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Supporting Information

Asymmetric Cross-Aldol Reaction of α-Keto Hydrazones and α,ß-Unsaturated γ-Keto Hydrazones with Trifluoromethyl Ketones

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Contents

1. General information

^{1}H NMR spectra were recorded at 300 MHz or 500 MHz (internal reference; $CDCl_3$ = 7.26; CD_2Cl_2 = 5.32; DMSO-d_6 = 2.50). ^{13}C NMR spectra were recorded at 75.5 MHz or 126 MHz (internal reference; $CDCl_3$ = 77.0; CD_2Cl_2 = 54.0; DMSO-d_6 = 39.5); ^{19}F NMR spectra were recorded at 282.5 MHz or 471 MHz. Column chromatography was performed on silica gel (Merck Kieselgel 60). Analytical TLC was performed on aluminium backed plates (1.5 × 5 cm) pre-coated (0.25 mm) with silica gel (Merck, Silica Gel 60 F254). Compounds were visualized by exposure to UV light or by dipping the plates in solutions of $KMnO_4$, vainilline or phosphomolibdic acid stains followed by heating. Melting points were recorded in a metal block and are uncorrected. Optical rotations were measured on a JASCO *P-2000* polarimeter. The enantiomeric excess (ee) of the products was determined by chiral stationary phase HPLC (Daicel Chiralpak IA/IB/IC/ID and OJ-H Chiralcel columns). Unless otherwise noted, analytical grade solvents and commercially available reagents were used without further purification. Jones reagent was prepared as follows: Concentrated H_2SO_4 (3 mL, 56 mmol) was dropwise added to a solution of $Na_2Cr_2O_7 \cdot H_2O$ (3 g, 10 mmol) in H_2O (10 mL) at 0 ºC. Togni Reagent II [1-trifluoromethyl-1,2-benziodoxol-3-(1*H*)-one] was purchased from Sigma-Aldrich (60 wt. %, contains 40 wt. % Celatom® FW-80 as additive). Not-commercially available hydrazone reagents **1A**[1], **1D**[1], **1F**[1], **1H**[1], **4**[1], **8E**[1], trifluoromethyl ketones **2g**[2], **2h**[3], **2i**[4], **2j**[5] and organocatalysts **III**[6], **Ia-c**[7], **II**[7], **VI**[8] were synthesized according to literature procedures. Crystals of suitable size were covered with FOMBLIN oil and mounted on a glass fiber. Data collection has been performed on a Bruker SMART APEX II CCD area detector on a D8 goniometer at 100 K, using a graphite monochromator Cu Kα1 (λ = 1.54178 Å) and a Bruker Cryo-Flex low-temperature device. Data collection was processed with APEX-W2D-NT,[9] cell refinement and data reduction with SAINT-Plus1 and the absorption was corrected by multiscan method applied by SADABS.[10] The structure was solved by direct method and refined on F^2 (SHELXTL).[11] Non-hydrogen atoms were refined with anisotropic displacement parameters and hydrogen atoms attached to refined atoms were placed in geometrically idealized positions and refined by using a riding model.

[1] E. Matador, M. G. Retamosa, D. Rohal'ová, J. Iglesias-Sigüenza, P. Merino, R. Fernández, J. M. Lassaletta, D. Monge, *Org. Chem. Front.* 2021, **8**, 3446.
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[8] F. Yu, X. Sun, Z. Jin, S. Wen, X. Liang, J. Ye, *Chem. Commun.* 2010, **46**, 4589.
[9] APEX2 (version 2009.11_0). Program for Bruker CCD X-Ray Diffractometer Control, Bruker AXS Inc., Madison, WI, 2009.
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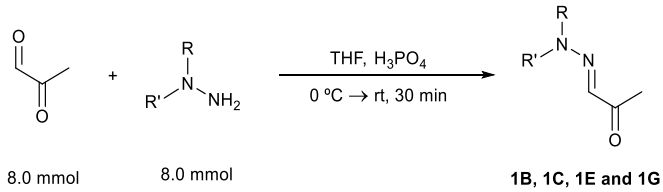
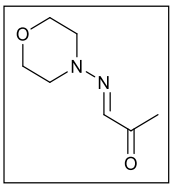
2. General procedure for the synthesis of ketones 1B, 1C, 1E and **1G**

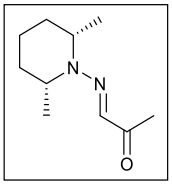


Free hydrazine (8.0 mmol) was dropwise added to a solution of pyruvaldehyde (1.25 mL, 8.0 mmol, 40 wt. % in H_2O) and H_3PO_4 (0.39 g, 4.0 mmol) in THF (5 mL) at 0 °C. The resulting mixture was allowed to warm to room temperature and stirred until the consumption of the starting material (15-30 min, TLC monitoring). After this time, the solvent was eliminated under reduced pressure. The mixture was then neutralized with a saturated aqueous solution of $NaHCO_3$ and extracted with Et_2O (3 x 25 mL). The combined organic layers were washed with brine (1 x 50 mL), dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (pure *n*-hexanes to *n*-hexanes/EtOAc 3/1) to afford pure product **1B**, **1C**, **1E**, and **1G**.

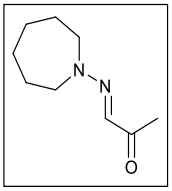
(*E*)-1-(Morpholinoimino)propan-2-one, 1B. Following the general procedure **2**, starting from 1,1-morpholin-4-amine (0.82 g, 8.0 mmol), compound **1B** was obtained as a white solid (1.08 g, 86%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 6.88 (s, 1H), 3.87 – 3.80 (m, 4H), 3.31 – 3.25 (m, 4H), 2.29 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 198.0, 132.0, 66.1, 50.6, 24.4. **HRMS** (ESI): m/z calcd for $C_7H_{12}O_2N_2Na$ [M^++Na] 179.0791, found 179.0788.



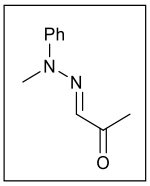
(*E*)-1-[(*cis*-2,6-Dimethylpiperidin-1-yl)imino]propan-2-one, 1C. Following the general procedure **2**, starting from 1-amino-*cis*-2,6-dimethylpiperidine (1.03 g, 8.0 mmol), compound **1C** was obtained as a light yellow solid (1.61 g, 80%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 6.75 (d, J = 0.8 Hz, 1H), 4.02 – 3.89 (m, 2H), 2.27 (s, 3H), 1.87 – 1.73 (m, 3H), 1.71 – 1.61 (m, 2H), 1.59 – 1.50 (m, 1H), 1.15 (d, J = 6.9 Hz, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 198.0, 127.3, 53.5, 30.2, 24.1, 18.1, 14.2. **HRMS** (ESI): m/z calcd for $C_{10}H_{19}ON_2$ [M^++H] 183.1492, found 183.1490.



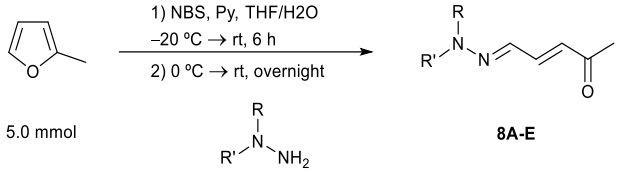
(*E*)-1-(Azepan-1-ylimino)propan-2-one, 1E. Following the general procedure **2**, starting from azepan-1-amine (0.96 g, 8.0 mmol), compound **1E** was obtained as a light yellow oil (0.69 g, 51%). **^{1}H NMR** (500 MHz, 60 ºC, DMSO-d_6) δ 6.58 (s, 1H), 3.63 – 3.38 (m, 4H), 2.15 (s, 3H), 1.78 – 1.66 (m, 4H), 1.59 – 1.49 (m, 4H). **^{13}C NMR** (75.5 MHz, 60 ºC, DMSO-d_6) δ 194.9, 125.6, 53.7, 27.5, 26.2, 23.5. **HRMS** (ESI): m/z calcd for $C_9H_{16}ON_2Na$ [M^++Na] 191.1155, found 191.1152.



(*E*)-1-(2-Methyl-2-phenylhydrazineylidene)propan-2-one, 1G. Following the general procedure **2**, starting from 1-methyl-1-phenylhydrazine (0.98 g, 8.0 mmol), compound **1G** was obtained as a yellow solid (0.97 g, 69%). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.44 – 7.31 (m, 4H), 7.14 – 7.05 (m, 1H), 6.97 (q, J = 0.9 Hz, 1H), 3.39 (s, 3H), 2.44 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 198.1, 146.7, 131.3, 129.4, 123.6, 117.0, 34.3, 24.7. **HRMS** (ESI): m/z calcd for $C_{10}H_{12}ON_2Na$ [M^++Na] 199.0842, found 199.0839.

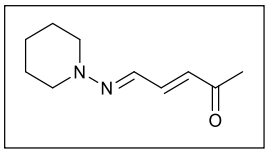


3. General procedure for the *one pot* synthesis of α,β-unsaturated ketones 8A-E

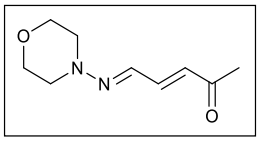


N-Bromosuccinimide (1.35 g, 7.5 mmol) and pyridine (809 µL, 10.0 mmol) were subsequently added to a solution of 2-methylfuran (456 µL, 5.0 mmol) in THF/H_2O (25 mL, 9/1) at −20 °C. The mixture was allowed to warm slowly to room temperature and stirred for 6 h. After this time, the reaction was cooled to 0 °C and the corresponding hydrazine (5.0 mmol) was added in one portion. The resulting mixture was allowed to warm to room temperature and stirred overnight. After this time, the solvent was eliminated under reduced pressure. The mixture was then diluted with CH_2Cl_2 (50 mL) and washed with aqueous $Na_2S_2O_3$ (3 x 50 mL, 10 wt. %) and brine (1 x 50 mL). The organic layer was dried over $MgSO_4$ and the solvent was eliminated under reduced pressure. The resulting residue was purified by flash chromatography (*n*-hexanes/EtOAc 3/1) to afford pure product **8A-E**.

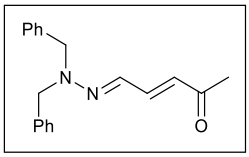
(3*E*,5*E*)-5-(Piperidin-1-ylimino)pent-3-en-2-one, 8A. Following the general procedure **3**, starting from piperidin-1-amine (500 µL, 5.0 mmol), ketone **8A** was obtained as a light orange oil (0.60 g, 67%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.30 – 7.16 (m, 2H), 6.18 – 6.03 (m, 1H), 3.28 – 3.19 (m, 4H), 2.28 (s, 3H), 1.77 – 1.64 (m, 4H), 1.63 – 1.51 (m, 2H). **^{13}C NMR** (75.5 MHz, $CDCl_3$): δ 198.6, 142.8, 130.9, 128.8, 51.2, 26.2, 24.7, 23.6. **HRMS** (ESI): m/z calcd for $C_{10}H_{17}ON_2$ [M^++H] 181.1335, found 181.1334.



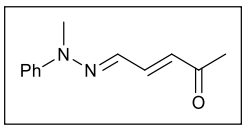
(3*E*,5*E*)-5-(Morpholinoimino)pent-3-en-2-one, 8B. Following the general procedure **3**, starting from 4-aminomorpholine (497 µL, 5.0 mmol), ketone **8B** was obtained as a light orange solid (0.43 g, 47%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.36 – 7.12 (m, 2H), 6.17 (d, *J* = 14.9 Hz, 1H), 3.98 – 3.72 (m, 4H), 3.35 – 3.09 (m, 4H), 2.30 (s, 3H). **^{13}C NMR** (75.5 MHz, $CDCl_3$): δ 198.4, 141.7, 133.1, 130.6, 66.0, 50.9, 26.5. **HRMS** (ESI): m/z calcd for $C_9H_{14}O_2N_2Na$ [M^++Na] 205.0947, found 205.0944.



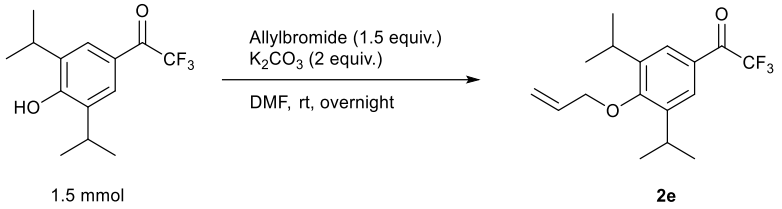
(3*E*,5*E*)-5-(2,2-Dibenzylhydrazineylidene)pent-3-en-2-one, 8C. Following the general procedure **3**, starting from *N*,*N*-dibenzylhydrazine (1.10 g, 5.0 mmol), ketone **8C** was obtained as a pale orange solid (0.82 g, 56%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.39 – 7.27 (m, 7H), 7.24 – 7.14 (m, 4H), 6.92 (d, *J* = 9.1 Hz, 1H), 5.96 (d, *J* = 15.9 Hz, 1H), 4.60 (s, 4H), 2.26 (s, 3H). **^{13}C NMR** (75.5 MHz, $CDCl_3$): δ 198.4, 142.7, 136.0, 129.2, 128.7, 127.8, 127.6, 127.2, 57.6, 26.4. **HRMS** (ESI): m/z calcd for $C_{19}H_{20}ON_2Na$ [M^++Na] 315.1468, found 315.1469.



(3*E*,5*E*)-5-(2-Methyl-2-phenylhydrazineylidene)pent-3-en-2-one, 8D. Following the general procedure **3**, starting from 1-methyl-1-phenyhydrazine (607 µL, 5.0 mmol), ketone **8D** was obtained as a light yellow solid (0.60 g, 59%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.48 – 7.29 (m, 5H), 7.29 – 7.19 (m, 1H), 7.08 – 6.96 (m, 1H), 6.24 (d, *J* = 15.8 Hz, 1H), 3.40 (s, 3H), 2.33 (s, 3H). **^{13}C NMR** (75.5 MHz, $CDCl_3$): δ 198.4, 146.8, 142.3, 130.9, 129.6, 129.1, 122.4, 116.2, 33.8, 26.6. **HRMS** (ESI): m/z calcd for $C_{12}H_{14}ON_2Na$ [M^++Na] 225.0998, found 225.0997.



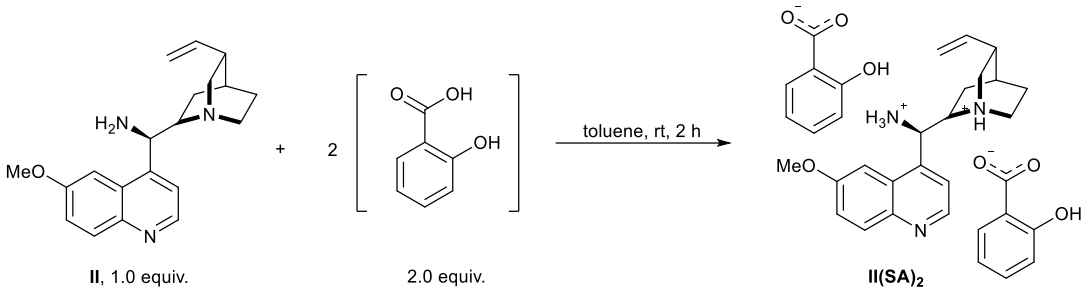
4. Synthesis of 1-[4-(allyloxy)-3,5-diisopropylphenyl]-2,2,2-trifluoroethan-1-one (2e)



1.5 mmol **2e**

Allyl bromide (190 µL, 2.25 mmol) and K_2CO_3 (0.42 g, 3.0 mmol) were subsequently added to a solution of 2,2,2-trifluoro-1-(4-hydroxy-3,5-diisopropylphenyl)ethan-1-one[12] (0.41 g, 1.5 mmol) in DMF (5 mL) at room temperature. The resulting mixture was stirred at the same temperature overnight. After this time, the solvent was eliminated under reduced pressure. The mixture was diluted with EtOAc (25 mL), washed with H_2O (6 x 5 mL) and brine (2 x 5 mL), dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (toluene/EtOAc 95/5) to afford pure product **2e** as a colorless oil (0.41 g, 87%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.85 (s, 2H), 6.22 – 6.03 (m, 1H), 5.48 (d, *J* = 17.2 Hz, 1H), 5.32 (d, *J* = 10.5 Hz, 1H), 4.35 (d, *J* = 5.3 Hz, 2H), 3.35 (hept, *J* = 6.8 Hz, 2H), 1.26 (d, *J* = 6.9 Hz, 12H). **^{13}C NMR** (75.5 MHz, CD_2Cl_2): δ 180.3 (q, $J_{C,F}$ = 34.0 Hz), 160.8, 144.1, 134.0, 127.3, 127.0, 117.8, 117.5 (q, $J_{C,F}$ = 291.7 Hz), 76.2, 27.4, 24.0. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –70.89 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{17}H_{22}O_2F_3$ [M^++H] 315.1566, found 315.1566.

5. Synthesis of II(SA)$_2$ salt



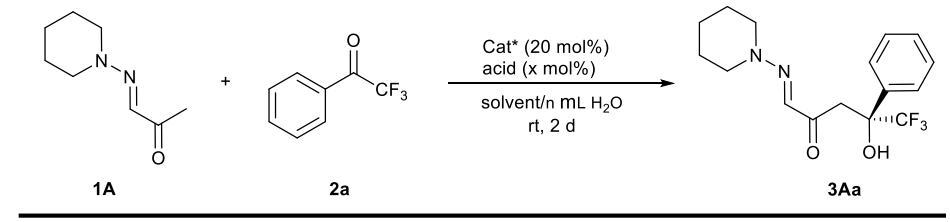
II, 1.0 equiv. 2.0 equiv. **II(SA)$_2$**

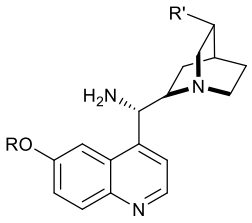
Salicylic acid (0.55 g, 4 mmol) was added to a solution of **II** (0.67 g, 2 mmol) in toluene (0.1 M, 20 mL) at room temperature. The mixture was stirred at the same temperature for 2 h. After this time, the solvent was eliminated under reduced pressure and Et_2O was added (5 mL). The resulting suspension was vigorously stirred for 15 min and the solvent was eliminated under reduced pressure to afford the pure salt **II(SA)$_2$** as a pale yellow solid (1.1 g, 92%); mp. = 138-140 ºC. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 9.81 (br s, 6H), 8.77 (d, *J* = 4.6 Hz, 1H), 8.08 (d, *J* = 9.3 Hz, 1H), 7.84 (dd, *J* = 7.8, 1.3 Hz, 2H), 7.75 – 7.59 (m, 2H), 7.58 – 7.42 (s, 2H), 7.41 – 7.30 (m, 4H), 6.90 (d, *J* = 8.2 Hz, 2H), 6.80 (t, *J* = 7.4 Hz, 2H), 5.84 – 5.73 (m, 1H), 5.32 – 5.14 (m, 2H), 3.93 (s, 3H), 3.69 – 3.52 (m, 3H), 3.42 – 3.25 (m, 1H), 2.72 – 2.56 (m, 1H), 1.96 – 1.79 (s, 3H), 1.41 – 1.31 (m, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 174.4, 161.8, 159.0, 146.9, 143.7, 136.5, 134.6, 132.2, 132.1, 131.1, 130.7, 129.4, 128.6, 128.5, 127.7, 123.1, 118.6, 117.5, 117.0, 115.2, 62.1, 56.5, 55.8, 48.6, 45.9, 36.5, 26.6, 24.1, 23.5. **HRMS** (ESI): m/z calcd for $C_{20}H_{26}ON_3^+$ [M^+] 324.2070, found 324.2066. $[\alpha]_D^{25}$ = +31.6 (c 1.0, $CHCl_3$).

Recrystallization of **II(SA)$_2$** by slow diffusion of *n*-hexanes in a solution of **II(SA)$_2$** in CH_2Cl_2 afforded suitable crystals for X-ray analysis.

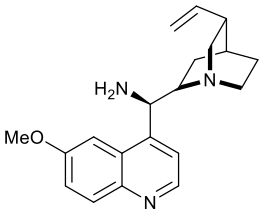
[12] D. S. Stewart, P. Y. Savechenkov, Z. Dostalova, D. C. Chiara, R. Ge, D. E. Raines, J. B. Cohen, S. A. Forman, K. S. Bruzik, K. W. Miller, *J. Med. Chem.* 2011, **54**, 8124.

6. Screening of chiral organocatalysts and preliminary optimization of the reaction parameters

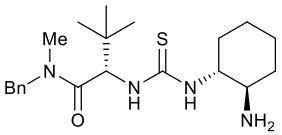




Ia, R = -CH=CH$_2$, R' = Me
Ib, R = -CH=CH$_2$, R' = H
Ic, R = Et, R' = Me



II



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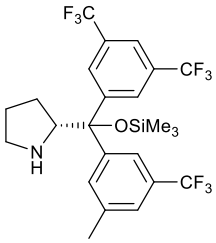
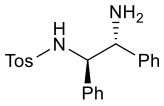
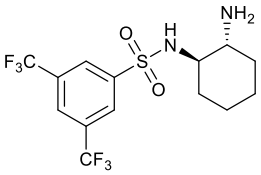


IV



V



VI

2,2,2-Trifluoro-1-phenylethan-1-one **2a** (14 µL, 0.1 mmol) was added to a solution of organocatalyst **I-VI** (0.02 mmol), the acid additive (0.02 mmol) and ketone **1A** (30 mg, 0.2 mmol) in the corresponding solvent (100 µL/n µL H_2O) at room temperature. The resulting mixture was stirred at this temperature for 2 d. Conversions were estimated by ^{1}H-NMR and enantiomeric ratios were determined by HPLC analysis.

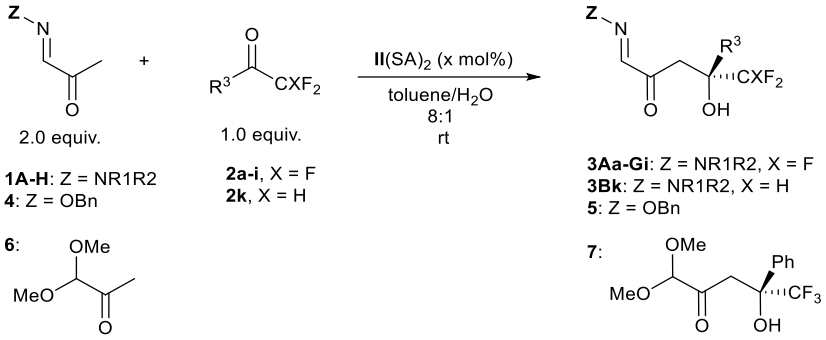
Table S1

Entry	Catalyst	Acid (mol%)	Solvent	Conv. (%)[a]	ee (%)[b]
1	**Ia**	BA (20)	Toluene	65	82
2	**Ib**	BA (20)	Toluene	<10[c]	66
3	**Ic**	BA (20)	Toluene	64	82
4	**II**	BA (20)	**Toluene**	**55**	**90**
5	**III**	BA (20)	Toluene	95[c]	54
6	**IV**	BA (20)	Toluene	<5[c]	nd
7	**V**	BA (20)	Toluene	35[c]	32
8	**VI**	BA (20)	Toluene	10[c]	*rac*
9	**II**	BA (20)	H_2O	>95[d]	84
10	**II**	BA (20)	$CHCl_3$	60	80
11	**II**	BA (20)	THF	<5	nd
12	**II**	BA (20)	MeOH	20	37
13	**II**	BA (20)	EtOAc	15	74
14	**II**	BA (20)	TFT	45	86
15	**II**	BA (20)	Toluene/H_2O (2:1)	>95	88
16	**II**	TFA (20)	Toluene/H_2O (2:1)	50	86
17	**II**	*m*-Br-PhOH (20)	Toluene/H_2O (2:1)	<5	nd
18	**II**	*m*-Cl-PhCO$_2$H (20)	Toluene/H_2O (2:1)	>95	88
19	**II**	*p*-NO$_2$-PhCO$_2$H (20)	Toluene/H_2O (2:1)	>95	89
20	**II**	*p*-Me-PhCO$_2$H (20)	Toluene/H_2O (2:1)	>95	88
21	**II**	*p*-OMe-PhCO$_2$H (20)	Toluene/H_2O (2:1)	>95	89

22	**II**	**SA (20)**	Toluene/H_2O (2:1)	**>95 (80)[c]**	**89**
23[e]	**II**	SA (20)	Toluene/H_2O (2:1)	>95	88
24[e]	**II**	SA (20)	Toluene/H_2O (4:1)	>95	87
25[e]	**II**	SA (20)	Toluene/H_2O (8:1)	>95	89
26[e]	**II**	SA (20)	Toluene/H_2O (16:1)	>95	87
27[e]	**II**	SA (10)	Toluene/H_2O (8:1)	84	84
28[e]	**II**	SA (40)	Toluene/H_2O (8:1)	>95	92
29[e],[f]	**II**	**SA (20)**	Toluene/H_2O (8:1)	**>95**	**92**
30[e],[g]	**II(SA)$_2$**	**-**	**Toluene/H_2O (8:1)**	**>95**	**92**

[a] Estimated by ^{1}H NMR in the crude mixture. [b] Determined by HPLC analysis after isolation of the product by semipreparative TLC (toluene/EtOAc 9/1). [c] Determined after 1 d. [d] Determined after 36 h. [e] Reaction was performed at 0.2 mmol scale. [f] Reaction was performed employing 10 mol% of catalyst loading. [g] Reaction was performed employing **II(SA)$_2$** salt (10 mol%). [BA = Benzoic Acid]. [TFA = Trifluoroacetic Acid]. [SA = Salicylic Acid]. [TFT = Trifluorotoluene]. [nd = not determined].

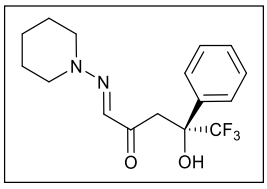
7. General procedure for the catalytic enantioselective reactions of ketones 1A-H, 4, and 6 with di- and trifluoromethyl ketones 2a-k



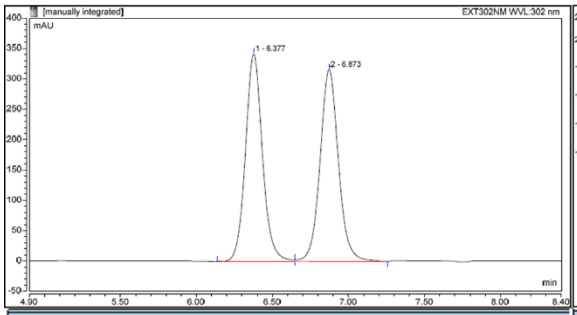
Di- or trifluoromethyl ketone **2a-k** (1.0 equiv.) was added to a solution of **II(SA)$_2$** salt (x mol%) and the corresponding ketone **1A-H, 4** or **6** (2.0 equiv.) in toluene/H_2O 8:1 (1.0 M) at room temperature. The resulting mixture was stirred at this temperature until the consumption of the starting material. After this time, the resulting mixture was directly purified by flash chromatography (toluene/EtOAc 9/1) to afford pure product **3Aa-Gi**, **3Bk**, **5** or **7**.

Racemic samples were prepared employing pyrrolidine (20 mol%) and benzoic acid (20 mol%) following the general procedure described above.

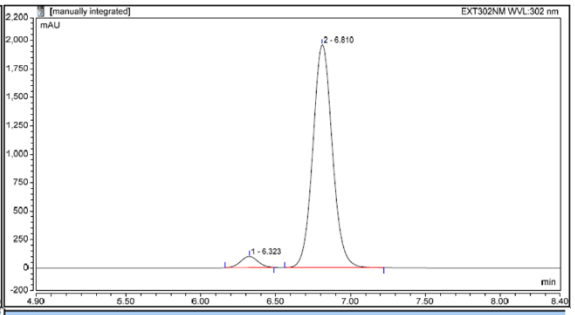
(*S*,*E*)-5,5,5-Trifluoro-4-hydroxy-4-phenyl-1-(piperidin-1-ylimino)pentan-2-one, (*S*)-**3Aa**.



Following the general procedure **7**, starting from **1A** (61 mg, 0.4 mmol), 2,2,2-trifluoro-1-phenylethan-1-one **2a** (28 µL, 0.2 mmol) and 10 mol% of **II(SA)$_2$** salt (12 mg, 0.02 mmol), compound (*S*)-**3Aa** was obtained as a colorless oil (65 mg, 98%; reaction performed at 2 mmol scale: 637 mg, 99%, 92% ee; reactions ran for 2 d). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.63 (d, *J* = 7.3 Hz, 2H), 7.36 – 7.28 (m, 4H), 6.72 (s, 1H), 6.30 (s, 1H), 3.91 (d, *J* = 16.0 Hz, 1H), 3.42 (t, *J* = 5.8 Hz, 4H), 3.29 (d, *J* = 16.0 Hz, 1H), 1.73 (dq, *J* = 11.4, 5.7 Hz, 4H), 1.67 – 1.58 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 198.0, 138.2, 128.5, 128.1, 126.9, 125.0 (q, $J_{C,F}$ = 285.0 Hz), 76.6 (q, $J_{C,F}$ = 28.9 Hz), 51.6, 38.0, 24.9, 23.5. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.33 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{16}H_{19}O_2N_2F_3Na$ [M^++Na] 351.1291, found 351.1287. The enantiomeric excess was determined by HPLC using a Chiralpak IA column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{minor} = 6.3 min, τ_{major} = 6.8 min (92% ee); $[\alpha]_D^{25}$ = +242.6 (c 1.0, $CHCl_3$).

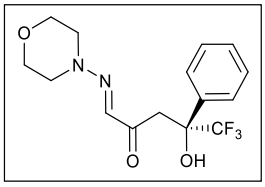


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	6.377	44.305	49.94
2	6.873	44.415	50.06



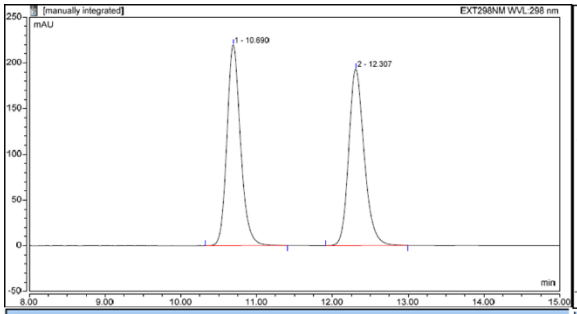
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	6.323	13.013	4.21
2	6.810	296.008	95.79

(*S*,*E*)-5,5,5-Trifluoro-4-hydroxy-1-(morpholinoimino)-4-phenylpentan-2-one, (*S*)-**3Ba**.

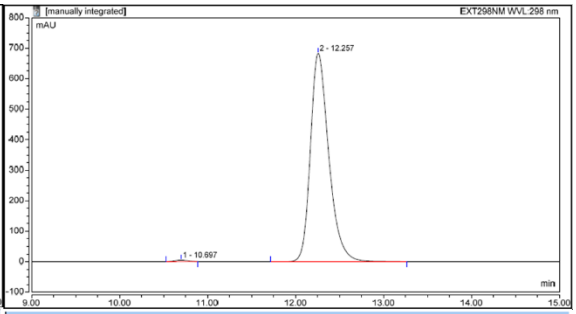


Following the general procedure **7**, starting from **1B** (62 mg, 0.4 mmol), 2,2,2-trifluoro-1-phenylethan-1-one **2a** (28 µL, 0.2 mmol) and 10 mol% of **II(SA)**$_2$ salt (12 mg, 0.02 mmol), compound (*S*)-**3Ba** was obtained as a white solid (65 mg, 98%, 92% ee; reaction performed at 2 mmol scale: 650 mg, 98%, 92% ee; after a single recrystallization: 310 mg, 47%, >99% ee; reactions ran for 2 d). mp. = 72-74 ºC. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.61 (d, *J* = 7.4 Hz, 2H), 7.43 – 7.28 (m, 3H), 6.78 (s, 1H), 5.98 (s, 1H), 3.92 (d, *J* = 16.3 Hz, 1H), 3.90 – 3.80 (m, 4H), 3.44 – 3.38 (m, 4H), 3.31 (d, *J* = 16.3 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 198.2, 138.0, 130.2, 128.7, 128.3, 126.8, 124.8 (q, $J_{C,F}$ = 284.7 Hz), 76.6 (q, $J_{C,F}$ = 29.2 Hz), 66.0, 50.7, 38.3.**^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.37 (s, 3F). **HRMS** (ESI): m/z calcd for $C_{15}H_{17}F_3N_2O_3Na$ [M^++Na] 353.1083, found 353.1078. The enantiomeric excess was determined by HPLC using a Chiralpak IB column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{minor} = 10.7 min, τ_{major} = 12.3 min (>99% ee); $[\alpha]_D^{20}$ = +261.5 (c 1.0, $CHCl_3$).

Recrystallization of (*S*)-**3Ba** by slow diffusion of *n*-hexanes in a solution of (*S*)-**3Ba** in Et_2O afforded suitable crystals for X-ray analysis.

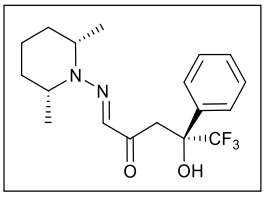


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	10.690	45.630	49.98
2	12.307	45.662	50.02



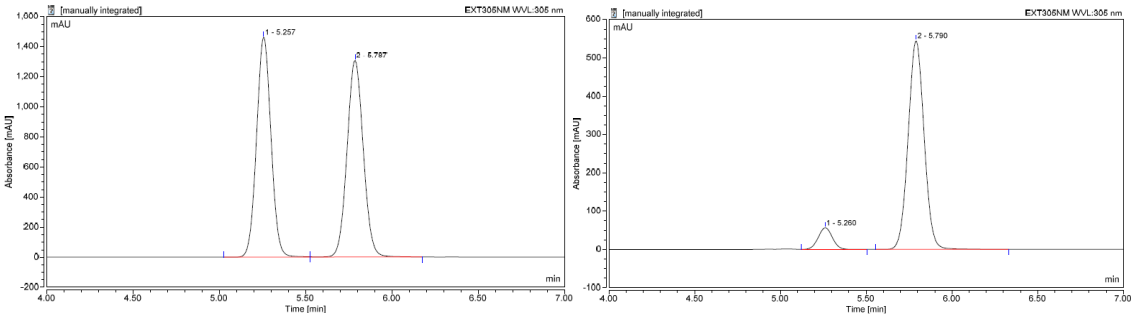
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	10.697	0.806	0.49
2	12.257	165.086	99.51

(*S*,*E*)-1-[(*cis*-2,6-Dimethylpiperidin-1-yl)imino]-5,5,5-trifluoro-4-hydroxy-4-phenylpentan-2-one, (*S*)-**3Ca**.



Following the general procedure **7**, starting from **3C** (73 mg, 0.4 mmol), 2,2,2-trifluoro-1-phenylethan-1-one **2a** (28 µL, 0.2 mmol) and 20 mol% of **II(SA)**$_2$ salt (24 mg, 0.04 mmol), compound (*S*)-**3Ca** was obtained as a pale yellow oil (70 mg, 98%, reaction ran for 7 d). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.72 – 7.52 (m, 2H), 7.42 – 7.26 (m, 3H), 6.67 (s, 1H), 6.44 (s, 1H), 4.12 – 3.97 (m, 2H), 3.92 (d, *J* = 15.8 Hz, 1H), 3.27 (d, *J* = 15.7 Hz, 1H), 1.92 – 1.79 (m, 3H), 1.77

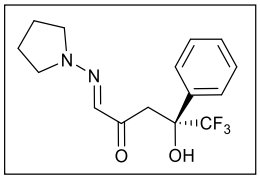
– 1.68 (m, 2H), 1.61 (tt, J = 7.7, 4.1 Hz, 1H), 1.23 (d, J = 7.0 Hz, 3H), 1.17 (d, J = 7.0 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 197.9, 138.3, 128.5, 128.1, 127.0, 126.5, 125.0 (q, $J_{C,F}$ = 285.0 Hz), 76.7 (q, $J_{C,F}$ = 28.8 Hz), 54.7, 54.1 37.5, 30.1, 18.6, 18.1, 14.0. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.34 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{18}H_{23}F_3N_2O_2Na$ [M^++Na] 379.1604, found 379.1598. The enantiomeric excess was determined by HPLC using a Chiralpak IB column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{minor} = 5.3 min, τ_{major} = 5.8 min (83% ee); $[\alpha]_D^{25}$ = +335.0 (c 1.0, $CHCl_3$).



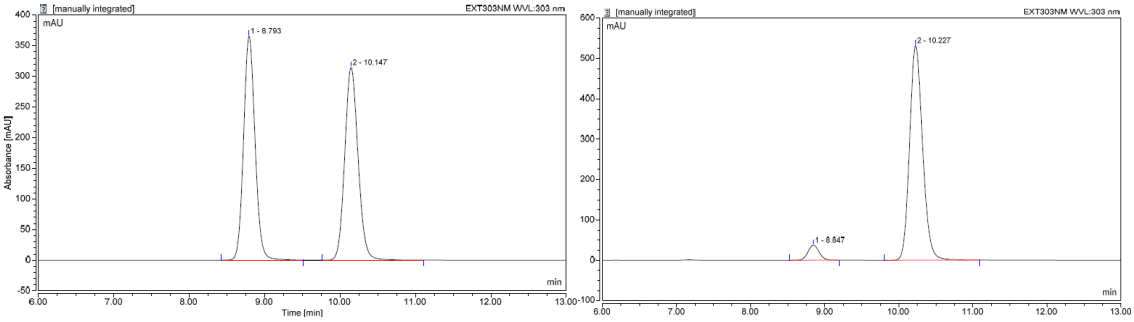
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	5.257	142.040	49.88
2	5.787	142.706	50.12

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	5.260	5.432	8.46
2	5.790	58.774	91.54

(*S*,*E*)-5,5,5-Trifluoro-4-hydroxy-4-phenyl-1-(pyrrolidin-1-ylimino)pentan-2-one, (*S*)-**3Da**.



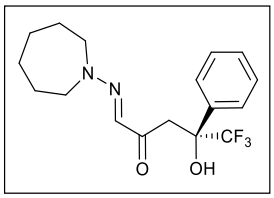
Following the general procedure **7**, starting from **1D** (56 mg, 0.4 mmol), 2,2,2-trifluoro-1-phenylethan-1-one **2a** (28 µL, 0.2 mmol) and 20 mol% of **II(SA)$_2$** salt (24 mg, 0.04 mmol), compound (*S*)-**3Da** was obtained as a pale yellow oil (60 mg, 95%, reaction ran for 7 d). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.63 (d, J = 7.6 Hz, 2H), 7.39 – 7.28 (m, 3H), 6.44 (t, J = 1.0 Hz, 1H), 3.86 (d, J = 16.1 Hz, 1H), 3.45 (s, 4H), 3.28 (d, J = 16.1 Hz, 1H), 2.13 – 1.93 (m, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 197.4, 138.3, 128.5, 128.1, 128.1, 126. 9, 125.0 (q, $J_{C,F}$ = 285.0 Hz), 76.6 (q, $J_{C,F}$ = 28.8 Hz), 51.1, 37.5, 23.9. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.31 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{15}H_{17}F_3N_2O_2Na$ [M^++Na] 337.1134, found 337.1129. The enantiomeric excess was determined by HPLC using a Chiralpak IB column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{minor} = 6.6 min, τ_{major} = 10.2 min (89% ee); $[\alpha]_D^{25}$ = +391.6 (c 1.0, $CHCl_3$).



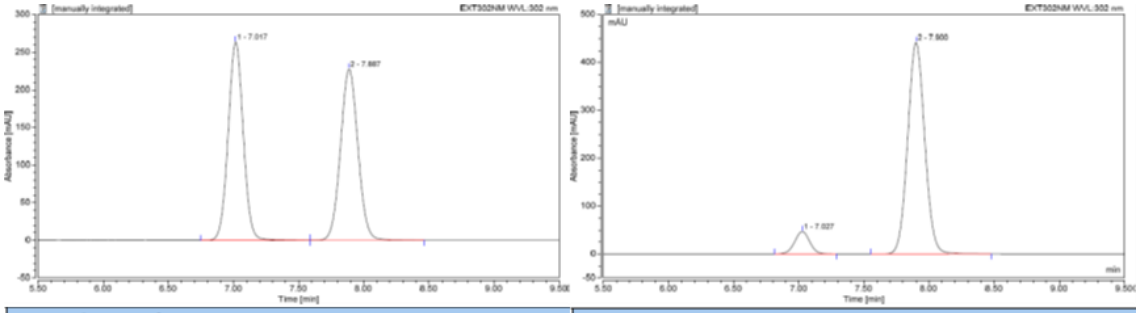
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	8.793	64.459	50.01
2	10.147	64.434	49.99

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	8.847	6.563	5.70
2	10.227	108.653	94.30

(*S*,*E*)-1-(Azepan-1-ylimino)-5,5,5-trifluoro-4-hydroxy-4-phenylpentan-2-one, (*S*)-**3Ea**.



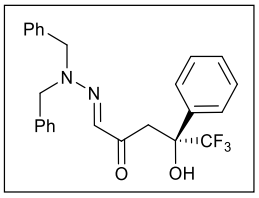
Following the general procedure **7**, starting from **1E** (67 mg, 0.4 mmol), 2,2,2-trifluoro-1-phenylethan-1-one **2a** (28 µL, 0.2 mmol) and 20 mol% of **II(SA)**$_2$ salt (24 mg, 0.04 mmol), compound (*S*)-**3Ea** was obtained as a pale yellow oil (68 mg, 99%, reaction ran for 7 d). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.63 (d, *J* = 7.4 Hz, 2H), 7.41 – 7.27 (m, 3H), 6.54 (s, 1H), 3.92 (d, *J* = 15.8 Hz, 1H), 3.82 (s, 2H), 3.31 (s, 2H), 3.24 (d, *J* = 15.9 Hz, 1H), 1.86 – 1.74 (m, 4H), 1.70 – 1.53 (m, 4H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 197.7, 138.3, 128.5, 128.1, 127.0, 125.9, 125.0 (q, $J_{C,F}$ = 284.9 Hz), 76.7 (q, $J_{C,F}$ = 28.8 Hz), 59.3, 50.8, 37.5, 28.3. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.37 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{17}H_{21}F_3N_2O_2Na$ [M^++Na] 365.1447, found 365.1444. The enantiomeric excess was determined by HPLC using a Chiralpak IB column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{minor} = 7.0 min, τ_{major} = 7.9 min (83% ee); $[\alpha]_D^{25}$ = +320.1 (c 1.0, $CHCl_3$).



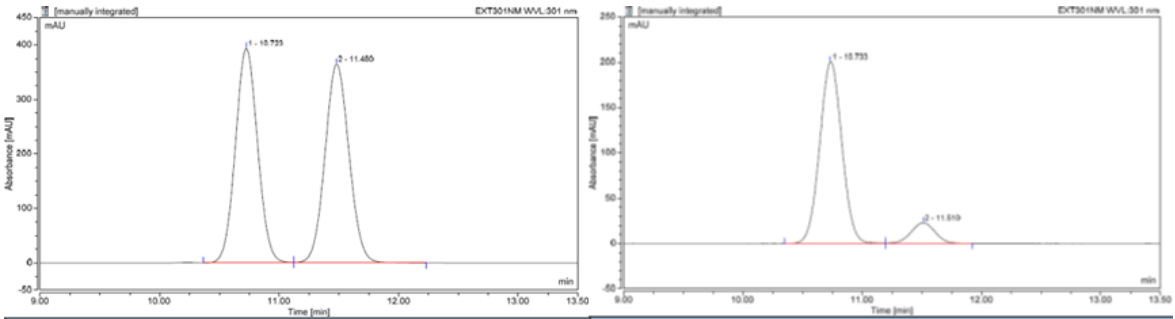
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	7.017	35.417	50.04
2	7.887	35.358	49.96

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	7.027	6.307	8.59
2	7.900	67.119	91.41

(*S*,*E*)-1-(2,2-Dibenzylhydrazineylidene)-5,5,5-trifluoro-4-hydroxy-4-phenylpentan-2-one, (*S*)-**3Fa**.



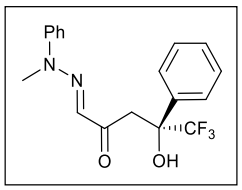
Following the general procedure **7**, starting from **1F** (106 mg, 0.4 mmol), 2,2,2-trifluoro-1-phenylethan-1-one **2a** (28 µL, 0.2 mmol) and 20 mol% of **II(SA)**$_2$ salt (24 mg, 0.04 mmol), compound (*S*)-**3Fa** was obtained as a pale yellow oil (88 mg, 99%; reaction ran for 3 d). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.64 – 7.56 (m, 2H), 7.40 – 7.30 (m, 9H), 7.14 (s, 4H), 6.59 (s, 1H), 6.13 (s, 1H), 4.69 (s, 4H), 4.01 (d, *J* = 15.8 Hz, 1H), 3.24 (d, *J* = 15.8 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 198.1, 138.1, 129.2, 128.7, 128.6, 128.3, 128.2, 127.5, 127.0, 124.9 (q, $J_{C,F}$ = 285.0 Hz), 76.7 (q, $J_{C,F}$ = 28.9 Hz), 37.6. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.37 (s, 3F). **HRMS** (ESI): m/z calcd for $C_{25}H_{23}F_3N_2O_2Na$ [M^++Na] 463.1604, found 463.1598. The enantiomeric excess was determined by HPLC using a Chiralpak IB column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{major} = 10.7 min, τ_{minor} = 11.5 min (78% ee); $[\alpha]_D^{20}$ = +234.9 (c 1.0, $CHCl_3$).



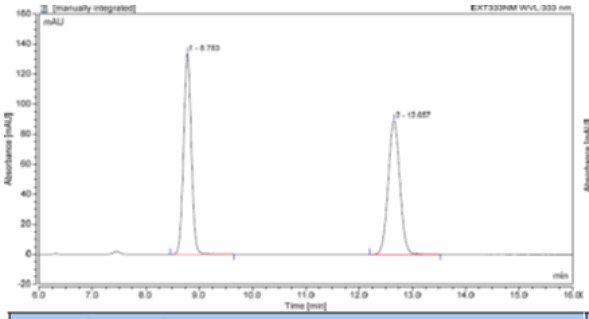
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	10.723	84.716	49.89
2	11.480	85.083	50.11

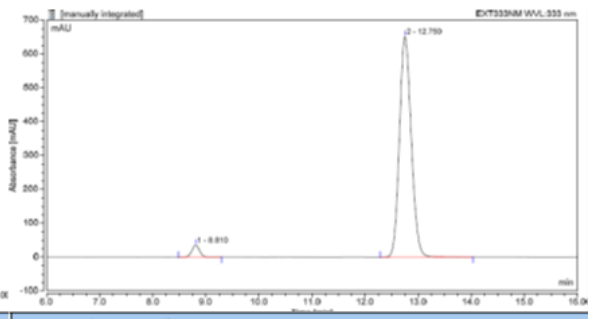
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	10.733	43.305	89.00
2	11.510	5.350	11.00

(*S*,*E*)-5,5,5-Trifluoro-4-hydroxy-1-(2-methyl-2-phenylhydrazineylidene)-4-phenylpentan-2-one, (*S*)-**3Ga**.



Following the general procedure **7**, starting from **1G** (70 mg, 0.4 mmol), 2,2,2-trifluoro-1-phenylethan-1-one **2a** (28 µL, 0.2 mmol) and 10 mol% of **II(SA)**$_2$ salt (12 mg, 0.02 mmol), compound (*S*)-**3Ga** was obtained as a yellow solid (70 mg, 99%; reaction performed at 2 mmol scale: 584 mg, 84%, 93% ee; reactions ran for 2 d); mp. = 88-90 °C. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.64 (d, *J* = 7.4 Hz, 2H), 7.49 – 7.40 (m, 4H), 7.38 – 7.29 (m, 3H), 7.22 (tt, *J* = 7.0, 1.5 Hz, 1H), 6.88 (d, *J* = 0.5 Hz, 1H), 6.01 (s, 1H), 4.05 (d, *J* = 16.4 Hz, 1H), 3.45 (d, *J* = 16.3 Hz, 1H), 3.42 (d, *J* = 0.5 Hz, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 198.4, 146.2, 137.9, 130.4, 129.5, 128.6, 128.2, 126.7, 124.7, 124.8 (q, $J_{C,F}$ = 285.4 Hz), 117.7, 76.6 (q, $J_{C,F}$ = 29.0 Hz), 38.1, 35.3. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.25 (s, 3F). **HRMS** (ESI): m/z calcd for $C_{18}H_{17}F_3N_2O_2Na$ [M^++Na] 373.1134, found 373.1129. The enantiomeric excess was determined by HPLC using a Chiralpak IB column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{minor} = 8.8 min, τ_{major} = 12.8 min (93% ee); $[\alpha]_D^{20}$ = +584.2 (c 1.0, $CHCl_3$).
Recrystallization of (*S*)-**3Ga** by slow evaporation of a solution of (*S*)-**3Ga** in CH_2Cl_2 afforded suitable crystals for X-ray analysis.

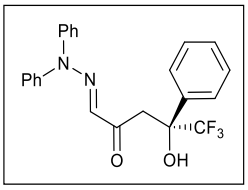




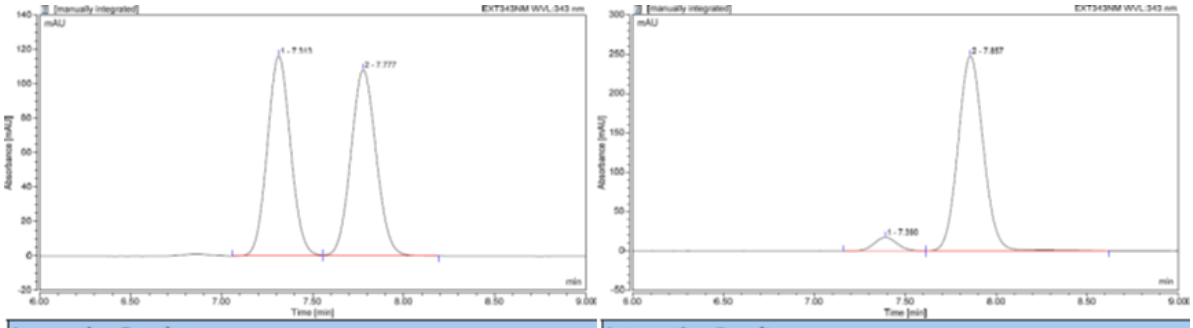
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	8.783	22.547	50.04
2	12.657	22.510	49.96

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	8.810	5.961	3.43
2	12.750	167.864	96.57

(*S*,*E*)-1-(2,2-Diphenylhydrazineylidene)-5,5,5-trifluoro-4-hydroxy-4-phenylpentan-2-one, (*S*)-**3Ha**.



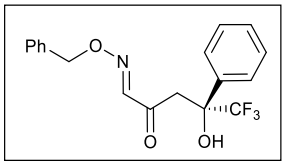
Following the general procedure **7**, starting from **1H** (95 mg, 0.4 mmol), 2,2,2-trifluoro-1-phenylethan-1-one **2a** (28 µL, 0.2 mmol) and 10 mol% of **II(SA)**$_2$ salt (12 mg, 0.02 mmol), compound (*S*)-**3Ha** was obtained as a pale pink solid (82 mg, 99%; reaction ran for 2 d). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.68 (d, *J* = 7.2 Hz, 2H), 7.48 (s, 5H), 7.41 – 7.28 (m, 4H), 7.19 (d, *J* = 7.9 Hz, 4H), 6.55 (s, 1H), 5.82 (s, 1H), 4.15 (d, *J* = 16.3 Hz, 1H), 3.51 (d, *J* = 16.4 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 198.7, 137.9, 130.3, 128.7, 128.4, 126.8, 124.9 (q, $J_{C,F}$ = 284.9 Hz), 76.7 (q, $J_{C,F}$ = 29.0 Hz), 38.5. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.23 (s, 3F). **HRMS** (ESI): m/z calcd for $C_{23}H_{19}F_3N_2O_2Na$ [M^++Na] 435.1291, found 435.1285. The enantiomeric excess was determined by HPLC using a Chiralpak IC column [*n*-hexanes/*i*PrOH (95:5)]; flow rate 1 mL/min; τ_{minor} = 7.4 min, τ_{major} = 7.9 min (88% ee); $[\alpha]_D^{20}$ = +403.2 (c 1.0, $CHCl_3$).



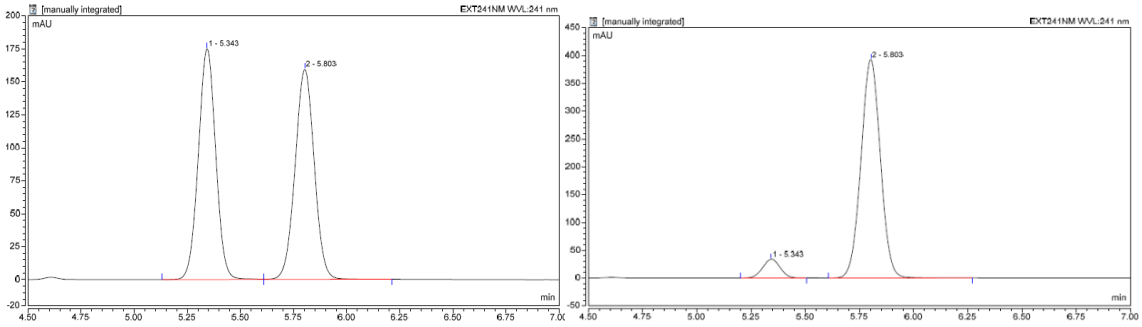
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	7.313	17.260	49.70
2	7.777	17.467	50.30

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	7.390	2.511	5.93
2	7.857	39.853	94.07

(*S*,*E*)-5,5,5-Trifluoro-4-hydroxy-2-oxo-4-phenylpentanal *O*-benzyl oxime, (*S*)-**5**.



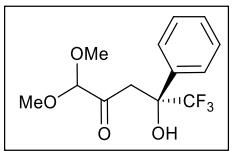
Following the general procedure **7**, starting from **4** (71 mg, 0.4 mmol), 2,2,2-trifluoro-1-phenylethan-1-one **2a** (28 µL, 0.2 mmol) and 20 mol% of **II(SA)**$_2$ salt (24 mg, 0.04 mmol), compound (*S*)-**5** was obtained as a pale yellow oil (70 mg, 99%, reaction ran for 3 d). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.55 – 7.49 (m, 2H), 7.47 – 7.39 (m, 6H), 7.36 – 7.27 (m, 3H), 5.35 (s, 2H), 5.06 (s, 1H), 3.99 (d, J = 16.8 Hz, 1H), 3.33 (d, J = 16.8 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 197.5, 137.1, 135.8, 129.0, 128.9, 128.5, 126.7, 124.5 (q, $J_{C,F}$ = 288.9 Hz), 78.8, 76.5 (q, $J_{C,F}$ = 29.4 Hz), 40.1. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.55 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{18}H_{16}F_3NO_3Na$ [M^++Na] 374.0974, found 374.0968. The enantiomeric excess was determined by HPLC using a Chiralpak IB column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{minor} = 5.3 min, τ_{major} = 5.8 min (86% ee); $[\alpha]_D^{25}$ = +161.21 (c 1.0, $CHCl_3$).



Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	5.343	16.613	49.93
2	5.803	16.662	50.07

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	5.343	3.194	7.25
2	5.803	40.855	92.75

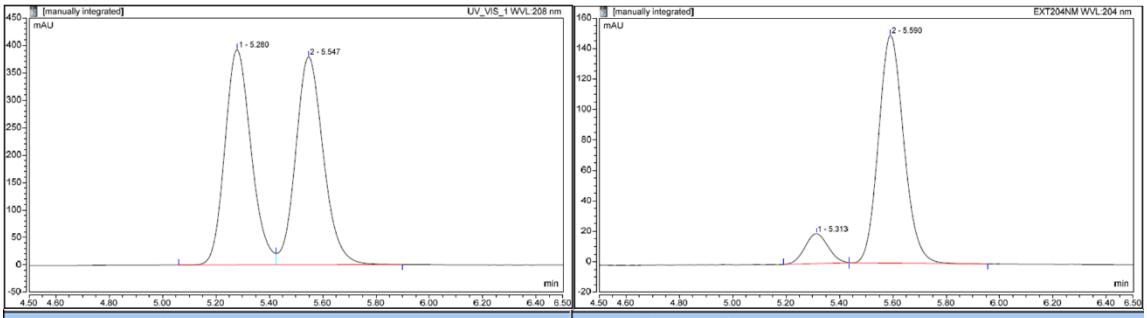
(*S*)-5,5,5-Trifluoro-4-hydroxy-1,1-dimethoxy-4-phenylpentan-2-one, (*S*)-**7**.



Following the general procedure **7**, starting from **6** (50 µL, 0.4 mmol), 2,2,2-trifluoro-1-phenylethan-1-one **2a** (28 µL, 0.2 mmol) and 20 mol% of **II(SA)**$_2$ salt (24 mg, 0.04 mmol), compound (*S*)-**7** was obtained as a colorless oil (54 mg, 92%, reaction ran for 3 d). The experimental data is in accordance with those reported in the literature.[13] **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.64 – 7.55 (m, 2H), 7.43 – 7.31 (m, 3H), 5.00 (s, 1H), 4.28 (s, 1H), 3.66 (d, J = 17.8 Hz, 1H), 3.40 (s, 3H), 3.31 (s, 3H), 3.29 (d, J = 17.8 Hz, 1H). **^{13}C NMR** (75.5 MHz, $CDCl_3$): δ 204.8, 137.1, 128.8, 128.3, 126.4, 124.4 (d, $J_{C,F}$ = 284.7 Hz), 104.4, 76.0 (d, $J_{C,F}$ = 29.3 Hz), 55.2, 39.9. The enantiomeric excess was determined by HPLC using a

[13] S. Luo, H. Xu, L. Chen, J. -P. Cheng, *Org. Lett.* 2008, **10**, 1775.

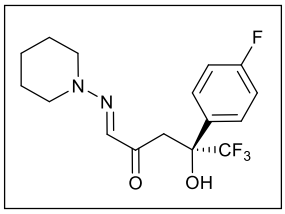
Chiralpak IB column [*n*-hexanes/*i*PrOH (95:5)]; flow rate 1 mL/min; τ_{minor} = 5.3 min, τ_{major} = 5.6 min (79% ee); $[\alpha]_D^{25}$ = +26.4 (c 2.0, EtOAc). Literature: $[\alpha]_D^{20}$ = +17.5 (c 2.0, EtOAc), 59% ee (*S*).



