Electronic Supplementary Information (ESI) for:

trans-1,2-Diaminocyclohexane-based sulfonamides as effective hydrogen-bonding organocatalysts for asymmetric Michael-hemiacetalization reaction

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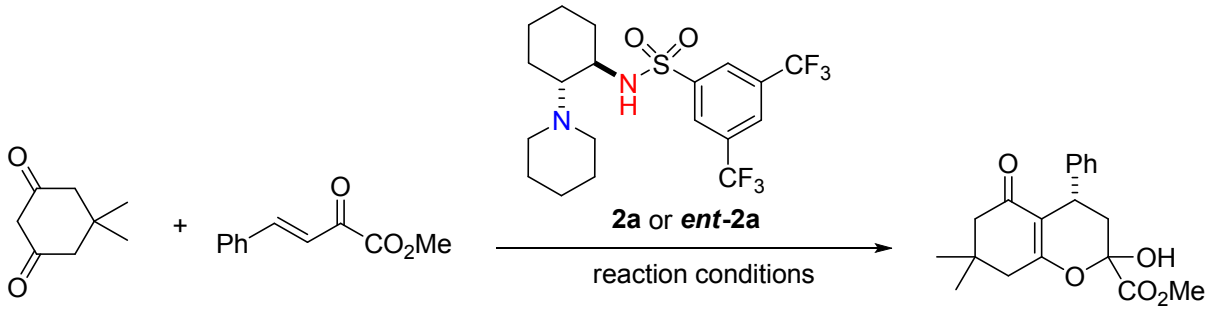
Additional catalytic experiments

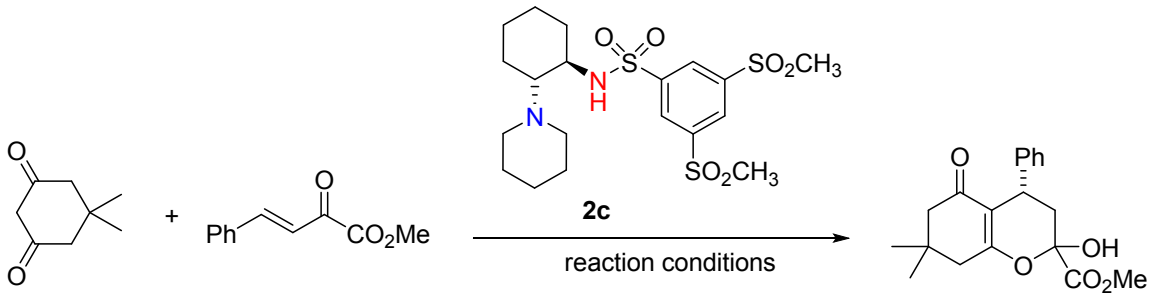
Table S1. Summary of results for the reaction of dimedone **10** and benzylidenepyruvate **9a** catalyzed by **2a** and ***ent*-2a**



Entry	Source data label	catalyst	Loading, % mol	solvent	Time, h	Temp, °C	Scale, mmol	Ee, %	Yield, %[a]
1	RK	**2a**	10	toluene	20	RT	0.1	93.2	
2	MD180	**2a**	10	toluene	18	RT	0.1	95.4	
3	MD139	***ent*-2a**	10	toluene	17	RT	0.1	89.6[b]	
4	MD140A	**2a**	10	DCM	20	RT	0.1	95.6	
5	MD179A	**2a**	1.0	DCM	72	−20	0.1	94.7	
6	MD140C	**2a**	10	trifluorotoluene	20	RT	0.1	92.7	
7	MD140B	**2a**	10	chlorobenzene	20	RT	0.1	95.8	
8	MD158	*crude* **2a**[c]	10	chlorobenzene	19	RT	0.1	88.8	
9	MD186	*crude* **2a**[d]	10	chlorobenzene	19	RT	0.1	94.3	
10	MD145A	**2a**	5.0	chlorobenzene	23	RT	0.1	96.8	
11	MD145B	**2a**	2.5	chlorobenzene	23	RT	0.1	95.3	
12	MD145C	**2a**	1.0	chlorobenzene	23	RT	0.1	95.4	
13	MD150	**2a**	1.0	chlorobenzene	46	RT	3.0	87.8 (99.3)[e]	90 (43)[e]
14	MD152	**2a**	1.0	chlorobenzene	336	−20	0.1	99.4	
15	MD159	**2a**	1.0	chlorobenzene	120	−20	3.0	99.3	98
16	MD145D	**2a**	0.5	chlorobenzene	23	RT	0.1	93.7	
17	MD147A	**2a**	0.5	chlorobenzene	96	RT	0.1	91.6	
18	MD157	***ent*-2a**	0.5	chlorobenzene	44	RT	0.1	91.4[b]	
19	MD147B	**2a**	0.25	chlorobenzene	96	RT	0.1	93.5	
20	MD147C	**2a**	0.10	chlorobenzene	96	RT	0.1	86.8	
21	MD147D	**2a**	0.05	chlorobenzene	96	RT	0.1	66.7	

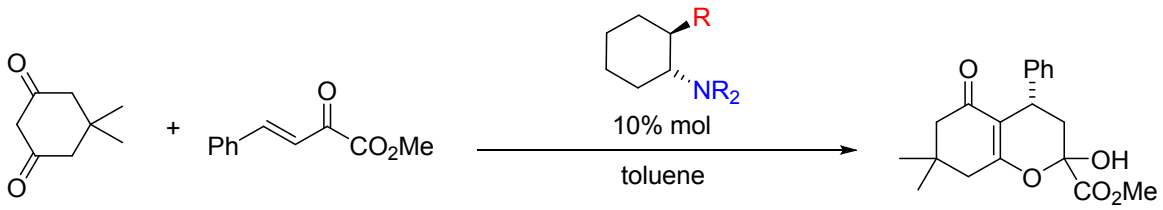
a) Given yields are preparative, observed conversions for all reactions were high; b) Different major enantiomer was obtained; c) using catalyst sample that was neither washed in EtOAc with $NaHCO_3$ soln. nor previously recrystallized and contained ca. 13 %mol sulfonic acid triethylamine salt by NMR integration; d) using catalyst sample that was washed in EtOAc with $NaHCO_3$ soln. but not recrystallized; e) Values in parentheses were obtained after single recrystallization from *tert*-butyl methyl ether

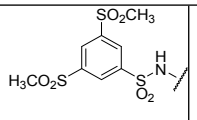
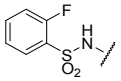
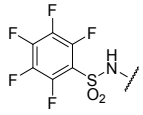
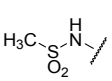
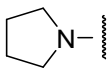
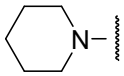
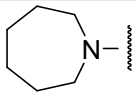
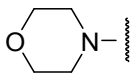
Table S2. Summary of results for the reaction of dimedone **10** and benzylidenepyruvate **9a** catalyzed by **2c**



Entry	Source data label	Loading, %mol	solvent	Time, h	Temp, °C	Scale, mmol	Ee, %
1	MD133	10	toluene	26	RT	0.1	83.9
2	MD138A	10	DCM	24	RT	0.1	90.6
3	MD138B	10	chlorobenzene	24	RT	0.1	93.6
4	MD138C	10	trifluorotoluene	24	RT	0.1	89.1
5	MD149A	1.0	chlorobenzene	22	RT	0.1	86.4
6	MD149B	0.5	chlorobenzene	22	RT	0.1	88.1

Table S3. Enantioselectivities obtained using matrix of catalysts **1**-**4** × **c**,**m**,**p**,**t** in the reaction of dimedone **10** and benzylidenepyruvate **9a** [a)]



R= / NR_2=	 **c**	 **m**	 **p**	 **t**
	Enantioselectivities, %[a)]			
1 	nd [c)]	54.2	nd [c)]	76.4
2 	93.6[b)]	55.6	39.2	77.6
3 	nd [c)]	33.4	21.8	66.8
4 	88.7[b)]	29.6	9.6	46.6

a) Reaction conditions: 10 %mol catalyst in toluene at room temperature for 20 h; The experiments were run in parallel; b) Reactions run separately, and in chlorobenzene; c) Not determined, and the

synthesis of appropriate catalyst was not attempted. Note: the values shown here and those in Table 1 entries 15, 18, and 22 from the main text for **2m**, **2p**, and **2t** originate from different experiments

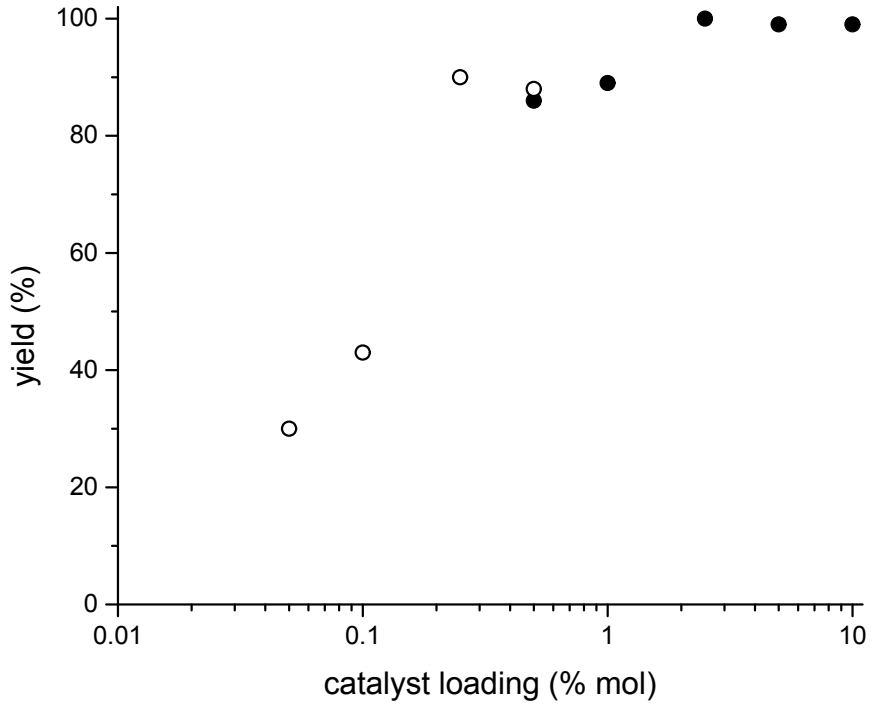


Figure S1. Effect of catalyst **2a** loading on the yield of product **11a** for reactions performed at room temperature in chlorobenzene for 24 h (●) and 96 h (○). The corresponding enantioselectivity values are shown in Figure 6 from the main text.

NMR titration experiments

Samples of compound **2a** (12.7 mg, 28 μmol) were disssolved in $CDCl_3$ (0.5 mL, 56 mM) and titrated separately with $CDCl_3$ solutions of dimedone (**10**, 111 mM) and methyl benzylidenepyruvate (**9a**, 278 mM). Consecutive spectra taken after addition of 0.2 equiv aliquots of the reactants are shown in the following Figures S2-S4.

The titration experiment was expected to show interactions between the catalyst **2a**, which was supposed to act as an H-bond donor, and 1,2-dicarbonyl compound **9a**. Unfortunately this experiment failed to demonstrate such an interaction while it revealed no spectral changes (Figure S4). An additional part of this experiment was the titration with dimedone **10**. It again did not change any of the observed signals (Figure S3) apart from the single rather broad resonance (Figure S2). The SO_2N-H signal gradually shifted and merged with the OH signal corresponding to dimedone tautomer.
The observed spectral change is likely a consequence of acid-mediated exchange with dimedone as an acid source (pKa 5.2). The resonance attributed to NH increases in integration from the initial 0.51H

to nearly 1.35H after addition of 1 equiv of dimedone. This indicates a combined OH/NH signal of a dynamic system. Substantial protonation of the amine group in **2a** was not observed, since the adjacent NCH/CH_2 signals remained at their position throughout the titration.

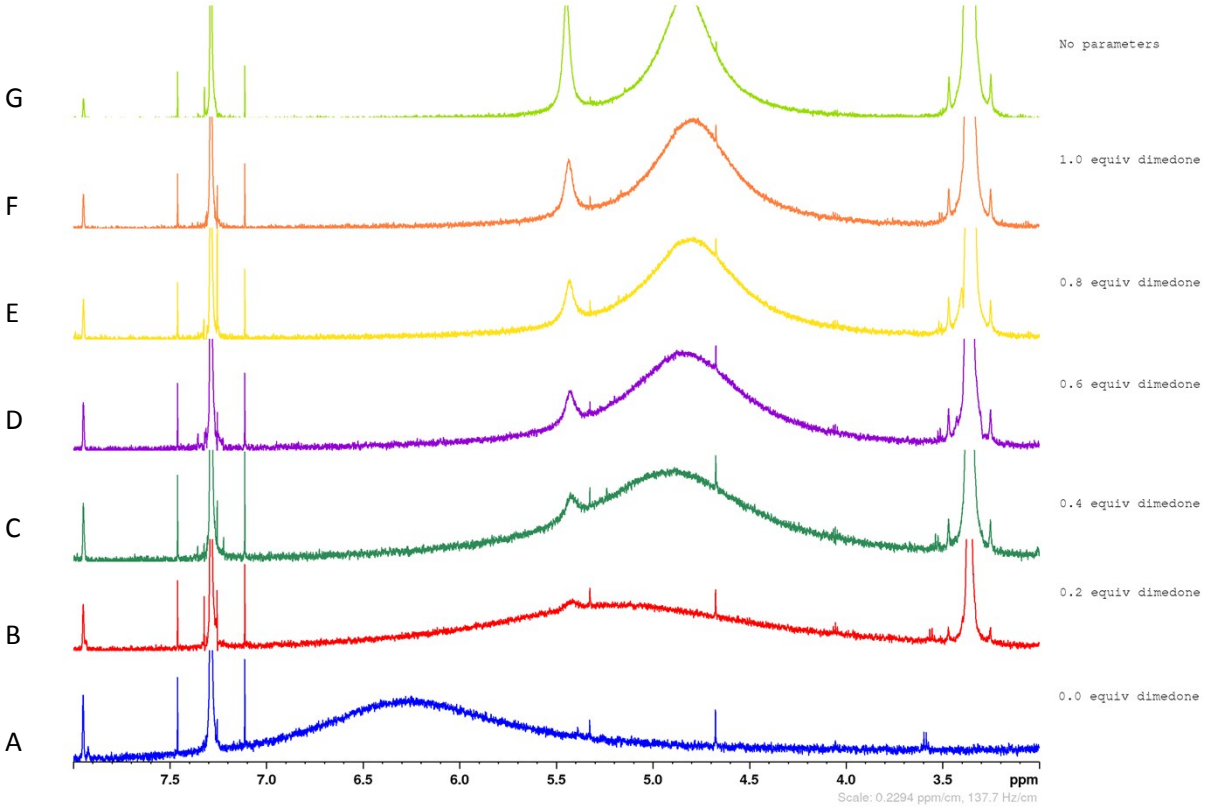


Figure S2. Plots of ^{1}H NMR spectra (600 MHz, $CDCl_3$) in range of 8 to 3 ppm for titration of **2a** with dimedone (**10**): from bottom: a) no dimedone, b) 0.2 equiv c) 0.4 equiv, d) 0.6 equiv, e) 0.8 equiv, f) 1.0 equiv, and g) 2.0 equiv dimedone. In spectrum a) broad signal was assigned to sulfonamide NH. For full range spectra see the following Figure S3.

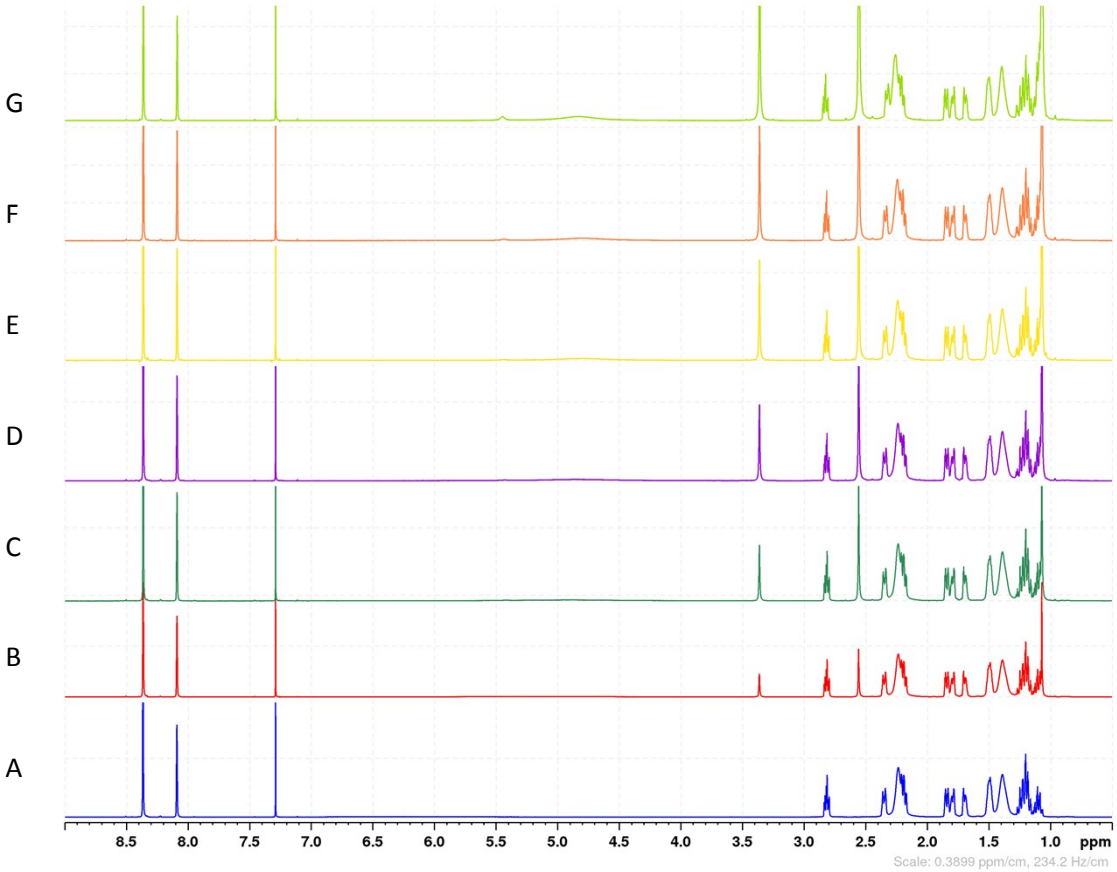


Figure S3. Plots of ^{1}H NMR spectra (600 MHz, $CDCl_3$) for titration of **2a** with dimedone (**10**): from bottom: a) no dimedone, b) 20 %mol dimedone, c) 40 %mol dimedone, d) 60 %mol dimedone, e) 80 %mol dimedone, f) 100 %mol dimedone, g) 150 %mol dimedone. For a magnified view of the broad signal at 4.5-6.5 ppm, see the preceeding Figure S2.

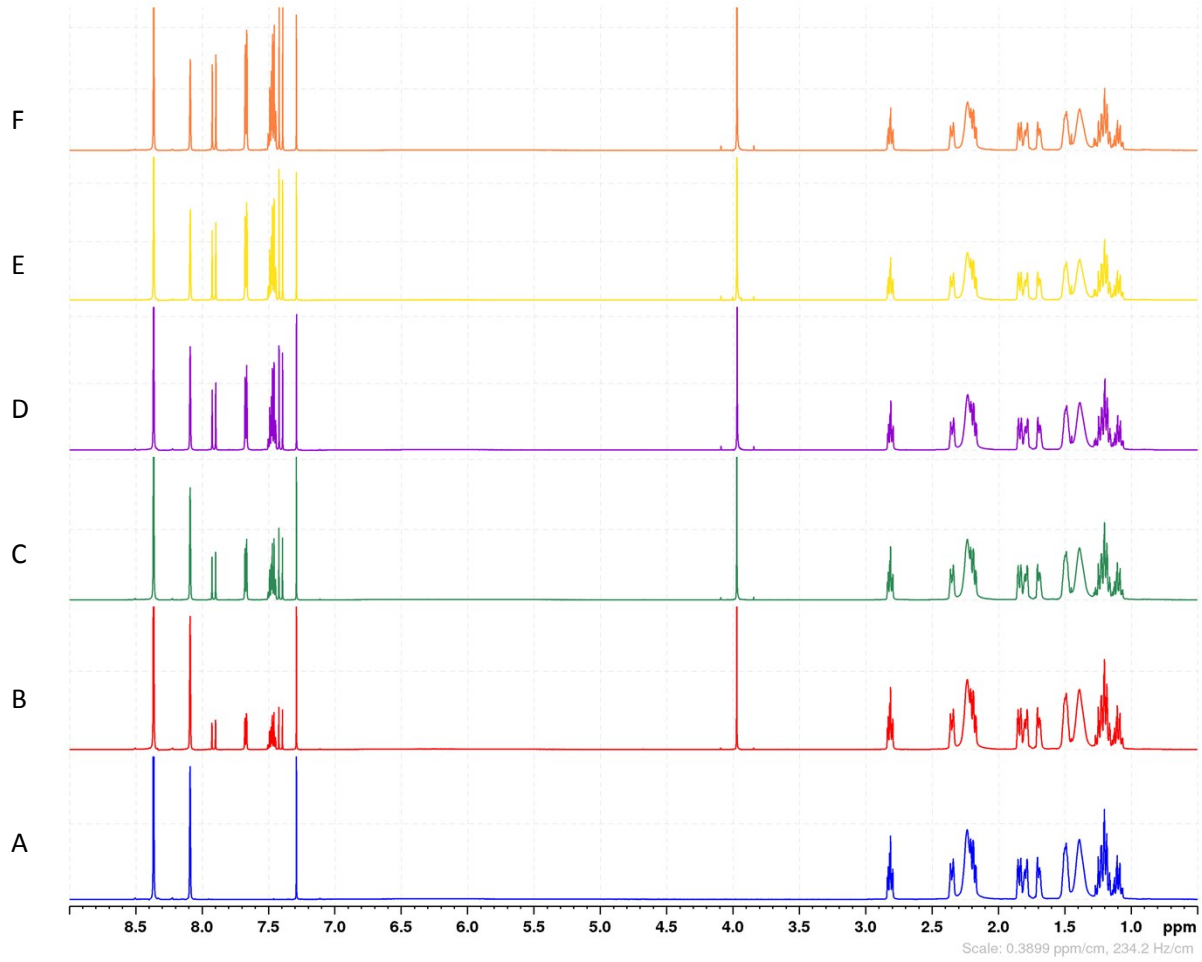


Figure S4. Plots of ^{1}H NMR spectra (600 MHz, $CDCl_3$) for titration of **2a** with methyl benzylidenepyruvate (acceptor **9a**) from bottom: a) no acceptor, b) 20 %mol acceptor, c) 40 %mol acceptor, d) 60 %mol acceptor, e) 80 %mol acceptor, f) 100 %mol acceptor.

DFT computations for catalysts[S1]

For *N*-(1*R*,2*R*)-(2-pyrrolidin-1-yl)-cyclohexyl-benzenesulfonamide **1i** geometry was optimized at the DFT/B3LYP/CC-pVDZ level of theory[S2] in vacuum starting from initial geometries corresponding to rotations along major degrees of freedom, as well as different configurations of pyramidal N1 nitrogen atom. Selected geometries and their energies were listed in Table S4.

Table S4. Lowest energy conformations for **2i**, and their energies determined at the DFT/B3LYP/CC-pVDZ level of theory

Conformation	N1 configuration	Dihedral angle, °		E, hartree	Relative energy, kcal/mol
		C2-C1-N1-S	C1-N1-S-C		

1	*R*	138.8	95.4	−1282.2759054	0.000
2	*R*	157.4	−62.7	−1282.2739087	1.253
3	*S*	133.8	69.9	−1282.2680098	4.955
4	*S*	140.9	74.5	−1282.2674033	5.335
5	*S*	81.0	139.4	−1282.2666547	5.805
6	*S*	−75.7	−98.2	−1282.2665644	5.862

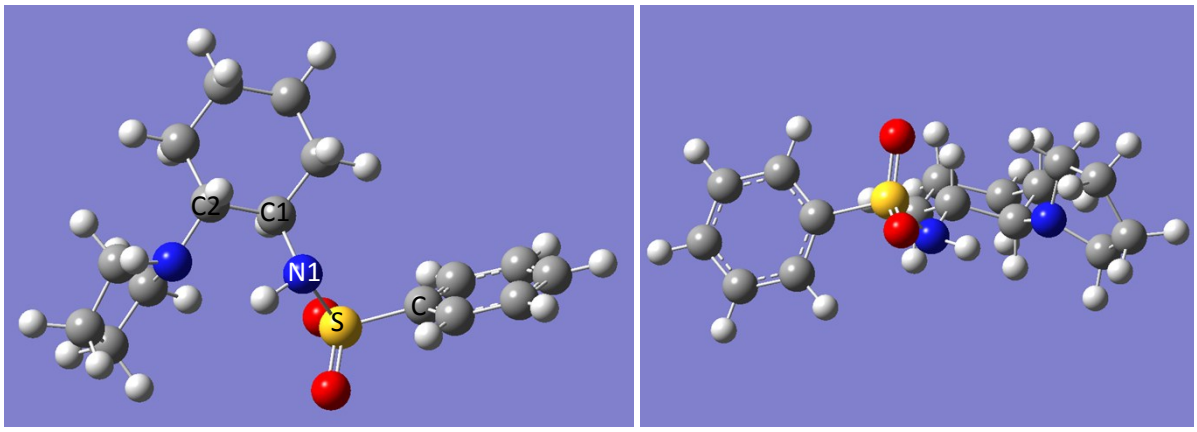
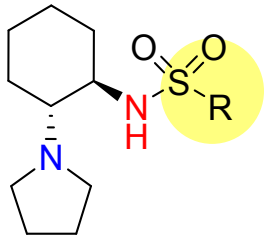


Figure S5. Projections of the lowest energy conformation (Conformation 1, Table S4) for **1i**.

Structures of different sulfonamine derivatives **1**, were optimized using the Conformation 1 Table S4 of **1i** as the initial input. All the geometries were optimized to local minima as confirmed by no imaginary frequencies. Table S5 lists some of molecular properties calculated for these conformations as well as highest vibration frequency corresponding mostly to N-H stretching IR band. These values were then taken to construct Figure 5 from the main text. Small experimental difference between compounds of type **1** and **2** justifies using simplified model.

[S1] We thank Wrocław Center for Networking and Supercomputing for allotment of computer time (No. 362)
[S2] Gaussian 16, Revision B.01, 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.

Table S5. DFT calculated dipole moment, highest oscillation frequency and N-H bond length for sulfonamide structures **1a**-**y**.



Entry	label	R=	Dipole moment, Debye	$\nu_{(N-H)}$, cm^{-1}	$d_{(N-H)}$, Å
1	**1a**	3,5-$(CF_3)_2C_6H_3$	4.48	3313.34	1.03484
2[a)]	**1b**	3-FC_6H_4	4.01 3.93	3327.99 3329.46	1.03395 1.03388
3	**1c**	3,5-$(MeSO_2)_2C_6H_3$	11.09	3311.99	1.03502
4	**1d**	3,5-$F_2C_6H_3$	3.99	3324.56	1.03413
5	**1e**	3,5-$Cl_2C_6H_3$	4.13	3320.39	1.03439
6	**1f**	4-$CH_3C_6H_4$	4.15	3339.90	1.03327
7	**1g**	3-$NO_2C_6H_4$	5.11	3315.89	1.03456
9	**1h**	4-$NO_2C_6H_4$	5.52	3316.71	1.03471
9	**1i**	C_6H_5	3.92	3335.08	1.03365
10	**1j**	4-FC_6H_4	3.76	3332.47	1.03377
11	**1k**	3,5-$(CH_3)_2C_6H_3$	4.01	3337.32	1.03319
12	**1l**	2-Naphthyl	4.00	3332.32	1.03342
13	**1m**	2-FC_6H_4	3.82	3350.61	1.03232
14	**1n**	2,3,4-$F_3C_6H_2$	3.94	3353.21	1.03208
15	**1o**	2,4-$F_2C_6H_3$	3.66	3343.25	1.03287
16	**1p**	C_6F_5	4.59	3369.27	1.03119
17	**1q**	8-quinolinyl	5.19	3326.86	1.03435
18	**1r**	2,6-$Cl_2C_6H_3$	4.14	3372.33	1.03067
19	**1s**	2,4,6-(*i*Pr)$_2C_6H_3$	3.76	3319.23	1.03462
20	**1t**	CH_3	3.57	3332.96	1.03334
21	**1u**	CF_3	5.04	3345.90	1.03253
22	**1v**	cyclohexyl	3.28	3344.14	1.03273
23	**1w**	benzene-1,3-diyl	0.06	3333.08	1.03365
24	**1x**	biphenyl-4,4'-diyl	3.21	3328.37	1.03409
25	**1y**	sulfamide	2.58	3352.88	1.03249

a) Two orientations of 3-fluorophenyl ring were considered giving almost equal energy

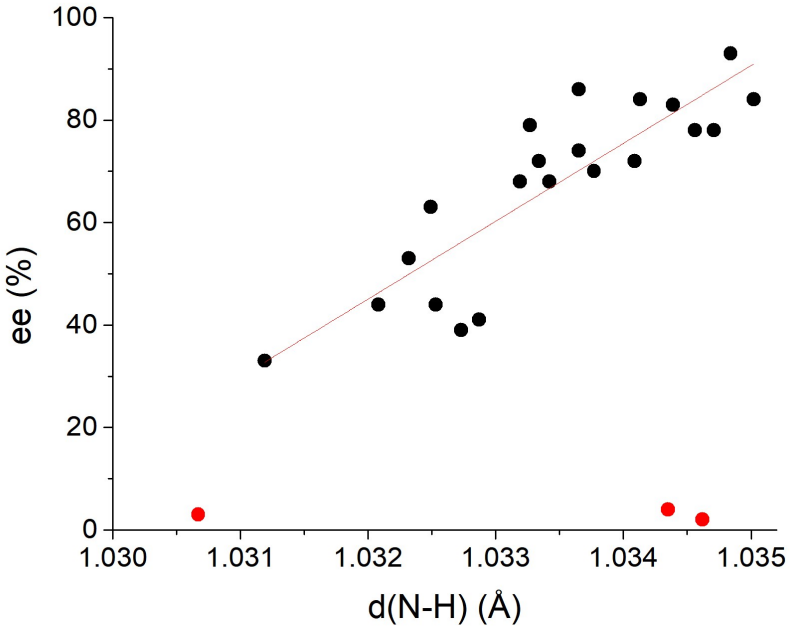


Figure S6. Correlation of experimental enantioselectivities for **11a** obtained in reaction of dimedone (**10**) with methyl benzylidenepyruvate (**9a**) (in toluene at room temperature, 10 %mol catalyst) with DFT calculated N-H distance in the catalysts. Pearson correlation coefficient was 0.863. Points corresponding to experiments where nearly racemic samples were obtained were excluded from the fit (red).

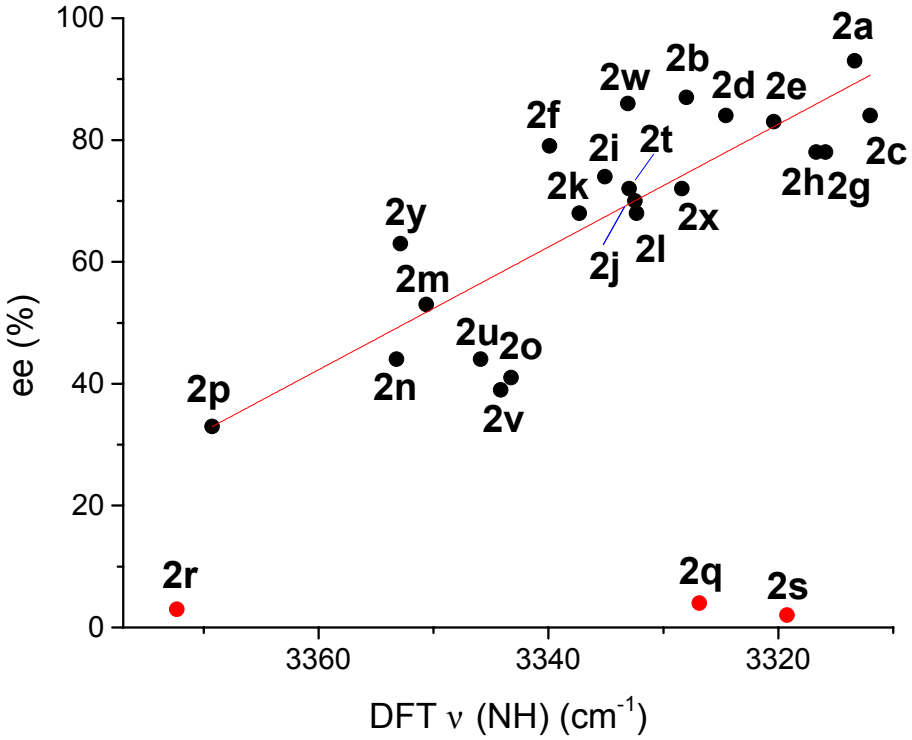


Figure S7. Correlation between enantiomeric excess for reaction of dimedone (**10**) with methyl benzylidenepyruvate (**9a**) (in toluene at room temperature, 10 %mol catalyst) and DFT calculated unscaled frequency of the N-H stretching band. The Pearson coefficient for the fitted line is −0.83. Results for 2,6-disubstituted benzenesulfonates and quinoline sulfonamide providing nearly racemic products were excluded from the fit (marked in red). This is a magnified version of Figure 5 from the main text with points associated with catalyst labels.

Determination of relative stereochemistry of end product **13**

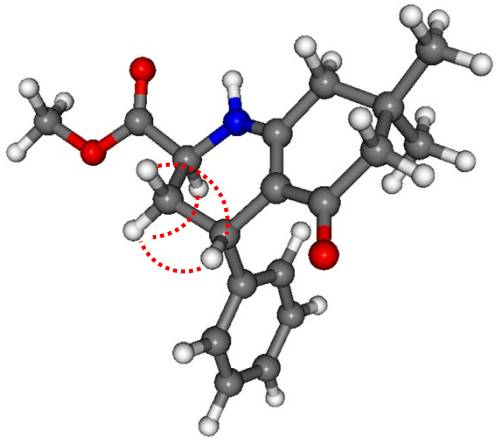


Figure S8. Lowest energy diastereomer of **13** determined at the DFT/B3LYP/CC-pVDZ level of theory. Dashed lines indicate contacts of less than 2.58 Å within the tetrahydropyridine unit and observed NOESY interactions. For plot of NOESY experiment see the following Figure S9.

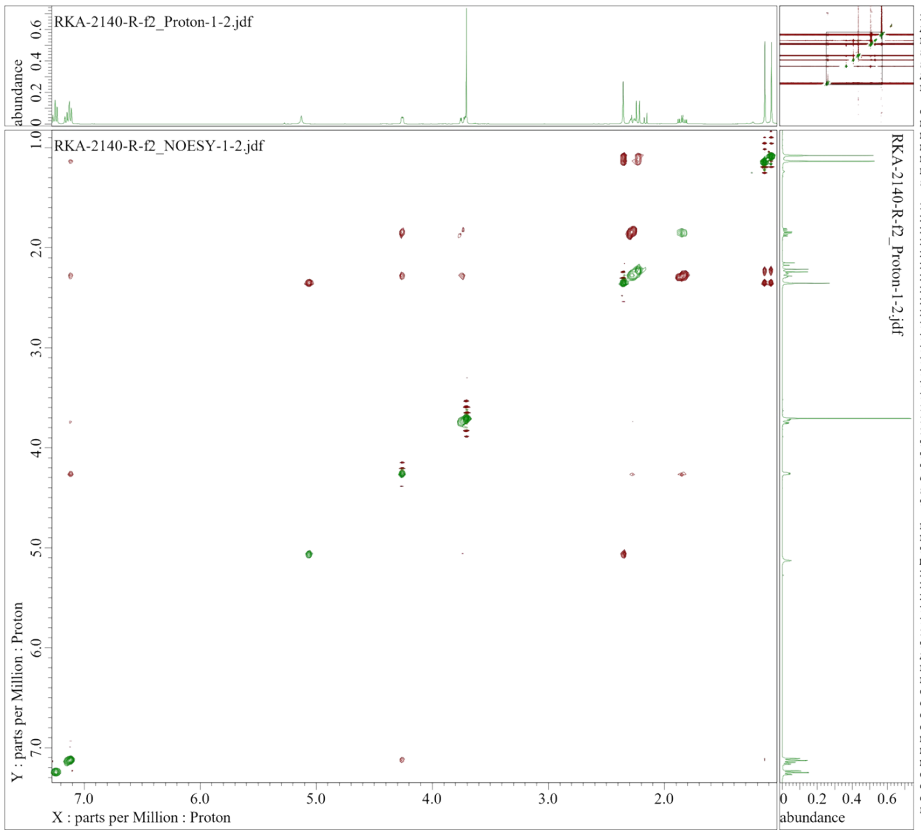
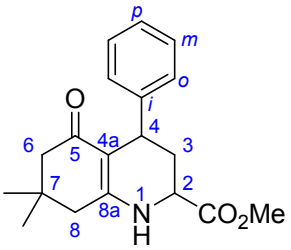


Figure S9. NOESY experiment (400 MHz, $CDCl_3$) for **13**. For interpretation refer to the preceding Figure S8.

Table S6. Comparison of DFT computed and scaled chemical shifts for two possible diastereomers of **13** and experimental data[a)]

Atom, signal	DFT chemical shift, ppm[a)]		Experiment, ppm[b)]
	Like (2*S*,4*S*)	Unlike (2*R*,4*S*)	
Carbon, ^{13}C			
C-2	51.68	55.32	49.82
C-3	34.34	37.78	32.53
C-4a	107.53	111.37	105.76
C-4	38.78	40.65	34.40
C-5	189.66	190.70	193.31
C-6	50.48	52.36	50.54
C-7	36.50	38.45	32.57
C-8	43.05	44.73	43.07
C-8a	157.22	158.95	155.84
7-CH_3(a)	25.28	25.01	28.44
7-CH_3(b)	31.18	31.11	28.78
CO_2	175.93	174.94	172.76
OMe	53.37	53.27	52.59
C-*ipso*	148.42	150.31	145.08
C-*ortho*	128.95	127.78	128.40
C-*meta*	128.52	128.41	127.80
C-*para*	126.39	125.32	126.28
RMSD[c)]	**2.40**	**3.73**	
Proton			
H-2	4.054	4.159	3.755
H-3a	2.250	2.763	2.291
H-3b	1.889	1.943	1.862
H-4	4.356	3.791	4.275
H-6a	2.186	2.021	2.16 – 2.38
H-6b	2.384	2.375	2.16 – 2.38
H-8a	2.806	2.973	2.356
H-8b	2.314	2.105	2.356
7-CH_3(a)	1.327	1.199	1.094
7-CH_3(b)	1.318	1.288	1.151
OMe	3.765	3.795	3.723
ortho	6.562	6.408	7.135
meta	6.184	6.139	7.268
para	7.306	7.205	7.163
NH	5.056	4.708	5.145
RMSD[c)]	**0.384**	**0.488**	



Atom numbering scheme for **13**

[a)] Geometries were optimized at the DFT/B3LYP/CC-pVDZ level of theory in vacuum,[S2] two conformers were considered for each diastereomer (2*S*,4*S* and 2*S*,4*R*) and their contribution was Boltzmann averaged. Isotropic shieldings were calculated at the mPW1PW91/6-311+G(2d,p) level of theory using chloroform universal solvent model (SMD) and following

scaling factors were taken from http://cheshirenmr.info/ScalingFactors.htm: ^{1}H slope: −1.0933, intercept: 31.9088; ^{13}C slope: −1.0449, intercept: 187.1018 as reported by Tantillo *et al.*[S3]

[b] The assignment of NMR signals was made based on HSQC and NOESY experiments (Figures S9 and S10)

[c] Root mean square deviation between the experimental and theoretical data (ppm). Lower value indicates better agreement of data. Unresolved signals of 6-CH_2 were not included in calculation of RMSD. For comparison, RMSD values obtained by Tantilo *et al.* on a probe set were 0.160 and 2.60 ppm for ^{1}H and ^{13}C.[S3]

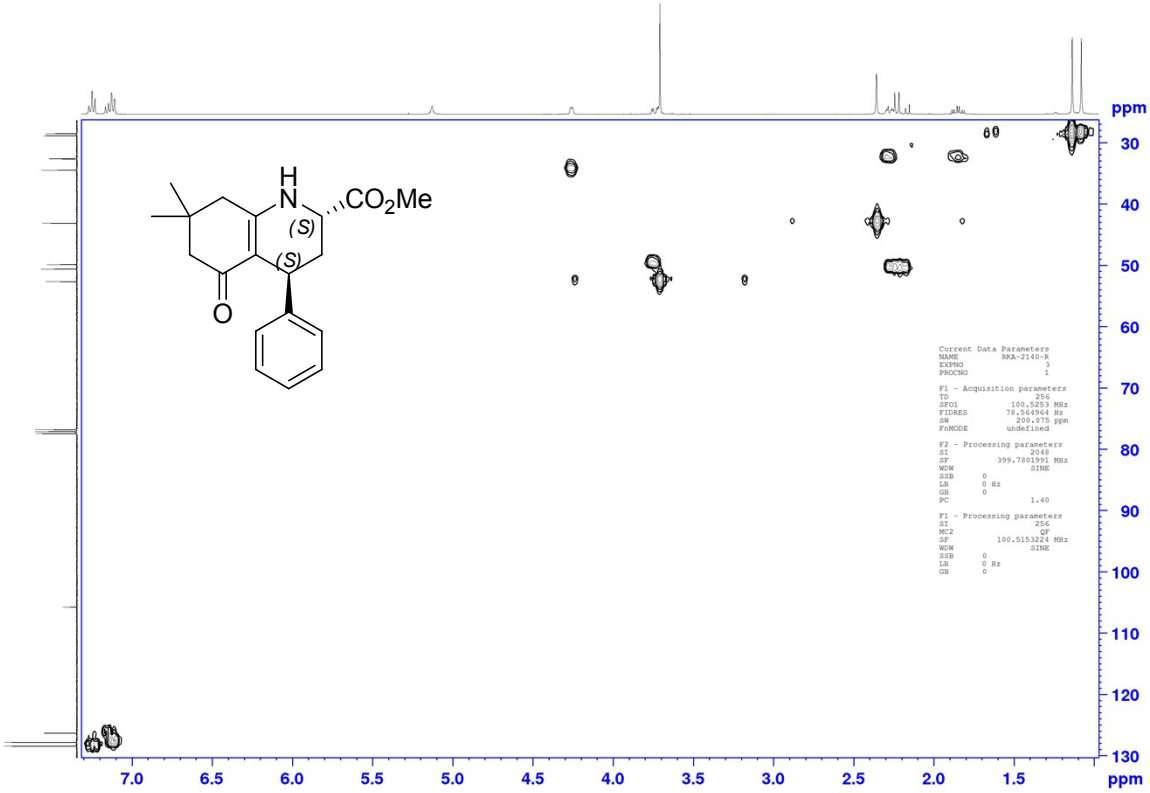


Figure S10. ^{1}H,^{13}C HSQC experiment (400, 101 MHz) for **13**.

[S3] Lodewyk, M. W.; Siebert, M. R.; Tantillo, D. J. *Chem. Rev.* **2012**, *112*, 1839-1862

Experimental

General

Enantiomeric 1,2-*trans*-diaminocyclohexanes (DACH) were obtained by crystallization of tartaric acid salts with L-tartaric acid and D-tartaric acid for 1*R*,2*R* and 1*S*,2*S* isomers, respectively according to the literature procedure.[S4] The salts were triple recrystallized from water, and liberated diamines were distilled before use. Mono Boc-DACH was obtained according to a literature procedure.[S5] 2-Oxo-butenoates were prepared according to literature procedures.[S6]

Sulfonyl chlorides and triflic anhydride were purchased from commercial suppliers and used as received.

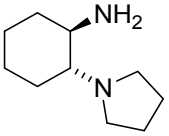
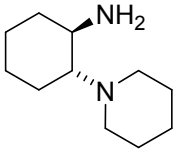
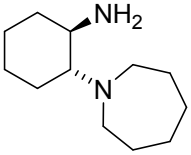
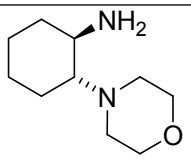
Catalysts

Synthesis of primary-tertiary amines

Mono Boc protected enantiomeric 1,2-*trans*-diaminocyclohexane (22.66 g, 106 mmol, 1.0 equiv) was dissolved in MeCN (220 mL), and K_2CO_3 (74.5 g, 539 mmol, 5.1 equiv) and dihalide (36.84 g, 160 mmol, 1.5 equiv) were added. The suspension was stirred at rt for 24 h then at 80 °C for 24-48 h, and cooled to room temperature. The mixture was filtered and the solids were washed with MeCN and combined filtrates were concentrated *in vacuo*. The residue was suspended in 6.5M aqueous HCl (117 mL) with vigorous stirring while evolution of gas was observed. After 12 h, the mixture was washed with diethyl ether (2 × 70 mL) to remove excess of dihalide. The aqueous phase was cooled to 0 °C and carefully alkalized with solid NaOH. The product was extracted with dichloromethane (4 × 30 mL), dried over Na_2SO_4, evaporated and vacuum distilled in kugelrohr to produce clear colorless liquids / low-melting solids. See Table S7 below.

[S4] (a) Guo, C.; Qiu, J.; Zhang, X.; Verdugo, D.; Larter, M. L.; Christie, R.; Kenney, P.; Walsh, P. J. *Tetrahedron*, **1997**, *53*, 4145; (b) Jaeger, F. M.; Bijkerk, L. Z. *Anorg. Allg. Chem*. **1937**, *233*, 97.
[S5] Darwish, M. O.; Wallace, A.; Clakrson, G. J.; Wills, M. *Tetrahedron Lett.* **2013**, *54*, 4250-4253.
[S6] (a) Feng, J.; Fu, X.; Chen, Z.; Lin, L.; Liu, X.; Feng. X. *Org. Lett.* **2013**, *15*, 2640-2643; (b) Huw, Y.-Z.; Liu, M.-M.; Huang, P.-J.; Song, X.; Wang, M. C.; Chankg, J.-B. *Chem. Eur. J.* **2015**, *21*, 11994-11998.

Table S7.

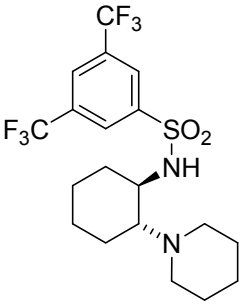
Entry	Product	Distillation conditions: oven temp / pressure	Reaction scale	Yield, %
1 [a)]		100 °C / 0.5 mmHg	65 mmol	70
2 [b)]		110 °C / 0.5 mmHg	65 mmol 106 mmol	86 86 (mp. 19-21°C)
3 [c)]		125°C / 0.07 mmHg	1.4 mmol 20 mmol	50 44
4 [d)]		130 °C / 0.5 mmHg	40 mmol	70

Dihalide used: [a)] 1,4-dibromobutane, [b)] 1,5-dibromopentane, [c)] 1,6-diiodohexane, [d)] di(2-bromoethyl) ether

General procedure for the synthesis of sulfonamides 1-5

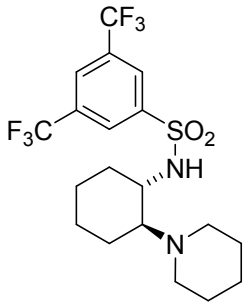
Primary-tertiary diamine (2.00 mmol, 1.0 equiv, 0.365 g for 2-piperidine-cyclohexylamine) was dissolved in dichloromethane (20 mL), and triethylamine (3.00 mmol, 0.42 mL, 1.5 equiv) was added followed by the respective sulfonyl chloride (2.20 mmol, 1.1 equiv). The mixture was stirred at room temperature for 12 h. Then aqueous $NaHCO_3$ (10%, 10 mL) was added and the mixture extracted with dichloromethane (2 × 10 mL). The extracts were evaporated, redissolved in ethyl acetate (20 mL), and washed with aqueous $NaHCO_3$ (2 × 10 mL). The solution was dried over Na_2SO_4, and concentrated *in vacuo* giving products in nearly quantitative yields. Solid products were then recrystallized usually from 2-propanol in various yields.

Piperidine catalysts 2



***N*-((1*R*,2*R*)-2-(Piperidin-1-yl)cyclohexyl)-3,5-bis(trifloromethyl)benzenesulfonamide, 2a.** According to the general procedure using 0.575 g (3.15 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 1.08 g (3.46 mmol, 1.1 equiv) of 3,5-bis(trifluoromethyl)benzenesulfonyl chloride, 1.40 g of product was obtained as pale solid (97%). After recrystallization from 2-propanol 1.04 g of white solid was received (72% yield).

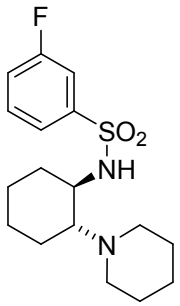
Mp 111.5-112 °C (2-propanol) (for ***ent*-2a** lit.[S7] mp. 110-111 °C); $[\alpha]_D^{22}$= −71.6 (*c* 1, CH_2Cl_2), (for ***ent*-2a** lit. $[\alpha]_D^{22}$ +60.1 (*c* 1.39, $CHCl_3$)[S7]); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 8.34 (s, 2H), 8.06 (s, 1H), 6.3 (br., 1H), 2.79 (td, *J* = 10.2, 3.7 Hz, 1H), 2.30 – 2.35 (m, 1H), 2.12 – 2.26 (m, 5H), 1.79 – 1.84 (m, 1H), 1.74 – 1.78 (m, 1H), 1.65 – 1.69 (m, 1H), 1.44 – 1.50 (m, 2H), 1.36 (br. 4H), 1.13 – 1.24 (m, 3H), 1.03 – 1.11 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.4, 132.8 (q, $J_{C\text{-}F}$ = 34.4 Hz), 127.4 (q, $J_{C\text{-}F}$ = 7.7 Hz), 126.0 (sept., $J_{C\text{-}F}$ = 3.4 Hz), 122.5 (q, $J_{C\text{-}F}$ = 273.2 Hz), 67.3, 53.8, 49.0, 32.5, 26.4, 25.2, 24.5, 24.1, 22.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.82 (s, 6H);



***N*-((1*S*,2*S*)-2-(Piperidin-1-yl)cyclohexyl)-3,5-bis(trifloromethyl)benzenesulfonamide, *ent*-2a.**[S7]

According to the general procedure using 0.174 g (0.956 mmol, 1.0 equiv) of (1*S*,2*S*)-2-(1-piperidinyl)cyclohexylamine and 0.329 g (1.05 mmol, 1.1 equiv) of 3,5-bis(trifluoromethyl)benzenesulfonyl chloride, 0.247 g of product was obtained after recrystallization from 2-propanol as white solid (56% yield).

Mp 110.5-112 °C (2-propanol). (lit.[S7] mp 110-111 °C); $[\alpha]_D^{21}$= +72.9 (*c* 1, CH_2Cl_2) (lit.[S7] $[\alpha]_D^{22}$ +60.1 (*c* 1.39, $CHCl_3$)).

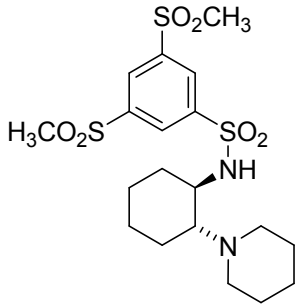


***N*-((1*R*,2*R*)-2-(Piperidin-1-yl)cyclohexyl)-3-fluorobenzenesulfonamide, 2b**

According to the general procedure using 0.364 g (2.00 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.290 mL (2.18 mmol, 1.1 equiv) of 3-fluorobenzenesulfonyl chloride, 0.435 g of product was obtained after recrystallization from 2-propanol as pale orange solid (64% yield).

mp 78.5 – 80.5 °C (2-propanol); $[\alpha]_D^{21}$= −109 (*c* 0.996, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 7.68 – 7.70 (m, 1H), 7.60 (dt, *J* = 8.1, 2.0 Hz, 1H), 7.51 (td, *J* = 8.0, 5.3 Hz, 1H), 7.27 (td, *J* = 8.0, 2.2 Hz, 1H), 6.25 (br., 1H), 2.68 (td, *J* = 10.5, 3.7 Hz, 1H), 2.41 – 2.46 (m, 1H), 2.05 – 2.19 (m, 5H), 1.73 – 1.81 (m, 2H), 1.64 – 1.68 (m, 1H), 1.43 (br., 2H), 1.35 (br., 4H), 1.10 – 1.29 (m, 3H), 1.00 – 1.06 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.4 (d, $J_{C\text{-}F}$ = 252 Hz), 141.9 (d, $J_{C\text{-}F}$ = 6.6 Hz), 130.7 (d, $J_{C\text{-}F}$ = 7.7 Hz), 123.0 (d, $J_{C\text{-}F}$ = 3.3 Hz), 119.6 (d, $J_{C\text{-}F}$ = 21.2 Hz), 114.6 (d, $J_{C\text{-}F}$ = 24.1 Hz), 67.4, 53.5, 49.1, 32.7, 26.5, 25.3, 24.5, 24.2, 22.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ −109.71 (td, $J_{F\text{-}H}$ = 8.2, 5.3 Hz); FT-IR (ATR) ν 3162, 2937, 1347, 1217, 1155 (S=O), 712, 586 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{17}H_{25}FN_2O_2S+H]^+$ 341.1694 found 341.1698

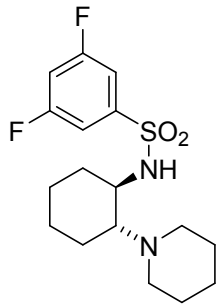
[S7] Schmitt, E.; Schiffers, I.; Bolm, C. *Tetrahedron* **2010**, *66*, 6349-6357. (Ref. 4b from the main text)



_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)-3,5-di(methylsulfonyl)benzenesulfonamide, 2c

According to the general procedure using 0.182 g (0.998 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.366 g (1.10 mmol, 1.1 equiv) of 3,5-bis(methylsulfonyl)benzenesulfonyl chloride, 0.331 g of product was obtained after recrystallization from 2-propanol as pale orange solid (69% yield).

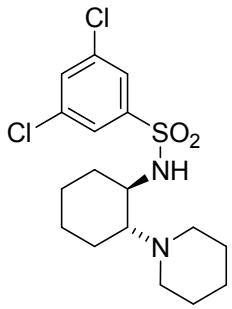
mp 206.5 – 209.0 °C (2-propanol); $[\alpha]_D^{21}$ = −66.7 (*c* 0.384, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 8.69 – 8.70 (m, 2H), 8.67 (t, *J* = 1.5 Hz, 1H), 5.52 (br., 1H), 3.18 (s, 6H), 2.95 – 3.00 (m, 1H), 2.30 – 2.36 (m, 2H), 2.15 – 2.27 (m, 4H), 1.81 – 1.85 (m, 1H), 1.77 (d, *J* = 5.9 Hz, 1H), 1.63 – 1.67 (m, 1H), 1.48 – 1.54 (m, 2H), 1.39 (br., 4H), 1.09 – 1.21 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 145.2, 143.6, 130.6, 129.8, 67.3, 54.0, 49.1, 44.3, 32.5, 26.5, 25.2, 24.5, 24.1, 22.8; FT-IR (ATR) ν 3133, 3063, 2928, 1310 (S=O), 1144 (S=O), 964, 812 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{19}H_{30}N_2O_6S_3+H]^+$ 479.1339 found 479.1344



_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)-3,5-difluorobenzenesulfonamide, 2d

According to the general procedure using 0.364 g (2.00 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.469 g (2.21 mmol, 1.1 equiv) of 3,5-difluorobenzenesulfonyl chloride, 0.279 g of product was obtained after recrystallization from 2-propanol as white solid (39% yield).

mp 72.0 – 74.0 °C (2-propanol); $[\alpha]_D^{20}$ = −103.6 (*c* 1.01, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 7.41 – 7.45 (m, 2H), 7.02 (tt, *J* = 8.4, 2.3 Hz, 1H), 6.26 (br., 1H), 2.72 (td, *J* = 10.5, 3.8 Hz, 1H), 2.38 – 2.42 (m, 1H), 2.12 – 2.22 (m, 5H), 1.74 – 1.83 (m, 2H), 1.65 – 1.69 (m, 1H), 1.43 – 1.50 (m, 2H), 1.38 (br., 4H), 1.12 – 1.29 (m, 3H), 1.03 – 1.10 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 162.8 (dd, $J_{C\text{-}F}$ = 255, 11 Hz), 143.4 (t, $J_{C\text{-}F}$ = 8.1 Hz), 110.8 (dd, *J* = 21.6, 6.3 Hz), 108.0 (t, $J_{C\text{-}F}$ = 25 Hz), 67.4, 53.6, 48.9, 32.7, 26.4, 25.3, 24.5, 24.1, 22.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ −105.71 – (−105.64) (m, 2F); FT-IR (ATR) ν 3132 (N-H), 2933, 1602 (N-H), 1351 (S=O), 1160 (S=O), 986 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{17}H_{24}F_2N_2O_2S+H]^+$ 359.1599 found 359.1609



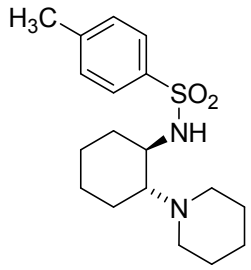
_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)-3,5-dichlorobenzenesulfonamide, 2e

According to the general procedure using 0.364 g (2.00 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.559 g (2.28 mmol, 1.1 equiv)

of 3,5-dichlorobenzenesulfonyl chloride, 0.744 g of product was obtained after recrystallization from 2-propanol as pale yellow solid (95% yield).

mp 147.7 – 149.2 °C (2-propanol); $[\alpha]_D^{21}$ = −110.8 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 7.76 – 7.77 (m, 2H), 7.54 – 7.55 (m, 1H), 6.31 (br., 1H), 2.68 (td, *J* = 10.5, 4.0 Hz, 1H), 2.37 – 2.42 (m, 1H), 2.12 – 2.23 (m, 5H), 1.74 – 1.83 (m, 2H), 1.65 – 1.69 (m, 1H), 1.45 – 1.53 (m, 2H), 1.39 (br., 4H), 1.12 – 1.28 (m, 3H), 1.03 – 1.10 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 142.9, 135.9, 132.4, 125.6, 67.4, 53.6, 48.4, 32.6, 26.5, 25.3, 24.6, 24.1, 22.7; FT-IR (ATR) ν 3110 (N-H), 2930, 1567 (N-H), 1346, 1171 (S=O), 801, 721 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{17}H_{24}Cl_2N_2O_2S+H]^+$ 391.1008 found 391.1003

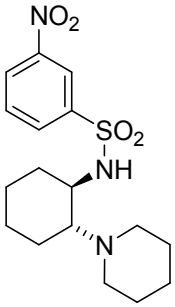
_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)-4-toluenesulfonamide, 2f[S8]



According to the general procedure using 0.424 g (2.33 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.460 g (2.42 mmol, 1.04 equiv) of tosyl chloride, 0.670 g of product was obtained after recrystallization from 2-propanol as white solid (86% yield). The spectra were in accordance with literature data.[S8]

Mp 98 – 99.5 °C (2-propanol) (lit.[S8] Mp 82–84 °C), FT-IR (ATR) $\tilde{\nu}$ 3195 (N-H), 2919, 1401, 1319, 1163 (S=O), 810, 690 cm^{-1} (lit.[S8] IR: 3195, 2919, 1401, 1319, 1163, 810, 689 cm^{-1})

_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)-3-nitrobenzenesulfonamide, 2g

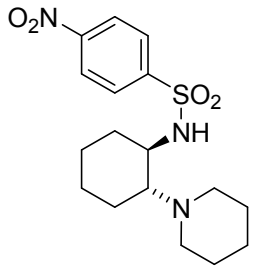


According to the general procedure using 0.364 g (2.00 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.489 g (2.21 mmol, 1.1 equiv) of 3-nitrobenzenesulfonyl chloride, 0.695 g of product was obtained after recrystallization from 2-propanol as white solid (95% yield).

