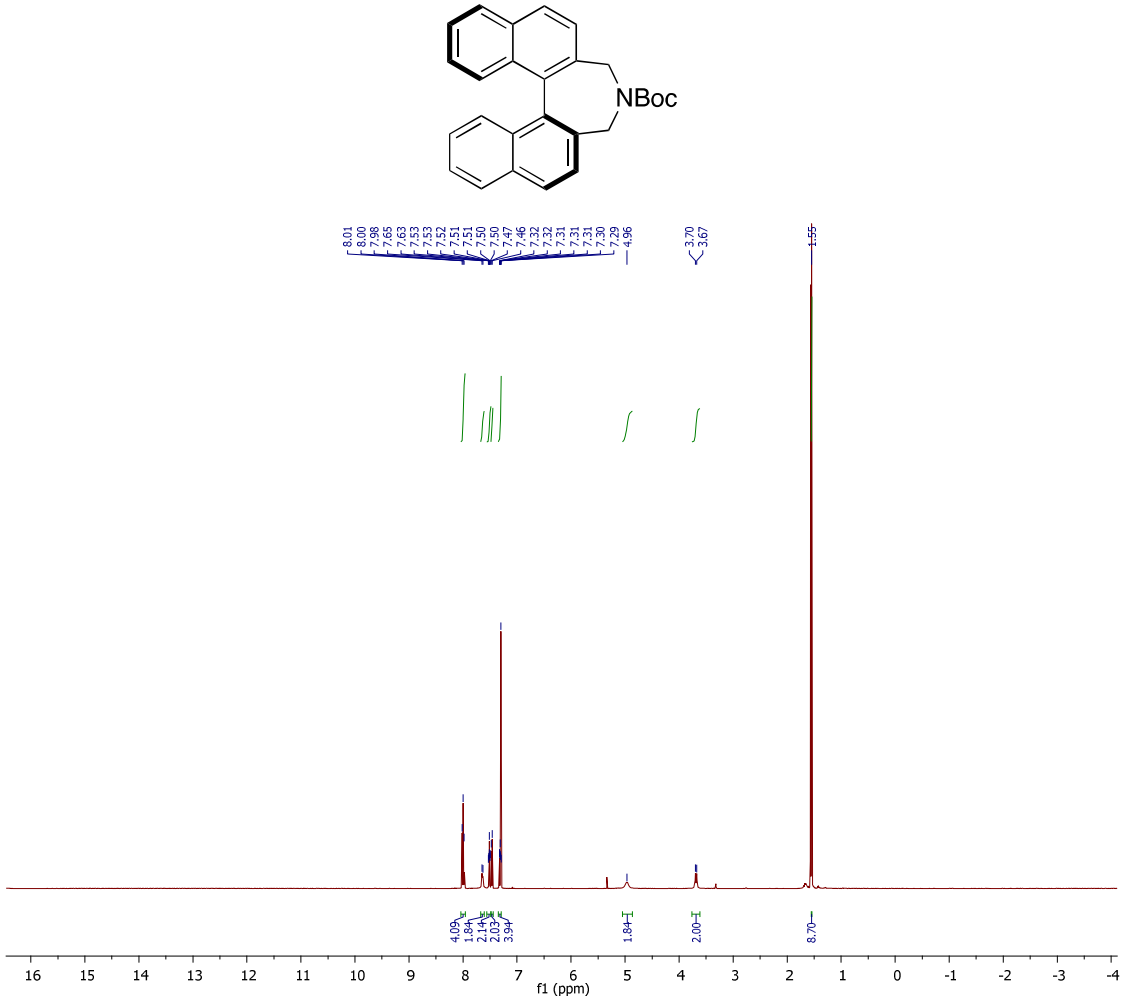
(*S*)-Tert-butyl 3H-dinaphtho[2,1-c:1',2'-e]azepine-4(5H)-carboxylate (–)-13



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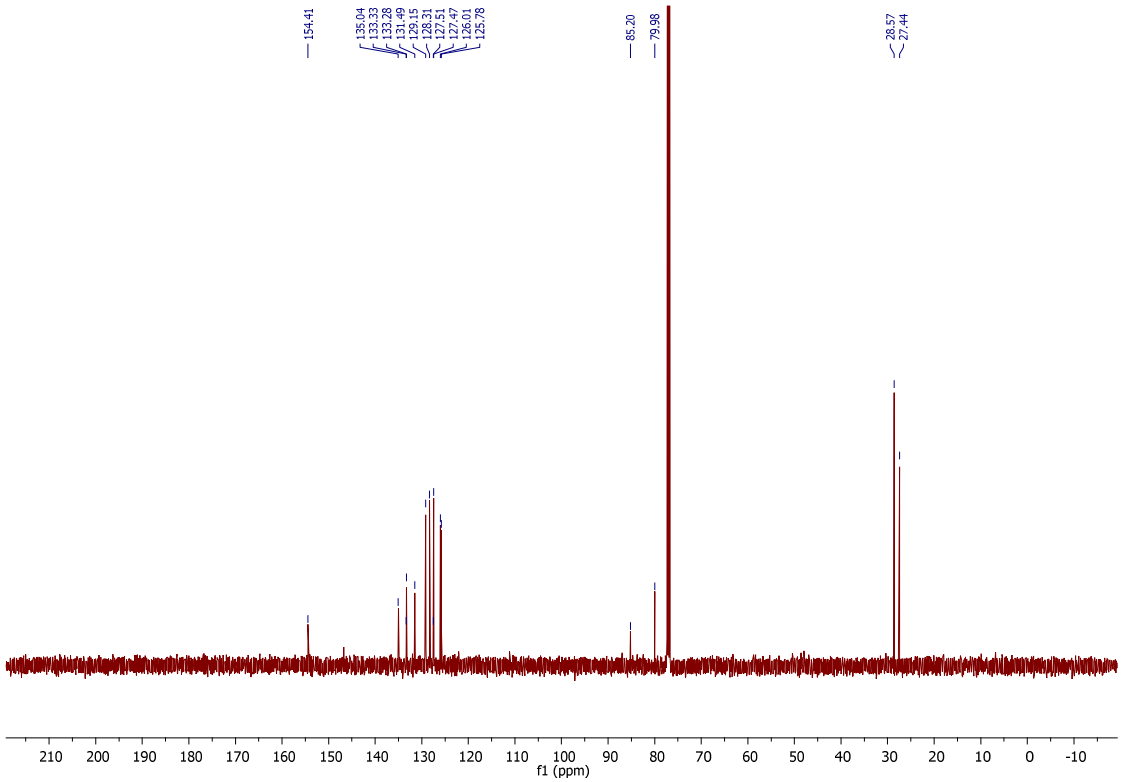
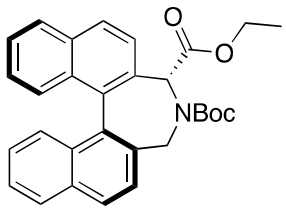


(3R,11cS)-4-Tert-butyl 3-ethyl 3H-dinaphtho[2,1-c:1',2'-e]azepine-3,4(5H)-dicarboxylate (–)-15



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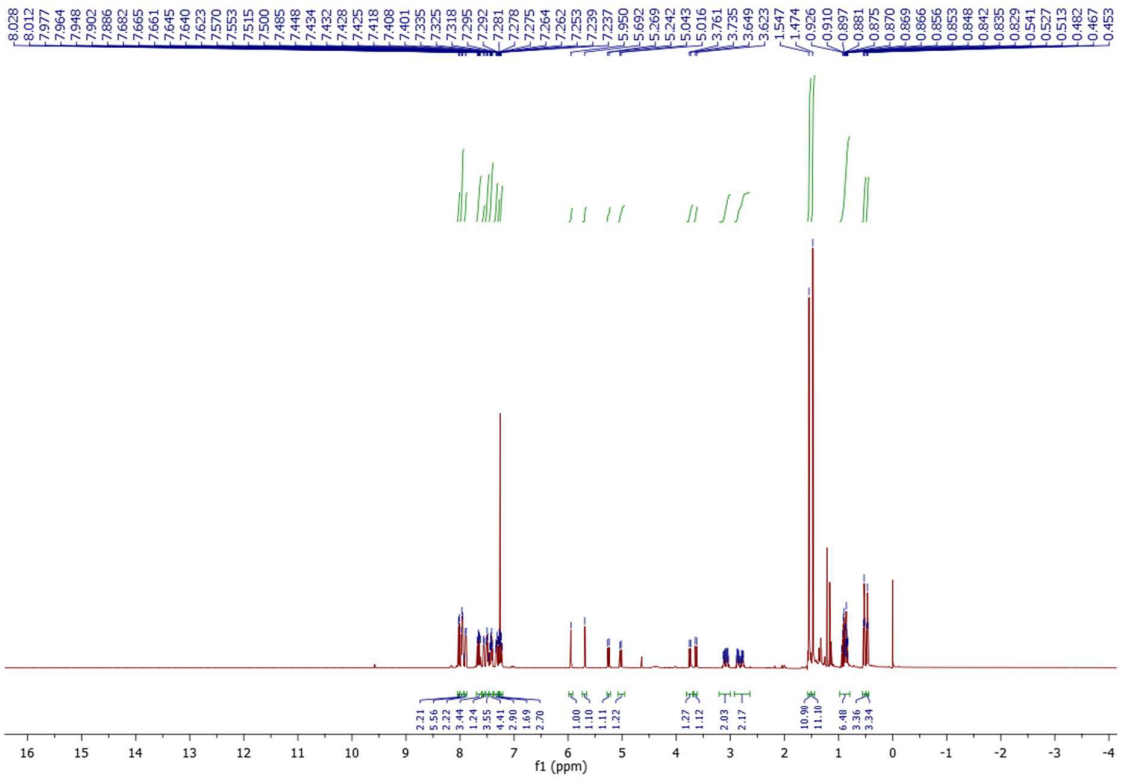

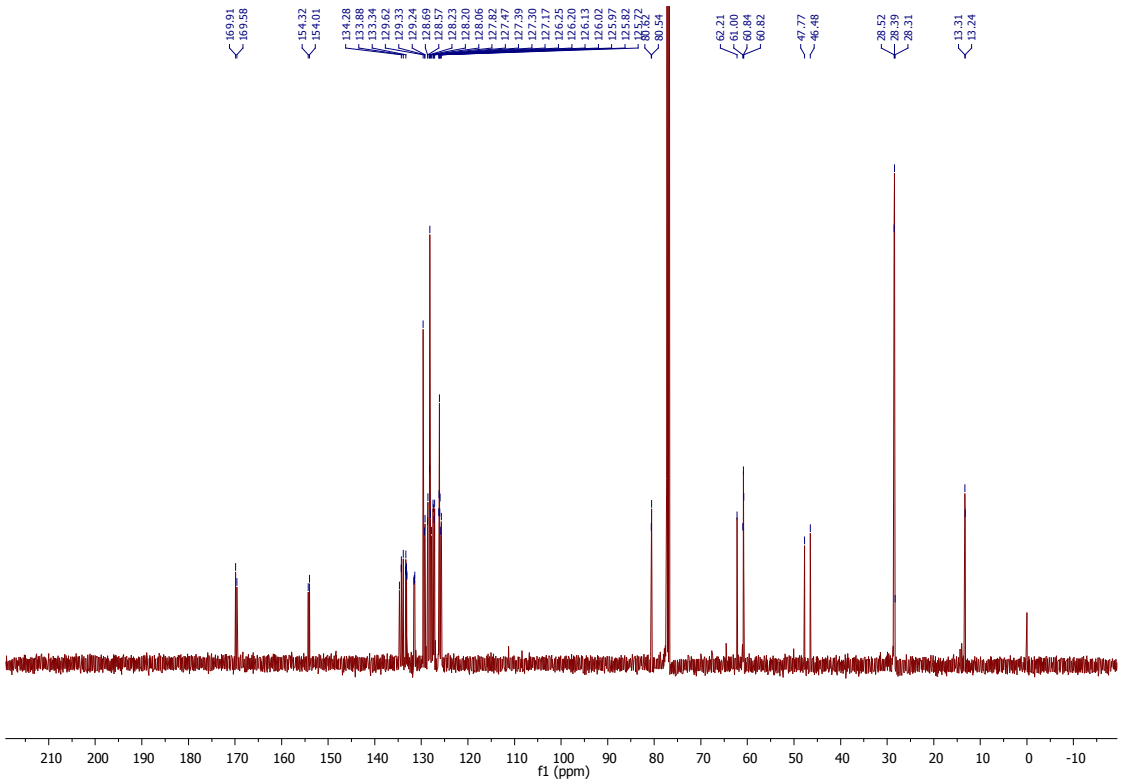

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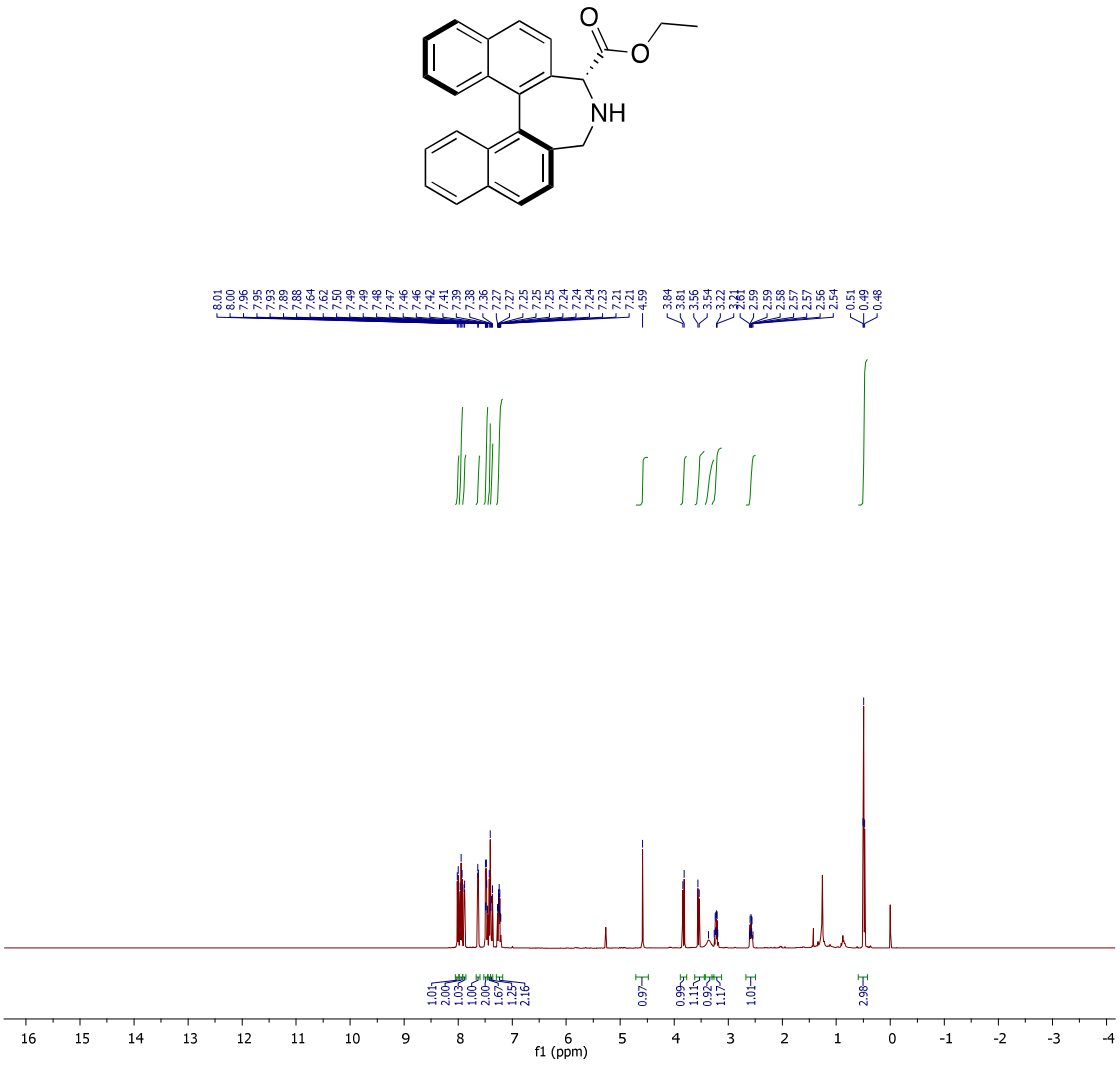
(3R,11cS)-Ethyl 4,5-dihydro-3H-dinaphtho[2,1-c:1',2'-e]azepine-3-carboxylate (+)-17



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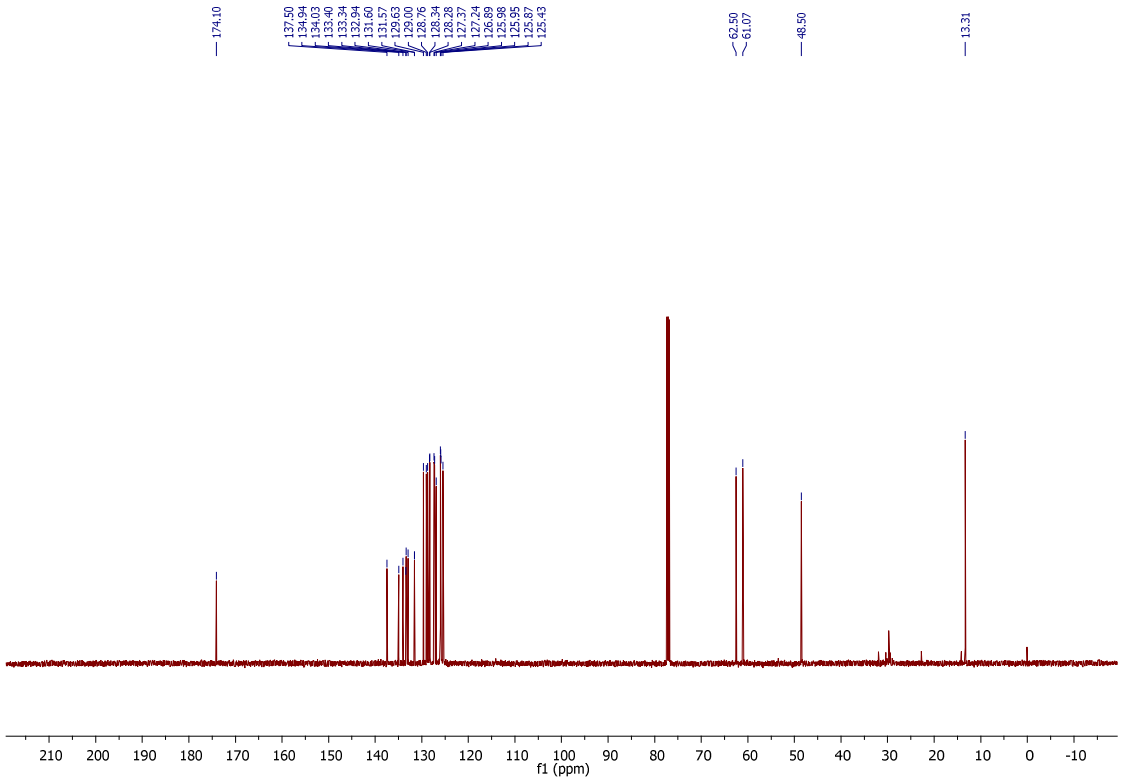
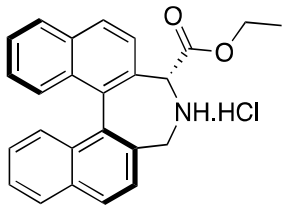


(3R,11cS)-Ethyl 4,5-dihydro-3H-dinaphtho[2,1-c:1',2'-e]azepine-3-carboxylate hydrochloride (+)-17.HCl



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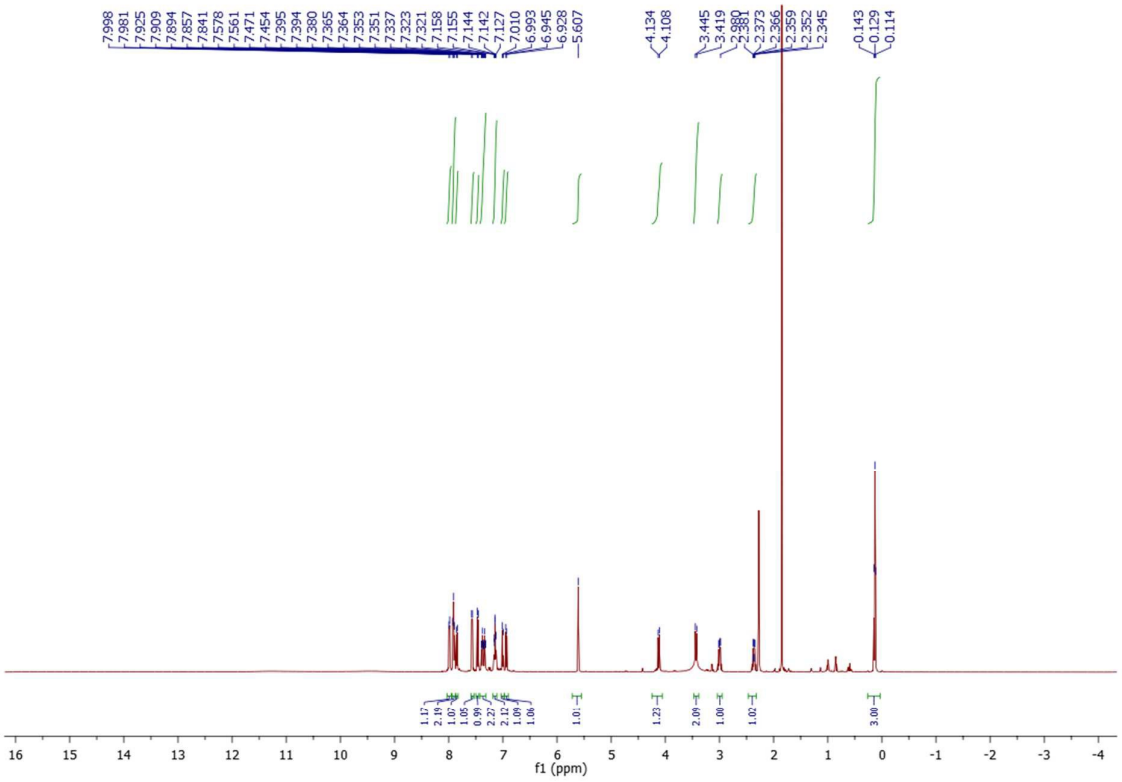

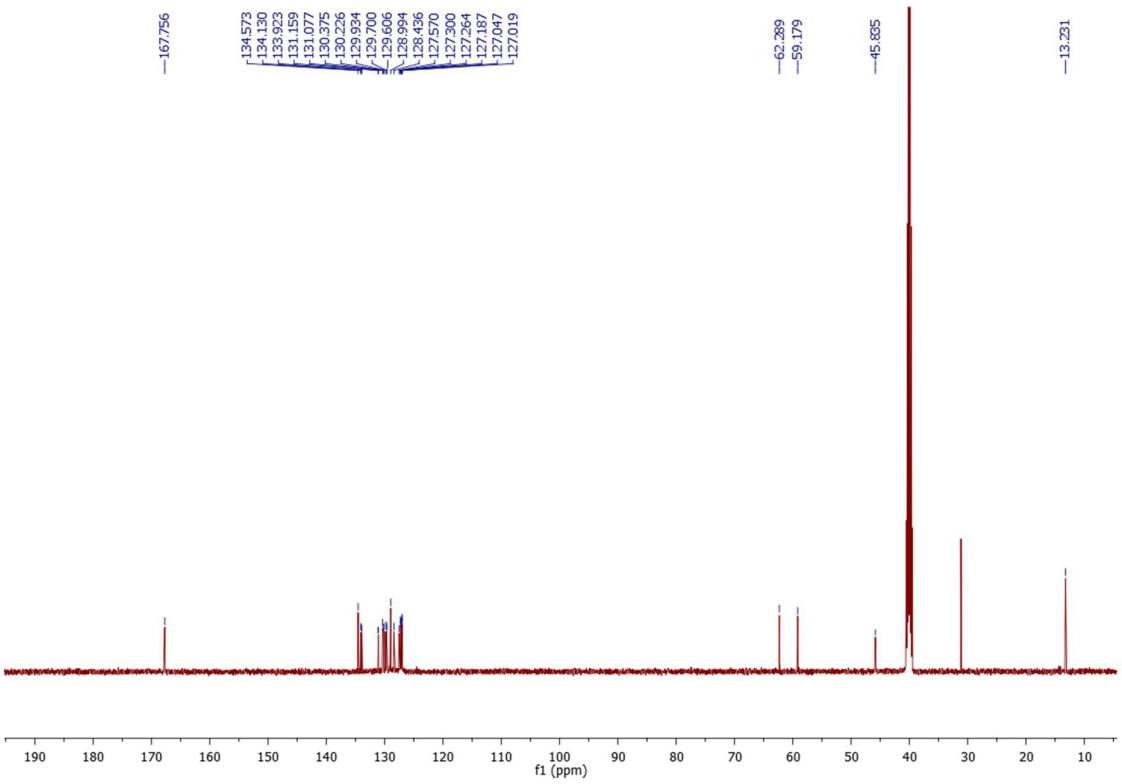

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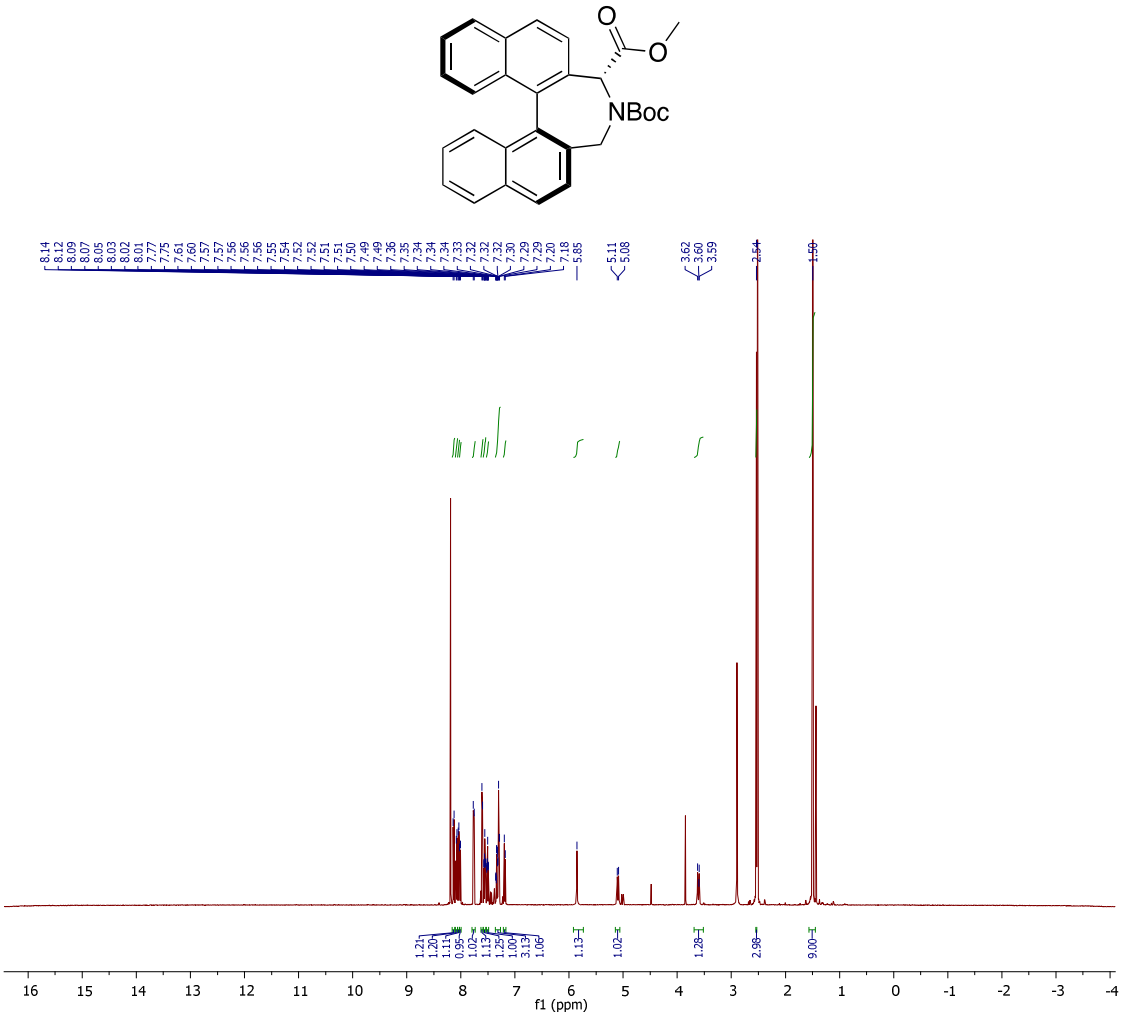
(3R,11cS)-4-Tert-butyl 3-methyl 3H-dinaphtho[2,1-c:1',2'-e]azepine-3,4(5H)-dicarboxylate (–)-14



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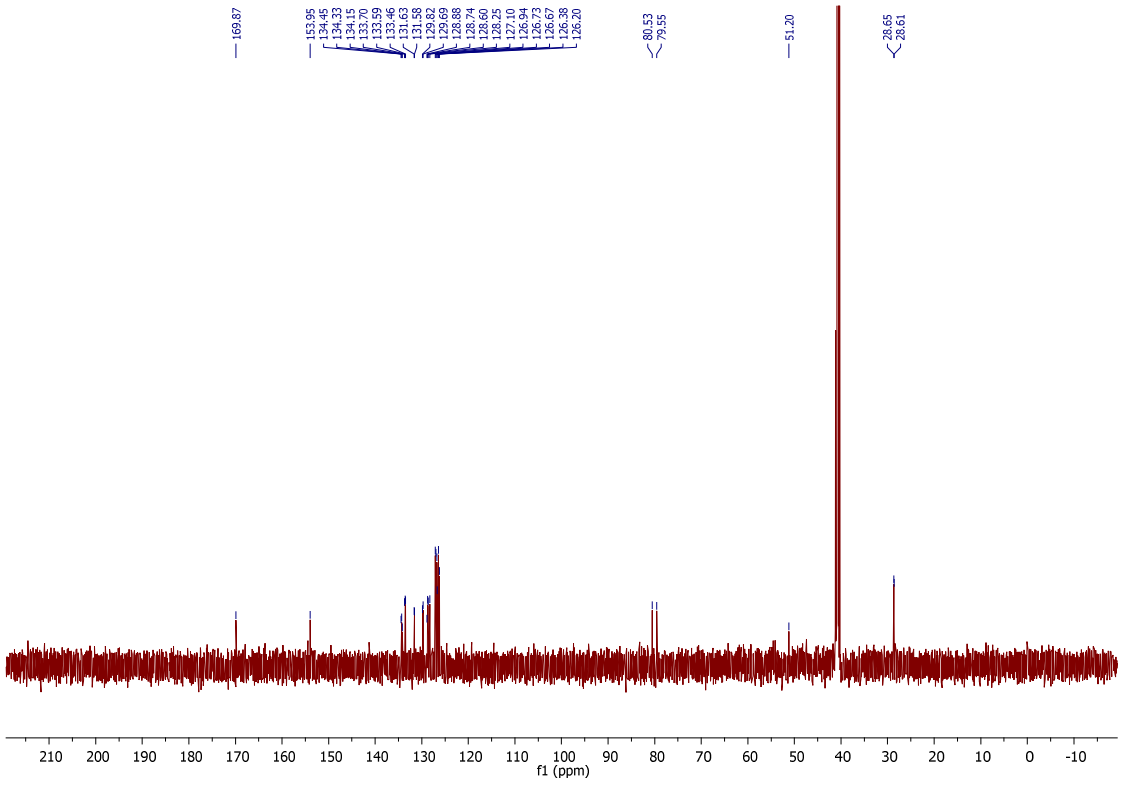
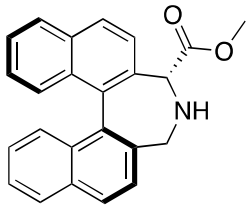


(3R,11cS)-Methyl 4,5-dihydro-3H-dinaphtho[2,1-c:1',2'-e]azepine-3-carboxylate (+)-16



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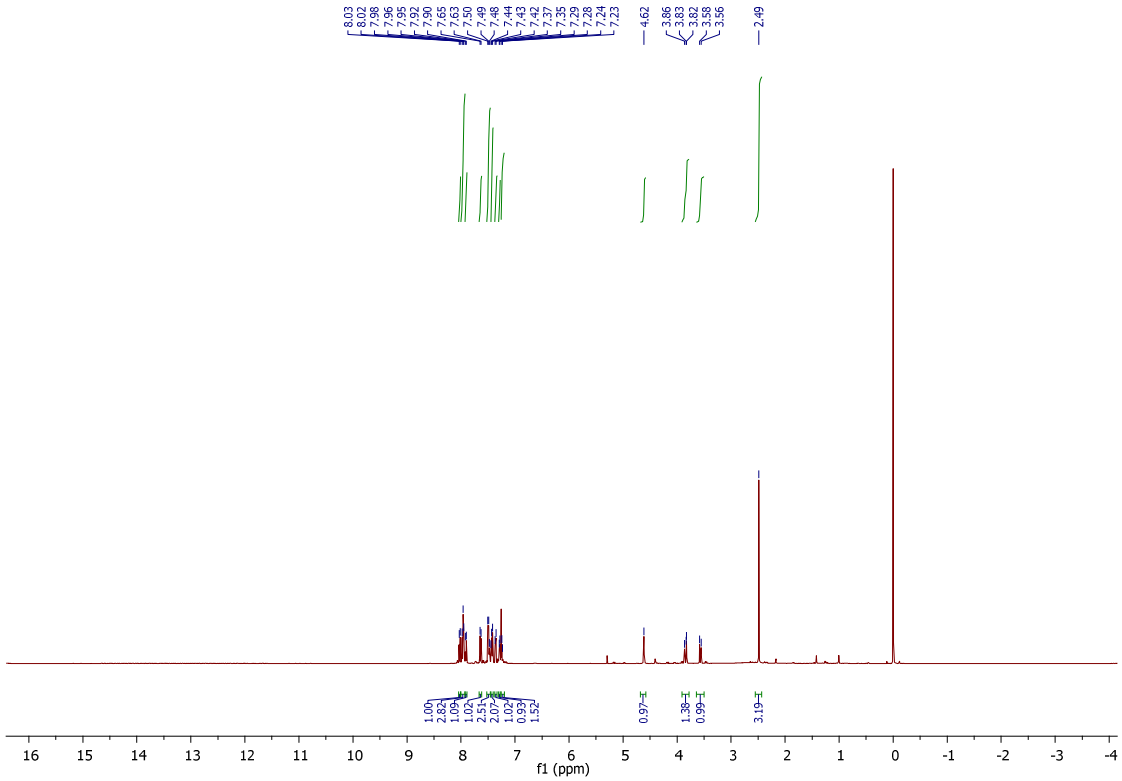

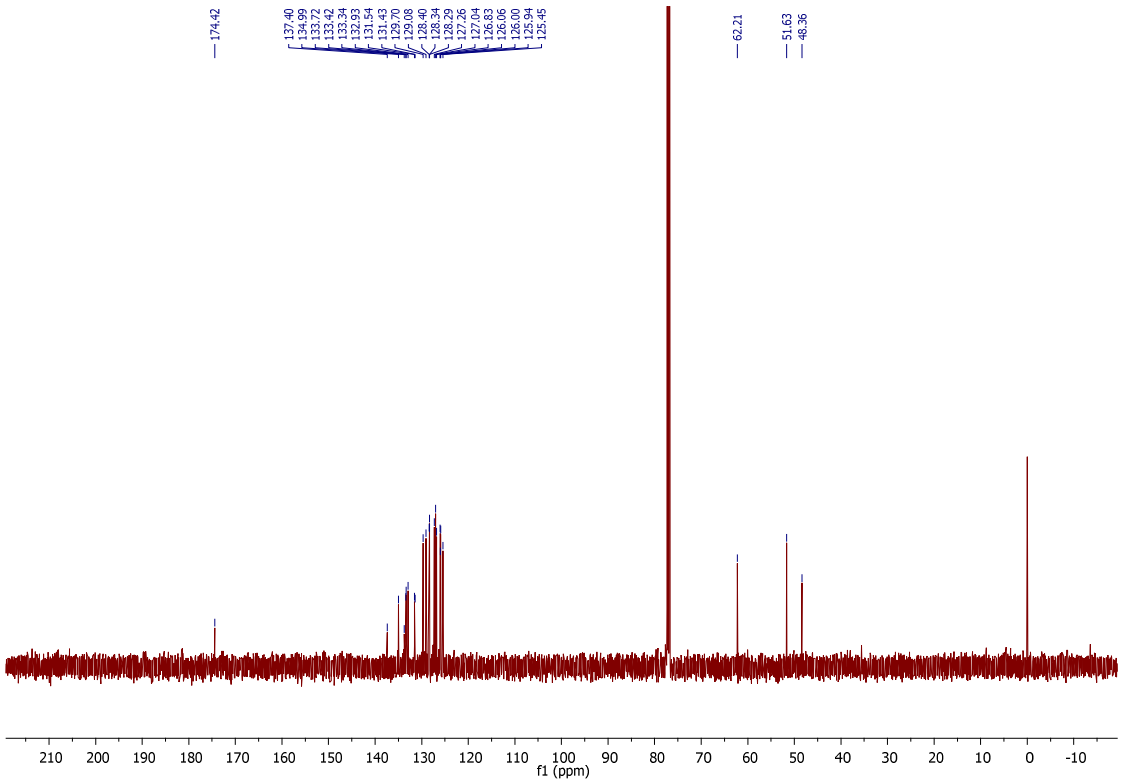

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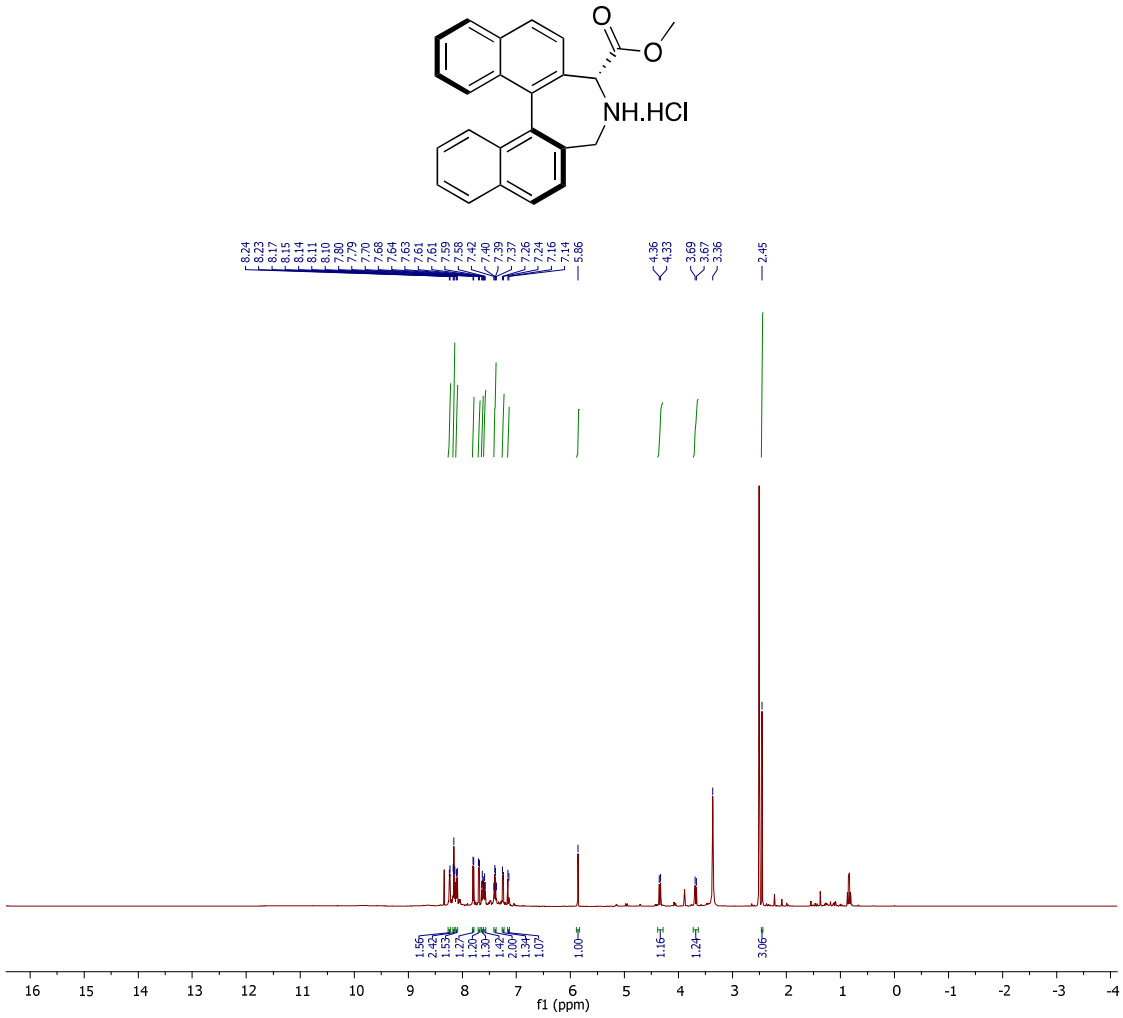
3R,11cS)-Methyl 4,5-dihydro-3H-dinaphtho[2,1-c:1',2'-e]azepine-3-carboxylate hydrochloride (+)-16.HCl



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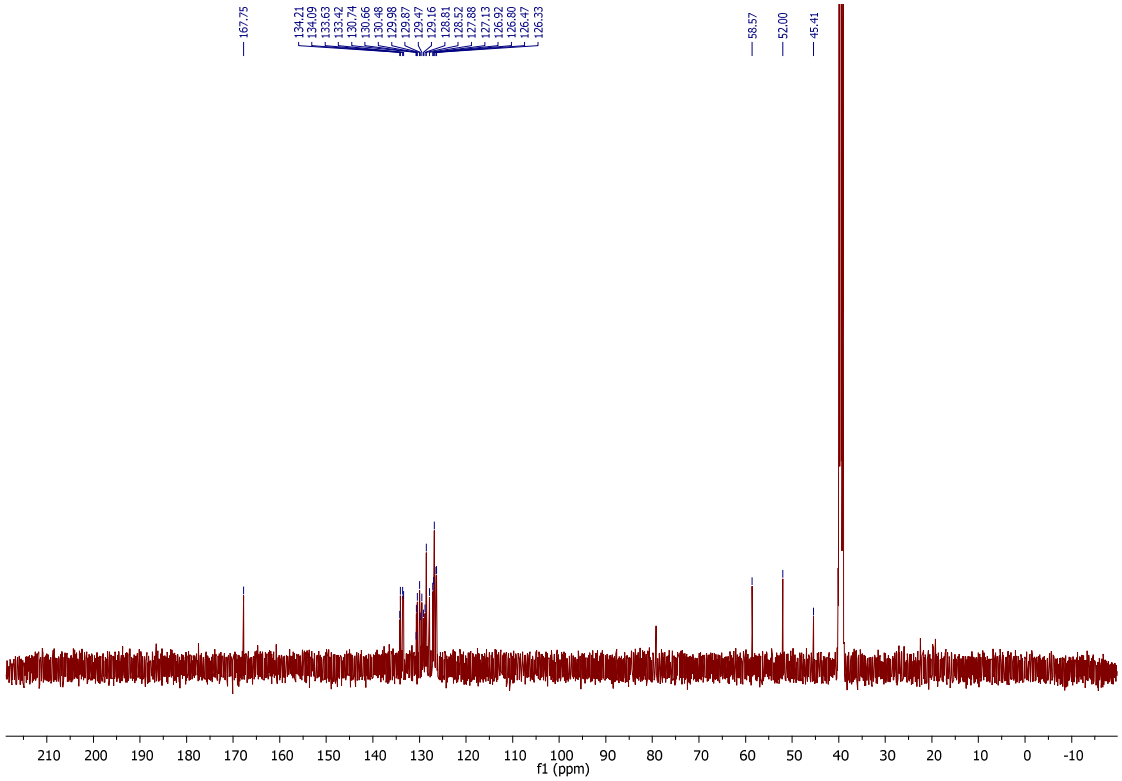
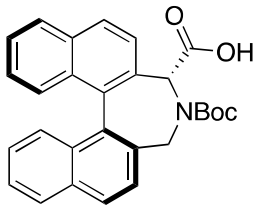


1st eluting diastereoisomer (3R,11cS)-4-(Tert-butoxycarbonyl)-4,5-dihydro-3H-dinaphtho[2,1-c:1',2'-e]azepine-3-carboxylic acid (–)-18a



