Advanced Synthesis & Catalysis

Supporting Information

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General methods and materials

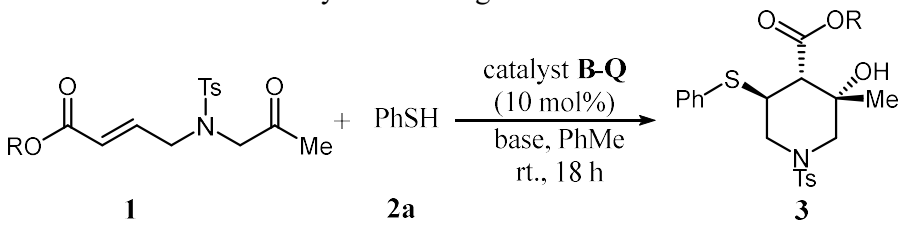
General Methods. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Inova 300, Mercury 400 or Inova 600 spectrometer. Chemical shifts (δ) are reported in ppm relative to residual solvents signals[1] for ^{1}H and ^{13}C NMR. ^{13}C NMR were acquired with 1 H broad-band decoupled mode. Chromatographic purifications were performed using 70-230 mesh silica gel. Mass spectra were recorded on a Waters Xevo Q-TOF spectrometer. Optical rotations were measured on a Perkin Elmer 241 Polarimeter provided with a sodium lamp and are reported as follows: $[\alpha]_{\lambda}^{T(^{\circ}C)}$ (c = g/100 mL, solvent). The enantiomeric excesses of the products (*ee*) were determined by chiral stationary phase HPLC (Daicel Chiralpak AD-H and AS-H or Chiralcel OD-H columns), using a UV detector operating at 254 nm.

Materials. Analytical grade solvents and commercially available reagents were used as received, unless otherwise stated. Catalysts **A-Q** were synthesized following literature procedures.[2] For catalyst **G**, see the dedicated section. Racemic products **3** were prepared using TBABr (10 mol%) instead of **G** as catalyst.

[1] H. E. Gottlieb, V. Kottlyar, A. Nudelman, *J. Org. Chem.* **1997**, *62*, 7512-7515.
[2] a) E. J. Corey, F. Xu, M. C: Noe, *J. Am. Chem. Soc.* **1997**, *119*, 12414-12415; b) E. J. Corey, M. C. Noe, *Org. Synth* **2003**, *80*, 38-45.

Additional screenings for the enantioselective sulfa-Michael/aldol reaction for the synthesis of piperidines 3

Table S1 Additional bases and catalysts screenings.[a)]



1 **2a** **3**

Entry	R	Catalyst	Base	Conversion[b)]	d.r.[b)]	ee[c)]
1	Me	**B**	$K_2CO_{3(aq)}$ 50% wt.	>99	80:20	36
2	Me	**B**	$K_2CO_{3(aq)}$ 5% wt.	>99	80:20	38
3	Me	**B**	$NaHCO_{3(aq)}$ 10% wt.	90	81:19	40
4	Me	**B**	**$K_2CO_{3(aq)}$ 10% wt.**	**>99**	**86:14**	**50**
5	Me	**H**	$K_2CO_{3(aq)}$ 10% wt.	33	80:20	6
6	Me	**I**	$K_2CO_{3(aq)}$ 10% wt.	<5	n.d.	n.d.
7	Me	**J**	$K_2CO_{3(aq)}$ 10% wt.	96	>20:1	48
8	Me	**K**	$K_2CO_{3(aq)}$ 10% wt.	90	>20:1	14
9	Me	**L**	$K_2CO_{3(aq)}$ 10% wt.	98	83:17	57
10	Me	**M**	$K_2CO_{3(aq)}$ 10% wt.	97	82:18	60
11	Me	**N**	$K_2CO_{3(aq)}$ 10% wt.	61	84:16	62
12	Me	**O**	$K_2CO_{3(aq)}$ 10% wt.	>99	82:18	50
13	Me	**P**	$K_2CO_{3(aq)}$ 10% wt.	>99	83:17	55
14	Me	**Q**	$K_2CO_{3(aq)}$ 10% wt.	97	84:16	46
15	Me	**G**	**$K_2CO_{3(aq)}$ 10% wt.**	**>99**	**83:17**	**68**
16	iPr	**B**	$K_2CO_{3(aq)}$ 50% wt.	72	90:10	44

[a)] Reaction conditions: **1** (0.05 mmol), **2a** (1.2 equiv, 0.06 mmol), base (100 μL), catalyst (0.005 mmol), PhMe (1000 μL, 0.05 M), 18 h. [b)] Calculated on the crude mixture by ^{1}H NMR analysis. [c)] Calculated on crude **3** by Chiral Stationary Phase (CSP) HPLC.

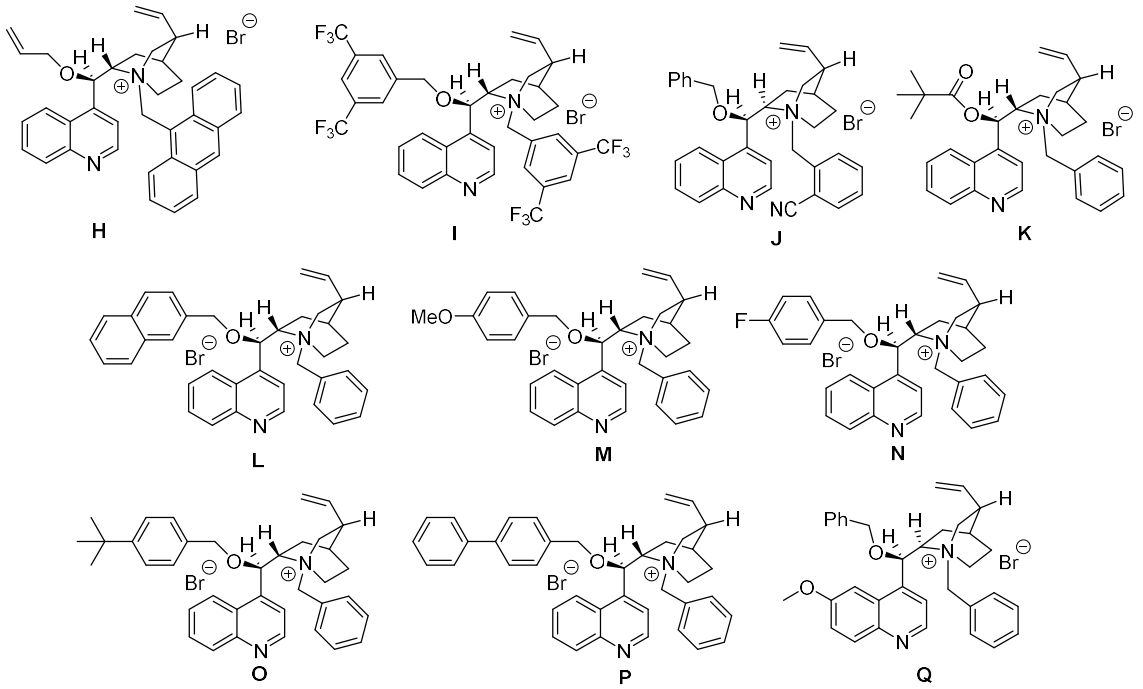


Figure S1. Catalysts screened in Table S1.

Different concentrations of the aqueous base, as well as $NaHCO_3$ instead of K_2CO_3 caused a detriment in the enantioselectivity (Table S1, compare entries 1-3 with entry 4) keeping almost the same high conversion and good diastereoselectivity.

A number of catalysts (H-P, compare entries 5-13 with entry 15), displaying different substitution at the "*N*" or "*O*" portion were screened, giving worse results compared to optimal catalyst **G**. Quinine derivative **Q** gave almost the same results than the analogue Cinchonidine **B** (compare entries 14 and 4). A substrate **1** showing a bulkiy ester, bearing an isopropyl group, underwent the desired reaction less efficiently (entry 16).

Preparation of Starting Materials

Substrates **1** used in the present study are reported in Figure S2.

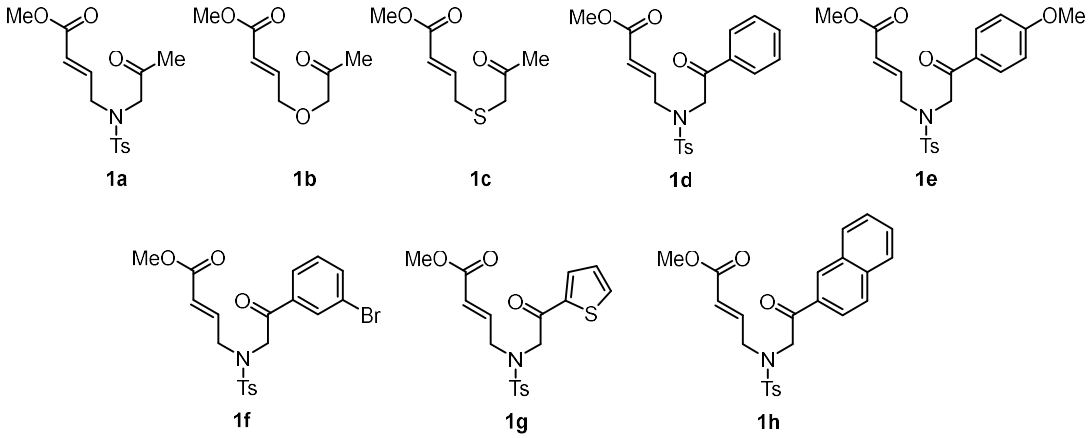
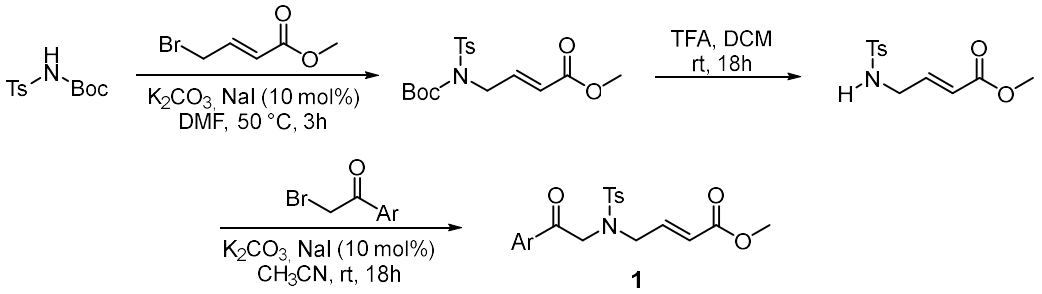


Figure S2. Structures of substrates **1**

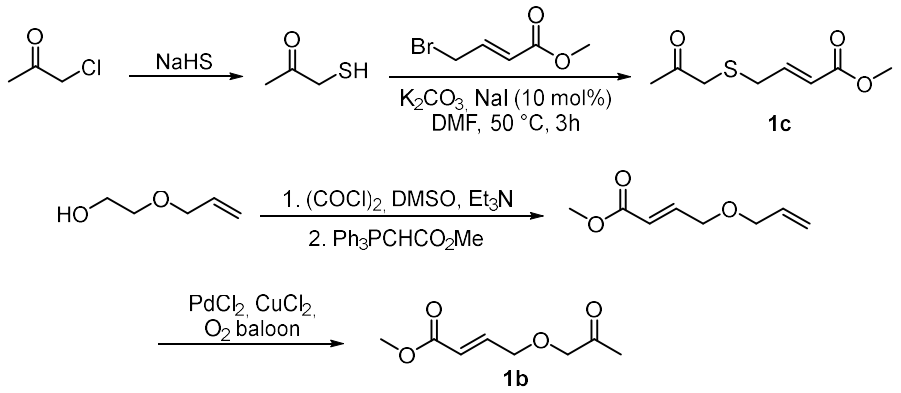
Substrates **1a** and **1d** were prepared following unmodified literature procedures[3] depicted in Scheme S1. Substrates **1e-h** were prepared following the same procedures with the appropriate α-bromo acetophenones. For these substrates, characterization is given below.



Scheme S1. Preparation of substrates **1a** and **1d-h**.

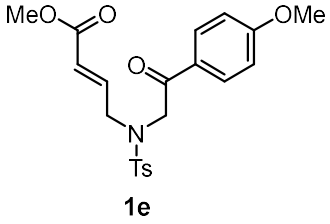
Substrates **1b**[4] and **1c**[5] were prepared following unmodified literature procedures (Scheme S2).

[3] a) F. Serpier, B. Flamme, J.-L. Brayer, B. Folléas, S. Darses, *Org. Lett.* **2015**, *17*, 1720-1723; b) F. Serpier, J.-L. Brayer, B. Folléas, S. Darses, *Org. Lett.* **2015**, *17*, 5496-5499.
[4] G. H. Lee, E. B. Choi, E. Lee, C. S. Pak, *J. Org. Chem.* **1994**, *59*, 1428-1443.
[5] M. D. Brown, D. W. Gillon, G. D. Meakins, G. H. Whitham, *J. Chem. Soc. Perkin Trans* **1985**, *1*, 1623-1625.



Scheme S2. Preparation of substrates **1b** and **1c**.

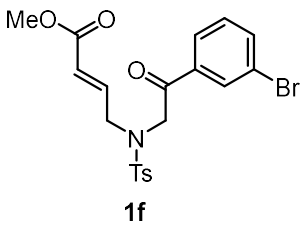
Methyl (*E*)-4-((*N*-(2-(4-methoxyphenyl)-2-oxoethyl)-4-methylphenyl)sulfonamido)but-2-enoate



1e

Following the reported procedure (employing 2-bromo-4'-methoxyacetopehenone), product **1e** was obtained as a light brown solid in 95% yield (792 mg, reaction run on 2.0 mmol scale). **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.91 – 7.81 (m, 2H), 7.76 – 7.67 (m, 2H), 7.32 – 7.27 (m, 2H), 6.98 – 6.87 (m, 2H), 6.78 (dt, *J* = 15.7, 5.8 Hz, 1H), 5.91 (dt, *J* = 15.7, 1.6 Hz, 1H), 4.70 (s, 2H), 4.08 (dd, *J* = 5.8, 1.7 Hz, 2H), 3.87 (s, 3H), 3.70 (s, 3H), 2.42 (s, 3H). **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 191.8, 165.9, 164.1, 143.7, 142.3, 136.6, 130.3 (2C), 129.6 (2C), 127.7, 127.5 (2C), 123.8, 114.0 (2C), 55.5, 52.0, 51.7, 48.7, 21.6. **ESI-MS**: 440 [M + Na^+].

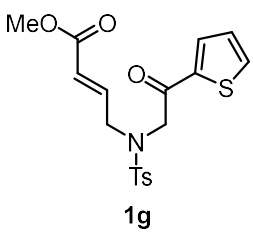
Methyl (*E*)-4-((*N*-(2-(3-bromophenyl)-2-oxoethyl)-4-methylphenyl)sulfonamido)but-2-enoate 1f



1f

Following the reported procedure (employing 2,3'-dibromoacetopehenone), product **1f** was obtained as a light yellow solid in 50% yield (233 mg, reaction run on 2.0 mmol scale). **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 7.97 (t, *J* = 1.8 Hz, 1H), 7.80 (ddd, *J* = 7.8, 1.7, 1.0 Hz, 1H), 7.74 – 7.67 (m, 3H), 7.35 (d, *J* = 7.9 Hz, 1H), 7.32 – 7.26 (m, 2H), 6.75 (dt, *J* = 15.7, 5.9 Hz, 1H), 5.90 (dt, *J* = 15.7, 1.6 Hz, 1H), 4.70 (s, 2H), 4.06 (dd, *J* = 5.9, 1.7 Hz, 2H), 3.69 (s, 3H), 2.42 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 192.4, 165.9, 143.9, 142.1, 136.8, 136.4, 136.3, 131.0, 130.5, 129.7 (2C), 127.4 (2C), 126.5, 124.0, 123.2, 52.5, 51.8, 48.8, 21.6. **ESI-MS**: 488 [M(^{79}Br) + Na^+], 490 [M(^{81}Br) + Na^+].

Methyl (*E*)-4-((*N*-(2-(thiophen-2-yl)-2-oxoethyl)-4-methylphenyl)sulfonamido)but-2-enoate 1g

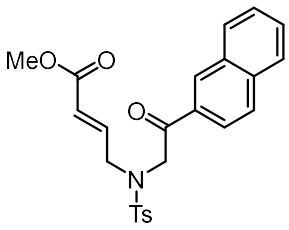


1g

Following the reported procedure (employing 2-bromo-1-(thiophen-2-yl)ethan-1-one), product **1g** was obtained as a light yellow solid in 25% yield (393 mg, reaction run on 4.0 mmol scale). **^{1}H NMR** (300

MHz, $CDCl_3$) δ = 7.80 – 7.77 (m, 1H), 7.73 – 7.70 (m, 2H), 7.69 – 7.67 (m, 1H), 7.30 – 7.27 (m, 2H), 7.16 – 7.13 (m, 1H), 6.77 (dt, J = 15.7, 5.9 Hz, 1H), 5.92 (dt, J = 15.7, 1.4 Hz, 1H), 4.64 (s, 2H), 4.08 (dd, J = 5.9, 1.4 Hz, 2H), 3.69 (s, 3H), 2.42 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 186.8, 166.1, 144.1, 142.2, 141.1, 136.5, 134.85, 132.8, 129.9 (2C), 128.7, 127.7 (2C), 124.2, 52.6, 51.9, 49.0, 21.8. **ESI-MS**: 416 [M + Na^+].

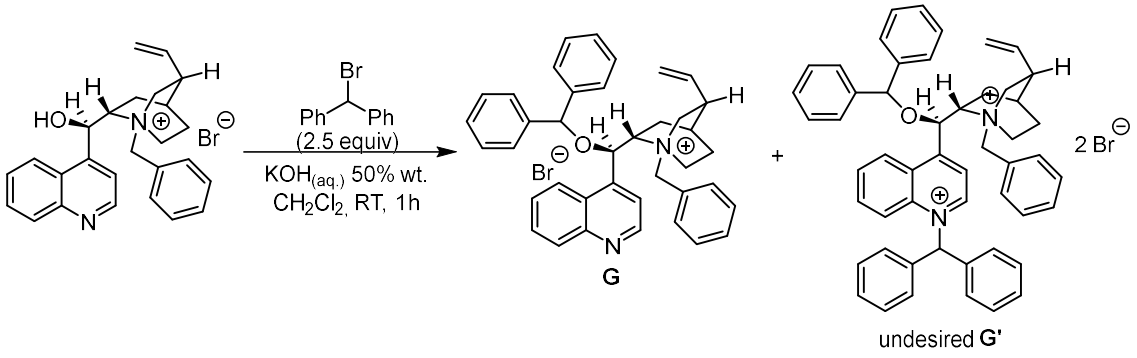
Methyl (*E*)-4-((*N*-(2-(hapthalen-2-yl)-2-oxoethyl)-4-methylphenyl)sulfonamido)but-2-enoate 1h



1h

Following the reported procedure (employing 2-bromo-acetonaphthone), product **1h** was obtained as a yellow solid in 40% yield (351 mg, reaction run on 2.0 mmol scale). **^{1}H NMR** (300 MHz, $CDCl_3$) δ = 8.42 (s, 1H), 8.05 – 7.83 (m, 4H), 7.78 – 7.73 (m, 2H), 7.68 – 7.51 (m, 2H), 7.36 – 7.28 (m, 2H), 6.82 (dt, J = 15.7, 5.8 Hz, 1H), 5.95 (dt, J = 15.7, 1.6 Hz, 1H), 4.90 (s, 2H), 4.15 (dd, J = 5.8, 1.6 Hz, 2H), 3.68 (s, 3H), 2.42 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 193.6, 166.1, 144.0, 142.5, 136.8, 136.1, 132.5, 132.1, 130.1, 129.9, 129.8 (2C), 129.2, 129.0, 128.0 (2C), 127.7, 127.31, 124.1, 123.5, 52.6, 51.9, 49.0, 21.8. **ESI-MS**: 460 [M + Na^+]

Preparation of *O*-benzhydryl-*N*-benzylcinchonidinium bromide (Catalyst G)



The following procedure is adapted from the literature,[6] optimized for the specific preparation of **G**. A Schlenck tube equipped with a magnetic stirring bar and under N_2 flow is charged with 466 mg (1.0 mmol) of *N*-benzylcinchonidinium bromide and 5 mL of CH_2Cl_2. Aqueous potassium hydroxide (625 μL, 50% wt.) is then added and the resulting biphasic mixture is vigorously stirred for 5 min. Then, benzhydryl bromide (2.23 g, 2.5 mmol) is added in one portion. Note that if benzhydryl bromide is added before the KOH solution, the undesired formation of **G'**, which is very difficult to separate from **G**, is generally observed. The mixture is vigorously stirred for 1 h, then diluted with 5 mL of water and stirred for 5 min. After separation of the phases, the organic phase is washed with a solution of 300 mg of sodium bromide in 3 mL of water, dried over Na_2SO_4 and filtered using the minimum quantity of CH_2Cl_2 as a rinse. This solution is immediately added dropwise (2 min) into a stirred mixture of *n*-hexane and Et_2O (1:5, 15 mL) producing, over 1 h of stirring, a fluffy mass. Note that prolonged standing of the crude CH_2Cl_2 solution results in the undesired formation of **G'**. After stirring for 1 h, the solids are collected by filtration, washed with 10 mL of Et_2O and 10 mL of *n*-hexane and dried under vacuum to afford 316 mg (0.50 mmol, 50% yield) of *O*-benzhydryl-*N*-benzylcinchonidinium bromide as a fluffy off-white powder. **$[\alpha]_D^{25}$** = -31 (c = 0.5 in CH_3OH). **^{1}H NMR** (400 MHz, CD_3OD) δ = 8.87 (d, *J* = 4.6 Hz, 1H), 8.22 – 8.17 (m, 1H), 8.13 – 8.07 (m, 1H), 7.93 (ddd, *J* = 8.4, 6.9, 1.3 Hz, 1H), 7.87 – 7.80 (m, 2H), 7.58 – 7.27 (m, 15H), 6.35 (s, 1H), 5.66 (ddd, *J* = 17.3, 10.5, 7.0 Hz, 1H), 5.53 (s, 1H), 5.09 (dt, *J* = 17.1, 1.2 Hz, 1H), 4.98 (dt, *J* = 10.4, 1.1 Hz, 1H), 4.52 (d, *J* = 12.1 Hz, 1H), 4.29 – 4.12 (m, 1H), 3.94 – 3.86 (m, 1H), 3.82 (d, *J* = 12.1 Hz, 1H), 3.52 – 3.46 (m, 1H), 3.40 – 3.32 (m, 2H), 2.74 – 2.60 (m, 2H), 2.49 – 2.37 (m, 1H), 2.22 – 2.16 (m, 1H), 2.05 – 1.93 (m, 1H), 1.72 – 1.62 (m, 1H). **^{13}C NMR** (101 MHz, CD_3OD) δ = 149.5, 147.7, 141.3, 140.6, 139.8, 137.1, 133.3, 130.4, 130.2, 129.3, 129.3, 129.2, 128.9, 128.4, 128.3, 127.5, 126.4, 125.8, 125.4, 122.2, 120.2, 116.3, 81.6, 70.1, 67.9, 63.3, 60.8, 51.3, 37.4, 26.6, 24.7, 21.8. **HRMS**: calculated for $[C_{39}H_{39}N_2O^+]$: 630.2246; found: 630.2245.

[6] E. J. Corey, M. C. Noe, *Org. Synth* **2003**, *80*, 38-45.

Preliminary Structural Assignment of Compounds 4 and 5

The structure of compound **3aa**, along with the relative and absolute stereochemistry, are reported in the dedicated section.
The structure of compound **4a** was confirmed by means of DEPT NMR experiments. Indeed, it is possible to distinguish between the two possible isomers (**4a** and **4''a**), simply by counting the number of CH and CH_2 carbons in the aliphatic region.

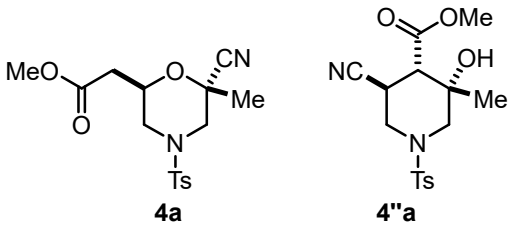


Figure S3. Possible structures **4a** and **4''a**.

In a 135 DEPT experiment, structure **4a** should have 3 negative signals (3xCH_2) and 4 positive signals (1CH and 3xCH_3). On the other hand, structure **4''a** should have 2 negative signals (2xCH_2) and 5 positive signals (1CH and 3xCH_3). The spectrum shown in Figure S4 clearly shows structure **4a** to be the correct one.

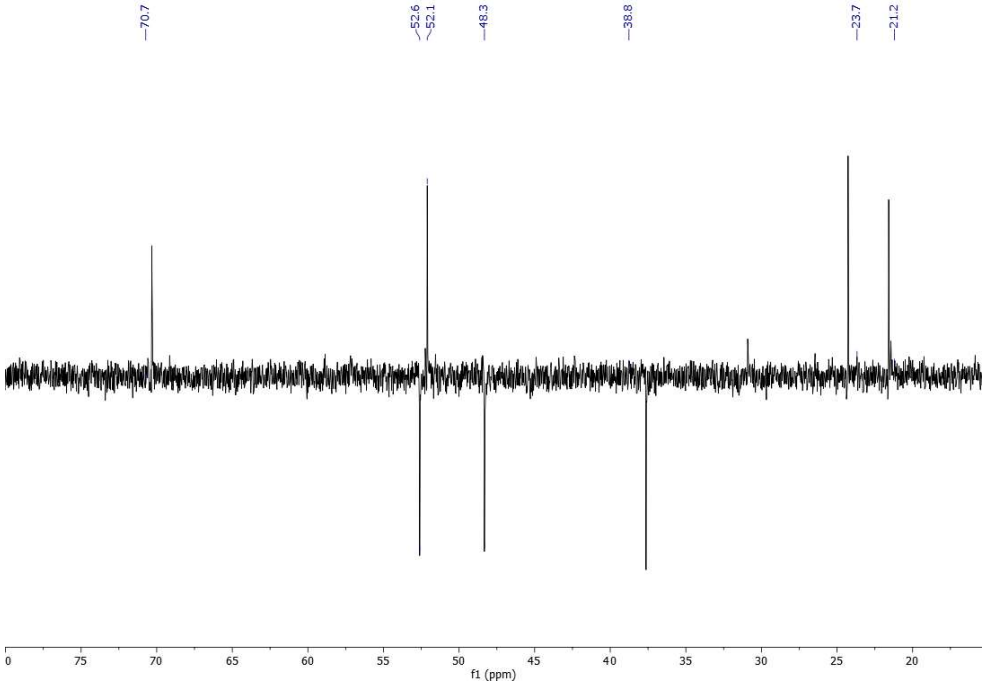


Figure S4. Expansion of the 135 DEPT NMR and ^{13}C NMR experiments of product **4a** in $CDCl_3$.

The structure of compound **5a** was confirmed by means of DEPT NMR experiments as well. Indeed, it is possible to distinguish between the three possible isomers (**5a** and **5'a** and **5''a**), simply by counting the number of CH and CH_2 carbons in the aliphatic region. It is also possible to exclude the presence of a mixture of structural isomers.

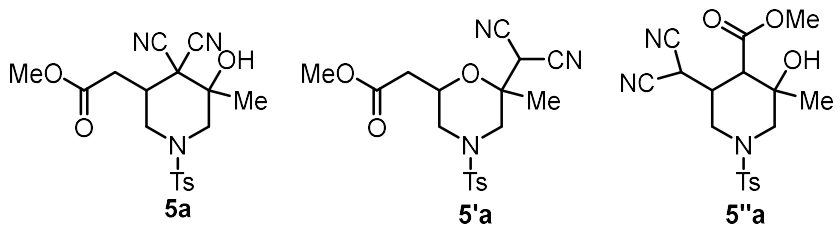


Figure S5. Possible structures **5a**, **5'a** and **5''a**.

In a 135 DEPT experiment, a mixture of two diastereoisomers with structure **5a** should have 6 negative signals (3xCH_2 each) and 8 positive signals (1CH and 3xCH_3 each).
A mixture of two diastereoisomers with structure **5'a** should have 6 negative signals (3xCH_2 each) and 10 positive signals (2CH and 3xCH_3 each).
A mixture of two diastereoisomers with structure **5''a** should have 4 negative signals (2xCH_2 each) and 12 positive signals (3CH and 3xCH_3 each).
Any mixture of structural isomers should have an odd number of positive or negative signals.
The spectrum shown in Figure S6 clearly shows structure **5a** to be the correct one. Moreover, the presence of four signals in the ^{13}C NMR indicated as quaternary carbons (by comparison with the DEPT spectrum) confirms this assignment.

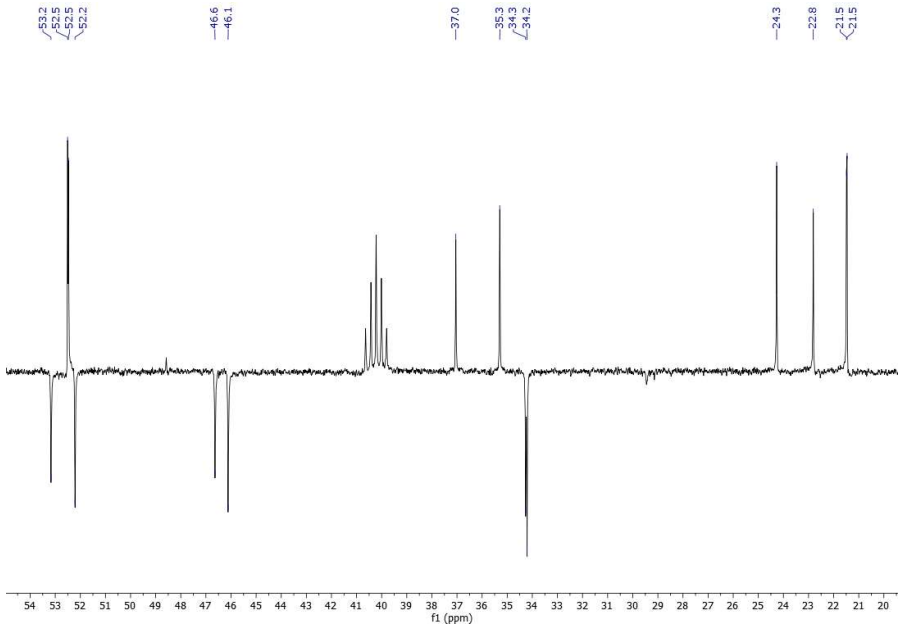


Figure S6. Expansion of the 135 DEPT NMR experiment of product **5a** in DMSO-d_6.

Stereochemical assignments

Compound 3aa

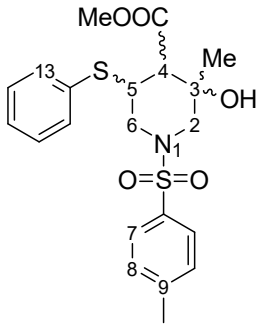


Figure S7. Compound **3aa** numbering

Relative configuration

Full assignment of the hydrogen chemical shifts of compound **3aa** was obtained by 2D COSY experiments, starting from the H-4 hydrogen at 2.32 ppm (doublet, numbering as from Figure S7). H-5 was found at 3.57 ppm by correlation with H-4. H-6' and H6" were found at 3.87 and 2.25 ppm by COSY from H-5. The remaining H-2' and H2" were found at 3.50 and 2.23 ppm. The diastereotopic pairs were then confirmed by HSQC. Careful investigation of the coupling constants value showed that a very large coupling constant takes place between H-4 and H-5 (12.4 Hz). H-5 has also a very large J-coupling with H-6" (12.3 Hz). This combination suggests that H-4, H-5 and H-6" occupy three axial position of the six-membered ring of piperidine, than can be conformationally related to a cyclohexane. Thus, the COOMe and the SPh moiety occupy two equatorial positions on the ring. The very large values of the coupling constants also suggest that the compound has a strongly preferred conformation. This hypothesis is further supported by the observation of a small ^4J coupling between H-6' and H-2' hydrogens, i.e. those in the C-2 and C-6 equatorial positions. The ^4J takes place because of the "W" disposition between the two hydrogens.
NOE spectra were recorded to assign the relative stereochemistry of the quaternary carbon in position 3. On saturation of the methyl signal at 1.15 ppm (assigned by HMBC correlation with the sp^3 quaternary carbon) yields strong NOE on H-2', H-2" and H-4 (Figure S9, control signals) but no enhancement was observed on H-5.

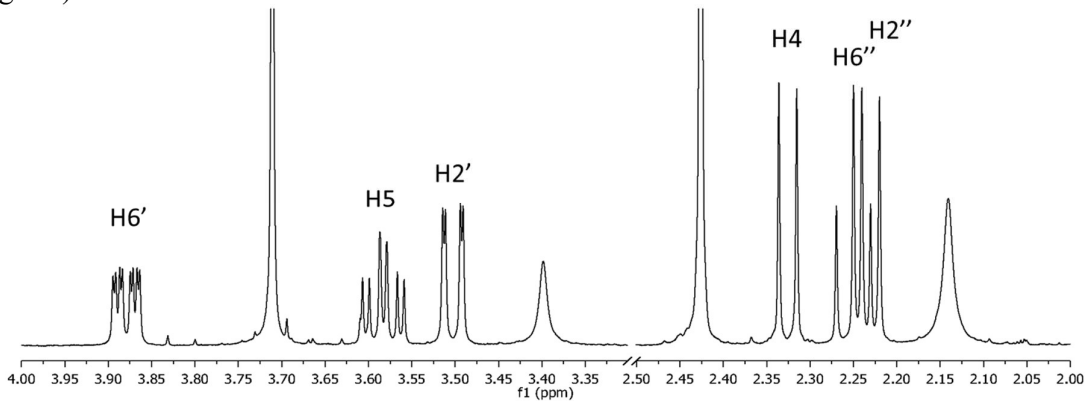


Figure S8. ^1H aliphatic region of compound **3aa** (600 MHz in CD_3CN)

This implies that H-5 is far from the methyl. Being H-5 in the axial position, the Methyl has to be placed in the equatorial position of the ring. As a whole, the *J* coupling analysis and NOE allow to assign the relative stereochemistry of **3aa** as 3*R**, 4*R**, 5*R**.

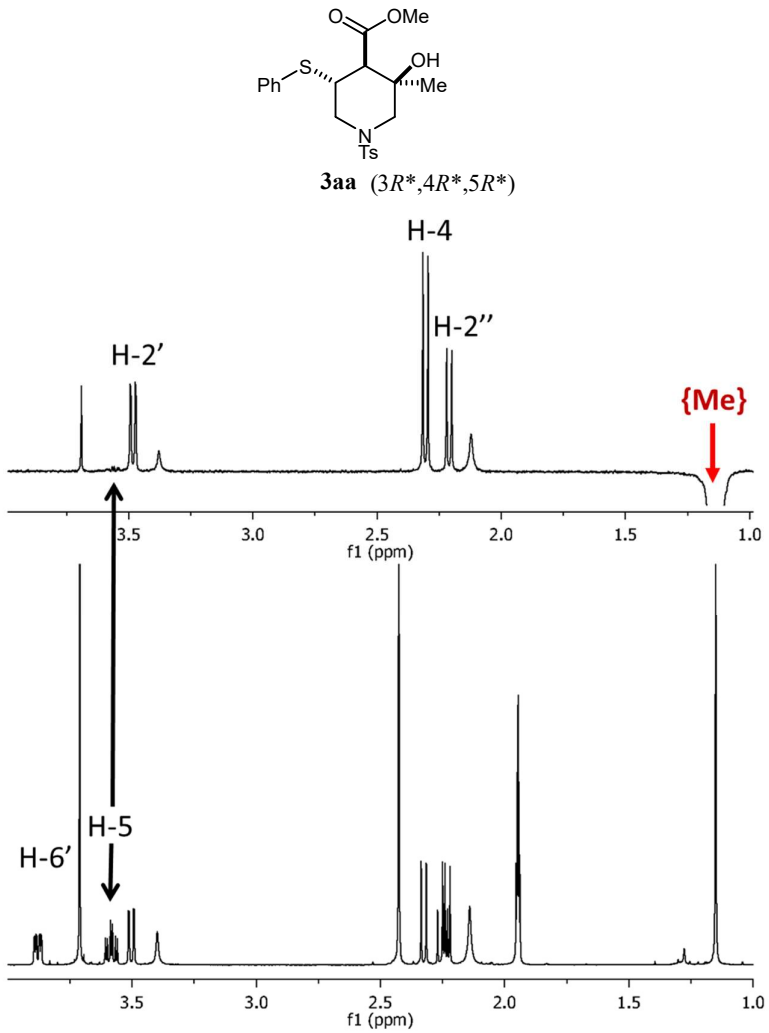


Figure S9. DPFGSE-NOE spectra of compound **3aa** (600 MHz in CD_3CN). Bottom: control spectrum. Top: NOE spectrum on saturation of the Methyl in position 3.

NOE spectra were also acquired to investigate the disposition of the SPh and tosyl exocyclic substituents (Figure S10). On saturation of the ortho hydrogens of the tosyl group, NOE enhancement were observed for all the hydrogens in position 2 and 6. This outcome suggests that the preferred conformation has the phenyl ring in a pseudo-axial position (see below for 3D structures). Saturation of the ortho hydrogens of the SPh moiety yields strong NOE only on H-5 and H-6', whereas NOEs on H-4 and H-6" are small. This suggest that the phenyl ring is mainly located in a pseudo equatorial disposition.

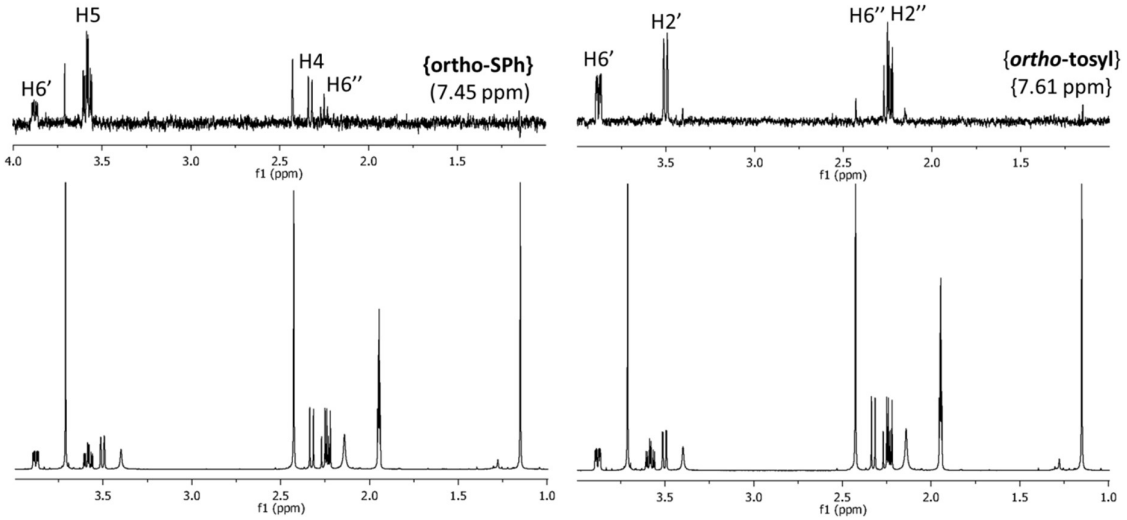


Figure S10. DPFGSE NOE of **3aa**. Left: NOE spectrum on saturation of the ortho hydrogens of the SPh moiety. Right: NOE spectrum on saturation of the ortho hydrogens of the tosyl moiety. Bottom is reported the control spectrum

The minor diastereoisomer **3'aa** could not be isolated. However, in the second fraction of the column chromatography performed for the purification of ***rac*-3aa** a certain amount of this compound could be recovered as inseparable mixture with **3aa**. The structure was assigned on the basis of the great similarity of the H-5 signals. Being these two almost identical in shape and value of the J coupling constants, it is assumed that the relative configuration of H-4 and H-5 should be the same for both **3aa** and **3'aa**. Therefore, the relative configuration of **3'aa** is 3*R**,4*S**,5*S**.

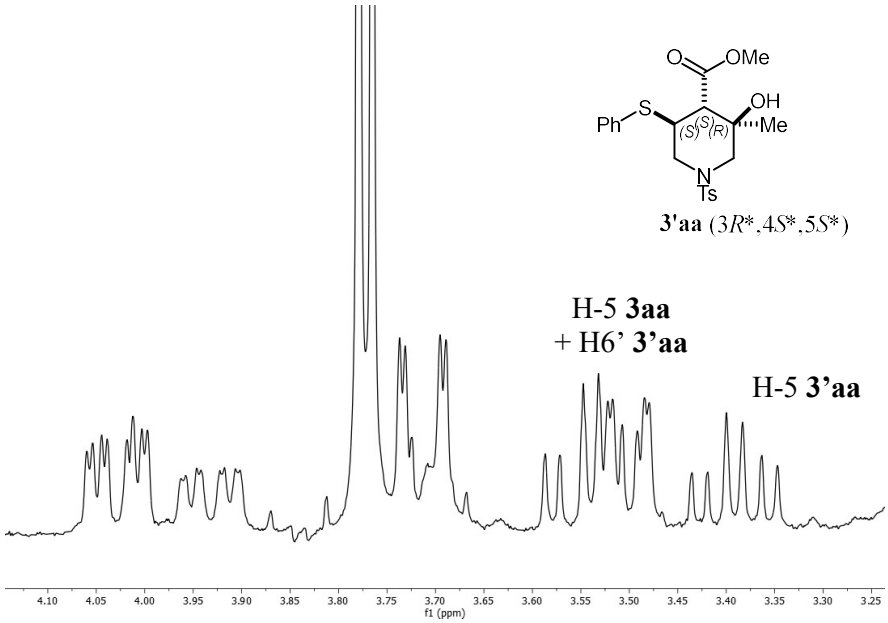


Figure S11. H-5 signals of **3aa** and **3'aa** in the ^{1}H NMR spectrum in $CDCl_3$.

Conformational analysis

Starting from the assigned relative configuration of **3aa**, a complete conformational analysis was performed in order to find all the low-energy conformations. A full scan of the potential energy surface (PES) was performed using molecular mechanics and the MMFF force field (Macromodel, MMFF force field, SPMC method). All the energy minima enclosed in the lowest 10 kcal/mol range (52 conformations) were then optimized using DFT calculations at the B3LYP/6-31G(d) level of theory including the solvent (acetonitrile) with the SMD approach.[7] Frequency analysis was performed to check whether they corresponded to energy minima (no imaginary frequencies observed). After this step, the energies of 16 conformations comprised within the 3 kcal/mol energy range from the global minimum were calculated at the SMD-B3LYP/6-311++G(2d,2p) level. The final energies for the evaluation of the conformational ratio were then obtained by adding the thermal correction to enthalpy extracted from the B3LYP/6-31G(d) calculation to the electronic energy at the higher calculation level. The enthalpic correction was preferred to the free energy because of the presence of many low-energy vibration that hamper a correct evaluation of the entropic factor.[8] After the second DFT step, 14 conformations were found to be enclosed in a ≈ 2.5 kcal/mol range, and 6 within the first 1.5 kcal threshold (Table S2). Those accounts for a 80% population and were considered for the following analysis.

Table S2. relative energies of the conformations of 3aa.

	SMD-B3LYP/6-31G(d)			SMD-B3LYP/6-311++g(2d,2p) SP			
Conf. #	**H°(a.u.)**	**Rel H° (kcal/mol)**	**H_corr. (a.u.)**	**EE (a.u.)**	**EE+H_corr (a.u.)**	**Rel. E (kcal/mol)**	**Pop %**
#5	-2042.055604	0.00	0.46485	-2042.999012	-2042.534162	**0.00**	47
#27	-2042.055486	0.08	0.463819	-2042.996971	-2042.533152	**0.63**	16
#13	-2042.054612	0.63	0.463783	-2042.996484	-2042.532701	**0.92**	10
#1	-2042.053761	1.16	0.4646	-2042.996842	-2042.532242	**1.20**	6
#29	-2042.052883	1.71	0.464681	-2042.996544	-2042.531863	**1.44**	4
#2	-2042.052782	1.77	0.464602	-2042.996405	-2042.531803	**1.48**	4
#11	-2042.05412	0.93	0.464612	-2042.996188	-2042.531576	1.62	3
#15	-2042.052935	1.68	0.464561	-2042.995726	-2042.531165	1.88	2
#45	-2042.053354	1.42	0.463851	-2042.994908	-2042.531057	1.95	2
#3	-2042.051499	2.58	0.464714	-2042.995756	-2042.531042	1.96	2
#4	-2042.051499	2.58	0.464713	-2042.995755	-2042.531042	1.96	1
#32	-2042.052109	2.20	0.463695	-2042.994449	-2042.530754	2.14	1
#8	-2042.052405	2.01	0.464668	-2042.995211	-2042.530543	2.27	1
#17	-2042.054227	0.87	0.464804	-2042.995281	-2042.530477	2.31	1

All the low-energy conformations have the six-membered ring with chair shape, where the SPh, COOMe and the Me moieties are in the equatorial position, as experimentally suggested by *J*-coupling analysis and NOE spectra. Within the most stable conformations, the differences are due to the different relative dispositions of the SPh and the tosyl moieties,

[7] Marenich, A.V.; Cramer, C.J.; Truhlar, D.G. *J. Phys. Chem. B* **2009**, *113*, 6378-6396.