R_f = 0.457 (CH_2Cl_2/MeOH 10:1 v:v); $[\alpha]_D^{21}$ = −94.9 (*c* 0.990, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 8.74 (t, *J* = 1.9 Hz, 1H), 8.43 (ddd, *J* = 8.2, 2.2, 1.0 Hz, 1H), 8.22 – 8.24 (m, 1H), 7.75 (t, 8.0 Hz, 1H), 6.18 (br., 1H), 2.77 (td, *J* = 10.5, 4.0 Hz, 1H), 2.35 – 2.39 (m, 1H), 2.11 – 2.22 (m 5H), 1.78 – 1.82 (m, 1H), 1.74 – 1.78 (m, 1H), 1.64 – 1.68 (m, 1H), 1.40 – 1.47 (m, 2H), 1.36 (br., 4H), 1.14 – 1.24 (m, 3H), 1.01 – 1.08 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 148.3, 142.5, 132.8, 130.3, 126.9, 122.4, 67.4, 53.7, 49.1, 32.6, 26.5, 25.2, 24.5, 24.1, 22.7; FT-IR (ATR) ν 3137 (N-H), 2933, 1532 (NO), 1349, 1172 (S=O), 906, 877 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{17}H_{25}N_3O_4S+H]^+$ 368.1639 found 368.1629

[S8] Martins, J. E. D.; Wills, M. *Tetrahedron: Asymmetry* **2008**, *19*, 1250–1255.

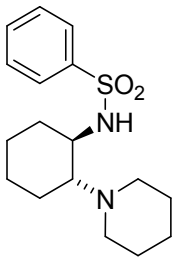
_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)-4-nitrobenzenesulfonamide, 2h



According to the general procedure using 0.364 g (2.00 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.484 g (2.21 mmol, 1.1 equiv) of 4-nitrobenzenesulfonyl chloride, 0.652 g of product was obtained after recrystallization from 2-propanol as white solid (89% yield).

mp 156.6 – 157.5 °C (2-propanol); $[\alpha]_D^{21}$ = −101.6 (*c* 1.25, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 8.37 (d, *J* = 8.9 Hz, 2H), 8.09 (d, *J* = 8.9 Hz, 2H), 6.28 (br., 1H), 2.76 (td, *J* = 10.4, 3.9 Hz, 1H), 2.35 – 2.40 (m, 1H), 2.12 – 2.20 (m, 5H), 1.78 – 1.83 (m, 1H), 1.73 – 1.78 (m, 1H), 1.63 – 1.68 (m, 1H), 1.41 – 1.48 (m, 2H), 1.37 (br., 4H), 1.11 – 1.26 (m, 3H), 1.02 – 1.08 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 149.9, 146.1, 128.5, 124.2, 67.4, 53.6, 48.9, 32.6, 26.5, 25.2, 24.5, 24.1, 22.7; FT-IR (ATR) ν 3157 (N-H), 2919, 1532 (NO), 1344, 1159 (S=O), 854, 736 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{17}H_{25}N_3O_4S+H]^+$ 368.1639 found 368.1628

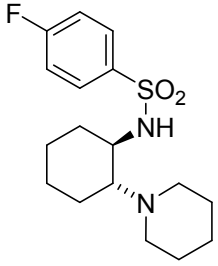
_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)-benzenesulfonamide, 2i



According to the general procedure using 0.571 g (3.14 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.42 mL (3.29 mmol, 1.05 equiv) of benzenesulfonyl chloride, 0.707 g of product was obtained after recrystallization from 2-propanol as white solid (70% yield).

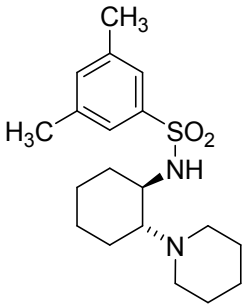
Mp 123.5 – 125 °C (2-propanol); $[\alpha]_D^{24}$ = −117 (*c* 1, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 7.87 – 7.90 (m, 2H), 7.55 – 7.58 (m, 1H), 7.49 – 7.53 (m, 2H), 6.19 (br., 1H), 2.60 – 2.66 (m, 1H), 2.44 – 2.49 (m, 1H), 2.00 – 2.25 (m, 5H), 1.71 – 1.78 (m, 2H), 1.62 – 1.67 (m, 1H), 1.22 – 1.44 (m, 7H), 1.11 – 1.18 (m, 2H), 0.96 – 1.03 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.6, 132.5, 128.9, 127.2, 67.4, 53.4, 49.0, 32.8, 26.6, 25.4, 24.5, 24.2, 22.7; FT-IR (ATR) ν 3195 (N-H), 2919, 1401, 1319, 1163 (S=O), 810, 690 cm^{-1};

_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)-4-fluorobenzenesulfonamide, 2j



According to the general procedure using 0.364 g (2.00 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.427 g (2.19 mmol, 1.1 equiv) of 4-fluorobenzenesulfonyl chloride, 0.580 g of product was obtained after recrystallization from 2-propanol as white solid (85% yield).

mp 125.0 – 127.5 °C (2-propanol); $[\alpha]_D^{19}$ = −109.3 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 7.91 (dd, *J* = 8.8, 5.1 Hz, 2H), 7.19 (dd, *J* = 8.8, 8.4 Hz, 2H), ~6.2 (br., 1H), 2.66 (td, *J* = 10.8, 4.2 Hz, 1H), 2.40 – 2.44 (m, 1H), 2.08 – 2.17 (m, 5H), 1.72 – 1.80 (m, 2H), 1.64 – 1.67 (m, 1H), 1.39 – 1.45 (m, 2H), 1.35 (br., 4H), 1.11 – 1.28 (m, 3H), 0.99 – 1.06 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.0 (d, $J_{C\text{-}F}$ = 255 Hz), 136.0 (d, $J_{C\text{-}F}$ = 2.8 Hz), 129.9 (d, $J_{C\text{-}F}$ = 9.2 Hz), 116.1 (d, $J_{C\text{-}F}$ = 22.4 Hz), 67.4, 53.5, 49.1, 32.7, 26.5, 25.3, 24.5, 24.2, 22.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ −105.67 (tt, $J_{F\text{-}H}$ = 8.4, 5.2 Hz, 1F); FT-IR (ATR) ν 3128 (N-H), 2929, 1591 (N-H), 1311, 1156 (S=O), 728 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{17}H_{25}FN_2O_2S+H]^+$ 341.1694 found 341.1699

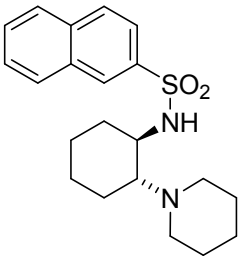


_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)-3,5-dimethylbenzenesulfonamide, 2k

According to the general procedure using 0.364 g (2.00 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.448 g (2.21 mmol, 1.1 equiv) of 3,5-dimethylbenzenesulfonyl chloride, 0.606 g of product was obtained after recrystallization from 2-propanol as white solid (86% yield).

mp 142.0 – 143.6 °C (2-propanol); $[\alpha]_D^{21}$ = −118.3 (*c* 0.994, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 7.49 (s, 2H), 7.18 (s, 1H), 6.18 (br., 1H), 2.59 (td, *J* = 10.6, 4.1 Hz, 1H), 2.45 – 2.50 (m, 1H), 2.38 (s, 6H), 2.03 – 2.18 (m, 5H), 1.71 – 1.79 (m, 2H), 1.63 – 1.67 (m, 1H), 1.41 (br., 2H), 1.36 (br., 4H), 1.23 – 1.30 (m, 1H), 1.09 – 1.20 (m, 2H), 1.01 (dq, *J* = 12.2, 3.2 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 139.1, 138.9, 134.2, 124.8, 67.4, 53.3, 48.9, 32.7, 26.6, 25.4, 24.6, 24.2, 22.7, 21.3; FT-IR (ATR) ν 3127 (N-H), 2930, 1454, 1342 (S=O), 1159 (S=O), 857, 734 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{19}H_{30}N_2O_2S+H]^+$ 351.2101 found 351.2099

_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)-2-naphthalenesulfonamide, 2l

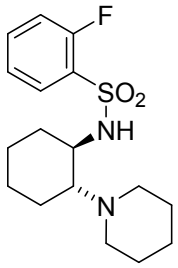


According to the general procedure using 0.364 g (2.00 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.500 g (2.21 mmol, 1.1 equiv) of 2-naphthalenesulfonyl chloride, 0.642 g of product was obtained after recrystallization from 2-propanol as white solid (86% yield).

mp 105.0 – 106.3 °C (2-propanol); $[\alpha]_D^{21}$ = −69.7 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 8.45 (d, *J* = 0.8 Hz, 1H), 7.98 (d, *J* = 7.9 Hz, 1H), 7.96 (d, *J* = 8.8 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.87 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.64 (ddd, *J* = 8.0, 7.0, 1.5 Hz, 1H), 7.61 (ddd, *J* = 8.0, 7.0, 1.5 Hz, 1H) 6.33 (br., 1H), 2.66 (td, *J* = 10.5, 3.7 Hz, 1H), 2.48 – 2.52 (m, 1H), 2.14 (t, *J* = 11.0 Hz, 1H), 2.06 (br., 4H), 1.69 – 1.75 (m, 2H), 1.62 – 1.66 (m, 1H), 1.24 – 1.40 (m,

7H), 1.07 – 1.19 (m, 2H), 0.92 – 0.98 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 136.6, 134.8, 132.2, 129.25, 129.15, 128.7, 128.4, 127.9, 127.5, 122.8, 67.4, 53.4, 48.8, 32.7, 26.5, 25.3, 24.5, 24.2, 22.7; FT-IR (ATR) ν 3183 (N-H), 2917, 1332 (S=O), 1316, 1160 (S=O), 830, 753 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{21}H_{28}N_2O_2S+H]^+$ 373.1944 found 373.1954

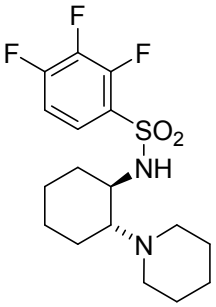
_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)-2-fluorobenzenesulfonamide, 2m



According to the general procedure using 0.600 g (3.29 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.707 g (3.63 mmol, 1.1 equiv) of 2-fluorobenzenesulfonyl chloride, 1.01 g of product was obtained as orange oil that crystallized over 12 months of storage (90% yield).

R_f = 0.839 (CH_2Cl_2/MeOH 10:1 v:v); $[\alpha]_D^{22}$ = −93.4 (*c* 1, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 7.91 (td, *J* = 7.5, 1.6 Hz, 1H), 7.55 – 7.59 (m, 1H), 7.28 (td, *J* = 7.7, 1.1 Hz, 1H), 7.18 – 7.22 (m, 1H), 6.4 (br., 1H), 2.70 (td, *J* = 10.6, 4.0 Hz, 1H), 2.44 – 2.49 (m, 1H), 2.14 – 2.26 (m, 5H), 1.78 – 1.82 (m, 1H), 1.71 – 1.75 (m, 1H), 1.61 – 1.66 (m, 1H), 1.44 – 1.49 (m, 4H) 1.37 (br., 2H), 1.23 – 1.30 (m, 1H), 1.07 – 1.21 (m, 2H), 1.01 – 1.08 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.1 (d, $J_{C\text{-}F}$ = 255 Hz), 134.9 (d, $J_{C\text{-}F}$ = 8.2 Hz), 130.8, 127.7 (d, $J_{C\text{-}F}$ = 13.9 Hz), 124.4 (d, $J_{C\text{-}F}$ = 3.8 Hz), 117.0 (d, $J_{C\text{-}F}$ = 21.0 Hz); 67.6, 53.6, 49.4, 32.9, 26.3, 25.4, 24.7, 24.2, 22.8; ; ^{19}F NMR (376 MHz, $CDCl_3$) δ −108.22 (s, 1F); FT-IR (ATR) ν 3198 (N-H), 2933, 1599 (N-H), 1345 (S=O), 1165 (S=O), 763 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{17}H_{25}FN_2O_2S+H]^+$ 341.1694 found 341.1685

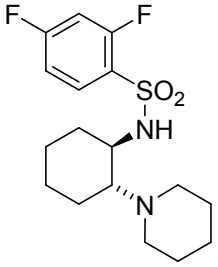
_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)-2,3,4-trifluorobenzenesulfonamide, 2n



According to the general procedure using 0.364 g (2.00 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.504 g (2.19 mmol, 1.1 equiv) of 2,3,4-trifluorobenzenesulfonyl chloride, 0.635 g of product was obtained after recrystallization from 2-propanol as white solid (84% yield).

mp 158.0 – 160.0 °C (2-propanol); $[\alpha]_D^{20}$ = −91.1 (*c* 1.01, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS; label: MD-110A-solid1) δ 7.67 – 7.71 (m, 1H), 7.10 – 7.14 (m, 1H), 6.48 (br., 1H), 2.75 (dd, *J* = 10.5, 4.0 Hz, 1H), 2.37 – 2.41 (m, 1H), 2.26 – 2.32 (m, 2H), 2.20 – 2.26 (m, 2H), 2.15 – 2.19 (m, 1H), 1.81 – 1.85 (m, 1H), 1.73 – 1.78 (m, 1H), 1.62 – 1.67 (m, 1H), 1.49 – 1.52 (m, 2H), 1.43 – 1.49 (m, 2H), 1.40 (br., 2H), 1.05 – 1.28 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) sp^2 region not interpreted due to complicated C-F couplings, δ sp^3: 67.6, 53.7, 49.5, 32.7, 26.3, 25.4, 24.7,

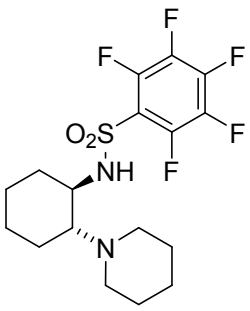
24.2, 22.9; $^{13}C\{^{19}F\}$ NMR (101 MHz, $CDCl_3$) δ sp^2: 154.1 (dd, J_{C-H} = 13.3, 5.2 Hz), 148.7 (dd, J_{C-H} = 11.5, 1.7 Hz), 140.4 (dd, J_{C-H} = 8.1, 1.9 Hz), 126.1 (m), 124.3 (d, J_{C-H} = 172 Hz), 112.4 (d, J_{C-H} = 170 Hz); sp^3 uninterpretable due to complicated C–H coupling; ^{19}F NMR (376 MHz, $CDCl_3$) δ −124.94 – (−125.06) (m, 1F), −128.35 – (−128.46) (m, 1F), −156.57 – (−156.71) (m, 1F); FT-IR (ATR) ν 3171 (N-H), 2927, 1607 (N-H), 1348 (S=O), 1161 (S=O), 1033 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{17}H_{23}F_3N_2O_2S+H]^+$ 377.1505 found 377.1504



_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)-2,4-difluorobenzenesulfonamide, 2o

According to the general procedure using 0.364 g (2.00 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.469 g (2.21 mmol, 1.1 equiv) of 2,4-difluorobenzenesulfonyl chloride, 0.319 g of product was obtained after recrystallization from 2-propanol as white solid (44% yield).

mp 100.0 – 101.5 °C (2-propanol); $[\alpha]_D^{19}$ = −101.0 (*c* 0.995, CH_2Cl_2); ^1H NMR (600 MHz, $CDCl_3$, TMS) δ 7.93 (td, *J* = 8.4, 6.3 Hz, 1H), 7.00 – 7.03 (m, 1H), 6.95 (ddd, *J* = 10.7, 8.4, 2.4 Hz, 1H), 6.46 (br., 1H), 2.71 (td, *J* = 10.6, 4.0 Hz, 1H), 2.40 – 2.44 (m, 1H), 2.25 – 2.30 (m, 2H), 2.18 – 2.25 (m, 3H), 1.80 – 1.84 (m, 1H), 1.72 – 1.77 (m, 1H), 1.62 – 1.66 (m, 1H), 1.42 – 1.54 (m, 4H), 1.38 (br., 2H), 1.03 – 1.28 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.6 (dd, J_{C-F} = 257, 10.4 Hz), 159.7 (dd, J_{C-F} = 258, 12.7 Hz), 132.4 (dd, J_{C-F} = 10.3, 1.3 Hz), 124.4 (dd, J_{C-F} = 14.1, 3.8 Hz), 111.7 (dd, J_{C-F} = 21.8, 3.8 Hz), 105.5 (t, J_{C-F} = 25.4 Hz), 67.5, 53.5, 49.3, 32.6, 26.2, 25.3, 24.6, 24.1, 22.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ −101.07 – (−100.98) (m, 1F), −103.18 – (−103.10) (m, 1F); FT-IR (ATR) ν 3190 (N-H), 2920, 1603 (N-H), 1166 (S=O), 967, 845 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{17}H_{24}F_2N_2O_2S+H]^+$ 359.1599 found 359.1608



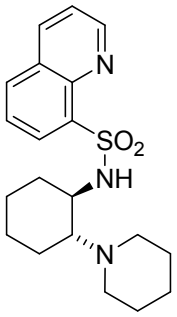
_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)-pentafluorobenzenesulfonamide, 2p

According to the general procedure using 0.359 g (1.96 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.320 mL (2.15 mmol, 1.1 equiv) of pentafluorobenzenesulfonyl chloride, 0.524 g of product was obtained after recrystallization from 2-propanol as white solid (64% yield).

mp 182.0 – 183.4 °C (2-propanol); $[\alpha]_D^{21}$ = −88.6 (*c* 1.00, CH_2Cl_2); ^1H NMR (600 MHz, $CDCl_3$, TMS) δ 6.54 (br., 1H), 2.89 (td, *J* = 10.5, 4.0 Hz, 1H), 2.46 – 2.51 (m, 1H), 2.29 – 2.37 (m, 2H), 2.26 (br., 2H), 2.16 – 2.21 (m, 1H), 1.83 – 1.87 (m, 1H), 1.76 – 1.81 (m, 1H), 1.66 –

1.71 (m, 1H), 1.50 – 1.56 (m, 2H), 1.36 – 1.50 (m, 4H), 1.24 – 1.31 (m, 1H), 1.09 – 1.22 (m, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) sp^2 not interpreted due to complicated C-F coupling, δ sp^3: 67.6, 54.0, 49.5, 32.4, 26.2, 25.4, 24.6, 24.2, 22.9; ^{13}C {^{19}F} NMR (101 MHz, $CDCl_3$) δ 144.7, 143.8, 137.9, 116.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ −135.48 – (−135.35) (m, 2F), −105.67 (tt, *J* = 8.4, 5.2 Hz, 1F), −158.71 – (−158.55) (m, 2F); FT-IR (ATR) ν 3133, 2941, 1648 (N-H), 1500, 1361, 1172, 1097, 990, 715 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{17}H_{21}F_5N_2O_2S+H]^+$ 413.1317 found 413.1317

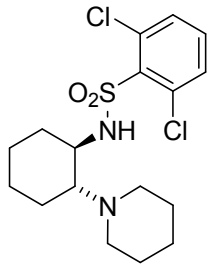
_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)-8-quinolinesulfonamide, 2q



According to the general procedure using 0.674 g (3.70 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.923 g (4.06 mmol, 1.1 equiv) of quinoline-8-sulfonyl chloride, 1.35 g of product was obtained after recrystallization from 2-propanol as white solid (98% yield).

mp 242 °C (dec., 2-propanol); $[\alpha]_D^{21}$ = −272.7 (*c* 0.902, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.12 (dd, *J* = 4.2, 1.6 Hz, 1H), 8.41 (dd, *J* = 7.3, 1.3 Hz, 1H), 8.24 (dd, *J* = 8.3, 1.6 Hz, 1H), 8.01 (dd, *J* = 8.2, 1.2 Hz, 1H), 7.62 (t, *J* = 7.7 Hz, 1H), 7.53 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.10 (br., 1H), 2.90 – 2.96 (m, 1H), 2.60 (d, *J* = 12.3 Hz, 1H), 2.16 (t, *J* = 9.8 Hz, 1H), 2.03 (br., 3H), 1.60-1.75 (m, 3H), 1.32 – 1.41 (m, 1H), 1.09 – 1.16 (m, 2H), 0.94 – 1.09 (m, 5H), 0.52 (br., 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 151.3, 143.8, 137.4, 136.6, 132.8, 130.3, 129.0, 125.5, 122.1; 67.5, 54.2, 49.2, 34.7, 25.4 (2C overlapped), 24.5, 24.3, 22.9; FT-IR (ATR) ν 3196 (N-H), 2932, 1332 (S=O), 1165 (S=O), 838 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{20}H_{27}N_3O_2S+H]^+$ 374.1897 found 374.1905

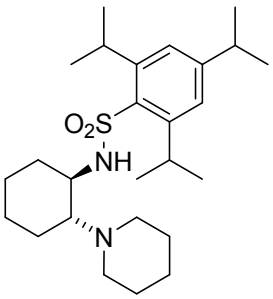
_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)-2,6-dichlorobenzenesulfonamide, 2r



According to the general procedure using 0.364 g (2.00 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.547 g (2.23 mmol, 1.1 equiv) of 2,6-dichlorobenzenesulfonyl chloride, 0.695 g of product was obtained after recrystallization from 2-propanol as pale yellow solid (89% yield).

mp 164.5 – 166.2 °C (2-propanol); $[\alpha]_D^{20}$ = −108.5 (*c* 1.02, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 7.47 (d, *J* = 8.0 Hz, 2H), 7.33 (t, *J* = 8.0 Hz, 1H), 6.73 (br., 1H), 2.95 (td, *J* = 10.5, 4.0 Hz, 1H), 2.55 – 2.59 (m, 1H), 2.29 – 2.33 (m, 2H), 2.22 (br., 2H), 2.16 (td, *J* = 11.0, 3.1 Hz, 1H), 1.80 – 1.84 (m, 1H), 1.73 – 1.77 (m, 1H), 1.63 – 1.67 (m, 1H), 1.40 – 1.48 (m, 4H), 1.36 (br., 2H), 1.08 – 1.27 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 136.1, 135.1, 132.1, 131.4, 67.7, 53.8,

49.4, 32.7, 26.1, 25.4, 24.6, 24.3, 22.8; FT-IR (ATR) ν 3186 (N-H), 2940, 1558 (N-H), 1425, 1175 (S=O), 736 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{17}H_{24}Cl_2N_2O_2S+H]^+$ 391.1008 found 391.1003

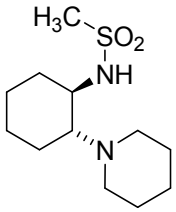


_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)-2,4,6-triisopropylbenzenesulfonamide, 2s

According to the general procedure using 0.595 g (3.27 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 1.08 g (3.63 mmol, 1.1 equiv) of 2,4,6-triisopropylbenzenesulfonyl chloride, 1.30 g of product was obtained as orange oil (90% yield).

R_f = 0.869 (CH_2Cl_2/MeOH 10:1 v:v); $[\alpha]_D^{21}$ = −48.5 (*c* 0.957, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 7.14 (s, 2H), 6.1 (br., 1H), 4.31 (sep, *J* = 6.8 Hz, 2H), 3.36 (td, *J* = 10.7, 3.8 Hz, 1H), 2.89 (sept., *J* = 6.9 Hz, 1H), 2.62 – 2.66 (m, 2H), 2.22 – 2.26 (m, 2H), 2.11 (td, *J* = 10.9, 2.9 Hz, 1H),1.97 – 2.02 (m, 1H), 1.82 – 1.86 (m, 1H), 1.73 – 1.77 (m, 1H), 1.53 – 1.60 (m, 4H), 1.46 – 1.51 (m, 2H), 1.37 – 1.43 (m, 2H), 1.27 (d, *J* = 6.6 Hz, 12H), 1.24 (d, *J* = 7.0 Hz, 6H), 1.10 – 1.23 (m, 4H), 0.97 – 1.04 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$), δ 152.6, 150.1, 134.6, 123.8; 67.6, 53.4, 49.0, 34.3, 33.0, 29.6, 26.6, 25.6, 25.2, 24.8, 24.7, 24.4, 23.77, 23.75, 23.0; FT-IR (ATR) ν 3154, 2931, 1600 (N-H), 1308 (S=O), 1149 (S=O) cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{26}H_{44}N_2O_2S+H]^+$ 449.3196 found 449.3196

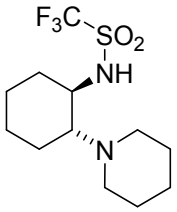
_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)-methanesulfonamide, 2t



According to the general procedure using 0.555 g (3.05 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.26 mL (3.36 mmol, 1.1 equiv) of methanesulfonyl chloride, 0.528 g of product was obtained after recrystallization from 2-propanol as white solid (67% yield).

mp 141.7 – 143.8 °C (2-propanol); $[\alpha]_D^{21}$ = −89.3 (*c* 0.996, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 6.0 (br., 1H), 3.14 (td, *J* = 10.4, 4.2 Hz, 1H), 2.96 (s, 3H), 2.58 – 2.62 (m, 2H), 2.39 – 2.42 (m, 1H), 2.27 – 2.32 (m, 2H), 2.15 (td, *J* = 10.9, 3.4 Hz, 1H), 1.86 – 1.89 (m, 1H), 1.78 – 1.83 (m, 1H), 1.68 – 1.71 (m, 1H), 1.57 – 1.63 (m, 2H), 1.48 – 1.54 (m, 2H) 1.43 (br., 2H), 1.17 – 1.31 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 67.5, 53.7, 49.4, 41.7, 33.1, 26.7, 25.5, 24.8, 24.3, 23.0; FT-IR (ATR) ν 3178 (N-H), 2934, 1313 (S=O), 1143 (S=O), 779 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{12}H_{24}N_2O_2S+H]^+$ 261.1631 found 261.1629

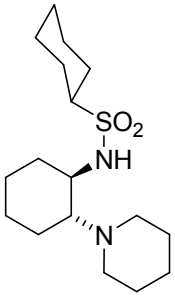
_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)- trifloromethanesulfonamide, 2u



According to the general procedure using 0.369 g (2.02 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.375 mL (2.23 mmol, 1.1 equiv) of trifluoromethanesulfonyl anhydride, 0.497 g of product was obtained after crystallization by slow evaporation from MTBE and cyclohexane mixture as a yellow solid (59% yield).

R_f = 0.582 (CH_2Cl_2/MeOH 10:1 v:v); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 6.16 (br., 1H), 3.30 (td, J = 10.5, 3.9 Hz, 1H), 2.64 – 2.69 (m, 2H), 2.42 – 2.48 (m, 1H), 2.36 (br., 2H), 2.21 – 2.26 (m, 1H), 1.87 – 1.92 (m, 1H), 1.80 – 1.85 (m, 1H), 1.70 – 1.74 (m, 1H), 1.61 – 1.67 (m, 2H), 1.57 (br., 2H), 1.46 (br., 2H), 1.27 – 1.35 (m, 1H), 1.19 – 1.26 (m, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 119.9 (q, J_{C-F} = 241 Hz), 68.4, 54.7, 49.3, 32.6, 26.1, 25.2, 24.3, 24.1, 22.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ −76.95 (s, 3F); FT-IR (ATR) ν 3220, 3107, 2936, 1361, 1182, 1148, 953, 901 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{12}H_{21}F_3N_2O_2S+H]^+$ 315.1349 found 315.1346

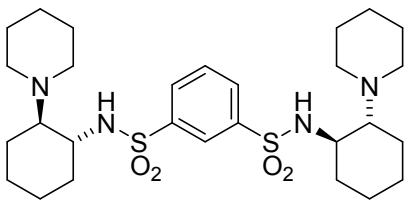
_N_-((1_R_,2_R_)-2-(Piperidin-1-yl)cyclohexyl)-cyclohexanesulfonamide, 2v



According to the general procedure using 0.181 g (1.00 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.165 mL (1.15 mmol, 1.1 equiv) of cyclohexanesulfonyl chloride, 0.073 g of product was obtained after recrystallization from 2-propanol as pale yellow solid (22% yield).

mp 149.8 – 151.3 °C (2-propanol); $[\alpha]_D^{21}$ = −64.9 (*c* 1, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 5.76 (br., 1H), 3.21 (td, J = 10.0, 4.0 Hz, 1H), 2.81 (tt, J = 12.1, 3.3 Hz, 1H), 2.59 – 2.64 (m, 2H), 2.35 – 2.39 (m, 1H), 2.17 – 2.32 (m, 4H), 2.12 – 2.17 (m, 1H), 1.84 – 1.93 (m, 3H), 1.76 – 1.83 (m, 1H), 1.65 – 1.73 (m, 2H), 1.50 – 1.62 (m, 6H), 1.42 (br., 2H), 1.16 – 1.32 (m, 7H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 67.7, 61.6, 53.0, 49.2 (br., 2C), 33.4, 26.5 (3C), 26.3, 25.5, 25.33, 25.28, 25.25, 24.7, 24.3, 22.9; FT-IR (ATR) ν 3216 (N-H), 2924, 1335, 1310, 1140, 892, 770 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{17}H_{32}N_2O_2S+H]^+$ 329.2257 found 329.2265

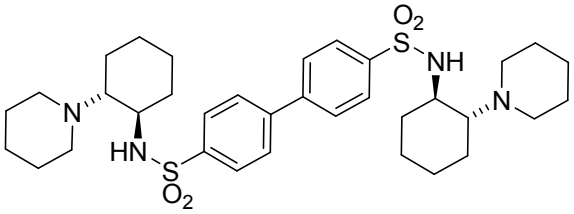
_N'_,_N_-Bis((1_R_,2_R_)-2-(piperidin-1-yl)cyclohexyl)-1,3-benzenedisulfonamide, 2w



According to the general procedure using 0.309 g (1.70 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.199 g (0.723 mmol, 0.43 equiv) of benzene-1,3-disulfonyl

chloride, 0.377 g of product was obtained as white solid sparingly soluble in 2-propanol (92% yield). The compound melts in very broad temperature range 75 – 108 °C.

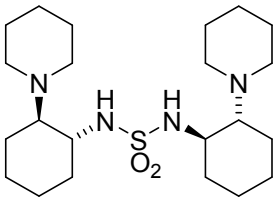
R_f = 0.234 (CH_2Cl_2/MeOH 10:1 v:v); $[\alpha]_D^{21}$ = −91.5 (*c* 1.02, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.40 (t, *J* = 1.4 Hz, 1H), 8.08 (dd, *J* = 7.8, 1.7 Hz, 2H), 7.68 (t, *J* = 7.8 Hz, 1H), 6.30 (br., 2H), 2.76 (td, *J* = 10.4, 3.9 Hz, 2H), 2.33 – 2.38 (m, 2H), 2.11 – 2.22 (m, 10H), 1.76 – 1.81 (m, 2H), 1.72 – 1.76 (m, 2H), 1.61 – 1.66 (m, 2H), 1.43 – 1.49 (m, 4H), 1.36 (br., 8H), 1.12 – 1.23 (m, 6H), 1.01 – 1.09 (m,2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 141.7, 130.7, 129.8, 126.0, 67.4, 53.6, 49.1, 32.6, 26.5, 25.3, 24.6, 24.1, 22.7; FT-IR (ATR) ν 3176 (N-H), 2931, 1343 (S=O), 1155 (S=O), 959, 905, 794 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{28}H_{46}N_4O_4S_2+H]^+$ 567.3033, found 567.3020



***N',N*-Bis((1*R*,2*R*)-2-(piperidin-1-yl)cyclohexyl)-4,4'-biphenyldisulfonamide, 2x**

According to the general procedure using 0.309 g (1.70 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.248 g (0.706 mmol, 0.42 equiv) of biphenyl-4,4'-disulfonyl chloride, 0.435 g of product was obtained after recrystallization from 2-propanol as white solid (80% yield).

mp 207.7 – 209.5 °C; $[\alpha]_D^{21}$ = −109.9 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 8.00 (d, *J* = 7.9 Hz, 4H), 7.74 (d, *J* = 8.4 Hz, 4H), 6.25 (br., 2H), 2.74 (td, *J* = 10.5, 3.7 Hz, 2H), 2.45 – 2.50 (m, 2H), 2.05 – 2.19 (m, 10H), 1.79 (d, *J* = 13.0 Hz, 2H), 1.73 – 1.77 (m, 2H), 1.65 – 1.69 (m, 2H), 1.32 – 1.44 (m, 12H), 1.24 – 1.32 (m, 2H), 1.12 – 1.22 (m, 4H), 1.01 – 1.07 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.4, 139.7, 128.0, 127.8, 67.4, 53.5, 49.0, 32.9, 26.6, 25.3, 24.5, 24.2, 22.7; FT-IR (ATR) ν 3169 (N-H), 2929, 1594 (N-H), 1337 (S=O), 1165 (S=O), 827, 713 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{34}H_{50}N_4O_4S_2+H]^+$ 643.3346 found 643.3353



***N',N*-Bis((1*R*,2*R*)-2-(piperidin-1-yl)cyclohexyl)-sulfamide, 2y**

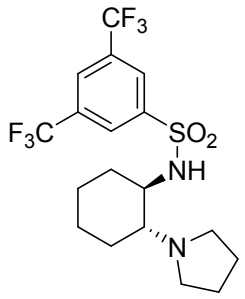
According to the general procedure using 0.308 g (1.69 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(1-piperidinyl)cyclohexylamine and 0.057 mL (0.705 mmol, 0.42 equiv) of sulfuryl chloride, 0.062 g of product was obtained after recrystallization from 2-propanol as pale yellow solid (21% yield).

mp 179.5-181°C (dec., 2-propanol); $[\alpha]_D^{21}$ = −96.1 (*c* 1.02, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 5.93 (br., 2H), 3.17 (td, *J* = 10.2, 3.9 Hz, 2H), 2.63 – 2.68 (m, 4H), 2.47 – 2.52 (m, 2H), 2.26 (br., 4H), 2.12 (td, *J* = 10.4, 3.2 Hz, 2H), 1.83 – 1.87 (m, 2H), 1.76 – 1.81 (m, 2H), 1.65 – 1.70 (m,

2H), 1.50 – 1.62 (m, 8H), 1.42 (br., 4H), 1.15 – 1.26 (m, 8H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 67.8, 53.9, 49.3, 33.0, 26.7, 25.7, 24.9, 24.5, 23.0; FT-IR (ATR) ν 3183, 3161, 2927, 1308, 1153, 1147, 960, 771 cm^{-1}; HRMS (ESI-TOF) calcd. for $[C_{22}H_{42}N_4O_2S+H]^+$ 427.3101 found 427.3100.

Catalysts 1 and 3-5

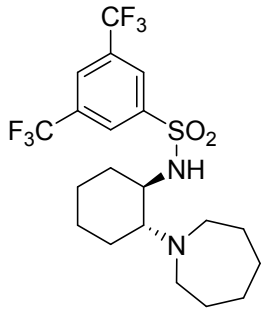
N-((1*R*,2*R*)-2-(Pyrrolidin-1-yl)cyclohexyl)-3,5-bis(trifloromethyl)benzenesulfonamide, 1a



According to the general procedure using 0.605 g (3.59 mmol) of (1*R*,2*R*)-2-(1-pyrrolidinyl)cyclohexylamine and 1.24 g (3.96 mmol, 1.1 equiv) of 3,5-bis(trifluoromethyl)benzenesulfonyl chloride, 1.50 g of product was obtained as orange oil (94% yield).

R_f = 0.515 (CH_2Cl_2/MeOH 10:1 v:v); $[\alpha]_D^{22}$ = −66.2 (*c* 1.00, CH_2Cl_2) ; ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 8.33 (s, 2H), 8.07 (s, 1H), 4.8 (br., 1H), 2.75 (td, *J* = 10.4, 4.1 Hz, 1H), 2.46 (td, *J* = 10.3, 2.6 Hz, 1H), 2.38 – 2.42 (m, 2H), 2.28 – 2.32 (m, 1H), 2.18 – 2.23 (m, 2H), 1.75 – 1.80 (m, 2H), 1.64 – 1.70 (m, 3H), 1.55 – 1.62 (m, 2H), 1.10 – 1.24 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.5, 132.8 (q, J_{C-F} = 34.5 Hz), 127.4 (m), 125.9 (m), 122.5 (q, J_{C-F} = 273 Hz), 61.5, 55.8, 46.6, 32.5, 24.9, 24.1, 23.5, 21.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.84 (s, 6F); HRMS (ESI-TOF) calcd. for $[C_{18}H_{22}F_6N_2O_2S+H]^+$ 445.1379 found 445.1384

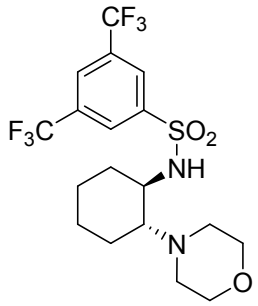
N-((1*R*,2*R*)-2-(Azepan-1-yl)cyclohexyl)-3,5-bis(trifloromethyl)benzenesulfonamide, 3a



According to the general procedure using 0.203 g (1.04 mmol) of (1*R*,2*R*)-2-(1-azepanyl)cyclohexylamine and 0.356 g (1.14 mmol, 1.1 equiv) of 3,5-bis(trifluoromethyl)benzenesulfonyl chloride, 0.374 g of product was obtained after recrystallization from 2-propanol as white solid (76% yield).

mp 116.6 – 119.0 °C (2-propanol); $[\alpha]_D^{23}$ = −55.6 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 8.35 (s, 2H), 8.06 (s, 1H), 5.6 (br., 1H), 2.88 (td, *J* = 10.3, 4.1 Hz, 1H), 2.34 – 2.52 (m, 4H), 2.21 – 2.30 (m, 2H), 1.72 – 1.83 (m, 2H), 1.62 – 1.69 (m, 1H), 1.48 – 1.61 (m, 6H), 1.44 (br., 2H), 1.11 – 1.22 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 144.0, 132.9 (q, J_{C-F} = 34.6 Hz), 127.5 (m), 126.0 (quin., J_{C-F} = 3.5 Hz), 122.7 (q, J_{C-F} = 273 Hz), 68.7, 54.8, ~50 (br.), 32.5, 29.4, 26.9, 25.4, 24.2, 23.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.81 (s, 6F); HRMS (ESI-TOF) calcd. for $[C_{20}H_{26}F_6N_2O_2S+H]^+$ 473.1692 found 473.1702

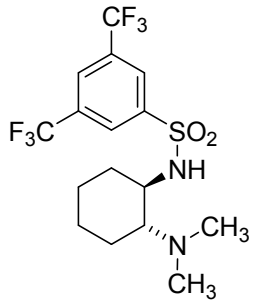
N-((1*R*,2*R*)-2-(Morpholin-4-yl)cyclohexyl)-3,5-bis(trifloromethyl)benzenesulfonamide, 3a



According to the general procedure using 0.402 g (2.18 mmol) of (1*R*,2*R*)-2-(4-morpholinyl)cyclohexylamine and 0.750 g (2.40 mmol, 1.1 equiv) of 3,5-bis(trifluoromethyl)benzenesulfonyl chloride, 0.786 g of product was obtained after recrystallization from 2-propanol as white solid (78% yield).

mp 103.6 – 106.4 °C (2-propanol); $[\alpha]_D^{23} = -71.9$ (*c* 0.997, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 8.34 (s, 2H), 8.07 (s, 1H), 6.29 (br., 1H), 3.62 – 3.66 (m, 2H), 3.56 (br., 2H), 2.94 (td, *J* = 10.3, 4.1 Hz, 1H), 2.30 – 2.42 (m, 4H), 2.19 – 2.28 (m, 2H), 1.85 – 1.90 (m, 1H), 1.78 – 1.83 (m, 1H), 1.65 – 1.69 (m, 1H), 1.11 – 1.22 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.9, 133.0 (q, $J_{C\text{-}F}$ = 34.5 Hz), 127.4 (m), 126.2 (quin, $J_{C\text{-}F}$ = 3.4 Hz), 122.6 (q, $J_{C\text{-}F}$ = 274 Hz), 67.2, 66.9, 53.7, 48.2, 32.6, 25.1, 24.1, 22.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.80 (s, 6F).

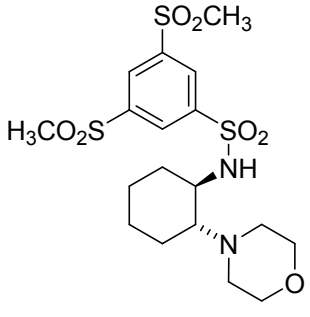
_N_-((1_R_,2_R_)-2-(dimethylamino)cyclohexyl)-3,5-bis(trifloromethyl)benzenesulfonamide, 5a [S7]



According to the general procedure using 0.303 g (2.13 mmol) of (1*R*,2*R*)-2-(*N*,*N*-dimethylamino)cyclohexylamine[S9] and 0.733 g (2.34 mmol, 1.1 equiv) of 3,5-bis(trifluoromethyl)benzenesulfonyl chloride, 0.923 g of product was obtained as crude solid (quantitative yield). Spectra were in accordance with literature data.[S7]

^{19}F NMR (376 MHz, $CDCl_3$; label: MD-160A-cr) δ −62.86 (s, 6H).

_N_-((1_R_,2_R_)-2-(Morpholin-4-yl)cyclohexyl)-3,5-di(methylsulfonyl)benzenesulfonamide, 4c



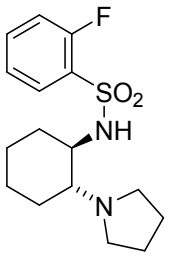
According to the general procedure using 0.178 g (0.968 mmol, 1.0 equiv) of (1*R*,2*R*)-2-(morpholin-4-yl)cyclohexylamine and 0.354 g (1.07 mmol, 1.1 equiv) of 3,5-3,5-bis(methylsulfonyl)benzenesulfonyl chloride, 0.323 g of product was obtained after recrystallization from *sec*-butanol as white solid (69% yield).

mp 168 – 171 °C (*sec*-butanol); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 8.69 (d, *J* = 1.5 Hz, 2H), 8.67 (t, *J* = 1.4 Hz, 1H), 6.42 (br., 1H), 3.65 – 3.70 (m, 2H), 3.56 – 3.62 (m, 2H), 3.20 (s, 6H), 3.09 (td, *J* =

[S9] Kaik, K.; Gawroński, J. *Tetrahedron: Asymmetry* **2003**, *14*, 1559-1563.

10.5, 4.0 Hz, 1H), 2.48 (br., 2H), 2.33 – 2.39 (m, 2H), 2.22 (td, *J* = 10.5, 3.0 Hz, 1H), 2.14 – 2.19 (m, 1H), 1.86 – 1.91 (m, 1H), 1.78 – 1.82 (m, 1H), 1.62 – 1.67 (m, 1H), 1.08 – 1.22 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$; label) δ 145.5, 143.8, 130.6, 129.9, 67.3, 66.8, 53.8, 48.3, 44.3, 32.5, 25.1, 24.0, 22.9;

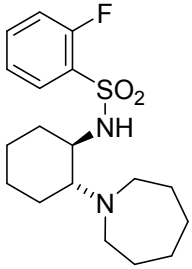
_N_-((1_R_,2_R_)-2-(Pyrrolidin-1-yl)cyclohexyl)-2-fluorobenzenesulfonamide, 1m



According to the general procedure using 0.542 g (3.22 mmol) of (1*R*,2*R*)-2-(1-pyrrolidinyl)cyclohexylamine and 0.718 g (3.69 mmol, 1.1 equiv) of 2-fluorobenzenesulfonyl chloride, 0.737 g of product was obtained after recrystallization from 2-propanol as yellow solid (70% yield).

mp 89.3 – 92.3 °C (2-propanol); $[\alpha]_D^{23}$ = −117.3 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 7.92 (td, *J* = 7.5, .1.8 Hz, 1H), 7.55 – 7.59 (m, 1H), 7.28 (td, *J* = 7.6, 1.0 Hz, 1H), 7.18 – 7.21 (m, 1H), 6.4 (br., 1H), 2.65 (td, *J* = 10.4, 3.9 Hz, 1H), 2.41 – 2.49 (m, 2H), 2.35 – 2.40 (m, 2H), 2.19 – 2.25 (m, 2H), 1.79 – 1.77 (m, 2H), 1.62 – 1.70 (m, 4H), 1.23 – 1.31 (m, 1H), 1.07 – 1.22 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 159.2 (d, $J_{C\text{-}F}$ = 256 Hz), 134.9 (d, $J_{C\text{-}F}$ = 8.2 Hz), 130.8, 127.8 (d, $J_{C\text{-}F}$ = 13.8 Hz), 124.4 (d, $J_{C\text{-}F}$ = 3.8 Hz), 116.8 (d, $J_{C\text{-}F}$ = 21.2 Hz), 61.5, 55.5, 46.9, 32.9, 25.0, 24.2, 23.4, 22.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ −109.49 – (−108.80) (m, 1F); HRMS (ESI-TOF) calcd. for $[C_{16}H_{23}FN_2O_2S+H]^+$ 327.1537 found 327.1545

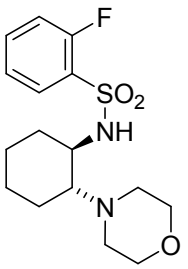
_N_-((1_R_,2_R_)-2-(Azepan-1-yl)cyclohexyl)-2-fluorobenzenesulfonamide, 3m



According to the general procedure using 0.190 g (0.965 mmol) of (1*R*,2*R*)-2-(1-azepanyl)cyclohexylamine and 0.211 g (1.08 mmol, 1.1 equiv) of 2-fluorobenzenesulfonyl chloride, 0.320 g of product was obtained as orange oil (94% yield).

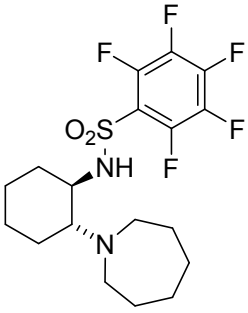
R_f = 0.413 (CH_2Cl_2/MeOH 10:1 v:v); $[\alpha]_D^{24}$ = −65.6 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 7.92 (td, J = 7.7, 1.8 Hz, 1H), 7.53 – 7.58 (m, 1H), 7.27 (td, *J* = 7.8, 1.0 Hz, 1H), 7.19 (ddd, *J* = 9.6, 8.4, 1.0 Hz, 1H), 6.37 (br., 1H), 2.84 (td, *J* = 10.2, 3.7 Hz, 1H), 2.44 – 2.51 (m, 2H), 2.34 – 2.43 (m, 3H), 2.24 – 2.28 (m, 1H), 1.47 – 1.79 (m, 11 H), 1.09 – 1.25 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$; label: MD-091A-cr) δ 159.2 (d, $J_{C\text{-}F}$ = 255 Hz), 134.8 (d, $J_{C\text{-}F}$ = 8 Hz), 130.5, 128.6, 124.4 ($J_{C\text{-}F}$ = 3 Hz), 117.1($J_{C\text{-}F}$ = 21 Hz), 69.0, 54.3, 51.1 (br.), 32.6, 29.0, 27.0, 25.5, 24.3, 23.6; ^{19}F NMR (376 MHz, $CDCl_3$; label: MD-091A-cr) δ −108.35 – (−108.27) (m, 1F); HRMS (ESI-TOF) calcd. for $[C_{18}H_{27}FN_2O_2S+H]^+$ 355.1850 found 327. 355.1855

***N*-((1*R*,2*R*)-2-(Morpholin-4-yl)cyclohexyl)-2-fluorobenzenesulfonamide 4m**



According to the general procedure using 0.402 g (2.18 mmol) of (1*R*,2*R*)-2-(4-morpholinyl)cyclohexylamine and 0.478 g (2.46 mmol, 1.1 equiv) of 2-fluorobenzenesulfonyl chloride, 0.582 g of product was obtained as white solid after recrystallization from 2-propanol (78% yield).

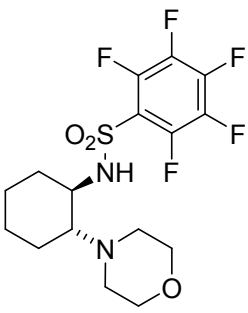
mp 115.5 – 118.0 °C (2-propanol); $[\alpha]_D^{24} = -126.0$ (*c* 0.997, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 7.92 (td, *J* = 7.5, 1.6 Hz, 1H), 7.57 – 7.61 (m, 1H), 7.30 (td, *J* = 7.6, 0.6 Hz, 1H), 7.18 – 7.22 (m, 1H), 6.30 (br., 1H), 3.58 – 3.65 (m, 4H), 2.73 (td, *J* = 10.6, 4.1 Hz, 1H), 2.44 – 2.49 (m, 1H), 2.26 – 2.33 (m, 4H), 2.18 – 2.23 (m, 1H), 1.82 – 1.87 (m, 1H), 1.74 – 1.79 (m, 1H), 1.63 – 1.67 (m, 1H), 1.25 – 1.32 (m, 1H), 1.05 – 1.23 (m, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 158.9 (d, $J_{C\text{-}F}$ = 255 Hz), 135.1 (d, $J_{C\text{-}F}$ = 8.2 Hz), 130.8, 127.7 (d, $J_{C\text{-}F}$ = 13.8 Hz), 124.6 (d, $J_{C\text{-}F}$ = 3.8 Hz), 116.9 (d, $J_{C\text{-}F}$ = 21.0 Hz), 67.07, 67.06, 53.3, 48.5, 32.9, 25.2, 24.1, 22.9; ^{19}F NMR (376 MHz, $CDCl_3$) δ −108.75 – (−108.67) (m, 1F);



***N*-((1*R*,2*R*)-2-(Azepan-1-yl)cyclohexyl)-pentafluorobenzenesulfonamide, 3p**

According to the general procedure using 0.199 g (1.01 mmol) of (1*R*,2*R*)-2-(1-azepanyl)cyclohexylamine and 0.165 mL (1.11 mmol, 1.1 equiv) of pentafluorobenzenesulfonyl chloride, 0.300 g of product was obtained after recrystallization from 2-propanol as white solid (70% yield).

mp 149.1 – 152.3 °C (2-propanol); $[\alpha]_D^{23} = -54.5$ (*c* 1.00, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 5.2 (br,. 1H), 2.99 – 3.05 (m, 1H), 2.54 – 2.60 (m, 2H), 2.38 – 2.51 (m, 3H), 2.25 – 2.31 (m, 1H), 1.81 – 1.85 (m, 1H), 1.74 – 1.79 (m, 1H), 1.65 – 1.69 (m, 1H), 1.51 – 1.63 (m, 8H), 1.16 – 1.25 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 68.9, 54.9, 51.4, 32.0, 29.0, 26.9, 25.4, 24.2, 23.6; ^{13}C{^{19}F} NMR (101 MHz, $CDCl_3$) δ 144.6, 143.7, 137.9, 117.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ −135.70 – (−135.58) (m, 2F), −146.59 (tt, *J* = 21.0, 6.1 Hz, 1F), −158.89 – (−158.73) (m, 2F); HRMS (ESI-TOF) calcd. for $[C_{18}H_{23}F_5N_2O_2S+H]^+$ 427.1473 found 427.1476.



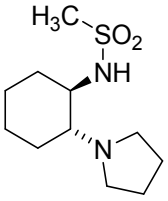
***N*-((1*R*,2*R*)-2-(Morpholin-4-yl)cyclohexyl)-pentafluorobenzenesulfonamide, 4p**

According to the general procedure using 0.402 g (2.18 mmol) of (1*R*,2*R*)-2-(4-morpholinyl)cyclohexylamine and 0.356 mL (2.40 mmol, 1.1 equiv) of

pentafluorobenzenesulfonyl chloride, 0.701 g of product was obtained after recrystallization from 2-propanol as white solid (78% yield).

mp 161.4 – 163.6 °C (2-propanol); $[\alpha]_D^{20}$ = −86.6 (*c* 0.997, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 6.59 (br., 1H), 3.61 – 3.71 (m, 4H), 3.00 (td, *J* = 10.6, 4.0 Hz, 1H), 2.41 – 2.49 (m, 3H), 2.36 – 2.40 (m, 2H), 2.23 (td, *J* = 10.9, 2.9 Hz, 1H), 1.88 – 1.93 (m, 1H), 1.80 – 1.84 (m, 1H), 1.67 – 1.72 (m, 1H), 1.14 – 1.31 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 67.2, 67.1, 53.8, 48.4, 32.3, 25.1, 24.1, 23.0; ^{13}C{^{19}F} NMR (101 MHz, $CDCl_3$) 144.6, 143.8, 137.9, 117.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ −135.98 – (−135.85) (m, 2F), −145.80 (tt, *J* = 21.0, 6.2 Hz, 1F), −158.54 – (−158.37) (m, 2F);

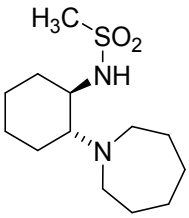
_N_-((1_R_,2_R_)-2-(Pyrrolidin-1-yl)cyclohexyl)-methanesulfonamide, 1t



According to the general procedure using 0.534 g (3.20 mmol) of (1*R*,2*R*)-2-(1-pyrrolidinyl)cyclohexylamine and 0.300 mL (3.88 mmol, 1.1 equiv) of methanesulfonyl chloride, 0.355 g of product was obtained after recrystallization from 2-propanol as white solid (45% yield).

mp 95.5 – 97.8°C (2-propanol); $[\alpha]_D^{22}$ = −101.5 (*c* 1.01, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 5.9 (br,. 1H), 3.12 (td, *J* = 10.1, 4.2 Hz, 1H), 2.97 (s, 3H), 2.60 – 2.65 (m, 2H), 2.51 – 2.55 (m, 2H), 2.43 – 2.48 (m, 1H), 2.37 – 2.41 (m, 1H), 1.80 – 1.85 (m, 2H), 1.69 – 1.77 (m, 5H), 1.23 – 1.31 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 61.5, 55.6, 46.8, 41.9, 32.8, 25.0, 24.2, 23.7, 21.7; HRMS (ESI-TOF) calcd. for $[C_{11}H_{22}N_2O_2S+H]^+$ 247.1474 found 247.1482.

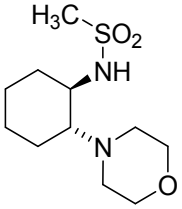
_N_-((1_R_,2_R_)-2-(Azepan-1-yl)cyclohexyl)-methanesulfonamide, 3t



According to the general procedure using 146 mg (0.741 mmol) of (1*R*,2*R*)-2-(1-azepanyl)cyclohexylamine and 63 μL (0.814 mmol, 1.1 equiv) of methanesulfonyl chloride, 83 mg of product was obtained after recrystallization from 2-propanol as white solid (41% yield).

mp 119.3 – 121.1 °C (2-propanol); $[\alpha]_D^{22}$ = −68.9 (*c* 1.00, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 6.05 (br., 1H), 3.13 (td, *J* = 10.2, 4.2 Hz, 1H), 2.97 (s, 3H), 2.70 – 2.75 (m, 2H), 2.43 – 2.51 (m, 2H), 2.36 – 2.41 (m, 1H), 2.21 – 2.26 (m, 1H), 1.82 – 1.87 (m, 1H), 1.77 – 1.82 (m, 1H), 1.53 – 1.72 (m, 9H), 1.20 – 1.30 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 68.6, 54.5, ~50 (br.), 42.4, 32.7, 29.6, 26.9, 25.5, 24.3, 23.5; HRMS (ESI-TOF) calcd. for $[C_{13}H_{26}N_2O_2S+H]^+$ 275.1788 found 275.1783.

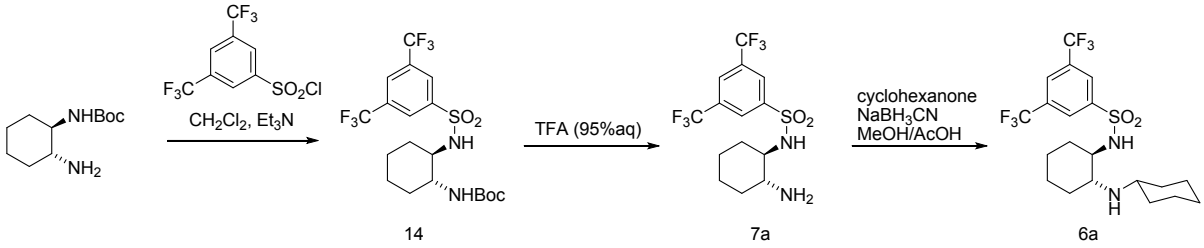
***N*-((1*R*,2*R*)-2-(Morpholin-4-yl)cyclohexyl)-methanesulfonamide, 4t**



According to the general procedure using 0.402 g (2.18 mmol) of (1*R*,2*R*)-2-(4-morpholinyl)cyclohexylamine and 0.186 mL (2.40 mmol, 1.1 equiv) of methanesulfonyl chloride, 0.483 g of product was obtained after recrystallization from 2-propanol as white solid (85% yield).

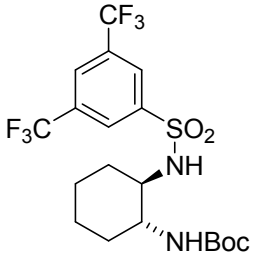
mp 141.7 – 143.8 °C (2-propanol); $[\alpha]_D^{23}$ = −85.4 (*c* 1.01, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 5.79 (br., 1H), 3.64 – 3.75 (m, 4H), 3.22 (td, *J* = 10.3, 4.2 Hz, 1H), 2.98 (s, 3H), 2.64 – 2.70 (m, 2H), 2.36 – 2.41 (m, 3H), 2.19 (td, *J* = 10.9, 3.3 Hz, 1H), 1.89 – 1.94 (m, 1H), 1.82 – 1.86 (m, 1H), 1.69 – 1.73 (m, 1H), 1.21 – 1.31 (m, 4H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 67.4, 66.9, 53.3, 48.3, 42.6, 32.9, 25.3, 24.1, 22.9.

Catalysts 6-8



Scheme S1. Synthesis of **6a** and **7a**

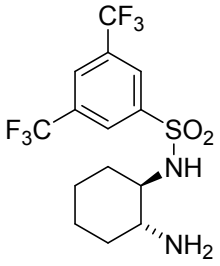
***N*-((1*R*,2*R*)-2-(*tert*-Butyloxycarbonylamino)cyclohexyl)-3,5-bis(trifloromethyl)benzenesulfonamide, 14**



According to the general procedure using 0.437 g (2.04 mmol) of *tert*-butyl ((1*R*,2*R*)-2-aminocyclohexyl)carbamate and 0.701 g (2.24 mmol, 1.1 equiv) of 3,5-bis(trifluoromethyl)benzenesulfonyl chloride, 0.877 g (89% yield) of product was obtained and used further without purification.

^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 8.31 (s, 2H), 8.04 (s, 1H), 6.35 (s, 1H), 4.52 (br., 1H), 3.30 – 3.41 (m, 1H), 3.04 – 3.10 (m, 1H), 1.93 – 2.00 (m, 2H), 1.63 – 1.77 (m, 2H). 1.40 (s, 9H), 1.16 – 1.31 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.6, 145.0, 132.7 (q, $J_{C\text{-}F}$ = 34 Hz), 127.0 – 127.2 (m), 125.7 (quint. $J_{C\text{-}F}$ = 3 Hz), 122.6 (q, $J_{C\text{-}F}$ = 274 Hz), 80.8, 60.8, 53.4, 33.8, 32.4, 28.2, 24.6, 24.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.72 (s, 6F).

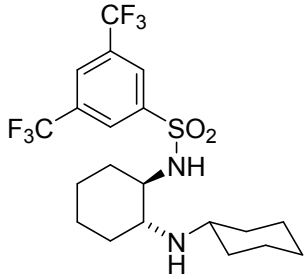
_N_-((1_R_,2_R_)-2-aminocyclohexyl)-3,5-bis(trifloromethyl)benzenesulfonamide, 6a [S10]



Boc-sulfonamide **14** (0.877 g, 1.79 mmol) was dissolved in 95% aqueous solution of trifluoroacetic acid (10 mL) and stirred at RT for 17 h. The solution was concentrated *in vacuo*, and the residue dissolved in a mixture of aqueous $NaHCO_3$ (10%, 25 mL) and DCM (25 mL). The mixture was alkalized with excess of NaOH and phases were separated. Aqueous phase was extracted with DCM (2 × 10 mL) and combined organic phases were dried over Na_2SO_4, and concentrated *in vacuo* to obtain 0.596 g of product as orange oil (85% yield). Spectra were in accordance to literature data.[S10]

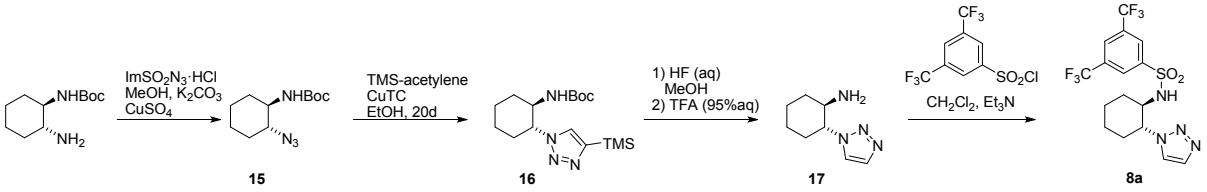
^{19}F NMR (376 MHz, $CDCl_3$; label: MD-141A-cr) δ −62.94 (s, 6F).