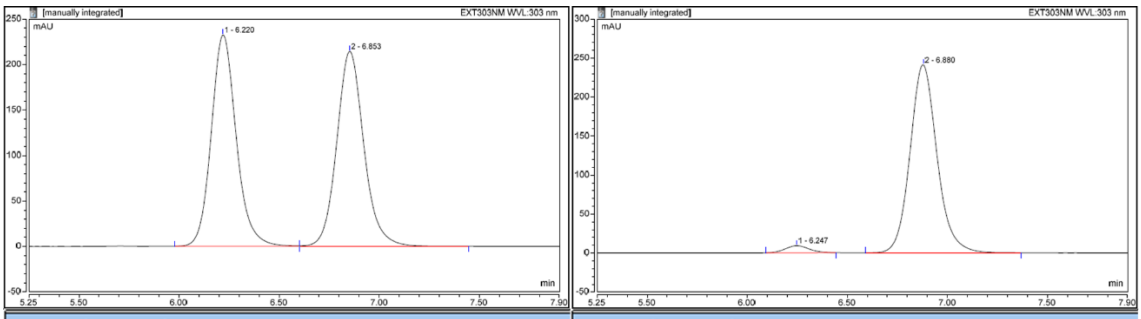
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	5.280	44.631	49.52
2	5.547	45.500	50.48

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	5.313	1.980	10.77
2	5.590	16.416	89.23

(*S*,*E*)-5,5,5-Trifluoro-4-(4-fluorophenyl)-4-hydroxy-1-(piperidin-1-ylimino)pentan-2-one, (*S*)-**3Ab**.



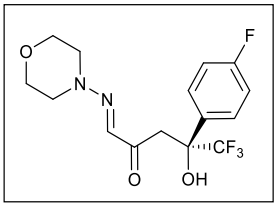
Following the general procedure **7**, starting from **1A** (61 mg, 0.4 mmol), 2,2,2-trifluoro-1-(4-fluorophenyl)ethan-1-one **2b** (28 µL, 0.2 mmol) and 10 mol% of **II(SA)**$_2$ salt (12 mg, 0.02 mmol), compound (*S*)-**3Ab** was obtained as a colorless oil (64 mg, 93%, reaction ran for 1 d). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.59 (dd, *J* = 8.5, 5.4 Hz, 1H), 7.08 – 6.94 (m, 2H), 6.73 (s, 1H), 6.30 (s, 1H), 3.90 (d, *J* = 16.0 Hz, 1H), 3.53 – 3.34 (m, 2H), 3.23 (d, *J* = 16.0 Hz, 1H), 1.82 – 1.63 (m, 6H). **^{13}C NMR** (75.5 MHz, $CDCl_3$): δ 197.7, 162.8 (d, $J_{C,F}$ = 247.2 Hz), 133.8 (d, $J_{C,F}$ = 2.8 Hz), 128.8 (d, $J_{C,F}$ = 8.3 Hz), 128.1, 124.6 (q, $J_{C,F}$ = 284.5 Hz), 114.9 (d, $J_{C,F}$ = 21.5 Hz), 76.2 (q, $J_{C,F}$ = 28.9 Hz), 51.4, 37.8, 24.8, 23.3. **^{19}F NMR** (282.5 MHz, $CDCl_3$): δ –80.69 (s, 3F), –114.15 (s, 1F). **HRMS** (ESI) m/z calcd. for $C_{16}H_{18}O_2N_2F_4Na$ [M^++Na] 369.1197, found 369.1195. The enantiomeric excess was determined by HPLC using a Chiralpak IA column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{minor} = 6.2 min, τ_{major} = 6.9 min (94% ee); $[\alpha]_D^{25}$ = +261.5 (c 1.0, $CHCl_3$).



Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	6.220	33.623	49.97
2	6.853	33.663	50.03

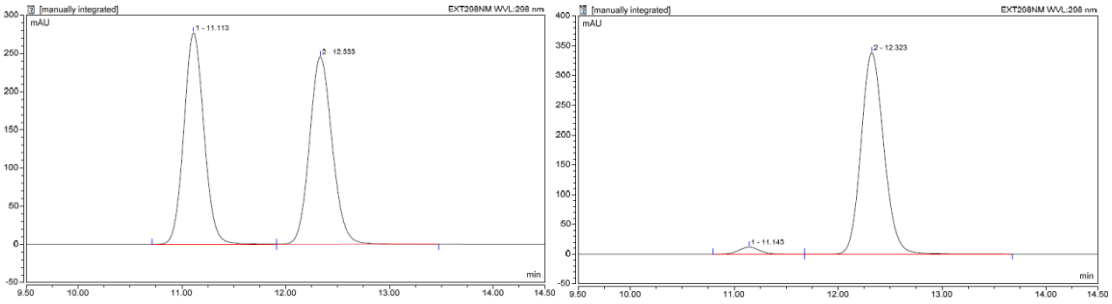
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	6.247	1.233	3.16
2	6.880	37.715	96.84

(*S*,*E*)-5,5,5-Trifluoro-4-(4-fluorophenyl)-4-hydroxy-1-(morpholinoimino)pentan-2-one, (*S*)-**3Bb**.



Following the general procedure **7**, starting from **1B** (62 mg, 0.4 mmol), 2,2,2-trifluoro-1-(4-fluorophenyl)ethan-1-one **2b** (28 µL, 0.2 mmol) and 10 mol% of **II(SA)**$_2$ salt (12 mg, 0.02 mmol), compound (*S*)-**3Bb** was obtained as a colorless oil (68 mg, 98%, reaction ran for 1 d). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.58 (dd, *J* = 8.6, 5.4 Hz, 2H), 7.10 – 6.94 (m, 2H), 6.78 (s, 1H), 6.04 (s, 1H), 3.95 – 3.79 (m, 5H), 3.46 – 3.35 (m, 4H), 3.27 (d, *J* = 16.3 Hz, 1H). **^{13}C NMR** (75.5 MHz, $CDCl_3$): δ

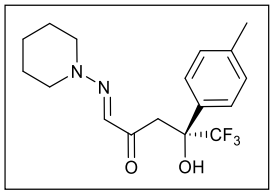
197.9, 162.8 (q, $J_{C,F}$ = 247.5 Hz), 133.6 (d, $J_{C,F}$ = 3.2 Hz), 129.9, 128.6 (d, $J_{C,F}$ = 8.8 Hz), 124.5 (d, $J_{C,F}$ = 284.9 Hz), 115.0 (d, $J_{C,F}$ = 21.5 Hz), 76.1 (d, $J_{C,F}$ = 29.2 Hz), 65.8, 50.5, 38.0. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.65 (s, 3F), –113.85 (s, 1F). **HRMS** (ESI) m/z calcd. for $C_{15}H_{16}F_4N_2O_3Na$ [M^++Na] 371.0989, found 371.0985. The enantiomeric excess was determined by HPLC using a Chiralpak IB column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{minor} = 11.1 min, τ_{major} = 12.3 min (94% ee); $[\alpha]_D^{25}$ = +311.5 (c 1.0, $CHCl_3$).



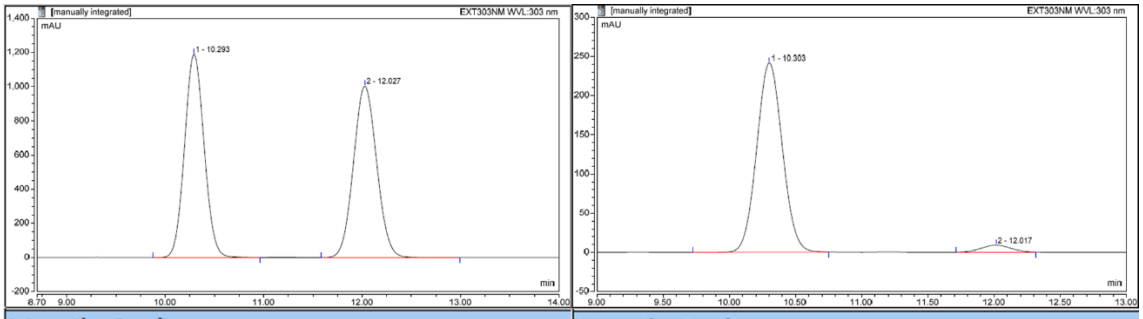
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	11.113	62.443	49.97
2	12.333	62.508	50.03

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	11.143	2.704	3.05
2	12.323	86.008	96.95

(*S*,*E*)-5,5,5-Trifluoro-4-hydroxy-1-(piperidin-1-ylimino)-4-(*p*-tolyl)pentan-2-one, (*S*)-**3Ac**.



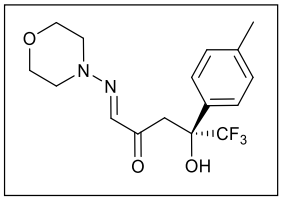
Following the general procedure **7**, starting from **1A** (61 mg, 0.4 mmol), 2,2,2-trifluoro-1-(*p*-tolyl)ethan-1-one **2c** (31 µL, 0.2 mmol) and 10 mol% of **II(SA)$_2$** salt (12 mg, 0.02 mmol), compound (*S*)-**3Ac** was obtained as a colorless oil (63 mg, 93%, reaction ran for 3 d). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.50 (d, *J* = 8.1 Hz, 2H), 7.15 (d, *J* = 8.2 Hz, 2H), 6.73 (s, 1H), 6.22 (s, 1H), 3.91 (d, *J* = 16.0 Hz, 1H), 3.42 (t, *J* = 6.5 Hz, 4H), 3.25 (d, *J* = 16.0 Hz, 1H), 2.33 (s, 3H), 1.81 – 1.62 (m, 6H). **^{13}C NMR** (75.5 MHz, $CDCl_3$): δ 198.0, 138.1, 135.1, 128.8, 128.3, 126.7, 124.8 (q, $J_{C,F}$ = 284.4 Hz), 76.4 (q, $J_{C,F}$ = 28.9 Hz), 51.4, 37.9, 24.8, 23.4, 21.0. **^{19}F NMR** (282.5 MHz, $CDCl_3$): δ –80.54 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{17}H_{21}O_2N_2F_3Na$ [M^++Na] 365.1447, found 365.1440. The enantiomeric excess was determined by HPLC using a Chiralpak IC column [*n*-hexanes/*i*PrOH (85:15)]; flow rate 1 mL/min; τ_{major} = 10.3 min, τ_{minor} = 12.0 min (92% ee); $[\alpha]_D^{25}$ = +295.5 (c 1.0, $CHCl_3$).



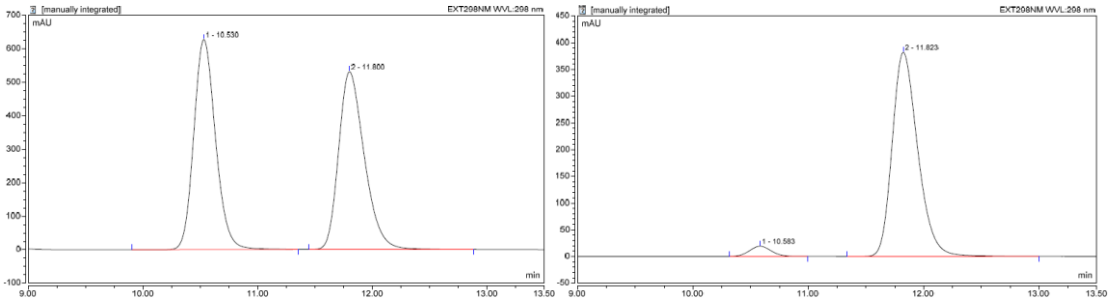
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	10.293	274.413	50.02
2	12.027	274.236	49.98

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	10.303	54.199	95.92
2	12.017	2.305	4.08

(*S*,*E*)-5,5,5-Trifluoro-4-hydroxy-1-(morpholinoimino)-4-(*p*-tolyl)pentan-2-one, (*S*)-**3Bc**.



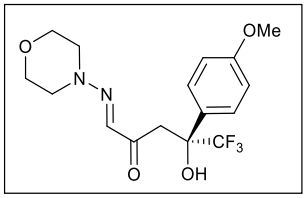
Following the general procedure **7**, starting from **1B** (62 mg, 0.4 mmol), 2,2,2-trifluoro-1-(*p*-tolyl)ethan-1-one **2c** (31 µL, 0.2 mmol) and 10 mol% of **II(SA)$_2$** salt (12 mg, 0.02 mmol), compound (*S*)-**3Bc** was obtained as a colorless oil (66 mg, 94%, reaction ran for 2 d). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.48 (d, *J* = 8.0 Hz, 2H), 7.15 (d, *J* = 8.0 Hz, 2H), 6.78 (s, 1H), 5.94 (s, 1H), 3.93 (d, *J* = 16.3 Hz, 1H), 3.89 – 3.83 (m, 4H), 3.42 – 3.36 (m, 4H), 3.27 (d, *J* = 16.3 Hz, 1H), 2.33 (s, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 198.3, 138.4, 135.0, 130.3, 129.0, 126.7, 124.9 (q, $J_{C,F}$ = 284.9 Hz), 76.5 (q, $J_{C,F}$ = 29.0 Hz), 66.0, 50.7, 38.3, 21.1.**^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.54 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{16}H_{19}F_3N_2O_3Na$ [M^++Na] 367.1240, found 367.1238. The enantiomeric excess was determined by HPLC using a Chiralpak IB column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{minor} = 10.6 min, τ_{major} = 11.8 min (92% ee); $[\alpha]_D^{25}$ = +340.7 (c 1.0, $CHCl_3$).



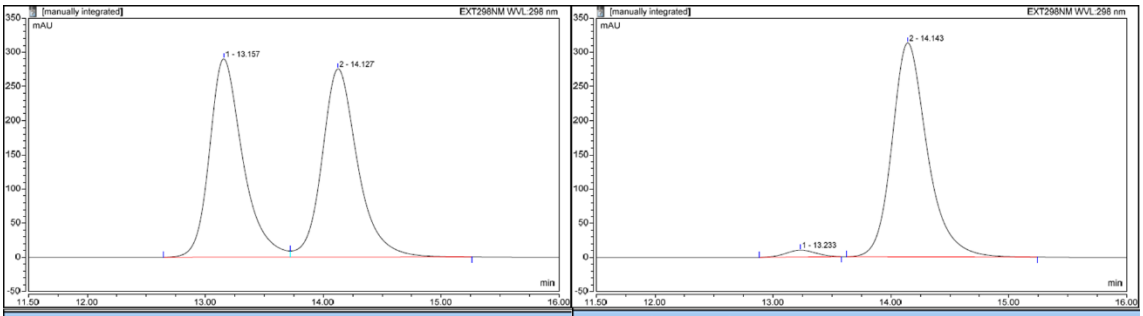
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	10.530	138.011	50.00
2	11.800	137.991	50.00

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	10.583	4.166	4.07
2	11.823	98.135	95.93

(*S*,*E*)-5,5,5-Trifluoro-4-hydroxy-4-(4-methoxyphenyl)-1-(morpholinoimino)pentan-2-one, (*S*)-**3Bd**.



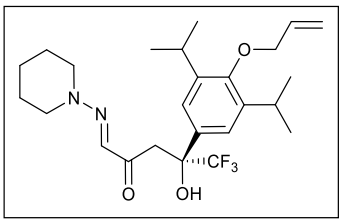
Following the general procedure **7**, starting from **1B** (62 mg, 0.4 mmol), 2,2,2-trifluoro-1-(4-methoxyphenyl)ethan-1-one **2d** (32 µL, 0.2 mmol) and 20 mol% of **II(SA)$_2$** salt (24 mg, 0.04 mmol), compound (*S*)-**3Bd** was obtained as a colorless oil (69 mg, 96%, reaction ran for 3 d). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.51 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.9 Hz, 2H), 6.78 (s, 1H), 5.93 (s, 1H), 3.92 (d, *J* = 16.2 Hz, 1H), 3.88 – 3.81 (m, 4H), 3.78 (s, 3H), 3.45 – 3.35 (m, 4H), 3.24 (d, *J* = 16.2 Hz, 1H). **^{13}C NMR** (75.5 MHz, $CDCl_3$): δ 198.1, 159.7, 130.4, 130.1, 129.8, 128.0, 126.6, 124.7 (q, $J_{C,F}$ = 284.5 Hz), 76.1 (q, $J_{C,F}$ = 29.0 Hz), 65.8, 55.1, 50.5, 38.1. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.74 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{16}H_{19}F_3N_2O_4Na$ [M^++Na] 383.1189, found 383.1184. The enantiomeric excess was determined by HPLC using a Chiralpak IA column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{minor} = 13.2 min, τ_{major} = 14.1 min (95% ee); $[\alpha]_D^{25}$ = +222.1 (c 1.0, $CHCl_3$).



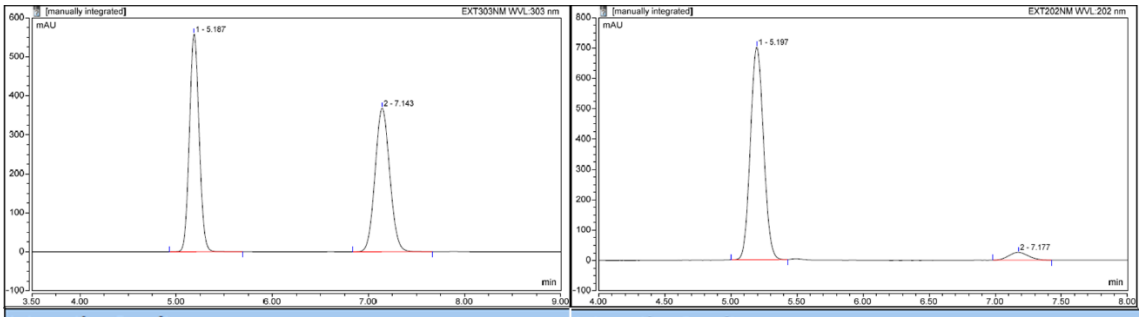
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	13.157	94.913	49.59
2	14.127	96.492	50.41

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	13.233	2.958	2.65
2	14.143	108.653	97.35

(*S*,*E*)-4-[4-(Allyloxy)-3,5-diisopropylphenyl]-5,5,5-trifluoro-4-hydroxy-1-(piperidin-1-ylimino)pentan-2-one, (*S*)-**3Ae**.



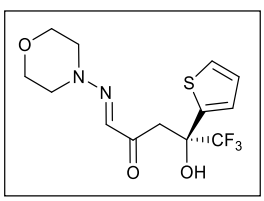
Following the general procedure **7**, starting from **1A** (61 mg, 0.4 mmol), 1-[4-(allyloxy)-3,5-diisopropylphenyl]-2,2,2-trifluoroethan-1-one **2e** (63 mg, 0.2 mmol) and 20 mol% of **II(SA)**$_2$ salt (24 mg, 0.04 mmol), compound (*S*)-**3Ae** was obtained as a white solid (78 mg, 83%, reaction ran for 5 d). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ 7.33 (s, 2H), 6.73 (s, 1H), 6.24 – 6.03 (m, 2H), 5.46 (dd, *J* = 17.2, 1.7 Hz, 1H), 5.27 (dd, *J* = 10.5, 1.4 Hz, 1H), 4.34 – 4.20 (m, 3H), 3.55 – 3.38 (m, 4H), 3.36 – 3.21 (m, 2H), 2.93 (d, *J* = 15.8 Hz, 1H), 1.83 – 1.59 (m, 6H), 1.19 (dd, *J* = 18.0, 6.9 Hz, 12H). **^{13}C NMR** (75.5 MHz, CD_2Cl_2): δ 199.1, 154.3, 141.9, 134.8, 134.3, 128.4, 125.4 (q, $J_{C,F}$ = 284.3 Hz) 123.6, 117.0, 77.4 (q, $J_{C,F}$ = 28.8 Hz), 75.9, 37.3, 27.2, 25.5, 24.4, 24.3, 23.9. **^{19}F NMR** (471 MHz, CD_2Cl_2): δ –81.26 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{25}H_{35}O_3N_2F_3Na$ [M^++Na] 491.2492, found 491.2490. The enantiomeric excess was determined by HPLC using a Chiralpak IC column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min); τ_{minor} = 5.2 min, τ_{major} = 7.1 min (90% ee); $[\alpha]_D^{20}$ = +240.3 (c 1.0, $CHCl_3$).



Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	5.187	65.154	50.01
2	7.143	65.123	49.99

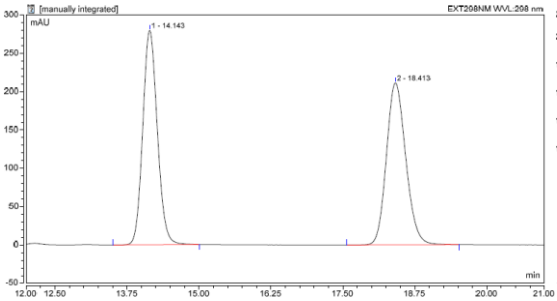
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	5.197	80.863	94.92
2	7.177	4.325	5.08

(*R*,*E*)-5,5,5-Trifluoro-4-hydroxy-1-(morpholinoimino)-4-(thiophen-2-yl)pentan-2-one, (*R*)-**3Bf**.

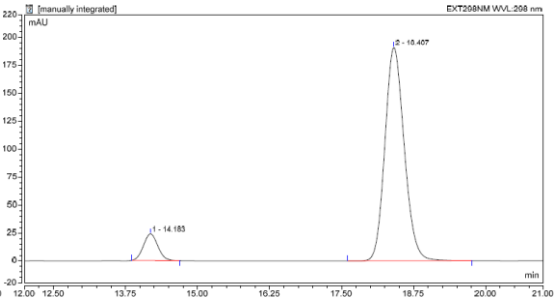


Following the general procedure **7**, starting from **1B** (62 mg, 0.4 mmol), 2,2,2-trifluoro-1-(thiophen-2-yl)ethan-1-one **2f** (26 µL, 0.2 mmol) and 10 mol% of **II(SA)**$_2$ salt (12 mg, 0.02 mmol), compound (*R*)-**3Bf** was obtained as a colorless oil (63 mg, 94%, reaction ran for 2 d). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.29 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.08 (d, *J* = 3.4 Hz, 1H), 6.96 (dd, *J* = 5.0, 3.7 Hz, 1H), 6.81 (s, 1H), 6.51 (s, 1H), 3.93 – 3.79 (m, 5H), 3.46 – 3.35 (m, 4H), 3.24 (d, *J* = 16.2 Hz, 1H). **^{13}C NMR** (75.5 MHz, $CDCl_3$): δ 197.6, 142.3, 129.8, 126.9, 126.3, 125.8, 124.0 (q, $J_{C,F}$ = 284.7 Hz), 75.8 (q, $J_{C,F}$ = 30.5 Hz) 65.8, 50.5, 38.9. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –81.40 (s, 3F). **HRMS**

(ESI) m/z calcd. for $C_{13}H_{15}F_3N_2O_3SNa$ [M^++Na] 359.0648, found 359.0646. The enantiomeric excess was determined by HPLC using a Chiralpak IB column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{minor} = 14.2 min, τ_{major} = 18.4 min (83% ee); $[\alpha]_D^{25}$ = +163.7 (c 1.0, $CHCl_3$).

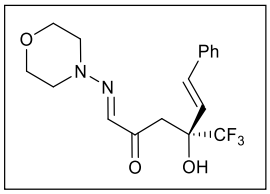


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	14.143	81.992	49.96
2	18.413	82.124	50.04

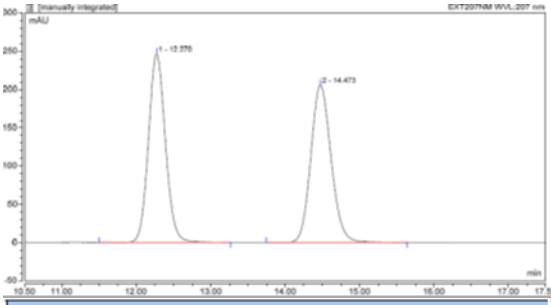


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	14.183	6.847	8.45
2	18.407	74.182	91.55

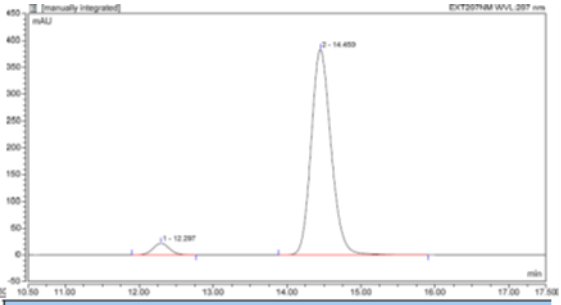
(*S*,1*E*,5*E*)-4-Hydroxy-1-(morpholinoimino)-6-phenyl-4-(trifluoromethyl)hex-5-en-2-one, (*S*)-**3Bg**.



Following the general procedure **7**, starting from **1B** (62 mg, 0.4 mmol), (*E*)-1,1,1-trifluoro-4-phenylbut-3-en-2-one **2g** (32 µL, 0.2 mmol) and 10 mol% of **II(SA)**$_2$ salt (12 mg, 0.02 mmol), compound (*S*)-**3Bg** was obtained as a colorless oil (61 mg, 85%, reaction ran for 2 d). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.35 – 7.28 (m, 2H), 7.24 (t, *J* = 7.4 Hz, 2H), 7.22 – 7.15 (m, 1H), 6.87 (d, *J* = 15.9 Hz, 1H), 6.79 (s, 1H), 6.10 (d, *J* = 15.8 Hz, 1H), 5.78 (s, 1H), 3.82 – 3.74 (m, 4H), 3.38 – 3.25 (m, 5H), 3.14 (d, *J* = 15.6 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 197.9, 136.0, 133.6, 130.3, 128.7, 128.4, 127.1, 125.1, 124.9 (q, $J_{C,F}$ = 285.4 Hz), 75.6 (q, $J_{C,F}$ = 29.2 Hz), 66.0, 50.7, 38.3. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.96 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{17}H_{19}F_3N_2O_3Na$ [M^++Na] 379.1240, found 379.1234. The enantiomeric excess was determined by HPLC using a Chiralpak IB column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{minor} = 12.3 min, τ_{major} = 14.5 min (91% ee); $[\alpha]_D^{25}$ = +237.3 (c 1.0, $CHCl_3$).

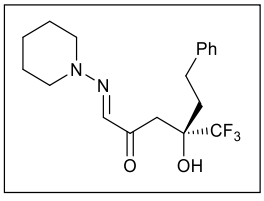


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	12.270	64.850	49.95
2	14.473	64.979	50.05



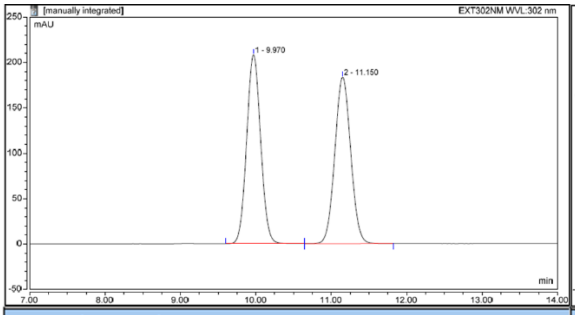
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	12.297	5.630	4.50
2	14.450	119.490	95.50

(***R*,*E***)-**4-Hydroxy-6-phenyl-1-(piperidin-1-ylimino)-4-(trifluoromethyl)hexan-2-one**, (*R*)-**3Ah**.



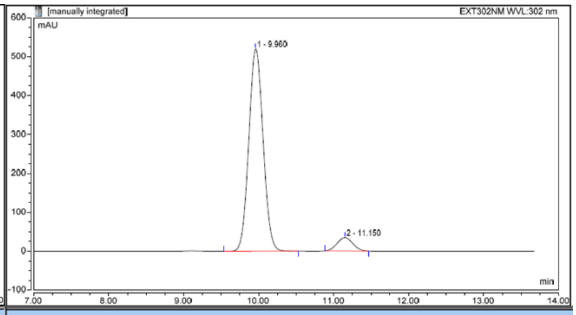
Following the general procedure **7**, starting from **1A** (61 mg, 0.4 mmol), 1,1,1-trifluoro-4-phenylbutan-2-one **2h** (40 mg, 0.2 mmol) and 20 mol% of **II(SA)**$_2$ salt (24 mg, 0.04 mmol), compound (*R*)-**3Ah** was obtained as a colorless oil (64 mg, 90%, reaction ran for 5 d). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.34 – 7.14 (m, 5H), 6.86 (s, 1H), 6.13 (s, 1H), 3.52 – 3.33 (m, 5H), 2.97 – 2.66 (m, 3H), 1.99 (dtd, *J* = 18.6, 14.0, 5.2 Hz, 2H), 1.81 – 1.61 (m, 6H). **^{13}C NMR** (75.5 MHz, $CDCl_3$): δ 198.7, 141.6, 128.41, 128.36, 128.1, 126.1 (q, $J_{C,F}$ = 286.9 Hz),

125.9, 75.2 (q, $J_{C,F}$ = 27.5 Hz), 51.4, 37.3, 36.1, 29.2, 24.7, 23.3. **^{19}F NMR** (282.5 MHz, $CDCl_3$): δ –80.12. **HRMS** (ESI) m/z calcd. for $C_{18}H_{23}O_2N_2F_3Na$ [M^++Na] 379.1604, found 379.1599. The enantiomeric excess was determined by HPLC using a Chiralpak IC column [*n*-hexanes/*i*PrOH (85:15)]; flow rate 1 mL/min); τ_{major} = 9.9 min, τ_{minor} = 11.1 min (87% ee); $[\alpha]_D^{25}$ = +47.8 (c 0.5, $CHCl_3$).



Integration Results

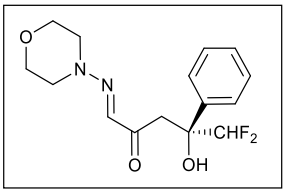
No.	Retention Time min	Area mAU*min	Relative Area %
1	9.970	44.741	50.00
2	11.150	44.748	50.00



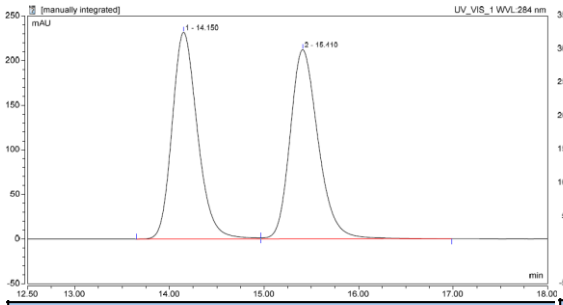
Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %
1	9.960	114.784	93.29
2	11.150	8.256	6.71

(*S*,*E*)-5,5-Difluoro-4-hydroxy-1-(morpholinoimino)-4-phenylpentan-2-one, (*S*)-**3Bk**.

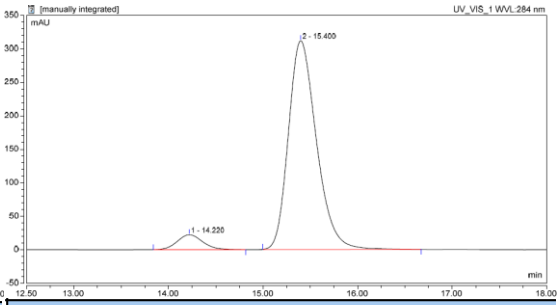


Following the general procedure **7**, starting from **1B** (62 mg, 0.4 mmol), 2,2-difluoro-1-phenylethan-1-one **2k** (61 mg, 0.2 mmol) and 20 mol% of **II(SA)$_2$** salt (24 mg, 0.04 mmol), compound (*S*)-**3Bk** was obtained as a pale yellow oil (61 mg, 98%; reaction ran for 2 d). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.54 (d, *J* = 7.5 Hz, 2H), 7.40 – 7.24 (m, 3H), 6.78 (s, 1H), 5.67 (dd, *J* = 55.8, 1.0 Hz, 1H), 5.59 (d, *J* = 1.2 Hz, 1H), 3.91 – 3.78 (m, 5H), 3.44 – 3.30 (m, 4H), 3.22 (d, *J* = 16.5 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 199.2, 139.59, 139.57, 130.6, 128.3, 128.2, 126.6, 116.4 (dd, $J_{C,F}$ = 251.6, 248.1 Hz), 76.0 (dd, $J_{C,F}$ = 22.7, 21.0 Hz), 66.0, 50.6, 37.7 (t, $J_{C,F}$ = 2.2 Hz). **^{19}F NMR** (471 MHz, $CDCl_3$): δ –128.38 (d, *J* = 275.5 Hz, 1F), –130.50 (d, *J* = 275.5 Hz, 1F). **HRMS** (ESI): m/z calcd for $C_{15}H_{18}F_2N_2O_3Na$ [M^++Na] 335.1178, found 335.1174. The enantiomeric excess was determined by HPLC using a Chiralpak IB column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{minor} = 14.2 min, τ_{major} = 15.4 min (88% ee); $[\alpha]_D^{20}$ = +237.3 (c 1.0, $CHCl_3$).



Integration Results

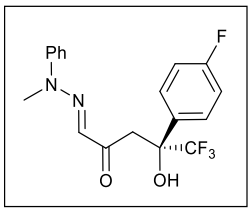
No.	Retention Time min	Area mAU*min	Relative Area %
1	14.150	72.156	49.71
2	15.410	72.989	50.29



Integration Results

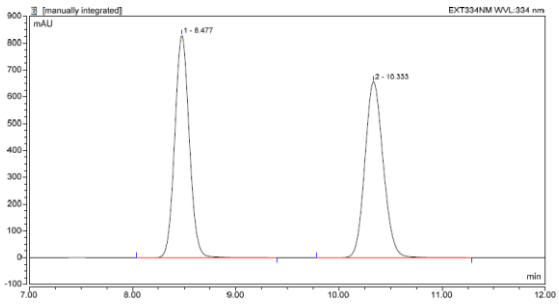
No.	Retention Time min	Area mAU*min	Relative Area %
1	14.220	6.878	6.04
2	15.400	107.049	93.96

(*S*,*E*)-5,5,5-Trifluoro-4-(4-fluorophenyl)-4-hydroxy-1-(2-methyl-2-phenylhydrazineylidene)pentan-2-one, (*S*)-**3Gb**.

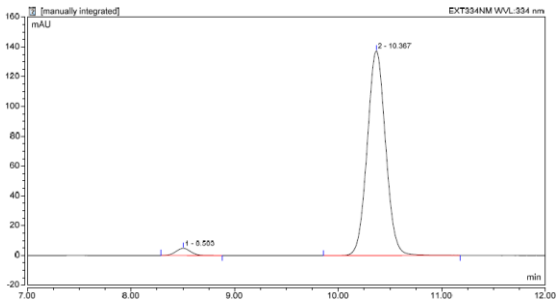


Following the general procedure **7**, starting from **1G** (70 mg, 0.4 mmol), 2,2,2-trifluoro-1-(4-fluorophenyl)ethan-1-one **2b** (28 µL, 0.2 mmol) and 10 mol% of **II(SA)$_2$** salt (12 mg, 0.02 mmol), compound (*S*)-**3Gb** was obtained as a pale brown solid (68 mg, 92%, reaction ran for 1 d). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.61 (dd, *J* = 8.7, 5.3 Hz, 2H), 7.54 – 7.38 (m, 4H), 7.22 (t, *J* = 7.2 Hz, 1H), 7.08

– 6.98 (m, 2H), 6.88 (s, 1H), 6.03 (s, 1H), 4.03 (d, J = 16.3 Hz, 1H), 3.44 (s, 3H), 3.41 (d, J = 16.3 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 198.2, 162.9 (d, $J_{C,F}$ = 247.4 Hz), 146.2, 133.7 (d, $J_{C,F}$ = 3.2 Hz), 130.4, 129.6, 128.7 (d, $J_{C,F}$ = 8.3 Hz), 124.8, 124.6 (q, $J_{C,F}$ = 284.6 Hz), 117.7, 115.2 (d, $J_{C,F}$ = 21.6 Hz), 76.3 (q, $J_{C,F}$ = 29.2 Hz), 38.0, 35.4. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.55 (s, 3F), –113.81 (s, 1F). **HRMS** (ESI) m/z calcd. for $C_{18}H_{16}F_4N_2O_2Na$ [M^++Na] 391.1040, found 391.1036. The enantiomeric excess was determined by HPLC using a Chiralpak IB column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{minor} = 8.5 min, τ_{major} = 10.4 min (95% ee); $[\alpha]_D^{25}$ = +584.4 (c 1.0, $CHCl_3$).

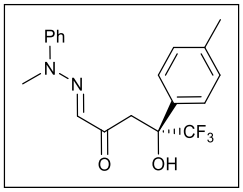


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	8.477	134.745	49.99
2	10.333	134.794	50.01

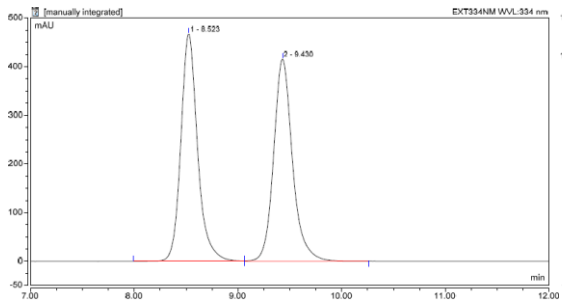


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	8.503	0.777	2.68
2	10.367	28.161	97.32

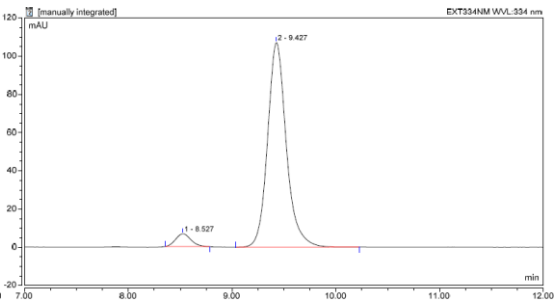
(*S*,*E*)-5,5,5-Trifluoro-4-hydroxy-1-(2-methyl-2-phenylhydrazineylidene)-4-(*p*-tolyl)pentan-2-one, (*S*)-**3Gc**.



Following the general procedure **7**, starting from **1G** (70 mg, 0.4 mmol), 2,2,2-trifluoro-1-(*p*-tolyl)ethan-1-one **2c** (31 µL, 0.2 mmol) and 10 mol% of **II(SA)$_2$** salt (12 mg, 0.02 mmol), compound (*S*)-**3Gc** was obtained as a brown pale solid (54 mg, 99%, reaction ran for 2 d). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.59 – 7.36 (m, 6H), 7.26 – 7.10 (m, 3H), 6.89 (s, 1H), 5.96 (s, 1H), 4.07 (d, J = 16.4 Hz, 1H), 3.49 – 3.36 (m, 4H), 2.33 (s, 3H). **^{13}C NMR** (75.5 MHz, $CDCl_3$): δ 198.4, 146.2, 138.3, 134.9, 130.4, 129.5, 128.9, 126.5, 124.7 (q, $J_{C,F}$ = 284.8 Hz), 124.6, 117.6, 76.5 (q, $J_{C,F}$ = 28.9 Hz), 38.0, 35.2, 21.0. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.41 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{19}H_{19}F_3N_2O_2Na$ [M^++Na] 387.1291, found 387.1287. The enantiomeric excess was determined by HPLC using a Chiralpak IB column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{minor} = 8.5 min, τ_{major} = 9.4 min (90% ee); $[\alpha]_D^{25}$ = +584.4 (c 1.0, $CHCl_3$).

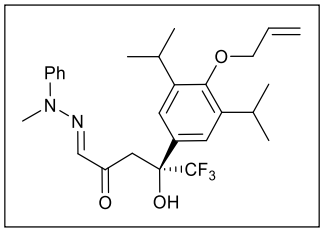


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	8.523	87.188	49.92
2	9.430	87.482	50.08

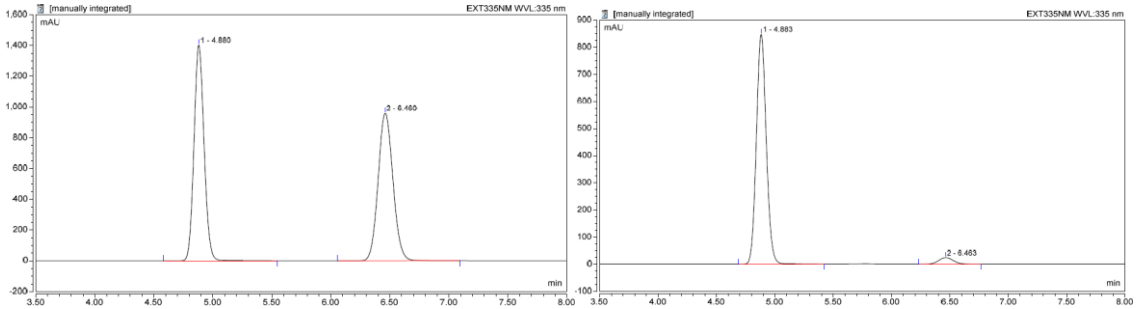


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	8.527	1.141	4.84
2	9.427	22.434	95.16

(*S*,*E*)-4-[4-(Allyloxy)-3,5-diisopropylphenyl]-5,5,5-trifluoro-4-hydroxy-1-(2-methyl-2-phenylhydrazineylidene)pentan-2-one, (*S*)-**3Ge**.



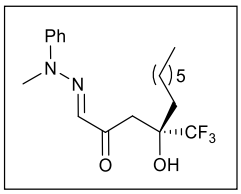
Following the general procedure **7**, starting from **1G** (70 mg, 0.4 mmol), 1-[4-(allyloxy)-3,5-diisopropylphenyl]-2,2,2-trifluoroethan-1-one **2e** (63 mg, 0.2 mmol) and 20 mol% of **II(SA)$_2$** salt (24 mg, 0.04 mmol), compound (*S*)-**3Ge** was obtained as a yellow solid (90 mg, 92%, reaction ran for 5 d). **^{1}H NMR** (300 MHz, CD_2Cl_2): δ 7.54 – 7.40 (m, 3H), 7.35 (s, 2H), 7.26 – 7.16 (m, 2H), 6.91 (s, 1H), 6.21 – 6.03 (m, 1H), 5.93 (s, 1H), 5.45 (dd, *J* = 17.2, 1.7 Hz, 1H), 5.26 (dd, *J* = 10.5, 1.5 Hz, 1H), 4.35 – 4.23 (m, 3H), 3.43 (s, 3H), 3.34 – 3.20 (m, 3H), 1.13 (dd, *J* = 19.2, 6.9 Hz, 12H). **^{13}C NMR** (75.5 MHz, CD_2Cl_2): δ 199.4, 154.3, 146.9, 142.2, 134.8, 134.2, 131.0, 130.0, 125.4 (q, $J_{C,F}$ = 284.5 Hz), 125.1, 123.4, 118.1, 117.0, 77.4 (q, $J_{C,F}$ = 28.8 Hz) 75.9, 38.0, 35.7, 27.2, 24.22, 24.17. **^{19}F NMR** (471 MHz, CD_2Cl_2): δ –78.98 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{27}H_{33}F_3N_2O_3Na$ [M^++Na] 513.2335, found 513.2330. The enantiomeric excess was determined by HPLC using a Chiralpak IC column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{major} = 4.9 min, τ_{minor} = 6.5 min (92% ee); $[\alpha]_D^{25}$ = +504.2 (c 1.0, $CHCl_3$).



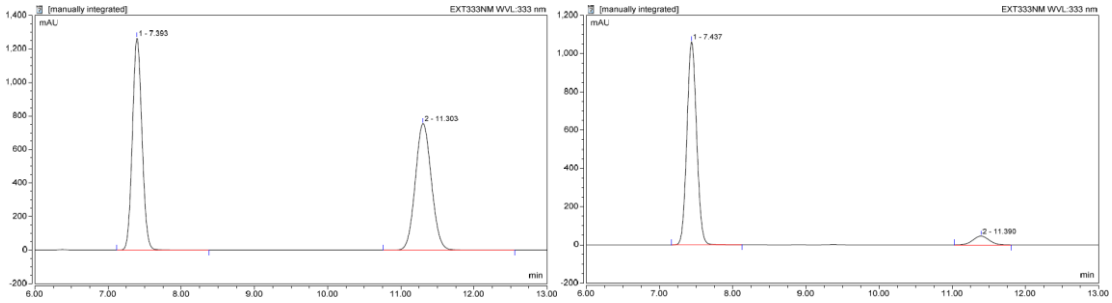
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	4.880	139.279	49.94
2	6.460	139.596	50.06

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	4.883	83.999	95.99
2	6.463	3.511	4.01

(*R*,*E*)-4-Hydroxy-1-(2-methyl-2-phenylhydrazineylidene)-4-(trifluoromethyl)heptan-2-one, (*R*)-**3Gi**.



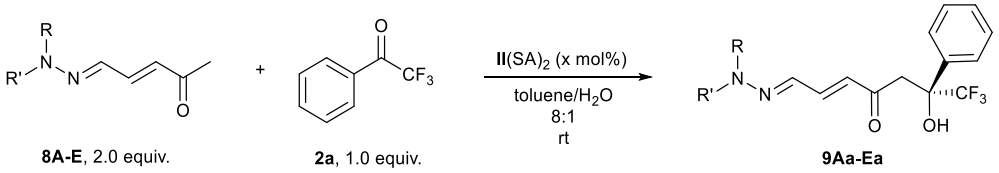
Following the general procedure **7**, starting from **1G** (70 mg, 0.4 mmol), 1,1,1-trifluorononan-2-one **2i** (40 mg, 0.2 mmol) and 20 mol% of **II(SA)$_2$** salt (24 mg, 0.04 mmol), compound (*R*)-**3Gi** was obtained as a pale yellow solid (60 mg, 81%, reaction ran for 7 d). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.51 – 7.32 (m, 4H), 7.17 (tt, *J* = 7.1, 1.4 Hz, 1H), 6.98 (d, *J* = 0.6 Hz, 1H), 5.72 (s, 1H), 3.59 (d, *J* = 15.9 Hz, 1H), 3.46 (s, 3H), 2.82 (d, *J* = 15.9 Hz, 1H), 1.78 (td, *J* = 13.3, 12.7, 4.3 Hz, 1H), 1.66 (td, *J* = 13.6, 13.0, 4.6 Hz, 1H), 1.55 (ddd, *J* = 26.0, 12.4, 5.2 Hz, 2H), 1.40 (td, *J* = 14.8, 13.4, 6.2 Hz, 1H), 1.32 – 1.25 (m, 9H), 0.94 – 0.82 (m, 3H).**^{13}C NMR** (126 MHz, $CDCl_3$): δ 199.7, 146.4, 130.5, 129.5, 126.4 (q, $J_{C,F}$ = 287.1 Hz), 124.6, 117.7, 75.8 (q, $J_{C,F}$ = 27.3 Hz), 36.0, 35.4, 31.9, 31.0, 30.0, 29.8, 29.3, 22.9, 22.8, 14.2. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.12 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{19}H_{28}F_3N_2O_2$ [M^++H] 373.2097, found 373.2093. The enantiomeric excess was determined by HPLC using a Chiralpak IC column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{major} = 7.4 min, τ_{minor} = 11.4 min (87% ee); $[\alpha]_D^{25}$ = +71.3 (c 1.0, $CHCl_3$).



Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	7.393	191.129	49.90
2	11.303	191.892	50.10

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	7.437	162.972	93.40
2	11.390	11.516	6.60

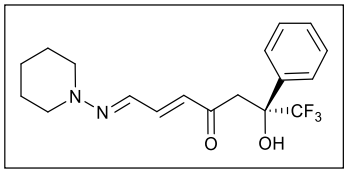
8. General procedure for the catalytic enantioselective reactions of α,β-unsaturated ketones 8A-E with trifluoromethyl ketone 2a



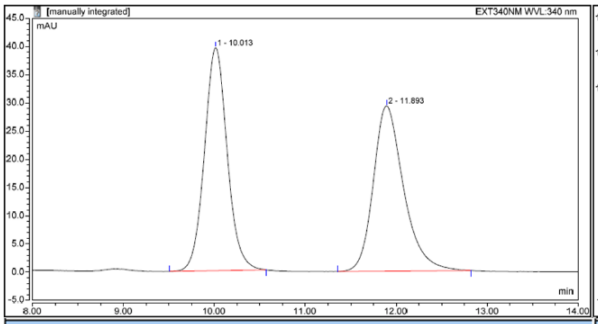
2,2,2-Trifluoro-1-phenylethan-1-one **2a** (1.0 equiv.) was added to a solution of **II(SA)$_2$** salt (x mol%) and the corresponding α,β-unsaturated ketone **8A-E** (2.0 equiv.) in toluene/H_2O 8:1 (1.0 M) at room temperature. The resulting mixture was stirred at this temperature until consumption of the starting material. Then, the resulting crude mixture was directly purified by flash chromatography (toluene/EtOAc 9/1) to afford pure product **9Aa-Ea**.

Racemic samples were prepared employing (±)-*trans*-1,2-diaminocyclohexane (20 mol%) and benzoic acid (20 mol%) following the general procedure described above.

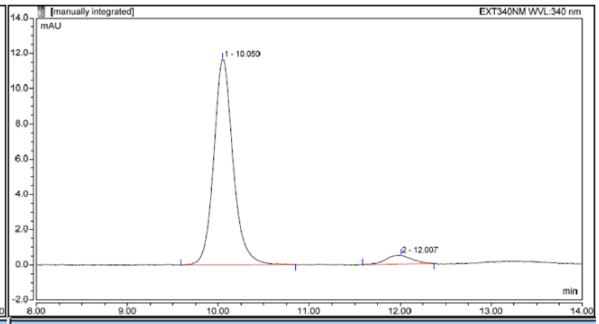
(*S*,1*E*,2*E*)-7,7,7-Trifluoro-6-hydroxy-6-phenyl-1-(piperidin-1-ylimino)hept-2-en-4-one, (*S*)-**9Aa**.



Following the general procedure **8**, starting from **8A** (72 mg, 0.4 mmol), 2,2,2-trifluoro-1-phenylethan-1-one **2a** (28 µL, 0.2 mmol) and 20 mol% of **II(SA)$_2$** salt (24 mg, 0.04 mmol), compound (*S*)-**9Aa** was obtained as a yellow oil (19 mg, 26%; reaction ran for 7 d). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.59 (d, *J* = 7.5 Hz, 2H), 7.45 – 7.29 (m, 4H), 7.14 (d, *J* = 9.1 Hz, 1H), 6.09 (s, 1H), 6.06 (d, *J* = 15.9 Hz, 1H), 3.55 (d, *J* = 16.6 Hz, 1H), 3.32 (t, *J* = 5.7 Hz, 3H), 3.27 (d, *J* = 16.6 Hz, 1H), 1.77 – 1.68 (m, 4H), 1.66 – 1.54 (m, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 199.3, 145.1, 137.9, 129.1, 128.5, 128.3, 126.5, 126.4, 124.6 (q, $J_{C,F}$ = 284.9 Hz), 76.4 (q, $J_{C,F}$ = 28.8 Hz), 51.3, 40.2, 24.8, 23.6. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.22 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{18}H_{22}O_2N_2F_3$ [M^++H] 355.1628, found 355.1627. The enantiomeric excess was determined by HPLC using a Chiralpak IA column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{major} = 10.0 min, τ_{minor} = 12.0 min (89% ee); $[\alpha]_D^{25}$ = +275.8 (c 1.0, $CHCl_3$).

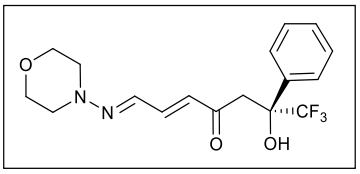


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	10.013	11.458	50.33
2	11.893	11.308	49.67

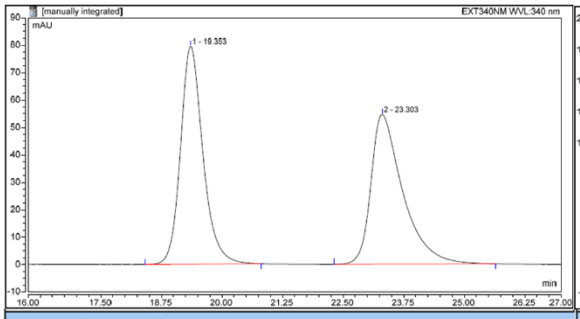


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	10.050	2.872	94.48
2	12.007	0.168	5.52

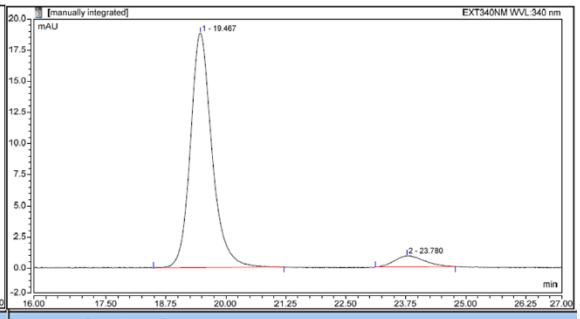
(*S*,1*E*,2*E*)-7,7,7-Trifluoro-6-hydroxy-1-(morpholinoimino)-6-phenylhept-2-en-4-one, (*S*)-**9Ba**.



Following the general procedure **8**, starting from **8B** (73 mg, 0.4 mmol), 2,2,2-trifluoro-1-phenylethan-1-one **2a** (28 µL, 0.2 mmol) and 20 mol% of **II(SA)**$_2$ salt (24 mg, 0.04 mmol), compound (*S*)-**9Ba** was obtained as a yellow oil (42 mg, 58%; reaction ran for 3 d). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.58 (d, *J* = 7.5 Hz, 2H), 7.42 – 7.29 (m, 4H), 7.21 (d, *J* = 9.1 Hz, 1H), 6.14 (d, *J* = 15.9 Hz, 1H), 5.90 (s, 1H), 3.85 (t, *J* = 5.1 Hz, 4H), 3.56 (d, *J* = 16.7 Hz, 1H), 3.32 – 3.23 (m, 5H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 199.3, 143.8, 137.1, 131.4, 128.6, 128.4, 128.3, 126.3, 124.6 (q, $J_{C,F}$ = 284.8 Hz), 76.4 (q, $J_{C,F}$ = 29.0 Hz), 66.0, 50.7, 40.7. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.19 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{17}H_{19}O_3N_2F_3Na$ [M^++Na] 379.1240, found 379.1236. The enantiomeric excess was determined by HPLC using a Chiralpak IA column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{major} = 19.4 min, τ_{minor} = 23.8 min (88% ee); $[\alpha]_D^{25}$ = +189.5 (c 0.5, $CHCl_3$).

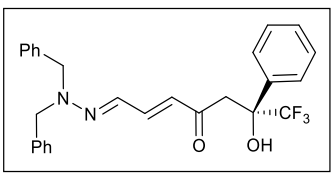


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	19.353	42.612	50.65
2	23.303	41.523	49.35



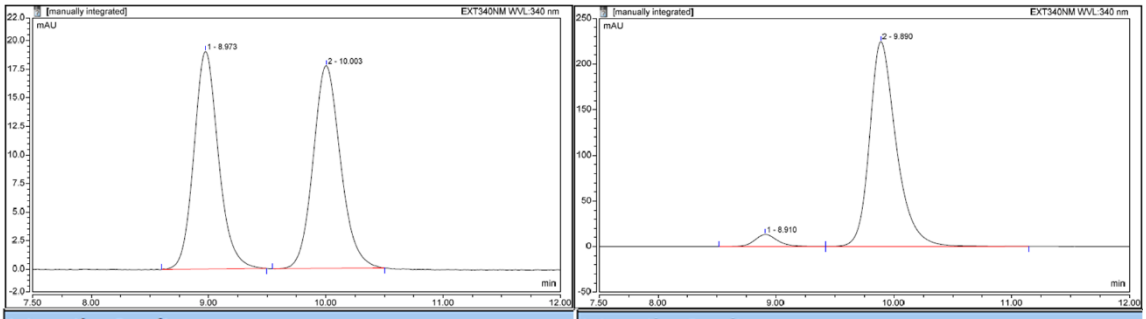
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	19.467	9.782	93.90
2	23.780	0.635	6.10

(*S*,1*E*,2*E*)-1-(2,2-Dibenzylhydrazineylidene)-7,7,7-trifluoro-6-hydroxy-6-phenylhept-2-en-4-one, (*S*)-**9Ca**.



Following the general procedure **8**, starting from **8C** (73 mg, 0.4 mmol), 2,2,2-trifluoro-1-phenylethan-1-one **2a** (28 µL, 0.2 mmol) and 10 mol% of **II(SA)**$_2$ salt (12 mg, 0.02 mmol), compound (*S*)-**9Ca** was obtained as a yellow oil (88 mg, 94%; reaction performed at 2 mmol scale: 904 mg, 97%, 90% ee; reactions ran for 2 d). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.55 (d, *J* = 7.0 Hz, 2H), 7.46 – 7.24 (m, 10H), 7.14 (d, *J* = 6.5 Hz, 4H), 6.86

(d, *J* = 9.2 Hz, 1H), 6.09 (s, 1H), 5.89 (d, *J* = 15.8 Hz, 1H), 4.60 (s, 4H), 3.46 (d, *J* = 16.6 Hz, 1H), 3.21 (d, *J* = 16.6 Hz, 1H). **^{13}C NMR** (75.5 MHz, $CDCl_3$): δ 199.1, 144.8, 137.9, 135.5, 128.9, 128.5, 128.2, 127.8, 127.3, 126.3, 125.8, 124.6 (q, $J_{C,F}$ = 285.0 Hz), 76.4 (q, $J_{C,F}$ = 28.9 Hz), 57.9, 40.6. **^{19}F NMR** (282.5 MHz, $CDCl_3$): δ –80.10 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{27}H_{25}O_2N_2F_3Na$ [M^++Na] 489.1760, found 489.1756. The enantiomeric excess was determined by HPLC using a Chiralpak IA column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{minor} = 8.9 min, τ_{major} = 9.9 min (90% ee); $[\alpha]_D^{25}$ = +204.2 (c 1.0, $CHCl_3$).