[8] (a) R. F. Ribeiro, A. V. Marenich, C. J. Cramer, D. G. Truhlar, *J. Phys. Chem. B* **2011**, *115*, 14556-14562; (b) S. Grimme, *Chemistry-Eur. J.* **2012**, *18*, 9955-9964; (c) M. L. Laury, S. E. Boesch, I. Haken, P. Sinha, R. A. Wheeler, A. K. Wilson. *J. Comput. Chem.* **2011**, *32*, 2339-2347. M. Mancinelli, R. Franzini, A. Renzetti, E. Marotta, C. Villani, A. Mazzanti *RSC Adv.* **2019**, *9*,18165-18175.

while the spatial disposition of the COOMe group is kept fixed by the intramolecular hydrogen bond with the OH (Figure S12), with the exception of conformation #29. Conformation #5 and #13 are in a very good agreement with the experimental data from NOE.

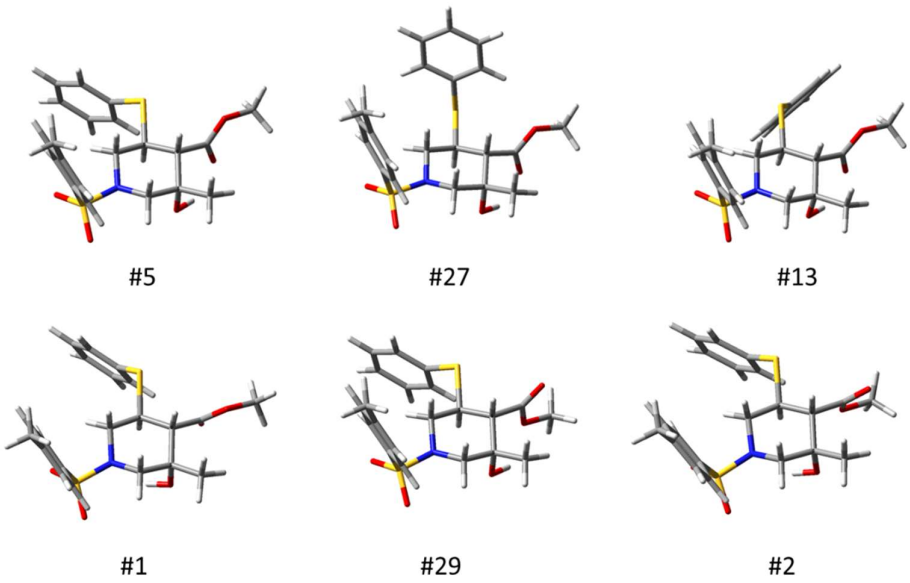


Figure S12. The six best conformations of **3aa.** Geometry optimization at the SMD-B3LYP/6-31G(d) level.

Absolute configuration.

All compounds **3** are amorphous solids and every attempt of crystallization failed, giving in some case gelatinous mixtures or amorphous solids. Thus, anomalous dispersion X-ray crystallography[9] is unfeasible. For this reason, the absolute configuration of compound **3aa** was determined by the theoretical simulations of chiro-optical spectra.[10] In the present case, the theoretical calculation of the ECD spectra of **3aa** was selected for the absolute configuration assignment.

[9] For a review see: H. D. Flack, G. Bernardinelli, *Chirality,* **2008**, *20*, 681-690

[10] For reviews see: a) G. Bringmann, T. Bruhn, K. Maksimenka, Y. Hemberger, *Eur. J. Org. Chem*. **2009**, 2717-2727. b)T. D. Crawford, M. C. Tam, M. L. Abrams, *J. Chem. Phys. A* **2007**, *111*,12057–12068. c) G. Pescitelli, L. Di Bari, N. Berova, *Chem. Soc. Rev.* **2011**, *40*, 4603-4625. d) A. Mazzanti, D. Casarini, D. *WIRES Comput. Mol. Sci.***2012**, *2*, 613-641 e) S. Superchi, P. Scafato, M. Górecki, G. Pescitelli. *Curr. Med. Chem.* **2018**, *25*, 287-320.

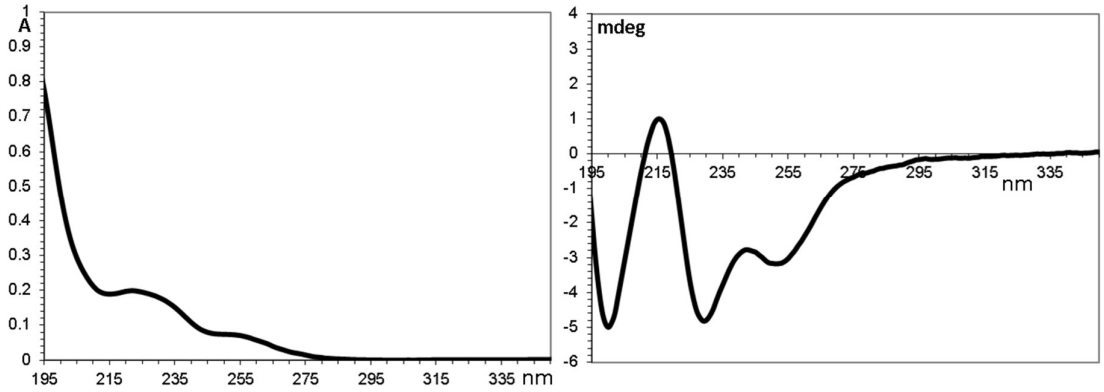


Figure S13. UV and ECD spectrum of **3aa** in acetonitrile.

The ECD spectrum of **3aa** was acquired in HPLC-grade acetonitrile solution ($1 \cdot 10^{-4}$ M) with a cell path of 0.2 cm in the 190-400 nm region by the average of 16 scans at 50 nm/min scan rate (Figure S13). Albeit rather weak, the experimental ECD spectrum exhibits two negative Cotton effects centred at 255 and 228 nm, a positive branch at 216 and a negative one at 200 nm. The TD-DFT simulations of the ECD spectra were performed using the geometries of the best 6 conformations (Table S1). Calculations were performed with CAM-B3LYP[11] that includes long range correction using the Coulomb Attenuating Method and the 6-311++G(2d,p) basis set, that is known to yield good performances at a reasonable computational cost.[12] The results of the TD-DFT calculations for CAM-B3LYP, assuming the 3*S*,4*S*,5*S* absolute configuration are shown in Figure S14.

[11] T. Yanai, D. Tewand, N. Handy, *Chem. Phys. Lett.* **2004**, *393*, 51-57.

[12] a) M. Meazza, M. E. Light, A. Mazzanti, R. Rios. *Chem. Sci.* **2016**, *7*, 984-988; b) P. Gunasekaran, S. Perumal, J. Carlos Menéndez, M. Mancinelli, S. Ranieri, A. Mazzanti, *J. Org. Chem.* **2014**, *79,* 11039-11050.

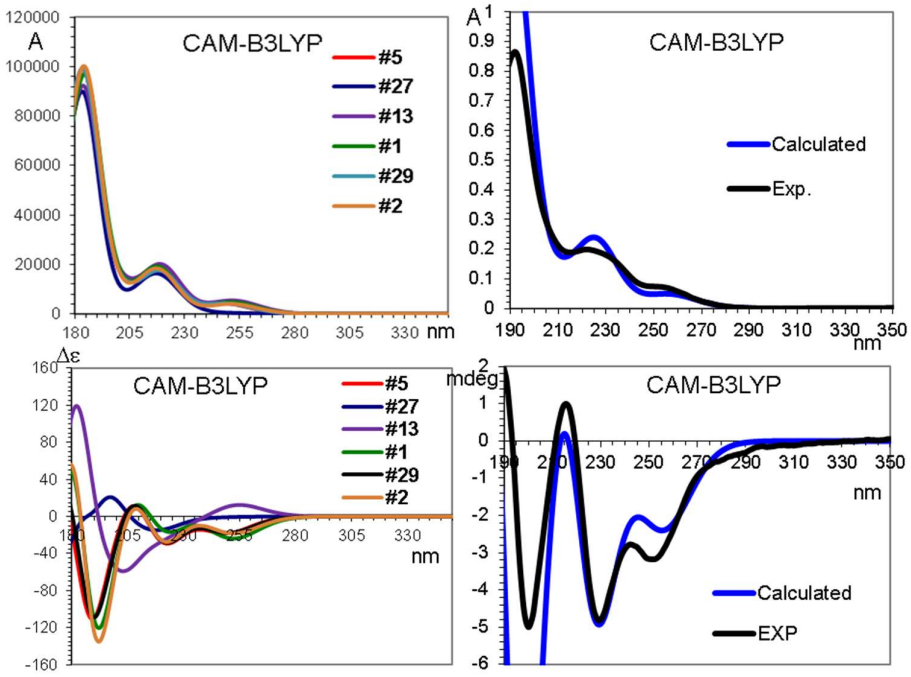
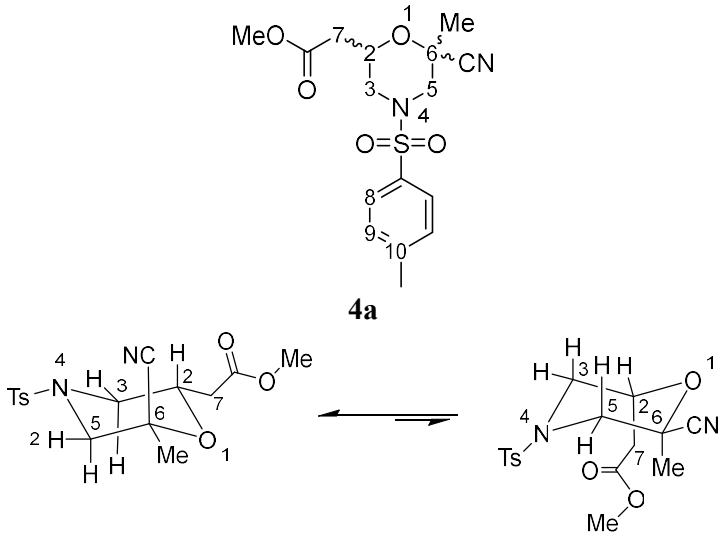


Figure S14. Left: TD-DFT simulated spectra calculated for the six conformations of **3aa**, (3*S*, 4*S*, 5 absolute configuration) using CAM-B3LYP/6-311++G(2d,p) basis set. For each conformation, the first 50 excited states were calculated, and the spectra were obtained using a 0.25 eV line width at half height. The red shift to be applied to simulations was evaluated on the UV spectrum as +7 nm. Scale factors were applied to the UV simulated spectrum ($1.4 \cdot 10^{-5}$) and to the ECD simulation (0.17) to match the experimental spectra (black lines in the right quadrants).

The simulation of the weighted spectrum was obtained by using the populations obtained from Boltzmann distribution using the population of Table S2. The simulated spectra were vertically scaled and red-shifted to get the best match with the experimental spectrum The simulation is in a good agreement with the experimental spectrum, and it correctly match the sign and sequence of the Cotton effects. It is thus safe to assign the 3*S*, 4*S*, 5*S* absolute configuration to **3aa**. It has to be underlined that the absolute configuration of the analogue compounds with the phenyl group in position 3 is 3*R*, 4*S*, 5*S* because of the change in the CIP priorities on changing from the 3-methyl to the 3-phenyl moiety.

Relative configuration of 4a



4a

Figure S15. Atom numbering and the two possible chair conformations of **4a** (2*R**,6*S** relative configuration)

The relative configuration of **4a** was determined by NOE as for compound **3aa**. Preliminary assignment of the hydrogens was achieved with 2D-COSY, HSQC and HMBC. The very large coupling constant of H-2 with H-3" (10.5 Hz) suggests that H-2 occupies mainly the axial position. On saturation of the methyl signal, strong NOE effects are observed on the two hydrogens H-5' and H-5", and a very small NOE on H-2. Saturation of H-2 yields strong NOE only on H-3' and on the two hydrogens in position 7. These data imply that the methyl has to occupy the equatorial position, whereas the cyano group is in the axial one. In this conformation, the CH_2COOMe and the methyl occupy both the equatorial position, whereas the less hindered CN moiety is in the axial position. This arrangement corresponds to the 2*R**, 6*S** relative configuration.

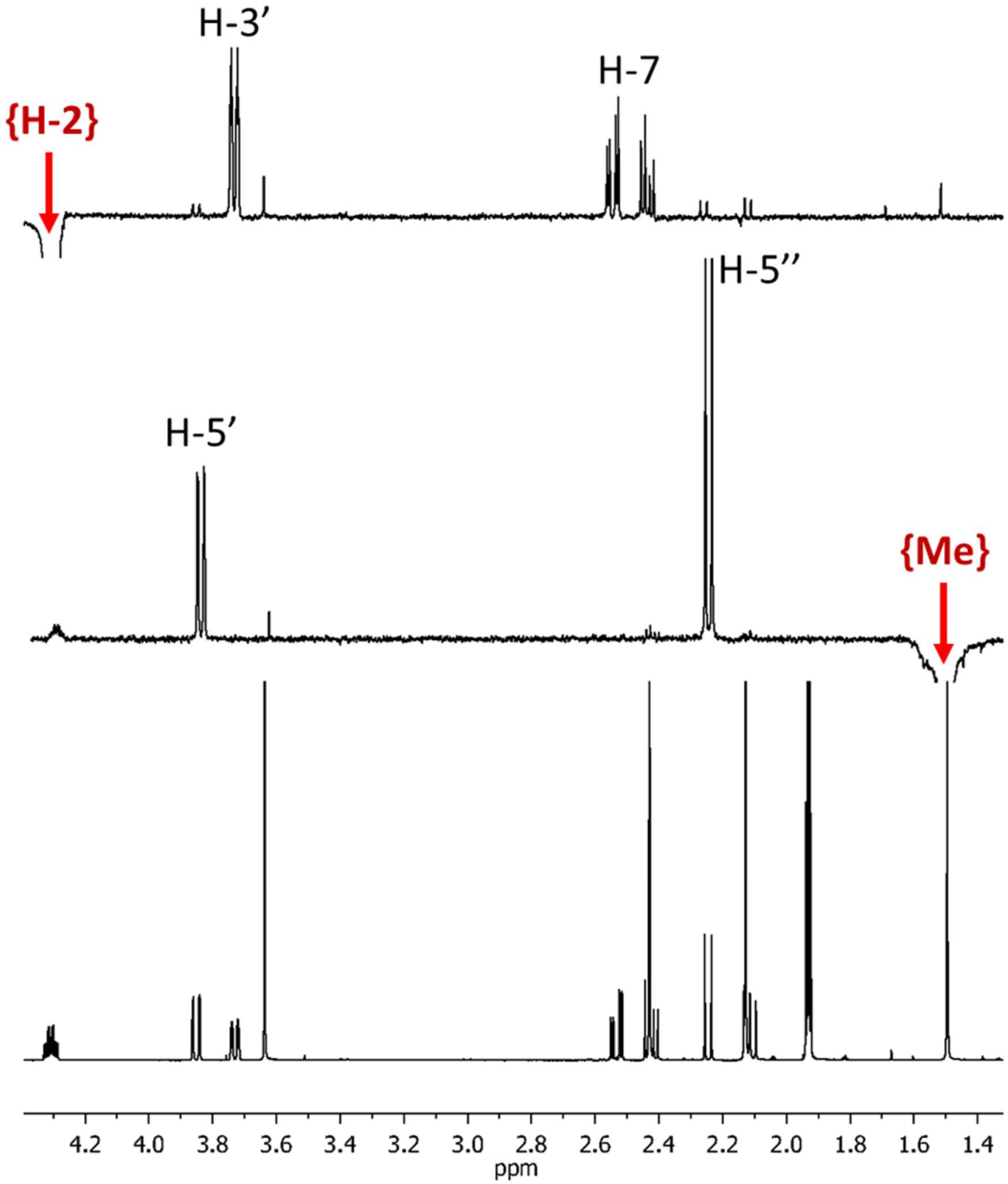


Figure S16. DPFGSE-NOE spectra of compound **4a** (600 MHz in CD_3CN). Bottom: control spectrum. Middle: NOE spectrum on saturation of the methyl in position 6. Top: NOE spectrum on saturation of the H-2 signal.

Computational study

A computational study based on DFT calculations was performed to investigate the catalytic cycle. All the calculations were performed with the Gaussian 16 suite of programs[13] on model compounds where the *p*-tolyl group of the tosyl moiety was replaced by a methyl (mesyl), in order to reduce the computational times. To the same aim, the ammonium ion of the organocatalyst was replaced by tetramethylammonium (TMA). Geometry optimization of the ground states (GS) and transition states (TS) were obtained using the B3LYP functional and the 6-31G(d) basis set. Each optimized structure was validated by frequency analysis showing no imaginary frequency for GS geometries, and a single imaginary frequency for the TS. Visual inspection of the corresponding normal mode was used to confirm that the wanted TS was found. Single point energies were then obtained with M06-2X/6-311+G(d) and the final energies to be compared for the determination of the best reaction pathway were obtained by adding the ZPE contribution to the Enthalpies evaluated at the lower calculation level to the single point energy.[14] The choice to use enthalpy instead of the Gibbs free energy was dictated by the presence of many low-energy vibrators that hamper a suitable evaluation of the entropic factor, even if correction were applied.[15] The use of enthalpy provides less accurate absolute energy for the TS with respect to GS, but a more reliable comparison within them.

Reaction with thiophenol.

The experimental outcome of the reaction is the exclusive formation of the piperidine ring, that derives from the Michael addition of PhS^- to the α,β-unsaturated system, followed by intramolecular cyclization. As a first attempt, the intramolecular TS was searched starting from the cyclized compound (with *S*, *S*, *S* absolute configuration) by a relaxed scan of the potential energy surface (PES) that accounted for the elongation of the C3-C4 bond. The geometry corresponding to the energy maximum was then used as input for the optimization of the TS geometry. The geometry of the transition state is shown in Figure S17. It was found that the reaction coordinate related to the imaginary frequency involved also the formation of the S-C_β bond. The C3-C4 distance in the TS was 2.32Å and the C5-S was 1.91 Å. Starting from this geometry, an IRC calculation confirmed that the TS connect the cyclized compound and the starting reagents. Thus, DFT calculations suggest that the formation of the piperidine ring is due to a concerted, albeit asynchronous, reaction with a single TS. In the GS of the cyclized compound the C3-C4 bond distance is 1.61 Å whereas the C5-S is 1.86 Å, thus the C-S bond is almost already formed when the cyclization starts. Several attempts were made to localize the TS for the alternative pathway where the PhS^- nucleophile adds to the ketone and

[13] Gaussian 16, rev A.03. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, G. A. Petersson, H. Nakatsuji, X. Li, M. Caricato, A. V. Marenich, J. Bloino, B. G. Janesko, R. Gomperts, B. Mennucci, H. P. Hratchian, J. V. Ortiz, A. F. Izmaylov, J. L. Sonnenberg, D. Williams-Young, F. Ding, F. Lipparini, F. Egidi, J. Goings, B. Peng, A. Petrone, T. Henderson, D. Ranasinghe, V. G. Zakrzewski, J. Gao, N. Rega, G. Zheng, W. Liang, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, K. Throssell, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. J. Bearpark, J. J. Heyd, E. N. Brothers, K. N. Kudin, V. N. Staroverov, T. A. Keith, R. Kobayashi, J. Normand, K. Raghavachari, A. P. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, J. M. Millam, M. Klene, C. Adamo, R. Cammi, J. W. Ochterski, R. L. Martin, K. Morokuma, O. Farkas, J. B. Foresman, and D. J. Fox, Gaussian, Inc., Wallingford CT, **2016**.

[14] P. Yu, C. Q. He, A. Simon, W. Li, R. Mose, M. K. Thøgersen, K.A. Jørgensen, K. N. Houk. *J. Am. Chem. Soc.* 2018, **140**, 13726-13735.

[15] a) Y. Zhao, D.G Truhlar, *Phys. Chem. Chem. Phys.* **2008**, *10*, 2813-2818; b) R. F. Ribeiro, A. V. Marenich, C. J. Cramer, D. G. Truhlar, *J. Phys. Chem. B* **2011**, ***115***, 14556-14562; c) S. Grimme, *Chemistry-Eur. J.* **2012**, ***18***, 9955-9964.

the intermediate then cyclizes to yield a morpholine derivative. However, we cannot find any effective geometry for this TS. This is in agreement with similar cases known in the literature.[16]

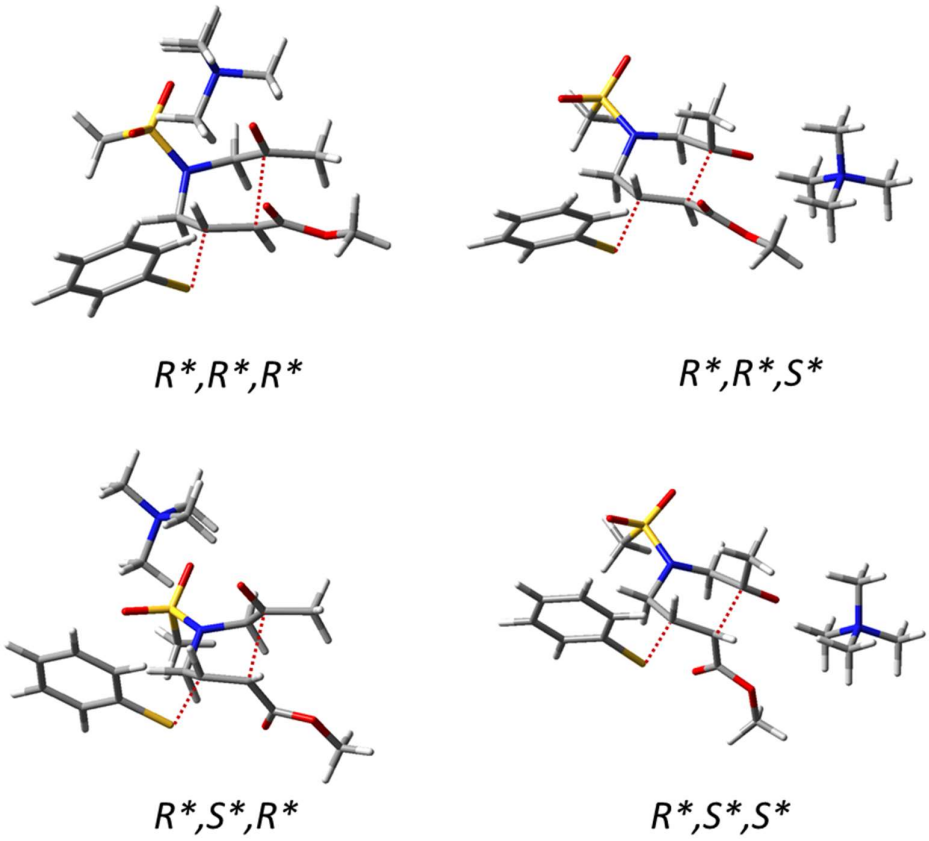


Figure S17. 3D structures of the cyclization TS for compound **3aa***. Distances in Å.

Scheme S3. Possible pathways for the formation of compound **3aa***.

Once the TS for cyclization was found, we searched for the TS geometries leading to the three remaining diastereoisomers, in order to check whether the observed major diastereoisomer (*R**,*R**,*R** relative configuration) was indeed the one corresponding to the lowest energy TS.

[16] Reference 10 in the manuscript

All the three TS were successfully optimized (Figure S17) and a summary of the calculations is reported in Table S3. The TS for the 3*S*, 4*S*, 5*S* configuration was calculated as the most stable one and, in agreement with the experimental outcome, the 3*R*,4*S*,5*S* TS was calculated as the second in energy, with 0.7 kcal/mol difference with respect to the best one. This energy difference corresponds to a 78:22 ratio at 0°C, in very good agreement with the experimentally observed dr (72:28).

Table S3. Summary of the relative energies of the four TS for the concerted cyclization to compound 3aa*.

	Opt EE (B3LYP)[a] (a.u.)	H_corr (a.u.)	SP EE (M06-2X)[b] (a.u.)	SP+H_corr (a.u.)	Rel. E. (kcal/mol)
AC	-2025.174365	0.538571	-2024.994546	-2024.455975	-7.9
R,R*,R**	-2025.154888	0.537665	-2024.981022	-2024.443357	0.00
R,S*,S**	-2025.151895	0.537752	-2024.980034	-2024.442282	0.7
R,R*,S**	-2025.146750	0.537872	-2024.976547	-2024.438675	2.9
R,S*,R**	-2025.148712	0.538166	-2024.978309	-2024.440143	2.0
GS R,R*,R**	-2025.174669	0.539680	-2025.003465	-2024.463785	-12.8
GS R,S*,S**	-2025.151895	0.537752	-2024.995082	-2024.457330	-8.8
GS - R,R*,S**	-2025.164061	0.539817	-2024.995752	-2024.455935	-7.9
GS R,S*,R**	-2025.148712	0.538166	-2025.002416	-2024.464250	-13.1

[a] B3LYP/6-31G(d). [b] SMD-M06-2X/6-311+G(d)

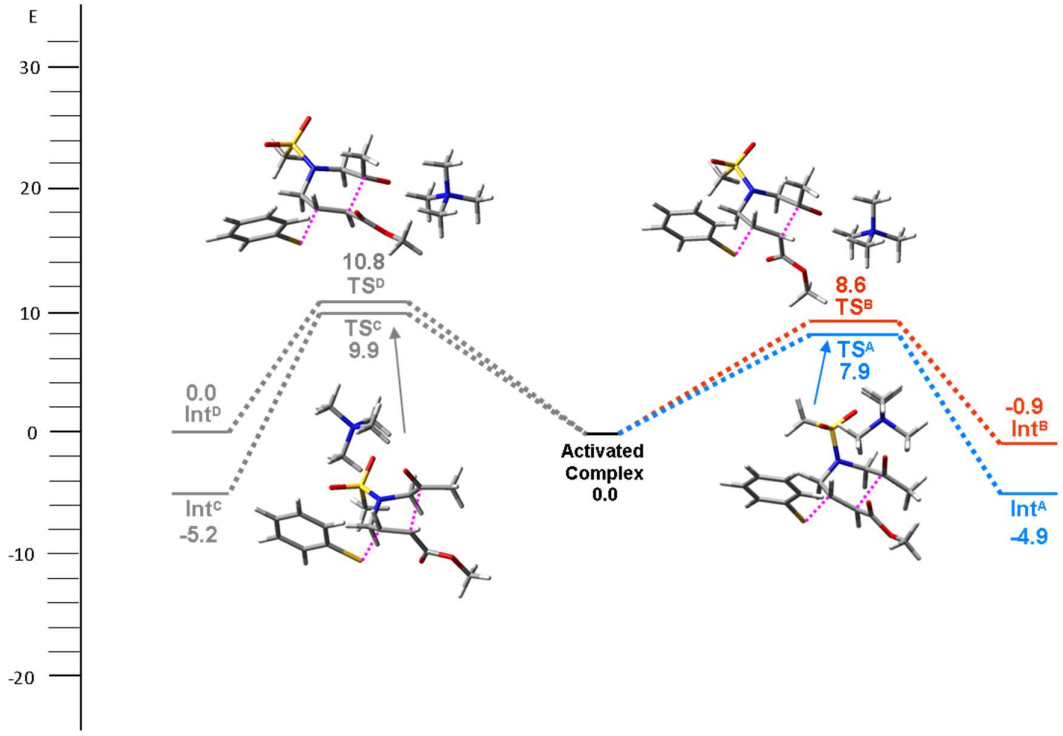
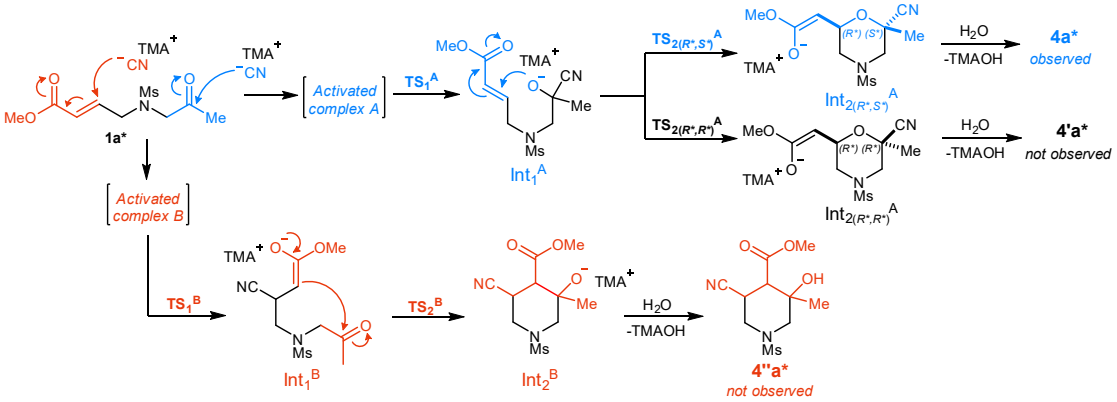


Figure S17. Available reaction pathways for the formation of the four diastereoisomers of **3aa***. Energies in kcal/mol.

Reaction with acetone cyanohydrin

In the case of the reaction with CN^- as nucleophile, a morpholine ring was obtained instead of piperidine. The two reaction pathways leading to the two possible compounds are sketched in Scheme S4. Pathway named A leads to the formation of the observed compound, while pathway B yields a piperidine derivative analogous to that observed with PhS^- as nucleophile.



Scheme S4. Possible reaction pathways. The A pathway is shown in blue, while B pathway is shown in orange.

The first reaction step for the formation of the morpholine ring involves the nucleophilic addition of CN^- to the ketone, followed by the nucleophilic addition of the oxygen on the β carbon of the α,β-unsaturated ester. The First TS for the formation of morpholine ($\mathbf{TS_1^A}$) was successfully localized, and subsequent relaxed IRC calculation allowed to connect it with an

activated complex and to intermediate **Int1^{A}**. The pathway to **Int1^{B}** by way of $TS_1{}^{B}$ was modeled in the same way. Figure S18 shows the geometries of the two TS.

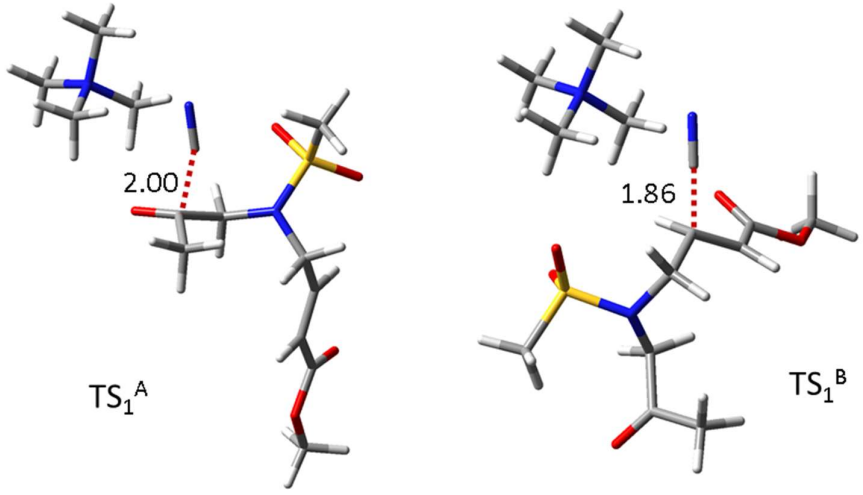


Figure S18. Optimized structures of **TS1^{A}** and **TS1^{B}**. Distances are reported in Å

A direct comparison of the energies of $TS_1{}^{A}$ vs $TS_1{}^{B}$ suggested that the former is much more stable than the latter (5.4 kcal/mol).

Table S4. Summary of the relative energies of the ground states and transition states for the two pathways reported in scheme S3.

	Opt EE (B3LYP) (a.u.)	H_corr (a.u.)	SP EE (M06-2x) (a.u.)	SP+H_corr (a.u.)	Rel E (kcal /mol)
AC^{A}	-1488.151749	0.450066	-1488.014437	-1487.564371	0
AC^{B}	-1488.150941	0.449793	-1488.013469	-1487.563676	0.4
$TS_1{}^{A}$	-1488.131421	0.449261	-1487.996377	-1487.547116	10.8
$TS_1{}^{B}$	-1488.121723	0.448724	-1487.987185	-1487.538461	16.2
$TS_{2(RS)}{}^{A}$	-1488.123089	0.448962	-1487.991059	-1487.542097	14.0
$TS_{2(RR)}{}^{A}$	-1488.119706	0.449122	-1487.986434	-1487.537312	17.0
$TS_2{}^{B}$	-1488.140398	0.449923	-1488.012121	-1487.562198	1.4
$Int_1{}^{A}$	-1488.146006	0.449945	-1488.009194	-1487.559246	3.2
$Int_1{}^{B}$	-1488.160677	0.450335	-1488.024988	-1487.574653	-6.5

When the two intermediates **Int1^{A}** and **Int1^{B}** are formed, subsequent cyclization leads to morpholine or piperidine. In the case of pathway A the two possible diastereomeric TS that yields the two diastereomeric morpholines have different energies, and the best one (**$TS_{2(R^*,S^*)}{}^{A}$**) has activation energy again lower than that of the first step of pathway B (**TS1^{B}**) (Figure S19). Comfortably, this transition state yields the experimentally observed diastereoisomer. The main reason for the higher stability of **$TS_{2(R^*,S^*)}{}^{A}$** has to be assigned to the lower steric hindrance of the cyano group with respect to the methyl in the pseudo-axial position of the six-membered-shaped transition state. On the contrary, the TS following **Int1^{B}** and yielding the piperidine compound have much lower energy with respect to **TS1^{B}** (for this reason only the **TS2^{B}** yielding the most stable diastereoisomer has been shown). However, this pathway is forbidden by the high energy of **TS1^{B}** in the first stage. After cyclization, the enolate can be protonated by a water molecule to obtain the final compound **4a***. Figure S20 summarizes the whole reaction pathway.

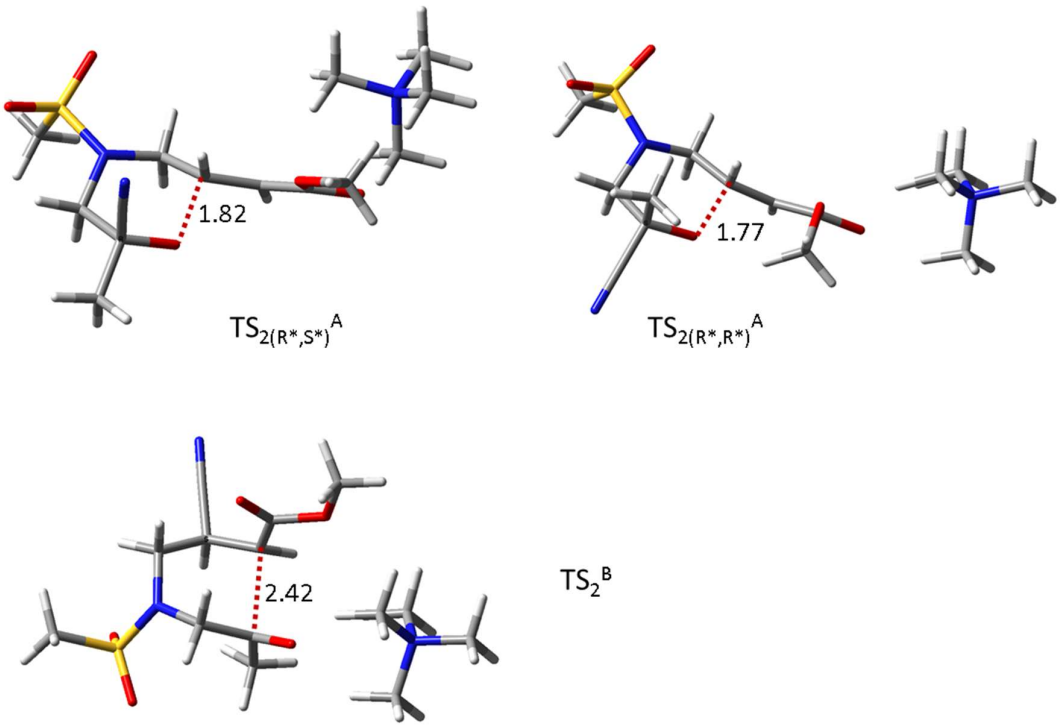


Figure S19. Optimized structures of $\mathbf{TS_2^A}$ and $\mathbf{TS_2^B}$. Distances are reported in Å

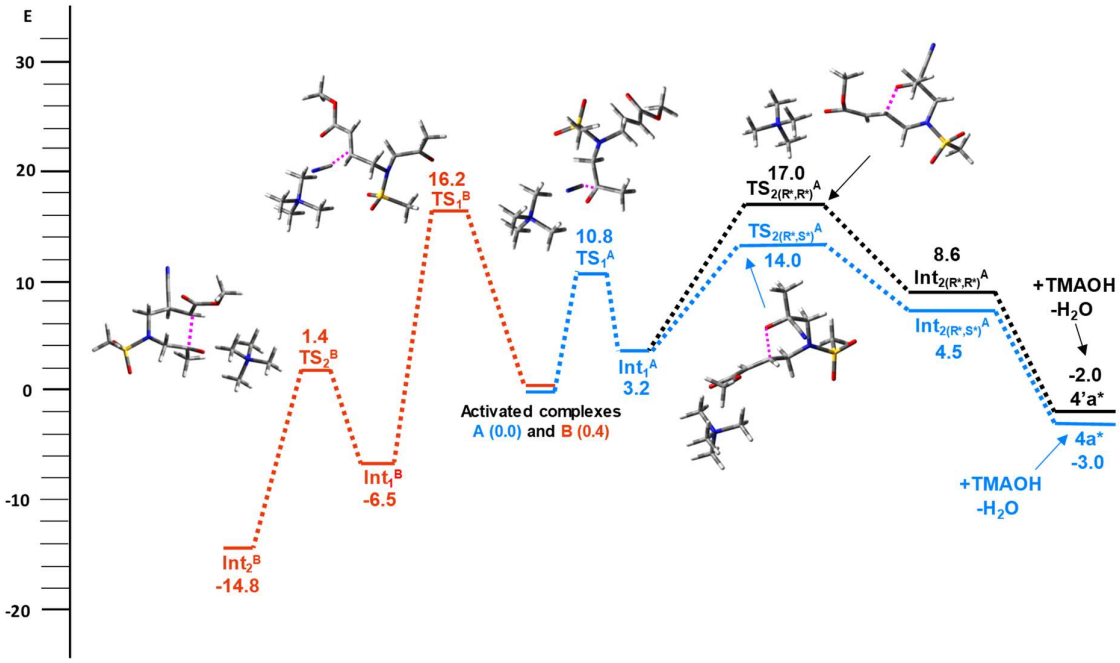
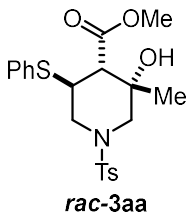


Figure S20. Available reaction pathways for the formation of 4a* and for the unobserved piperidine ring. Energies in kcal/mol.

General procedure for the synthesis of products *rac*-3, 4 and 5

In a test tube, equipped with a magnetic stir bar, substrates **1** (0.1 mmol) and TBABr (3.2 mg, 0.01 mmol, 10 mol%) were suspended in toluene (500 µL) and the reaction mixture was cooled to 0 °C. Then, Cs_2CO_3 (40.0 mg, 0.12 mmol) and the corresponding nucleophile (0.12 mmol) were added in this order. The resulting suspension was vigorously stirred for 1 h at 0 °C, diluted with CH_2Cl_2 (1 mL), passed through a small plug of silica, eluted with CH_2Cl_2 (3x1 mL) and Et_2O (3x1 mL) and evaporated *in vacuo*. The resulting crude mixture was analyzed by means of ^{1}H NMR spectroscopy to determine the diastereomeric ratio and finally purified by column chromatography on silica gel (CH_2Cl_2/Et_2O mixtures) to obtain products ***rac*-3**, **4** or **5**.

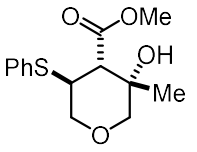
Methyl (3*R,4*R**,5*R**)-3-hydroxy-3-methyl-5-(phenylthio)-1-tosylpiperidine-4-carboxylate *rac*-3aa**



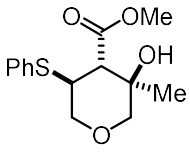
***rac*-3aa**

Following the general procedure from substrate **1a** and thiophenol **2a**, product ***rac*-3aa** was obtained as a white solid in 77% yield (33.5 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = from 50:1 to 20:1). The diastereomeric ratio was found to be 2.5:1 in the crude mixture; 2 fractions were isolated from the column chromatography, the first having 3.7:1 dr (82% of the isolated product) and the second having 1.5:1 dr (18% of the isolated product). Full characterization is given for enantioenriched **3aa** in the corresponding section.

Methyl (3*S,4*S**,5*S**) and (3*R**,4*S**,5*S**)-3-hydroxy-3-methyl-5-(phenylthio)tetrahydro-*2H*-pyran-4-carboxylate 3ba**



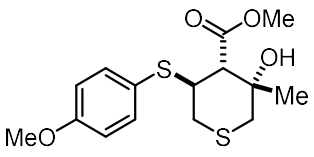
3ba (M)



3ba (m)

Following the general procedure from substrate **1b** and thiophenol **2a**, product **3ba** (1.4:1 dr in the crude mixture and after column chromatography) was obtained as a colorless oil in 86% yield (24.3 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 80:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.49 – 7.42 (m, 2H M + m), 7.34 – 7.27 (m, 3H M + m), 4.11 – 4.09 (m, 1H m), 4.08 – 4.06 (m, 1H M), 3.81 (s, 3H M), 3.81 (s, 3H m), 3.70 – 3.59 (m, 2H M + m), 3.38 – 3.12 (m, 3H M + m), 2.62 (d, *J* = 11.2 Hz, 1H m), 2.49 (d, *J* = 12.3 Hz, 1H M), 1.28 (s, 3H m), 1.13 (s, 3H M). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 172.8 (M), 171.2 (m), 133.8 (2C m), 133.3 (2C M), 132.2 (m), 132.0 (M), 129.1 (2C m), 129.1 (2C M), 128.3 (m), 128.1 (M), 76.5 (m), 75.2 (M), 71.3 (m), 71.1 (M), 69.8 (m), 69.2 (M), 56.9 (m), 55.0 (M), 52.15 (m), 52.13 (M), 43.9 (m), 43.0 (M), 24.1 (M), 22.3 (m). ["M" stands for the major diastereoisomer (3*S**,4*S**,5*S**) and "m" for the minor diastereoisomer (3*R**,4*S**,5*S**)]. **HRMS**: calculated for [$C_{14}H_{18}O_4S$ + Na^+]: 305.0818; found: 305.0823.

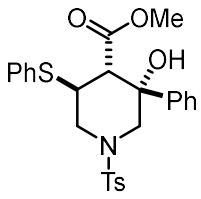
Methyl (3*S,4*S**,5*S**)-3-hydroxy-3-methyl-5-(4-methoxyphenylthio) tetrahydro-*2H*-thiopyran-4-carboxylate 3cb**



3cb

Following the general procedure, but using aqueous K_2CO_3 (10% wt., 200 μL) instead of solid Cs_2CO_3, from substrate **1c**, 4-methoxythiophenol **2b** and catalyst **F** instead of TBABr, product **3cb** (>20:1 dr in the crude mixture and after column chromatography) was obtained as a colorless oil in 52% yield (17.1 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 60:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.44 – 7.39 (m, 2H), 6.88 – 6.83 (m, 2H), 3.84 (s, 3H), 3.81 (s, 3H), 3.61 (very broad s, 1H), 3.45 (td, *J* = 12.0, 3.8 Hz, 1H), 2.73 (ddd, *J* = 13.6, 3.8, 2.0 Hz, 1H), 2.62 – 2.45 (m, 3H), 2.34 (d, *J* = 12.2 Hz, 1H), 1.29 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 172.7, 160.3, 136.9 (2C), 121.8, 114.6 (2C), 68.5, 57.4, 55.3, 51.9, 46.5, 40.4, 32.7, 28.5. **HRMS**: calculated for [$C_{15}H_{20}O_4S_2$ + Na^+]: 351.0695; found: 351.0698.