_N_-((1_R_,2_R_)-2-(_N_-cyclohexylamino)cyclohexyl)-3,5-bis(trifloromethyl)benzenesulfonamide, 7a



Amine **6a** (0.201 g, 0.649 mmol) was dissolved in MeOH (2.7 mL) and cyclohexanone (0.201 mL, 1.95 mmol, 3.0 equiv) was added followed by acetic acid (0.606 mL). The mixture was stirred at RT for 30 minutes and sodium cyanoborohydride was added portionwise (102 mg, 1.62 mmol, 2.5 equiv) and the solution was stirred at RT for 22 h. The mixture was concentrated *in vacuo*, residues were alkalized with 10 mL of saturated NaOH. The mixture was extracted with dichloromethane (3 × 10 mL). The combined extracts were dried over K_2CO_3, and evaporated to obtain 0.199 g of white solid (85% yield).

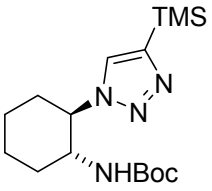
Mp 134-138 °C; ^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 8.37 (s, 2H), 8.08 (s, 1H), 2.48 – 2.53 (m, 2H), 2.28 (td, J = 10.6, 3.7 Hz, 1H), 2.21 – 2.26 (m, 1H), 2.11 – 2.16 (m, 1H), 1.83 – 1.88 (m, 1H), 1.66 – 1.76 (m, 4H), 1.61 – 1.65 (m, 1H), 1.55 – 1.60 (m, 1H), 1.12 – 1.32 (m, 7H), 1.02 – 1.08 (m, 1H), 0.92 – 0.98 (m, 1H), 0.84 – 0.90 (m, 1H) (1 signal for NH observed due to coalescence); ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.3, 132.7 (q, $J_{C\text{-}F}$ = 34.3 Hz), 127.6 (m), 125.9 (m), 122.6 (q, $J_{C\text{-}F}$ = 273 Hz), 58.7, 57.2, 53.1, 34.9, 33.5, 32.5, 32.4, 25.9, 25.0 (overlapping 2 signals), 24.5, 24.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.77 (s, 6F).



[10] Feng, Y.; Zhichao, J.; Huicai, H.; Tingting, Y.; Jinxing, L. Xinmiao Y. *Org. Biomol. Chem.* **2010**, *8,* 4767-4774.

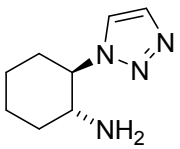
Scheme S2. Synthesis of **8a**.

tert-Butyl ((1*R*,2*R*)-2-(4-trimethylsilyl-1,2,3-triazol-1-yl)cyclohexylcarbamate, 16



tert-Butyl ((1*R*,2*R*)-2-azidocyclohexyl)carbamate (**15**, 1.98 g, 8.24 mmol) was dissolved in EtOH (15 mL). Copper(I) thiophene-2-carboxylate (79.4 mg, 0.416 mmol, 5 %mol) was added followed by the addition of trimethylsilylacetylene (3.0 mL, 21.7 mmol, 2.6 equiv). The suspension was stirred at room temperature for 480 h. Then 20 mg of NaHS was added and mixture was stirred vigorously. The suspension was filtered through layer of silica gel and washed with a mixture of DCM/EtOH (2:1 v:v, 75 mL), the solution was concentrated *in vacuo*. The residue was redissolved in ca. 10 mL of AcOEt and filtered through layer of silica gel and eluted with AcOEt (110 mL). After concentration *in vacuo*. 2.22 g of crude product **16** was obtained as white solid also containing product **17** without TMS group (approx. 80% yield).

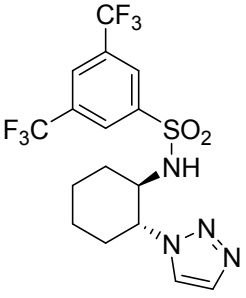
(1*R*,2*R*)-2-(1,2,3-triazol-1-yl)cyclohexylamine, 17



Crude _tert_-Butyl ((1*R*,2*R*)-2-(4-trimethylsilyl-1,2,3-triazol-1-yl)cyclohexylcarbamate (**16**, 0.202 g, 0.598 mmol) was dissolved in MeOH (3.7 mL) in a polypropylene tube and 40% aqueous solution of HF (0.5 mL) was added slowly, and the mixture was stored at room temperature for 2 h. The solution was alkalized by carefully adding saturated aqueous $NaHCO_3$, and extracted with dichloromethane (3 × 7 mL), dried over Na_2SO_4 and evaporated. In the residue, TMS group was completely removed and approx. 5% of Boc groups were cleaved. The mixture was dissolved in 95% aqueous solution of trifluoroacetic acid (10 mL) and stirred at room temperature for 20 h and concentrated *in vacuo*. The residue was alkalized by saturated aqueous solution of $NaHCO_3$ (10 mL) and solid NaOH to pH > 13 and extracted with dichloromethane (4 × 10 mL), dried over Na_2SO_4 and evaporated. The product was obtained as orange oil (37.5 mg, 38% yield).

^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.73 (d, *J* = 1.0 Hz, 1H), 7.60 (d, *J* = 1.0 Hz, 1H), 4.10 (ddd, *J* = 12.2, 10.0, 4.2 Hz, 1H), 3.19 (ddd, *J* = 11.1, 10.1, 4.2 Hz, 1H), 2.04 – 2.14 (m, 2H), 1.82 – 1.96 (m, 3H), 1.24-1.54 (m, 5H).

***N*-((1*R*,2*R*)-2-(1,2,3-triazol-1-yl)cyclohexyl)-3,5-bis(trifloromethyl)benzenesulfonamide, 8a,**



According to the general procedure using 35.0 mg (0.211 mmol) of (1*R*,2*R*)-2-(1,2,3-triazol-1-yl)cyclohexylamine and 72.4 mg (0.232 mmol, 1.1 equiv) of

3,5-bis(trifluoromethyl)benzenesulfonyl chloride, 62.1 mg of product was obtained as orange oil (67% yield).

^{1}H NMR (600 MHz, $CDCl_3$, TMS) δ 8.09 (s, 2H), 8.00 (s, 1H), 7.49 (s, 1H), 7.44 (s, 1H), 6.40 (d, J = 8.2 Hz, 1H), 4.48 (td, J = 11.4, 3.7 Hz, 1H), 3.59 – 3.65 (m, 1H), 2.11 – 2.21 (m, 2H), 1.84 – 1.95 (m, 3H), 1.57 – 1.64 (m, 1H), 1.41 – 1.51 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 143.9, 133.6, 132.7 (q, J_{C-F} = 34.3 Hz), 126.8 (m), 126.0 (m), 122.5 (q, J_{C-F} = 274 Hz), 122.0, 63.2, 58.1, 34.2, 32.8, 24.6, 24.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ −62.80 (s, 6F).

General procedure for Michael-hemiacetalization reaction

Diketone **9** (0.1 mmol, 1 equiv, 19 mg for methyl benzylidenepyruvate **9a**) and the catalyst (0.01 mmol, 10 %mol, 4.5 mg for **2a**) were dissolved in 1 mL of solvent (chlorobenzene), and stirred at room temperature for 15 minutes. Then, the mixture was brought to the desired temperature (room temperature, −20 °C, or −40 °C) and nucleophile was added (0.11 mmol, 1.1 equiv, 15.4 mg for dimedone, **10**). The mixture was stirred at that temperature for 1 day (or up to 5 days for reactions performed at low temperatures). Then 1.5 mL of chloroform was added, and the mixture was passed through a pad of silica gel (15 g) and eluted with 100 mL ethyl acetate. The solution was evaporated to yield essentially pure product **11** for which enantiomeric composition was determined by chiral HPLC.

Analytically pure samples were obtained by chromatography on silica gel with hexane/AcOEt/CH_2Cl_2 7:3:1 (v/v/v). Column was loaded with a sample dissolved in CH_2Cl_2. Chromatography did not change enantiomeric composition.

For reactions requiring less than 3 mg of catalyst, the required catalyst was added as a solution in the reaction solvent.

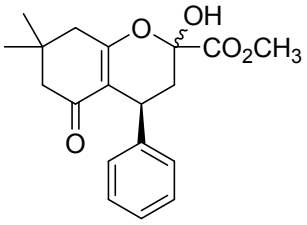
The reaction was repeated on a 3-mmol scale by multiplying all the quantities by 30. However, the workup included filtration through a pad of silica gel (20 g) and elution with 150 mL of ethyl acetate. Product was purified by chromatography as described above.

Note on NMR and HPLC chromatograms of hemiacetal products 11

The Michael addition end products **11** were all (as reported in the literature for known examples **11a**, **11c**, **11f**, **11g**, and **11h**) mixtures of the cyclic and linear anomers in equilibrium. This process was slow on an NMR timescale and presented as separate compounds in ^{1}H and ^{13}C NMR spectroscopy (Figures S76-S85), but fast enough that they did not resolve by HPLC chromatography (Figures S88-S99). (See ref. 11 from main text: Calter, P. A.; Wang, J. *Org. Lett*. **2009**, *11*, 2205–2208).

In some HPLC chromatograms partial resolution of epimeric hemiacetals was observed as peak asymmetry or partially overlapped peaks. The extent of resolution of anomers depended on the solvent from which the sample was dissolved prior to injection.. More symmetrical peaks were observed for samples dissolved in 2-propanol. The observed rartio of enantiomers was unaffected.

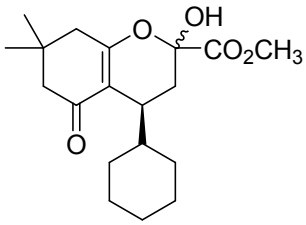
Catalytic products:



Methyl (4*S*)-2-hydroxy-7,7-dimethyl-5-oxo-4-phenyl-3,4,5,6,7,8-hexahydro-2H-chromene-2-carboxylate 11a

$[\alpha]_D^{22}$ = +14.8 (*c* 0.85, CH_2Cl_2; >99 %ee);

HPLC AD-H, 7:3, 1 mL/min, λ = 254 nm; tr = 6.5 – 7 (minor), 10.5 (major);

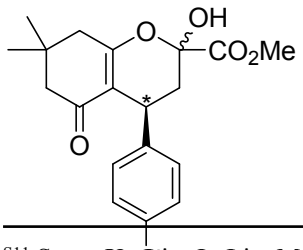


Methyl (4*S*)-4-cyclohexyl-2-hydroxy-7,7-dimethyl-5-oxo-3,4,5,6,7,8-hexahydro-2H-chromene-2-carboxylate, 11b

Modification of the general procedure (increased time, 96h) , product (45 % yield) was obtained as a colorless oil. Product was found to decompose on standing and during purification on silica gel.

$[\alpha]_D^{23}$ = 0 (*c* 0.1, CH_2Cl_2; 78 %ee); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 4.74 (br., 0.3H), 4.42 (br., 0.45H), 3.90 – 3.92 (m, 1.7H), 3.83 – 3.84 (m, 1.3H), 2.77 – 2.79 (m, 0.4H), 2.58 – 2.71 (m, 0.8H), 2.19 – 2.35 (m, 4H), 2.05 – 2.11 (m, 1H), 1.91 – 1.98 (m, 1H), 1.57 – 1.73 (m, 4H), 0.83 – 1.46 (m, 13H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.7, 170.5, 170.1, 166.7, 114.7, 114.5, 96.7, 95.3, 53.7, 51.5, 51.1, 42.8, 42.5, 39.4, 36.8, 32.0, 31.8, 31.75, 31.34, 31.31, 31.1, 30.0, 29.9, 29.6, 29.0, 28.8, 28.0, 27.5, 27.0, 26.8, 26.79, 26.75, 26.6, 26.58; HRMS (ESI-TOF) calcd. for $[C_{19}H_{28}O_5+H]^+$ 337.2010; found: 337.2029.

HPLC IC-3, 9:1, 1 mL/min, λ = 254 nm; tr = 15.39 (minor), 22.76 (major); 89:11 e.r.

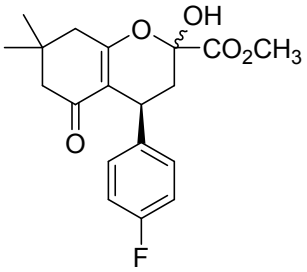


Methyl (4*S*)-4-(4-chlorophenyl)-2-hydroxy-7,7-dimethyl-5-oxo-3,4,5,6,7,8-hexahydro-2H-chromene-2-carboxylate, 11c

The title compound is known and characterized in the literature.[S11]

[S11] Song, X.; Liu, J.; Liu, M.-M.; Wang, X.; Zhang, Z.-F.; Wang, M. C. *Tetrahedron* **2014**, *70*, 5468-5474.

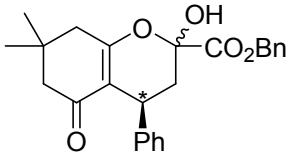
HPLC AD-H, 7:3, 0.7 mL/min, λ = 254 nm; tr = 8.08 (minor), 14.79 (major); 2:98 e.r.



Methyl (4*S*)-4-(4-fluorophenyl)-2-hydroxy-7,7-dimethyl-5-oxo-3,4,5,6,7,8-hexahydro-2H-chromene-2-carboxylate 11d

$[\alpha]_D^{22}$ = +18.6 (*c* 0.85, CH_2Cl_2; 96 %ee); ^{1}H NMR (400 MHz, $CDCl_3$, TMS, major/minor anomer, ca. 6:4 ratio) δ 7.08 – 7.13 (m, 2H), 6.89 – 6.95 (m, 2H), 4.42 (br., 0.6H), 4.23 (br., 0.4H), 4.05 (d, *J* = 7.0 H, 0.4H), 3.88 (btt, *J* = 9.0, 1.9 Hz, 0.6H), 3.85 (s, 1.1H), 3.78 (s, 1.9H), 2.55 (d, *J* = 7.7 Hz, 0.2H), 2.53 (d, *J* = 7.3 Hz, 0.2H), 2.47 (d, *J* = 17.6 Hz, 0.4H), 2.24 – 2.43 (m, 2.7H), 2.23 (d, *J* = 8.8Hz, 1.3H), 2.19 (s, 1.2H), 1.18 (s, 1.1H), 1.15 (s, 1.9H), 1.10 (s, 1H), 1.08 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$, major/minor anomer, ca. 6:4 ratio) δ 196.0 / 196.5, 169.3 / 169.4, 166.8 / 167.4, 161.30 / 161.33 (d, $J_{C\text{-}F}$ = 244 Hz), 139.7 / 138.8 (d, $J_{C\text{-}F}$ = 3 Hz), 128.4 / 128.9 (d, $J_{C\text{-}F}$ = 8 Hz), 115.1 / 114.9 (d, $J_{C\text{-}F}$ = 21.5 Hz), 114.0 / 112.2, 94.9 / 95.7, 53.48 / 53.56, 50.94 / 50.92, 42.53 / 42.47, 38.3/ 35.9, 32.7 / 32.0, 31.7 / 31.4, 29.1 / 28.8, 27.7/ 28.2; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −117.13 (tt, *J* =8.6, 5.2 Hz, 0.62 F), −117.17 (tt, *J* =8.6, 5.2 Hz, 0.38 F). HRMS (ESI-TOF) calcd. for $[C_{19}H_{21}FO_5+H]^+$ 349.1446 found 349.1458.

HPLC AD-H, 7:3, 0.7 mL/min, λ = 254 nm; tr = 7.29 (minor), 12.79 (major); 2:98 e.r.

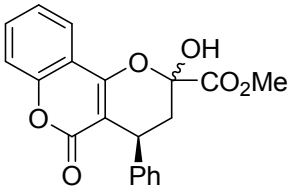


Benzyl (4*S*)-2-hydroxy-7,7-dimethyl-5-oxo-4-phenyl-3,4,5,6,7,8-hexahydro-2H-chromene-2-carboxylate, 11e

Applying the general procedure, product (93.5 % yield) was obtained as an off-white foam.

$[\alpha]_D^{23}$ = +14.5 (*c* 0.80, CH_2Cl_2; 96.4 %ee); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.26 – 7.39 (m, 5H), 7.22 – 7.24 (m, 2H), 7.13 – 7.17 (m, 3H), 5.25 (s, 0.8H), 5.18 (d, *J* = 12.2, 0.6H), 5.05 (d, *J* = 12.2 Hz, 0.6H), 4.67 (br., 0.6H), 4.36 (br., 0.3H), 4.03 (m, 0.4H), 3.89 (dd, *J* = 9.5, 8.3Hz, 0.6H), 2.57 (dd, *J* = 14.2, 7.4 Hz, 0.4H), 2.39 – 2.47 (m, 1H), 2.24 – 2.35 (m, 3H), 2.15-2.22 (m, 1.6H), 1.17 (s, 1.2H), 1.15 (s, 1.8H), 1.07 (s, 1.8H), 1.06 (s, 1.2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.7, 196.3, 168.8, 168.6, 167.6, 167.0, 144.0, 143.0, 134.5, 134.4, 128.84, 128.78, 128.76, 128.7, 128.4, 128.38, 128.36, 128.3, 127.3, 127.1, 126.2, 126.1, 114.0, 112.2, 95.9, 95.0, 68.5, 68.4, 50.8, 50.7, 42.4, 42.3, 38.1, 36.1, 33.4, 32.2, 32.0, 31.7, 29.3, 28.6, 28.5, 27.7. HRMS (ESI-TOF) calcd. for $[C_{25}H_{26}O_5+H]^+$ 407.1853 found 407.1854.

HPLC AD-H, 7:3, 0.7 mL/min, λ = 254 nm; tr = 9.75 (minor), 15.37 (major); 98.2:1.78 e.r.

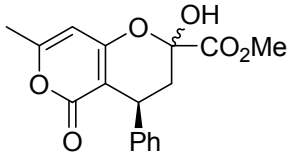


Methyl (4*S*)-3,4-dihydro-2-hydroxy-5-oxo-4-phenyl-2*H*,5*H*-pyrano[3,2-c][1]benzopyran-2-carboxylic acid, 11f

The (*R*)-isomer of the title compound is known and characterized in the literature[S12]

Applying a modification of the general procedure (−40 °C, 48 h) the product was obtained in a 99% yield;

HPLC AD-H, 8:2, 0.75 mL/min, λ = 254 nm; tr = 12.75 (minor), 22.03 (major); 97.5:2.5 e.r.

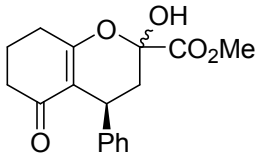


Methyl (4*S*)-2-hydroxy-7-methyl-5-oxo-4-phenyl-2,3,4,5-tetrahydropyrano[4,3-b] pyran-2-carboxylate, 11g

The title compound is known and characterized in the literature[S13] and the (*R*)-isomer of the title compound is also known[S12]

Applying a modification of the general procedure (−40 °C, 48 h) the product was obtained in a >99% yield;

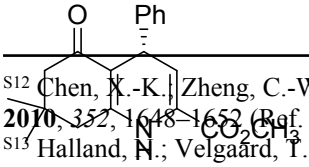
HPLC AD-H, 8:2, 0.75 mL/min, λ = 254 nm; tr = 11.97 (minor), 17.96 (major); 98:2 e.r.



Methyl (4*S*)-2-hydroxy-5-oxo-4-phenyl-3,4,5,6,7,8-hexahydro-2H-chromene-2-carboxylate, 11h

(*R*)-Isomer of the title compound is known and characterized in ref.[S12]

Applying a modification of the general procedure (−40 °C, 48 h) the product was obtained in a >99% yield; HPLC AD-H, 8:2, 0.75 mL/min, λ = 254 nm; tr = 10.55 (minor), 14.43 (major); 99:1 e.r.



Methyl (4*S*) 1,4,5,6,7,8-hexahydro-7,7-dimethyl-5-oxo-4-phenyl-quinoline-2-carboxylate, 12

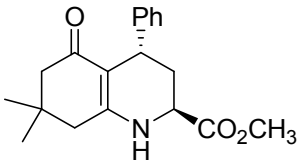
[S12] Chen, X.-K.; Zheng, C.-W.; Chai, S.-L. Zhao,; Z.; Zhao, Y.-Q. Yang,; G.; Cao, W.-G. *Adv. Synth. Cat.* **2010**, *352*, 1648–1652 (Ref. 13 from the main text)

[S13] Halland, N.; Velgaard, T.; Jørgensen, K. A. *J. Org. Chem.* **2003**, *68*, 5067–5074 (Ref. 10c from the main text)

Ammonium acetate (47 mg, 6 mmol, 10 equiv) was added to the solution of chiral adduct **11a** (199.5 mg, 0.6 mmol, 1.0 equiv; 99.65:0.35 e.r.) in MeOH (4 mL) at rt and the resulted mixture was refluxed for 3h. Then, next portion of ammonium acetate (50 mg) was added at once and the reaction was continued until the total consumption of the substrate (TLC, hexanes/AcOEt, 3:1, v/v). Then the greenish solution was cooled and the solvent was evaporated to give an oily residue. Further purification using silica gel chromatography (hexanes/Et_2O, 1:1, v/v) gave an off-white solid (110 mg, 59% yield).

$[\alpha]_D^{23}$ = −473.0 (*c* 0.40, MeOH; 96.1 %ee); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.24 – 7.29 (m, 4H), 7.14 – 7.18 (m, 1H), 6.46 (br., 1H), 6.12 (dd, *J* = 5.5, 1.8 Hz, 1H), 4.74 (d, *J* = 5.8 Hz, 1H), 3.80 (s, 3H), 2.37 (d, *J* = 16.5 Hz, 1H), 2.31 (dd, *J* = 16.5, 0.6 Hz, 1H), 2.24 (d, *J* = 16.2, Hz, 1H), 2.17 (dd, *J* = 16.5, 0.6 Hz, 1H), 1.09 (s, 3H), 1.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.3, 163.4, 150.1, 146.1, 128.5, 127.8, 126.6, 125.7, 117.5, 107.2, 52.6, 50.7, 41.7, 37.8, 32.6, 29.2, 27.5, HRMS calcd. for $[C_{19}H_{21}NO_3+H]^+$ requires 312.1594; found: 312.1606.

HPLC AD-H, 9:1, 0.7 mL/min, λ=254 nm, tr = 31.0 (major), 34.47 (minor), 98.05:1.95 e.r.



Methyl (2*S*,4*S*) 1,2,3,4,5,6,7,8-octahydro-7,7-dimethyl-5-oxo-4-phenyl-quinoline-2-carboxylate, 13

Solution of adduct **11a** (330 mg, 1.0 mmol, 1.0 equiv) in dichloroethane (3 mL) and 4-chlorobenzylamone (420 mg, 3.0 mmol, 3.0 equiv) was stirred at 50°C (oil bath) for 16 h. Then DBU (76 mg, 0.5 mmol, 0.5 equiv) was added at once at 50°C and reaction was performed for the next 20 h. Solvent was removed *in vacuo* and the residue was loaded onto silica gel column (CH_2Cl_2/Acetone, 15:1, v/v). Elution in gradient of CH_2Cl_2/Acetone, 10:1 to 5:1, v/v, gave 238 mg product (76% of yield) as an off-white solid.

$[\alpha]_D^{23}$ = +148.7 (*c* 0.26, MeOH; 97.5 %ee); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 7.23 – 7.27 (m, 2H), 7.11 – 7.16 (m, 3H), 5.23 (br., 1H), 4.27 (d, *J* = 4.3 Hz, 1H), 3.74 (dd, *J* = 12.5, 3.7 Hz, 1H), 3.70 (d, *J* = 1.2 Hz, 3H), 2.34 (s, 2H), 2.17 – 2.30 (m, 3H), 1.86 (ddd, *J* = 12.5, 4.9, 1.2 Hz, 1H), 1.14 (s, 3H), 1.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.2, 172.5, 156.2, 144.8, 128.2, 127.6, 126.1, 105.0, 52.5, 50.2, 49.5, 42.6, 34.1, 32.4, 32.1, 28.5, 28.3; HRMS calcd. for $[C_{19}H_{23}NO_3+H]^+$ 314.1751; found: 314.1747.

HPLC AD-H, 8:2, 1 mL/min, λ=254 nm, tr = 8.36 (minor), 14.60 (major), 98.74:1.26 e.r.

Plots of ^{1}H, ^{13}C, and ^{19}F NMR spectra

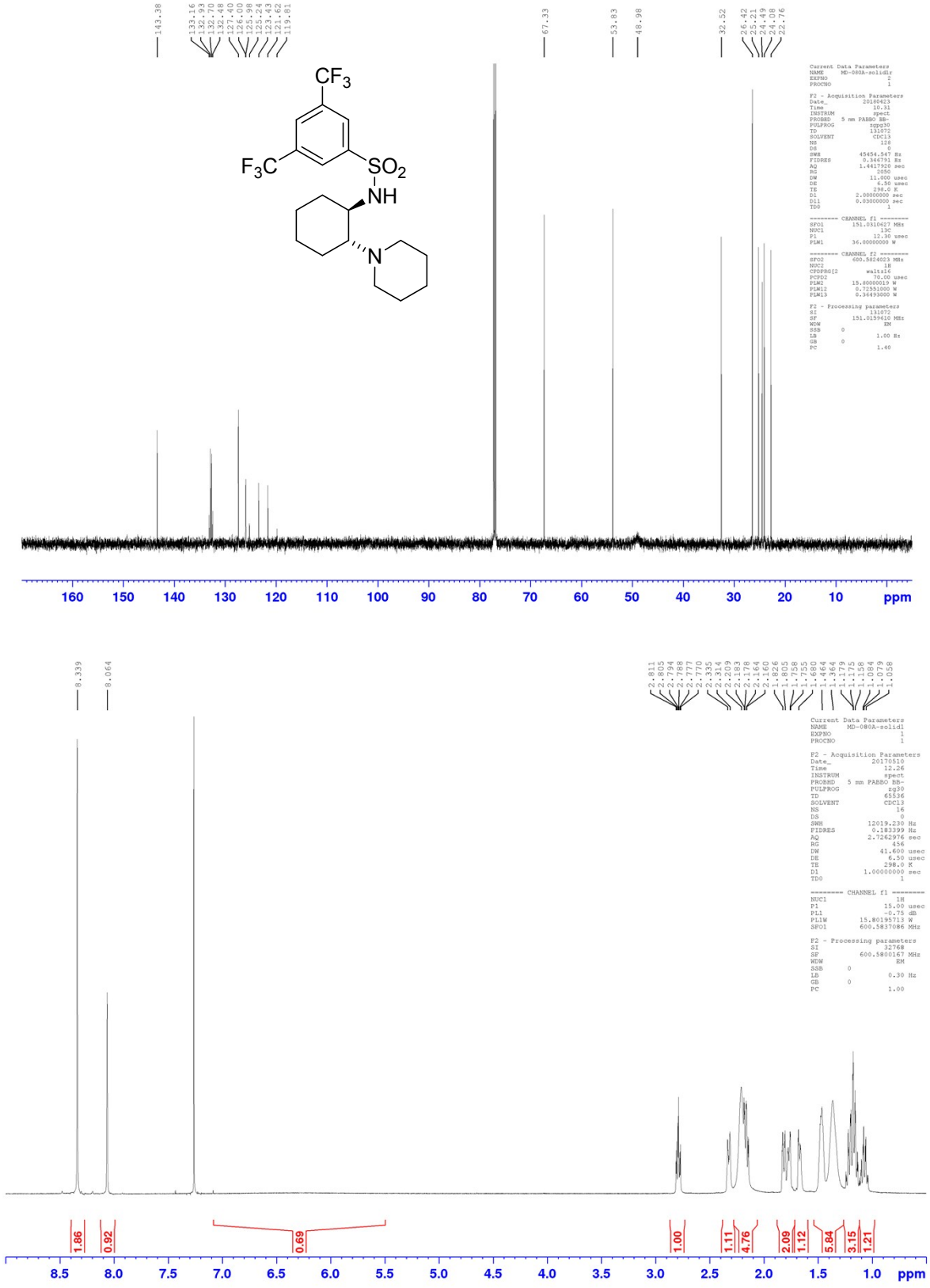


Figure S11. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2a**

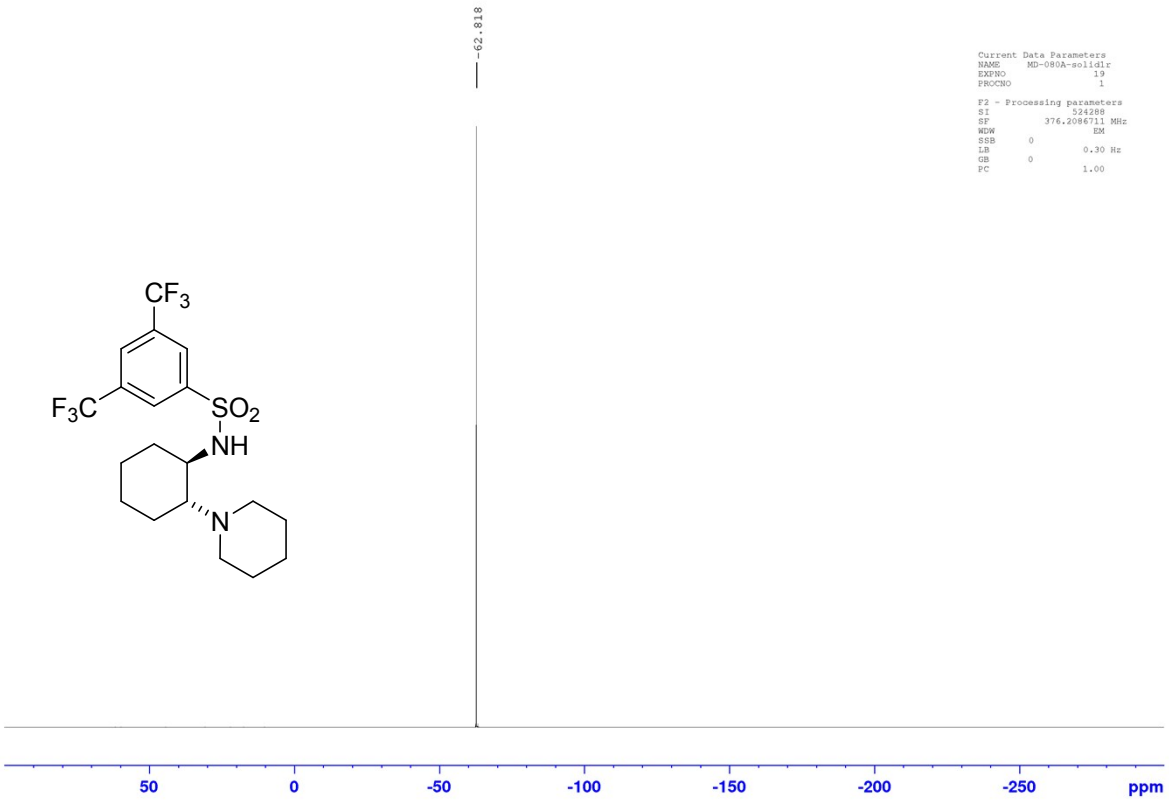


Figure S12. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for catalyst **2a**

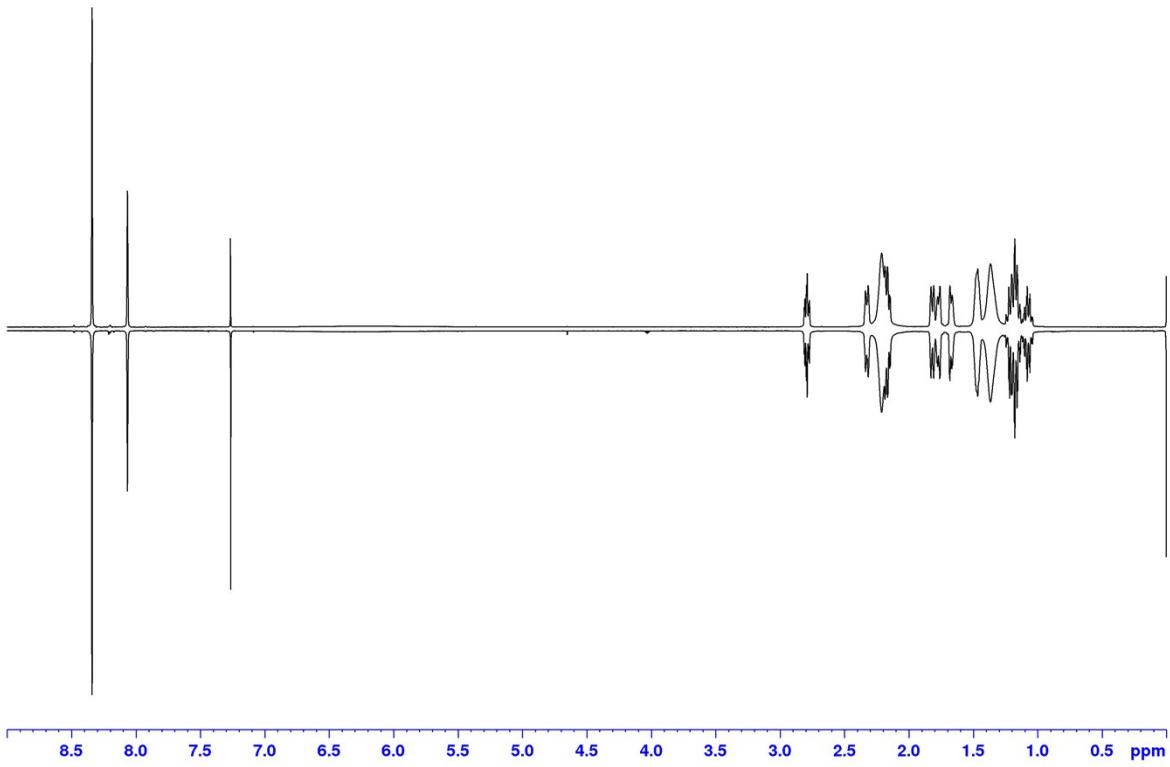


Figure S13. Overlay of ^{1}H NMR spectra (600 MHz, $CDCl_3$, TMS) for catalysts **2a** (positive phase) and ***ent*-2a** (negative phase)

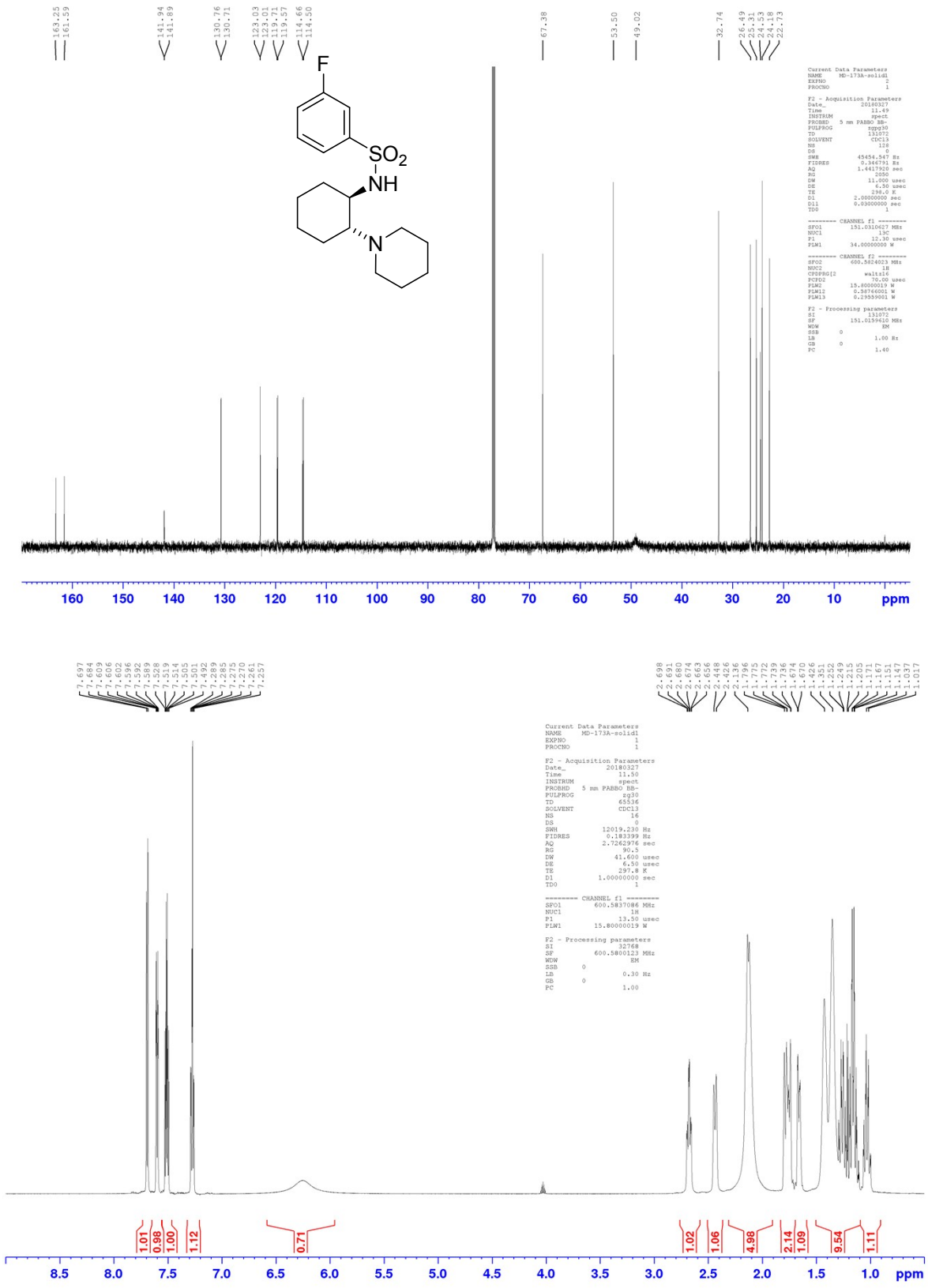


Figure S14. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2b**

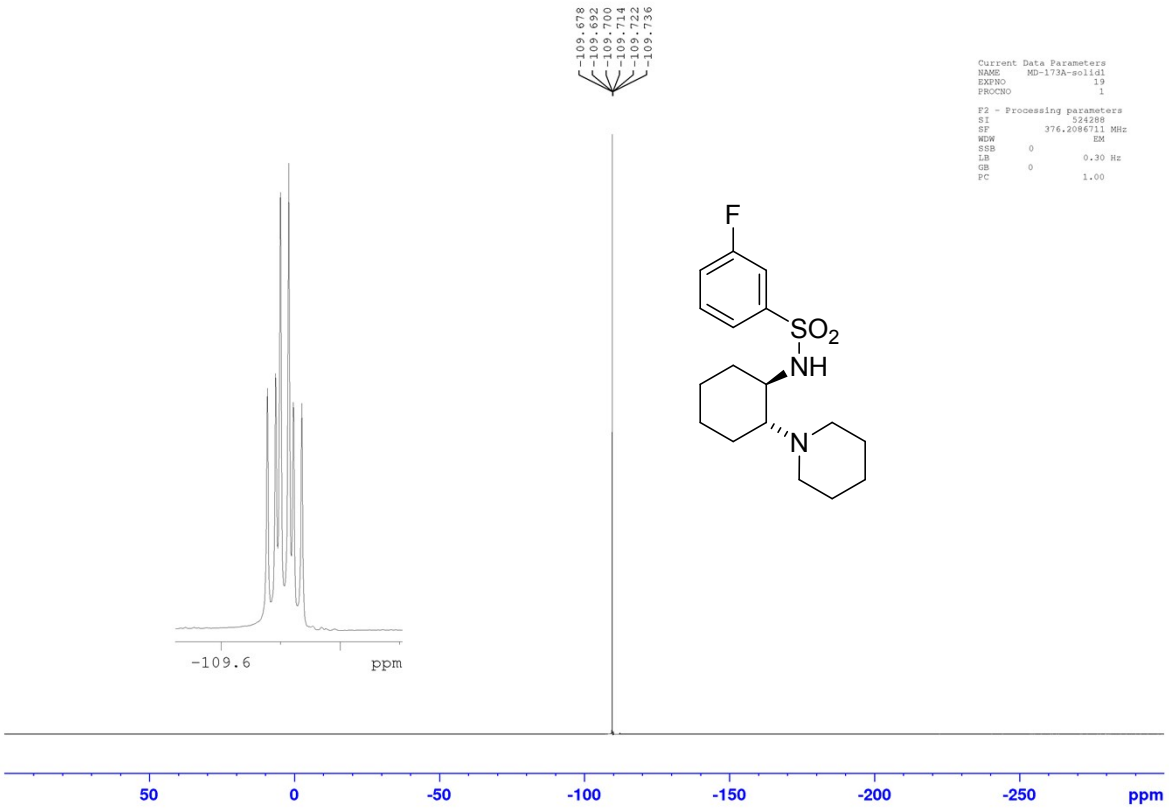


Figure S15. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for catalyst **2b**

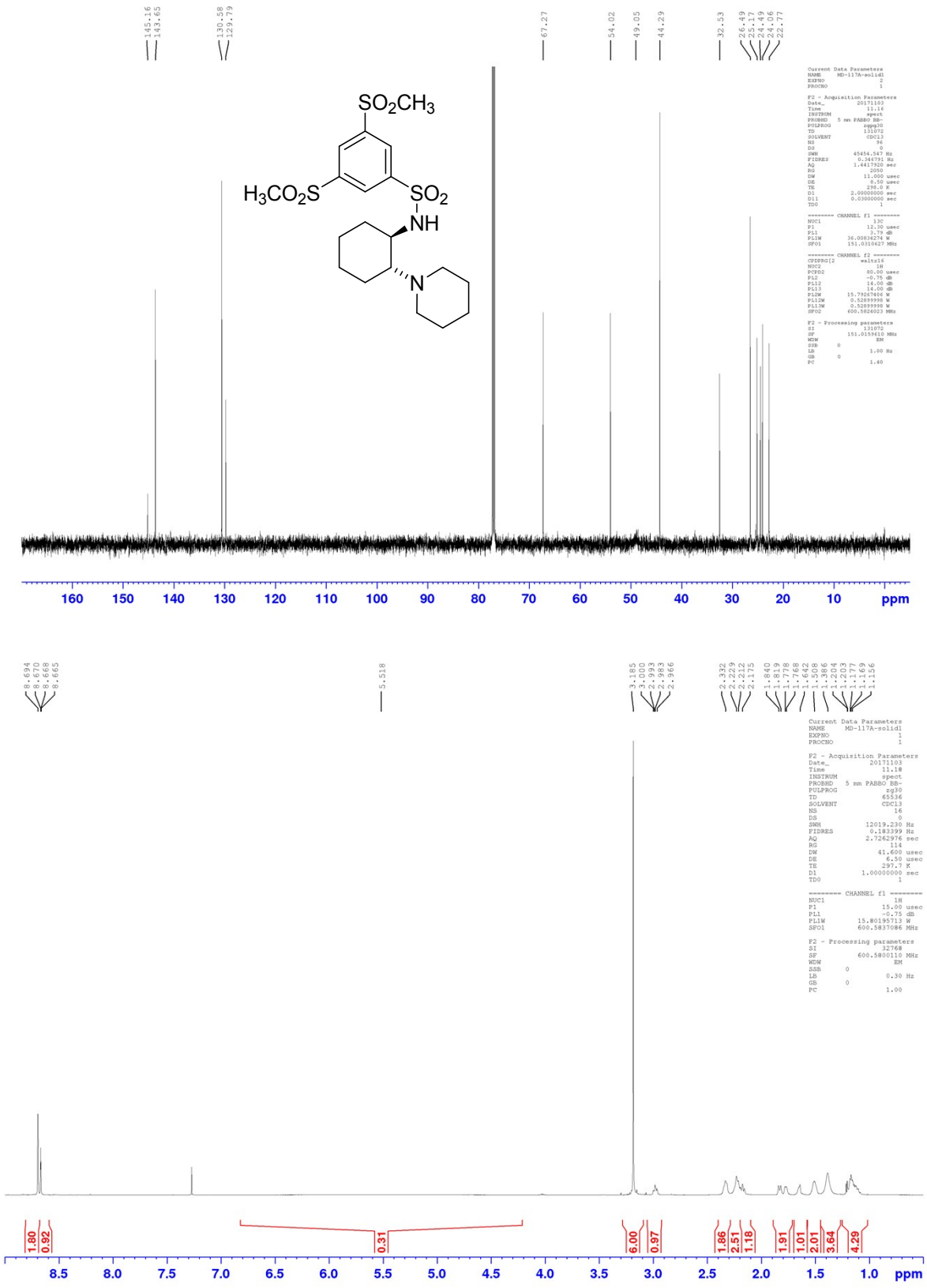


Figure S16. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2c**

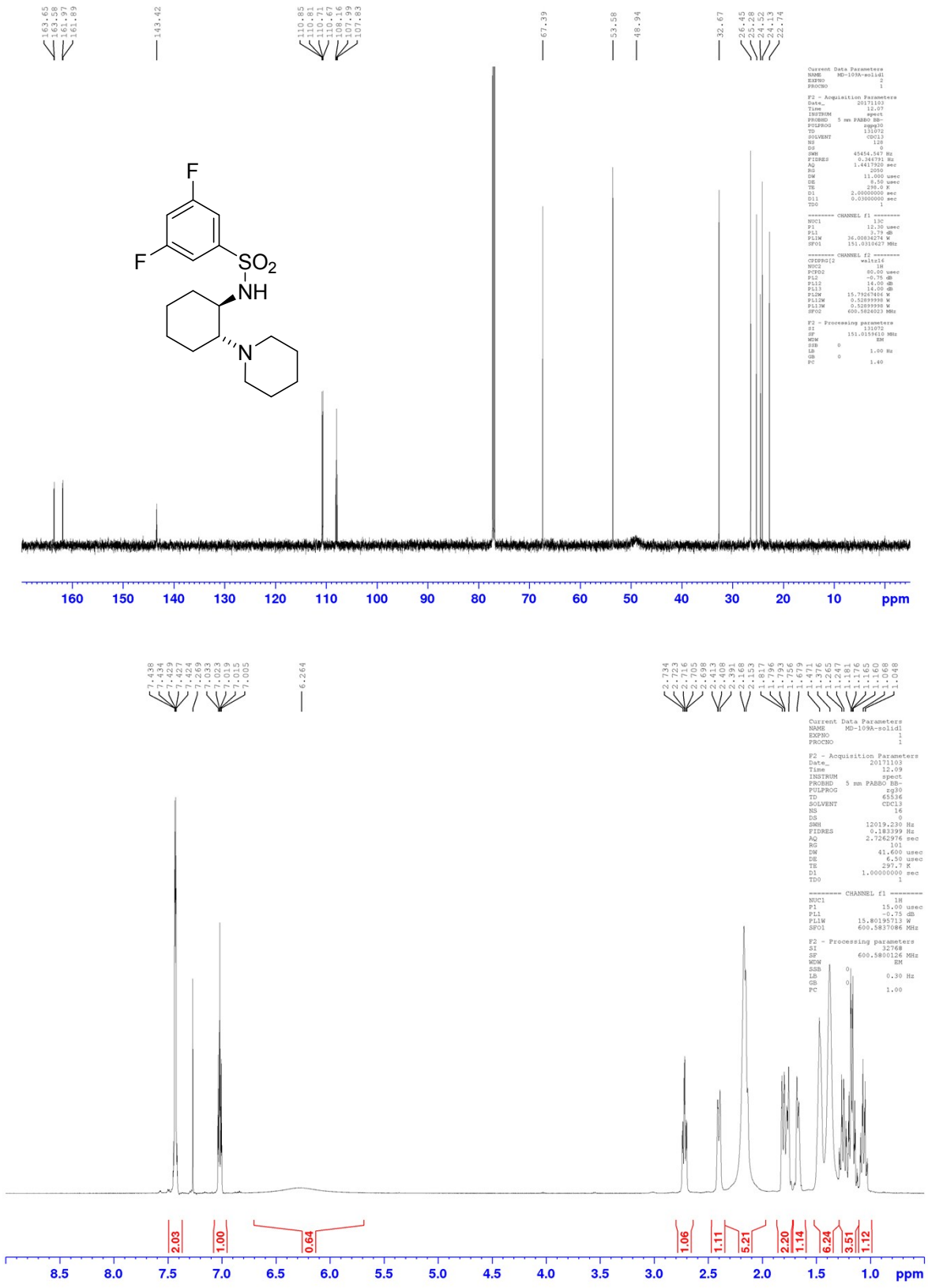


Figure S17. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2d**

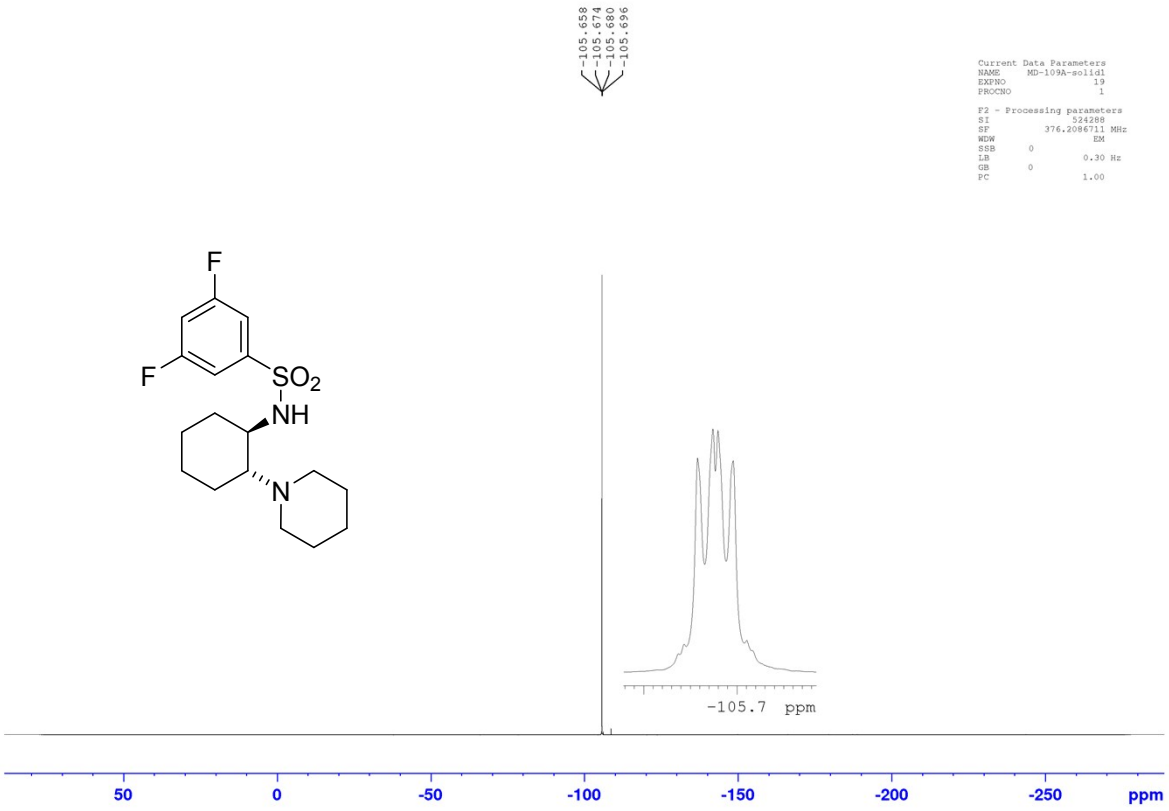


Figure S18. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for catalyst **2d**