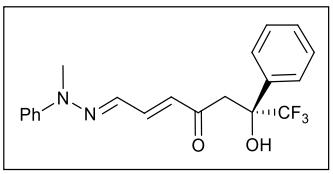
Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %
1	8.973	4.632	49.03
2	10.003	4.814	50.97

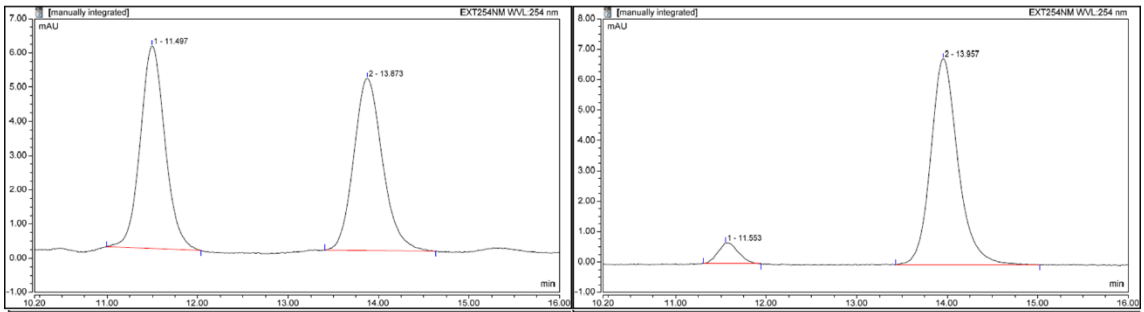
Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %
1	8.910	2.989	4.82
2	9.890	59.014	95.18

(*S*,1*E*,2*E*)-7,7,7-Trifluoro-6-hydroxy-1-(2-methyl-2-phenylhydrazineylidene)-6-phenylhept-2-en-4-one, (*S*)**-9Da**.



Following the general procedure **8**, starting from **8D** (81 mg, 0.4 mmol) 2,2,2-trifluoro-1-phenylethan-1-one **2a** (28 µL, 0.2 mmol) and 10 mol% of **II(SA)$_2$** salt (12 mg, 0.02 mmol), compound (*S*)-**9Da** was obtained as a yellow solid (56 mg, 75%; reaction ran for 2 d). **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.61 (d, *J* = 7.6 Hz, 2H), 7.53 (dd, *J* = 15.9, 9.1 Hz, 1H), 7.44 – 7.31 (m, 7H), 7.23 (d, *J* = 9.1 Hz, 1H), 7.11 – 7.04 (m, 1H), 6.22 (d, *J* = 15.9 Hz, 1H), 6.01 (s, 1H), 3.60 (d, *J* = 16.6 Hz, 1H), 3.43 (s, 3H), 3.32 (d, *J* = 16.6 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 199.2, 146.5, 144.3, 137.8, 130.1, 129.2, 128.6, 128.3, 127.8, 126.4, 124.6 (q, $J_{C,F}$ = 284.9 Hz), 123.2, 121.2, 76.4 (q, $J_{C,F}$ = 28.9 Hz), 40.8, 34.3. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.14 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{20}H_{19}O_2N_2F_3Na$ [M^++Na] 399.1291, found 399.1288. The enantiomeric excess was determined by HPLC using a Chiralpak IA column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{minor} = 11.5 min, τ_{major} = 13.9 min (86% ee); $[\alpha]_D^{25}$ = +419.1 (c 1.0, $CHCl_3$).



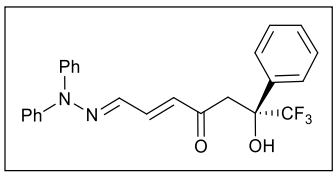
Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %
1	11.497	1.877	50.26
2	13.873	1.857	49.74

Integration Results

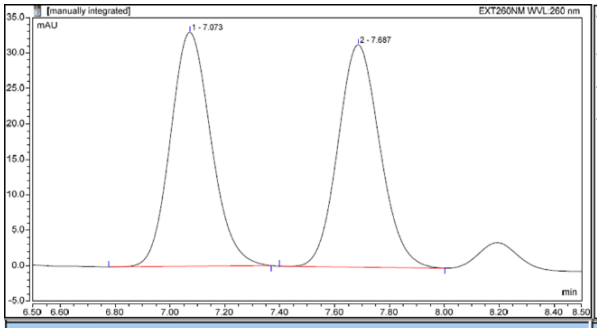
No.	Retention Time min	Area mAU*min	Relative Area %
1	11.553	0.177	6.91
2	13.957	2.378	93.09

(*S*,1*E*,2*E*)-1-(2,2-Diphenylhydrazineylidene)-7,7,7-trifluoro-6-hydroxy-6-phenylhept-2-en-4-one, (*S*)-**9Ea**.



Following the general procedure **8**, starting from **8E** (106 mg, 0.4 mmol), 2,2,2-trifluoro-1-phenylethan-1-one **2a** (28 µL, 2 mmol) and 10 mol% of **II(SA)**$_2$ salt (12 mg, 0.02 mmol), compound (*S*)-**9Ea** was obtained as a yellow solid (82 mg, 94%; reaction performed at 2 mmol scale: 851 mg, 97%, 90% ee; reactions ran for 2 d); mp: 118-120 ºC. **^{1}H NMR** (500 MHz, $CDCl_3$): δ 7.59 (d, *J* = 7.5 Hz, 2H), 7.52 (dd, *J* = 15.9, 9.3 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 4H), 7.40 – 7.26 (m, 5H), 7.17 (d, *J* = 7.6 Hz, 4H), 6.89 (d, *J* = 9.3 Hz, 1H), 6.02 (d, *J* = 15.9 Hz, 1H), 5.92 (s, 1H), 3.54 (d, *J* = 16.7 Hz, 1H), 3.28 (d, *J* = 16.7 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 199.0, 143.4, 137.8, 133.3, 130.0, 128.8, 128.6, 128.3, 126.3, 124.6 (q, $J_{C,F}$ = 284.9 Hz), 76.4 (q, $J_{C,F}$ = 28.8 Hz), 41.0. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.14 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{25}H_{22}O_2N_2F_3$ [M^++H] 439.1628 found 439.1633. The enantiomeric excess was determined by HPLC using a Chiralpak IB column [*n*-hexanes/*i*PrOH (90:10)]; flow rate 1 mL/min; τ_{minor} = 7.2 min, τ_{major} = 7.8 min (90% ee); $[\alpha]_D^{25}$ = +350.4 (c 1.0, $CHCl_3$).

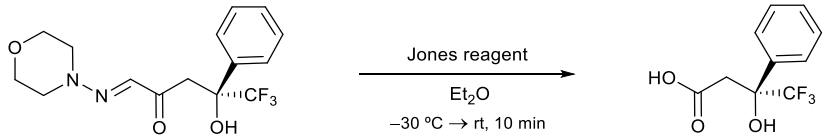
Recrystallization of (*S*)-**3Ga** by slow evaporation of a solution of (*S*)-**3Ga** in Et_2O afforded suitable crystals for X-ray analysis.



Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	7.073	5.656	50.42
2	7.687	5.561	49.58

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	7.220	0.145	4.83
2	7.813	2.858	95.17

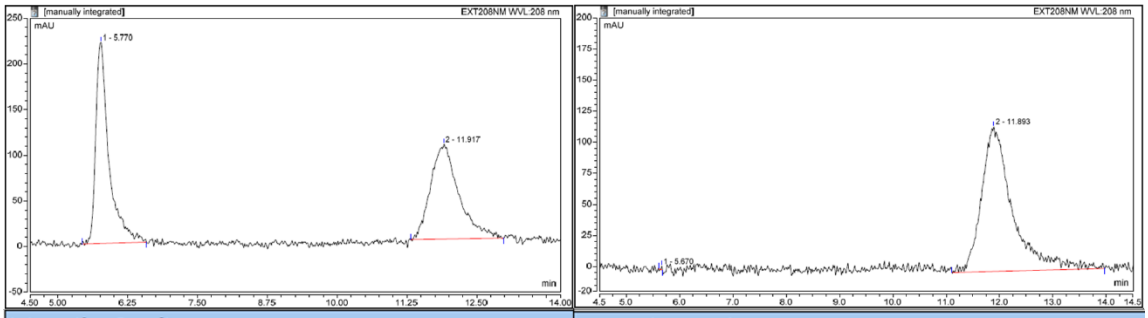
9. Synthesis of (*S*)-4,4,4-trifluoro-3-hydroxy-3-phenylbutanoic acid, (*S*)-**10**



(S)-**3Ba**, 0.45 mmol (S)-**10**

Jones reagent (6.75 mL, 4.5 mmol) was dropwise added to a solution of (*S*)-**3Ba** (150 mg, 0.45 mmol, >99% ee) in Et_2O (4.5 mL) at –30 °C. The reaction mixture was allowed to warm to room temperature and stirred for 10 min. After this time, the mixture was filtered through a short silica gel pad (50 x 40 mm) and eluted with Et_2O until the product could no longer be detected (TLC monitoring). The solvent was eliminated under reduced pressure and the residue was diluted with aqueous NaOH (5 mL, 1.0 M) and washed with Et_2O (2 x 5 mL). The aqueous phase was acidified with aqueous H_2SO_4 (2.0 N) until pH 0-1 and extracted with EtOAc (7 x 5 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was eliminated under reduced pressure to afford the product (*S*)-**10** as a white solid (61 mg, 58%). The

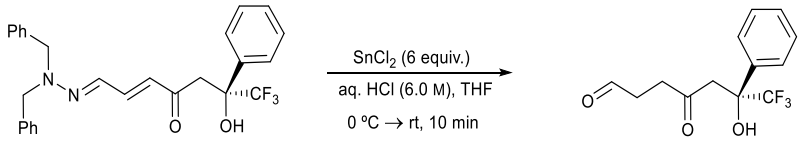
experimental data is in accordance with those reported in the literature.[14] **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.64 (br s, 1H), 7.63 – 7.33 (m, 5H), 4.89 (s, 1H), 3.34 – 3.10 (m, 2H). **^{19}F NMR** (282.5 MHz, $CDCl_3$): δ –80.47 (s, 3F). The enantiomeric excess was determined by HPLC using a Chiralcel OJ-H column [*n*-hexanes/*i*PrOH/TFA (85:15:0.2)], flow rate 1 mL/min; τ_{minor} = 5.7 min, τ_{major} = 11.9 min (>99% ee); $[\alpha]_D^{25}$ = +12.6 (c 0.5, $CHCl_3$). Literature: $[\alpha]_D^{26}$ = +7.6 (c 0.98, $CHCl_3$), >99% ee (*S*).



Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	5.770	60.165	49.88
2	11.917	60.455	50.12

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	5.670	0.024	0.03
2	11.893	78.037	99.97

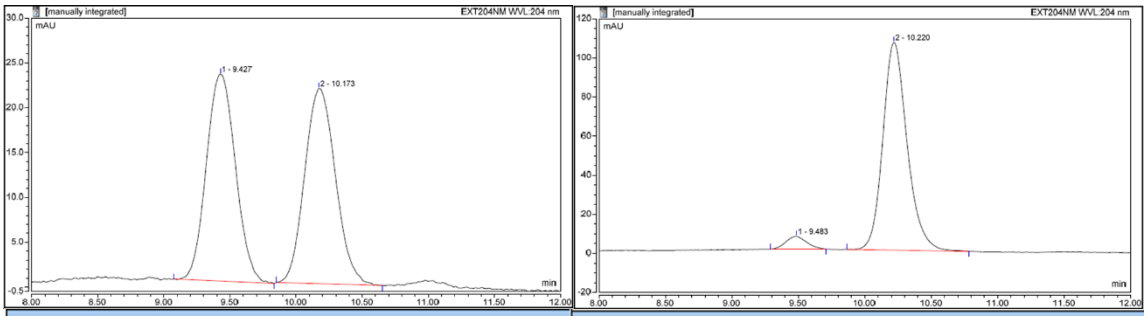
10. Synthesis of (*S*)-7,7,7-trifluoro-6-hydroxy-4-oxo-6-phenylheptanal, (*S*)-**11**



(S)-**9Ca**, 0.28 mmol (S)-**11**

A solution of (*S*)-**9Ca** (130 mg, 0.28 mmol, 90% ee) in THF (1.70 mL) was dropwise added to a solution of $SnCl_2$ (340 mg, 1.70 mmol) in aqueous HCl (1.6 mL, 6.0 M) at 0 °C. The mixture was allowed to warm to room temperature and stirred for 10 min. After this time, the mixture was diluted with H_2O (12 mL) and extracted with CH_2Cl_2/*i*PrOH (4 x 5 mL, 9/1). The combined organic layers were washed with water (1 x 10 mL) and brine (1 x 10 mL), dried over anhydrous $MgSO_4$ and the solvent was eliminated under reduced pressure. The resulting residue was purified by flash chromatography (CH_2Cl_2/Et_2O 10/1) to afford pure product (*S*)-**11** as a colorless oil (70 mg, 91%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 9.68 (s, 1H), 7.57 (d, *J* = 7.1 Hz, 2H), 7.46 – 7.31 (m, 3H), 5.25 (s, 1H), 3.43 (d, *J* = 17.0 Hz, 1H), 3.28 (d, *J* = 17.0 Hz, 1H), 2.93 – 2.53 (m, 4H). **^{13}C NMR** (75.5 MHz, $CDCl_3$): δ 208.7, 199.4, 137.2, 128.8, 128.4, 126.1, 124.5 (q, $J_{C,F}$ = 285.0 Hz), 76.0 (q, $J_{C,F}$ = 29.2 Hz), 44.8, 37.0, 36.6. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –80.27 (s, 3F)**. HRMS** (ESI) m/z calcd. for $C_{13}H_{13}O_3F_3Na$ $[M^+ + Na]$ 297.0709, found 297.0713. HPLC Chiralpak ID column [*n*-hexanes/*i*PrOH (90:10)], flow rate 1 mL/min; τ_{minor} = 9.5 min, τ_{major} = 10.2 min (90% ee); $[\alpha]_D^{25}$ = +163.7 (c 1.0, $CHCl_3$).

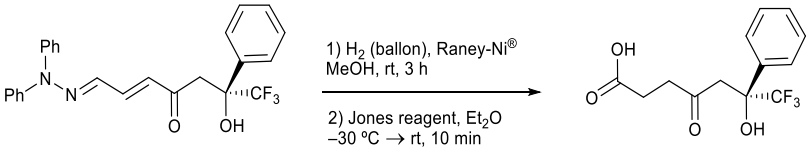
[14] Z. Jing, X. Bai, W. Chen, G. Zhang, B. Zhu, Z. Jiang, *Org. Lett.* 2016, **18**, 2, 260.



Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	9.427	5.886	50.06
2	10.173	5.873	49.94

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	9.483	1.194	5.04
2	10.220	22.489	94.96

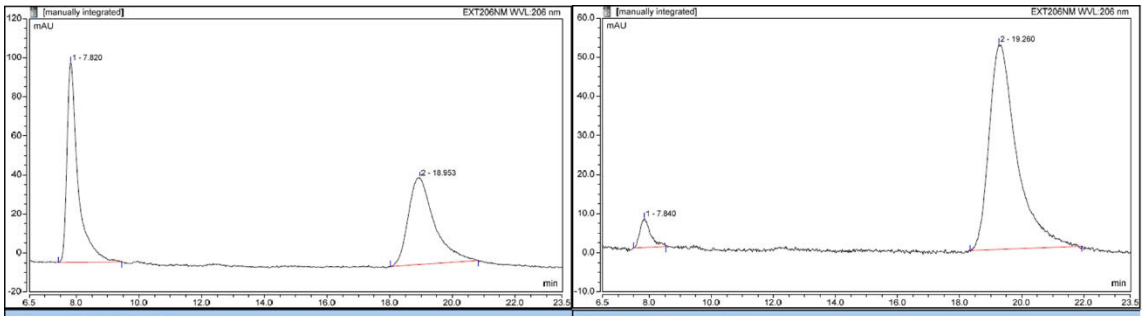
11. Synthesis of (*S*)-7,7,7-trifluoro-6-hydroxy-4-oxo-6-phenylheptanoic acid, (*S*)-**12**



(S)-**9Ea**, 0.25 mmol (S)-**12**

Step 1: A suspension of (*S*)-**9Ea** (110 mg, 0.25 mmol, 90% ee) and Raney-Ni® (0.30 g, 50% in H_2O) in MeOH (3 mL) was stirred under hydrogen atmosphere (1 atm) at room temperature for 3 h. After this time, the mixture was filtered through a celite pad and the solvent was eliminated under reduced pressure to afford (*S*)-7-(2,2-diphenylhydrazineylidene)-1,1,1-trifluoro-2-hydroxy-2-phenylheptan-4-one (**9Ea'**) as a yellow oil, which was used in the next step without further purification.

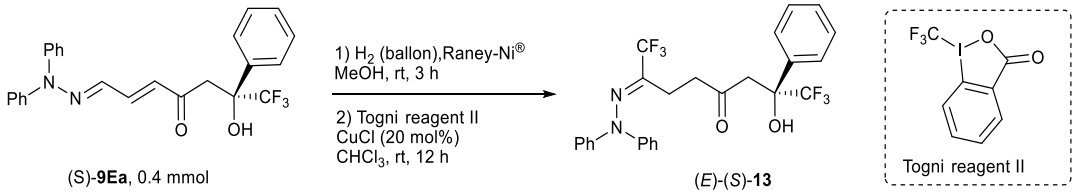
Step 2: Jones reagent (4 mL, 2.67 mmol) was dropwise added to a solution of crude (*S*)-**9Ea'** (~0.25 mmol) in Et_2O (2.5 mL) at –30 ºC. The reaction mixture was allowed to warm to rt and stirred for 10 min. The mixture was then filtered through a short silica gel pad (30 x 40 mm) and eluted with Et_2O until the product could no longer be detected (TLC monitoring). The solvent was eliminated under reduced pressure and the residue was dissolved in aqueous NaOH (5 mL, 1.0 M) and washed with Et_2O (2 x 5 mL). The aqueous phase was acidified with aqueous H_2SO_4 (2.0 N) until pH 0-1 and extracted with EtOAc (7 x 5 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure to afford (*S*)-**12** as a yellow oil (46 mg, 63%). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.96 (br s, 1H), 7.56 – 7.48 (m, 2H), 7.44 – 7.29 (m, 3H), 5.35 (br s, 1H), 3.41 (d, J = 17.0 Hz, 1H), 3.25 (d, J = 17.0 Hz, 1H), 2.89 – 2.75 (m, 1H), 2.73 – 2.50 (m, 3H). **^{13}C NMR** (75.5 MHz, $CDCl_3$): δ 208.7, 177.9, 137.1, 128.8, 128.4, 126.1, 124.4 (q, $J_{C,F}$ = 285.0 Hz), 76.0 (q, $J_{C,F}$ = 29.2 Hz), 44.8, 38.7, 27.2. **^{19}F NMR** (282.5 MHz, $CDCl_3$): δ –80.29 (s, 3F)**. HRMS** (ESI) m/z calcd. for $C_{13}H_{13}O_4F_3Na$ [M^++Na] 313.0658, found 313.0657. The enantiomeric excess was determined by HPLC using a Chiralcel OJ-H column [*n*-hexanes/*i*PrOH/TFA (80:20:0.2)], flow rate 1 mL/min; τ_{minor} = 7.8 min, τ_{major} = 19.0 min (90% ee); $[\alpha]_D^{25}$ = +22.4 (c 0.5, $CHCl_3$).



Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	7.820	41.733	49.37
2	18.953	42.793	50.63

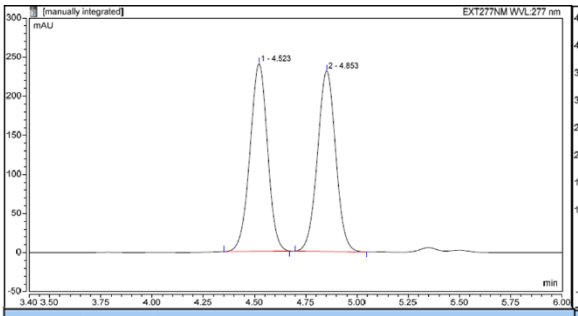
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	7.840	2.951	5.19
2	19.260	53.952	94.81

12. Synthesis of (*E*)-(*S*)-7-(2,2-diphenylhydrazineylidene)-1,1,1,8,8,8-hexafluoro-2-hydroxy-2-phenyloctan-4-one, (*E*)-(*S*)-**13**.



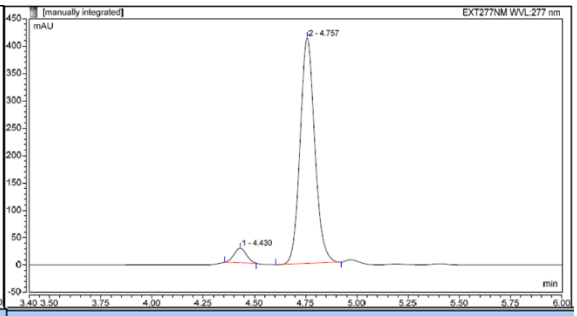
Step 1: A suspension of (*S*)-**9Ea** (180 mg, 0.4 mmol, 90% ee) and Raney-Ni® (0.40 g, 50% in H_2O) in MeOH (3 mL) was stirred under hydrogen atmosphere (1 atm) at room temperature for 3 h. After this time, the mixture was filtered through a celite pad and the solvent was eliminated under reduced pressure to afford (*S*)-7-(2,2-diphenylhydrazineylidene)-1,1,1-trifluoro-2-hydroxy-2-phenylheptan-4-one (**9Ea'**) as a yellow oil, which was used in the next step without further purification.

Step 2: Togni reagent II (366 mg, 0.7 mmol) and copper chloride (8 mg, 0.08 mmol) were subsequently added to a solution of crude (*S*)-**9Ea'** (~0.4 mmol) in $CHCl_3$ (3 mL). The reaction was flushed with argon and sealed. The reaction mixture was stirred at room temperature overnight and then washed with a saturated solution of $NaHCO_3$ (3 × 7 mL). The organic layer was dried over MgSO4 and the solvent was eliminated under reduced pressure. The resulting residue was purified by flash chromatography (*n*-hexanes/EtOAc 6/1) to afford pure (*E*)-(*S*)-**13** as a yellow oil (148 mg, 73%). **^{1}H NMR** (500 MHz, CDCl3): δ 7.57 – 7.49 (m, 2H), 7.45 – 7.37 (m, 3H), 7.20 – 7.19 (m, 4H), 7.19 (t, *J* = 7.4 Hz, 2H), 7.10 – 7.00 (m, 4H), 5.21 (s, 1H), 3.14 (d, *J* = 17.1 Hz, 1H), 2.98 (d, *J* = 17.0 Hz, 1H), 2.46 – 2.22 (m, 2H), 2.19 – 2.03 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$): δ 207.7, 146.3, 138.9 (q, $J_{C,F}$ = 32.2 Hz), 137.2, 129.6, 128.9, 128.5, 126.1, 125.5, 125.0, 124.3 (q, $J_{C,F}$ = 284.8 Hz), 122.3, 121.7 (q, $J_{C,F}$ = 275.4 Hz), 75.9 (q, $J_{C,F}$ = 29.3 Hz), 44.3, 39.6, 20.9. **^{19}F NMR** (471 MHz, $CDCl_3$): δ –68.55 (s, 3F), –80.28 (s, 3F). **HRMS** (ESI) m/z calcd. for $C_{26}H_{22}O_2N_2F_6Na$ [M^++Na] 531.1478, found 531.1473. The enantiomeric excess was determined by HPLC using a Chiralpak IB column [*n*-hexanes/*i*PrOH (90:10)], flow rate 1 mL/min; τ_{minor} = 4.5 min, τ_{major} = 4.8 min (90% ee); $[\alpha]_D^{25}$ = +46.3 (c 1.0, $CHCl_3$).



Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %
1	4.523	23.855	50.05
2	4.853	23.805	49.95

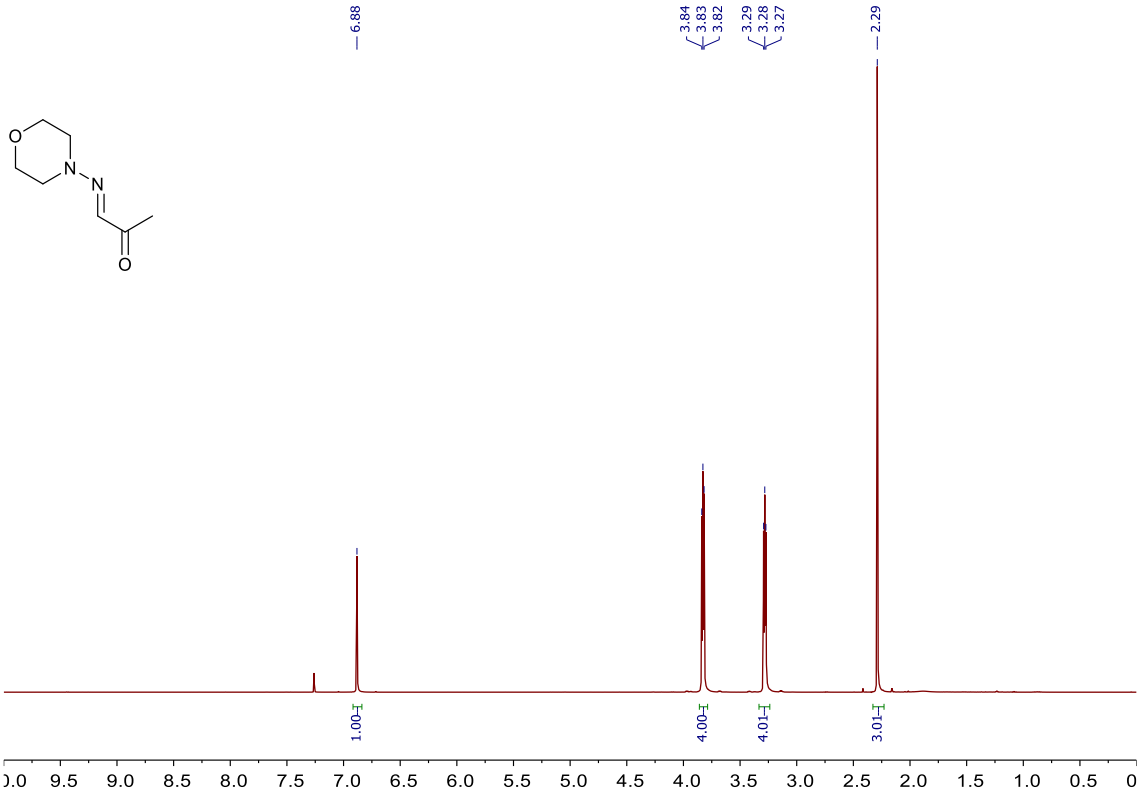


Integration Results

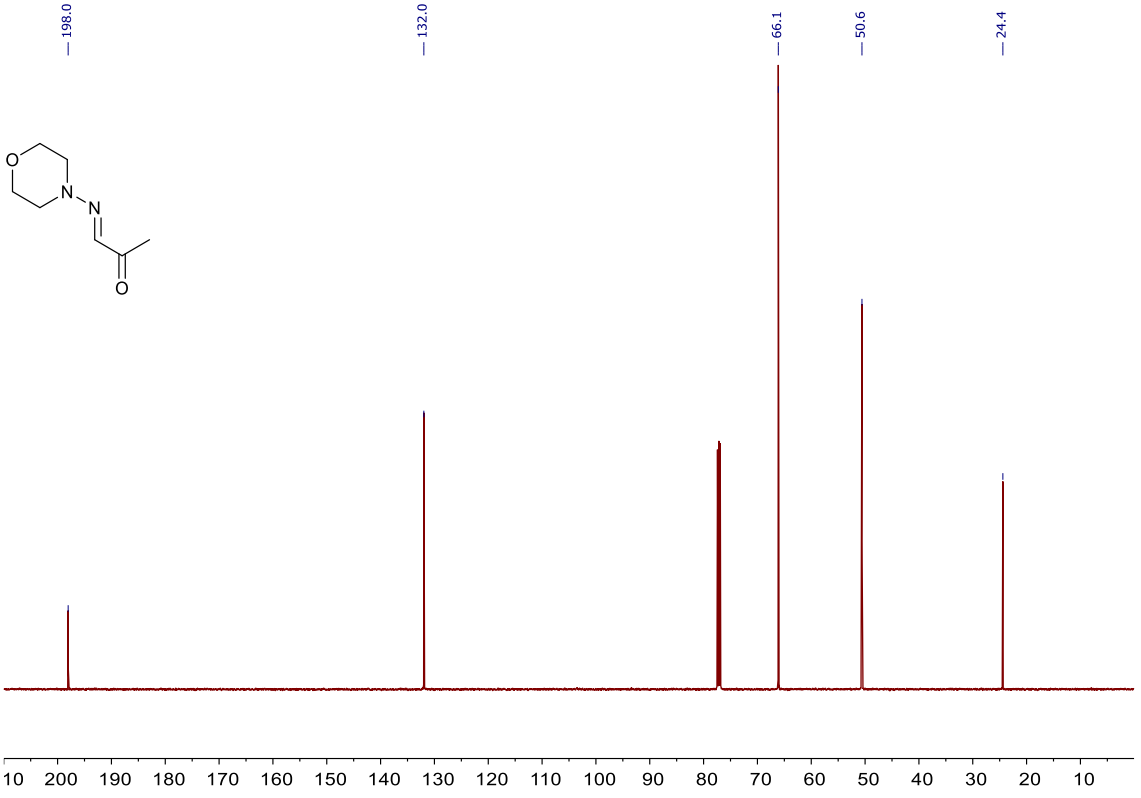
No.	Retention Time min	Area mAU*min	Relative Area %
1	4.430	1.882	5.24
2	4.757	34.049	94.76

13. NMR spectra of all compounds

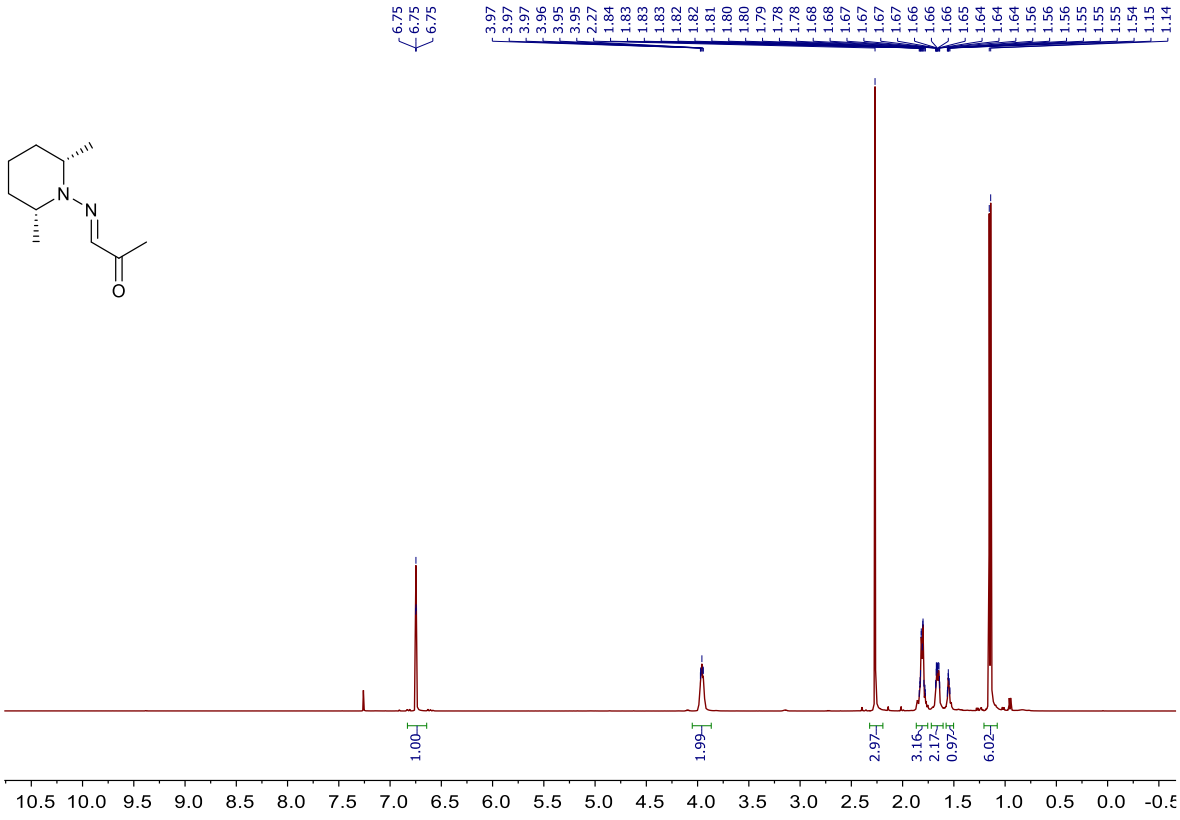
^{1}H NMR (500 MHz, $CDCl_3$) of **1B**



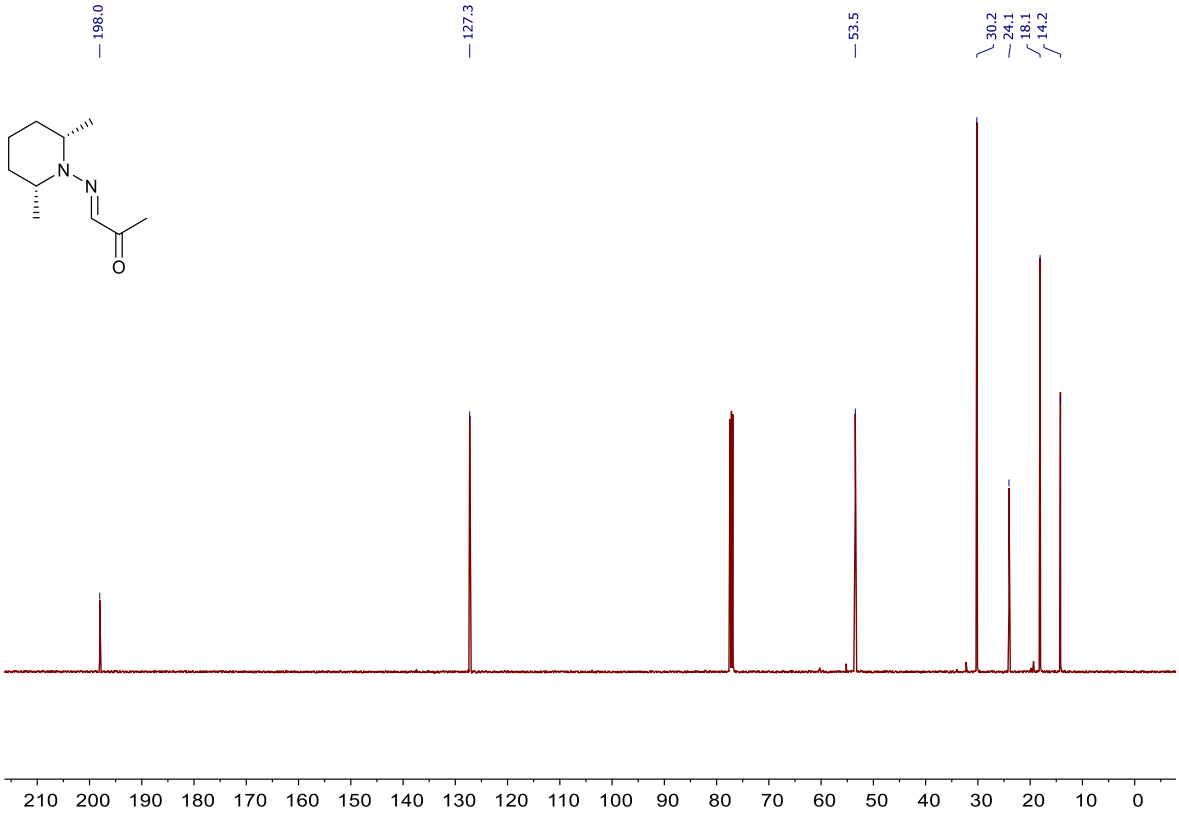
^{13}C NMR (126 MHz, $CDCl_3$) of **1B**



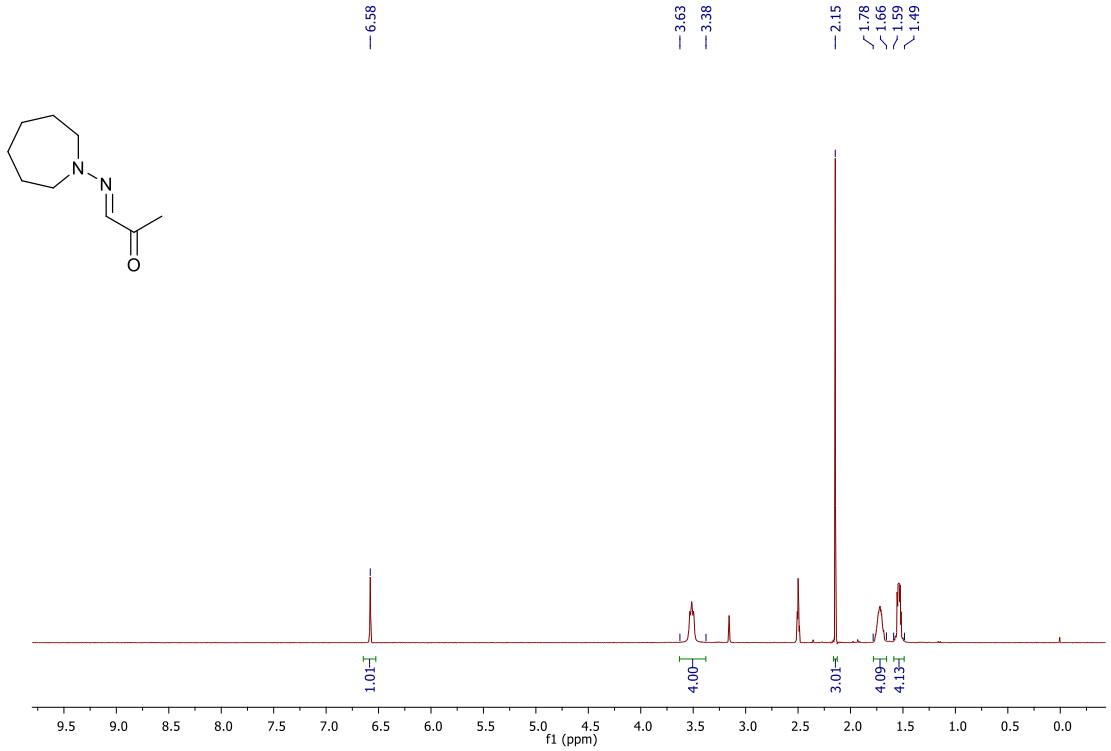
^{1}H NMR (500 MHz, $CDCl_3$) of **1C**



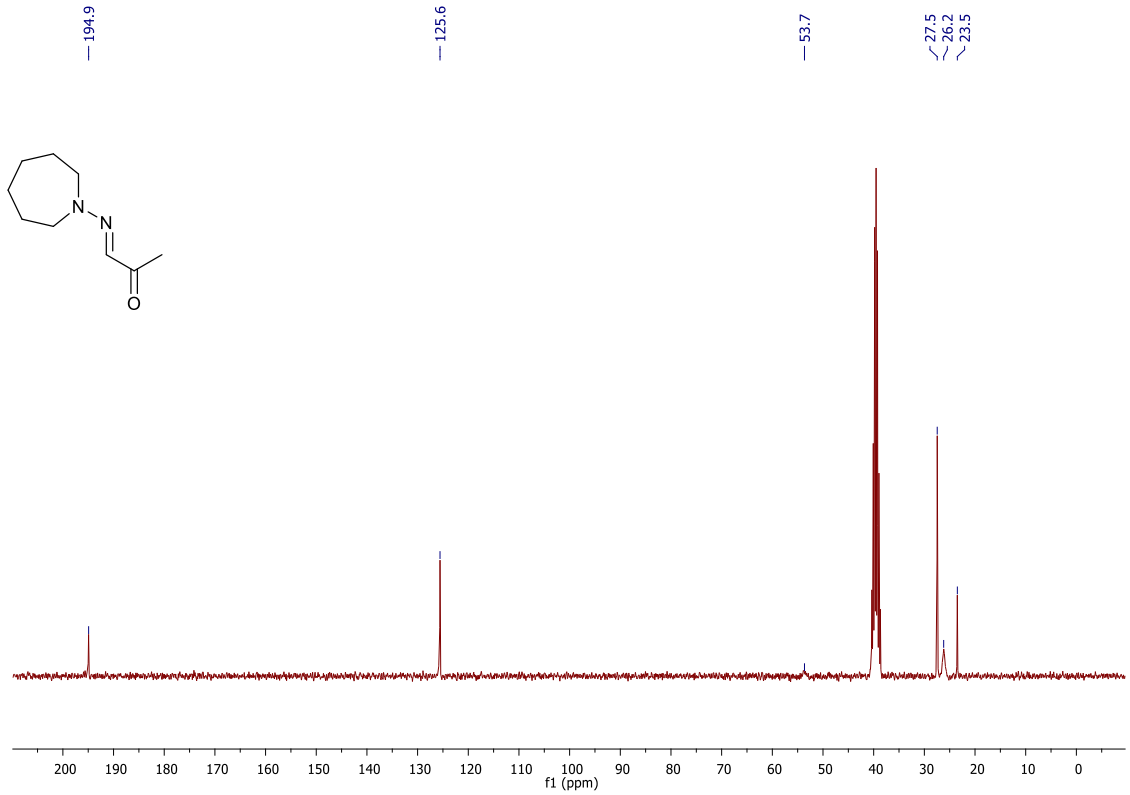
^{13}C NMR (126 MHz, $CDCl_3$) of **1C**



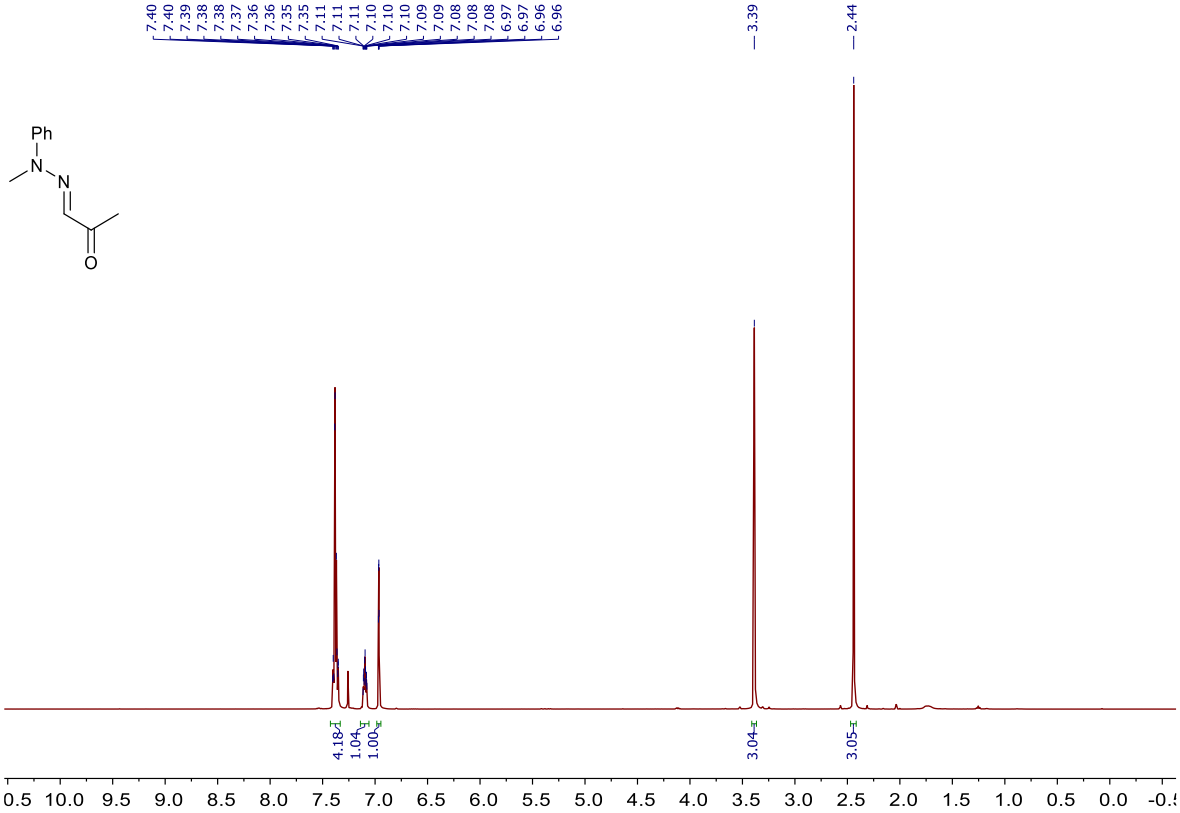
^{1}H NMR (300 MHz, 60 ºC, DMSO-d_6) of **1E**



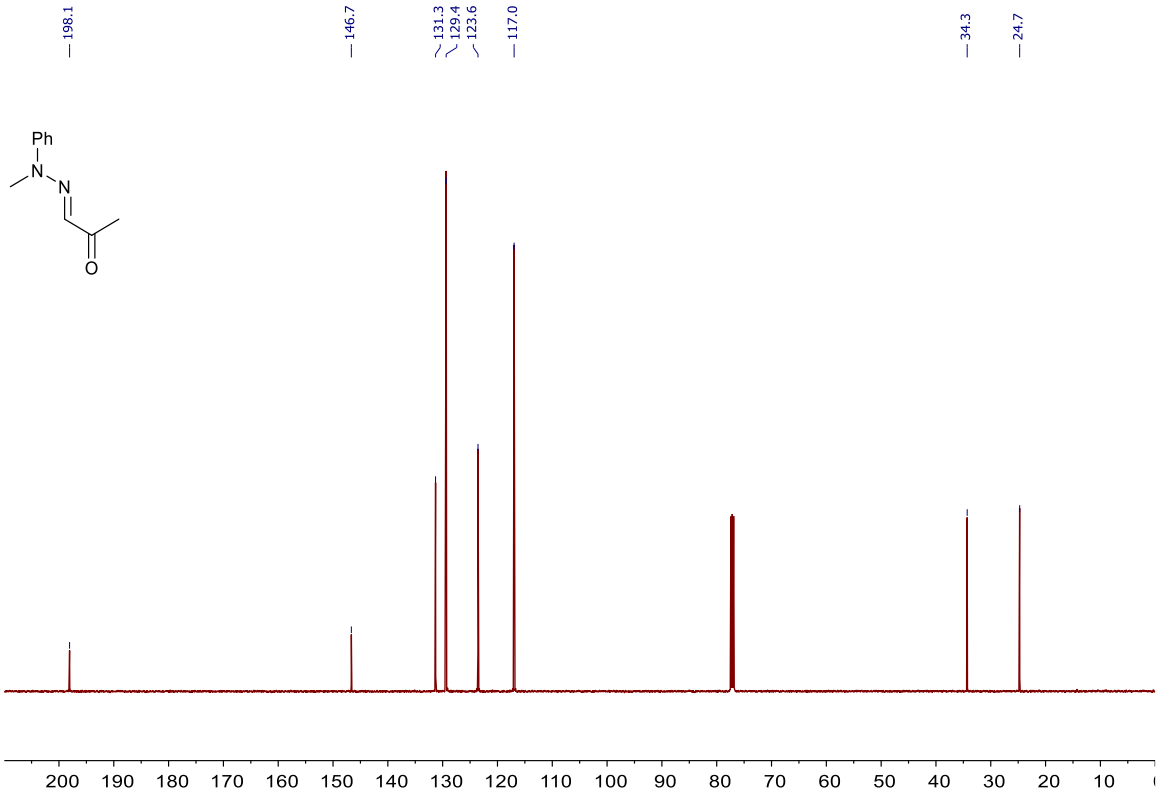
^{13}C NMR (75.5 MHz, 60 ºC, DMSO-d_6) of **1E**



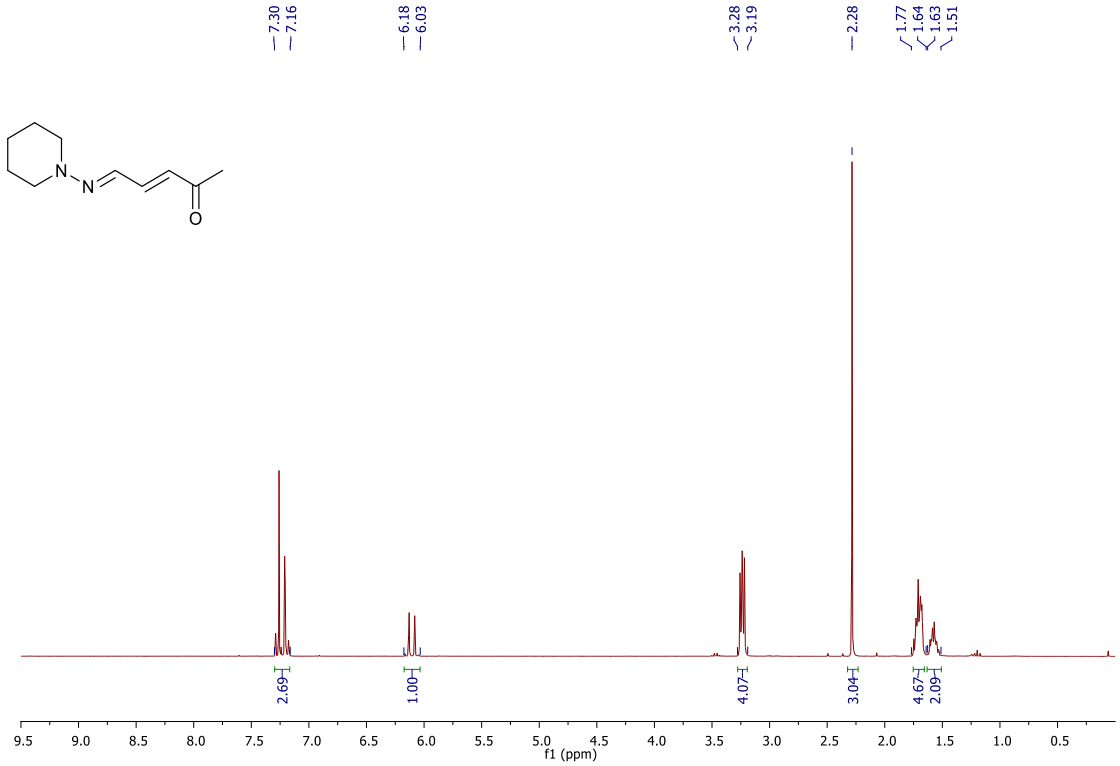
^{1}H NMR (500 MHz, $CDCl_3$) of **1G**



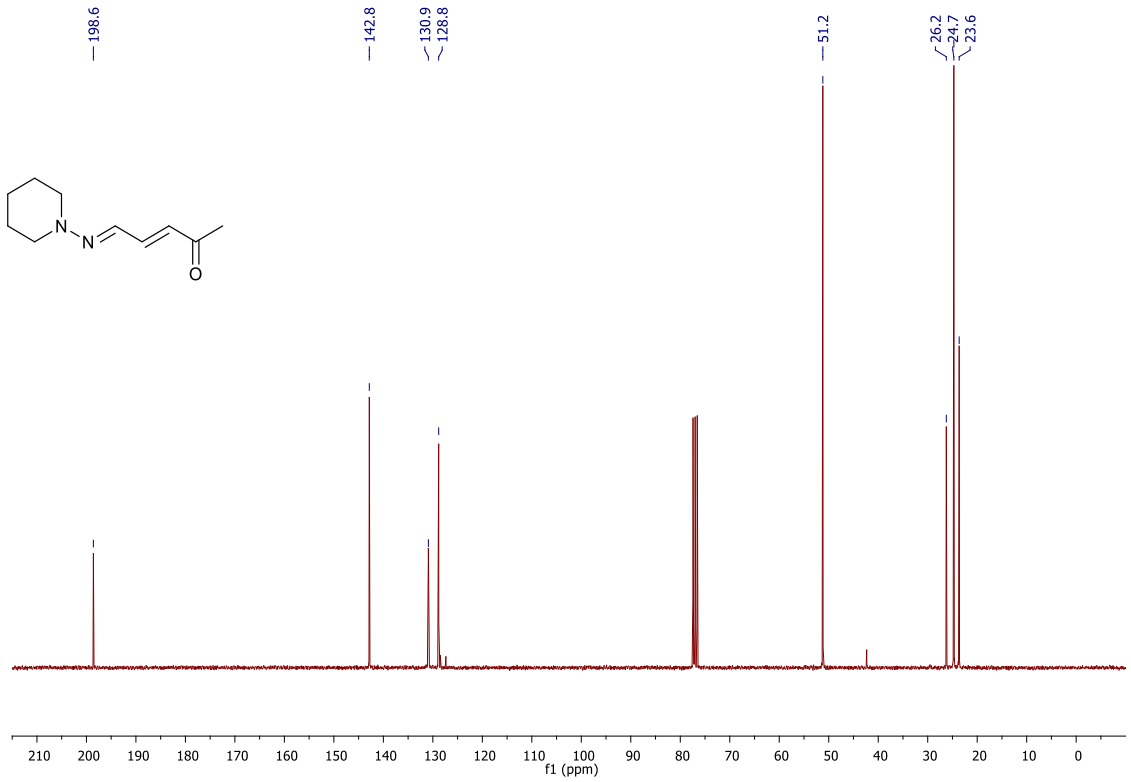
^{13}C NMR (126 MHz, $CDCl_3$) of **1G**



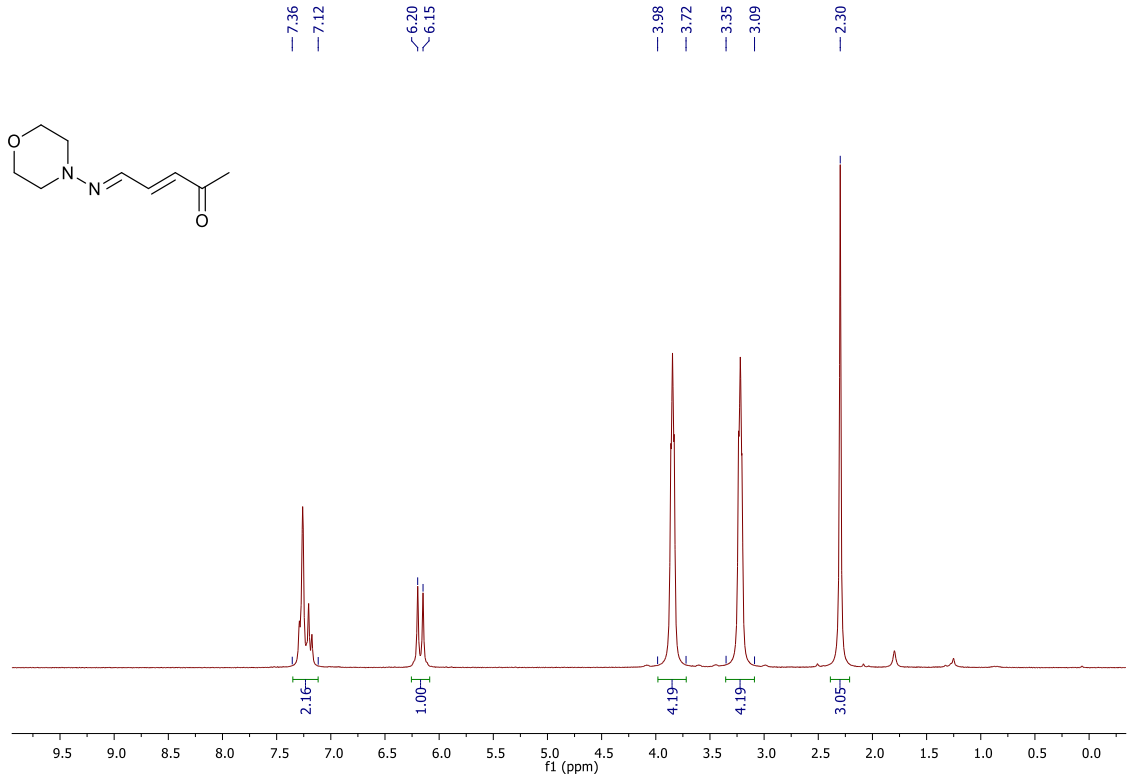
^{1}H NMR (300 MHz, $CDCl_3$) of **8A**



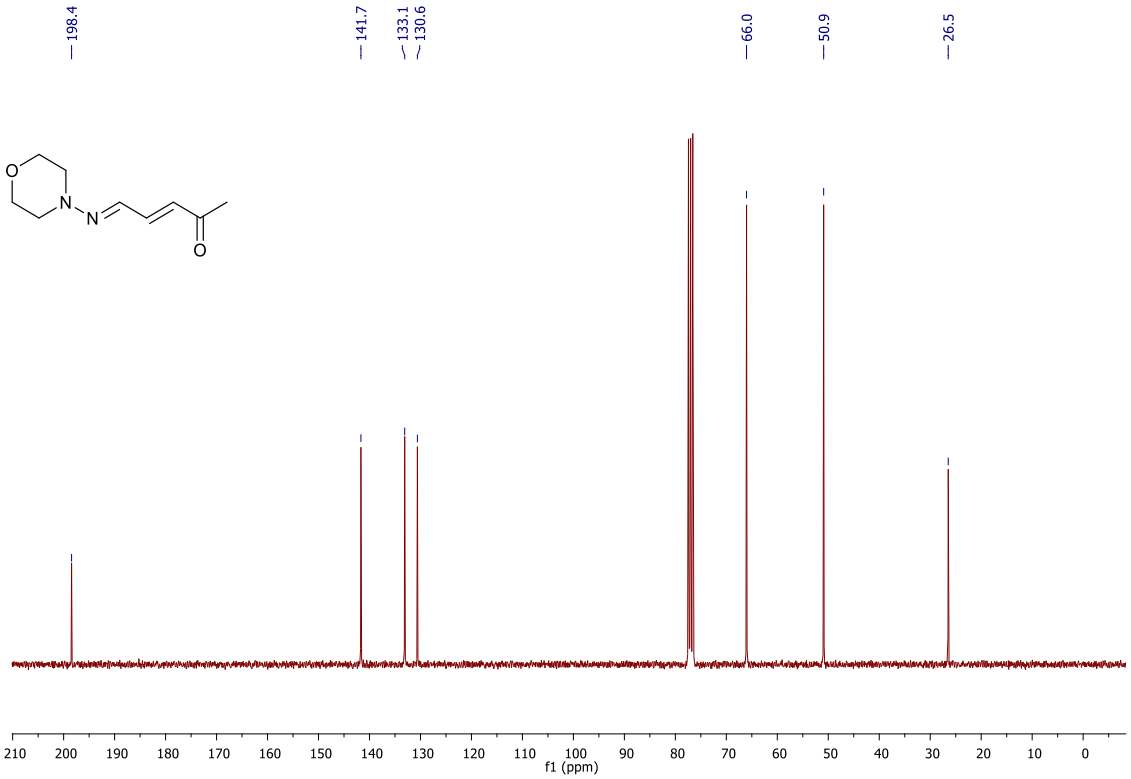
^{13}C NMR (75.5 MHz, $CDCl_3$) of **8A**