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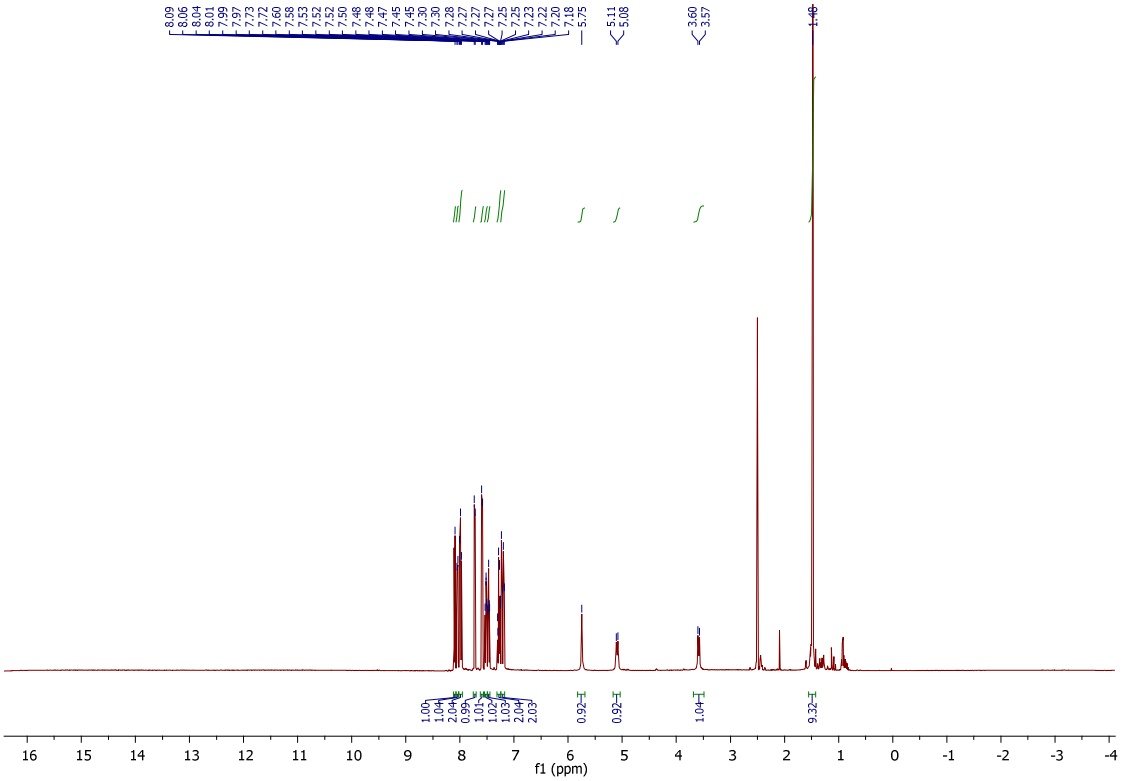

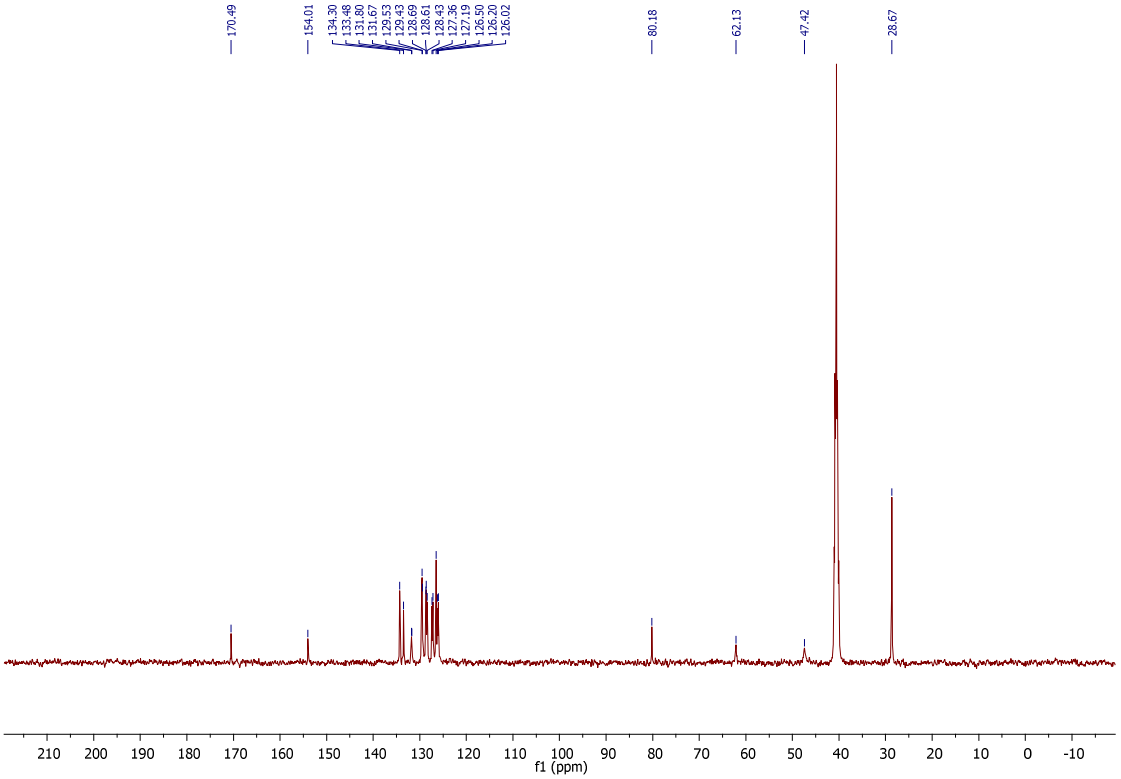

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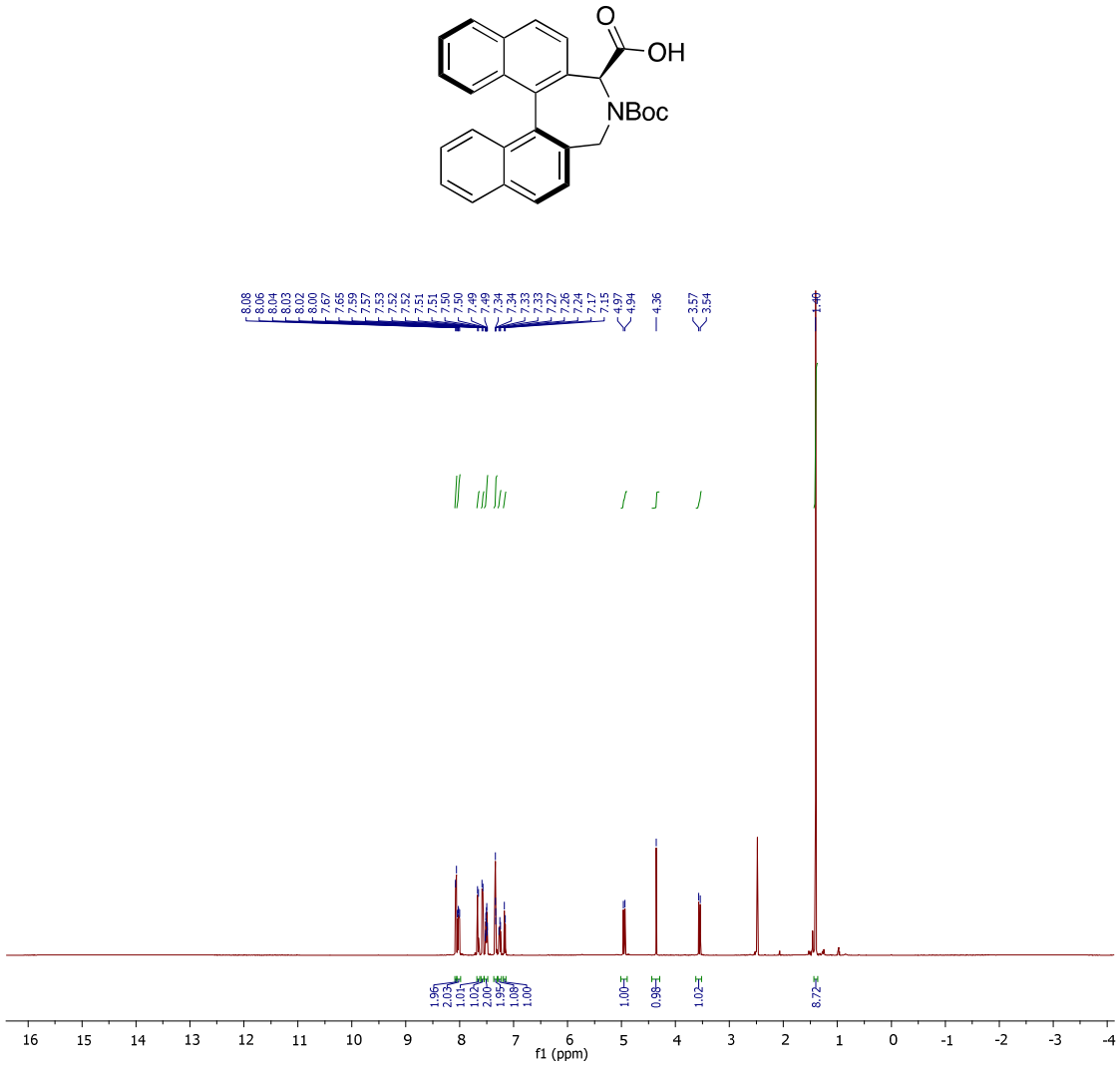
2nd eluting diastereoisomer (3S,11cS)-4-(Tert-butoxycarbonyl)-4,5-dihydro-3H-dinaphtho[2,1-c:1',2'-e]azepine-3-carboxylic acid (+)-18b



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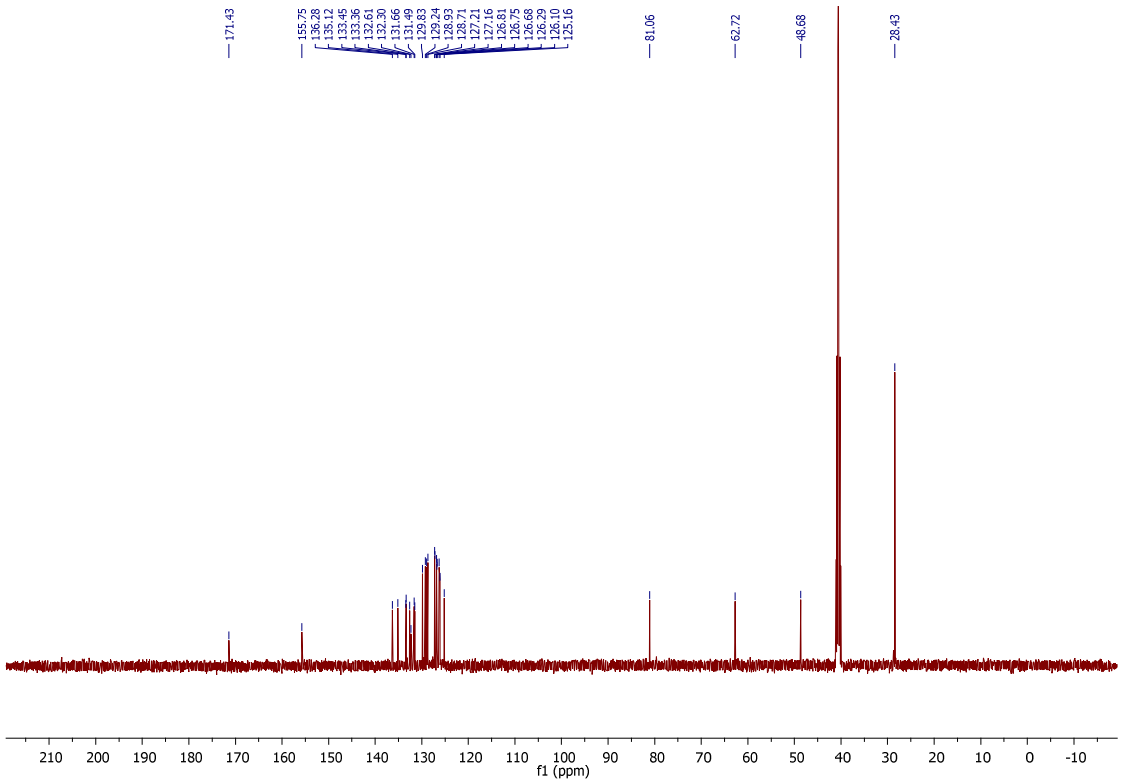
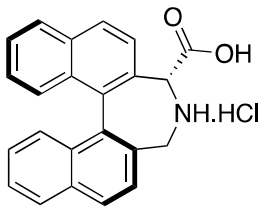


(3R,11cS)-4,5-dihydro-3H-dinaphtho[2,1-c:1',2'-e]azepine-3-carboxylic acid hydrochloride (+)-19a.HCl



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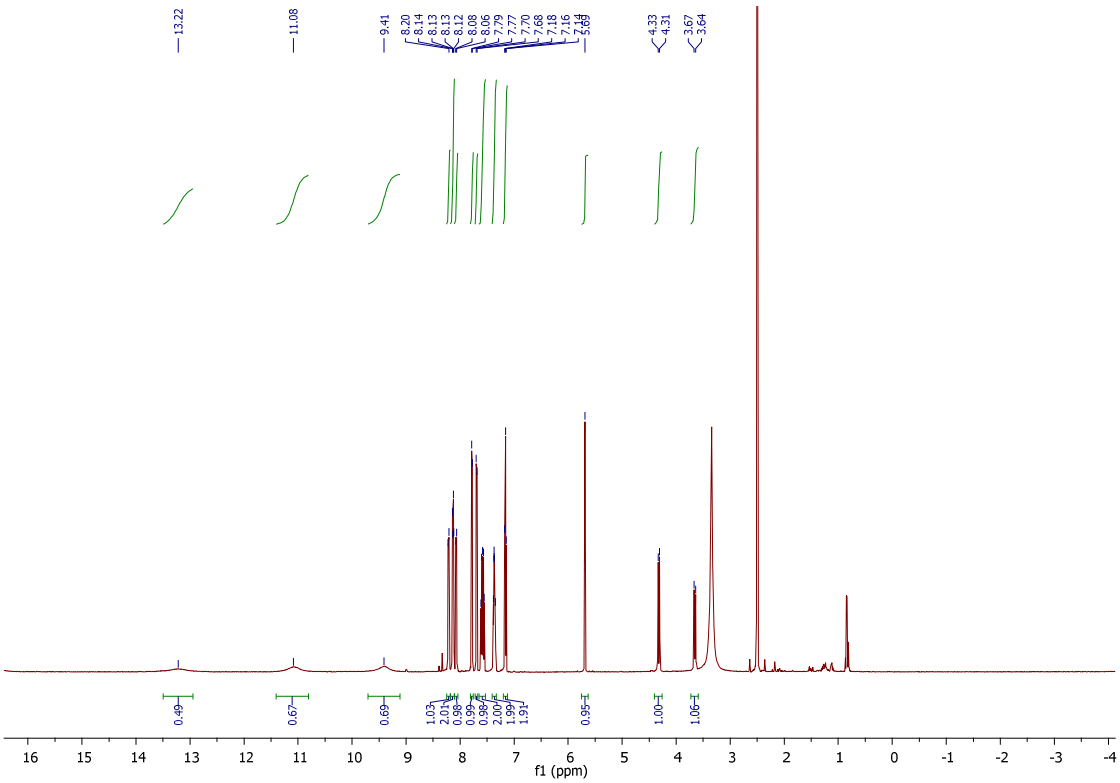

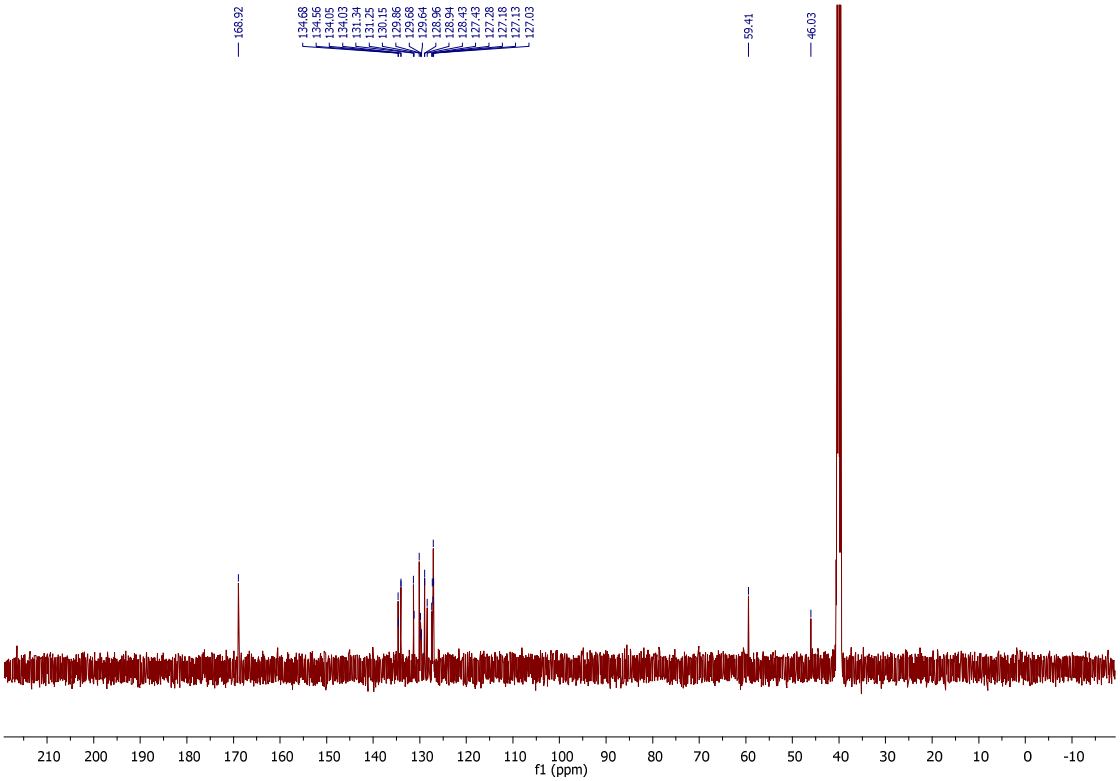

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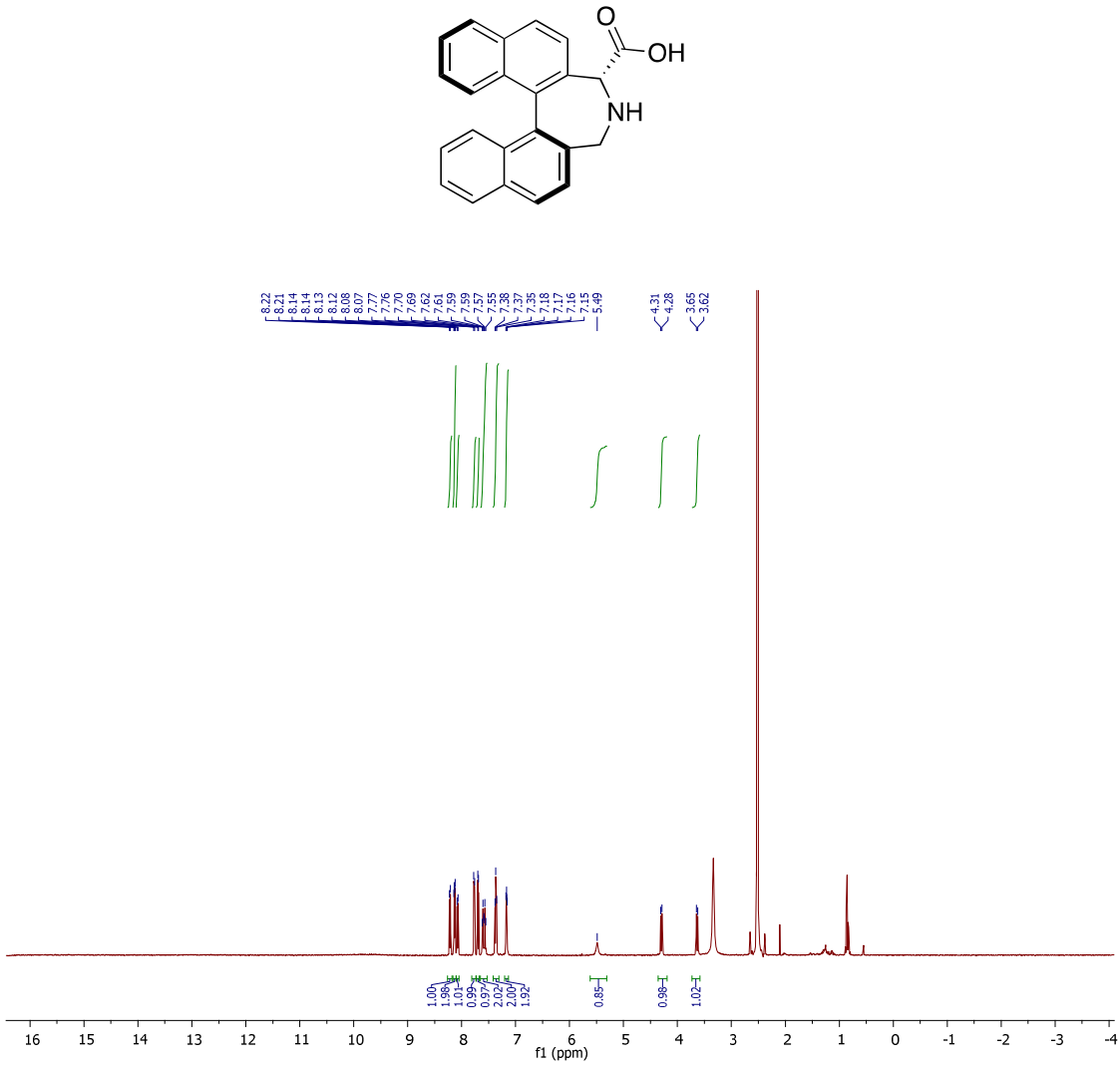
(3R,11cS)-4,5-dihydro-3H-dinaphtho[2,1-c:1',2'-e]azepine-3-carboxylic acid (+)-19a



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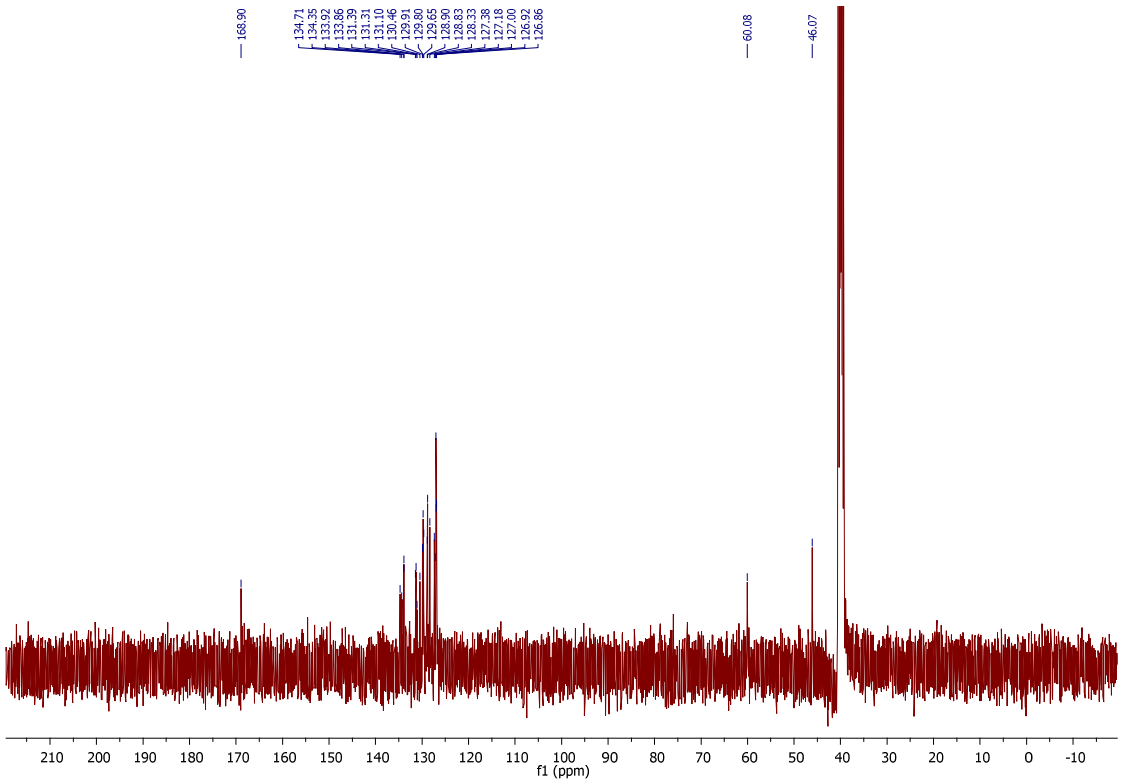
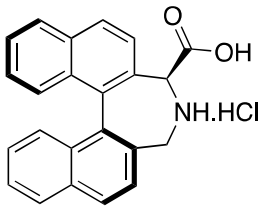


(3S,11cS)-4,5-dihydro-3H-dinaphtho[2,1-c:1',2'-e]azepine-3-carboxylic acid hydrochloride (+)-19b.HCl



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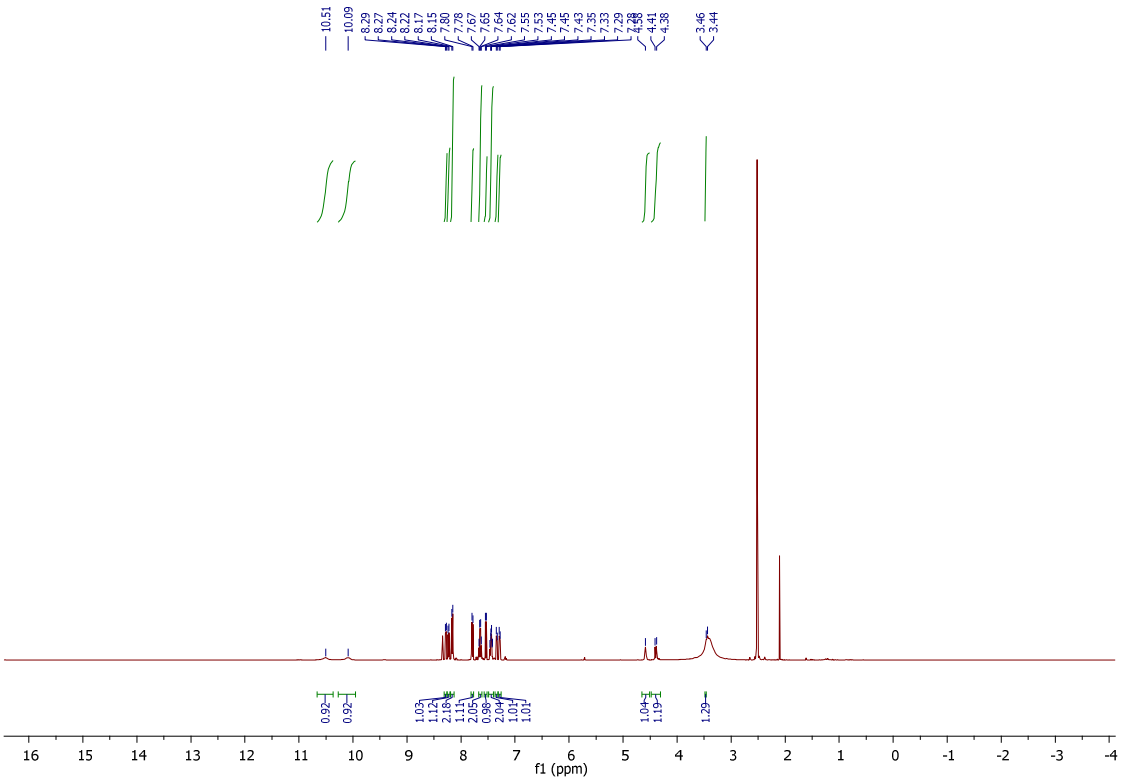
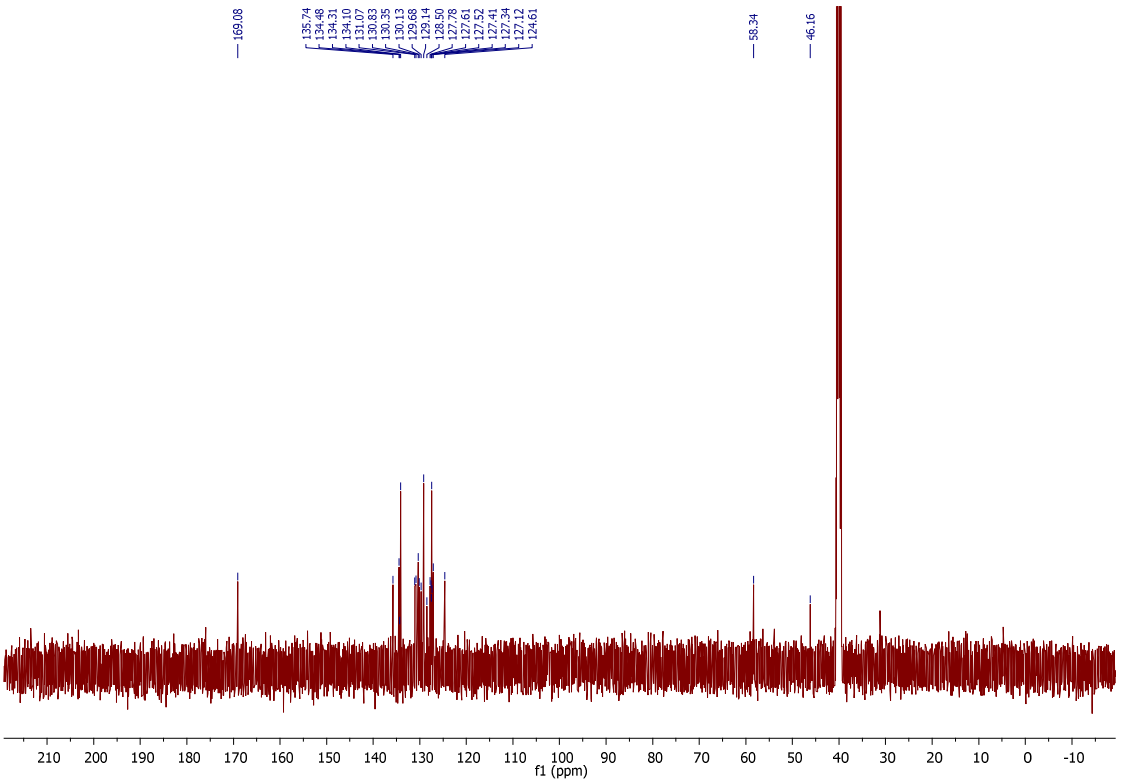
DOI: 10.1039/C8OB01795F





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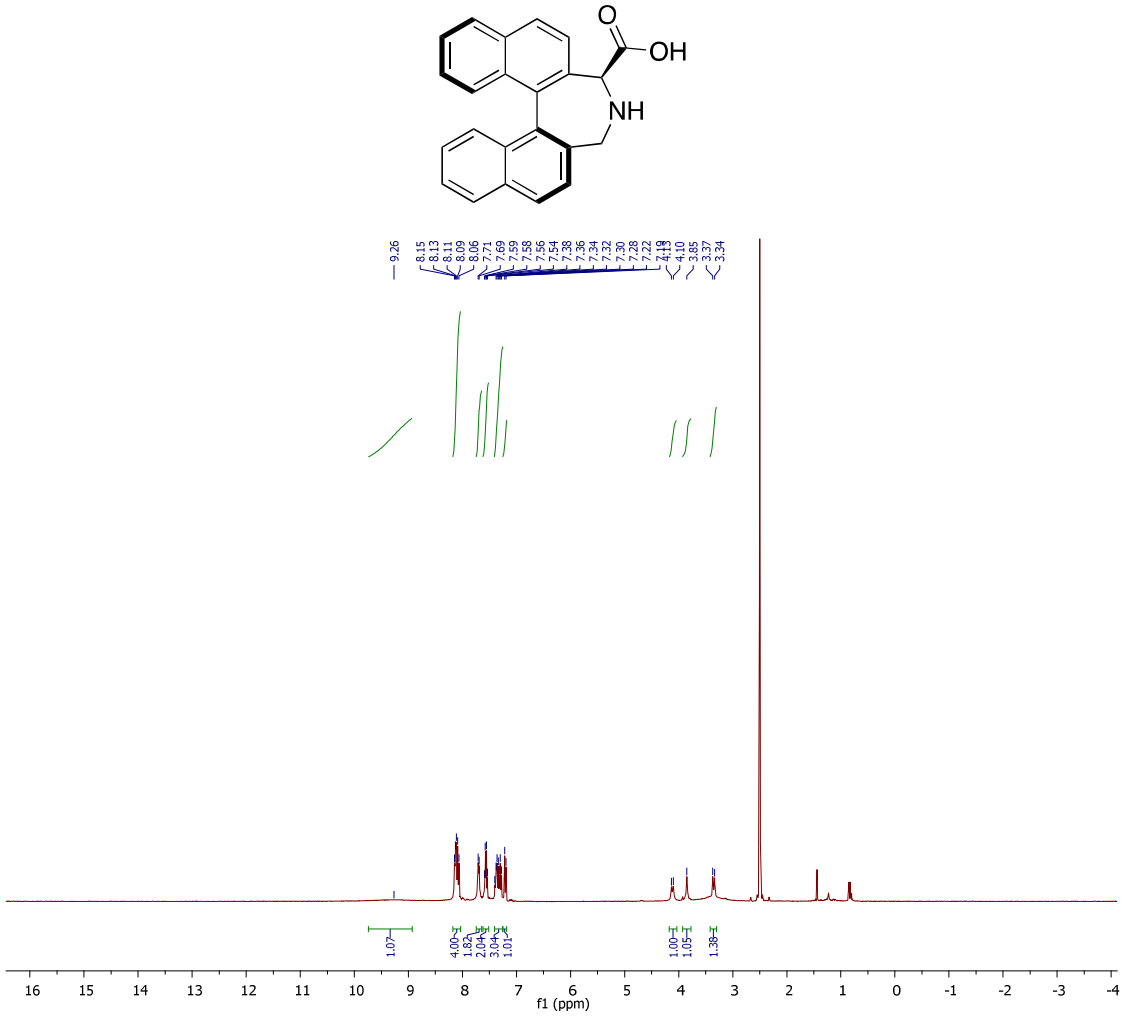
DOI: 10.1039/C8OB01795F

(3S,11cS)-4,5-dihydro-3H-dinaphtho[2,1-c:1',2'-e]azepine-3-carboxylic acid (+)-19b



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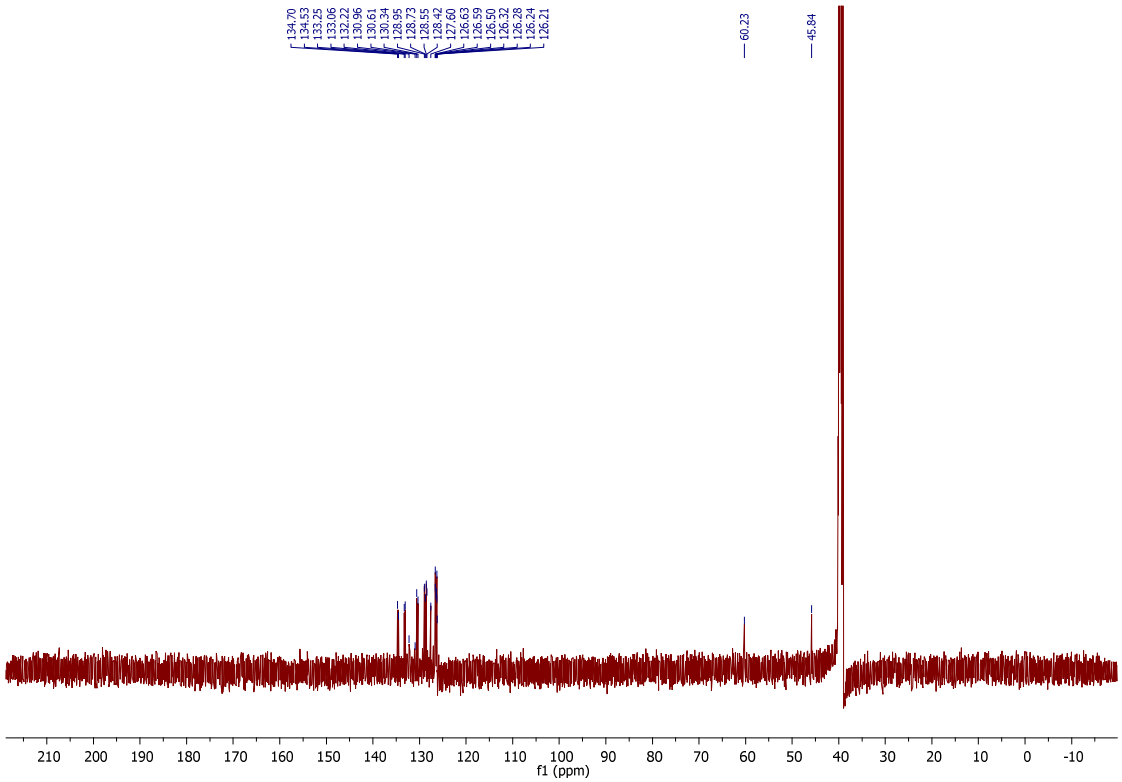
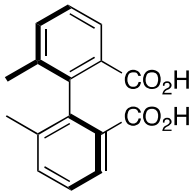
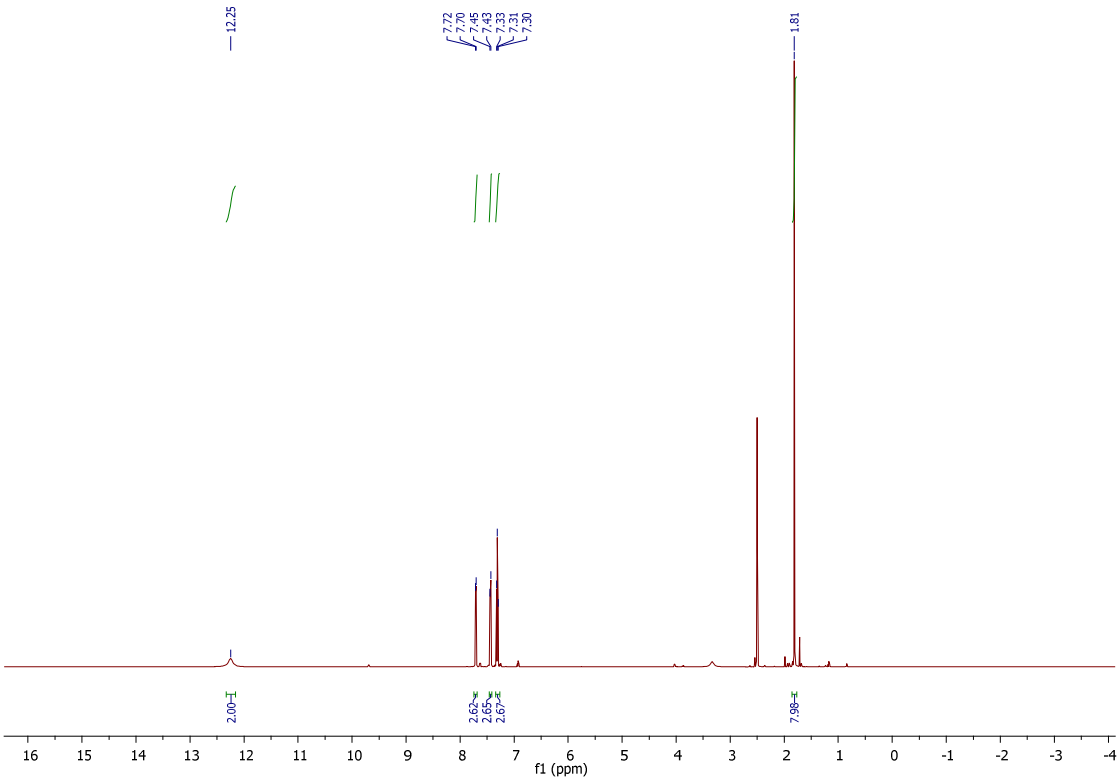
DOI: 10.1039/C8OB01795F

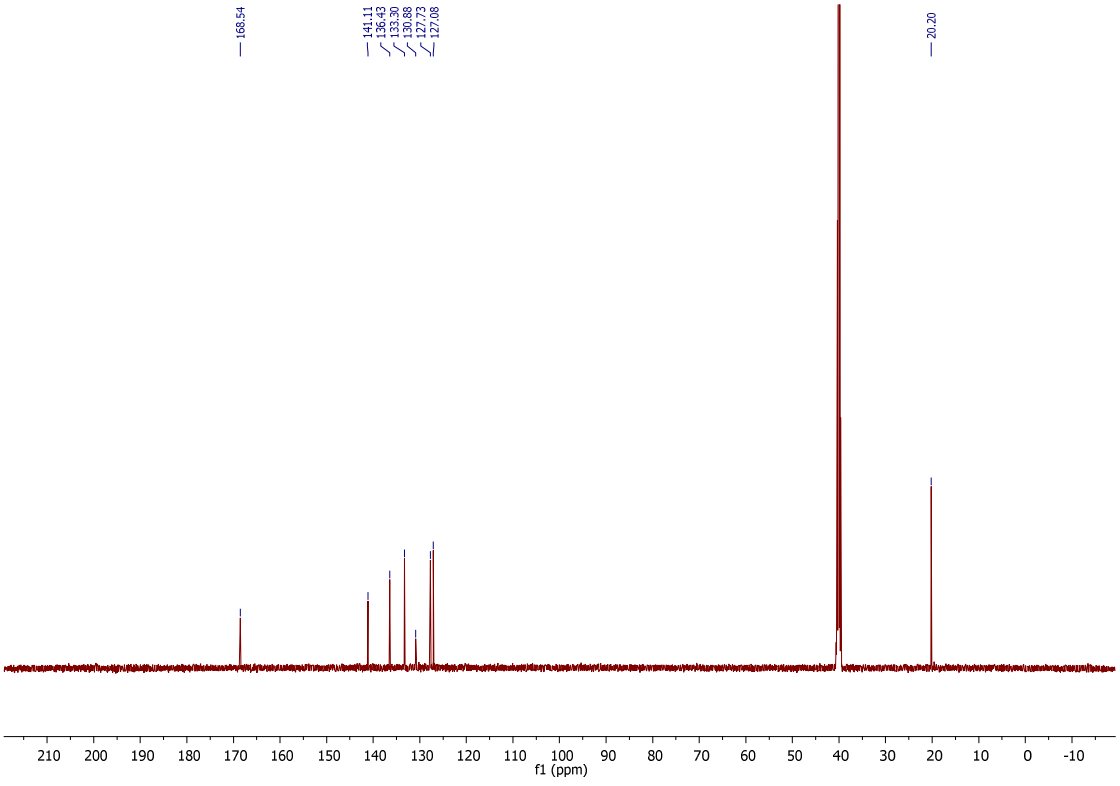


(S)-6,6'-dimethyl-[1,1'-biphenyl]-2,2'-dicarboxylic acid 31 (+)-21



View Article Online
DOI: 10.1039/C8OB01795F





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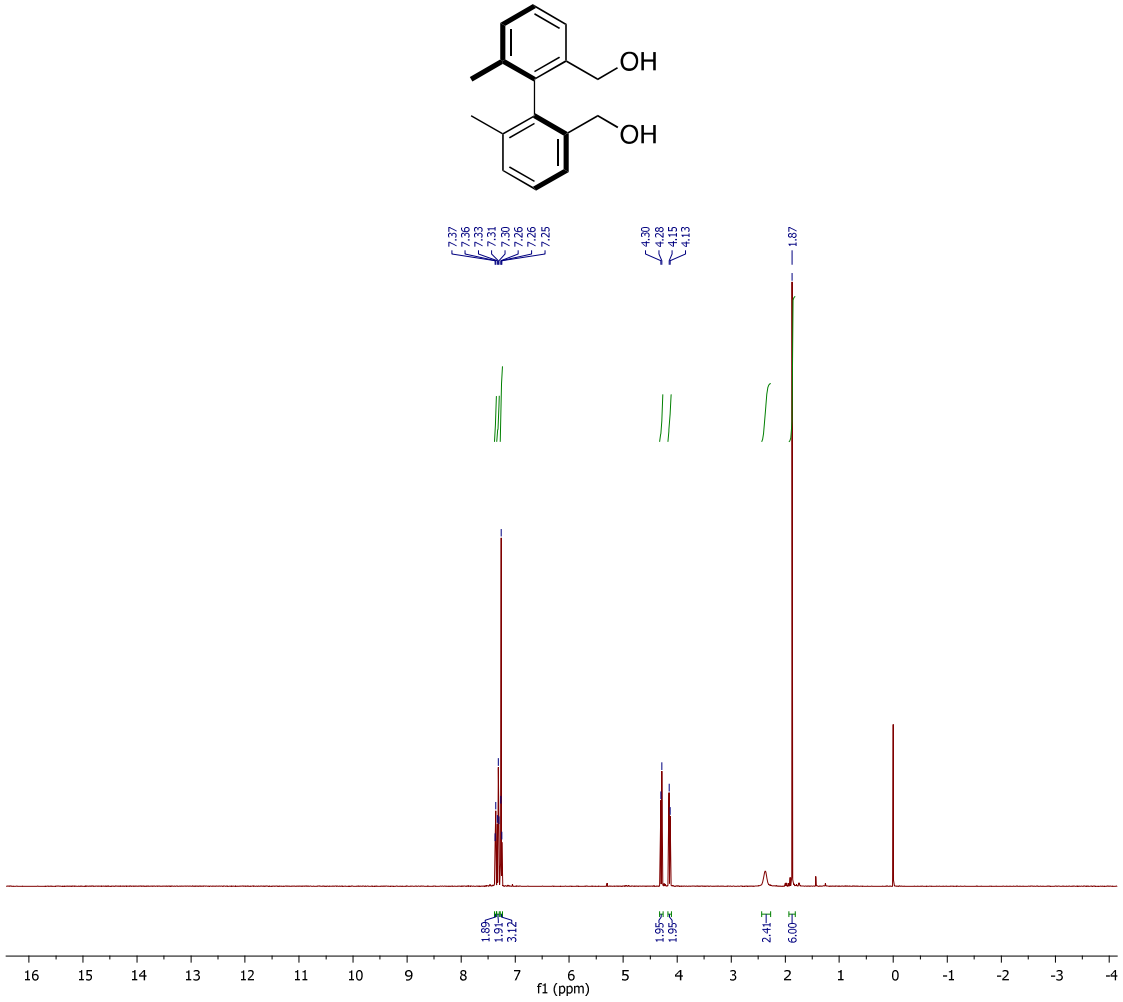
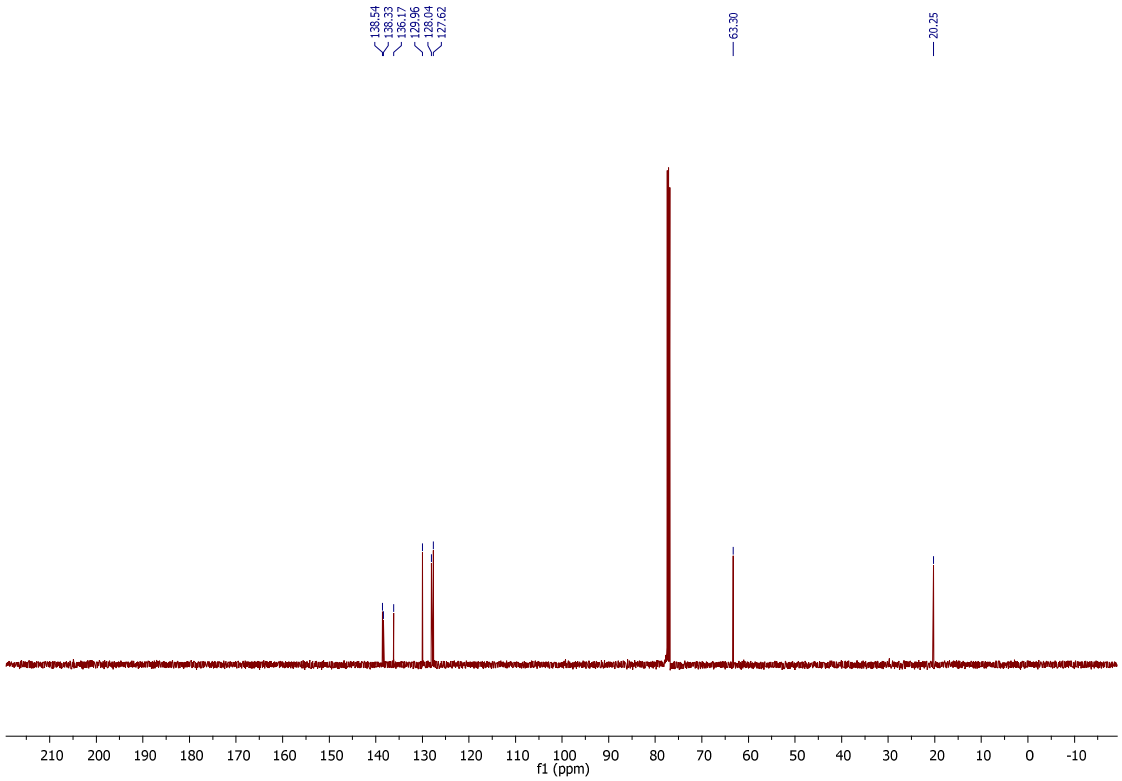
DOI: 10.1039/C8OB01795F