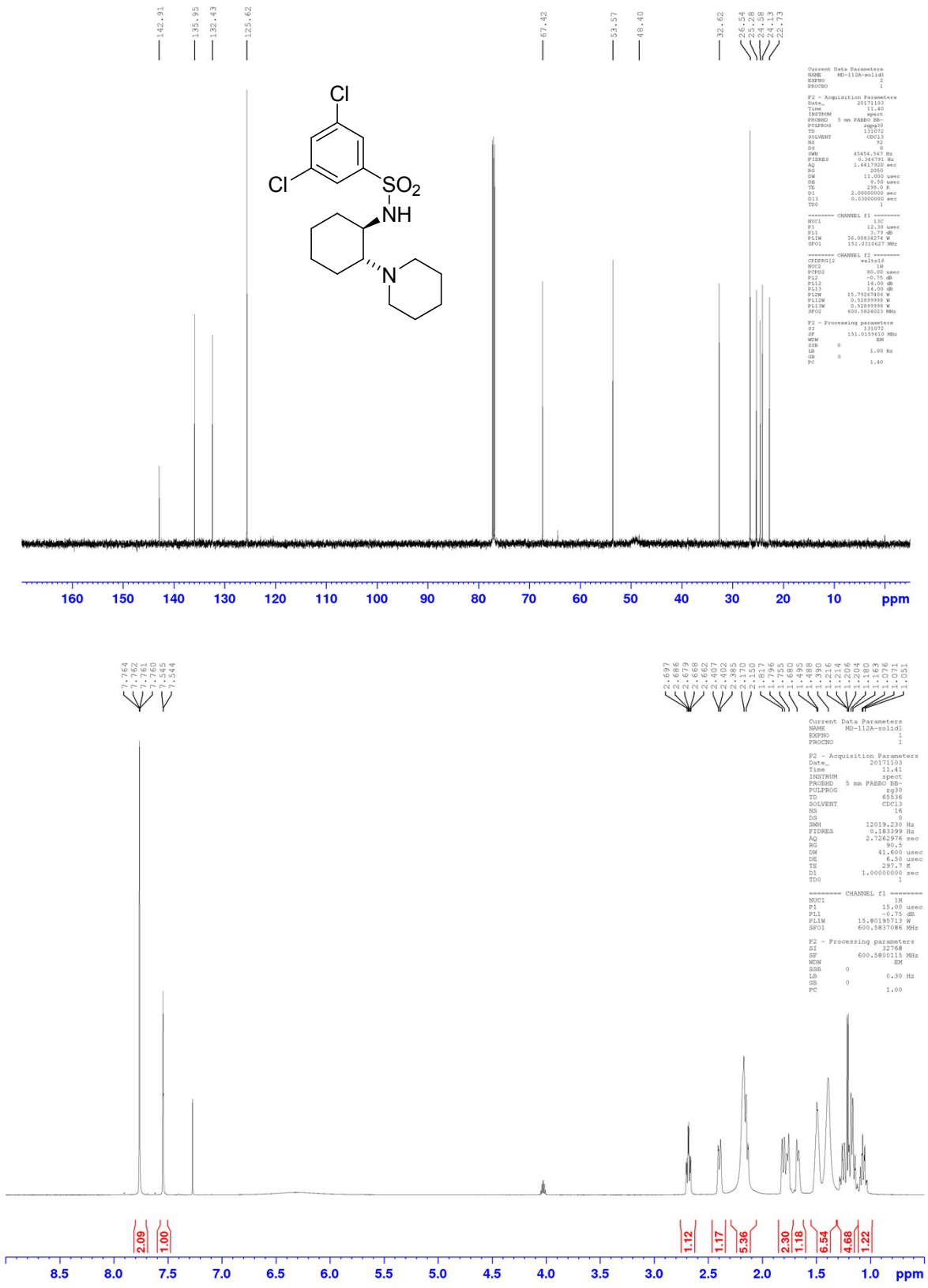


Figure S19. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2e**

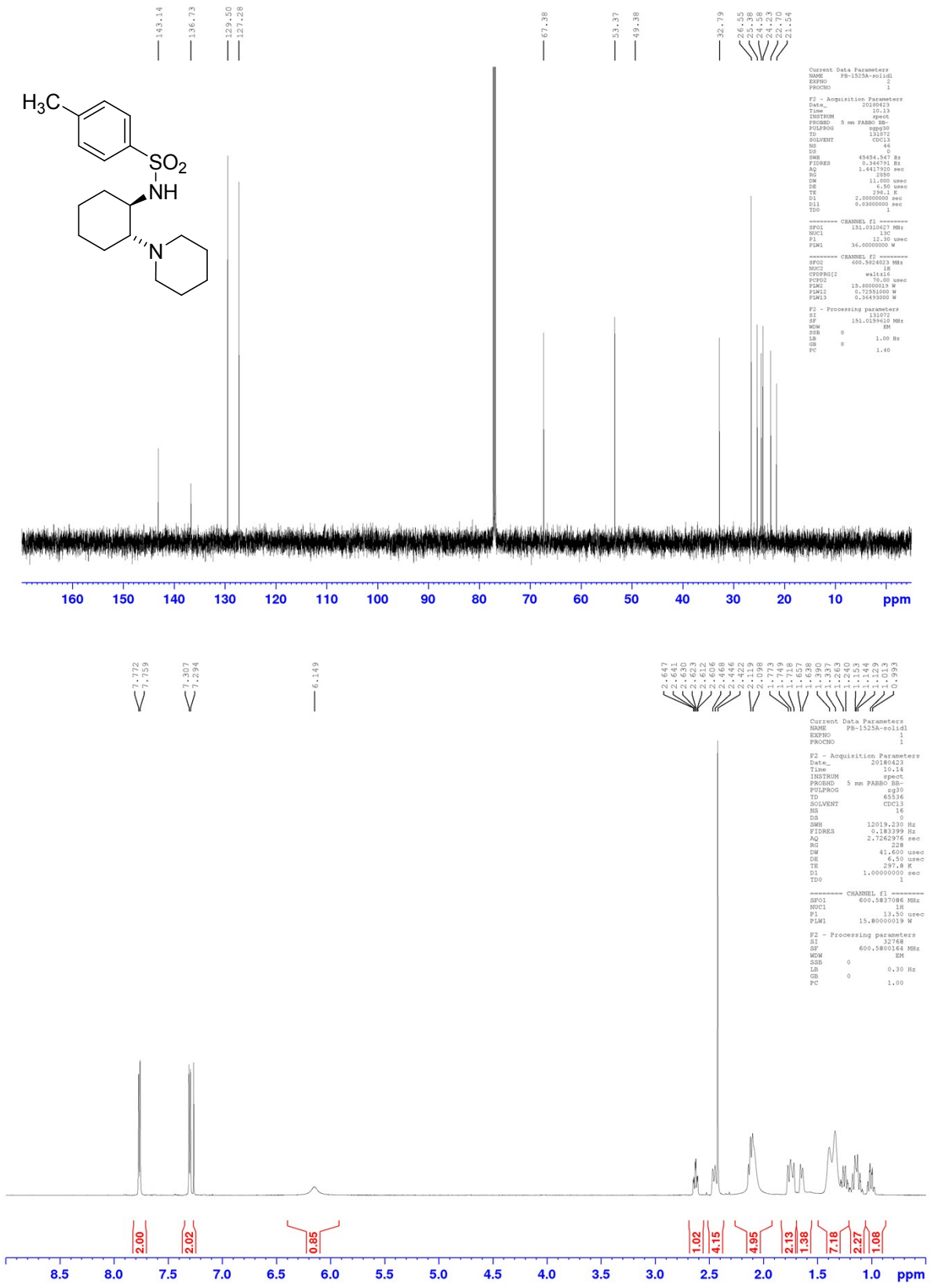


Figure S20. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2f**

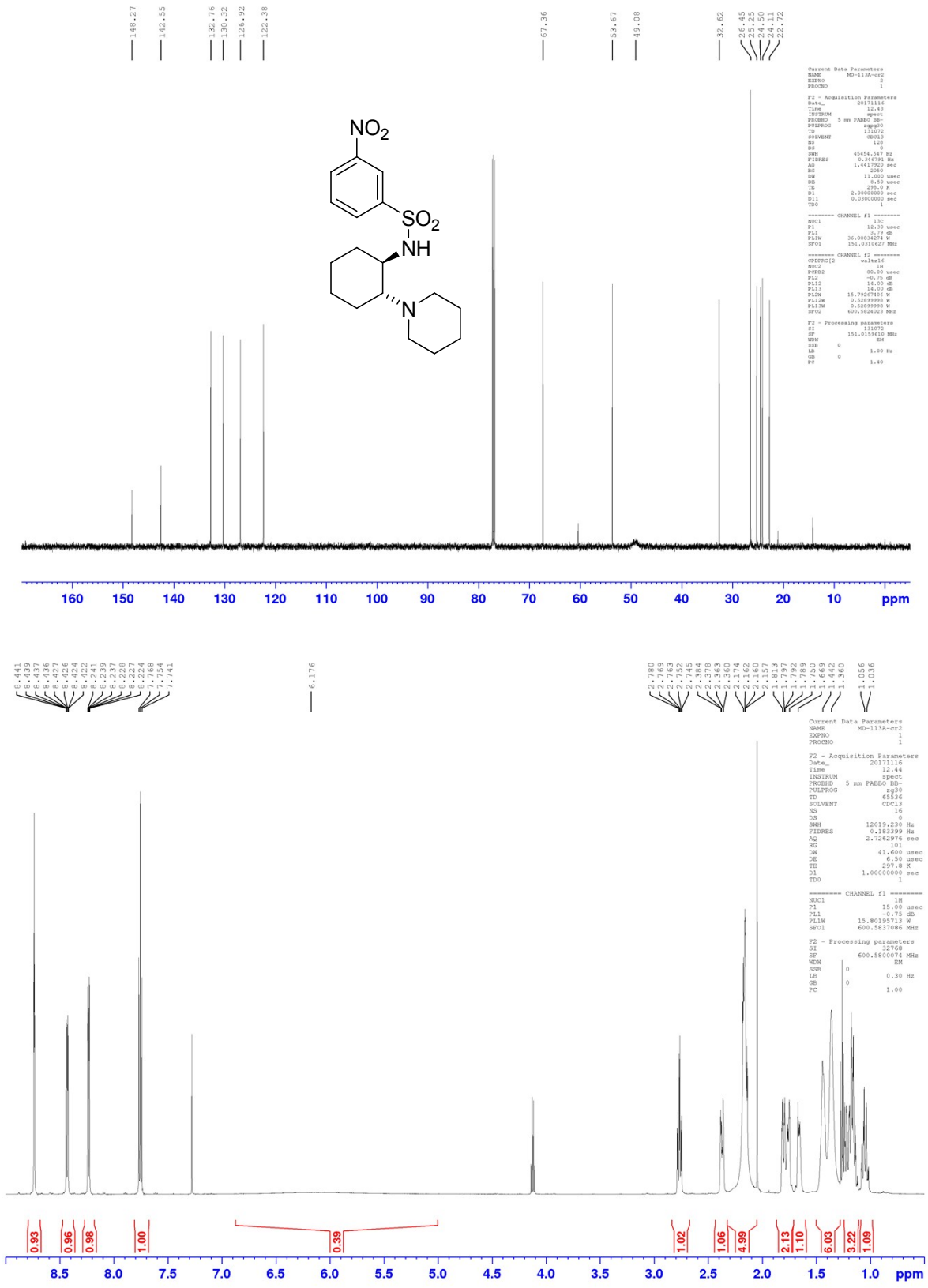


Figure S21. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2g**

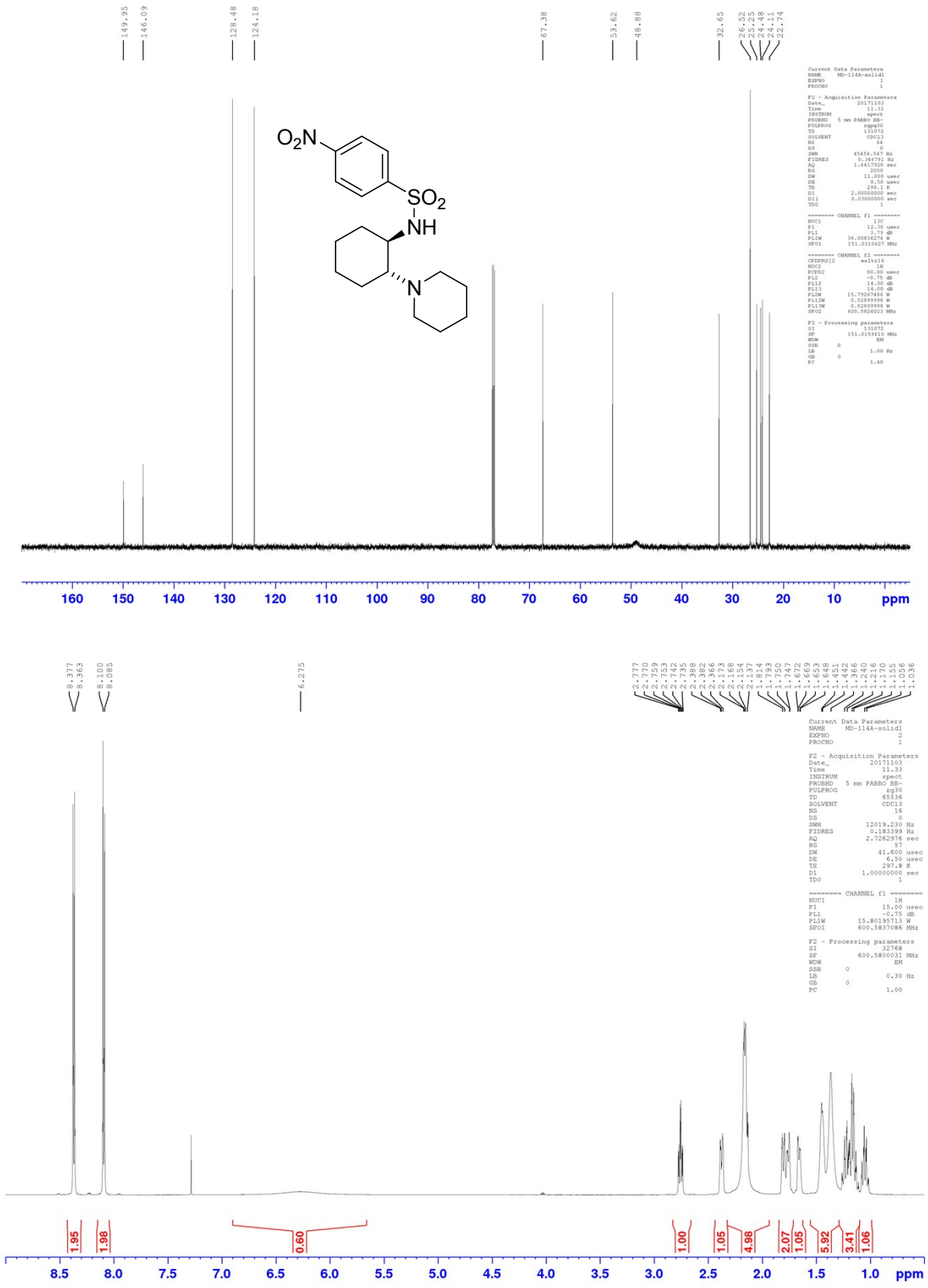


Figure S22. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2h**

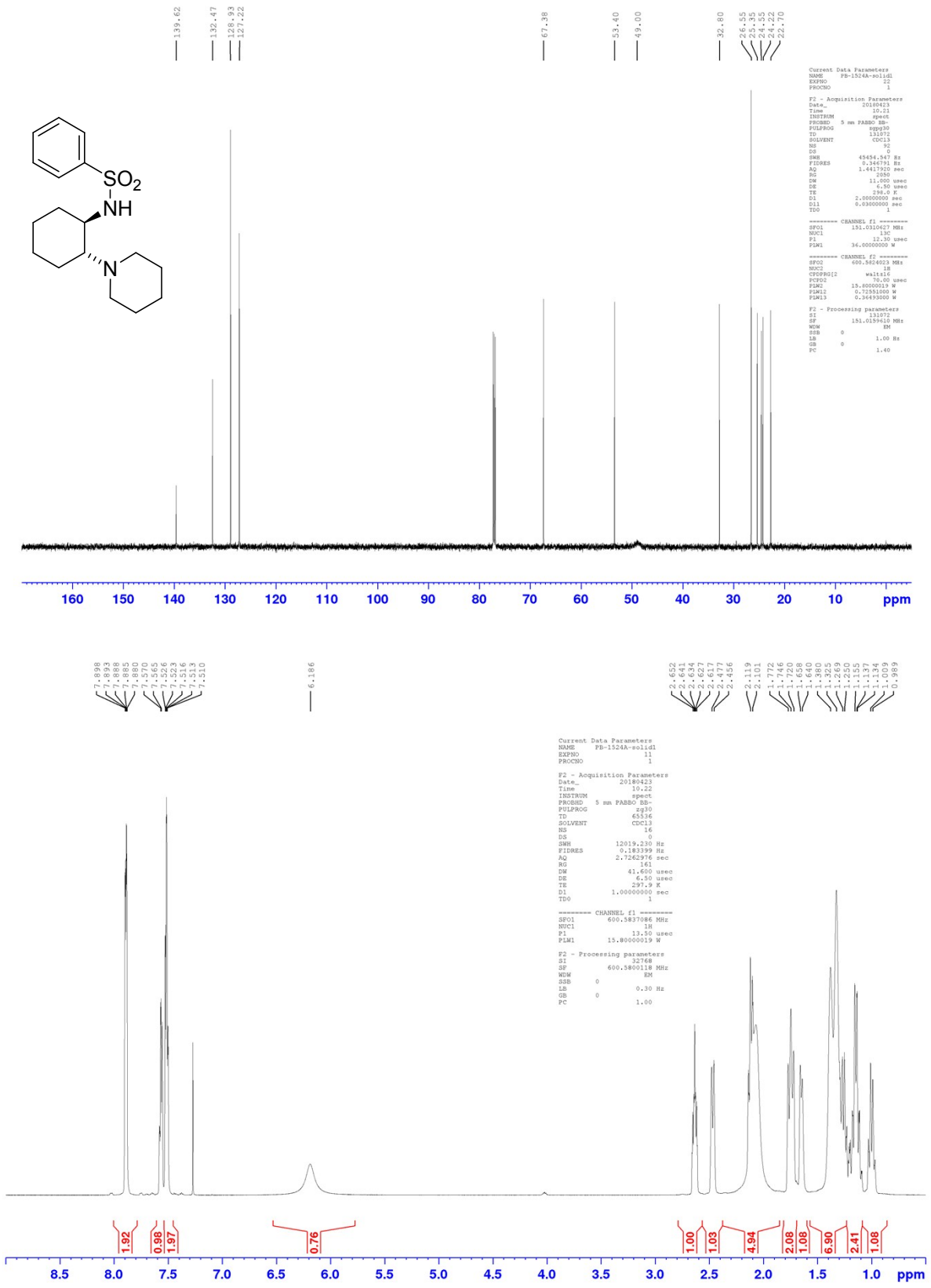


Figure S23. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2i**

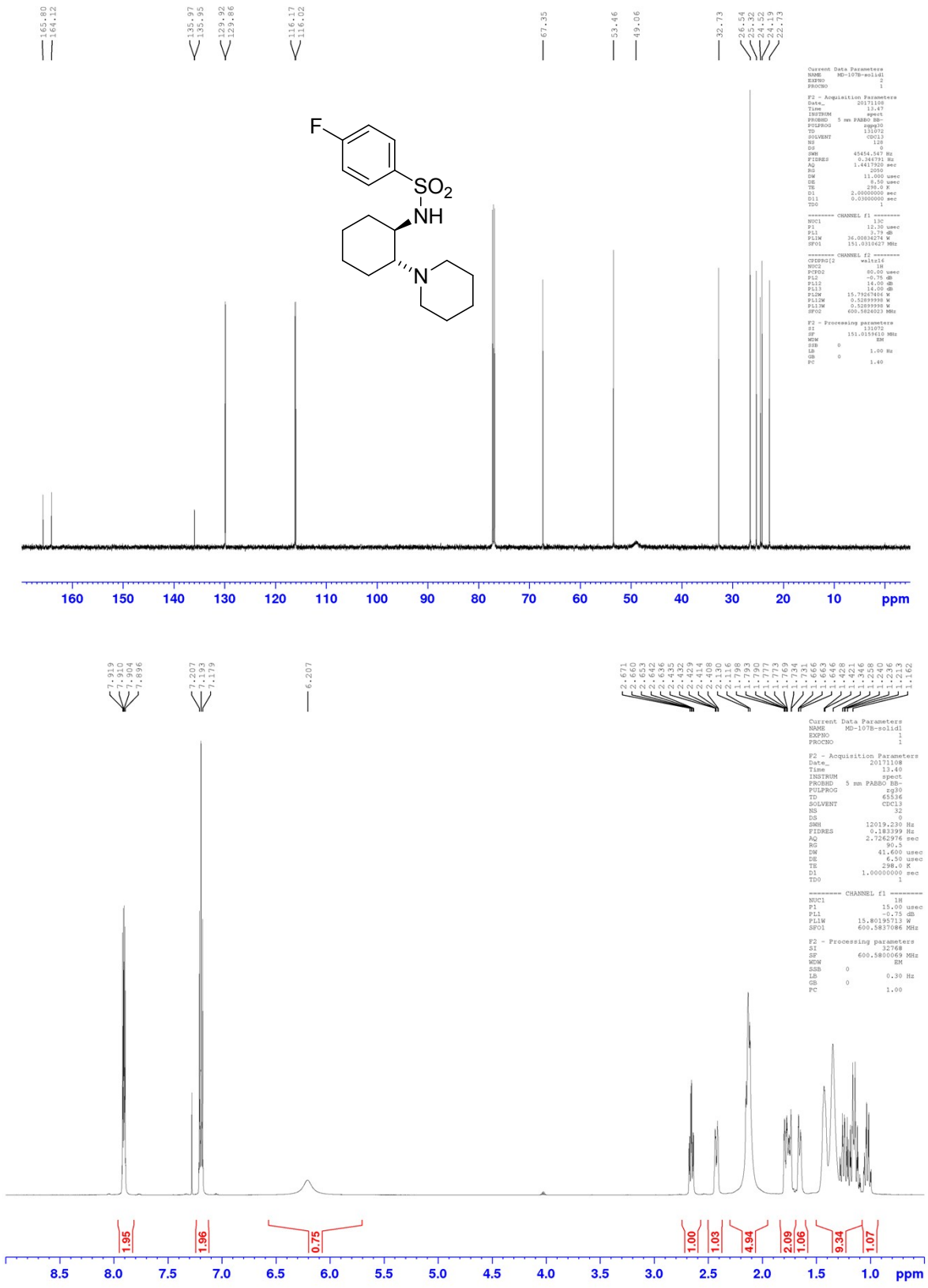


Figure S24. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2j**

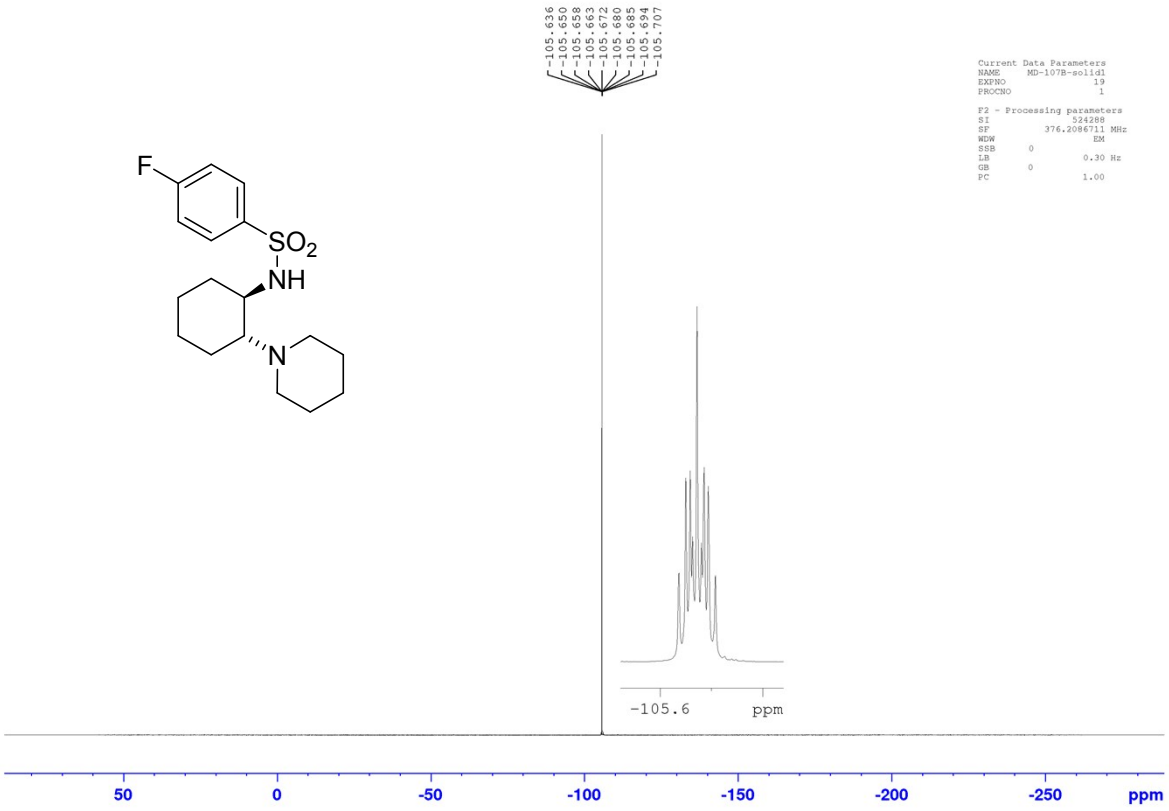


Figure S25. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for catalyst **2j**

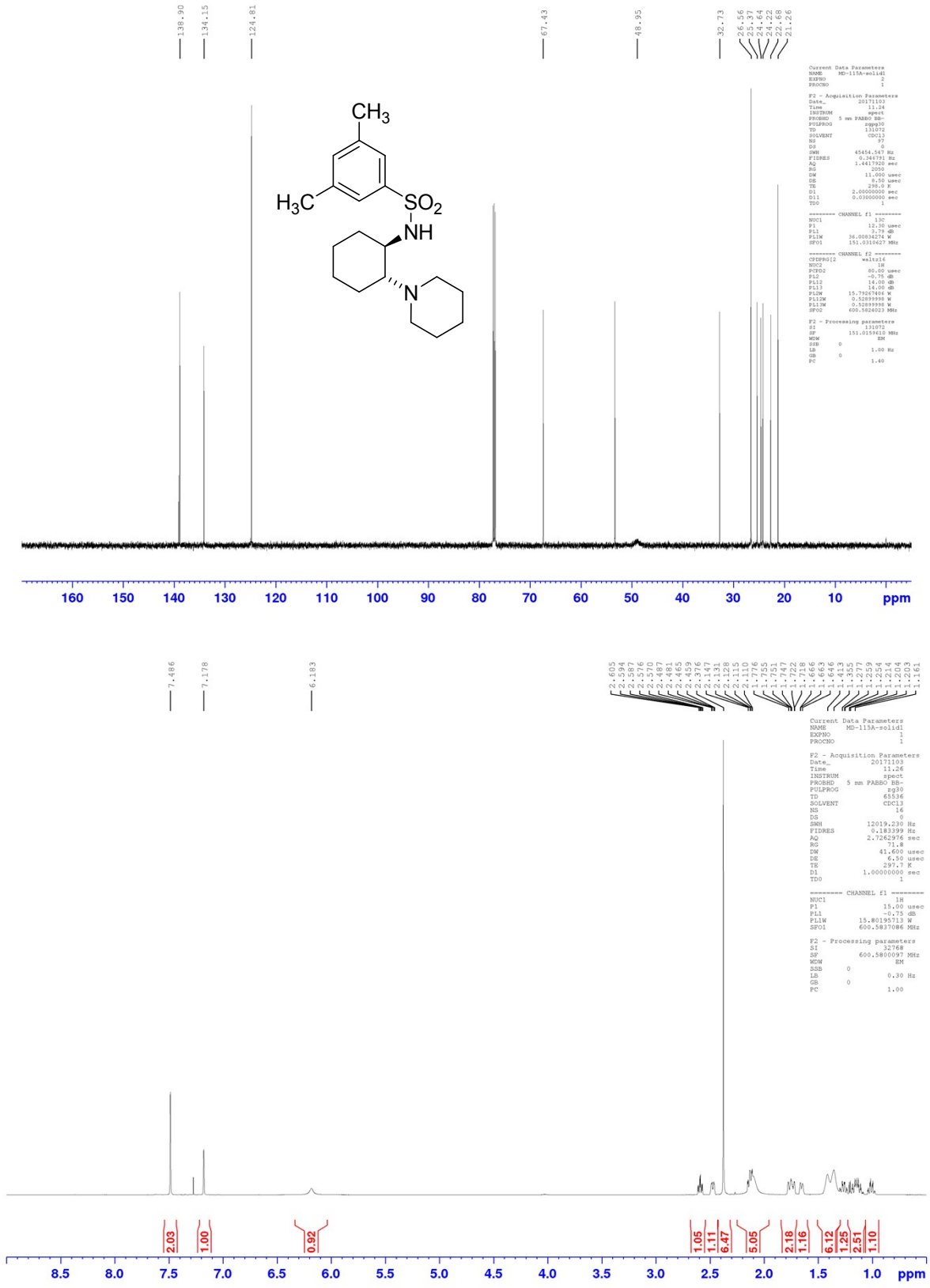


Figure S26. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2k**

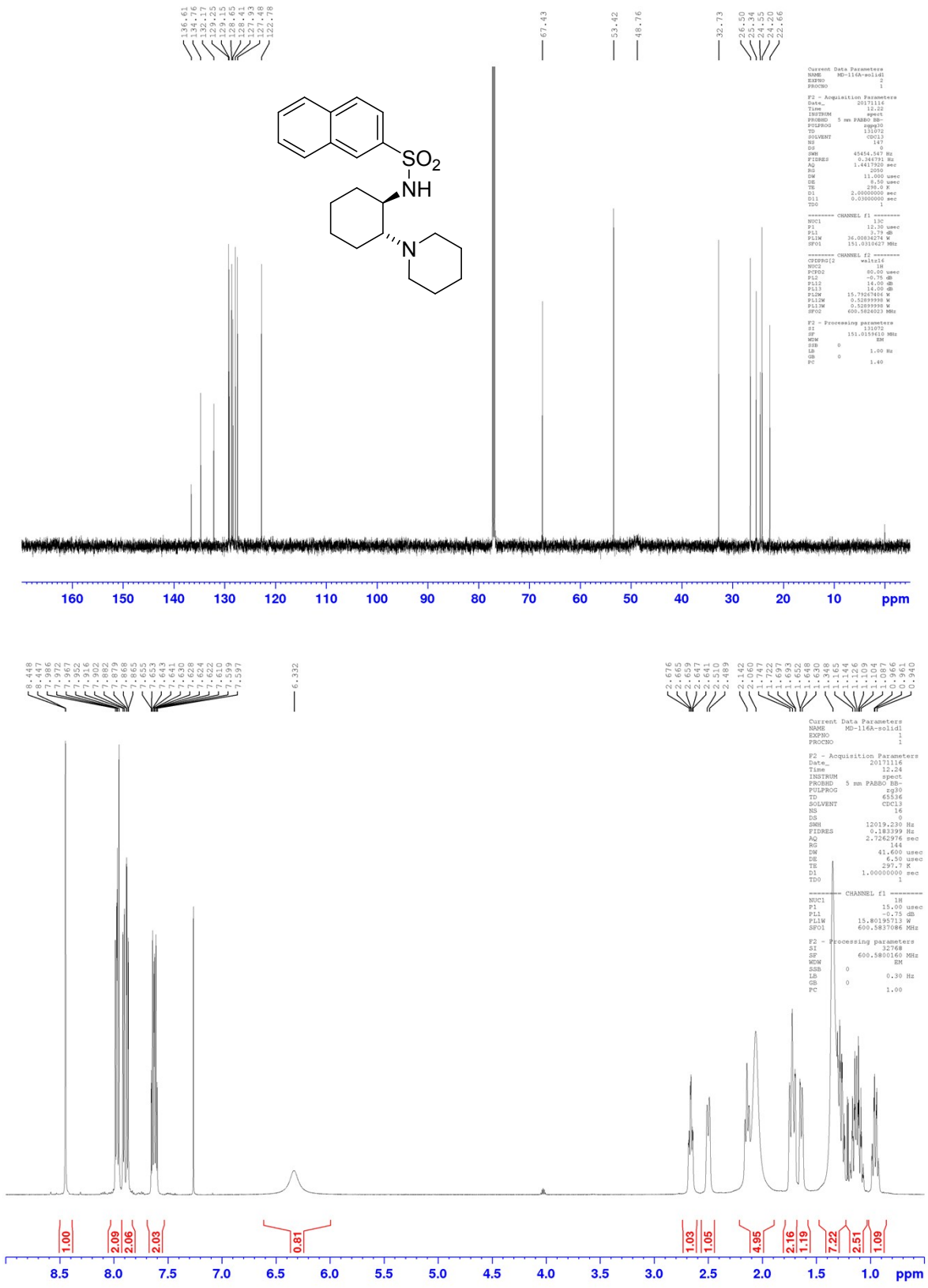


Figure S27. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2l**

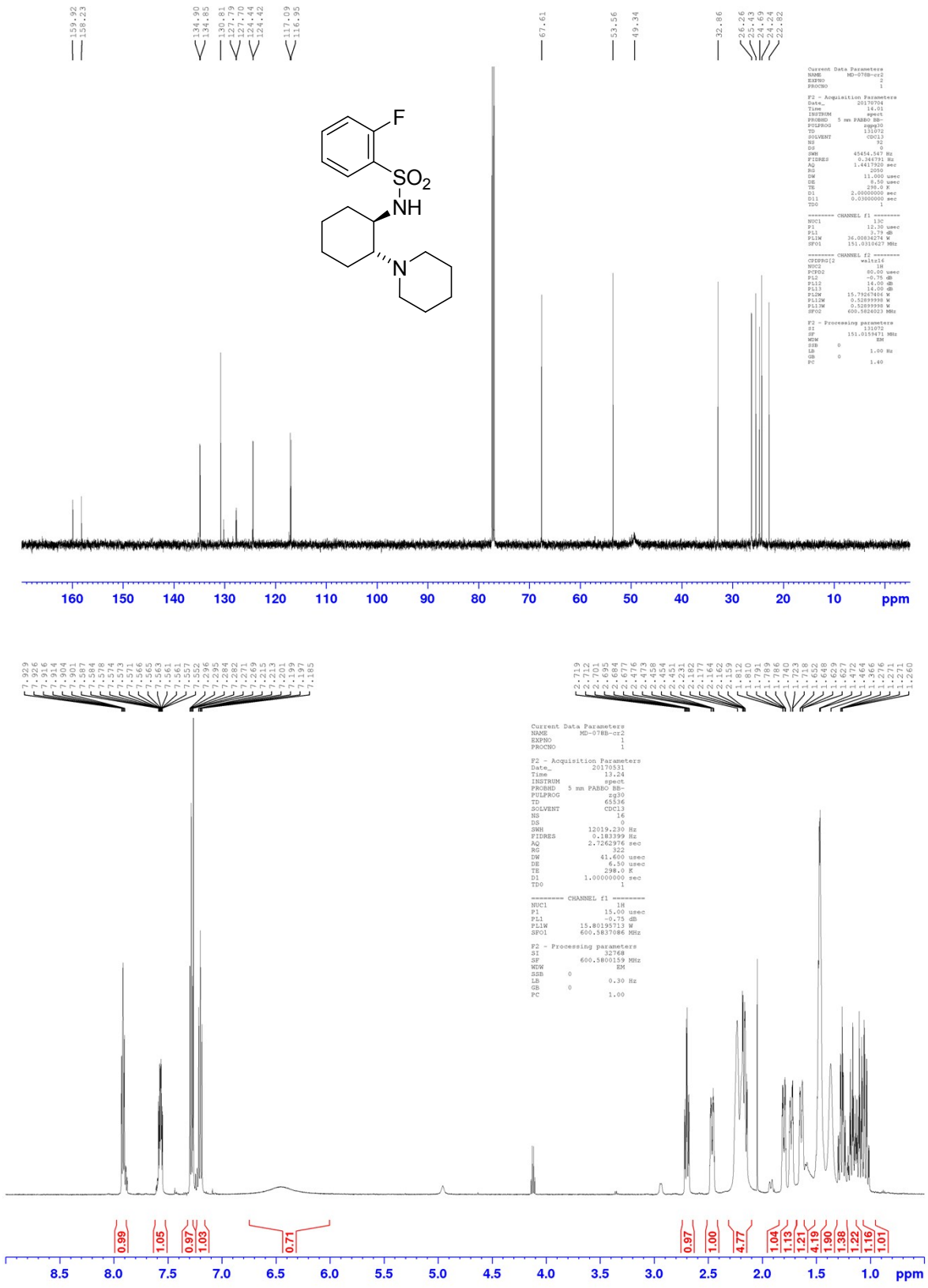


Figure S28. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2m**

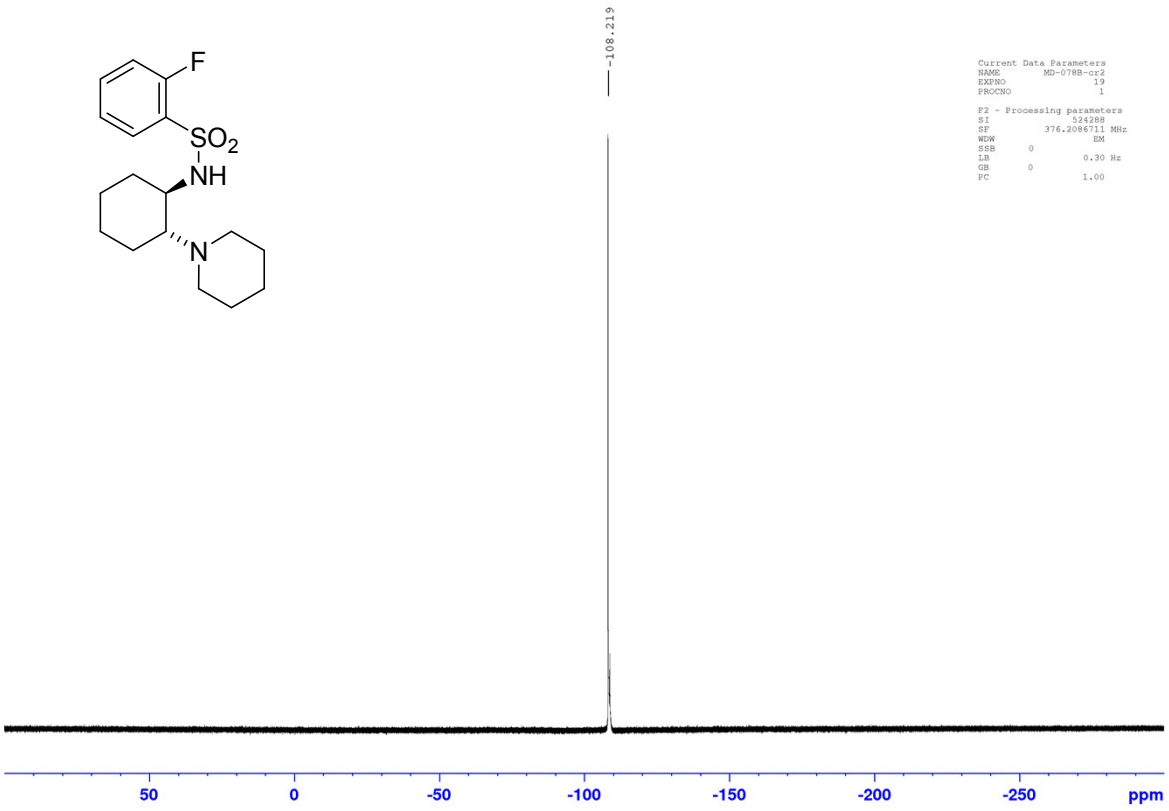


Figure S29. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for catalyst **2m**

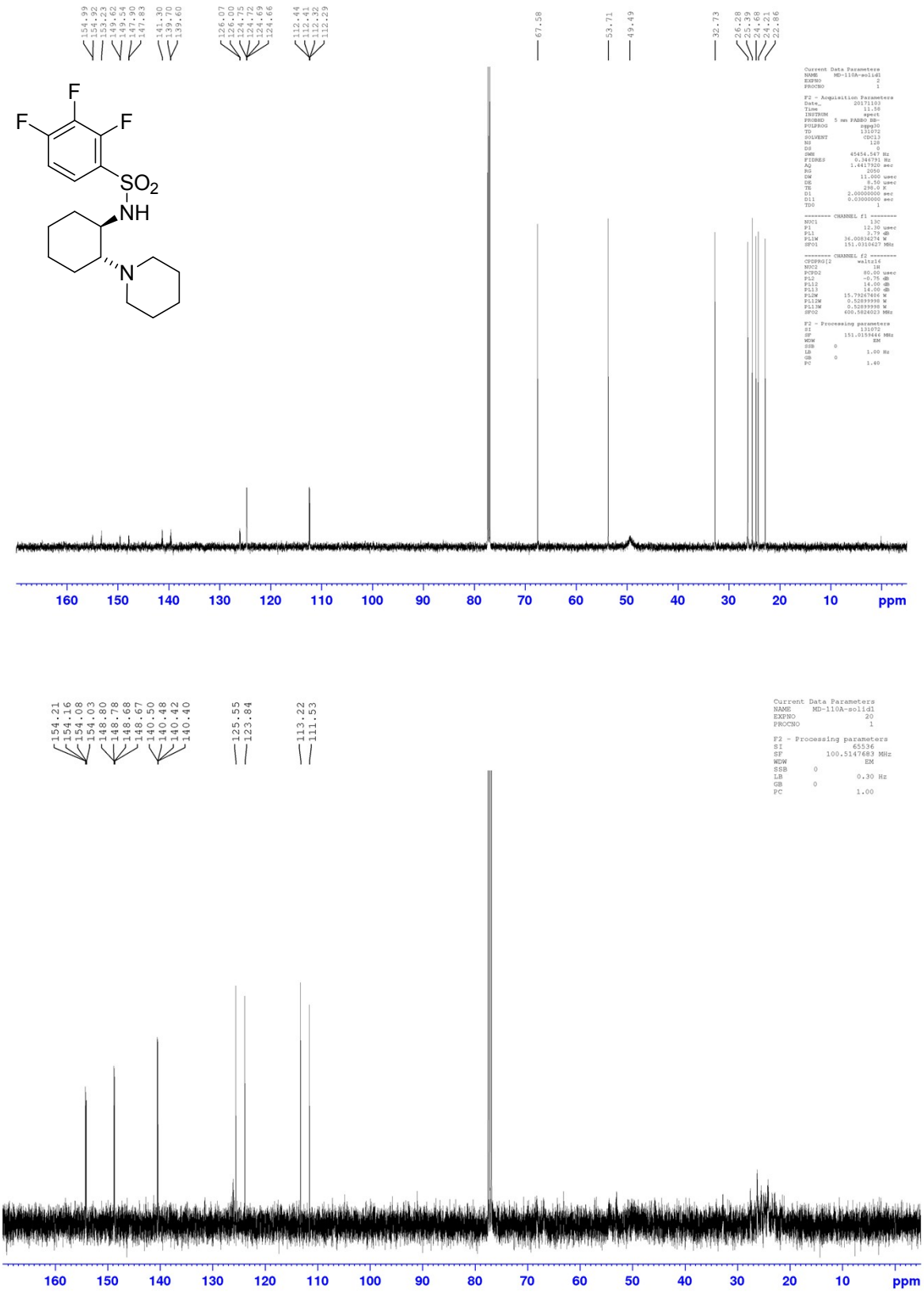


Figure S30. $^{13}C\{^{1}H\}$ and $^{13}C\{^{19}F\}$ NMR spectra (151 MHz, 101 MHz, $CDCl_3$) for catalyst **2n**

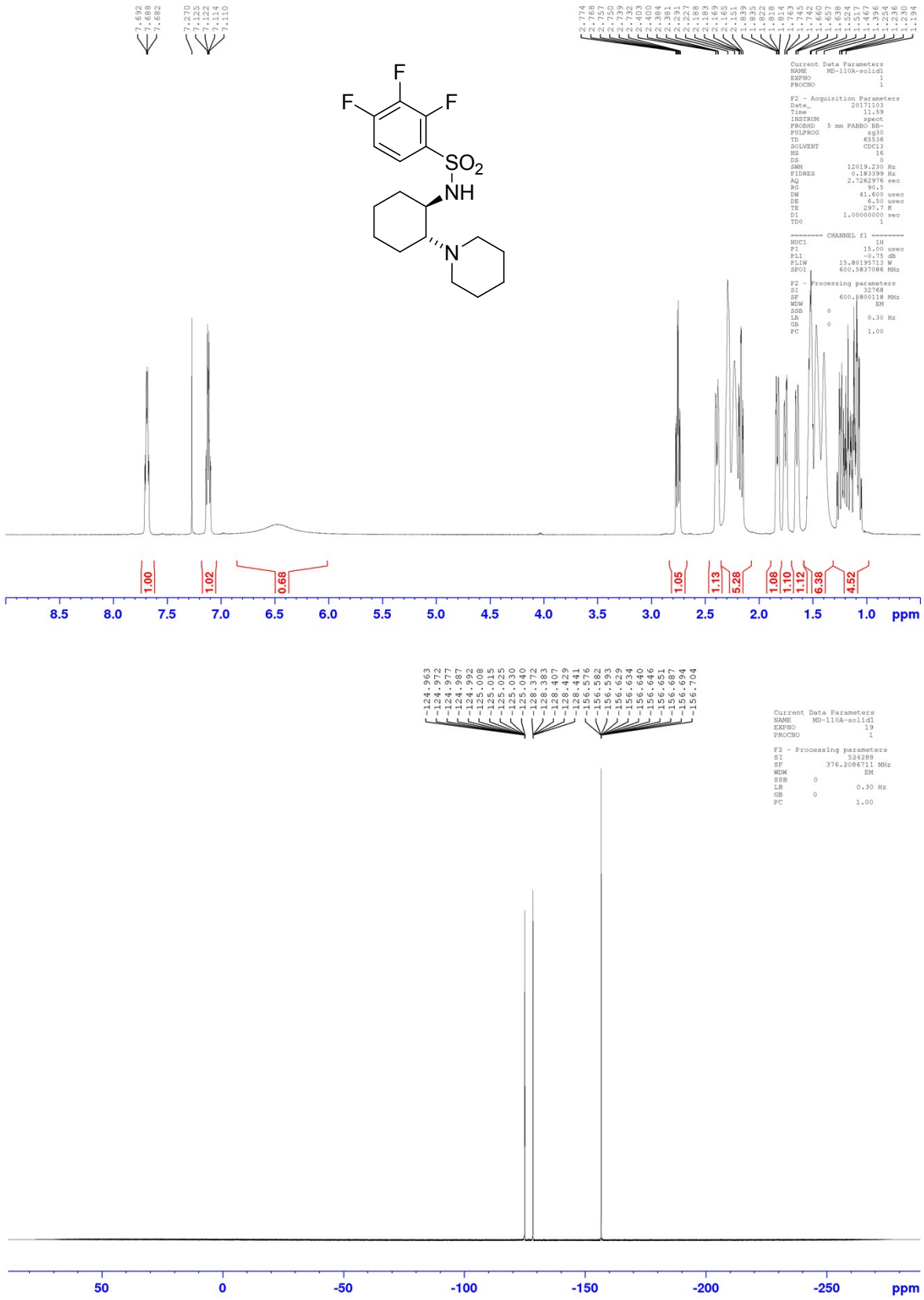


Figure S31. ^{1}H and ^{19}F NMR spectrum (600 MHz, 376 MHz, $CDCl_3$) for catalyst **2n**

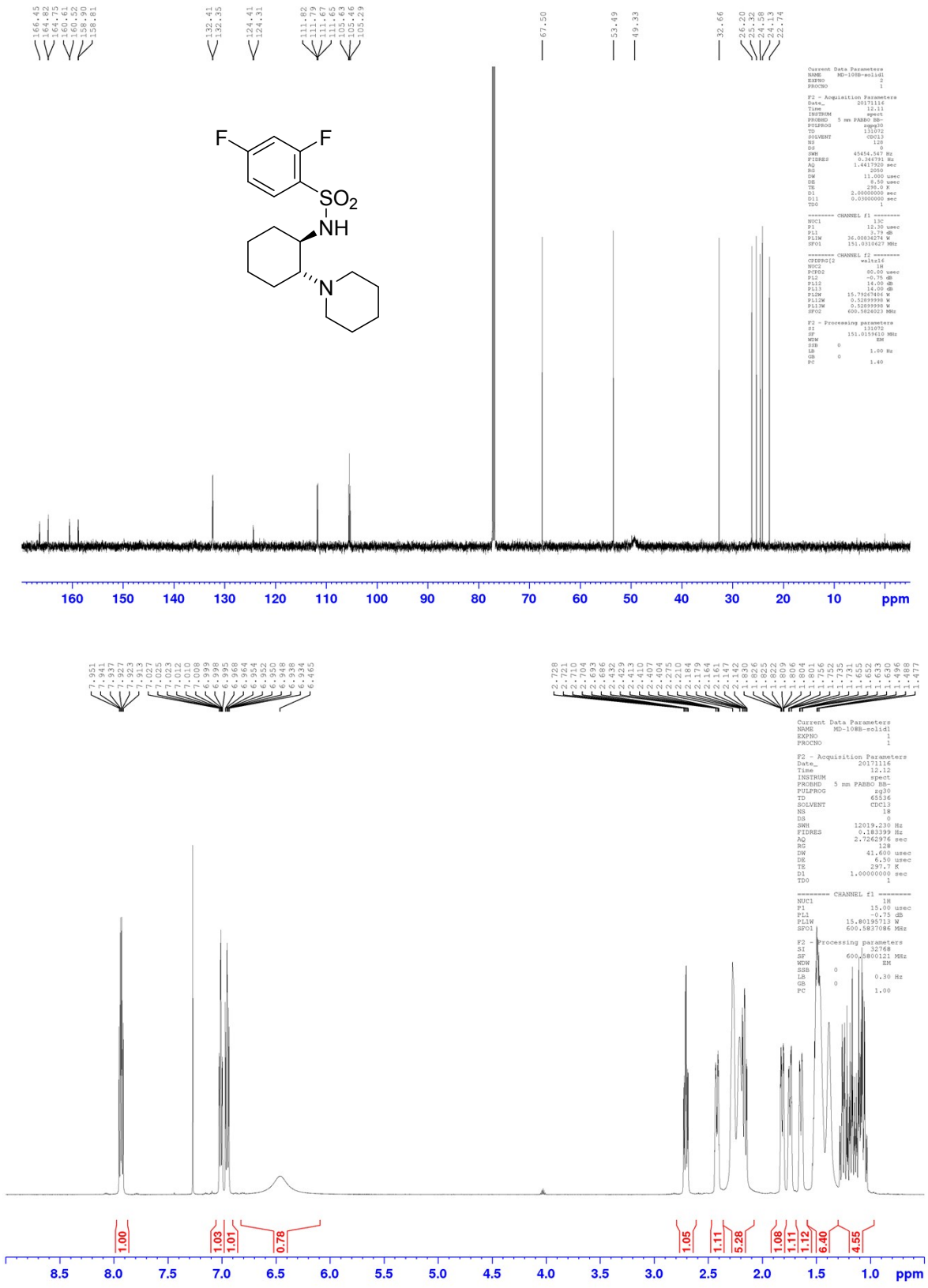


Figure S32. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2o**

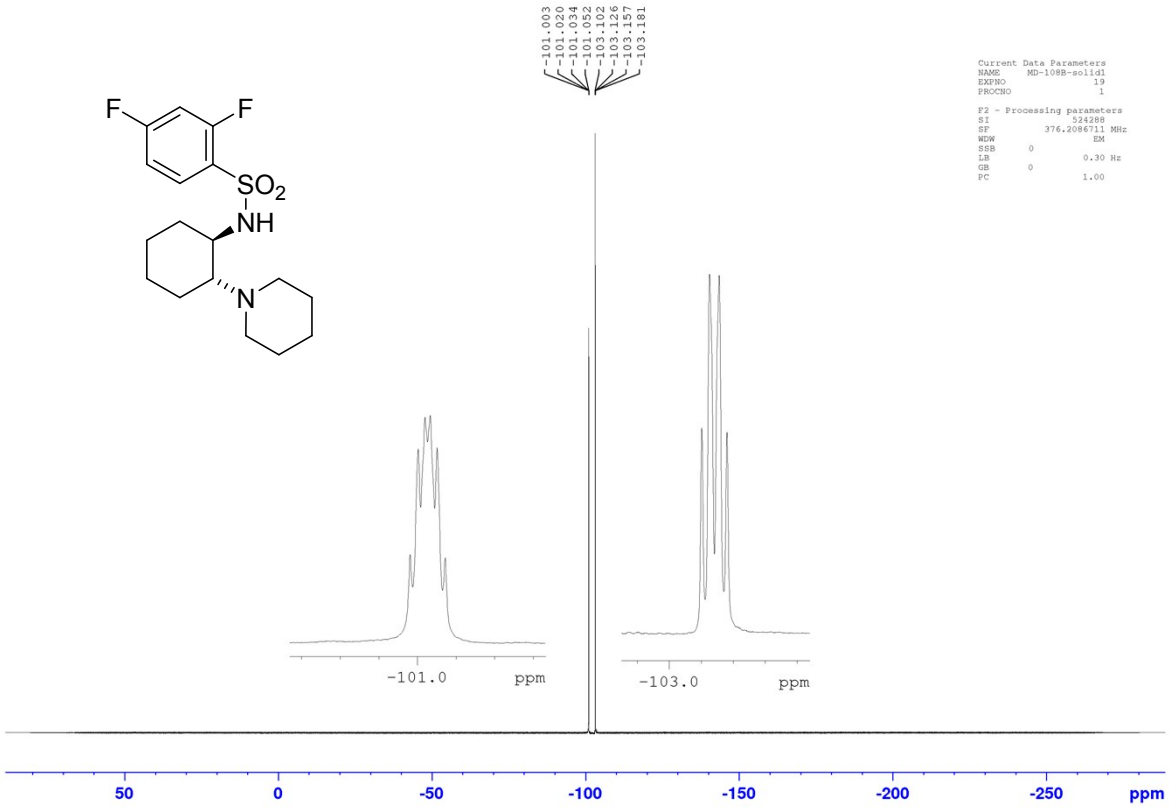


Figure S33. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for catalyst **2o**

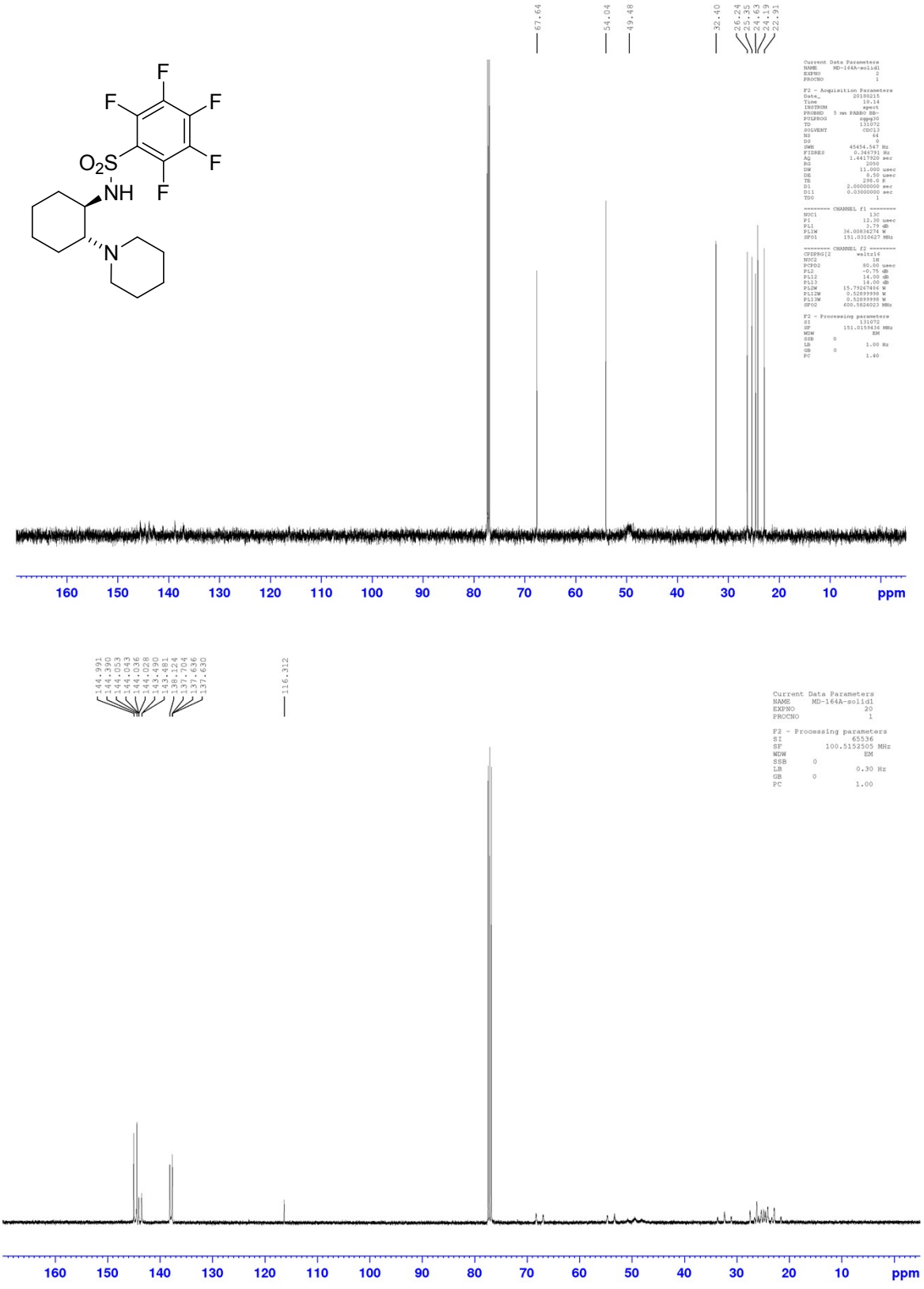


Figure S34. $^{13}C\{^{1}H\}$ and $^{13}C\{^{19}F\}$ NMR spectra (151 MHz, 101 MHz, $CDCl_3$) for catalyst **2p** (note: incomplete ^{19}F decoupling)

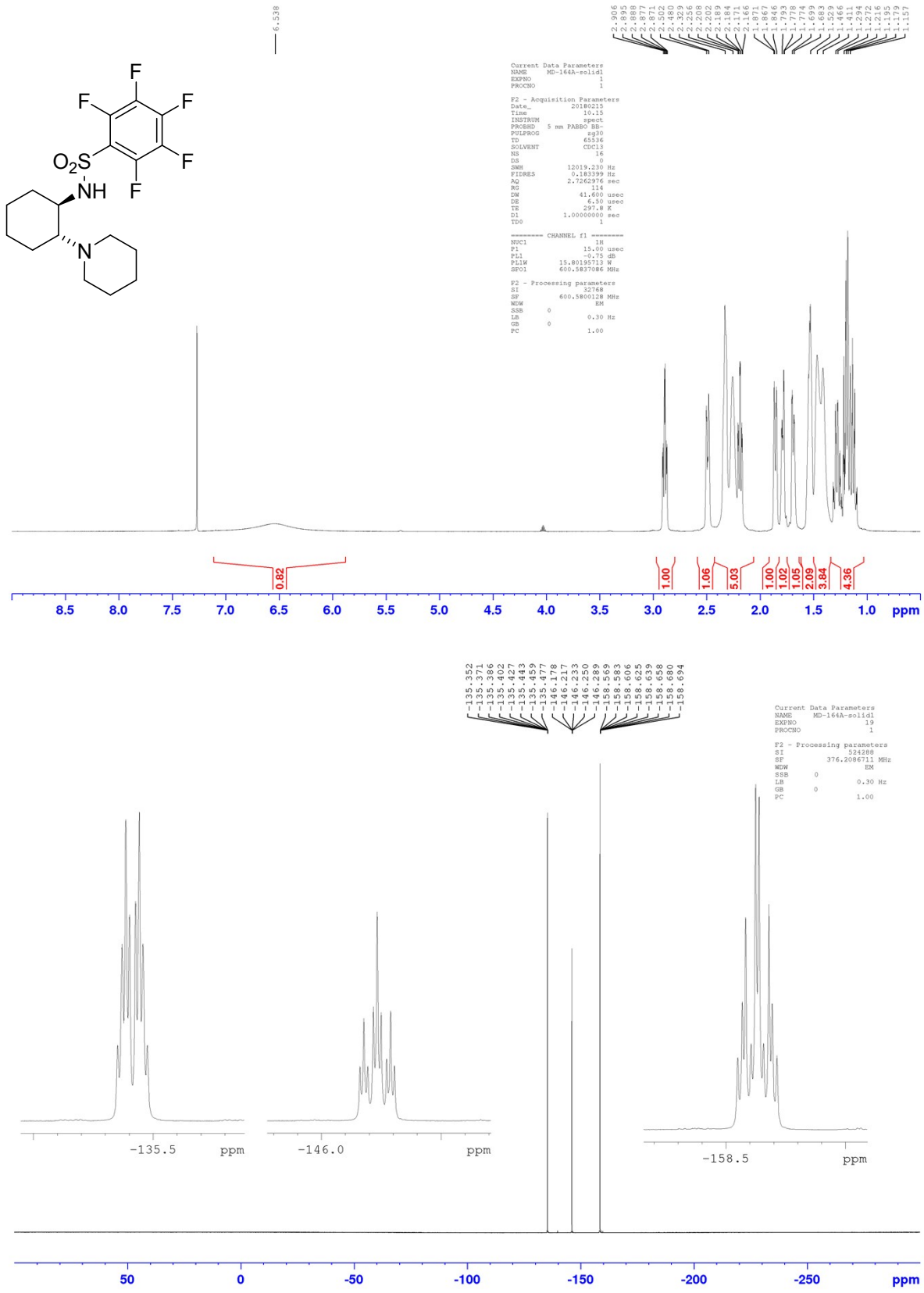


Figure S35. ^{1}H and ^{19}F NMR spectra (600 MHz, 376 MHz, $CDCl_3$) for catalyst **2p**