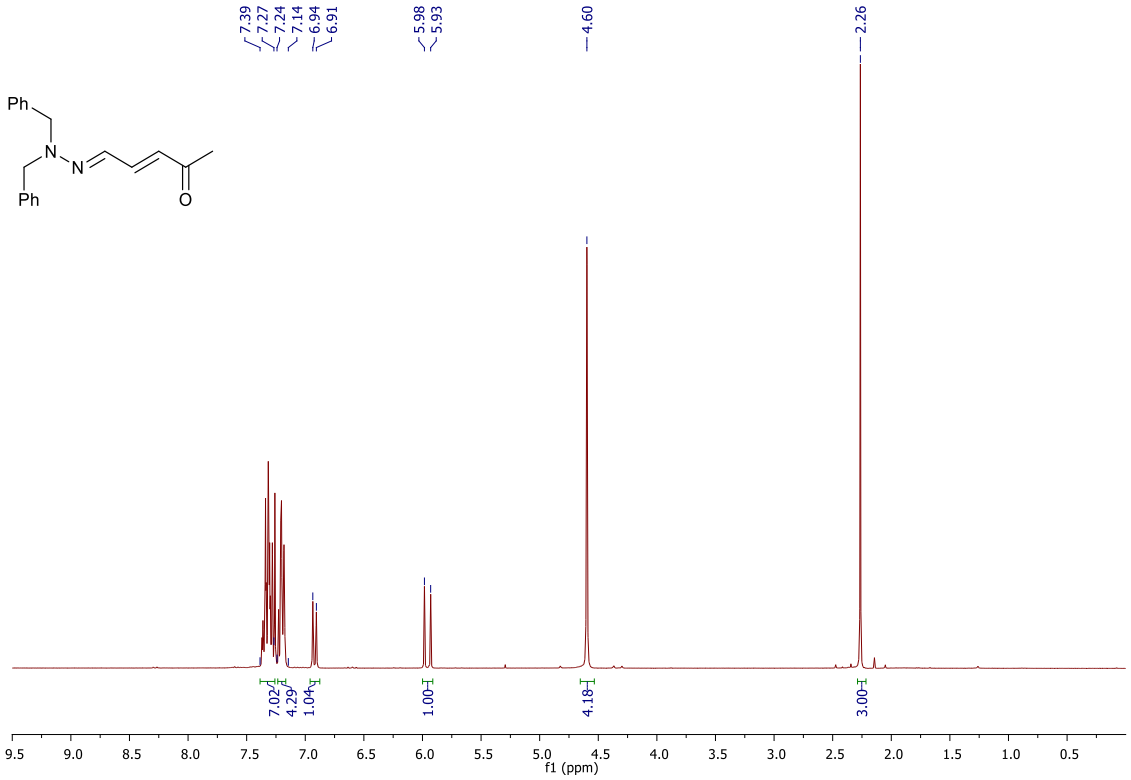
^{1}H NMR (300 MHz, $CDCl_3$) of **8B**



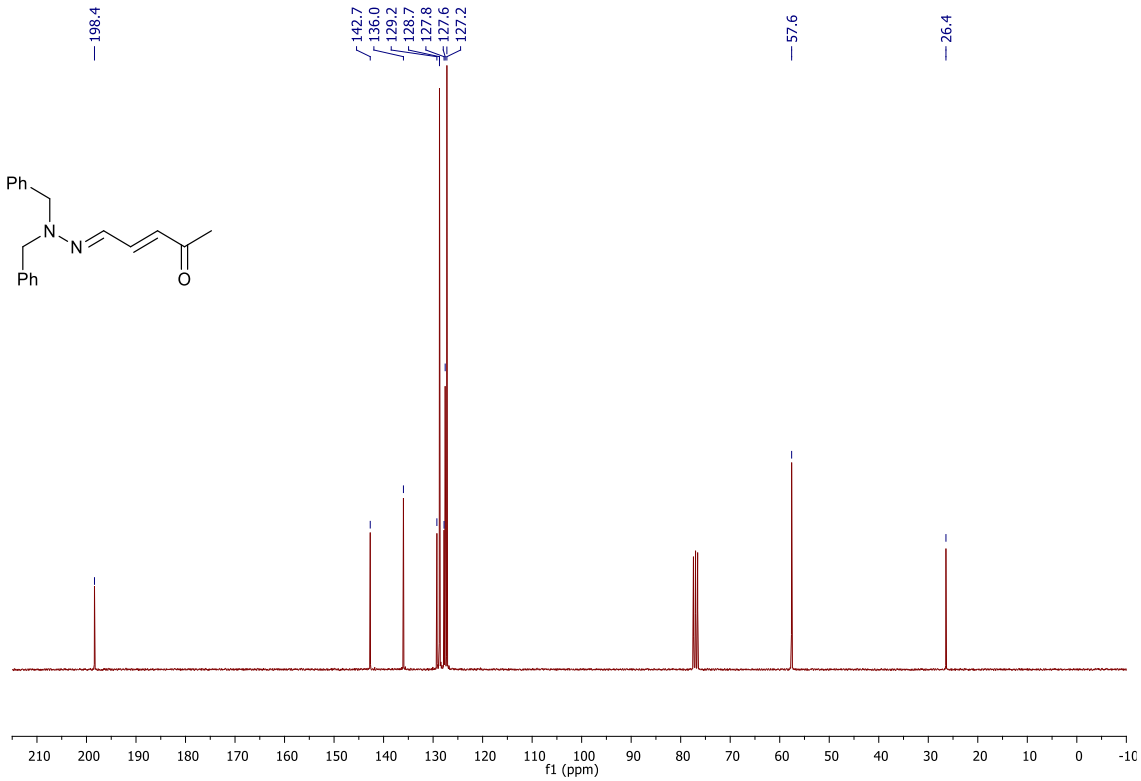
^{13}C NMR (75.5 MHz, $CDCl_3$) of **8B**



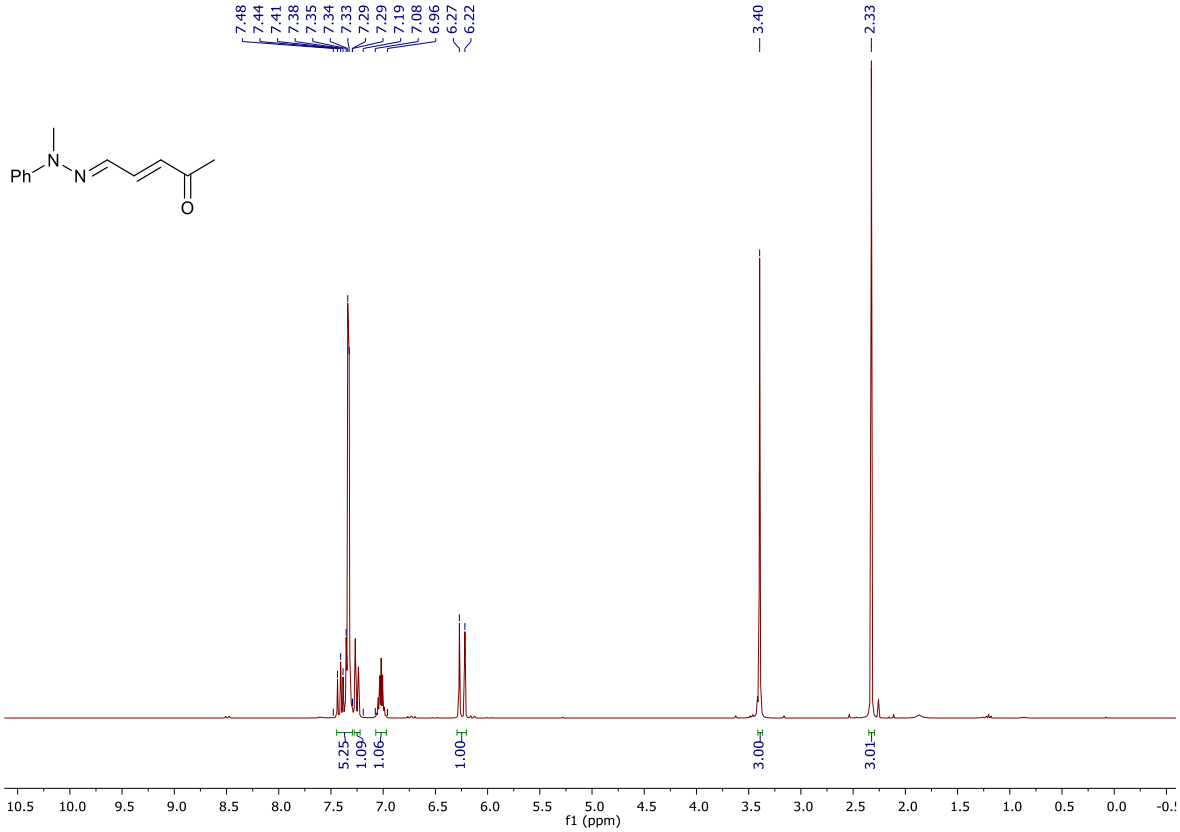
^{1}H NMR (300 MHz, $CDCl_3$) of **8C**



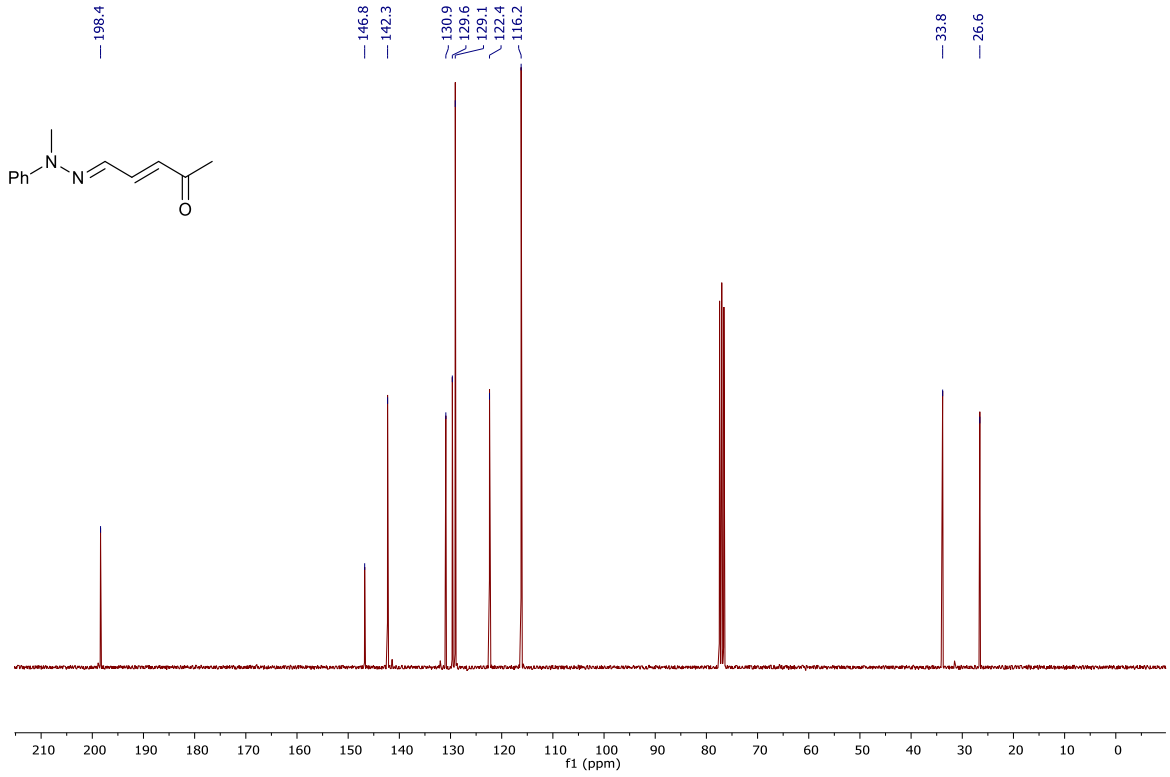
^{13}C NMR (75.5 MHz, $CDCl_3$) of **8C**



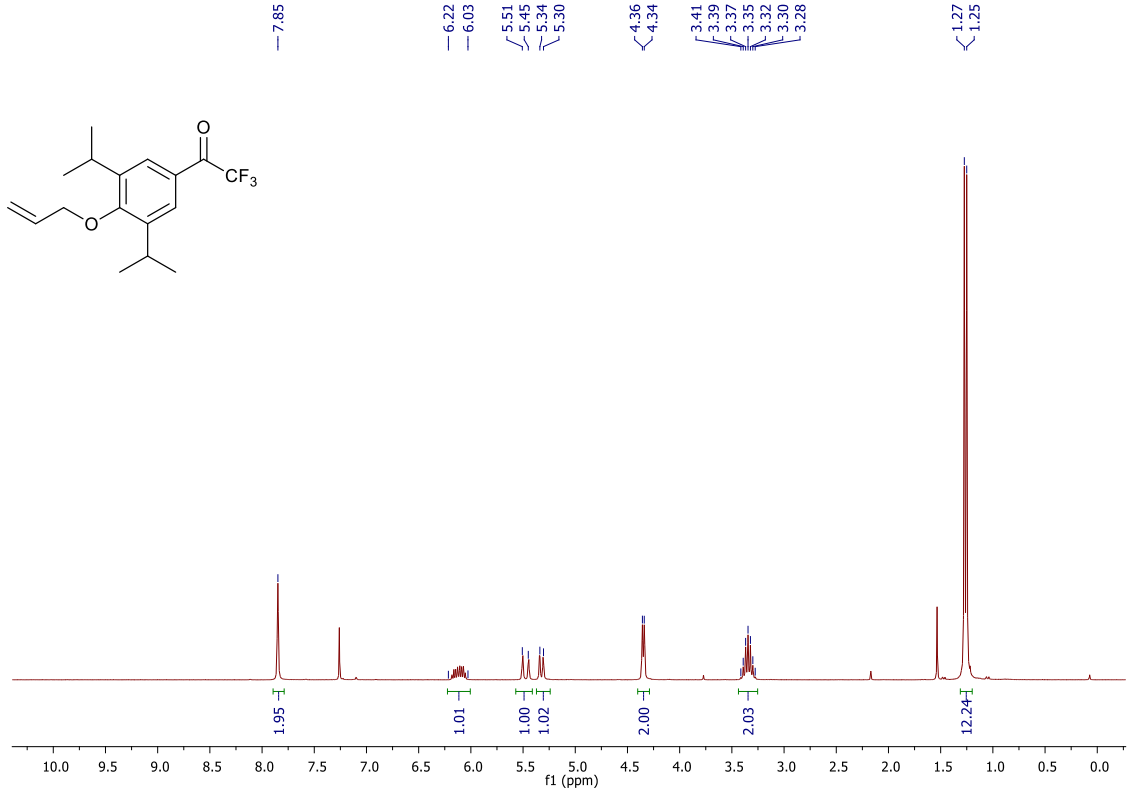
^{1}H NMR (300 MHz, $CDCl_3$) of **8D**



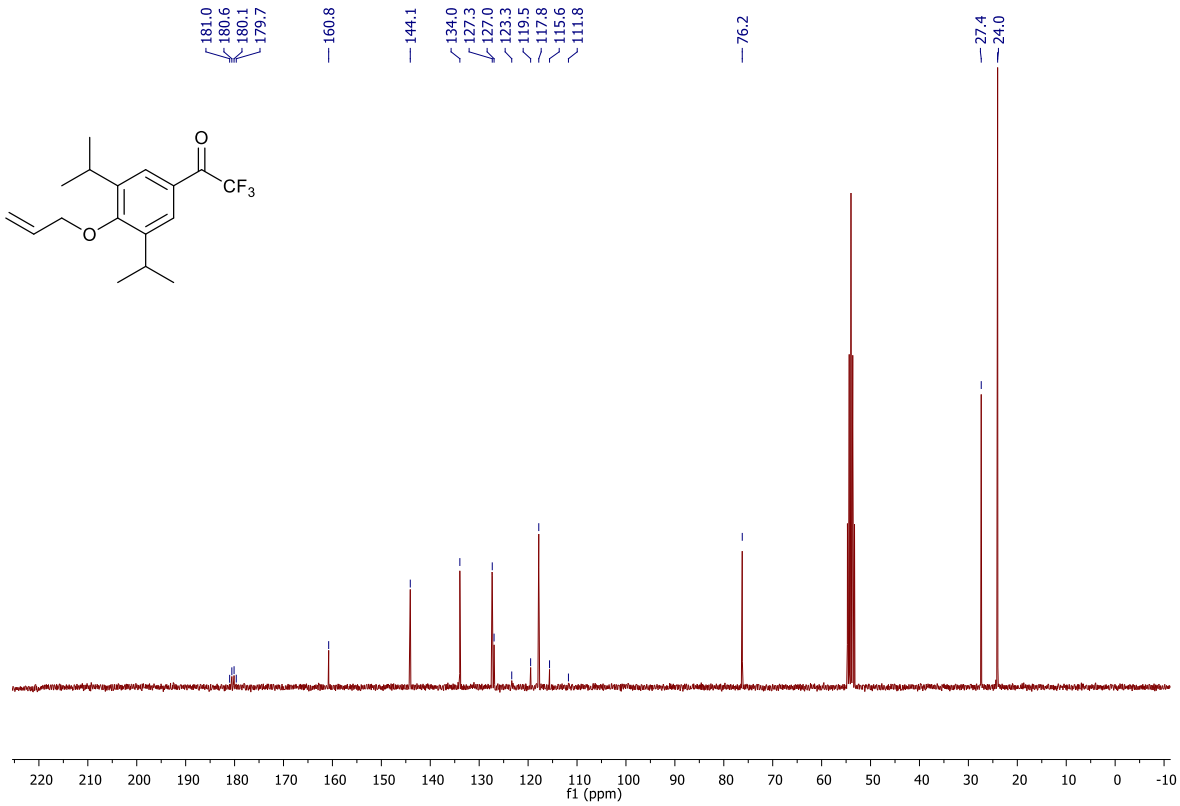
^{13}C NMR (75.5 MHz, $CDCl_3$) of **8D**



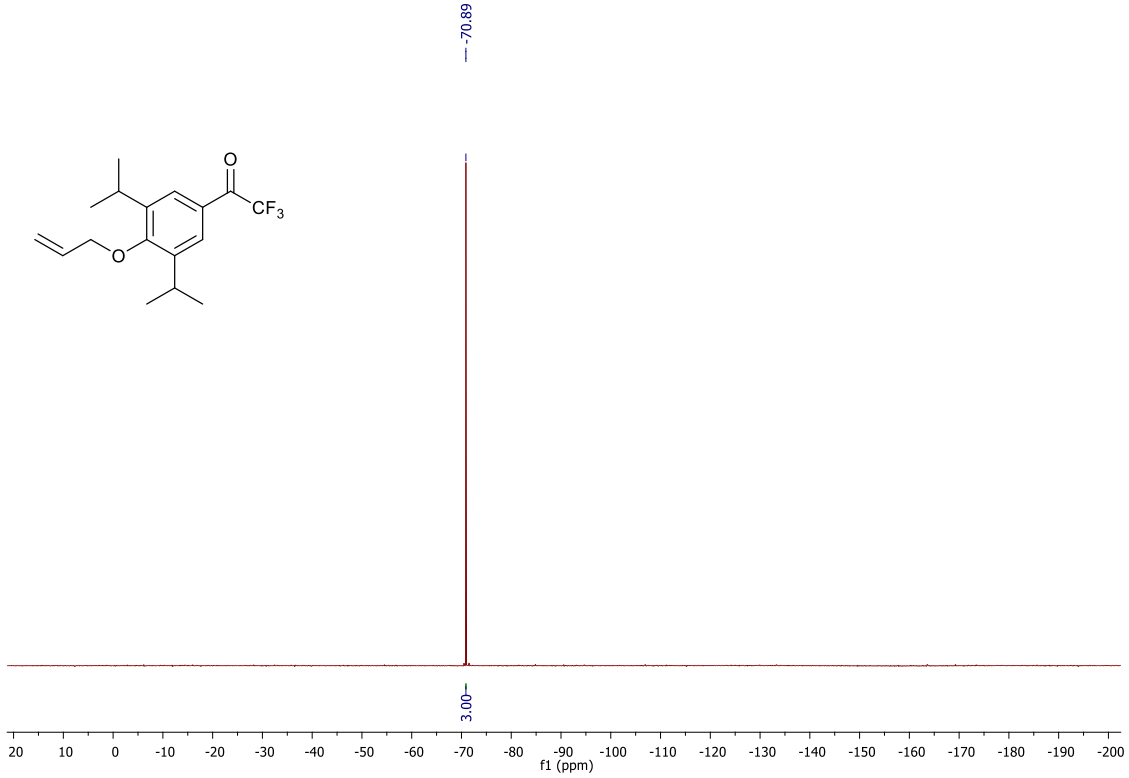
^{1}H NMR (300 MHz, $CDCl_3$) of **2e**



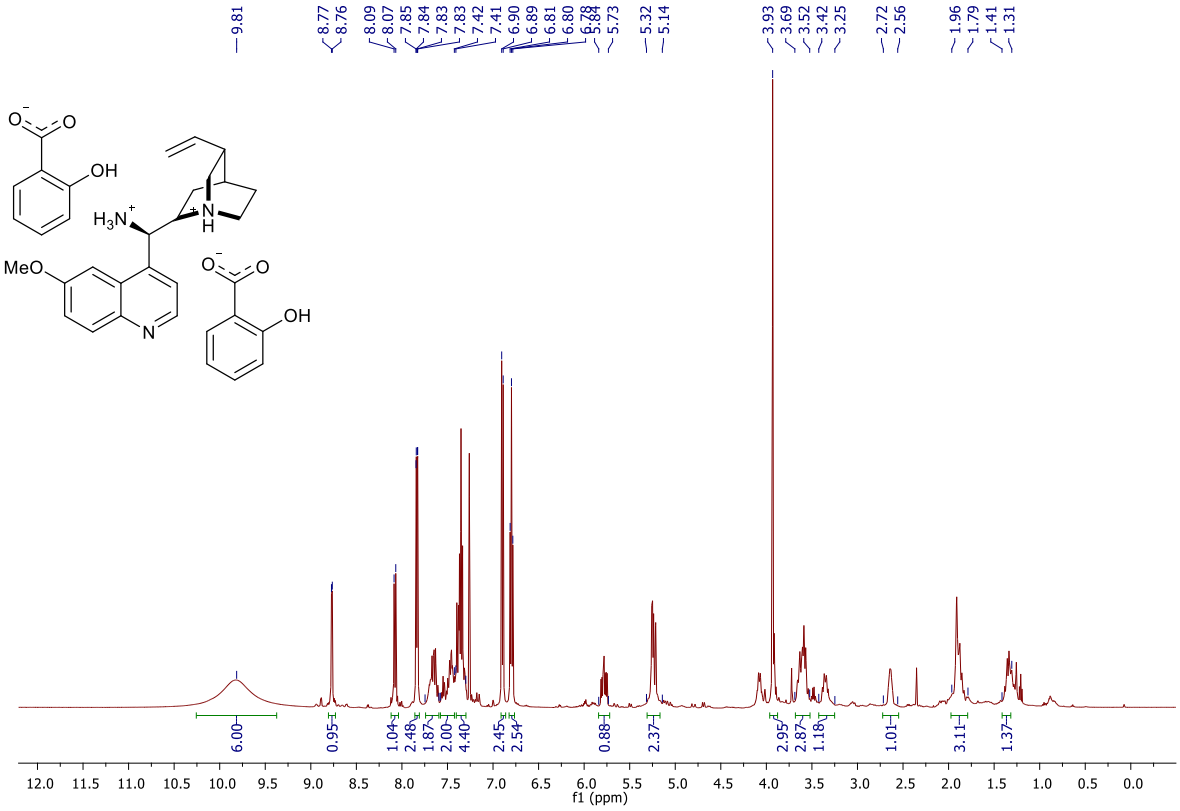
^{13}C NMR (75.5 MHz, CD_2Cl_2) of **2e**



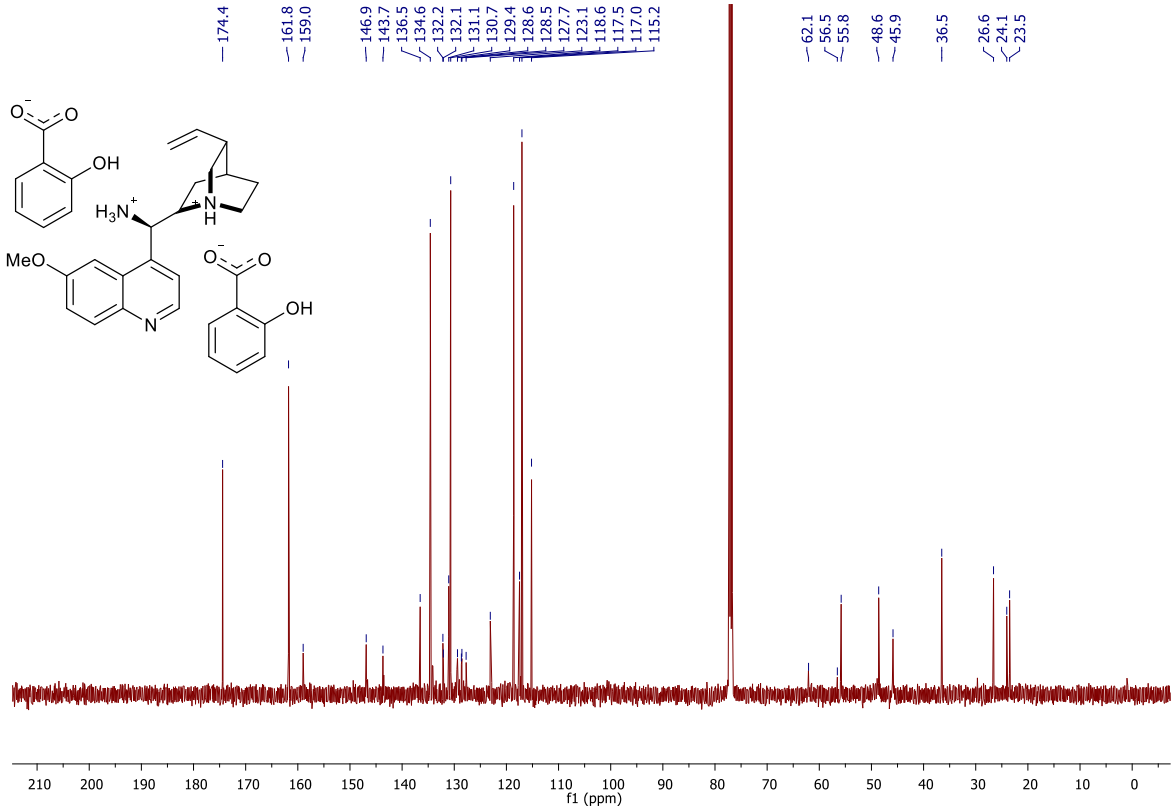
^{19}F NMR (471 MHz, $CDCl_3$) of **2e**



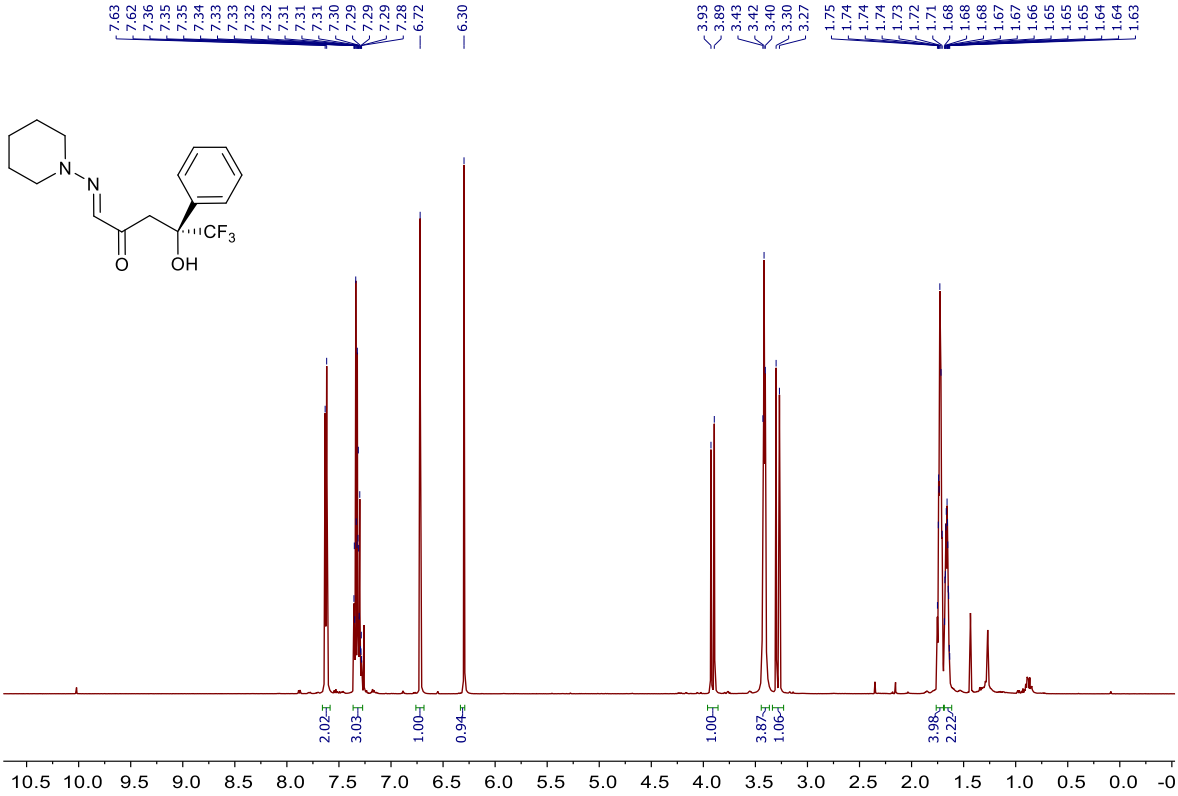
^{1}H NMR (500 MHz, $CDCl_3$) of **II(SA)$_2$**



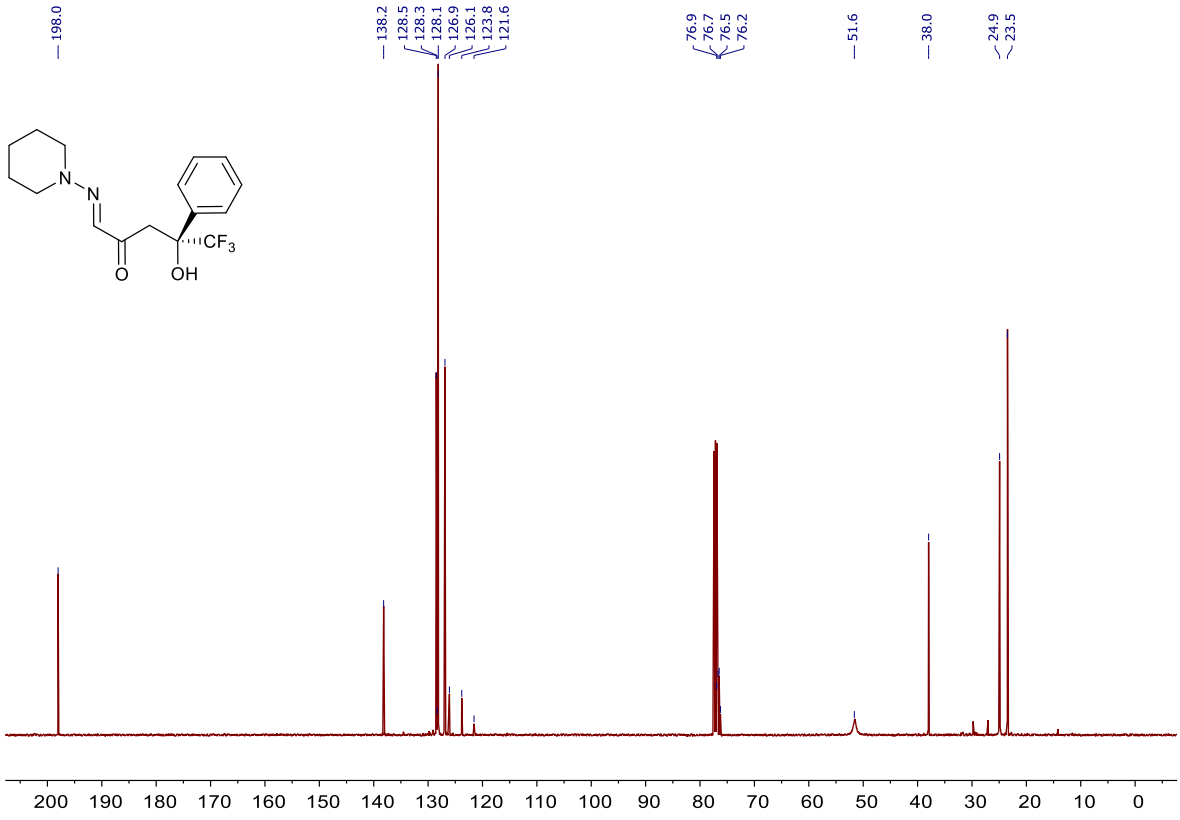
^{13}C NMR (126 MHz, $CDCl_3$) of **II(SA)$_2$**



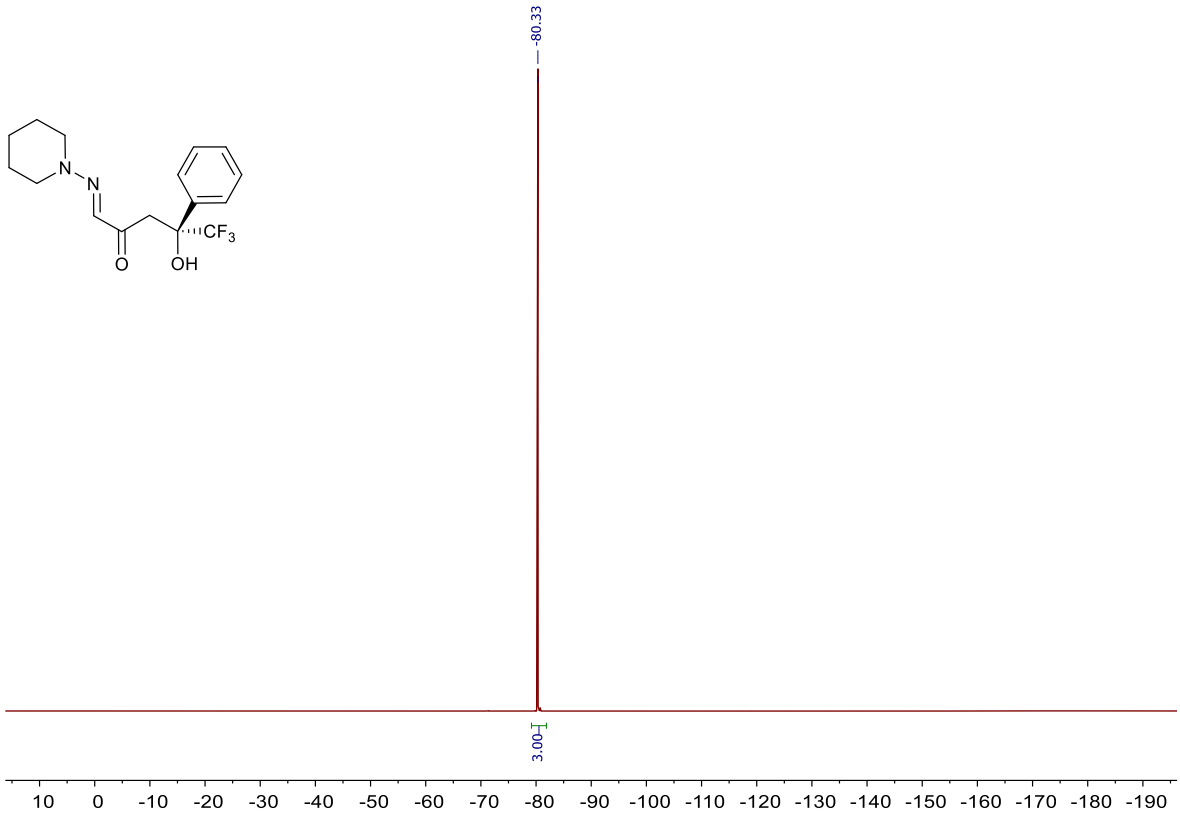
^{1}H NMR (500 MHz, $CDCl_3$) of (*S*)-**3Aa**



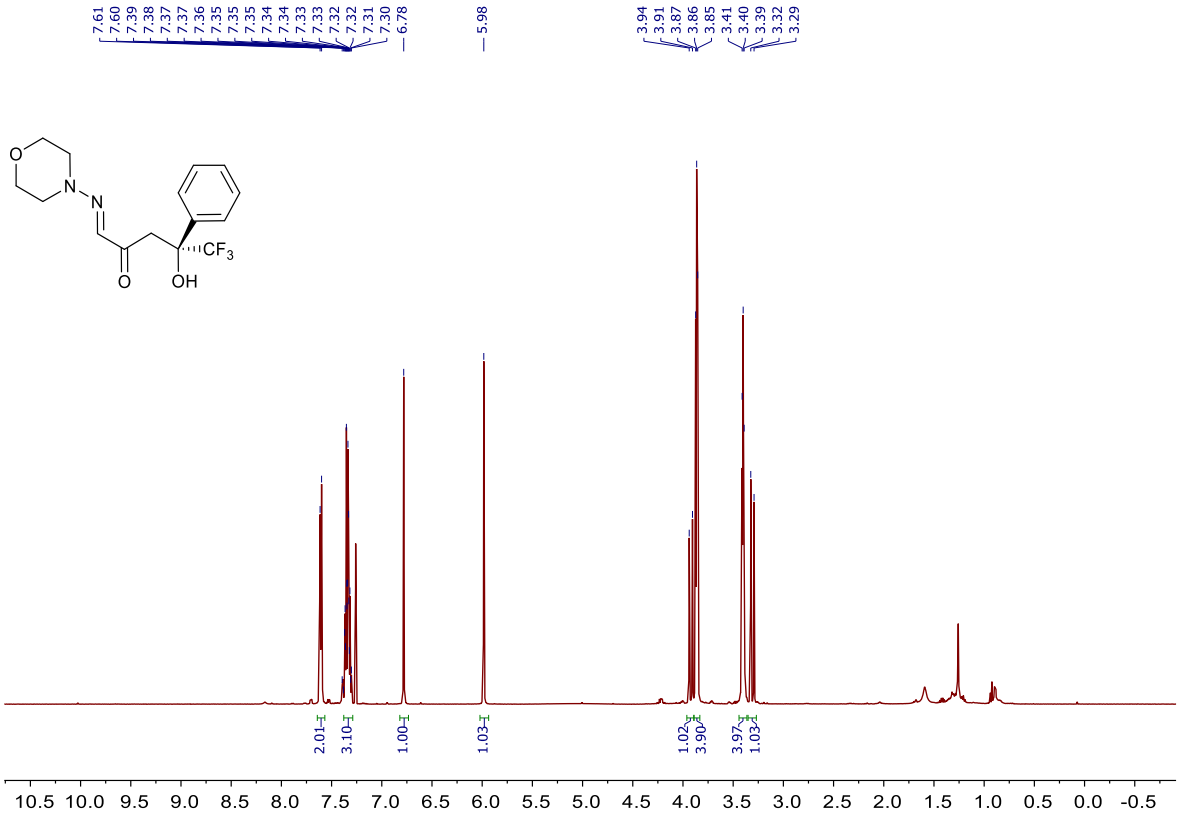
^{13}C NMR (126 MHz, $CDCl_3$) of (*S*)-**3Aa**



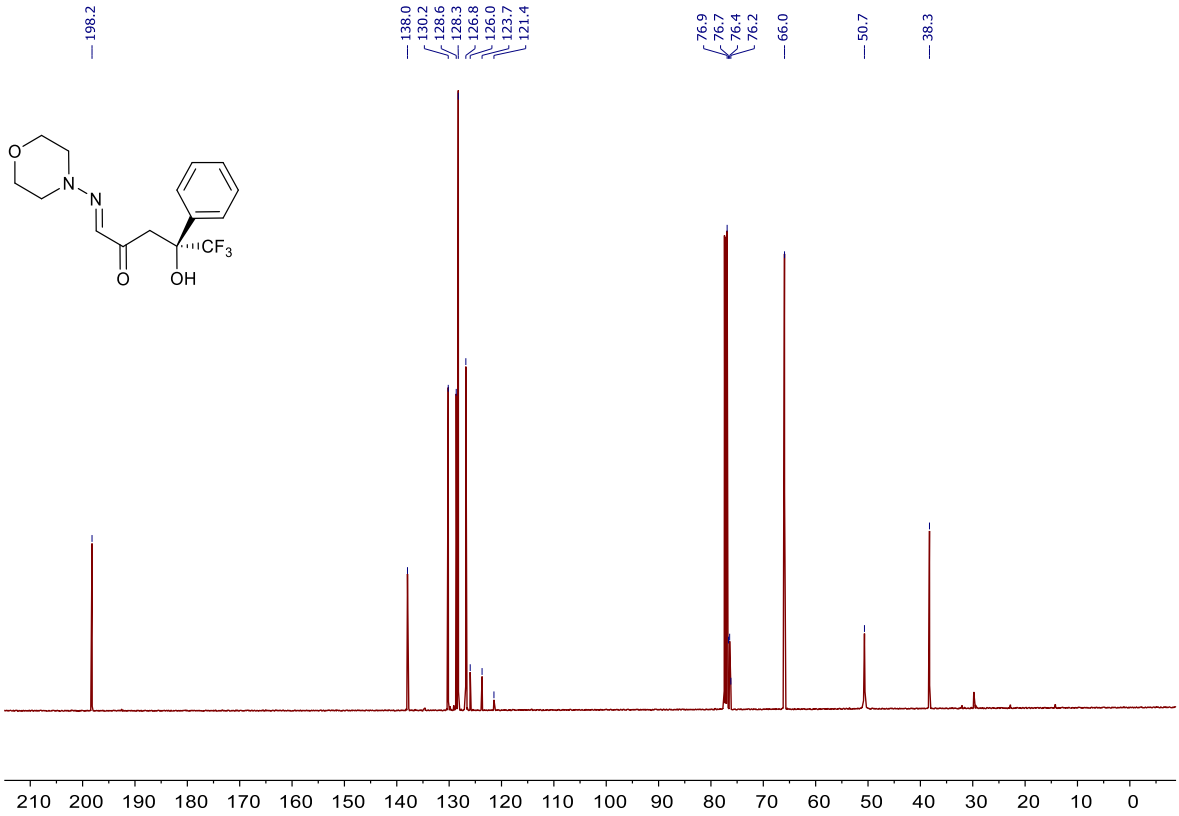
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)-**3Aa**



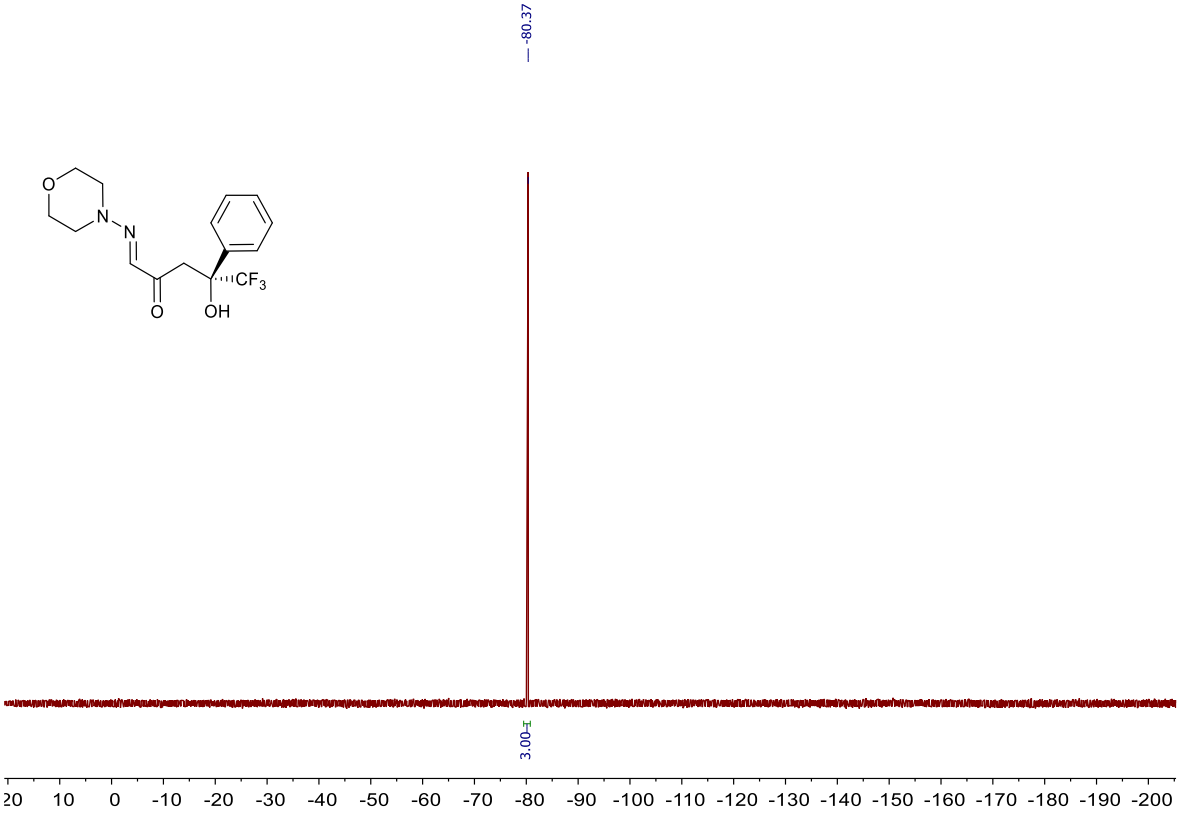
^{1}H NMR (500 MHz, $CDCl_3$) of (*S*)-**3Ba**



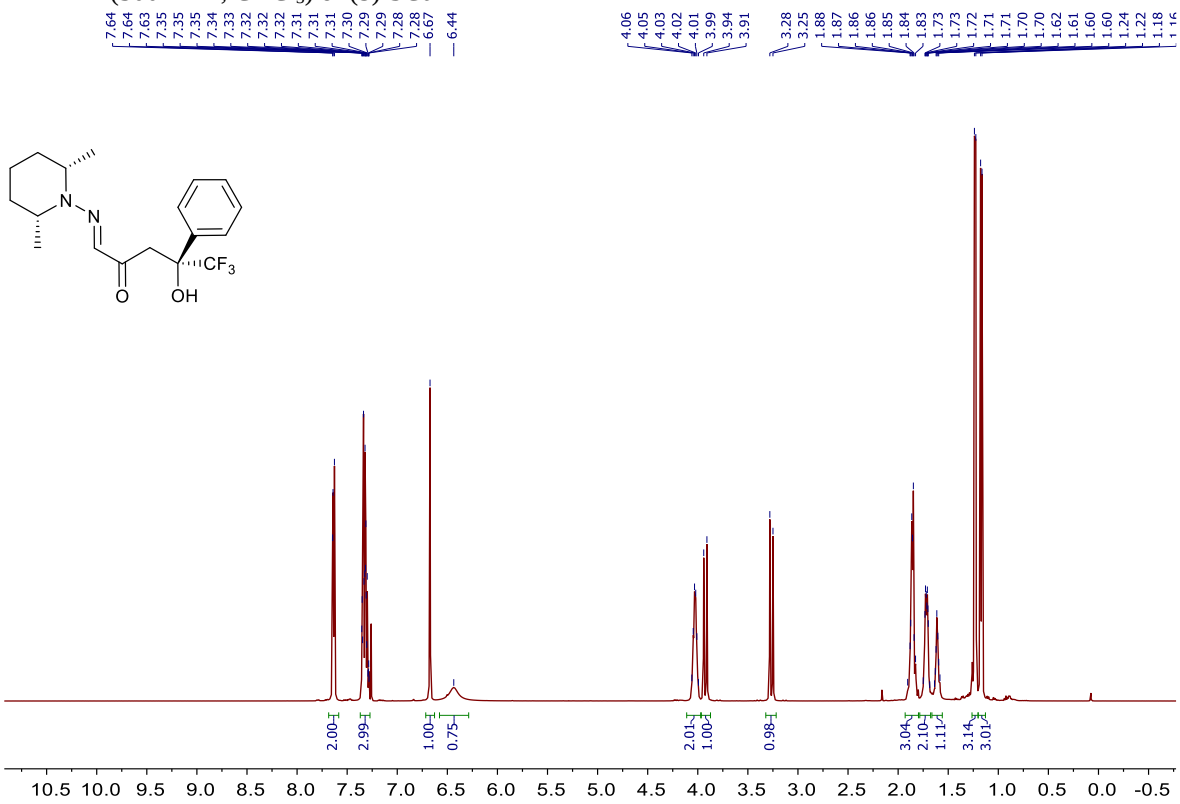
^{13}C NMR (126 MHz, $CDCl_3$) of (*S*)-**3Ba**



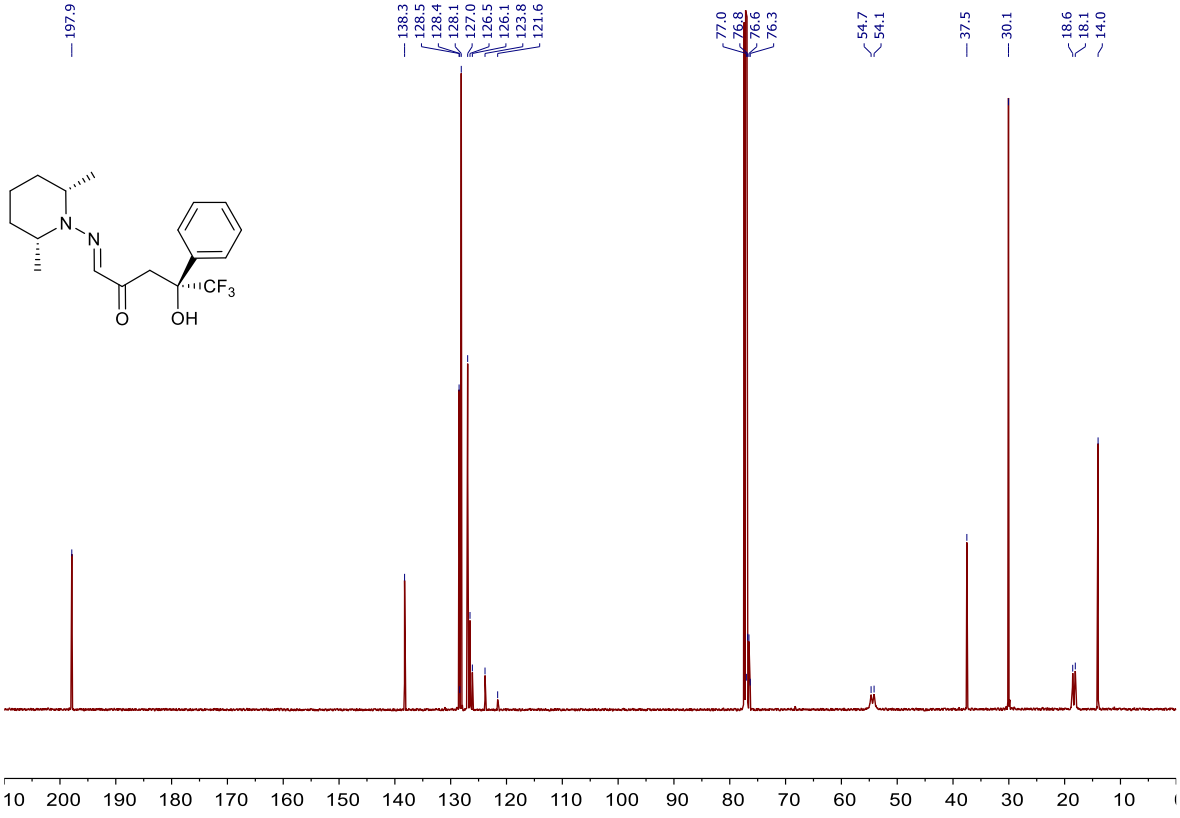
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)-**3Ba**



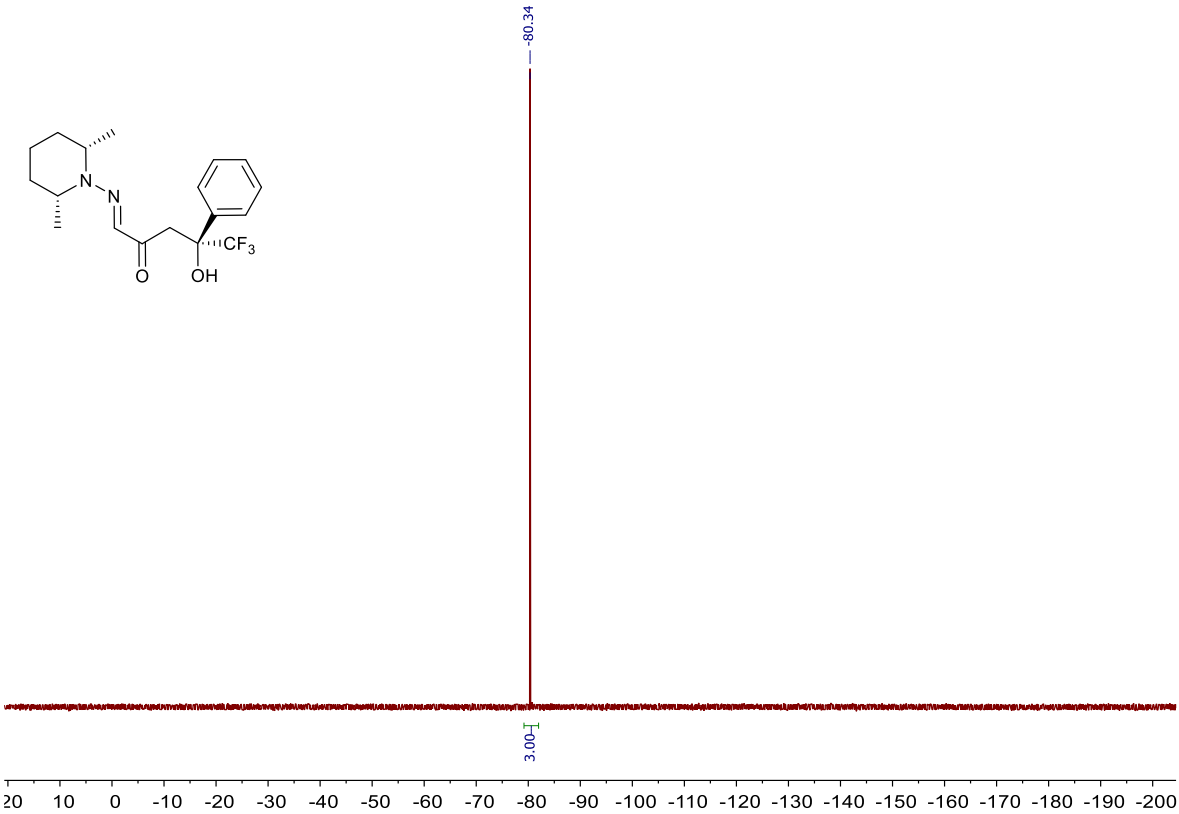
^{1}H NMR (500 MHz, $CDCl_3$) of (*S*)-**3Ca**



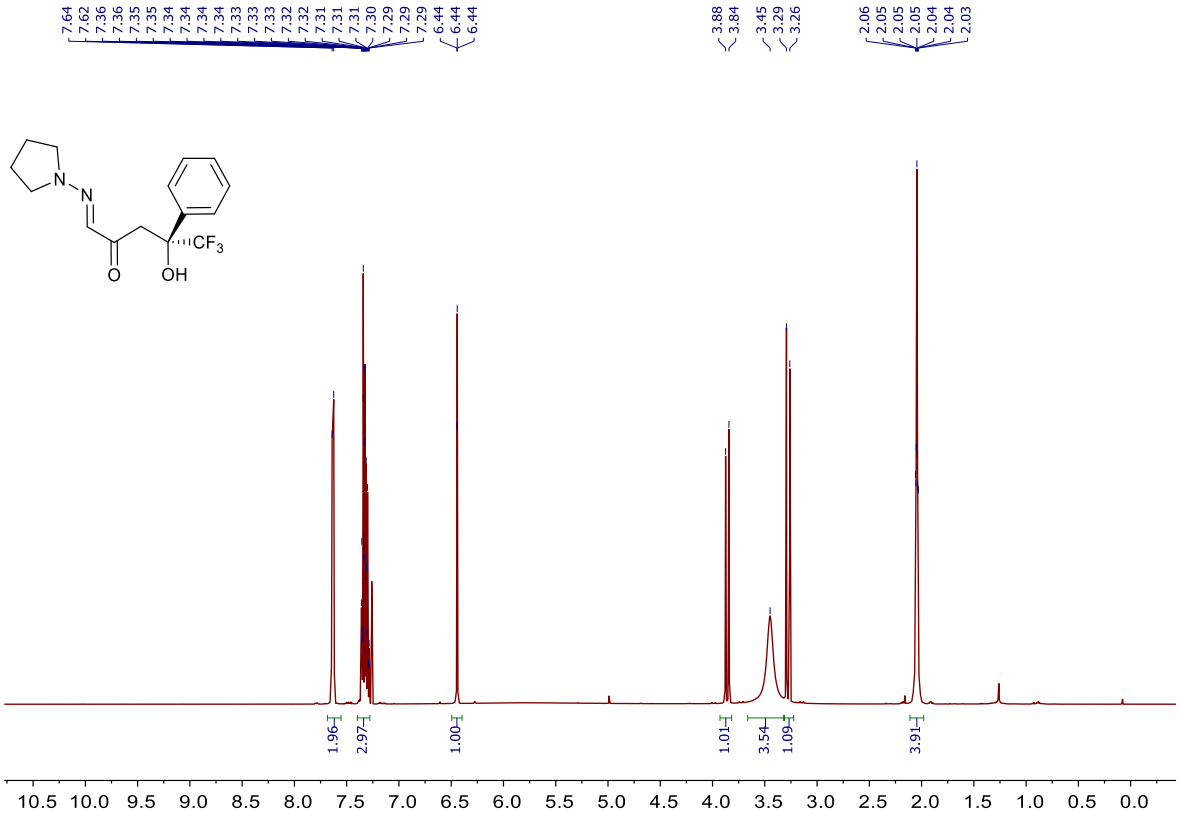
^{13}C NMR (126 MHz, $CDCl_3$) of (*S*)-**3Ca**