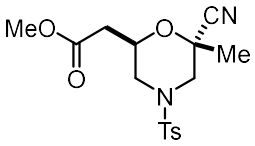
Methyl (3*R,4*S**,5*S**)-3-hydroxy-3-phenyl-5-(phenylthio)-1-tosylpiperidine-4-carboxylate *rac*-3da**



***rac*-3da**

Following the general procedure from substrate **1d** and thiophenol **2a**, product ***rac*-3da** (>20:1 dr in the crude mixture and after column chromatography) was obtained as a white solid in 87% yield (43.2 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 50:1). Full characterization is given for enantioenriched **3da** in the corresponding section.

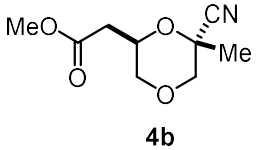
Methyl (2*R,6*S**)-2-(6-cyano-6-methyl-4-tosylmorpholin-2-yl)acetate 4a**



4a

Following the general procedure from substrate **1a** and acetone cyanohydrin, product **4a** (>20:1 dr in the crude mixture and after column chromatography) was obtained as a white solid in 90% yield (31.7 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 70:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.73 – 7.64 (m, 2H), 7.40 – 7.32 (m, 2H), 4.41 (dtd, *J* = 10.6, 6.3, 2.6 Hz, 1H), 3.83 (dd, *J* = 12.1, 1.6 Hz, 1H), 3.80 – 3.73 (m, 1H), 3.71 (s, 3H), 2.54 (dd, *J* = 15.9, 6.6 Hz, 1H), 2.45 (s, 3H) overlapped with 2.44 (dd, *J* = 15.9, 6.0 Hz, 1H), 2.29 (d, *J* = 12.1 Hz, 1H), 2.23 (dd, *J* = 11.7, 10.6 Hz, 1H), 1.55 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 169.4, 144.5, 132.6, 130.0 (2C), 127.8 (2C), 117.7, 70.6, 70.3, 52.6, 52.1, 48.3, 37.6, 24.3, 21.6. **HRMS**: calculated for [$C_{16}H_{20}N_2O_5S$ + Na^+]: 375.0985; found: 375.0991.

Methyl (2*R,6*R**)-2-(6-cyano-6-methyl-1,4-dioxan-2-yl)acetate 4b**

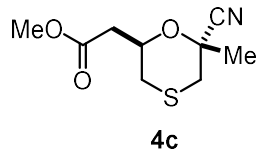


4b

Following the general procedure from substrate **1b** and acetone cyanohydrin, product **4b** (>20:1 dr in the crude mixture and after column chromatography) was obtained as a colorless oil in 86% yield (17.1 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 70:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 4.44 (dtd, *J* = 10.5, 6.5, 2.7 Hz, 1H), 3.96 (ddd, *J* = 11.6, 2.7, 0.6 Hz, 1H), 3.93 – 3.88 (m, 1H), 3.71 (s, 3H), 3.30 (d, *J* = 11.9 Hz, 1H) partially overlapped with 3.26 (dd, *J* = 11.7, 10.5 Hz, 1H), 2.52 (dd, *J* = 15.9,

6.5 Hz, 1H), 2.41 (dd, *J* = 15.9, 6.5 Hz, 1H), 1.48 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 169.8, 118.8, 72.6, 70.5, 69.8, 69.7, 52.0, 36.4, 31.6. **HRMS**: calculated for [$C_9H_{13}NO_4$ + Na^+]: 222.0737; found: 222.0739.

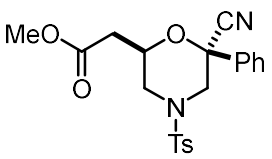
Methyl (2*R,6*R**)-2-(6-cyano-6-methyl-1,4-oxathian-2-yl)acetate 4c**



4c

Following the general procedure, but using aqueous K_2CO_3 (10% wt., 200 μL) instead of solid Cs_2CO_3, from substrate **1c** and acetone cyanohydrin, product **4c** (>20:1 dr in the crude mixture and after column chromatography) was obtained as a colorless oil in 50% yield (10.7 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 70:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 4.48 (dtd, *J* = 9.3, 6.5, 3.4 Hz, 1H), 3.71 (s, 3H), 2.74 (d, *J* = 13.9 Hz, 1H), 2.66 – 2.46 (m, 5H), 1.64 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 170.0, 118.5, 72.6, 72.3, 51.9, 40.7, 35.0, 29.7, 27.9. **HRMS**: calculated for [$C_9H_{13}NO_3S$ + Na^+]: 238.0508; found: 238.0508.

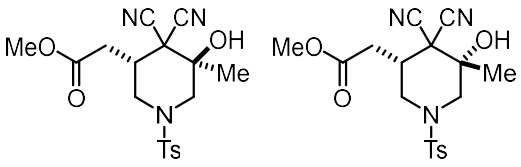
Methyl (2*R,6*S**)-2-(6-cyano-6-phenyl-4-tosylmorpholin-2-yl)acetate 4d**



4d

Following the general procedure, from substrate **1d** and acetone cyanohydrin, product **4d** (>20:1 dr in the crude mixture and after column chromatography) was obtained as a white solid in 92% yield (37.2 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 60:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.69 – 7.62 (m, 2H), 7.54 – 7.46 (m, 2H), 7.44 – 7.38 (m, 3H), 7.36 – 7.28 (m, 2H), 4.66 (dtd, *J* = 10.6, 6.2, 2.7 Hz, 1H), 4.03 (dd, *J* = 12.3, 1.7 Hz, 1H), 3.87 (ddd, *J* = 11.8, 2.8, 1.8 Hz, 1H), 3.72 (s, 3H), 2.69 (dd, *J* = 15.8, 6.4 Hz, 1H), 2.61 (dd, *J* = 15.8, 6.1 Hz, 1H), 2.43 (s, 3H), partially overlapped with 2.41 (d, *J* = 11.7 Hz, 1H) partially overlapped with 2.38 (dd, *J* = 11.8, 10.7 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 169.4, 144.5, 135.2, 132.6, 130.0 (2C), 129.9, 129.0 (2C), 127.8 (2C), 125.2 (2C), 116.7, 75.7, 70.5, 54.3, 52.2, 48.4, 37.7, 21.6. **HRMS**: calculated for [$C_{21}H_{22}N_2O_5S$ + Na^+]: 437.1142; found: 437.1144.

Methyl (3*R,5*R**)- and (3*R**,5*S**)-2-(4,4-dicyano-5-hydroxy-5-methyl-1-tosylpiperidin-3-yl)acetate 5a**

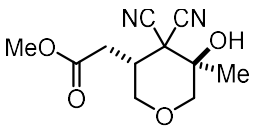


5a

Following the general procedure from substrate **1a** and malononitrile, product **5a** (1.1:1 dr in the crude mixture and after column chromatography) was obtained as a colorless oil in 66% yield (28.8 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 60:1). **^{1}H NMR** (400 MHz, DMSO-*d*$_6$) δ = 7.71 – 7.61 (m, 2H + 2H), 7.51 – 7.40 (m, 2H + 2H), 6.93 (s, 1H), 6.72 (s, 1H), 4.02 – 3.87 (m, 1H + 1H), 3.66 (dd, *J* = 12.2, 1.1 Hz, 1H) partially overlapped with 3.65 (s, 3H), 3.64 (s, 3H), 3.50 (dd, *J* = 12.2, 1.5 Hz, 1H), 3.01 (dddd, *J* = 11.2, 7.3, 6.1, 3.9 Hz, 1H), 2.82 (dddd, *J* = 10.8, 7.6, 5.4, 4.2 Hz, 1H), 2.63 – 2.52 (m, 2H + 2H), 2.40 (s, 3H), 2.39 (s, 3H) partially overlapped with 2.398 (d, *J* = 12.6 Hz, 1H), 2.31 (d, *J* = 12.7 Hz, 1H), 2.27 – 2.10 (m, 1H +1H), 1.50 (s, 3H), 1.45 (s, 3H). **^{13}C NMR** (101 MHz, DMSO-*d*$_6$) δ = 170.5, 170.4, 144.7, 144.4, 133.2, 132.8, 130.6 (2C), 130.5 (2C), 127.9 (2C), 127.8 (2C), 114.2, 114.0, 113.1, 112.8, 71.7, 71.2, 53.2, 52.51, 52.48, 52.2, 50.8, 48.6, 46.6, 46.1, 37.0, 35.3, 34.3, 34.2, 24.3, 22.8, 21.49, 21.46. All peaks are

given without assignation. **HRMS**: calculated for [$C_{18}H_{21}N_3O_5S$ - H^+]: 390.1129; found: 390.1124.

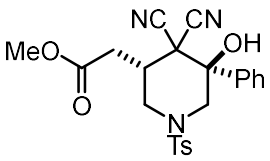
Methyl (3*R,5*R**)-2-(4,4-dicyano-5-hydroxy-5-methyltetrahydro-*2H*-pyran-3-yl)acetate 5b**



5b

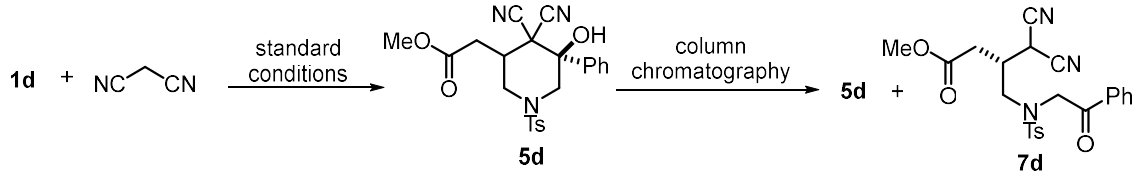
Following the general procedure from substrate **1b** and malononitrile, product **5b** (4.8:1 dr in the crude mixture and after column chromatography) was obtained as a colorless oil in 40% yield (9.5 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 50:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 4.16 (dd, *J* = 12.3, 4.2 Hz, 1H), 3.75 (s, 3H), 3.71 – 3.61 (m, 2H), 3.31 (dd, *J* = 12.4, 11.2 Hz, 1H), 3.22 (bs, 1H), 3.08 – 2.96 (m, 1H), 2.75 (dd, *J* = 16.8, 3.2 Hz, 1H), 2.43 (dd, *J* = 16.8, 10.7 Hz, 1H), 1.25 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 169.9, 112.8, 112.7, 71.6, 71.3, 67.1, 52.4, 36.0, 33.1, 29.7, 21.5. Only the NMR data of the major diastereoisomer are reported. The relative stereochemistry is given tentatively, in analogy with **4b**. **HRMS**: calculated for [$C_{11}H_{14}N_2O_4$ - H^+]: 237.0881; found: 237.0878.

Methyl 2-((3*R,5*R**)-4,4-dicyano-5-hydroxy-5-phenyl-1-tosylpiperidin-3-yl)acetate**



5d

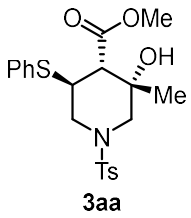
Following the general procedure, from substrate **1d** and malononitrile, product **5d** (along with **7d**, see main text) was obtained as a colorless oil in 41% yield (18.1 mg of **5d**, along with 13.9 mg of **7d**) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 50:1). This compound was found to be unstable over silica, as a 1.3:1 mixture of **5d** and **7d** was recovered after column chromatography, while the crude mixture contained almost exclusively **5d**. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.73 – 7.62 (m, 3H), 7.50 – 7.43 (m, 2H), 7.43 – 7.36 (m, 2H), 7.22 – 7.10 (m, 2H), 4.33 (ddd, *J* = 12.8, 4.1, 1.9 Hz, 1H), 4.25 (s, 1H), 3.91 (dd, *J* = 13.2, 1.9 Hz, 1H), 3.81 (s, 3H), 3.43 – 3.28 (m, 1H) partially overlapped with 3.31 (d, *J* = 13.6 Hz, 1H), 2.85 (dd, *J* = 16.8, 3.0 Hz, 1H), 2.49 (s, 3H) overlapped with 2.55 – 2.30 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 169.7, 145.1, 136.5, 132.9, 130.4 (2C), 130.0, 128.7 (2C), 127.5 (2C), 126.0 (2C), 112.2, 112.2, 73.2, 52.7, 51.1, 50.4, 46.1, 34.5, 24.8, 21.7. Only the NMR data of **5d** are reported. **HRMS**: calculated for [$C_{23}H_{23}N_3O_5S$ - H^+]: 452.1286; found: 452.1287.



General procedure for the synthesis of enantioenriched products 3

In a test tube, equipped with a magnetic stir bar, substrates **1** (0.1 mmol) and catalyst **G** (6.4 mg, 0.01 mmol, 10 mol%) were suspended in toluene (2 mL) and the reaction mixture was cooled to 0 °C. Then, Cs_2CO_3 (40.0 mg, 0.12 mmol) and the corresponding thiophenol (0.12 mmol) were added in this order. The resulting suspension was vigorously stirred for 1 h at 0 °C, diluted with CH_2Cl_2 (1 mL), passed through a small plug of silica, eluted with CH_2Cl_2 (3x1 mL) and Et_2O (3x1 mL) and evaporated *in vacuo*. The resulting crude mixture was analyzed by means of ^{1}H NMR spectroscopy to determine the diastereomeric ratio and finally purified by column chromatography on silica gel (CH_2Cl_2/Et_2O mixtures) to obtain products **3** as white amorphous solids.

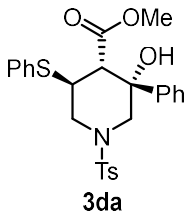
Methyl (3*S*,4*S*,5*S*)-3-hydroxy-3-methyl-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3aa



3aa

Following the general procedure from substrate **1a** and thiophenol **2a**, product **3aa** (>20:1 dr after column chromatography, 8:1 in the crude mixture) was obtained as a white solid in 80% yield (34.8 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = from 50:1 to 20:1). **[α]$_D^{25}$** = -89 (c = 0.7 in $CHCl_3$) for 88% *ee*. **^{1}H NMR** (600 MHz, CD_3CN) δ = 7.62 – 7.59 (m, 2H), 7.48 – 7.44 (m, 2H), 7.41 – 7.33 (m, 5H), 3.88 (ddd, *J* = 12.0, 4.7, 1.9 Hz, 1H), 3.71 (s, 3H), 3.58 (td, *J* = 12.0, 4.7 Hz, 1H), 3.50 (dd, *J* = 12.2, 1.9 Hz, 1H), 3.40 (bs, 1H), 2.43 (s, 3H), 2.33 (d, *J* = 12.4 Hz, 1H), 2.25 (dd, J_1 = J_2 = 11.8 Hz, 1H) partially overlapped with 2.23 (d, *J* = 12.2 Hz, 1H). **^{13}C NMR** (151 MHz, CD_3CN) δ = 171.5, 144.1, 133.5, 132.8 (2C), 132.4, 129.7 (2C), 129.3 (2C), 128.2, 127.5 (2C), 69.1, 55.4, 55.2, 51.5, 50.3, 43.2, 24.9, 20.5. **HRMS**: calculated for [$C_{21}H_{25}NO_5S_2$ + Na^+]: 458.1066; found: 458.1064. **HPLC**: OD-H (*n*-hexane/iPrOH 90:10, flow-rate 1.00 mL/min; t_{maj} = 18.4 min; t_{min} = 30.4 min).

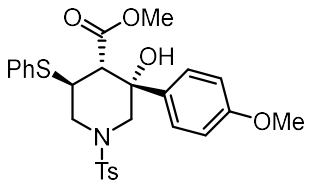
Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3da



3da

Following the general procedure from substrate **1d** and thiophenol **2a**, product **3da** (>20:1 dr in the crude mixture and after column chromatography) was obtained as a white solid in 71% yield (35.3 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 50:1). **[α]$_D^{25}$** = -24 (c = 1.0 in $CHCl_3$) for 91% *ee*. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.62 – 7.58 (m, 2H), 7.45 – 7.39 (m, 4H), 7.38 – 7.28 (m, 6H), 7.28 – 7.23 (m, 2H), 4.12 (ddd, *J* = 12.6, 4.4, 1.9 Hz, 1H), 3.80 (dd, *J* = 12.9, 1.8 Hz, 1H) overlapped with 3.80 (bs, 1H), 3.71 (td, *J* = 11.7, 4.5 Hz, 1H), 3.45 (s, 3H), 2.92 (d, *J* = 12.1 Hz, 1H), 2.56 (dd, *J* = 12.7, 11.5 Hz, 1H) overlapped with 2.56 (d, *J* = 13.0 Hz, 1H), 2.42 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 173.0, 143.6, 141.6, 134.6, 132.9 (2C), 131.7, 129.6 (2C), 129.3 (2C), 128.5 (2C), 128.3, 128.1, 127.6 (2C), 125.1 (2C), 73.3, 55.5, 54.4, 52.1, 50.4, 43.2, 21.6. **HRMS**: calculated for [$C_{26}H_{27}NO_5S_2$ + Na^+]: 520.1223; found: 520.1229. **HPLC**: AD-H (*n*-hexane/iPrOH 60:40, flow-rate 0.75 mL/min; t_{maj} = 69.2 min; t_{min} = 85.2 min).

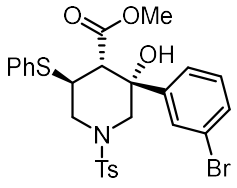
Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-(4-methoxyphenyl)-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3ea



3ea

Following the general procedure from substrate **1e** and thiophenol **2a**, product **3ea** (>20:1 dr in the crude mixture and after column chromatography) was obtained as a white solid in 57% yield (30.0 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 50:1). **[α]$_D^{25}$** = -13 (c = 0.9 in $CHCl_3$) for 67% *ee*. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.63 – 7.57 (m, 2H), 7.43 – 7.39 (m, 2H), 7.37 – 7.30 (m, 5H), 7.27 – 7.23 (m, 2H), 6.88 – 6.83 (m, 2H), 4.10 (ddd, *J* = 12.7, 4.4, 1.9 Hz, 1H) overlapped with 4.06 (bs, 1H), 3.80 (s, 3H), 3.76 (dd, *J* = 13.0, 1.8 Hz, 1H), 3.76 – 3.64 (m, 1H), 3.48 (s, 3H), 2.89 (d, *J* = 12.1 Hz, 1H), 2.54 (dd, *J* = 12.7, 11.5 Hz, 1H) overlapped with 2.50 (d, *J* = 13.0 Hz, 1H), 2.42 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 173.1, 159.3, 143.5, 134.6, 133.7, 132.9 (2C), 131.8, 129.6 (2C), 129.3 (2C), 128.2, 127.6 (2C), 126.4 (2C), 113.8 (2C), 73.0, 55.7, 55.2, 54.4, 52.1, 50.3, 43.2, 21.5. **HRMS**: calculated for [$C_{27}H_{29}NO_6S_2$ + Na^+]: 550.1329; found: 550.1333. **HPLC**: OD-H (*n*-hexane/iPrOH 90:10, flow-rate 1.00 mL/min; t_{maj} = 25.5 min; t_{min} = 38.6 min).

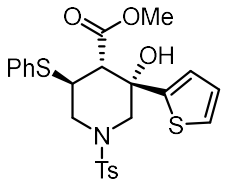
Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-(3-bromophenyl)-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3fa



3fa

Following the general procedure from substrate **1f** and thiophenol **2a**, product **3fa** (>20:1 dr in the crude mixture and after column chromatography) was obtained as a white solid in 65% yield (37.4 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 100:1). **[α]$_D^{25}$** = -13 (c = 1.0 in $CHCl_3$) for 59% *ee*. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.64 – 7.56 (m, 3H), 7.46 – 7.37 (m, 3H), 7.37 – 7.30 (m, 4H), 7.29 – 7.24 (m, 2H), 7.21 (t, *J* = 7.9 Hz, 1H), 4.12 (bs, 1H) overlapped with 4.11 (ddd, *J* = 12.8, 4.5, 1.8 Hz, 1H), 3.78 (dd, *J* = 13.1, 1.8 Hz, 1H), 3.67 (td, *J* = 11.8, 4.4 Hz, 1H), 3.49 (s, 3H), 2.87 (d, *J* = 12.1 Hz, 1H), 2.61 – 2.53 (m, 1H) overlapped with 2.53 (d, *J* = 13.0 Hz, 1H), 2.43 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 172.8, 144.0, 143.7, 134.6, 132.9 (2C), 131.6, 131.3, 130.0, 129.7 (2C), 129.3 (2C), 128.5, 128.4, 127.6 (2C), 123.8, 122.9, 73.1, 55.4, 54.1, 52.2, 50.3, 43.2, 21.6. **HRMS**: calculated for [$C_{26}H_{26}BrNO_5S_2$ + Na^+]: 598.0328 [M(^{79}Br) + Na^+], 600.0308 [M(^{81}Br) + Na^+]; found 598.0328 [M(^{79}Br) + Na^+], 600.0304 [M(^{81}Br) + Na^+]. **HPLC**: OD-H (*n*-hexane/iPrOH 90:10, flow-rate 1.00 mL/min; t_{maj} = 16.3 min; t_{min} = 20.4 min).

Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-(thiophen-2-yl)-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3ga

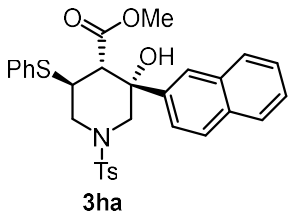


3ga

Following the general procedure from substrate **1g** and thiophenol **2a**, product **3ga** (>20:1 dr in the crude mixture and after column chromatography) was obtained as a white solid in 66% yield (33.2 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 100:1). **[α]$_D^{25}$** = -23 (c = 0.6 in CH_2Cl_2) for 67% *ee*. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.63 – 7.58 (m, 2H), 7.42 – 7.37 (m, 2H), 7.35 – 7.31 (m, 3H), 7.28 – 7.22 (m, 3H), 6.95 (dd, *J* = 5.0, 3.6 Hz, 1H), 6.92 (dd, *J* = 3.6, 1.3 Hz, 1H), 4.57 (very broad s, 1H), 4.07 (ddd, *J* = 12.8, 4.4, 1.9 Hz, 1H), 3.99 (dd, *J* = 13.0, 1.8 Hz, 1H), 3.60 (ddd, *J* = 12.5, 11.7, 4.6 Hz, 1H), 3.56 (s, 3H), 2.84 (d, *J* = 12.1 Hz, 1H), 2.57 (dd, *J* = 12.8, 11.5 Hz, 1H) overlapped with 2.57 (d, *J* = 13.1 Hz, 1H), 2.42 (s, 3H). **^{13}C NMR** (101

MHz, $CDCl_3$) δ = 173.1, 147.0, 143.6, 134.8, 132.9 (2C), 131.6, 129.6 (2C), 129.3 (2C), 128.3, 127.6 (2C), 127.1, 125.5, 123.6, 72.5, 56.2, 55.5, 52.3, 50.2, 43.0, 21.6. **HRMS**: calculated for [$C_{24}H_{25}NO_5S_3$ + Na^+]: 526.0787; found: 526.0793. **HPLC**: OD-H (*n*-hexane/iPrOH 90:10, flow-rate 1.00 mL/min; t_{maj} = 16.4 min; t_{min} = 26.1 min).

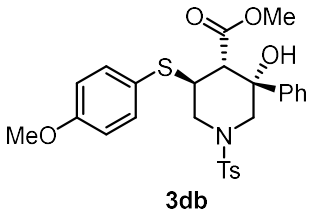
Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-(naphthalen-2-yl)-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3ha



3ha

Following the general procedure from substrate **1h** and thiophenol **2a**, product **3ha** (>20:1 dr in the crude mixture and after column chromatography) was obtained as a white solid in 87% yield (47.0 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 100:1). **[α]$_D^{25}$** = +15 (c = 1.0 in CH_2Cl_2) for 86% *ee*. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.98 (d, *J* = 1.9 Hz, 1H), 7.87 – 7.79 (m, 3H), 7.64 – 7.58 (m, 2H), 7.53 – 7.46 (m, 3H), 7.46 – 7.41 (m, 2H), 7.39 – 7.31 (m, 3H), 7.29 – 7.23 (m, 2H), 4.26 (bs, 1H), 4.15 (ddd, *J* = 12.7, 4.5, 1.8 Hz, 1H), 3.86 (dd, *J* = 13.0, 1.8 Hz, 1H), 3.77 (td, *J* = 11.7, 4.4 Hz, 1H), 3.40 (s, 3H), 3.08 (d, *J* = 12.1 Hz, 1H), 2.62 (dd, *J* = 12.8, 11.5 Hz, 1H) partially overlapped with 2.65 (d, *J* = 13.1 Hz, 1H), 2.43 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 173.1, 143.6, 139.0, 134.7, 133.0, 132.9 (3C), 131.8, 129.6 (2C), 129.3 (2C), 128.4, 128.3 (2C), 127.6 (2C), 127.5, 126.5, 126.4, 124.7, 122.8, 73.5, 55.5, 54.1, 52.1, 50.4, 43.3, 21.6. **HRMS**: calculated for [$C_{30}H_{29}NO_5S_2$ + Na^+]: 570.1379; found: 570.1385. **HPLC**: OD-H (*n*-hexane/iPrOH 90:10, flow-rate 1.00 mL/min; t_{min} = 34.3 min; t_{maj} = 50.1 min).

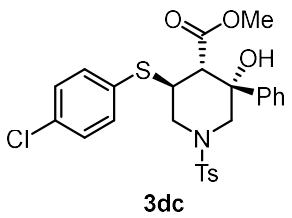
Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(4-methoxyphenylthio)-1-tosylpiperidine-4-carboxylate 3db



3db

Following the general procedure from substrate **1d** and 4-methoxythiophenol **2b**, product **3db** (>20:1 dr in the crude mixture and after column chromatography) was obtained as a white solid in 70% yield (36.9 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 50:1). **[α]$_D^{25}$** = -28 (c = 0.8 in $CHCl_3$) for 81% *ee*. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.62 – 7.56 (m, 2H), 7.42 – 7.36 (m, 4H), 7.36 – 7.27 (m, 3H), 7.27 – 7.23 (m, 2H), 6.91 – 6.84 (m, 2H), 4.09 (ddd, *J* = 12.6, 4.5, 1.8 Hz, 1H) partially overlapped with 4.03 (bs, 1H), 3.84 (s, 3H), 3.75 (dd, *J* = 12.9, 1.8 Hz, 1H), 3.50 (td, *J* = 11.6, 4.7 Hz, 1H) partially overlapped with 3.48 (s, 3H), 2.87 (d, *J* = 12.1 Hz, 1H), 2.52 (dd, *J* = 12.6, 11.6 Hz, 1H) partially overlapped with 2.51 (d, *J* = 13.0 Hz, 1H), 2.42 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 173.1, 160.3, 143.5, 141.6, 136.3 (2C), 134.6, 129.6 (2C), 128.5 (2C), 128.1, 127.6 (2C), 125.1 (2C), 121.4, 114.8 (2C), 73.3, 55.5, 55.4, 54.3, 52.0, 50.2, 43.8, 21.6. **HRMS**: calculated for [$C_{27}H_{29}NO_6S_2$ + Na^+]: 550.1329; found: 550.1326. **HPLC**: OD-H (*n*-hexane/iPrOH 90:10, flow-rate 1.00 mL/min; t_{maj} = 26.2 min; t_{min} = 27.7 min).

Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(4-chlorophenylthio)-1-tosylpiperidine-4-carboxylate 3dc

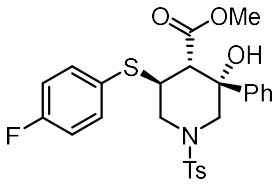


3dc

Following the general procedure from substrate **1d** and 4-chlorothiophenol **2c**, product **3dc** (>20:1 dr in the crude mixture and after column chromatography) was obtained as a white solid in 57% yield (30.4 mg) after column chromatography on silica gel

(CH_2Cl_2/Et_2O = 50:1). **[α]D25** = -3 (c = 1.0 in $CHCl_3$) for 89% *ee*. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.63 – 7.58 (m, 2H), 7.45 – 7.39 (m, 2H), 7.37 – 7.28 (m, 7H), 7.28 – 7.24 (m, 2H), 4.06 (ddd, *J* = 12.6, 4.4, 1.9 Hz, 1H) overlapped with 4.05 (very broad s, 1H), 3.80 (dd, *J* = 13.0, 1.8 Hz, 1H), 3.66 (td, *J* = 11.6, 4.7 Hz, 1H), 3.45 (s, 3H), 2.90 (d, *J* = 12.1 Hz, 1H), 2.57 (d, *J* = 13.1 Hz, 1H), 2.55 (dd, *J* = 12.8, 11.4 Hz, 1H) 2.43 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 172.9, 143.7, 141.4, 134.6, 134.5, 134.3 (2C), 130.2, 129.6 (2C), 129.5 (2C), 128.5 (2C), 128.2, 127.6 (2C), 125.1 (2C), 73.3, 55.4, 54.4, 52.1, 50.2, 43.5, 21.6. **HRMS**: calculated for [$C_{26}H_{26}ClNO_5S_2$ + Na^+]: 554.0833 [M(^{35}Cl) + Na^+], 556.0804 [M(^{37}Cl) + Na^+]; found 554.0831 [M(^{35}Cl) + Na^+], 556.0804 [M(^{37}Cl) + Na^+]. **HPLC**: OD-H (*n*-hexane/iPrOH 90:10, flow-rate 1.00 mL/min; t_{maj} = 15.2 min; t_{min} = 23.2 min).

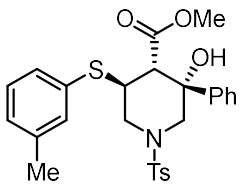
Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(4-fluorophenylthio)-1-tosylpiperidine-4-carboxylate 3dd



3dd

Following the general procedure from substrate **1d** and 4-fluorothiophenol **2d**, product **3dd** (>20:1 dr in the crude mixture and after column chromatography) was obtained as a white solid in 74% yield (38.1 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 100:1). **[α]D25** = -6 (c = 0.3 in $CHCl_3$) for 91% *ee*. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.63 – 7.57 (m, 2H), 7.46 – 7.39 (m, 4H), 7.38 – 7.28 (m, 3H), 7.28 – 7.24 (m, 2H), 7.08 – 7.00 (m, 2H), 4.07 (ddd, *J* = 12.6, 4.5, 1.8 Hz, 1H) overlapped with 4.07 (bs, 1H), 3.78 (dd, *J* = 12.9, 1.8 Hz, 1H), 3.60 (td, *J* = 11.7, 4.4 Hz, 1H), 3.46 (s, 3H), 2.89 (d, *J* = 12.1 Hz, 1H), 2.54 (d, *J* = 13.0 Hz, 1H), 2.53 (dd, *J* = 12.6, 11.6 Hz, 1H), 2.43 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 171.9, 162.0 (d, *J* = 249.4 Hz), 142.6, 140.5, 134.9 (d, *J* = 8.4 Hz, 2C), 133.5, 128.6 (2C), 127.5 (2C), 127.2, 126.6 (2C), 125.6 (d, *J* = 3.4 Hz), 124.0 (2C), 115.4 (d, *J* = 22.0 Hz, 2C), 72.3, 54.4, 53.4, 51.1, 49.2, 42.9, 20.5. **HRMS**: calculated for [$C_{26}H_{26}FNO_5S_2$ + Na^+]: 538.1129; found: 538.1134. **HPLC**: OD-H (*n*-hexane/iPrOH 90:10, flow-rate 1.00 mL/min; t_{maj} = 15.2 min; t_{min} = 21.0 min).

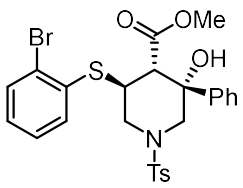
Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(3-methylphenylthio)-1-tosylpiperidine-4-carboxylate 3de



3de

Following the general procedure from substrate **1d** and 3-methylthiophenol **2e**, product **3de** (>20:1 dr in the crude mixture and after column chromatography) was obtained as a white solid in 71% yield (36.3 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 70:1). **[α]D25** = -29 (c = 1.0 in $CHCl_3$) for 91% *ee*. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.63 – 7.57 (m, 2H), 7.47 – 7.40 (m, 2H), 7.37 – 7.28 (m, 3H), 7.28 – 7.18 (m, 5H), 7.16 – 7.10 (m, 1H), 4.12 (ddd, *J* = 12.6, 4.5, 1.9 Hz, 1H) overlapped with 4.10 (very broad s, 1H) 3.80 (dd, *J* = 13.0, 1.8 Hz, 1H), 3.72 (td, *J* = 11.8, 4.5 Hz, 1H), 3.44 (s, 3H), 2.91 (d, *J* = 12.1 Hz, 1H), 2.56 (dd, *J* = 12.6, 11.6 Hz, 1H) overlapped with 2.56 (d, *J* = 12.9 Hz, 1H), 2.42 (s, 3H), 2.36 (d, *J* = 0.7 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 173.0, 143.5, 141.6, 139.1, 134.6, 133.4, 131.5, 129.8, 129.6 (2C), 129.09, 129.08, 128.5 (2C), 128.1, 127.6 (2C), 125.1 (2C), 73.3, 55.5, 54.3, 52.0, 50.4, 43.1, 21.5, 21.3. **HRMS**: calculated for [$C_{27}H_{29}NO_5S_2$ + Na^+]: 534.1379; found: 534.1383. **HPLC**: OD-H (*n*-hexane/iPrOH 90:10, flow-rate 1.00 mL/min; t_{maj} = 14.9 min; t_{min} = 22.9 min).

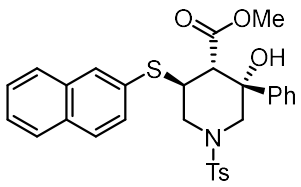
Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(2-bromophenylthio)-1-tosylpiperidine-4-carboxylate 3df



3df

Following the general procedure (but running the reaction at room temperature and for 18 h) from substrate **1d** and 2-bromothiophenol **2f**, product **3df** (>20:1 dr in the crude mixture and after column chromatography) was obtained as a white solid in 68% yield (39.2 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 70:1). **[α]D^{25}** = -20 (c = 1.0 in $CHCl_3$) for 71% *ee*. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.64 – 7.59 (m, 3H), 7.48 – 7.42 (m, 3H), 7.38 – 7.29 (m, 4H), 7.29 – 7.24 (m, 2H), 7.19 – 7.12 (m, 1H), 4.18 (bs, 1H), 4.11 (ddd, *J* = 12.8, 4.4, 1.8 Hz, 1H) partially overlapped with 3.90 (td, *J* = 11.5, 4.6 Hz, 1H), 3.85 (dd, *J* = 13.0, 1.8 Hz, 1H), 3.44 (s, 3H), 3.00 (d, *J* = 12.1 Hz, 1H), 2.65 (dd, *J* = 12.8, 11.4 Hz, 1H) overlapped with 2.61 (d, *J* = 13.0 Hz, 1H), 2.43 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 172.8, 143.7, 141.5, 134.5, 133.7, 133.5, 132.3, 129.7 (2C), 129.0, 128.5 (2C), 128.3, 128.2, 127.6 (2C), 126.6, 125.1 (2C), 73.4, 55.6, 53.8, 52.2, 50.2, 42.7, 21.6. **HRMS**: calculated for [$C_{26}H_{26}BrNO_5S_2$ + Na^+]: 598.0328 [M(^{79}Br) + Na^+], 600.0308 [M(^{81}Br) + Na^+]; found 598.0329 [M(^{79}Br) + Na^+], 600.0303 [M(^{81}Br) + Na^+]. **HPLC**: OD-H (*n*-hexane/iPrOH 90:10, flow-rate 1.00 mL/min; t_{maj} = 23.5 min; t_{min} = 40.9 min).

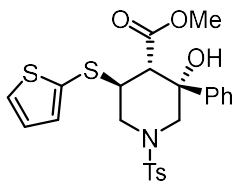
Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(naphthalen-2-ylthio)-1-tosylpiperidine-4-carboxylate 3dg



3dg

Following the general procedure from substrate **1d** and 2-naphthalenethiol **2g**, product **3dg** (>20:1 dr in the crude mixture and after column chromatography) was obtained as a white solid in 84% yield (45.9 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 50:1). **[α]D^{25}** = -34 (c = 0.6 in $CHCl_3$) for 94% *ee*. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.95 – 7.90 (m, 1H), 7.88 – 7.77 (m, 3H), 7.58 – 7.50 (m, 4H), 7.49 – 7.41 (m, 3H), 7.37 – 7.27 (m, 3H), 7.18 – 7.12 (m, 2H), 4.15 (ddd, *J* = 12.7, 4.4, 1.8 Hz, 1H) overlapped with 4.15 (very broad s, 1H), 3.91 – 3.74 (m, 2H), 3.46 (s, 3H), 2.97 (d, *J* = 12.1 Hz, 1H), 2.62 (dd, *J* = 12.8, 11.5 Hz, 1H) partially overlapped with 2.58 (d, *J* = 13.1 Hz, 1H), 2.37 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 173.1, 143.5, 141.6, 134.6, 133.6, 132.7, 132.1, 129.7, 129.5 (2C), 128.97, 128.96, 128.5 (2C), 128.1, 127.7, 127.62, 127.56 (2C), 126.80, 126.76, 125.1 (2C), 73.4, 55.5, 54.4, 52.1, 50.4, 43.2, 21.5. **HRMS**: calculated for [$C_{30}H_{29}NO_5S_2$ + Na^+]: 570.1379; found: 570.1385. **HPLC**: OD-H (*n*-hexane/iPrOH 90:10, flow-rate 1.00 mL/min; t_{maj} = 21.7 min; t_{min} = 27.5 min).

Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(thiophen-2-ylthio)-1-tosylpiperidine-4-carboxylate 3dh

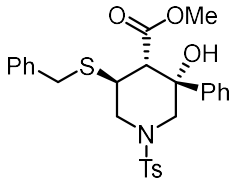


3dh

Following the general procedure from substrate **1d** and 2-thiophenethiol **2h**, product **3dh** (>20:1 dr in the crude mixture and after column chromatography) was obtained as a white solid in 71% (35.7 mg) yield after column chromatography on silica gel (CH_2Cl_2/Et_2O = 50:1). **[α]D^{25}** = -18 (c = 0.3 in $CHCl_3$) for 83% *ee*. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.65 – 7.60 (m, 2H), 7.46 (dd, *J* = 5.4, 1.2 Hz, 1H), 7.41 – 7.37 (m, 2H), 7.36 – 7.26 (m, 5H), 7.20 (dd, *J* = 3.6, 1.3 Hz, 1H), 7.05 (dd, *J* = 5.4, 3.6 Hz, 1H), 4.20 (ddd, *J* = 12.5, 4.4, 1.8 Hz, 1H), 4.03 (d, *J* = 2.3 Hz, 1H), 3.74 (dd, *J* = 12.9,

1.9 Hz, 1H), 3.52 (s, 3H), 3.44 (td, *J* = 11.7, 4.4 Hz, 1H), 2.93 (d, *J* = 12.0 Hz, 1H), 2.56 (dd, *J* = 12.6, 11.6 Hz, 1H), 2.48 (dd, *J* = 13.0, 2.4 Hz, 1H), 2.42 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 171.8, 142.6, 140.6, 136.3, 133.6, 130.7, 128.6 (2C), 127.5 (2C), 127.1, 127.0, 126.9, 126.6 (2C), 124.0 (2C), 72.4, 54.4, 53.0, 51.1, 48.9, 43.0, 20.5. **HRMS**: calculated for [$C_{24}H_{25}NO_5S_3$ + Na^+]: 526.0787; found: 526.0793. **HPLC**: OD-H (*n*-hexane/iPrOH 90:10, flow-rate 1.00 mL/min; t_{maj} = 21.1 min; t_{min} = 25.0 min).

Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(benzylthio)-1-tosylpiperidine-4-carboxylate 3di

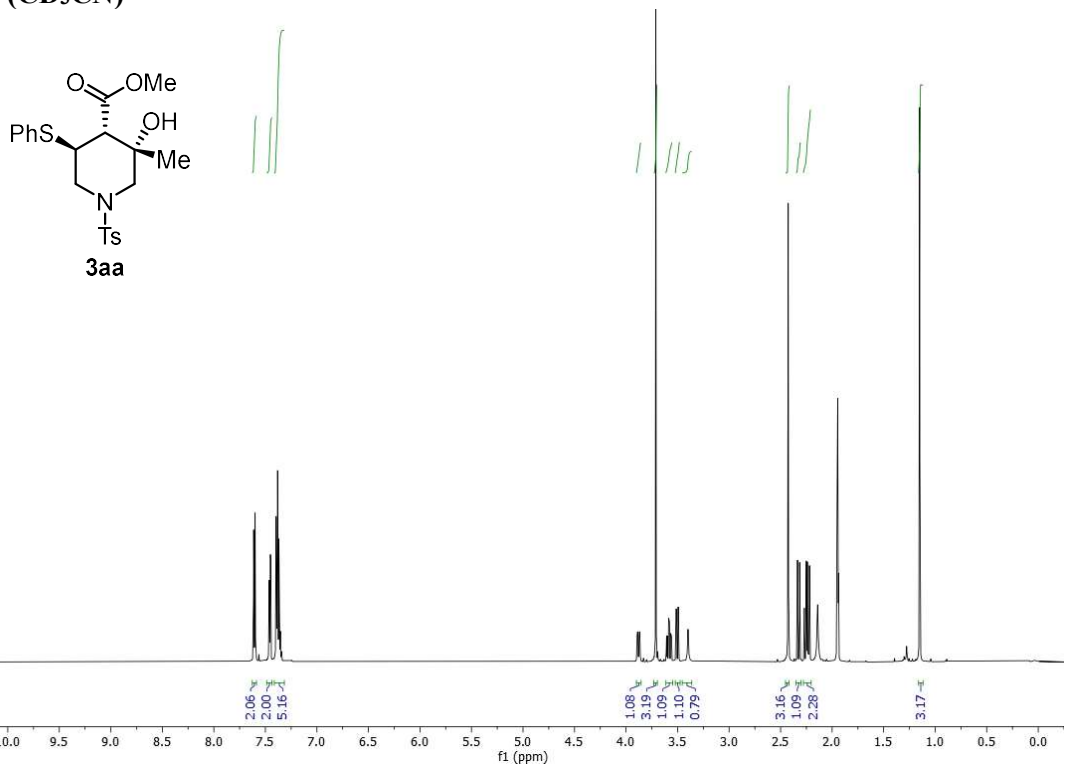


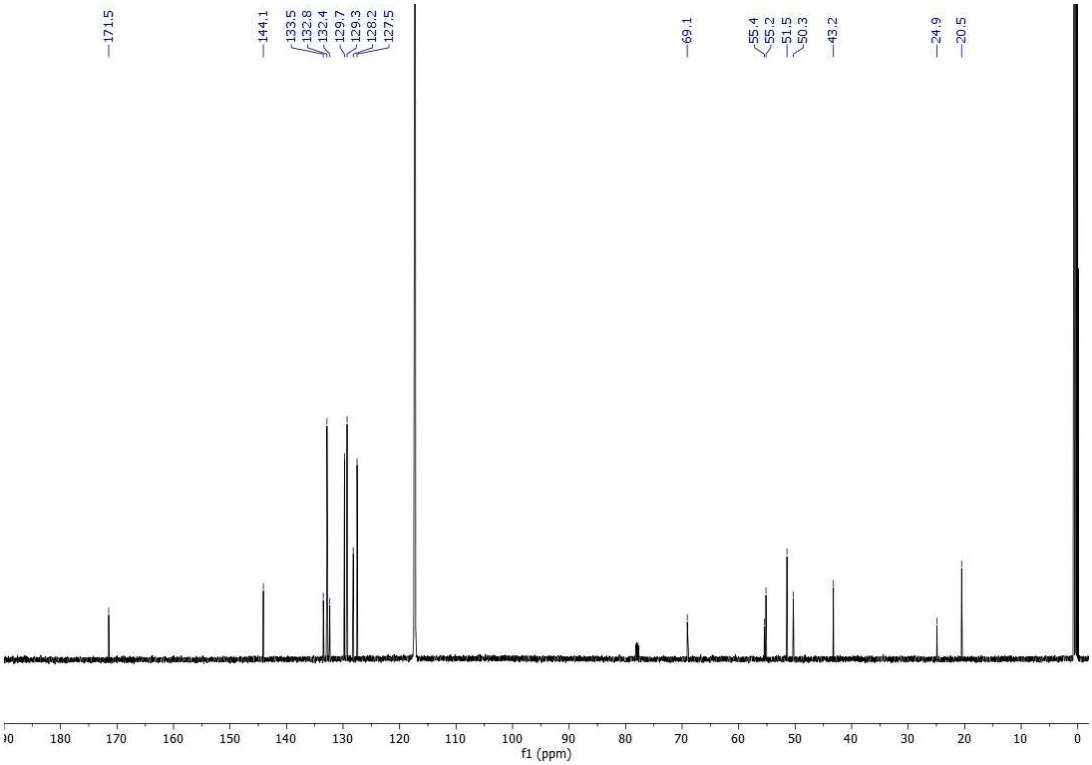
3di

Following the general procedure from substrate **1d** and benzylthiol **2i**, product **3di** (>20:1 dr in the crude mixture and after column chromatography) was obtained as a white solid in 67% yield (34.2 mg) after column chromatography on silica gel (CH_2Cl_2/Et_2O = 100:1). **[α]$_D^{25}$** = -4 (c = 1.0 in $CHCl_3$) for 37% *ee*. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 7.59 – 7.55 (m, 2H), 7.43 – 7.37 (m, 2H), 7.36 – 7.31 (m, 3H), 7.31 – 7.25 (m, 7H), 4.02 (ddd, *J* = 12.4, 4.5, 1.8 Hz, 1H), 3.80 (d, *J* = 13.7 Hz, 1H) overlapped with 3.80 (bs, 1H), 3.79 (d, *J* = 13.7 Hz,1H), 3.73 (dd, *J* = 12.7, 1.9 Hz, 1H), 3.40 (s, 3H) overlapped with 3.44 – 3.35 (m, 1H), 2.83 (d, *J* = 12.2 Hz, 1H), 2.47 (d, *J* = 12.7 Hz, 1H), 2.43 (s, 3H), 2.41 – 2.36 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 172.8, 143.6, 141.6, 137.5, 134.3, 129.7 (2C), 128.8 (2C), 128.7 (2C), 128.4 (2C), 128.1, 127.5 (2C), 127.4, 125.1 (2C), 73.1, 55.5, 54.7, 52.0, 50.7, 40.2, 36.3, 21.6. **HRMS**: calculated for [$C_{27}H_{29}NO_5S_2$ + Na^+]: 534.1379; found: 534.1377. **HPLC**: AS-H (*n*-hexane/iPrOH 90:10, flow-rate 1.00 mL/min; t_{maj} = 12.3 min; t_{min} = 34.7 min).