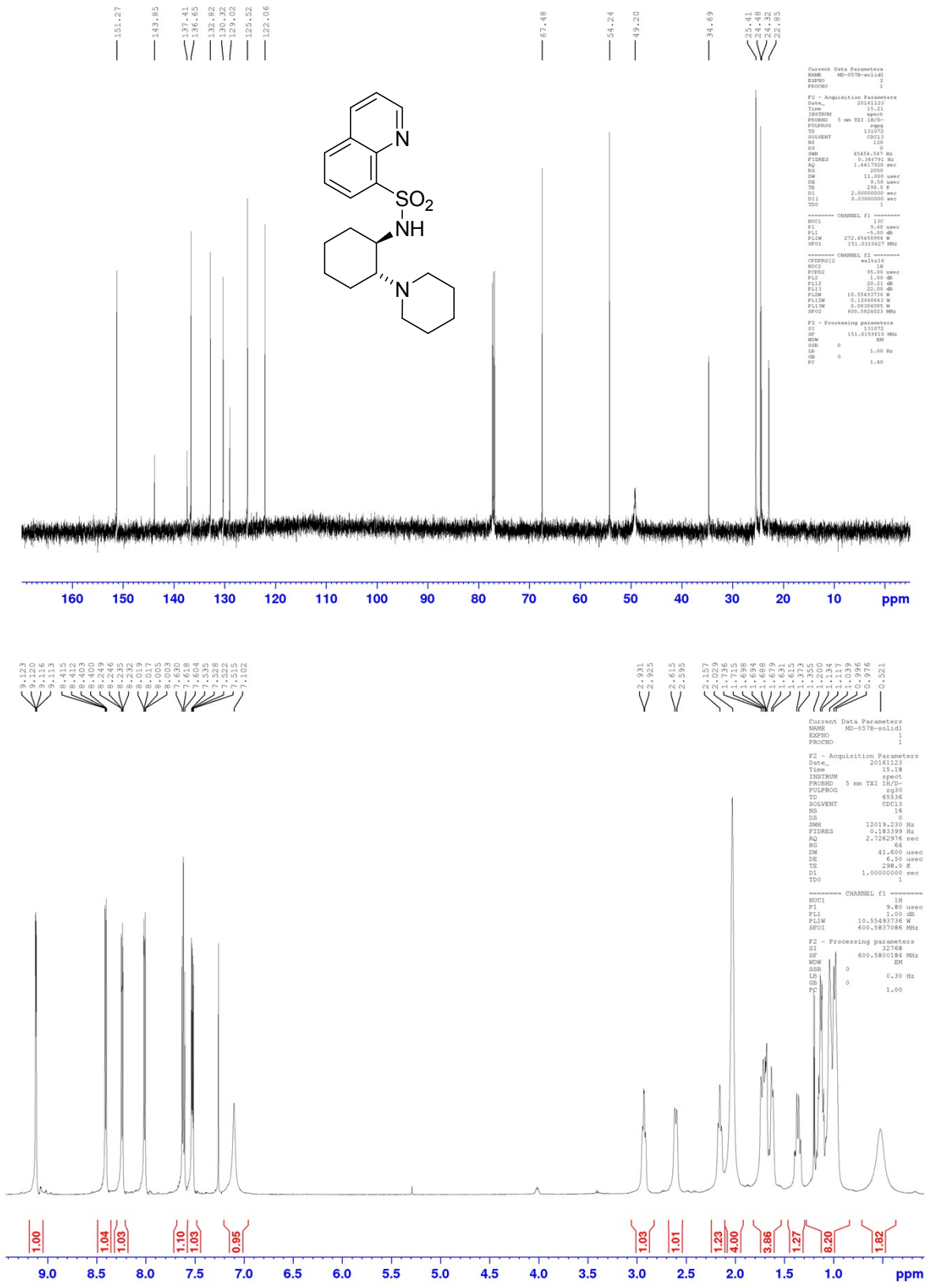


Figure S36. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2q**

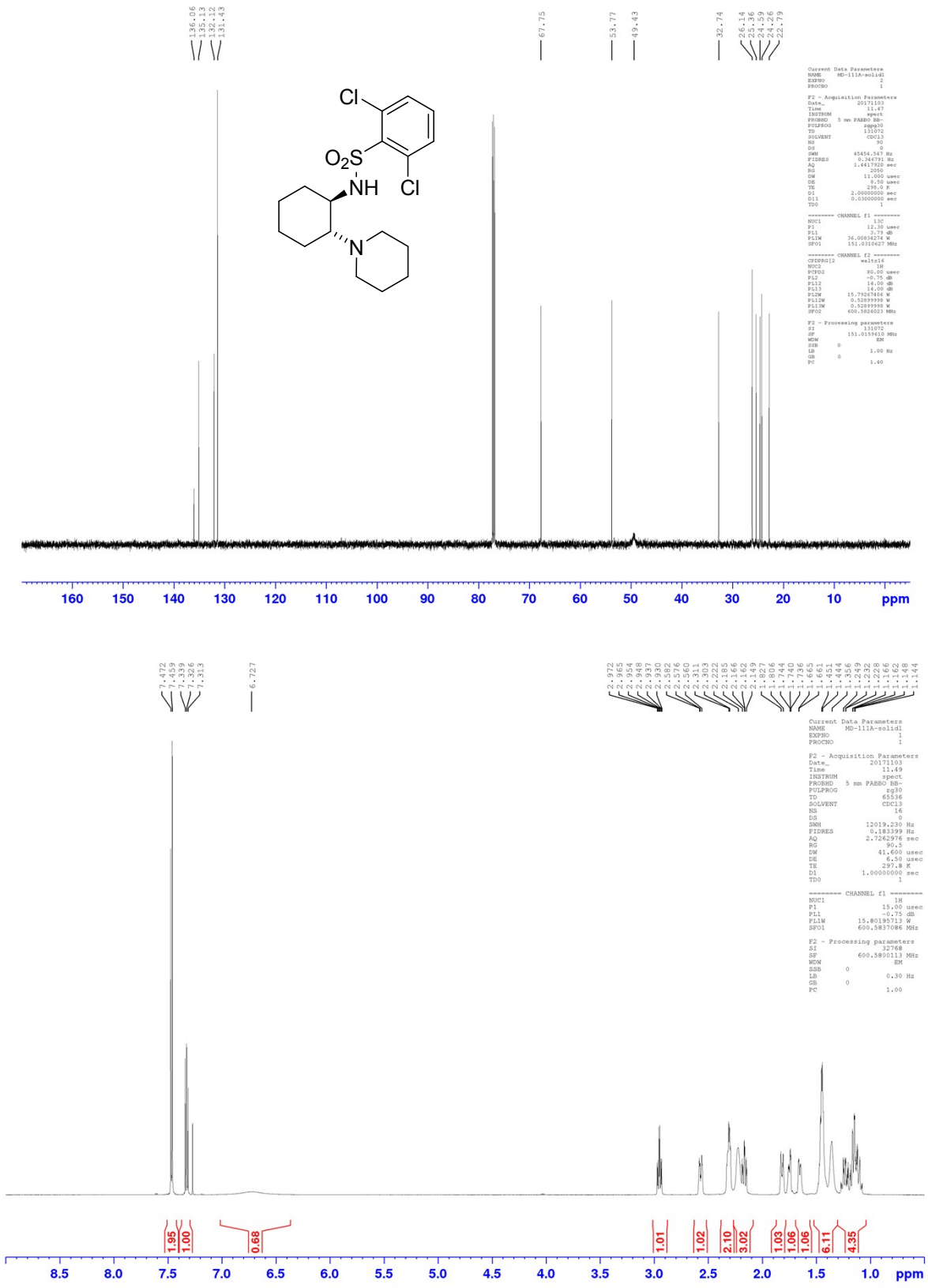


Figure S37. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2r**

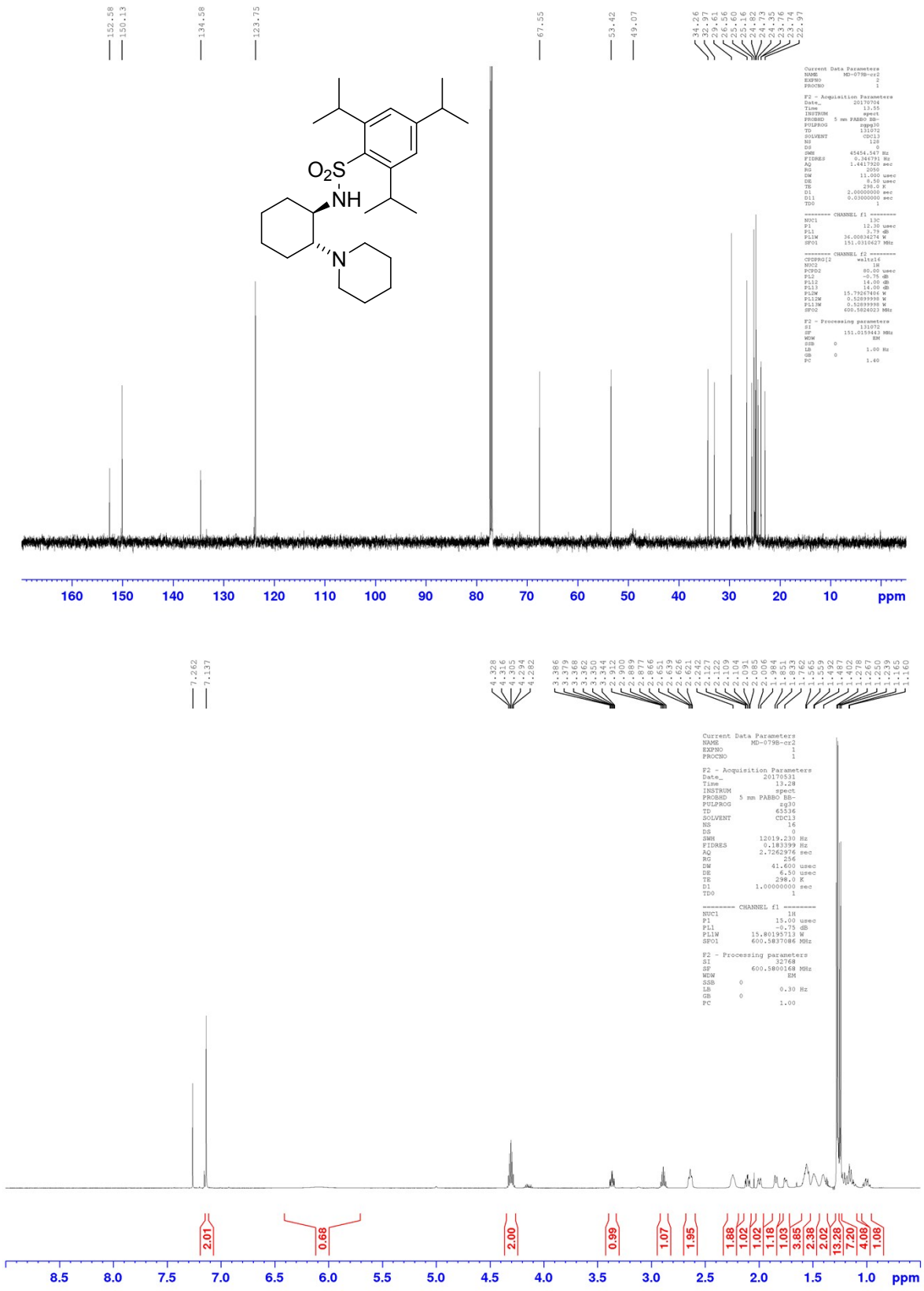


Figure S38. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2s**

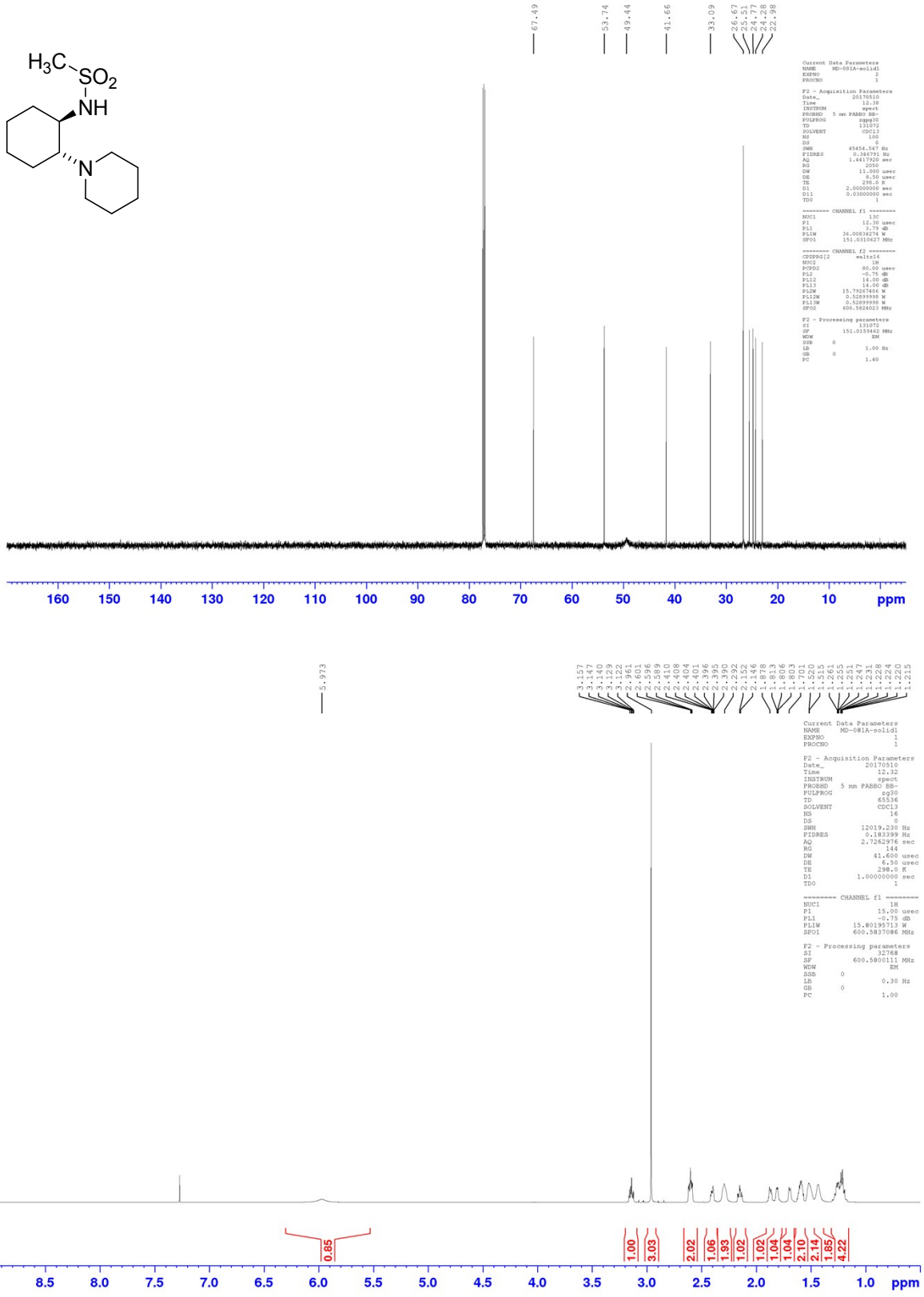


Figure S39. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2t**

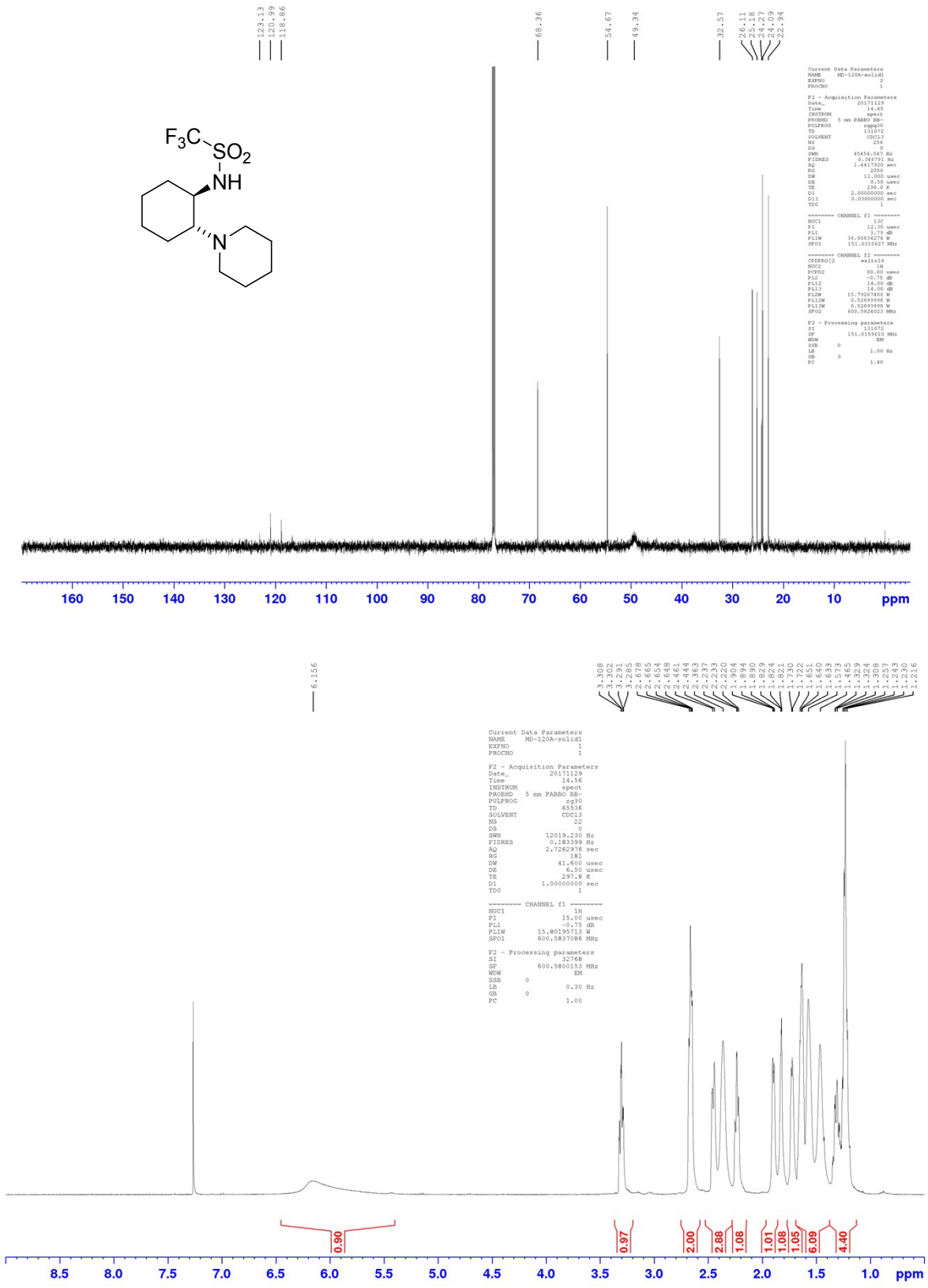


Figure S40. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2u**

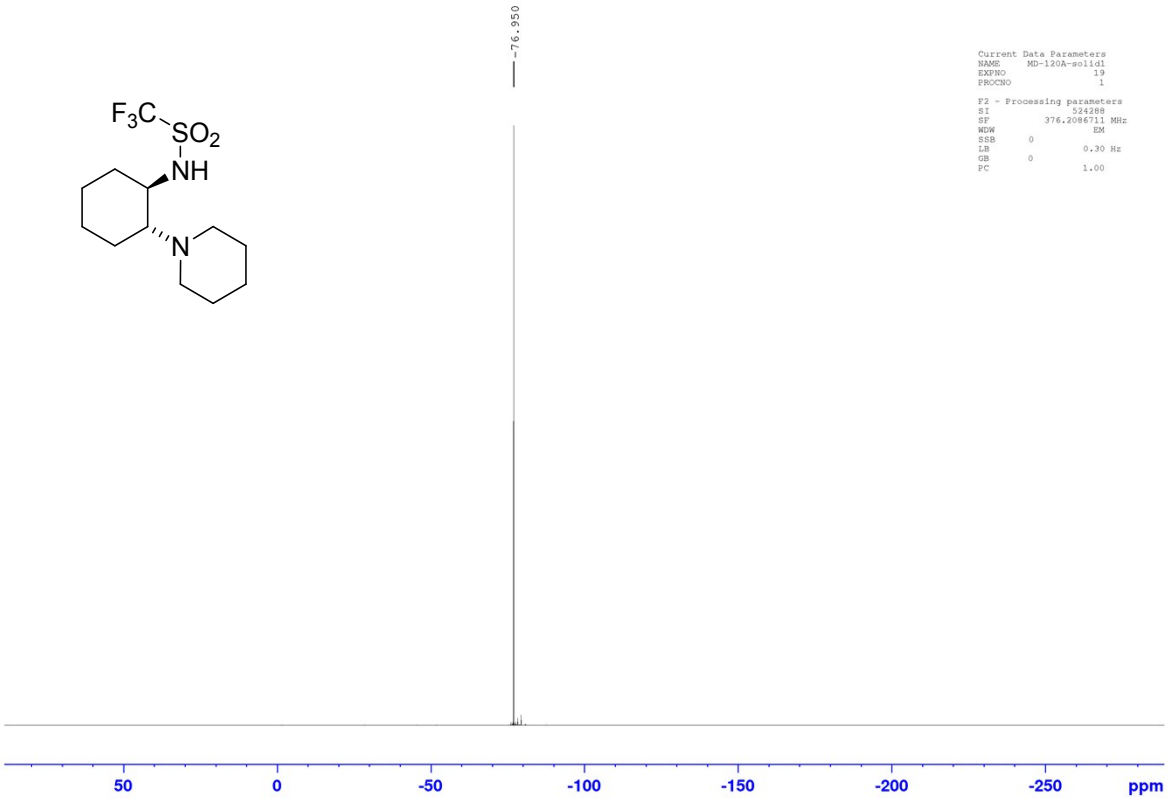


Figure S41. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for catalyst **2u**

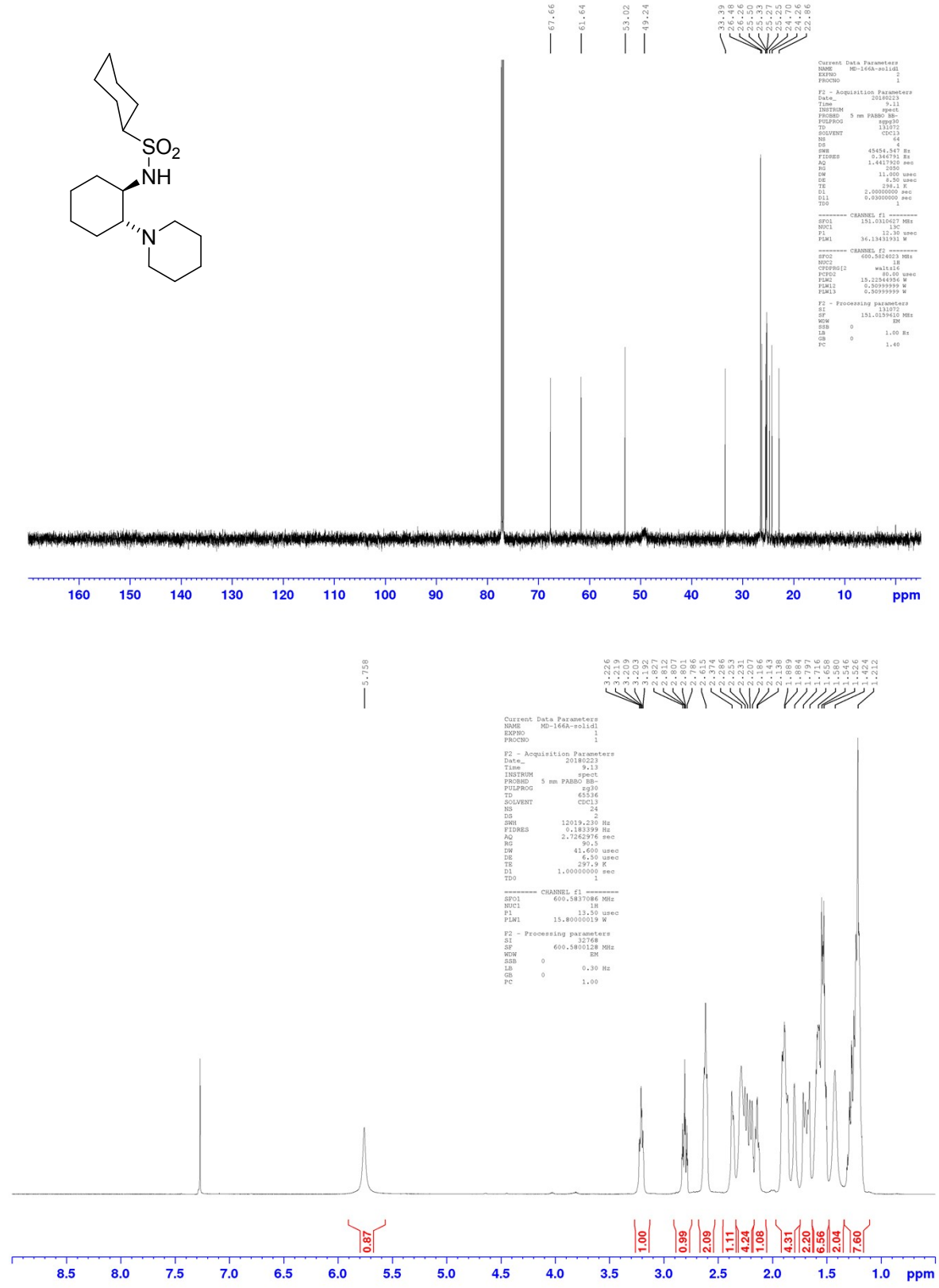


Figure S42. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2v**

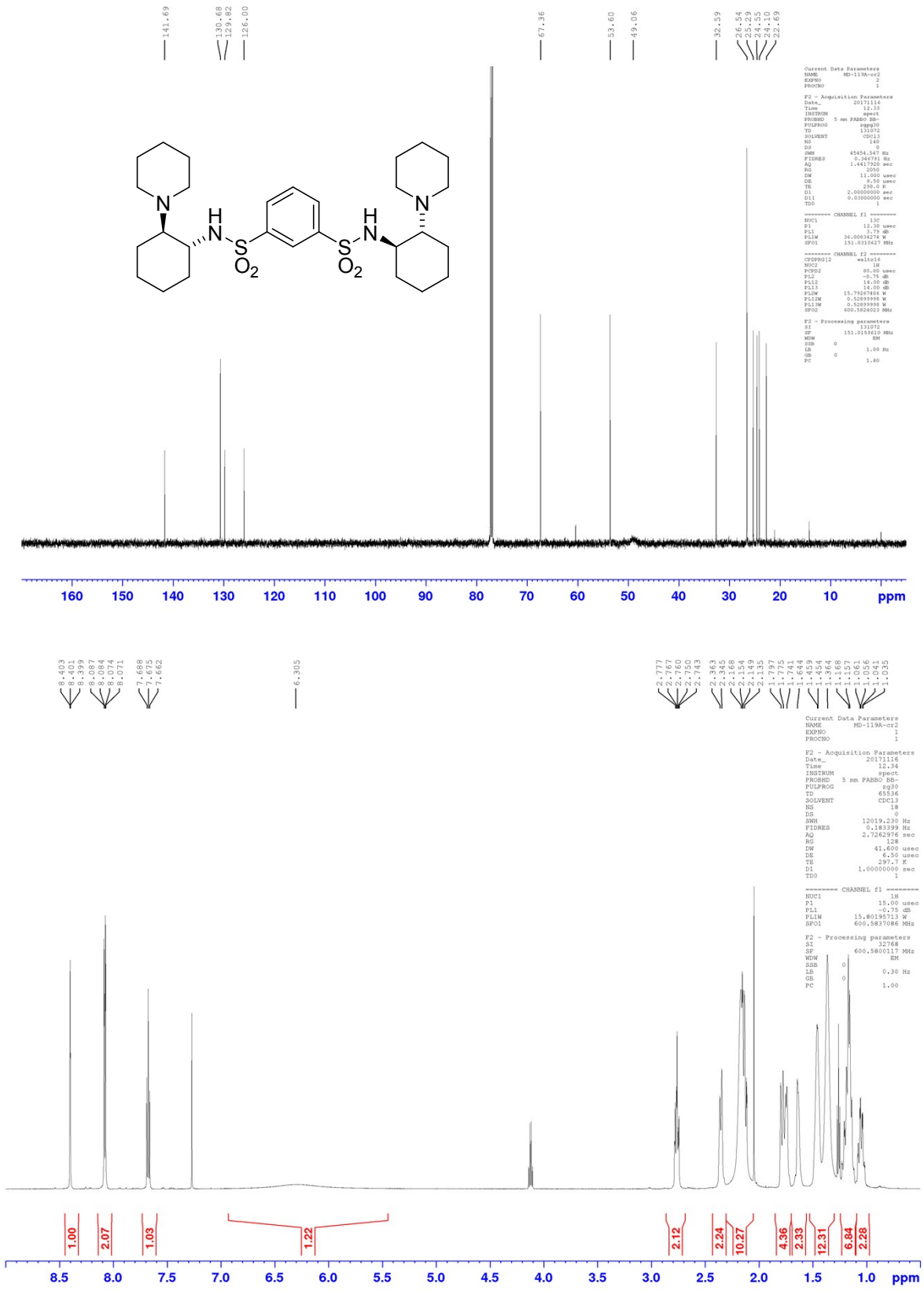


Figure S43. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2w**

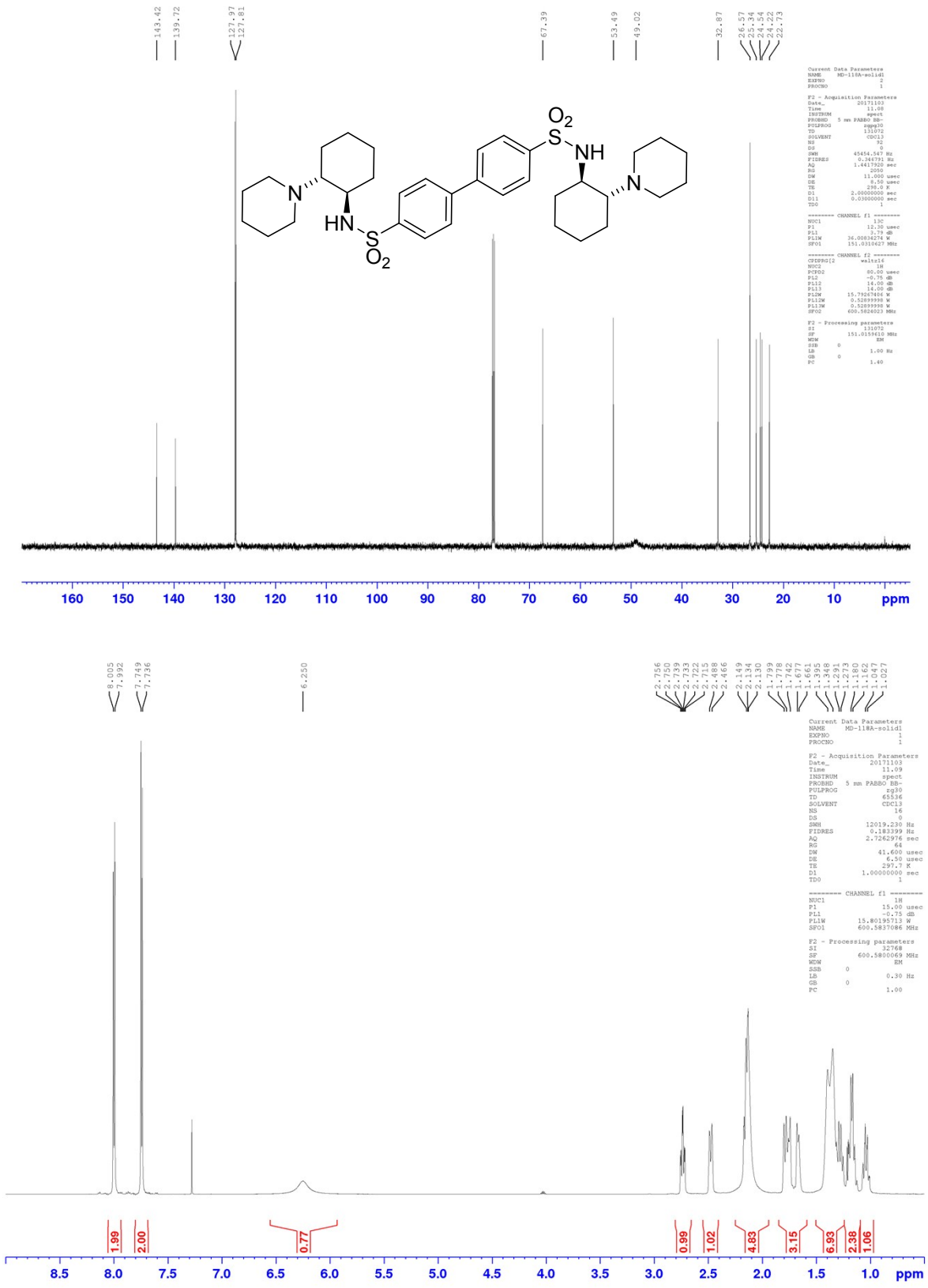


Figure S44. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2x**

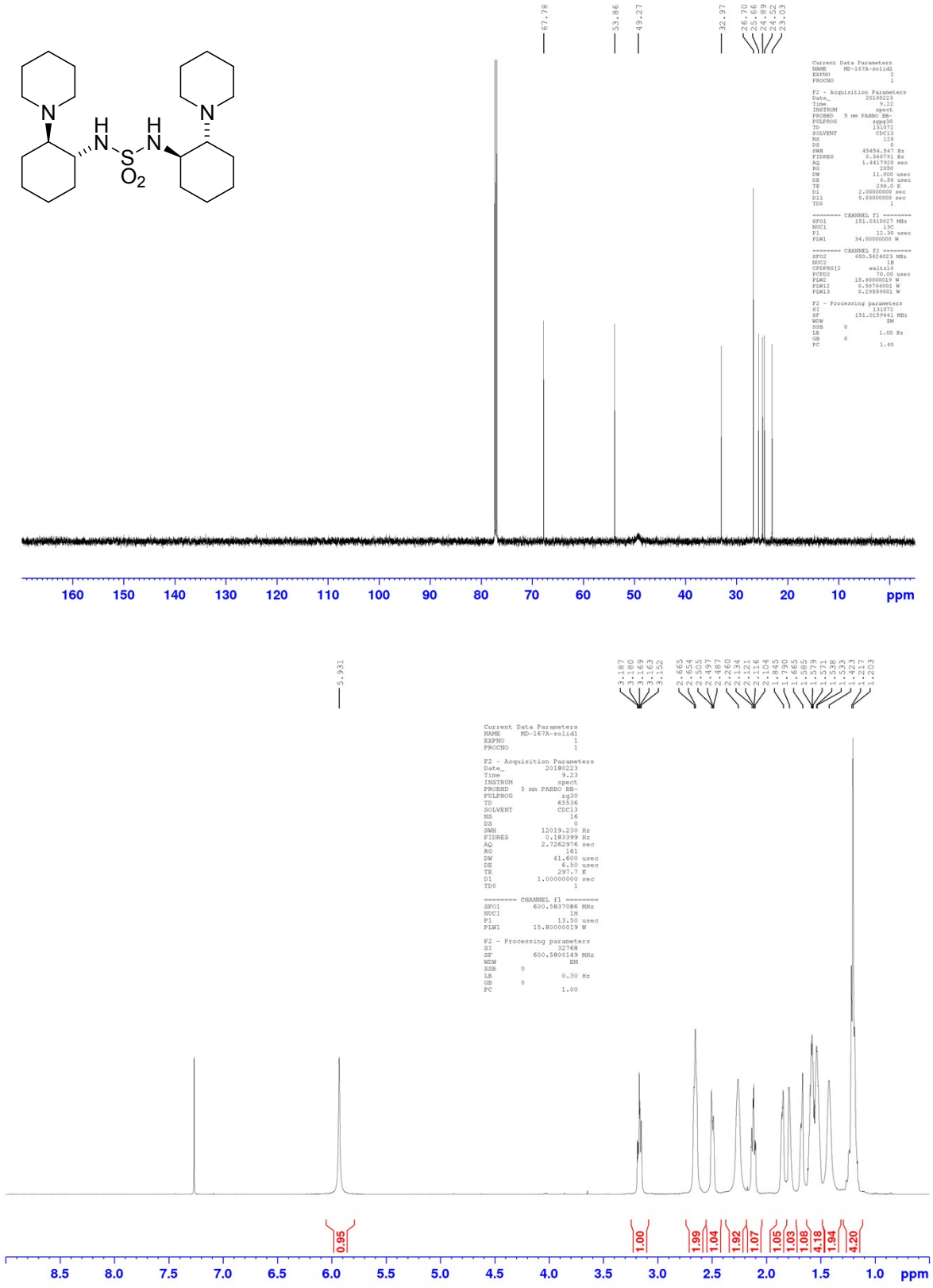


Figure S45. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **2y**

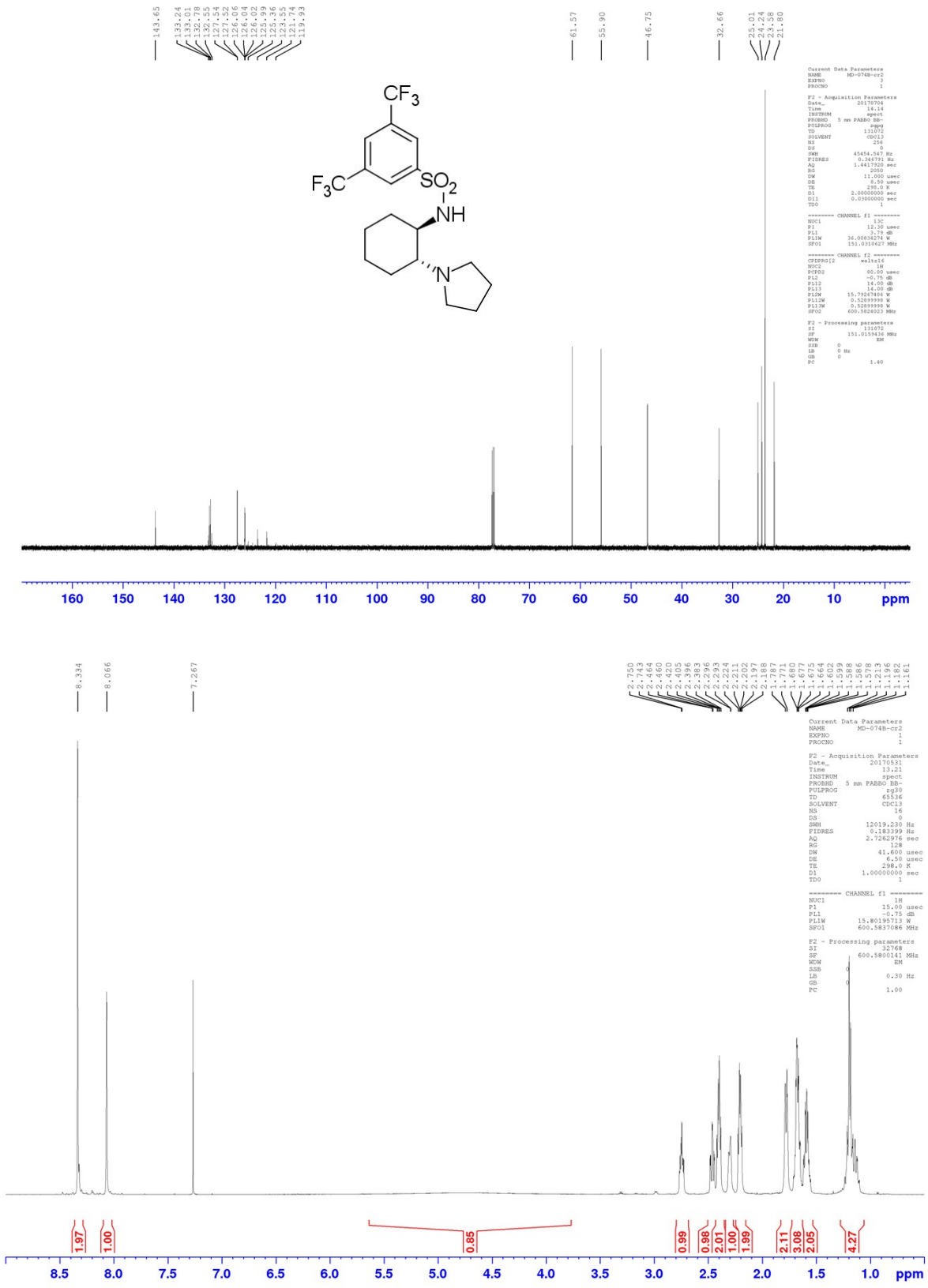


Figure S46. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **1a**

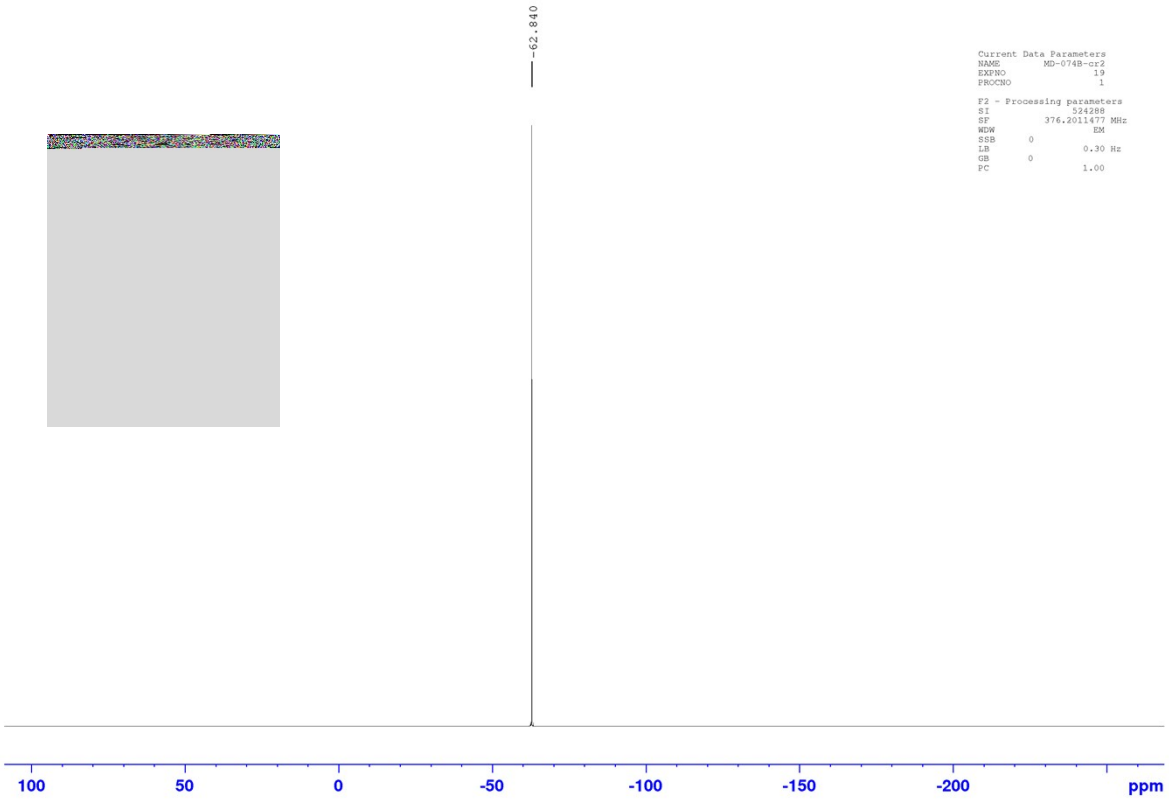


Figure S47. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for catalyst **1a**

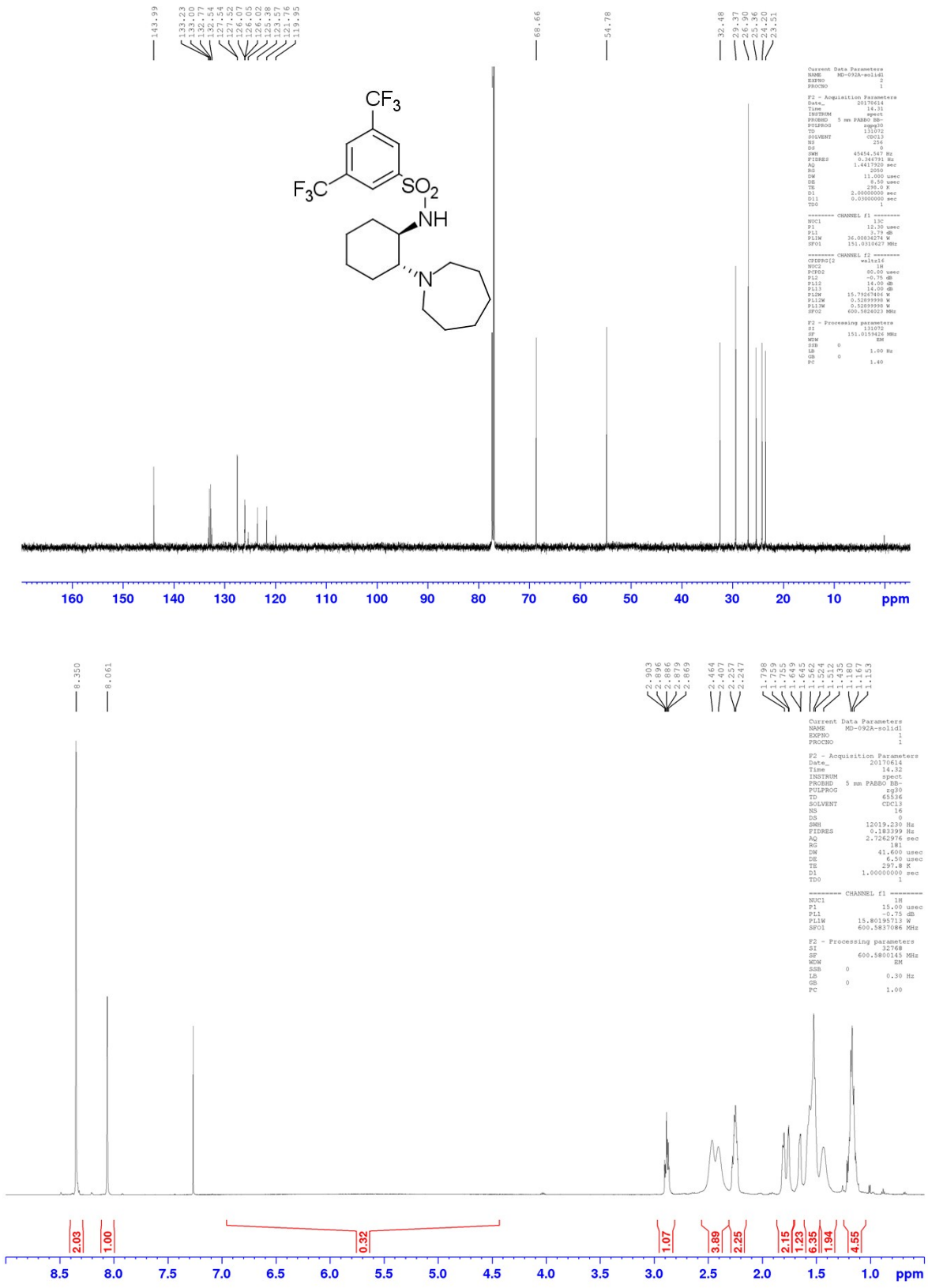


Figure S48. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **3a**

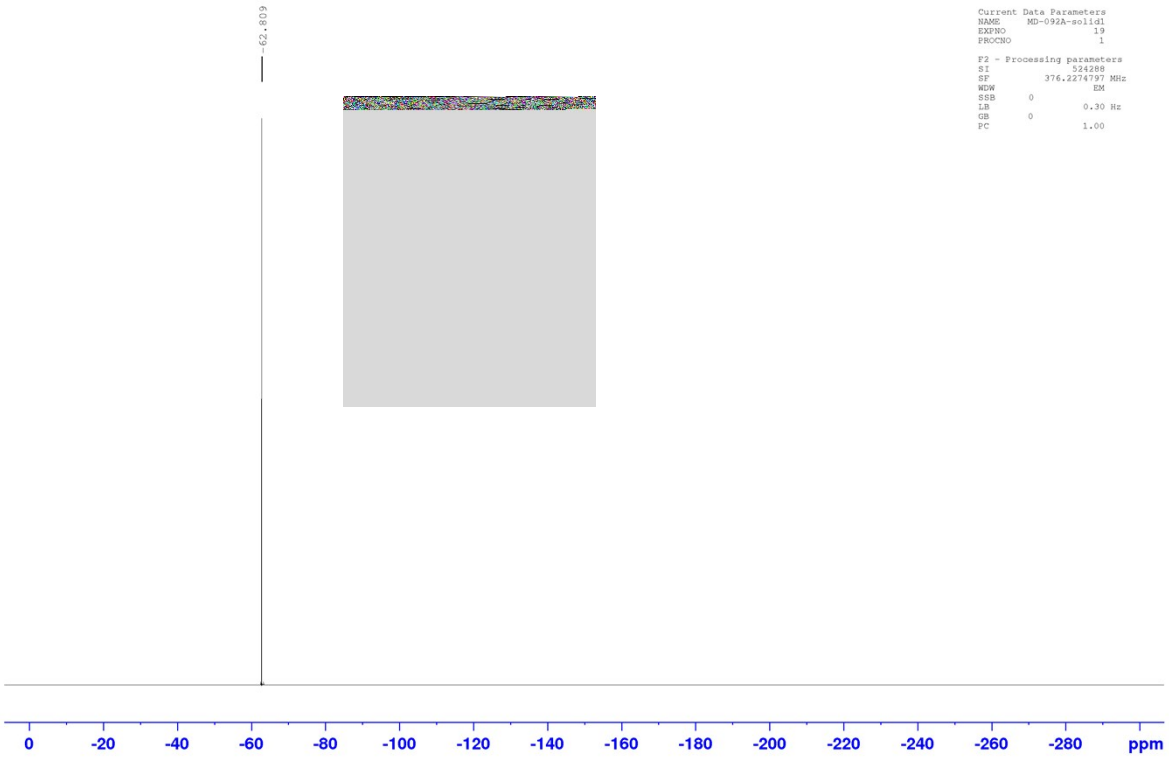


Figure S49. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for catalyst **3a**

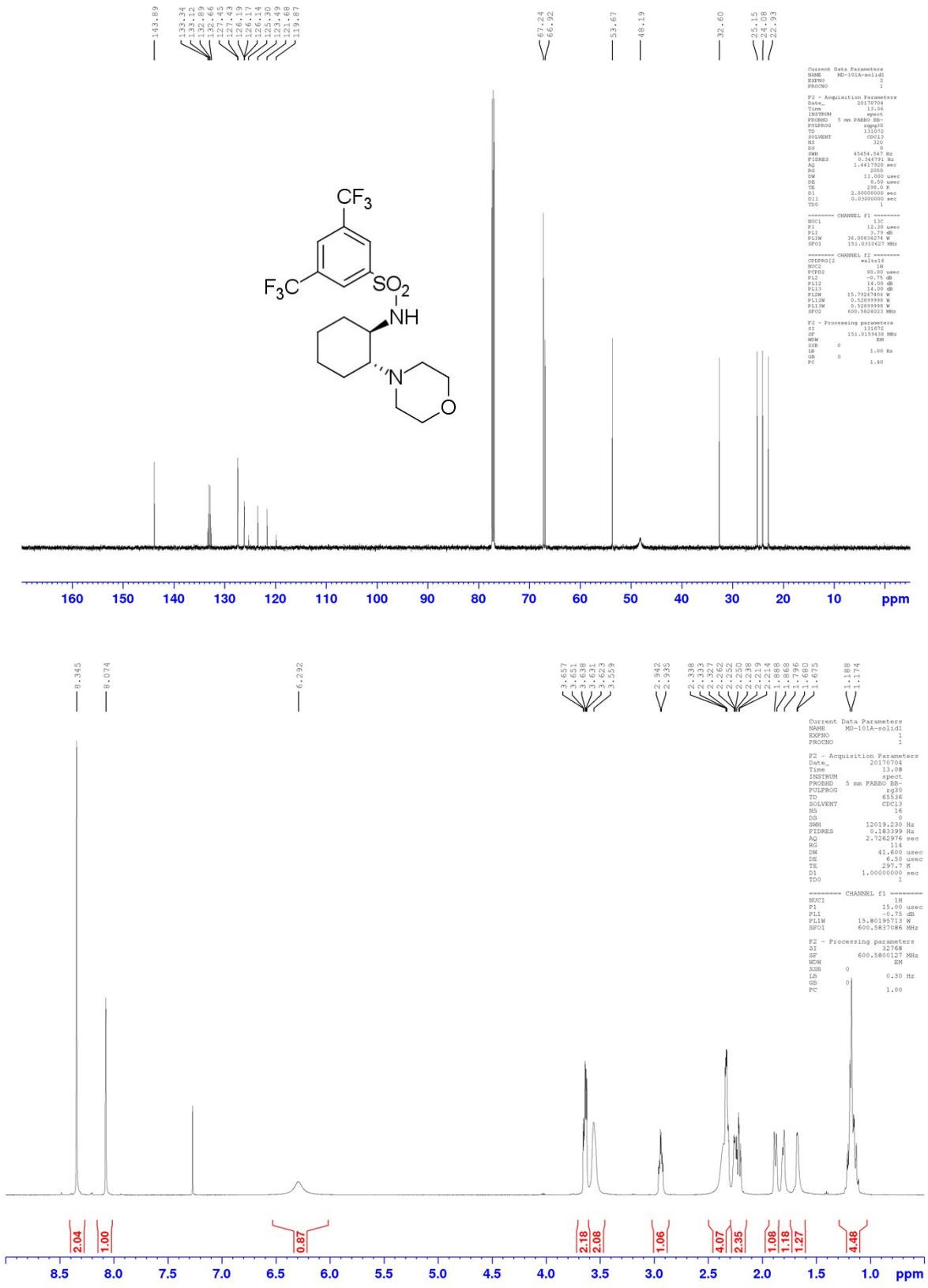


Figure S50. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **4a**

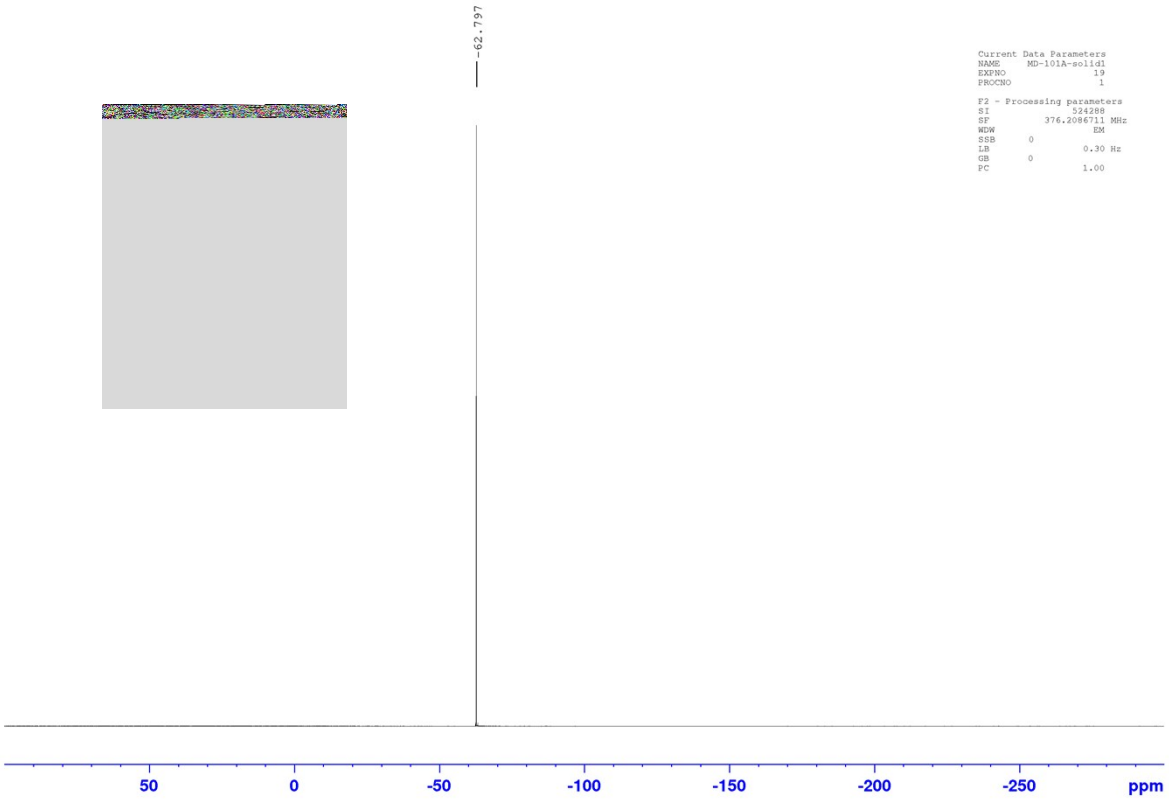


Figure S51. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for catalyst **4a**

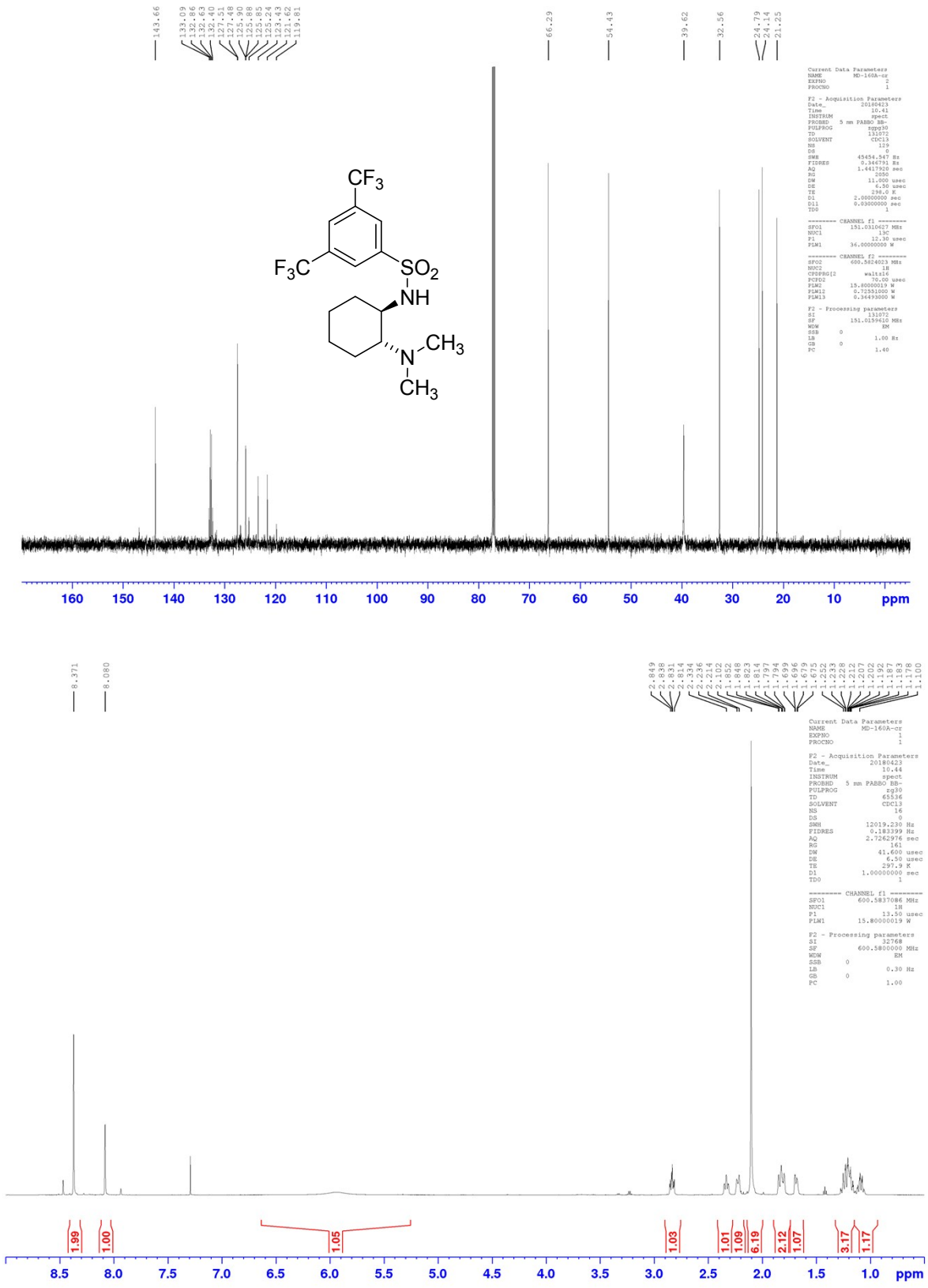


Figure S52. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **5a**

Figure S53. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for catalyst **5a**

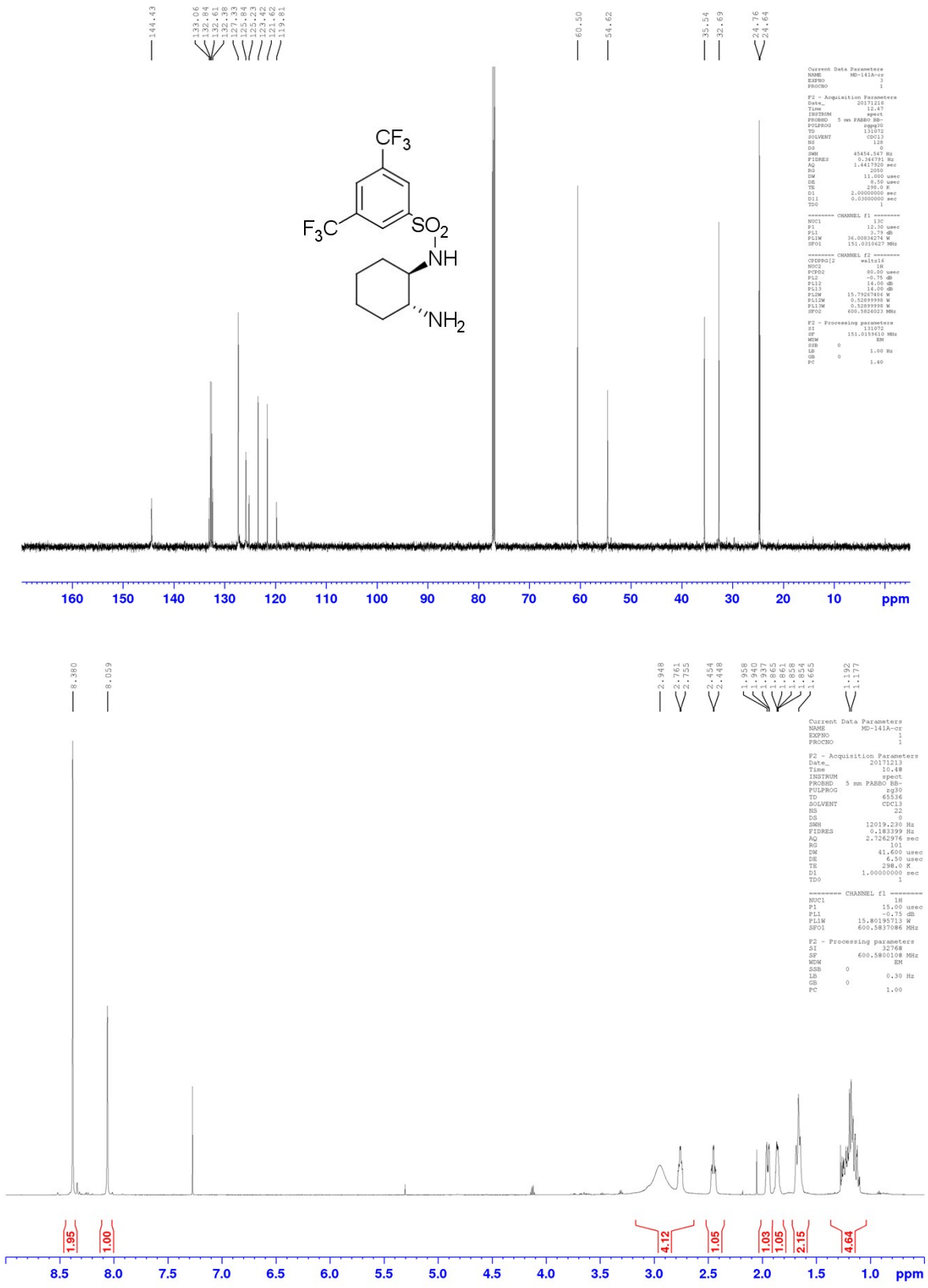


Figure S54. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **6a**

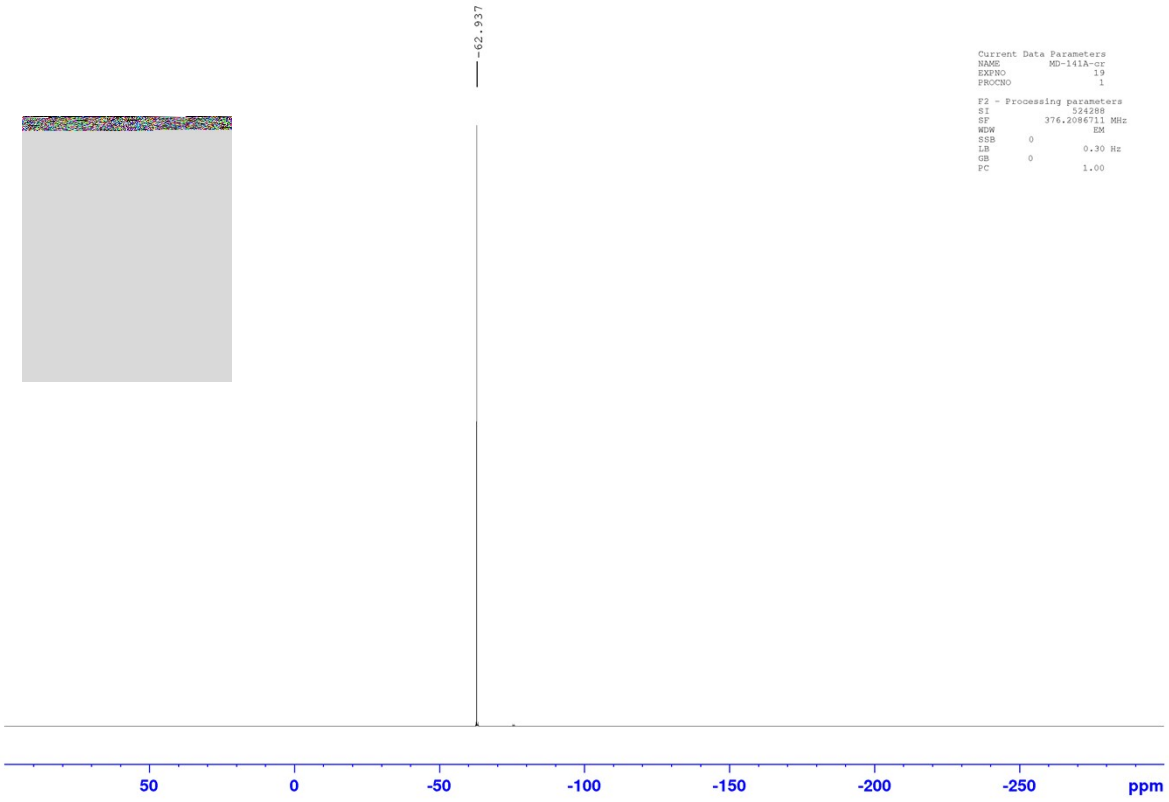


Figure S55. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for catalyst **6a**