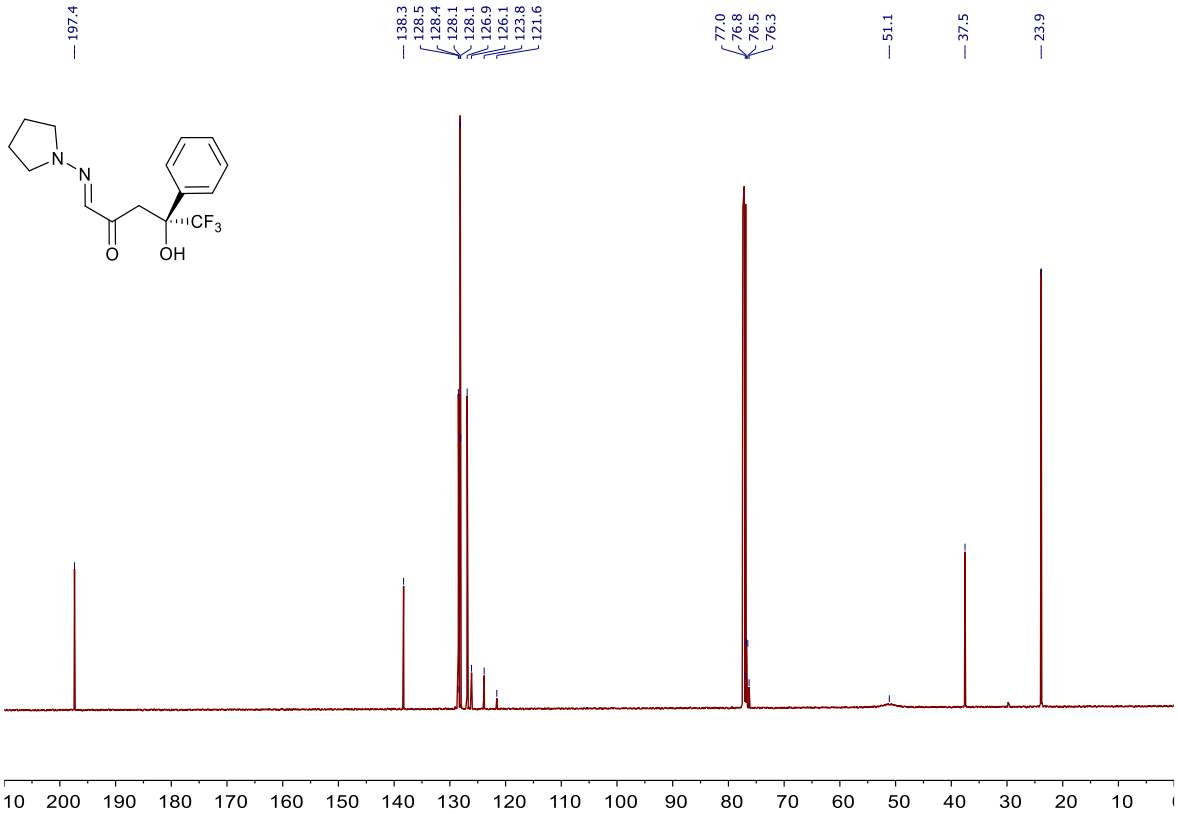
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)-**3Ca**



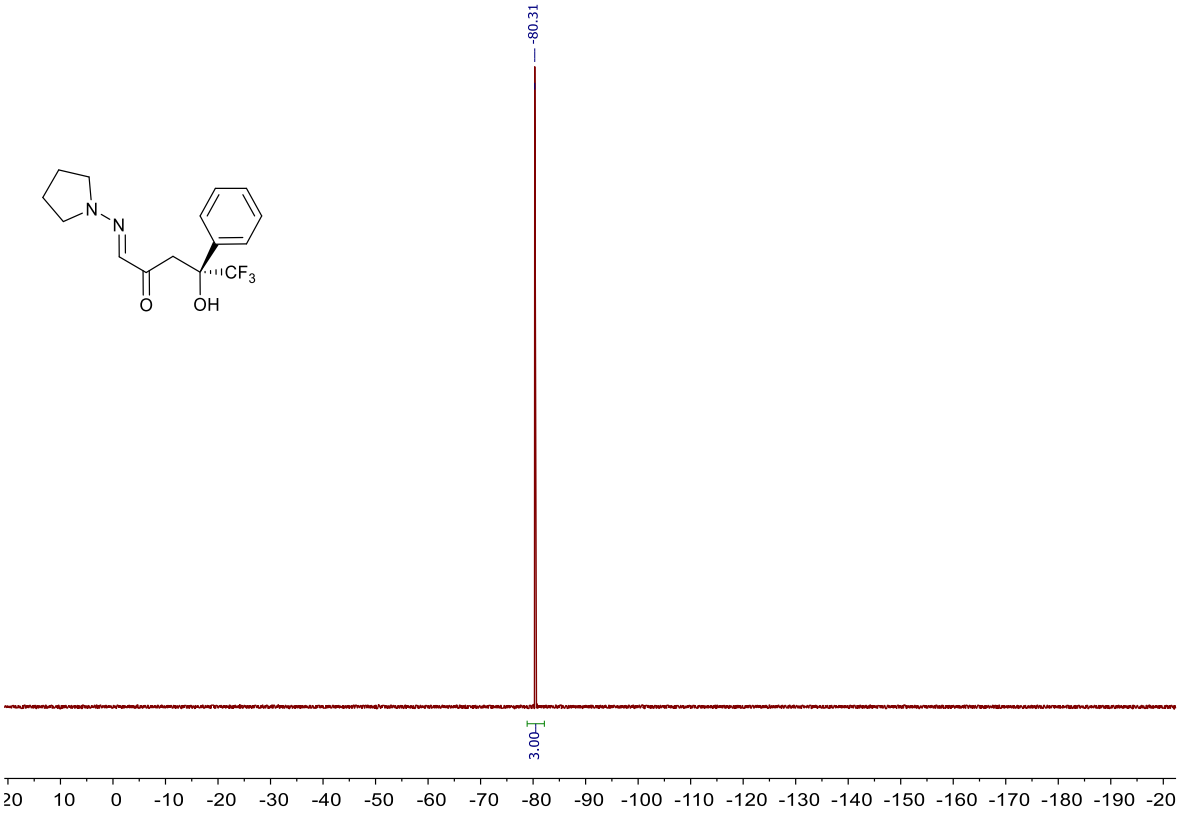
^{1}H NMR (500 MHz, $CDCl_3$) of (*S*)-**3Da**



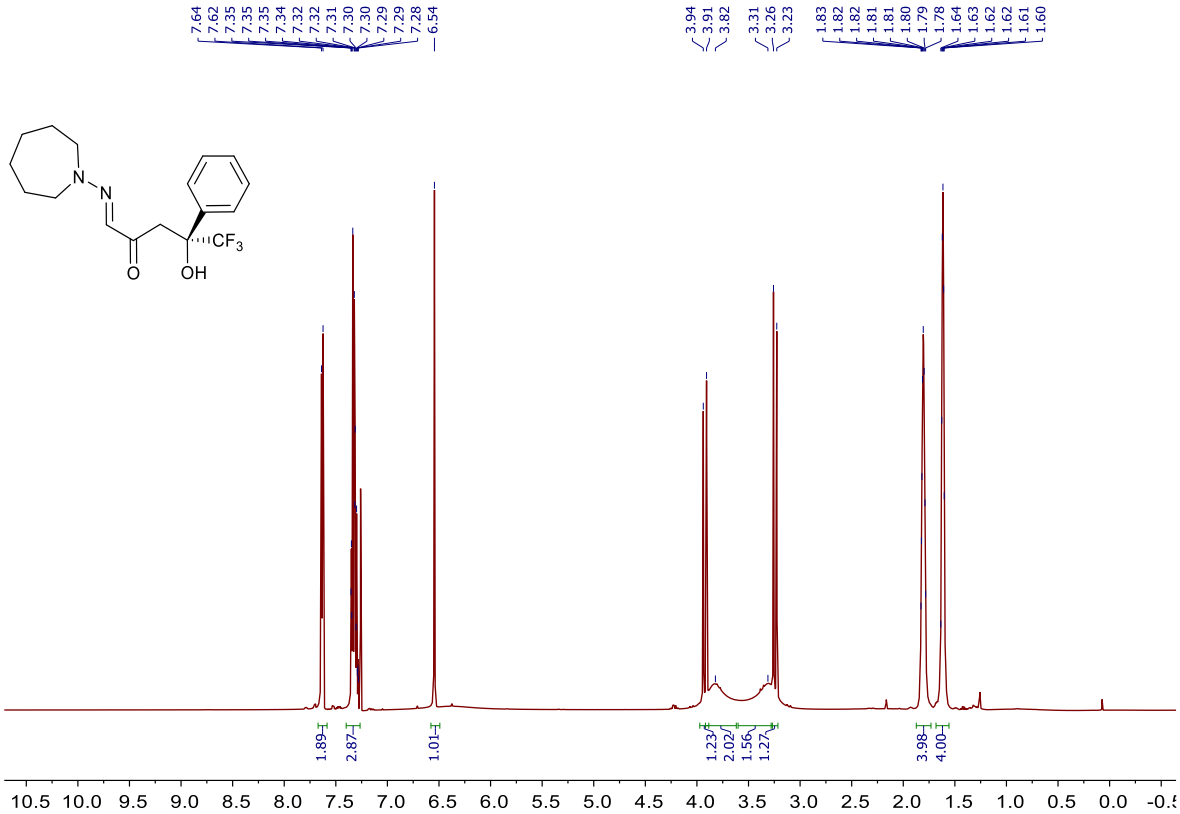
^{13}C NMR (126 MHz, $CDCl_3$) of (*S*)-**3Da**



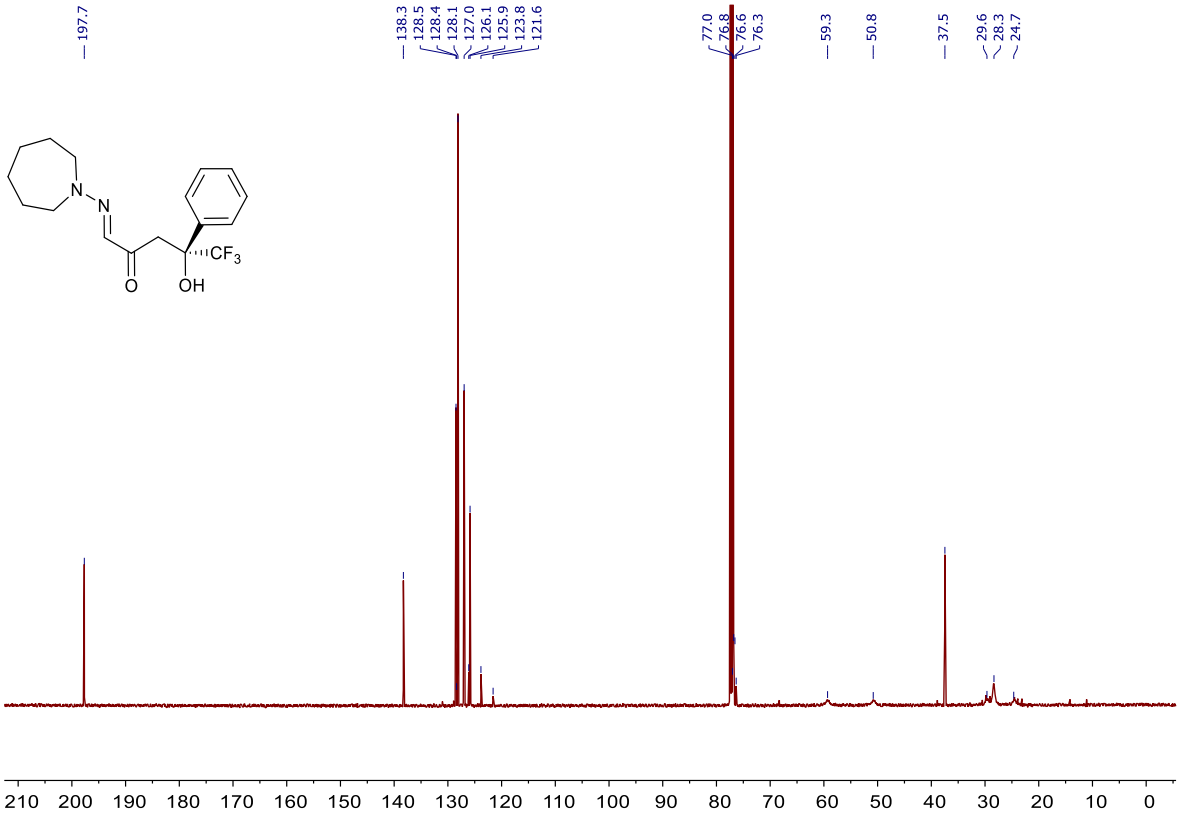
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)-**3Da**



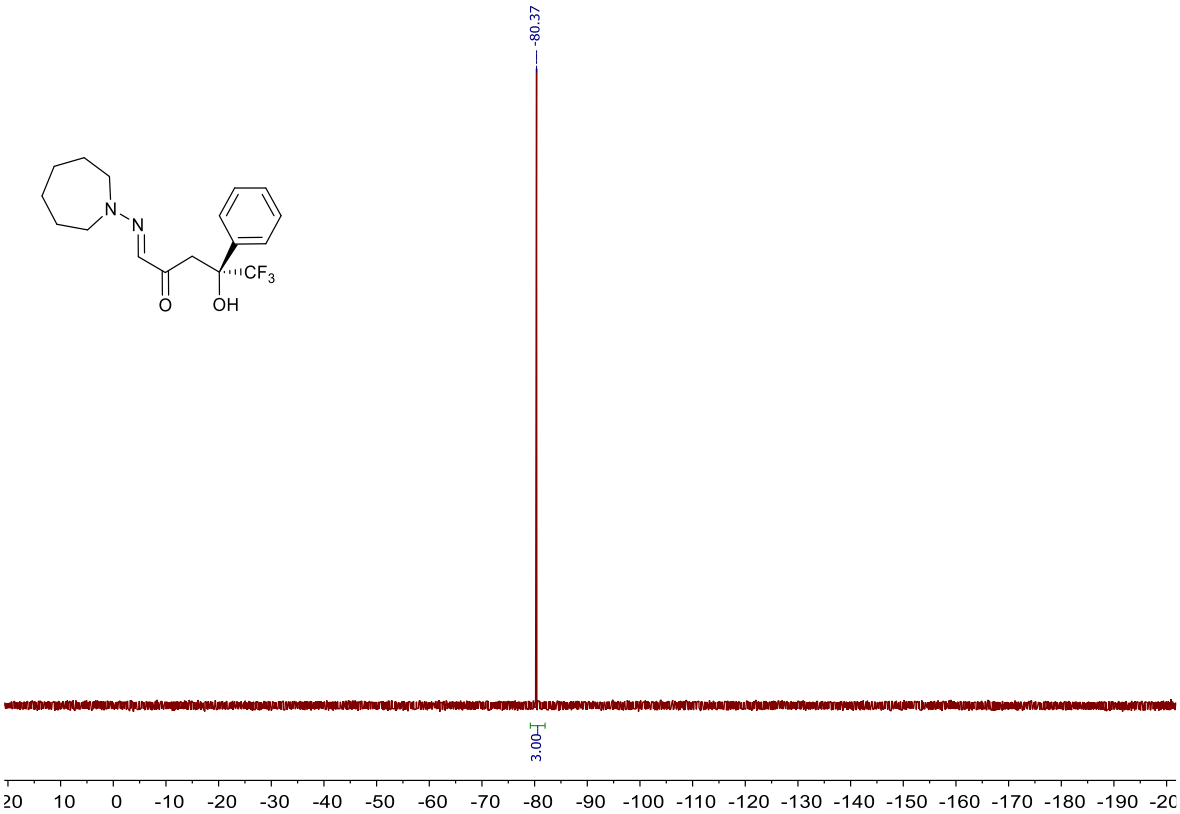
^{1}H NMR (500 MHz, $CDCl_3$) of (*S*)-**3Ea**



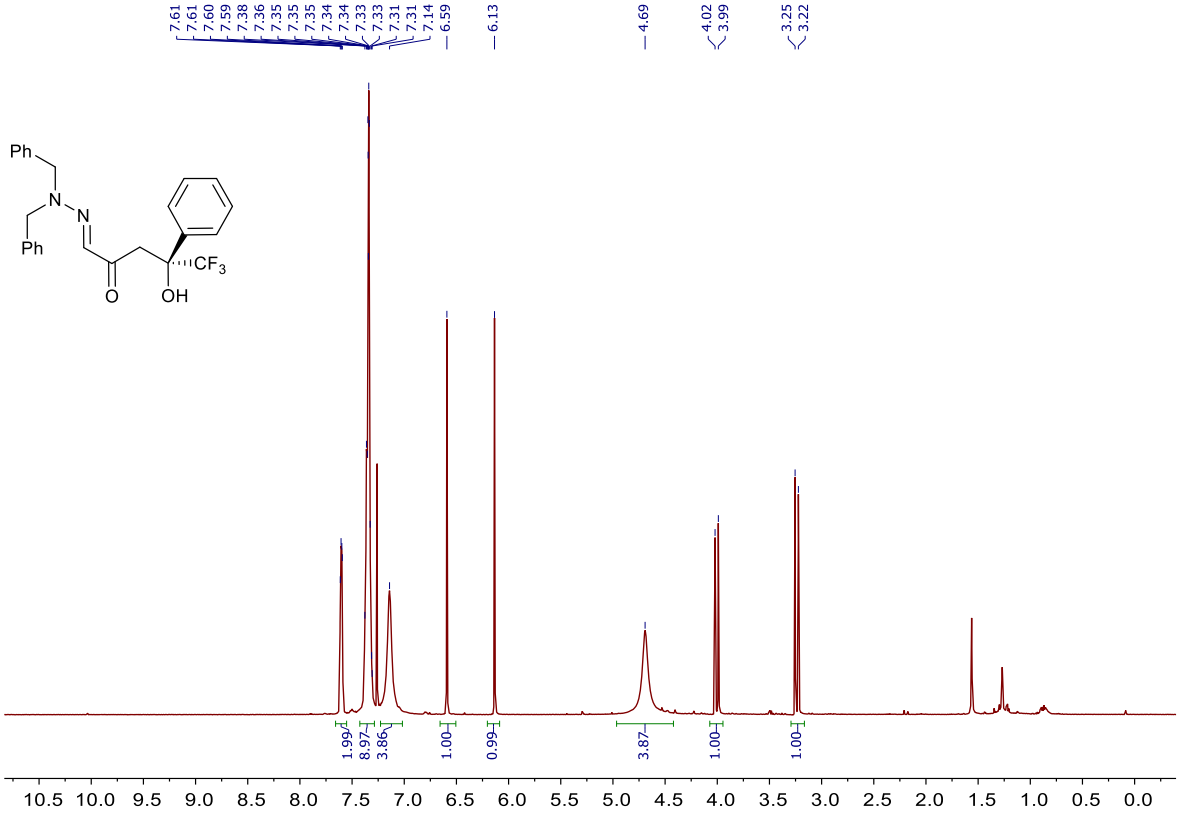
^{13}C NMR (126 MHz, $CDCl_3$) of (*S*)-**3Ea**



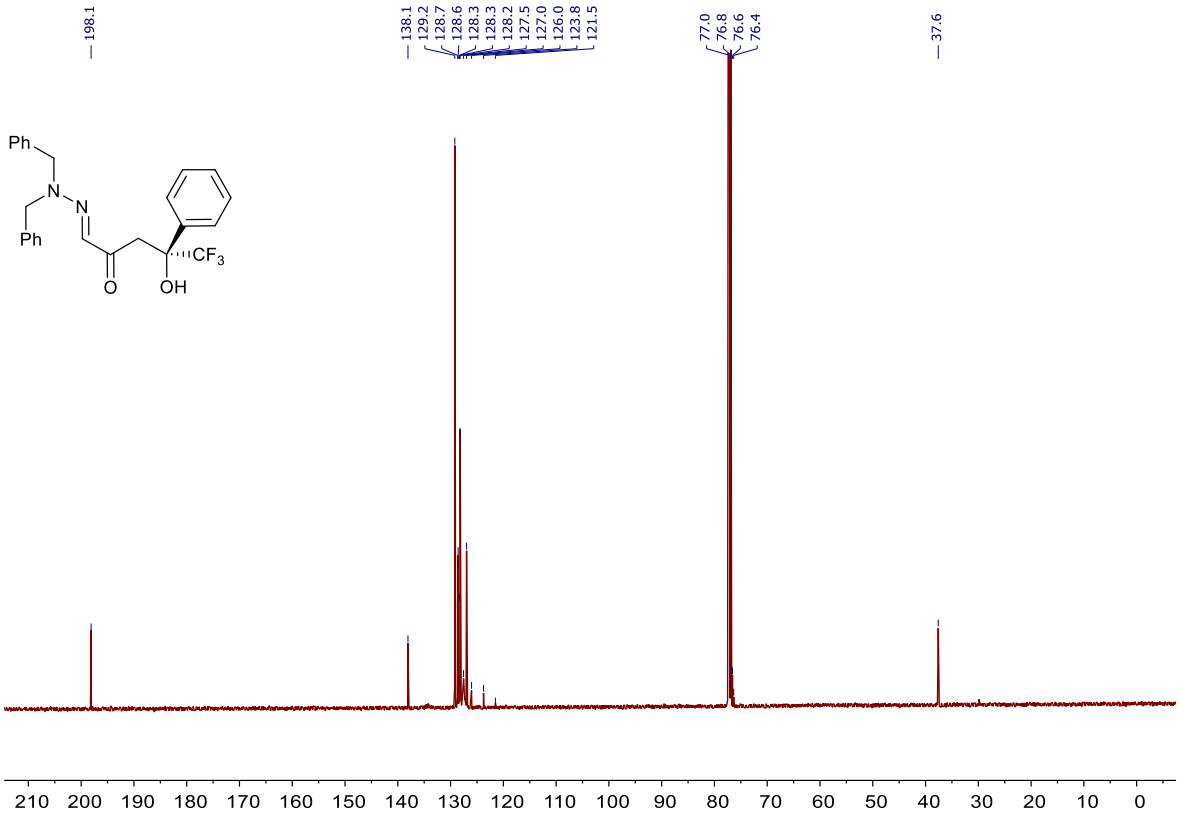
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)-**3Ea**



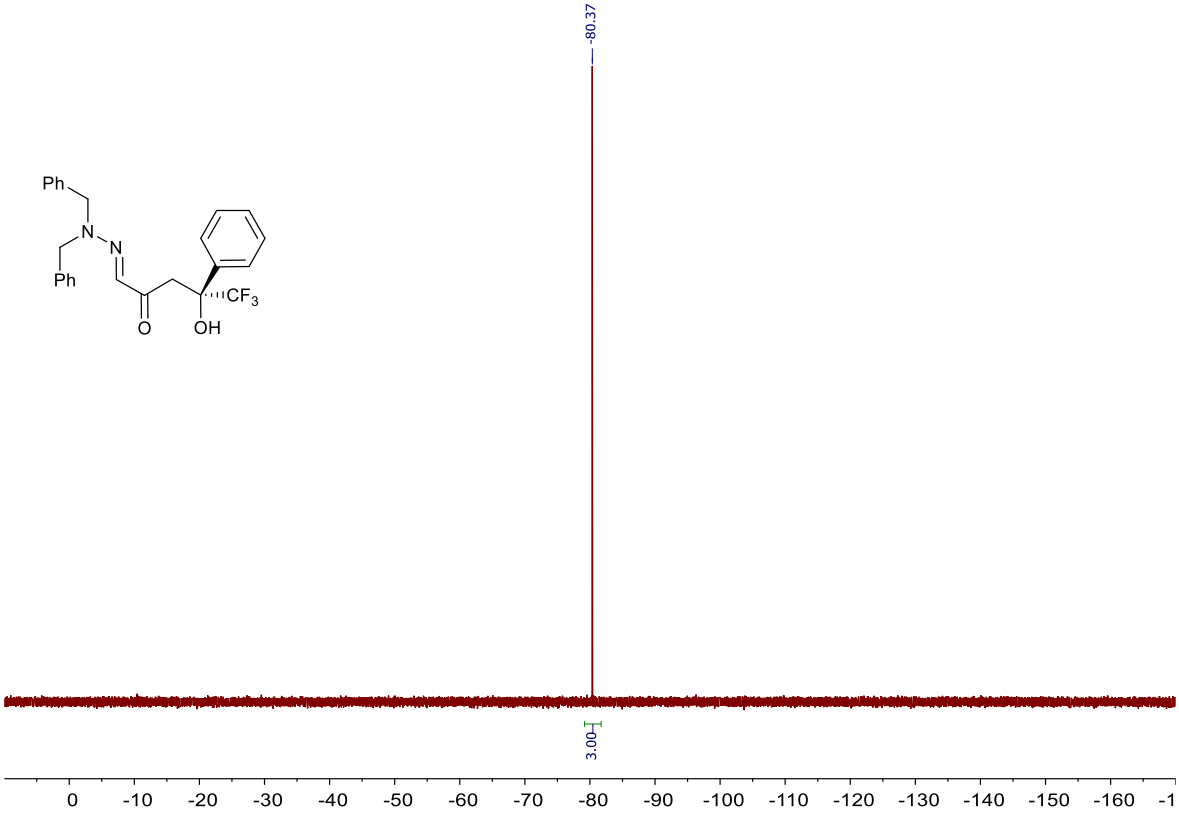
^{1}H NMR (500 MHz, $CDCl_3$) of (*S*)-**3Fa**



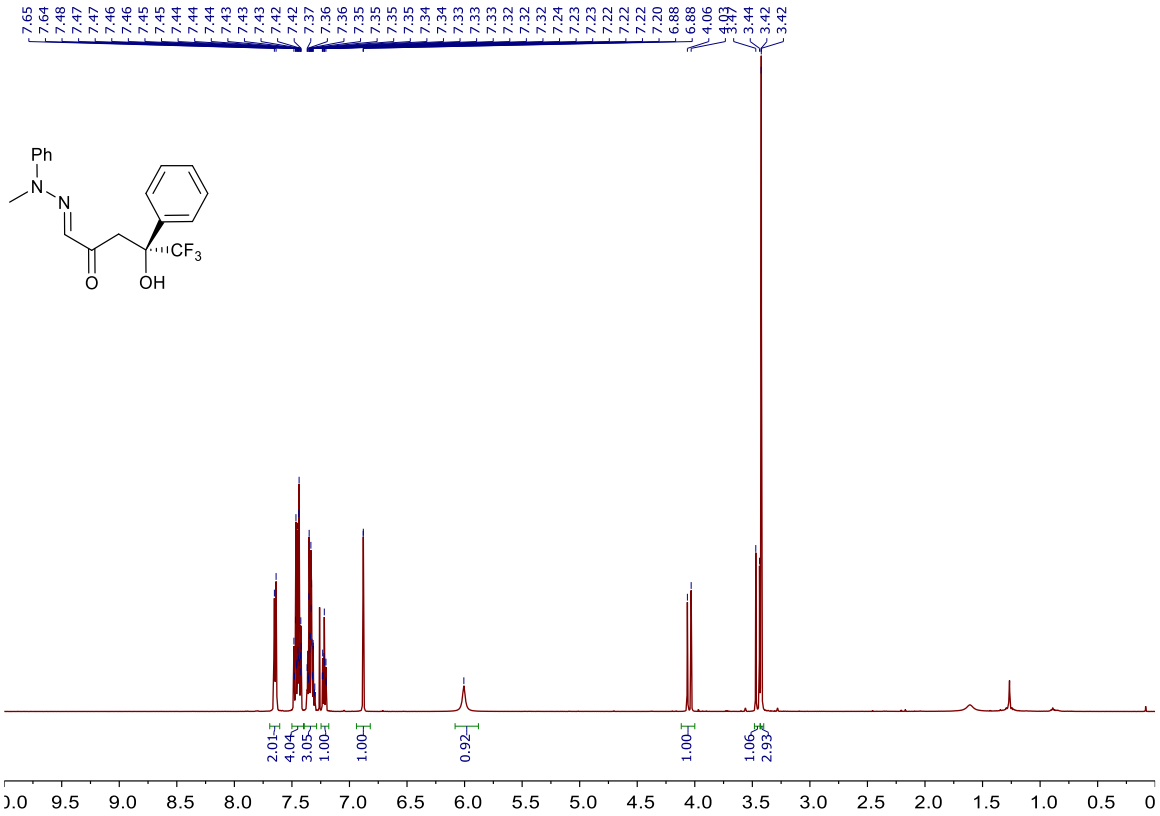
^{13}C NMR (126 MHz, $CDCl_3$) of (*S*)-**3Fa**



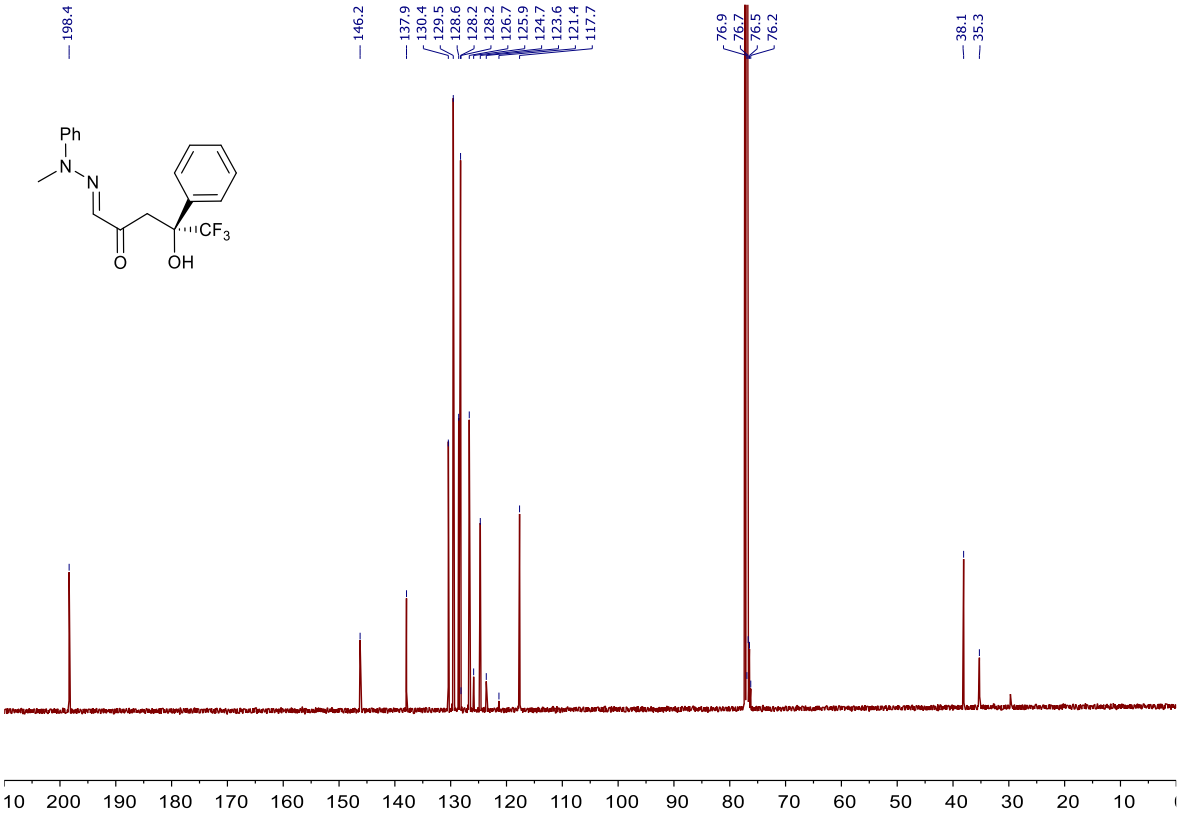
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)-**3Fa**



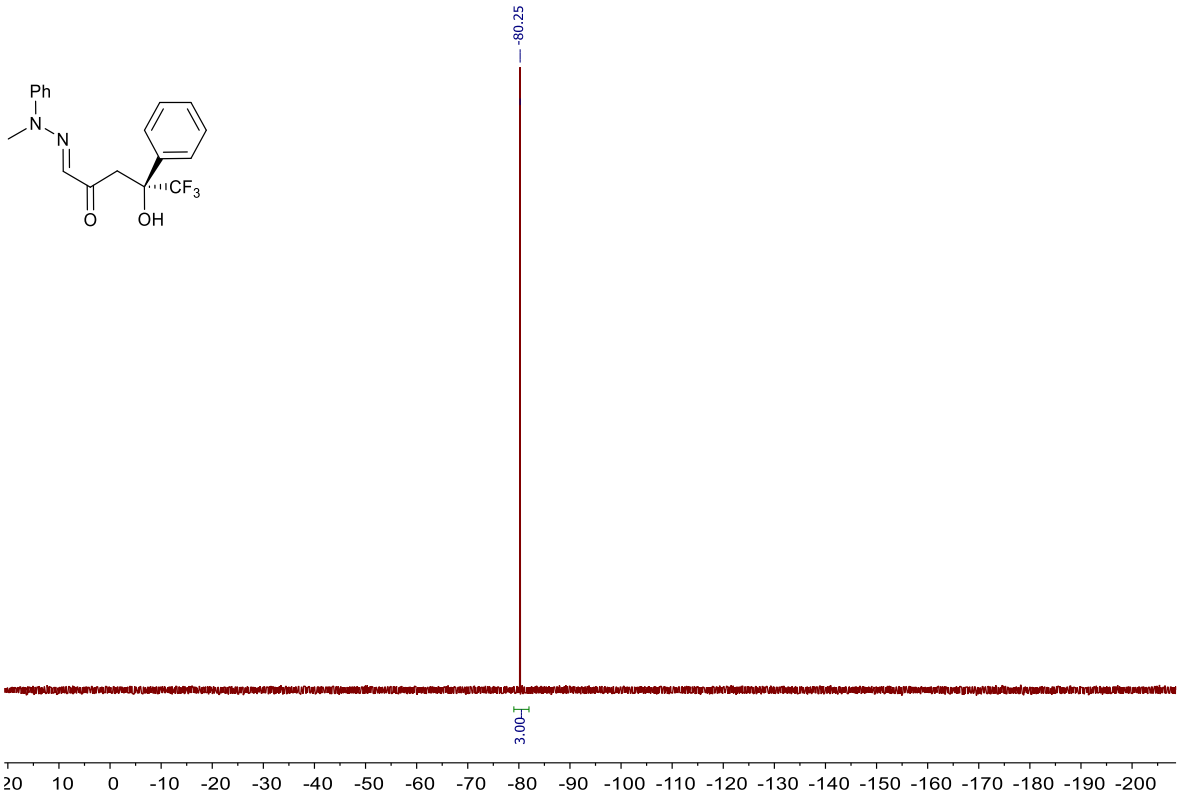
^{1}H NMR (500 MHz, $CDCl_3$) of (*S*)-**3Ga**



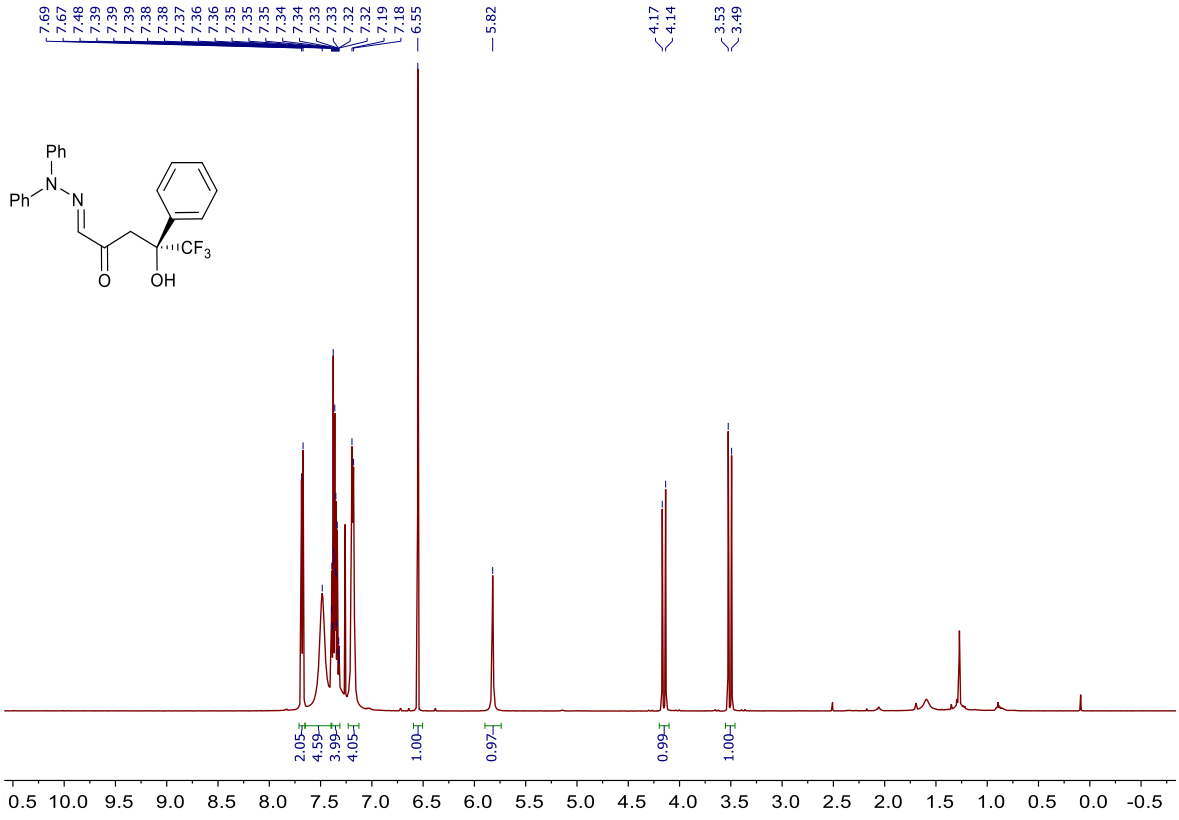
^{13}C NMR (126 MHz, $CDCl_3$) of (*S*)-3**Ga**



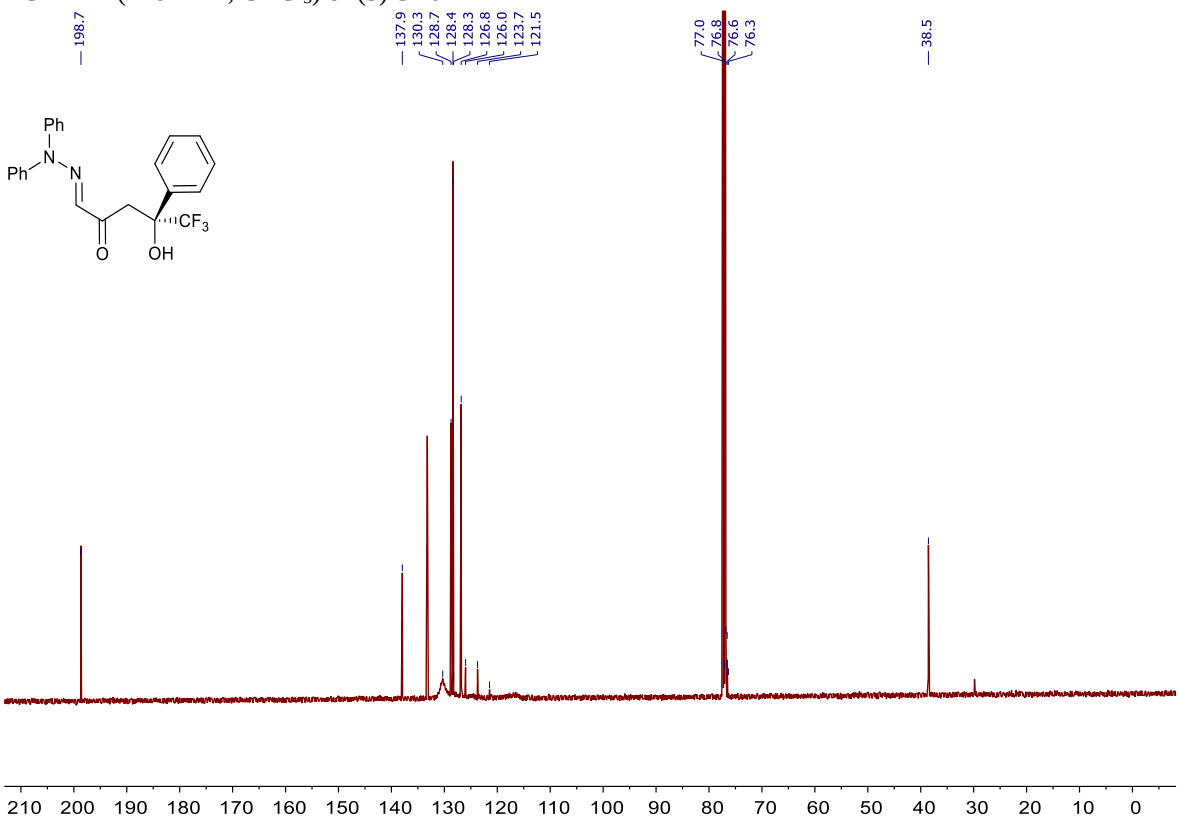
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)-**3Ga**



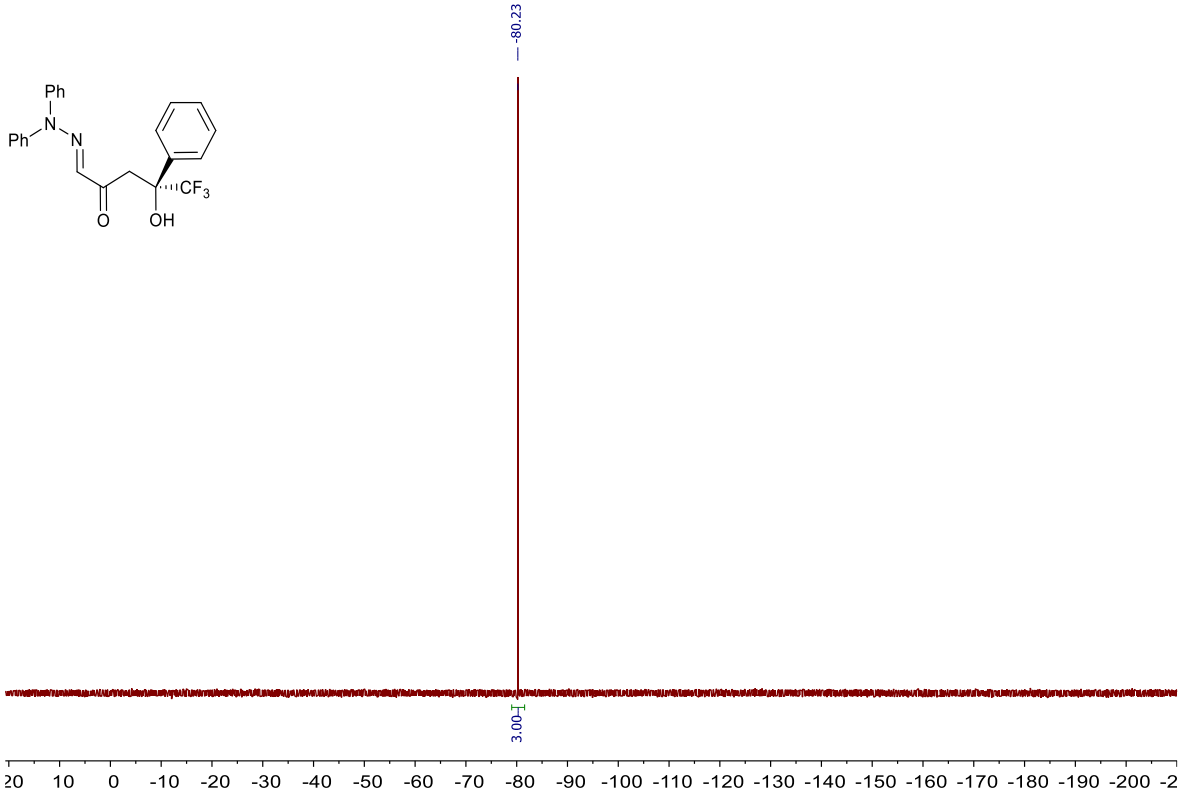
^{1}H NMR (500 MHz, $CDCl_3$) of (*S*)-**3Ha**



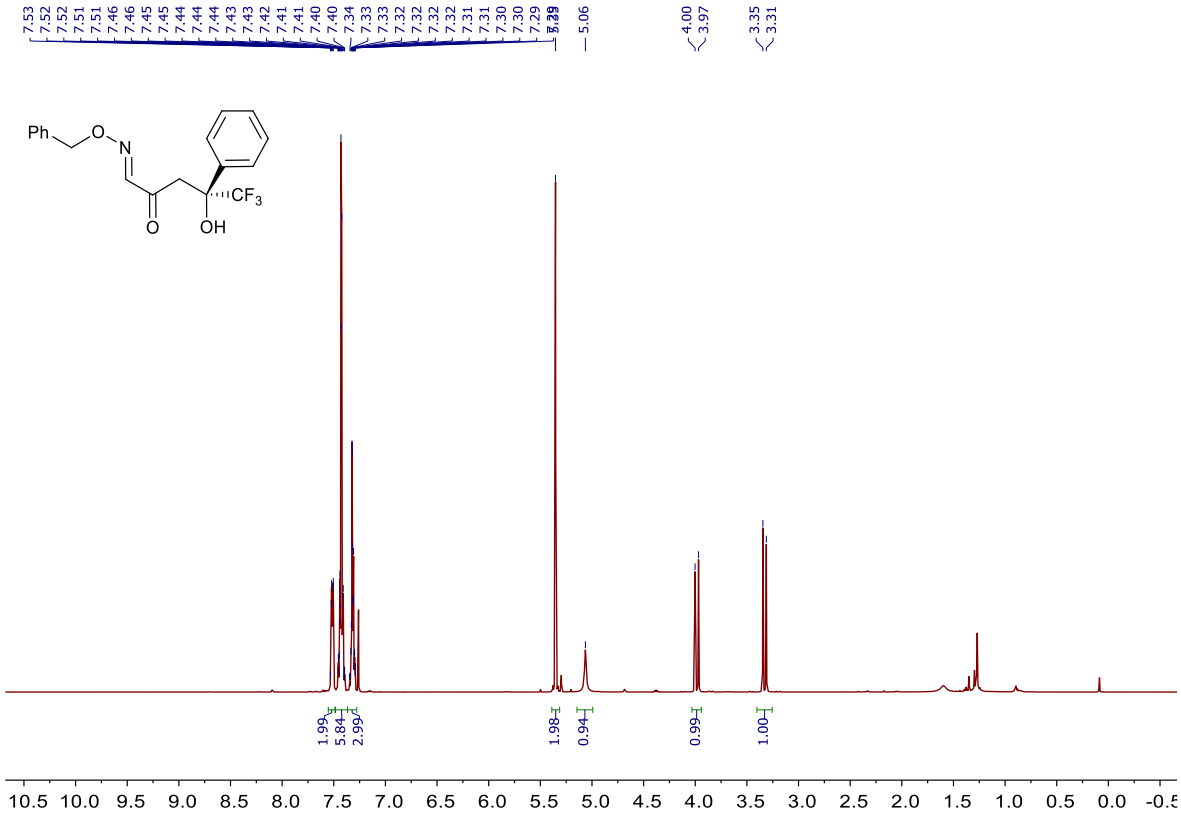
^{13}C NMR (126 MHz, $CDCl_3$) of (*S*)-**3Ha**



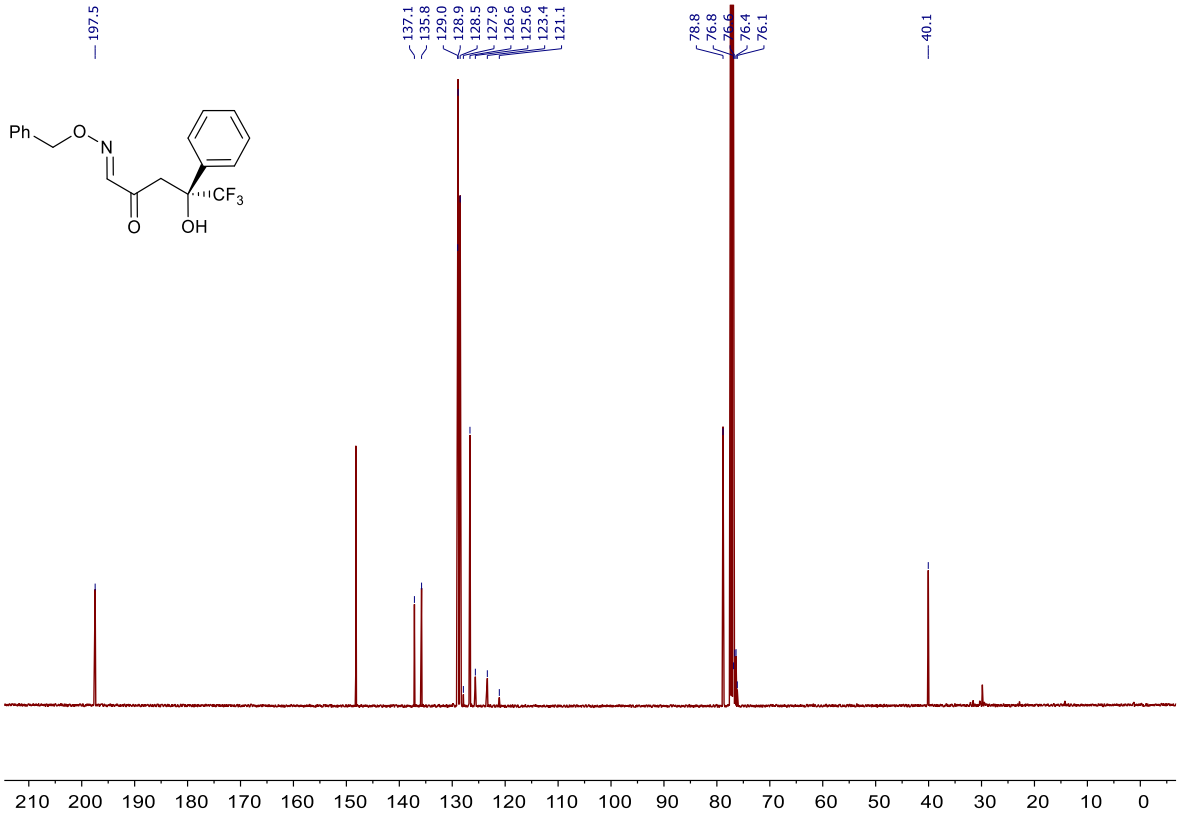
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)-**3Ha**



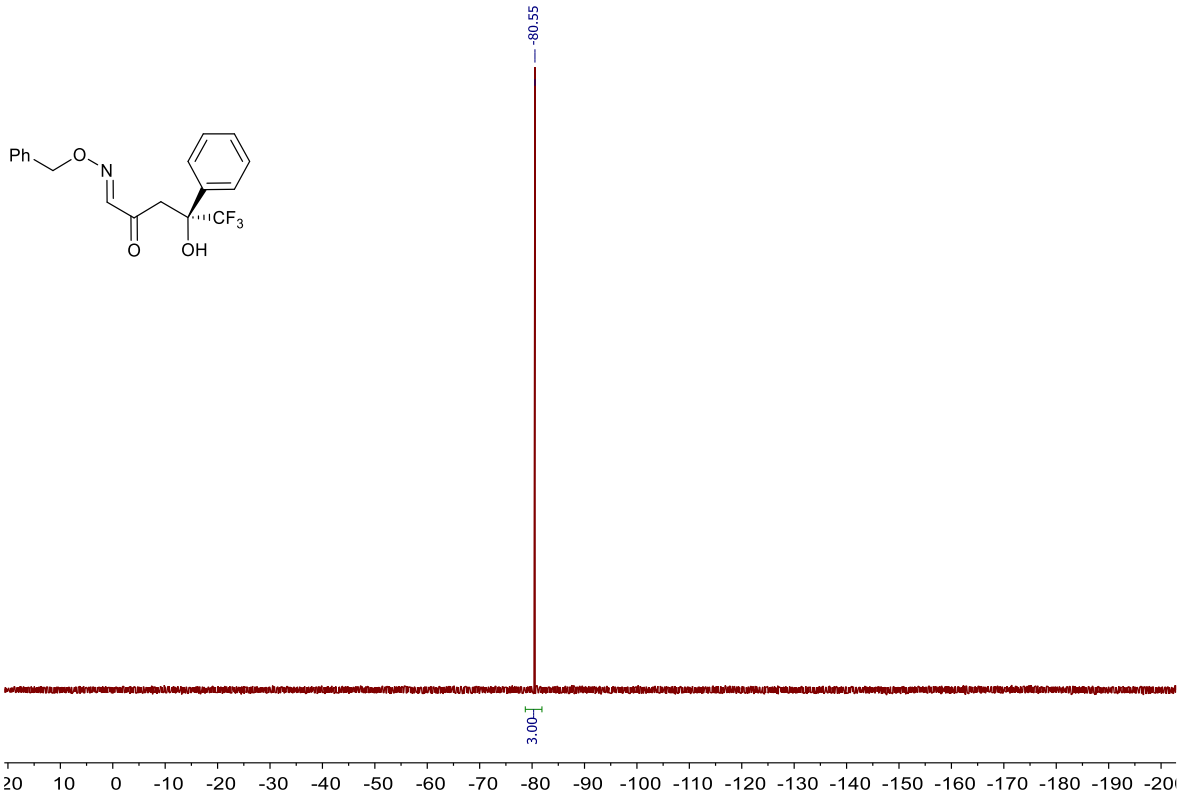
^{1}H NMR (500 MHz, $CDCl_3$) of (*S*)-**5**



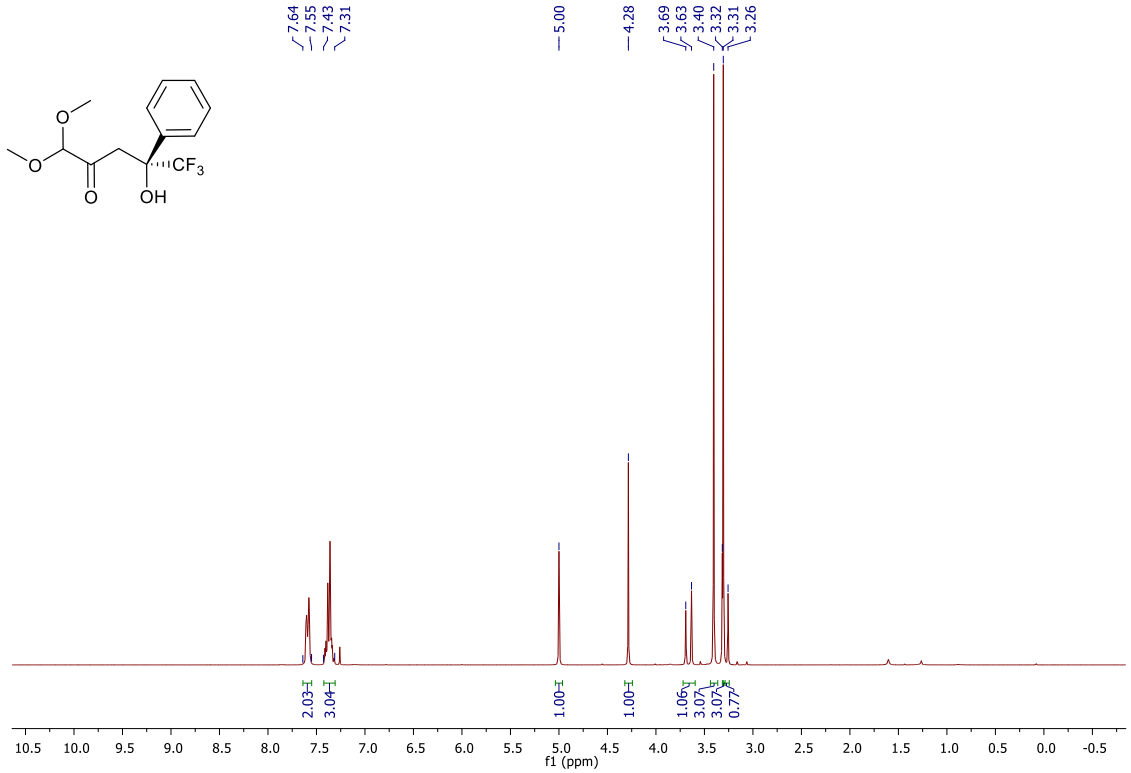
^{13}C NMR (126 MHz, $CDCl_3$) of (*S*)-**5**



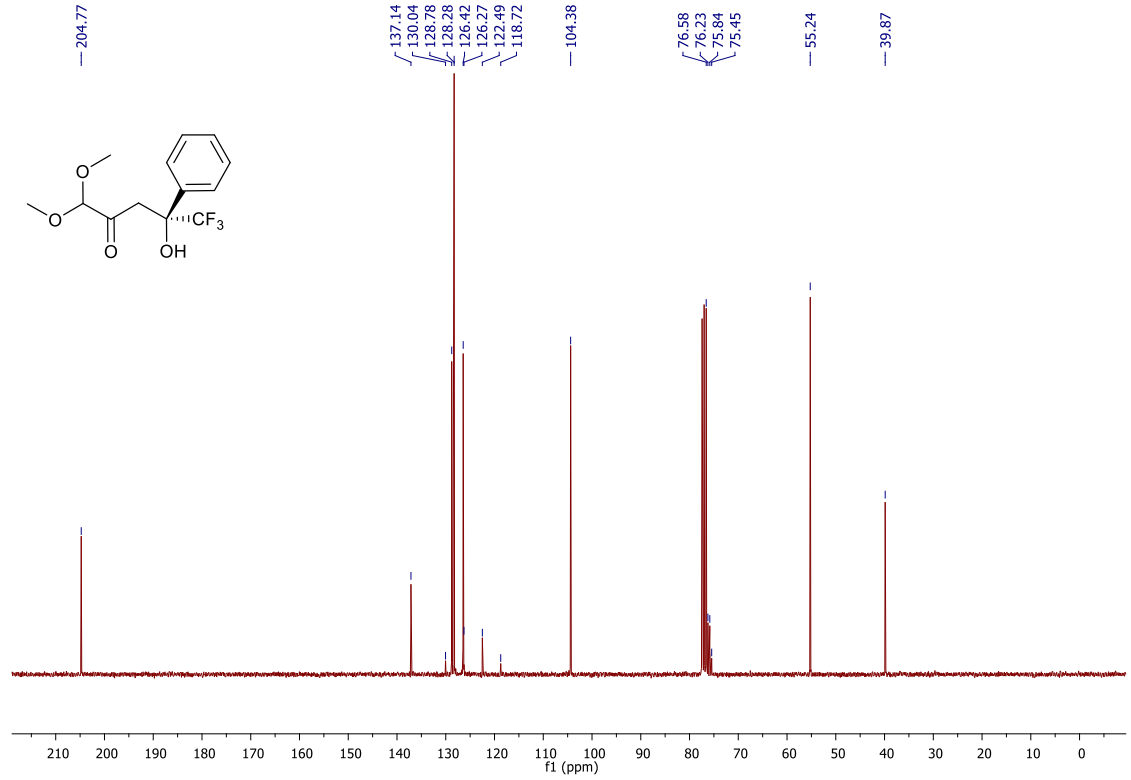
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)-**5**



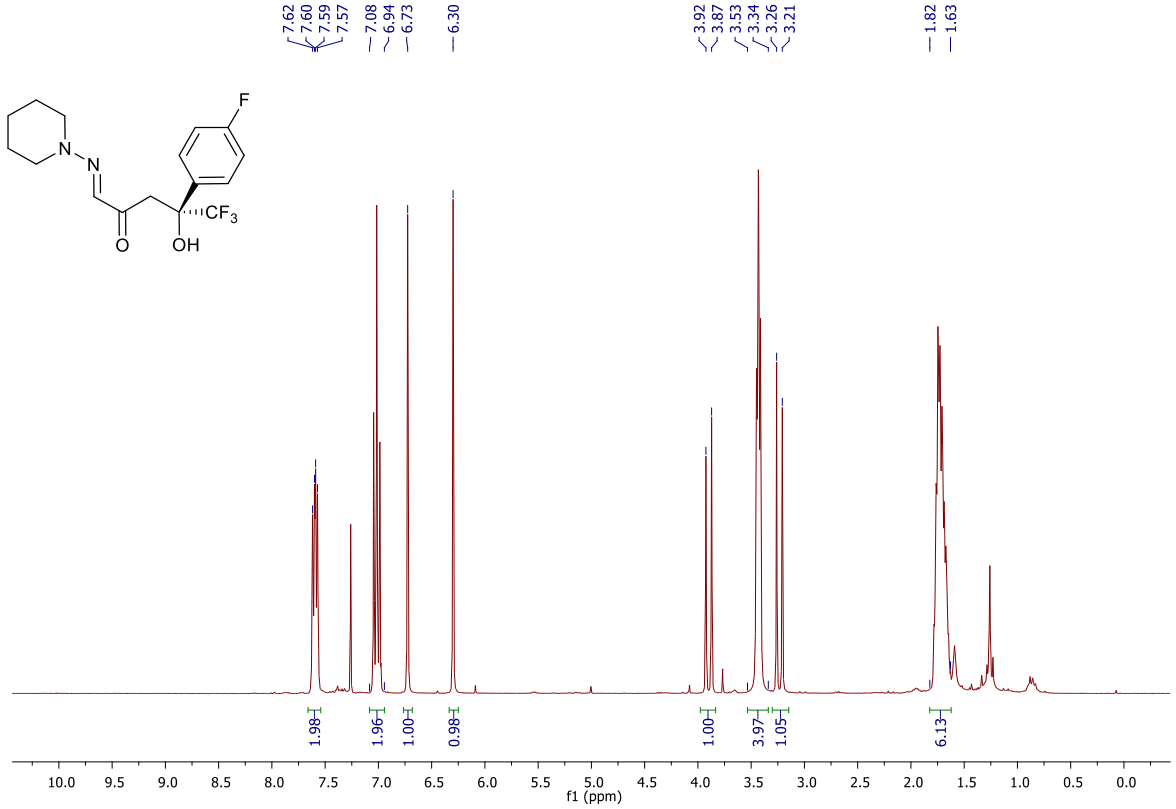
^{1}H NMR (300 MHz, $CDCl_3$) of (*S*)-**7**.