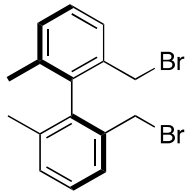
***(−)-(S)*-(6,6'-dimethyl-[1,1'-biphenyl]-2,2'-diyl)dimethanol (–)-22**



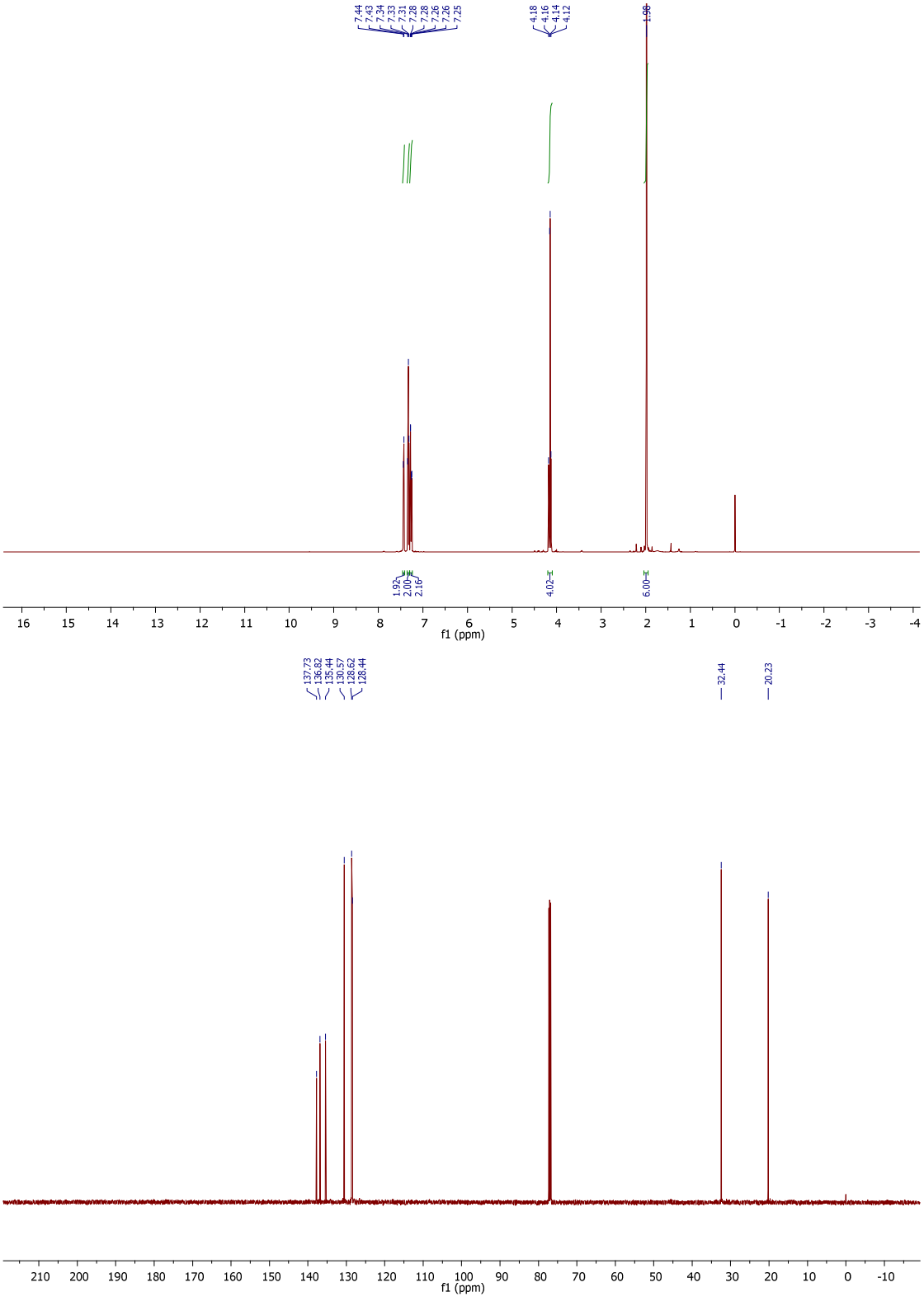
View Article Online
DOI: 10.1039/C8OB01795F



(+)-2,2'-bis(bromomethyl)-6,6'-dimethyl-1,1'-biphenyl (+)-20



View Article Online
DOI: 10.1039/C8OB01795F



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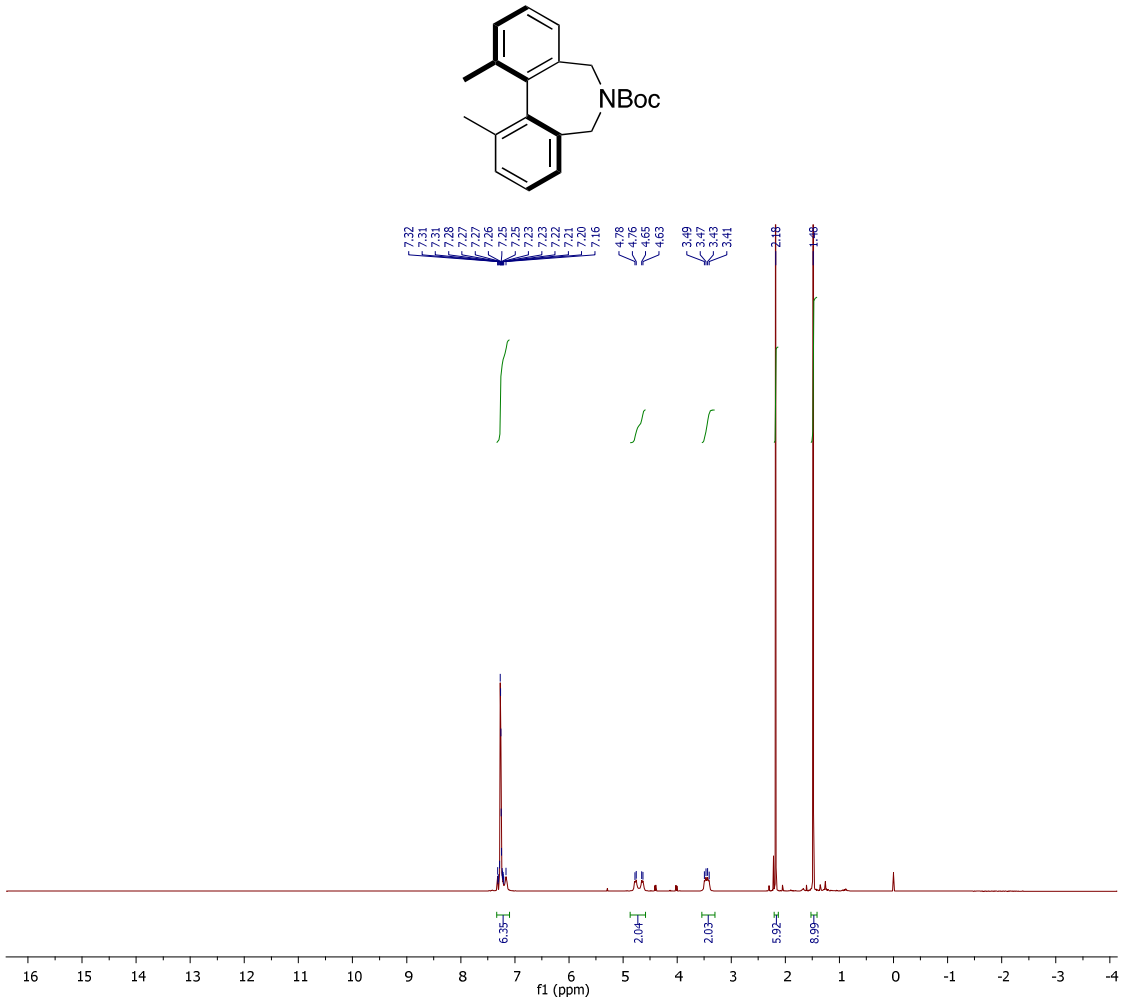
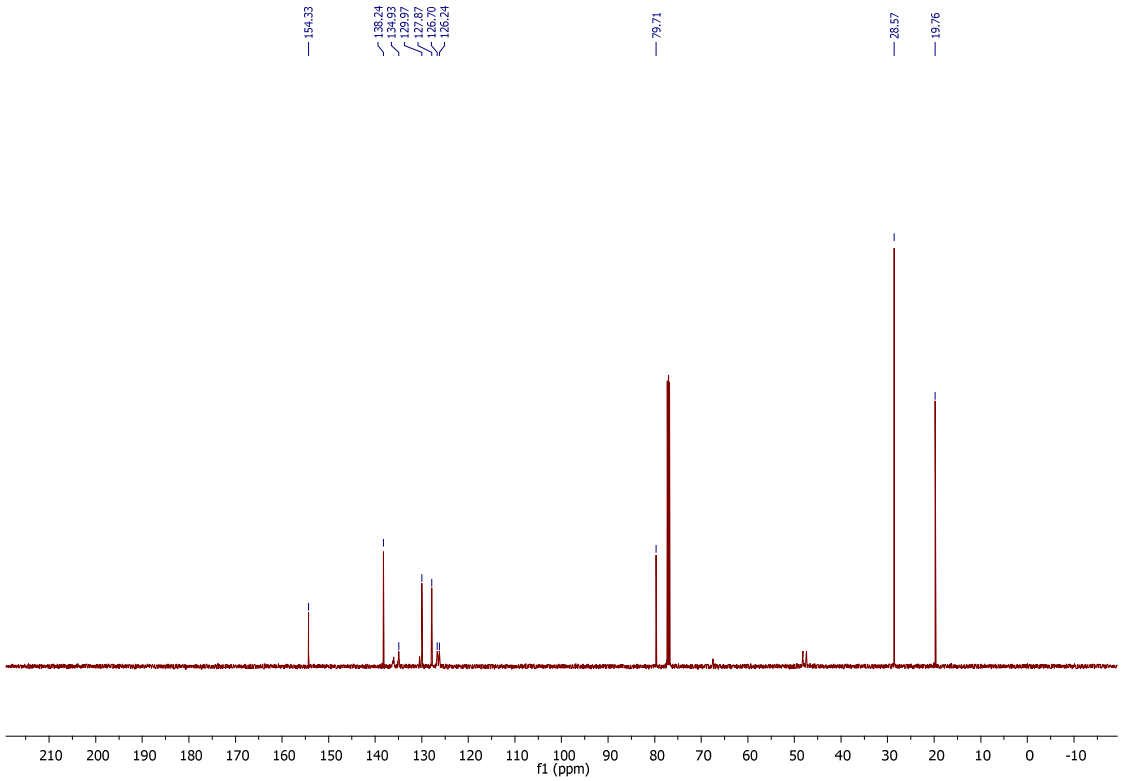
DOI: 10.1039/C8OB01795F

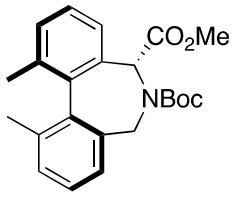
(+)-(*S*)-tert-butyl 1,11-dimethyl-5H-dibenzo[c,e]azepine-6(7H)-carboxylate (–)-23



View Article Online
DOI: 10.1039/C8OB01795F



(5R,11bS)-6-tert-butyl 5-methyl 1,11-dimethyl-5H-dibenzo[c,e]azepine-5,6(7H)-dicarboxylate (–)-24



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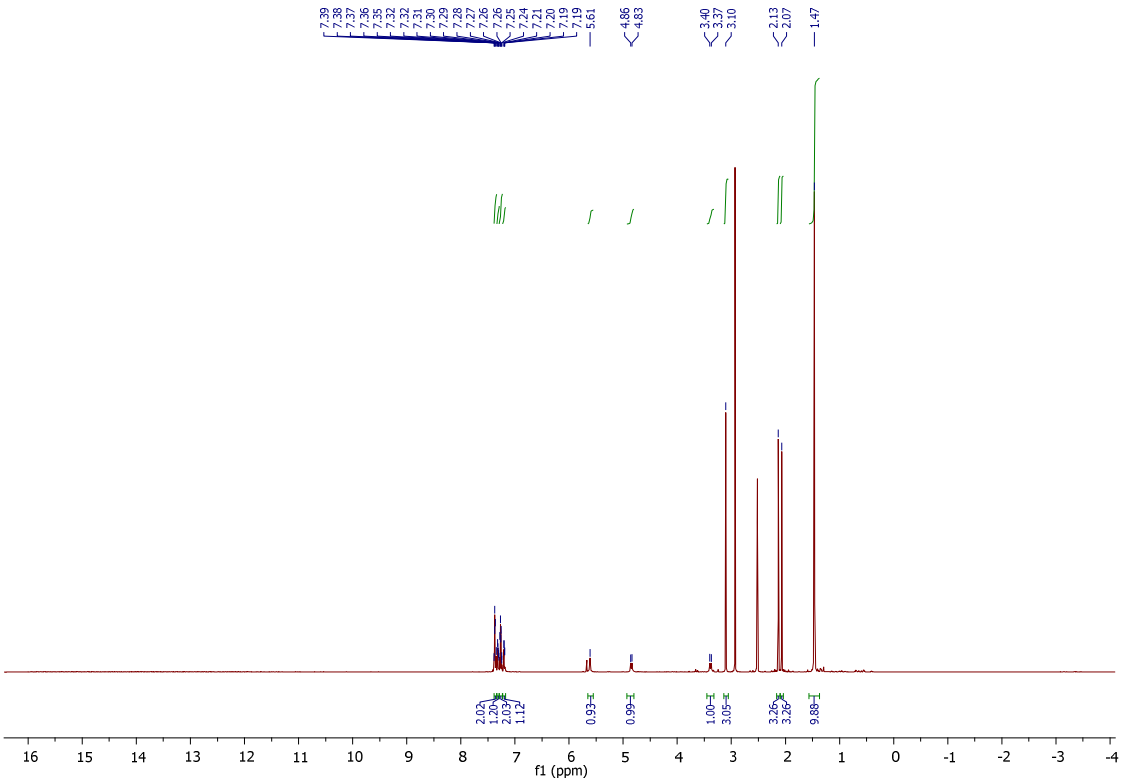
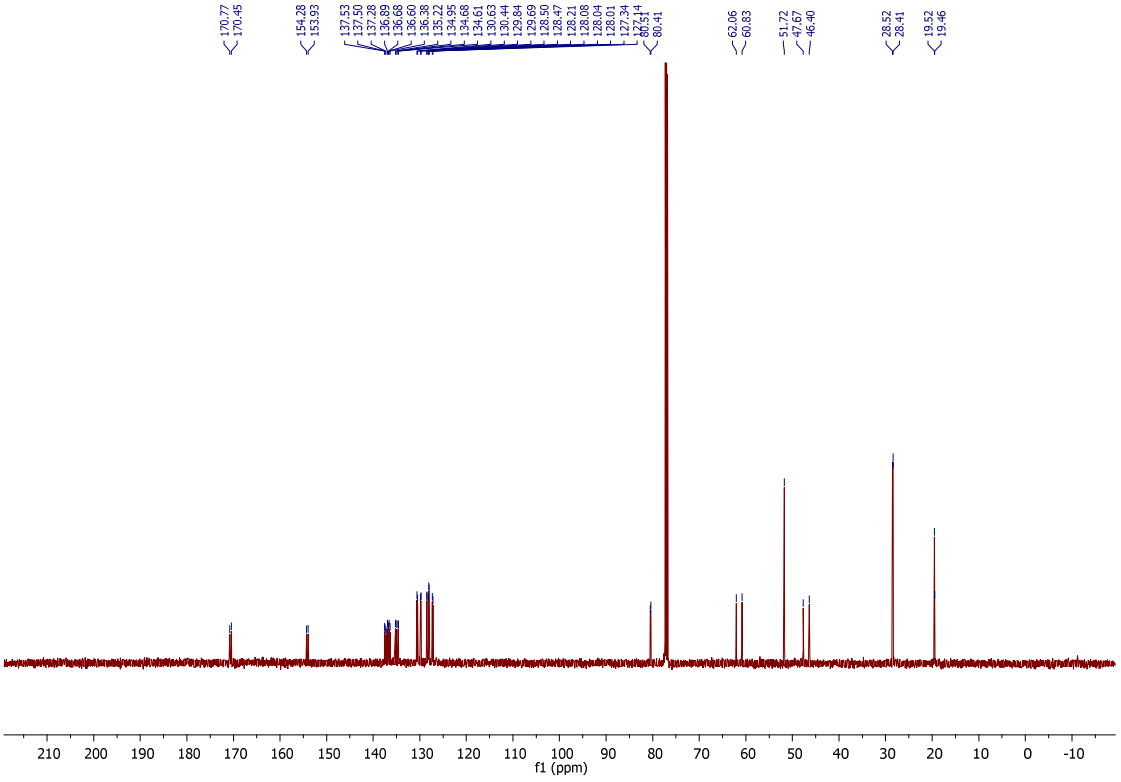
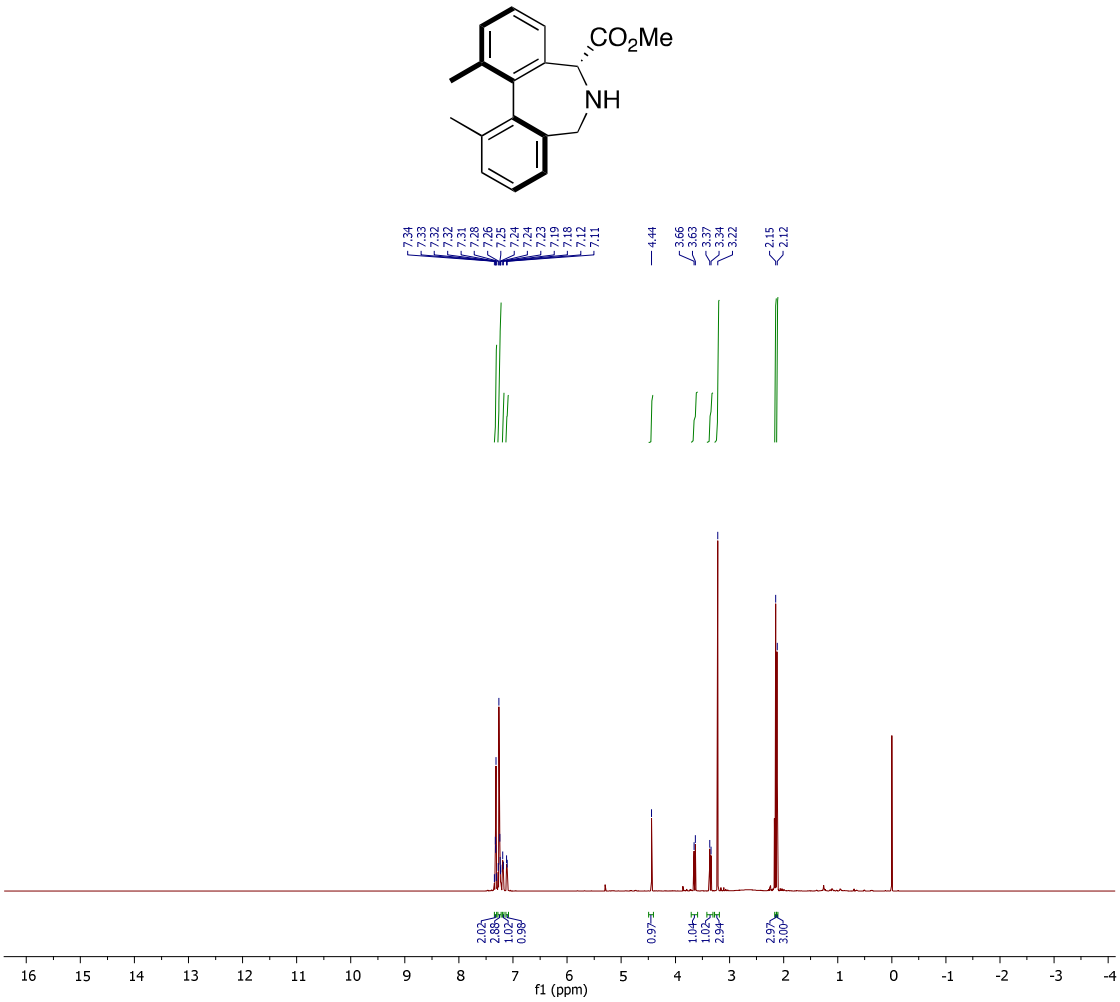
DOI: 10.1039/C8OB01795F





View Article Online
DOI: 10.1039/C8OB01795F

(5R,11bS)-Methyl 1,11-dimethyl-6,7-dihydro-5H-dibenzo[c,e]azepine-5-carboxylate (+)-25



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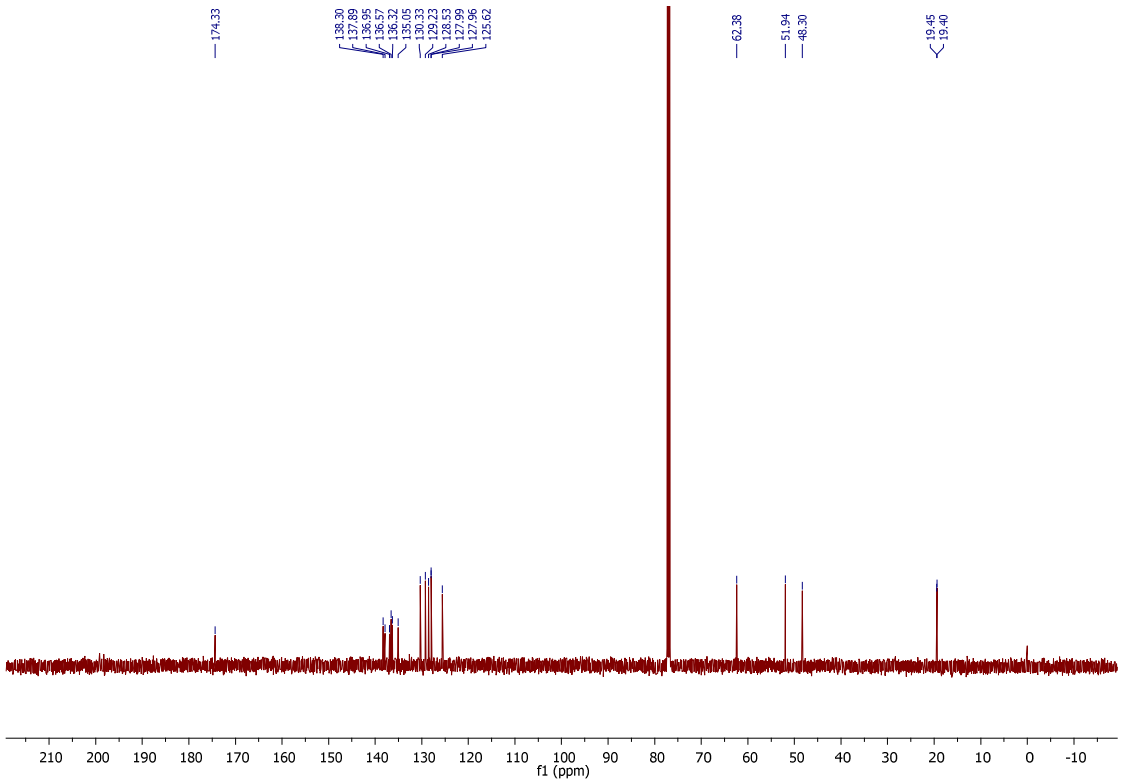
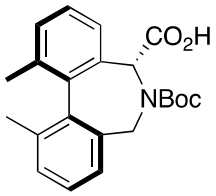


(5R,11bS)-6-(tert-butoxycarbonyl)-1,11-dimethyl-6,7-dihydro-5Hdibenzo[c,e] azepine-5-carboxylic acid (–)-26



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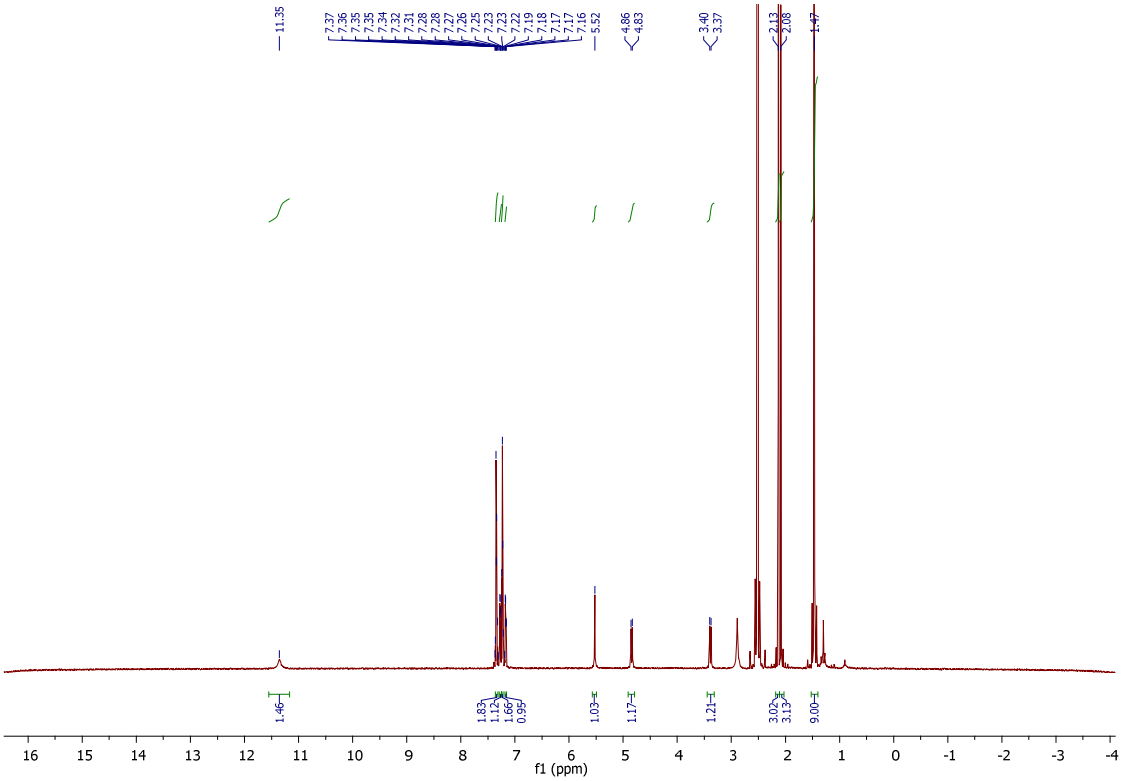

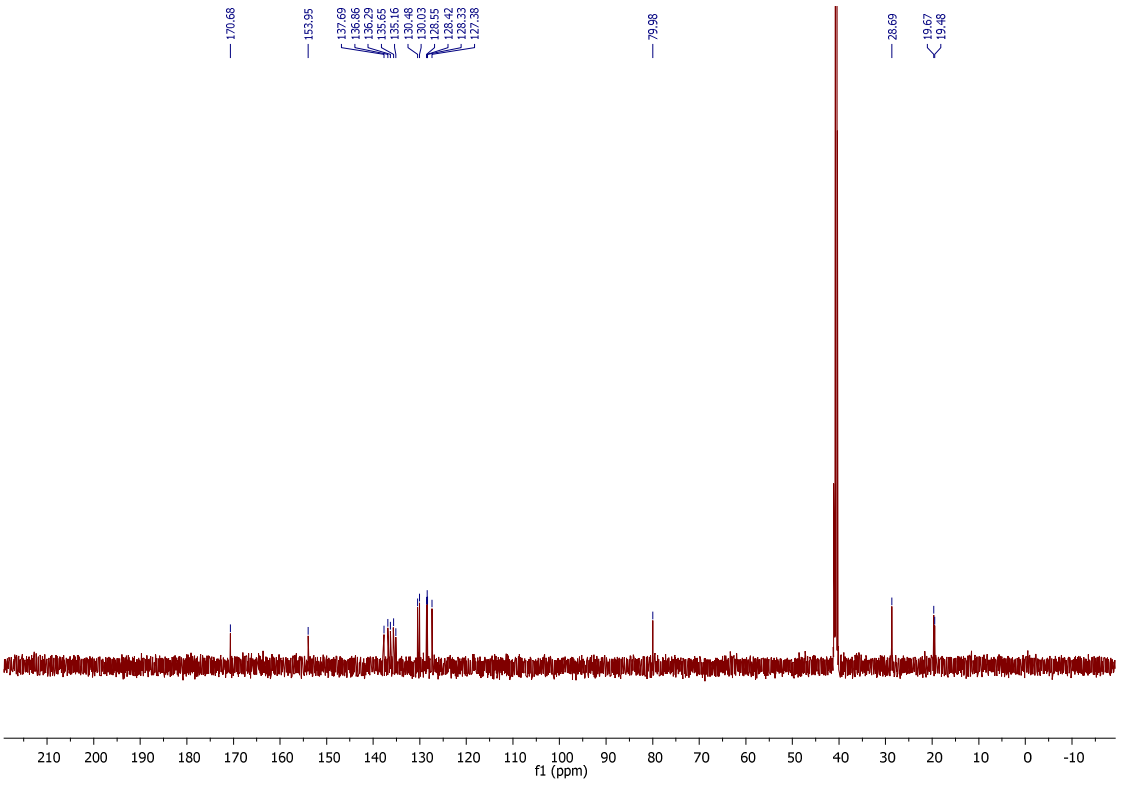

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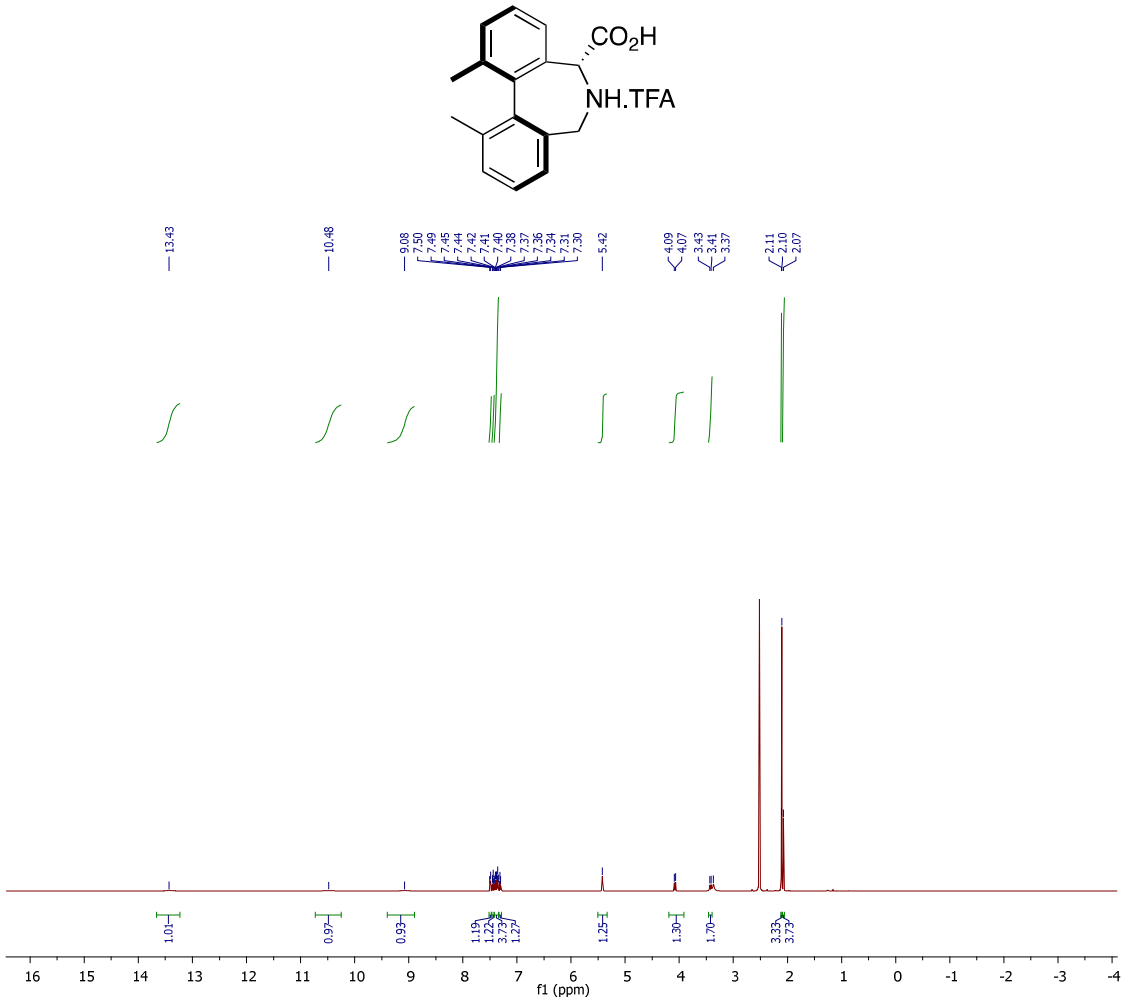
DOI: 10.1039/C8OB01795F

(5R,11bS)-1,11-dimethyl-6,7-dihydro-5H-dibenzo[c,e]azepine-5-carboxylic acid trifluoroacetic acid (−)-27.TFA



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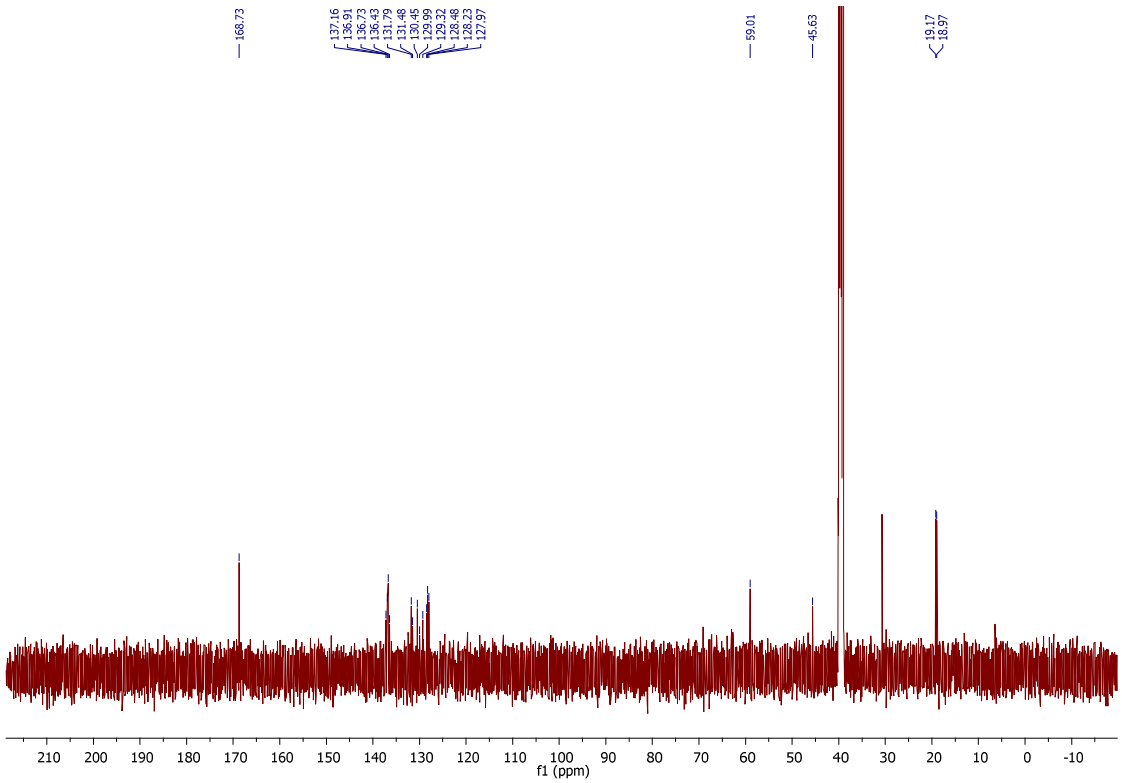

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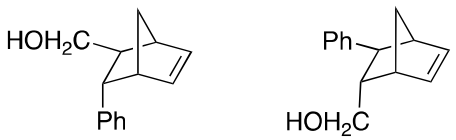
DOI: 10.1039/C8OB01795F

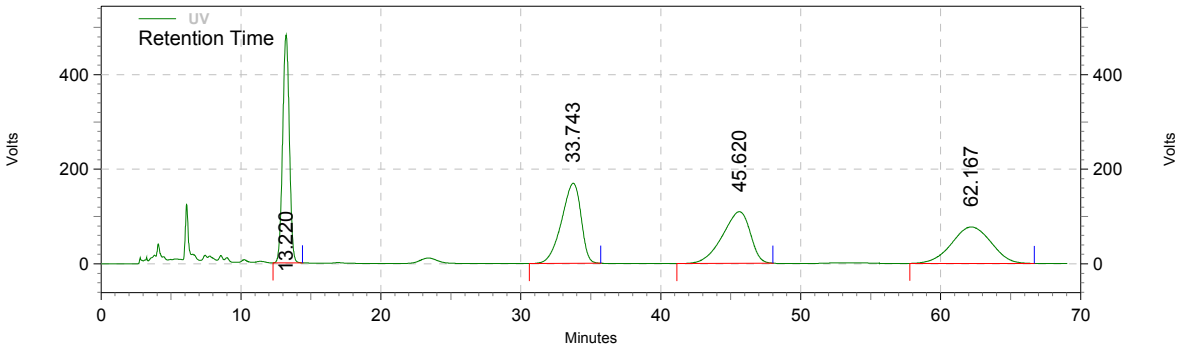
Racemic trace

Table 1: Entry 1

3-Phenylbicyclo[2.2.1]hept-5-en-2-yl)methanol



Enantiomeric excesses were determined using HPLC with Chiralcel® OJ column (hexane/iPrOH=90:10, λ=222 nm), 1.0 mL; ***endo*** isomer (t_R1 15 min, 35 min) ***exo*** isomer (t_R1 47 min, 65 min))



UV Results

Retention Time	Area	Area %	Height	Height %
13.220	64536756	25.71	1928102	57.55
33.743	65498431	26.09	677564	20.22
45.620	60424958	24.07	436586	13.03
62.167	60578598	24.13	308081	9.20
Totals	251038743	100.00	3350333	100.00

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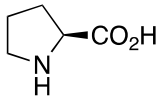
Table 1: Entry 2

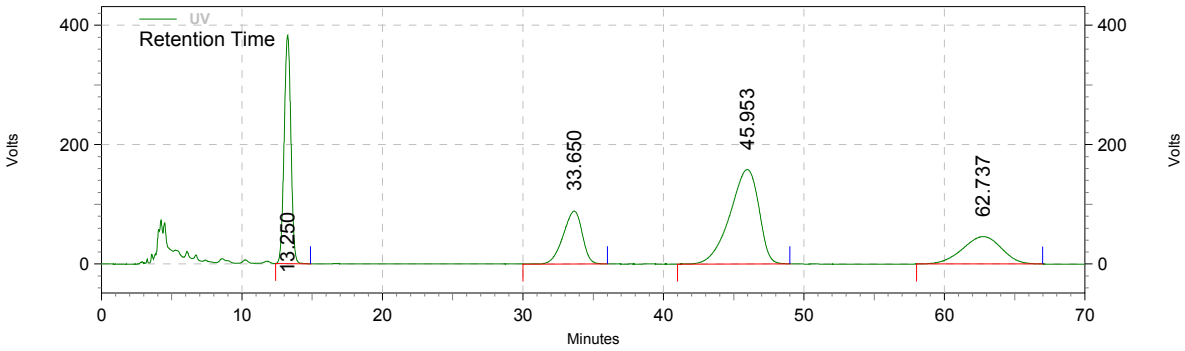


Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\fk81a 80.20 70 min ojnew col 222nm new OJ.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 60 min.met

Acquired: 12/08/2015 12:06:25

Printed: 12/08/2015 16:07:04



UV Results

Retention Time	Area	Area %	Height	Height %
13.250	51007629	24.22	1529611	56.64
33.650	33510346	15.91	354250	13.12
45.953	90381098	42.92	632596	23.43
62.737	35702246	16.95	183908	6.81

Totals	210601319	100.00	2700365	100.00

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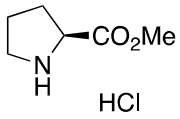
DOI: 10.1039/C8OB01795F

Table 1: Entry 3

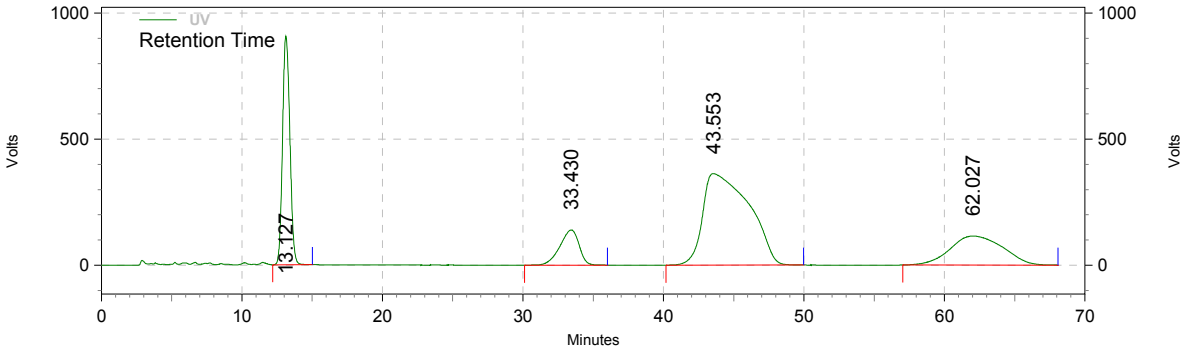


Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\fk146A 80.20 70 min OJ 222nm 1 ml.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 70 min.met

Acquired: 27/08/2015 12:31:30

Printed: 27/08/2015 13:42:30



UV Results

Retention Time	Area	Area %	Height	Height %
13.127	131888924	20.65	3629379	59.51
33.430	52971200	8.29	558125	9.15
43.553	333423380	52.21	1451480	23.80
62.027	120378914	18.85	460042	7.54

Totals	638662418	100.00	6099026	100.00

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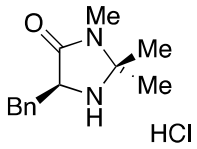
Table 1: Entry 4