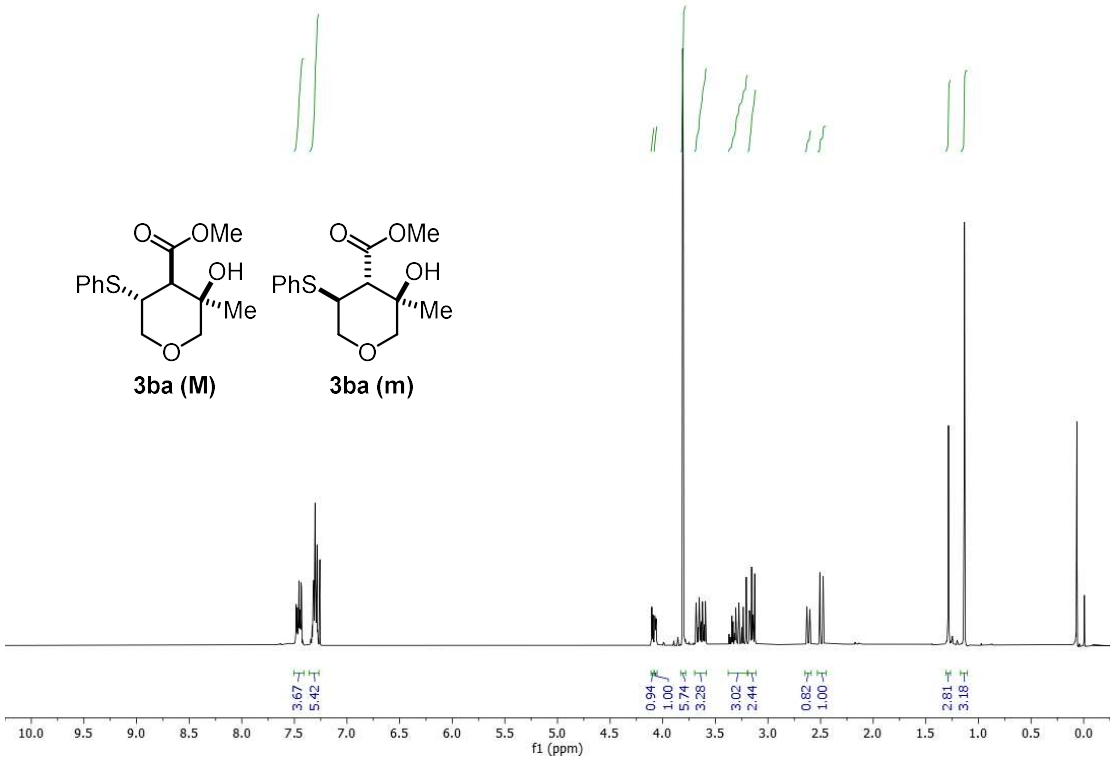
Copies of ^{1}H and ^{13}C NMR spectra of products 3, 4 and 5

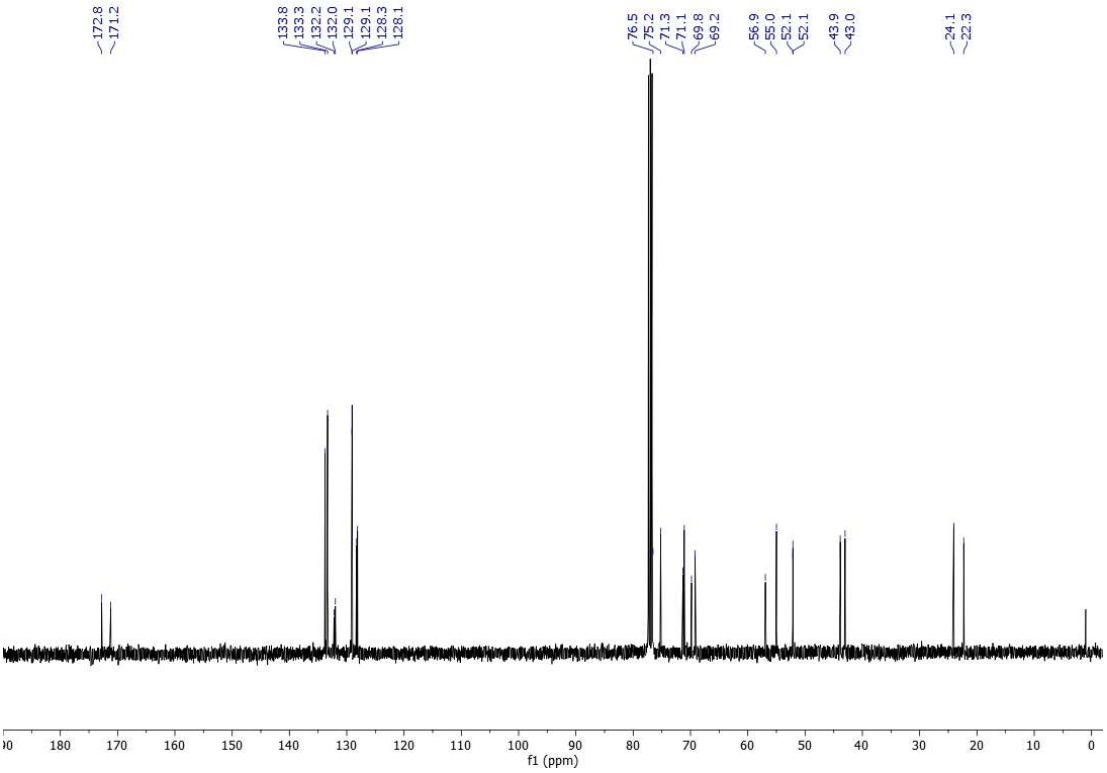
Methyl (3*S*,4*S*,5*S*)-3-hydroxy-3-methyl-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3aa (CD_3CN)



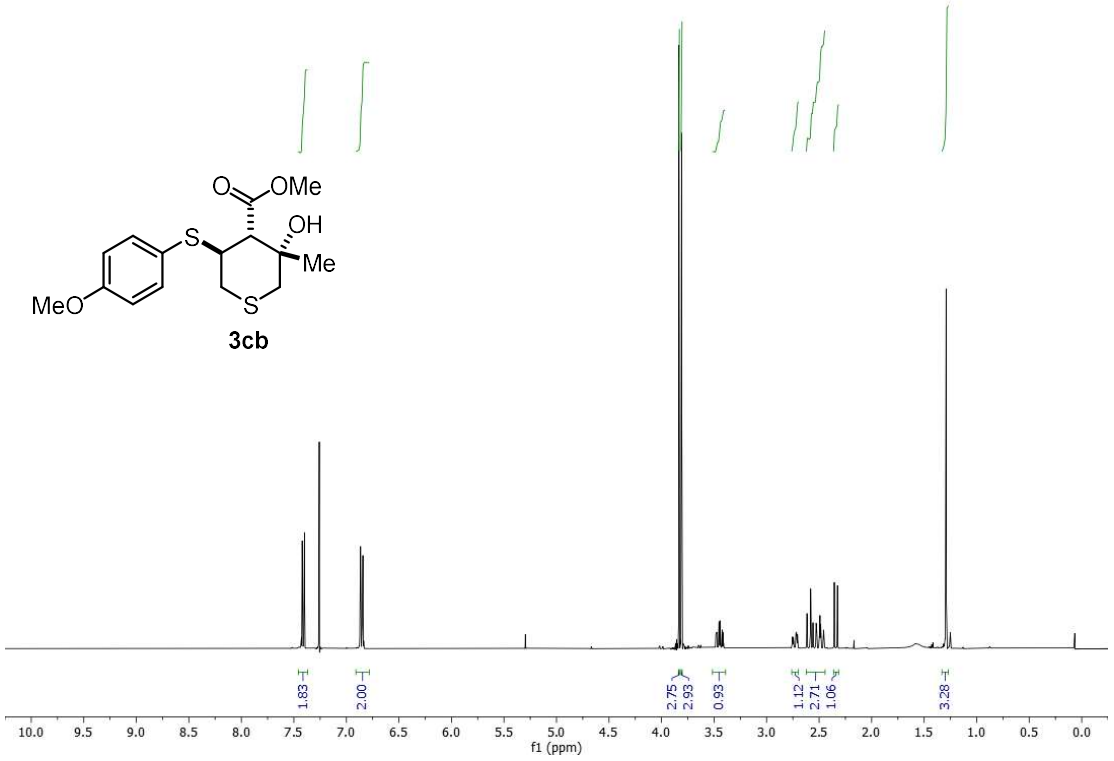


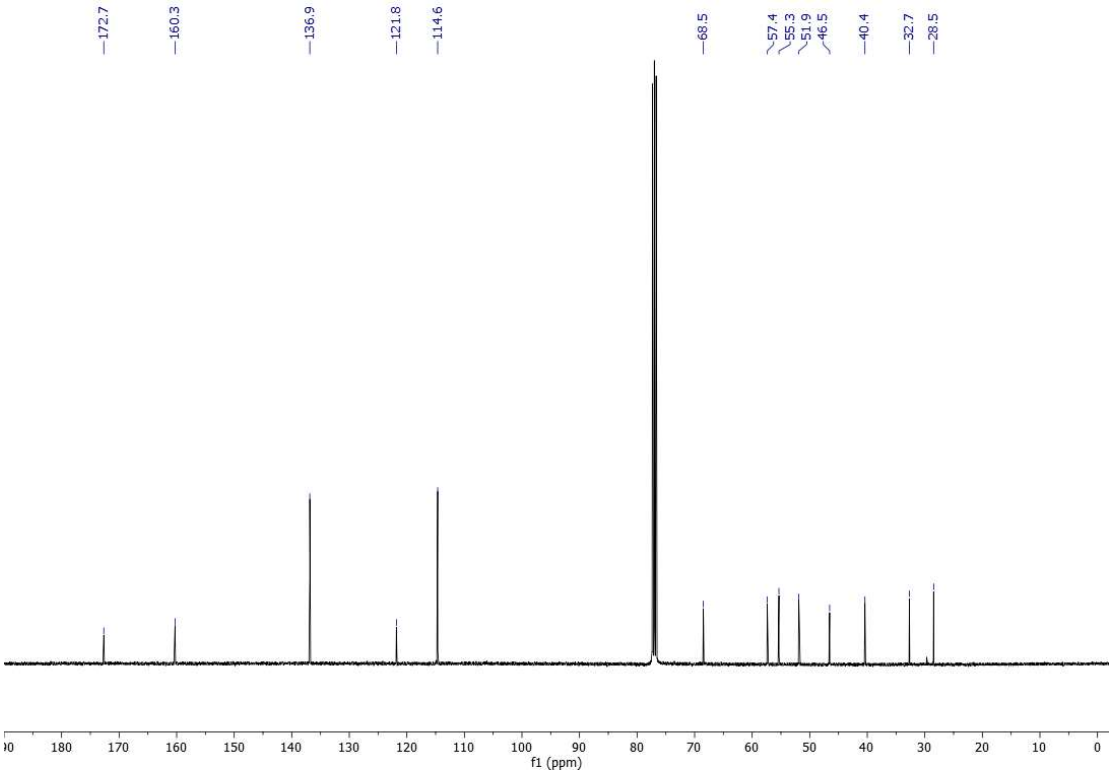
Methyl (3*R,4*R**,5*R**) and (3*R**,4*S**,5*S**)-3-hydroxy-3-methyl-5-(phenylthio)tetrahydro-*2H*-pyran-4-carboxylate 3ba ($CDCl_3$)**



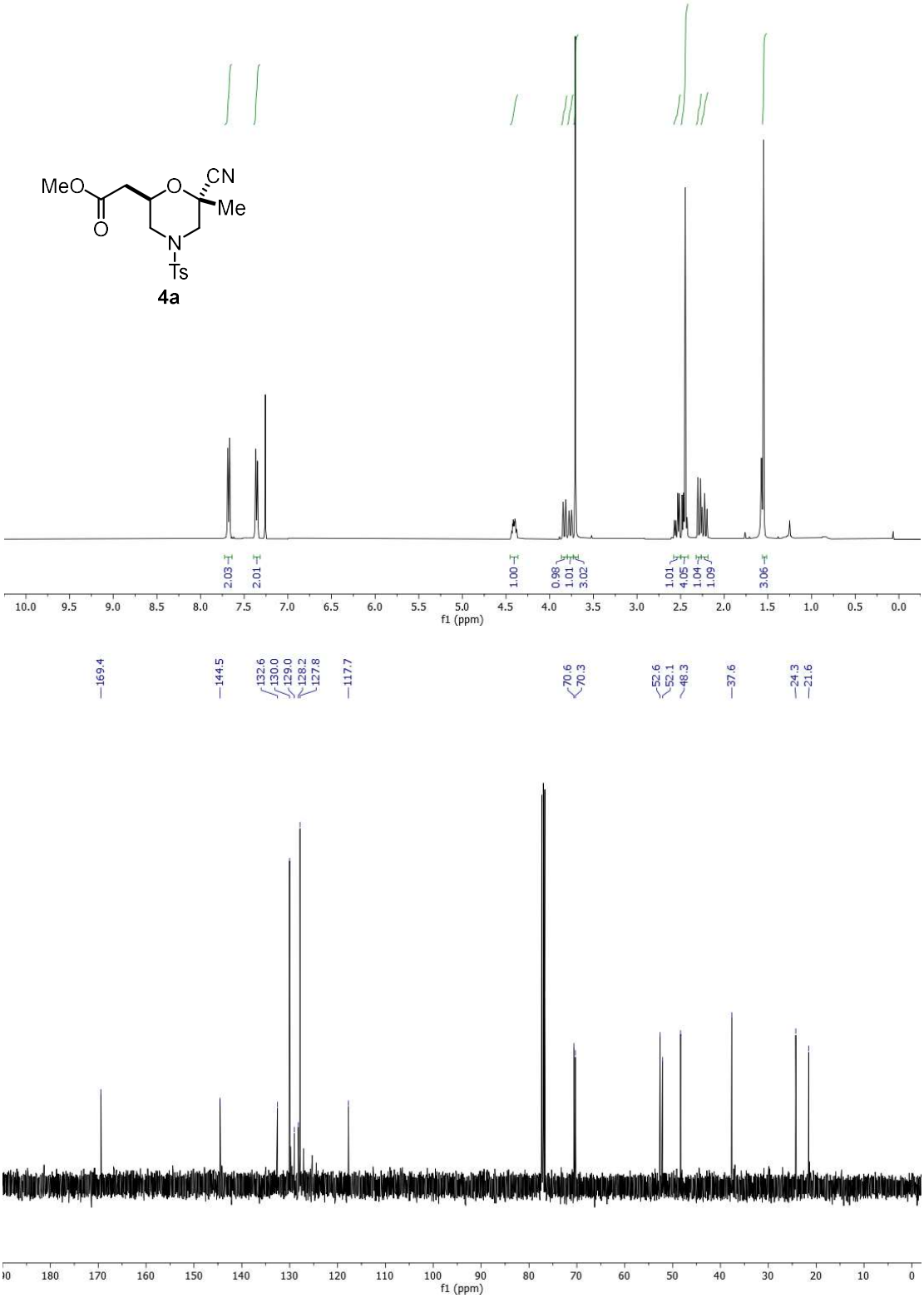


Methyl (3*R,4*R**,5*R**)-3-hydroxy-3-methyl-5-(4-methoxyphenylthio)tetrahydro-*2H*-thiopyran-4-carboxylate 3cb ($CDCl_3$)**

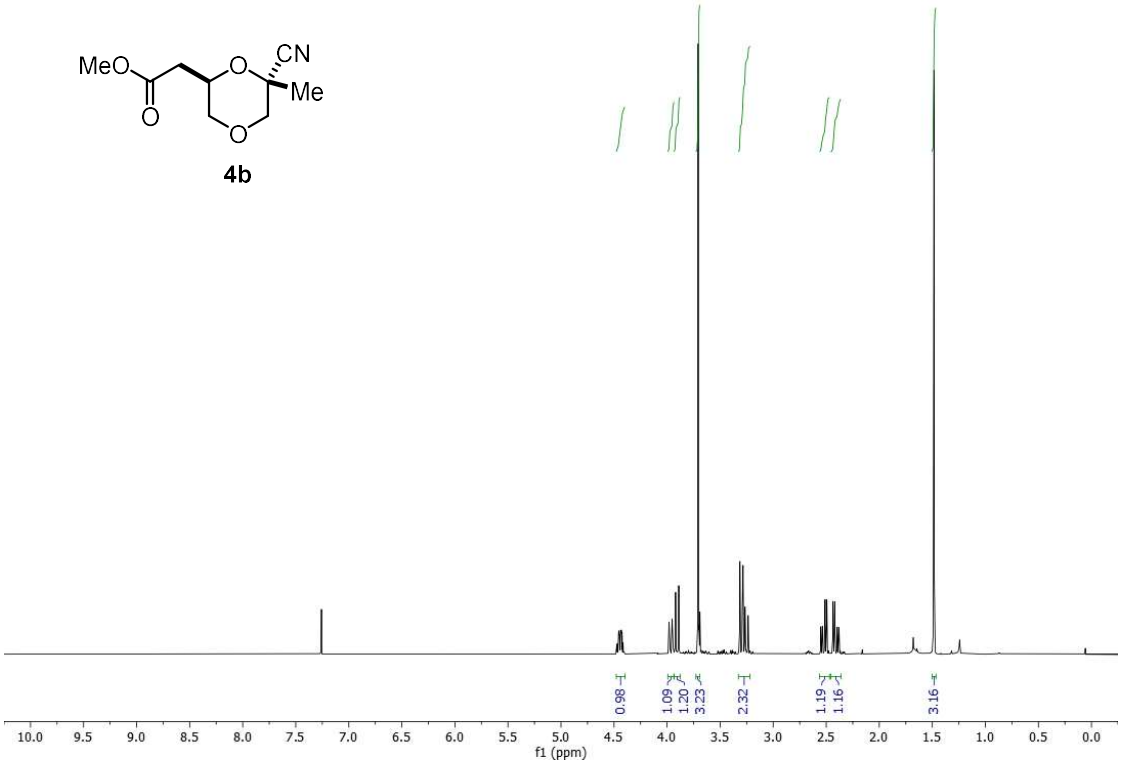


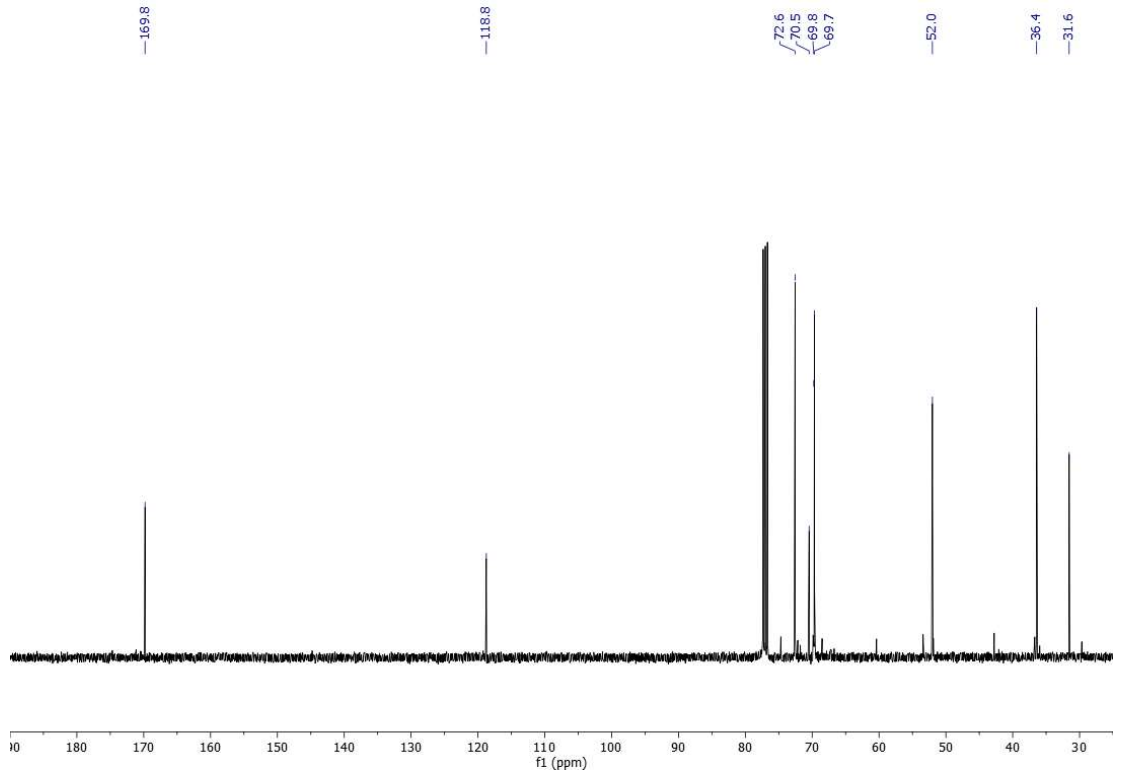


Methyl (2*R,6*S**)-2-(6-cyano-6-methyl-4-tosylmorpholin-2-yl)acetate 4a ($CDCl_3$)**

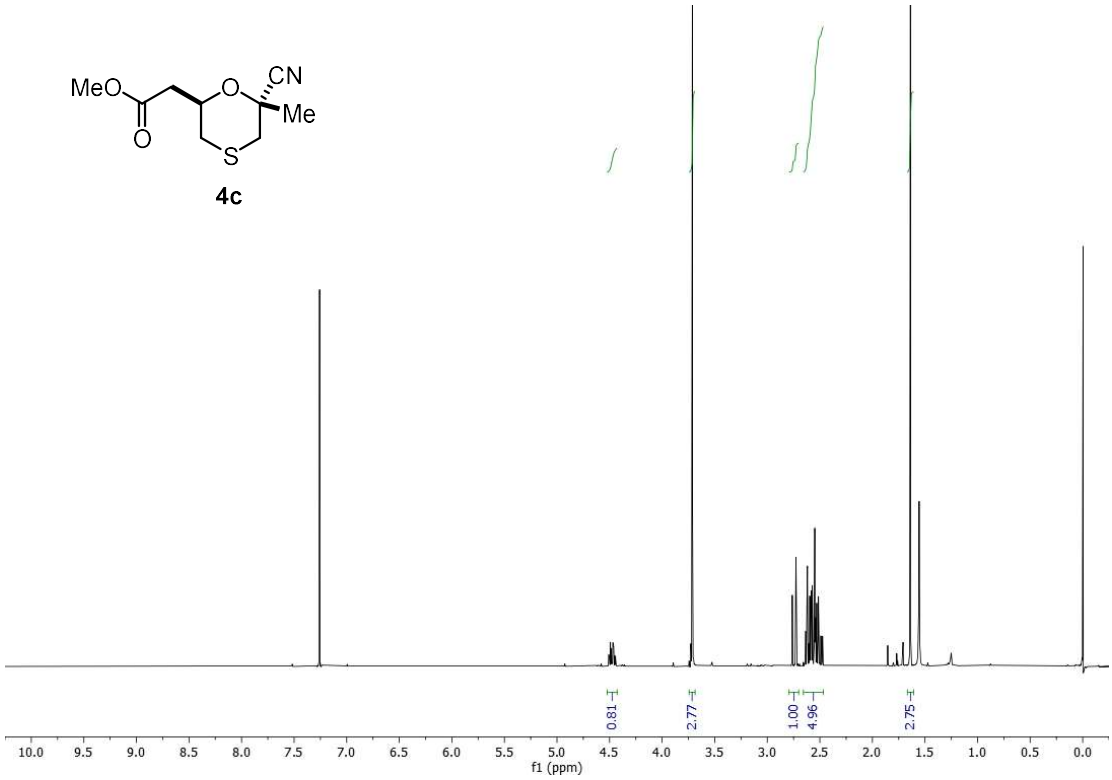


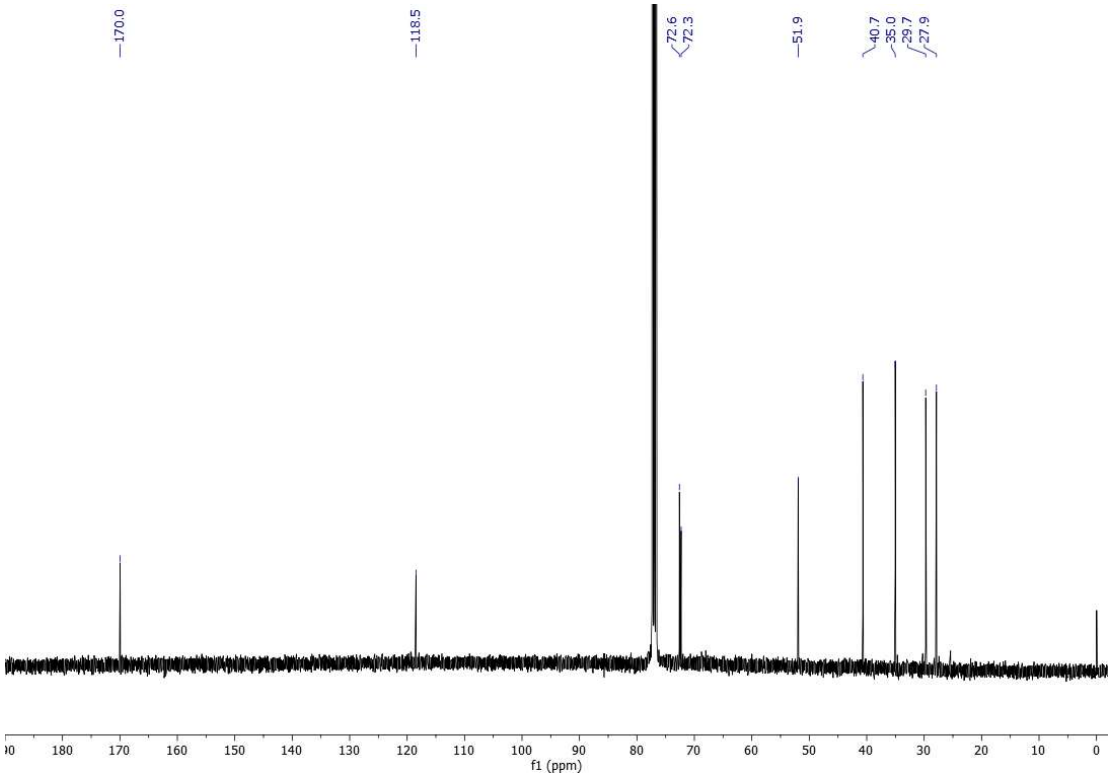
Methyl (2*R,6*R**)-2-(6-cyano-6-methyl-1,4-dioxan-2-yl)acetate 4b ($CDCl_3$)**



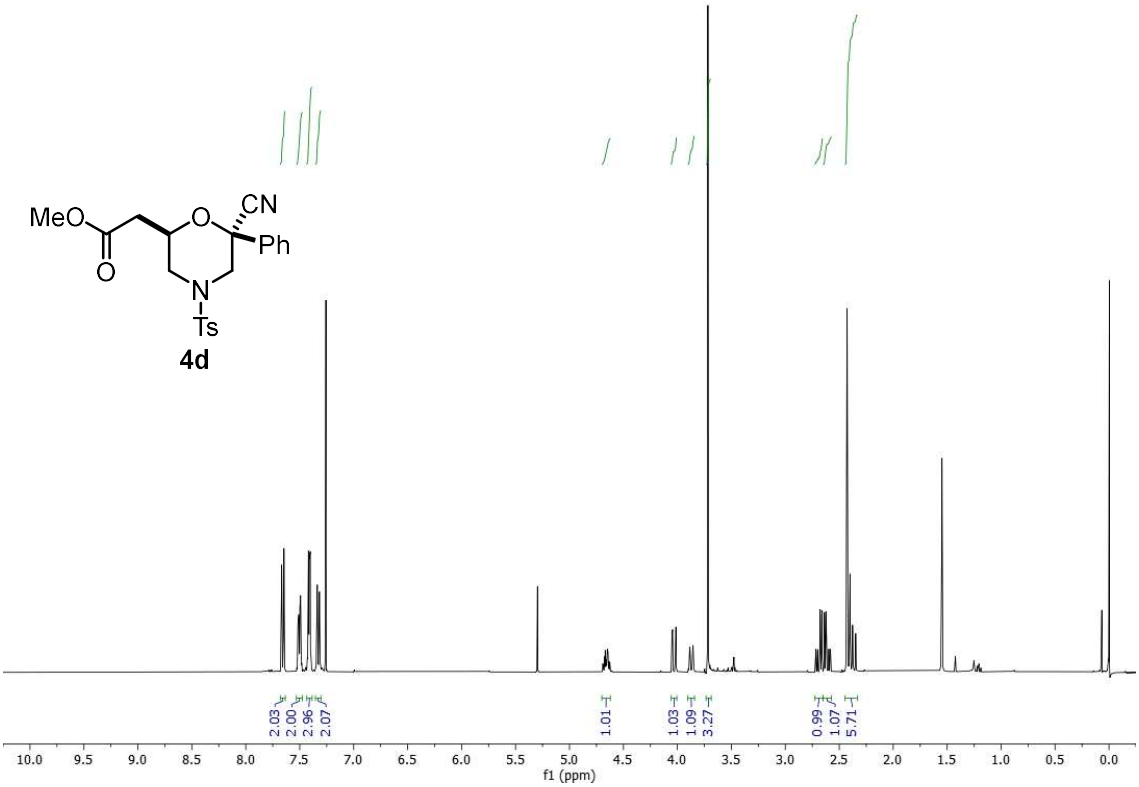


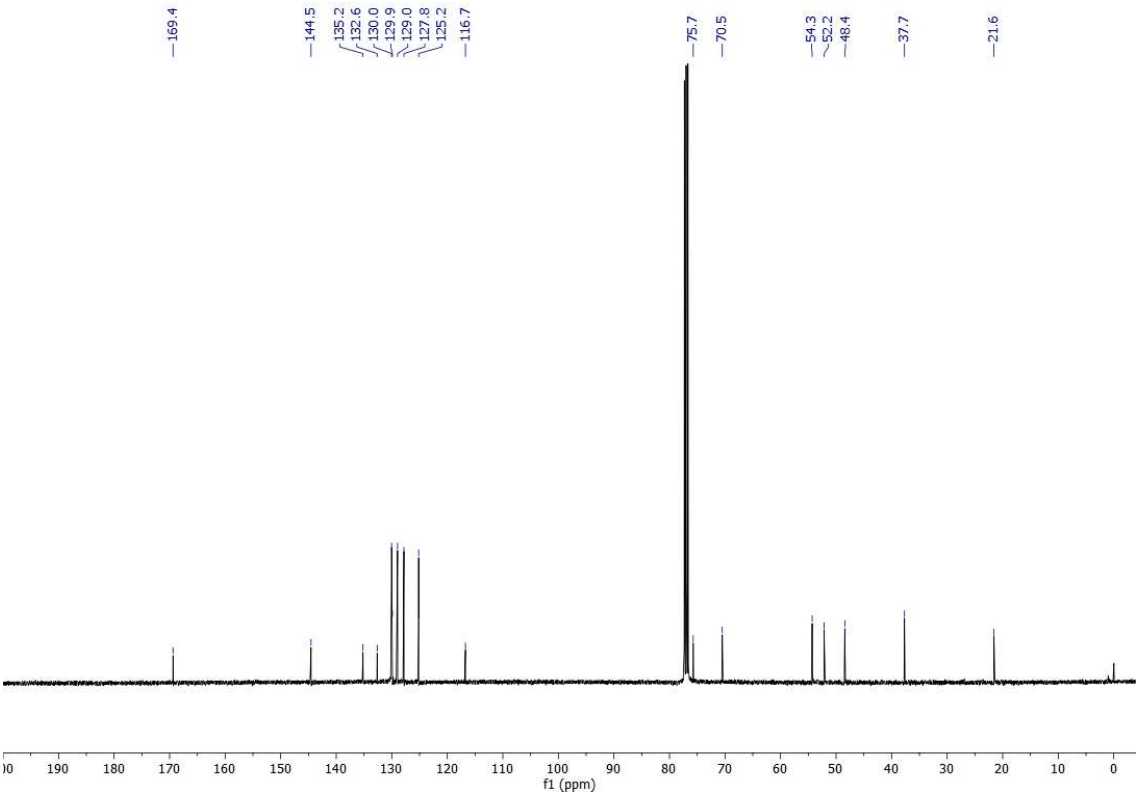
Methyl (2*R,6*R**)-2-(6-cyano-6-methyl-1,4-oxathian-2-yl)acetate 4c ($CDCl_3$)**



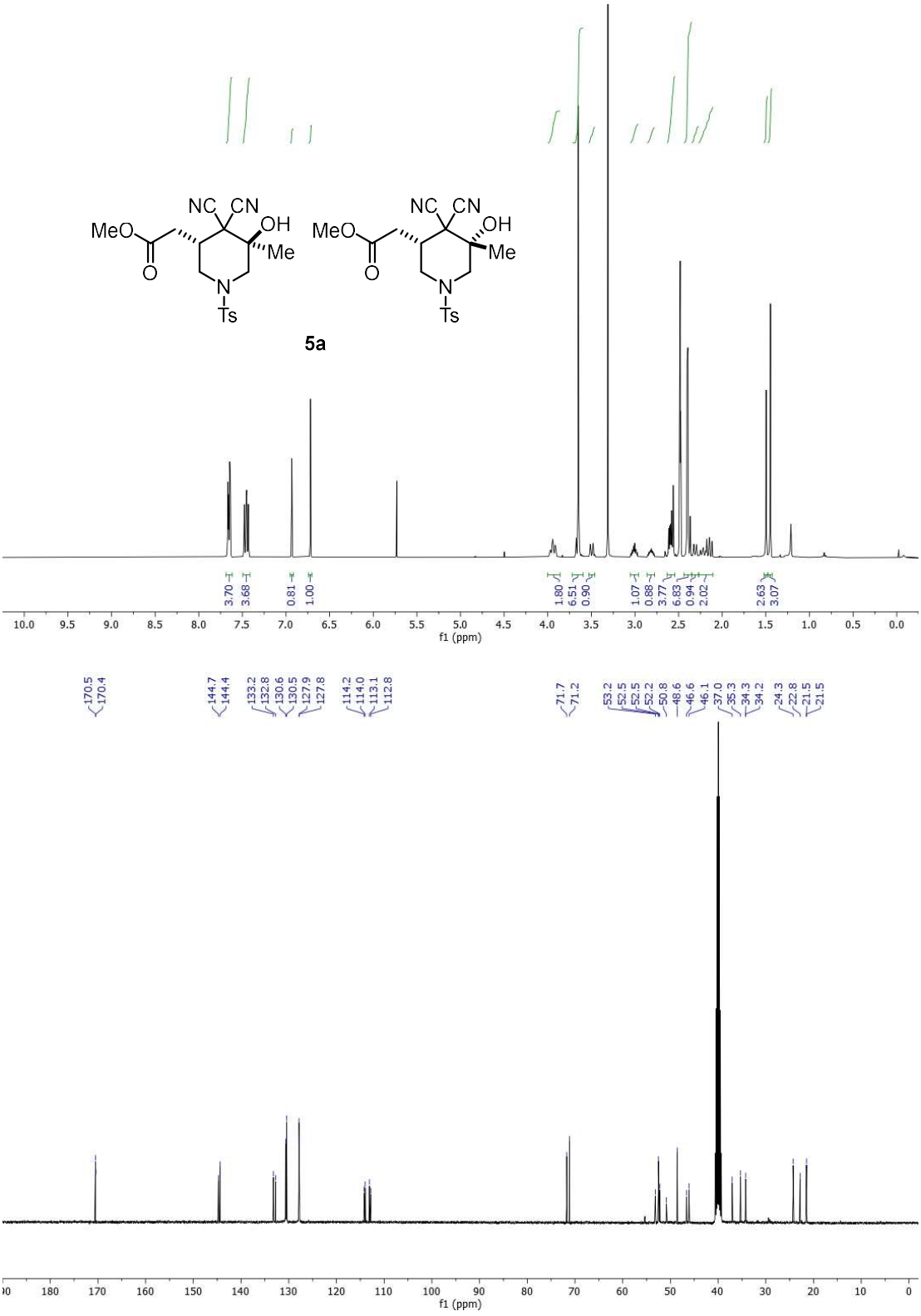


Methyl (2*R,6*S**)-2-(6-cyano-6-phenyl-4-tosylmorpholin-2-yl)acetate 4d**

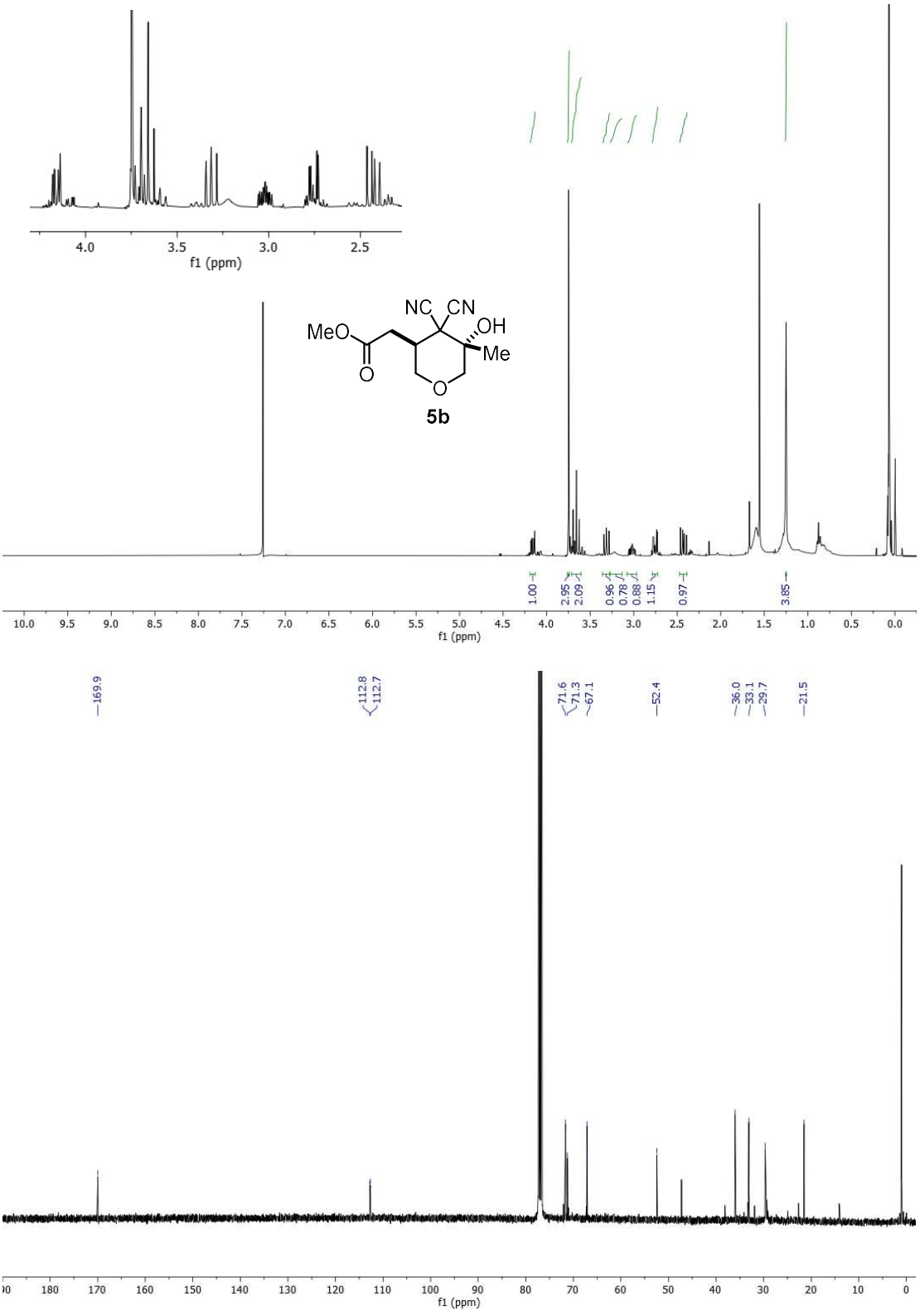




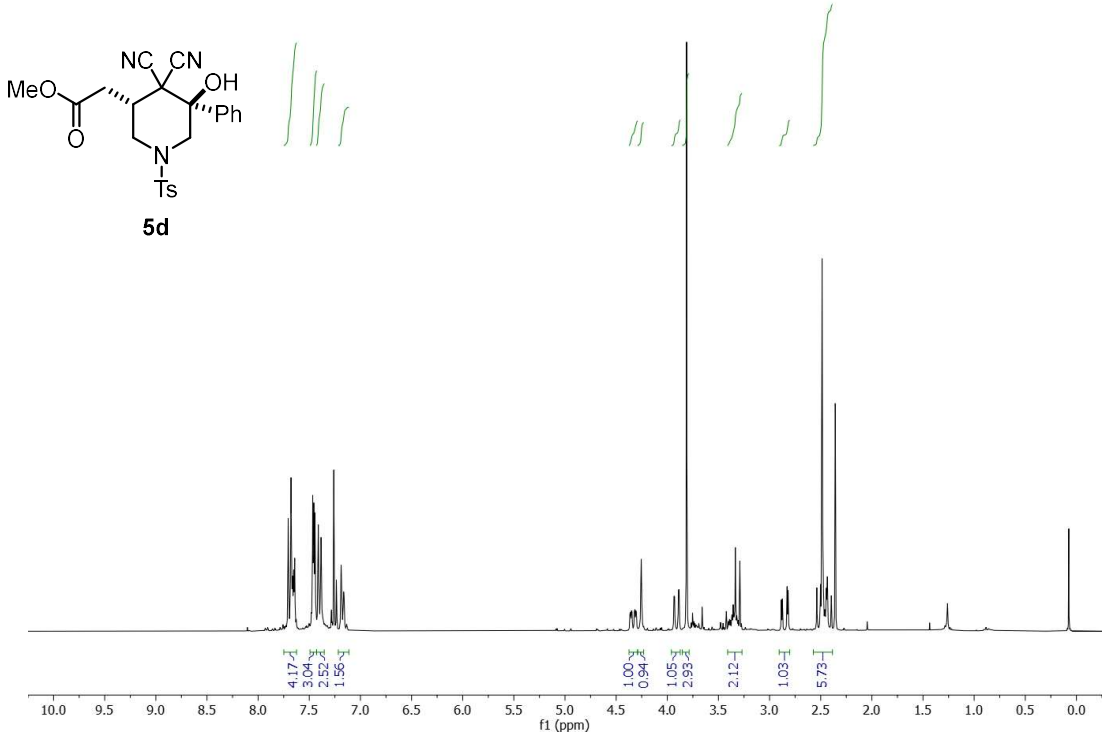
Methyl (3*R,5*R**)- and (3*R**,5*S**)-2-(4,4-dicyano-5-hydroxy-5-methyl-1-tosylpiperidin-3-yl)acetate 5a (DMSO-d_6)**