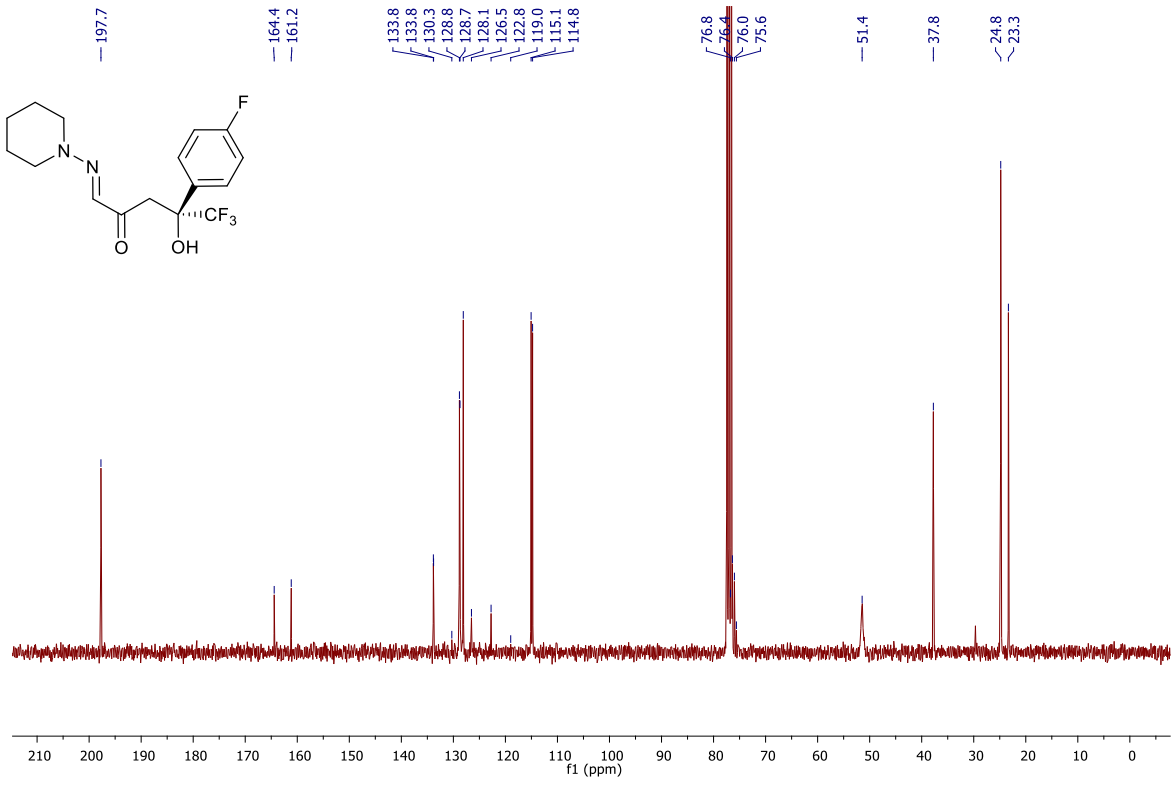
^{13}C NMR (75.5 MHz, $CDCl_3$) of (*S*)-**7**.



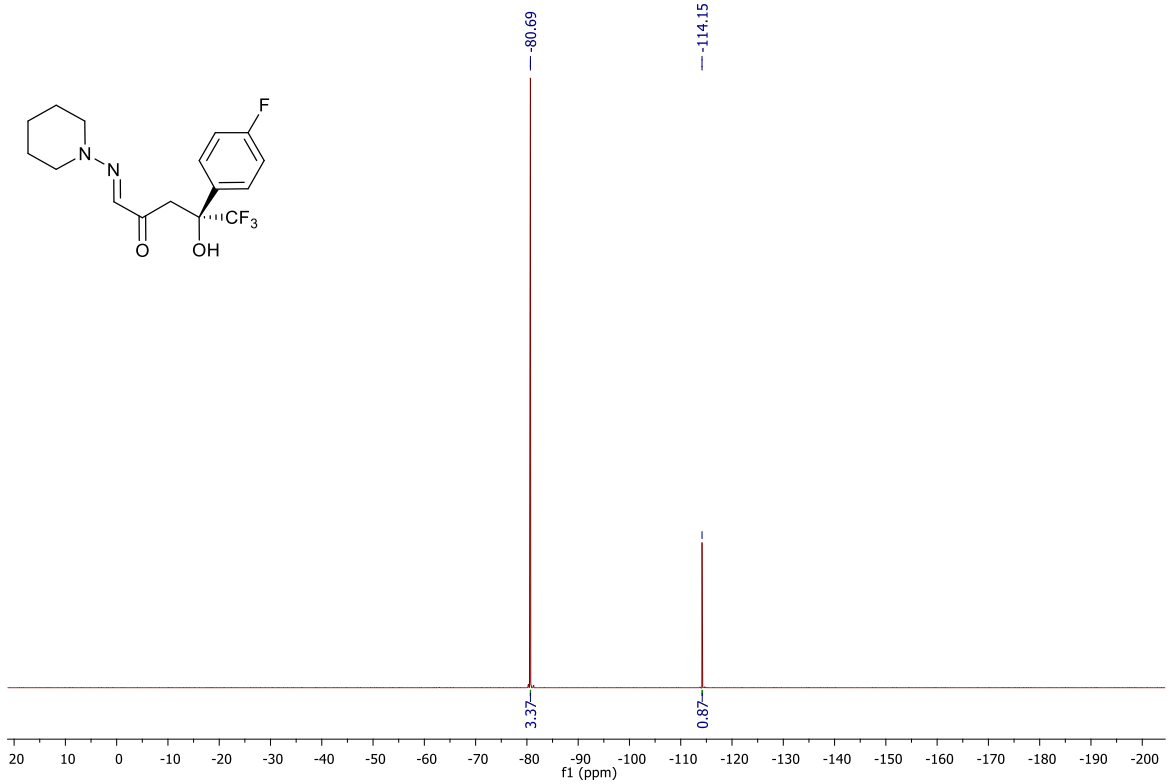
^{1}H NMR (300 MHz, $CDCl_3$) of (*S*)-**3Ab**



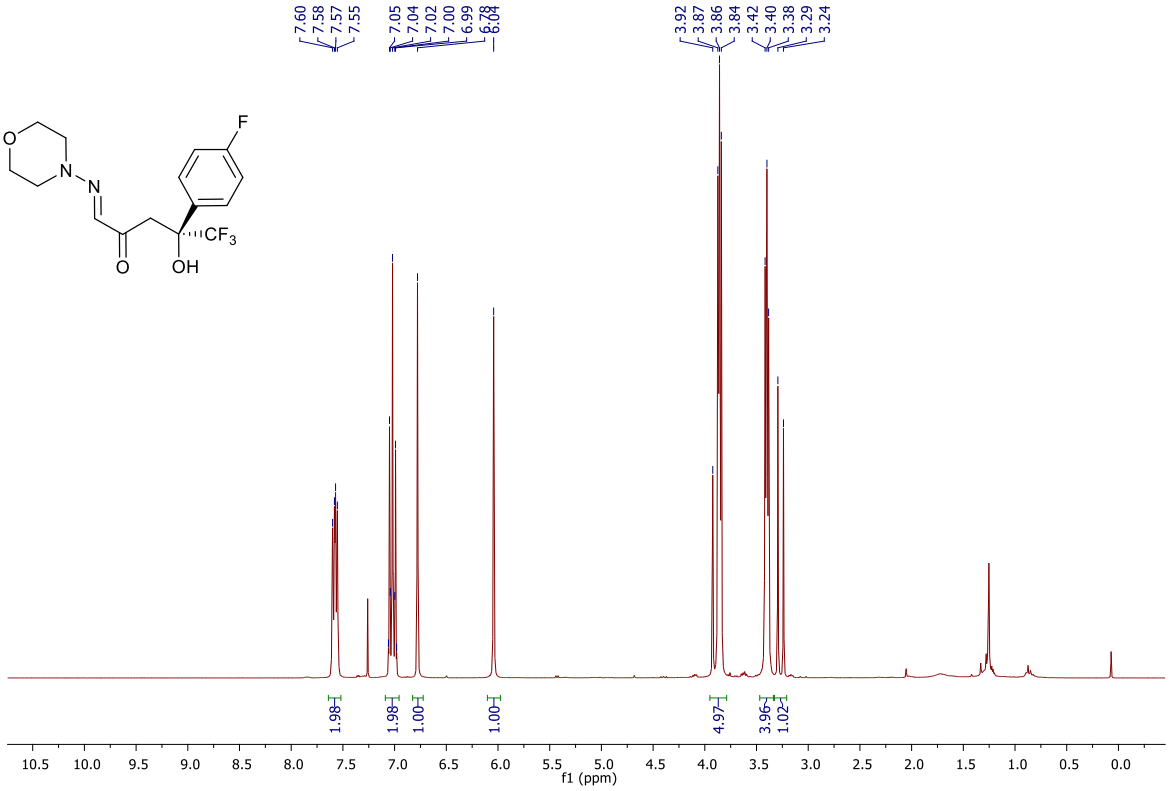
^{13}C NMR (75.5 MHz, $CDCl_3$) of (*S*)- **3Ab**



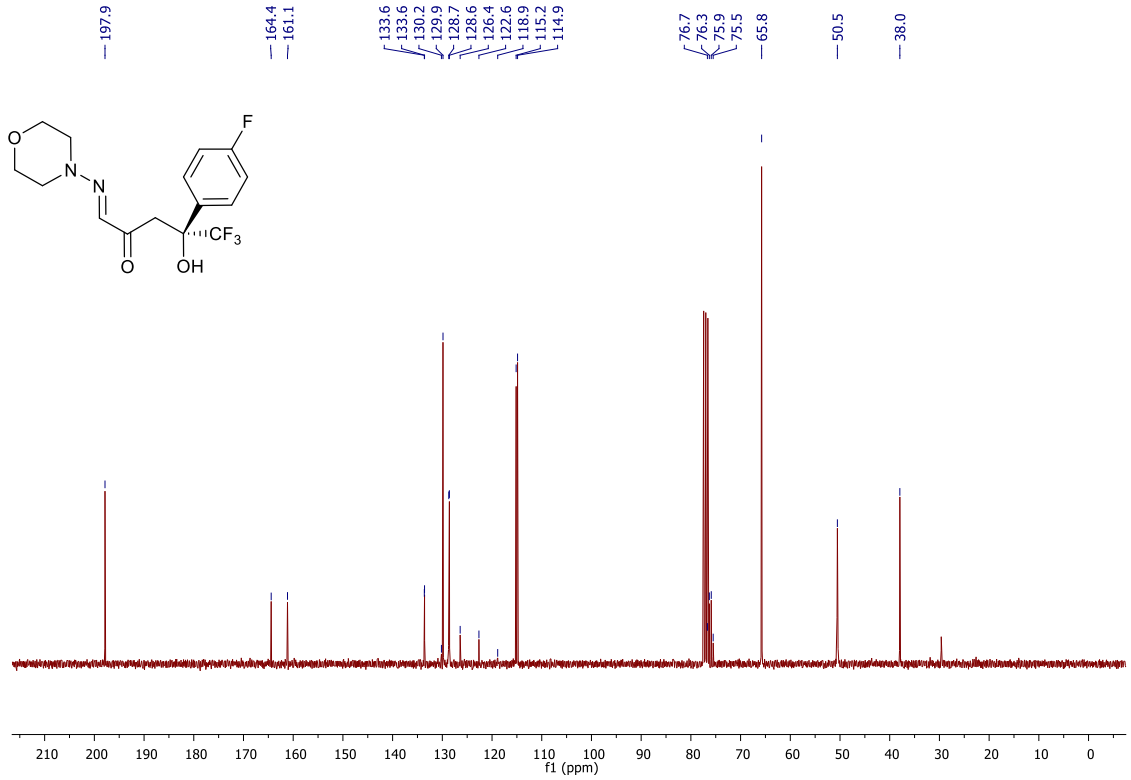
^{19}F NMR (282.5 MHz, $CDCl_3$) of (*S*)- **3Ab**



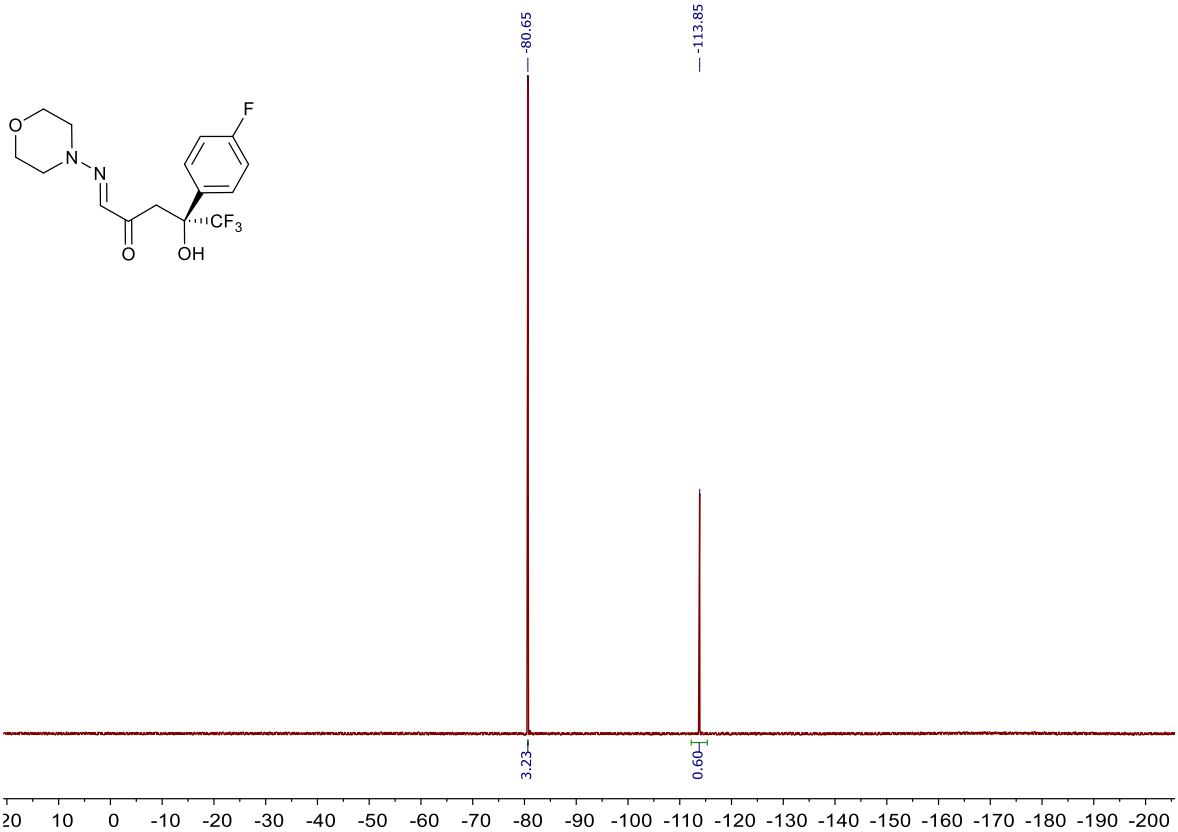
^{1}H NMR (500 MHz, $CDCl_3$) of (*S*)-**3Bb**



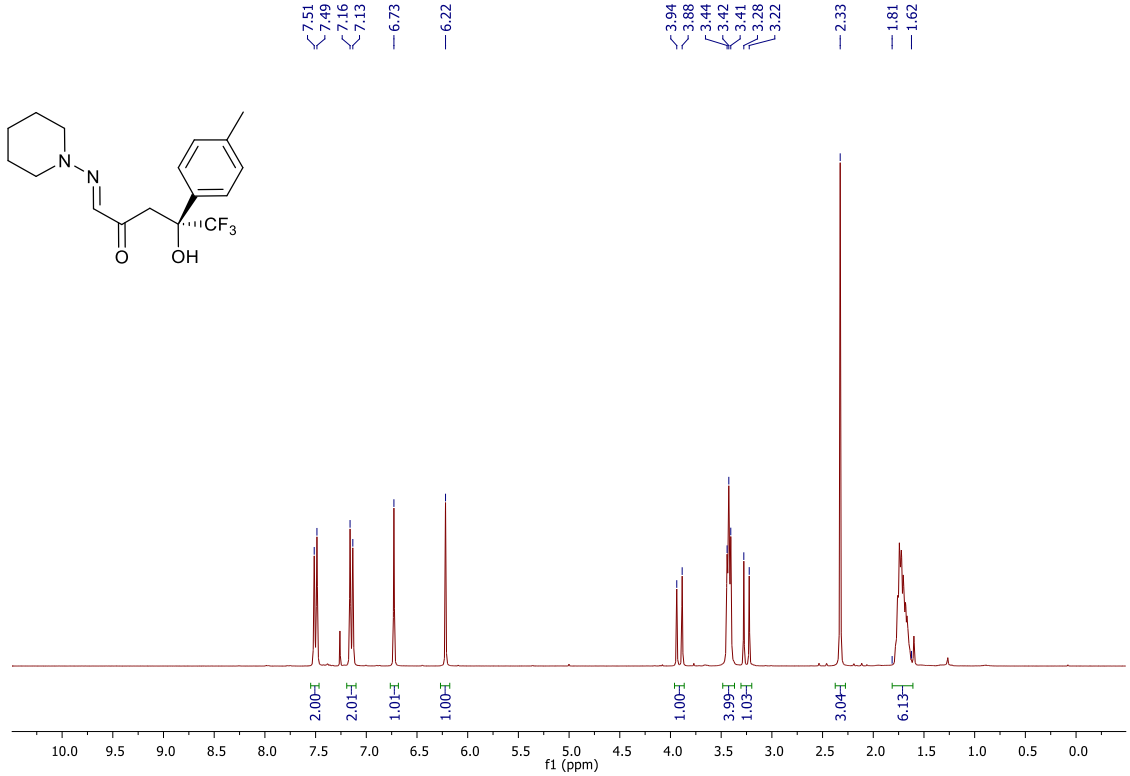
^{13}C NMR (126 MHz, $CDCl_3$) of (*S*)-**3Bb**



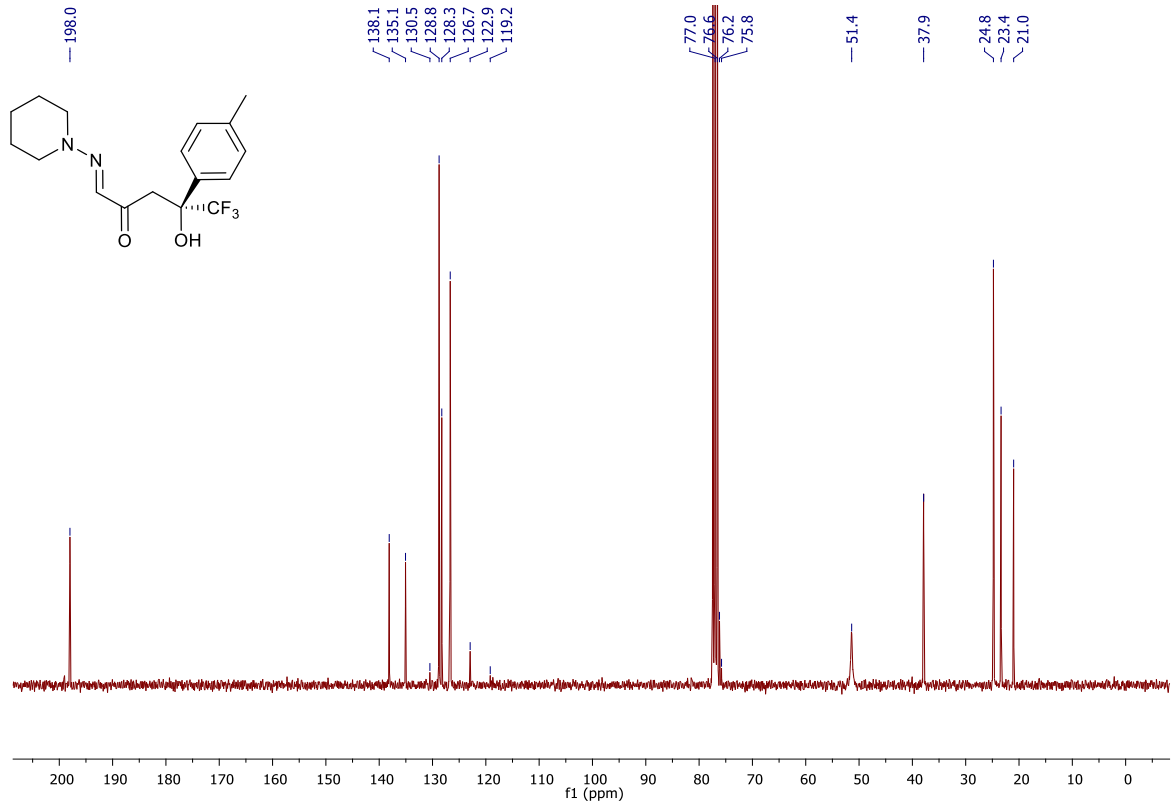
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)-**3Bb**



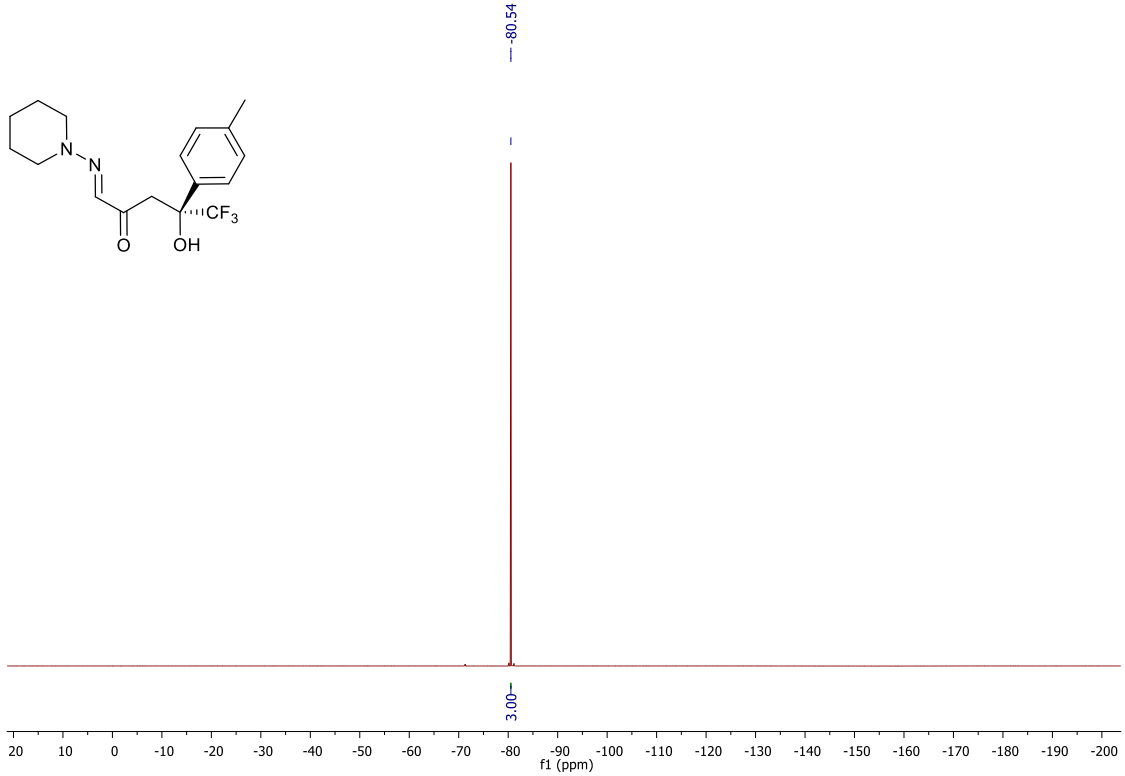
^{1}H NMR (300 MHz, $CDCl_3$) of (*S*)-**3Ac**



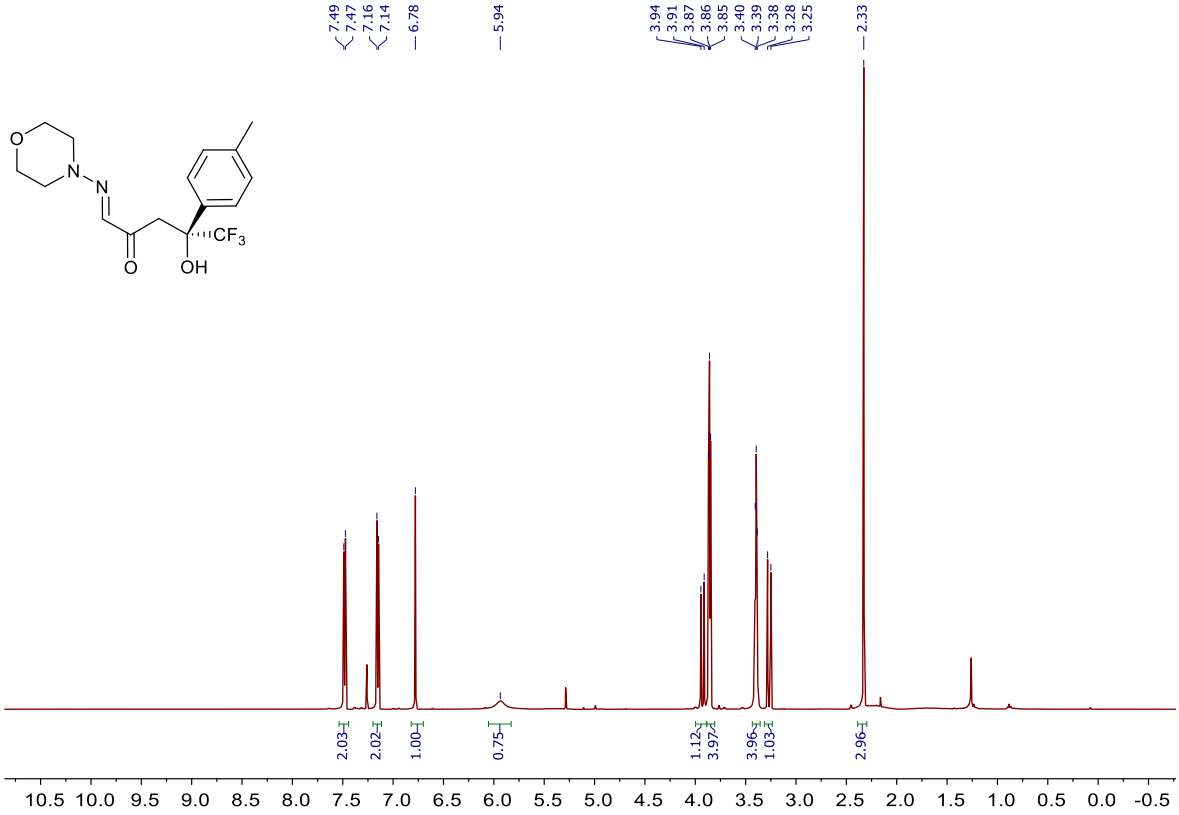
^{13}C NMR (75.5 MHz, $CDCl_3$) of (*S*)- **3Ac**



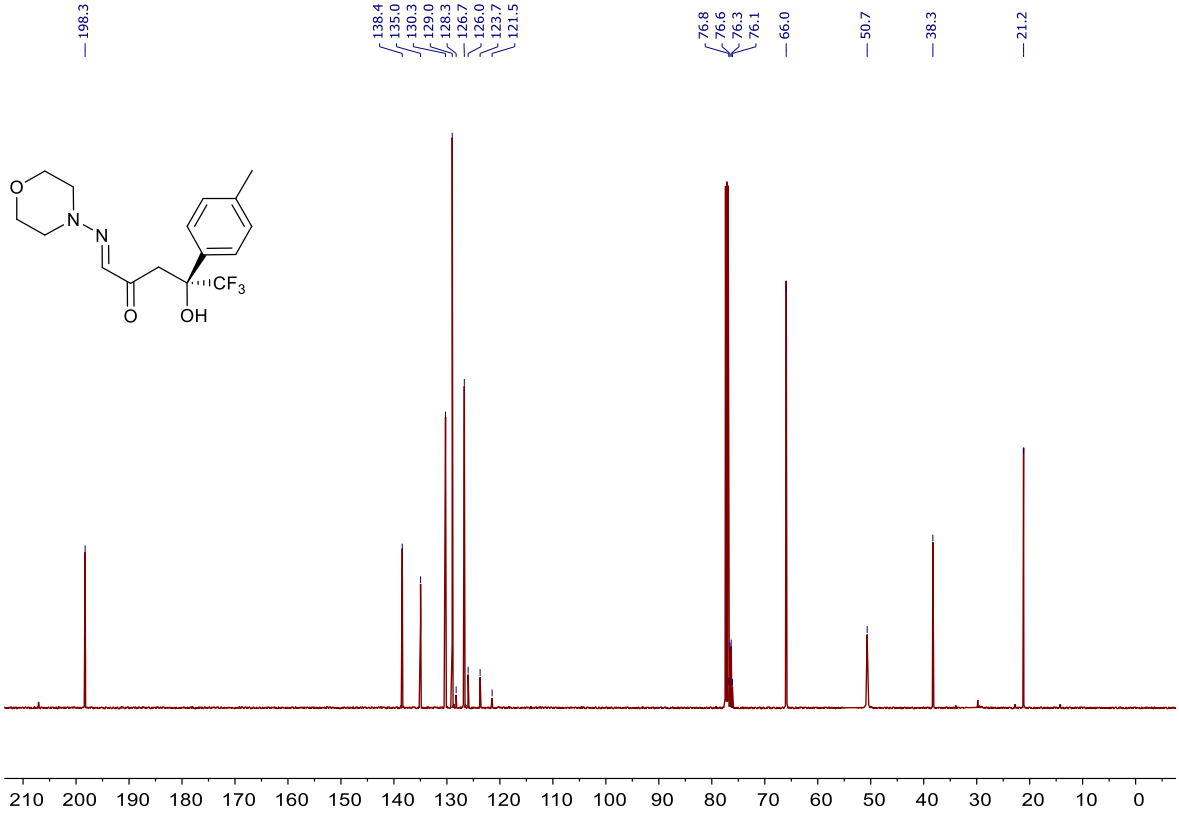
^{19}F NMR (282.5 MHz, $CDCl_3$) of (*S*)- **3Ac**



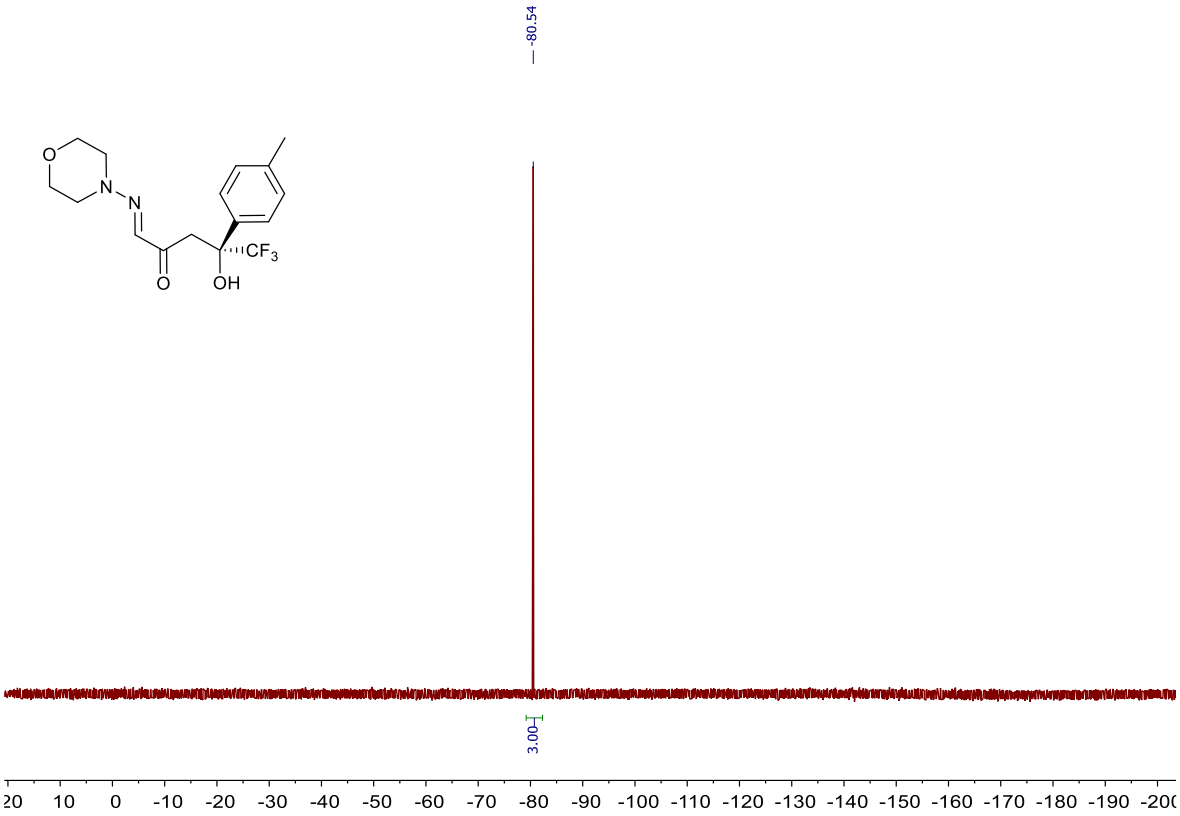
^{1}H NMR (500 MHz, $CDCl_3$) of (*S*)-**3Bc**



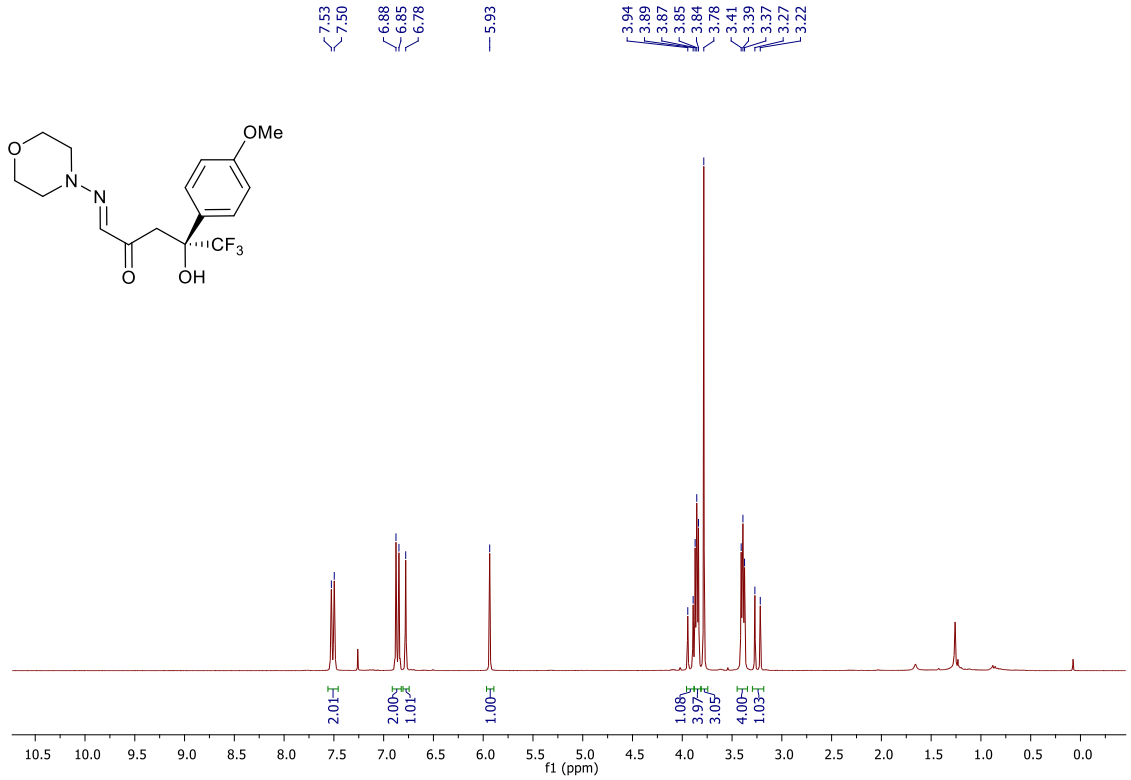
^{13}C NMR (126 MHz, $CDCl_3$) of (*S*)-**3Bc**



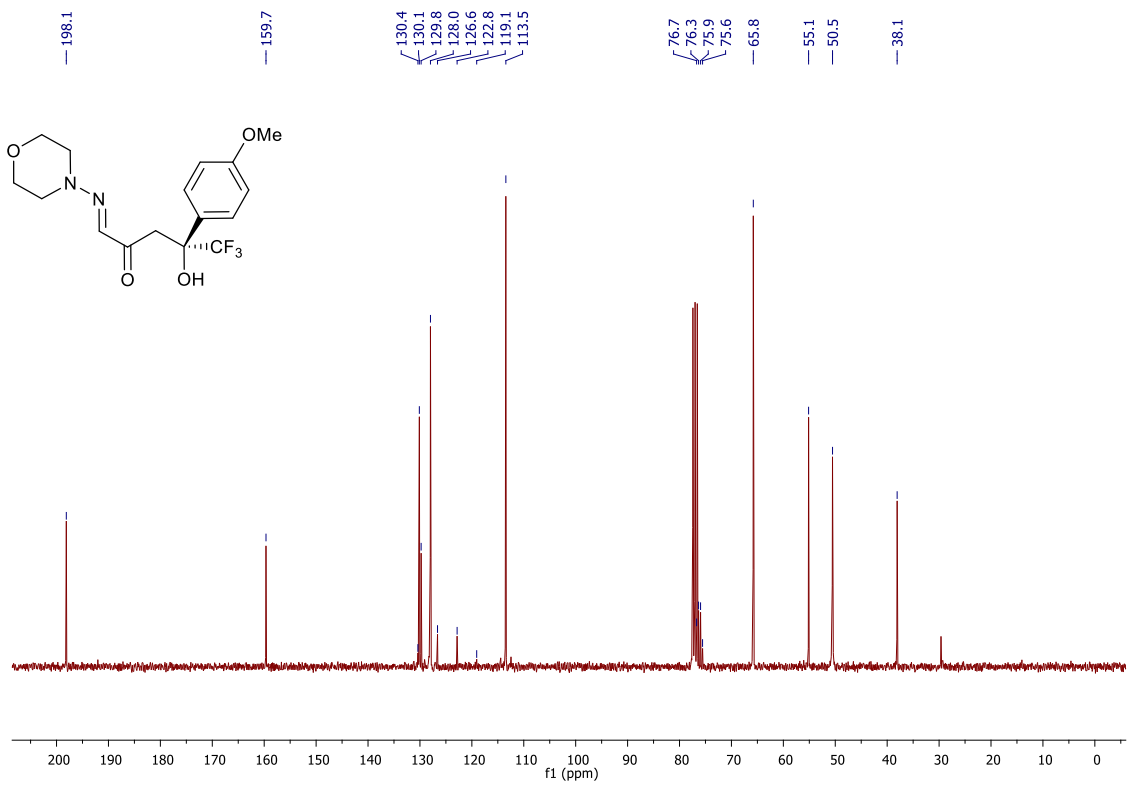
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)-**3Bc**



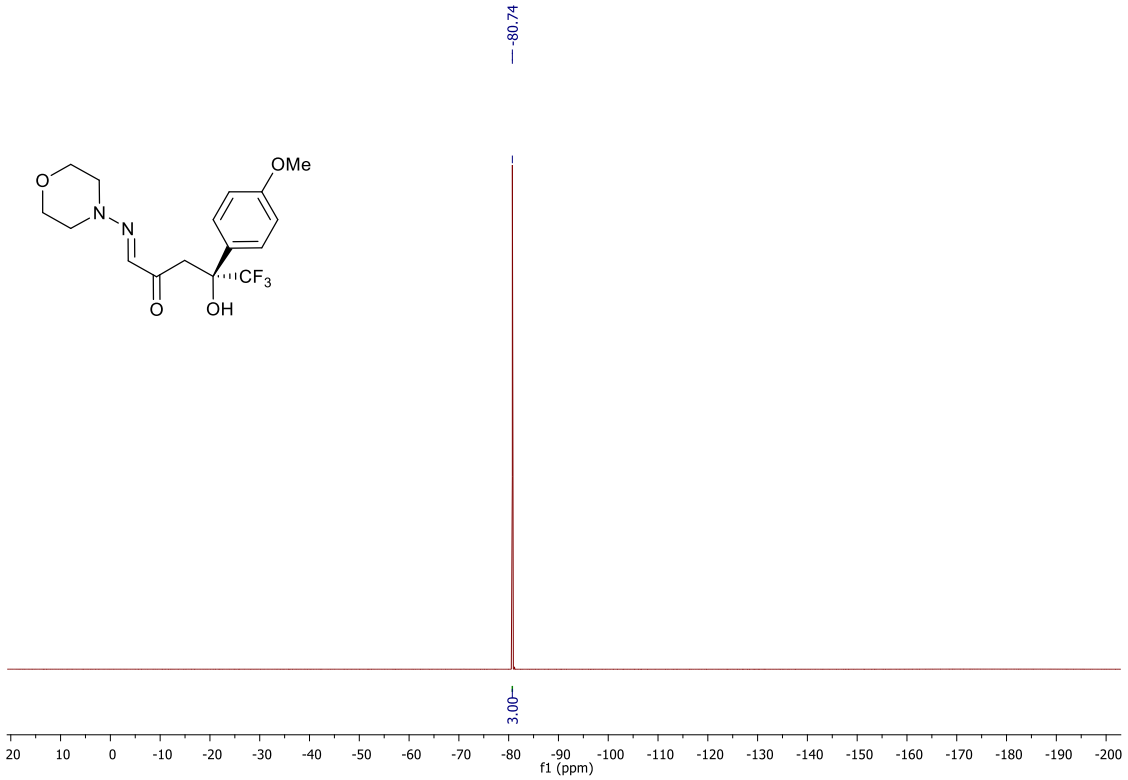
^{1}H NMR (300 MHz, $CDCl_3$) of (*S*)-**3Bd**



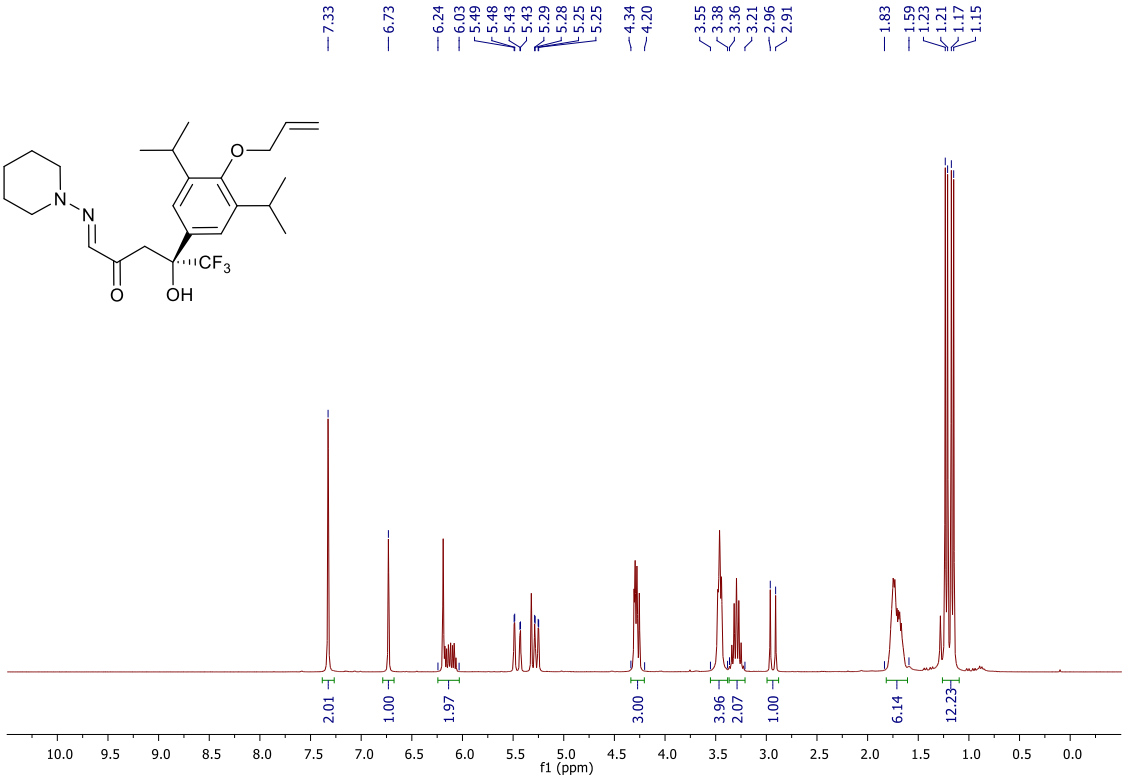
^{13}C NMR (7.5 MHz, $CDCl_3$) of (*S*)- **3Bd**



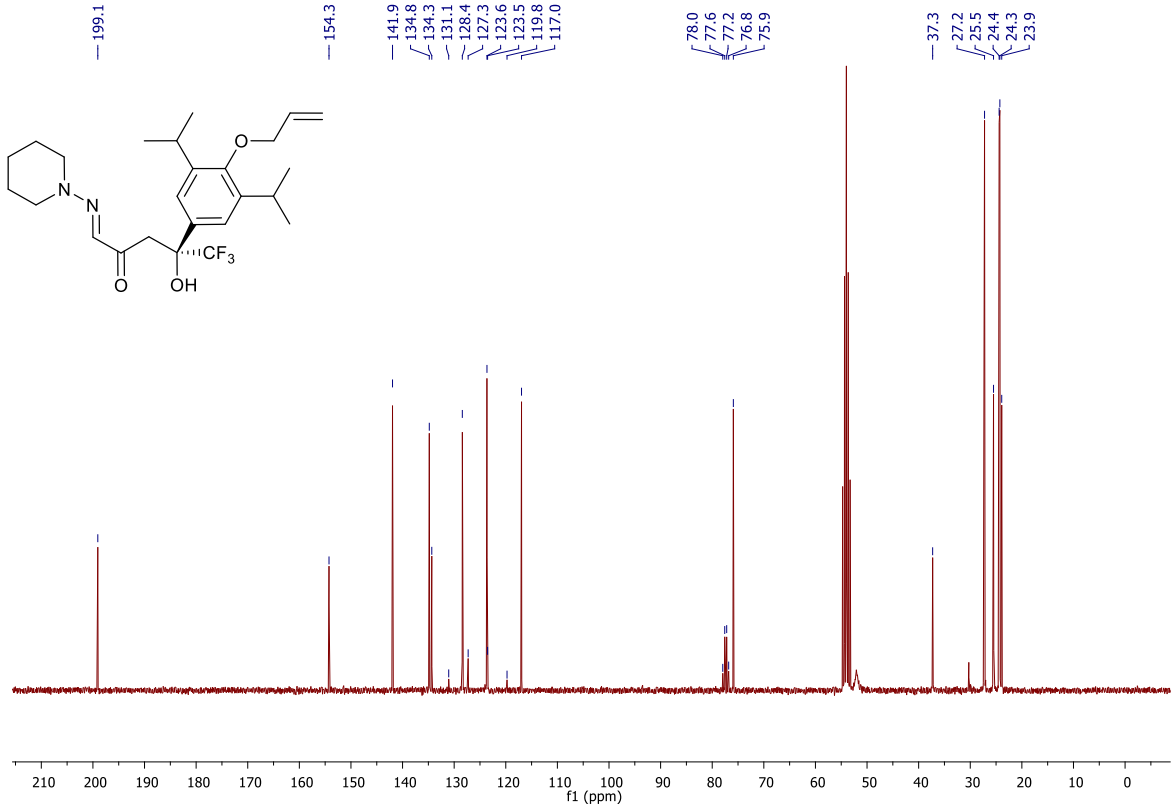
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)- **3Bd**



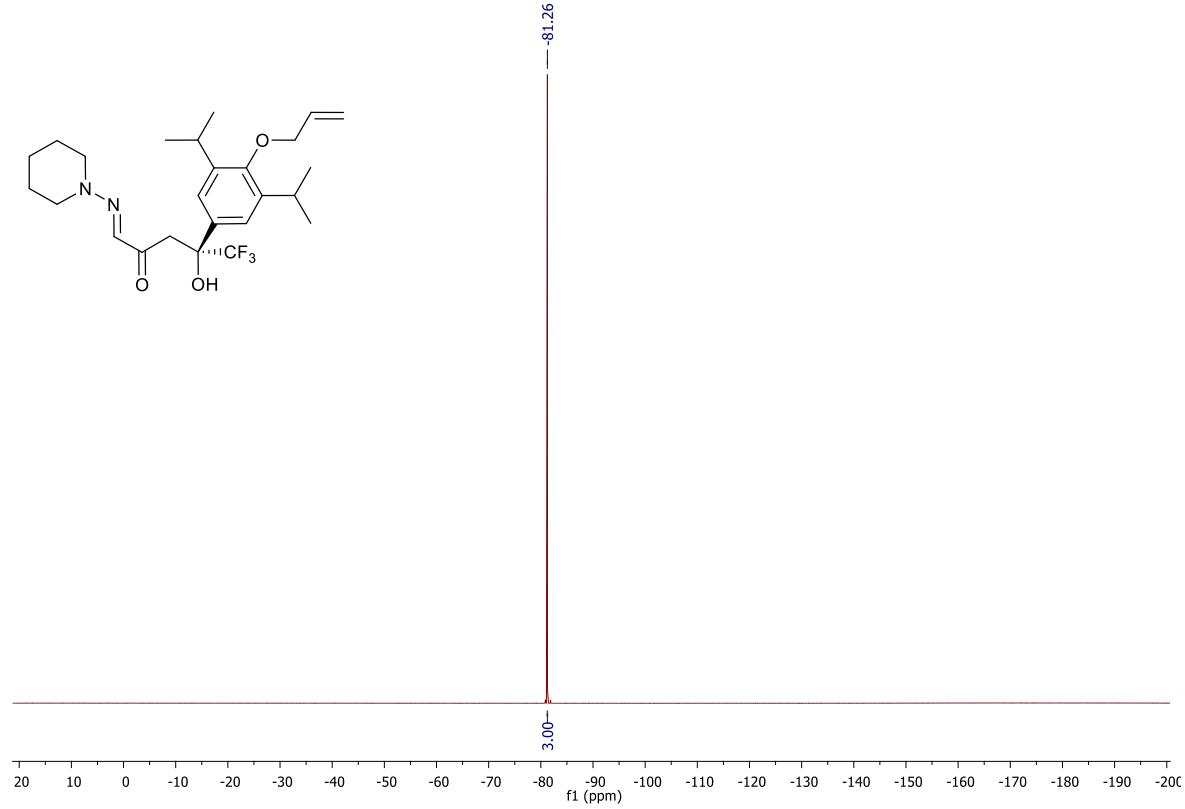
^{1}H NMR (300 MHz, CD_2Cl_2) (*S*)-**3Ae**



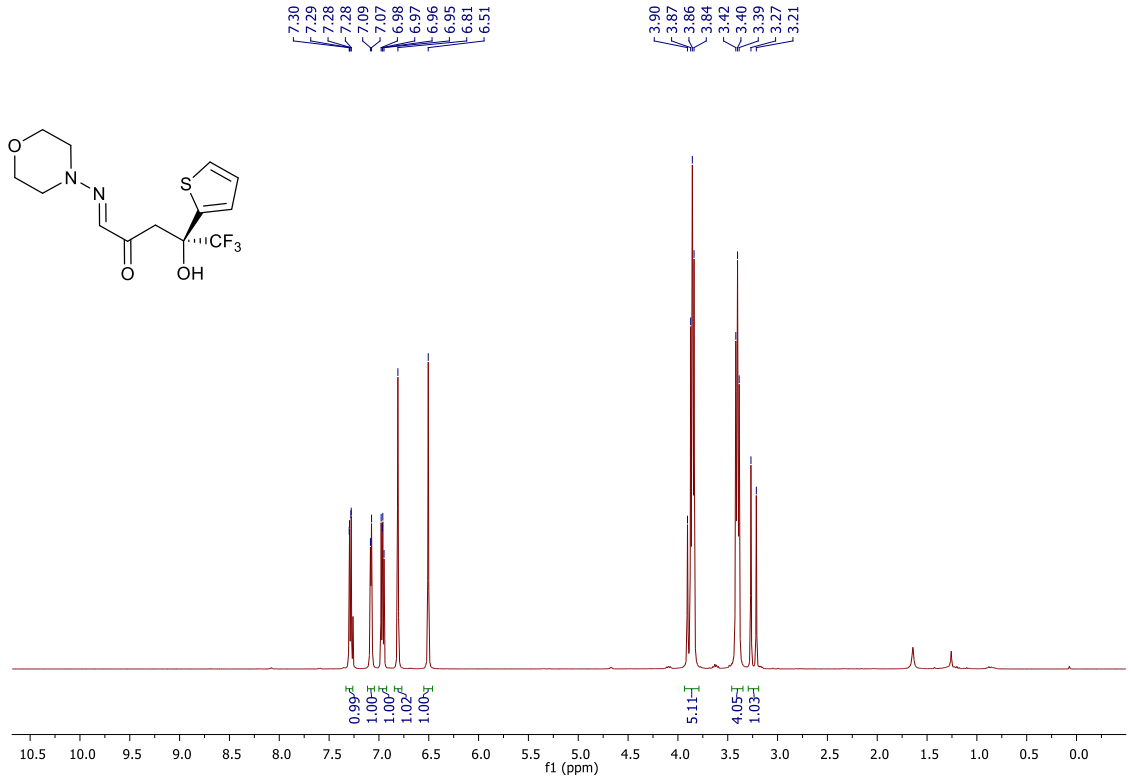
^{13}C NMR (75.5 MHz, CD_2Cl_2) (*S*)-**3Ae**