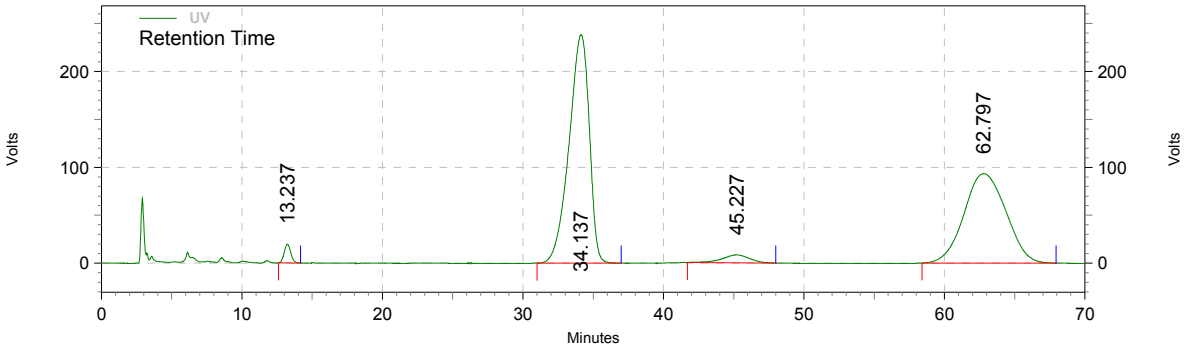


Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\fk111a 80.20 70 min ojnew col 222nm new OJ.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 60 min.met

Acquired: 12/08/2015 06:10:02

Printed: 12/08/2015 10:04:20



UV Results

Retention Time	Area	Area %	Height	Height %
13.237	2535884	1.41	77678	5.40
34.137	95500448	53.13	953999	66.36
45.227	4462090	2.48	33011	2.30
62.797	77264272	42.98	372904	25.94

Totals	179762694	100.00	1437592	100.00

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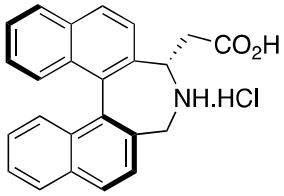
DOI: 10.1039/C8OB01795F

Table 1: Entry 9



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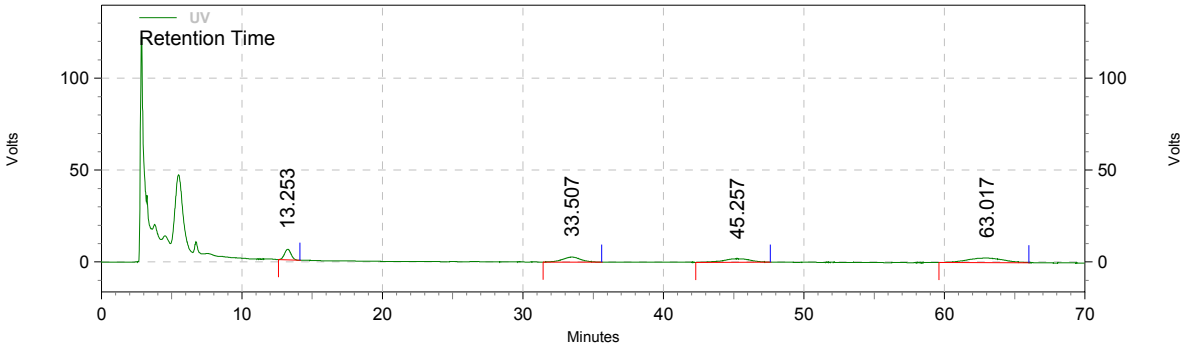
Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 60 min.met

Acquired: 12/08/2015 10:55:10

Printed: 12/08/2015 16:12:07



UV Results

Retention Time	Area	Area %	Height	Height %
13.253	751905	16.38	23162	44.59
33.507	1001477	21.82	10940	21.06
45.257	1047410	22.82	7748	14.92
63.017	1789119	38.98	10092	19.43

Totals	4589911	100.00	51942	100.00

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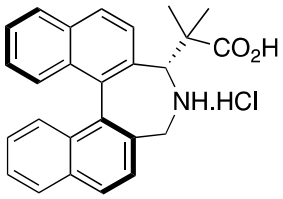
Table 1: Entry 10

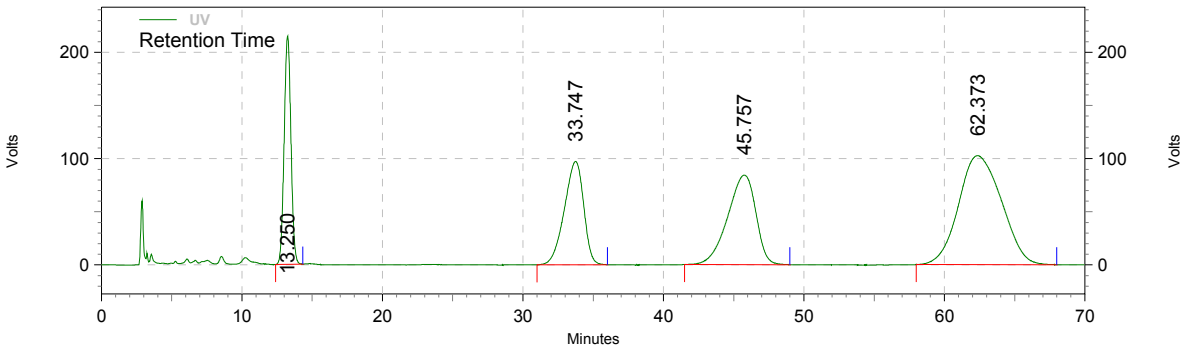


Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\fk106a 80.20 70 min ojnew col 222nm new OJ.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 60 min.met

Acquired: 12/08/2015 08:32:35

Printed: 12/08/2015 10:01:41



UV Results

Retention Time	Area	Area %	Height	Height %
13.250	28787746	14.39	859465	43.07
33.747	37159913	18.57	388520	19.47
45.757	47032218	23.51	337013	16.89
62.373	87102801	43.53	410333	20.56

Totals	200082678	100.00	1995331	100.00

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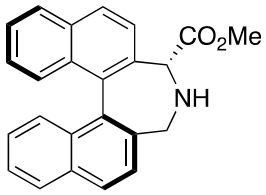
DOI: 10.1039/C8OB01795F

Table 1: Entry 11

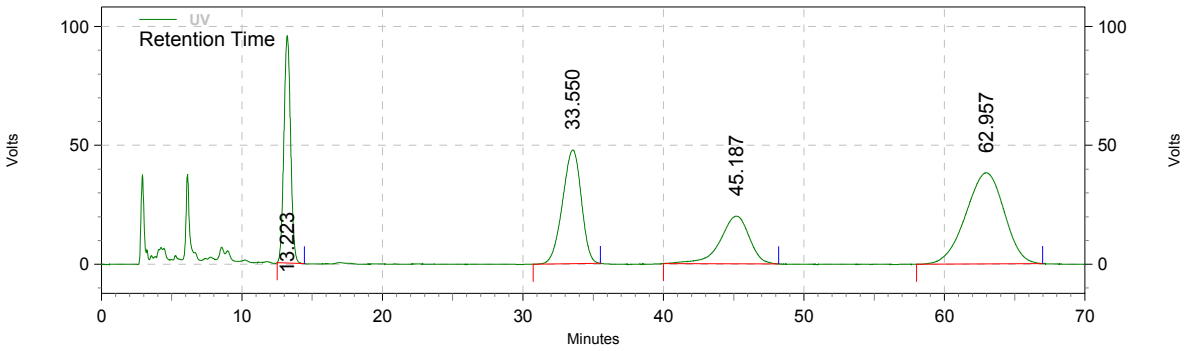


Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\fk115a 80.20 70 min ojnew col 222nm new OJ.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 60 min.met

Acquired: 11/08/2015 21:51:29

Printed: 12/08/2015 10:25:56



UV Results

Retention Time	Area	Area %	Height	Height %
13.223	12692405	17.83	382644	47.37
33.550	17808685	25.01	191505	23.71
45.187	11576366	16.26	80270	9.94
62.957	29122669	40.90	153312	18.98

Totals	71200125	100.00	807731	100.00

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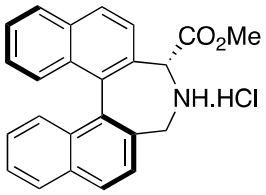
Table 1: Entry 12



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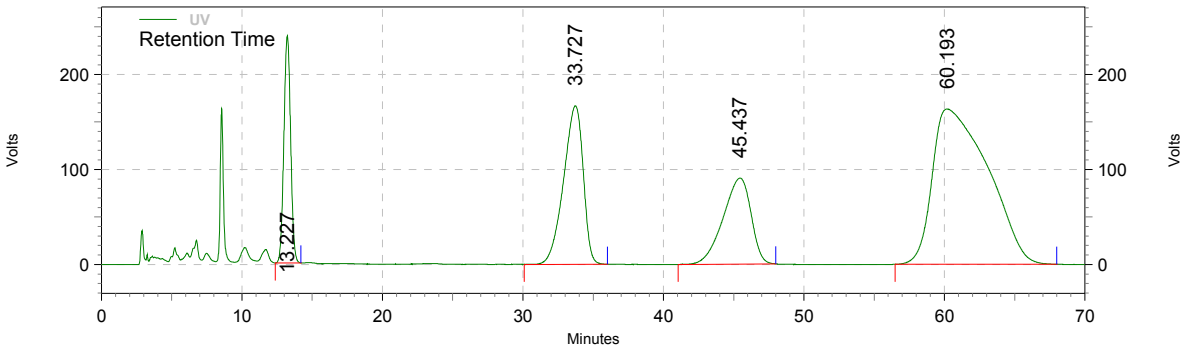
Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 60 min.met

Acquired: 12/08/2015 02:36:15

Printed: 12/08/2015 10:36:00



UV Results

Retention Time	Area	Area %	Height	Height %
13.227	31895315	9.75	956531	36.24
33.727	64867738	19.83	667327	25.28
45.437	50082498	15.31	362259	13.72
60.193	180191602	55.10	653465	24.76

Totals	327037153	100.00	2639582	100.00

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DOI: 10.1039/C8OB01795F

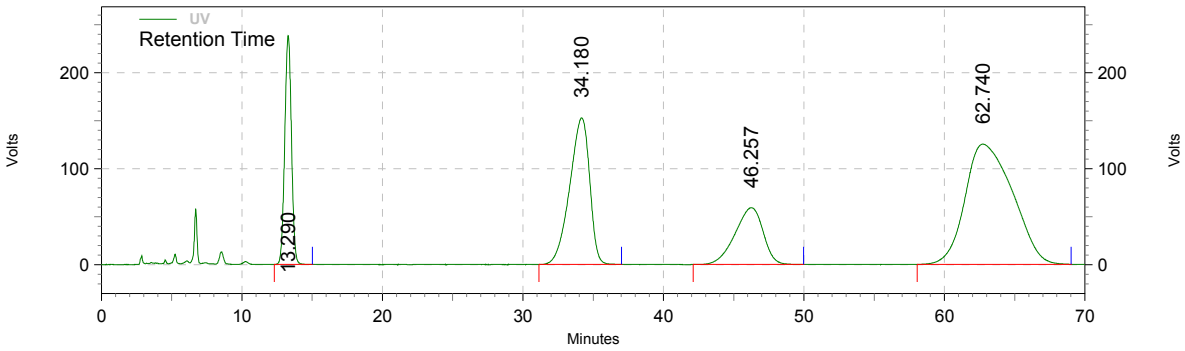
Table 1: Entry 13

Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\fk155a OJ col 70min 80.20 1ml 222nm.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 70 min.met

Acquired: 18/09/2015 21:49:54

Printed: 19/09/2015 10:11:22



UV Results

Retention Time	Area	Area %	Height	Height %
13.290	31628773	13.03	954437	41.43
34.180	60283005	24.83	611146	26.53
46.257	33002472	13.59	236572	10.27
62.740	117891887	48.55	501415	21.77

Totals	242806137	100.00	2303570	100.00

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DOI: 10.1039/C8OB01795F

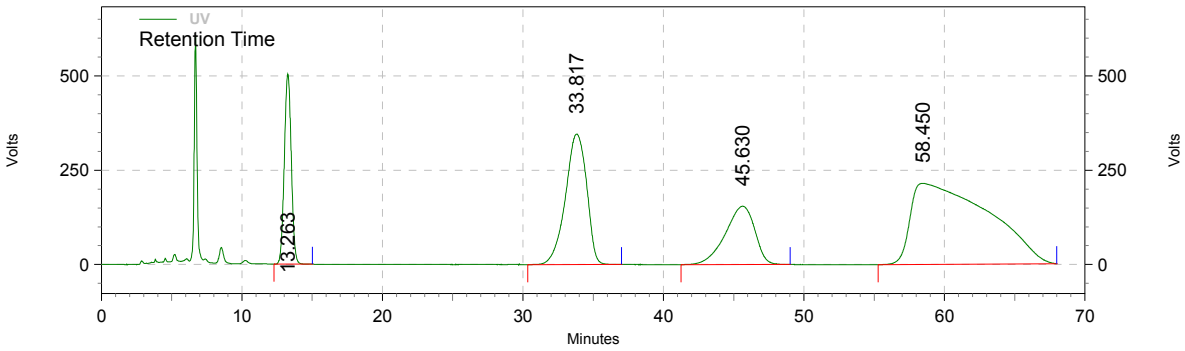
Table 1: Entry 14

Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\fk150a 80.20 70 min OJ new col 222nm 1 ml.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 70 min.met

Acquired: 25/08/2015 19:15:15

Printed: 26/08/2015 10:32:28



UV Results

Retention Time	Area	Area %	Height	Height %
13.263	69612656	10.93	2016253	41.33
33.817	145199395	22.80	1383630	28.36
45.630	90385111	14.20	618673	12.68
58.450	331523585	52.07	859872	17.63

Totals	636720747	100.00	4878428	100.00

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DOI: 10.1039/C8OB01795F

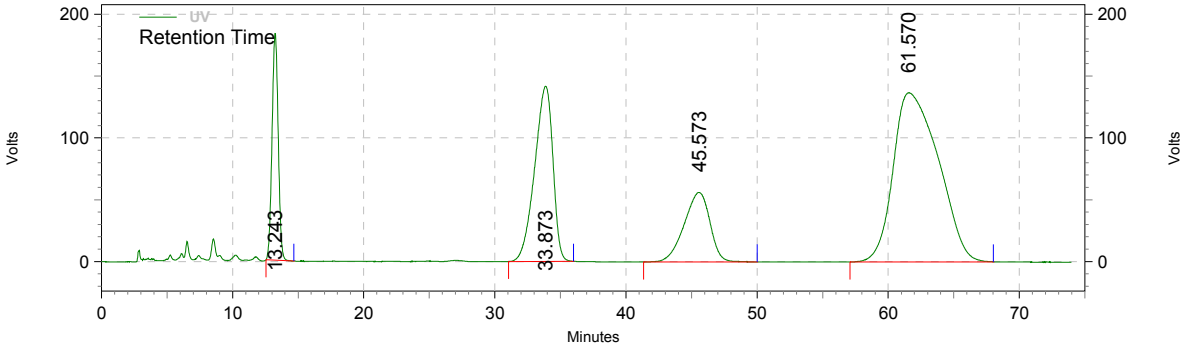
Table 1: Entry 15

Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\fk141A 80.20 70 min OJ 222nm 1 ml.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 70 min.met

Acquired: 27/08/2015 13:40:54

Printed: 27/08/2015 15:01:49



UV Results

Retention Time	Area	Area %	Height	Height %
13.243	24066176	10.00	733768	35.40
33.873	54790835	22.76	567050	27.36
45.573	30757918	12.78	224860	10.85
61.570	131091183	54.46	546904	26.39

Totals	240706112	100.00	2072582	100.00

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DOI: 10.1039/C8OB01795F

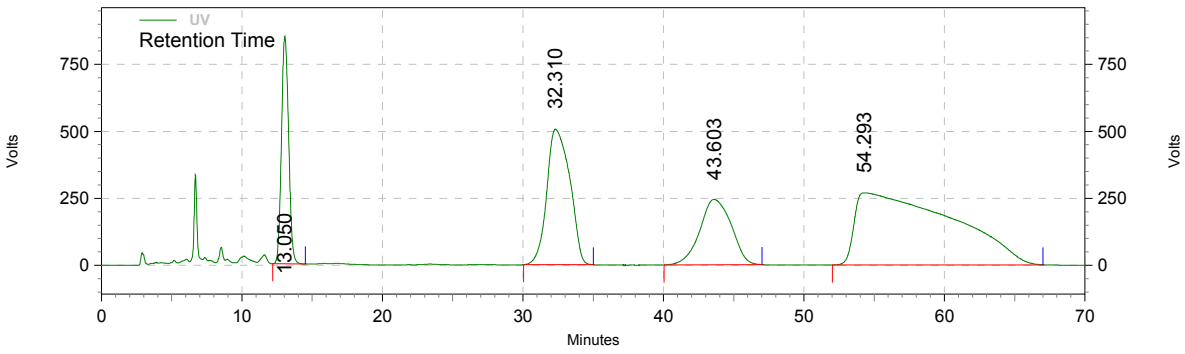
Table 1: Entry 16

Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\fk149A 80.20 70 min OJ 222nm 1 ml.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 70 min.met

Acquired: 27/08/2015 14:56:04

Printed: 27/08/2015 16:49:34



UV Results

Retention Time	Area	Area %	Height	Height %
13.050	120621900	11.76	3397867	45.46
32.310	230889588	22.51	2021312	27.04
43.603	151872631	14.81	976340	13.06
54.293	522194865	50.92	1078936	14.43

Totals	1025578984	100.00	7474455	100.00

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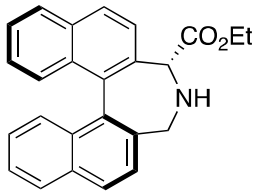
DOI: 10.1039/C8OB01795F

Table 1: Entry 17

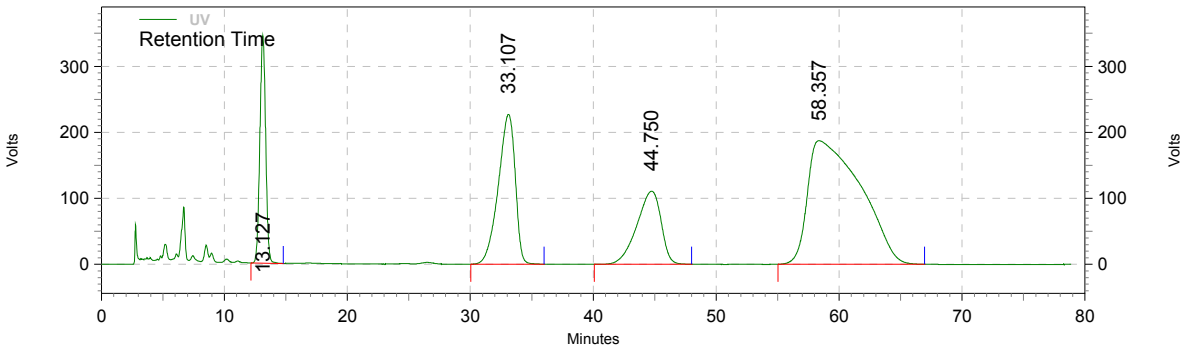


Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\fk143A 80.20 70 min OJ 222nm 1 ml.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 70 min.met

Acquired: 11/09/2015 11:51:35

Printed: 11/09/2015 13:13:14



UV Results

Retention Time	Area	Area %	Height	Height %
13.127	45428356	10.87	1379101	39.64
33.107	86833598	20.78	907986	26.10
44.750	60782790	14.55	443364	12.74
58.357	224756662	53.80	749036	21.53

Totals	417801406	100.00	3479487	100.00

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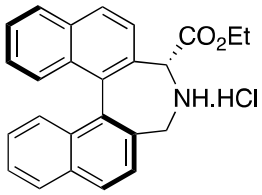
DOI: 10.1039/C8OB01795F

Table 1: Entry 18

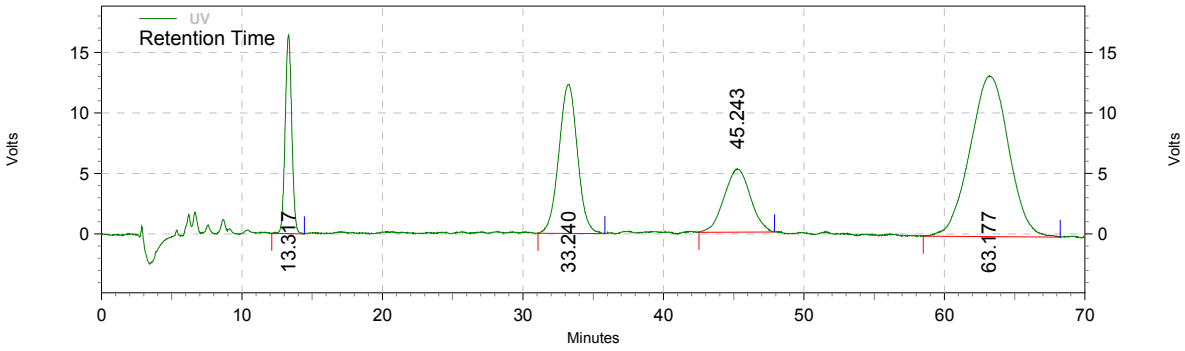


Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\fk156a OJ col 70min 80.20 1ml 222nm.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 70 min.met

Acquired: 18/09/2015 19:27:44

Printed: 19/09/2015 10:13:59



UV Results

Retention Time	Area	Area %	Height	Height %
13.317	2133020	10.89	65686	34.77
33.240	4530531	23.13	49242	26.07
45.243	2725000	13.91	20940	11.09
63.177	10200716	52.07	53026	28.07
Totals	19589267	100.00	188894	100.00

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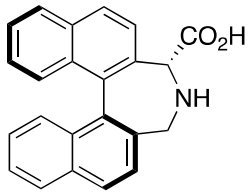
Table 1: Entry 19

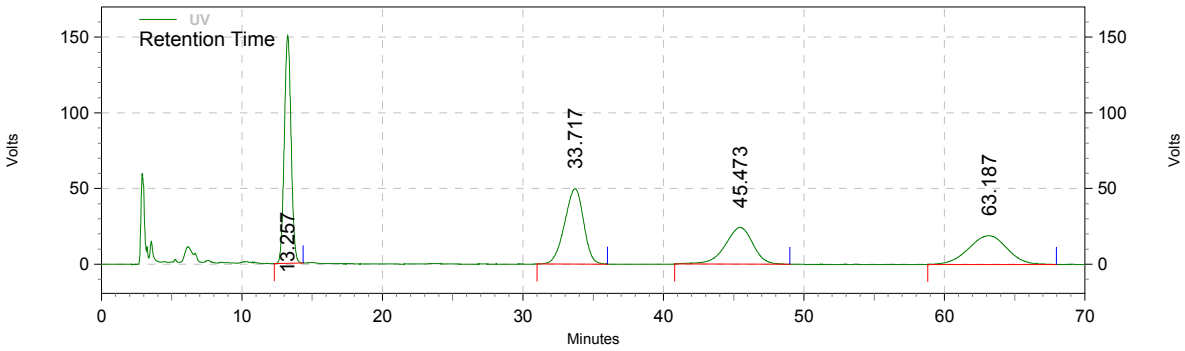


Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\fk102a 80.20 70 min ojnew col 222nm new OJ.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 60 min.met

Acquired: 12/08/2015 07:21:19

Printed: 12/08/2015 09:53:31



UV Results

Retention Time	Area	Area %	Height	Height %
13.257	20188052	30.19	601719	61.78
33.717	18694599	27.96	199148	20.45
45.473	13453070	20.12	97064	9.97
63.187	14536308	21.74	76069	7.81

Totals	66872029	100.00	974000	100.00

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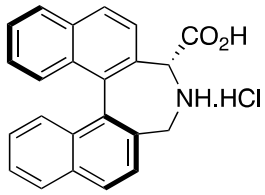
Table 1: Entry 20

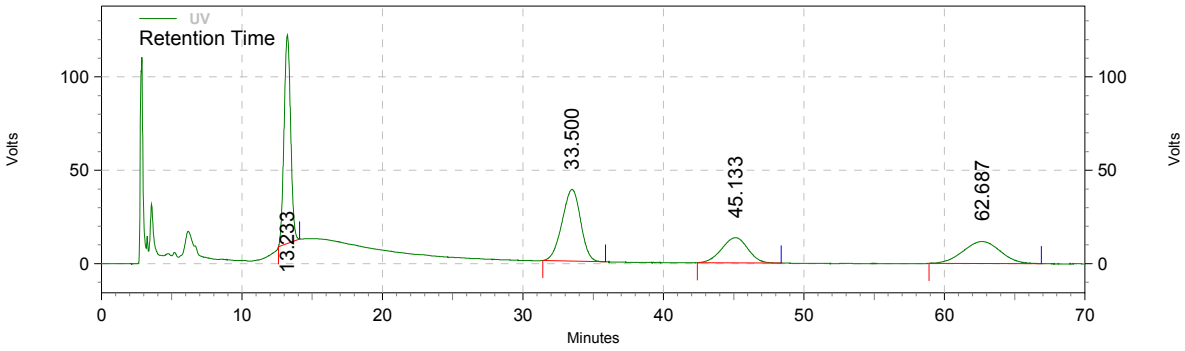


Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\fk103a 80.20 70 min ojnew col 222nm new OJ.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 60 min.met

Acquired: 11/08/2015 19:29:10

Printed: 12/08/2015 09:56:25



UV Results

Retention Time	Area	Area %	Height	Height %
13.233	14518200	32.72	446867	63.67
33.500	14116232	31.81	153656	21.89
45.133	6995705	15.77	54006	7.69
62.687	8739819	19.70	47353	6.75

Totals	44369956	100.00	701882	100.00

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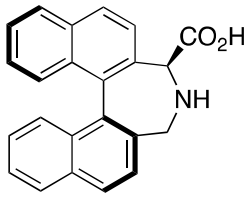
Table 1: Entry 21

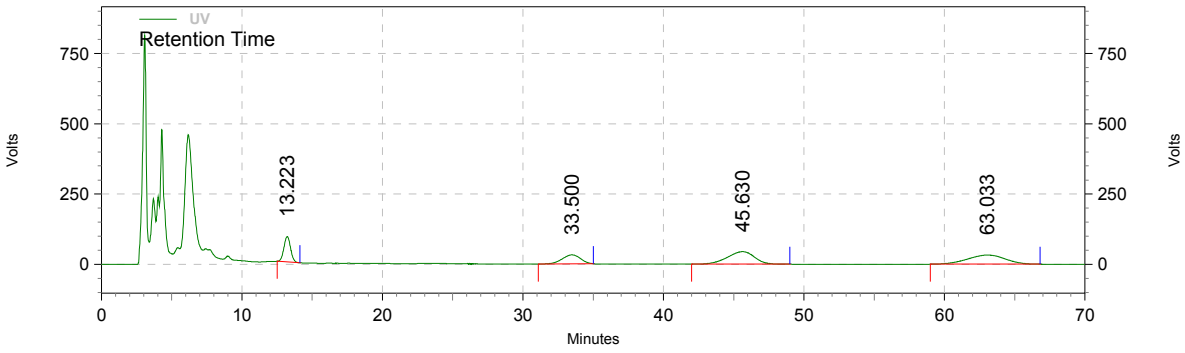


Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\fk89a 80.20 70 min ojnew col 222nm new OJ.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 60 min.met

Acquired: 12/08/2015 01:25:06

Printed: 12/08/2015 09:47:20



UV Results

Retention Time	Area	Area %	Height	Height %
13.223	11911109	16.55	361581	45.33
33.500	11440553	15.90	127837	16.03
45.630	24172440	33.59	178657	22.40
63.033	24440004	33.96	129629	16.25

Totals	71964106	100.00	797704	100.00

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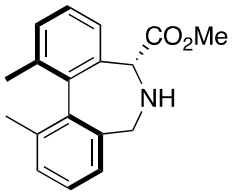
DOI: 10.1039/C8OB01795F

Table 1: Entry 23

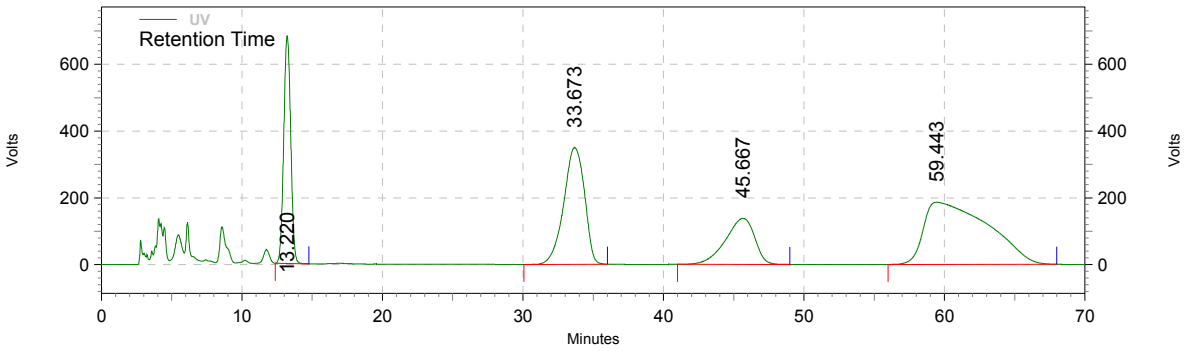


Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\fk88a 80.20 70 min ojnew col 222nm new OJ.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 60 min.met

Acquired: 12/08/2015 09:43:55

Printed: 12/08/2015 16:09:15



UV Results

Retention Time	Area	Area %	Height	Height %
13.220	94254496	16.94	2729897	50.31
33.673	143949344	25.88	1398691	25.78
45.667	80006616	14.38	551984	10.17
59.443	238099322	42.80	745216	13.73

Totals				
	556309778	100.00	5425788	100.00

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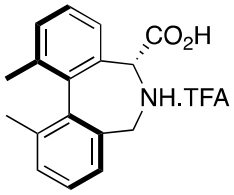
Table 1: Entry 24

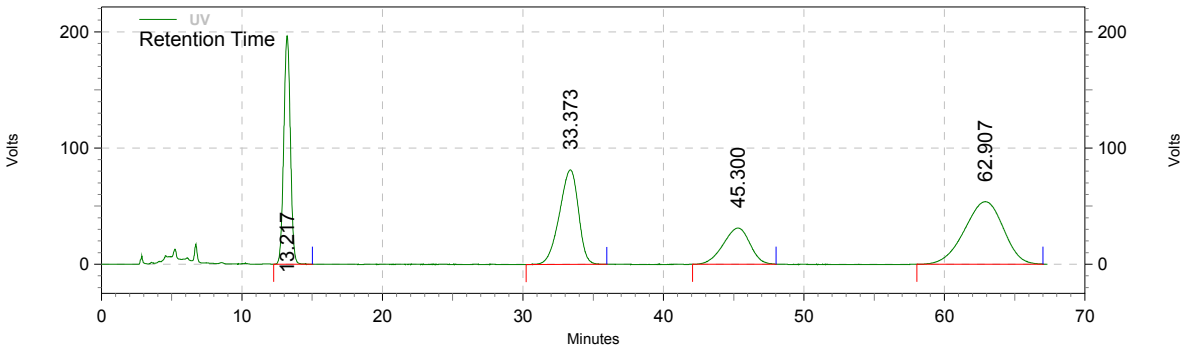


Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\fk144a OJ col 70min 80.20 1ml 222nm.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 70 min.met

Acquired: 18/09/2015 18:18:48

Printed: 18/09/2015 19:28:04



UV Results

Retention Time	Area	Area %	Height	Height %
13.217	25698863	22.49	786582	54.18
33.373	30578984	26.76	325339	22.41
45.300	16499502	14.44	124453	8.57
62.907	41500099	36.32	215390	14.84

Totals	114277448	100.00	1451764	100.00

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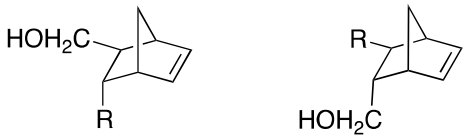
DOI: 10.1039/C8OB01795F

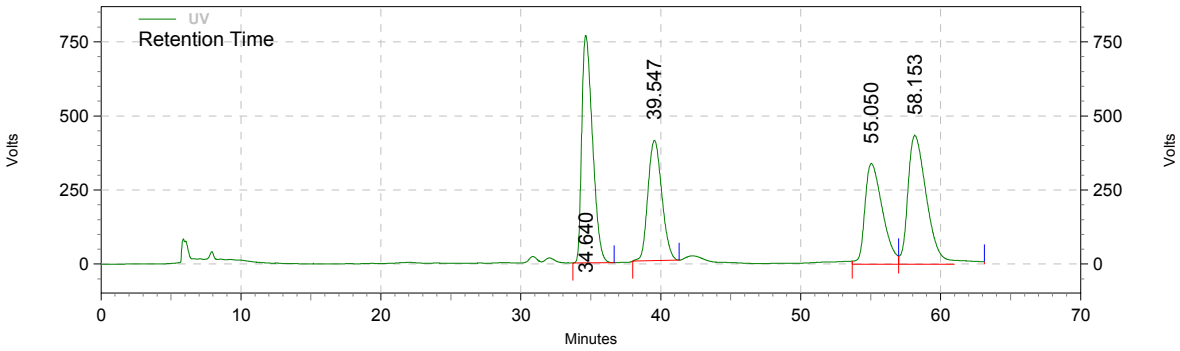
Table 2:

Racemic trace

3-(4-Methoxyphenyl)bicyclo[2.2.1]hept-5-en-2-yl)methanol



Enantiomeric excesses were determined using Chiralcel® AS-3 column (hexane/iPrOH=95:5, λ=222 nm), 0.5 mL; ***endo*** isomer (t_R1 35 min, 59 min) ***exo*** isomer (t_R1 39 min, 56 min)).



UV Results

Retention Time	Area	Area %	Height	Height %
34.640	163558053	29.20	3072756	39.40
39.547	112346323	20.06	1624898	20.84
55.050	118755971	21.20	1360526	17.45
58.153	165465336	29.54	1739711	22.31
Totals	560125683	100.00	7797891	100.00

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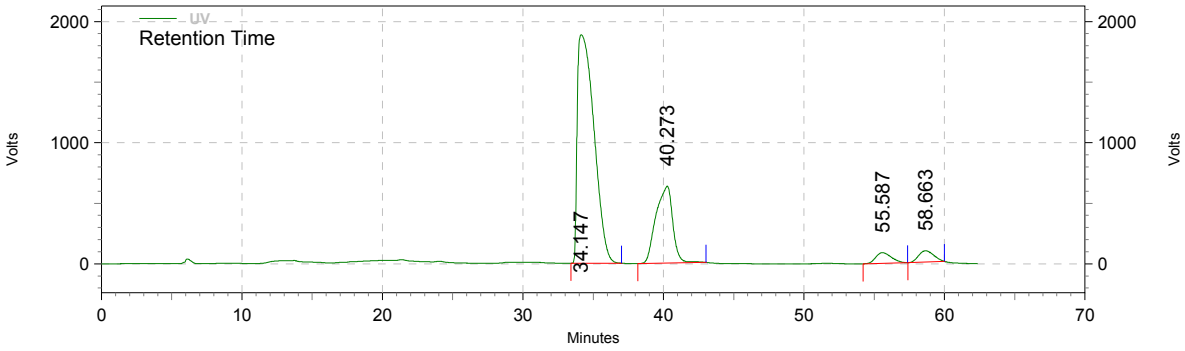
Table 2: Entry 1

Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\fk127a 95.5 60 min AS-3 222nm 0.5ml.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\95.5 0.5ml 254nm 70 min.met

Acquired: 25/08/2015 11:53:47

Printed: 25/08/2015 15:08:53



UV Results

Retention Time	Area	Area %	Height	Height %
34.147	621306304	70.07	7545500	69.80
40.273	209866962	23.67	2536428	23.46
55.587	27427539	3.09	354425	3.28
58.663	28036378	3.16	374410	3.46

Totals	886637183	100.00	10810763	100.00

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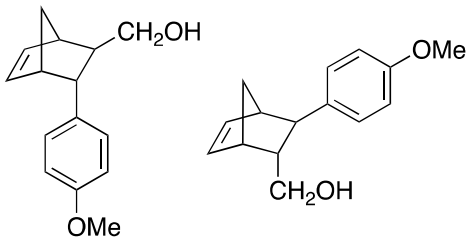
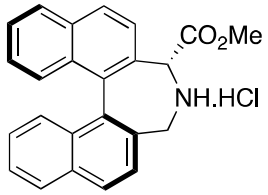
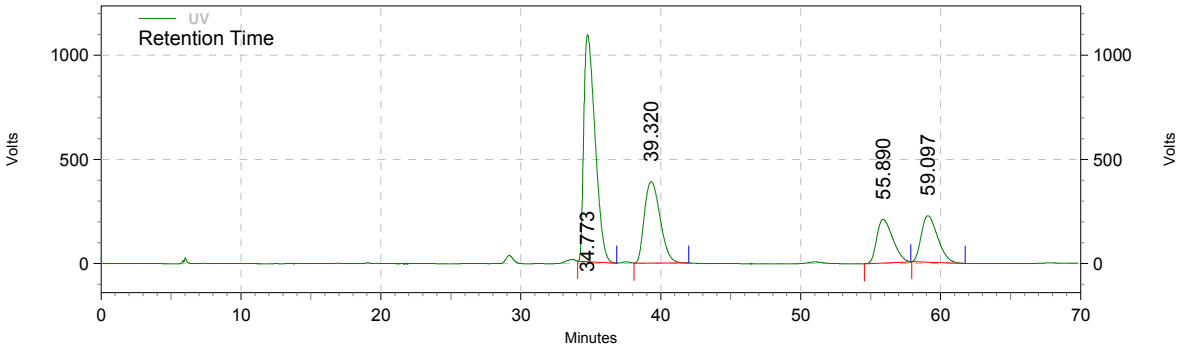
Table 2: Entry 2







UV Results

Retention Time	Area	Area %	Height	Height %
34.773	244782841	48.39	4362457	56.96
39.320	122076450	24.13	1563928	20.42
55.890	66366689	13.12	838484	10.95
59.097	72598464	14.35	894406	11.68
Totals	505824444	100.00	7659275	100.00

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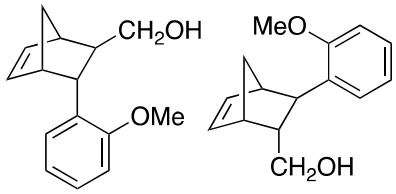
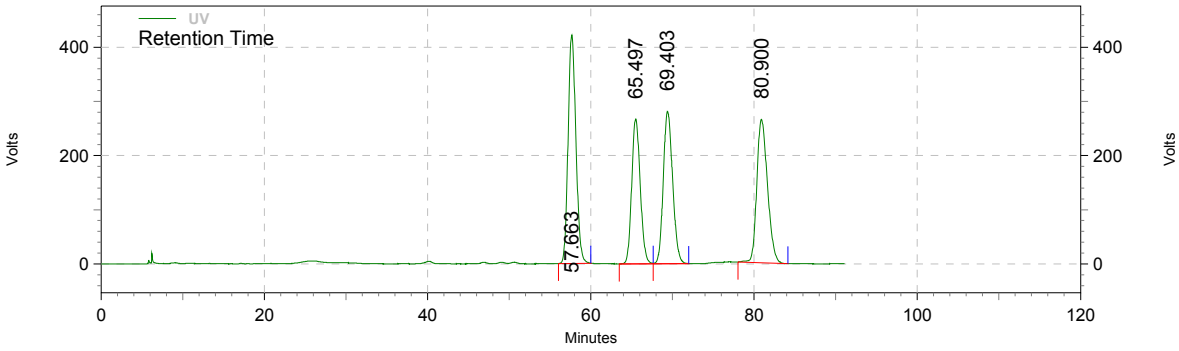
DOI: 10.1039/C8OB01795F

Racemic trace

3-(2-Methoxyphenyl)bicyclo[2.2.1]hept-5-en-2-yl)methanol



Enantiomeric excesses were determined using Chiralcel® AD-H column (hexane/iPrOH=98:2, λ=222 nm), 0.5 mL; ***endo*** isomer (t_R1 65 min, 80 min) ***exo*** isomer (t_R1 57 min, 69 min)).



UV Results

Retention Time	Area	Area %	Height	Height %
57.663	112116054	29.82	1687969	34.15
65.497	77688234	20.67	1069444	21.64
69.403	89562179	23.82	1125462	22.77
80.900	96566392	25.69	1059634	21.44
Totals	375932859	100.00	4942509	100.00

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DOI: 10.1039/C8OB01795F

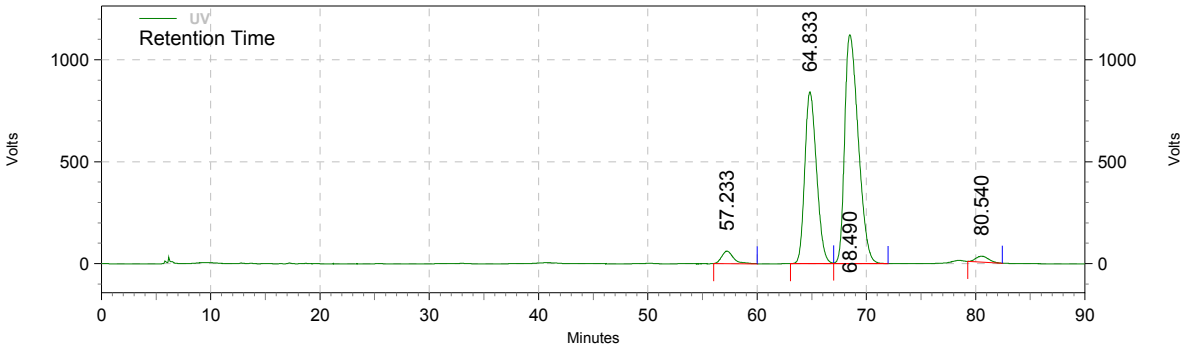
Table 2: Entry 3

Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\fk126A 98.2 90 min AD-H 222nm 0.5 ml.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\98.2 0.5ml 222nm 90 min.met

Acquired: 26/08/2015 17:04:04

Printed: 26/08/2015 18:38:23



UV Results

Retention Time	Area	Area %	Height	Height %
57.233	18253405	2.74	245313	2.98
64.833	251635736	37.71	3368507	40.97
68.490	387917941	58.13	4490546	54.62
80.540	9517660	1.43	117705	1.43

Totals	667324742	100.00	8222071	100.00

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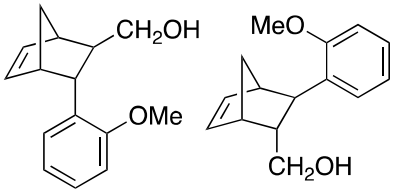
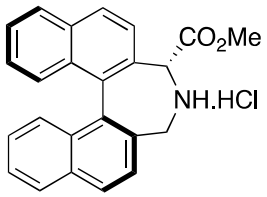
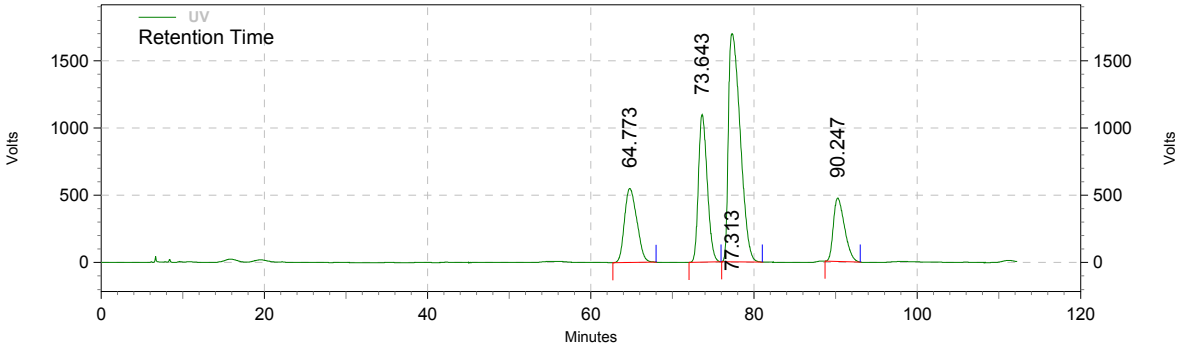
Table 2: Entry 4







UV Results

Retention Time	Area	Area %	Height	Height %
64.773	232326523	16.35	2201612	14.42
73.643	329047246	23.16	4387511	28.74
77.313	679753155	47.85	6788242	44.47
90.247	179479029	12.63	1887803	12.37
Totals	1420605953	100.00	15265168	100.00

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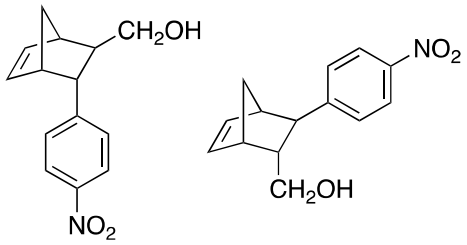
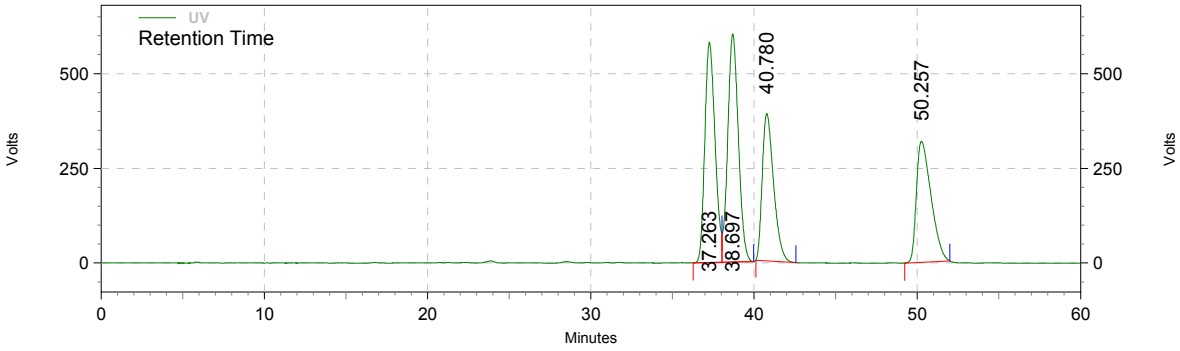
Racemic trace

3-(4-Nitrophenyl)bicyclo[2.2.1]hept-5-en-2-yl)methanol



Enantiomeric excesses were determined using Chiralcel® AD-H column (hexane/iPrOH=90:10, λ=254 nm), 0.5 mL; ***endo*** isomer (t_R1 49 min, 57 min) ***exo*** isomer (t_R1 43 min, 53 min)).