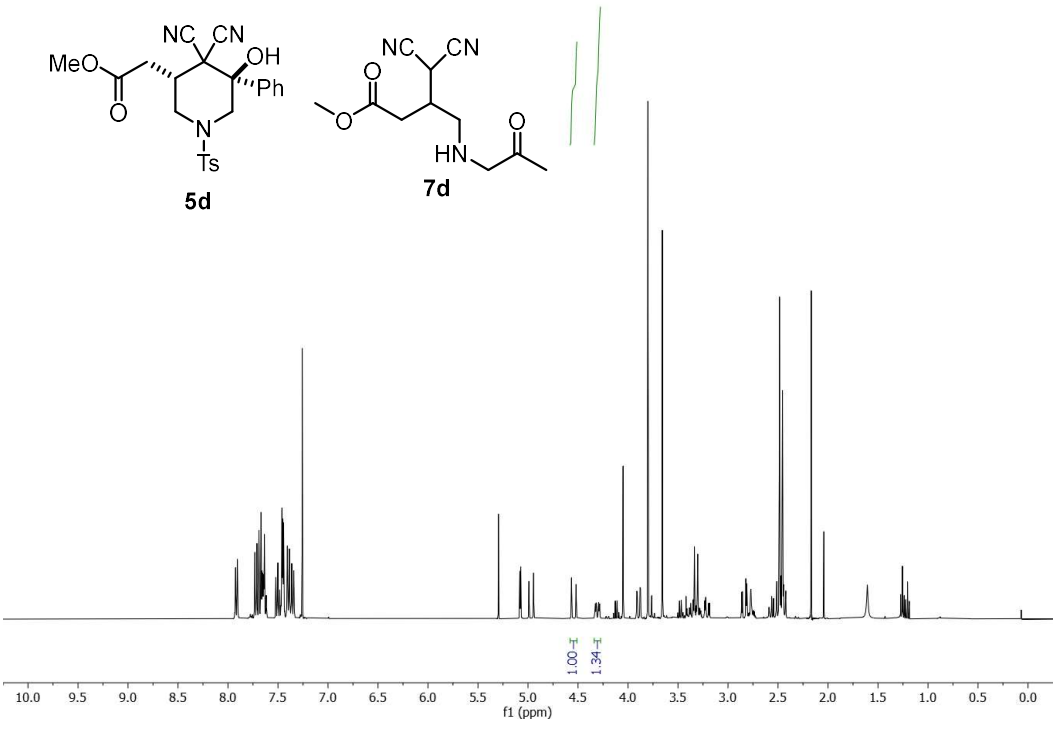
Methyl (3*R,5*R**)-2-(4,4-dicyano-5-hydroxy-5-methyltetrahydro-2*H*-pyran-3-yl)acetate 5b ($CDCl_3$)**



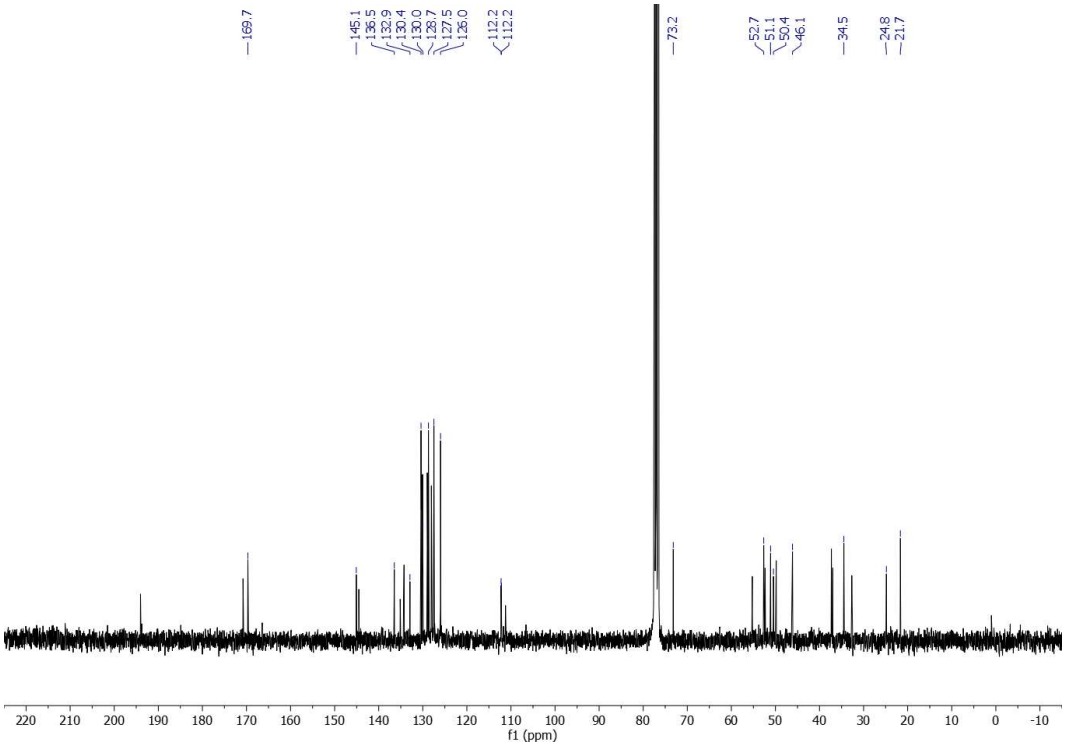
Methyl (3*R,5*R**)-2-(4,4-dicyano-5-hydroxy-5-phenyl-1-tosylpiperidin-3-yl)acetate 5d (¹H NMR crude)**



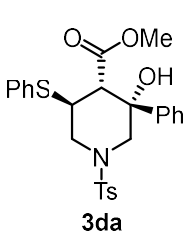
Methyl (3*R,5*R**)-2-(4,4-dicyano-5-hydroxy-5-phenyl-1-tosylpiperidin-3-yl)acetate 5d and methyl 4,4-dicyano-3-(((2-oxopropyl)amino)methyl)butanoate 7d (¹H NMR after column chromatography)**



Methyl (3*R,5*R**)-2-(4,4-dicyano-5-hydroxy-5-phenyl-1-tosylpiperidin-3-yl)acetate 5d and methyl 4,4-dicyano-3-(((2-oxopropyl)amino)methyl)butanoate 7d (^{13}C NMR after column chromatography)**

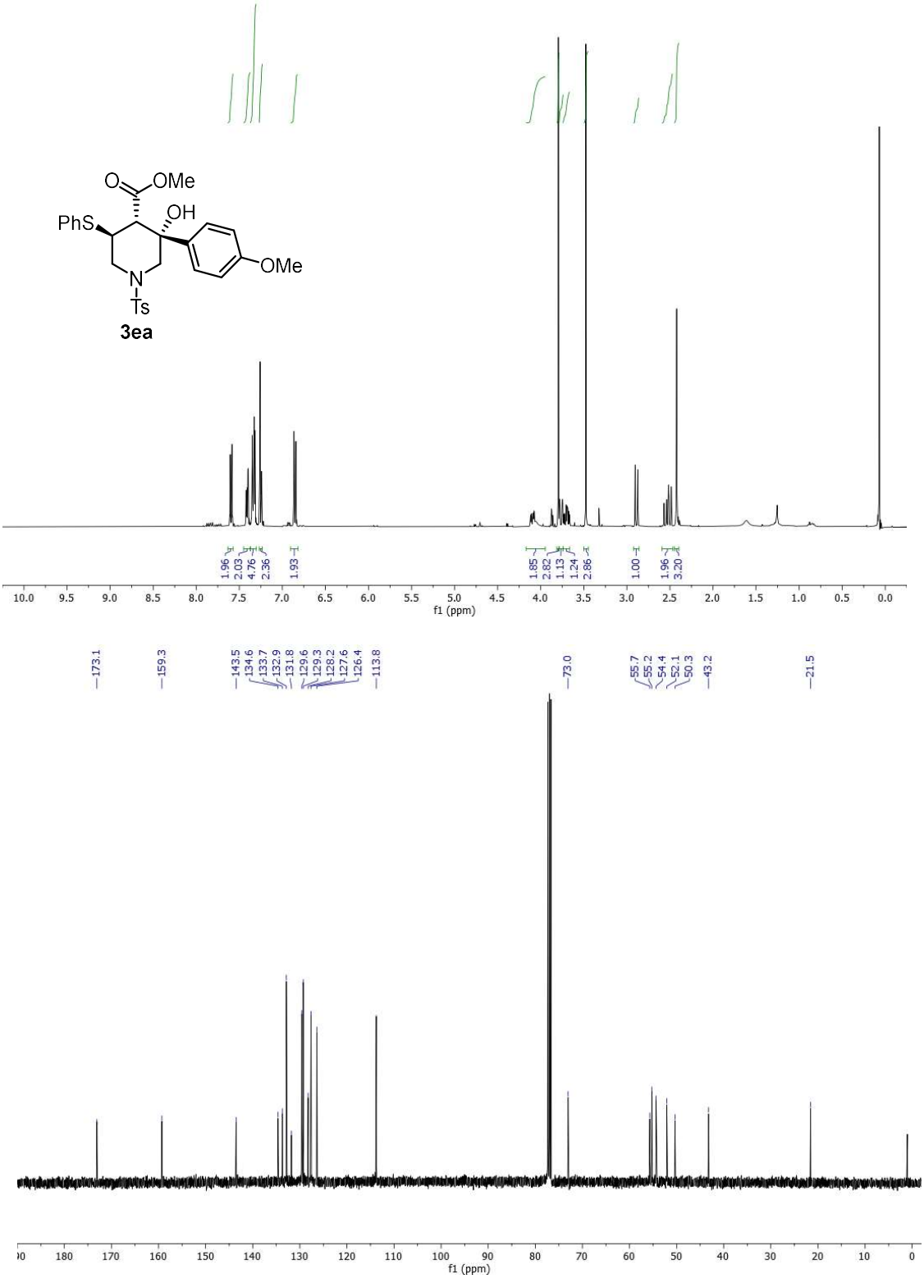


Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3da ($CDCl_3$)

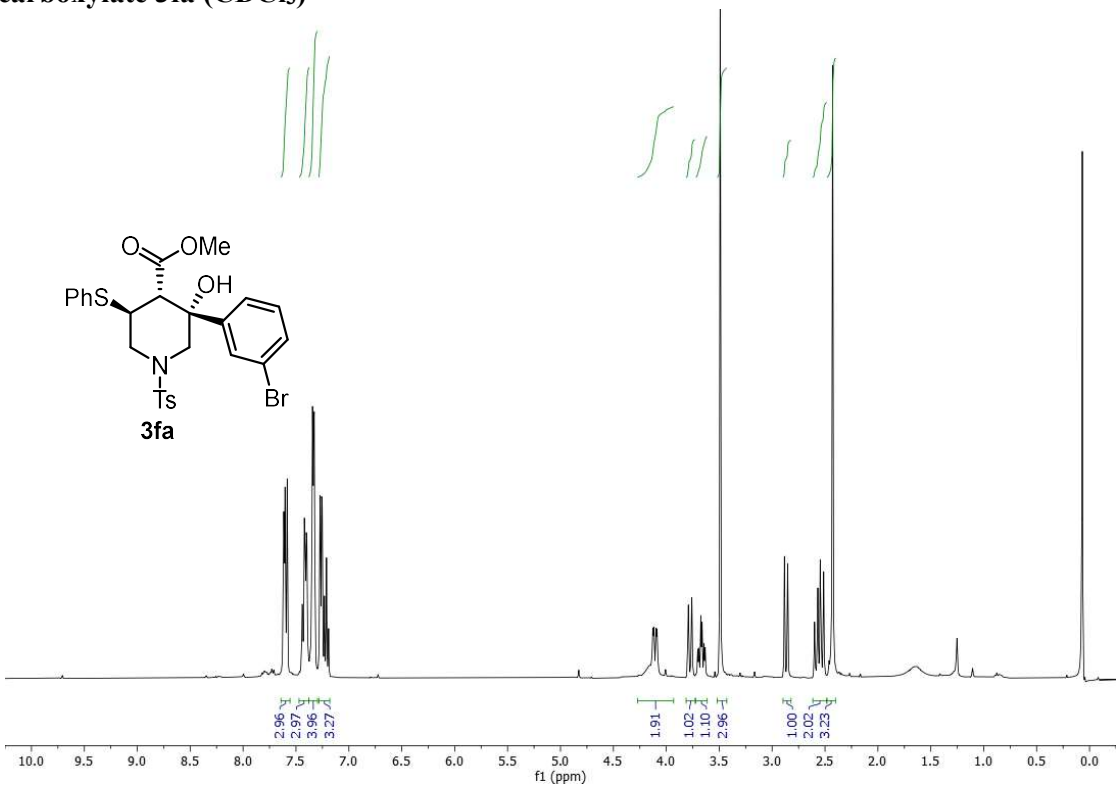


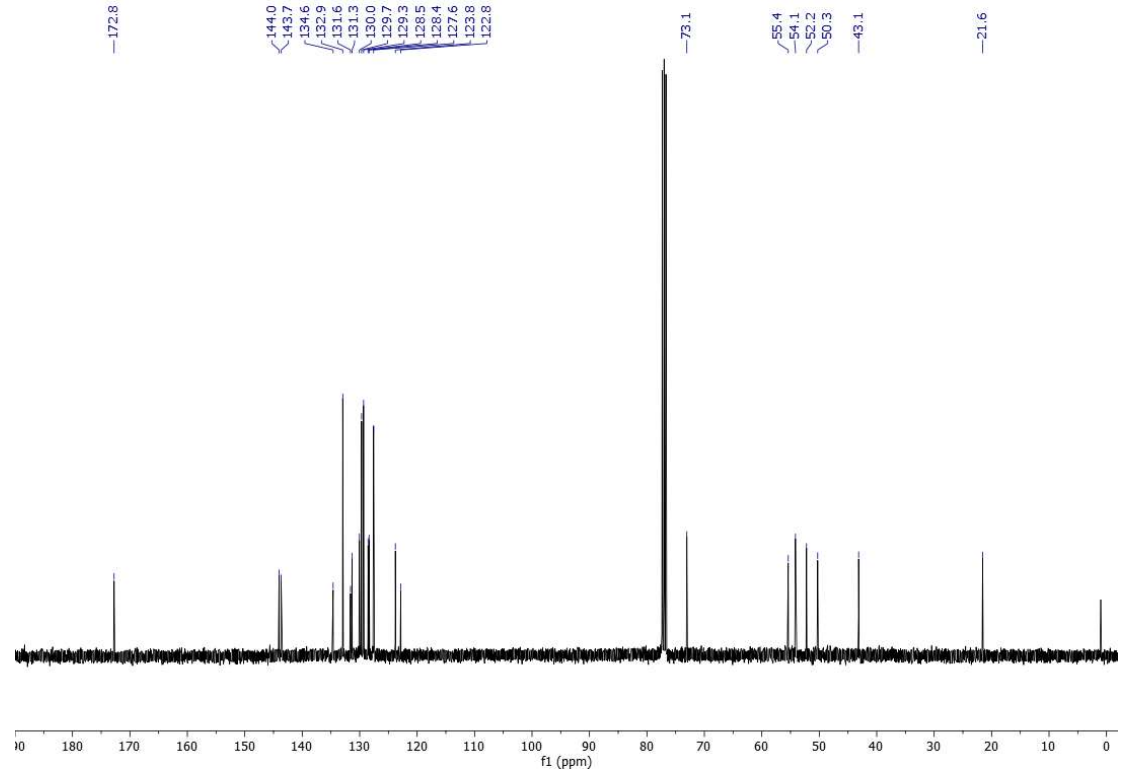
3da

Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-(4-methoxyphenyl)-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3ea ($CDCl_3$)

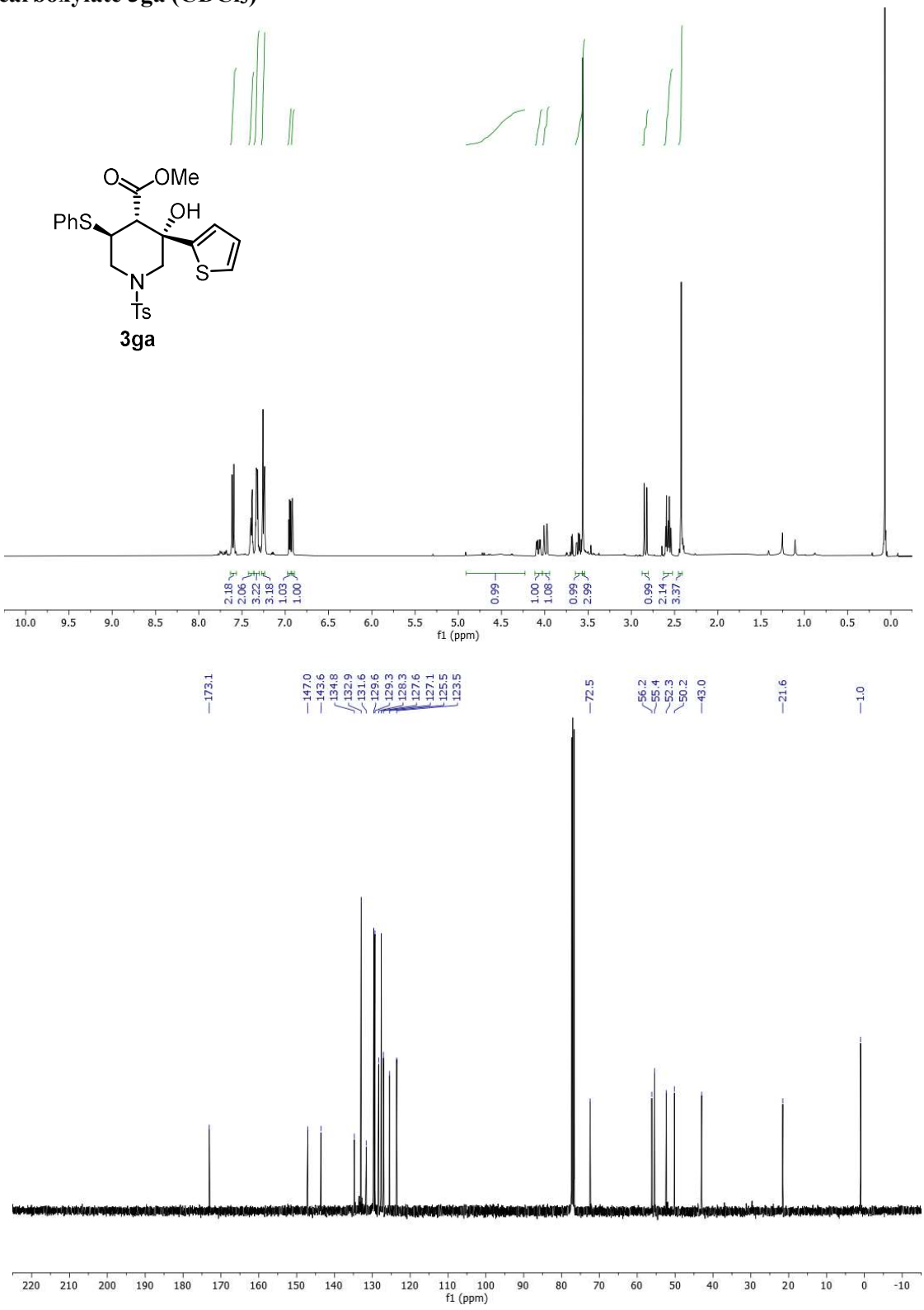


Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-(3-bromophenyl)-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3fa ($CDCl_3$)

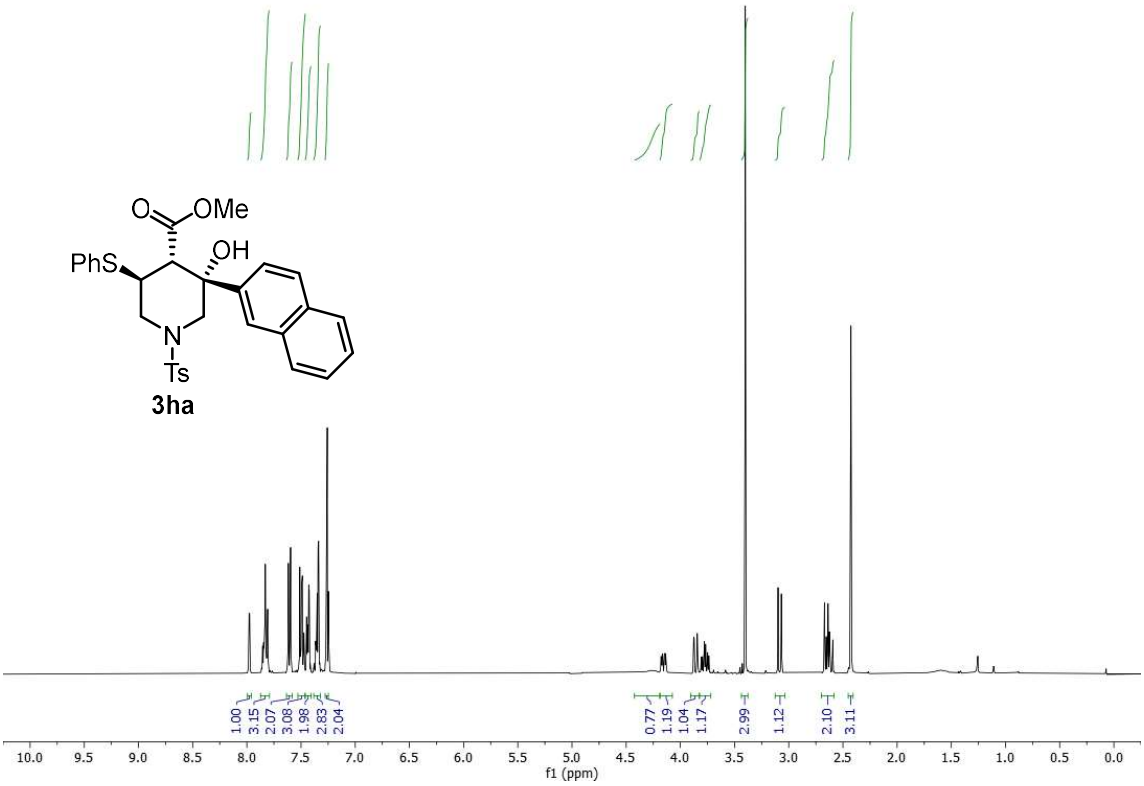


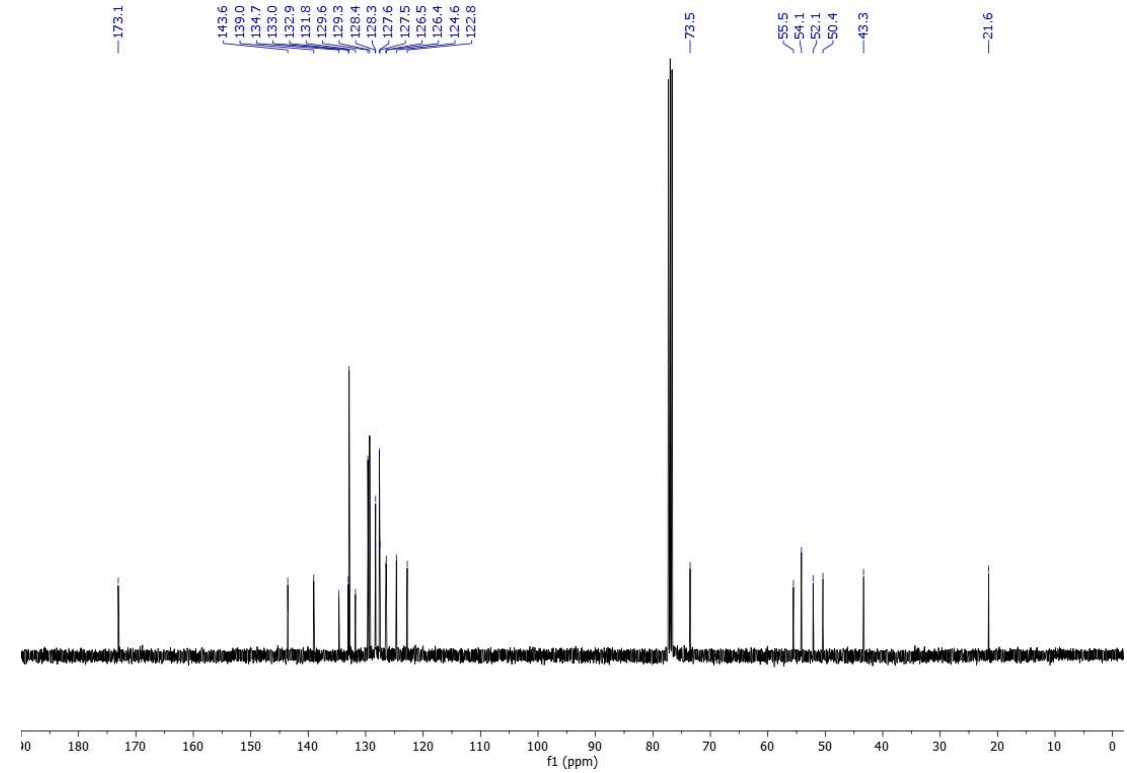


Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-(thiophen-2-yl)-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3ga ($CDCl_3$)

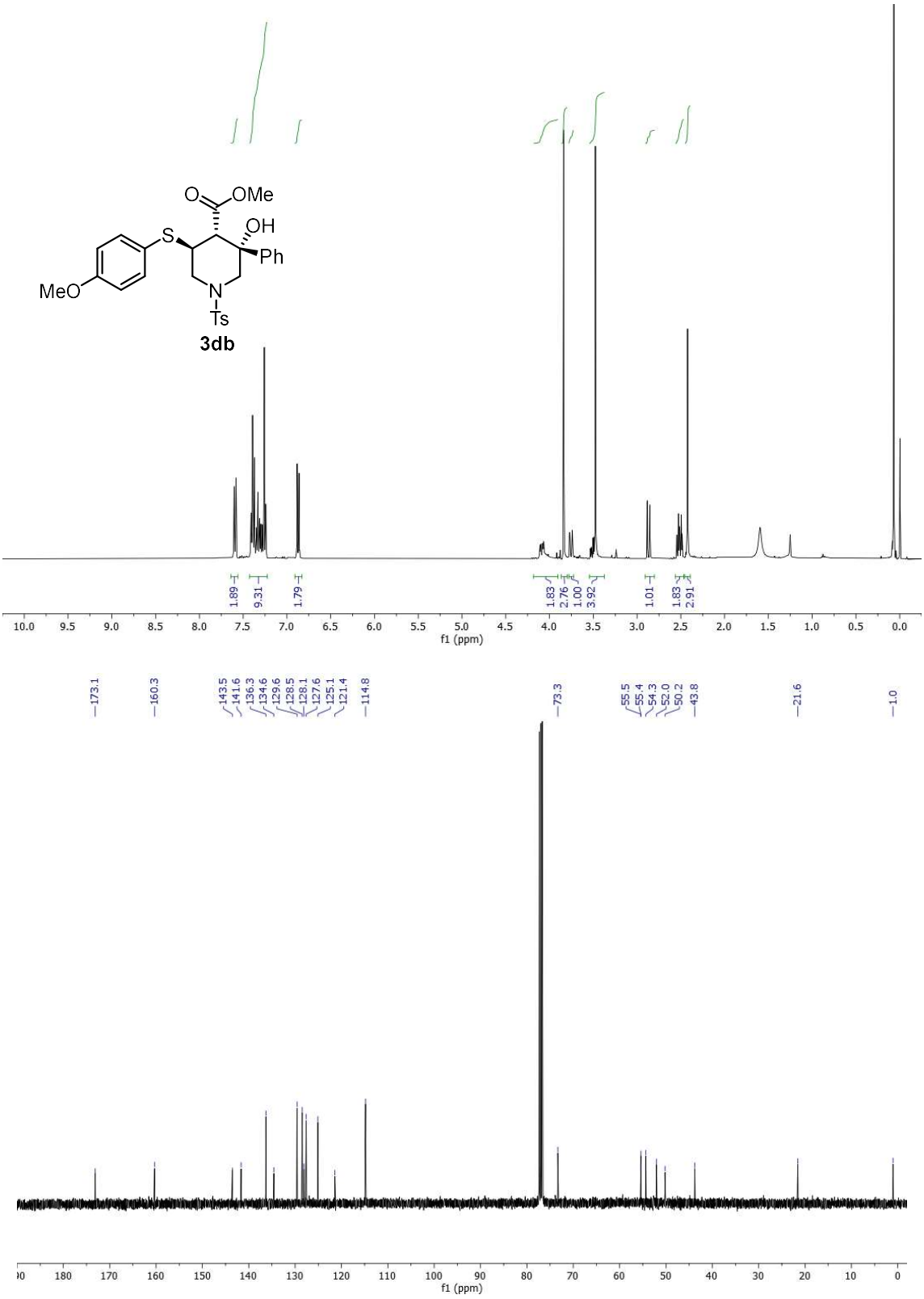


Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-(naphthalen-2-yl)-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3ha($CDCl_3$)

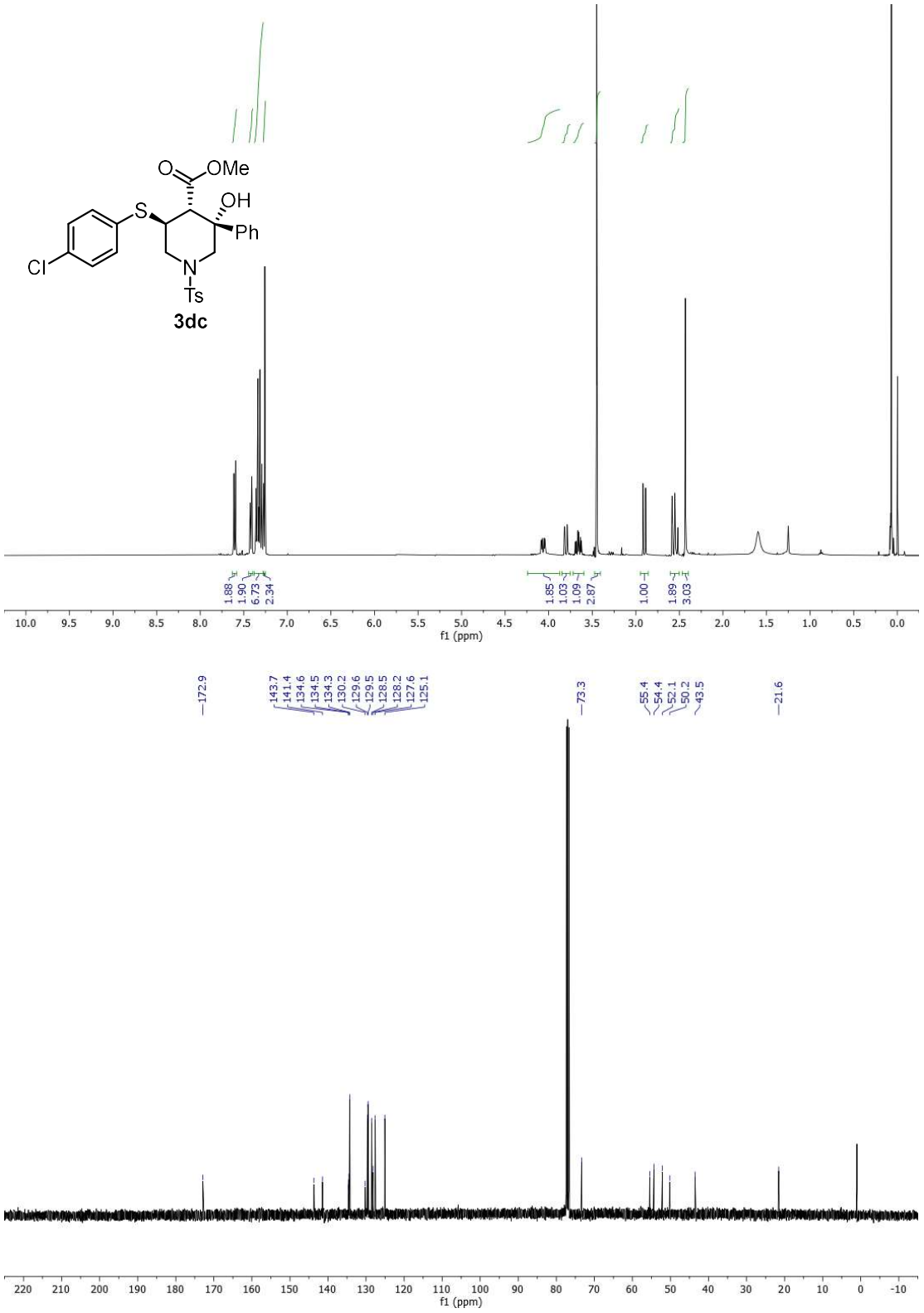




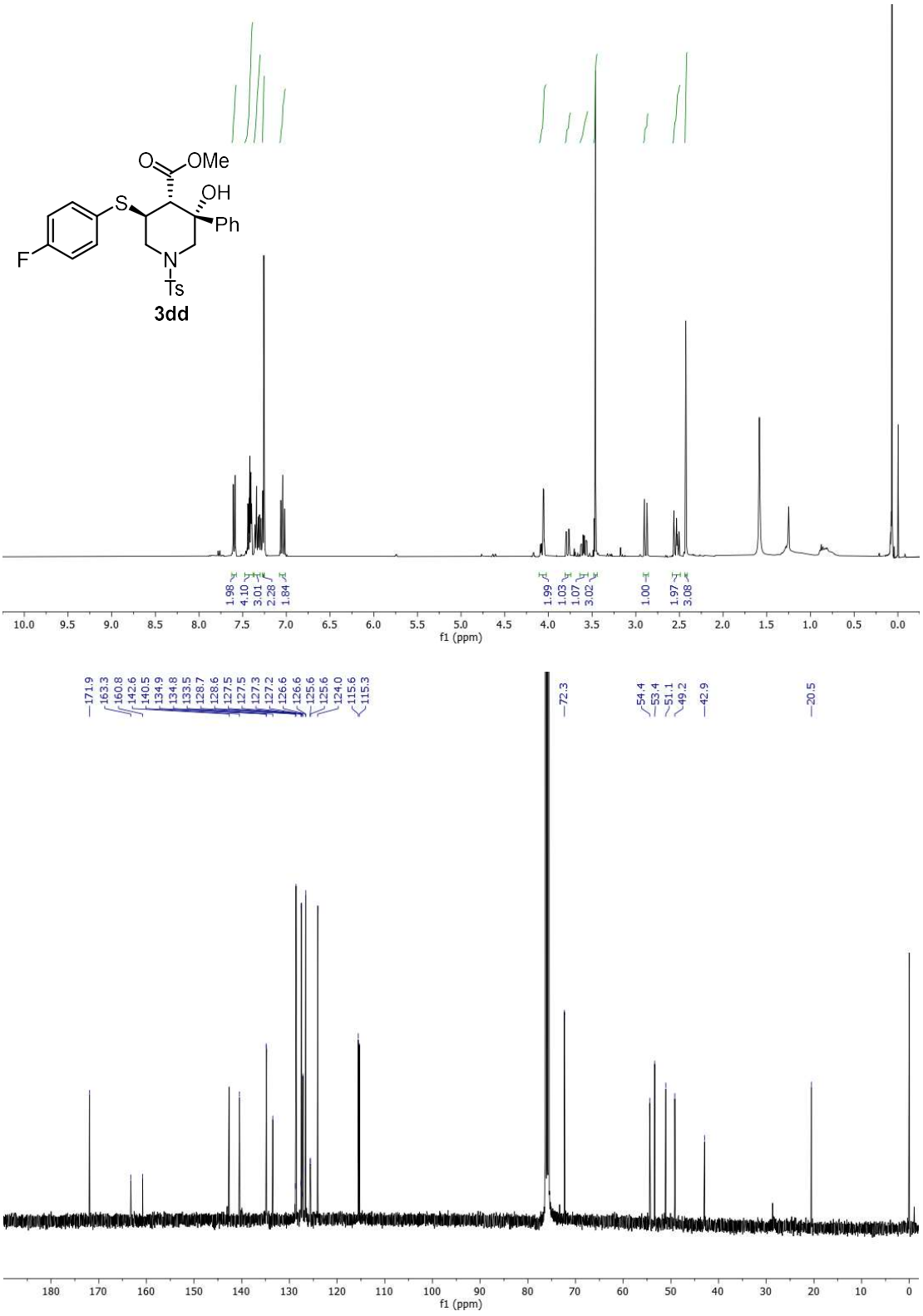
Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(4-methoxyphenylthio)-1-tosylpiperidine-4-carboxylate 3db ($CDCl_3$)



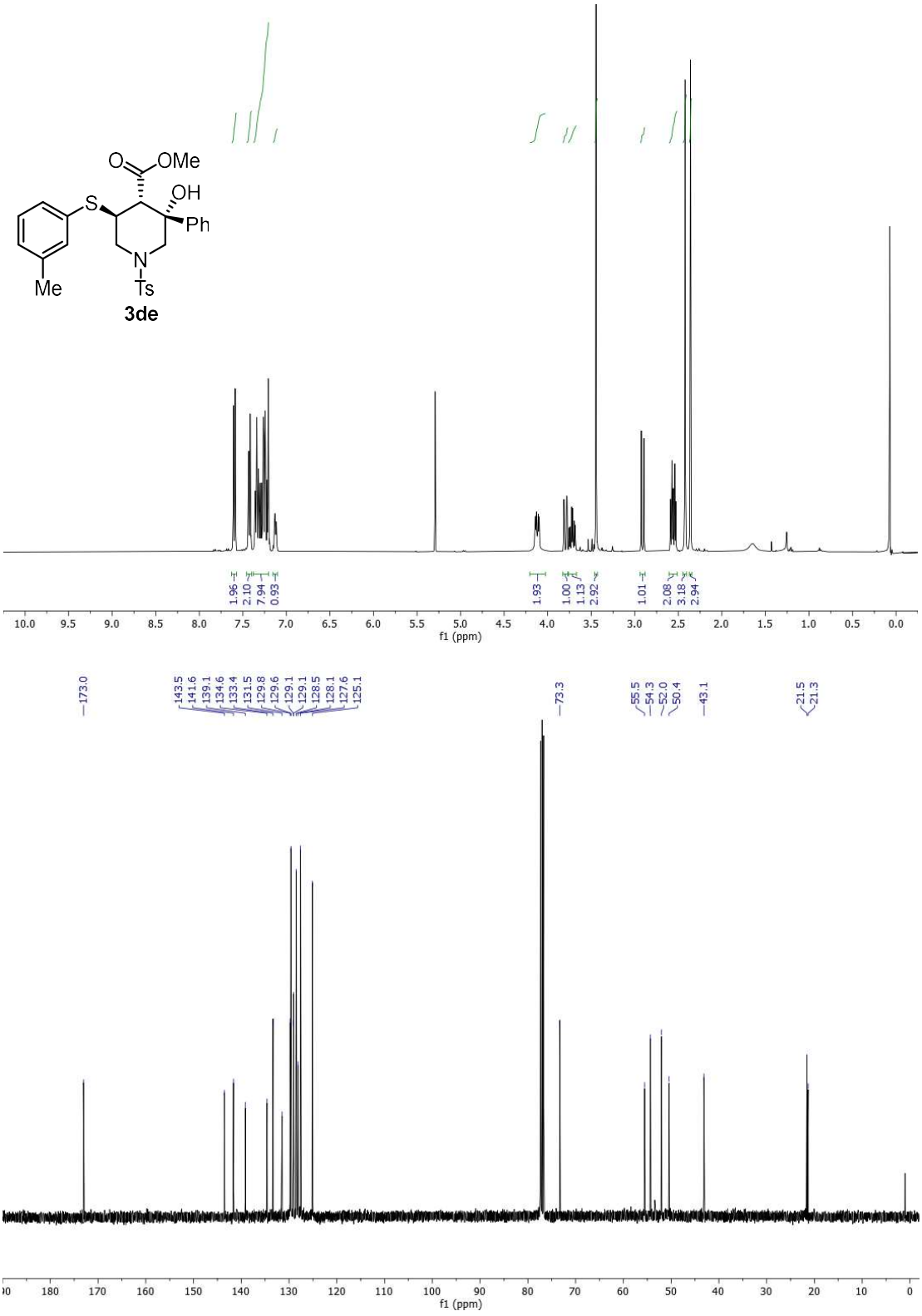
Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(4-chlorophenylthio)-1-tosylpiperidine-4-carboxylate 3dc ($CDCl_3$)



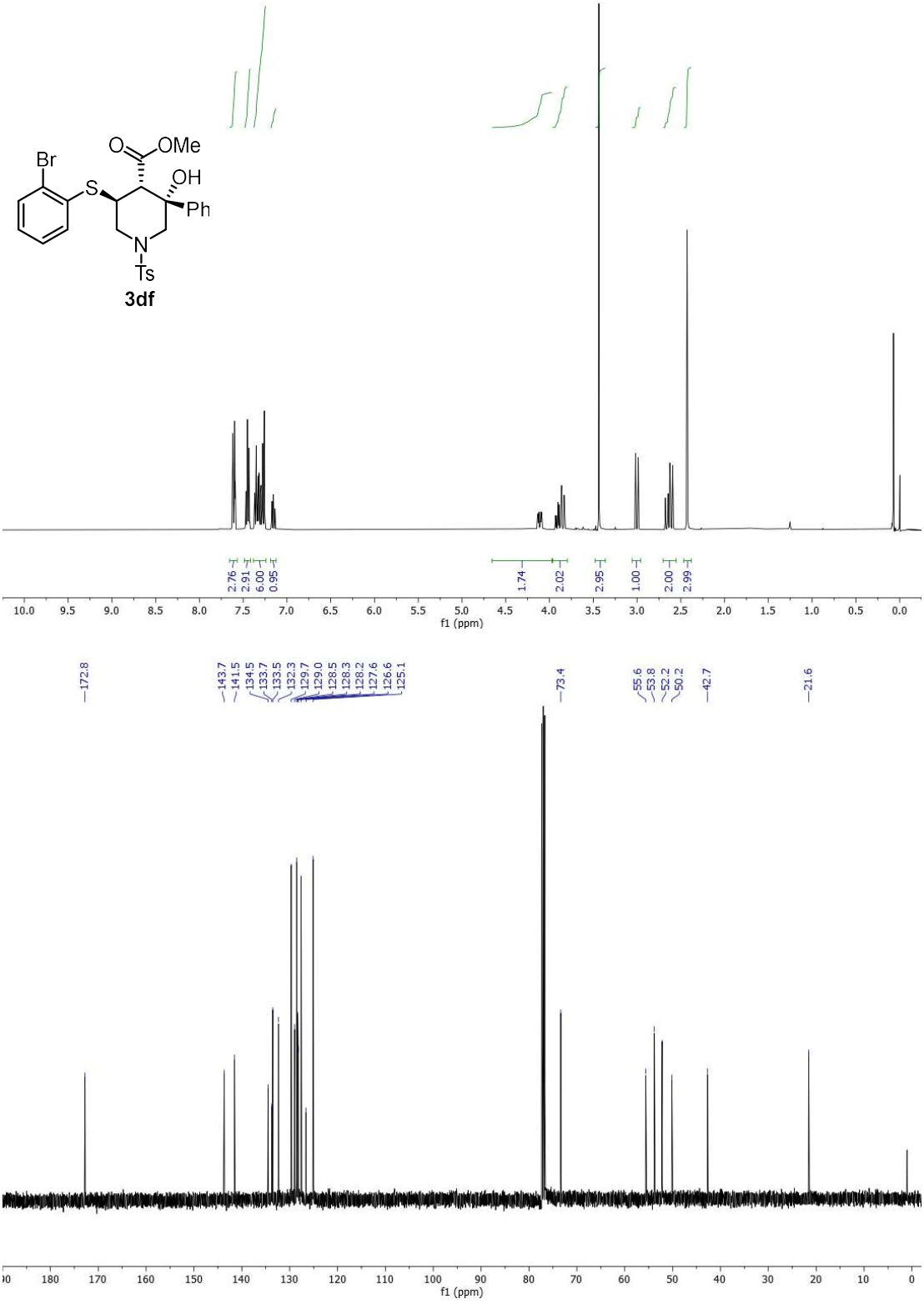
Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(4-fluorophenylthio)-1-tosylpiperidine-4-carboxylate 3dd ($CDCl_3$)