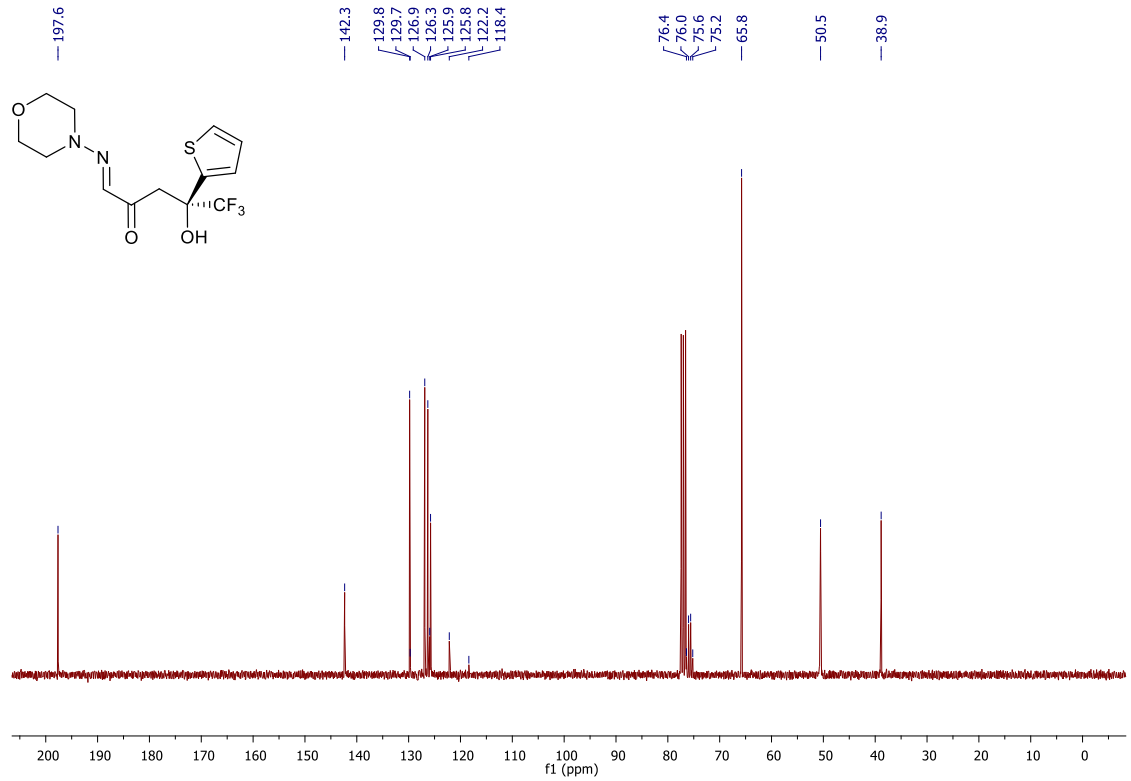
^{19}F NMR (471 MHz, CD_2Cl_2) of (*S*)-**3Ae**



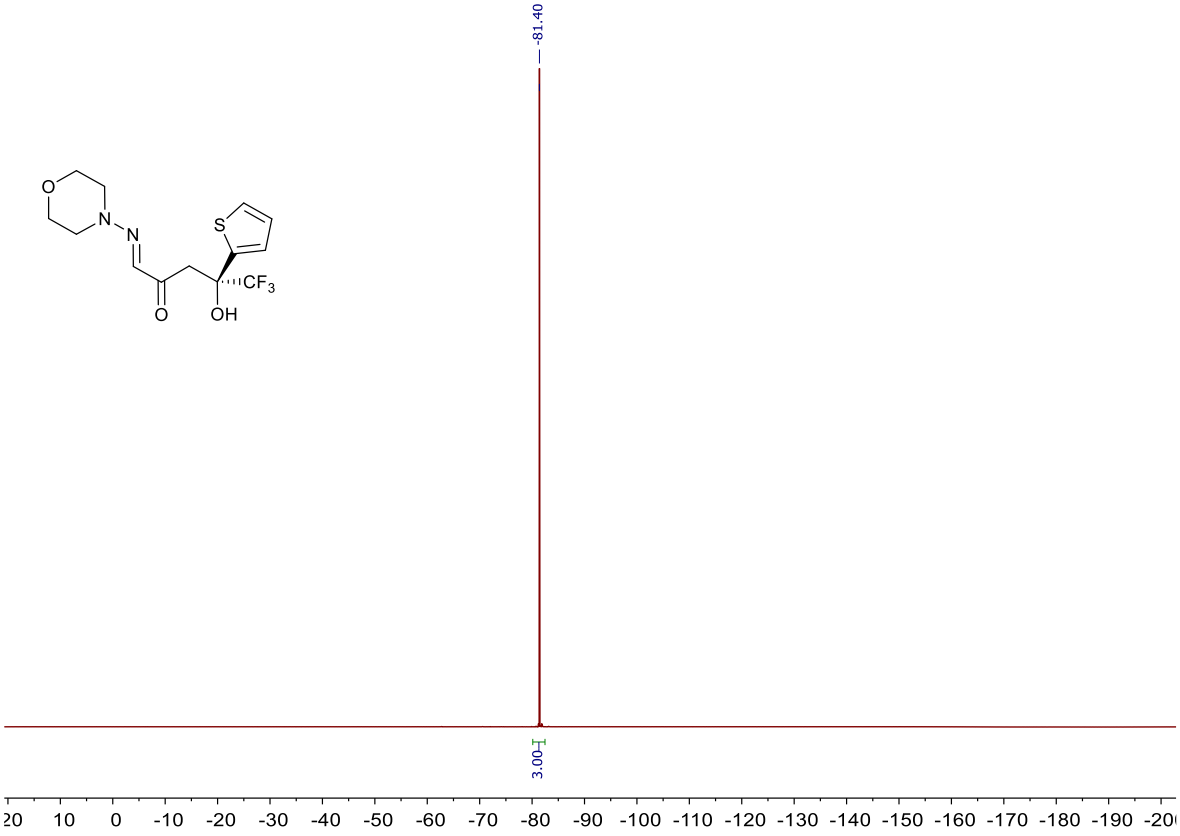
^{1}H NMR (500 MHz, $CDCl_3$) of (*R*)-**3Bf**



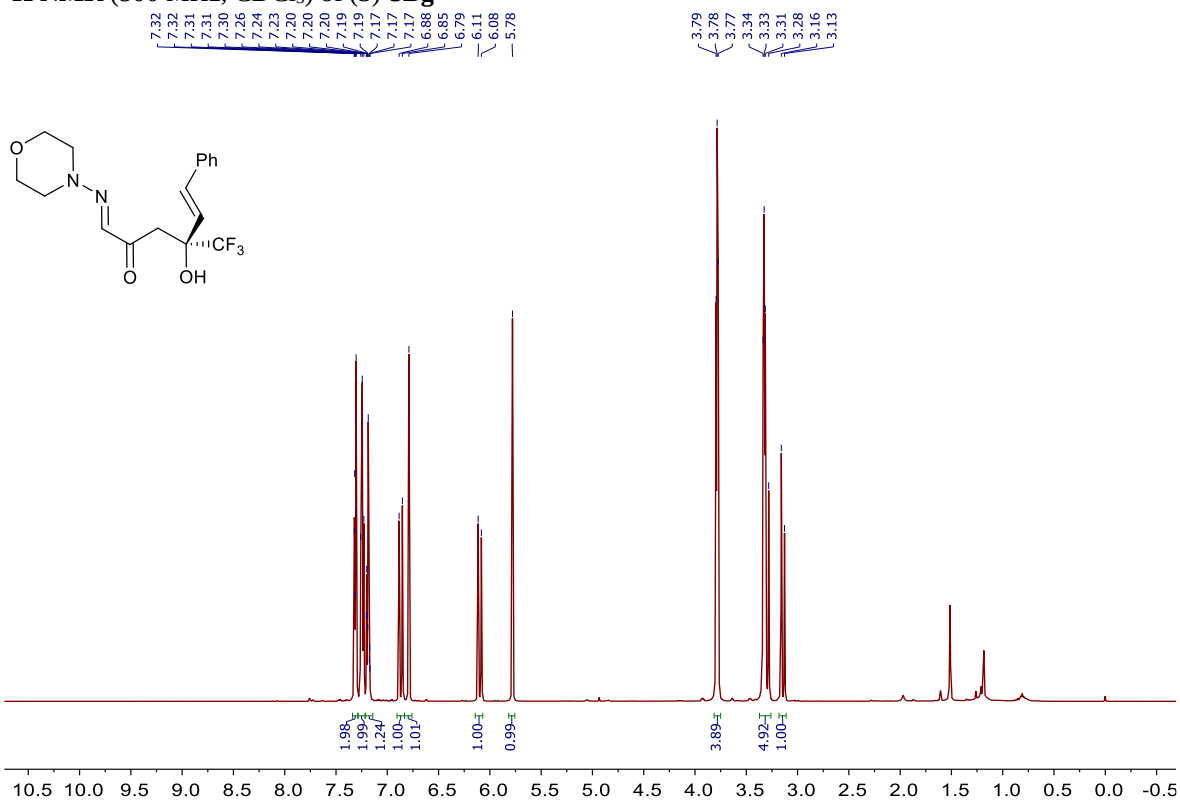
^{13}C NMR (126 MHz, $CDCl_3$) of (*R*)- **3Bf**



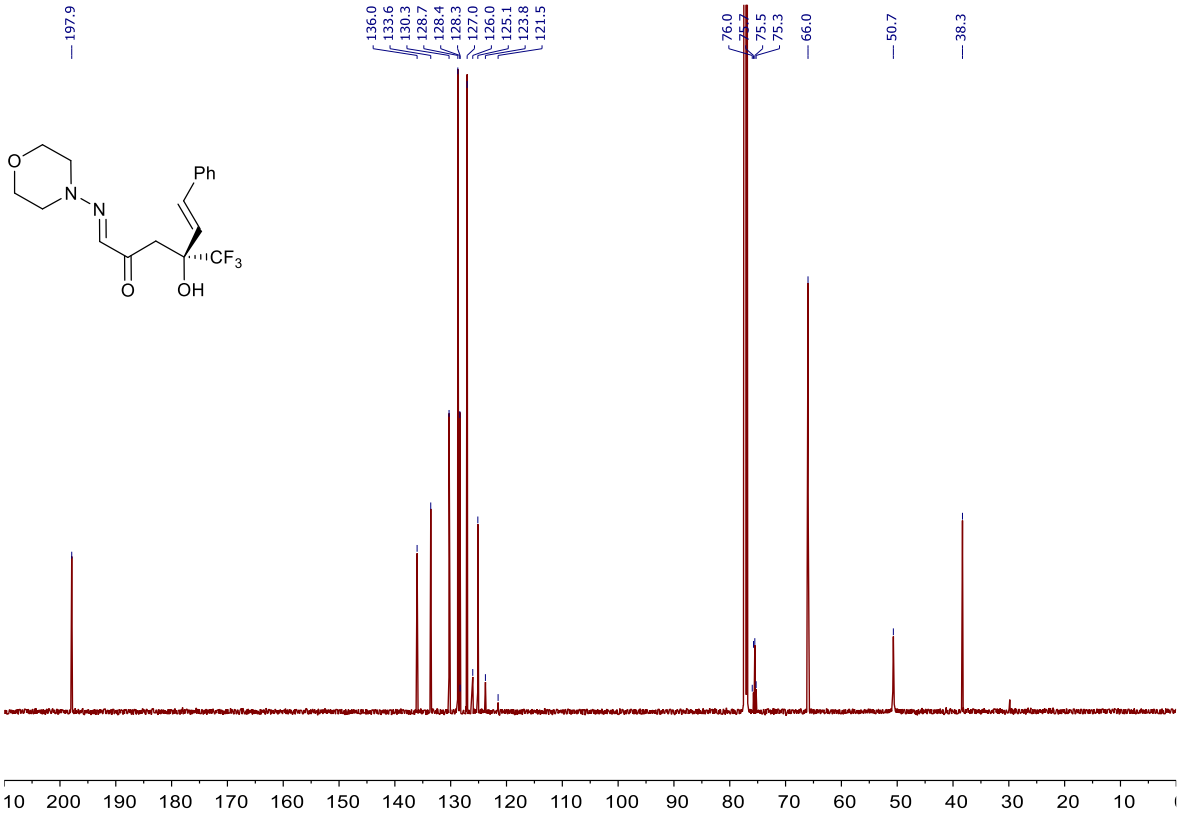
^{19}F NMR (471 MHz, $CDCl_3$) of (*R*)- **3Bf**



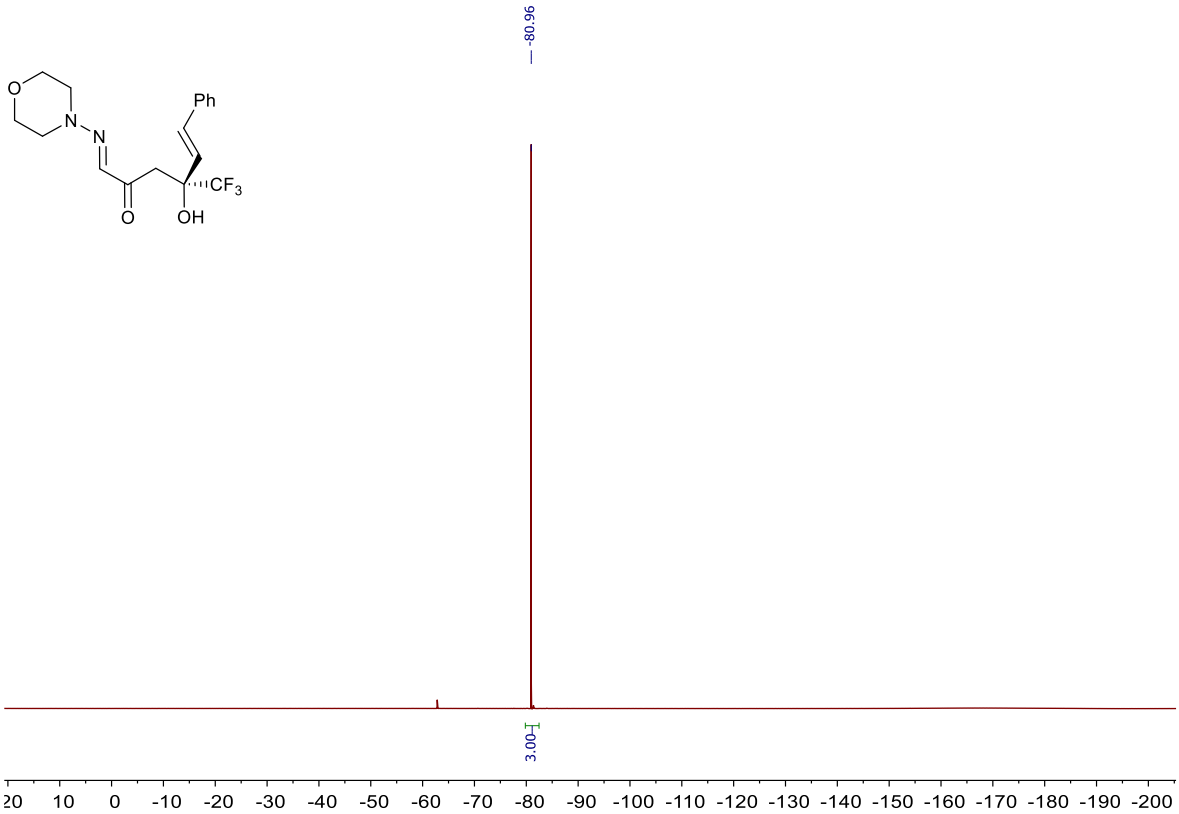
^{1}H NMR (500 MHz, $CDCl_3$) of (*S*)-**3Bg**



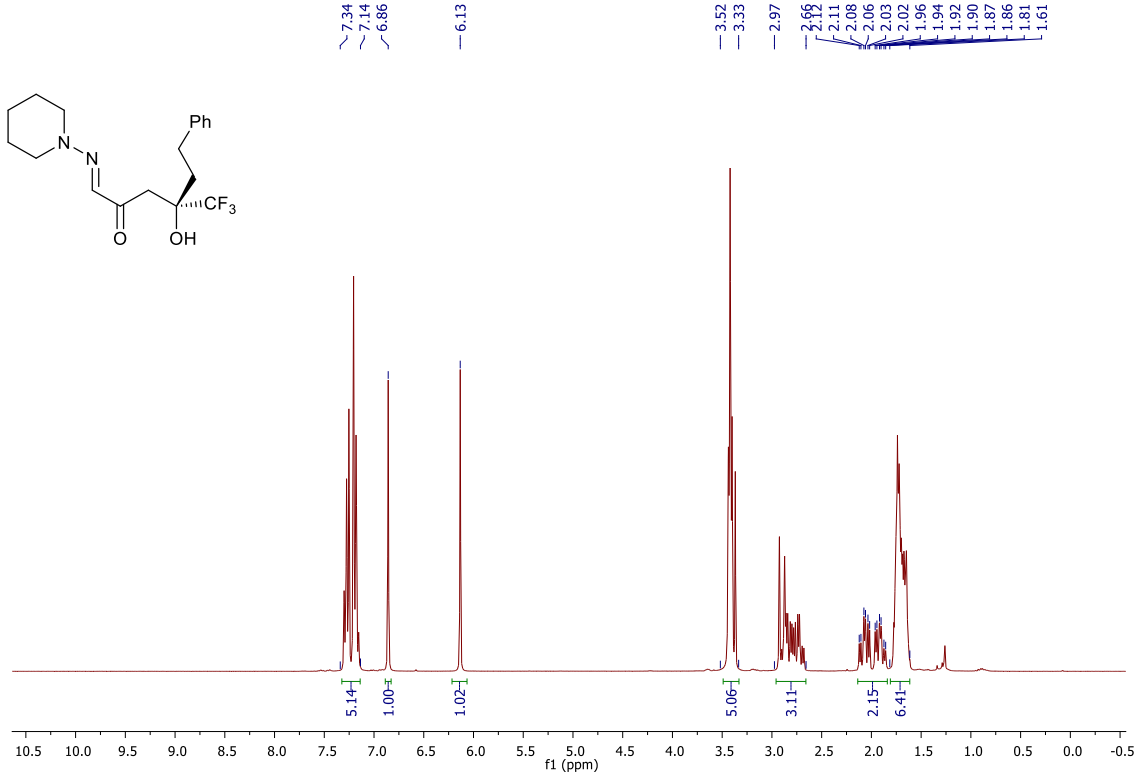
^{13}C NMR (126 MHz, $CDCl_3$) of (*S*)- **3Bg**



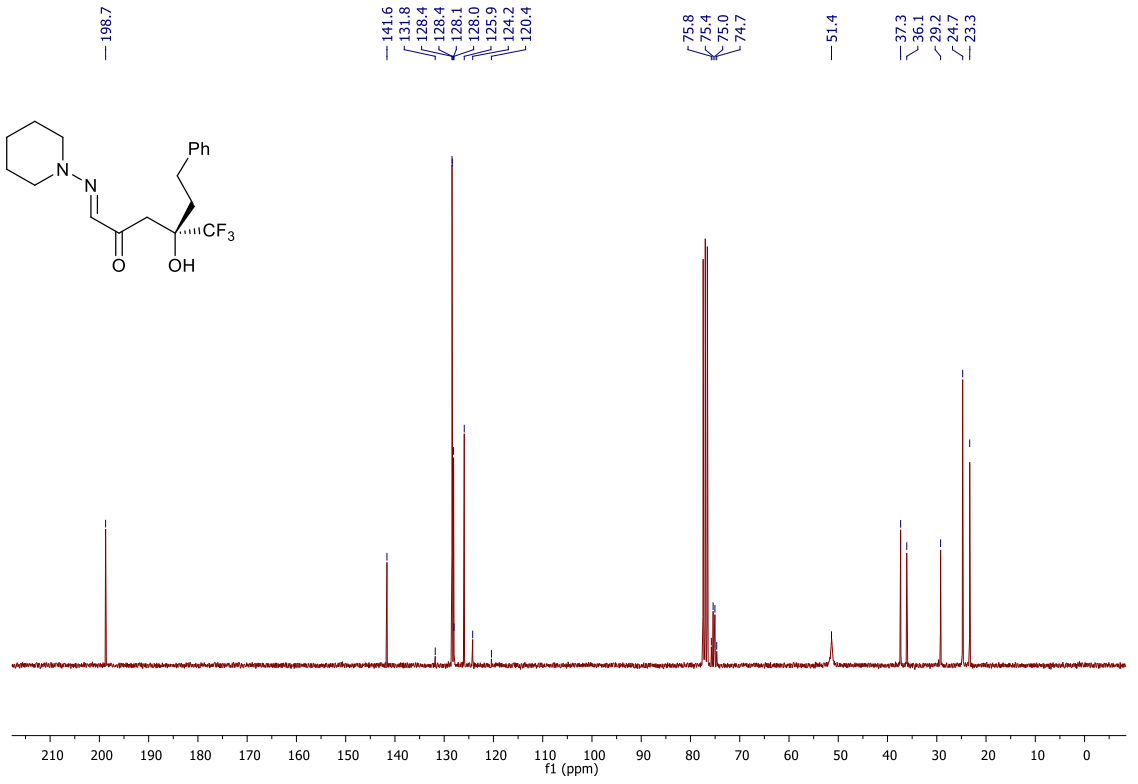
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)- **3Bg**



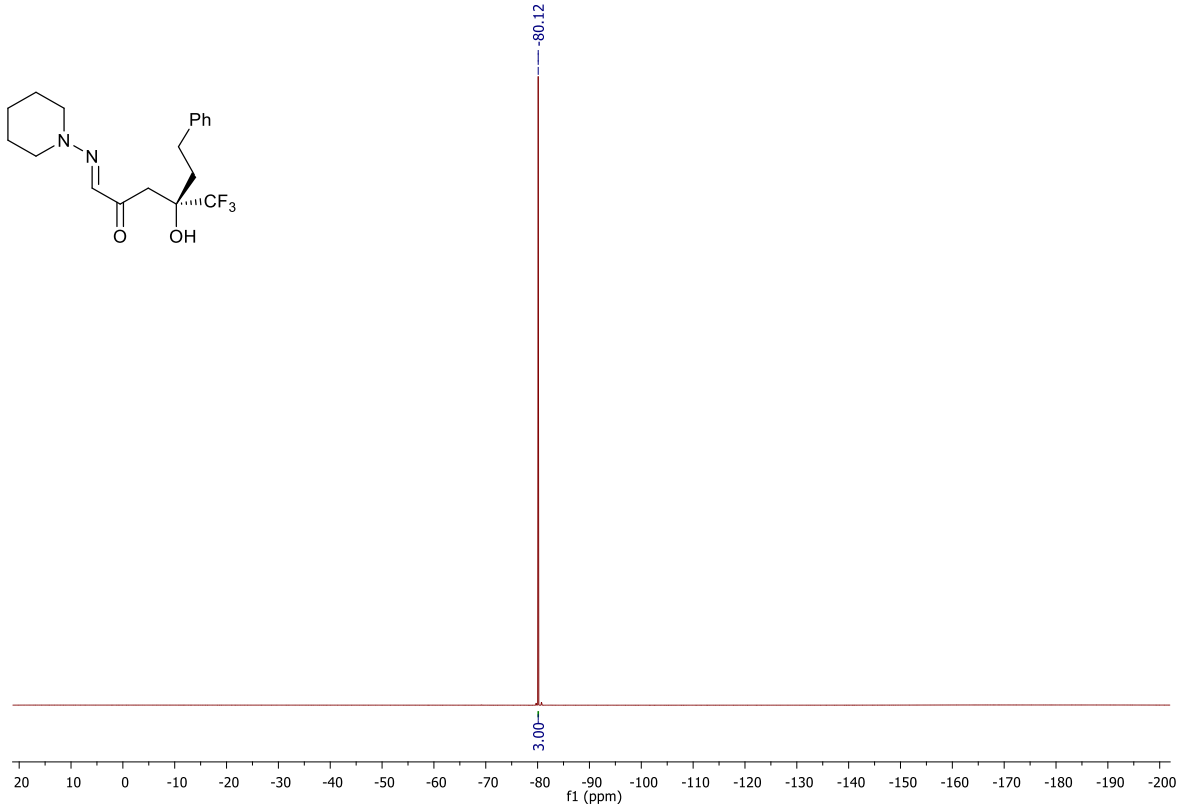
^{1}H NMR (300 MHz, $CDCl_3$) of (*R*)-**3Ah**



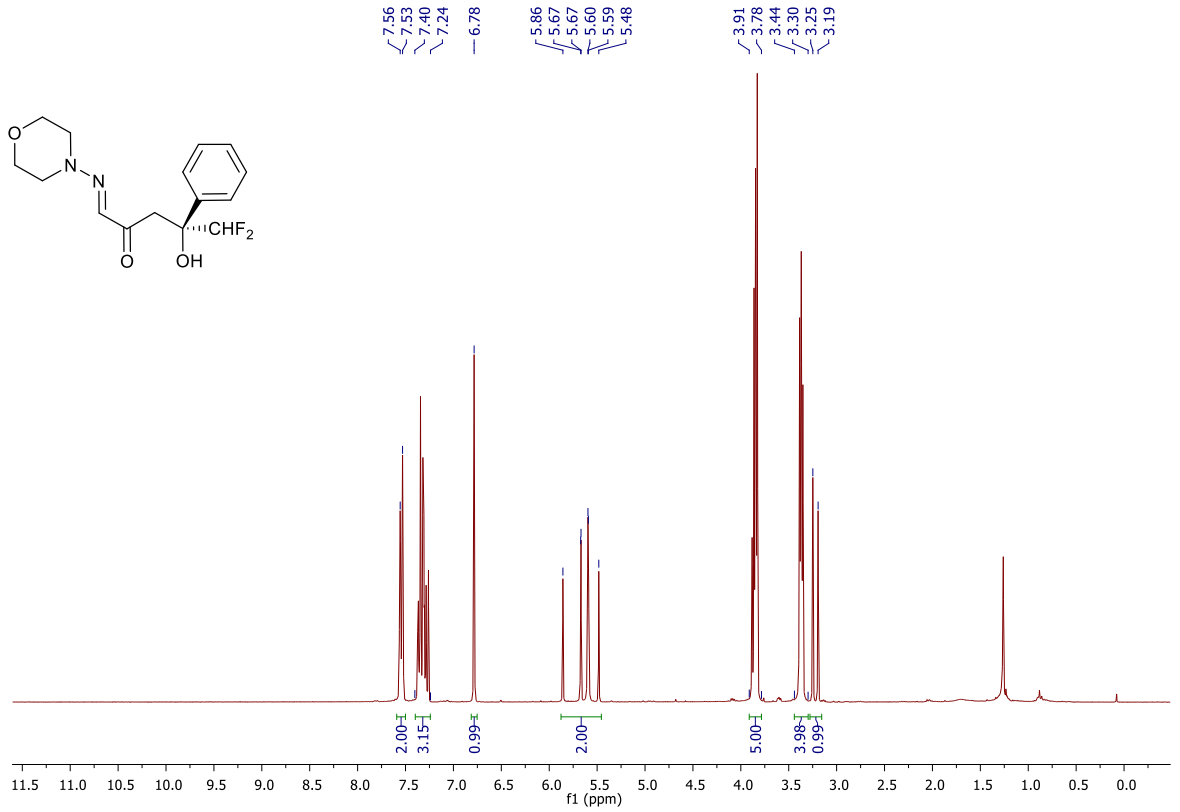
^{13}C NMR (75.5 MHz, $CDCl_3$) of (*R*)- **3Ah**



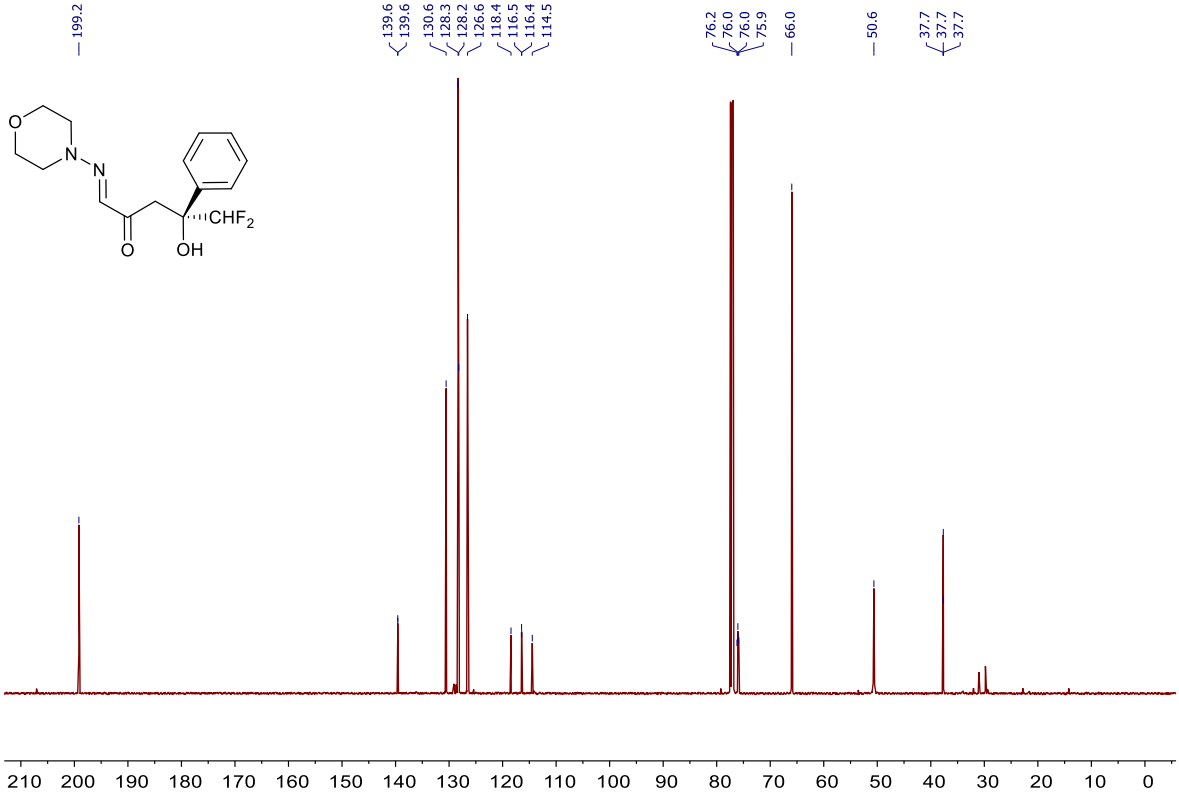
^{19}F NMR (282.5 MHz, $CDCl_3$) of (*R*)- **3Ah**



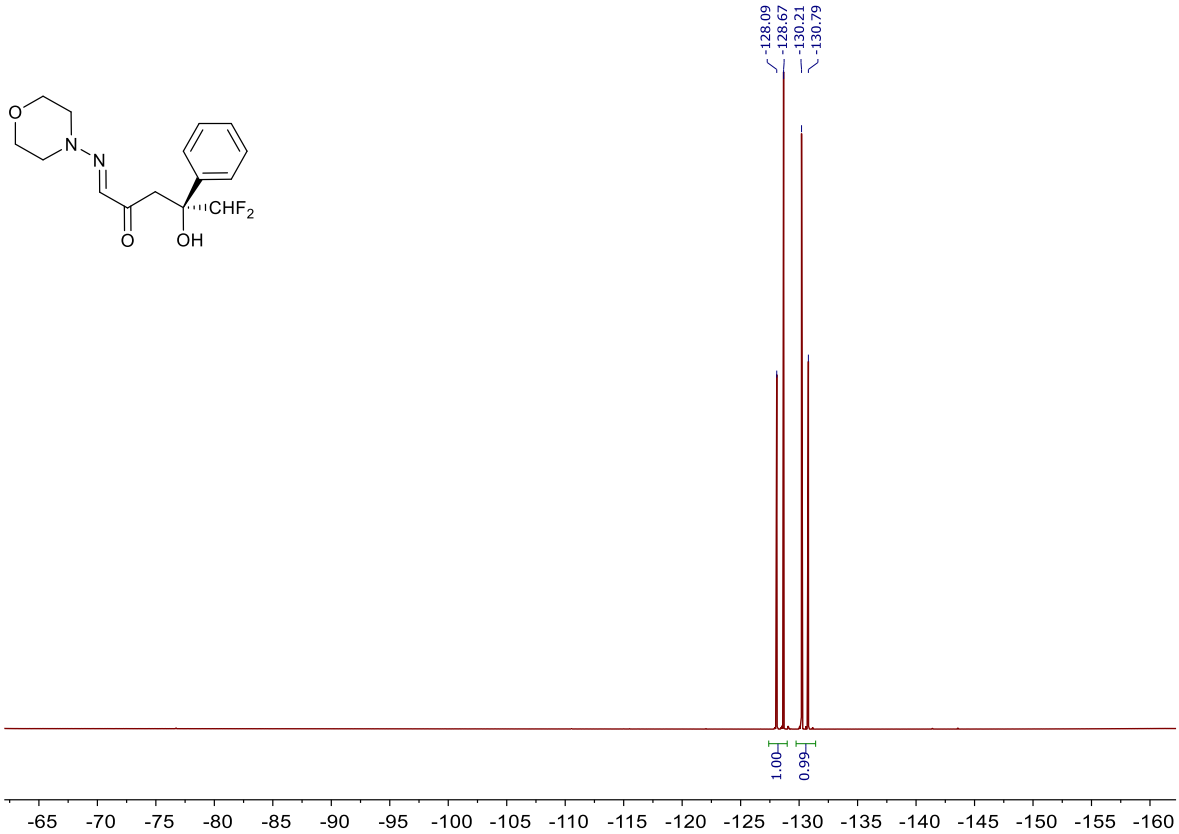
^{1}H NMR (300 MHz, $CDCl_3$) of (*S*)-**3Bk**



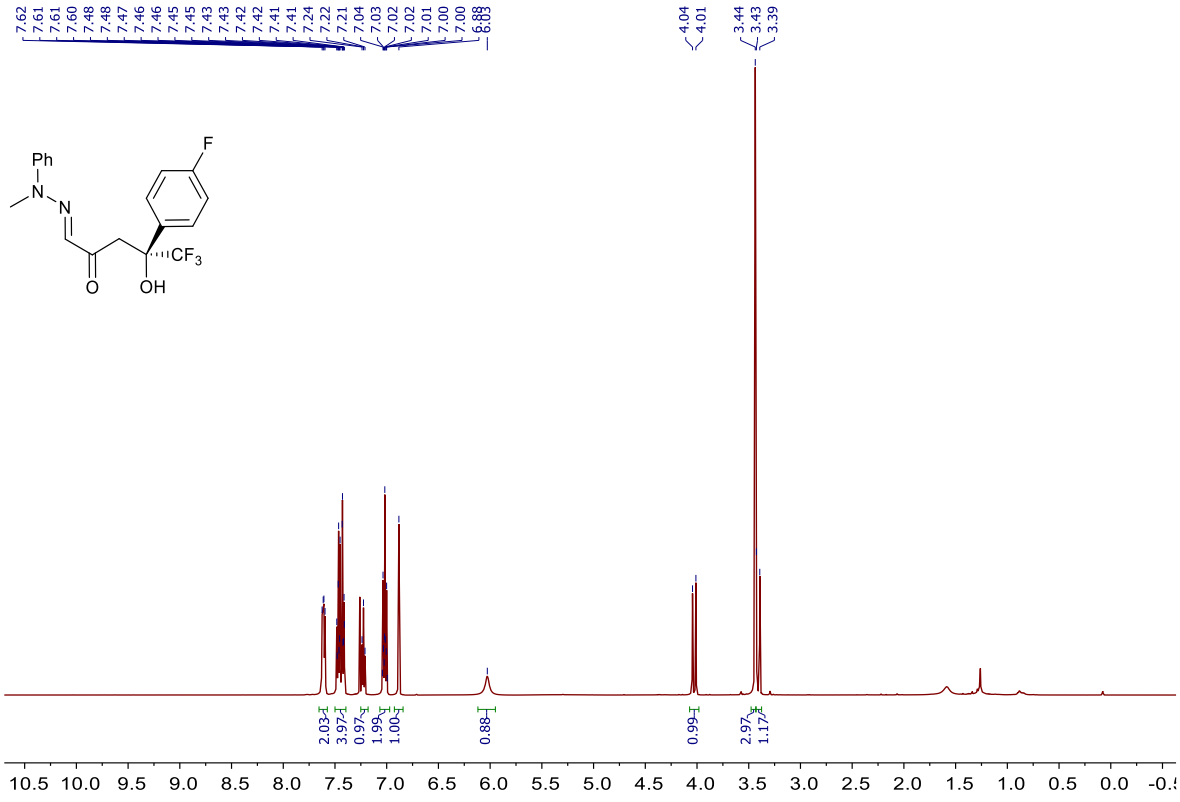
^{13}C NMR (126 MHz, $CDCl_3$) of (*S*)- **3Bk**



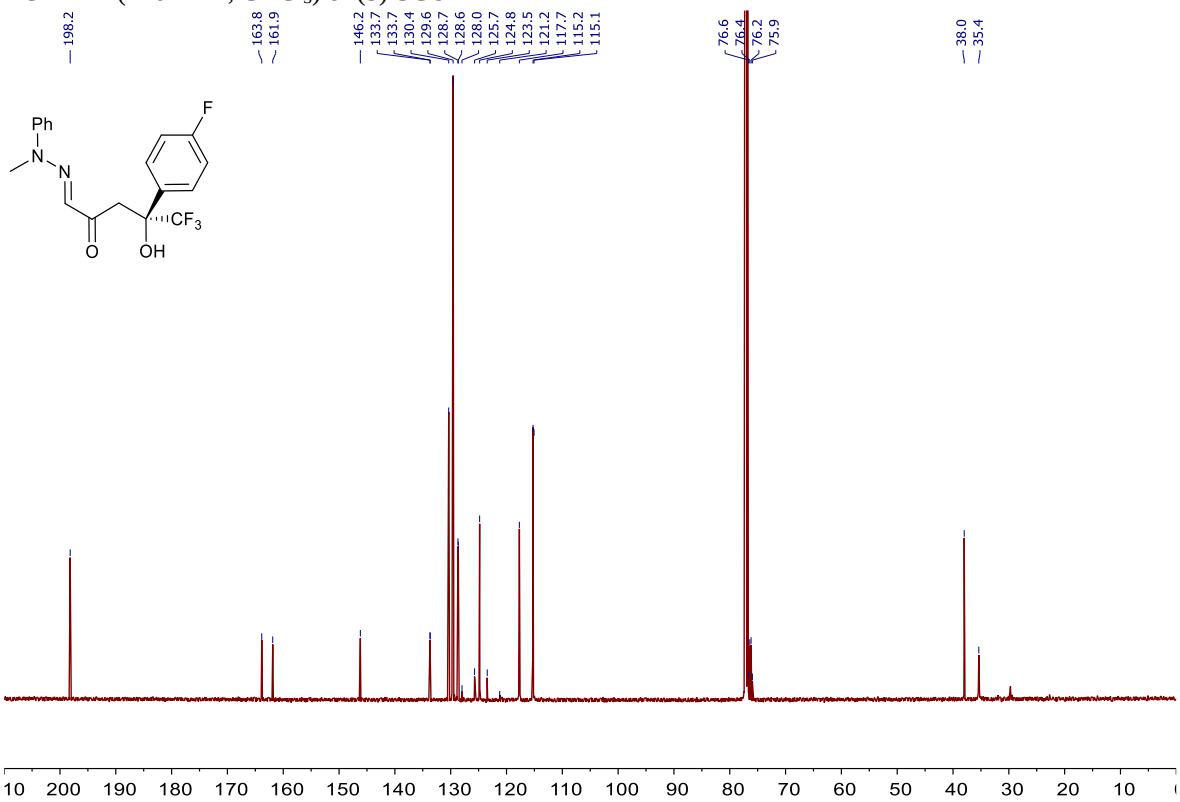
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)- **3Bk**



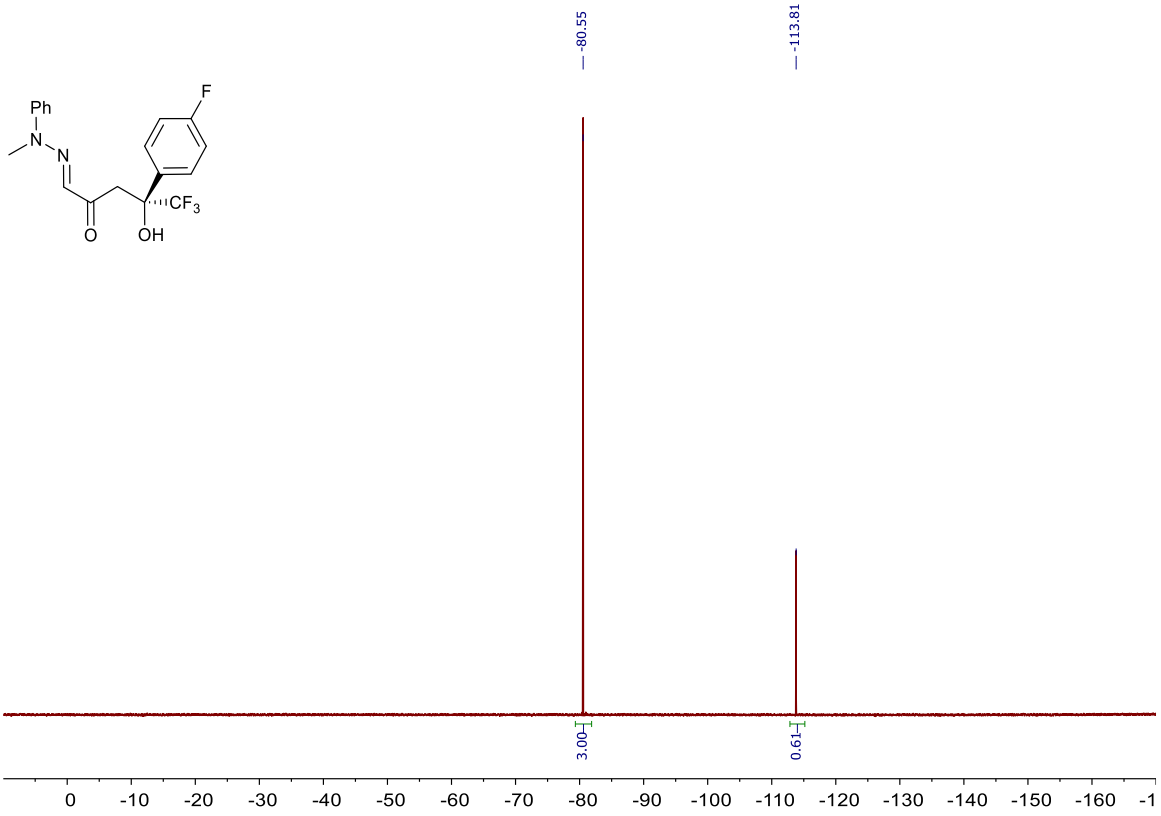
^{1}H NMR (500 MHz, $CDCl_3$) of (*S*)-**3Gb**



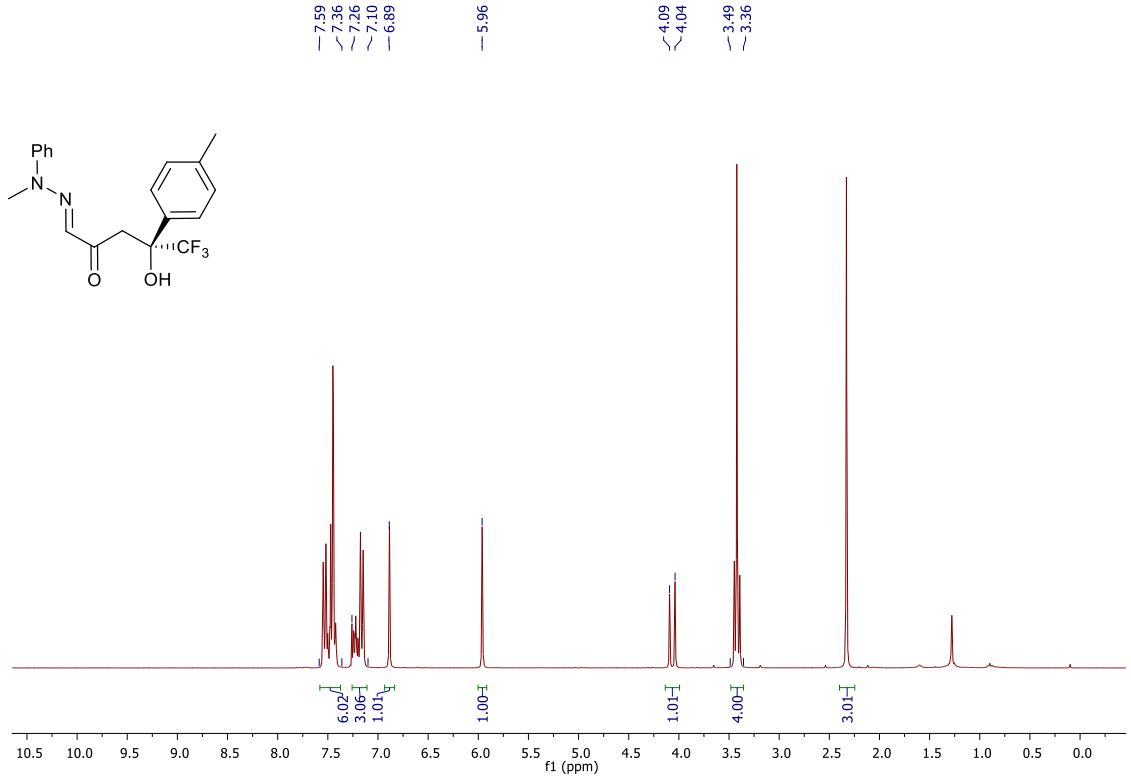
^{13}C NMR (126 MHz, $CDCl_3$) of (*S*)-**3Gb**



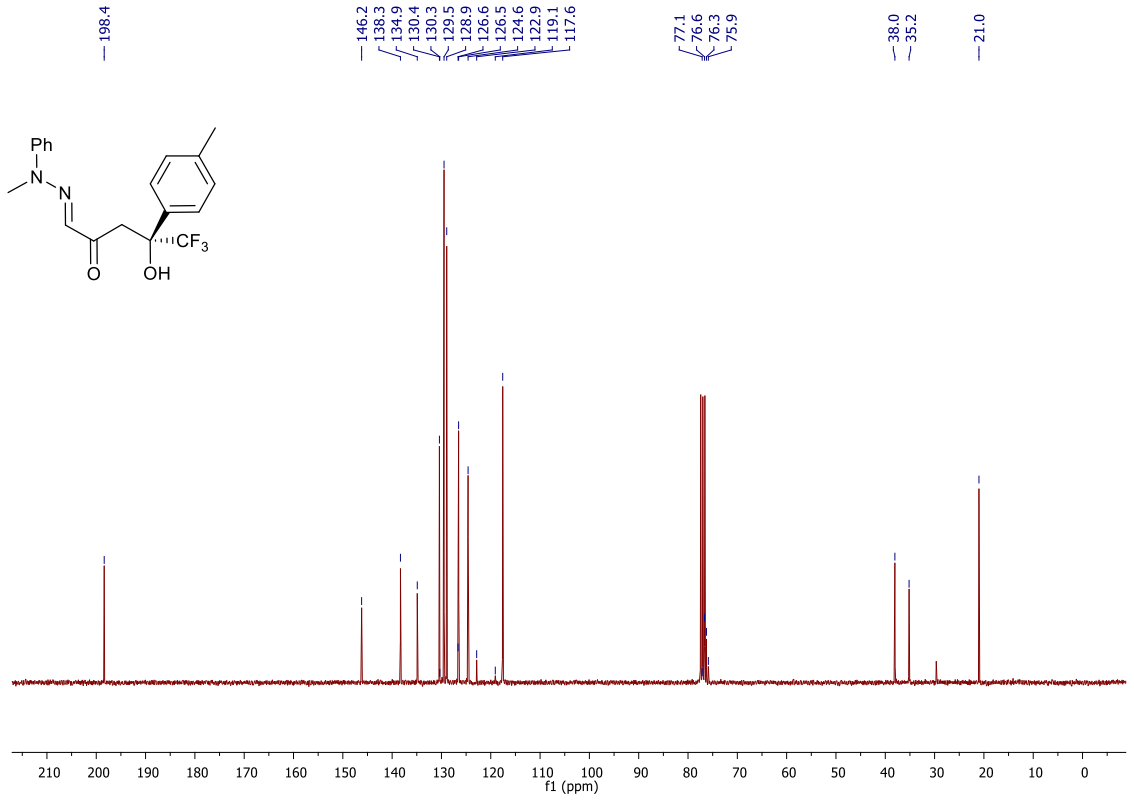
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)-**3Gb**



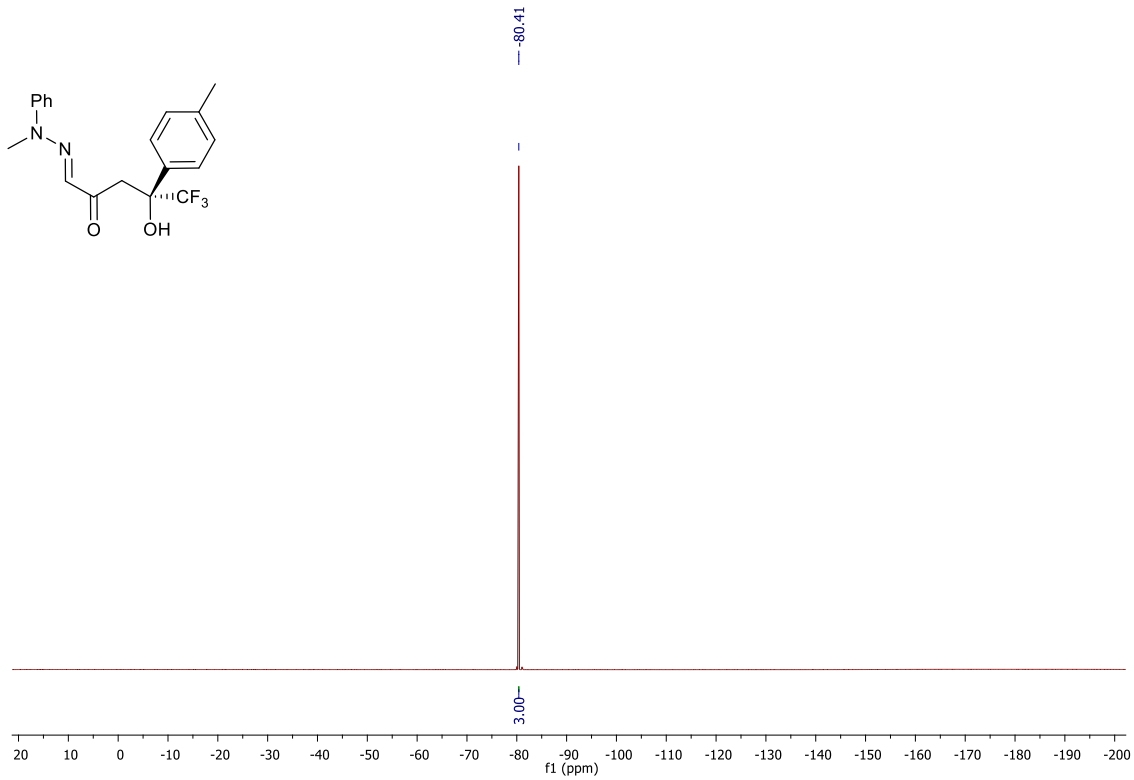
^{1}H NMR (300 MHz, $CDCl_3$) of (*S*)-**3Gc**



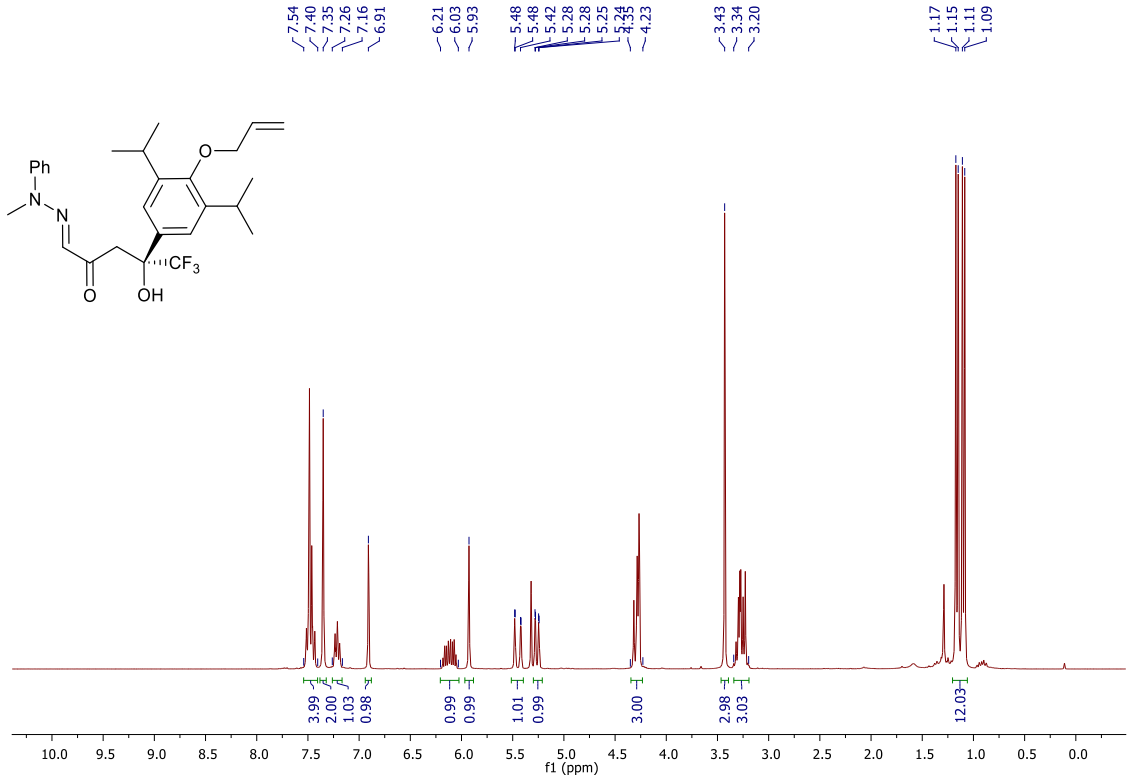
^{13}C NMR (75.5 MHz, $CDCl_3$) of (*S*)-**3Gc**



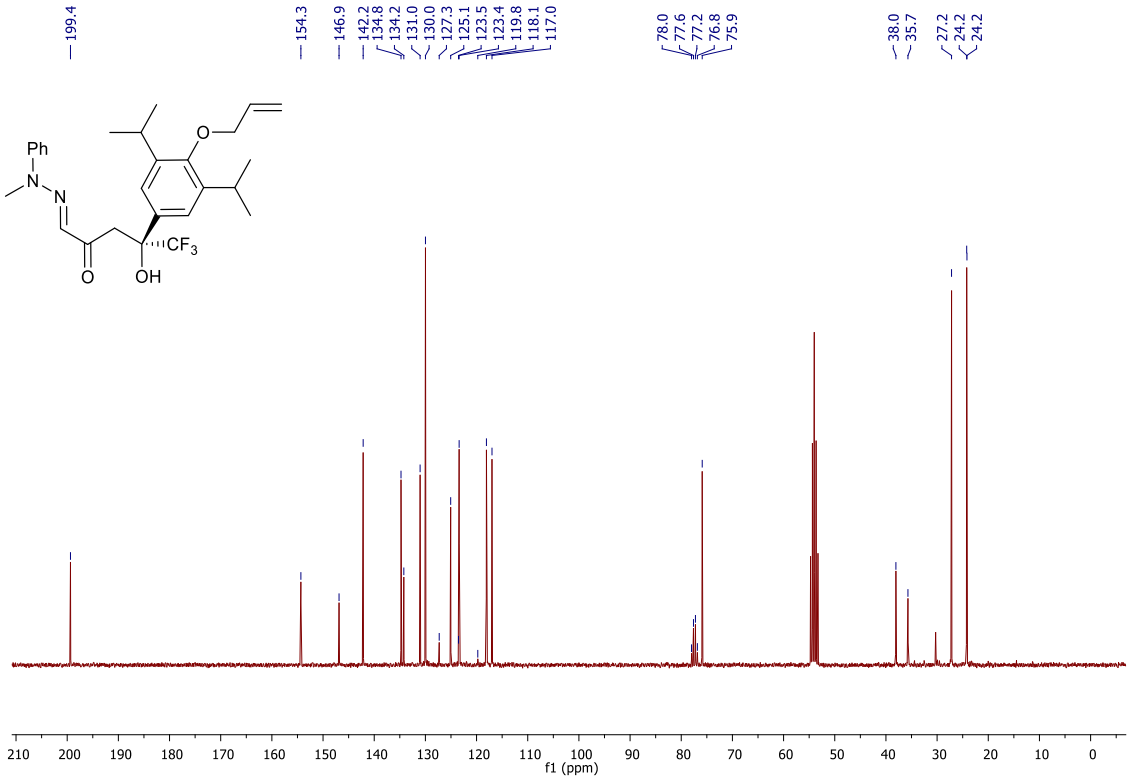
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)-**3Gc**