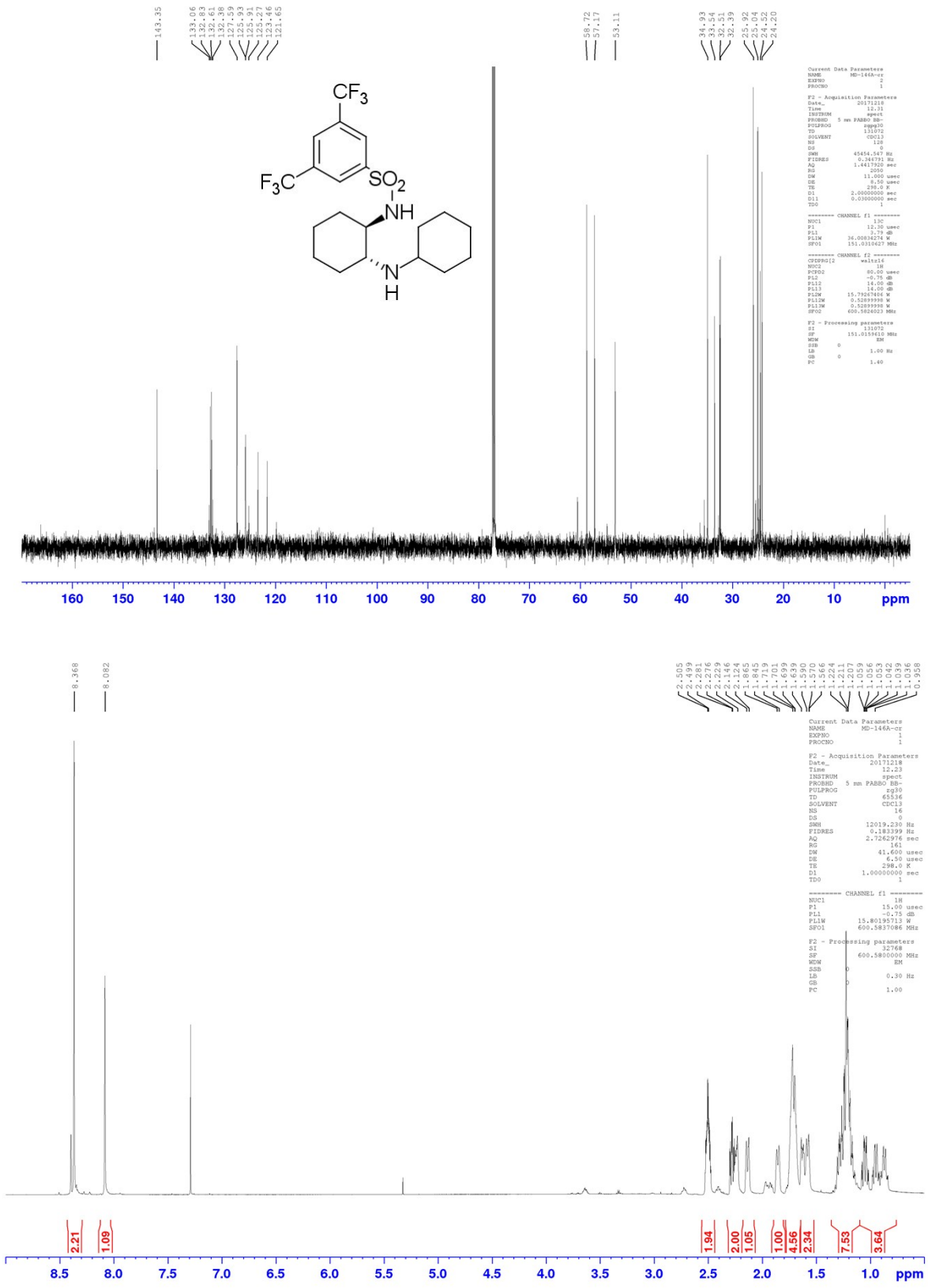


Figure S56. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **7a**

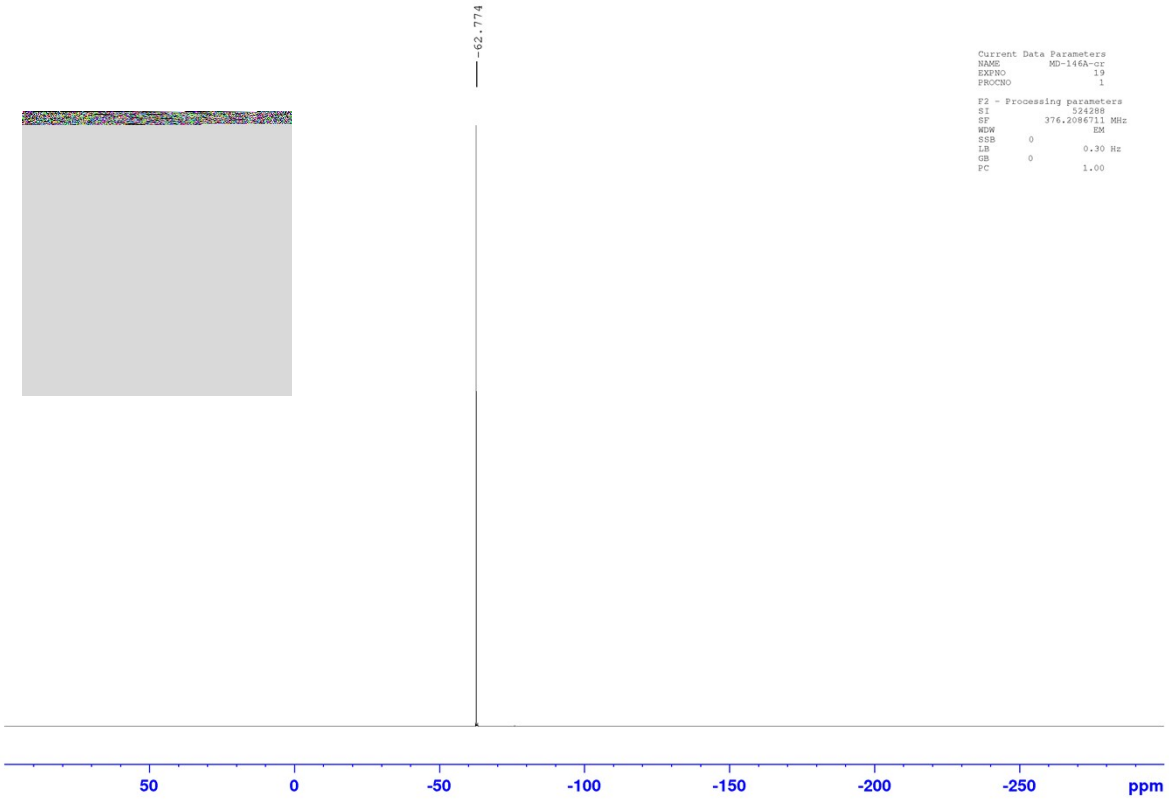


Figure S57. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for catalyst **7a**

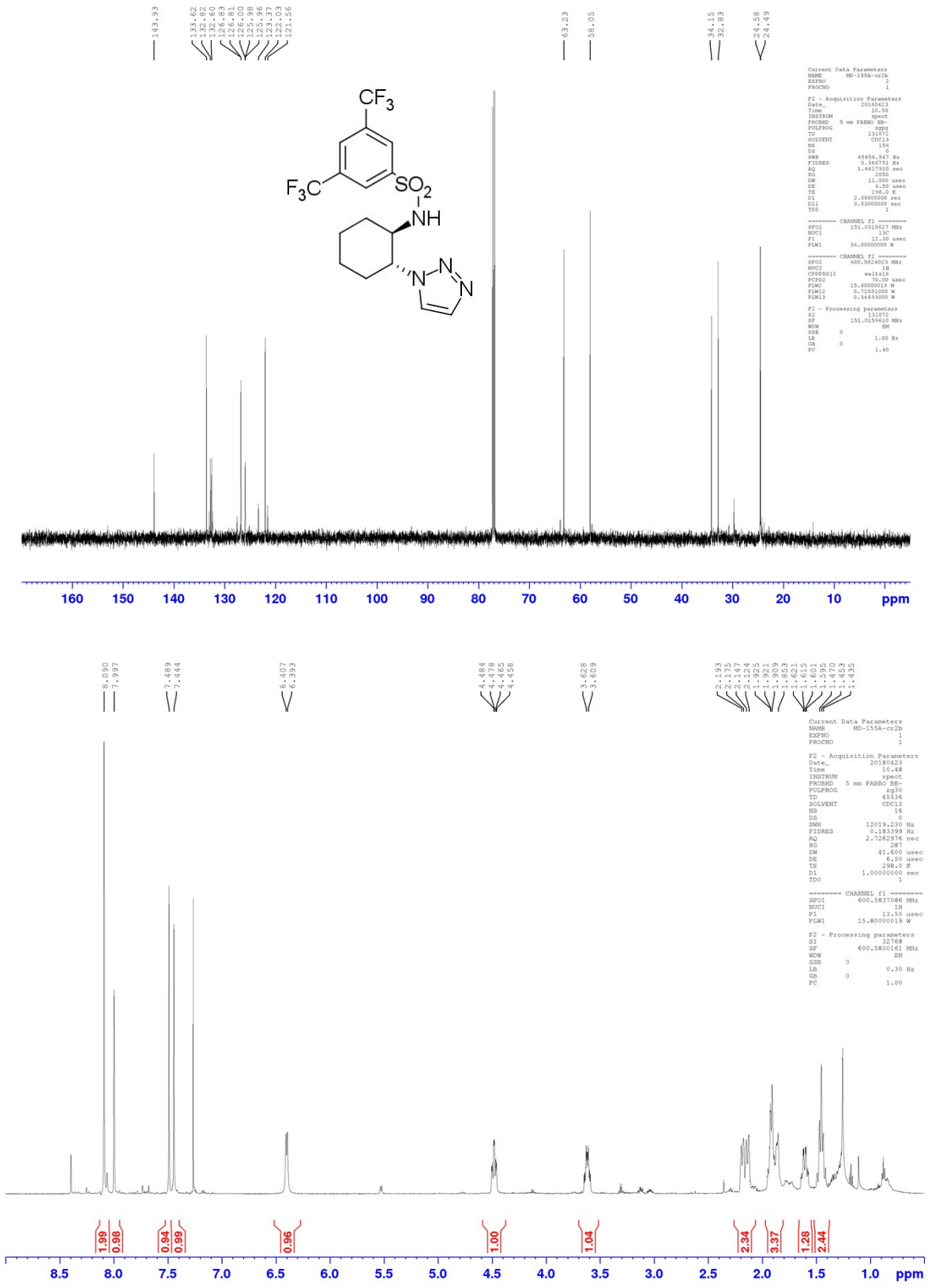


Figure S58. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **8a**

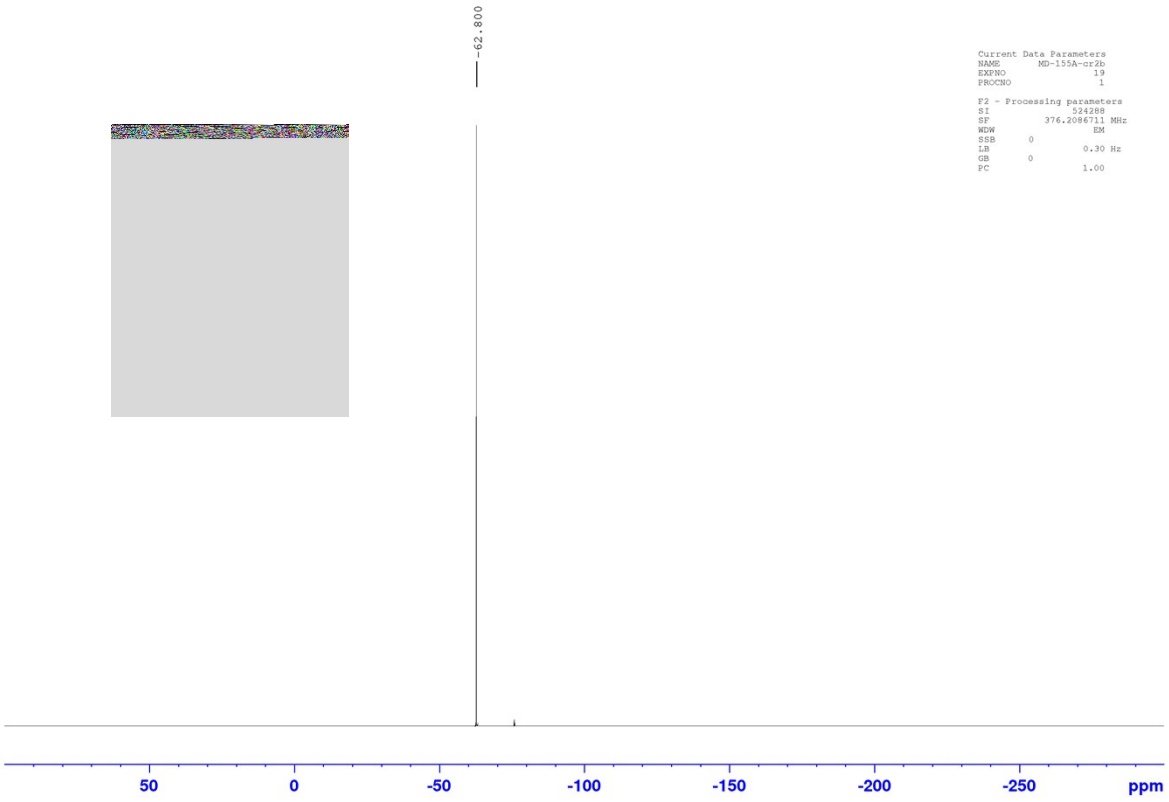


Figure S59. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for catalyst **8a**

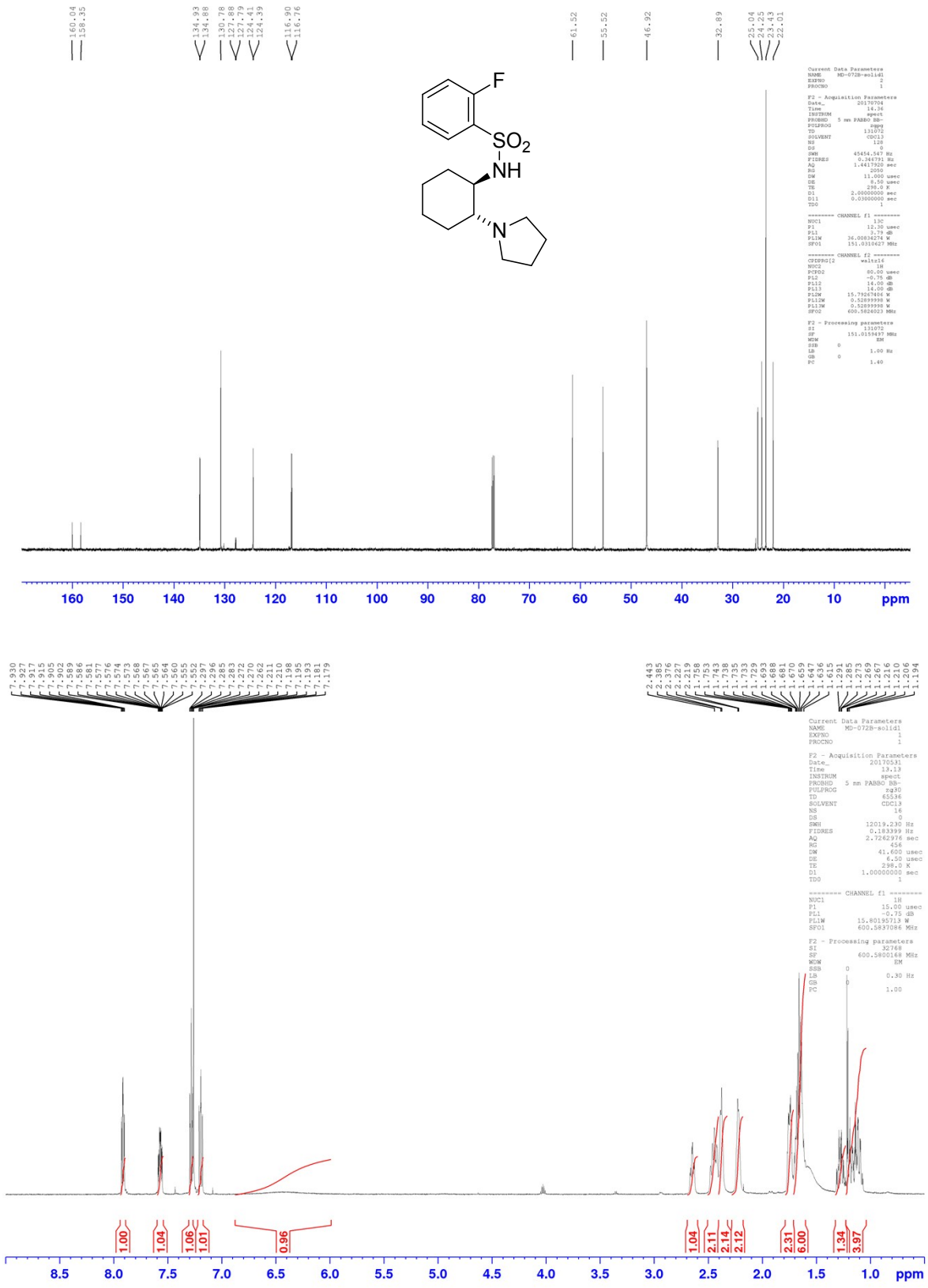


Figure S60. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **1m**

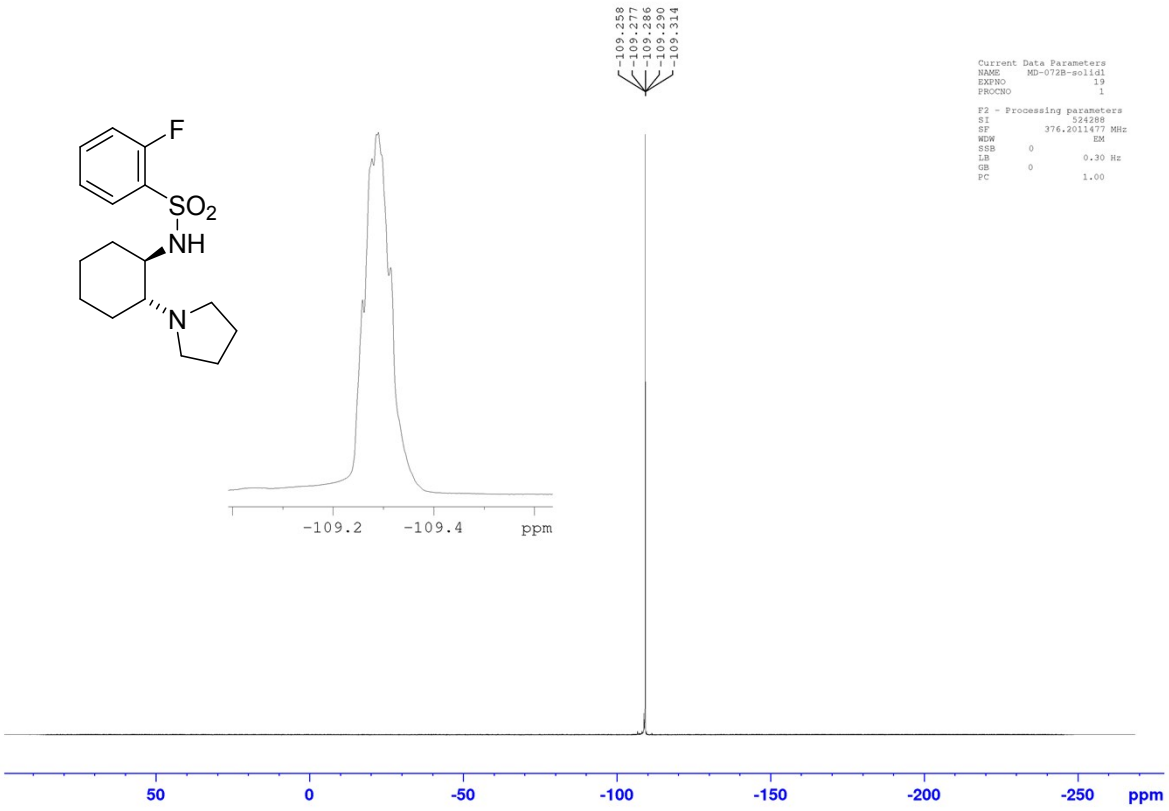


Figure S61. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for catalyst **1m**

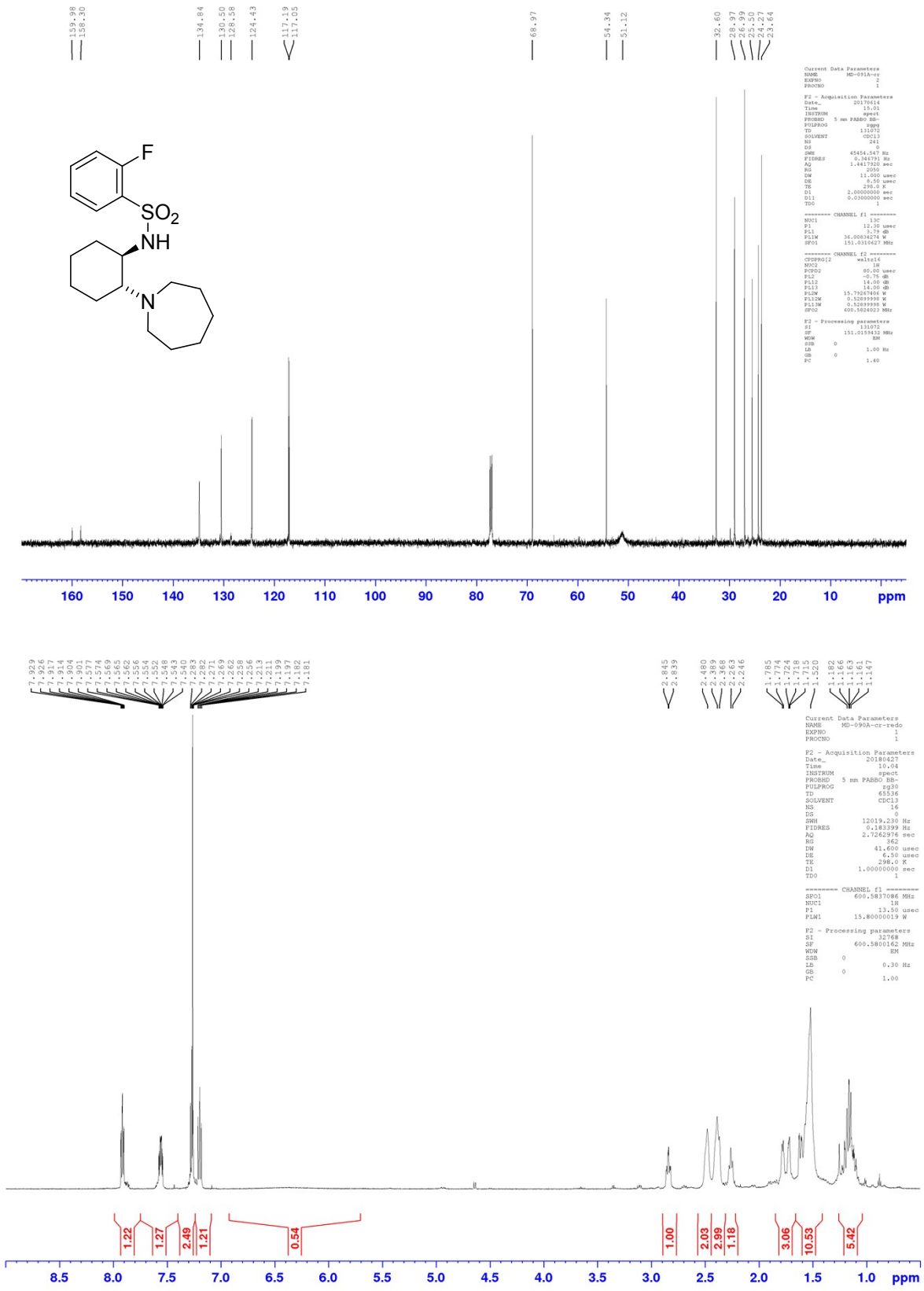


Figure S62. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **3m**

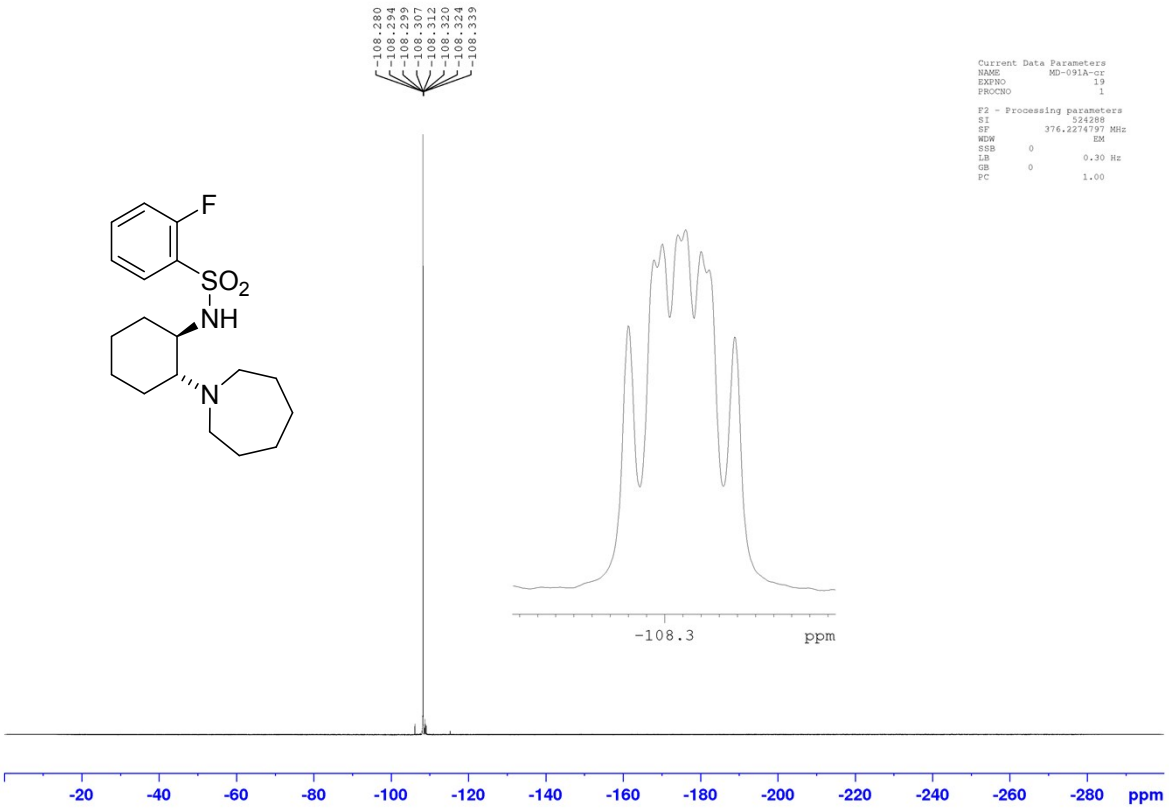


Figure S63. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for catalyst **3m**

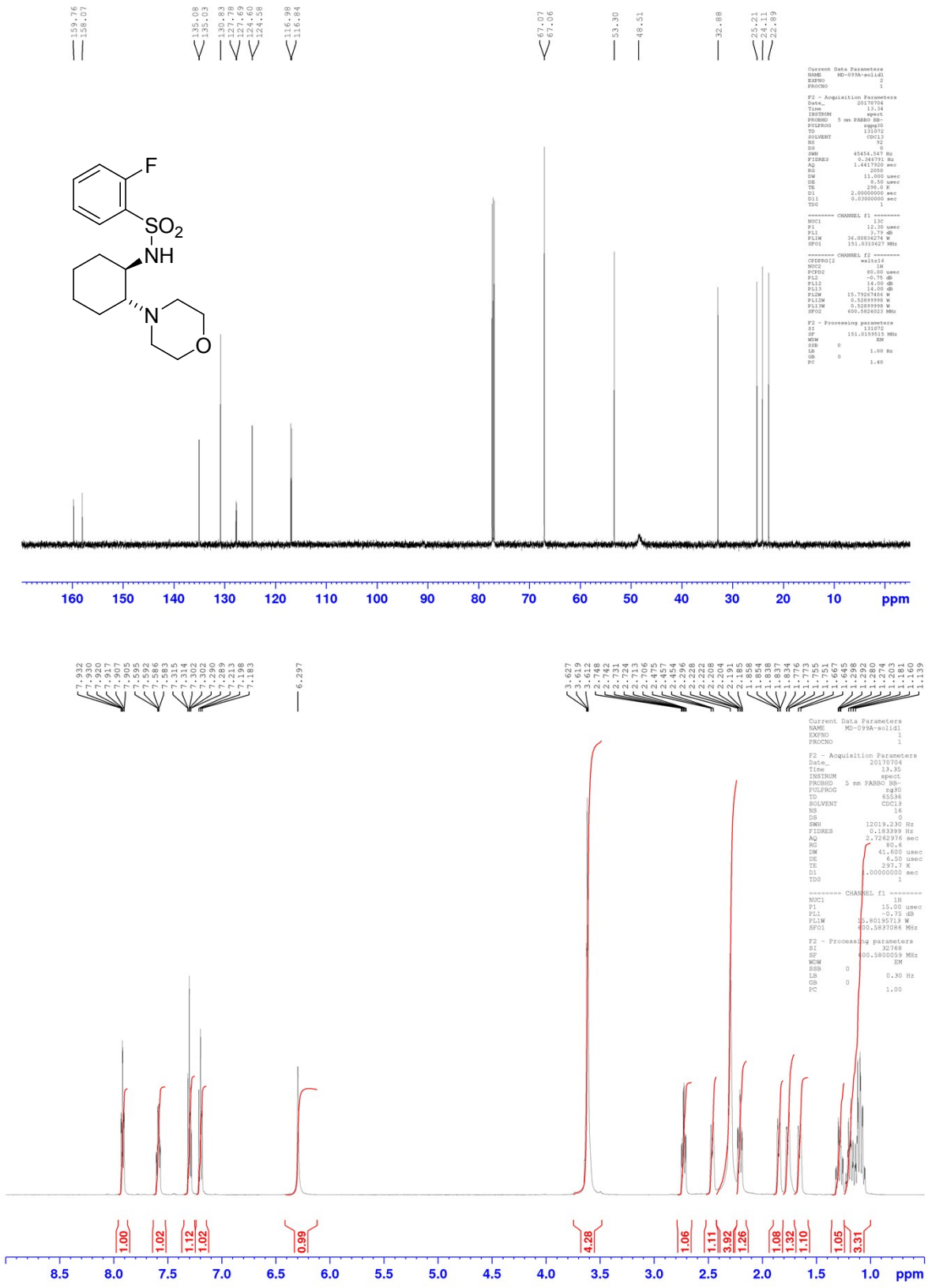


Figure S64. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **4m**

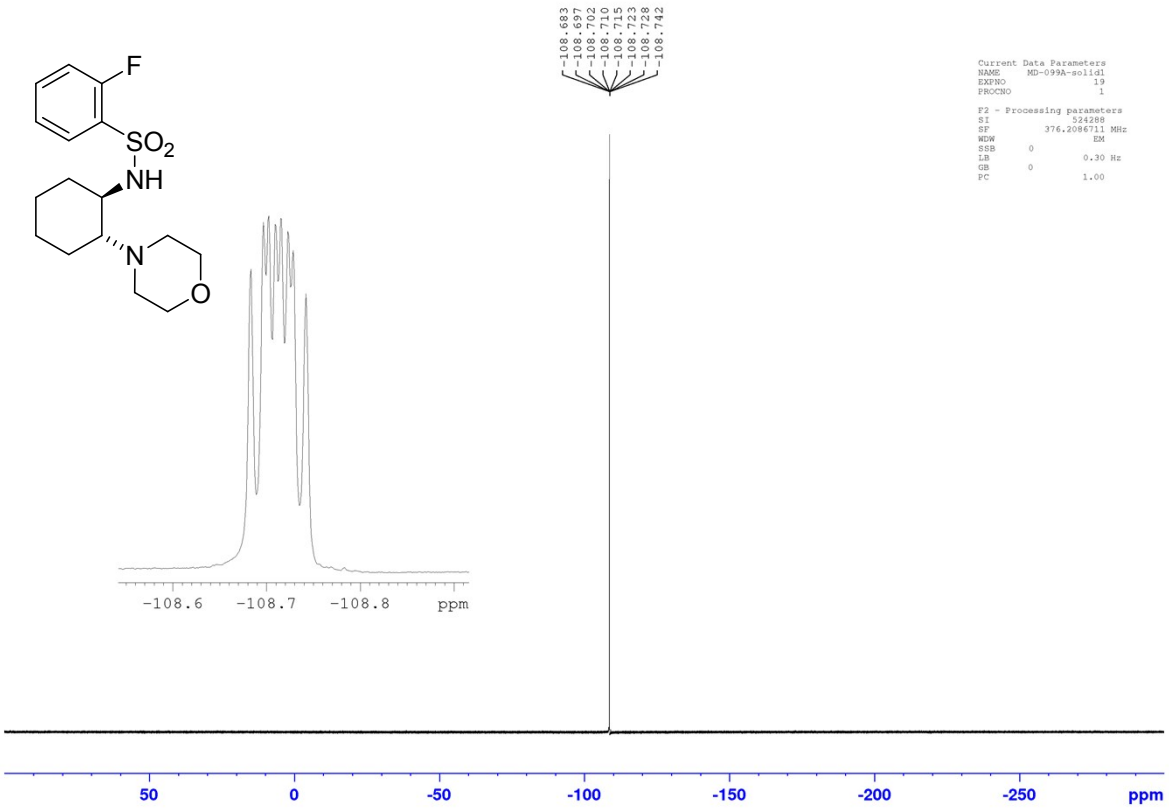


Figure S65. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for catalyst **4m**

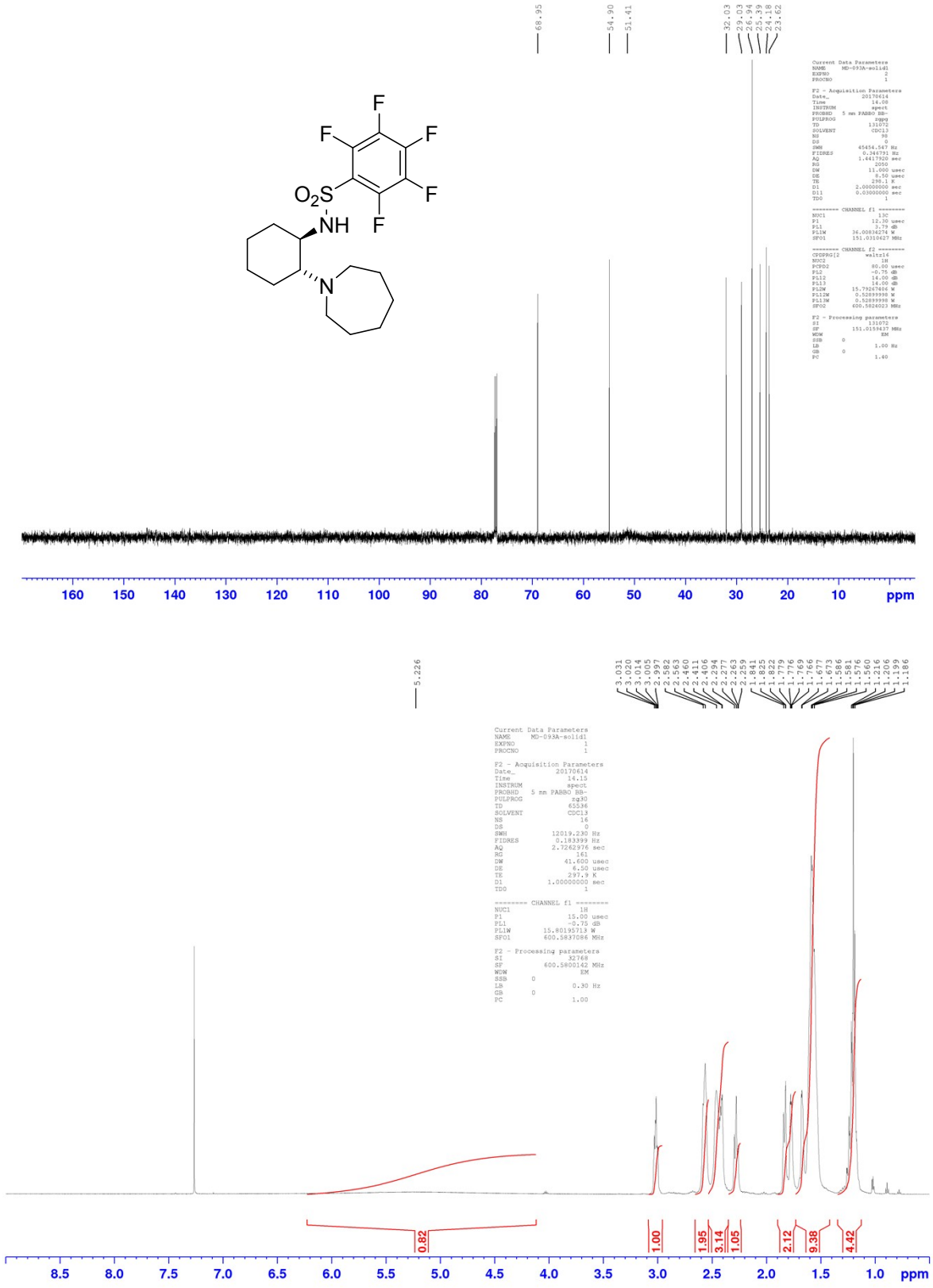


Figure S66. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **3p**

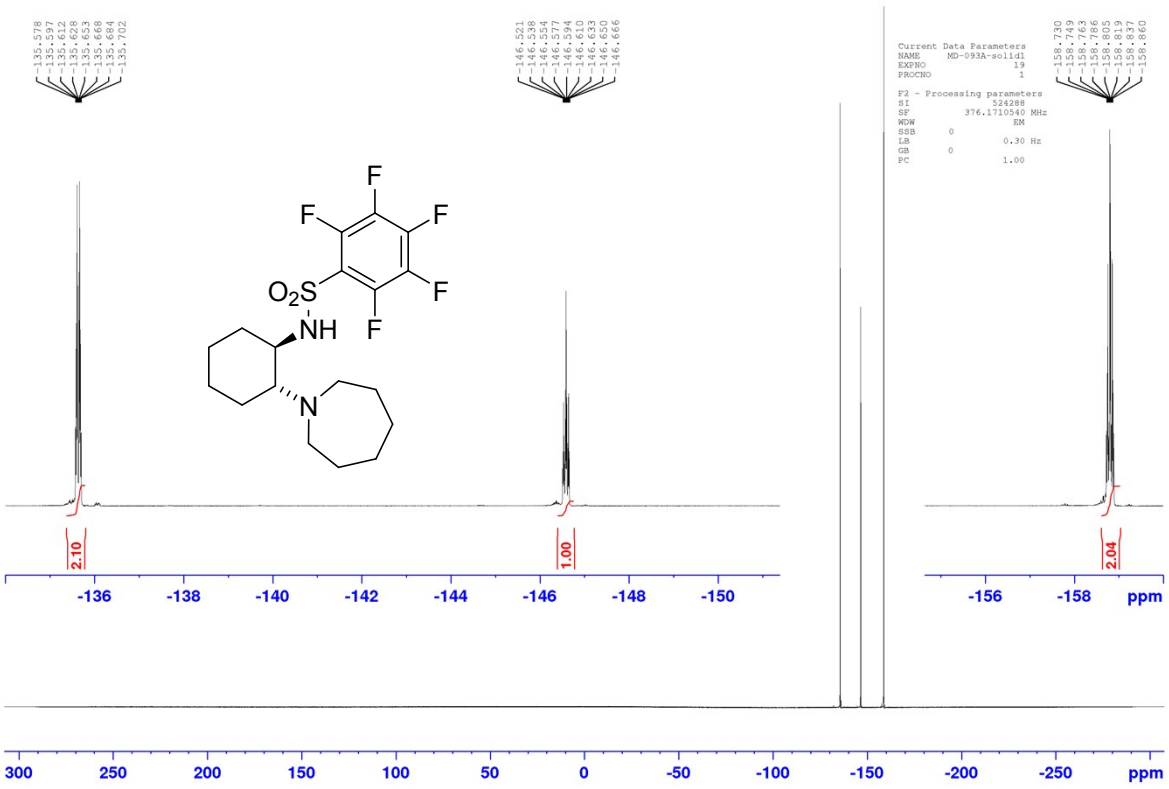


Figure S67. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for catalyst **3p**

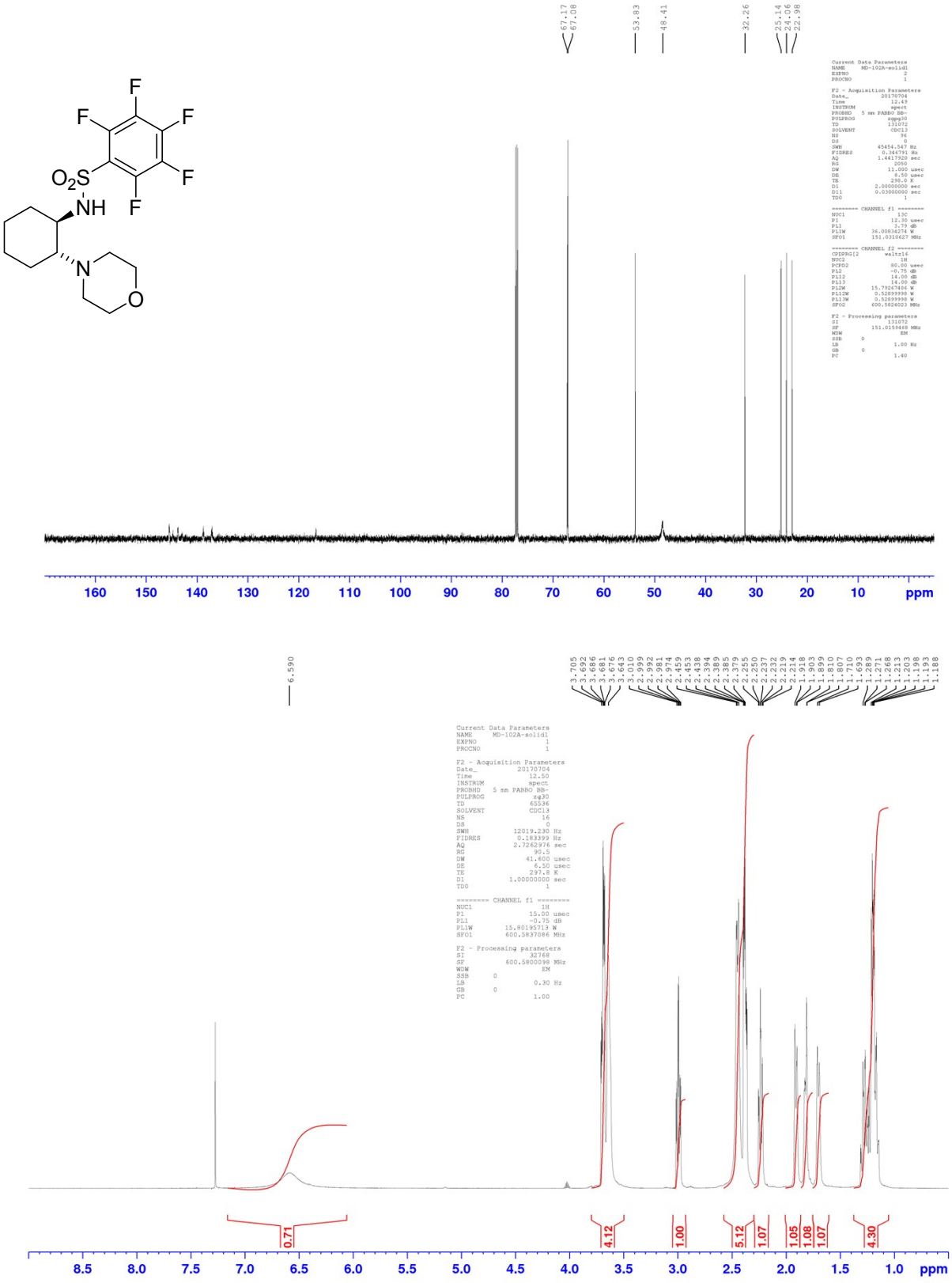


Figure S68. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **4p**

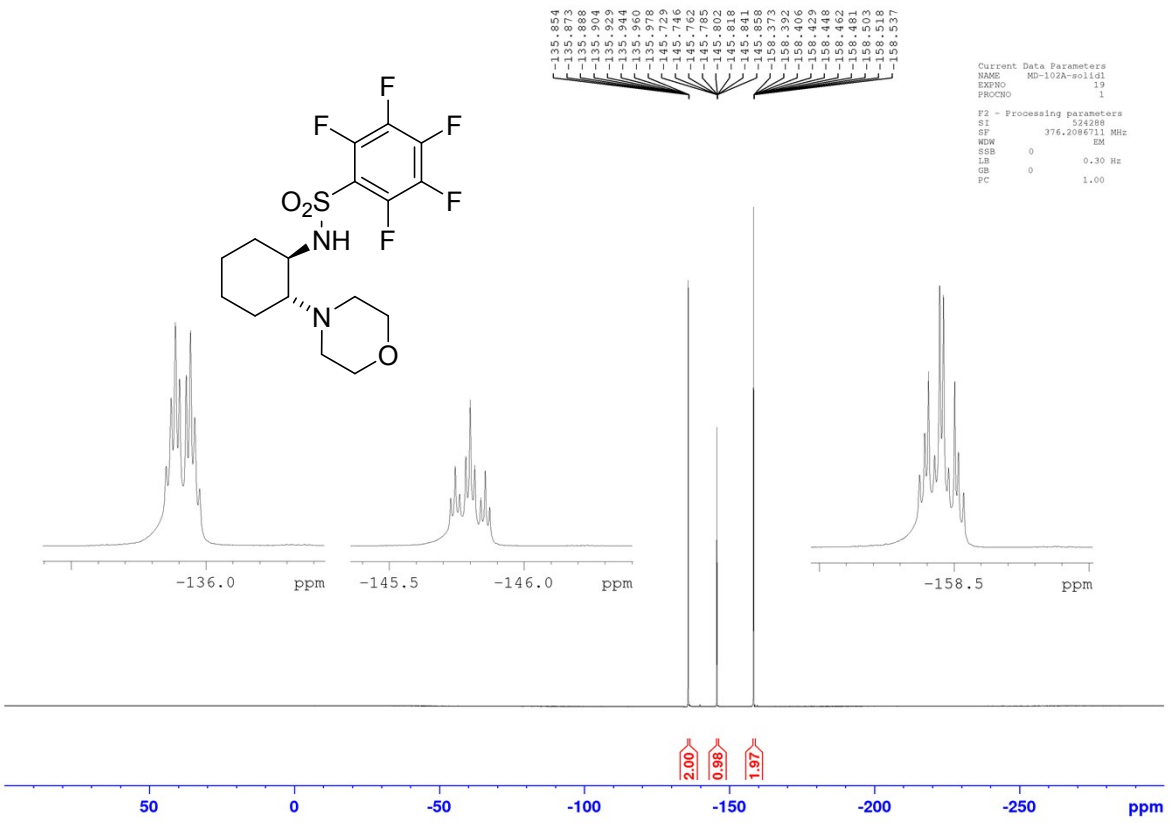


Figure S69. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for catalyst **4b**

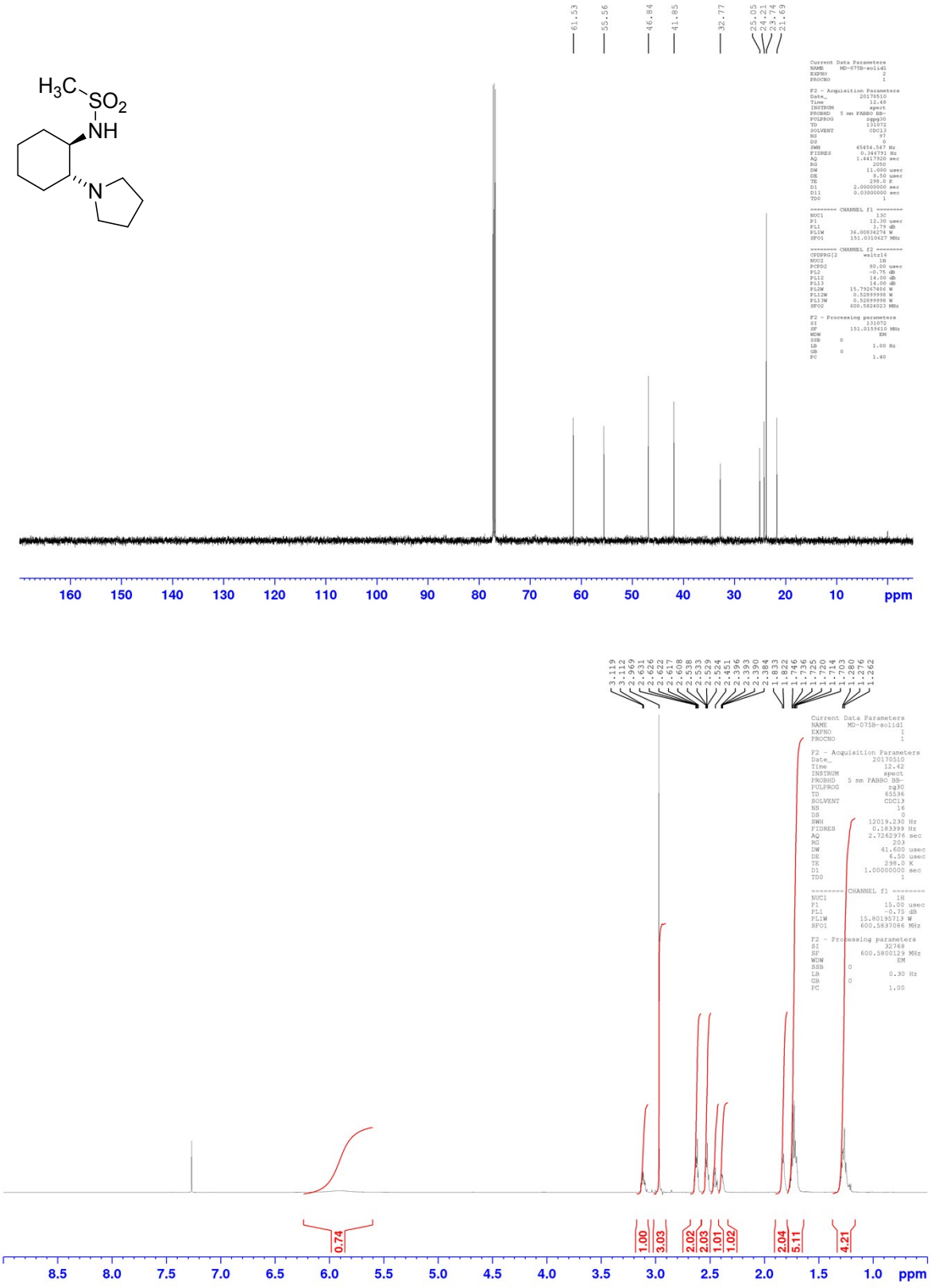


Figure S70. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **1t**

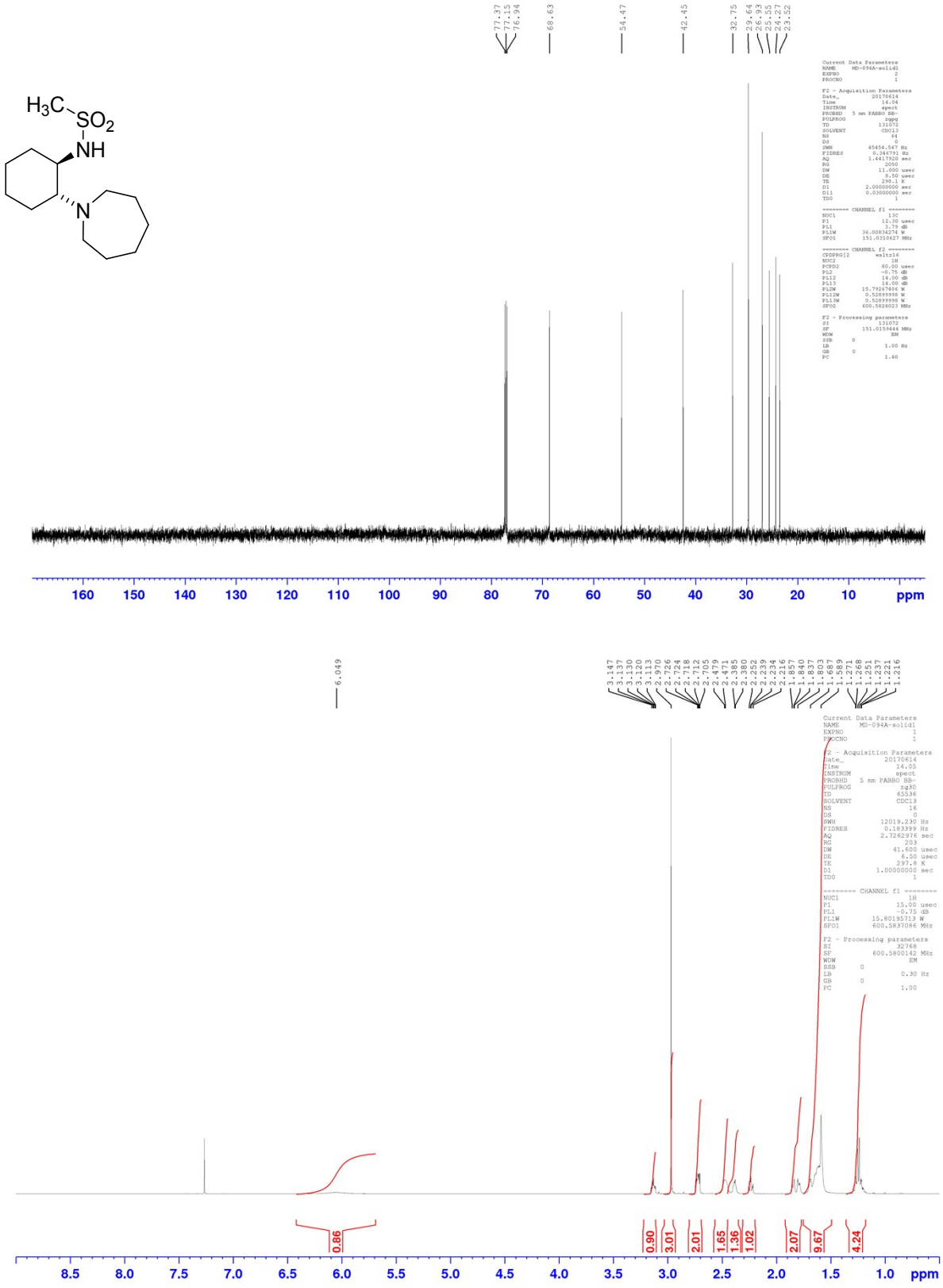


Figure S71. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **3t**

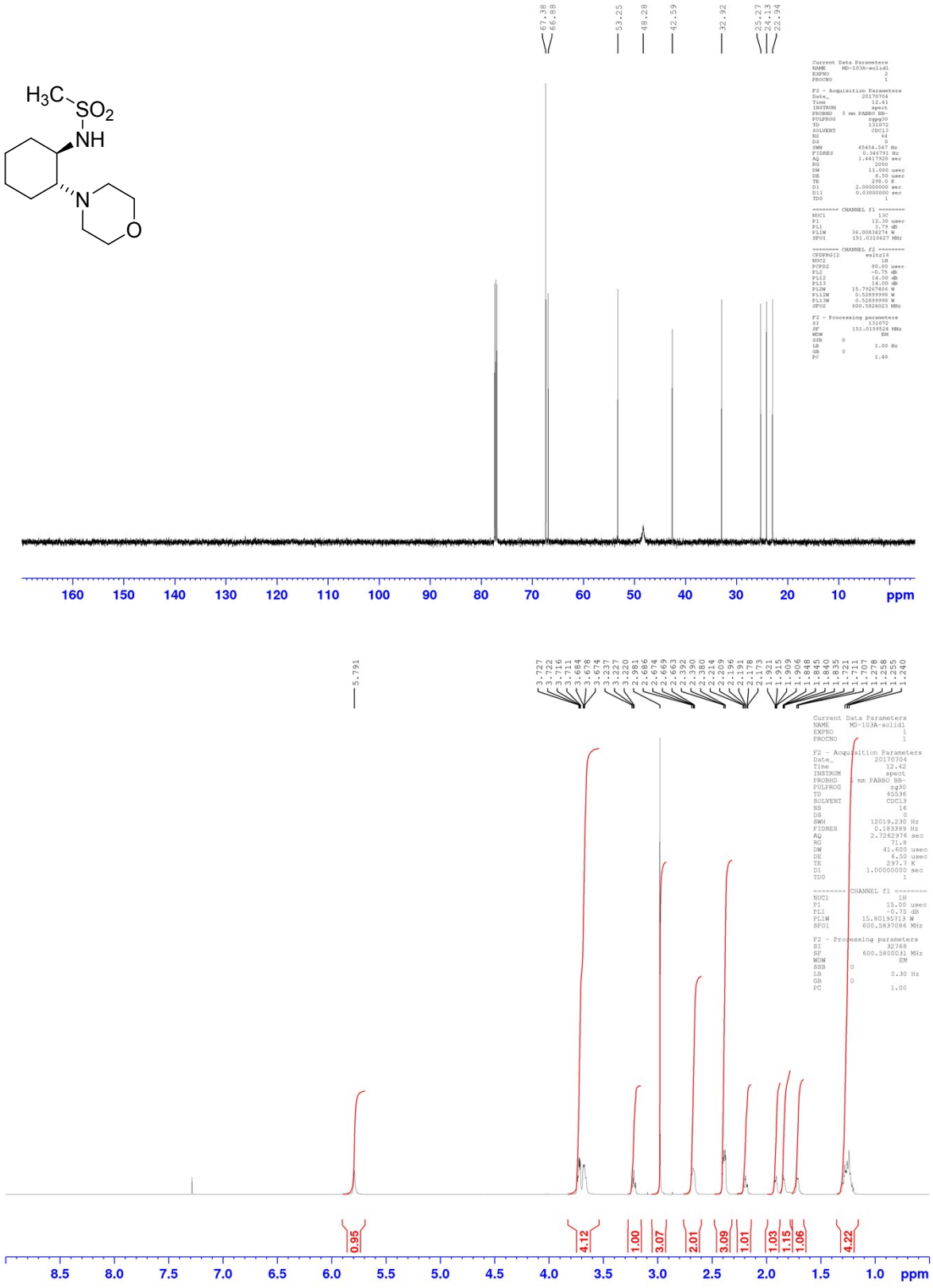


Figure S72. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalyst **4t**

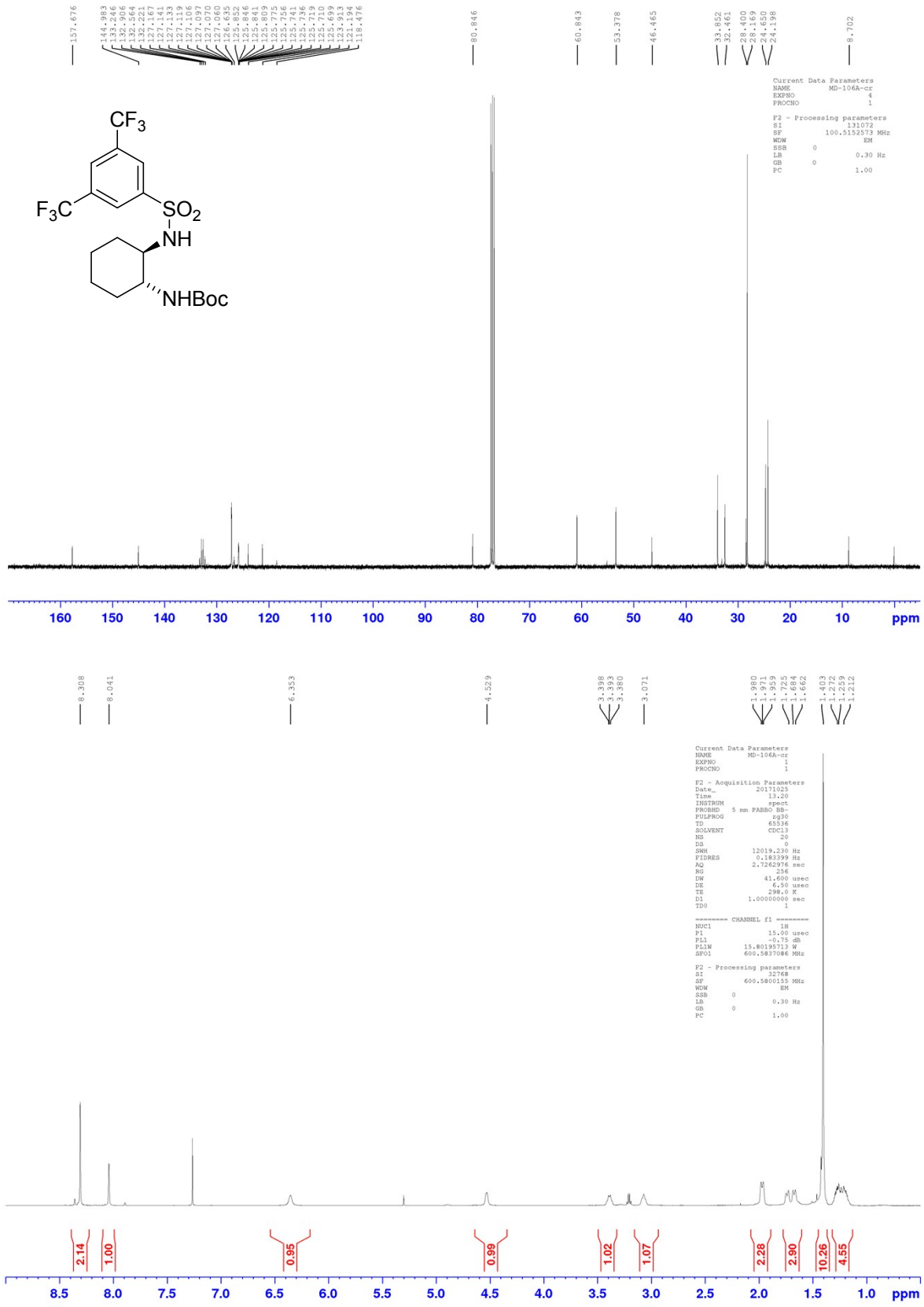


Figure S73. ^{13}C and ^{1}H NMR spectra (101 MHz, 600 MHz, $CDCl_3$) for intermediate **14**: *N*-((1*R*,2*R*)-2-(Boc-amino)cyclohexyl-3,5-bis(trifluoromethyl)benzenesulfonamide