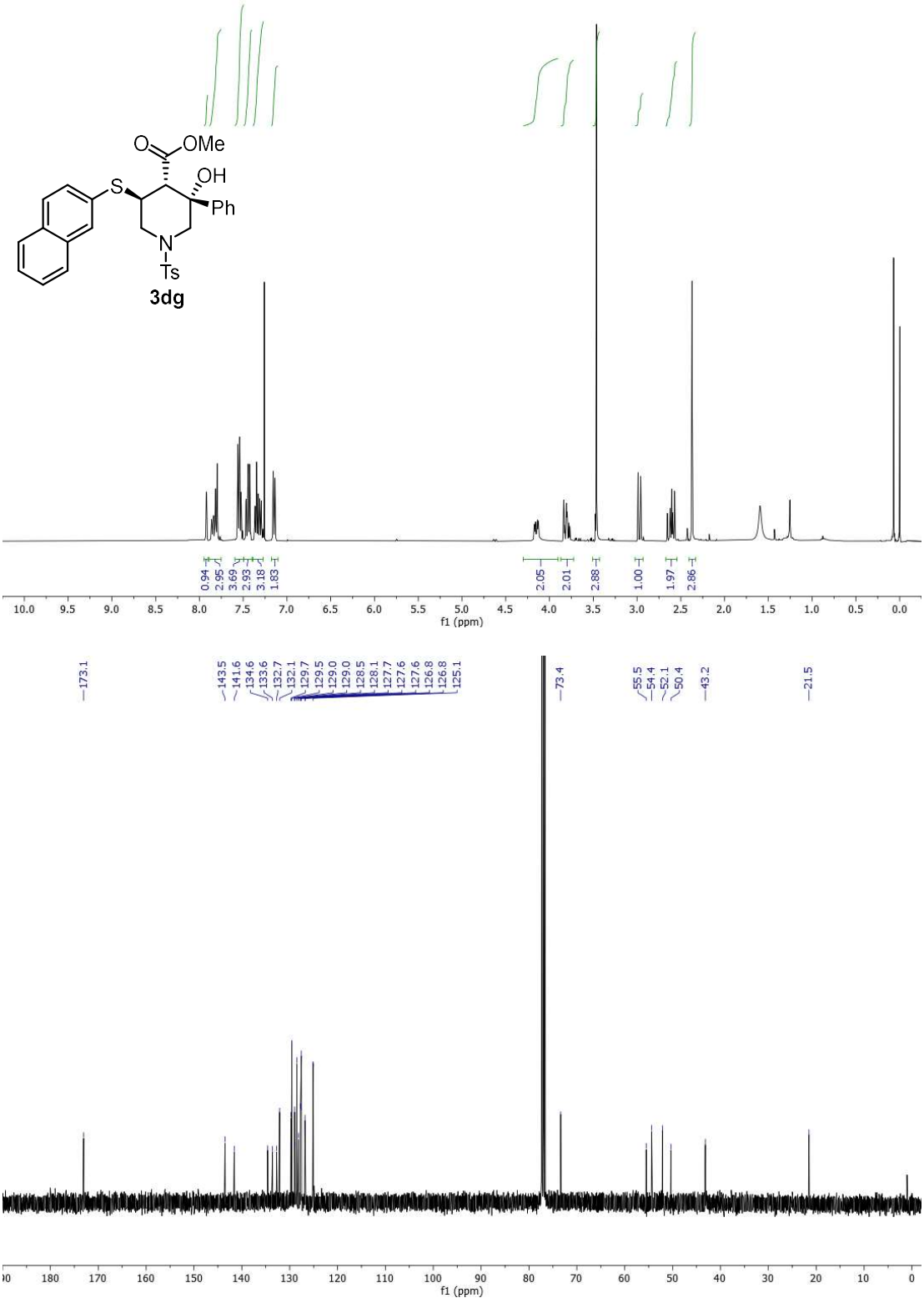
Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(3-methylphenylthio)-1-tosylpiperidine-4-carboxylate 3de ($CDCl_3$)



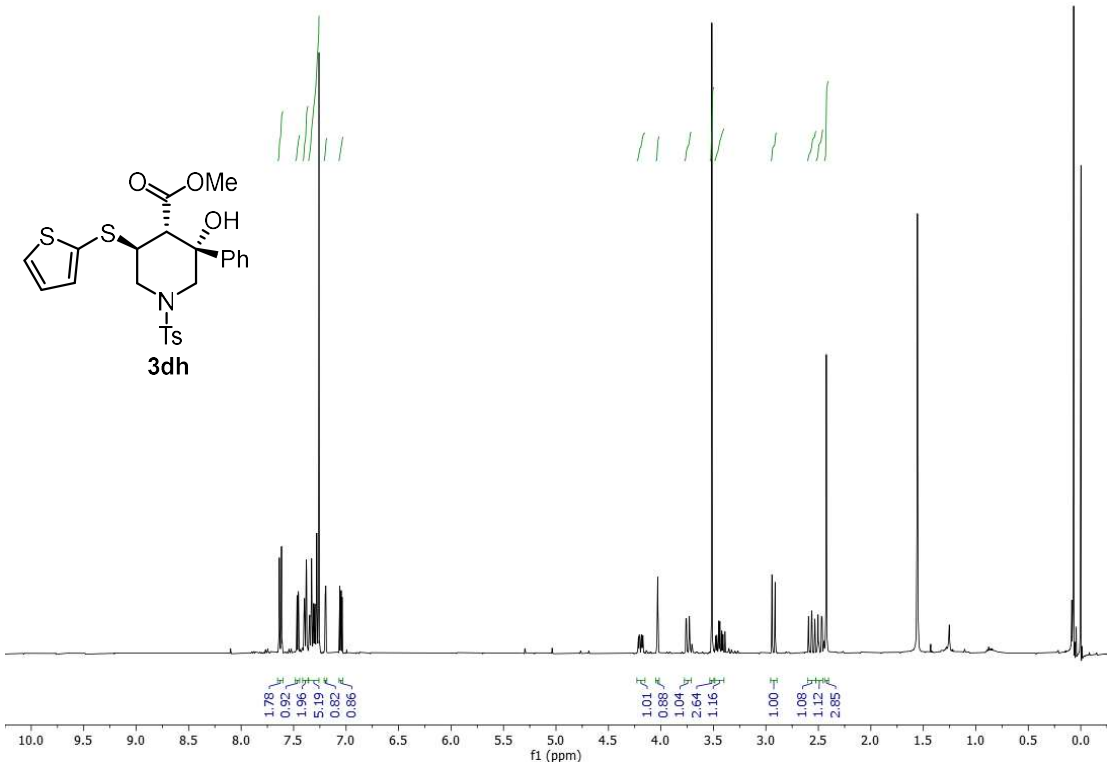
Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(2-bromophenylthio)-1-tosylpiperidine-4-carboxylate 3df ($CDCl_3$)

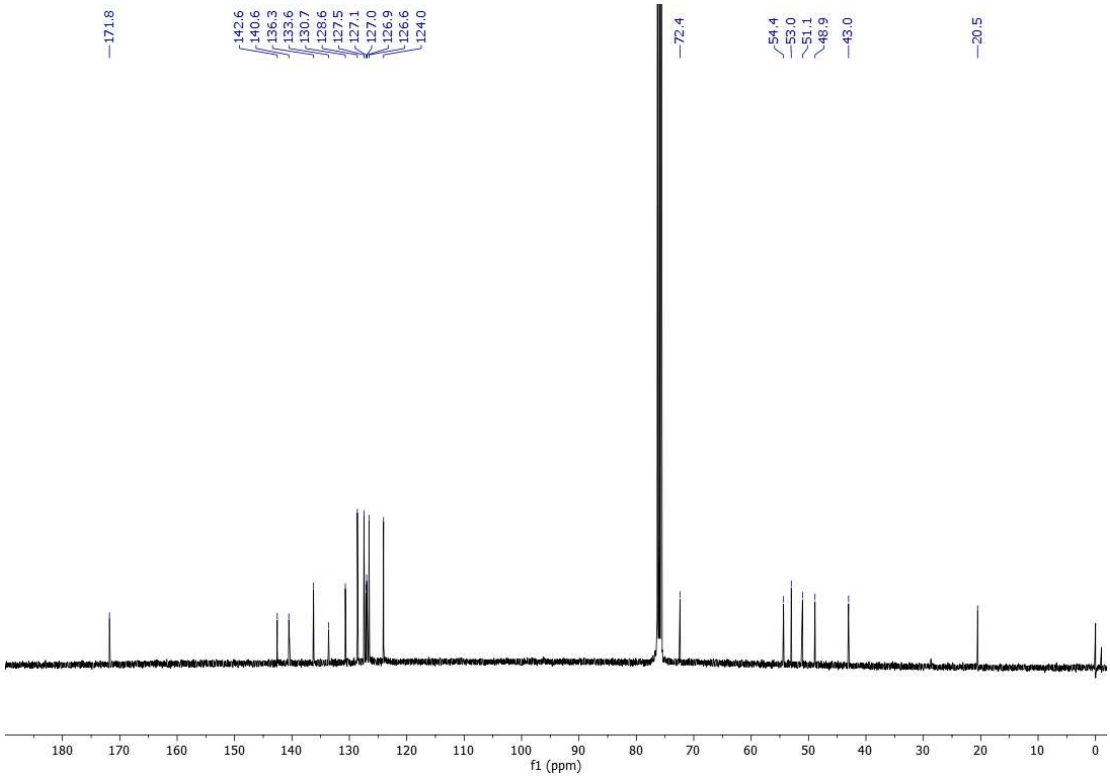


Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(naphthalen-2-yl)-1-tosylpiperidine-4-carboxylate 3dg ($CDCl_3$)

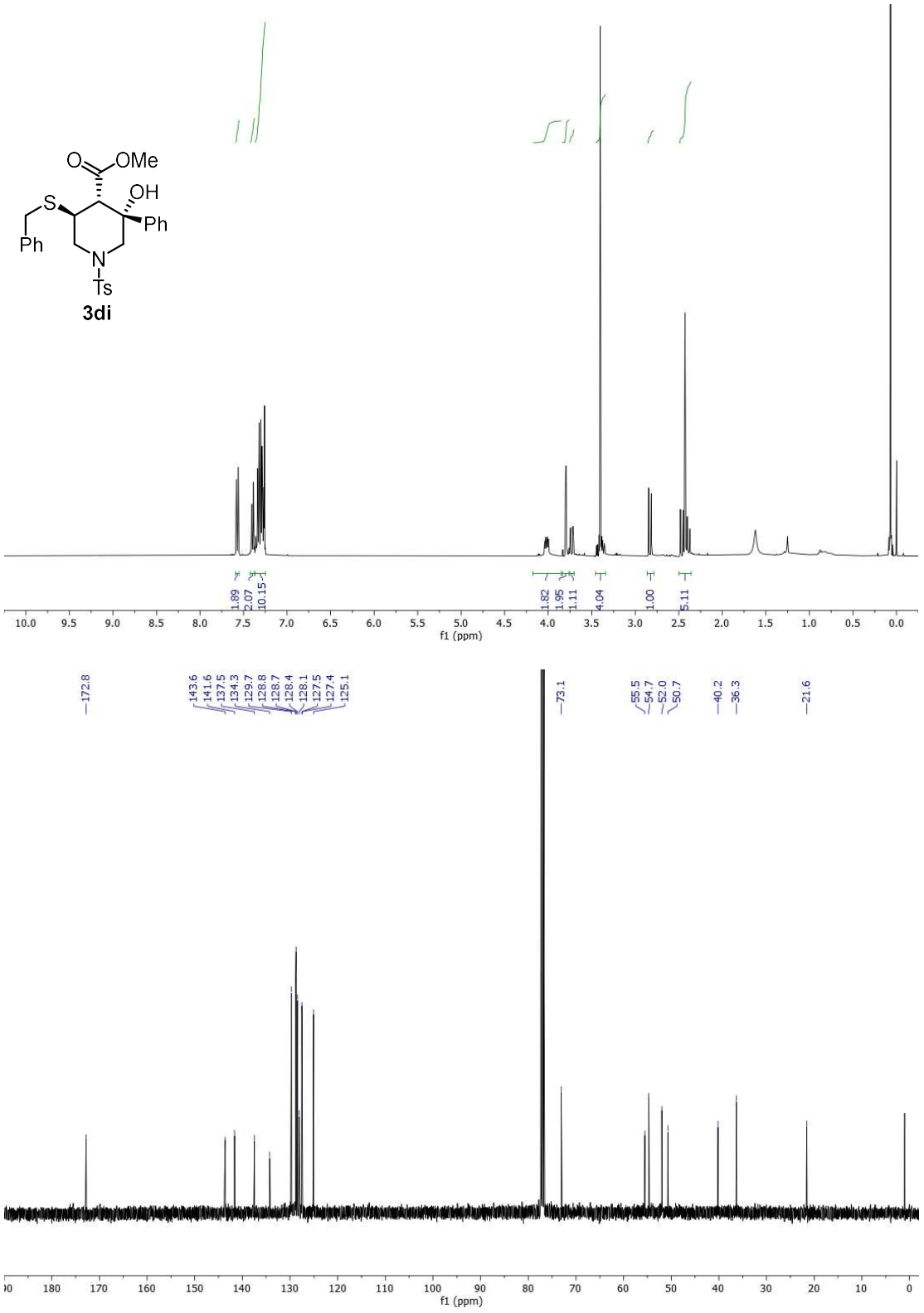


Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(thiophen-2-yl)-1-tosylpiperidine-4-carboxylate 3dh ($CDCl_3$)



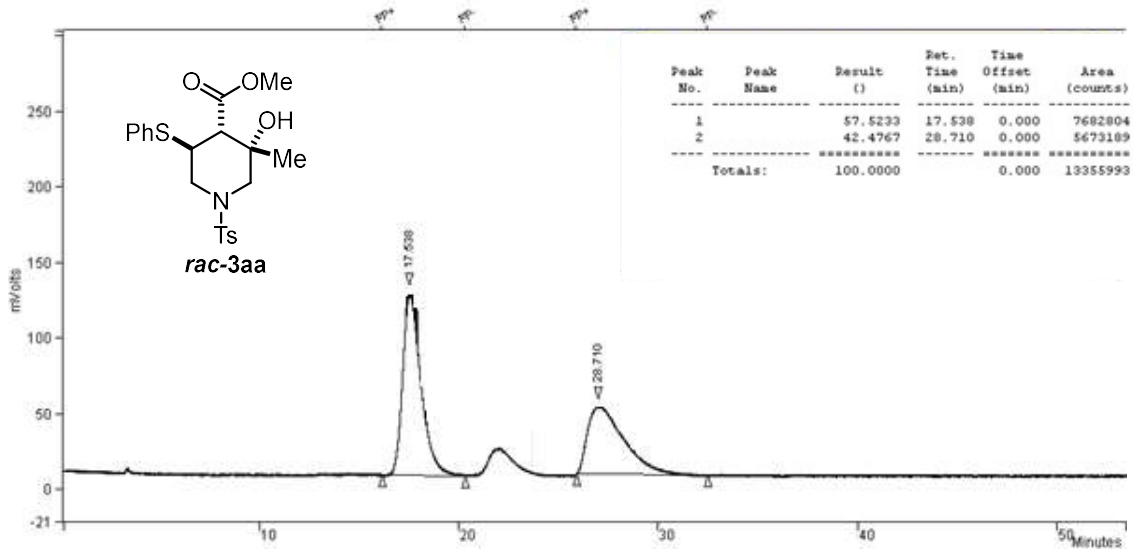


Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(benzylthio)-1-tosylpiperidine-4-carboxylate 3di ($CDCl_3$)



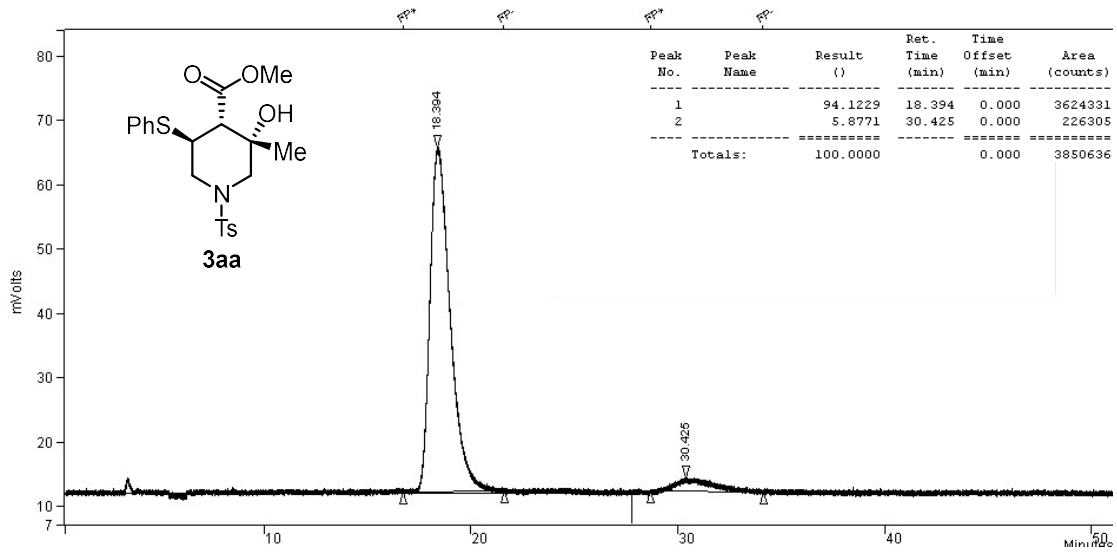
Copies of HPLC traces of products 3

Methyl (3*S,4*S**,5*S**)-3-hydroxy-3-methyl-5-(phenylthio)-1-tosylpiperidine-4-carboxylate *rac*-3aa**



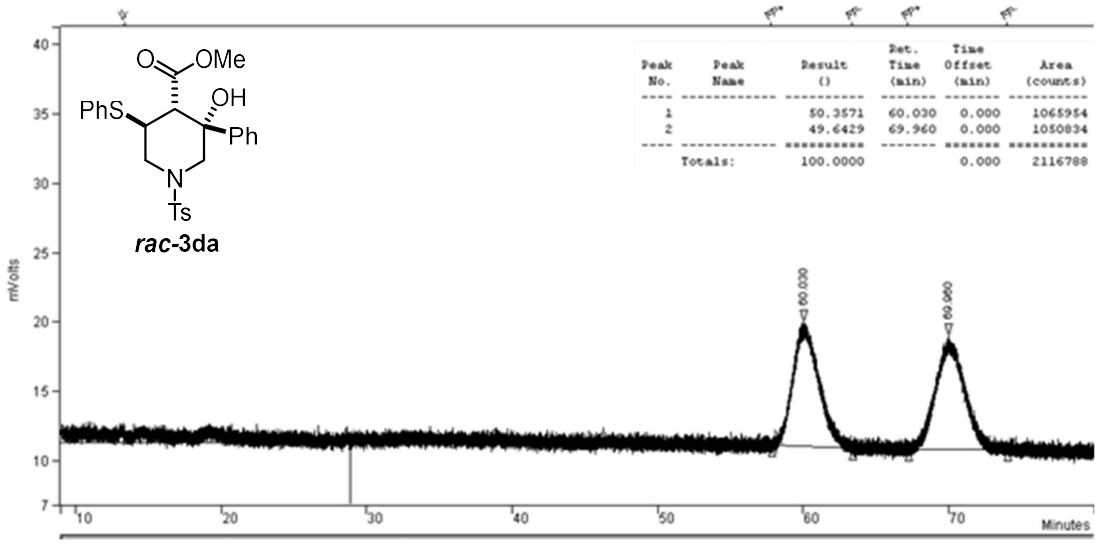
Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		57.5233	17.538	0.000	7682804
2		42.4767	28.710	0.000	5673189
	Totals:	100.0000		0.000	13355993

Methyl (3*S*,4*S*,5*S*)-3-hydroxy-3-methyl-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3aa



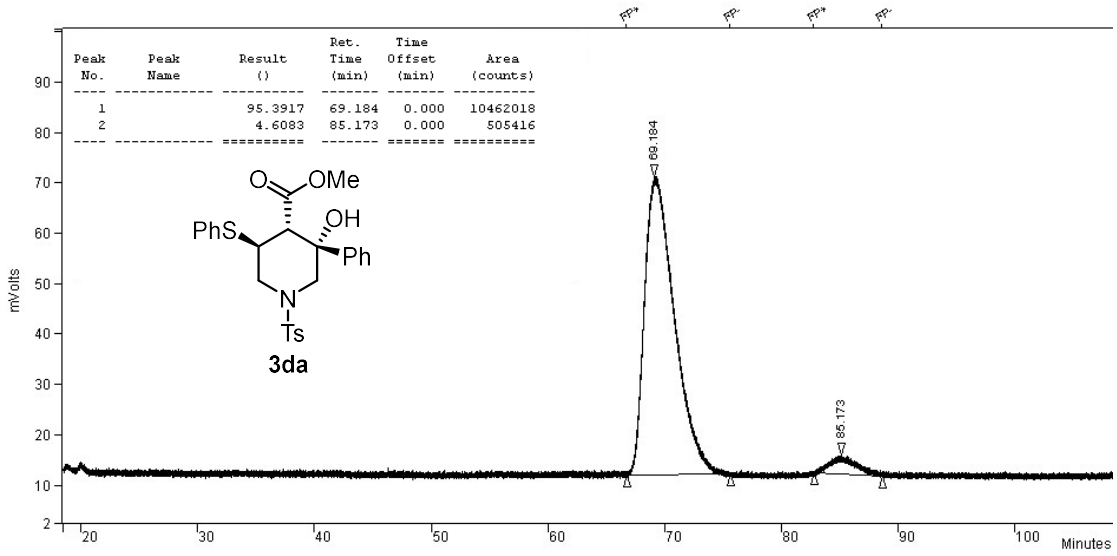
Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		94.1229	18.394	0.000	3624331
2		5.8771	30.425	0.000	226305
	Totals:	100.0000		0.000	3850636

Methyl (3*R,4*S**,5*S**)-3-hydroxy-3-phenyl-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3da**



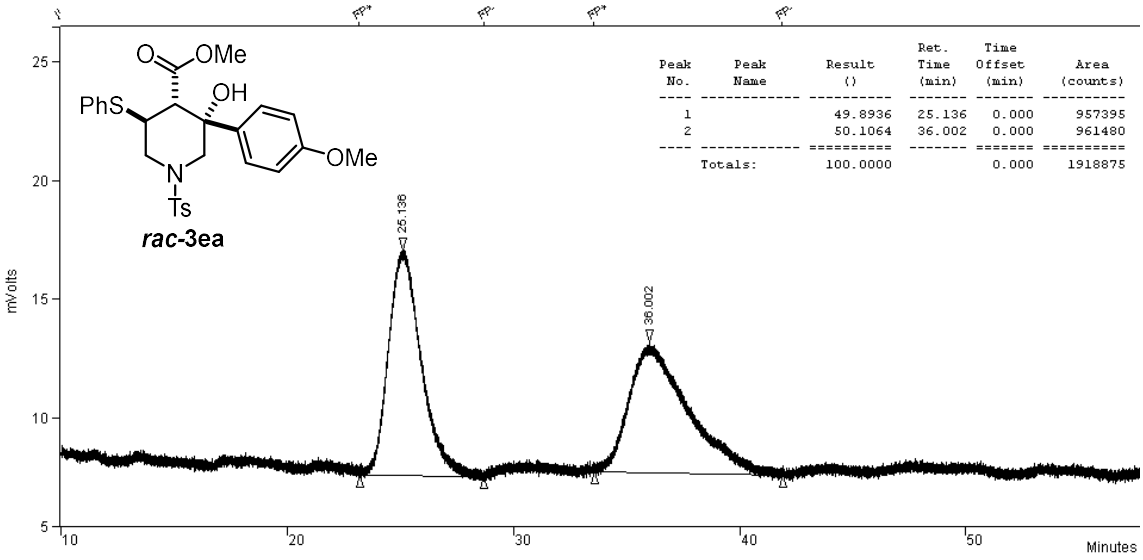
Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		50.3571	60.030	0.000	1065954
2		49.6429	69.960	0.000	1050834
	Totals:	100.0000		0.000	2116788

Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3da



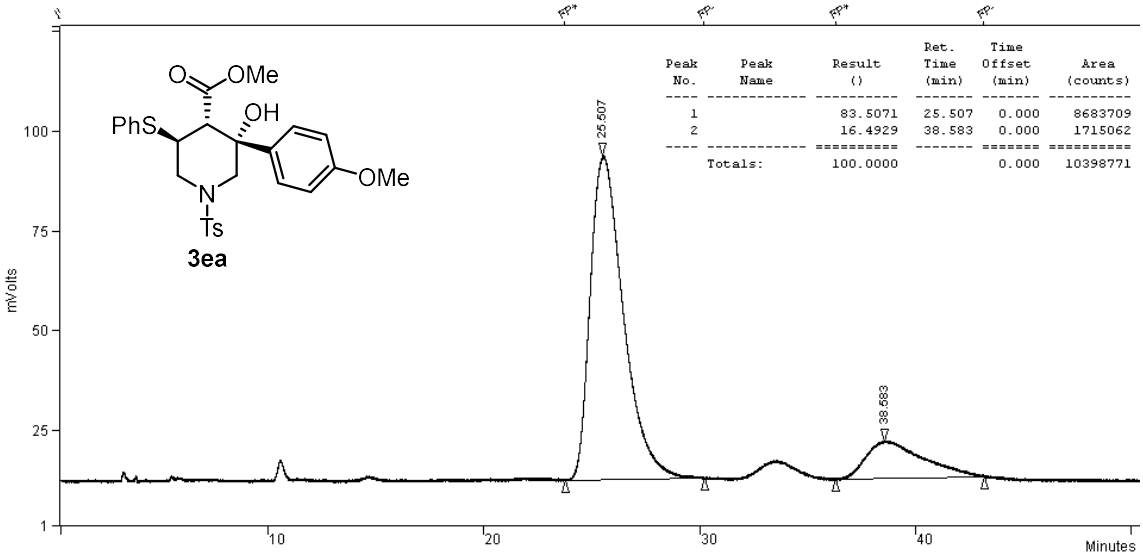
Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		95.3917	69.184	0.000	10462018
2		4.6083	85.173	0.000	505416

Methyl (3*R,4*S**,5*S**)-3-hydroxy-3-(4-methoxyphenyl)-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3ea**



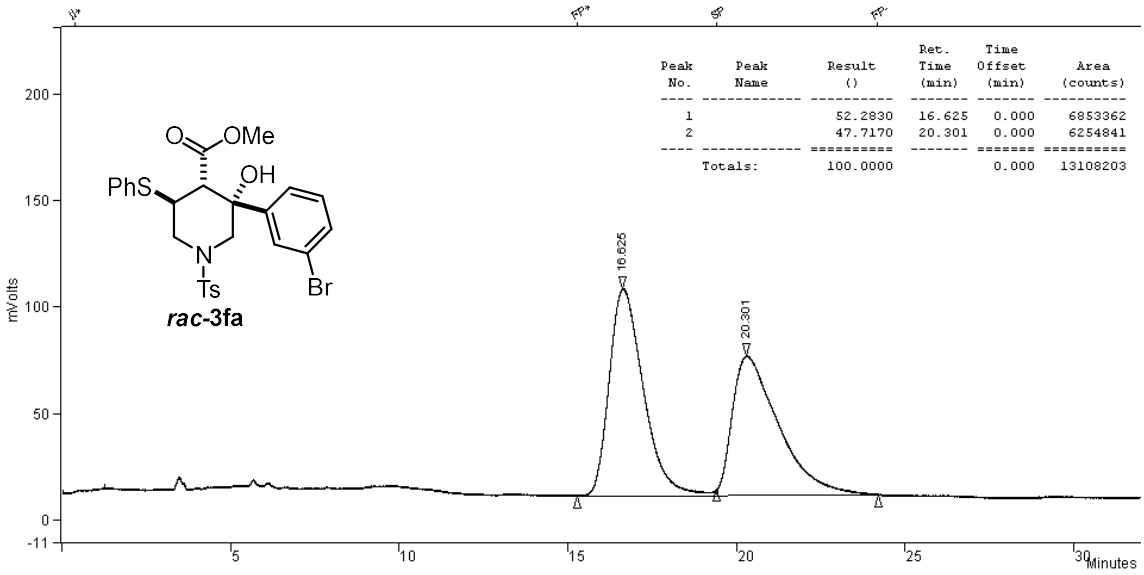
Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		49.8936	25.136	0.000	957395
2		50.1064	36.002	0.000	961480
Totals:		100.0000		0.000	1918875

Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-(4-methoxyphenyl)-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3ea

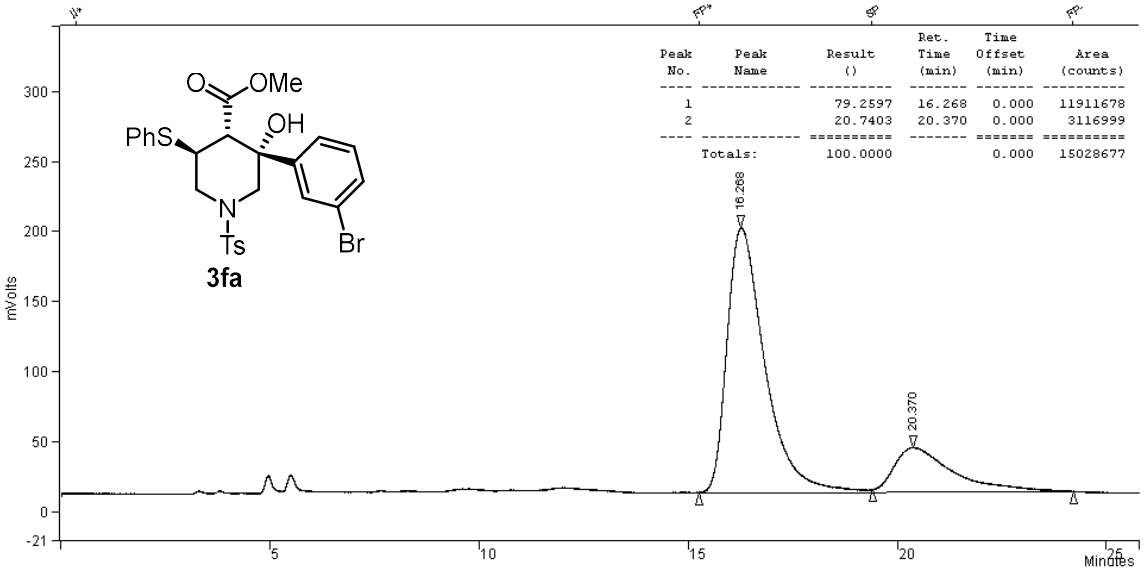


Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		83.5071	25.507	0.000	8683709
2		16.4929	38.583	0.000	1715062
Totals:		100.0000		0.000	10398771

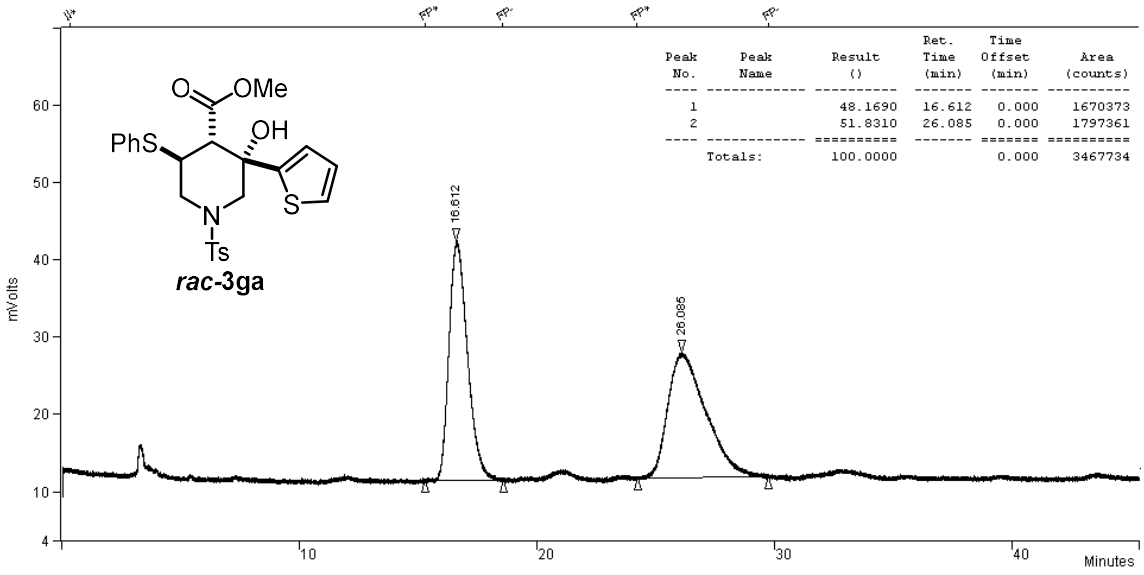
Methyl (3*R,4*S**,5*S**)-3-hydroxy-3-(3-bromophenyl)-5-(phenylthio)-1-tosylpiperidine-4-carboxylate *rac*-3fa**



Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-(3-bromophenyl)-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3fa

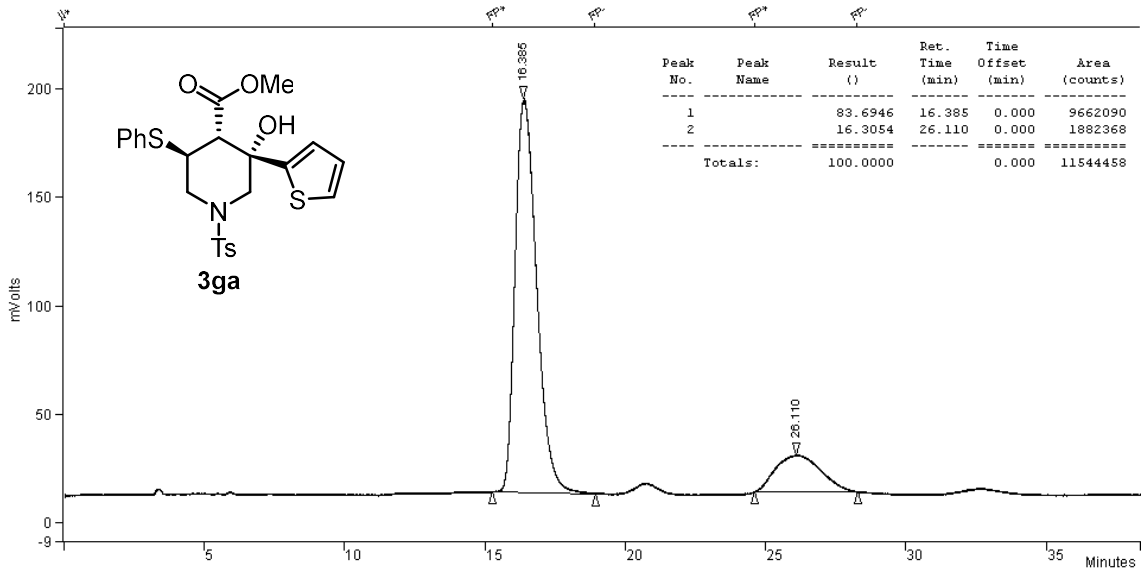


Methyl (3*R,4*S**,5*S**)-3-hydroxy-3-(thiophen-2-yl)-5-(phenylthio)-1-tosylpiperidine-4-carboxylate *rac*-3ga**



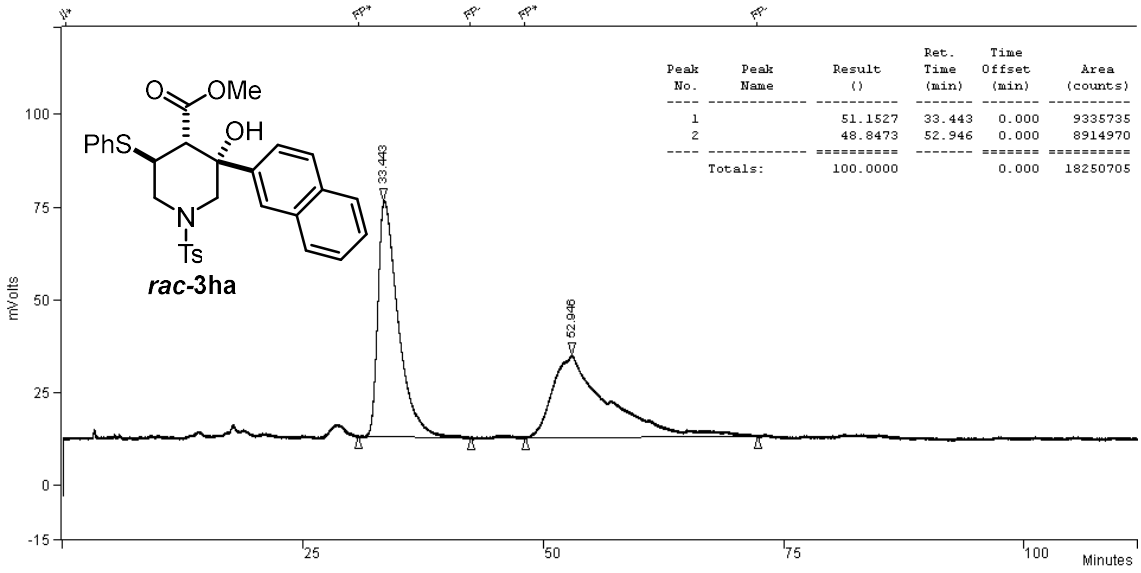
Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		48.1690	16.612	0.000	1670373
2		51.8310	26.085	0.000	1797361
	Totals:	100.0000		0.000	3467734

Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-(thiophen-2-yl)-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3ga



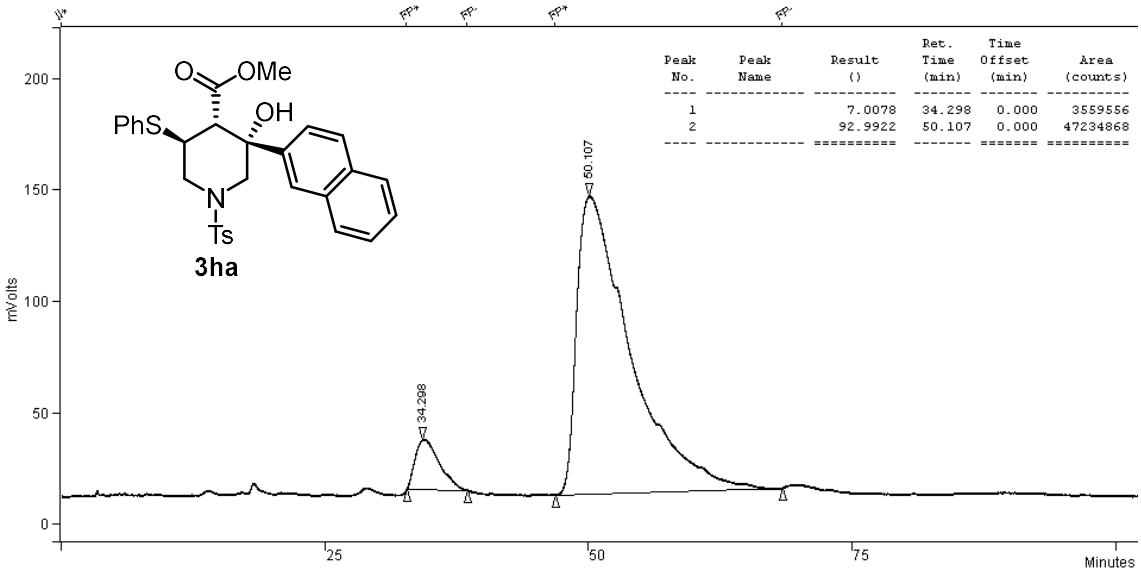
Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		83.6946	16.385	0.000	9662090
2		16.3054	26.110	0.000	1882368
	Totals:	100.0000		0.000	11544458

Methyl (3*R,4*S**,5*S**)-3-hydroxy-3-(naphthalen-2-yl)-5-(phenylthio)-1-tosylpiperidine-4-carboxylate *rac*-3ha**



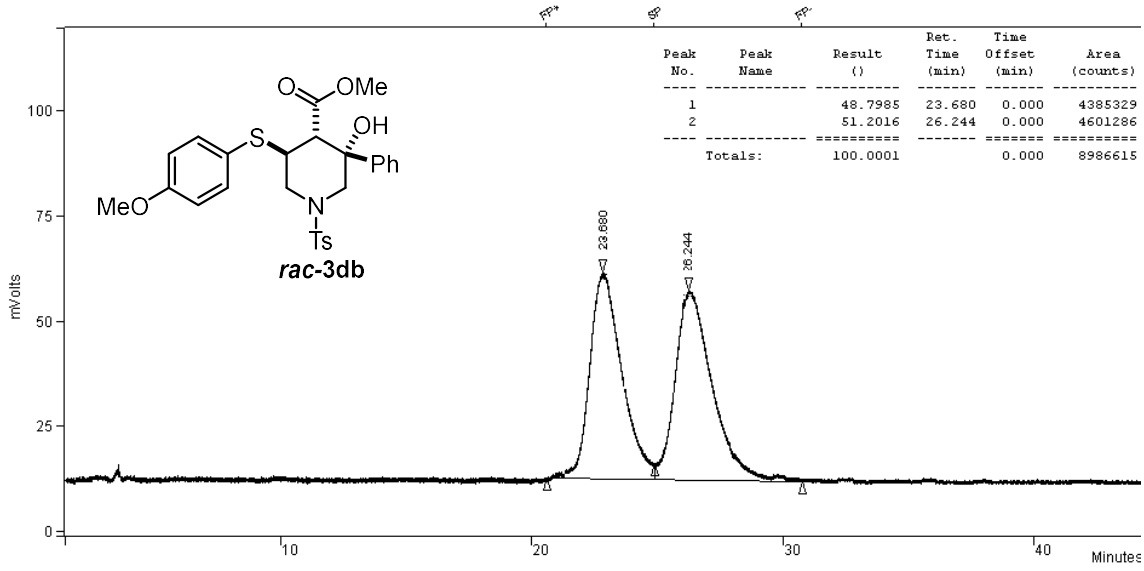
Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		51.1527	33.443	0.000	9335735
2		48.8473	52.946	0.000	8914970
	Totals:	100.0000		0.000	18250705

Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-(naphthalen-2-yl)-5-(phenylthio)-1-tosylpiperidine-4-carboxylate 3ha



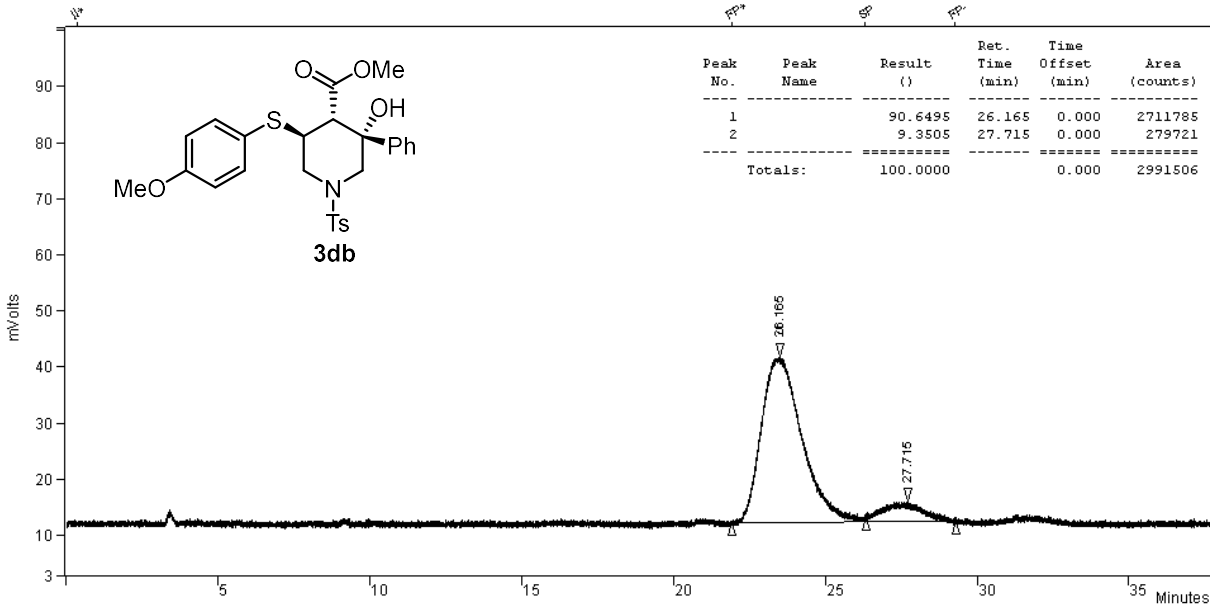
Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		7.0078	34.298	0.000	3559556
2		92.9922	50.107	0.000	47234868

Methyl (3*R,4*S**,5*S**)-3-hydroxy-3-phenyl-5-(4-methoxyphenylthio)-1-tosylpiperidine-4-carboxylate *rac*-3db**