UV Results

Retention Time	Area	Area %	Height	Height %
37.263	101429900	27.78	2325141	30.72
38.697	109077192	29.88	2409635	31.84
40.780	75191423	20.60	1555653	20.55
50.257	79372910	21.74	1278614	16.89
Totals	365071425	100.00	7569043	100.00

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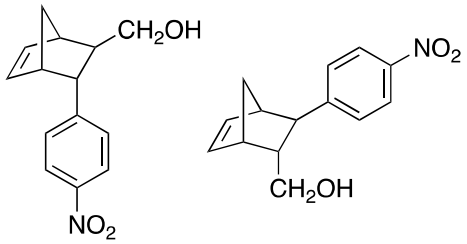
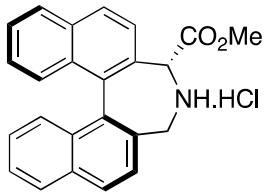
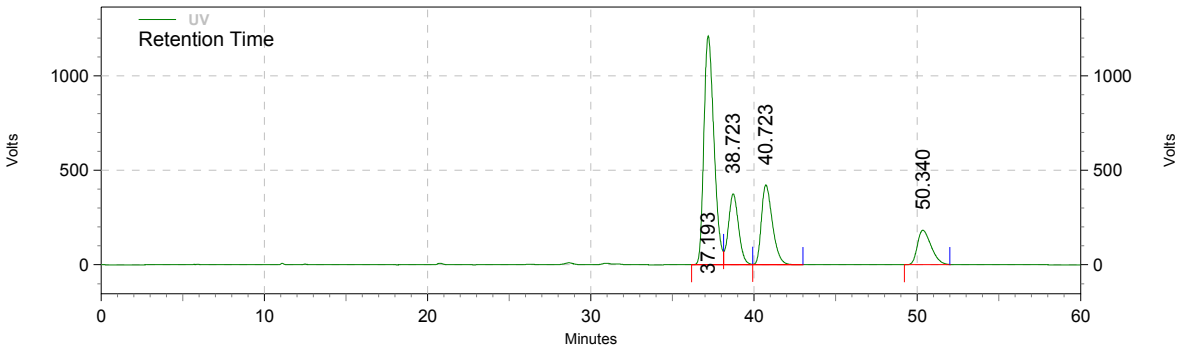
DOI: 10.1039/C8OB01795F

Table 2: Entry 5







UV Results

Retention Time	Area	Area %	Height	Height %
37.193	208648627	52.80	4848600	55.28
38.723	64947736	16.43	1503547	17.14
40.723	79165321	20.03	1688706	19.25
50.340	42443003	10.74	729707	8.32
Totals	395204687	100.00	8770560	100.00

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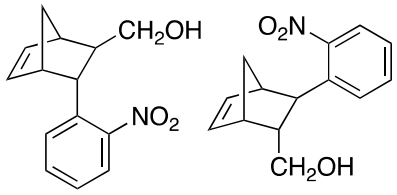
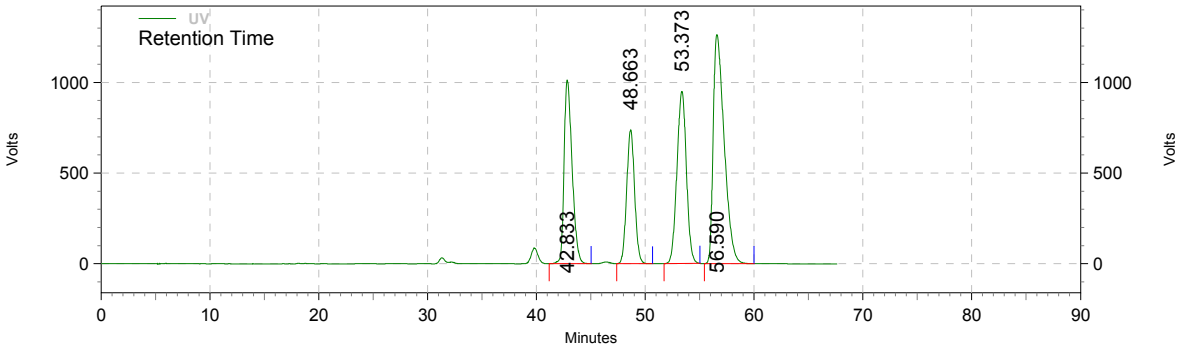
DOI: 10.1039/C8OB01795F

Racemic trace

3-(2-Nitrophenyl)bicyclo[2.2.1]hept-5-en-2-yl)methanol



Enantiomeric excesses were determined using Chiralcel® AD-H column (hexane/iPrOH=95:5, λ=254 nm), 0.5 mL; ***endo*** isomer (t_R1 37 min, 39 min) *exo* isomer (t_R1 41 min, 50 min)).



UV Results

Retention Time	Area	Area %	Height	Height %
42.833	206808907	21.99	4048777	25.56
48.663	150125042	15.96	2952648	18.64
53.373	229614645	24.41	3792924	23.94
56.590	354062576	37.64	5049003	31.87
Totals	940611170	100.00	15843352	100.00

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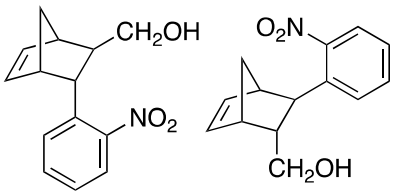
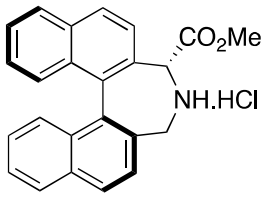
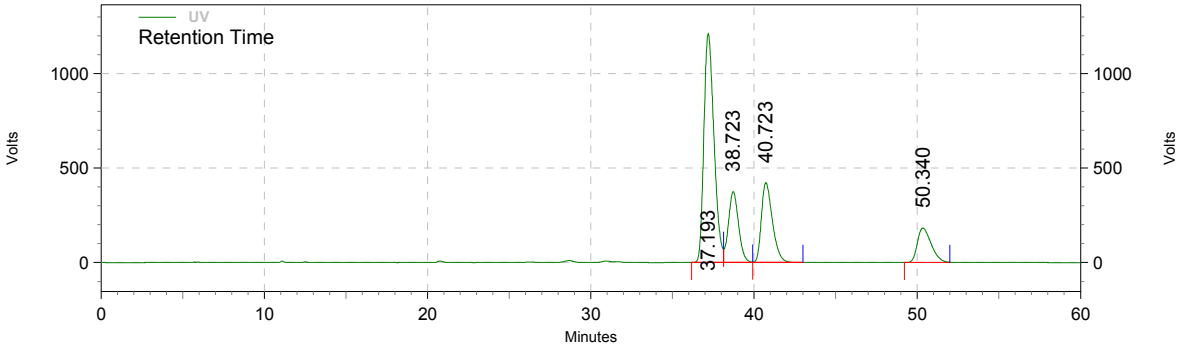
DOI: 10.1039/C8OB01795F

Table 2: Entry 6







UV Results

Retention Time	Area	Area %	Height	Height %
37.193	208648627	52.80	4848600	55.28
38.723	64947736	16.43	1503547	17.14
40.723	79165321	20.03	1688706	19.25
50.340	42443003	10.74	729707	8.32
Totals	395204687	100.00	8770560	100.00

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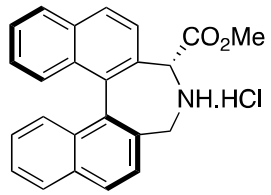
DOI: 10.1039/C8OB01795F

Extras

DMSO

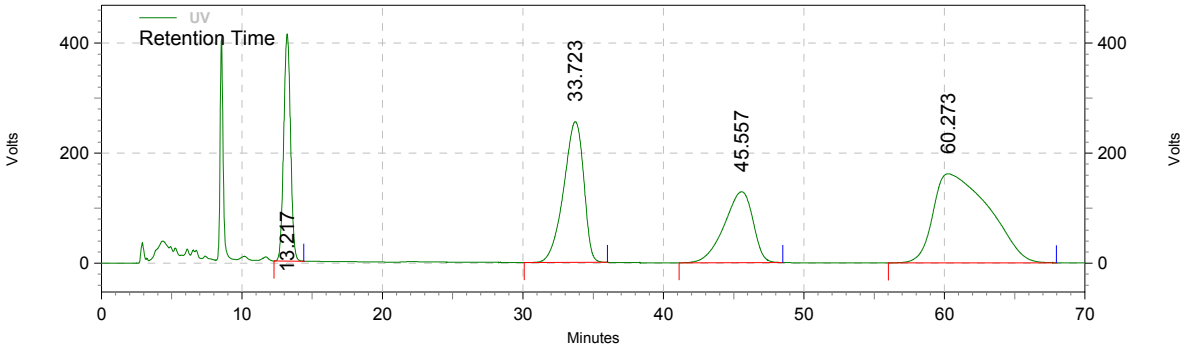


Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\fk119a 80.20 70 min ojnew col 222nm new OJ.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 60 min.met

Acquired: 12/08/2015 00:13:56

Printed: 12/08/2015 10:28:22



UV Results

Retention Time	Area	Area %	Height	Height %
13.217	55890096	13.68	1651198	43.01
33.723	101626015	24.87	1024026	26.67
45.557	73475052	17.98	516098	13.44
60.273	177699782	43.48	647663	16.87

Totals				
	408690945	100.00	3838985	100.00

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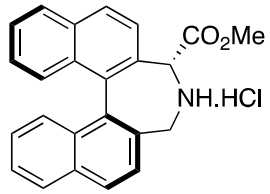
DOI: 10.1039/C8OB01795F

Area % Report

MeOH



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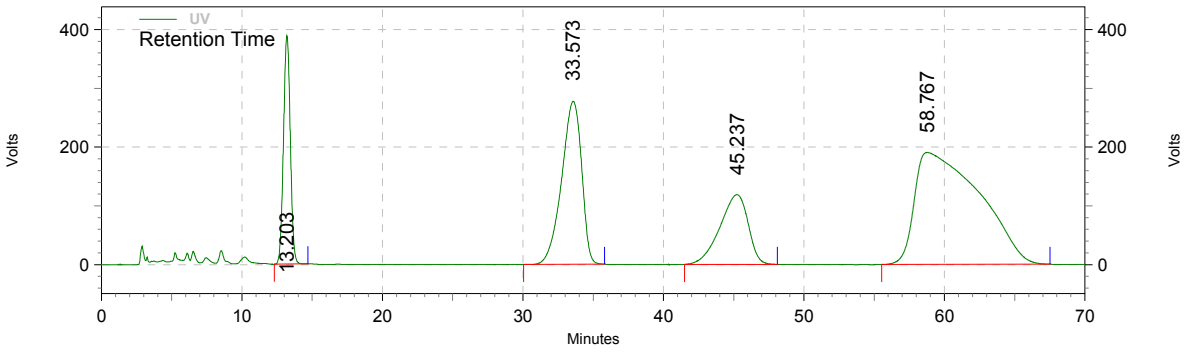
Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 60 min.met

Acquired: 11/08/2015 23:02:42

Printed: 12/08/2015 10:30:47



UV Results

Retention Time	Area	Area %	Height	Height %
13.203	52399515	11.06	1555104	39.86
33.573	109823275	23.18	1109560	28.44
45.237	66181909	13.97	474323	12.16
58.767	245313138	51.78	762016	19.53
Totals	473717837	100.00	3901003	100.00

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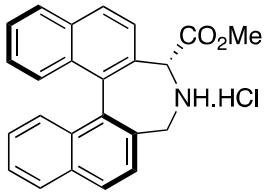
DOI: 10.1039/C8OB01795F

Area % Report

DCM



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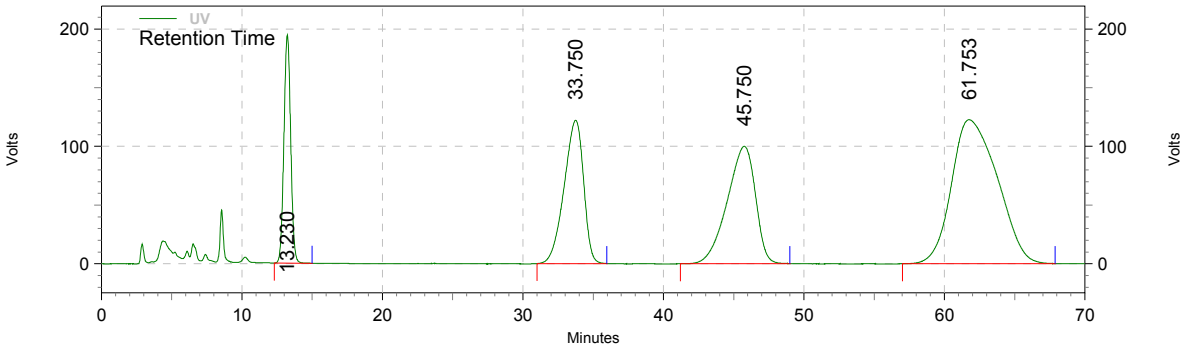
Acquired: 12/08/2015 03:47:31

Printed: 12/08/2015 10:33:05



UV Results

Retention Time	Area	Area %	Height	Height %
13.230	26024299	10.83	778147	36.07
33.750	46967516	19.55	488398	22.64
45.750	55930542	23.28	400235	18.55
61.753	111333006	46.34	490645	22.74

Totals	240255363	100.00	2157425	100.00

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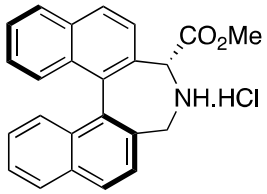
DOI: 10.1039/C8OB01795F

Area % Report

MeOH:H_2O



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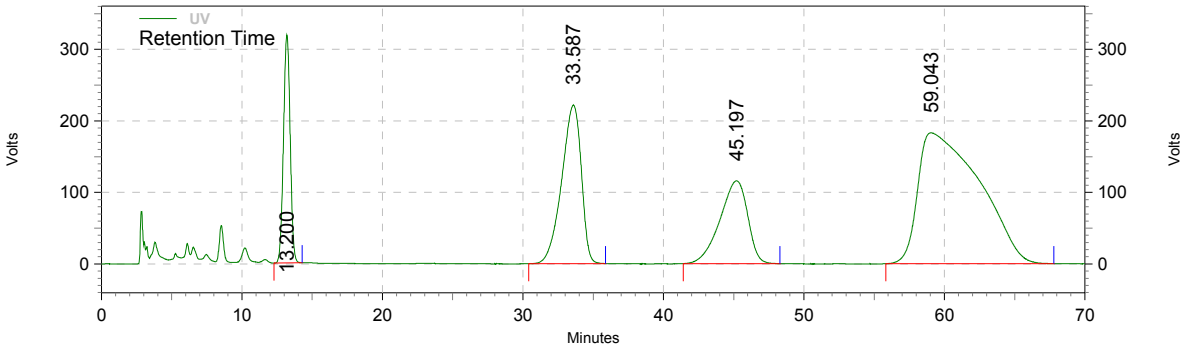
Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 60 min.met

Acquired: 11/08/2015 20:40:19

Printed: 12/08/2015 09:50:32



UV Results

Retention Time	Area	Area %	Height	Height %
13.200	42115716	10.15	1276100	38.00
33.587	86078004	20.75	886733	26.40
45.197	63615376	15.34	463155	13.79
59.043	223016583	53.76	732413	21.81

Totals	414825679	100.00	3358401	100.00

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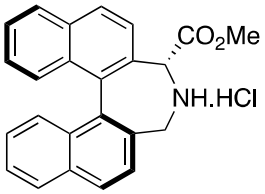
DOI: 10.1039/C8OB01795F

Area % Report

EtOH:H_2O



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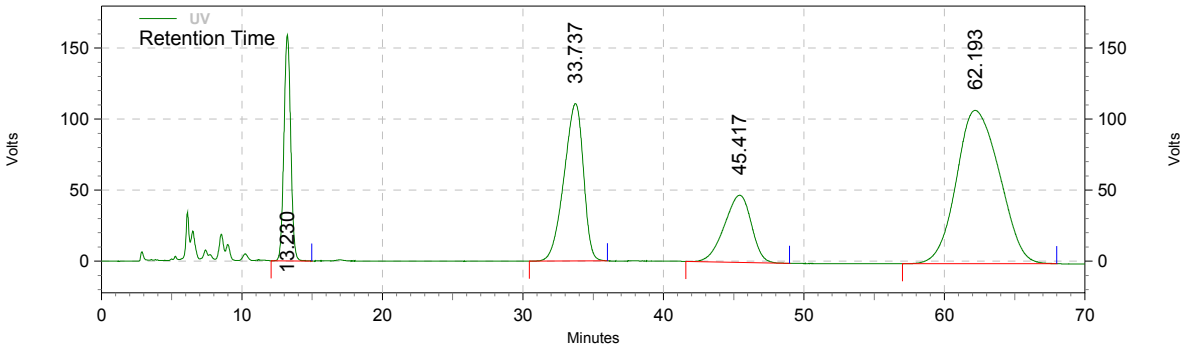
Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 70 min.met

Acquired: 13/08/2015 12:31:21

Printed: 13/08/2015 13:50:39



UV Results

Retention Time	Area	Area %	Height	Height %
13.230	21307907	11.75	636421	37.42
33.737	42518471	23.44	443333	26.06
45.417	25355990	13.98	189325	11.13
62.193	92178605	50.83	431894	25.39

Totals	181360973	100.00	1700973	100.00

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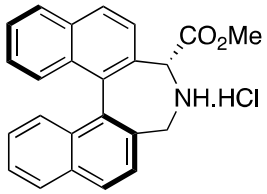
DOI: 10.1039/C8OB01795F

Area % Report

THF:H_2O



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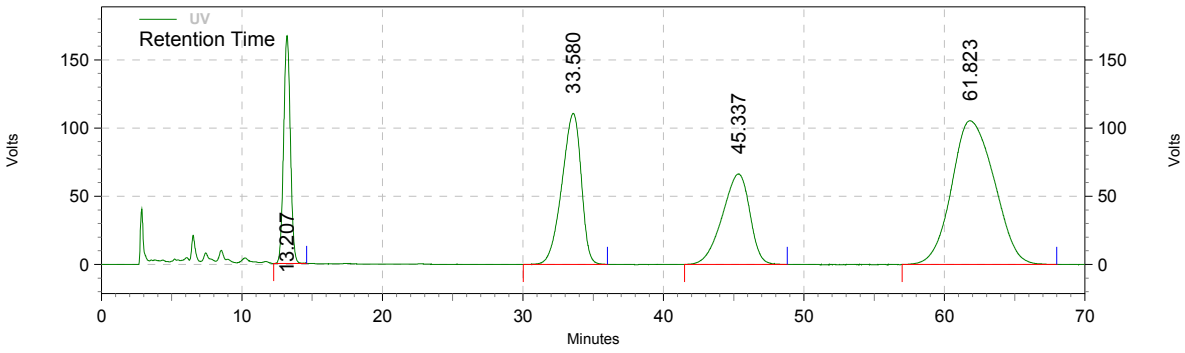
Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 60 min.met

Acquired: 12/08/2015 13:17:43

Printed: 12/08/2015 15:51:40



UV Results

Retention Time	Area	Area %	Height	Height %
13.207	22225410	11.73	668225	37.17
33.580	42284116	22.32	442747	24.63
45.337	36111913	19.07	265336	14.76
61.823	88787139	46.88	421628	23.45

Totals	189408578	100.00	1797936	100.00

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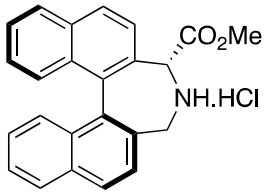
DOI: 10.1039/C8OB01795F

Area % Report

DMF:H_2O

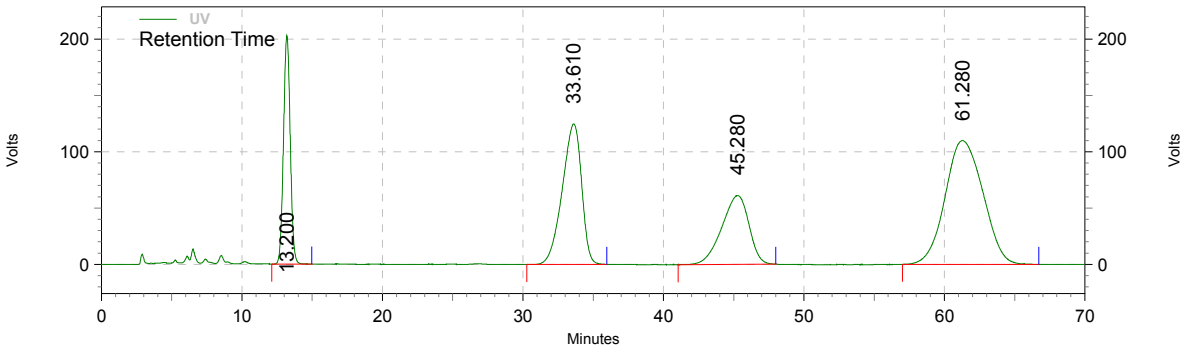


Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\fk133a 80.20 70 min ojnew col 222nm new OJ.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 60 min.met

Acquired: 12/08/2015 14:28:56

Printed: 12/08/2015 15:53:59



UV Results

Retention Time	Area	Area %	Height	Height %
13.200	27068837	14.26	811312	40.69
33.610	47814006	25.18	499001	25.02
45.280	32831882	17.29	244522	12.26
61.280	82159769	43.27	439294	22.03

Totals	189874494	100.00	1994129	100.00

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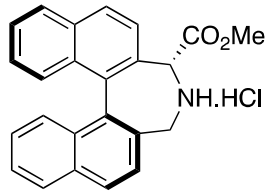
DOI: 10.1039/C8OB01795F

Area % Report

CH_2NO_2:H_2O

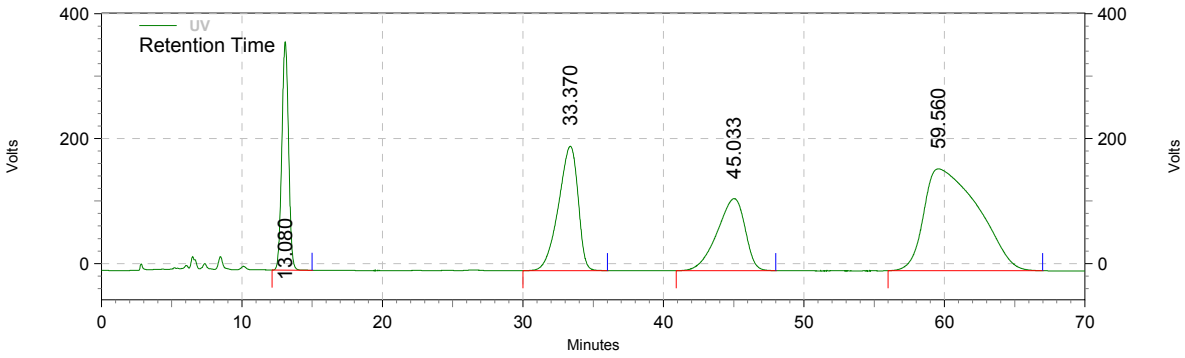


Data File: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\fk128a 80.20 70 min ojnew col 222nm new OJ.dat

Method: C:\EZChrom Elite\Enterprise\Projects\Fran\diels alder\80.20 1ml 222nm 60 min.met

Acquired: 12/08/2015 16:05:19

Printed: 12/08/2015 17:35:11



UV Results

Retention Time	Area	Area %	Height	Height %
13.080	48745952	13.35	1463413	43.36
33.370	77109017	21.12	796852	23.61
45.033	63875285	17.50	461735	13.68
59.560	175361503	48.03	652775	19.34

Totals	365091757	100.00	3374775	100.00

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Computational Supplementary Information

Cartesian coordinates for all 16 transition structures calculated at B3LYP/6-31G*

z-endo-si-a

1	6	0	-2.489319	-0.519059	0.621655
2	6	0	-1.559452	-0.681484	1.645625
3	6	0	-0.017063	0.413801	-0.578955
4	6	0	-0.536043	0.399879	1.897124
5	1	0	0.738119	0.919854	-1.188198
6	1	0	-1.006209	1.387405	1.951693
7	1	0	-0.005911	0.220752	2.834818
8	7	0	0.484814	0.436553	0.813862
9	6	0	-1.307332	1.205111	-0.723901
10	6	0	-2.491191	0.770410	-0.132765
11	6	0	-1.266683	2.413552	-1.461716
12	1	0	-0.339244	2.711566	-1.945212
13	6	0	-3.657090	1.609255	-0.199621
14	6	0	-3.601173	2.826054	-0.959805
15	6	0	-2.389394	3.191860	-1.598253
16	6	0	-4.752411	3.655462	-1.038700
17	6	0	-1.534118	-1.863552	2.425248
18	6	0	-3.370610	-1.605882	0.292338
19	6	0	-2.426377	-2.878416	2.181348
20	6	0	-3.347275	-2.789390	1.104543
21	1	0	-0.810472	-1.955172	3.231341
22	6	0	-4.225887	-3.863110	0.797401
23	6	0	1.782277	0.470467	1.108052
24	1	0	1.990377	0.479119	2.176129
25	6	0	-0.117773	-1.010774	-1.178554
26	8	0	-0.739149	-1.238715	-2.187536
27	8	0	0.625126	-1.900573	-0.506499
28	6	0	0.601110	-3.247068	-1.034495
29	1	0	-0.414769	-3.644670	-0.988331
30	1	0	0.948444	-3.254099	-2.069794
31	1	0	1.271461	-3.819329	-0.394346
32	6	0	2.875233	0.470936	0.243327
33	6	0	3.128030	3.164011	0.344850
34	6	0	4.227517	0.290250	0.734581
35	1	0	2.706214	0.399502	-0.823473
36	6	0	4.387087	2.719729	-0.325967
37	6	0	3.346615	3.220598	1.718997
38	1	0	2.261859	3.562909	-0.171800
39	6	0	5.060453	1.954868	0.811153
40	1	0	4.258489	-0.008863	1.781506
41	1	0	4.996610	3.615512	-0.532057
42	1	0	4.268515	2.187371	-1.269423
43	6	0	4.550662	2.568867	2.001017
44	1	0	6.117643	1.712524	0.748208
45	1	0	4.975755	2.439942	2.991509
46	1	0	2.672091	3.653419	2.449211

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57	1	0	7.740269	-2.765041	-2.011049
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68	1	0	-4.918056	0.418106	1.106311
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73	1	0	4.909605	0.259741	-1.227333

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68	6	0	-5.781669	-1.678297	0.293377
69	1	0	-4.788500	-0.038314	-0.640917
70	1	0	-2.081856	-3.253598	3.007831
71	1	0	-4.430699	-3.807648	2.585475
72	1	0	-6.552749	-3.391469	1.379764
73	1	0	-6.703684	-1.519860	-0.258277

e-endo-si-b

1	6	0	2.197624	-0.173203	-0.686678
2	6	0	0.938014	-0.339882	-1.256686
3	6	0	0.393109	0.360900	1.511983
4	6	0	-0.166848	0.640327	-0.931173
5	1	0	-0.073359	0.702310	2.443615
6	1	0	0.171641	1.676003	-1.036849
7	1	0	-1.011169	0.496582	-1.602880
8	7	0	-0.646188	0.464651	0.461964
9	6	0	1.577485	1.270082	1.237243
10	6	0	2.434126	1.031416	0.165141
11	6	0	1.768712	2.390039	2.083132
12	1	0	1.098508	2.543746	2.925141
13	6	0	3.469232	1.983871	-0.131941
14	6	0	3.657799	3.105985	0.743542
15	6	0	2.796885	3.271391	1.857931
16	6	0	4.684837	4.047173	0.462701
17	6	0	0.665281	-1.441450	-2.104692
18	6	0	3.199332	-1.186454	-0.884193
19	6	0	1.632813	-2.379632	-2.366936
20	6	0	2.908648	-2.292945	-1.751191
21	1	0	-0.316308	-1.528064	-2.564580
22	6	0	3.894805	-3.294966	-1.958497

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23	6	0	-1.925702	0.262996	0.788449
24	1	0	-2.090489	0.162556	1.858996
25	6	0	0.728187	-1.129665	1.770317
26	8	0	-0.017486	-2.044477	1.486814
27	8	0	1.874954	-1.252790	2.434565
28	6	0	2.263158	-2.599647	2.791449
29	1	0	1.493550	-3.062240	3.413265
30	1	0	2.414580	-3.192772	1.887500
31	1	0	3.195537	-2.491398	3.343299
32	6	0	-3.045622	0.211494	-0.033101
33	6	0	-2.940985	-2.532830	0.154164
34	6	0	-4.390770	0.225280	0.499368
35	1	0	-2.925123	0.291940	-1.106150
36	6	0	-4.235671	-2.249720	-0.535697
37	6	0	-3.158084	-2.573604	1.525782
38	1	0	-2.012990	-2.805187	-0.334574
39	6	0	-5.015709	-1.560935	0.581525
40	1	0	-4.431292	0.501494	1.551588
41	1	0	-4.733586	-3.212561	-0.739438
42	1	0	-4.167284	-1.718590	-1.485047
43	6	0	-4.439304	-2.071754	1.785062
44	1	0	-6.093113	-1.446414	0.505595
45	1	0	-4.884381	-1.969967	2.770225
46	1	0	-2.424020	-2.880362	2.260047
47	6	0	-5.470215	0.934878	-0.268553
48	6	0	-6.468191	1.611826	0.449404
49	6	0	-5.535629	0.937437	-1.670674
50	6	0	-7.496056	2.282895	-0.211802
51	1	0	-6.434622	1.620659	1.536667
52	6	0	-6.564330	1.605767	-2.332519
53	1	0	-4.781723	0.424152	-2.261514
54	6	0	-7.547995	2.280879	-1.606233
55	1	0	-8.253253	2.808056	0.362945
56	1	0	-6.596171	1.601260	-3.418189
57	1	0	-8.347516	2.801727	-2.124490
58	6	0	5.479407	3.912492	-0.651115
59	6	0	4.295229	1.892167	-1.287801
60	6	0	5.271396	2.829972	-1.538887
61	1	0	4.821756	4.884798	1.141648
62	1	0	2.948008	4.120207	2.519360
63	1	0	6.258046	4.640207	-0.859777
64	1	0	5.885685	2.741215	-2.430257
65	1	0	4.145675	1.075284	-1.983975
66	6	0	4.457135	-1.169076	-0.218632
67	6	0	5.109668	-3.232934	-1.316534
68	6	0	5.384920	-2.165152	-0.429411
69	1	0	4.681435	-0.361917	0.468885
70	1	0	1.426740	-3.212604	-3.033925
71	1	0	3.665824	-4.119470	-2.628798
72	1	0	5.855122	-4.005686	-1.479767
73	1	0	6.337736	-2.131884	0.091158

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2	6	0	1.094584	-1.113482	-0.893322
3	6	0	0.429847	0.291329	1.535256
4	6	0	-0.125853	-0.221276	-0.884573
5	1	0	-0.075495	0.805683	2.359762
6	1	0	0.072036	0.729908	-1.395353
7	1	0	-0.942337	-0.723481	-1.404474
8	7	0	-0.600596	0.092331	0.487421
9	6	0	1.534007	1.200933	1.028209
10	6	0	2.409989	0.774990	0.032443
11	6	0	1.604912	2.519256	1.541803
12	1	0	0.932343	2.814791	2.343867
13	6	0	3.331836	1.718245	-0.539710
14	6	0	3.397982	3.047367	-0.001079
15	6	0	2.530604	3.411616	1.060130
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17	6	0	0.961907	-2.441036	-1.372361
18	6	0	3.444908	-1.535538	-0.376782
19	6	0	2.042588	-3.287059	-1.396454
20	6	0	3.299815	-2.868853	-0.887485
21	1	0	-0.004867	-2.781991	-1.733747
22	6	0	4.407293	-3.757789	-0.844537
23	6	0	-1.884813	0.308335	0.760218
24	1	0	-2.087053	0.511775	1.809995
25	6	0	0.930444	-1.027661	2.165350
26	8	0	1.973963	-1.108215	2.765149
27	8	0	0.014531	-2.002341	2.061646
28	6	0	0.373926	-3.253106	2.692931
29	1	0	0.546701	-3.101351	3.760638
30	1	0	-0.475401	-3.914774	2.526217
31	1	0	1.277587	-3.657088	2.232181
32	6	0	-2.974229	0.285826	-0.108607
33	6	0	-4.335421	0.286553	0.390674
34	6	0	-2.989612	2.983200	-0.374965
35	1	0	-2.810437	0.099854	-1.162569
36	6	0	-5.013874	2.018597	0.249647
37	1	0	-4.389260	0.127148	1.466802
38	6	0	-4.289067	2.561808	-0.979512
39	6	0	-3.185172	3.238096	0.979602
40	1	0	-2.099276	3.232828	-0.941667
41	6	0	-4.437045	2.735662	1.347542
42	1	0	-6.089051	1.865391	0.220420
43	1	0	-4.822012	3.470203	-1.306799
44	1	0	-4.226152	1.898024	-1.841421
45	1	0	-2.466944	3.704190	1.644731
46	1	0	-4.859635	2.776891	2.346602

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47	6	0	-5.367718	-0.557898	-0.308026
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49	6	0	-5.367464	-0.781987	-1.693305
50	6	0	-7.376867	-1.920193	-0.128341
51	1	0	-6.405003	-0.973280	1.538954
52	6	0	-6.357086	-1.565111	-2.286314
53	1	0	-4.590907	-0.358438	-2.324480
54	6	0	-7.365094	-2.136532	-1.506964
55	1	0	-8.152873	-2.364025	0.488318
56	1	0	-6.337793	-1.732087	-3.359355
57	1	0	-8.133534	-2.747289	-1.971213
58	6	0	5.603113	-3.366691	-0.289114
59	6	0	4.686362	-1.177974	0.218134
60	6	0	5.735038	-2.069375	0.259822
61	1	0	6.671247	-1.776392	0.725925
62	1	0	1.941451	-4.297393	-1.784045
63	1	0	4.286264	-4.759747	-1.248288
64	1	0	6.442288	-4.055314	-0.255741
65	1	0	4.800572	-0.194866	0.658671
66	6	0	4.159696	1.407553	-1.655523
67	6	0	5.114350	3.638256	-1.619365
68	6	0	5.024578	2.341634	-2.179684
69	1	0	2.597147	4.413932	1.474888
70	1	0	4.362319	4.979515	-0.126858
71	1	0	5.808340	4.360903	-2.038440
72	1	0	5.643509	2.081960	-3.033656
73	1	0	4.102387	0.421411	-2.101133

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1	6	0	-2.151472	0.661228	-0.484571
2	6	0	-0.872417	0.876799	-0.990722
3	6	0	-0.455839	-0.902720	1.272343
4	6	0	0.090504	-0.283885	-1.114362
5	1	0	-0.047886	-1.640521	1.972765
6	1	0	-0.378974	-1.147188	-1.596704
7	1	0	0.955076	0.007821	-1.707795
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9	6	0	-1.747616	-1.473262	0.718436
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11	6	0	-2.100410	-2.795606	1.085907
12	1	0	-1.470684	-3.340094	1.785398
13	6	0	-3.698352	-1.366668	-0.746789
14	6	0	-4.048062	-2.702319	-0.353589
15	6	0	-3.234318	-3.385670	0.585291
16	6	0	-5.185737	-3.326908	-0.932517
17	6	0	-0.441784	2.176882	-1.351533
18	6	0	-3.012850	1.787639	-0.244949
19	6	0	-1.277905	3.255044	-1.201577
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22	6	0	-3.415128	4.215427	-0.408600
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26	8	0	0.342131	1.192719	2.213448
27	8	0	-1.721405	0.449197	2.771692
28	6	0	-1.894291	1.584764	3.651956
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30	1	0	-2.861149	1.431845	4.128991
31	1	0	-1.092153	1.612744	4.392516
32	6	0	2.989649	-0.547147	-0.224969
33	6	0	4.294554	-0.346364	0.371817
34	6	0	3.441250	-3.192503	-0.514165
35	1	0	2.872008	-0.340729	-1.281477
36	6	0	5.253799	-1.949666	0.248440
37	1	0	4.248639	-0.210613	1.451125
38	6	0	4.696520	-2.567841	-1.030499
39	6	0	3.594441	-3.448615	0.845551
40	1	0	2.635891	-3.561384	-1.139795
41	6	0	4.730300	-2.769590	1.298158
42	1	0	6.289969	-1.625888	0.288768
43	1	0	5.379859	-3.378223	-1.335054
44	1	0	4.586475	-1.901695	-1.885740
45	1	0	2.918196	-4.033273	1.459166
46	1	0	5.092048	-2.766498	2.321592
47	6	0	5.223816	0.668595	-0.237974
48	6	0	6.063709	1.400071	0.615937
49	6	0	5.302487	0.906712	-1.618797
50	6	0	6.951104	2.348263	0.108708
51	1	0	6.014908	1.232136	1.689516
52	6	0	6.191963	1.852280	-2.127268
53	1	0	4.665306	0.365473	-2.313045
54	6	0	7.019625	2.576122	-1.266303
55	1	0	7.585449	2.909478	0.788477
56	1	0	6.235630	2.026136	-3.198553
57	1	0	7.710168	3.313196	-1.665017
58	6	0	-4.640473	4.063545	0.197257
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60	6	0	-5.065511	2.780399	0.616538
61	1	0	-6.024446	2.668714	1.114532
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63	1	0	-3.069685	5.198425	-0.718168
64	1	0	-5.278781	4.925981	0.365385
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66	6	0	-4.485089	-0.739459	-1.754102
67	6	0	-5.936048	-2.680226	-1.886023
68	6	0	-5.571384	-1.379170	-2.307325
69	1	0	-3.508510	-4.393315	0.885933
70	1	0	-5.444344	-4.333537	-0.614269
71	1	0	-6.800615	-3.168185	-2.326319
72	1	0	-6.152938	-0.882060	-3.078324

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73	1	0	-4.217849	0.253626	-2.095742

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1	6	0	2.352698	-0.233326	-0.537144
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4	6	0	-0.098133	0.229768	-0.892764
5	1	0	-0.077355	0.589336	2.479710
6	1	0	0.089329	1.278962	-1.147197
7	1	0	-0.901780	-0.136390	-1.531334
8	7	0	-0.580743	0.180239	0.510825
9	6	0	1.515211	1.271464	1.251871
10	6	0	2.411385	1.060027	0.207244
11	6	0	1.545033	2.471594	2.002897
12	1	0	0.850167	2.602482	2.828644
13	6	0	3.317952	2.112083	-0.163254
14	6	0	3.344412	3.317520	0.616091
15	6	0	2.453145	3.458644	1.709771
16	6	0	4.244008	4.359102	0.262060
17	6	0	1.029333	-1.824666	-1.834638
18	6	0	3.485538	-1.113508	-0.637247
19	6	0	2.121083	-2.638059	-2.011803
20	6	0	3.364598	-2.320201	-1.405342
21	1	0	0.074944	-2.088387	-2.284468
22	6	0	4.482167	-3.189830	-1.520810
23	6	0	1.014849	-1.135104	1.975296
24	8	0	2.063677	-1.268449	2.553937
25	8	0	0.154725	-2.139579	1.706880
26	6	0	0.617730	-3.447780	2.119338
27	1	0	-0.187350	-4.136952	1.864162
28	1	0	1.532215	-3.705330	1.581453
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31	6	0	-4.318422	0.143564	0.534511
32	6	0	-3.024252	-2.684400	-0.060060
33	1	0	-2.851718	0.212332	-1.072447
34	6	0	-5.013548	-1.640954	0.575071
35	1	0	-4.332280	0.275487	1.618039
36	6	0	-3.837823	-2.413019	1.163618
37	6	0	-3.846488	-2.613025	-1.171969
38	1	0	-1.991645	-3.014188	-0.044983
39	6	0	-5.080526	-2.061604	-0.782589
40	1	0	-5.928269	-1.501340	1.145581
41	1	0	-4.230316	-3.374110	1.535653
42	1	0	-3.302724	-1.943594	1.989847
43	6	0	-1.871414	0.104360	0.832388
44	1	0	-2.051591	0.067220	1.905045
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46	1	0	-5.919596	-1.878407	-1.444345

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50	6	0	-7.329541	2.406778	0.128264
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53	1	0	-4.727083	0.678854	-2.168511
54	6	0	-7.391191	2.579700	-1.254171
55	1	0	-8.056623	2.891305	0.773191
56	1	0	-6.487892	2.084722	-3.149812
57	1	0	-8.167800	3.198431	-1.693646
58	6	0	4.167033	2.034509	-1.303350
59	6	0	5.066527	4.238674	-0.832950
60	6	0	5.015738	3.068638	-1.627818
61	1	0	2.484215	4.369747	2.301097
62	1	0	4.137961	1.149683	-1.928337
63	1	0	5.651093	2.987723	-2.505070
64	1	0	5.747171	5.042430	-1.097714
65	1	0	4.260881	5.259953	0.869913
66	6	0	5.664240	-2.906125	-0.877376
67	6	0	4.713962	-0.868470	0.036252
68	6	0	5.772418	-1.741415	-0.081246
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1	6	0	2.177444	-0.244709	-0.629210
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7	1	0	-0.989371	0.510367	-1.628644
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9	6	0	1.659673	1.479864	1.083613
10	6	0	2.494019	1.044265	0.056258
11	6	0	1.926683	2.689224	1.771069
12	1	0	1.271233	2.997458	2.581715
13	6	0	3.585936	1.879696	-0.363403
14	6	0	3.851226	3.094828	0.353678
15	6	0	3.008423	3.463910	1.432412
16	6	0	4.935188	3.921603	-0.047869
17	6	0	0.567112	-1.584774	-1.885239
18	6	0	3.113202	-1.335313	-0.689278
19	6	0	1.474241	-2.607087	-2.020071
20	6	0	2.753166	-2.523175	-1.410086

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21	1	0	-0.418326	-1.665697	-2.337455
22	6	0	3.674320	-3.603075	-1.480721
23	6	0	0.682159	-0.761793	1.968897
24	8	0	-0.131422	-1.656585	1.856958
25	8	0	1.840004	-0.857623	2.615679
26	6	0	2.147274	-2.150984	3.187075
27	1	0	3.101287	-2.018891	3.694933
28	1	0	1.367184	-2.446168	3.892093
29	1	0	2.230985	-2.896173	2.393630
30	6	0	-3.007934	0.312163	-0.014770
31	6	0	-4.324031	0.255185	0.567038
32	6	0	-2.772268	-2.533608	0.202783
33	1	0	-2.918733	0.332654	-1.093764
34	6	0	-4.829752	-1.583612	0.784457
35	1	0	-4.322052	0.474966	1.636038
36	6	0	-3.578680	-2.190522	1.409970
37	6	0	-3.612626	-2.618896	-0.893338
38	1	0	-1.716182	-2.773557	0.236317
39	6	0	-4.880259	-2.128034	-0.528258
40	1	0	-5.745045	-1.476354	1.361180
41	1	0	-3.880023	-3.133480	1.896544
42	1	0	-3.054053	-1.601093	2.161782
43	6	0	-1.882518	0.474653	0.780370
44	1	0	-2.032329	0.474809	1.857495
45	1	0	-3.335238	-2.967484	-1.881820
46	1	0	-5.741703	-2.073064	-1.184580
47	6	0	-5.481941	0.916771	-0.115616
48	6	0	-6.465699	1.530602	0.673649
49	6	0	-5.622561	0.953338	-1.511758
50	6	0	-7.556431	2.173349	0.087000
51	1	0	-6.372875	1.513639	1.757491
52	6	0	-6.711822	1.593372	-2.098876
53	1	0	-4.881631	0.480292	-2.151380
54	6	0	-7.682594	2.206540	-1.301412
55	1	0	-8.304120	2.647827	0.715688
56	1	0	-6.803183	1.616173	-3.180989
57	1	0	-8.530312	2.705220	-1.761672
58	6	0	4.397778	1.580976	-1.494280
59	6	0	5.713094	3.587765	-1.131189
60	6	0	5.430634	2.411687	-1.866192
61	1	0	3.216462	4.382865	1.973651
62	1	0	4.193661	0.689924	-2.076361
63	1	0	6.032682	2.164769	-2.735893
64	1	0	6.535592	4.229280	-1.433435
65	1	0	5.129374	4.832346	0.512627
66	6	0	4.890938	-3.535402	-0.842669
67	6	0	4.370274	-1.311114	-0.022552
68	6	0	5.233442	-2.381917	-0.097601
69	1	0	1.217220	-3.502578	-2.579949
70	1	0	3.393807	-4.490481	-2.042351
71	1	0	5.586279	-4.367687	-0.900004