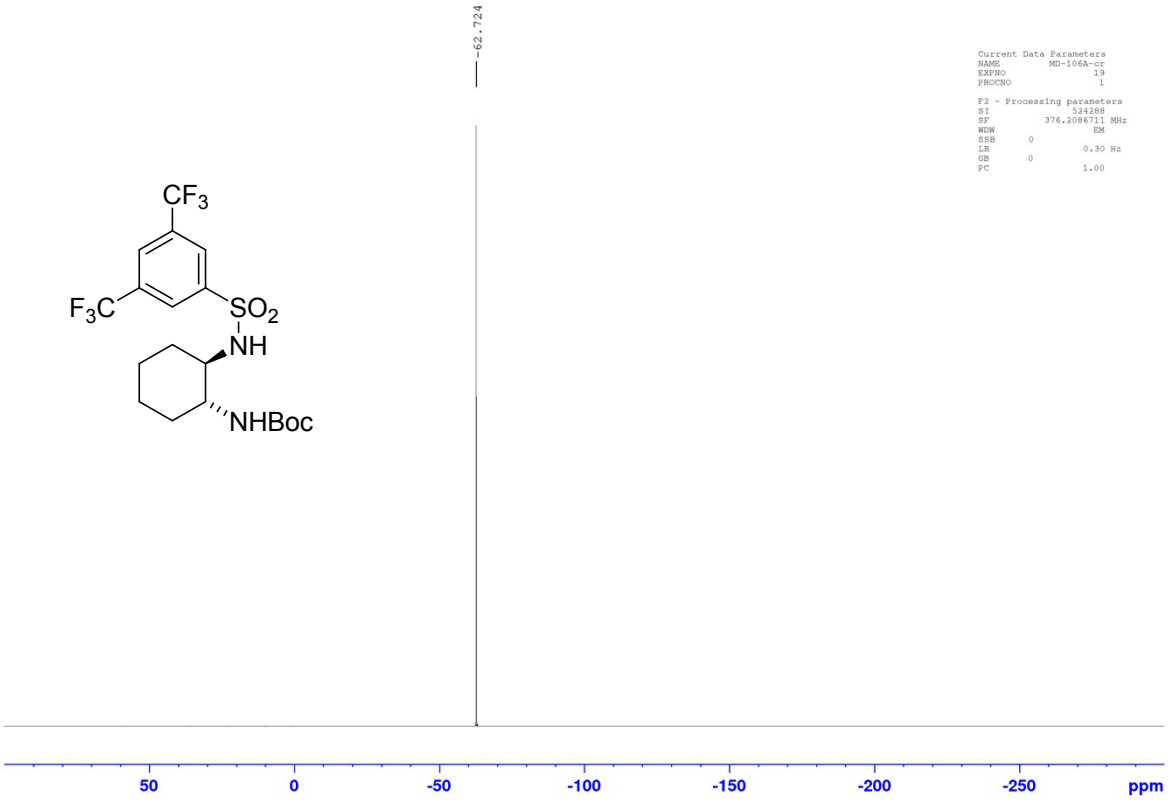


Figure S74. ^{19}F NMR spectrum (376 MHz, $CDCl_3$) for intermediate **14**: *N*-((1*R*,2*R*)-2-(Boc-amino)cyclohexyl-3,5-bis(trifluoromethyl)benzenesulfonamide

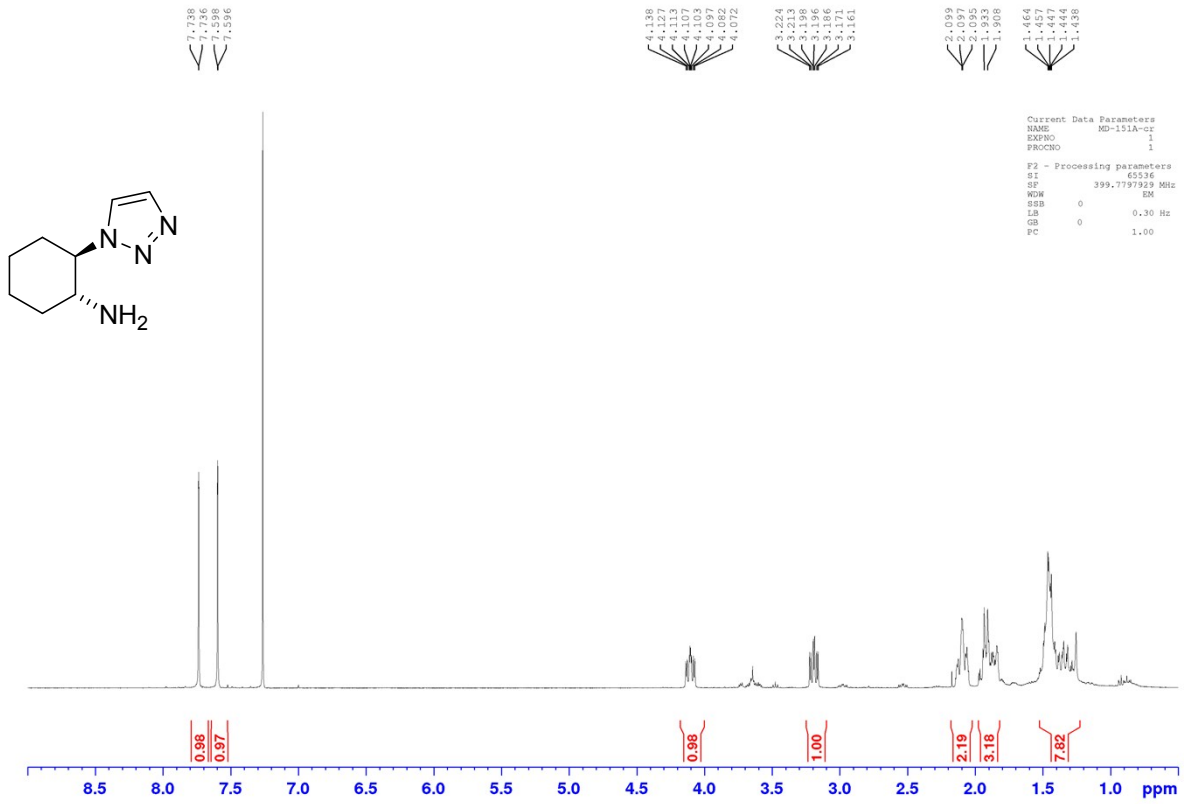


Figure S75. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) for intermediate **17**: (1*R*,2*R*)-2-(1,2,3-triazol-1-yl)-cyclohexaneamine

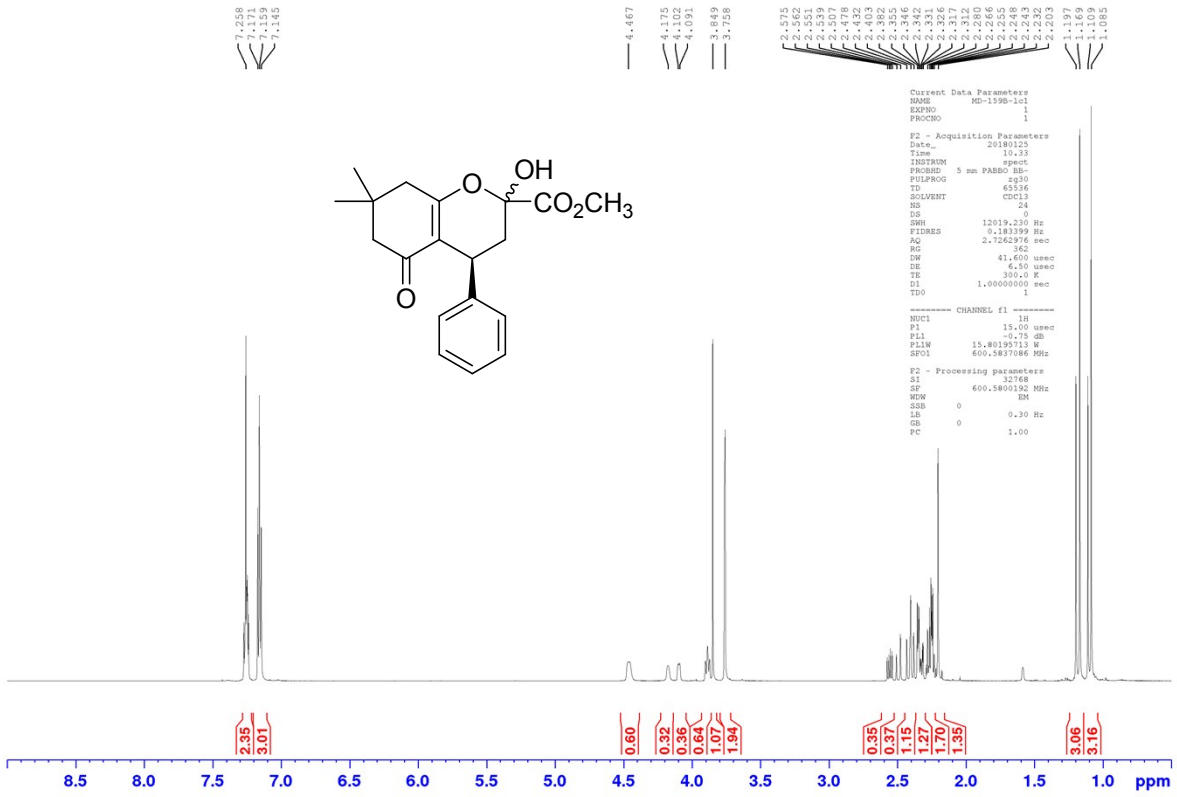


Figure S76. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) for catalytic product **11a** (*cf.* Note on page S36)

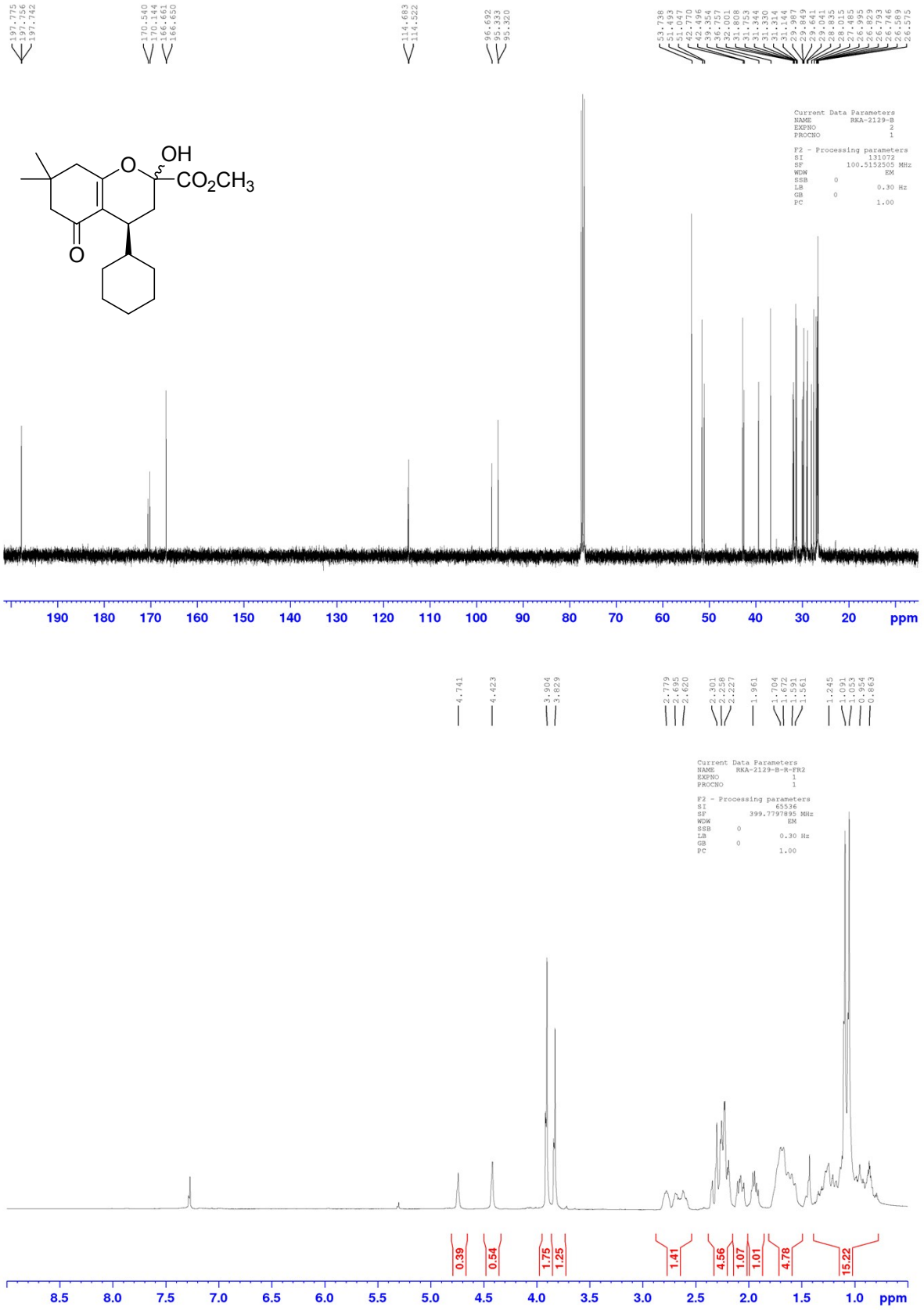


Figure S77. ^{13}C and ^{1}H NMR spectra (101 MHz, 400 MHz, $CDCl_3$) for catalytic product **11b** (*cf.* Note on page S36)

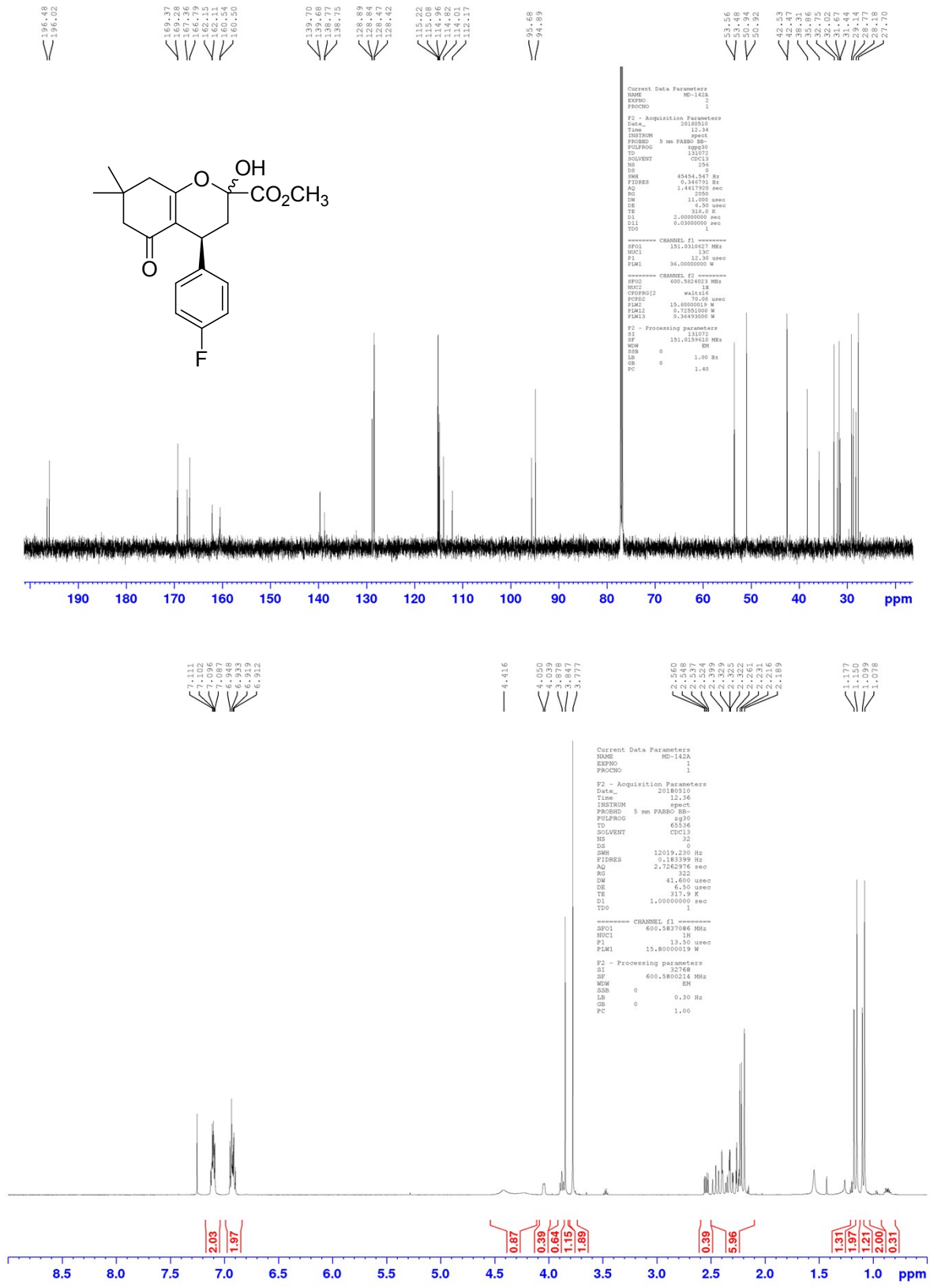


Figure S78. ^{13}C and ^{1}H NMR spectra (151 MHz, 600 MHz, $CDCl_3$) for catalytic product **11c** (*cf.* Note on page S36)

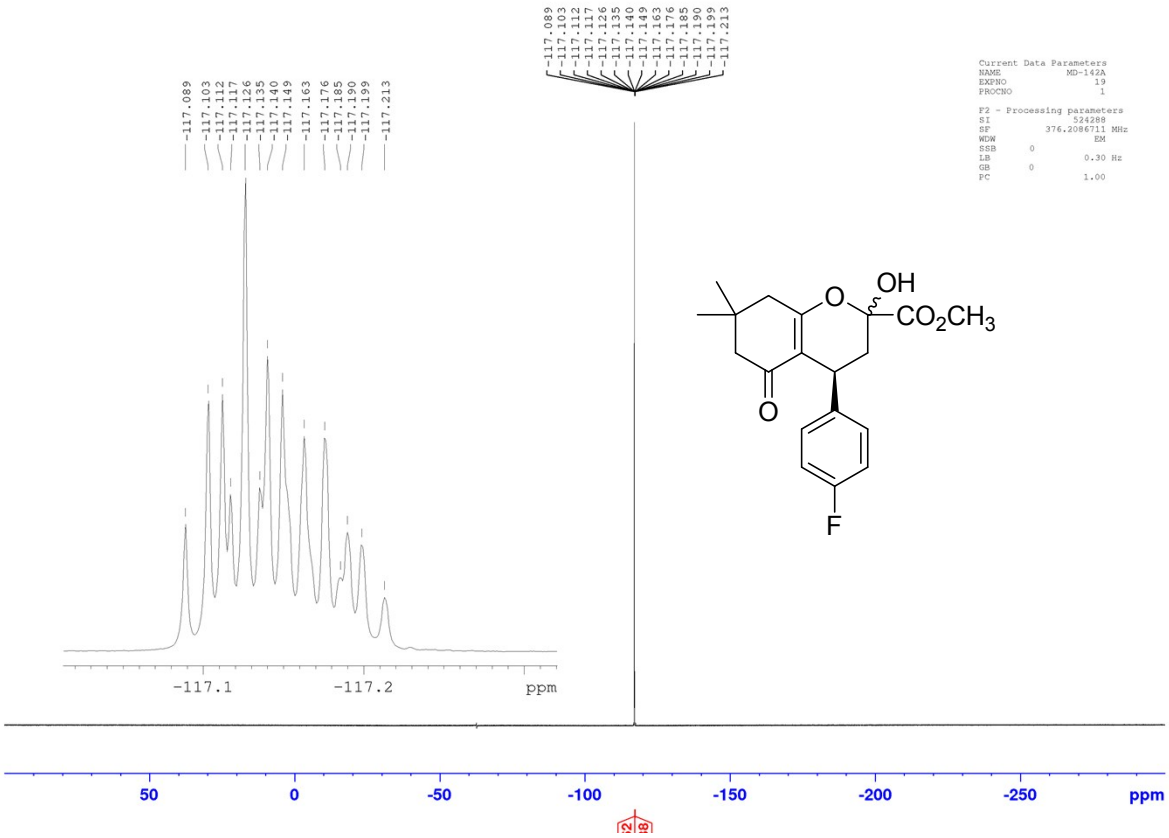


Figure S79. ^{19}F NMR (376MHz, $CDCl_3$) spectrum for **11c**

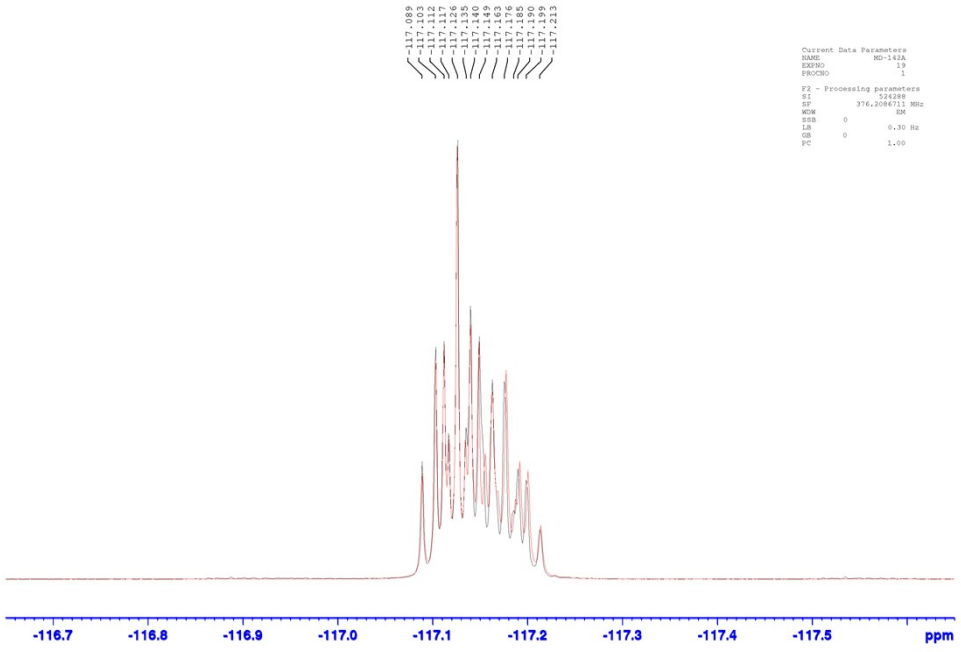


Figure S80. Overlay of experimental ^{19}F NMR (376 MHz, $CDCl_3$) spectrum for **11c** (black) and NMR simulation assuming following parameters: -117.126 (tt, J =8.6, 5.2 Hz, 1 F, linewidth 1.1 Hz), -117.176 (tt, J =8.6, 5.2 Hz, 0.66 F, 1.4 Hz), corresponding to two anomers (*cf*. Note on page S36)

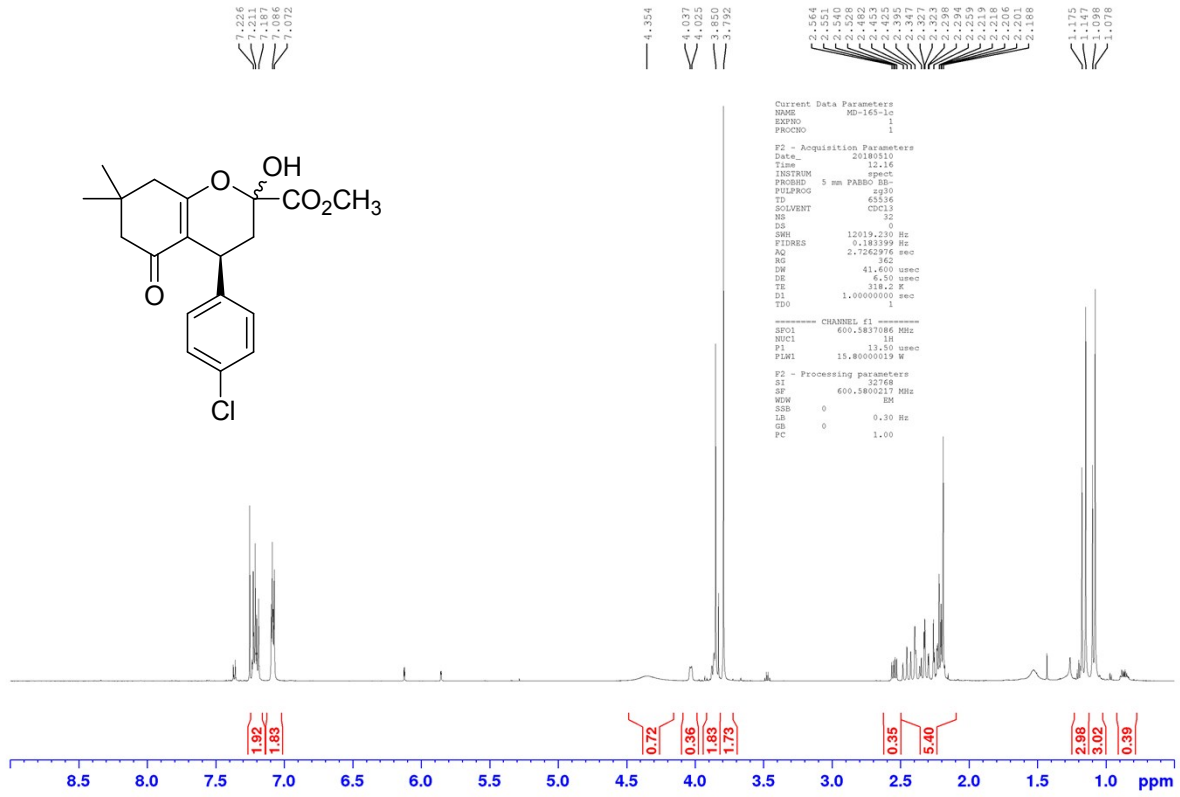


Figure S81. ^{1}H NMR spectrum (600 MHz, $CDCl_3$) for catalytic product **11d** (*cf.* Note on page S36)

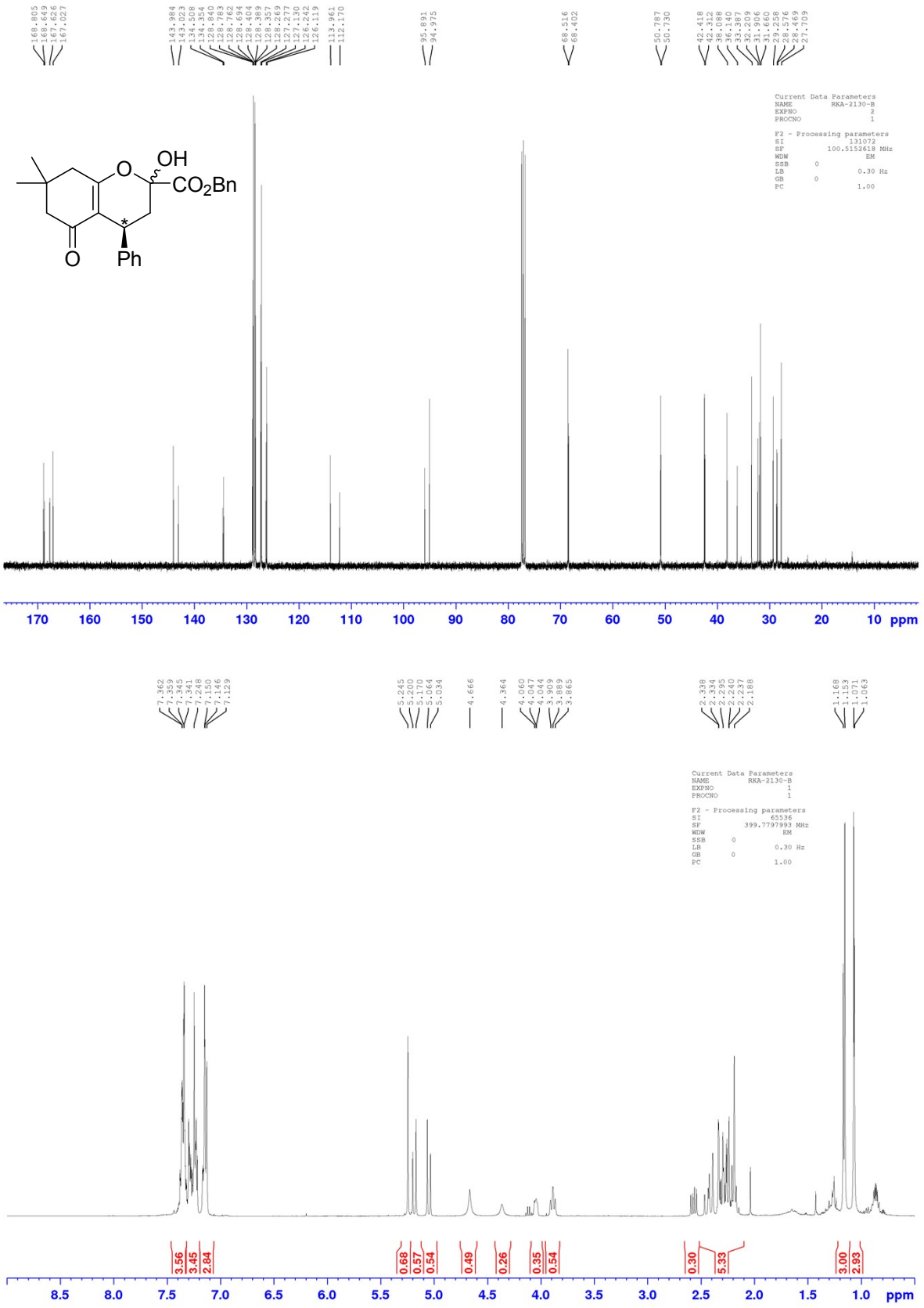


Figure S82. ^{13}C and ^{1}H NMR spectra (101 MHz, 400 MHz, $CDCl_3$) for catalytic product **11e** (*cf.* Note on page S36)

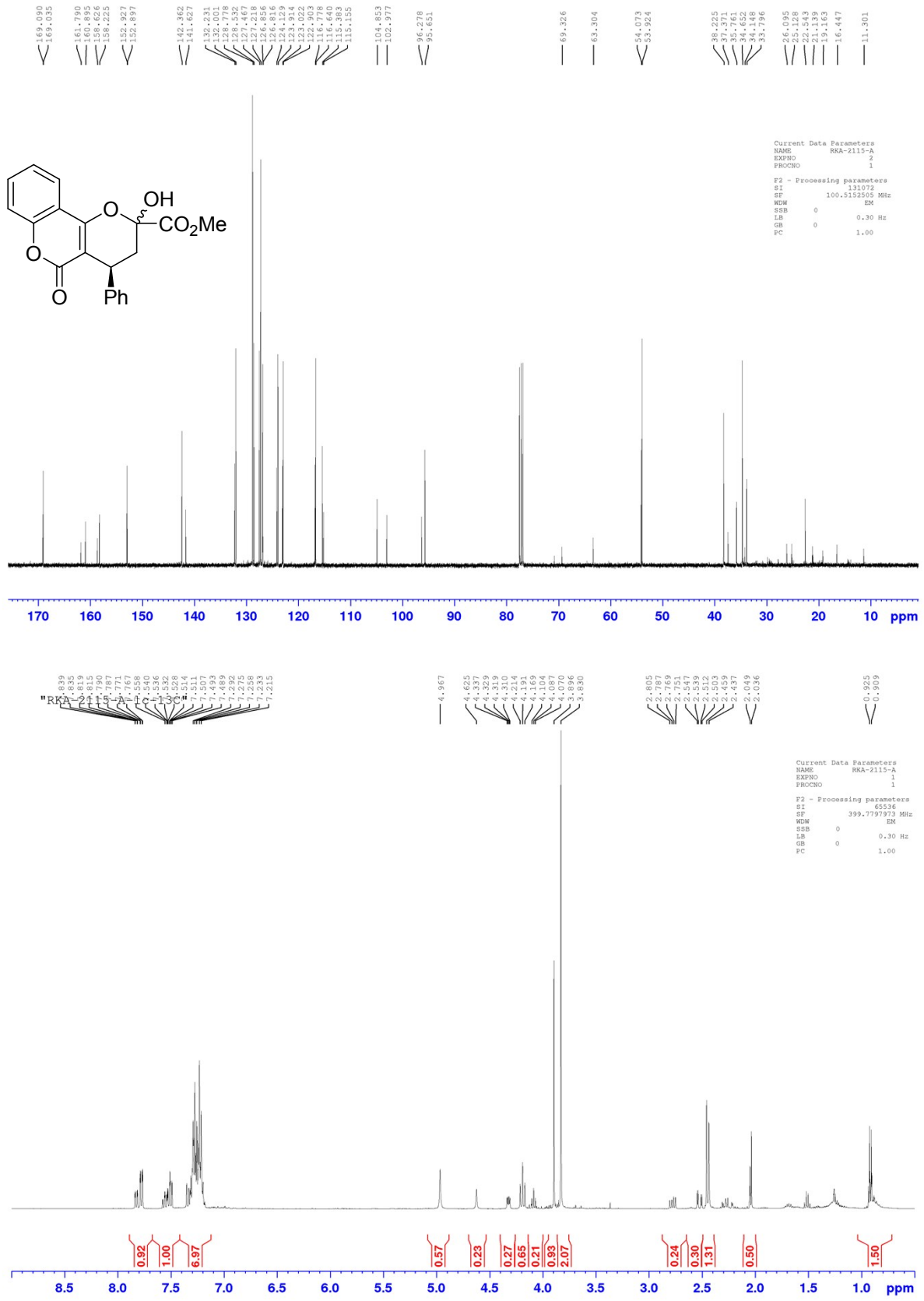


Figure S83. ^{13}C and ^{1}H NMR spectra (101 MHz, 400 MHz, $CDCl_3$) for catalytic product **11f** (*cf*. Note on page S36)

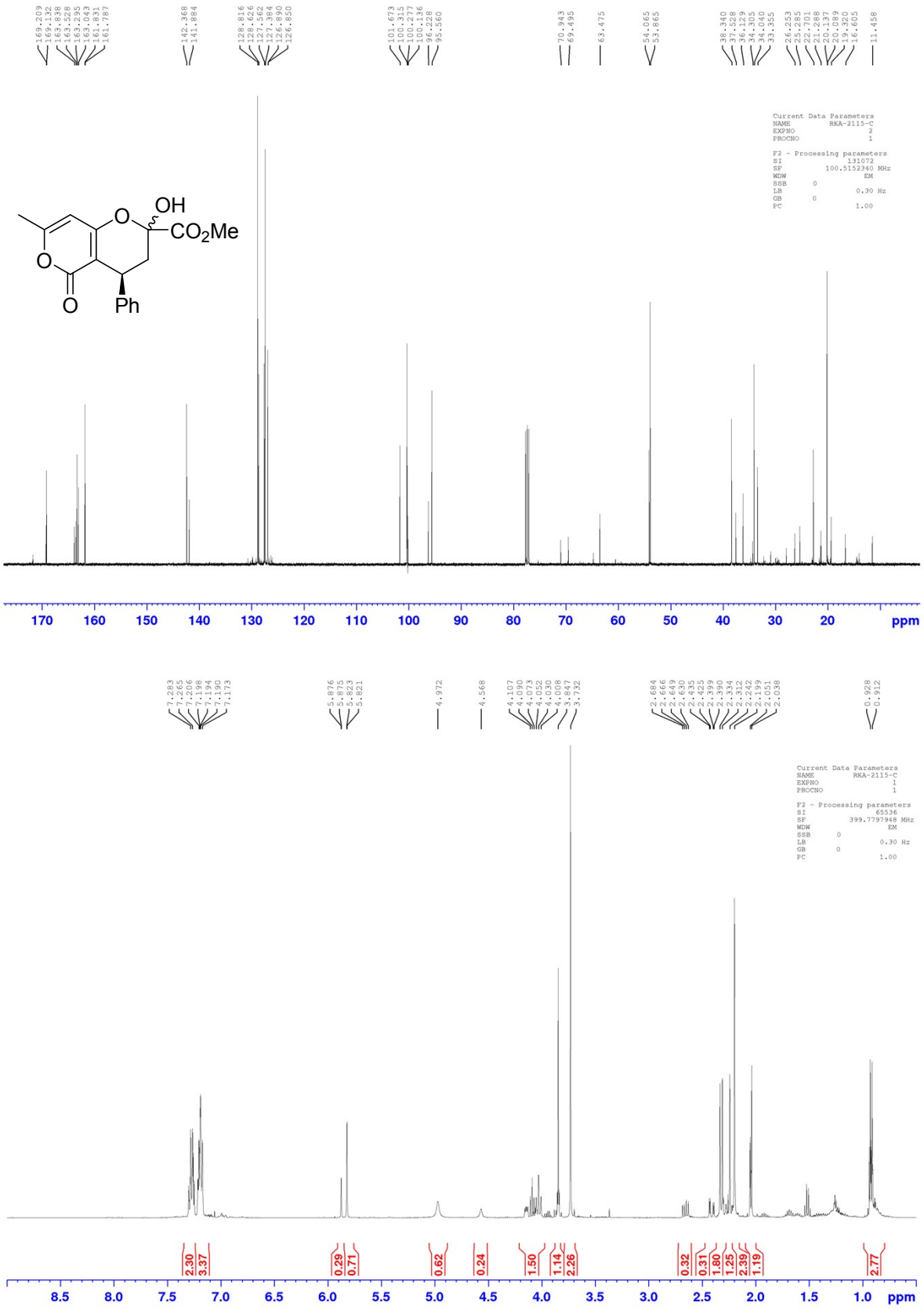


Figure S84. ^{13}C and ^{1}H NMR spectra (101 MHz, 400 MHz, $CDCl_3$) for catalytic product **11g** (*cf.* Note on page S36)

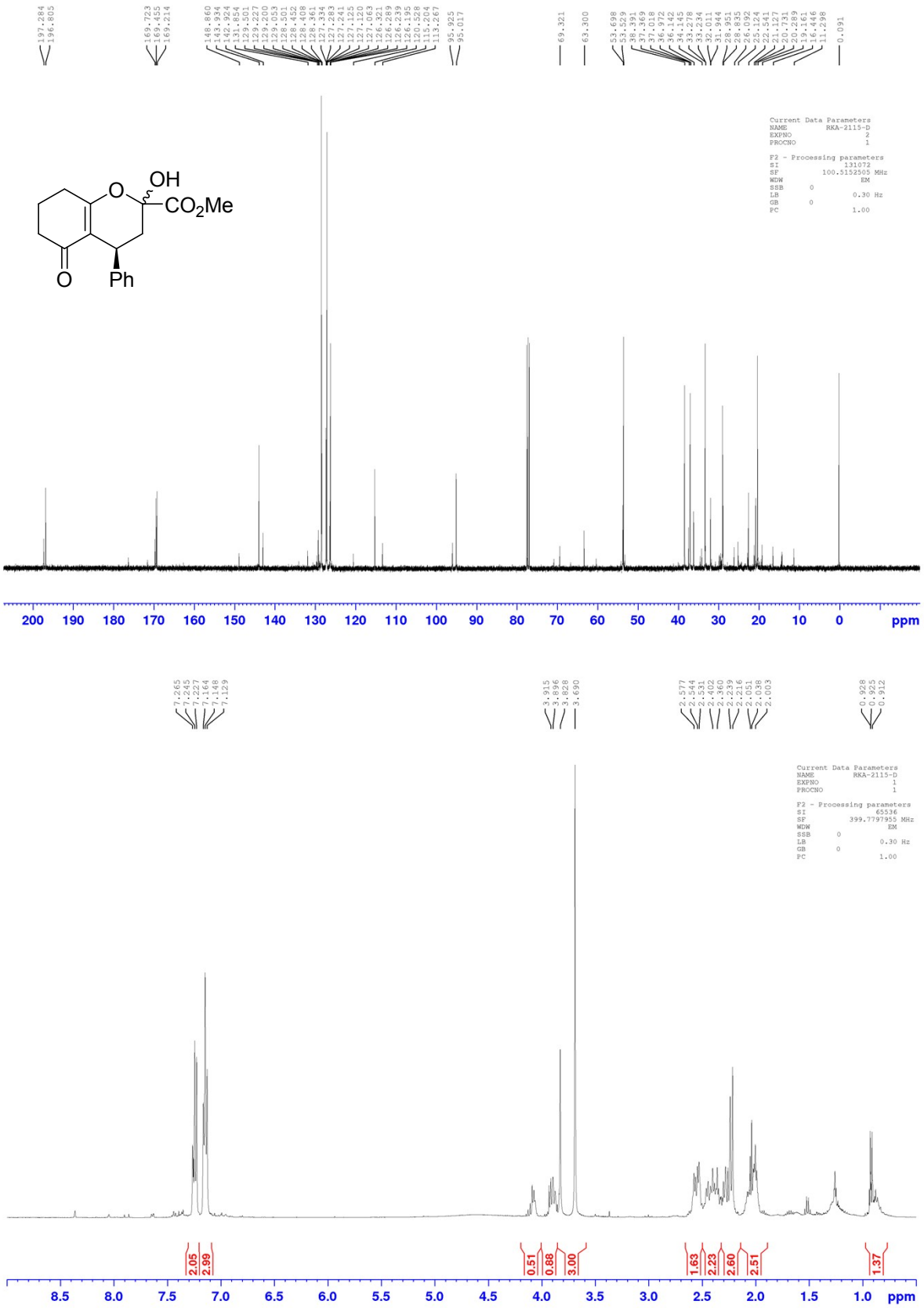


Figure S85. ^{13}C and ^{1}H NMR spectra (101 MHz, 400 MHz, $CDCl_3$) for catalytic product **11h** (*cf.* Note on page S36)

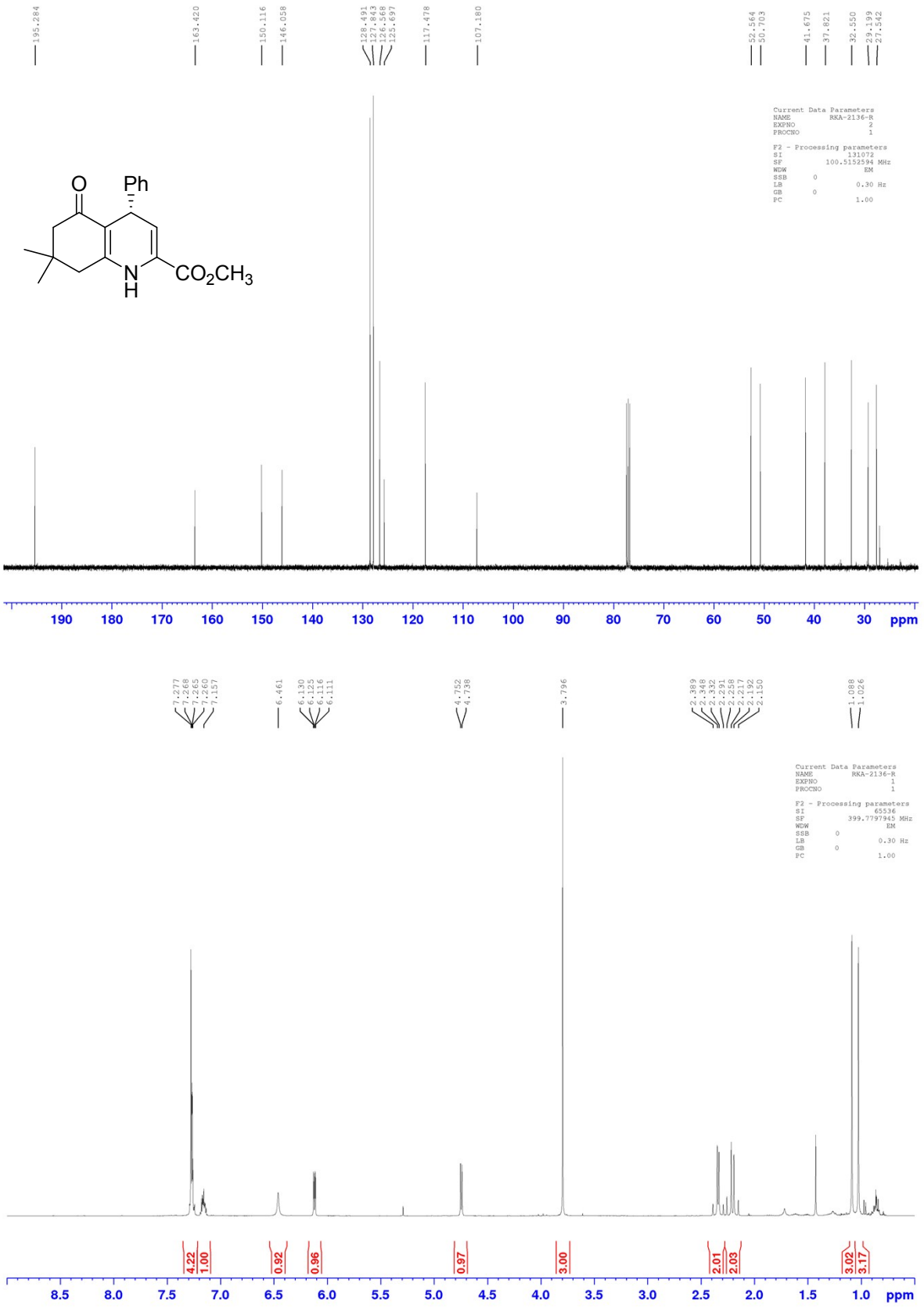


Figure S86. ^{13}C and ^{1}H NMR spectra (101 MHz, 400 MHz, $CDCl_3$) for end product **12**

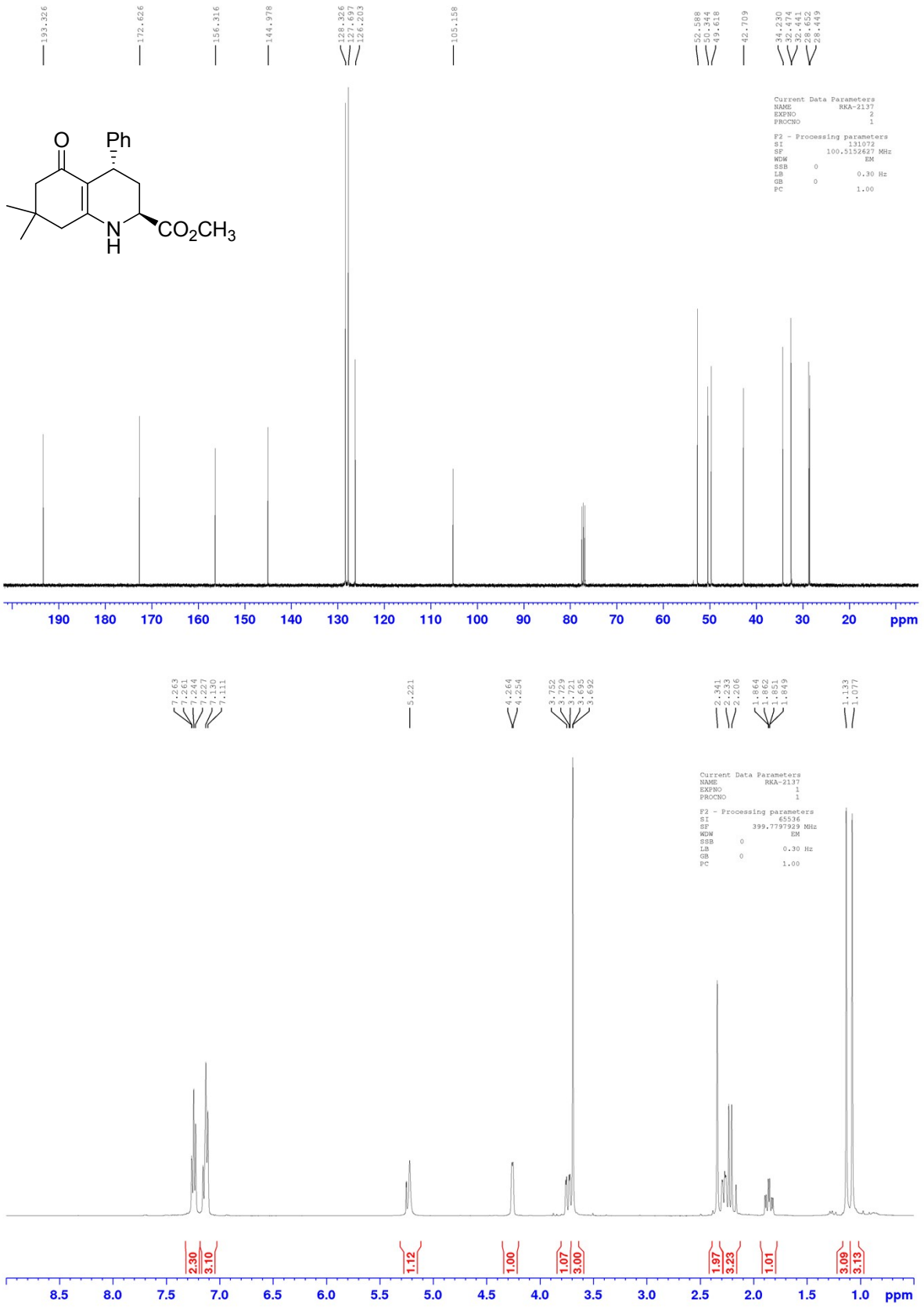
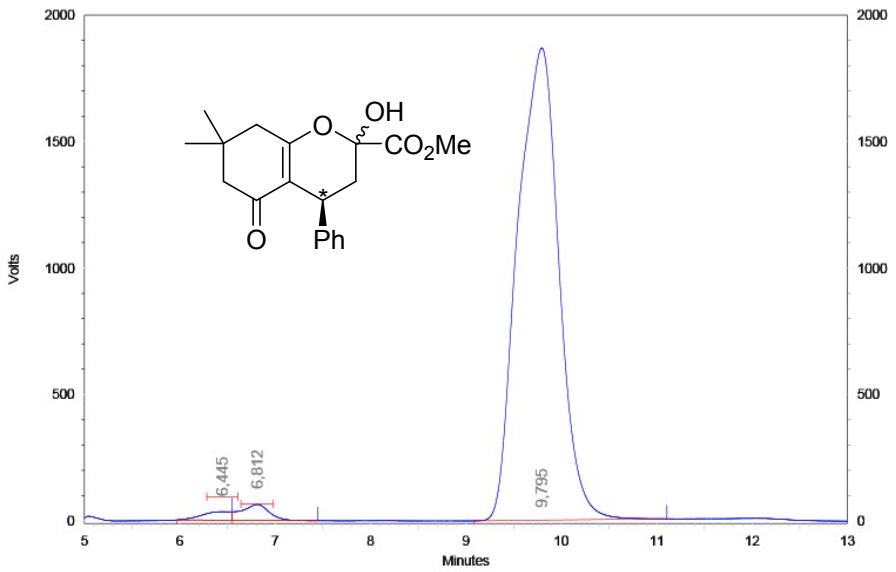


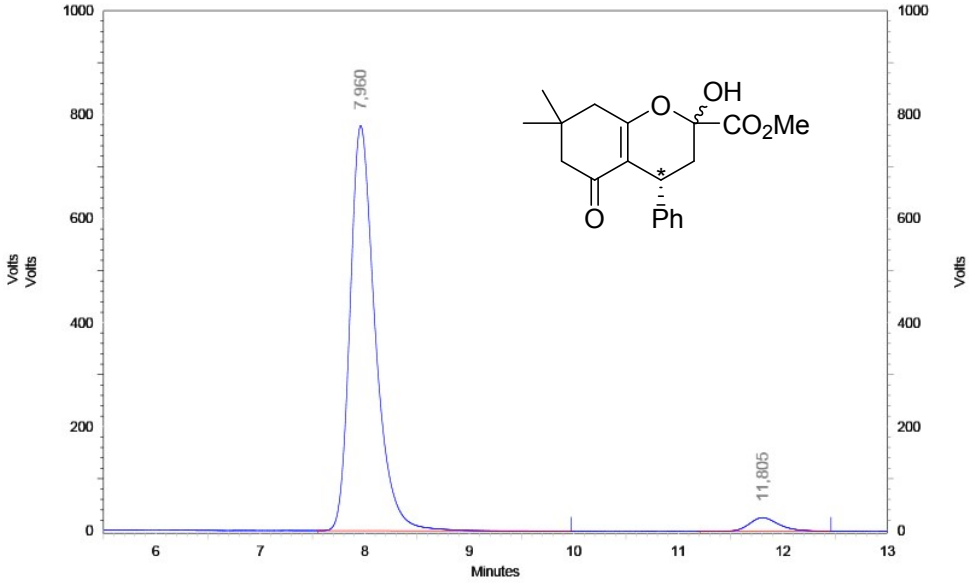
Figure S87. ^{13}C and ^{1}H NMR spectra (101 MHz, 400 MHz, $CDCl_3$) for end product **13**

Chiral HPLC chromatograms



UV2000-254nm Results (System (2018-05-04 10:04:05) (Reprocessed))

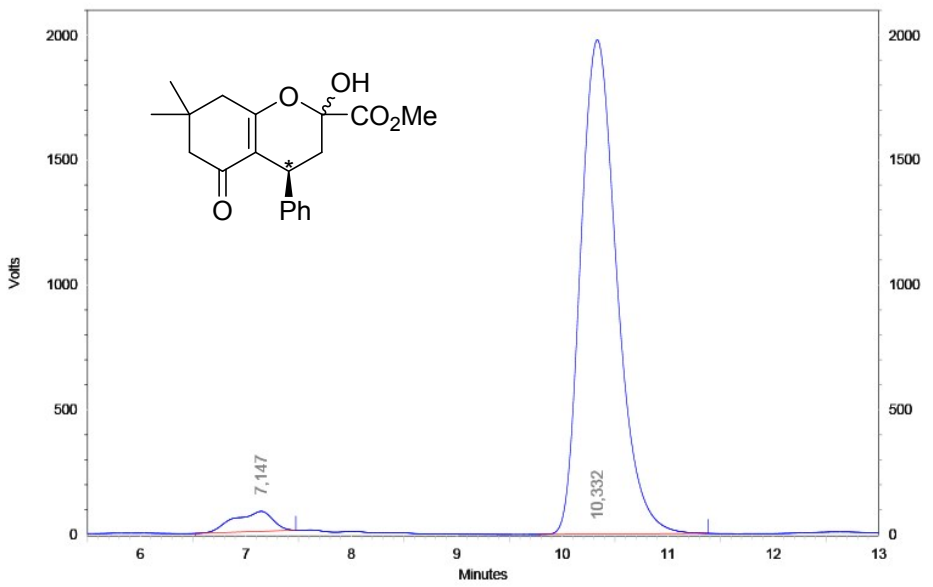
Retention Time	Area	Area %	Height	Height %
6,445	692329	1,20	33396	1,70
6,812	1276038	2,20	62926	3,20
9,795	55909361	96,60	1867053	95,09
Totals	57877728	100,00	1963375	100,00

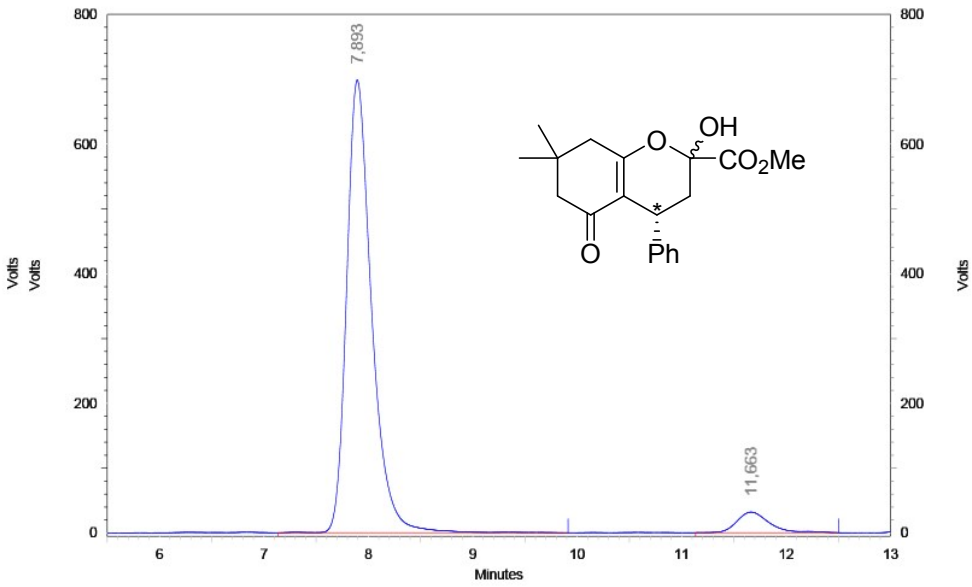


UV2000-254nm Results (System (2018-06-08 15:38:49) (Original))

Retention Time	Area	Area %	Height	Height %
7,960	13004919	96,20	778829	96,76
11,805	514200	3,80	26089	3,24
Totals	13519119	100,00	804918	100,00

Figure S88. HPLC chromatograms (Chiralpak AD-H, 4.6 mm ID × 250 mm, hexane/2-propanol 7:3, 0.7 mL/min) for adduct **11a** obtained from methyl benzylidenepyruvate (**9a**) and dimedone (**10**) using 10% mol catalysts **2a** (left) and ***ent*-2a** (right) in toluene. The results shown correspond to Table 1 entries 2 and 3. For HPLC chromatogram of a racemic sample, see Figure S91.