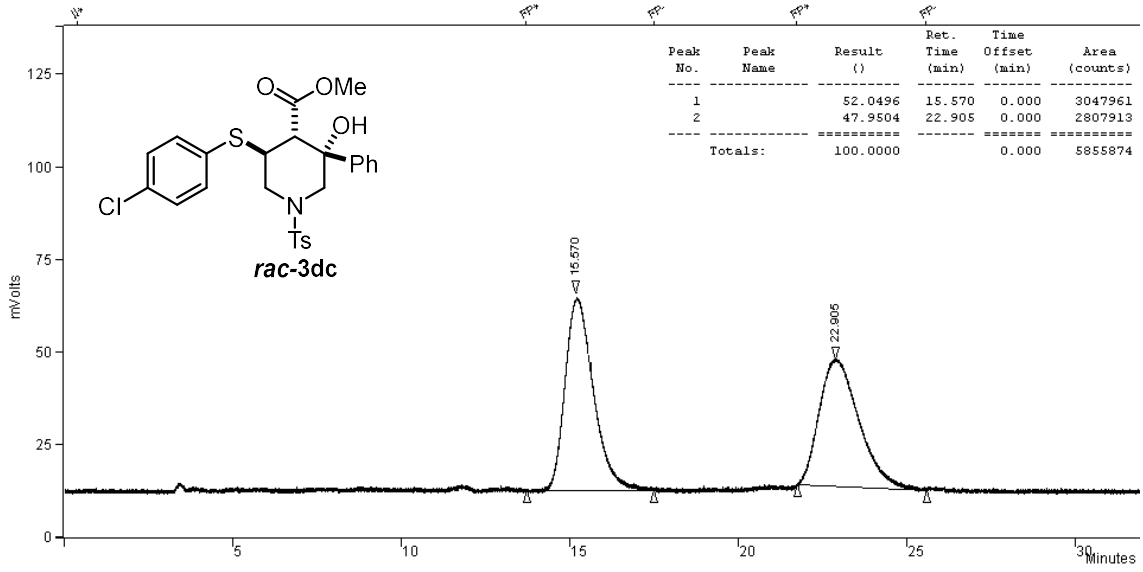
Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		48.7985	23.680	0.000	4385329
2		51.2016	26.244	0.000	4601286
	Totals:	100.0001		0.000	8986615

Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(4-methoxyphenylthio)-1-tosylpiperidine-4-carboxylate 3db



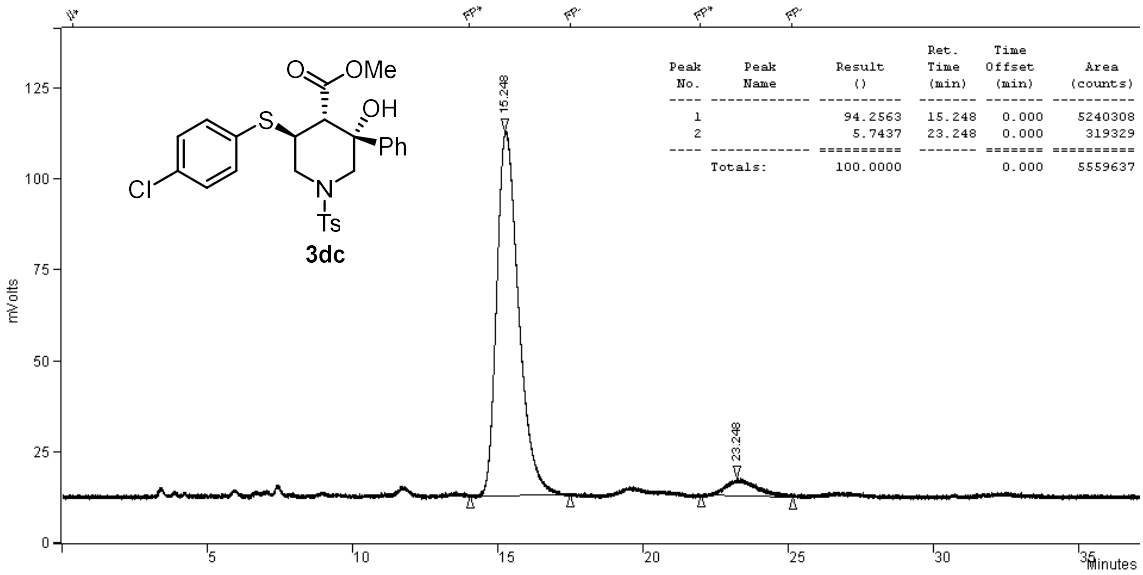
Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		90.6495	26.165	0.000	2711785
2		9.3505	27.715	0.000	279721
	Totals:	100.0000		0.000	2991506

Methyl (3*R,4*S**,5*S**)-3-hydroxy-3-phenyl-5-(4-chlorophenylthio)-1-tosylpiperidine-4-carboxylate *rac*-3dc**



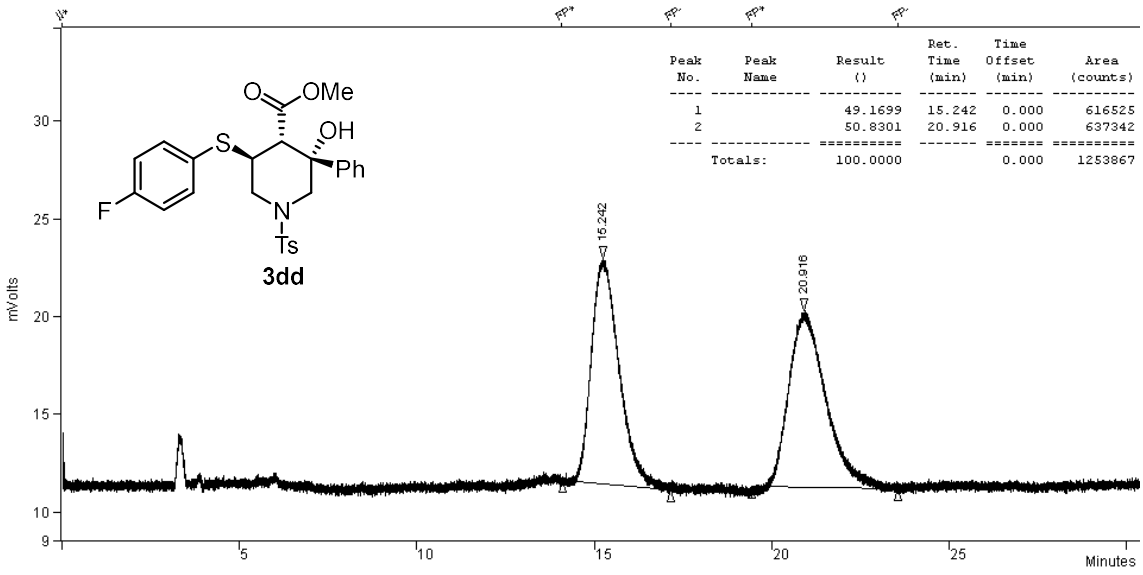
Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		52.0496	15.570	0.000	3047961
2		47.9504	22.905	0.000	2807913
	Totals:	100.0000		0.000	5855874

Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(4-chlorophenylthio)-1-tosylpiperidine-4-carboxylate 3dc

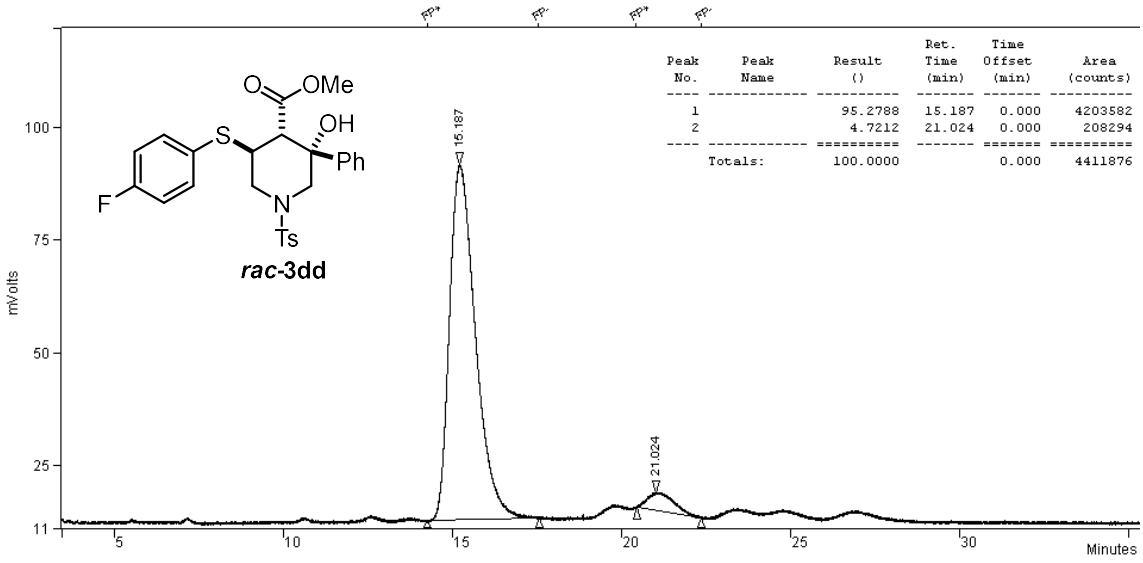


Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		94.2563	15.248	0.000	5240308
2		5.7437	23.248	0.000	319329
	Totals:	100.0000		0.000	5559637

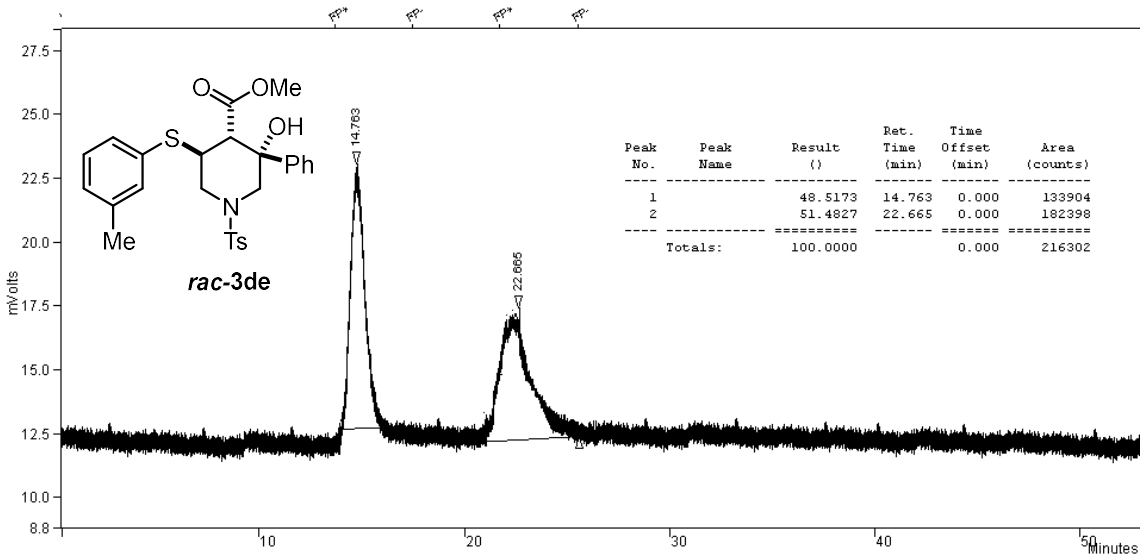
Methyl (3*R,4*S**,5*S**)-3-hydroxy-3-phenyl-5-(4-fluorophenylthio)-1-tosylpiperidine-4-carboxylate *rac*-3dd**



Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(4-fluorophenylthio)-1-tosylpiperidine-4-carboxylate 3dd

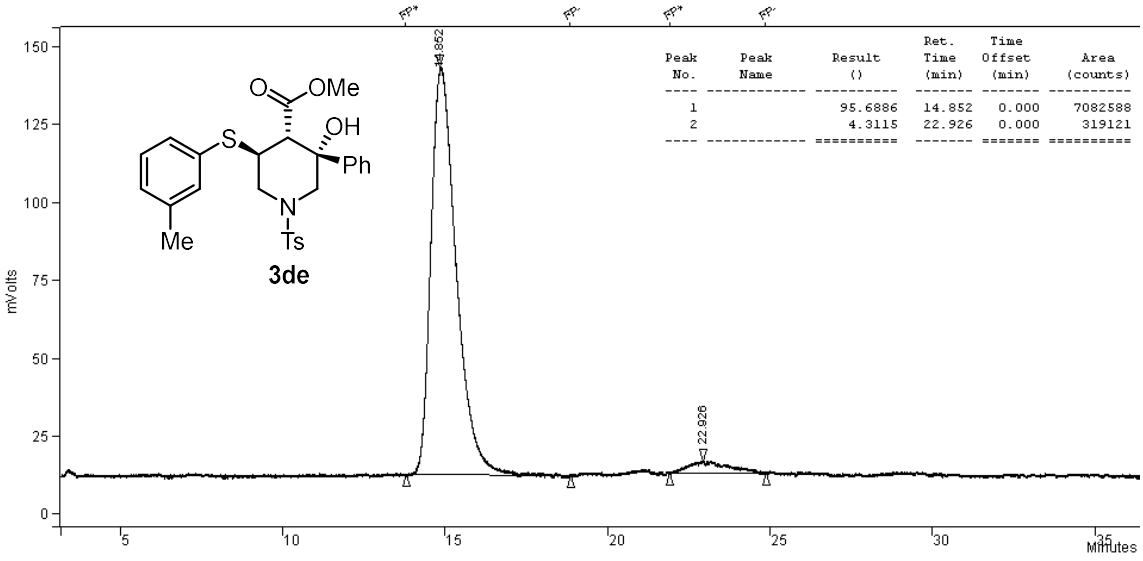


Methyl (3*R,4*S**,5*S**)-3-hydroxy-3-phenyl-5-(3-methylphenylthio)-1-tosylpiperidine-4-carboxylate 3de**



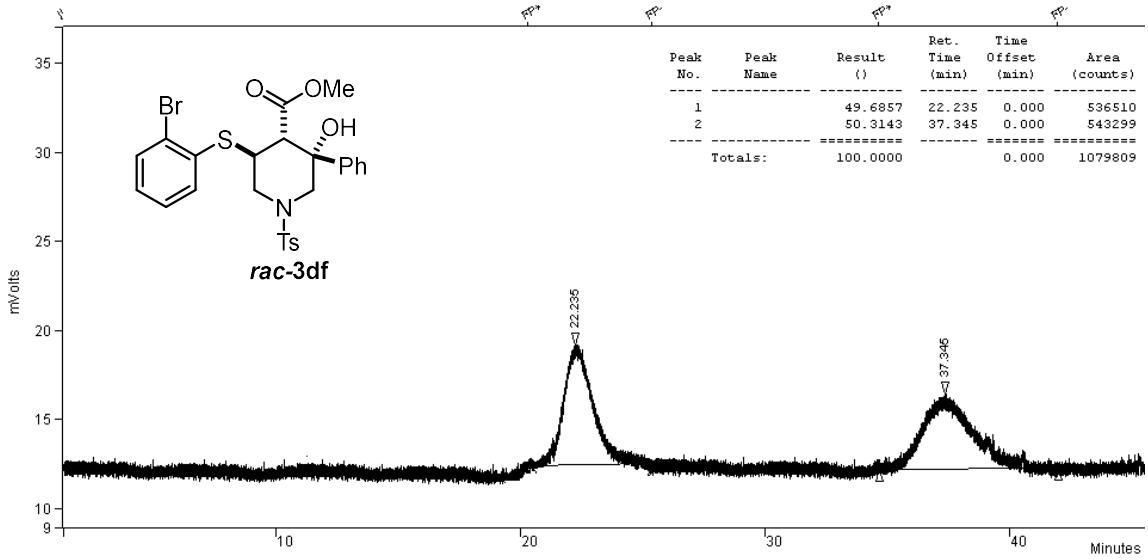
Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		48.5173	14.763	0.000	133904
2		51.4827	22.665	0.000	182398
Totals:		100.0000		0.000	216302

Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(3-methylphenylthio)-1-tosylpiperidine-4-carboxylate 3de



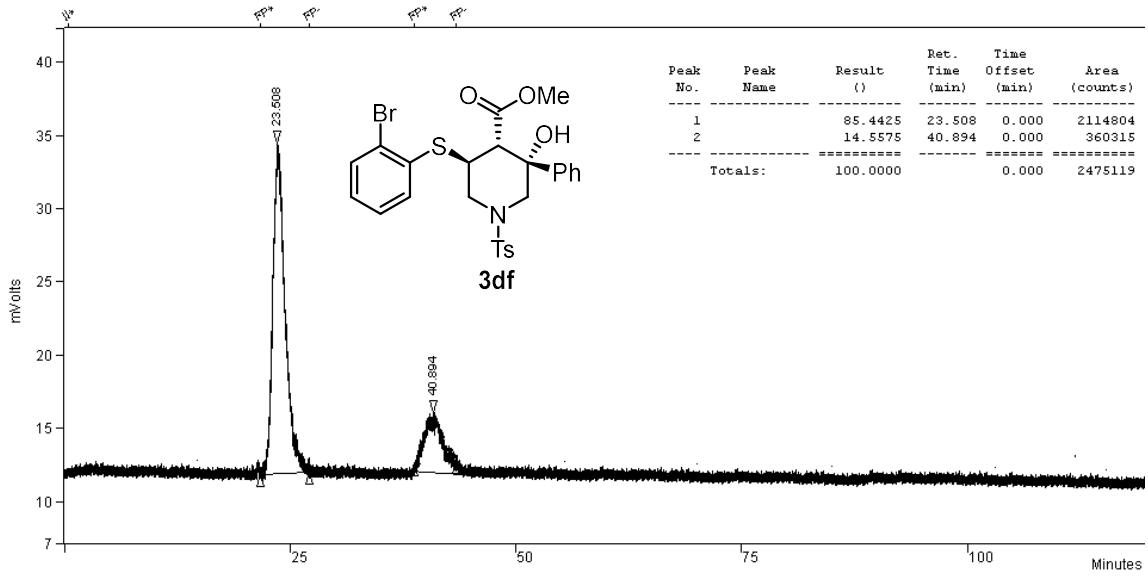
Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		95.6886	14.852	0.000	7082588
2		4.3115	22.926	0.000	319121

Methyl (3*R,4*S**,5*S**)-3-hydroxy-3-phenyl-5-(2-bromophenylthio)-1-tosylpiperidine-4-carboxylate *rac*-3df**



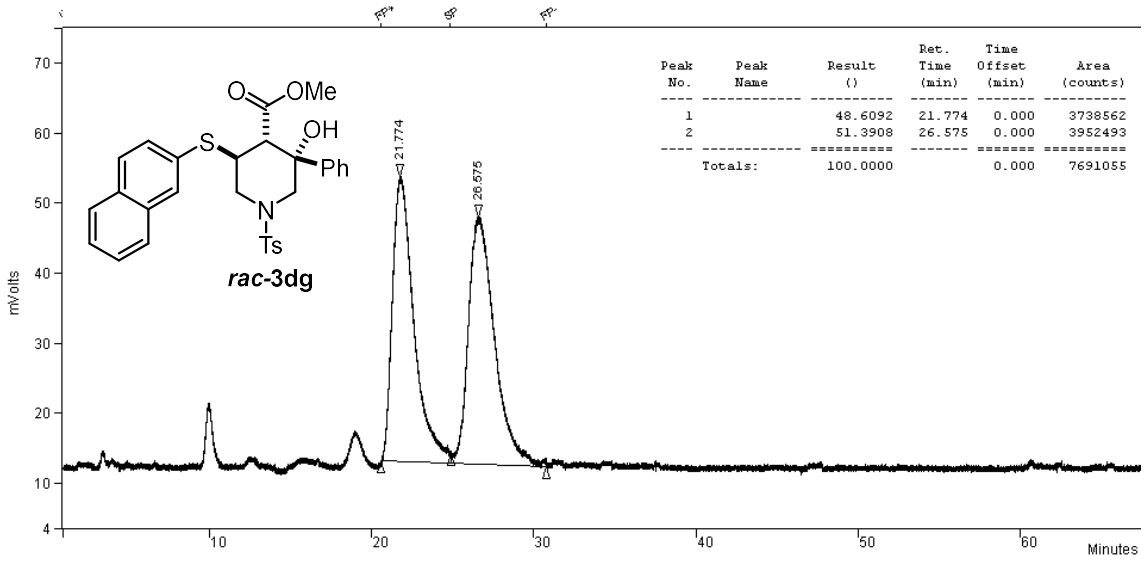
Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		49.6857	22.235	0.000	536510
2		50.3143	37.345	0.000	543299
Totals:		100.0000		0.000	1079809

Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(2-bromophenylthio)-1-tosylpiperidine-4-carboxylate 3df



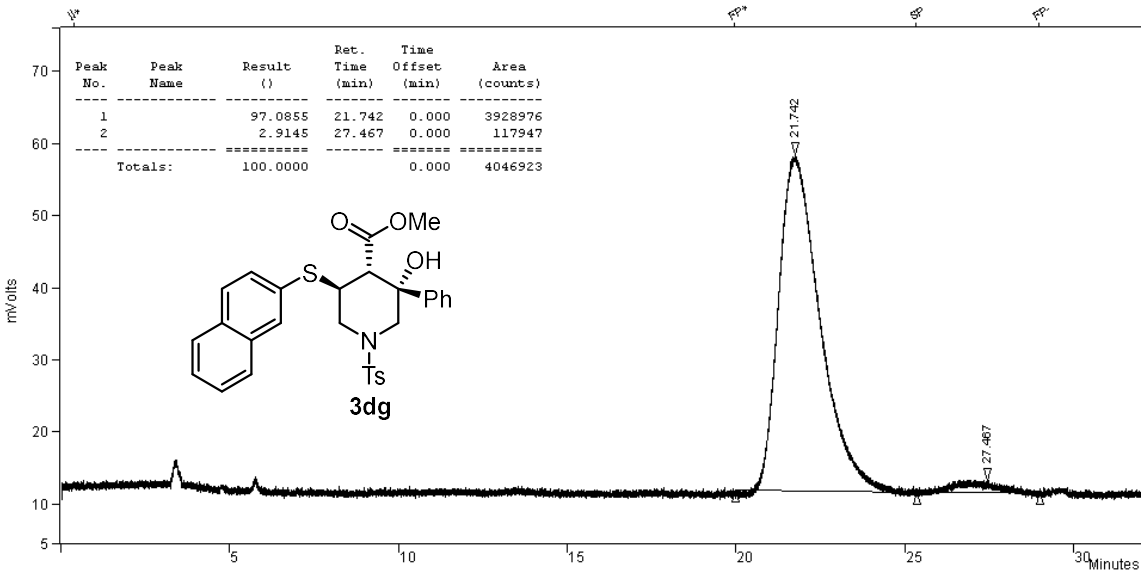
Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		85.4425	23.508	0.000	2114804
2		14.5575	40.894	0.000	360315
Totals:		100.0000		0.000	2475119

Methyl (3*R,4*S**,5*S**)-3-hydroxy-3-phenyl-5-(naphthalen-2-yl)-1-tosylpiperidine-4-carboxylate *rac*-3dg**



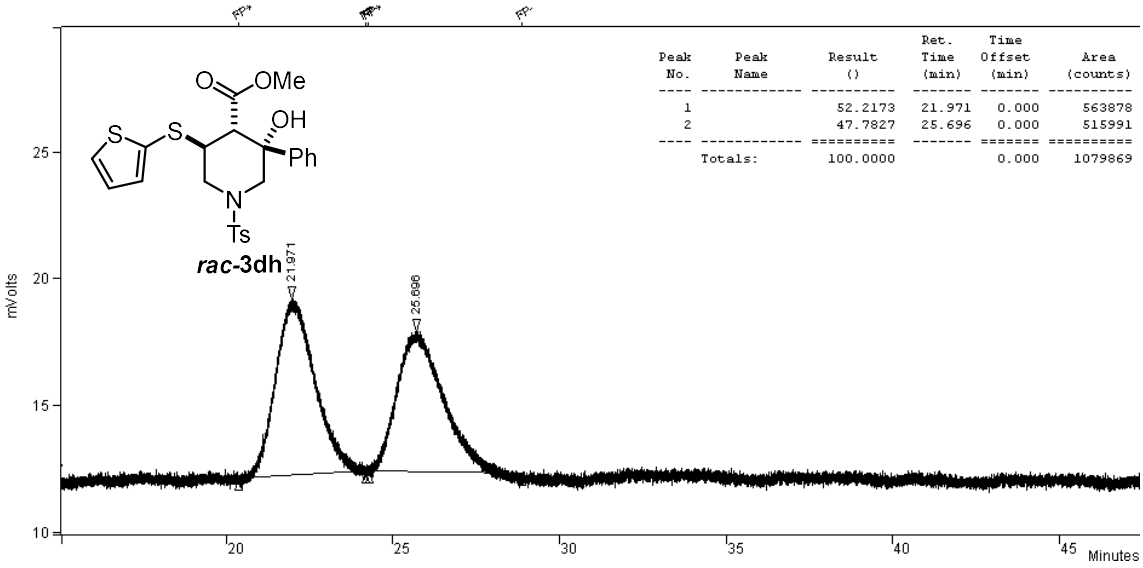
Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		48.6092	21.774	0.000	3738562
2		51.3908	26.575	0.000	3952493
Totals:		100.0000		0.000	7691055

Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(naphthalen-2-yl)-1-tosylpiperidine-4-carboxylate 3dg



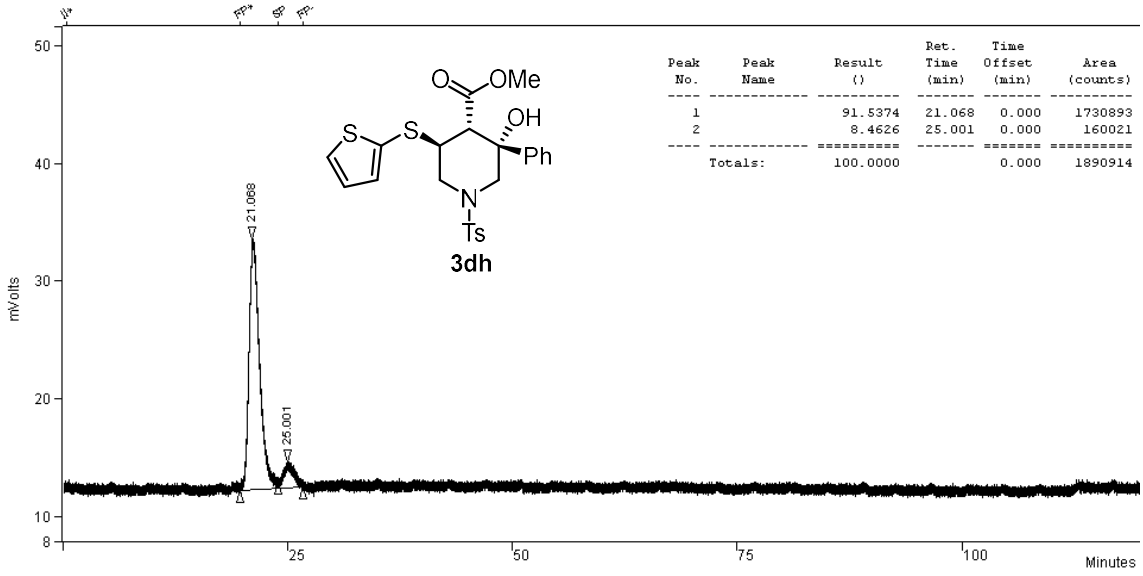
Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		97.0855	21.742	0.000	3928976
2		2.9145	27.467	0.000	117947
Totals:		100.0000		0.000	4046923

Methyl (3*R,4*S**,5*S**)-3-hydroxy-3-phenyl-5-(thiophen-2-yl)-1-tosylpiperidine-4-carboxylate *rac*-3dh**



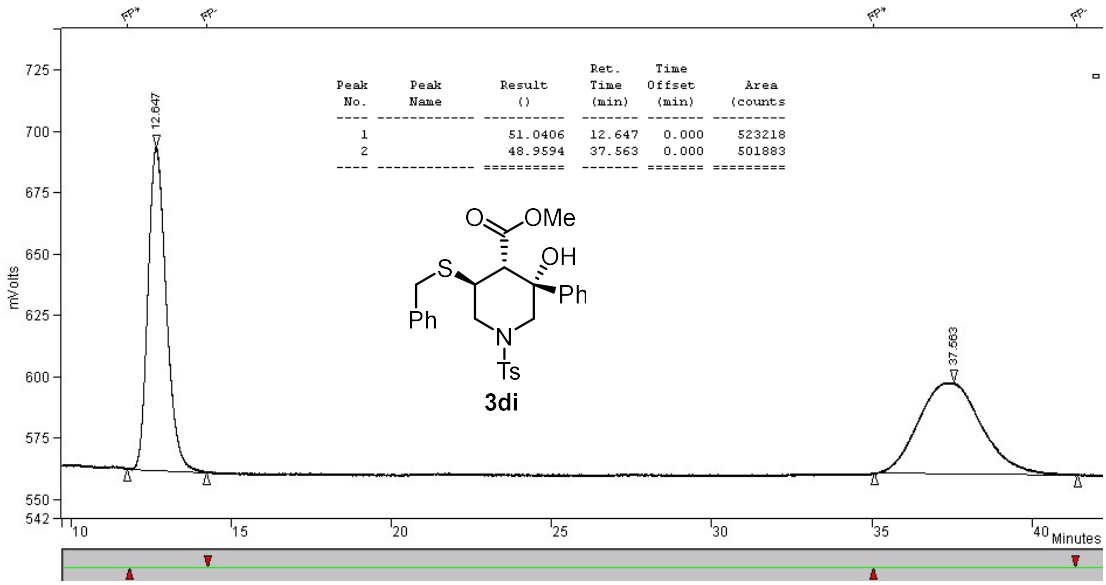
Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		52.2173	21.971	0.000	563878
2		47.7827	25.696	0.000	515991
Totals:		100.0000		0.000	1079869

Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(thiophen-2-yl)-1-tosylpiperidine-4-carboxylate 3dh

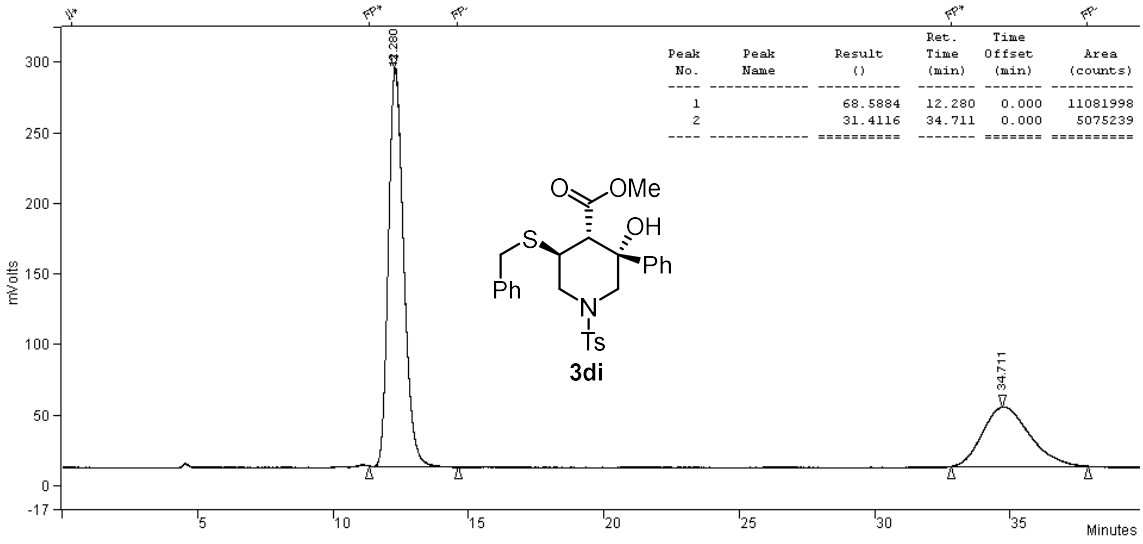


Peak No.	Peak Name	Result ()	Ret. Time (min)	Time Offset (min)	Area (counts)
1		91.5374	21.068	0.000	1730893
2		8.4626	25.001	0.000	160021
Totals:		100.0000		0.000	1890914

Methyl (3*R,4*S**,5*S**)-3-hydroxy-3-phenyl-5-(benzylthio)-1-tosylpiperidine-4-carboxylate 3di**



Methyl (3*R*,4*S*,5*S*)-3-hydroxy-3-phenyl-5-(benzylthio)-1-tosylpiperidine-4-carboxylate 3di



Calculations Coordinates

All Calculation have been performed whit Charge=0 and Spin Multiplicity=1

Ciano-addition

Activated complexes A

C	2.02014	1.50898	-0.48139
C	2.8286	0.29824	-0.85337
C	3.96413	-0.06539	-0.24709
C	0.59114	1.12147	2.30819
C	0.34615	0.36914	0.99605
H	2.45734	-0.3026	-1.68182
H	2.44621	2.02172	0.38869
H	2.02232	2.20312	-1.32748
H	0.96634	-0.53506	0.96976
H	-0.68721	0.00117	1.01344
H	4.37585	0.4926	0.58988
C	4.72142	-1.25632	-0.70201
O	4.40873	-1.99295	-1.61655
C	0.54572	0.26958	3.54715
H	0.56759	0.90023	4.43867
H	-0.35638	-0.36422	3.51119
H	1.40788	-0.41122	3.56215
O	0.76971	2.33008	2.31705
O	5.8339	-1.42832	0.05112
C	6.64147	-2.56151	-0.30127
H	6.9926	-2.4773	-1.33341
H	7.48248	-2.54944	0.39267
H	6.07	-3.48791	-0.19719
S	-0.59016	2.0366	-0.9471
O	-1.83537	1.25766	-0.81713
O	-0.09897	2.41684	-2.27496
N	0.61627	1.13744	-0.21977
C	-0.83511	3.56165	-0.01234
H	-1.61988	4.11903	-0.5295
H	-1.12191	3.31791	1.00927
H	0.09909	4.12466	-0.01126
N	-4.41253	-1.44324	-0.7404
C	-5.12198	-2.61415	-0.10782
H	-4.61404	-2.81898	0.84345
H	-6.16798	-2.34035	0.04808
H	-5.05563	-3.46606	-0.78839
C	-4.49393	-0.26061	0.19939
H	-3.93248	0.56502	-0.2373
H	-5.54863	-0.00277	0.3207
H	-4.04563	-0.56838	1.14777
C	-2.96326	-1.8157	-0.9631

H	-2.93609	-2.64443	-1.67432
H	-2.44033	-0.94213	-1.35345
H	-2.55274	-2.10749	0.00687
C	-5.04285	-1.08655	-2.04919
H	-6.08733	-0.81656	-1.88048
H	-4.50215	-0.2414	-2.47895
H	-4.98505	-1.9467	-2.71927
C	-2.1263	-1.59981	2.49916
N	-3.042	-2.29258	2.22495

Activated complexes B

C	1.20531	0.49801	0.75812
C	-0.55601	2.31752	0.57935
C	4.45385	0.8822	0.51767
C	3.32587	0.98039	-0.5193
H	1.70095	1.11542	1.51471
H	0.83104	-0.39865	1.28584
H	2.97825	2.02136	-0.58722
H	3.74663	0.73168	-1.49956
H	-0.14947	2.908	1.39591
C	-1.7973	2.80622	-0.0509
O	-2.51924	2.17211	-0.81009
C	5.563	1.91004	0.38757
H	5.95279	1.93711	-0.6374
H	5.17694	2.9133	0.61001
H	6.36971	1.67269	1.08358
O	4.45767	0.02467	1.37816
O	-2.07377	4.07345	0.32835
C	-3.27074	4.64227	-0.22164
H	-4.14675	4.05804	0.07438
H	-3.32961	5.65142	0.18686
H	-3.21707	4.67219	-1.31321
S	2.1093	-1.4042	-0.96824
O	3.18191	-1.43975	-1.97204
O	0.71361	-1.61826	-1.38351
N	2.19504	0.11724	-0.26
C	2.4784	-2.57999	0.34106
H	2.5391	-3.56175	-0.13598
H	3.43199	-2.29545	0.78756
H	1.65898	-2.55276	1.07179
C	0.01994	1.18647	0.15049
H	-0.41334	0.66954	-0.7011
C	-0.40307	-2.1598	2.1236
N	-1.5012	-2.56299	2.27449
N	-3.68219	-1.59634	-0.15581
C	-4.72607	-1.18248	-1.14441
H	-4.46938	-0.19332	-1.52835
H	-4.7507	-1.90783	-1.9602

H	-5.69686	-1.1512	-0.64536
C	-3.99868	-2.95349	0.41957
H	-4.00194	-3.68066	-0.39537
H	-3.22214	-3.17824	1.16206
H	-4.98612	-2.90756	0.88486
C	-3.62342	-0.58948	0.96978
H	-2.86262	-0.93682	1.67583
H	-3.36666	0.38015	0.54048
H	-4.6082	-0.55402	1.44194
C	-2.3345	-1.65127	-0.83951
H	-2.38529	-2.38722	-1.64399
H	-2.12369	-0.66182	-1.24405
H	-1.58765	-1.93922	-0.09849

TS^{1}_{B}

C	1.22821	0.07012	1.55168
C	0.20314	2.25599	0.77644
C	4.1643	0.32383	-0.40937
C	2.63789	0.35138	-0.54712
H	1.91109	0.72092	2.10777
H	0.92142	-0.73648	2.21669
H	2.22205	1.35388	-0.38901
H	2.37111	0.03866	-1.55997
H	0.82997	2.86494	1.42094
C	-0.65359	2.90577	-0.15238
O	-1.54165	2.3919	-0.85202
C	4.77068	1.1117	0.73154
H	4.52733	2.17652	0.62667
H	4.34513	0.78138	1.68697
H	5.85427	0.97896	0.74558
O	4.84607	-0.32616	-1.18363
O	-0.38904	4.25899	-0.25312
C	-1.19613	4.96343	-1.18811
H	-2.25995	4.88966	-0.93652
H	-0.87252	6.00611	-1.13533
H	-1.05984	4.5819	-2.20642
S	1.38925	-1.99579	-0.16545
O	0.64467	-1.7728	-1.42263
O	0.69293	-2.67704	0.93587
N	2.02738	-0.55183	0.46163
C	2.8804	-2.91459	-0.5786
H	2.55183	-3.82718	-1.08104
H	3.51196	-2.31322	-1.23592
H	3.40395	-3.14844	0.34941
C	0.03163	0.86966	1.03713
H	-0.45505	0.35691	0.20619
C	-1.33417	0.44356	2.22254
N	-2.44786	0.29933	2.55961

N	-3.66853	-1.36078	-0.41677
C	-4.27055	-2.07267	-1.58797
H	-3.51441	-2.16238	-2.36976
H	-4.60091	-3.06456	-1.27335
H	-5.1203	-1.49535	-1.95692
C	-4.68622	-1.21192	0.68402
H	-5.02019	-2.20689	0.98628
H	-4.20787	-0.69097	1.51906
H	-5.52935	-0.63406	0.29982
C	-3.2017	0.01463	-0.84498
H	-2.83754	0.56	0.02168
H	-2.39667	-0.09164	-1.57058
H	-4.04715	0.54261	-1.28946
C	-2.4901	-2.15299	0.10017
H	-2.83486	-3.15779	0.35299
H	-1.7212	-2.19324	-0.67214
H	-2.10374	-1.65133	0.98653

TS^{1}_{A}

C	2.03853	1.09981	1.05189
C	3.11824	0.54406	0.16032
C	3.92503	-0.46486	0.51056
C	-0.85193	-0.89557	1.24505
C	0.10269	-0.27374	0.19418
H	3.23485	1.00985	-0.81574
H	2.00523	0.55364	2.00012
H	2.27025	2.14358	1.28754
H	0.92466	-0.9928	0.07102
H	-0.42957	-0.24096	-0.75459
H	3.84306	-0.95923	1.47553
C	4.9839	-0.95498	-0.4022
O	5.22113	-0.53528	-1.51727
C	-0.34817	-0.91762	2.68977
H	-1.14465	-1.27838	3.34566
H	0.48855	-1.62804	2.75319
H	-0.01807	0.06557	3.03598
O	-1.47381	-1.91039	0.81908
O	5.68071	-1.96561	0.17777
C	6.73469	-2.51558	-0.62423
H	7.47342	-1.74753	-0.87005
H	7.18633	-3.30162	-0.01777
H	6.33572	-2.92957	-1.55457
S	0.26453	2.34118	-0.55229
O	-0.70404	1.8496	-1.54161
O	1.50031	3.00687	-0.99251
N	0.68536	1.04982	0.46403
C	-0.58903	3.49364	0.53764
H	-0.8352	4.37046	-0.06637

H	-1.48625	3.0077	0.92237
H	0.08827	3.77477	1.3467
N	-4.65465	-1.31944	-0.75626
C	-5.11299	-2.50413	-1.54914
H	-6.05564	-2.86939	-1.13692
H	-5.25067	-2.20765	-2.59072
H	-4.35002	-3.28115	-1.48074
C	-4.48427	-1.73076	0.69318
H	-3.60529	-2.37055	0.78074
H	-4.29897	-0.82755	1.27381
H	-5.405	-2.22831	1.00627
C	-3.34448	-0.81839	-1.33379
H	-3.12018	0.14762	-0.88475
H	-2.55397	-1.51684	-1.0494
H	-3.46783	-0.72889	-2.415
C	-5.67007	-0.21399	-0.82759
H	-6.62106	-0.57959	-0.43385
H	-5.29724	0.61493	-0.22225
H	-5.7872	0.09274	-1.86911
C	-2.16288	0.60397	1.43164
N	-3.20011	1.15187	1.35967

Int^1_A

C	1.9991	1.44614	0.84439
C	2.95828	0.73201	-0.06979
C	3.92158	-0.0963	0.35112
C	-1.03059	-0.24472	1.94224
C	0.09527	-0.21883	0.84189
H	2.84532	0.91812	-1.13618
H	2.1929	1.18431	1.89041
H	2.14062	2.52547	0.74075
H	0.96282	-0.82289	1.13179
H	-0.3017	-0.64608	-0.08147
H	4.07513	-0.31159	1.40573
C	4.83861	-0.75655	-0.60618
O	4.80913	-0.65193	-1.81656
C	-0.43337	0.103	3.32934
H	-1.22633	0.05204	4.08088
H	0.38853	-0.56044	3.6304
H	-0.06875	1.13523	3.29302
O	-2.09805	0.50578	1.62921
O	5.74586	-1.52054	0.05372
C	6.68647	-2.20758	-0.78279
H	7.27079	-1.49533	-1.37213
H	7.33295	-2.76403	-0.1031
H	6.17026	-2.88846	-1.46546
S	-0.21244	2.09492	-0.57426
O	-1.04348	1.23174	-1.43587

O	0.80111	2.96114	-1.19598
N	0.58437	1.1416	0.56647
C	-1.31213	3.11798	0.41194
H	-1.96126	3.66357	-0.27803
H	-1.85334	2.41649	1.06188
H	-0.69532	3.81456	0.98389
N	-4.12764	-1.1531	-1.1351
C	-4.69875	-2.14818	-0.16029
H	-4.05216	-2.19016	0.71825
H	-5.70659	-1.82848	0.11119
H	-4.73166	-3.12858	-0.64043
C	-4.08001	0.21553	-0.48721
H	-3.7241	0.92302	-1.23722
H	-5.09651	0.46384	-0.17213
H	-3.36353	0.20239	0.36429
C	-2.72923	-1.58004	-1.51043
H	-2.79757	-2.47437	-2.13364
H	-2.23866	-0.76076	-2.03631
H	-2.18949	-1.80444	-0.59223
C	-4.97969	-1.10085	-2.36577
H	-5.97687	-0.75242	-2.09078
H	-4.52671	-0.40614	-3.07486
H	-5.04049	-2.0982	-2.80674
C	-1.475	-1.71487	1.96482
N	-1.98659	-2.75642	1.84013

Int^1_B

C	1.64551	0.54483	1.32562
C	-0.01681	2.38957	0.55298
C	3.28907	0.52181	-1.4858
C	1.80505	0.34905	-1.17584
H	2.5177	1.19763	1.21114
H	1.84209	-0.11319	2.17682
H	1.29604	1.32565	-1.15621
H	1.34199	-0.23242	-1.97943
H	0.56927	3.29766	0.46092
C	-1.22646	2.30492	-0.10734
O	-2.10537	1.38332	-0.04497
C	3.60813	1.36978	-2.70117
H	2.98785	1.08643	-3.55973
H	3.38573	2.422	-2.48038
H	4.6657	1.27346	-2.95453
O	4.15937	0.0277	-0.79029
O	-1.45813	3.37757	-0.97083
C	-2.69678	3.37426	-1.65183
H	-3.54916	3.3689	-0.96095
H	-2.7153	4.29539	-2.24162
H	-2.79987	2.51352	-2.32703