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72	1	0	6.186962	-2.341806	0.421216
73	1	0	4.645394	-0.437966	0.557574

e-exo-re-a

1	6	0	2.333624	-0.599136	-0.463990
2	6	0	1.097078	-1.022730	-0.943904
3	6	0	0.463525	0.200213	1.591712
4	6	0	-0.112402	-0.119469	-0.856083
5	1	0	-0.030926	0.660863	2.453748
6	1	0	0.093543	0.868227	-1.287820
7	1	0	-0.936766	-0.567909	-1.411075
8	7	0	-0.575456	0.083633	0.540150
9	6	0	1.572435	1.134660	1.142538
10	6	0	2.440242	0.773038	0.115051
11	6	0	1.656570	2.412604	1.748140
12	1	0	0.989209	2.656613	2.571469
13	6	0	3.370526	1.745718	-0.390850
14	6	0	3.450595	3.032430	0.240926
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17	6	0	0.945340	-2.307315	-1.523652
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22	6	0	4.374269	-3.706109	-1.113372
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26	6	0	0.395455	-3.420796	2.481217
27	1	0	0.575368	-3.352701	3.556311
28	1	0	-0.457598	-4.064489	2.269215
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31	6	0	-2.958011	3.120520	-0.148940
32	6	0	-4.302659	0.302394	0.507705
33	1	0	-2.811369	0.174694	-1.074563
34	6	0	-3.795152	2.877007	1.064718
35	6	0	-3.753490	3.012192	-1.275815
36	1	0	-1.932824	3.473560	-0.125307
37	6	0	-4.964030	2.097269	0.474073
38	1	0	-4.336546	0.205185	1.594505
39	1	0	-4.187866	3.847567	1.411029
40	1	0	-3.280468	2.421556	1.912092
41	6	0	-4.997576	2.474399	-0.897119
42	1	0	-5.892352	1.986181	1.028583
43	6	0	-1.859629	0.265513	0.844855
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50	6	0	-7.355923	-1.909267	0.127852
51	1	0	-6.315866	-0.958817	1.753151
52	6	0	-6.434713	-1.541392	-2.073125
53	1	0	-4.685940	-0.308146	-2.183155
54	6	0	-7.402853	-2.123191	-1.249395
55	1	0	-8.102018	-2.358042	0.776929
56	1	0	-6.464164	-1.705297	-3.146465
57	1	0	-8.186999	-2.738153	-1.680707
58	6	0	5.171213	3.720075	-1.334126
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63	1	0	5.872243	4.463749	-1.701522
64	1	0	5.683447	2.263182	-2.856381
65	1	0	4.125979	0.556374	-2.042538
66	6	0	5.576753	-3.375115	-0.533877
67	6	0	4.691635	-1.219447	0.143029
68	6	0	5.728030	-2.125511	0.112288
69	1	0	1.898854	-4.138536	-2.082701
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71	1	0	6.406492	-4.075504	-0.556658
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e-exo-re-b

1	6	0	-2.166137	0.600447	-0.529424
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4	6	0	0.079554	-0.407605	-1.032995
5	1	0	-0.087309	-1.419994	2.182817
6	1	0	-0.388467	-1.317514	-1.422254
7	1	0	0.949572	-0.185010	-1.647905
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9	6	0	-1.775028	-1.392064	0.900554
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26	6	0	-1.948541	1.970004	3.477823
27	1	0	-1.927688	2.823135	2.796951
28	1	0	-2.925117	1.875749	3.950211
29	1	0	-1.160264	2.076676	4.226181
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31	6	0	3.380199	-3.311592	-0.296975
32	6	0	4.270015	-0.378188	0.511559
33	1	0	2.870567	-0.397659	-1.153581
34	6	0	4.105880	-3.008258	0.973892
35	6	0	4.222101	-3.064658	-1.367160
36	1	0	2.412332	-3.797712	-0.349705
37	6	0	5.189342	-2.057271	0.478885
38	1	0	4.226380	-0.309519	1.599890
39	1	0	4.606188	-3.930773	1.312505
40	1	0	3.488582	-2.657112	1.802203
41	6	0	5.357455	-2.380438	-0.895804
42	1	0	6.056566	-1.834938	1.095385
43	6	0	1.834183	-0.693909	0.704309
44	1	0	1.984206	-0.809484	1.775129
45	1	0	4.021794	-3.314696	-2.402839
46	1	0	6.186870	-2.048873	-1.510115
47	6	0	5.233474	0.623290	-0.050539
48	6	0	6.049370	1.339012	0.837658
49	6	0	5.353140	0.877703	-1.425604
50	6	0	6.956151	2.290304	0.368634
51	1	0	5.967569	1.158206	1.907229
52	6	0	6.259700	1.825653	-1.895398
53	1	0	4.739483	0.335793	-2.140932
54	6	0	7.064410	2.535956	-0.999738
55	1	0	7.574498	2.838144	1.073529
56	1	0	6.337393	2.012958	-2.962538
57	1	0	7.769455	3.274799	-1.368741
58	6	0	-5.943997	-2.871647	-1.592426
59	6	0	-4.493638	-0.927051	-1.656607
60	6	0	-5.577026	-1.621600	-2.145619
61	1	0	-3.535938	-4.280271	1.362353
62	1	0	-5.459972	-4.381675	-0.150786
63	1	0	-6.806008	-3.403636	-1.984031
64	1	0	-6.154394	-1.208114	-2.967457
65	1	0	-4.224086	0.025177	-2.098073
66	6	0	-4.652407	4.058914	-0.226016
67	6	0	-4.294235	1.702072	0.229462
68	6	0	-5.083576	2.827025	0.321213
69	1	0	-0.951446	4.060670	-1.902533
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71	1	0	-5.289782	4.935225	-0.152845

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72	1	0	-6.046304	2.769450	0.821095
73	1	0	-4.636459	0.769315	0.662111

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1	6	0	-2.511552	-0.579222	0.608365
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4	6	0	-0.573150	0.221125	1.982342
5	1	0	0.734788	1.021112	-1.025050
6	1	0	-1.045145	1.199412	2.121008
7	1	0	-0.051882	-0.041768	2.905069
8	7	0	0.456888	0.353725	0.915670
9	6	0	-1.318301	1.260771	-0.561912
10	6	0	-2.507756	0.774347	-0.024779
11	6	0	-1.270292	2.533016	-1.182661
12	1	0	-0.337567	2.874156	-1.625598
13	6	0	-3.673532	1.615961	-0.026290
14	6	0	-3.610394	2.897863	-0.669855
15	6	0	-2.391813	3.321468	-1.257567
16	6	0	-4.761651	3.730883	-0.684181
17	6	0	-1.571815	-2.083530	2.289318
18	6	0	-3.385430	-1.632582	0.168690
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21	1	0	-0.857372	-2.248245	3.091952
22	6	0	-4.232532	-3.931911	0.445651
23	6	0	1.753298	0.368808	1.222527
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25	6	0	-0.120993	-0.900979	-1.212306
26	8	0	-0.719101	-1.027515	-2.252791
27	8	0	0.602889	-1.855840	-0.612284
28	6	0	0.590841	-3.143765	-1.270620
29	1	0	0.971133	-3.050908	-2.290193
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31	1	0	-0.426986	-3.537999	-1.296783
32	6	0	2.849044	0.406400	0.364210
33	6	0	4.193464	0.300121	0.869745
34	6	0	3.018838	3.218264	0.399540
35	1	0	2.690673	0.342925	-0.704719
36	6	0	4.956279	2.041560	0.961483
37	1	0	4.223202	0.118562	1.945933
38	6	0	3.831558	2.850196	1.598728
39	6	0	3.818231	3.143821	-0.728144
40	1	0	2.014830	3.626443	0.441778
41	6	0	5.025672	2.511698	-0.380668
42	1	0	5.872942	1.842079	1.510943
43	1	0	4.278346	3.772415	2.006138
44	1	0	3.284686	2.372289	2.412869

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50	6	0	7.102090	-2.063666	0.303524
51	1	0	6.126499	-1.177199	2.003131
52	6	0	6.200762	-1.473614	-1.856736
53	1	0	4.531836	-0.130024	-1.861645
54	6	0	7.132761	-2.175031	-1.086203
55	1	0	7.820506	-2.605125	0.911869
56	1	0	6.217582	-1.556858	-2.939620
57	1	0	7.876431	-2.802448	-1.568294
58	6	0	-4.240528	-1.505315	-0.960871
59	6	0	-5.066328	-3.763728	-0.635178
60	6	0	-5.057429	-2.542871	-1.350795
61	1	0	-2.452565	-4.025180	2.466138
62	1	0	-4.216811	-4.872181	0.990854
63	1	0	-5.722633	-4.569579	-0.950459
64	1	0	-5.696844	-2.425947	-2.220899
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67	6	0	-5.924262	3.337367	-0.064878
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71	1	0	-6.797353	3.983101	-0.077896
72	1	0	-6.893118	1.795622	1.112680
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1	6	0	2.442309	-0.553488	-0.714094
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5	1	0	-0.737047	1.115509	0.991493
6	1	0	1.039831	1.347022	-2.133056
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8	7	0	-0.490296	0.494323	-0.970844
9	6	0	1.324764	1.281339	0.535153
10	6	0	2.493844	0.771179	-0.025061
11	6	0	1.330912	2.525316	1.213719
12	1	0	0.411989	2.888317	1.667978
13	6	0	3.693414	1.563275	0.012081
14	6	0	3.684502	2.815360	0.714348
15	6	0	2.484454	3.261619	1.323351
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23	6	0	-1.790220	0.443559	-1.260667
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25	6	0	-0.030393	-0.884302	1.031780
26	8	0	-0.678893	-1.796759	0.575681
27	8	0	0.673832	-0.920059	2.165593
28	6	0	0.682112	-2.190137	2.857912
29	1	0	1.150708	-2.951394	2.231082
30	1	0	1.266257	-2.019821	3.761183
31	1	0	-0.338019	-2.493787	3.103115
32	6	0	-2.876218	0.429991	-0.389983
33	6	0	-4.218727	0.249720	-0.879846
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39	6	0	-3.962199	3.122731	0.682564
40	1	0	-2.202861	3.676920	-0.522952
41	6	0	-5.143263	2.429883	0.362407
42	1	0	-5.986211	1.695795	-1.507401
43	1	0	-4.497696	3.699677	-2.046031
44	1	0	-3.446154	2.344621	-2.460651
45	1	0	-5.940375	2.198491	1.059707
46	1	0	-3.690457	3.481317	1.668996
47	6	0	-5.173677	-0.645263	-0.147739
48	6	0	-6.077036	-1.416359	-0.893327
49	6	0	-5.202608	-0.742746	1.251750
50	6	0	-6.981302	-2.270192	-0.260517
51	1	0	-6.067266	-1.355990	-1.979546
52	6	0	-6.105789	-1.593636	1.884889
53	1	0	-4.518128	-0.155078	1.858228
54	6	0	-6.998433	-2.360981	1.130834
55	1	0	-7.668907	-2.863385	-0.856081
56	1	0	-6.111808	-1.661255	2.968967
57	1	0	-7.700838	-3.024064	1.626899
58	6	0	4.137833	-1.613974	0.808802
59	6	0	4.850400	-3.898166	0.402363
60	6	0	4.905603	-2.702774	1.158051
61	1	0	2.217378	-3.924934	-2.692166
62	1	0	3.940357	-4.905757	-1.255806
63	1	0	5.468167	-4.745362	0.685414
64	1	0	5.559124	-2.644756	2.023856
65	1	0	4.187252	-0.708847	1.402957
66	6	0	4.889998	1.182249	-0.658690
67	6	0	6.014115	3.185577	0.123511
68	6	0	6.016682	1.971487	-0.603909

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69	1	0	2.485702	4.206131	1.860844
70	1	0	4.849976	4.537509	1.310368
71	1	0	6.913249	3.793364	0.163338
72	1	0	6.916210	1.661518	-1.127807
73	1	0	4.909640	0.259910	-1.227062

z-exo-re-a

1	6	0	2.592000	-0.320101	-0.543194
2	6	0	1.733370	-0.899838	-1.473961
3	6	0	-0.041030	0.331864	0.484287
4	6	0	0.516562	-0.136882	-1.938874
5	1	0	-0.890472	0.792248	0.995920
6	1	0	0.779654	0.882161	-2.241865
7	1	0	0.050882	-0.636936	-2.790781
8	7	0	-0.514746	-0.043838	-0.865874
9	6	0	1.055600	1.386053	0.409836
10	6	0	2.314153	1.080436	-0.102540
11	6	0	0.747187	2.696933	0.847325
12	1	0	-0.235403	2.903442	1.263693
13	6	0	3.279212	2.133718	-0.264769
14	6	0	1.681804	3.699419	0.767904
15	6	0	1.967843	-2.208040	-1.963698
16	6	0	3.673177	-1.098748	-0.002786
17	6	0	3.045216	-2.936108	-1.522548
18	6	0	3.908405	-2.416466	-0.522228
19	1	0	1.295807	-2.625807	-2.709339
20	6	0	4.985124	-3.187084	-0.006396
21	6	0	-1.805850	-0.182435	-1.169176
22	1	0	-1.986348	-0.341836	-2.230881
23	6	0	0.357558	-0.862636	1.379839
24	8	0	0.941235	-0.705593	2.423711
25	8	0	-0.074386	-2.051411	0.918253
26	6	0	0.323832	-3.184101	1.727009
27	1	0	-0.095864	-3.101123	2.732025
28	1	0	-0.065610	-4.062597	1.212375
29	1	0	1.412366	-3.230130	1.792054
30	6	0	-2.917306	-0.103047	-0.334982
31	6	0	-3.148807	-2.900530	-0.166209
32	6	0	-4.246210	-0.002060	-0.876205
33	1	0	-2.778209	0.030909	0.730901
34	6	0	-3.952336	-2.622178	-1.394428
35	6	0	-3.947855	-2.714833	0.947186
36	1	0	-2.142988	-3.301204	-0.169458
37	6	0	-5.071234	-1.754823	-0.832591
38	1	0	-4.257825	0.071009	-1.964929
39	1	0	-4.406914	-3.569111	-1.730325
40	1	0	-3.397726	-2.219098	-2.243294
41	6	0	-5.147301	-2.098231	0.542398

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42	1	0	-5.976924	-1.569773	-1.403884
43	1	0	-5.962491	-1.824222	1.202625
44	1	0	-3.678932	-2.956949	1.968996
45	6	0	-5.249179	0.923859	-0.261667
46	6	0	-6.168186	1.569682	-1.102256
47	6	0	-5.310927	1.173411	1.118485
48	6	0	-7.120082	2.447240	-0.582213
49	1	0	-6.133851	1.390367	-2.174766
50	6	0	-6.262158	2.048056	1.638954
51	1	0	-4.617732	0.684047	1.797893
52	6	0	-7.170113	2.688554	0.790437
53	1	0	-7.819256	2.941192	-1.250409
54	1	0	-6.294440	2.232678	2.708836
55	1	0	-7.909964	3.370226	1.199129
56	6	0	2.956635	3.453929	0.198289
57	6	0	4.533930	1.940280	-0.909314
58	6	0	3.909112	4.498448	0.052370
59	6	0	5.121494	4.267777	-0.553359
60	6	0	5.427822	2.977873	-1.048812
61	1	0	1.446299	4.699298	1.122207
62	1	0	3.654218	5.488964	0.420139
63	1	0	5.840598	5.074001	-0.664252
64	1	0	6.376997	2.806144	-1.548156
65	1	0	4.784554	0.962326	-1.302976
66	6	0	4.498133	-0.639447	1.061235
67	6	0	5.780607	-2.698768	1.003932
68	6	0	5.522783	-1.418872	1.549870
69	1	0	3.238025	-3.929662	-1.918943
70	1	0	5.162256	-4.176483	-0.420399
71	1	0	6.598663	-3.297307	1.393899
72	1	0	6.136108	-1.050208	2.366857
73	1	0	4.305032	0.332487	1.499598

z-exo-re-b

1	6	0	2.523454	-0.366152	-0.632343
2	6	0	1.630354	-0.871353	-1.574193
3	6	0	-0.058251	0.475565	0.385210
4	6	0	0.474995	-0.013287	-2.033572
5	1	0	-0.876821	0.997320	0.891321
6	1	0	0.810816	0.990744	-2.312238
7	1	0	-0.018374	-0.459986	-2.899181
8	7	0	-0.549144	0.121797	-0.962215
9	6	0	1.114479	1.443195	0.323235
10	6	0	2.350434	1.048378	-0.183609
11	6	0	0.903884	2.771100	0.769369
12	1	0	-0.064666	3.049775	1.176809
13	6	0	3.393480	2.026645	-0.330569
14	6	0	1.912039	3.700782	0.703993
15	6	0	1.760630	-2.193399	-2.063551

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16	6	0	3.532906	-1.231277	-0.084840
17	6	0	2.765978	-3.010465	-1.609028
18	6	0	3.658730	-2.565213	-0.599667
19	1	0	1.062860	-2.554171	-2.815127
20	6	0	4.658980	-3.425500	-0.071604
21	6	0	-1.841427	-0.075874	-1.233047
22	1	0	-2.037476	-0.257717	-2.288225
23	6	0	0.182942	-0.805243	1.219337
24	8	0	-0.258312	-1.898590	0.938399
25	8	0	0.858753	-0.513062	2.331200
26	6	0	1.116610	-1.617520	3.227447
27	1	0	1.736447	-2.364737	2.727970
28	1	0	1.644515	-1.181452	4.074266
29	1	0	0.176651	-2.072677	3.547832
30	6	0	-2.935663	-0.024383	-0.378590
31	6	0	-3.006351	-2.871736	-0.151185
32	6	0	-4.277262	-0.016786	-0.894417
33	1	0	-2.781538	0.132429	0.682120
34	6	0	-3.845931	-2.645768	-1.365705
35	6	0	-3.786067	-2.689964	0.975347
36	1	0	-1.977556	-3.208497	-0.157987
37	6	0	-4.998002	-1.827268	-0.797493
38	1	0	-4.315398	0.025277	-1.984018
39	1	0	-4.259724	-3.617369	-1.683660
40	1	0	-3.324540	-2.229393	-2.229251
41	6	0	-5.022874	-2.139370	0.585446
42	1	0	-5.924666	-1.702121	-1.351057
43	1	0	-5.835451	-1.888915	1.258474
44	1	0	-3.477419	-2.892886	1.994148
45	6	0	-5.326453	0.855740	-0.281794
46	6	0	-6.299448	1.423484	-1.118202
47	6	0	-5.378469	1.134011	1.093392
48	6	0	-7.293735	2.253386	-0.599469
49	1	0	-6.273869	1.220618	-2.186732
50	6	0	-6.371913	1.960914	1.612734
51	1	0	-4.643972	0.703344	1.769110
52	6	0	-7.333045	2.524268	0.768027
53	1	0	-8.034409	2.687411	-1.264603
54	1	0	-6.396262	2.168490	2.678645
55	1	0	-8.105973	3.168959	1.175571
56	6	0	3.169132	3.363861	0.141267
57	6	0	4.634137	1.742855	-0.968811
58	6	0	4.199140	4.334051	0.009483
59	6	0	5.394571	4.016176	-0.590644
60	6	0	5.605337	2.710444	-1.094485
61	1	0	1.749222	4.713729	1.062121
62	1	0	4.017498	5.338654	0.382519
63	1	0	6.173397	4.766319	-0.691360
64	1	0	6.541889	2.470948	-1.589738
65	1	0	4.811894	0.751551	-1.368995
66	6	0	4.389672	-0.841327	0.982931

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67	6	0	5.485417	-3.006727	0.944958
68	6	0	5.338318	-1.705881	1.482826
69	1	0	2.875639	-4.018412	-2.000346
70	1	0	4.751599	-4.428024	-0.481318
71	1	0	6.244360	-3.673538	1.343573
72	1	0	5.980326	-1.386785	2.298950
73	1	0	4.287117	0.149565	1.410007

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ARTICLE

Novel Binaphthyl and Biphenyl α- and β-Amino Acids and Esters: Organocatalysis of Asymmetric Diels Alder Reactions. A Combined Synthetic and Computational Study.

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Experimental Detail

Melting points were recorded using a Büchi B-545 Melting Point apparatus. Optical rotations were obtained using a Bellingham and Stanley Ltd ADP440 polarimeter and the solvents used for these measurements were of HPLC-grade quality. IR spectra were recorded on a Perkin-Elmer 100 FT-IR spectrophotometer; samples were used as thin films on KBr plates. NMR spectra were recorded on a Bruker 500 MHz Spectrometer. Chemical shifts were recorded in parts per million (ppm), *J* values are given in Hertz (Hz) and are referenced against tetramethylsilane or the residual deuteriated solvents peak. High-resolution mass spectra were obtained from the EPSRC Mass Spectrometry Unit at the University of Swansea. Enantiomeric excesses were determined by chiral high performance liquid chromatography using a Hitachi Elite LaChrom HPLC system using an L-2200 autosampler, L-2130 pump and L-2400 UV detector. All HPLC samples were run against racemic mixture as a standard and using a hexane-isopropanol mixture; conditions varied and are provided in detail below. Unless otherwise stated, all starting materials were sourced from commercial suppliers and were used without any purification. THF and Et_2O were distilled from the sodium-benzophenone ketyl radical. Toluene, CH_2Cl_2 and CH_3CN were distilled over CaH_2; DMF was distilled over $MgSO_4$. Needles and glassware were oven-dried and allowed to cool under a positive pressure of nitrogen gas prior to use. Light petroleum ether was distilled at 40-60 °C to remove impurities. Dicyclopentadiene was cracked on the day of use to produce cyclopentadiene.

_(S)_-(+)-[1,1']-Binaphthalene-2,2'-diol _bis_-trifluoromethane sulfonate [21]

_(S)_-[1,1]-2-2'-Binaphthalene diol (10.00 g, 35 mmol) and 4-dimethylaminopyridine (1.71 g, 14 mmol, 0.4 equiv.) were dissolved in anhydrous dichloromethane (300 mL). The solution was cooled to –78 °C. 2,6-Lutidine (12.2 mL, 104 mmol, 3.0 equiv.) and

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trifluoromethanesulfonic anhydride (18.0 mL, 104 mmol, 3.0 equiv.) were added to the mixture. The solution turned from yellow to pink and was allowed to reach room temperature overnight. Over this time period the reaction mixture turned from pale pink to dark brown. Silica gel (~10 g) was added and the solvent was removed under reduced pressure. The residue was placed on a sintered funnel and washed repeatedly with petroleum ether (~2 L). The petroleum ether fractions were combined and the solvents removed under reduced pressure to yield the title compound as a colourless solid (19.2 g, 100%), which was employed in the next step without further purification.

m.p. 86-88 °C (Lit[21] 83-85 °C); $[\alpha]_D^{23}$ +144 ° (*c*=1.00, $CHCl_3$) [Lit[21] $[\alpha]_D^{21}$: +148 º, (*c* 1.00, $CHCl_3$)]; ν_{max} (CH_2Cl_2)/cm^{-1} 3060, 1592, 1509, 1423, 1219, 1140, 1066, 963, 941, 739, 704, 634; ^{1}H NMR (500 MHz; $CDCl_3$) 8.14 (2H, d, J= 9.0 Hz), 8.01 (2H, d, J= 8.2 Hz), 7.62 (2H, d, J= 9.0 Hz), 7.59 (2H, ddd, J= 8.1, 6.8, 1.1 Hz), 7.41 (2H, ddd, J= 8.1, 6.8, 1.1 Hz), 7.27-7.23 (2H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.5, 133.2, 132.4, 132.1, 128.4, 128.0, 127.4, 126.8, 123.5, 119.4, 116.9.

(S)-(+)-2,2'-Dimethyl-[1,1']-binaphthalene [41]

(S)-[1,1']-Binaphthalene-2,2'-diol-bis-trifluoromethanesulfonate (15.50 g, 28 mmol) and 1,3-bis(diphenylphosphino)propane nickel (II) chloride (1.07 g, 1.97 mmol, 0.07 equiv.) were dissolved in anhydrous Et_2O (300 mL). The mixture was cooled to –78 °C. A solution of methyl magnesium bromide (3M in Et_2O, 38 mL, 113 mmol, 4.0 equiv.) was added slowly and the reaction mixture was allowed to reach room temperature overnight. The excess Grignard reagent was quenched at 0 °C with H_2O (50 mL), and the mixture was diluted with Et_2O (100 mL). The solution was stirred for 30 min. The solids were filtered through a plug of celite and washed with Et_2O (~50 mL). The filtrate was transferred to a separating funnel and a few drops of aqueous HCl (37%) were added. The organic layer was washed with H_2O (5 x 50 mL) and saturated brine (2 x 30 mL), and dried over anhydrous $MgSO_4$. The solvents were removed under reduced pressure. The residue was recrystallized (hot methanol) to yield the title compound as a colourless crystalline solid (7.5 g, 95%).

m.p. 75–77 °C (Lit[41] 77–79 °C); $[\alpha]_D^{23}$ +36.5 ° (*c* 1.00, $CHCl_3$) [Lit[41] $[\alpha]_D^{21}$ +37.7 °, (*c* 1.00, $CHCl_3$)]; ν_{max} (CH_2Cl_2)/cm^{-1} 3049, 3007, 2858, 1506, 1443, 1421, 1351, 1219; ^{1}H NMR (500 MHz, $CDCl_3$) 7.88 (4H, t, *J*= 8.0 Hz) 7.50 (2H, d, *J*= 8.5 Hz), 7.38 (2H, ddd, *J*= 8.0, 6.8, 1.1 Hz), 7.20 (2H, ddd, *J*= 8.0, 6.8, 1.1 Hz), 7.04 (2H, d, *J*= 8.1 Hz), 2.03 (6H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.1, 134.3, 132.8, 132.2, 128.7, 127.9, 127.4, 126.1, 125.6, 124.9, 20.0.

(S)-(–)-2,2'-Bis-bromomethyl-[1,1']-binaphthalene (–)-7 [21]

(S)-2,2'-Dimethyl-[1,1']-binaphthalene (4.00 g, 14.2 mmol), *N*-bromosuccinimide (6.30 g, 35.4 mmol, 2.5 equiv.) and azobisisobutyronitrile (0.23 g, 1.4 mmol, 0.1 equiv.) were dissolved in cyclohexane (28 mL, 14 % *w/v* solution). The mixture was heated at reflux for 4 h until completion was observed using TLC. The reaction mixture was cooled to 0 °C, and EtOAc (9 mL) and distilled water (56 mL) were added. The mixture was stirred for 1 h to allow for precipitation, and filtration yielded the title compound as a beige solid (4.76 g, 77%).

m.p. 188-190 °C (Lit[21] 180-183 °C) $[\alpha]_D^{23}$ –174.4 ° (*c* 1.00, $CHCl_3$) [Lit[21] for (*R*)-2,2'-*Bis*-bromomethyl-[1,1']binaphthalene $[\alpha]_D^{20}$ +186.4 °, (*c* 1.00, benzene)]; ν_{max} (CH_2Cl_2)/cm^{-1} 3054, 2986, 2305, 1723, 1421, 1265, 896, 740, 705; ^{1}H NMR (500 MHz, $CDCl_3$) 8.02 (2H, d, *J*= 8.6 Hz), 7.92 (2H, d, *J*= 8.2 Hz), 7.75 (2H, d, *J*= 8.6 Hz), 7.49 (2H, ddd, *J*= 8.0, 6.8, 1.0 Hz), 7.27 (2H, ddd, *J*= 8.0, 6.8, 1.1 Hz), 7.08-7.07 (2H, d, *J*= 8.5 Hz), 4.25 (4H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.2, 134.1, 133.3, 132.5, 129.4, 128.0, 127.8, 126.9, 126.8, 126.8, 32.7.

(S)-(+)-3,5-Dihydrodinaphtho-[2,1-c:1',2'-e]-oxepine (+)-9 [21]

(S)-2,2'-Bis(bromomethyl)-[1-1']-binaphthalene (3.20 g, 7.3 mmol) was suspended in a mixture of saturated aqueous sodium carbonate and 1,4-dioxane (1:1, 100 mL), and the mixture heated at reflux for 12 h. The mixture was allowed to cool to room temperature and extracted with Et_2O (3 x 30 mL). The combined organic layers were washed with H_2O (20 mL) and saturated brine (2 x 40 mL), and dried over anhydrous $MgSO_4$. The solvents were removed under reduced pressure, and the resulting yellow oil was purified using column chromatography on silica gel (100:0-90:10 light petroleum ether/EtOAc) to give a colourless solid. Recrystallization of the solid ($CHCl_3$ in hexane) yielded the title compound as a colourless solid (1.88 g, 87%).

m.p. 170-173 °C (Lit[21] 180-183 °C); $[\alpha]_D^{20}$ +527.0 ° (*c* 1.00, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3054, 2986, 2304, 1420, 1265, 1055, 896, 820; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (4H, dd, *J*= 16.3, 8.3 Hz), 7.67 (2H, d, *J*= 8.3 Hz), 7.58 (2H, dd, *J*= 8.6, 0.6 Hz), 7.54 (2H, ddd, *J*= 8.1, 6.8, 1.2 Hz), 7.34 (2H, ddd, *J*= 8.3, 6.8, 1.3 Hz) 4.69 (2H, d, *J*= 11.4 Hz), 4.24 (2H, d, *J*= 11.4 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 135.5, 134.0, 133.6, 131.2, 129.2, 128.4, 127.7, 127.4, 126.0, 126.0, 67.5.

(*S*)-(–)-2'-Bromomethyl-[1,1']-binaphthalene-2-carboxaldehyde (–)-10 [21]

(*S*)-2,7-Dihydrodinaphtho-[2,1-c;1',2'-e]-oxepine (4.80 g, 16.2 mmol) was dissolved in cyclohexane (80 mL), and the solution cooled in an ice bath. Bromine (0.9 mL, 18.2 mmol, 1.125 equiv.) was added slowly. The ice bath was removed and the reaction mixture heated at reflux for 1 h, which caused the dark red reaction mixture to turn yellow. The solvent was removed under reduced pressure and the residue redissolved in Et_2O (70 mL). The solution was washed with saturated aqueous sodium hydrogen carbonate (2 x 50 mL) and saturated brine (2 x 60 mL), and dried over anhydrous $MgSO_4$. The solvents were removed under reduced pressure, and the residue was purified using column chromatography on silica gel (9:1 light petroleum/EtOAc) to yield the title compound as a colourless solid (3.04 g, 50%).

m.p. 147-149 °C (Lit[21] 151-153 °C); $[\alpha]_D^{23}$ –142.0 ° (*c* 1.00, $CHCl_3$) [Lit[2] for (*R*)-2'-Bromomethyl-[1,1']binaphthalene-2-carboxaldehyde $[\alpha]_D^{20}$ +144.7 ° (*c* 1.02, $CHCl_3$)]; ν_{max} (CH_2Cl_2)/cm^{-1} 3054, 2986, 2305, 1689, 1422, 1265, 896, 740, 705, 600; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.56 (1H, d, *J*= 1.0 Hz), 8.21 (1H, d, *J*= 8.5 Hz), 8.09 (1H, d, *J*= 8.5 Hz), 8.05 (1H, d, *J*= 8.5 Hz), 8.00 (1H, d, *J*= 8.5 Hz), 7.94 (1H, d, *J*= 8.0 Hz), 7.72 (1H, d, *J*= 8.5 Hz), 7.62 (1H, ddd, *J*= 8.0, 7.0, 1.0 Hz), 7.50 (1H, ddd, *J*= 8.0, 7.0, 1.0 Hz), 7.35 (1H, ddd, *J*= 8.5, 7.0, 1.5 Hz, 1H), 7.29 (1H, ddd, *J*= 8.5, 7.0, 1.5 Hz), 7.24 (1H, dd, *J*= 8.0, 0.5 Hz), 7.02 (1H, dd, *J*= 8.5, 0.5 Hz), 4.33 (1H, d, *J*= 10.0 Hz), 4.08 (1H, d, *J*= 10.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.8, 141.6, 136.3, 134.7, 133.6,

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133.0, 132.5, 132.4, 130.2, 129.9, 129.4, 129.2, 128.5, 128.2, 127.41, 127.40, 127.0, 126.6, 122.4, 31.9.

_(S)_-(+)-Allyl-4,5-dihydro-3H-4-aza-cyclohepta-[2,1-a;3,4-a']-dinaphthalene (+)-6 [19a]

_(S)_-2,2'-Bis-(bromomethyl)-[1-1']-binaphthalene (2.50 g, 5.7 mmol) and allylamine (0.5 mL, 6.25 mmol, 1.1 equiv.) were dissolved in acetonitrile (25 mL). Anhydrous potassium carbonate (2.36 g, 17.1 mmol, 3.0 equiv.) was added and the reaction mixture heated at reflux overnight or until completion was observed using TLC. The reaction mixture was cooled to room temperature, diluted with dichloromethane (40 mL) and filtered to remove potassium carbonate. The filtrate was washed with H_2O (3 x 10 mL) and saturated brine (2 x 20 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure yielding an orange solid. Recrystallization (hot acetone) yielded the title compound as a pale yellow solid (1.60 g, 84%).

m.p. 167-169 °C (Lit [19a] 148-149 °C); $[\alpha]_D^{23}$ +396.2 ° (_c_ 1.80, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3944, 3054, 2987, 2829, 2685, 2410, 2305, 1508, 1421, 1263, 1156, 896, 820; ^{1}H NMR (500 MHz, $CDCl_3$) 7.96 (4H, d, _J_= 8.3 Hz), 7.56 (2H, d, _J_= 8.2 Hz), 7.49-7.45 (4H, m), 7.31 (2H, ddd, _J_= 8.3, 6.8, 1.1 Hz), 6.07-5.95 (1H, m), 5.29 (1H, dd, _J_= 17.1, 1.3 Hz), 5.24 (1H, d, _J_= 10.0 Hz), 3.76 (2H, d, _J_= 12.5 Hz), 3.17 (2H, d, _J_= 12.5 Hz), 3.16-3.12 (2H, m); ^{13}C NMR (126 MHz, $CDCl_3$) 136.3, 135.1, 133.4, 133.2, 131.4, 128.4, 128.3, 127.8, 127.5, 125.8, 125.5, 118.1, 58.5, 54.8.

_(S)_-(+)-4-Allyl-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-4-ium tetraphenylborate (+)-8

Method A: (_S_)-Allyl-4,5-dihydro-3H-4-aza-cyclohepta-[2,1-a;3,4-a']-dinaphthalene (1.00 g, 3.0 mmol) was dissolved in dichloromethane (50 mL). The solution was cooled to 0 °C, and _N_-bromosuccimide (0.56 g, 3.13 mmol, 1.05 equiv.) added. The mixture was stirred for 1 h or until completion was observed using TLC. The solvent was removed under reduced pressure to yield the crude bromide salt as an orange foamy solid (3.83 g crude mass, not routinely isolated). The crude _(S)_-4-allyl-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-4-ium bromide was dissolved in a minimum volume of ethanol, and a solution of sodium tetraphenylborate (1.13 g, 3.3 mmol, 1.1 equiv.) in the minimum volume of acetonitrile added. The solution was stirred for 10 min. The bright yellow precipitate was collected by filtration and washed with cold ethanol to yield the title compound as a yellow solid, which was dried at 70 °C overnight (1.55 g, 80%).

Method B: (_S_)-Allyl-4,5-dihydro-3H-4-aza-cyclohepta-[2,1-a;3,4-a']-dinaphthalene (2.12 g, 6.3 mmol) was dissolved in anhydrous dichloromethane (100 mL). Dried crushed 4Å molecular sieve and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (2.87 g, 12.6 mmol, 2 equiv.) were added. The mixture was stirred at ambient temperature for 2 h or until completion was observed using TLC. A solution of sodium tetraphenylborate (2.37 g, 6.93 mmol, 1.1 equiv.), in the minimum volume of acetonitrile was added, and the reaction stirred for a further 10 min. The solvent was removed under reduced pressure and the orange residue triturated in hot EtOH to yield the title compound as a bright yellow solid (1.9 g, 46%).

Method C: (_S_)-2'-Bromomethyl-[1,1']-binaphthalene-2-carboxaldehyde (1.41 g, 3.76 mmol) was dissolved in EtOH (15 mL), and a solution of allylamine (0.3 mL, 3.76 mmol, 1 equiv.) in ethanol (0.5 mL) added dropwise. The mixture was warmed to 35 °C and stirred for 4 h or until consumption of starting material was observed by TLC. The mixture was allowed to reach room temperature, and a solution of sodium tetraphenylborate (1.42 g, 4.14 mmol, 1.10 equiv.) in the minimum volume of acetonitrile added. The solution was stirred for 10 min, the solvents were removed under reduced pressure, and the crude residue triturated in hot EtOH to yield the title compound as a bright yellow solid (1.59 g, 65%).

m.p.* 160 °C (*_decomp._); $[\alpha]_D^{23}$ +410.5 ° (_c_ 1.00, MeCN); ν_{max} (CH_2Cl_2)/cm^{-1} 3054, 2987, 2685, 2410, 2305, 1521, 1263, 1156, 896; ^{1}H NMR (500 MHz, d6-DMSO) δ 9.55 (1H, s), 8.38 (1H, d, _J_= 8.6 Hz), 8.25 (2H, t, _J_= 8.8 Hz), 8.08 (2H, dd, _J_= 14.3, 8.3 Hz), 7.85 (1H, d, _J_= 8.5 Hz), 7.79 (1H, t, _J_= 7.4 Hz), 7.55 (1H, t, _J_= 7.5 Hz), 7.49 (1H, t, _J_= 7.6 Hz), 7.44 (1H, d, _J_= 8.5 Hz), 7.29 (1H, t, _J_= 7.7 Hz), 7.18 (8H, s), 6.99 (1H, d, _J_= 8.7 Hz), 6.92 (8H, t, _J_= 7.3 Hz), 6.78 (4H, t, _J_= 7.1 Hz), 6.03–5.89 (1H, m), 5.65 (1H, d, _J_= 17.5 Hz), 5.53 (1H, d, _J_= 10.1 Hz), 5.14 (1H, d, _J_= 13.5 Hz), 4.84 (2H, d, _J_= 5.5 Hz), 4.69 (1H, d, _J_= 13.6 Hz); ^{13}C NMR (126 MHz, d6-DMSO) δ 169.6, 164.4, 141.0, 136.6, 136.0, 135.2, 133.8, 131.31, 131.24, 130.5, 129.8, 129.6, 129.5, 129.2, 128.1, 127.51, 127.46, 127.2, 126.8, 126.7, 125.80, 125.78, 125.76, 125.74, 124.3, 122.0, 64.1, 62.0 56.3; HRMS (NSI-FTMS) _m/z_: $[M\text{-}BPh_4]^+$ Calcd for $[C_{25}H_{20}N]^+$ 334.1596; Found 334.1595.

(3S,11cS)-(+)-4-Allyl-3-methyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine

(_S_)-4-Allyl-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-4-ium tetraphenylborate (843 mg, 1.29 mmol) was dissolved in anhydrous THF (20 mL). The solution was cooled to –78 °C, and a solution of methyl magnesium bromide (3M in Et_2O, 2.2 mL, 6.45 mmol, 5 equiv.) was added slowly. The mixture was allowed to reach room temperature overnight. The excess Grignard reagent was quenched with H_2O (5 mL), and the reaction mixture diluted with Et_2O (30 mL). The organic layer was washed with H_2O (20 mL) and saturated brine (10 mL), and dried over anhydrous $MgSO_4$. The solvents were removed under reduced pressure and the residue was purified using column chromatography on silica gel (7:3 light petroleum/EtOAc 3% TEA) to yield the title compound as a colourless oil (388 mg, 86%).

$[\alpha]_D^{25}$ +317 ° (_c_ 1.00, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3048, 3005, 2959, 2928, 2904, 2805, 2866, 1506, 1366, 1264, 1112, 819, 750, 738; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95-7.87 (4H, m), 7.65 (1H, d, _J_= 8.3 Hz), 7.48 (1H, dd, _J_= 8.6, 0.7 Hz), 7.44–7.38 (3H, m), 7.33 (1H, d, _J_= 8.3 Hz), 7.21 (2H, dddd, _J_= 8.1, 7.0, 5.7, 1.3 Hz), 6.00 (1H, dddd, _J_= 17.6, 10.1, 7.6, 5.5 Hz), 5.25 (1H, dd, _J_= 17.0, 1.5 Hz), 5.19 (1H, dd, _J_= 11.0, 1.0 Hz), 4.04 (1H, q, _J_= 7.3 Hz), 3.72 (1H, d, _J_= 11.0 Hz), 3.26 (1H, ddt, _J_= 13.6, 5.4, 1.4 Hz), 3.15 (1H, dd, _J_= 13.7, 7.6 Hz), 3.10 (1H, d, _J_= 11.0 Hz), 0.54 (3H, d, _J_= 7.4 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.4, 136.6, 135.8, 135.1, 133.3, 133.2, 132.9, 132.1, 132.0, 129.2, 128.8, 128.4, 128.1, 128.0, 127.42, 127.40, 125.9, 125.7, 125.5, 117.9, 61.9, 61.0, 56.8, 22.2; HRMS (NSI-FTMS) _m/z_: $[M+H]^+$ Calcd for $[C_{26}H_{24}N]^+$ 350.1909; Found 350.1902.

(3S,11cS)-(+)-3-Methyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine

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(3*S*,11cS)-4-Allyl-3-methyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine (700 mg, 2.00 mmol) was dissolved in anhydrous dichloromethane (20 mL). $Pd(PPh_3)_4$ (92 mg, 0.08 mmol, 0.04 equiv.) and 1,3-dimethylbarbituric acid (937 mg, 6.00 mmol, 3 equiv.) were added, and the reaction mixture was heated at reflux overnight or until TLC showed complete consumption of the starting material. The reaction was allowed to cool to room temperature, and washed with 1 M NaOH (2 x 15 mL), H_2O (2 x 10 mL), and saturated brine (2 x 10 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue purified using column chromatography on silica gel (10% MeOH in CH_2Cl_2) to yield the title compound as a yellow foam (341 mg, 55%).

m.p. 110-112 °C, $[\alpha]_D^{23}$ +498.0 ° (*c* 1.00, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3049, 2951, 2923, 2864, 1673, 1594, 1075, 819, 750; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99–7.89 (4H, m), 7.61 (1H, d, *J*= 8.3 Hz), 7.50–7.45 (3H, m), 7.41 (1H, d, *J*= 8.2 Hz), 7.37 (1H, d, *J*= 8.3 Hz) 7.29–7.21 (2H, m), 4.41 (1H, q, *J*= 7.3 Hz), 3.86 (1H, d, *J*= 12.4 Hz), 3.78 (1H, d, *J*= 12.3 Hz), 2.31 (1H, s), 0.72 (3H, d, *J*= 7.2 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.5, 135.4, 133.5, 133.3, 133.2, 132.20, 132.17, 129.2, 129.1, 128.4, 128.2, 127.3, 127.2, 127.0, 126.1, 125.8, 125.7, 125.7, 57.3, 48.4, 22.5; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{23}H_{20}N]^+$ 310.1596; Found 310.1589.

(+)-*tert*-Butyl 2-((3S,11cS)-4-allyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl) acetate (+)-28

A mixture of zinc dust (1.90 g, 29.1 mmol, 10 equiv.), anhydrous THF (40 mL) and TMSCl (0.37 mL, 2.9 mmol, 1 equiv.) was heated at reflux for 30 min. tert-Butyl bromoacetate (0.43 mL, 2.9 mmol) was added, and the mixture heated at reflux for a further 30 min. The mixture was cooled to –78 °C. (*S*)-4-Allyl-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-4-ium tetraphenylborate (1.90 g, 2.9 mmol) was dissolved in anhydrous THF (40 mL), and the solution transferred into the zinc slurry at –78 °C using a cannula. The mixture was stirred at –78 °C for 1 h, and t-butyl bromoacetate (4.3 mL, 29.1 mmol, 10 equiv.) added in small portions over 20 min, while maintaining the temperature. The mixture was allowed to reach room temperature and reaction progress monitored by TLC. Saturated aqueous ammonium chloride (5 mL) was added. Et_2O (50 mL) was added, and the mixture filtered through a pad of celite. The filtrate was washed with H_2O (3 x 20 mL) and saturated brine (3 x 20 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to give a yellow oil. The product was purified using column chromatography on silica gel (9:1 light petroleum ether/ EtOAc) to yield the title compound as a colourless oil (932 mg, 71%).

$[\alpha]_D^{22}$ +158 ° (*c* 1.00, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3052, 2978, 1724, 1507, 1367, 1264, 1150, 820;^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98-7.90 (4H, m), 7.62 (1H, d, *J*= 8.3 Hz), 7.48-7.41 (4H, m), 7.36 (1H, d, *J*= 8.1 Hz), 7.27-7.19 (2H, m), 5.97 (1H, m), 5.25 (1H, dd, *J*= 17.1, 1.5 Hz) 5.19 (1H, *appt* d, *J*= 10.2 Hz) 4.41 (1H, t, *J*= 7.8 Hz), 3.71 (1H, d, *J*= 10.9 Hz), 3.35–3.20 (2H, m), 3.08 (1H, d, *J*= 10.9 Hz), 1.73 (1H, dd, *J*= 15.1, 7.0 Hz), 1.51 (1H, dd, *J*= 15.1, 8.4 Hz), 1.15 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.3, 136.1, 135.5, 135.2, 135.0, 133.5, 133.3, 133.0, 131.9, 131.8, 129.9, 129.0, 128.4, 128.3, 128.1, 128.0, 127.6, 127.4, 125.9, 125.7, 125.6, 125.6, 118.0, 79.9, 64.1, 61.4, 56.1, 42.6, 27.9; HRMS (CI^+) *m/z*: $[M+H]^+$ Calcd for $[C_{31}H_{32}NO_2]^+$ 450.2433; Found for: 450.2424.