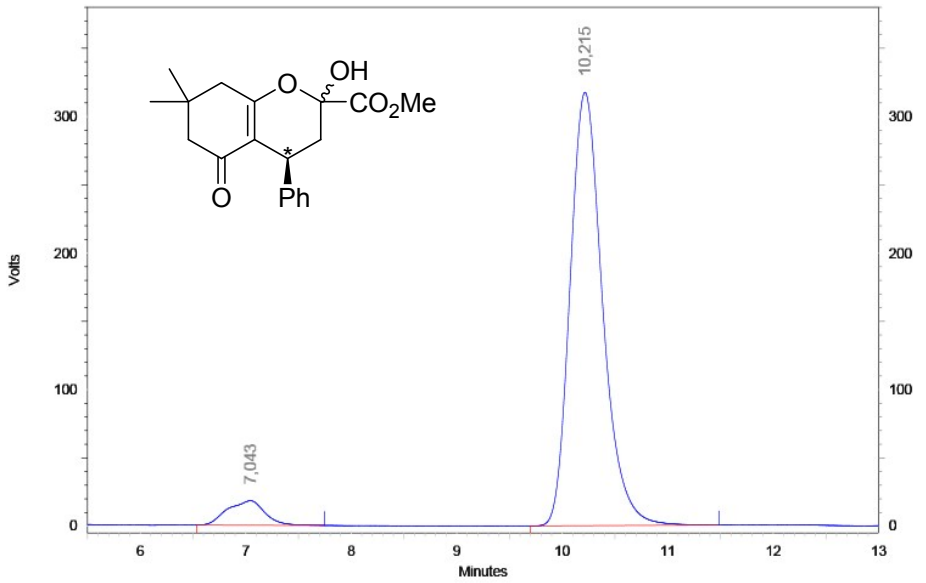
UV2000-254nm Results (System (2017-12-20 13:59:52) (Original))

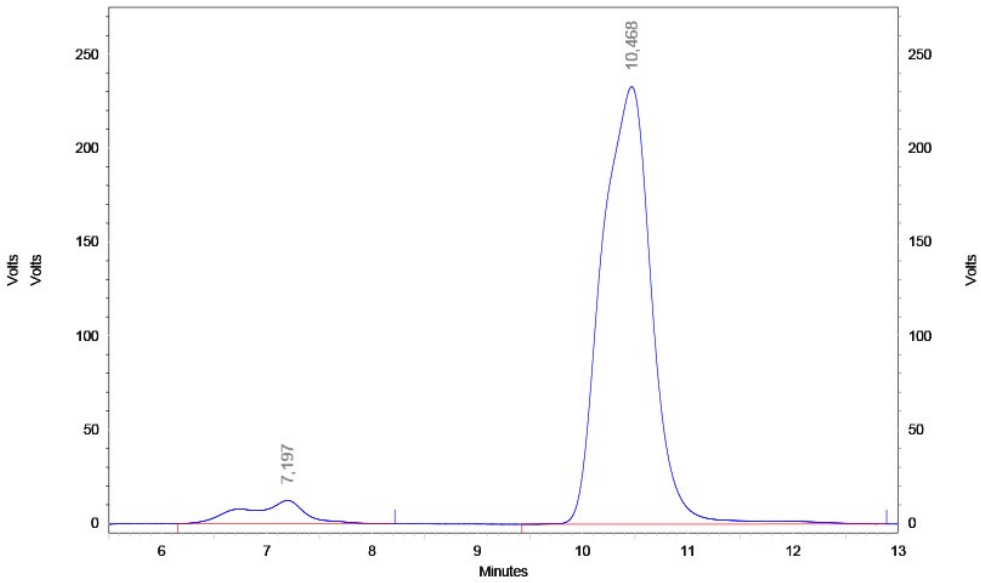
Retention Time	Area	Area %	Height	Height %
7,147	2055247	4,19	79954	3,88
10,332	47037655	95,81	1978627	96,12
Totals	49092902	100,00	2058581	100,00

UV2000-254nm Results (System (2018-06-08 15:55:45) (Original))

Retention Time	Area	Area %	Height	Height %
7,893	11590892	94,44	698117	95,65
11,663	682432	5,56	31724	4,35
Totals	12273324	100,00	729841	100,00

Figure S89. HPLC chromatograms (Chiralpak AD-H, 4.6 mm ID × 250 mm, hexane/2-propanol 7:3, 0.7 mL/min) for adduct **11a** obtained from methyl benzylidenepyruvate (**9a**) and dimedone (**10**) using 0.5 %mol catalysts **2a** (left) and ***ent*-2a** (right) in chlorobenzene at room temperature. For HPLC chromatogram of a racemic sample, see Figure S91.





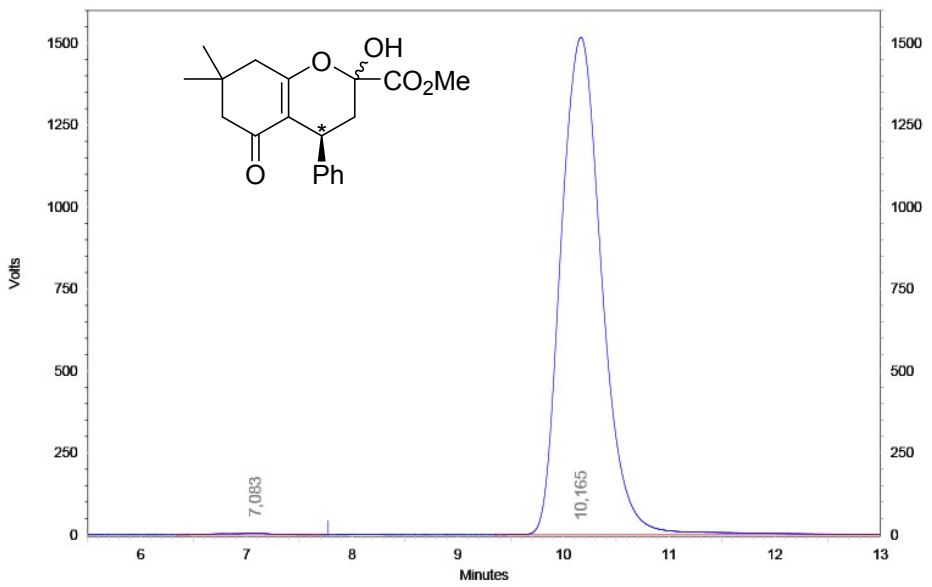
UV2000-254nm Results (System (2017-12-22 11:14:57) (Reprocessed))

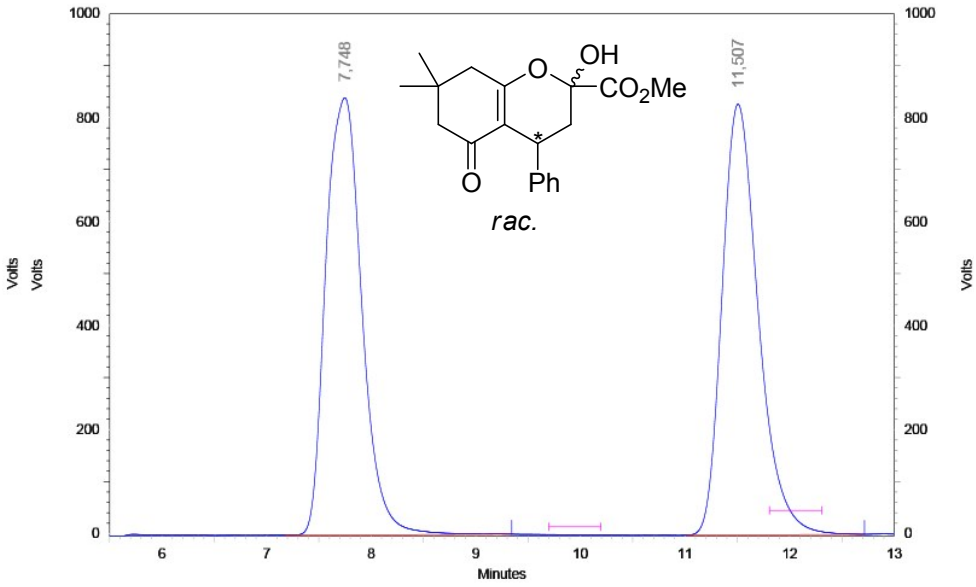
Retention Time	Area	Area %	Height	Height %
7,043	440417	6,09	17936	5,35
10,215	6792348	93,91	317374	94,65
Totals	7232765	100,00	335310	100,00

UV2000-254nm Results (System (2018-01-15 11:50:08) (Original))

Retention Time	Area	Area %	Height	Height %
7,197	496232	6,09	12419	5,06
10,468	7657564	93,91	233039	94,94
Totals	8153796	100,00	245458	100,00

Figure S90. HPLC chromatograms (Chiralpak AD-H, 4.6 mm ID × 250 mm, hexane/2-propanol 7:3, 0.7 mL/min) for adduct **11a** obtained on a 3-mmol scale from methyl benzylidenepyruvate (**9a**) and dimedone (**10**) using 1 %mol catalyst **2a** in chlorobenzene at room temperature: crude sample (left) and after purification by column chromatography (right). For chromatogram of a recrystallized sample and racemic **11a** see the following Figure S91.





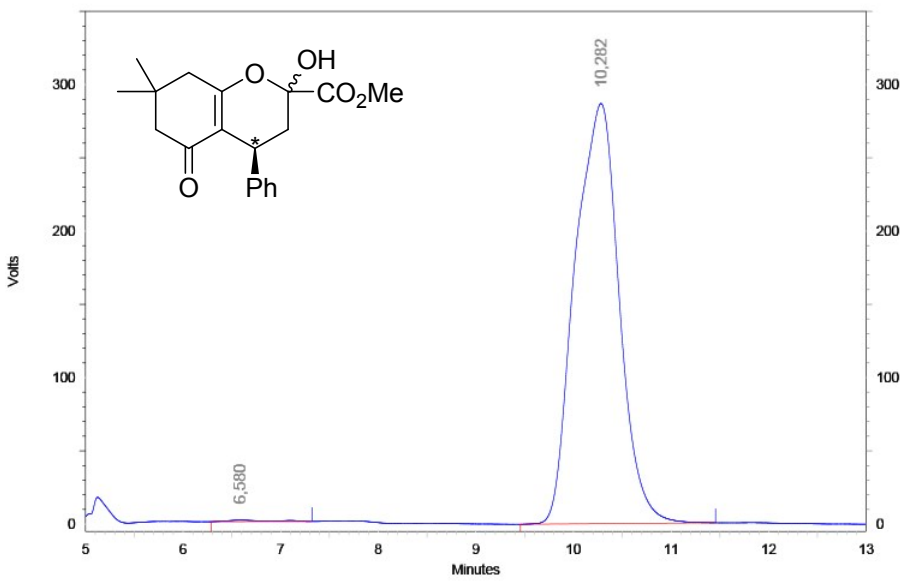
UV2000-254nm Results (System (2018-01-19 11:48:54) (Reprocessed))

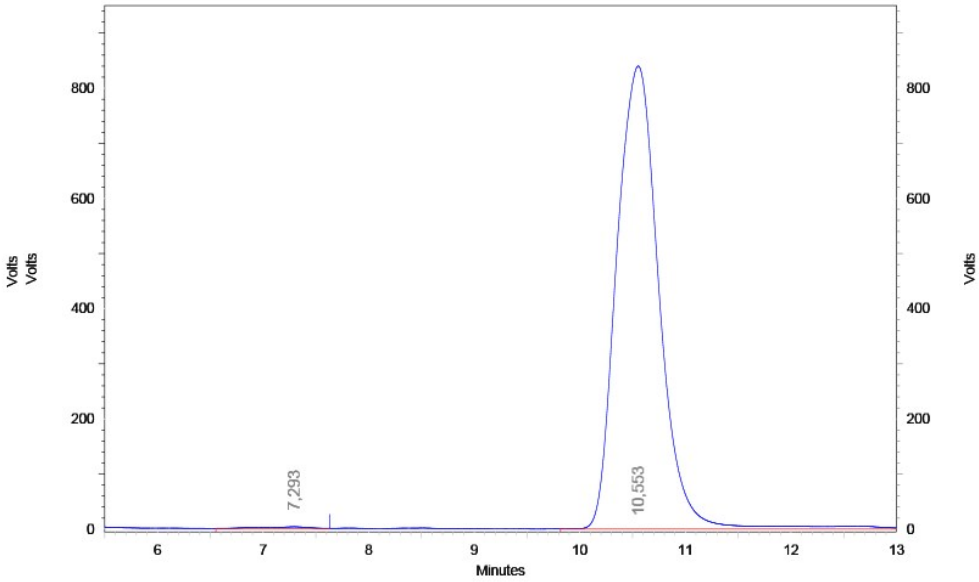
Retention Time	Area	Area %	Height	Height %
7,083	143096	0,35	4759	0,31
10,165	40733065	99,65	1518160	99,69
Totals	40876161	100,00	1522919	100,00

UV2000-254nm Results (System (2018-06-07 11:57:09) (Reprocessed))

Retention Time	Area	Area %	Height	Height %
7,748	20122513	50,25	840427	50,37
11,507	19923119	49,75	828242	49,63
Totals	40045632	100,00	1668669	100,00

Figure S91. HPLC chromatograms (Chiralpak AD-H, 4.6 mm ID × 250 mm, hexane/2-propanol 7:3, 0.7 mL/min) for adduct **11a**: obtained on a 3-mmol scale using 1 %mol catalyst **2a** in chlorobenzene after recrystallization from *tert*-butyl methyl ether (first crop; for uncrystallized sample see the preceeding Figure S90.) (left). Racemic product **11a** (right).





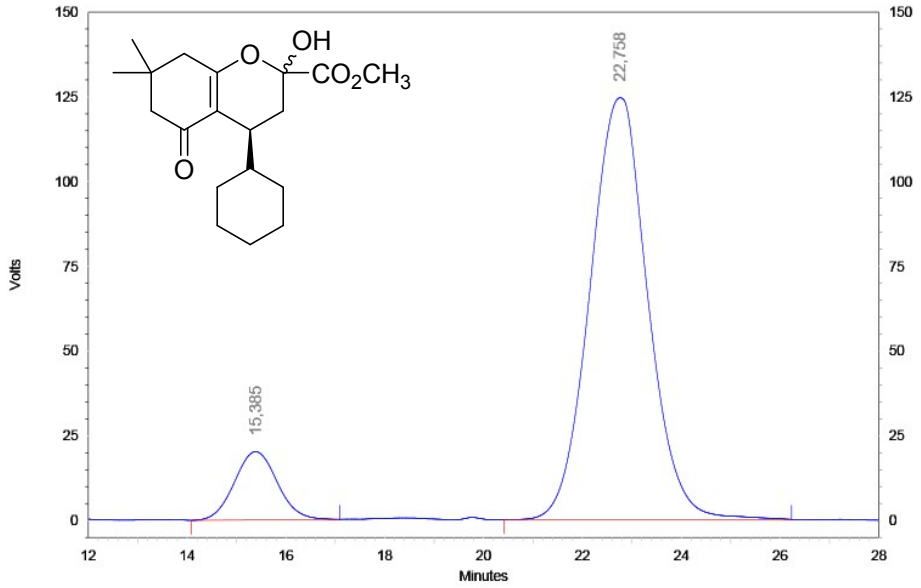
UV2000-254nm Results (System (2018-01-10 11:34:38) (Original))

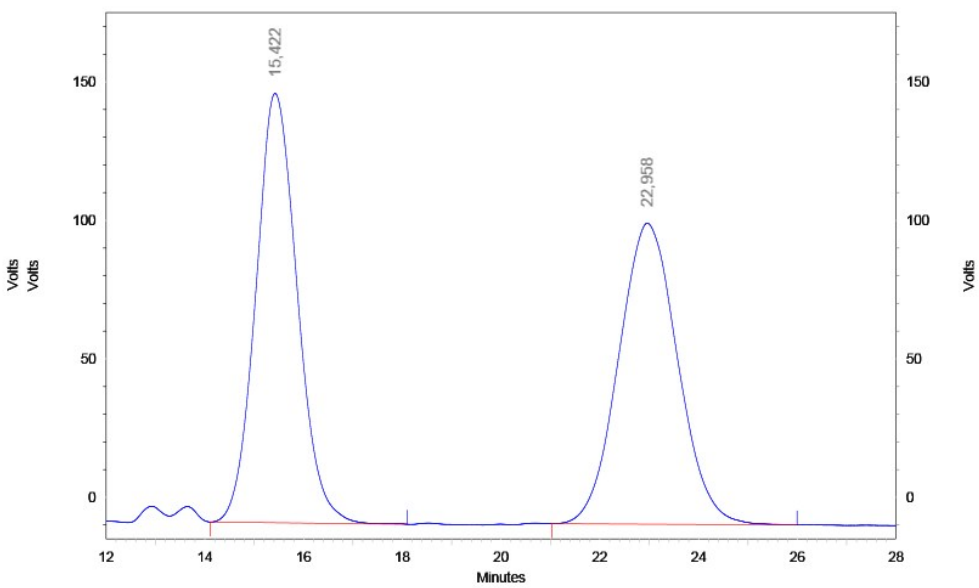
Retention Time	Area	Area %	Height	Height %
6,580	28693	0,32	982	0,34
10,282	8998898	99,68	286713	99,66
Totals	9027591	100,00	287695	100,00

UV2000-254nm Results (System (2018-01-17 14:34:31) (Reprocessed))

Retention Time	Area	Area %	Height	Height %
7,293	86656	0,37	2895	0,34
10,553	23494825	99,63	839923	99,66
Totals	23581481	100,00	842818	100,00

Figure S92. HPLC chromatograms (Chiralpak AD-H, 4.6 mm ID × 250 mm, hexane/2-propanol 7:3, 0.7 mL/min) for adduct **11a** obtained from methyl benzylidenepyruvate (**9a**) and dimedone (**10**) using 1 %mol catalyst **2a** in chlorobenzene at -20 °C: On a 0.1-mmol scale (left), and on a 3-mmol scale after purification by column chromatography (right).





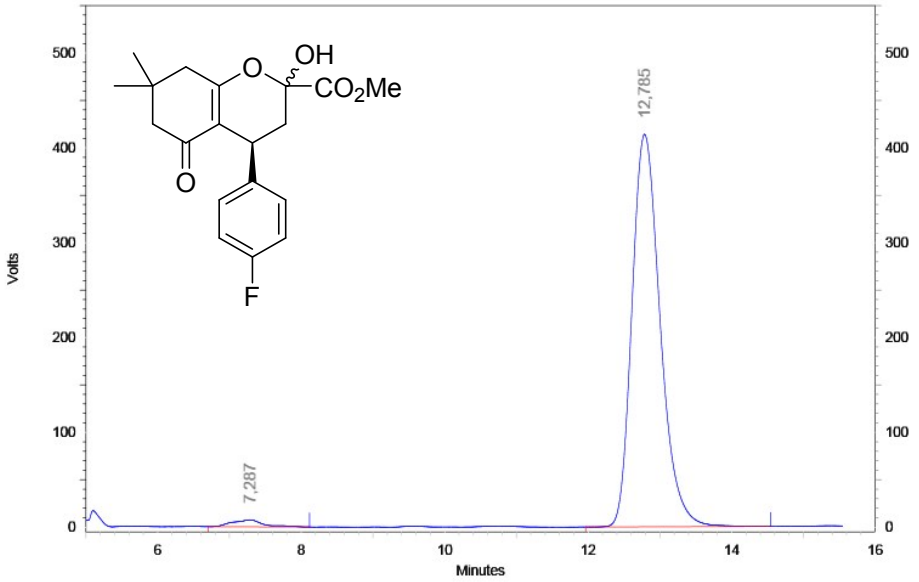
UV2000-254nm Results (System (2018-02-28 15:04:33) (Original))

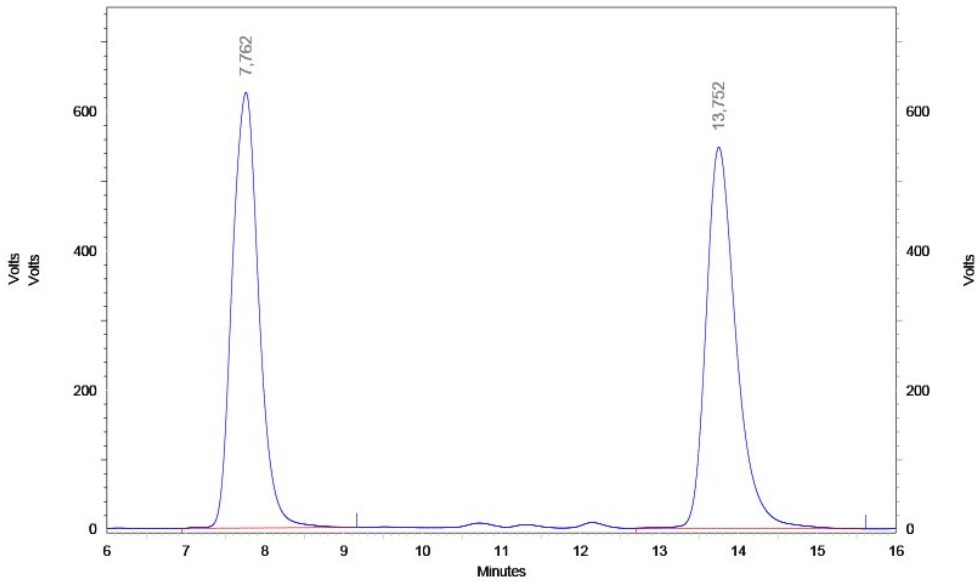
Retention Time	Area	Area %	Height	Height %
15,385	1209699	10,70	20147	13,94
22,758	10099466	89,30	124415	86,06
Totals	11309165	100,00	144562	100,00

UV2000-254nm Results (System (2018-02-28 14:34:29) (Original))

Retention Time	Area	Area %	Height	Height %
15,422	9039346	50,07	155004	58,80
22,958	9014745	49,93	108625	41,20
Totals	18054091	100,00	263629	100,00

Figure S93. HPLC chromatograms (Chiralpak IC-3, 4.6 mm ID × 250 mm, hexane/2-propanol 9:1, 1 mL/min) for adduct **11b** obtained from methyl 5-cyclohexyl-3-oxo-pent-4-enoate (**9b**) and dimedone (**10**) with 10 %mol catalyst **2a** in chlorobenzene at room temperature (left) and a racemic sample (right). The results shown correspond to Table 4 entry 1.





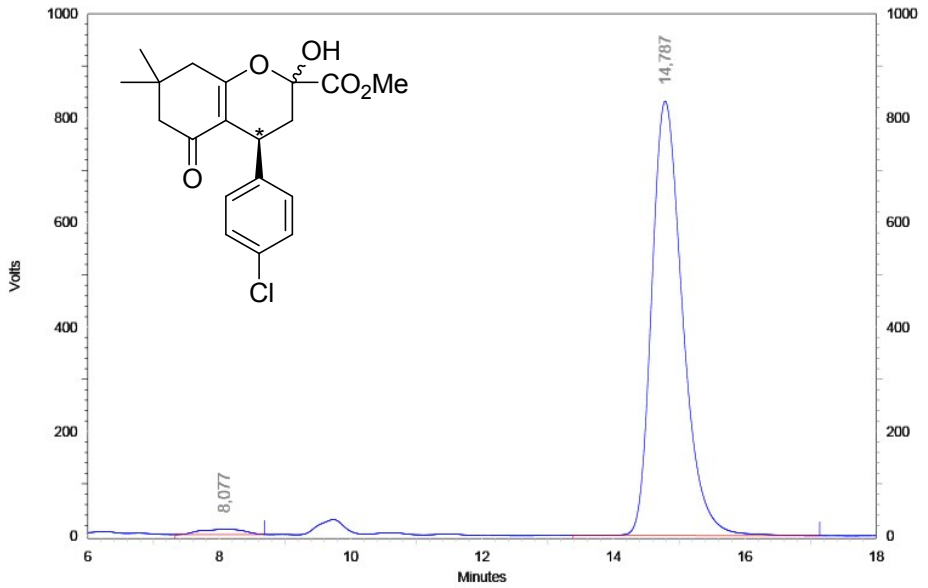
UV2000-254nm Results (System (2017-12-07 12:58:44) (Original))

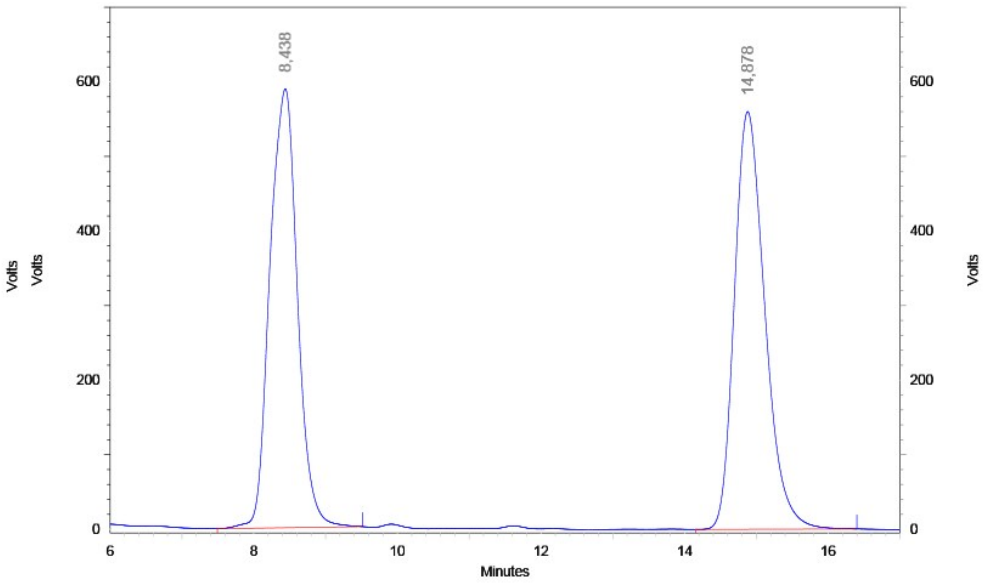
Retention Time	Area	Area %	Height	Height %
7,287	219038	1,90	7371	1,75
12,785	11292906	98,10	413949	98,25
Totals	11511944	100,00	421320	100,00

UV2000-254nm Results (System (2018-02-15 11:44:55) (Reprocessed))

Retention Time	Area	Area %	Height	Height %
7,762	14662165	50,27	625732	53,33
13,752	14504120	49,73	547485	46,67
Totals	29166285	100,00	1173217	100,00

Figure S94. HPLC chromatograms (Chiralpak AD-H, 4.6 mm ID × 250 mm, hexane/2-propanol 7:3, 1 mL/min) for adduct **11c** obtained from methyl 4-(fluorobenzylidene)pyruvate (**9c**) and dimedone (**10**) using 10 %mol catalyst **2a** in chlorobenzene at room temperature (left) and a racemic sample (right). The results shown correspond to Table 4 entry 2.





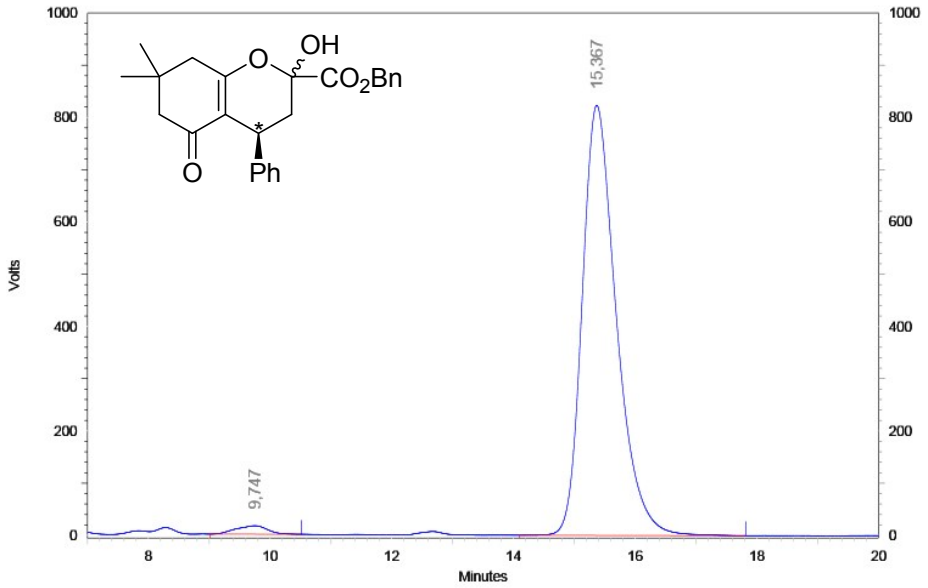
UV2000-254nm Results (System (2018-02-15 13:10:52) (Original))

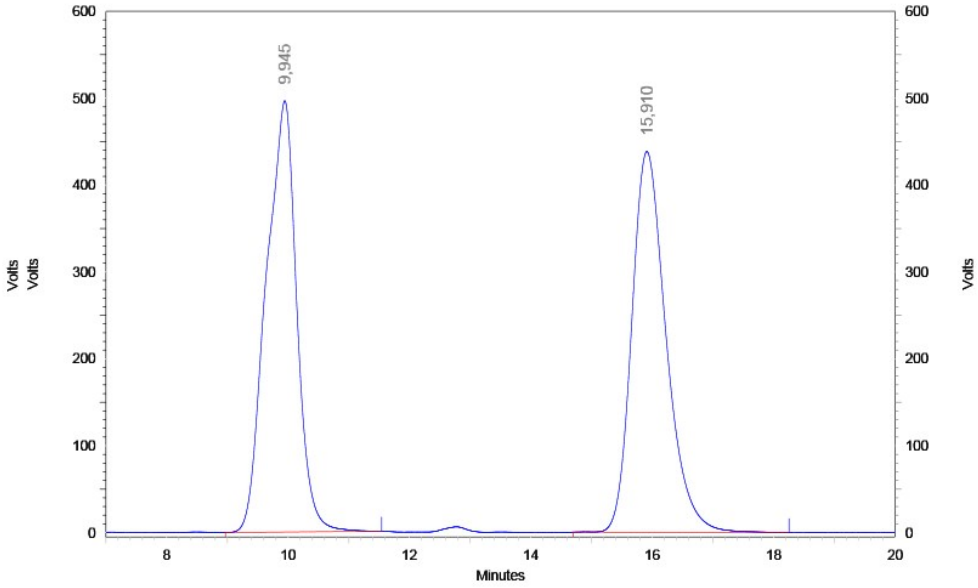
Retention Time	Area	Area %	Height	Height %
8,077	477924	1,73	10487	1,24
14,787	27075779	98,27	831975	98,76
Totals	27553703	100,00	842462	100,00

UV2000-254nm Results (System (2018-02-15 12:49:06) (Original))

Retention Time	Area	Area %	Height	Height %
8,438	15703357	48,78	588641	51,24
14,878	16487775	51,22	560134	48,76
Totals	32191132	100,00	1148775	100,00

Figure S95. HPLC chromatograms (Chiralpak AD-H, 4.6 mm ID × 250 mm, hexane/2-propanol 7:3, 1 mL/min) for adduct **11d** obtained from methyl 4-(chlorobenzylidene)pyruvate (**9d**) and dimedone (**10**) with 1 %mol catalyst **2a** in chlorobenzene at -20 °C (left) and a racemic sample (right). The results shown correspond to Table 4 entry 3.





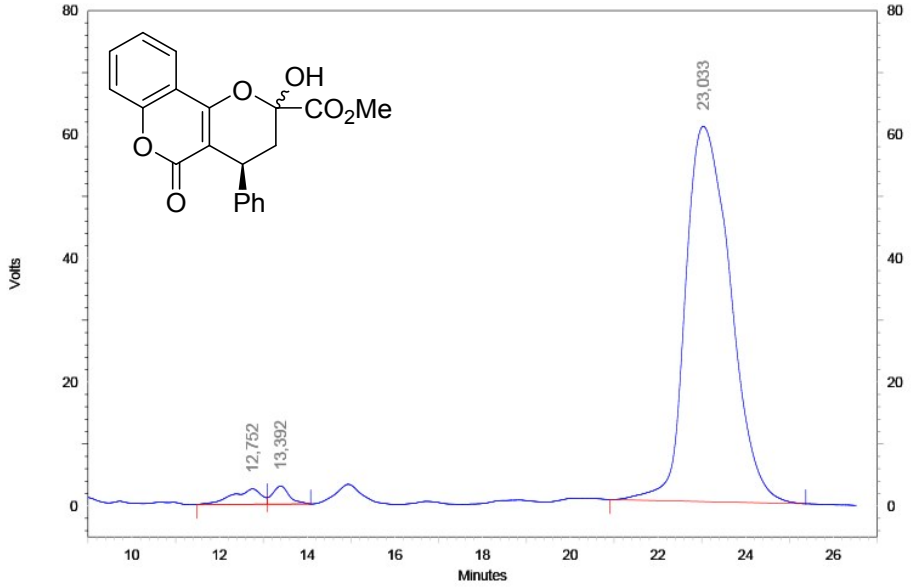
UV2000-254nm Results (System (2018-02-02 10:03:53) (Original))

Retention Time	Area	Area %	Height	Height %
9,747	578790	1,77	16115	1,92
15,367	32038492	98,23	823264	98,08
Totals	32617282	100,00	839379	100,00

UV2000-254nm Results (System (2018-02-02 09:36:48) (Reprocessed))

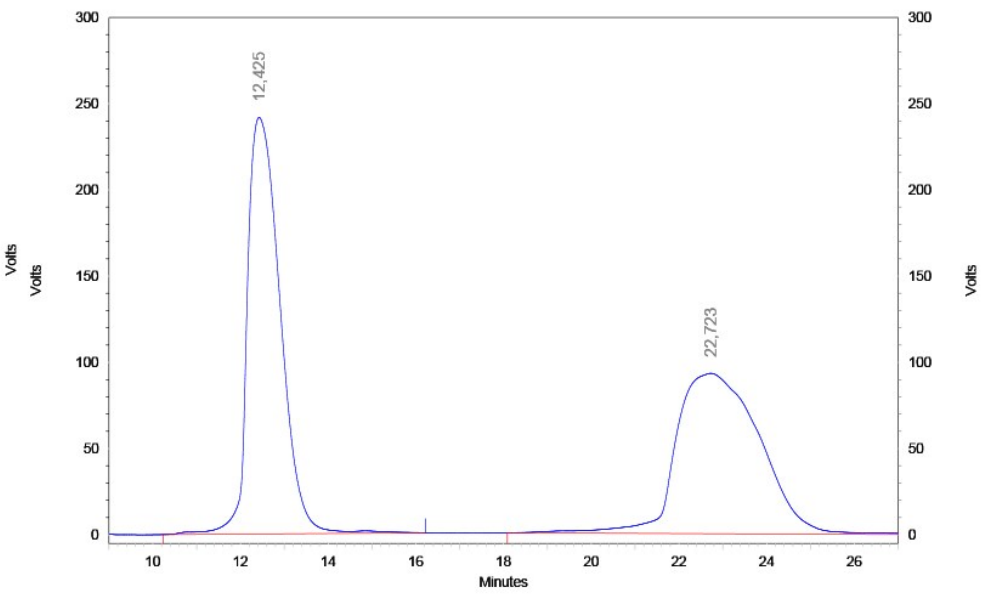
Retention Time	Area	Area %	Height	Height %
9,945	17335926	50,14	496252	53,11
15,910	17238716	49,86	438124	46,89
Totals	34574642	100,00	934376	100,00

Figure S96. HPLC chromatograms (Chiralpak AD-H, 4.6 mm ID × 250 mm, hexane/2-propanol 7:3, 0.7 mL/min) for adduct **11e** obtained from benzyl benzylidenepyruvate (**9e**) and dimedone (**10**) using 10 %mol catalyst **2a** in chlorobenzene at room temperature (left) and a racemic sample (right). The results shown correspond to Table 4 entry 4.



UV2000-254nm Results (System (2018-04-25 12:40:01) (Reprocessed))

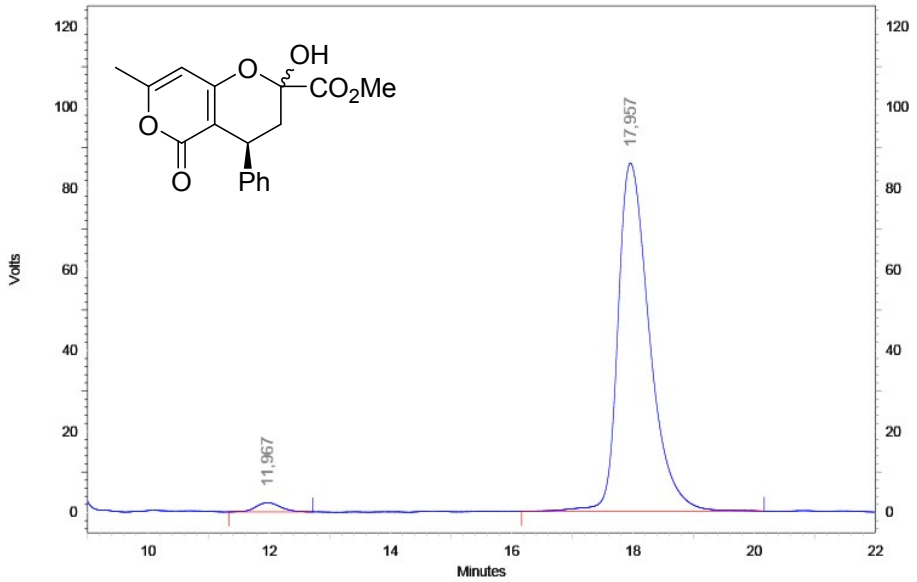
Retention Time	Area	Area %	Height	Height %
12,752	111853	2,48	2469	3,74
13,392	76188	1,69	2910	4,41
23,033	4320516	95,83	60609	91,85
Totals	4508557	100,00	65988	100,00

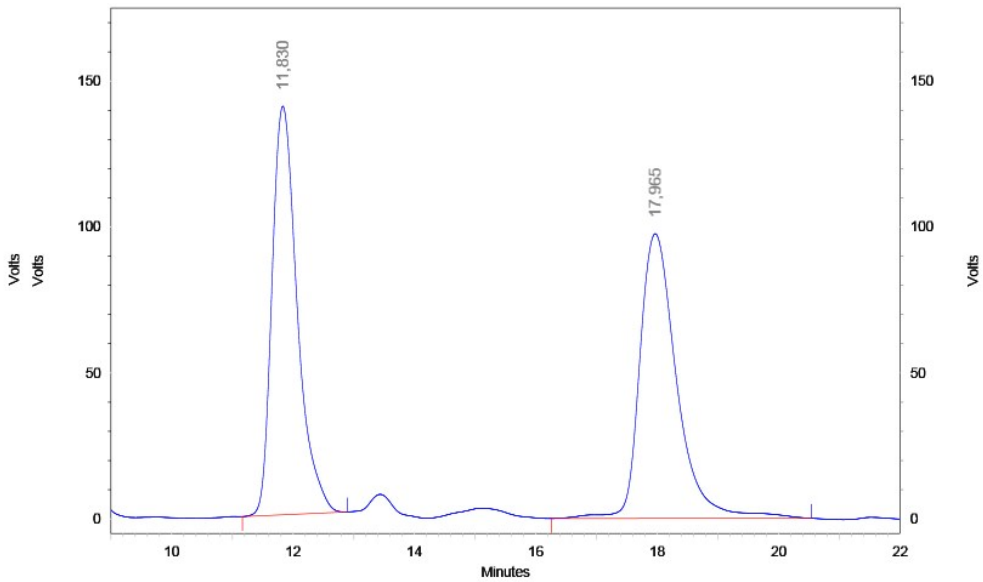


UV2000-254nm Results (System (2017-12-19 13:17:44) (Original))

Retention Time	Area	Area %	Height	Height %
12,425	12562809	50,45	241459	72,20
22,723	12338978	49,55	92983	27,80
Totals	24901787	100,00	334442	100,00

Figure S97. HPLC chromatograms (Chiralpak AD-H, 4.6 mm ID × 250 mm, hexane/2-propanol 8:2, 0.75 mL/min) for adduct **11f** obtained from methyl benzylidenepyruvate (**9a**) and 4-hydroxycoumarin with 10 %mol catalyst **2a** in chlorobenzene at -40 °C (left) and a racemic sample (right). The results correspond to values shown in Figure 7.





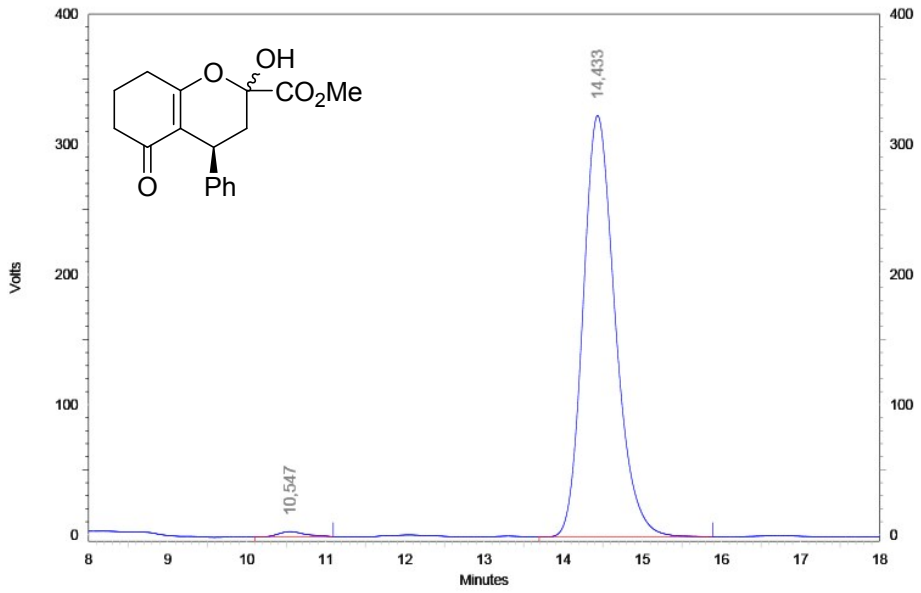
UV2000-254nm Results (System (2018-01-12 15:14:05) (Original))

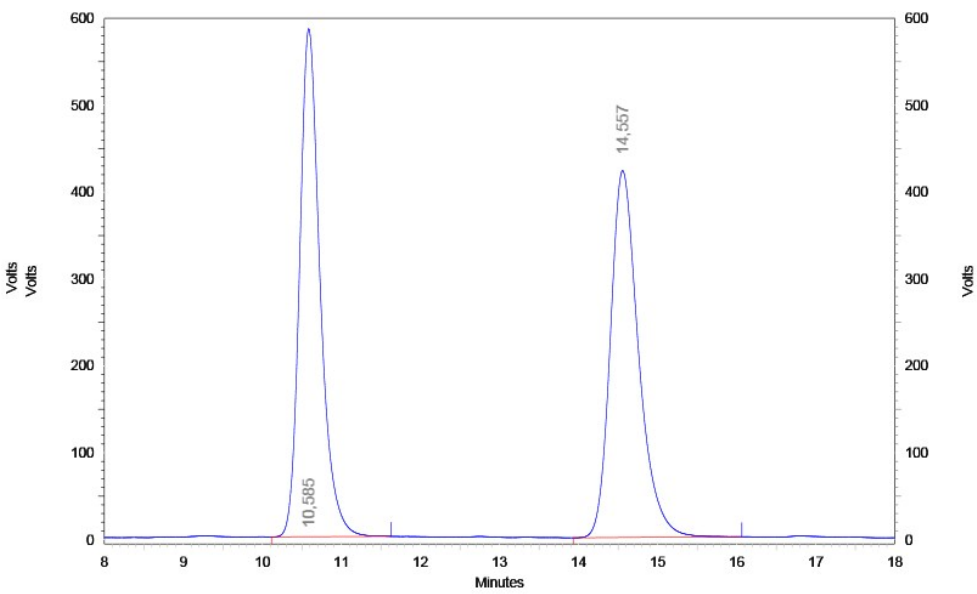
Retention Time	Area	Area %	Height	Height %
11,967	64725	2,04	2280	2,59
17,957	3102219	97,96	85878	97,41
Totals	3166944	100,00	88158	100,00

UV2000-254nm Results (System (2017-12-20 10:58:10) (Original))

Retention Time	Area	Area %	Height	Height %
11,830	4046813	49,44	139966	58,93
17,965	4139080	50,56	97548	41,07
Totals	8185893	100,00	237514	100,00

Figure S98. HPLC chromatograms (Chiralpak AD-H, 4.6 mm ID × 250 mm, hexane/2-propanol 8:2, 0.75 mL/min) for adduct **11g** obtained from methyl benzylidenepyruvate (**9a**) and triacetic acid lactone with 10 %mol catalyst **2a** in chlorobenzene at -40 °C (left) and a racemic sample (right). The results correspond to values shown in Figure 7.





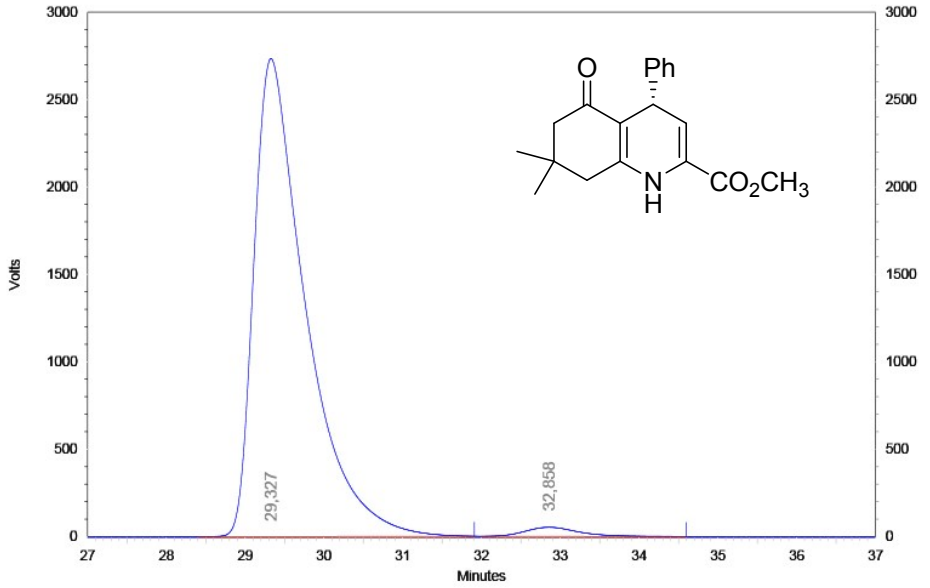
UV2000-220nm Results (System (2018-01-12 13:15:54) (Original))

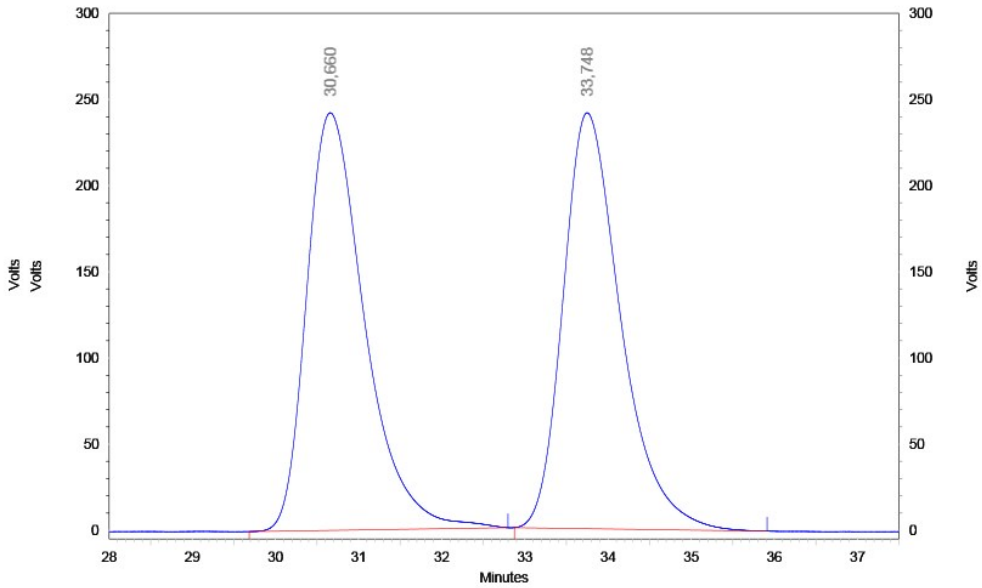
Retention Time	Area	Area %	Height	Height %
10,547	100364	1,09	4107	1,25
14,433	9126995	98,91	323711	98,75
Totals	9227359	100,00	327818	100,00

UV2000-220nm Results (System (2018-01-12 12:53:48) (Reprocessed))

Retention Time	Area	Area %	Height	Height %
10,585	10536524	50,14	584452	58,07
14,557	10476506	49,86	422089	41,93
Totals	21013030	100,00	1006541	100,00

Figure S99. HPLC chromatograms (Chiralpak AD-H, 4.6 mm ID × 250 mm, hexane/2-propanol 8:2, 0.75 mL/min) for adduct **11h** obtained from methyl benzylidenepyruvate (**9a**) and 1,3-cyclohexanedione with 10 %mol catalyst **2a** in chlorobenzene at -40 °C (left) and a racemic sample (right). The results correspond to values shown in Figure 7.





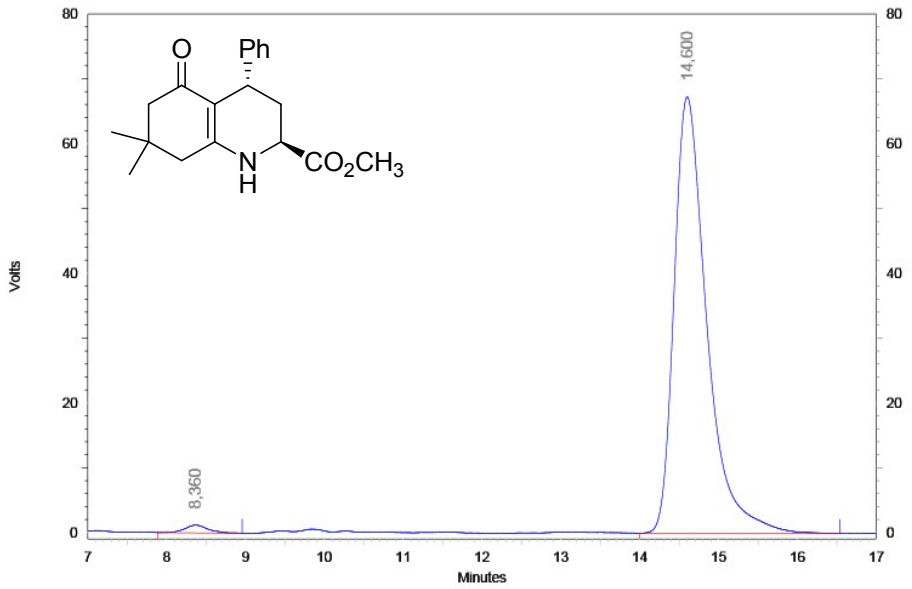
UV2000-254nm Results (System (2018-02-14 13:29:24) (Original))

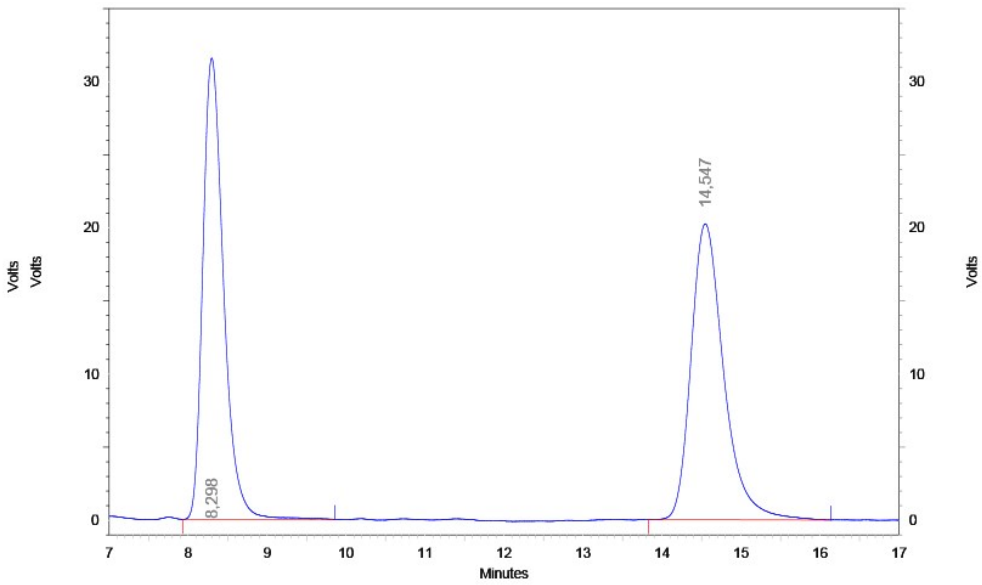
Retention Time	Area	Area %	Height	Height %
29,327	124150899	98,11	2733805	98,15
32,858	2391824	1,89	51595	1,85
Totals	126542723	100,00	2785400	100,00

UV2000-254nm Results (System (2018-02-14 10:06:23) (Original))

Retention Time	Area	Area %	Height	Height %
30,660	11730254	50,22	242283	50,10
33,748	11628910	49,78	241282	49,90
Totals	23359164	100,00	483565	100,00

Figure S100. HPLC chromatograms (Chiralpak AD-H, 4.6 mm ID × 250 mm, hexane/2-propanol 9:1, 0.7 mL/min) for methyl (2*S*,4*S*)-1,4,5,6,7,8-hexahydro-7,7-dimethyl-5-oxo-4-phenyl-quinoline-2-carboxylate (**12**) obtained starting from hemiacetal sample shown in Figure S92 (left) and a racemic sample (right). The results correspond to figures shown in Scheme 3.





UV2000-254nm Results (System (2018-03-05 12:54:10) (Original))

Retention Time	Area	Area %	Height	Height %
8,360	24707	1,26	1194	1,74
14,600	1936422	98,74	67314	98,26
Totals	1961129	100,00	68508	100,00

UV2000-254nm Results (System (2018-03-05 13:33:47) (Reprocessed))

Retention Time	Area	Area %	Height	Height %
8,298	575412	49,67	31545	60,92
14,547	583156	50,33	20240	39,08
Totals	1158568	100,00	51785	100,00

Figure S101. HPLC chromatograms (Chiralpak AD-H, 4.6 mm ID × 250 mm, hexane/2-propanol 8:2, 1 mL/min) for methyl 1,2,3,4,5,6,7,8-octahydro-7,7-dimethyl-5-oxo-4-phenyl-quinoline-2-carboxylate (**13**) obtained starting from hemiacetal sample shown in Figure S92 (left) and a racemic sample (right). The results correspond to figures shown in Scheme 3.

DFT computations listings

Listing of DFT/B3LYP/CC-pVDZ energies and atomic coordinates for **1i**

```
Zero-point correction=                           0.386279 (Hartree/Particle)
Thermal correction to Energy=                    0.406012
Thermal correction to Enthalpy=                  0.406956
Thermal correction to Gibbs Free Energy=         0.335649
SCF:  E(RB3LYP) =                           -1282.27590535
Sum of electronic and zero-point Energies=   -1281.889626
Sum of electronic and thermal Energies=      -1281.869893
Sum of electronic and thermal Enthalpies=    -1281.868949
Sum of electronic and thermal Free Energies= -1281.940256
Lowest frequencies: 18.4, 25.7 cm-1
```

Atom	X	Y	Z
C	-2.73483	-0.57964	0.03472
C	-3.44058	0.05428	1.05781
H	-2.9823	0.15477	2.04216
C	-4.72682	0.53548	0.79123
H	-5.29305	1.03384	1.58109
C	-5.28701	0.37246	-0.47873
H	-6.29211	0.74858	-0.68262
C	-4.56881	-0.27823	-1.49007
H	-5.01376	-0.4119	-2.47849
C	-3.28588	-0.76483	-1.23682
H	-2.71562	-1.28531	-2.00703
S	-1.09309	-1.24633	0.38291
O	-0.82893	-1.02346	1.83311
O	-0.99822	-2.60373	-0.20873
N	-0.0684	-0.2804	-0.58434
H	0.68589	-0.9335	-0.85437
C	0.576	0.88944	0.05067
H	0.59854	0.75091	1.14652
C	2.03615	0.95124	-0.46148
H	1.98767	1.15708	-1.54768
C	2.76393	2.13748	0.20305
H	3.80457	2.19062	-0.15676
H	2.81179	1.97869	1.2948
C	2.03524	3.45817	-0.08848
H	2.08097	3.66569	-1.17403
H	2.55348	4.29453	0.40957
C	0.56676	3.40063	0.3545
H	0.52302	3.32811	1.45728
H	0.04751	4.335	0.08421
C	-0.16198	2.19774	-0.26029
H	-0.23333	2.31127	-1.35692
H	-1.19535	2.14077	0.11784
N	2.66297	-0.36822	-0.35029
C	3.87308	-0.58964	-1.14546
C	2.9703	-0.89682	0.98504
C	4.34451	-1.99443	-0.71517
H	4.66188	0.16149	-0.92154
C	3.67092	-2.22824	0.66718
H	2.05421	-1.02866	1.57993
H	5.44238	-2.04386	-0.66144
H	4.39058	-2.5066	1.45111
H	3.64369	-0.51515	-2.2205

```
H       4.01874  -2.75559  -1.4395
H       2.92599  -3.03493   0.59947
H       3.65341  -0.22739   1.55149
```