S	1.43347	-1.92816	0.24165
O	1.10454	-2.44817	-1.0971
O	0.54447	-2.24331	1.37374
N	1.51073	-0.27509	0.10861
C	3.0673	-2.55217	0.6886
H	2.98255	-3.63903	0.75795
H	3.77921	-2.24589	-0.0763
H	3.34834	-2.13069	1.6554
C	0.36374	1.38668	1.60719
H	-0.45777	0.6692	1.70797
C	0.54154	2.02344	2.9326
N	0.70525	2.53859	3.96216
N	-3.212	-1.62141	-0.2396
C	-3.69354	-3.03462	-0.32666
H	-2.85543	-3.7028	-0.12192
H	-4.48288	-3.18932	0.41176
H	-4.08075	-3.21952	-1.33075
C	-4.34184	-0.65828	-0.49668
H	-5.10799	-0.80937	0.26686
H	-3.92206	0.35038	-0.44318
H	-4.75565	-0.8643	-1.48639
C	-2.13165	-1.38037	-1.26951
H	-1.8206	-0.33771	-1.14833
H	-1.30186	-2.06445	-1.08895
H	-2.56377	-1.55837	-2.2573
C	-2.65357	-1.35027	1.14021
H	-3.43295	-1.57821	1.87097
H	-1.77283	-1.97565	1.29437
H	-2.37803	-0.292	1.15579

TS^2_B

C	2.458	1.08659	-0.34974
C	1.6333	1.58753	0.86372
C	0.13437	1.34322	0.74088
C	-0.05446	-1.00017	0.17145
C	0.97305	-0.86436	-0.95547
H	2.00734	1.05217	1.74522
H	2.12974	1.6196	-1.24397
H	3.51641	1.29784	-0.1788
H	1.09418	-1.85634	-1.40603
H	0.5557	-0.19413	-1.7135
H	-0.40486	1.35933	1.68474
C	-0.55202	1.91596	-0.36601
O	-0.09766	2.22614	-1.47237
C	0.39778	-1.5128	1.52742
H	0.55963	-2.59715	1.44447
H	1.33042	-1.07323	1.88172
H	-0.38849	-1.33891	2.26768

O	-1.93088	2.05749	-0.14009
C	-2.60685	2.75045	-1.18448
H	-2.17513	3.74241	-1.35019
H	-2.56439	2.20515	-2.13416
H	-3.64642	2.85766	-0.8551
S	3.49435	-1.39523	-0.08203
O	2.95763	-2.75916	-0.1756
O	4.08264	-0.90214	1.17113
N	2.29665	-0.35297	-0.59103
C	4.77166	-1.23267	-1.35086
H	5.60875	-1.86854	-1.05341
H	4.35771	-1.56258	-2.305
H	5.09477	-0.19138	-1.40698
O	-1.24046	-1.22975	-0.19164
N	-4.40695	-1.05353	0.15029
C	-3.94	-2.47431	0.35144
H	-4.38503	-3.09921	-0.42562
H	-2.84852	-2.46297	0.28102
H	-4.2716	-2.80966	1.33639
C	-3.96358	-0.58047	-1.21607
H	-4.31162	0.44354	-1.35262
H	-2.87144	-0.62947	-1.24401
H	-4.41615	-1.2365	-1.96296
C	-3.77142	-0.18323	1.21082
H	-4.11847	-0.53269	2.18565
H	-2.69142	-0.2847	1.09844
H	-4.06593	0.85195	1.04208
C	-5.89838	-0.9818	0.25385
H	-6.34101	-1.61256	-0.51956
H	-6.20516	-1.33296	1.24087
H	-6.21342	0.05386	0.11468
C	1.94681	3.01726	1.09259
N	2.16961	4.14297	1.2797

$TS_{2(R^*,R^*)}^{A}$

C	0.51952	-0.01537	-0.31269
C	1.6725	-0.90977	-0.71338
C	3.44613	0.76335	-0.28737
C	2.39661	1.83335	0.12621
H	1.41641	-1.9431	-0.46689
H	0.34341	-0.00084	0.75931
H	4.37694	0.89923	0.26572
H	3.64053	0.87091	-1.36581
H	1.82831	-0.83202	-1.80137
N	2.90343	-0.56322	0.01698
O	1.17688	1.60813	-0.53114
S	3.99577	-1.7962	0.34885
O	5.01839	-1.23794	1.23606

O	3.21053	-2.97179	0.73392
C	-0.66092	-0.13249	-1.11469
H	-0.57453	-0.45997	-2.14692
C	-1.92646	0.22051	-0.67962
O	-3.01824	0.11126	-1.29821
O	-2.01566	0.72028	0.65436
C	-1.8946	2.14437	0.7232
H	-1.96871	2.41819	1.78058
H	-0.92792	2.46469	0.32114
H	-2.70507	2.63782	0.16646
C	4.81171	-2.19192	-1.21969
H	5.52817	-2.9916	-1.01914
H	4.06254	-2.53035	-1.93876
H	5.33281	-1.30534	-1.5873
N	-5.83408	-0.65481	0.17424
C	-5.24505	-1.75506	-0.67921
H	-4.26905	-1.40084	-1.0332
H	-5.15826	-2.65442	-0.06613
H	-5.92365	-1.9359	-1.51562
C	-5.89525	0.6156	-0.64263
H	-6.29849	1.40937	-0.0103
H	-4.87029	0.82862	-0.96997
H	-6.55604	0.44306	-1.49483
C	-7.20566	-1.04268	0.63182
H	-7.13856	-1.95824	1.22266
H	-7.61978	-0.23718	1.24122
H	-7.83819	-1.21007	-0.24186
C	-4.9432	-0.42061	1.37087
H	-3.95878	-0.08462	1.0261
H	-5.40964	0.34387	1.99627
H	-4.86372	-1.35652	1.92782
C	2.26755	1.92119	1.66375
H	2.00454	0.94197	2.07099
H	3.20715	2.24281	2.12612
H	1.48381	2.63924	1.92023
C	2.89788	3.14301	-0.37639
N	3.28837	4.16375	-0.76966

$TS_{2(R^*,S^*)}{}^{A}$

C	-0.30228	0.56105	0.16334
C	-1.05885	-0.72853	0.38753
C	-3.28738	0.34854	0.716
C	-2.63181	1.75269	0.66519
H	-0.60949	-1.51512	-0.22337
H	-0.46274	0.99507	-0.82053
H	-4.28624	0.35915	0.27575
H	-3.35837	0.07807	1.78294
H	-0.97291	-1.01242	1.44973

N	-2.47042	-0.62153	-0.02172
O	-1.32431	1.71235	1.12489
S	-3.23037	-2.03978	-0.5067
O	-4.53652	-1.67461	-1.05594
O	-2.25703	-2.80688	-1.29057
C	-3.42564	2.71743	1.56961
H	-2.96208	3.7063	1.53248
H	-4.47365	2.80192	1.26009
H	-3.37723	2.35152	2.60004
C	-2.70721	2.27549	-0.74197
N	-2.73417	2.71595	-1.81667
C	1.03806	0.59801	0.64179
H	1.29867	0.03284	1.5338
C	2.003	1.51948	0.19673
O	3.20726	1.57429	0.57059
O	1.56367	2.38751	-0.7719
C	2.51048	3.32477	-1.26579
H	1.94313	4.00719	-1.90205
H	2.99042	3.8761	-0.45195
H	3.29293	2.83801	-1.86362
C	-3.5467	-2.99064	1.00585
H	-4.04093	-3.91729	0.70589
H	-2.59753	-3.21332	1.49834
H	-4.20064	-2.41497	1.6643
N	4.77637	-1.32684	0.0753
C	4.68824	-0.89102	1.52049
H	4.05341	0.00494	1.54597
H	4.26456	-1.71275	2.10133
H	5.69803	-0.66604	1.87048
C	5.28018	-0.16536	-0.74943
H	5.29476	-0.46861	-1.79822
H	4.60246	0.67832	-0.57142
H	6.29152	0.07534	-0.41495
C	5.71034	-2.49039	-0.05929
H	5.34303	-3.31478	0.55467
H	5.7497	-2.79618	-1.10657
H	6.70401	-2.19038	0.2781
C	3.40114	-1.72713	-0.40456
H	2.69114	-0.90937	-0.23021
H	3.46329	-1.96656	-1.46796
H	3.09021	-2.61112	0.15614

Int2(R*,R*)A

C	0.56182	0.30788	-0.27819
C	1.53844	-0.81778	-0.63219
C	3.46103	0.66877	-0.26737
C	2.47464	1.8031	0.11914
H	1.12408	-1.77183	-0.30496

H	0.33906	0.26761	0.79137
H	4.39253	0.75994	0.29346
H	3.67327	0.74895	-1.34533
H	1.68321	-0.84117	-1.72551
N	2.82494	-0.60733	0.05903
O	1.22677	1.60988	-0.54098
S	3.82108	-1.93582	0.31926
O	4.95008	-1.47026	1.12834
O	2.9593	-3.0322	0.76615
C	-0.68181	0.21943	-1.06775
H	-0.61551	-0.07725	-2.11121
C	-1.9169	0.57818	-0.59775
O	-3.03826	0.55321	-1.19269
O	-1.96159	0.98515	0.78064
C	-2.08642	2.39471	0.9215
H	-2.17008	2.60982	1.99213
H	-1.20249	2.90336	0.5155
H	-2.97989	2.77426	0.40528
C	4.48289	-2.40626	-1.30051
H	5.12566	-3.27557	-1.14529
H	3.65599	-2.66468	-1.96541
H	5.06637	-1.57714	-1.7066
N	-5.64565	-0.81267	0.10447
C	-4.94396	-1.66036	-0.93372
H	-4.04812	-1.10325	-1.24455
H	-4.69667	-2.62175	-0.47877
H	-5.63127	-1.80714	-1.76991
C	-5.91923	0.55111	-0.48722
H	-6.41263	1.16037	0.27324
H	-4.94531	0.96288	-0.78087
H	-6.57653	0.42413	-1.35013
C	-6.92664	-1.46592	0.51803
H	-6.70535	-2.44655	0.94388
H	-7.42258	-0.84107	1.26341
H	-7.56786	-1.57816	-0.35819
C	-4.74526	-0.646	1.30529
H	-3.83756	-0.1165	0.99793
H	-5.28848	-0.07159	2.05911
H	-4.50616	-1.63733	1.69575
C	2.33652	1.9431	1.64882
H	2.06635	0.98283	2.0928
H	3.28134	2.27283	2.09276
H	1.5615	2.67926	1.87825
C	3.01423	3.06998	-0.42963
N	3.4655	4.05599	-0.8433

$Int_{2(R^*,S^*)}A$

C	-0.38364	0.69646	0.19472

C	-1.04284	-0.68531	0.26077
C	-3.22997	0.35746	0.75423
C	-2.53489	1.73682	0.70047
H	-0.57665	-1.34604	-0.4699
H	-0.45864	1.08251	-0.82733
H	-4.25213	0.41766	0.37653
H	-3.2492	0.05524	1.81535
H	-0.89479	-1.1025	1.27256
N	-2.47928	-0.59436	-0.06502
O	-1.17153	1.61399	1.05478
S	-3.26805	-2.00807	-0.51693
O	-4.62592	-1.63804	-0.91968
O	-2.36693	-2.73234	-1.41632
C	-3.16655	2.69721	1.71767
H	-2.65545	3.66183	1.67283
H	-4.23182	2.84742	1.51539
H	-3.04055	2.28296	2.72242
C	-2.68637	2.32157	-0.6653
N	-2.81432	2.8182	-1.70676
C	1.02256	0.65022	0.63649
H	1.25059	0.11199	1.55424
C	2.00668	1.51517	0.16885
O	3.22237	1.55831	0.53309
O	1.59311	2.37301	-0.84018
C	2.57815	3.24029	-1.37592
H	2.03919	3.93684	-2.02319
H	3.10676	3.78816	-0.58988
H	3.32299	2.69852	-1.97655
C	-3.42161	-3.01061	0.98747
H	-3.92282	-3.93843	0.70325
H	-2.42635	-3.22714	1.38145
H	-4.02343	-2.47199	1.72262
N	4.68736	-1.37299	0.09766
C	4.63379	-0.89322	1.53048
H	4.02207	0.02118	1.53406
H	4.19807	-1.68677	2.1411
H	5.655	-0.68573	1.858
C	5.20445	-0.24715	-0.76752
H	5.19054	-0.57908	-1.80771
H	4.54829	0.61709	-0.59435
H	6.2283	-0.02518	-0.45856
C	5.58907	-2.56243	-0.01923
H	5.21233	-3.36002	0.62391
H	5.60275	-2.89843	-1.05797
H	6.59591	-2.27894	0.29278
C	3.2936	-1.75036	-0.34674
H	2.60151	-0.91206	-0.17988
H	3.33175	-2.01797	-1.40476
H	2.97484	-2.61402	0.24114

Int$_2$B

C	-2.52639	0.8793	0.06104
C	-1.65178	1.68915	-0.9239
C	-0.13782	1.32817	-0.83297
C	0.1235	-0.23467	-0.91232
C	-0.85866	-0.95101	0.05996
H	-1.98339	1.43346	-1.93708
H	-2.28615	1.1809	1.08871
H	-3.58048	1.07529	-0.1403
H	-0.78145	-2.02607	-0.10775
H	-0.54596	-0.71888	1.08691
H	0.37974	1.79067	-1.67779
C	0.49436	1.8683	0.435
O	0.07761	1.71112	1.56699
C	-0.14331	-0.70746	-2.36045
H	0.06763	-1.78131	-2.42049
H	-1.17388	-0.55399	-2.70071
H	0.53924	-0.19078	-3.04569
O	1.60171	2.60266	0.16821
C	2.22264	3.19965	1.31355
H	1.52003	3.85403	1.83616
H	2.57052	2.4326	2.01268
H	3.06372	3.77681	0.92578
S	-3.47871	-1.62289	0.26137
O	-3.05471	-2.95199	-0.18563
O	-4.7502	-1.04214	-0.18044
N	-2.26316	-0.54638	-0.16608
C	-3.51359	-1.66114	2.07332
H	-4.29084	-2.36992	2.36737
H	-2.54086	-1.99267	2.44251
H	-3.75229	-0.66431	2.45026
O	1.40483	-0.50259	-0.52874
N	4.28886	-1.28665	0.0789
C	3.58434	-2.39969	-0.66339
H	3.61252	-3.29684	-0.04069
H	2.55574	-2.03532	-0.83041
H	4.11785	-2.57696	-1.59998
C	3.53471	-1.02112	1.36196
H	4.03432	-0.20493	1.88884
H	2.5086	-0.75431	1.06201
H	3.56357	-1.92921	1.96855
C	4.23997	-0.03823	-0.77399
H	4.7767	-0.24168	-1.7035
H	3.16993	0.16801	-0.94547
H	4.73288	0.76812	-0.22642
C	5.70377	-1.66491	0.37285

H	5.71262	-2.56679	0.9884
H	6.22579	-1.85337	-0.56745
H	6.18902	-0.84605	0.90807
C	-1.88025	3.12944	-0.74403
N	-2.04408	4.26997	-0.59674

4'a'

C	0.63454	0.54199	-0.18882
C	0.96762	-0.78976	-0.86259
C	3.29119	-0.04706	-1.12297
C	2.89796	1.32507	-0.49402
H	0.30497	-1.57077	-0.47612
H	0.77913	0.43999	0.89179
H	4.3191	-0.31037	-0.87102
H	3.20622	0.03877	-2.21263
H	0.78004	-0.70773	-1.94181
N	2.39402	-1.12711	-0.70678
O	1.50123	1.57593	-0.69898
S	2.83382	-2.10665	0.59601
O	4.29349	-2.01747	0.7198
O	1.97635	-1.85664	1.76477
C	-0.81015	0.89796	-0.47253
H	-1.38663	-0.02929	-0.18831
C	-1.43197	2.05481	0.25084
O	-2.53216	2.51079	-0.02548
O	-0.70257	2.50511	1.2926
C	-1.29023	3.57184	2.0504
H	-0.56257	3.81608	2.82501
H	-1.4776	4.43936	1.41226
H	-2.23478	3.2526	2.50045
C	2.40605	-3.74197	-0.03044
H	2.61352	-4.45287	0.7726
H	1.34436	-3.76276	-0.28411
H	3.0234	-3.95182	-0.90459
N	-4.93442	-0.8064	-0.34484
C	-4.06152	-0.35977	-1.49519
H	-3.96132	0.72657	-1.45487
H	-3.09137	-0.84094	-1.34819
H	-4.5392	-0.67616	-2.42571
C	-6.33483	-0.33337	-0.54893
H	-6.94609	-0.65337	0.29724
H	-6.33434	0.75665	-0.6147
H	-6.72838	-0.76229	-1.47332
C	-4.86785	-2.31392	-0.26566
H	-3.79418	-2.53697	-0.08921
H	-5.50698	-2.64184	0.55802
H	-5.23426	-2.72477	-1.20984
C	-4.36547	-0.24991	0.94273

H	-4.32618	0.83773	0.86353
H	-5.02012	-0.56152	1.76068
H	-3.35153	-0.70052	0.9976
C	3.29938	1.45269	0.98797
H	2.8646	0.64791	1.58496
H	4.3872	1.40482	1.09435
H	2.94205	2.41051	1.37545
C	3.59432	2.37896	-1.26722
N	4.17848	3.17803	-1.87267
H	-0.96876	1.05731	-1.54545
O	-2.02798	-1.74263	0.10448
H	-1.54906	-2.0756	0.88108

4a'

C	-0.5876	0.87001	-0.61464
C	-1.21402	-0.51961	-0.77557
C	-2.59974	-0.08221	1.21043
C	-1.94051	1.30838	1.33236
H	-1.31429	-0.75458	-1.83758
H	-1.13271	1.6085	-1.21593
H	-3.63778	-0.04897	1.54515
H	-2.0258	-0.76123	1.86324
H	-0.54246	-1.25238	-0.29489
N	-2.5666	-0.50847	-0.18728
O	-0.63666	1.27923	0.76849
S	-3.59348	-1.77492	-0.62463
O	-4.85919	-1.55163	0.07726
O	-3.52769	-1.8869	-2.08186
C	-1.7634	1.70212	2.80351
H	-1.2797	2.67981	2.8678
H	-2.72981	1.74885	3.3141
H	-1.12645	0.96193	3.29629
C	-2.77534	2.33899	0.6512
N	-3.406	3.1768	0.15405
C	0.88702	0.78164	-0.98206
H	1.33175	0.00052	-0.33059
C	1.7103	2.0429	-0.90942
O	2.93055	2.05274	-0.86678
O	0.97566	3.16969	-0.94084
C	1.71005	4.40213	-0.89116
H	0.9575	5.19057	-0.91361
H	2.30046	4.45998	0.02726
H	2.38112	4.48527	-1.7505
C	-2.85058	-3.27903	0.06026
H	-3.47372	-4.11612	-0.26215
H	-1.83513	-3.39158	-0.32551
H	-2.84624	-3.21404	1.15037
N	4.61311	-1.50286	0.27427

C	4.23799	-2.84202	0.8661
H	3.1302	-2.80248	0.96128
H	4.57675	-3.6264	0.18437
H	4.7424	-2.94176	1.83068
C	4.08676	-0.42471	1.19749
H	4.26149	0.5476	0.73469
H	3.00318	-0.654	1.27049
H	4.6154	-0.51212	2.15026
C	6.08981	-1.37771	0.10469
H	6.445	-2.1725	-0.55537
H	6.31505	-0.40228	-0.33166
H	6.5697	-1.46583	1.08147
C	3.9216	-1.37283	-1.06312
H	2.86173	-1.57002	-0.87687
H	4.06661	-0.35474	-1.42862
H	4.36439	-2.10212	-1.74604
H	0.97314	0.40876	-2.01294
O	1.56547	-1.73609	0.61565
H	1.00108	-1.61277	1.39593

Solfur Addition

Activated Complex

C	3.06105	0.55037	-0.59828
C	2.14592	1.72075	-0.36665
C	1.59974	2.4629	-1.3371
C	1.91711	-2.24926	-1.60848
C	1.55594	-1.45307	-0.35369
H	1.95461	1.9697	0.67508
H	3.12613	0.29246	-1.66061
H	4.06404	0.83135	-0.25966
H	0.67193	-0.83303	-0.57703
H	1.23047	-2.14277	0.43144
H	1.78227	2.25628	-2.38783
C	0.73275	3.61951	-1.0345
O	0.26747	3.91185	0.05968
C	0.77392	-2.99948	-2.2469
H	0.35536	-3.73053	-1.54342
H	-0.04347	-2.30214	-2.47886
H	1.11879	-3.51075	-3.14805
O	3.05224	-2.24827	-2.0592
O	0.50429	4.34699	-2.1462
C	-0.32506	5.50638	-1.98692
H	0.07336	6.16246	-1.20877
H	-0.31601	6.00682	-2.95527
H	-1.34606	5.21448	-1.72369
S	3.6651	-1.23438	1.34782
O	2.87869	-2.18381	2.14169

O	4.31661	-0.07653	1.97159
N	2.62992	-0.61937	0.17938
C	4.95718	-2.17472	0.50385
H	5.61482	-2.57076	1.2813
H	4.49773	-2.97565	-0.07383
H	5.5086	-1.50514	-0.15807
C	-2.94112	-1.66378	-0.75534
C	-2.57206	-2.53954	0.29165
C	-3.3942	-3.59601	0.68816
C	-4.61943	-3.819	0.05689
C	-5.00472	-2.9653	-0.98185
C	-4.18558	-1.91052	-1.37915
H	-1.61794	-2.38514	0.79103
H	-3.07048	-4.2513	1.495
H	-5.25903	-4.64267	0.36334
H	-5.95397	-3.12456	-1.49022
H	-4.49444	-1.25837	-2.19162
S	-1.91188	-0.31163	-1.26705
N	-2.43806	1.88027	1.89634
C	-1.01677	1.37578	1.78574
H	-0.98862	0.6817	0.93557
H	-0.36685	2.23187	1.60119
H	-0.75862	0.87375	2.72065
C	-2.80696	2.60004	0.61983
H	-2.74224	1.86892	-0.19743
H	-3.8236	2.98482	0.7288
H	-2.09277	3.41076	0.46921
C	-3.36304	0.70538	2.08264
H	-3.08635	0.18797	3.00324
H	-4.38779	1.07608	2.15262
H	-3.25012	0.04284	1.2221
C	-2.55111	2.81776	3.05748
H	-2.279	2.28627	3.97155
H	-1.87104	3.65608	2.89776
H	-3.5799	3.17717	3.12747

Int^{D} (3R*,4S*,5S*)

C	-1.46586	0.61741	-0.53706
C	-1.16023	-0.62125	0.31345
C	0.34849	-0.93445	0.39982
C	1.20243	0.32823	0.85806
C	0.76584	1.55614	0.00694
H	-1.5156	-0.43471	1.33018
H	-1.19704	0.41903	-1.58295
H	-2.52783	0.85792	-0.47186
H	1.23168	2.44813	0.42823
H	1.13422	1.40131	-1.01597
H	0.50309	-1.71834	1.14637

S	-2.08907	-2.116	-0.29874
C	0.9256	-1.44389	-0.90773
O	0.86091	-0.89917	-1.9931
C	0.91481	0.60306	2.3522
H	1.53491	1.44721	2.67552
H	-0.12942	0.85587	2.56751
H	1.20035	-0.27249	2.94774
C	-3.77767	-1.71082	0.16114
C	-4.72512	-1.44284	-0.83571
C	-4.17618	-1.71263	1.50577
C	-6.05191	-1.17696	-0.49114
H	-4.41648	-1.44138	-1.87672
C	-5.49838	-1.42928	1.84656
H	-3.44943	-1.94172	2.27994
C	-6.43976	-1.16406	0.8491
H	-6.77924	-0.96941	-1.27166
H	-5.796	-1.42549	2.8919
H	-7.4708	-0.94889	1.11655
O	1.53992	-2.64576	-0.74428
C	2.07443	-3.21861	-1.94215
H	1.28879	-3.35932	-2.68954
H	2.84895	-2.57492	-2.37178
H	2.49582	-4.18146	-1.64755
S	-1.2842	3.28978	-0.30447
O	-0.45197	4.2384	0.44175
O	-2.73914	3.25746	-0.12408
N	-0.7004	1.75117	0.01483
C	-0.97863	3.59694	-2.06583
H	-1.34299	4.60235	-2.28794
H	0.09412	3.53234	-2.25936
H	-1.52331	2.85949	-2.65923
O	2.52967	0.08779	0.64662
N	5.53241	-0.31913	0.40342
C	5.22896	0.83834	1.32792
H	5.7038	1.734	0.92068
H	4.12719	0.91613	1.34635
H	5.64507	0.60788	2.31136
C	4.93289	-0.01376	-0.95066
H	5.13844	-0.85799	-1.61284
H	3.85281	0.12643	-0.77873
H	5.40985	0.88933	-1.33857
C	4.8638	-1.55884	0.95552
H	5.29363	-1.76615	1.93831
H	3.78728	-1.32061	1.01069
H	5.06925	-2.3882	0.27501
C	7.00686	-0.52645	0.28799
H	7.46555	0.38025	-0.11196
H	7.41582	-0.7428	1.27707
H	7.19859	-1.36592	-0.38364

Int^{B} (3R*,4S*,5R*)

C	0.78114	-0.25428	1.23052
C	1.19185	-0.32387	-0.24877
C	0.88568	-1.6792	-0.90793
C	-0.70192	-1.93768	-0.74614
C	-1.01714	-1.923	0.78685
H	0.61143	0.40821	-0.81324
H	1.40203	-0.94216	1.81655
H	0.91165	0.76344	1.60109
H	-2.093	-2.05454	0.90933
H	-0.48704	-2.72015	1.32591
H	1.05034	-1.5888	-1.98377
S	2.98556	0.12376	-0.44912
C	1.73851	-2.81303	-0.39506
O	1.9423	-3.10142	0.77255
C	-1.0454	-3.34315	-1.29339
H	-0.77511	-3.39549	-2.35344
H	-0.54416	-4.16544	-0.76546
H	-2.12866	-3.49617	-1.2161
C	2.91311	1.91645	-0.3556
C	3.4641	2.58207	0.74722
C	2.35978	2.66765	-1.40339
C	3.45756	3.97763	0.80337
H	3.89484	2.00178	1.55757
C	2.34193	4.06055	-1.33701
H	1.95614	2.15454	-2.27172
C	2.89278	4.71925	-0.23467
H	3.8878	4.48343	1.66383
H	1.91182	4.63399	-2.15459
H	2.88525	5.80502	-0.18831
O	2.24662	-3.54872	-1.41639
C	3.0224	-4.68882	-1.02421
H	3.87948	-4.38332	-0.41781
H	2.41486	-5.3911	-0.44571
H	3.35672	-5.15018	-1.95451
S	-1.5869	0.11394	2.49191
O	-2.99529	-0.17881	2.17638
O	-1.14872	1.51105	2.61906
N	-0.64609	-0.60942	1.34183
C	-1.23308	-0.70099	4.06976
H	-1.85643	-0.23354	4.8353
H	-1.47404	-1.76224	3.97908
H	-0.17571	-0.5643	4.30663
O	-1.37132	-0.96244	-1.39498
N	-3.55386	1.24191	-1.62362
C	-2.99155	0.88416	-2.97796

H	-2.23761	0.10238	-2.81165
H	-3.81143	0.52617	-3.6055
H	-2.55434	1.78445	-3.41638
C	-2.4188	1.71317	-0.74203
H	-1.96938	2.5934	-1.20821
H	-2.81731	1.96165	0.24174
H	-1.72277	0.86297	-0.68919
C	-4.14637	-0.00825	-1.01294
H	-5.00381	-0.30895	-1.62027
H	-3.33084	-0.74686	-1.03077
H	-4.44531	0.21215	0.0124
C	-4.59191	2.30719	-1.74831
H	-4.13617	3.20245	-2.17693
H	-5.3958	1.95214	-2.39692
H	-4.98709	2.53207	-0.75596

Int^{C} (R*,R*,S*)

C	-1.36418	1.35322	-0.73853
C	-1.22582	-0.11635	-0.3155
C	0.23974	-0.57554	-0.34369
C	1.21119	0.37195	0.50842
C	0.94696	1.81711	-0.01072
H	-1.63633	-0.25625	0.68571
H	-1.11664	1.43941	-1.81123
H	-2.39255	1.686	-0.59324
H	1.5274	2.51138	0.59832
H	1.30761	1.86867	-1.0529
H	0.62577	-0.51238	-1.36755
S	-2.26736	-1.1597	-1.4637
C	0.35969	-2.01009	0.11063
O	-0.22014	-2.50401	1.05993
C	0.8837	0.31356	2.01791
H	1.5816	0.97861	2.53949
H	-0.13408	0.63659	2.26144
H	1.02635	-0.70089	2.40012
C	-3.75071	-1.44323	-0.4926
C	-4.99301	-1.07089	-1.02133
C	-3.68938	-2.08912	0.75145
C	-6.16535	-1.34214	-0.31282
H	-5.03656	-0.56509	-1.98137
C	-4.86367	-2.33485	1.46274
H	-2.72644	-2.39389	1.15157
C	-6.10342	-1.96803	0.93262
H	-7.12542	-1.0492	-0.73007
H	-4.80958	-2.82722	2.4304
H	-7.01557	-2.16874	1.48839
O	1.21921	-2.72521	-0.65836
C	1.34911	-4.10397	-0.28921

H	1.74382	-4.20173	0.72668
H	0.38078	-4.60959	-0.33635
H	2.04007	-4.54	-1.01336
S	-0.86538	3.81764	0.21839
O	0.0757	4.41015	1.17231
O	-2.31383	3.90447	0.42445
N	-0.4746	2.19236	0.07479
C	-0.51801	4.57071	-1.39533
H	-0.7579	5.6332	-1.31468
H	0.54046	4.4411	-1.63115
H	-1.14691	4.10189	-2.15538
O	2.50763	0.04346	0.26155
N	5.42778	-0.7169	-0.09925
C	5.30512	0.55795	0.70498
H	5.82681	1.35247	0.16629
H	4.22087	0.74976	0.79104
H	5.7753	0.39428	1.67738
C	6.86313	-1.08691	-0.28063
H	7.31992	-1.23882	0.6995
H	6.92398	-2.0078	-0.86433
H	7.37684	-0.27991	-0.80727
C	4.68409	-1.8124	0.6309
H	4.76385	-2.72885	0.04198
H	5.15468	-1.95065	1.60708
H	3.64217	-1.45729	0.71288
C	4.7611	-0.50183	-1.43944
H	5.29388	0.29791	-1.9594
H	4.83242	-1.43132	-2.00878
H	3.71479	-0.23271	-1.21317

TS^{B} (3R*,4S*,5R*)

C	-0.73874	-0.53498	1.09443
C	-0.87585	-1.13757	-0.31251
C	-2.11101	-0.78495	-1.05175
C	-1.58068	1.49667	-1.19151
C	-1.69996	1.67264	0.32953
H	-0.01554	-0.84169	-0.91904
H	-1.61133	-0.82292	1.68779
H	0.1751	-0.90083	1.5634
H	-1.58351	2.74067	0.54961
H	-2.67825	1.3386	0.69043
H	-2.08596	-1.00869	-2.11458
S	-0.65121	-3.04429	-0.14365
C	-3.41104	-0.88394	-0.45329
O	-3.71075	-0.84206	0.74623
C	-2.7851	1.95671	-1.99386
H	-2.69977	1.59195	-3.02051
H	-3.73532	1.61955	-1.57548

H	-2.78677	3.0581	-2.02842
C	1.13383	-3.16949	-0.01954
C	1.75612	-3.41804	1.21346
C	1.93661	-3.03443	-1.1654
C	3.14591	-3.52522	1.30032
H	1.142	-3.53037	2.10197
C	3.32617	-3.13345	-1.07554
H	1.45879	-2.8707	-2.1274
C	3.93541	-3.37943	0.15844
H	3.61129	-3.72104	2.26302
H	3.93312	-3.04308	-1.97402
H	5.01672	-3.46809	0.22669
O	-4.40892	-0.9409	-1.4113
C	-5.73659	-0.98239	-0.8949
H	-5.8898	-1.86298	-0.26252
H	-5.96521	-0.09175	-0.29945
H	-6.39268	-1.02848	-1.76744
S	0.16287	1.70928	2.27485
O	0.27916	3.13802	1.93427
O	1.38595	0.94582	2.57075
N	-0.61826	0.94866	1.01945
C	-0.90332	1.58993	3.73092
H	-0.38373	2.07003	4.563
H	-1.84379	2.10313	3.52011
H	-1.0819	0.53537	3.95046
O	-0.43652	1.54554	-1.71786
N	2.76637	2.22864	-1.42514
C	2.387	1.9826	-2.86325
H	1.31841	1.75485	-2.88913
H	2.61107	2.88291	-3.43984
H	2.97684	1.14345	-3.23772
C	2.44607	0.99041	-0.6181
H	3.01259	0.15127	-1.02704
H	2.71038	1.16403	0.42549
H	1.36992	0.83254	-0.70868
C	1.94371	3.38117	-0.89843
H	2.21472	4.27833	-1.45969
H	0.89567	3.11353	-1.04507
H	2.14528	3.50805	0.1651
C	4.22409	2.54575	-1.31812
H	4.80083	1.69601	-1.68842
H	4.44331	3.4344	-1.91366
H	4.46692	2.72957	-0.27025

TS^{C} (3R*,4R*,5S*)

C	-1.35387	1.22927	-0.81272
C	-1.21593	-0.23891	-0.39412
C	0.21298	-0.72652	-0.40544

C	1.37863	0.51219	0.56638
C	0.91745	1.85496	-0.0428
H	-1.64314	-0.37792	0.60029
H	-1.0508	1.3382	-1.86823
H	-2.39501	1.5391	-0.71687
H	1.43035	2.65158	0.50362
H	1.25196	1.87878	-1.09313
H	0.69178	-0.67274	-1.38484
S	-2.29126	-1.27059	-1.5533
C	0.38509	-2.04152	0.22499
O	-0.29443	-2.50853	1.12807
C	0.99543	0.36645	2.03975
H	1.57148	1.1015	2.61908
H	-0.06618	0.54749	2.22692
H	1.25131	-0.63261	2.40338
C	-3.79985	-1.47924	-0.60395
C	-5.02293	-1.07674	-1.15592
C	-3.77725	-2.09766	0.65584
C	-6.21276	-1.2924	-0.45748
H	-5.0375	-0.59206	-2.12779
C	-4.96801	-2.28793	1.35658
H	-2.82894	-2.42368	1.07452
C	-6.18815	-1.89208	0.80214
H	-7.15718	-0.97703	-0.89403
H	-4.94282	-2.75973	2.33572
H	-7.11363	-2.04962	1.34991
O	1.46985	-2.7273	-0.26571
C	1.68002	-4.00685	0.33846
H	1.89733	-3.91051	1.40705
H	0.79782	-4.64262	0.22278
H	2.53186	-4.4477	-0.18534
S	-1.061	3.65927	0.31156
O	-0.15166	4.27274	1.28373
O	-2.50458	3.60116	0.55296
N	-0.52893	2.08791	0.05159
C	-0.82592	4.54218	-1.25568
H	-1.16378	5.56968	-1.10349
H	0.23419	4.53002	-1.51836
H	-1.42531	4.06212	-2.03234
O	2.62687	0.24796	0.27328
N	5.55361	-0.55786	-0.26369
C	5.40756	0.04577	1.11432
H	6.03518	0.93828	1.16566
H	4.34016	0.28388	1.23191
H	5.74431	-0.69098	1.84692
C	6.97995	-0.92176	-0.52354
H	7.30555	-1.64676	0.22505
H	7.0609	-1.35796	-1.52116
H	7.59563	-0.0222	-0.46069
C	4.6734	-1.78431	-0.34695

H	4.76567	-2.20389	-1.35096
H	5.02614	-2.50558	0.39371
H	3.64638	-1.45699	-0.14017
C	5.07395	0.44726	-1.28527
H	5.70412	1.33654	-1.21163
H	5.17357	-0.00045	-2.27656
H	4.02468	0.66342	-1.03449

TS^{D} (3R*,4S*,5S*)

C	-1.48299	0.51572	-0.63755
C	-1.18839	-0.73026	0.20691
C	0.27264	-1.11396	0.27061
C	1.33042	0.52352	0.80411
C	0.73373	1.56453	-0.15882
H	-1.54197	-0.54535	1.22447
H	-1.2017	0.32337	-1.67936
H	-2.54653	0.75049	-0.57754
H	1.15434	2.53663	0.11465
H	1.06134	1.30633	-1.17533
H	0.49127	-1.80732	1.08144
S	-2.22061	-2.18312	-0.41635
C	0.92946	-1.51574	-0.97334
O	0.71705	-1.09351	-2.10326
C	0.91527	0.69904	2.26522
H	1.38259	1.61742	2.64918
H	-0.16394	0.79532	2.40465
H	1.28766	-0.14227	2.85883
C	-3.86706	-1.75116	0.15602
C	-4.86287	-1.41054	-0.77015
C	-4.18999	-1.79497	1.52075
C	-6.15798	-1.1179	-0.33819
H	-4.6151	-1.37592	-1.82687
C	-5.48003	-1.4851	1.95033
H	-3.42802	-2.0795	2.24094
C	-6.46821	-1.14896	1.02194
H	-6.92169	-0.85547	-1.06588
H	-5.7167	-1.51593	3.01088
H	-7.47445	-0.91306	1.35797
O	1.93724	-2.427	-0.74693
C	2.61679	-2.85643	-1.92497
H	1.92398	-3.32218	-2.63238
H	3.10567	-2.0182	-2.4335
H	3.35758	-3.58919	-1.59352
S	-1.41682	3.18393	-0.28384
O	-0.56516	4.14454	0.42602
O	-2.845	3.0723	0.02508
N	-0.734	1.66542	-0.08646
C	-1.28975	3.57366	-2.05034

H	-1.73113	4.56156	-2.19971
H	-0.23658	3.5827	-2.3393
H	-1.84087	2.82445	-2.62269
O	2.60113	0.31894	0.60438
N	5.62851	-0.27341	0.49512
C	5.34635	0.84436	1.47182
H	5.87488	1.73799	1.13272
H	4.2569	0.98573	1.46935
H	5.71507	0.54165	2.45429
C	5.11212	0.13338	-0.86668
H	5.30646	-0.68474	-1.56322
H	4.0357	0.32107	-0.74999
H	5.65165	1.02934	-1.1819
C	4.88239	-1.50907	0.94731
H	5.24944	-1.78258	1.93905
H	3.81751	-1.24365	0.95993
H	5.08725	-2.31159	0.23643
C	7.09681	-0.54774	0.43137
H	7.61563	0.35626	0.10616
H	7.44873	-0.84116	1.42236
H	7.27791	-1.35571	-0.28021

TS^{A} (3R*,4R*,5R*)

C	0.53322	-1.01517	-2.10965
C	0.80245	0.29053	-1.3523
C	-0.11227	1.41268	-1.73938
C	-2.04014	0.63573	-1.41205
C	-1.91545	-0.60587	-2.31765
H	0.72818	0.10461	-0.28128
H	0.68925	-0.86398	-3.18576
H	1.24276	-1.77951	-1.78455
H	-2.86214	-1.15437	-2.27066
H	-1.73665	-0.32135	-3.36173
H	-0.08877	1.69673	-2.79179
S	2.62935	0.73792	-1.64355
C	-0.10859	2.5375	-0.82413
O	0.13583	2.49652	0.38222
C	-2.92857	1.71068	-2.04083
H	-2.87901	2.63359	-1.45882
H	-2.65622	1.93995	-3.07639
H	-3.96964	1.35522	-2.02539
O	-2.17558	0.40919	-0.15992
C	3.42207	0.17093	-0.1381
C	4.47386	-0.75229	-0.20935
C	3.04923	0.69602	1.11011
C	5.14572	-1.14628	0.95004
H	4.76199	-1.15892	-1.17447
C	3.71259	0.28278	2.26537

H	2.24676	1.42782	1.1576
C	4.76399	-0.63529	2.19095
H	5.96243	-1.8608	0.88191
H	3.42092	0.69571	3.22865
H	5.2843	-0.94599	3.09336
O	-0.50566	3.70738	-1.42144
C	-0.57679	4.83936	-0.55602
H	0.39414	5.04233	-0.09332
H	-0.87607	5.67783	-1.18841
H	-1.31387	4.68719	0.23967
S	-1.11055	-2.67239	-0.7527
O	-2.56164	-2.83508	-0.58937
O	-0.26082	-2.45936	0.43425
N	-0.83861	-1.53236	-1.94848
C	-0.49459	-4.17984	-1.53812
H	-0.59936	-4.9871	-0.80964
H	-1.09801	-4.37831	-2.42484
H	0.55642	-4.05341	-1.8043
N	-2.0727	0.04202	2.99521
C	-2.07399	-0.14926	4.47721
H	-3.10541	-0.1765	4.83491
H	-1.5744	-1.09103	4.7122
H	-1.53984	0.68025	4.94466
C	-2.81862	-1.09239	2.33029
H	-2.82253	-0.90129	1.25469
H	-2.29367	-2.02326	2.54576
H	-3.8308	-1.11684	2.74128
C	-0.65077	0.07715	2.48172
H	-0.70133	0.30665	1.41812
H	-0.11605	0.86171	3.01934
H	-0.19634	-0.89949	2.64704
C	-2.74109	1.34537	2.63323
H	-2.71213	1.42032	1.5401
H	-3.76542	1.32351	3.01287
H	-2.18157	2.15959	3.09794

Int[A] (3R*,4R*,5R*)

C	0.64673800	-1.24585100	-1.88781900
C	0.94212500	0.06658000	-1.14873900
C	0.07822600	1.22746000	-1.65950200
C	-1.48623100	0.81760700	-1.58458500
C	-1.63446600	-0.49441000	-2.41478500
H	0.76381600	-0.06481300	-0.08229400
H	0.97686200	-1.16458800	-2.93190400
H	1.21542000	-2.05864400	-1.42964400
H	-2.67496600	-0.81761400	-2.35878700
H	-1.36876100	-0.35434400	-3.47351400
H	0.33749200	1.46621300	-2.69851400

S	2.75492200	0.46061700	-1.36118900
C	0.31108000	2.45609400	-0.81533200
O	0.50341900	2.47775900	0.38660700
C	-2.33330000	1.89680800	-2.30691000
H	-2.27246300	2.84869100	-1.77102300
H	-2.02940600	2.07347800	-3.34774500
H	-3.38195100	1.57569200	-2.29969500
O	-1.86939900	0.62215500	-0.30761200
C	3.47572000	-0.12980700	0.17280800
C	4.52366100	-1.05793100	0.12210600
C	3.06012100	0.37937300	1.41259200
C	5.15055100	-1.47432100	1.29851700
H	4.84214400	-1.45255000	-0.83838400
C	3.67730200	-0.05828800	2.58413300
H	2.26314400	1.11682400	1.44506900
C	4.72533400	-0.98133400	2.53246600
H	5.96411800	-2.19366600	1.24862700
H	3.34944200	0.33724100	3.54259700
H	5.20855400	-1.31147400	3.44834900
O	0.24630400	3.59165900	-1.55580600
C	0.42767500	4.81159400	-0.82711700
H	1.40136300	4.82192000	-0.32927300
H	0.36889500	5.60930300	-1.56903100
H	-0.35489600	4.93485500	-0.07247500
S	-1.36164400	-2.60828700	-0.71878100
O	-2.83007400	-2.56215100	-0.73085800
O	-0.62821200	-2.46492200	0.55269000
N	-0.78318400	-1.59064800	-1.92266300
C	-0.88588400	-4.22363500	-1.37923400
H	-1.18881800	-4.97360400	-0.64489700
H	-1.40547400	-4.37677500	-2.32590700
H	0.19601100	-4.25877400	-1.52124800
N	-2.71463300	0.42831700	2.65548100
C	-3.12830600	0.30872700	4.08429700
H	-4.18791200	0.55796300	4.17375500
H	-2.95966600	-0.71744500	4.41704500
H	-2.53298400	0.99656600	4.68851800
C	-3.52606400	-0.51409700	1.79380700
H	-3.20395000	-0.34829200	0.75724300
H	-3.31324000	-1.53723000	2.10531300
H	-4.58316200	-0.27987600	1.94366000
C	-1.24741700	0.09248500	2.50410400
H	-1.01235600	0.24311400	1.44391700
H	-0.67988600	0.76595500	3.15001300
H	-1.09806900	-0.94823700	2.79234500
C	-2.92835500	1.83512100	2.15381900
H	-2.59597400	1.82950600	1.10424700
H	-3.98966700	2.07697500	2.25077900
H	-2.32875600	2.51361000	2.76471600