(+)-*tert*-Butyl 2-((3S,11cS)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)acetate (+)-30

tert-Butyl 2-((3S,11cS)-4-allyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)-acetate (1.20 g, 2.67 mmol) was dissolved in anhydrous dichloromethane (60 mL). 1,3-Dimethylbarbituric acid (1.25 g, 8.00 mmol, 3 equiv.) and $Pd(PPh_3)_4$ (0.06 g, 0.05 mmol, 0.02 equiv.) were added, and the mixture heated at reflux overnight or until full consumption of the starting material was observed by TLC. The mixture was allowed to reach room temperature, and the solvent removed under reduced pressure. The residue was redissolved in Et_2O (50 mL) and the solution washed with 1 M NaOH solution (2 x 10 mL), H_2O (2 x 10 mL), and saturated brine (10 mL), and dried over anhydrous $MgSO_4$. The solvents were removed under reduced pressure, and the residue was purified using column chromatography on silica gel (6:4 light petroleum ether/EtOAc) to yield the title compound as a fluffy pale yellow foam (0.92 g, 84%).

m.p. 78-79 °C; $[\alpha]_D^{22}$ +206° (*c* 1.00, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3052, 2976, 1719, 1507, 1437, 1366, 1293, 1219, 1148, 1118; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02-7.91 (4H, m), 7.60 (1H, d, *J*= 8.3 Hz), 7.54 (1H, d, *J*= 8.4 Hz), 7.48-7.44 (2H, m), 7.40 (1H, d, *J*= 8.6 Hz), 7.34 (1H, d, *J*= 8.3 Hz), 7.26–7.22 (2H, m), 4.67 (1H, t, *J*= 7.6 Hz), 3.84 (1H, d, *J*= 12.2 Hz), 3.74 (1H, d, *J*= 12.2 Hz), 1.82 (1H, dd, *J*= 15.3, 7.6 Hz), 1.72 (1H, dd, *J*= 15.2, 7.7 Hz), 1.18 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.4, 137.5, 136.7, 135.0, 133.8, 133.2, 133.1, 132.1, 129.3, 129.1, 128.8, 128.5, 128.4, 128.1, 127.5, 127.4, 127.0, 125.9, 125.7, 125.6, 125.5, 80.2, 59.1, 48.8, 43.0, 27.9; HRMS (CI+) *m/z*: $[M+H]^+$ Calcd for $[C_{28}H_{28}NO_2]^+$ 410.2120; Found 410.2114.

(+)-2-((3S,11cS)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)acetic acid (+)-32

tert-Butyl 2-((3S,11cS)-4-allyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)acetate (660 mg, 1.6 mmol) was dissolved in dichloromethane (30 mL), and trifluoroacetic acid (1.5 mL, 19.3 mmol, 12 equiv.) added. The mixture was stirred until consumption of the starting material was observed by TLC. Saturated aqueous sodium hydrogen carbonate was added to bring the solution to neutral pH. The mixture was washed using H_2O (15 mL)and saturated brine (2 x 10 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue recrystallized (CH_2Cl_2 and light petroleum ether) to yield the title compound as a colourless solid (535 mg, 94%).

m.p. 228–230 °C; $[\alpha]_D^{22}$ +264 ° (*c* 1.00, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3345, 3072, 2971, 1719, 1597, 1507, 1375, 1204, 1152; ^{1}H NMR (400 MHz, *d6*-DMSO) δ 8.10 (2H, d, *J* = 8.3 Hz), 8.07 (2H, d, *J* = 8.3 Hz), 7.73 (1H, d, *J* = 8.3 Hz), 7.62 (1H, d, *J* = 8.4 Hz), 7.57-7.48 (2H, m), 7.37-7.28 (2H, m), 7.24 (1H, d, *J* = 8.5 Hz), 7.16 (1H, d, *J* = 8.4 Hz), 4.66 (1H, dd, *J* = 10.5, 5.8 Hz), 3.97 (1H, d, *J* = 12.0 Hz), 3.52 (1H, d, *J* = 11.9 Hz), 1.73 (1H, dd, *J* = 16.2, 5.8 Hz), 1.30 (1H, dd, *J* = 16.2, 5.8 Hz); ^{13}C NMR (101 MHz, *d6*-DMSO) δ 176.4, 136.5, 135.2, 133.4, 133.3, 133.2, 131.8, 131.7, 131.59, 129.67, 129.52, 129.28, 129.02, 128.77, 128.02, 126.90, 126.85, 126.81, 126.59, 126.43, 126.42, 57.12, 46.75, 38.32; HRMS (CI^+) *m/z*: $[M+H]^+$ Calcd for $[C_{24}H_{20}NO_2]^+$ 354.1494; Found 354.1487.

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(+)-2-((3S,11cS)-4,5-Dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)acetic acid (+)-32.HCl

tert-Butyl 2-((3S,11cS)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)acetate (481 mg, 1.2 mmol) was dissolved in dichloromethane (20 mL), and trifluoroacetic acid (1.3 mL, 16.4 mmol, 14 equiv.) added. The mixture was stirred until consumption of the starting material was observed by TLC. Saturated aqueous sodium hydrogen carbonate was added to bring the solution to neutral pH. The mixture was washed using H_2O (10 mL) and saturated brine (2 x 10 mL), and dried over anhydrous $MgSO_4$. Aqueous HCl (37%, 3 drops) was added, and the mixture stirred for 10 min. The solvent was removed under reduced pressure and the residue recrystallized (hot $CHCl_3$) to yield the title compound as a colourless solid (398 mg, 85%).

m.p. 293-295 °C; $[\alpha]_D^{23}$ +378 ° (*c* 0.5, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 2916, 2811, 2720, 2433, 1723, 1587, 1413, 1398, 1289, 1191, 899; ^{1}H NMR (500 MHz, *d6*-DMSO) δ 12.46 (1H, s), 10.21 (1H, s), 9.53 (1H, s) 8.21 (2H, dd, *J*= 19.0, 8.4 Hz), 8.14 (2H, dd, *J*= 13.0, 8.5 Hz), 7.79 (1H, d, *J*= 8.0 Hz), 7.72 (1H, d, *J*= 8.5 Hz), 7.62 (2H, dd, *J*= 15.6, 8.3 Hz), 7.46-7.34 (2H, m), 7.26-7.16 (2H, dd, *J*= 13.5, 8.5 Hz), 5.11 (1H, t, *J*= 7.0 Hz), 4.30 (1H, d, *J*= 13.0 Hz), 3.78 (1H, d, *J*= 13.0 Hz), 1.94 (2H, m); ^{13}C NMR (126 MHz, *d6*-DMSO) δ 171.3, 135.5, 134.00, 133.98, 133.8, 132.9, 131.6, 131.5, 130.0, 129.78, 129.76, 129.6, 129.1, 128.9, 128.68, 128.67, 127.41, 127.35, 127.1, 127.0, 126.9, 56.6, 46.1, 36.8; HRMS (NSI-FTMS) *m/z*: $[M-H]^-$ Calcd for $[C_{24}H_{19}ClNO_2]^-$ 388.1104; Found 388.1118.

(+)-*tert*-Butyl 2-((3R,11cS)-4-allyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)-2-methylpropanoate (+)-29

A mixture of zinc dust (2.0 g, 30.6 mmol, 10 equiv.), anhydrous THF (40 mL), and TMSCl (0.4 mL, 3.06 mmol, 1 equiv.) was heated at reflux for 30 min. tert-Butyl α-bromoisobutyrate (0.57 mL, 3.06 mmol, 1 equiv.) was added, and the mixture heated at reflux for a further 30 min. The mixture was cooled to –78 °C. (*S*)-4-Allyl-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-4-ium tetraphenylborate (2.0 g, 3.06 mmol) was dissolved in anhydrous THF (40 mL), and transferred into the activated zinc slurry using a cannula. The mixture was stirred for 1 h at –78 °C. *tert*-Butyl α-isobromobutyrate (5.7 mL, 30.6 mmol, 10 equiv.) was added in small portions over 20 min, maintaining the temperature at –78 °C. The mixture was allowed to reach room temperature and monitored by TLC. Saturated aqueous ammonium chloride (5 mL) and Et_2O (50 mL) were added, and the mixture filtered through a pad of celite. The filtrate was washed with H_2O (3 x 20 mL) and saturated brine (3 x 20 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue purified using column chromatography on silica gel (9:1 light petroleum ether/EtOAc) to yield the title compound as a colourless oil (1.1 g, 76%). $[\alpha]_D^{19}$ +102.8° (*c* 1.3, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2977, 2934, 2872, 1722, 1475, 1458, 1391, 1367, 1254, 1141, 1119, 918, 850, 819, 755, 667; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89-7.86 (4H, m), 7.54 (1H, d, *J*= 10.0 Hz), 7.45 (1H, d, *J*= 10.0 Hz), 7.42–7.36 (3H, m), 7.31 (1H, d, *J*= 10.0 Hz), 7.21 (1H, ddd, *J*= 8.3, 6.8, 1.5 Hz), 7.15 (1H, ddd, *J*= 8.3, 6.8, 1.5 Hz), 5.83-5.93 (1H, m), 5.24-5.20 (1H, m), 5.14-5.11 (1H, m), 4.55 (1H, s), 3.65 (1H, d, *J*= 11.5 Hz), 3.49-3.48 (2H, m), 3.41 (1H, d, *J*= 11.5 Hz), 1.29 (9H, s), 0.44 (3H, s), 0.30 (3H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.9, 136.5, 136.1, 136.0, 135.8, 134.2, 133.0, 133.0, 132.8, 132.2, 128.7, 128.3, 128.2, 128.2, 128.0, 127.8, 127.6, 125.8, 125.6, 125.3, 125.2, 117.1, 80.6, 79.8, 64.6, 55.1, 51.1, 28.0, 22.6, 22.4; HRMS (Cl^+) *m/z*: $[M+H]^+$ Calcd for $[C_{33}H_{36}NO_2]^+$ 478.2746; Found 478.2735.

(+)-*tert*-Butyl 2-((3R,11cS)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)-2-methylpropanoate (+)-31

tert-Butyl 2-((3R,11cS)-4-allyl-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)-2-methylpropanoate (1.12 g, 2.3 mmol) was dissolved in anhydrous dichloromethane (70 mL). 1,3-Dimethylbarbituric acid (1.08 g, 6.9 mmol, 3 equiv.) and $Pd(PPh_3)_4$ (0.05 g, 0.046 mmol, 0.02 equiv.) were added, and the mixture was heated at reflux overnight or until complete consumption of the starting material was observed by TLC. The reaction was allowed to cool to room temperature, and the solvent removed under reduced pressure. The residue was redissolved in Et_2O (60 mL), and the solution washed with 1M NaOH (2 x 15 mL), H_2O (2 x 20 mL), and saturated brine (2 x 20 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and column chromatography on silica gel (1:1 light petroleum ether/EtOAc) yielded the title compound as a colourless foam (623 mg, 62%).

m.p. 87-89 °C; $[\alpha]_D^{20}$ +314.0 ° (*c* 1.00, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3019, 2980, 2935, 2400, 1710, 1598, 1509, 1437, 1420, 1366, 1215, 1153, 1132, 1031, 928, 849, 819; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (4H, dd, *J*= 8.0, 5.0 Hz), 7.49 (1H, d, *J*= 8.0 Hz), 7.45 (1H, d, *J*= 8.0 Hz), 7.42-7.38 (2H, m), 7.26-7.24 (2H, m), 7.20 (1H, ddd, *J*= 8.2, 6.7, 1.5 Hz), 7.15 (1H, ddd, *J*= 8.2, 6.7, 1.5 Hz), 4.89 (1H, s), 3.95 (1H, d, *J*= 12.5 Hz), 3.73 (1H, d, *J*= 12.5 Hz), 1.35 (9H, s), 0.73 (3H, s), 0.23 (3H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 176.8, 138.9, 136.4, 134.8, 134.6, 133.4, 132.9, 132.8, 132.7, 132.4, 128.8, 128.4, 128.1, 127.9, 127.7, 127.5, 126.7, 125.8, 125.7, 125.4, 125.0, 80.1, 70.3, 50.7, 49.4, 28.0, 23.7, 19.6; HRMS (Cl^+) *m/z*: $[M+H]^+$ Calcd for $[C_{30}H_{32}NO_2]^+$ 438.2433; Found 438.2424.

(+)-2-((3R,11cS)-4,5-Dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)-2-methylpropanoic acid hydrochloride (+)-33.HCl

tert-Butyl 2-((3R,11cS)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)-2-methyl propanoate (643 mg, 1.47 mmol) was dissolved in dichloromethane (20 mL). Trifluoroacetic acid (1.3 mL, 17.6 mmol, 12 equiv.) was added, and the mixture stirred until complete consumption of the starting material was observed by TLC. Saturated aqueous sodium hydrogen carbonate was added to bring the solution to neutral pH. The mixture was washed with H_2O (15 mL) and saturated brine solution (2 x 15 mL), and dried over anhydrous $MgSO_4$. The residue was subjected to column chromatography on silica gel (EtOAc). Aqueous HCl (37%, 3 drops) was added, and the mixture stirred for 10 min. The solvent was then removed under reduced pressure and the residue recrystallized (Et_2O/light petroleum ether) to yield the title compound as a colourless solid (469 mg, 76%).

m.p. 222-225 °C; $[\alpha]_D^{23}$ +283° (*c* 0.5, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3500, 2928, 2833, 2728, 1703, 1566, 1460, 1189, 1154, 1134, 1034, 726; ^{1}H NMR (500 MHz, *d6*-DMSO) δ 13.01 (1H, s), 10.92 (1H, s), 9.05 (1H, s), 8.13 (2H, t, *J*= 8.5 Hz), 8.07 (2H, dd, *J*= 8.0, 4.5 Hz), 7.75 (1H, d, *J*= 8.5 Hz), 7.69 (1H, dd, *J*= 8.0, 3.3 Hz), 7.59-7.55 (2H, m), 7.35 (1H, t, *J*= 8.5 Hz), 7.27 (1H, t, *J*= 8.5 Hz), 7.15 (1H, d, *J*= 8.5 Hz), 7.08 (1H, d, *J*= 8.5 Hz), 5.24 (1H, s), 4.25 (1H, d, *J*= 13.5 Hz), 3.88 (1H, d,

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J= 13.0 Hz), 0.82 (3H, s), 0.18 (3H, s); ^{13}C NMR (126 MHz, DMSO) δ 176.6, 135.2, 133.4, 133.4, 133.2, 132.1, 131.6, 131.5, 129.5, 129.4, 129.1, 128.9, 128.7, 128.5, 128.5, 128.2, 127.2, 126.9, 126.7, 126.5, 126.3, 66.5, 47.4, 47.0, 25.0, 19.3; HRMS (NSI-FTMS) *m/z*: $[M-Cl]^+$ Calcd for $[C_{26}H_{24}NO_2]^+$ 382.1807; Found 382.1791.

(+)-2-((3S,11cS)-4,5-Dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)-2-methylpropanoic acid (+)-33

tert-Butyl2-((3R,11cS)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepin-3-yl)-2- methylpropanoate (300 mg, 0.69 mmol) was dissolved in dichloromethane (20 mL), and trifluoroacetic acid (0.63 mL, 8.2 mmol, 12 equiv.) added. The mixture was stirred until complete consumption of the starting material was observed by TLC. Saturated aqueous sodium hydrogen carbonate was added to bring the solution to neutral pH. The mixture was washed using H_2O (20 mL) and saturated brine (2 x 10 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue subjected to column chromatography (EtOAc). Recrystallization ($CHCl_3$/light petroleum ether) yielded the title compound as a beige solid (161 mg, 61%).

m.p. 192-194 °C; $[\alpha]_D^{25}$ +138.1°(*c* 0.9, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3400, 3054, 2979, 2850, 1673, 1598, 1470, 1200, 1135, 821, 751; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (1H, d, *J*= 8.5 Hz), 7.94 (1H, d, *J*= 8.2 Hz), 7.89 (1H, d, *J*= 8.2 Hz), 7.78 (1H, d, *J*= 7.8 Hz), 7.58 (5H, d, *J*= 8.1 Hz), 7.56-7.46 (3H, m), 7.26-7.30 (2H, m), 7.24-7.17 (2H, m), 5.35 (5H, s), 4.39 (2H, d, *J* = 12.9 Hz), 4.09 (2H, d, *J* = 12.8 Hz), 1.16 (3H, s), 0.01 (3H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 179.6, 136.1, 133.9, 133.9, 133.6, 132.9, 132.4, 131.7, 131.8, 129.6, 129.4, 129.2, 128.7, 128.1, 128.0, 127.6, 127.5, 126.8, 126.6, 126.3, 126.1, 77.2, 67.8, 47.2, 27.6, 26.6; HRMS (CI^+) *m/z*: $[M+H]^+$ Calcd for $[C_{26}H_{24}NO_2]^+$ 382.1807; Found 382.1803.

(–)-(*S*)-*tert*-Butyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-4(5H)-carboxylate (–)-13

Method A: (*S*)-4,5-Dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine (1.32 g, 4.5 mmol) was dissolved in warmed *t*-BuOH (30 mL). A solution of di-*tert*-butyl dicarbonate (1.02 g, 4.7 mmol, 1.05 equiv.) in *t*-BuOH (10 mL) was added, and the mixture stirred at room temperature for 3 h. A further portion of di-*tert*-butyl dicarbonate (0.12 equiv.) was added, and the mixture stirred until full consumption of the starting material was observed by TLC. EtOAc (50 mL) was added, and the solution washed with H_2O (2 x 20 mL) and saturated brine (20 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to yield the product as a pale yellow solid (1.65 g, 92%).

Method B: (*S*)-2,2'-Bis-bromomethyl-[1,1']binaphthalene (600 mg, 1.36 mmol) was dissolved in anhydrous DMF (30 mL). The pale yellow solution was cooled to 0 °C, and NaH (130 mg, 5.45 mmol, 4 equiv.) added in one portion. *t*-Butyl carbamate (160 mg, 1.36 mmol, 1 equiv.) was added slowly in small portions. The mixture was stirred for 4 days or until full consumption of the starting material was observed by TLC. The mixture was cooled to 0 °C, and saturated aqueous ammonium chloride (10 mL) added. The majority of the solvent was removed under reduced pressure. Et_2O (100 mL) was added, and the mixture washed with H_2O (5 x 20 mL) and saturated brine (3 x 20 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure, and the residue purified by recrystallization (acetone) to yield the title compound as a colourless solid (469 mg, 87%).

m.p. 219- 221 °C; $[\alpha]_D^{23}$ −7.0° (*c* 1.00, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3057, 2979, 2933, 2253, 1819, 1682, 1508, 1464, 1405, 1367, 1275, 1252, 1219, 1163, 1106, 908, 867, 819; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99-7.91 (4H, m), 7.60 (2H, d, *J*= 8.0 Hz), 7.47 (2H, ddd, *J*= 8.0, 7.0, 1.0 Hz), 7.43 (2H, d, *J*= 8.5 Hz), 7.26 (2H, ddd, *J*= 8.5, 7.0, 1.0 Hz), 4.93 (2H, br s), 3.65 (2H, d, *J*= 13.0 Hz), 1.51 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.4, 135.0, 133.33, 133.28, 131.5, 129.2, 128.3, 127.51, 127.47, 126.0, 125.8, 85.2, 80.0, 28.6, 27.4; ; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{27}H_{26}NO_2]^+$ 396.1964; Found 396.1955.

(–)-(3R,11cS)-4-*tert*-Butyl 3-ethyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3,4(5H)-dicarboxylate (–)-15

(*S*)-*tert*-Butyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-4(5H)-carboxylate (200 mg, 0.51 mmol) was dissolved in anhydrous Et_2O (20 mL), and the solution cooled to −78 °C. *sec*-BuLi (1.4 M solution in cyclohexane, 0.47 mL, 0.66 mmol, 1.3 equiv.) was added dropwise; the pale yellow solution instantly turned black on addition. The mixture was stirred at −78 °C for 1 h. Ethyl chloroformate (0.15 mL, 1.53 mmol, 3 equiv.) was added in one portion, causing the solution to turn from black to bright yellow. The mixture was allowed to reach room overnight, or until full consumption of the starting material was observed by TLC. The mixture was cooled to 0 °C, and saturated aqueous ammonium chloride (10 mL) added. The mixture was washed with H_2O (3 x 10 mL) and saturated brine (3 x 10 mL), dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The residue was purified by column chromatography on silica gel (7:3 light petroleum ether/EtOAc) to yield the title compound as a colourless solid (174 mg, 73%).

m.p. 101-103 °C; $[\alpha]_D^{22}$ −17.6 ° (*c* 1.00, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3052, 2976, 2931, 1748, 1695, 1508, 1475, 1461, 1392, 1366, 1297, 1252, 1243, 1217, 1164, 1155, 1107, 1027, 945, 911, 897, 864, 825, 814; 1H NMR (500 MHz, $CDCl_3$) δ 8.02 (2H, d, *J* = 8.2 Hz), 8.00–7.94 (4H, m), 7.89 (2H, d, *J* = 8.2 Hz), 7.69–7.60 (3H, m), 7.56 (1H, d, *J* = 8.3 Hz), 7.53–7.46 (3H, m), 7.42 (4H, ddd, *J* = 11.9, 8.3, 5.1 Hz), 7.33 (2H, dd, *J* = 8.3, 3.5 Hz), 7.30–7.27 (1H, m), 7.24 (2H, dd, *J* = 8.2, 7.2 Hz), 5.95 (1H, s), 5.69 (1H, s), 5.26 (1H, d, *J* = 13.4 Hz), 5.03 (1H, d, *J* = 13.3 Hz), 3.75 (2H, d, *J* = 13.3 Hz), 3.64 (1H, d, *J* = 13.4 Hz), 3.08 (2H, m), 2.93 – 2.64 (2H, m), 1.55 (9H, s), 1.47 (9H, s), 0.98–0.79 (6H, m), 0.53 (3H, t, *J* = 7.1 Hz), 0.47 (3H, t, *J* = 7.1 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.9, 169.6, 154.3, 154.0, 134.7, 134.32, 134.31, 134.28, 133.88, 133.37, 133.34, 133.32, 133.17, 133.13, 133.10, 131.64, 131.52, 131.50, 131.40, 129.6, 129.3, 129.2, 128.7, 128.6, 128.23, 128.20, 128.1, 127.8, 127.47, 127.39, 127.3, 127.2, 126.3, 126.2, 126.1, 126.02, 126.97, 125.8, 125.7, 80.6, 80.5, 62.2, 61.0, 60.84, 60.82, 47.8, 46.5, 28.5, 28.4, 13.3, 13.2; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{30}H_{30}NO_4]^+$ 468.2175; Found 468.2165.

(+)-(3R,11cS)-Ethyl 4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylate (+)-17

(3R,11cS)-4-*tert*-Butyl 3-ethyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3,4(5H)-dicarboxylate (90 mg, 0.2 mmol) was dissolved in dichloromethane (5 mL). Trifluoroacetic acid (0.2 mL, 2.8 mmol, 14 equiv.) was added, and the mixture stirred until complete

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consumption of the starting material was observed by TLC. Saturated aqueous sodium hydrogen carbonate was added to bring the pH of the solution to neutral. The solvent was removed reduced pressure and the residue redissolved in EtOAc (5 mL). The solution was washed with H_2O (3 x 5 mL) and saturated brine (3 x 5 mL), dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The residue was purified by column chromatography on silica gel (EtOAc), to yield the product as a yellow oil (60 mg, 81%).

$[\alpha]_D^{23}$ +386.0° (*c* 1.00, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3583, 2980, 2253, 1742, 1710, 1394, 1366, 1222, 1156, 1109, 1027, 909, 826; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (1H, d, *J*= 8.5 Hz), 7.98–7.91 (2H, m), 7.89 (1H, d, *J*= 8.5 Hz), 7.63 (1H, d, *J*= 8.5 Hz), 7.51-7.44 (2H, m), 7.44–7.34 (3H, m), 7.29-7.20 (2H, m), 4.59 (1H, s), 3.83 (1H, d, *J*= 13.5 Hz), 3.55 (1H, d, *J*= 13.5 Hz), 3.36 (1H, s), 3.22 (1H, dq, *J*= 10.7, 7.1 Hz), 2.58 (1H, dq, *J*= 10.7, 7.2 Hz), 0.49 (3H, t, *J*= 7.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.1, 137.5, 134.9, 134.0, 133.4, 133.3, 132.9, 131.60, 131.57, 129.6, 129.0, 128.8, 128.34, 128.28, 127.4, 127.2, 126.9, 125.98, 125.95, 125.9, 125.4, 62.5, 61.1, 48.5, 13.3; HRMS (ESI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{25}H_{22}NO_2]^+$ 368.1651; Found 368.1645.

(+)-(3R,11cS)-Ethyl 4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylate hydrochloride (+)-17.HCl

(3R,11cS)-4-*tert*-butyl 3-ethyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3,4(5H)-dicarboxylate (300 mg, 0.64 mmol) was dissolved in acetone (30 mL), concentrated aqueous HCl (3 drops) added, and the mixture heated at reflux overnight. The mixture was allowed to cool to room temperature, and the solvent removed under reduced pressure. The residue was purified by recrystallization (Et_2O and light petroleum ether) to yield the title compound as a yellow solid (260 mg, 100%).

m.p.* 219-221 °C (*decomp); $[\alpha]_D^{23}$ +340° (*c* 1.03, $CHCl_3$); ν_{max} (solid)/cm^{-1} 3394, 2928, 2661, 1736, 1671, 1595, 1545, 1443, 1369, 1299, 1236, 1195, 1055, 1027, 961, 897, 820, 796, 749, 705, 624; ^{1}H NMR (500 MHz, *d6*-DMSO) δ 8.02 (1H, d, *J*= 8.4 Hz), 7.94 (2H, dd, *J*= 8.3, 4.8 Hz), 7.88 (1H, d, *J*= 8.2 Hz), 7.58 (1H, d, *J*= 8.4 Hz), 7.48 (1H, d, *J*= 8.4 Hz), 7.45-7.40 (1H, m), 7.37 (1H, t, *J*= 7.5 Hz), 7.24-7.14 (2H, m), 7.03 (1H, d, *J*= 8.6 Hz), 6.96 (1H, d, *J*= 8.5 Hz), 5.63 (1H, s), 4.14 (1H, d, *J*= 13.5 Hz), 3.46 (1H, d, *J*= 13.0 Hz), 3.03 (1H, dq, *J*= 10.8, 7.1 Hz), 2.38 (1H, dq, *J*= 10.8, 7.1 Hz), 0.16 (3H, t, *J*= 7.1 Hz); ^{13}C NMR (126 MHz, DMSO) δ 167.76, 134.57, 134.13, 133.92, 131.16, 131.08, 130.38, 130.23, 129.93, 129.70, 129.61, 128.99, 128.44, 127.57, 127.30, 127.26, 127.19, 127.05, 127.02, 62.29, 59.18, 45.84, 13.23; HRMS (ESI-FTMS) *m/z*: $[M-Cl]^+$ Calcd for $[C_{25}H_{22}NO_2]^+$ 368.1651; Found 368.1645.

(–)-(3R,11cS)-4-tert-Butyl 3-methyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3,4(5H)-dicarboxylate (–)-14

(*S*)-*tert*-Butyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-4(5H)-carboxylate (900 mg, 2.3 mmol) was dissolved in anhydrous Et_2O (50 mL). The solution was cooled to −78 °C, and *sec*-BuLi (1.3 M in cyclohexane, 2.3 mL, 3.0 mmol, 1.3 equiv.) added dropwise, causing the pale yellow solution to turn black. The mixture was stirred at −78 °C for 1 h. Methyl chloroformate (0.53 mL, 6.8 mmol, 3 equiv.) was added, causing the solution to turn bright yellow. The mixture was allowed to reach room temperature over 12 h, or until complete consumption of the starting material was observed by TLC. The mixture was cooled to 0 °C, and saturated aqueous ammonium chloride (5 mL) added. The mixture was washed with H_2O (2 x 20 mL) and saturated brine (2 x 10 mL), dried over anhydrous $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (9:1 light petroleum ether/EtOAc) to yield title compound as a colourless fluffy solid (845 mg, 81%).

m.p. 124-126 °C; $[\alpha]_D^{23}$ −20.8° (*c* 0.5, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3053, 2975, 2946, 2884, 1751, 1696, 1508, 1456, 1392, 1366, 1296, 1164, 960, 823; ^{1}H NMR (500 MHz, *d6*-DMSO at 380 K) δ 8.13 (1H, d, *J*= 8.3 Hz), 8.08 (1H, d, *J*= 8.2 Hz), 8.04 (1H, d, *J*= 8.3 Hz), 8.01 (1H, d, *J*= 8.2 Hz), 7.76 (1H, d, *J*= 8.3 Hz), 7.60 (1H, d, *J*= 8.3 Hz), 7.56 (1H, ddd, *J*= 8.1, 6.6, 1.3 Hz), 7.51 (1H, ddd, *J*= 8.1, 6.8, 1.1 Hz), 7.37-7.32 (1H, m), 7.32–7.28 (2H, m), 7.19 (1H, d, *J*= 8.5 Hz), 5.85 (1H, s), 5.10 (1H, d, *J*= 13.3 Hz), 3.61 (1H, d, *J*= 13.4 Hz), 2.54 (3H, s), 1.50 (9H, s); ^{13}C NMR (126 MHz, *d6*-DMSO at 380 K) δ 169.9, 153.9, 134.5, 134.3, 134.2, 133.7, 133.6, 133.5, 131.63, 131.58, 129.8, 129.7, 128.9, 128.7, 128.6, 128.3, 127.1, 126.9, 126.73, 126.67, 126.4, 126.2, 80.5, 79.6, 51.2, 28.7, 28.6; HRMS (ESI-FTMS) *m/z*: $[M+Na]^+$ Calcd for $[C_{29}H_{27}NNaO_4]^+$ 476.1838; Found 476.1832.

(+)-(3R,11cS)-Methyl 4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylate (+)-16

(3*R*,11cS)-4-*tert*-Butyl 3-methyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3,4(5H)-dicarboxylate (600 mg, 1.32 mmol) was dissolved in dichloromethane (10 mL), and trifluoroacetic acid (1.4 mL, 18.5 mmol, 14 equiv.) added. The mixture was stirred for 30 min. Saturated aqueous sodium hydrogen carbonate was added to bring the pH to neutral. The solvent was removed under reduced pressure and the residue redissolved in EtOAc (30 mL). The solution was washed with H_2O (3 x 20 mL) and saturated brine (3 x 20 mL), dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The residue was purified by recrystallization ($CHCl_3$ and light petroleum ether) to yield the title compound as a colourless solid (364 mg, 78%).

m.p. 214-216 °C; $[\alpha]_D^{21}$ +420 ° (*c* 1.03, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3318, 3050, 2947, 2874, 1730, 1508, 1448, 1432, 1223, 1207, 1110, 992, 866, 822; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (1H, d, *J*= 8.0 Hz), 7.97-7.93 (2H, m), 7.91 (1H, d, *J*= 8.0 Hz), 7.64 (1H, d, *J*= 8.5 Hz), 7.52-7.47 (2H, m), 7.44-7.42 (2H, m), 7.36 (1H, d, *J*= 8.5 Hz), 7.28 (1H, d, *J*= 7.6 Hz), 7.24 (1H, d, *J*= 7.5 Hz), 4.62 (1H, s), 3.84 (1H, d, *J*= 14.0 Hz), 3.57 (1H, d, *J*= 13.7 Hz), 2.49 (3H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.4, 137.4, 135.0, 133.7, 133.4, 133.3, 132.9, 131.5, 131.4, 129.7, 129.1, 128.4, 128.34, 128.29, 127.3, 127.0, 126.8, 126.1, 126.0, 125.9, 125.5, 62.2, 51.6, 48.4; HRMS (ESIFTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{24}H_{20}NO_2]^+$ 354.1494; Found 354.1479.

(+)-(3R,11cS)-Methyl 4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylate hydrochloride (+)-16.HCl

(3R,11cS)-4-*tert*-Butyl 3-methyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3,4(5H)-dicarboxylate (258 mg, 0.57 mmol) was dissolved in acetone (30 mL), concentrated aqueous HCl (3 drops) added, and the mixture heated at reflux overnight. The mixture was allowed to cool to room temperature, and the solvent removed under reduced pressure. The residue was purified by recrystallization (MeOH and Et_2O) to yield the title compound as a beige solid (222 mg, 100%).

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m.p. 220-230 °C; $[\alpha]_D^{21}$ + 296.0 ° (*c* 1.00, $CHCl_3$); ν_{max} (solid)/cm^{-1} 3406, 3053, 2950, 2673, 1746, 1596, 1508, 1439, 1371, 1248, 1212, 1058, 864, 822; ^{1}H NMR (500 MHz, *d6*-DMSO) δ 9.67 (1H, s), 8.26 (1H, d, *J*= 8.0 Hz), 8.17-8.15 (2H, m), 8.12 (1H, d, *J*= 8.5 Hz), 7.81 (1H, d, *J*= 8.5 Hz), 7.71 (1H, d, *J*= 8.3 Hz), 7.65 (1H, ddd, *J*= 8.0, 6.6, 1.0 Hz), 7.61 (1H, ddd, *J*= 8.1, 6.8, 1.0 Hz), 7.42-7.37 (2H, m), 7.27 (1H, d, *J*= 8.4 Hz), 7.16 (1H, d, *J*= 8.5 Hz), 5.86 (1H, s), 4.36 (1H, d, *J*= 13.2 Hz), 3.70 (1H, d, *J*= 13.2 Hz), 2.45 (3H, s); ^{13}C NMR (126 MHz, *d6*-DMSO) δ 167.8, 134.2, 134.1, 133.6, 133.4, 130.74, 130.66, 130.5, 130.0, 129.9, 129.5, 129.2, 128.8, 128.5, 127.9, 127.1, 126.9, 126.8, 126.5, 126.3 58.6, 52.0, 45.4; HRMS (NSI-FTMS) *m/z*: $[M-Cl]^+$ Calcd for $[C_{24}H_{20}NO_2]^+$ 354.1494; Found 354.1488.

(–)-(3R,11cS)-4-(*tert*-Butoxycarbonyl)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid (–)-18a and (+)-(3S,11cS)-4-(*tert*-butoxycarbonyl)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid (+)-18b

(*S*)-*tert*-Butyl 3H-dinaphtho-[2,1-c:1',2'-e]-azepine-4(5H)-carboxylate (500 mg, 1.26 mmol) was dissolved in anhydrous Et_2O (30 mL) under a positive pressure of argon, and the mixture was cooled to −78 °C. *sec*-BuLi (1.4 M solution in cyclohexane, 1.2 mL, 1.6 mmol, 1.3 equiv.) was added, causing the solution to turn from a pale yellow to a black colour. The mixture was stirred at −78 °C for 1 h. CO_2 gas was bubbled directly into the solution *via* a drying tube filled with $CaCl_2$. The mixture was stirred overnight at −78 °C under an atmosphere of argon. Saturated aqueous ammonium chloride (10 mL) and EtOAc (20 mL) were added. The organic layer was washed with H_2O (2 x 20 mL) and saturated brine (2 x 20 mL), dried over anhydrous Na_2SO_4, and the solvent removed under reduced pressure. The residue was purified by column chromatography on silica gel (4:1 light petroleum ether/EtOAc).

For the first eluting diastereoisomer **18a**: isolated as a colourless solid (188 mg, 34%), m.p. 164-167 °C; $[\alpha]_D^{24}$ −47.2 ° (*c* 1.00, $CHCl_3$); $\nu_{max}(CHCl_3)$/cm^{-1} 3056, 2976, 2937, 1754, 1694, 1393, 1367, 1303, 1245, 1156, 912, 819, 749; ^{1}H NMR (500 MHz, *d6*-DMSO, 363 K) δ 8.07 (1H, d, *J*= 8.7 Hz), 8.02 (1H, d, *J*= 8.7 Hz), 7.98–7.94 (2H, m), 7.70 (1H, d, *J*= 8.6 Hz), 7.57 (1H, d, *J*= 8.2 Hz), 7.49 (1H, ddd, *J*= 8.1, 6.8, 1.5 Hz), 7.44 (1H, ddd, *J*= 8.1, 6.8, 1.5 Hz), 7.25 (2H, m), 7.20-7.15 (2H, m), 5.72 (1H, s), 5.07 (1H, d, *J*= 15.5 Hz), 3.56 (1H, d, *J*= 15.5 Hz), 1.45 (9H, s); ^{13}C NMR (126 MHz, *d6*-DMSO, 363 K) δ 170.5, 154.0, 134.3, 133.5, 131.8, 131.7, 129.5, 129.4, 128.7, 128.6, 128.4, 127.4, 127.2, 126.5, 126.2, 126.0, 80.2, 62.1, 47.4, 28.7; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{28}H_{26}NO_4]^+$ 440.1862; Found 440.1854.

For the first eluting diastereoisomer **18b**: isolated as a colourless solid (170 mg, 31%), m.p. 255-257 °C; $[\alpha]_D^{24}$ +58.4 ° (*c* 1.00, $CHCl_3$); $\nu_{max}(CHCl_3)$/cm^{-1} 3052, 3006, 2976, 2927, 1751, 1725, 1696, 1395, 1367, 1251, 1219, 1151, 820, 772, 759, 677; ^{1}H NMR (500 MHz, *d6*-DMSO, 353 K) δ 8.07 (2H, d, *J*= 8.3 Hz), 8.02 (2H, dd, *J*= 11.6, 8.3 Hz), 7.66 (1H, d, *J*= 9.0 Hz), 7.58 (1H, d, *J*= 9.0 Hz), 7.52-7.48 (2H, m), 7.35-7.31 (2H, m), 7.27-7.24 (1H, m), 7.16 (1H, d, *J*= 8.7 Hz), 4.95 (1H, d, *J* =15.0 Hz), 4.36 (1H, s), 3.55 (1H, d, *J* =15.0 Hz), 1.40 (9H, s); ^{13}C NMR (126 MHz, *d6*-DMSO, 353 K) δ 171.4, 155.75, 136.3, 135.1, 133.5, 133.4, 132.6, 132.3, 131.7, 131.5, 129.8, 129.2, 128.9, 128.7, 127.21, 127.16, 126.8, 126.8, 126.7, 126.3, 126.1, 125.2, 81.1, 62.7, 48.7, 28.4; ; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{28}H_{26}NO_4]^+$ 440.1862; Found 440.1852.

(+)-(3R,11cS)-4,5-Dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid hydrochloride (+)-19a.HCl

3R,11cS)-4-(*tert*-Butoxycarbonyl)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid (230 mg, 0.52 mmol) was dissolved in acetone (20 mL), concentrated aqueous HCl (3 drops) added, and the mixture heated at reflux overnight. The mixture was allowed to cool to room temperature and the solvent removed under reduced pressure. The residue was purified by recrystalization (MeOH and light petroleum ether) to yoeld the title compound as a pale yellow solid (197 mg, 100%).

m.p. 265-267 °C; $[\alpha]_D^{22}$ +294 ° (*c* 1.00, MeOH); ν_{max} (CH_2Cl_2)/cm^{-1} 3019, 2400, 1741, 1528, 1425, 1215, 928, 757, 669, 625; ^{1}H NMR (500 MHz, *d6*-DMSO) δ 13.26 (1H, s), 11.10 (1H, s), 9.43 (1H, s), 8.23 (1H, d, *J*= 8.4 Hz), 8.15 (2H, dd, *J*= 8.3, 3.7 Hz), 8.09 (1H, d, *J*= 8.2 Hz), 7.80 (1H, d, *J*= 8.4 Hz), 7.71 (1H, d, *J*= 8.4 Hz), 7.66-7.54 (2H, m), 7.43-7.34 (2H, m), 7.18 (2H, t, *J*= 8.0 Hz), 5.71 (1H, s), 4.34 (1H, d, *J*= 13.1 Hz), 3.67 (1H, d, *J*= 13.1 Hz); ^{13}C NMR (126 MHz, *d6*-DMSO) δ 168.9, 134.7, 134.6, 134.1, 134.0, 131.34, 131.25, 130.2, 129.9, 129.8, 129.68, 129.65, 129.6, 129.0, 128.9, 128.4, 127.4, 127.3, 127.2, 127.1, 127.0, 59.4, 46.0; HRMS (NSI-FTMS) *m/z*: $[M-Cl]^+$ Calcd for $[C_{23}H_{18}NO_2]^+$ 340.1338; Found 340.1333.

(+)-(3R,11cS)-4,5-Dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid (+)-19a

(3R,11cS)-4-(*tert*-Butoxycarbonyl)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid (1.55g, 3.53 mmol) was dissolved in dichloromethane (30 mL), trifluoroacetic acid (3.8 mL, 49.4 mmol, 14 equiv.) added, and the solution stirred for 30 min. Saturated aqueous sodium hydrogen carbonate was added to bring the pH to neutral. The solvent was removed under reduced pressure, and the residue redissolved in EtOAc (30 mL). The solution was washed with H_2O (3 x 20 mL) and saturated brine (3 x 20 mL), dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The residue was purified by recrystallization ($CHCl_3$ and light petroleum ether) to yield the title compound (983 mg, 82%).

m.p. 269-271 °C; $[\alpha]_D^{25}$ +272.8 ° (*c* 1.00, $CHCl_3$); ν_{max}(solid)/cm^{-1} 3400, 3067, 2926, 2876, 2521, 1722, 1670, 1367, 1367, 1194, 1139, 820, 749; ^{1}H NMR (500 MHz, *d6*-DMSO) δ 8.21 (1H, d, *J*= 8.0 Hz), 8.13 (2H, dd, *J*= 8.0, 2.0 Hz), 8.08 (1H, d, *J*= 8.0 Hz), 7.77 (1H, d, *J*= 8.0 Hz), 7.69 (1H, d, *J*= 8.0 Hz), 7.60 (2H, dt, *J*= 15.9, 7.5), 7.37 (2H, ddd, *J*= 8.0, 6.5, 1.0 Hz), 7.17 (2H, dd, *J*= 8.5, 5.3 Hz), 5.49 (1H, s), 4.30 (1H, d, *J*= 13.1 Hz), 3.63 (1H, d, *J*= 13.1 Hz); ^{13}C NMR (126 MHz, *d6*-DMSO) δ 168.9, 134.7, 134.4, 133.92, 133.86, 131.4, 131.3, 131.1, 130.5, 129.9, 129.8, 129.7, 128.9, 128.8, 128.3, 127.4, 127.2, 127.0, 126.92, 126.86, 60.1, 46.1; HRMS (NSI-FTMS) *m/z* $[M-H]^-$ Calcd for $[C_{23}H_{16}NO_2]^-$ 338.1181; Found 338.1181.

(+)-(3S,11cS)-4,5-Dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid hydrochloride (+)-19b.HCl

(3S,11cS)-4-(*tert*-Butoxycarbonyl)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid (346 mg, 0.79 mmol) was dissolved in acetone (35 mL), concentrated aqueous HCl (3 drops) added., and the reaction mixture heated at reflux overnight. The mixture was allowed to cool to room temperature, and the solvent removed under reduced pressure. The residue was purified by

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recrystalization (diethyl ether and light petroleum ether) to yield the title compound as a yellow solid (296 mg, 100%). m.p.* 290-292 °C (*decomp); $[\alpha]_D^{22}$ +282 ° (*c* 1.00, MeOH); ν_{max} (solid)/cm^{-1} 3247, 2737, 1961, 1714, 1594, 1461, 1430, 1310, 1276, 1235, 1028, 816, 780, 665, 640; ^{1}H NMR (500 MHz, *d6*-DMSO) δ 10.51 (1H, s), 10.09 (1H, s), 8.29 (1H, d, *J*= 8.5 Hz), 8.24 (1H, d, *J*= 8.0 Hz), 8.17 (2H, d, *J*= 8.0 Hz), 7.79 (1H, d, *J*= 8.5 Hz), 7.68–7.62 (2H, m), 7.54 (1H, d, *J*= 8.5 Hz), 7.47-7.42 (2H, m), 7.35 (1H d, *J*= 8.5 Hz), 7.29 (1H, d, *J*= 8.6 Hz), 4.61 (1H, s), 4.41 (1H, d, *J*= 13.0 Hz), 3.45 (1H, d, *J*= 13.0 Hz); ^{13}C NMR (126 MHz, *d6*-DMSO) δ 169.1, 135.7, 134.5, 134.3, 134.1, 131.1, 130.8, 130.4, 130.1, 129.7, 129.1, 128.5, 127.8, 127.6, 127.5, 127.41, 127.34, 127.3, 127.1, 124.6, 58.3, 46.2; HRMS (NSI-FTMS) *m/z*: $[M-Cl]^+$ Calcd for $[C_{23}H_{18}NO_2]^+$ 340.1338; Found 340.1336.

(+)-(3S,11cS)-4,5-Dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid (+)-19b

(3S,11cS)-4-(*tert*-Butoxycarbonyl)-4,5-dihydro-3H-dinaphtho-[2,1-c:1',2'-e]-azepine-3-carboxylic acid (1.60 g, 3.64 mmol) was dissolved in dichloromethane (30 mL), trifluoroacetic acid (3.9 mL, 50.96 mmol, 14 equiv.) added, and the solution stirred for 30 min. Saturated aqueous sodium hydrogen carbonate was added to bring the pH to neutral. The solvent was removed under reduced pressure, and the residue redissolved in EtOAc (30 mL). The solution was washed with H_2O (3 x 20 mL) and saturated brine solution (3 x 20 mL), dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The residue was purified by recrystallization ($CHCl_3$ and light petroleum ether) to yield the title compound (877 mg, 71%) as a colourless solid.

m.p. 276-280 °C; $[\alpha]_D^{25}$ +196.0 ° (*c* 1.00, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3408, 3053, 3009, 2974, 2974, 2784, 2595, 1760, 1633, 1400, 1392, 1340, 1201, 1029, 820, 739; ^{1}H NMR (500 MHz, *d6*-DMSO) δ 8.09 (4H, m), 7.70 (2H, d, *J*= 8.3 Hz), 7.58 (2H, m), 7.42–7.26 (3H, m), 7.22 (1H, d, *J*= 8.6 Hz), 4.10 (1H, d, *J*= 12.7 Hz), 3.85 (1H, s), 3.35 (1H, d, *J*= 12.7 Hz); ^{13}C NMR (126 MHz, DMSO) δ 134.7, 134.5, 133.3, 133.1, 132.2, 131.0, 130.6, 130.3, 129.0, 128.7, 128.6, 128.4, 127.6, 126.63, 126.59, 126.5, 126.32, 126.28, 126.24, 126.21, 60.2, 45.8; HRMS (NSI-FTMS) *m/z* $[M+H]^+$ Calcd for $[C_{23}H_{18}NO_2]^+$ 340.1338; Found 340.1335.

(S)-(+)-6,6'-Dimethyl-[1,1'-biphenyl]-2,2'-dicarboxylic acid (+)-21 [30]

NaOH (5.88 g, 147 mmol) and 2-amino-3-methylbenzoic acid (17 g, 113 mmol) were dissolved in water, and the solution cooled to 0 °C. $NaNO_2$ (7.8 g, 113 mol) was added. The mixture was stirred until homogeneous. Aqueous HCl (4M, 240 mL) was added dropwise, keeping the temperature below 8 °C. After addition, the mixture was stirred at 0 °C for 30 min. A solution of $CuSO_4.5H_2O$ (48 g, 192 mmol) in water (150 mL) was cooled to 0 °C, and aqueous ammonium hydroxide (95 mL, 215 mmol) was added. NH_2OH was added (prepared from $(NH_2OH)_2.H_2SO_4$ (17.6 g, 107 mmol) with 3M NaOH (75 mL)). The diazonium salt was added in 40 mL portions *via* syringe, with the needle kept below the surface of the reaction medium, while maintaining the temperature below 8 °C. The mixture was heated under reflux for 30 minutes, allowed to cool to room temperature, and aqueous HCl (12M, 80 mL) added. The mixture was allowed to stand overnight, and the precipitate removed by filtration. The residue (17.5 g) was dried at 60 °C for 12 h, and recrystallized (ethanol) to give a yellow solid. The solvents were removed from the filtrate under reduced pressure, and the residue purified by recrystallization (ethanol-H_2O) to yield (±)-6,6'-dimethyl-[1,1'-biphenyl]-2,2'-dicarboxylic acid as a red-brown solid (8.2 g, 30.3 mmol, 54%).

(±)-6,6'-Dimethyl-[1,1'-biphenyl]-2,2'-dicarboxylic acid (3.5 g, 12.9 mmol) was dissolved in boiling EtOH (16 mL), and quinine (4.2 g, 12.9 mmol, 1 equiv.) added in one portion. The solution was allowed to cool to room temperature, and the colourless precipitate of the quinine monohydrate salt (4.90 g) removed by filtration. The salt was dissolved in EtOAc (70 mL), and 3 M HCl (80 mL) added. The solution was washed with H_2O (3 x 20 mL) and saturated brine (2 x 10 mL), dried over anhydrous $MgSO_4$, and the solution concentrated under reduced pressure to yield the title compound as an orange solid (1.3 g, 37%).

$[\alpha]_D^{21}$ +20.8 ° [(*c* 1.00, MeOH) (Lit[30] $[\alpha]_D^{25}$ +19.2 °, *c* 1.00, MeOH)]; m.p. 225-227 °C (Lit[30] 220-230 °C), ν_{max} (CH_2Cl_2)/cm^{-1} 3054, 2986, 2923, 2832, 2685, 2560, 2411, 2305, 1702, 1682, 1592, 1579, 1421, 1296, 1264, 1187, 1159, 1111, 934, 896, 819; ^{1}H NMR (500 MHz, *d6*-DMSO) δ 12.39 (2H, s), 7.72 (2H, d, *J*= 7.6 Hz), 7.46 (2H, d, *J*= 7.4 Hz), 7.33 (2H, t, *J*= 7.6 Hz), 1.83 (6H, s); ^{13}C NMR (126 MHz, *d6*-DMSO) δ 168.5, 141.1, 136.4, 133.3, 130.9, 127.7, 127.1, 20.2; HRMS (NSI-FTMS) *m/z*: $[M-H]^-$ Calcd for $[C_{16}H_{13}O_4]^-$ 269.0814; Found 269.0812.

(S)- (–)-(6,6'-Dimethyl-[1,1'-biphenyl]-2,2'-diyl)dimethanol (–)-22 [30]

6,6'-Dimethyl-[1,1'-biphenyl]-2,2'-dicarboxylic acid (144 mg, 0.48 mmol) was dissolved in anhydrous Et_2O (10 mL), and the solution cooled to 0 °C. $LiAlH_4$ (73 mg, 1.93 mmol, 4 equiv.) was added. After 5 h the mixture was quenched with H_2O (10 mL). The mixture was filtered through a pad of celite, washed with H_2O (3 x 15 mL) and saturated brine (2 x 10 mL), and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to yield the product as an orange solid (117 mg, 100%), used without further purification.

m.p. 208-210 °C (Lit[30] 116-118 °C); $[\alpha]_D^{22}$ −74.7 ° [(*c* 1.00, $CHCl_3$); Lit[30] $[\alpha]_D$ −30 ° (*c* 0.4, $CHCl_3$)]; ν_{max} (CH_2Cl_2)/cm^{-1} 3064, 3018, 2970, 2918, 2856, 1459, 1437, 1381, 1246, 1210, 1166, 788, 755, 735, 626, 613; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36 (2H, dd, *J*= 7.4, 1.0 Hz), 7.31 (2H, t, *J*= 7.5 Hz), 7.26 (2H, t, *J*= 6.1 Hz), 4.29 (2H, d, *J*= 11.5 Hz), 4.14 (2H, d, *J*= 11.5 Hz), 2.27 (2H, br s, O*H*), 1.87 (6H, s, Ar*CH*$_3$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.4, 138.2, 136.0, 129.8, 127.9, 127.5, 63.0, 20.1.

(+)-2,2'-bis(Bromomethyl)-6,6'-dimethyl-1,1'-biphenyl (+)-20

(6,6'-Dimethyl-[1,1'-biphenyl]-2,2'-diyl)dimethanol (500 mg, 2.1 mmol) and pyridine (19 µL, 0.23 mmol, 0.11 equiv.) were dissolved in anhydrous toluene (50 mL). Phosphorus tribromide (0.6 mL, 6.3 mmol, 3 equiv.) was added dropwise. The mixture was heated at 60 °C for 3 h. H_2O (50 mL) was added, and the mixture washed with saturated aqueous sodium hydrogen carbonate (20 mL). The organic layer was dried over anhydrous $MgSO_4$, decolourized with carbon black, filtered, and the solvent removed under reduced pressure to yield the title compound as an orange solid (677 mg, 88%), used without further purification.

m.p. 45-47 °C; $[\alpha]_D^{19.4}$ +35.2 ° (*c* 1.00, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3064, 3018, 2970, 2918, 2856, 1593, 1459, 1437, 1381, 1246, 1210, 1166, 1005, 935, 788, 755, 735, 626, 613; ^{1}H NMR (500 MHz, $CDCl_3$)

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δ 7.43 (2H, d, *J*= 7.6 Hz), 7.32 (2H, t, *J*= 7.6 Hz), 7.26 (2H, d, *J*= 7.6 Hz), 4.15 (4H, q, *J*= 10.1 Hz), 1.98 (6H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 137.7, 136.7, 135.4, 130.5, 128.6, 128.4, 32.4, 20.2.

(–)-(*S*)-*tert*-Butyl 1,11-dimethyl-5H-dibenzo[c,e]azepine-6(7H)-carboxylate (–)-23

2,2'-bis(Bromomethyl)-6,6'-dimethyl-1,1'-biphenyl (500 mg, 1.36 mmol) was dissolved in anhydrous DMF (30 mL), and NaH (67 mg, 2.78 mmol, 2.05 equiv.) added. The mixture was cooled to 0 °C, and *tert*-butyl carbamate (159 mg, 1.36 mmol, 1 equiv.) added in one portion. On completion of the reaction (TLC), DMF was removed under reduced pressure and the residue redissolved in EtOAc (60 mL). The solution was washed with H_2O (5 x 10 mL) and saturated brine (2 x 20 mL), dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The residue was purified by column chromatography (9:1 light petroleum ether/EtOAc) to yield the product as a colourless oil (385 mg, 88%).

$[\alpha]_D^{22}$ −238 ° (*c* 1.50, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3063, 2974, 2927, 2866, 1691, 1459, 1400, 1364, 1036, 1247, 1216, 1158, 1100, 869; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42-7.10 (6H, m), 4.71 (2H, d, *J*= 9.7 Hz), 3.45 (2H, d, *J*= 13.1 Hz), 2.18 (6H, s), 1.48 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.3, 138.2, 136.1, 134.9, 130.0, 127.9, 126.5, 79.7, 47.8, 28.6, 19.7; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{21}H_{26}NO_2]^+$ 324.1964; Found 324.1960.

(–)-(5R,11bS)-6-tert-Butyl 5-methyl 1,11-dimethyl-5H-dibenzo[c,e]azepine-5,6(7H)-dicarboxylate (–)-24

tert-Butyl 1,11-dimethyl-5H-dibenzo[c,e]azepine-6(7H)-carboxylate (645 mg, 1.99 mmol) was dissolved in anhydrous Et_2O (60 mL), and the solution cooled to −78 °C. *s*-BuLi (1.4 M in cyclohexane, 2.85 mL, 3.99 mmol, 2 equiv.) was added, and the mixture stirred for 1 h. Methyl chloroformate (0.23 mL, 2.99 mmol, 1.5 equiv.) was added, and the mixture stirred for 1 h at −78 °C. Saturated aqueous ammonium chloride was added. The mixture was washed with H_2O (2 x 30 mL) and saturated brine (2 x 10 mL), dried over anhydrous $MgSO_4$, and the solvents removed under reduced pressure. The residue was purified by column chromatography (9:1 light petroleum ether/EtOAc) to yield the product as a colourless fluffy solid (600 mg, 79%).

m.p. 74-76 °C; $[\alpha]_D^{23}$ −248 ° (*c* 1.00, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3065, 3002, 2975, 2948, 2930, 2872, 2250, 1752, 1686, 1600, 1474, 1458, 1433, 1392, 1366, 1355, 1308, 1255, 1221, 1206, 1161, 1105, 1004, 912, 875; ^{1}H NMR (500 MHz, *d6*-DMSO, 373 K) δ 7.42-7.16 (6H, m), 5.61 (1H, s), 4.85 (1H, d, *J*= 13.3 Hz), 3.38 (1H, d, *J*= 13.1 Hz), 3.10 (3H, s), 2.13 (3H s), 2.07 (3H, s), 1.47 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ ^{3}C NMR (126 MHz, $CDCl_3$) δ 170.8, 170.5, 154.3, 153.9, 137.5, 137.5, 137.3, 137.2, 136.9, 136.7, 136.6, 136.4, 135.2, 134.9, 134.7, 134.6, 130.6, 130.4, 129.8, 129.7, 128.50, 128.47, 128.2, 128.1, 128.04, 128.01, 127.3, 127.1, 80.5, 80.4, 62.1, 60.8, 51.7, 47.7, 46.4, 28.5, 28.4, 19.52, 19.46; ^{1}HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{23}H_{28}NO_4]^+$ 382.2018; Found 382.2013.

(+)-(5R,11bS)-Methyl 1,11-dimethyl-6,7-dihydro-5H-dibenzo[c,e]azepine-5-carboxylate (+)-25

(5R,11bS)-6-tert-Butyl 5-methyl 1,11-dimethyl-5H-dibenzo[c,e]azepine-5,6(7H)-dicarboxylate (100 mg, 0.26 mmol) was dissolved in dichloromethane (8 mL), trifluoroacetic acid (0.28 mL, 3.64 mmol, 14 equiv.) added in one portion, and the solution stirred for 30 minutes. Saturated aqueous sodium hydrogen carbonate was added to bring the pH to neutral. The solvent was removed under reduced pressure, and the residue redissolved in EtOAc (10 mL). The solution was washed with H_2O (3 x 10 mL) and saturated brine (3 x 5 mL), and dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The residue was purified by recrystallization ($CHCl_3$) to yield the title compound as a colourless solid (55 mg, 75%).

$[\alpha]_D^{26}$ +37.7 ° (*c* 0.70, $CHCl_3$); ν_{max} (CH_2Cl_2)/cm^{-1} 3316, 3062, 3017, 2948, 2926, 2867, 1732, 1493, 1432, 1378, 1302, 1265, 1228, 1211, 1122, 1099, 994, 785, 770, 741, 680; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36-7.29 (2H, m), 7.29-7.22 (2H, m), 7.18 (1H, d, *J*= 7.4 Hz), 7.11 (1H, d, *J*= 7.3 Hz), 4.44 (1H, s), 3.64 (1H, d, *J*= 13.6 Hz), 3.35 (1H, d, *J*= 13.6 Hz), 3.22 (3H, s), 2.64 (1H, s), 2.15 (3H, s), 2.12 (3H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.3, 138.3, 137.9, 136.9, 136.6, 136.3, 135.1, 130.3, 129.2, 128.5, 128.0, 127.9, 125.6, 62.4, 51.9, 48.3, 19.5, 19.4; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{18}H_{20}NO_2]^+$ 282.1494; Found 282.1489.

(–)-(5R,11bS)-6-(*tert*-Butoxycarbonyl)-1,11-dimethyl-6,7-dihydro-5Hdibenzo[c,e]azepine-5-carboxylic acid (–)-26

tert-Butyl 1,11-dimethyl-5H-dibenzo[c,e]azepine-6(7H)-carboxylate (645 mg, 1.99 mmol) was dissolved in anhydrous Et_2O (60 mL), and the solution cooled to −78 °C. *s*-BuLi (1.4 M in cyclohexane, 2.85 mL, 4.00 mmol, 2 equiv.) was added. After stirring for 1 h at −78 °C, CO_2 gas was bubbled into the mixture through a drying tube of $CaCl_2$ over 1 h. The mixture was allowed to reach ambient temperature overnight. Saturated aqueous ammonium chloride was added at 0 °C. The mixture was washed with H_2O (2 x 20 mL) and saturated brine (2 x 10 mL), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was purified by column chromatography (4:1 light petroleum ether/EtOAc) to yield the title compound as a colourless solid (330 mg, 45%).

m.p. 117-119 °C; $[\alpha]_D^{24}$ −250 ° (*c* 1.00, $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3066, 3009, 2976, 2928, 2782, 1751, 1717, 1601, 1456, 1394, 1367, 1310, 1254, 1219, 1160, 883, 760, 744; ^{1}H NMR (500 MHz, *d6*-DMSO, 380 K) δ 11.35 (1H, s), 7.37-7.32 (2H, m), 7.29-7.21 (3H, m), 7.17 (1H dd, *J*= 6.7, 2.0 Hz), 5.52 (1H, s), 4.84 (1H, d, *J*= 13.1 Hz), 3.39 (1H, d, *J*= 13.2 Hz), 2.13 (3H, s), 2.08 (3H, s), 1.47 (9H, s); ^{13}C NMR (126 MHz, *d6*-DMSO, 380 K) δ 170.7, 153.9, 137.8, 137.7, 136.9, 136.3, 135.7, 135.2, 130.5, 130.0, 128.6, 128.4, 128.3, 127.4, 80.0, 63.4, 28.7, 28.7, 19.7, 19.5; HRMS (NSI-FTMS) *m/z*: $[M-H]^-$ Calcd for $[C_{22}H_{24}NO_4]^-$ 366.1705; Found 366.1702.

(–)-(5R,11bS)-1,11-Dimethyl-6,7-dihydro-5H-dibenzo[c,e]azepine-5-carboxylic acid trifluoroacetic acid (–)-27.TFA

(5R,11bS)-6-(*tert*-Butoxycarbonyl)-1,11-dimethyl-6,7-dihydro-5H dibenzo[c,e]azepine-5-carboxylic acid (250 mg, 0.68 mmol) was dissolved in dichloromethane (10 mL), trifluoroacetic acid (0.71 mL, 9.53 mmol, 14 equiv.) added in one portion, and the solution stirred for 30 minutes. The solvent was removed under reduced pressure, and the residue redissolved in EtOAc (10 mL). The solution was washed with H_2O (3 x 10 mL) and saturated brine (3 x 5 mL), dried over anhydrous $MgSO_4$, and the solvent removed under reduced pressure. The residue was purified by recrystallization ($CHCl_3$) to yield the title compound as a colourless solid (128 mg, 50%).

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m.p. 250-252 °C; $[\alpha]_D^{24}$ −34.8 ° (*c* 1.02, MeOH); ν_{max} (solid)/cm^{-1} 3169, 2800, 1729, 1643, 1566, 1433, 1379, 1348, 1285, 1249, 1150, 1136, 1059, 839, 786, 725, 675; ^{1}H NMR (500 MHz, *d6*-DMSO) δ 13.49 (1H, s), 10.10 (1H, s), 9.13 (1H, s), 7.52-7.28 (6H, m), 5.43 (1H, s), 4.09 (1H, d, *J* = 12.9 Hz), 3.43 (1H, d, *J* = 12.9 Hz), 2.11 (3H, s), 2.08 (3H, s); ^{13}C NMR (126 MHz, *d6*-DMSO) δ ^{13}C NMR (126 MHz, DMSO) δ 168.7, 137.2, 136.9, 136.7, 136.4, 131.8, 131.48, 130.45, 130.0, 129.3, 128.5, 128.2, 128.0, 59.0, 45.6, 19.2, 19.0; HRMS (NSI-FTMS) *m/z*: $[M-CF_3CO_2H_2]^-$ Calcd for $[C_{17}H_{16}NO_2]^-$ 266.1181; Found 266.1187.

General procedure for the organocatalytic Diels-Alder reaction

The catalyst (10 mol%) was dissolved in MeOH:H_2O (95:5, 1 mL), and an α-β unsaturated aldehyde (1.0 mmol) was added. After 5 minutes the diene was added (3 mmol, 3 equiv.). The reaction was monitored by TLC, and upon complete consumption of cinnamaldehyde the mixture was diluted with Et_2O (5 mL), washed with H_2O (3 x 5 mL) and saturated brine (2 x 5 mL), and concentrated under reduced pressure. Hydrolysis of the dimethyl acetal adduct was performed by stirring in TFA:H_2O:$CHCl_3$ (1:1:2) for 2 h. The mixture was neutralized with aqueous sodium hydrogen carbonate, and extracted with Et_2O (2 x 10 mL). The combined organic layers were washed with saturated brine (2 x 5 mL), dried over anhydrous $MgSO_4$, and the solvents were removed under reduced pressure. The residue was purified by column chromatography. Reduction to the corresponding alcohol was performed using $LiAlH_4$ in anhydrous Et_2O to allow separation on HPLC media.

(1R,2S,3S,4S)-3-Phenylbicyclo[2.2.1]hept-5-ene-2-carbaldehyde and **(1S,2S,3S,4R)-3-phenylbicyclo[2.2.1]hept-5-ene-2-carbaldehyde** [42]

The reaction was performed according to the general procedure using (*E*)-cinnamaldehyde (126 µL, 1.0 mmol) and freshly distilled cyclopentadiene (252 µL, 3 mmol). After hydrolysis of the acetal, crude NMR analysis allowed conversion to be calculated and assignment of the diastereoisomeric ratio (*exo* δ 9.86 (1H, d, *J*= 2.0 Hz); *endo* δ 9.59 (1H, d, *J*= 2.2 Hz)). Column chromatography (15% EtOAc in petroleum ether) afforded the product, an inseparable mixture of diastereoisomers, as a colourless oil. ν_{max} ($CHCl_3$)/cm^{-1} 3059, 3026, 2970, 2950, 2898, 2828, 1718, 1600, 1496, 1450, 1333, 1131, 1059, 720, 699; ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.5, 202.8, 143.6, 142.6, 139.2, 136.6, 136.3, 133.8, 128.6, 128.2, 127.9, 127.4, 126.3, 126.2, 60.9, 59.5, 48.5, 48.4, 47.6, 47.2, 45.7, 45.48, 45.50, 45.2; HRMS (NSI-FTMS) *m/z*: $[M-H]^-$ Calcd for $[C_{14}H_{13}O]^-$ 197.0966; Found 197.0960.

For the *exo* compound: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.86 (1H, d, *J*= 2.0 Hz), 7.30-7.10 (5H, m), 6.29 (1H, dd, *J*= 5.5, 3.5 Hz), 6.03 (1H, dd, *J*= 5.5, 3.0 Hz), 3.69 (1H, dd, *J*= 5.0, 3.5 Hz), 3.18-3.16 (2H, m), 2.55 (1H, m), 1.61-1.54 (2H, m).

For the *endo* compound: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.55 (1H, d, *J*= 2.2 Hz), 7.30-7.10 (5H, m), 6.37 (1H, dd, *J*= 5.7, 3.2 Hz), 6.13 (1H, dd, *J*= 5.7, 2.8 Hz), 3.30-3.26 (1H, m), 3.08- 3.07 (1H, m), 3.06 (1H, dd, *J*= 4.5, 1.0 Hz), 2.93-2.90 (1H, m), 1.79-1.74 (1H, m), 1.51 (1H, m).

((1R,2S,3S,4S)-3-Phenylbicyclo[2.2.1]hept-5-en-2-yl)methanol and **((1S,2S,3S,4R)-3-phenylbicyclo[2.2.1]hept-5-en-2-yl)methanol** [36]

Following purification, the adduct (150 mg, 0.76 mmol) was dissolved in anhydrous Et_2O (10 mL). $LiAlH_4$ (30 mg, 0.76 mmol) was added, and the mixture stirred until completion of the reaction was observed by TLC. Purification by column chromatography (4:1 light petroleum ether/EtOAc) afforded the product, an inseparable mixture of diastereoisomers, as a colourless oil. ν_{max} ($CHCl_3$)/cm^{-1} 3339 (br), 3058, 2965, 2872, 1030, 717, 698; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32-7.14 (10H, m), 6.37 (1H, dd, *J*= 5.5, 3.0 Hz), 6.34 (1H, dd, *J*= 5.5, 3.0 Hz), 6.16 (1H, dd, *J*= 5.7, 3.0 Hz), 5.94 (1H, dd, *J*= 5.5, 3.0 Hz), 3.90 (1H, dd, *J*= 10.5, 6.0 Hz), 3.70- 3.62 (2H, m), 3.40 (1H, dd, *J*= 10.5, 9.0 Hz), 3.03 (2H, br m), 2.87 (2H, br m) 2.84 (1H, dd, *J*= 5.0, 3.5 Hz), 2.40-2.32 (1H, m), 2.14 (1H, dd, *J*= 5.5, 2.0 Hz), 1.94-1.90 (1H, m), 1.80-1.77 (1H, m), 1.66-1.64 (1H, m), 1.61-1.57 (1H, m), 1.54 (2H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 145.0, 144.0, 138.7, 137.6, 134.6, 134.3, 128.5, 128.0, 127.5, 126.0, 125.9, 66.9, 66.5, 50.3, 49.9, 49.0, 48.7, 48.4, 47.8, 47.08, 47.10, 44.8, 44.1; HRMS (NSI-FTMS) *m/z*: $[M+NH_4]^+$ Calcd for $[C_{14}H_{20}NO]^+$ 218.1545; Found 218.1541. Enantiomeric excesses were determined using HPLC with Chiralcel® OJ column (hexane/iPrOH=90:10, λ=222 nm), 1.0 mL; *endo* isomer (t_R1 15 min, 35 min); *exo* isomer (t_R1 47 min, 65 min)).

(1R,2S,3S,4S)-3-(2-Methoxyphenyl)bicyclo[2.2.1]hept-5-ene-2-carbaldehyde and **(1S,2S,3S,4R)-3-(2-methoxyphenyl)bicyclo[2.2.1]hept-5-ene-2-carbaldehyde** [36]

The reaction was performed according to the general procedure using (*E*)-2-methoxycinnamaldehyde (162 mg, 1.0 mmol) and freshly distilled cyclopentadiene (252 µL, 3 mmol). After hydrolysis of the acetal, crude NMR analysis allowed conversion to be calculated and assignment of the diastereoisomeric ratio (*exo* δ 9.93 (1H, d, *J*= 3.0 Hz); *endo* δ 9.50 (1H, d, *J*= 4.0 Hz)). Column chromatography (15% EtOAc in petroleum ether) afforded the product, an inseparable mixture of diastereoisomers, as a colourless oil. ν_{max} ($CHCl_3$)/cm^{-1} 2969, 2716, 1717, 1490, 1243, 1111, 1028, 753, 719; ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.3, 204.2, 157.6, 157.5, 138.5, 136.9, 136.4, 134.2, 132.4, 131.0, 127.3, 127.2, 127.2, 125.6, 120.4, 120.0, 110.0, 109.9, 59.7, 58.0, 55.0, 54.9, 47.8, 47.4, 47.0, 46.3, 46.2, 45.6, 40.8, 40.2; HRMS (NSI-FTMS) *m/z*: $[M-H]^-$ Calcd for $[C_{15}H_{15}O_2]^-$ 227.1072; Found 227.1065.

For the *exo* compound: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.93 (1H, d, *J*= 3.0 Hz), 7.26-6.79 (4H, m), 6.27 (1H, dd, *J*= 6.0, 3.5 Hz), 6.17 (1H, dd, *J*= 6.0, 3.0 Hz), 3.88 (1H, dd, *J*= 5.5, 3.0 Hz), 3.78 (3H, s), 3.29 (1H, m), 3.10-3.07 (1H, m), 2.38-2.31 (1H, m), 1.61 (1H, ddd, *J*= 8.5, 3.5, 1.5 Hz), 1.55 (1H, ddd, *J*= 8.5, 3.5, 1.5 Hz).

For the *endo* compound: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.50 (1H, d, *J*= 4.0 Hz), 7.26 – 6.79 (4H, m), 6.42 (1H, dd, *J*= 6.0, 3.5 Hz), 6.17 (1H, dd, *J*= 6.0, 3.0 Hz), 3.73 (3H, s), 3.26-3.22 (1H, m), 3.20 (1H, s), 3.16 (1H, d, *J*= 4.0 Hz), 2.55 (1H, dt, *J*= 5.0, 3.8 Hz), 1.72 (1H, s) 1.57-1.55 (1H, m).

((1R,2S,3S,4S)-3-(2-Methoxyphenyl)bicyclo[2.2.1]hept-5-en-2-yl)methanol and **((1S,2S,3S,4R)-3-(2-methoxyphenyl)bicyclo[2.2.1]hept-5-en-2-yl)methanol**

Following purification, the adduct (210 mg, 0.92 mmol) was dissolved in anhydrous Et_2O (10 mL). $LiAlH_4$ (35 mg, 0.92 mmol) was added, and the mixture stirred until completion of the reaction was

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observed by TLC. Purification by column chromatography (4:1 light petroleum ether/EtOAc) afforded the product, an inseparable mixture of diastereoisomers, as a colourless oil. ν_{max} ($CHCl_3$)/cm^{-1} 3368, 2962, 2941, 1598, 1490, 1463, 1242, 1029, 752, 736, 716; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (1H, dd, *J*= 8.0, 1.5 Hz), 7.22-7.16 (1H, m), 7.16-7.12 (1H, m), 7.05 (1H, dd, *J*= 8.0, 2.0 Hz), 6.96 (1H, td, *J*= 7.5, 1.0 Hz), 6.86 (1H, dd, *J*= 8.2, 1.0 Hz), 6.83-6.80 (2H, m), 6.36 (2H, dt, *J*= 5.8, 3.0 Hz), 6.13 (1H, dd, *J*= 6.0, 3.0 Hz), 5.84 (1H, dd, *J*= 6.0, 3.0 Hz), 3.84 (6H, s), 3.83 (1H, m), 3.80 (1H, m) 3.62 (1H, dd, *J*= 10.6, 8.5 Hz), 3.54 (1H, dd, *J*= 10.8, 7.5 Hz), 3.45 (1H, dd, *J*= 10.8, 6.8 Hz), 3.27 (1H, dd, *J*= 5.4, 3.2 Hz), 3.00 (1H, s), 2.96 (1H, s), 2.86 (2H, s), 2.50 (1H, dd, *J*= 5.0, 1.0 Hz), 2.24-2.15 (1H, m), 1.97-1.89 (1H, m), 1.82 (1H, d, *J*= 8.4 Hz), 1.73 (1H, br s), 1.68 (1H, d, *J*= 8.6 Hz), 1.58 (1H, ddd, *J*= 8.4, 3.3, 1.6 Hz), 1.50 (1H, ddd, *J*= 8.6, 3.4, 1.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.6, 156.80, 138.7, 137.3, 134.9, 134.6, 133.7, 131.8, 127.5, 126.8, 126.8, 126.6, 121.1, 120.0, 110.4, 109.9, 67.2, 67.0, 55.4, 50.89, 48.7, 48.6, 47.6, 47.5, 47.4, 44.9, 44.8, 40.9, 40.3; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{15}H_{19}O_2]^+$ 231.1385; Found 231.1380. Enantiomeric excesses were determined using Chiralcel® AD-H column (hexane/iPrOH=98:2, λ=222 nm), 0.5 mL; *endo* isomer (t_R1 65 min, 80 min); *exo* isomer (t_R1 57 min, 69 min)).

(1R,2S,3S,4S)-3-(4-Methoxyphenyl)bicyclo[2.2.1]hept-5-ene-2-carbaldehyde and (1S,2S,3S,4R)-3-(4-methoxyphenyl)bicyclo[2.2.1]hept-5-ene-2-carbaldehyde [36]

The reaction was performed according to the general procedure using (*E*)-4-methoxycinnamaldehyde (162 mg, 1.0 mmol) and freshly distilled cyclopentadiene (252 µL, 3 mmol). After hydrolysis of the acetal, crude NMR analysis allowed conversion to be calculated and assignment of the diastereoisomeric ratio (*exo* δ 9.88 (1H, d, *J*= 2.0 Hz); *endo* δ 9.56 (1H, d, *J*= 2.3 Hz)). Column chromatography (15% EtOAc in petroleum ether) afforded the product, an inseparable mixture of diastereoisomers, as a colourless oil. ν_{max} ($CHCl_3$)/cm^{-1} 2968, 2835, 2718, 1715, 1611, 1513, 1463, 1247, 1180, 1035, 726; ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.7, 202.9, 158.2, 158.0, 139.3, 136.6, 136.3, 135.6, 134.7, 133.7, 128.8, 128.3, 114.0, 113.6, 61.0, 59.7, 55.3, 55.2, 48.7, 48.6, 47.6, 47.1, 45.5, 45.07, 45.10, 44.7.

For the *exo* compound: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.88 (1H, d, *J*= 2.0 Hz), 7.08-7.03 (2H, m), 6.79-6.76 (2H, m), 6.31 (1H, dd, *J*= 5.6, 3.0 Hz), 6.05 (1H, dd, *J*= 5.6, 3.0 Hz), 3.75 (3H, s), 3.64 (1H, dd, *J*= 5.2, 3.5 Hz), 3.19-3.16 (1H, m), 3.16-3.14 (1H, m), 2.51 (1H, dt, *J*= 5.3, 2.0 Hz), 1.61-1.56 (1H, m), 1.53 (1H, m);
For the *endo* compound: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.56 (1H, d, *J*= 2.3 Hz), 7.19-7.15 (2H, m), 6.87-6.82 (2H, m), 6.39 (1H, dd, *J*= 5.6, 3.0 Hz), 6.14 (1H, dd, *J*= 5.6, 3.0 Hz), 3.76 (3H, s), 3.31-3.28 (1H, m), 3.06-3.03 (1H, m), 3.02-2.99 (1H, m), 2.91 (1H, ddd, *J*= 5.0, 3.4, 2.4 Hz), 1.78-1.76 (1H, m), 1.61-1.58 (1H, m).

((1S,2S,3S,4R)-3-(4-Methoxyphenyl)bicyclo[2.2.1]hept-5-en-2-yl)methanol

Following purification, the adduct (158 mg, 0.69 mmol) was dissolved in anhydrous Et_2O (10 mL). $LiAlH_4$ (26 mg, 0.69 mmol) was added, and the mixture stirred until competition of the reaction was observed by TLC. Purification by column chromatography (9:1, light petroleum ether/EtOAc) afforded the product, an inseparable mixture of diastereoisomers, as a colourless oil. ν_{max} ($CHCl_3$)/cm^{-1} 3400, 3056, 2964, 1611, 1580, 1511, 1464, 1265, 1246, 1034, 910, 743; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.25-7.07 (4H, m), 6.90-6.73 (4H, m), 6.37- 6.32 (1H, m), 6.14 (1H, dd, *J*= 5.7, 2.8 Hz), 5.94 (1H, dd, *J*= 5.7, 2.8 Hz), 3.88 (1H, dd, *J*= 10.5, 6.0 Hz), 3.79 (3H, m), 3.76 (3H, m), 3.66 (1H, dd, *J*= 10.5, 9.0 Hz) 3.61 (1H, dd, *J*= 10.5, 6.0 Hz), 3.38 (1H, dd, *J*= 10.5, 9.0 Hz), 3.01 (2H, br d, *J*= 17.5 Hz), 2.84 (1H, dd, *J*= 14.6, 1.5 Hz), 2.79 (1H, dd, *J*= 5.0, 3.5 Hz), 2.37-2.27 (1H, m), 2.11-2.07 (1H, m), 1.88-1.84 (2H, m), 1.75 (1H, d, *J*= 8.5 Hz), 1.63 (1H, d, *J*= 8.5 Hz), 1.59-1.54 (2H, m), 1.54-1.50 (1H, m), 1.26 (1H, s), 1.21 (1H, d, *J*= 6.1 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 157.9, 157.8, 138.7, 137.5, 137.0, 136.1, 134.6, 134.1, 129.0, 128.9, 128.4, 113.8, 113.4, 66.9, 66.6, 55.3, 55.2, 50.8, 50.4, 50.1, 49.4, 49.2, 48.8, 47.5, 47.1, 47.06, 47.09, 44.8, 44.1. HRMS (NSI-FTMS) *m/z*: $[M+NH_4]^+$ Calcd for $[C_{15}H_{22}NO_2]^+$ 248.1651; Found 248.1646. Enantiomeric excesses were determined using Chiralcel® AS-3 column (hexane/iPrOH=95:5, λ=222 nm), 0.5 mL; *endo* isomer (t_R1 35 min, 59 min); *exo* isomer (t_R1 39 min, 56 min)).

(1R,2S,3S,4S)-3-(2-Nitrophenyl)bicyclo[2.2.1]hept-5-ene-2-carbaldehyde and (1S,2S,3S,4R)-3-(2-nitrophenyl)bicyclo[2.2.1]hept-5-ene-2-carbaldehyde [37]

The reaction was performed according to the general procedure using (*E*)-2-nitrocinnamaldehyde (177 mg, 1.0 mmol) and freshly distilled cyclopentadiene (252 µL, 3 mmol). After hydrolysis of the acetal, crude NMR analysis allowed conversion to be calculated and assignment of the diastereoisomeric ratio (*exo* δ 9.80 (1H, d, *J*= 2.2 Hz); *endo* δ 9.40 (1H, d, *J*= 3.5 Hz)). Column chromatography (15% EtOAc in petroleum ether) afforded the product, an inseparable mixture of diastereoisomers, as a yellow oil. ν_{max} ($CHCl_3$)/cm^{-1} 3054, 2986, 2825, 2305, 2254, 1717, 1687, 1527, 1421, 1351, 1263, 746, 705; ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.6, 201.5, 139.2, 137.3, 137.0, 136.3, 136.1, 134.2, 132.8, 131.8, 128.9, 127.9, 127.4, 127.3, 124.8, 124.0, 59.3, 59.0, 49.8, 49.2, 48.2, 47.2, 46.6, 46.3, 41.7, 40.1; HRMS (NSI-FTMS) *m/z*: $[M-H]^-$ Calcd for $[C_{14}H_{12}NO_3]^-$ 242.0817; Found 242.0811.

For the *exo* compound ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.81 (1H, d, *J*= 2.2 Hz), 7.72 (1H, dd, *J*= 8.0, 1.5 Hz), 7.45-7.41 (1H, m), 7.36-7.30 (1H, m), 7.18 (1H, dd, *J*= 8.0, 1.0 Hz), 6.47 (1H, dd, *J*= 5.6, 3.2 Hz), 6.02 (1H, dd, *J*= 5.6, 3.0 Hz), 4.09 (1H, dd, *J*= 5.2, 3.3 Hz), 3.37 (1H, br s), 3.31-3.26 (1H, m), 2.63-2.58 (1H, m), 1.67-1.60 (1H, m), 1.60-1.57 (1H, m).
For the *endo* compound: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.40 (1H, d, *J*= 3.5 Hz), 7.82 (1H, dd, *J*= 8.0, 1.5 Hz), 7.59-7.52 (2H, m), 7.39 (1H, ddd, *J*= 8.4, 7.3, 1.5 Hz), 6.50 (1H, dd, *J*= 5.6, 3.2 Hz), 6.22 (1H, dd, *J*= 5.7, 2.8 Hz), 3.44 (1H, dd, *J*= 5.0, 1.0 Hz), 3.34-3.30 (1H, m), 3.13-3.11 (1H, m), 2.95 (1H, dt, *J*= 5.2, 3.6 Hz), 1.84 (1H, dt, *J*= 9.0, 1.5 Hz), 1.69-1.68 (1H, m).

((1R,2S,3S,4S)-3-(2-Nitrophenyl)bicyclo[2.2.1]hept-5-en-2-yl)methanol compound and ((1S,2S,3S,4R)-3-(2-nitrophenyl)bicyclo[2.2.1]hept-5-en-2-yl)methanol

Following purification, the adduct (140 mg, 0.58 mmol) was dissolved in anhydrous Et_2O (10 mL). $LiAlH_4$ (22 mg, 0.58 mmol, 1 equiv.) was added, and the mixture stirred until competition of the reaction was observed by TLC. Purification by column

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chromatography (9:1, light petroleum ether/EtOAc) afforded the product, an inseparable mixture of diastereoisomers, as a pale yellow oil. ν_{max} ($CHCl_3$)/cm^{-1} 3064, 2973, 1717, 1523, 1351, 723; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (1H, dd, *J* = 8.0, 1.4 Hz), 7.63 (2H, ddd, *J* = 8.0, 3.5, 1.1 Hz), 7.54 (1H, td, *J* = 7.8, 1.4 Hz), 7.40 (1H, dd, *J* = 7.3, 1.0 Hz), 7.36-7.26 (3H, m), 6.47 (1H, dd, *J* = 5.6, 3.2 Hz), 6.42 (1H, dd, *J* = 5.6, 3.1 Hz), 6.15 (1H, dd, *J* = 5.7, 2.9 Hz), 5.89 (1H, dd, *J* = 5.6, 2.9 Hz), 3.76 (1H, dd, *J* = 10.6, 6.3 Hz), 3.63 (1H, dd, *J* = 10.5, 8.2 Hz), 3.45 (1H, dd, *J* = 10.6, 6.0 Hz), 3.35 (1H, dd, *J* = 10.6, 8.0 Hz), 3.18 (1H, dd, *J* = 5.2, 3.2 Hz), 3.11 (2H, dd, *J* = 7.5, 1.8 Hz), 2.91 (1H, d, *J* = 1.4 Hz), 2.80 (1H, d, *J* = 1.4 Hz), 2.58-2.50 (2H, m), 2.00-1.93 (2H, m), 1.77 (2H, d, *J* = 8.9 Hz), 1.69 (2H, d, *J* = 8.8 Hz), 1.58-1.52 (2H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 138.3, 137.4, 134.0, 131.5, 129.1, 126.8, 123.4, 66.5, 50.7, 49.3, 48.0, 45.1, 42.6, 14.2; HRMS (NSI-FTMS) *m/z*: $[M+H]^+$ Calcd for $[C_{14}H_{16}NO_3]^+$ 246.1130; Found 246.1124. Enantiomeric excesses were determined using Chiralcel® AD-H column (hexane/iPrOH=95:5, λ=254 nm), 0.5 mL: *endo* isomer (t_R1 37 min, 39 min); *exo* isomer (t_R1 41 min, 50 min)).

(1R,2S,3S,4S)-3-(4-Nitrophenyl)bicyclo[2.2.1]hept-5-ene-2-carbaldehyde and **(1S,2S,3S,4R)-3-(4-nitrophenyl)bicyclo[2.2.1]hept-5-ene-2-carbaldehyde** [36]

The reaction was performed according to the general procedure using (*E*)-4-nitrocinnamaldehyde (177 mg, 1.0 mmol) and freshly distilled cyclopentadiene (252 μL, 3 mmol). After hydrolysis of the acetal, crude NMR analysis allowed conversion to be calculated and assignment of the diastereoisomeric ratio (*exo* δ 9.92 (1H, d, *J*= 2.0 Hz); *endo* δ 9.65 (1H, d, *J*= 2.0 Hz)). Column chromatography (15% EtOAc in petroleum ether) afforded the product, an inseparable mixture of diastereoisomers, as a yellow oil. ν_{max} ($CHCl_3$)/cm^{-1} 2972, 1715, 1596, 1515, 1495, 1345, 1107, 721; ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.1, 201.6, 171.1, 151.7, 150.6, 146.5, 146.3, 139.0, 137.0, 135.9, 134.0, 128.7, 128.2, 123.7, 123.3, 61.1, 60.3, 59.5, 48.4, 47.9, 47.6, 47.1, 45.6, 45.5, 45.1, 45.0, 21.0, 14.2; HRMS (NSI-FTMS) *m/z*: $[M-H]^-$ Calcd for $[C_{14}H_{12}NO_3]^-$ 242.0817; Found 242.0811.

For the *exo* compound: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.92 (1H, d, *J*= 2.0 Hz), 8.12-8.01 (2H, m), 7.36-7.26 (2H, m), 6.41 (1H, dd, *J*= 5.5, 3.0 Hz), 6.05 (1H, dd, *J*= 5.5, 3.0 Hz), 3.89 (1H, dd, *J*= 5.0, 3.5 Hz), 3.34-3.29 (1H, m), 3.26 (1H, br s), 2.64 (1H, d, *J*= 5.2 Hz), 1.62-1.59 (2H, m).

For the *endo* compound: ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.65 (1H, d, *J*= 2.0 Hz), 8.22-8.12 (2H, m), 7.48-7.35 (2H, m), 6.44 (1H, dd, *J*= 6.0, 3.5 Hz), 6.20 (1H, dd, *J*= 6.0, 3.0 Hz), 3.44 (1H, br s), 3.21-3.19 (2H, m), 2.98 (1H, ddd, *J*= 5.0, 3.5, 1.7 Hz), 1.78-1.68 (2H, m).

((1R,2S,3S,4S)-3-(4-Nitrophenyl)bicyclo[2.2.1]hept-5-en-2-yl)methanol and ((1S,2S,3S,4R)-3-(4-nitrophenyl)bicyclo[2.2.1]hept-5-en-2-yl)methanol

Following purification, the adduct (210 mg, 0.86 mmol) was dissolved in anhydrous Et_2O (10 mL). $LiAlH_4$ (32 mg, 0.86 mmol, 1 equiv.) was added, and the mixture stirred until competition of the reaction was observed by TLC. Purification by column chromatography (9:1, light petroleum ether/EtOAc) afforded the product, an inseparable mixture of diastereoisomers, as a colourless oil. ν_{max} ($CHCl_3$)/cm^{-1} 3418, 3054, 2986, 1265, 739; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18-8.12 (2H, m), 8.10-8.06 (2H, m), 7.51-7.46 (2H, m), 7.38-7.34 (2H, m), 6.40-6.37 (2H, m), 6.19 (1H, dd, *J*= 6.0, 3.0 Hz), 5.91 (1H, dd, *J*= 6.0, 3.0 Hz), 3.85 (1H, dd, *J*= 10.5, 7.0 Hz), 3.75 (1H, dd, *J*= 10.5, 8.0 Hz), 3.58 (1H, dd, *J*= 10.5, 7.0 Hz), 3.51 (1H, dd, *J*= 10.5, 8.0 Hz), 3.09 (1H, s), 3.07 (1H, s), 3.04-2.98 (1H, m), 2.97-2.95 (1H, br m), 2.90-2.89 (1H, br m), 2.38-2.31 (1H, m), 2.31-2.28 (1H, br m), 1.98-1.92 (1H, m), 1.72 (2H, br dd, *J*= 15.5, 8.5 Hz), 1.64 (1H, ddd, *J*= 8.8, 3.3, 1.7 Hz), 1.59 (1H, ddd, *J*= 8.8, 3.3, 1.6 Hz), 1.53 (2H, br s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 153.3, 152.2, 146.4, 146.2, 138.3, 138.3, 134.8, 134.0, 128.8, 128.3, 123.6, 123.2, 66.7, 66.4, 50.8, 50.0, 48.9, 48.8, 48.7, 48.1, 47.4, 47.1, 45.0, 44.4; HRMS (NSI-FTMS) *m/z*: $[M+NH_4]^+$ Calcd for $[C_{14}H_{19}N_2O_3]^+$ 263.1396; Found 263.1390. Enantiomeric excesses were determined using Chiralcel® AD-H column (hexane/iPrOH=90:10, λ=254 nm), 0.5 mL; *endo* isomer (t_R1 49 min, 57 min); *exo* isomer (t_R1 43 min, 53 min)).

Conflicts of interest

There are no conflicts to declare.

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