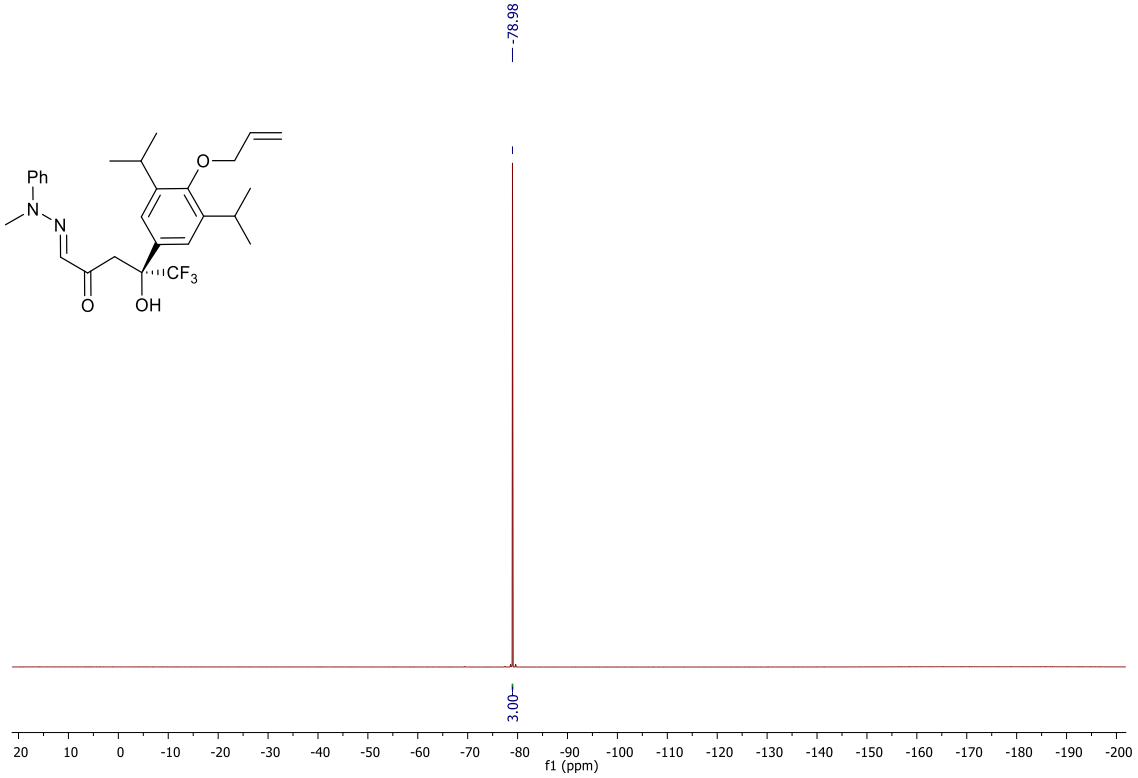
^{1}H NMR (300 MHz, CD_2Cl_2) of (*S*)-**3Ge**



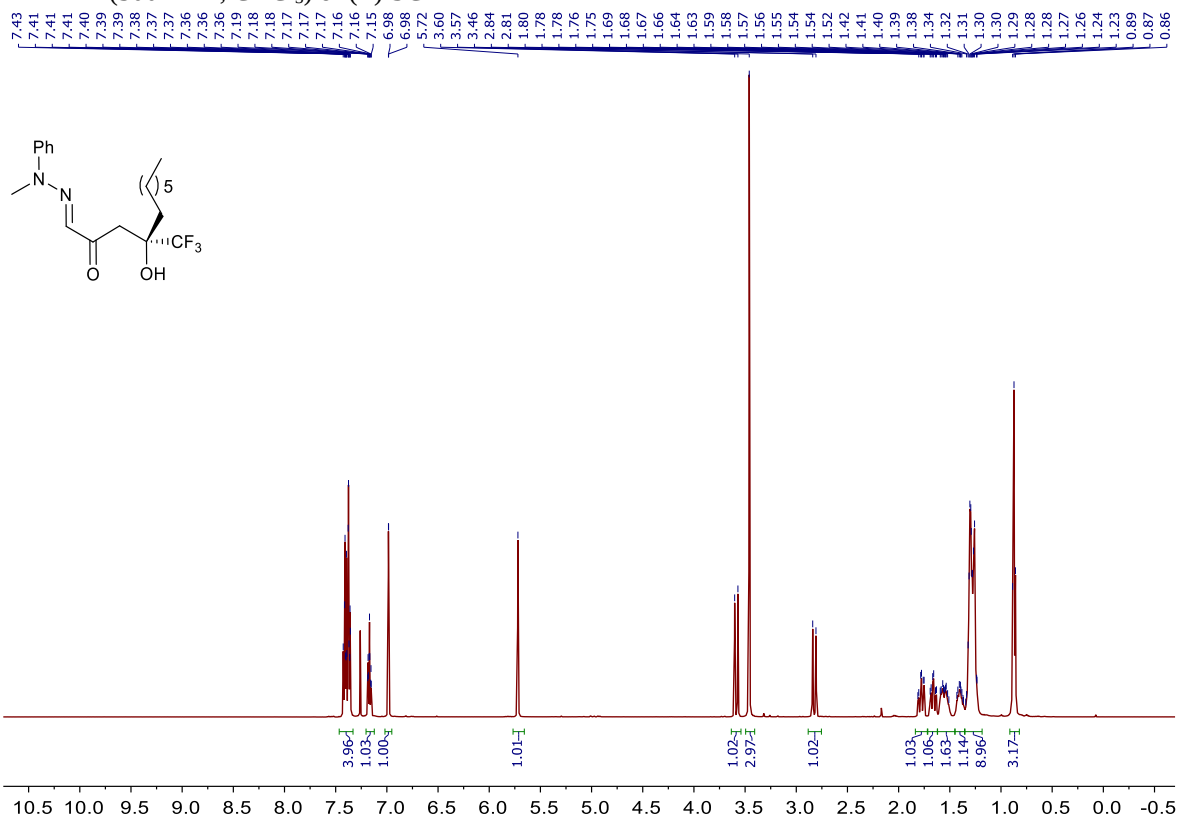
^{13}C NMR (75.5 MHz, CD_2Cl_2) of (*S*)-**3Ge**



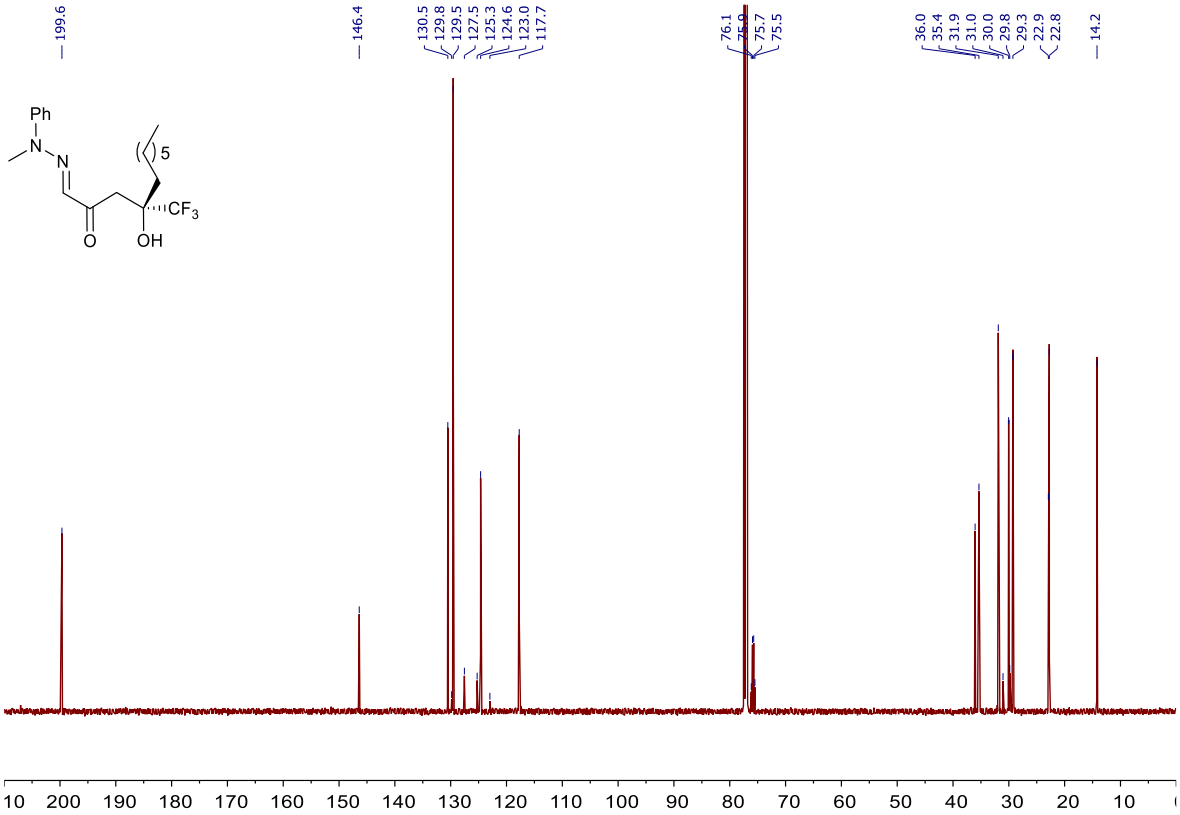
^{19}F NMR (471 MHz, CD_2Cl_2) of (*S*)-**3Ge**



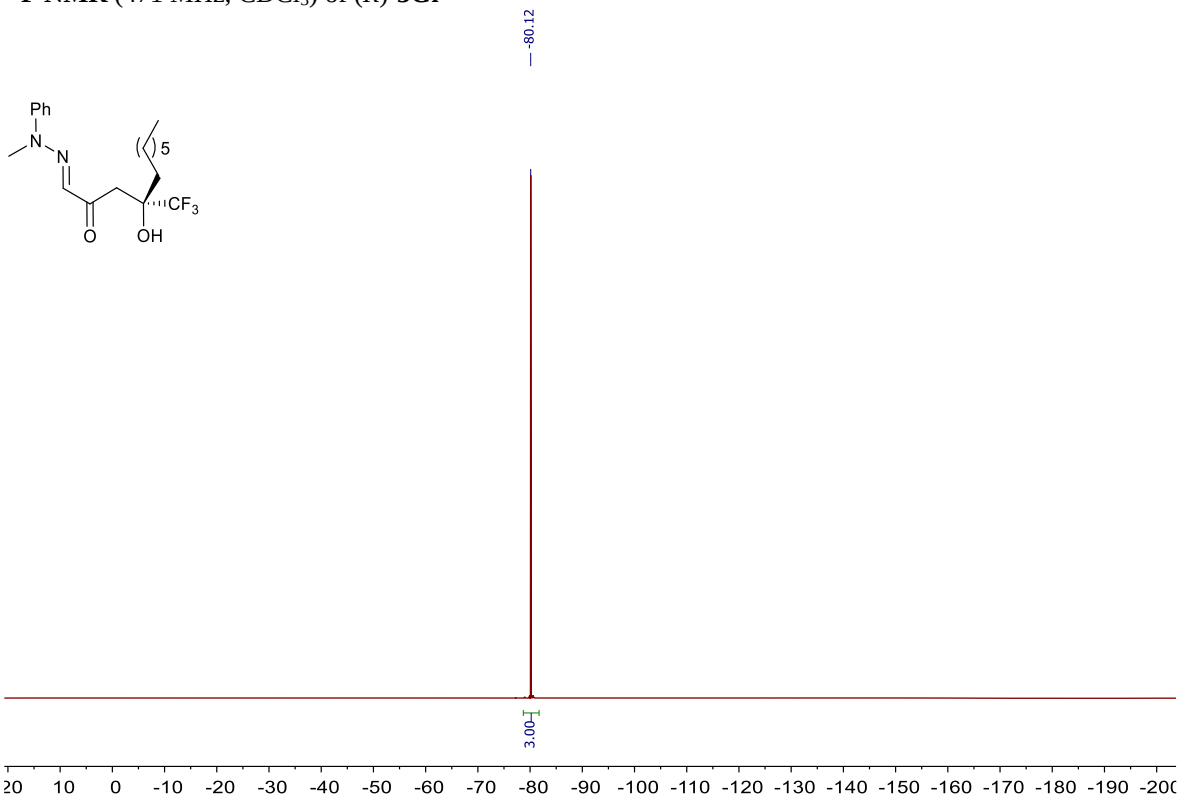
^{1}H NMR (500 MHz, $CDCl_3$) of (*R*)-**3Gi**



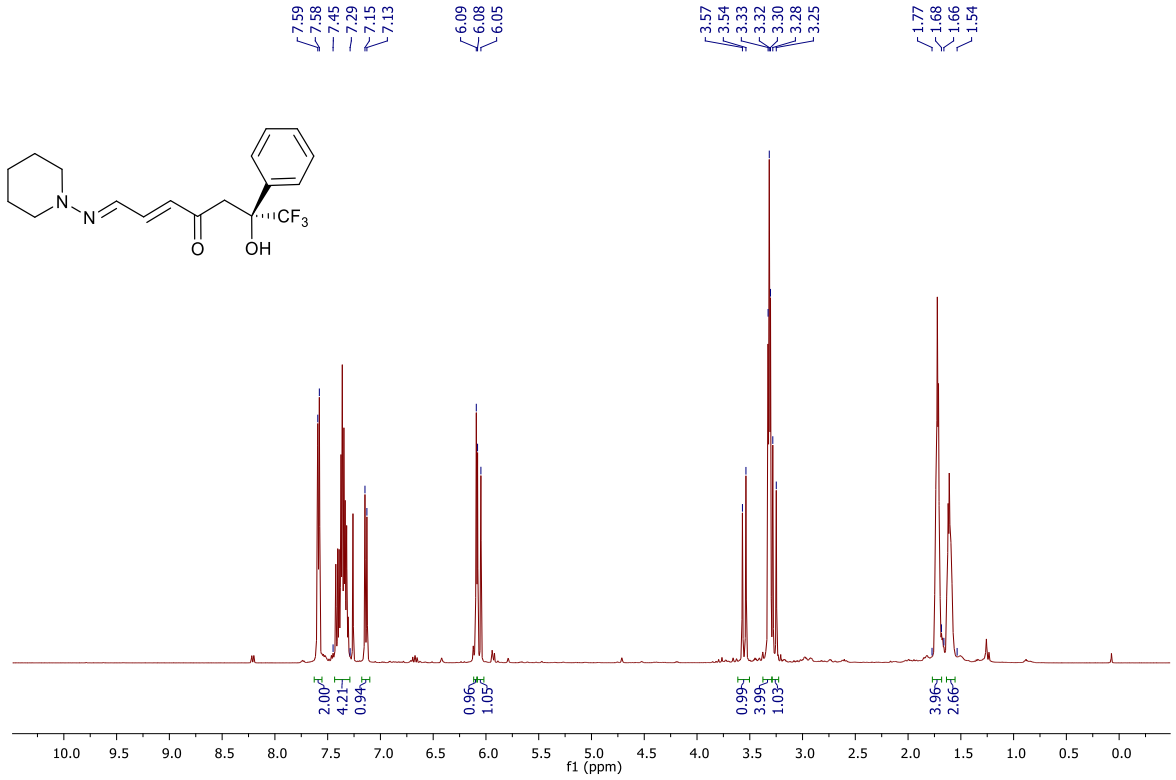
^{13}C NMR (126 MHz, $CDCl_3$) of (*R*)-**3Gi**



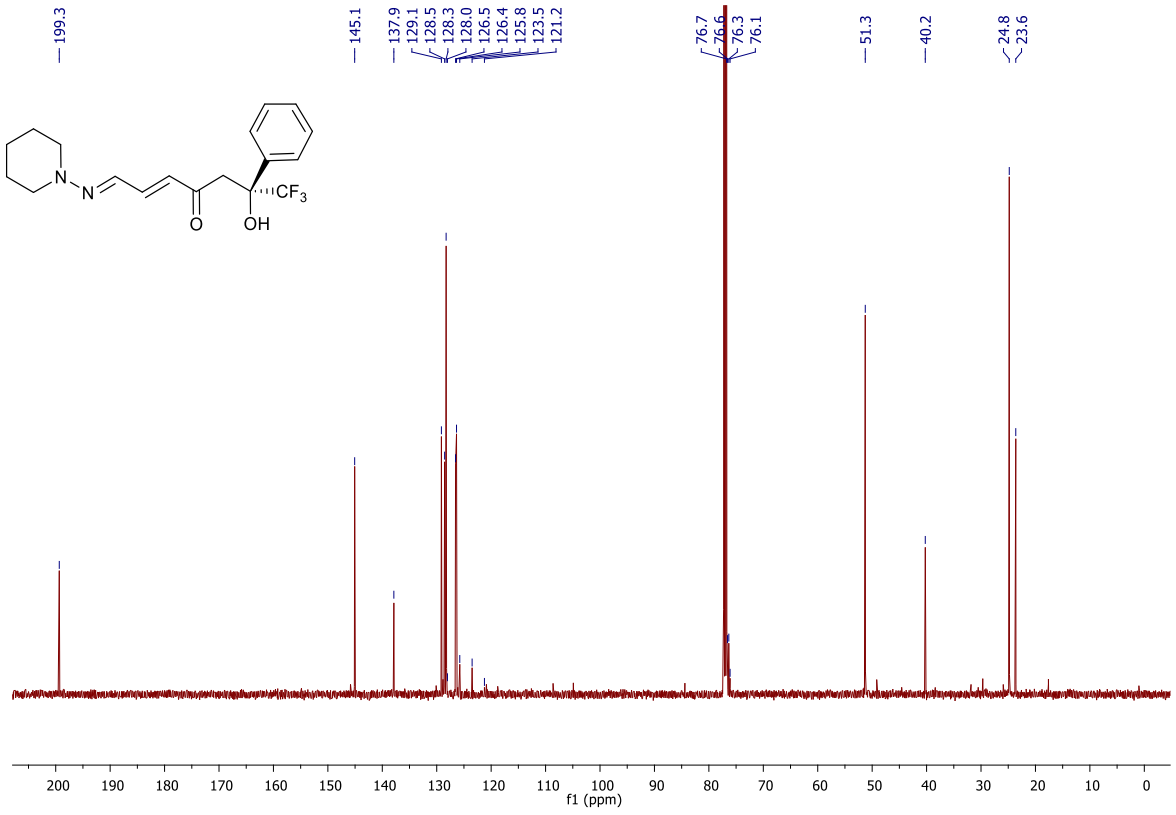
^{19}F NMR (471 MHz, $CDCl_3$) of (*R*)-**3Gi**



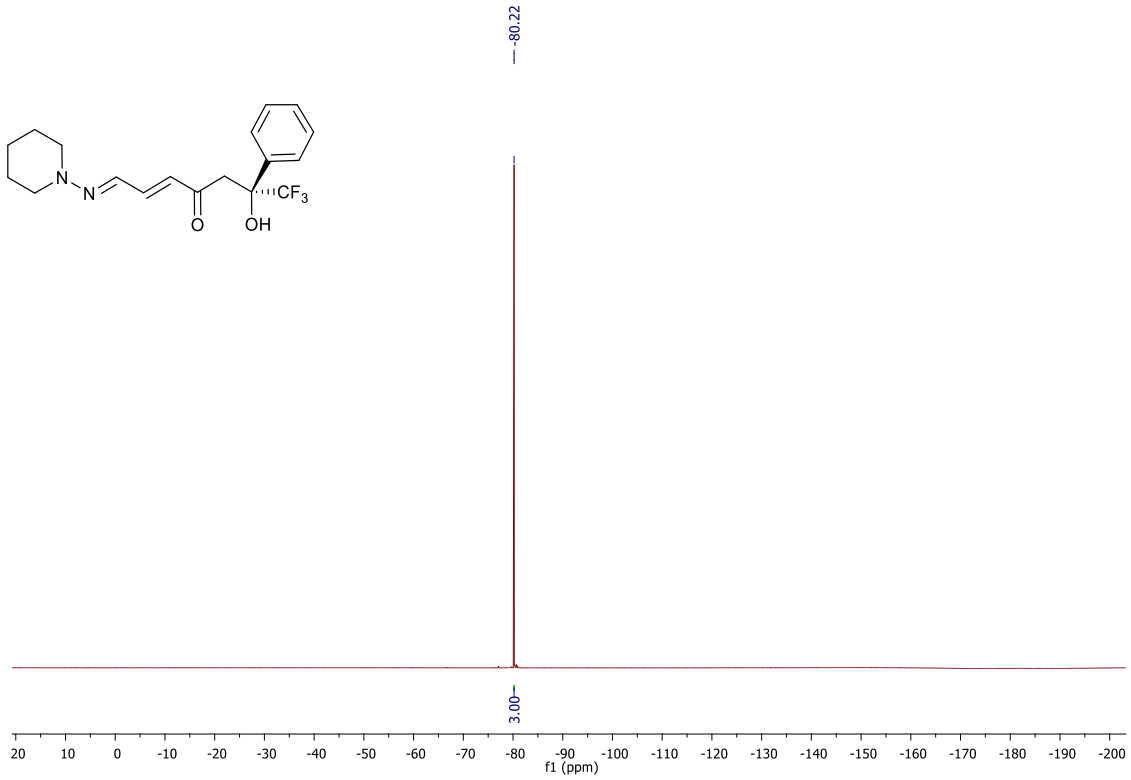
^{1}H NMR (500 MHz, $CDCl_3$) of (*S*)-**9Aa**



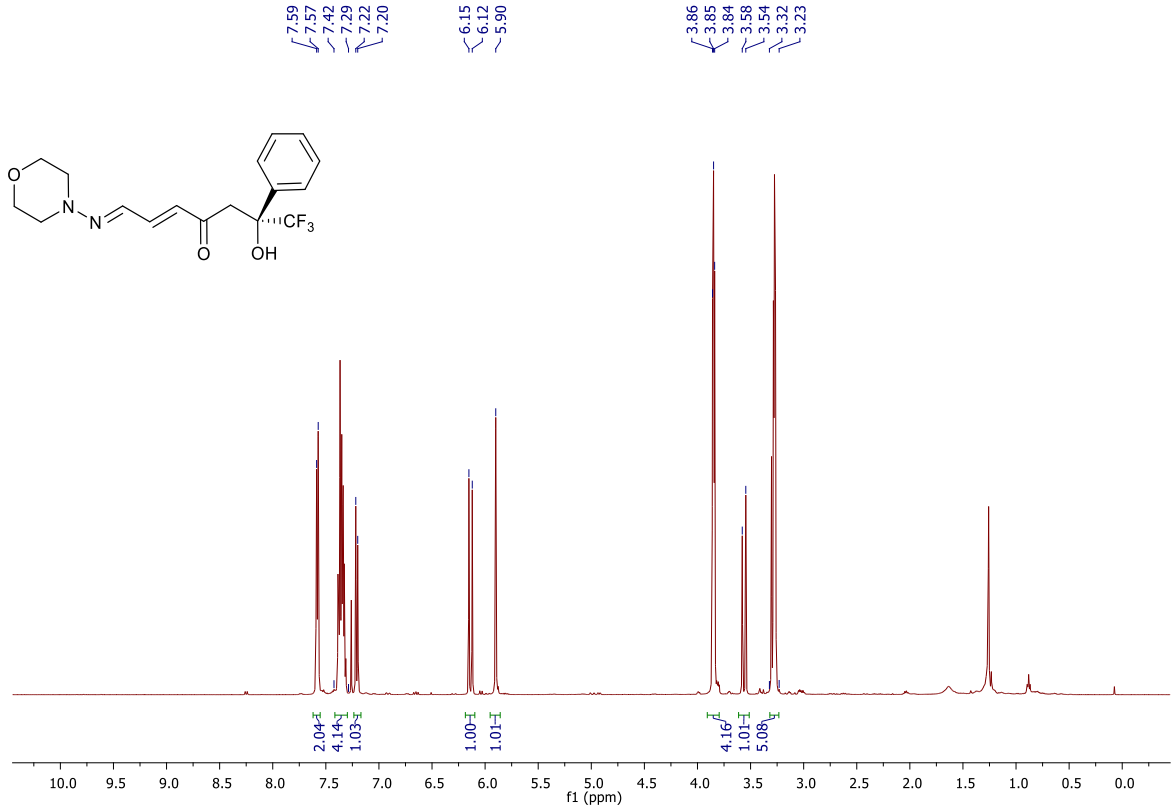
^{13}C NMR (126 MHz, $CDCl_3$) of (*S*)-**9Aa**



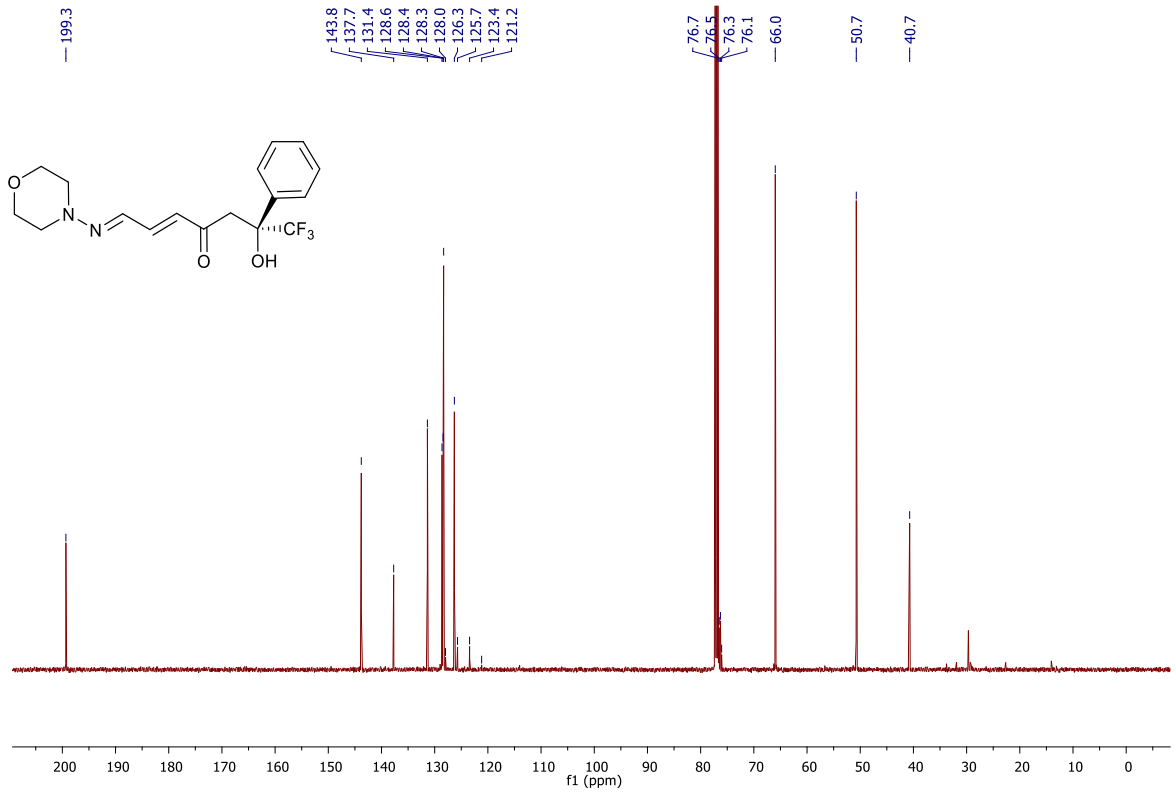
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)-**9Aa**



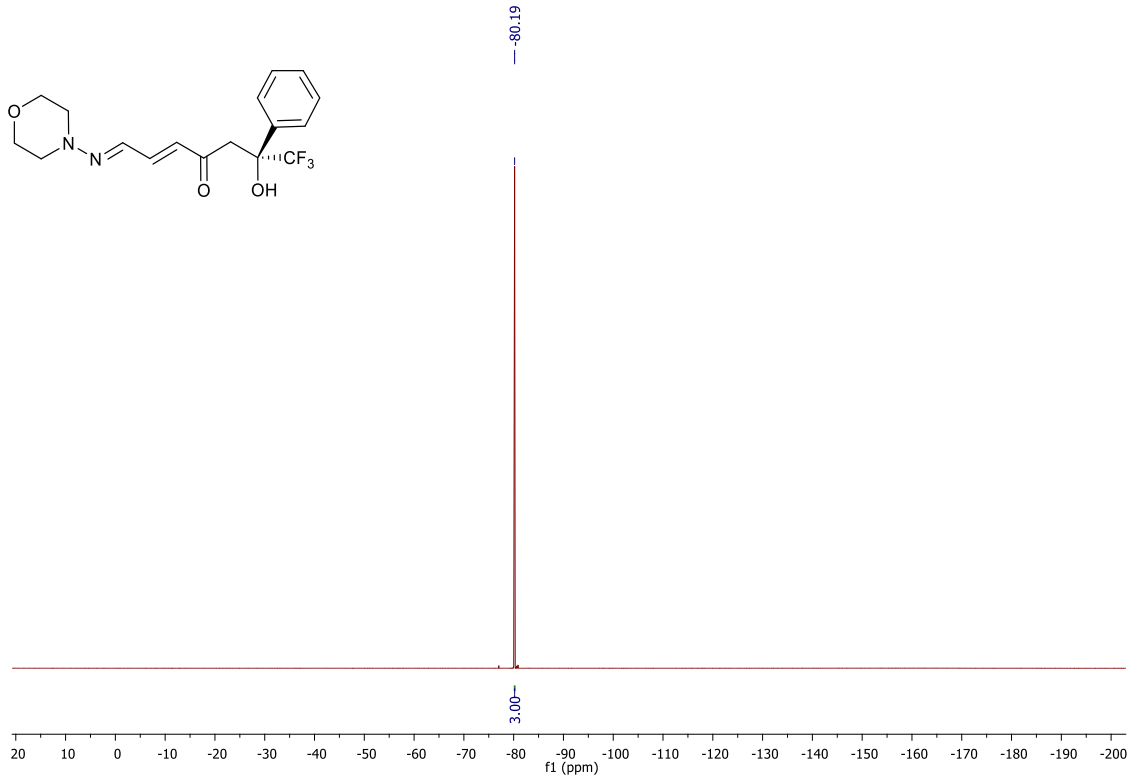
^{1}H NMR (500 MHz, $CDCl_3$) of (*S*)-**9Ba**



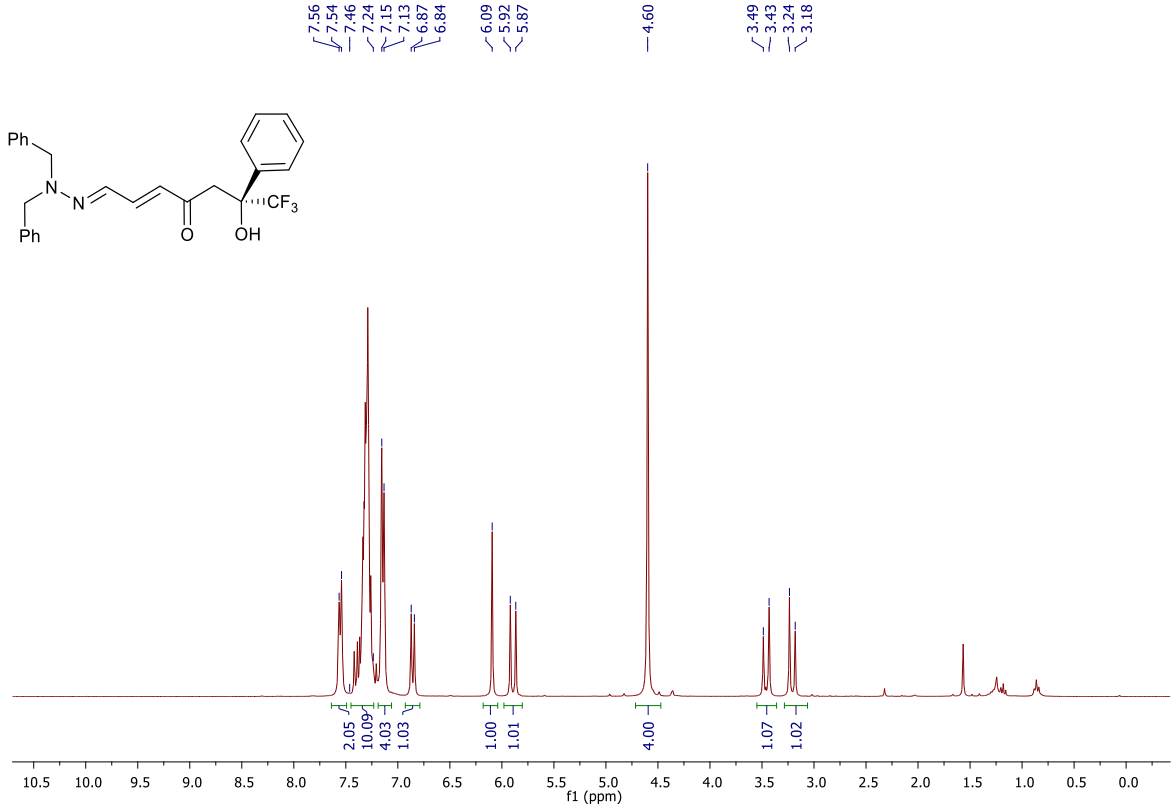
^{13}C NMR (126 MHz, $CDCl_3$) of (*S*)-**9Ba**



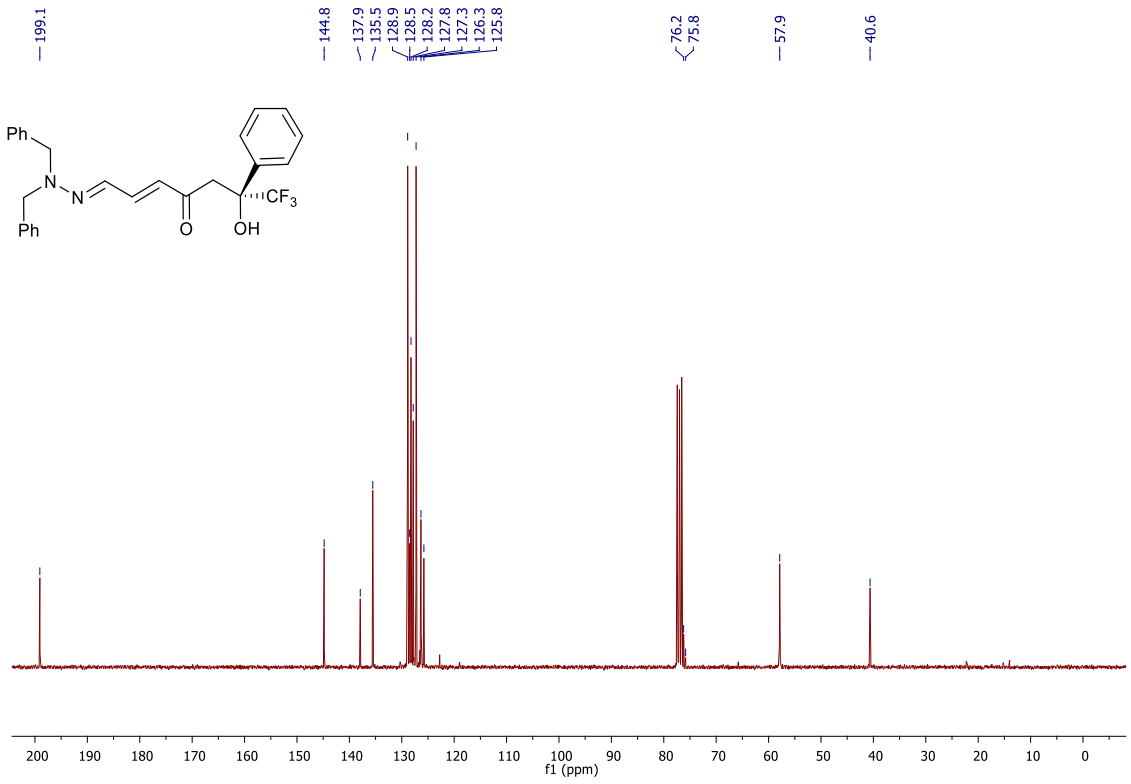
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)-**9Ba**



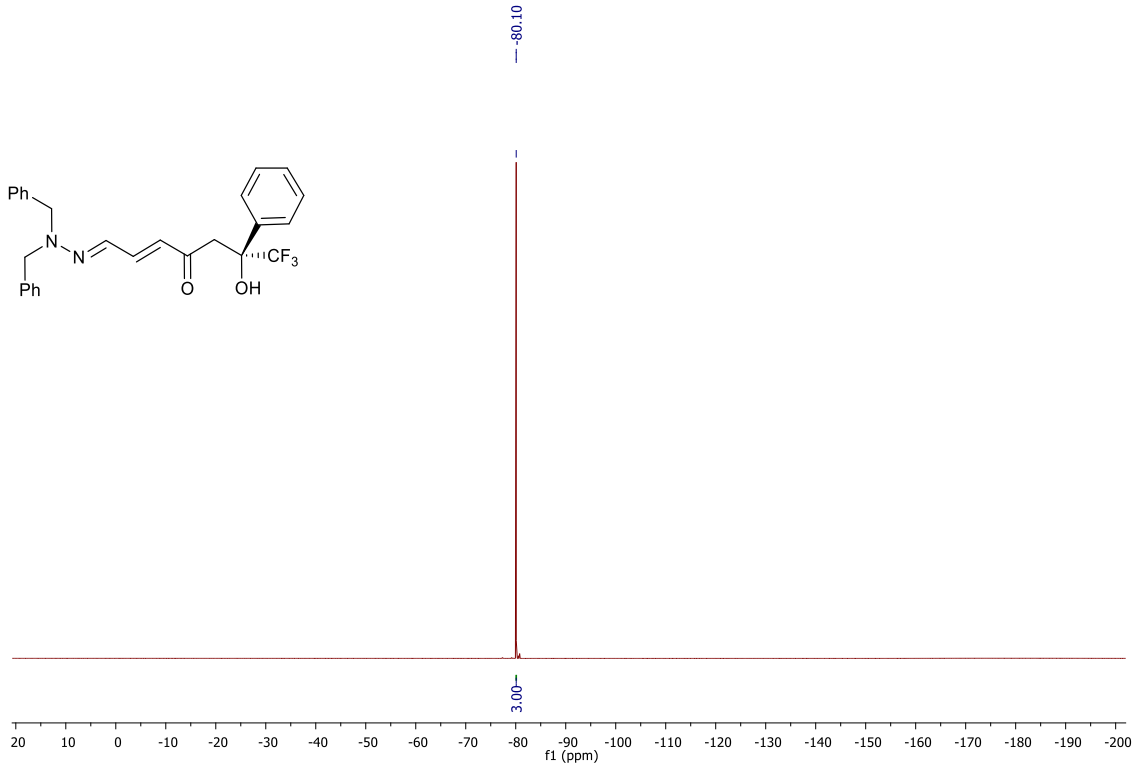
^{1}H NMR (300 MHz, $CDCl_3$) of (*S*)-**9Ca**



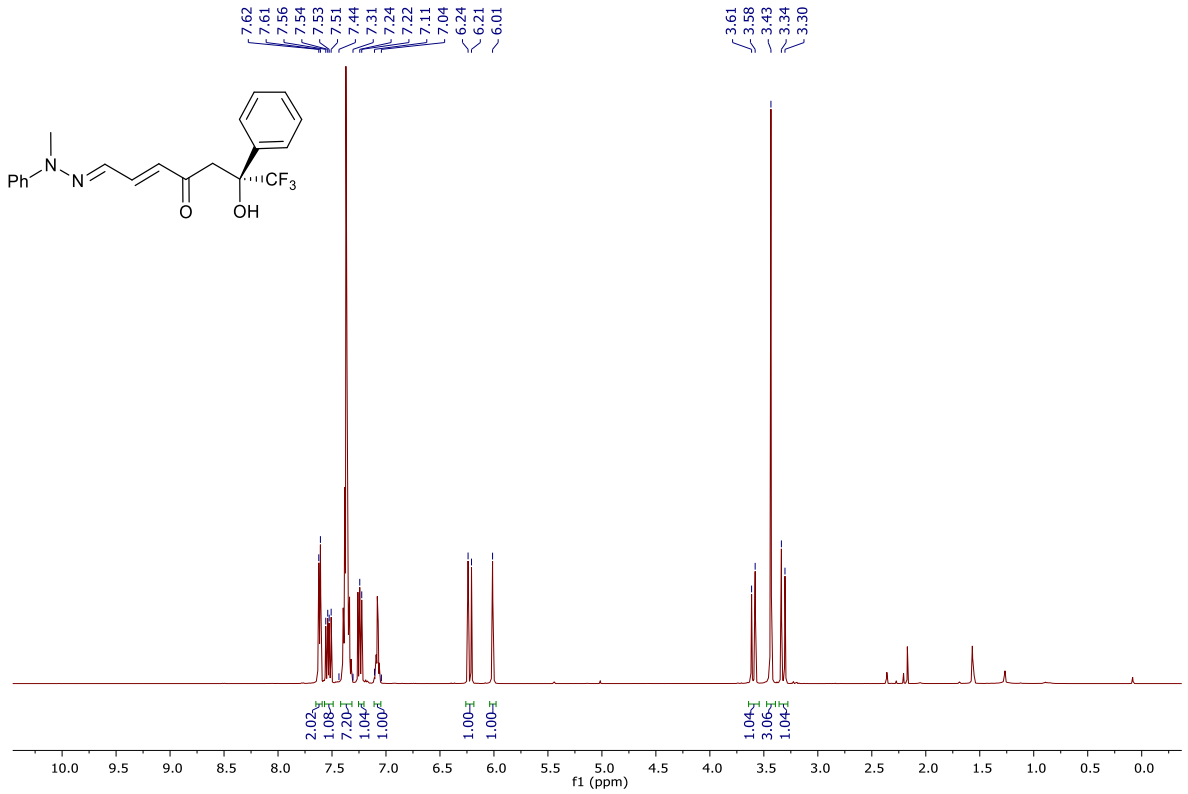
^{13}C NMR (75.5 MHz, $CDCl_3$) of (*S*)-**9Ca**



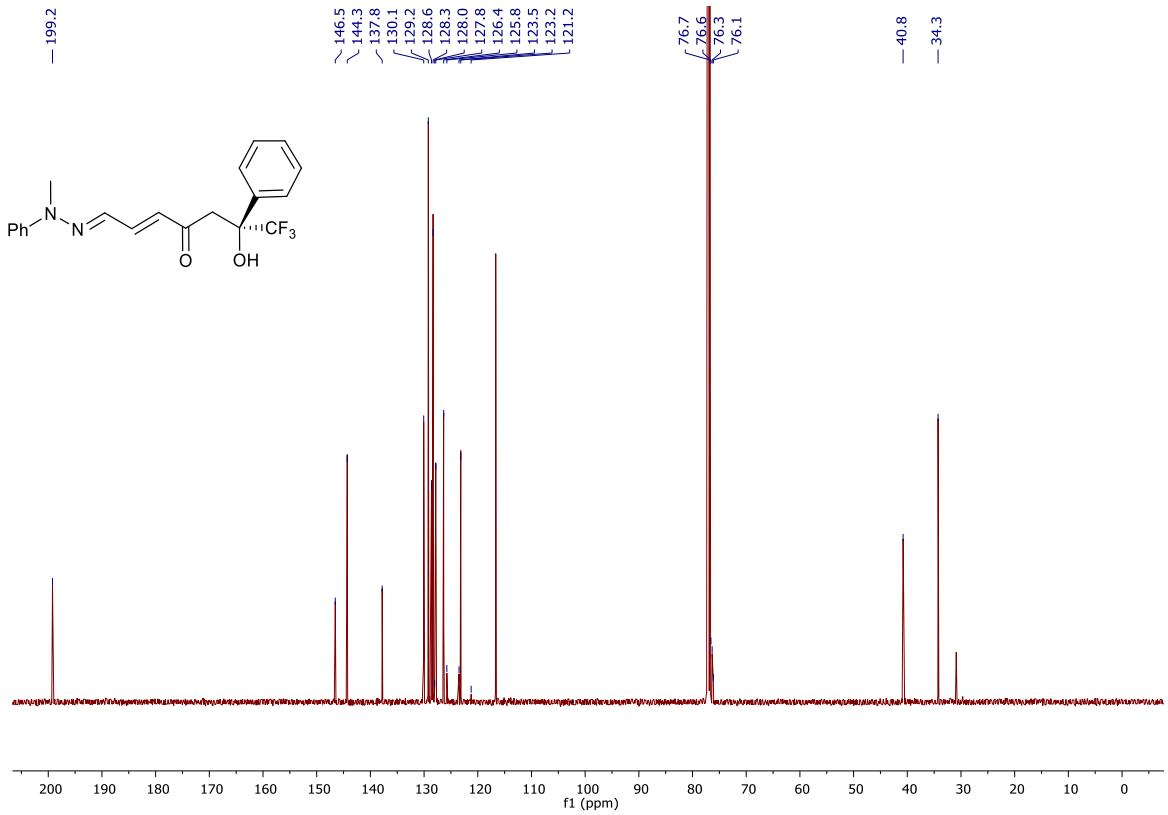
^{19}F NMR (282.5 MHz, $CDCl_3$) of (*S*)-**9Ca**



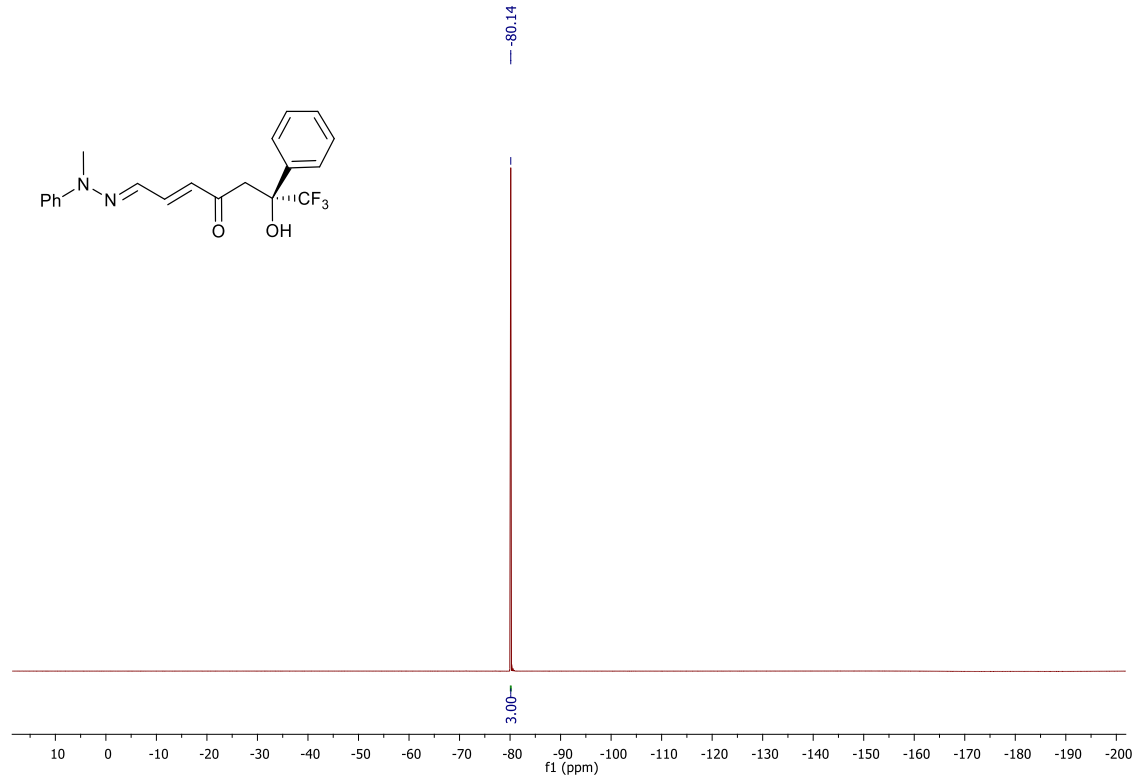
^{1}H NMR (500 MHz, $CDCl_3$) of (*S*)-**9Da**



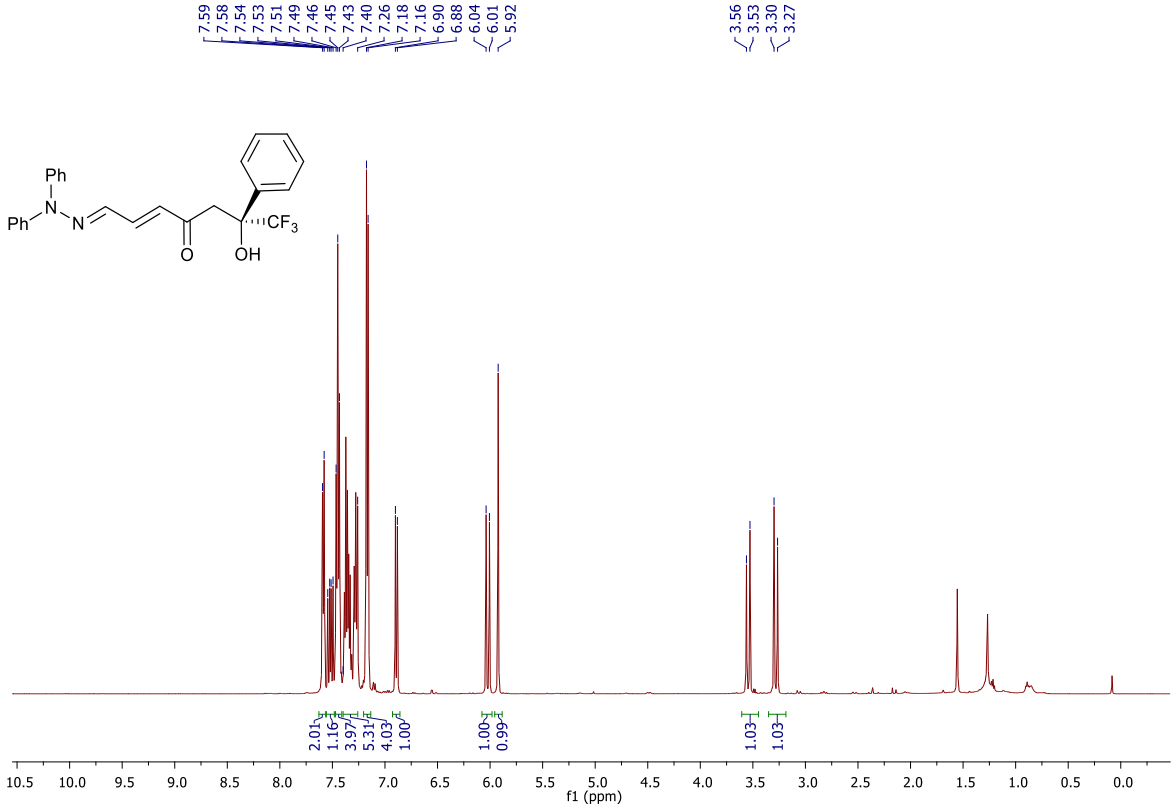
^{13}C NMR (126 MHz, $CDCl_3$) of (*S*)-**9Da**



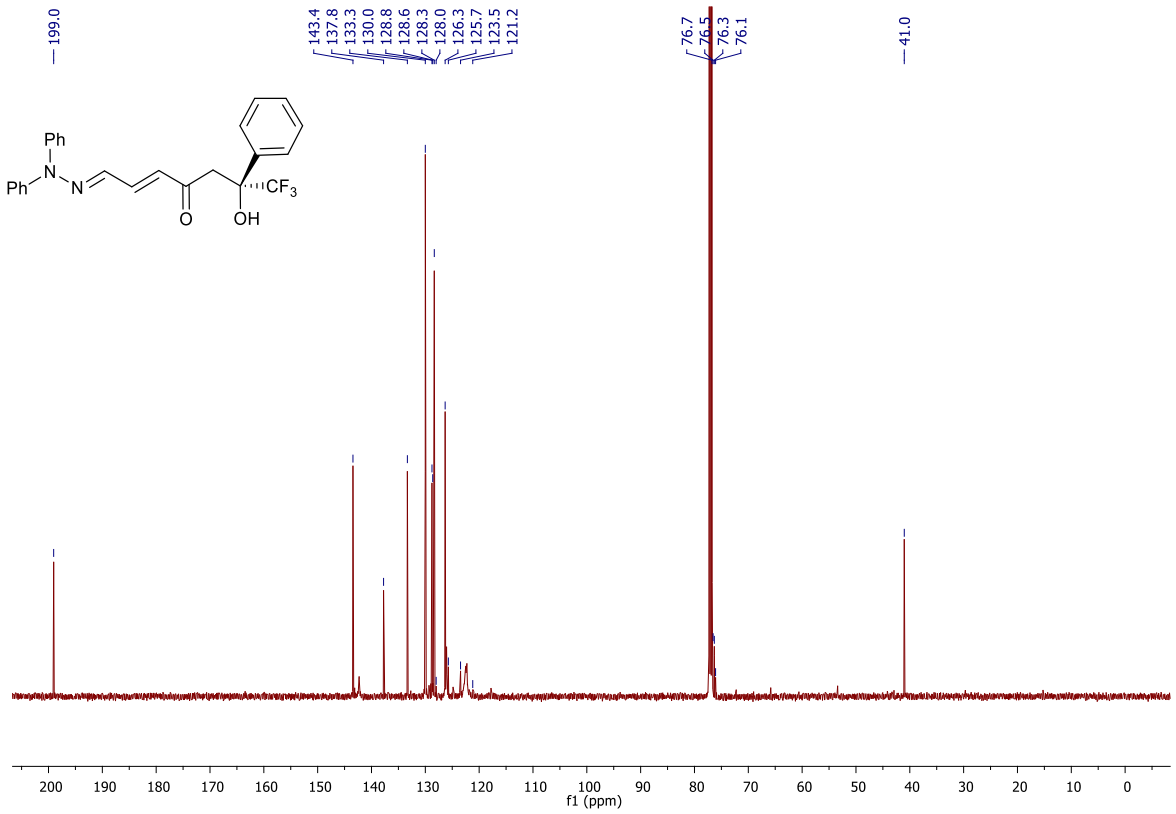
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)-**9Da**



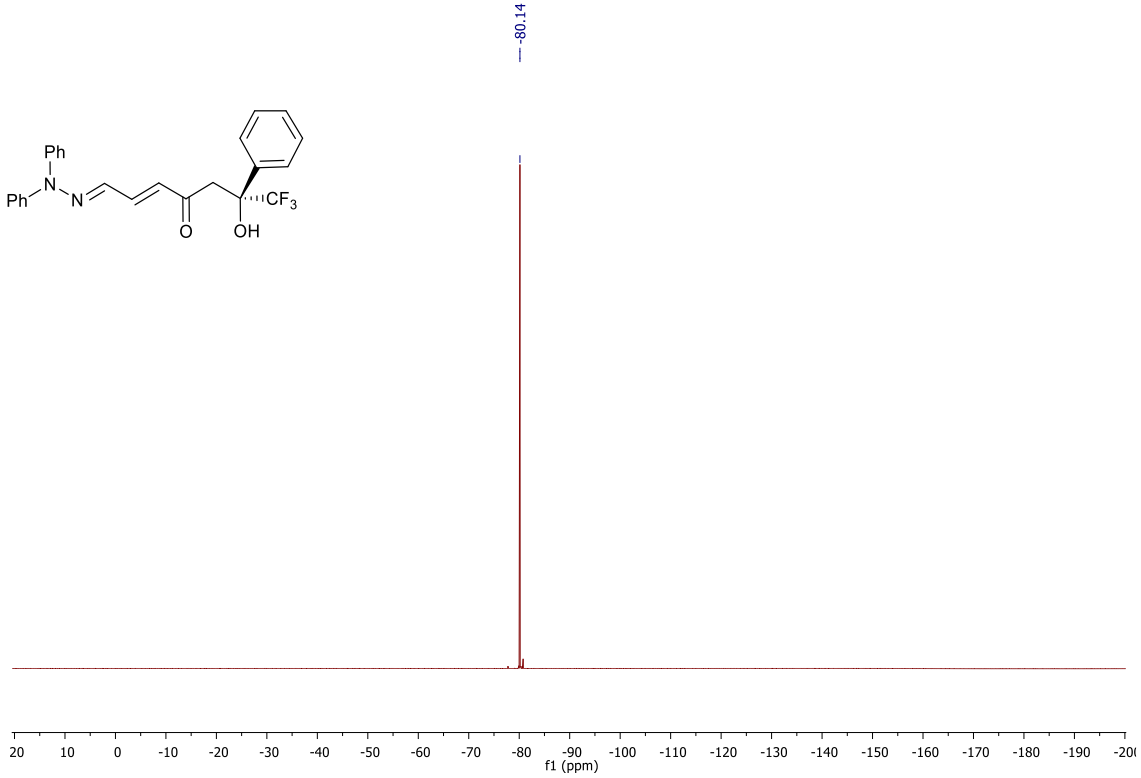
^{1}H NMR (500 MHz, $CDCl_3$) of (*S*)-**9Ea**



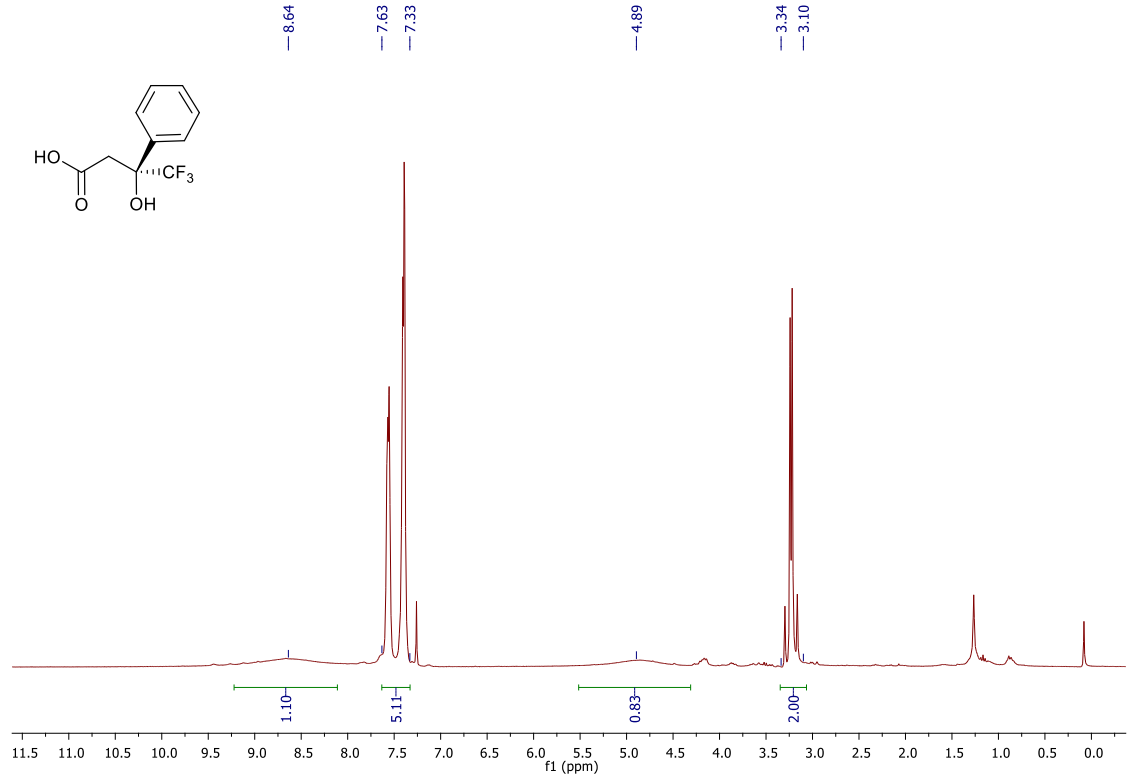
^{13}C NMR (126 MHz, $CDCl_3$) of (*S*)-**9Ea**



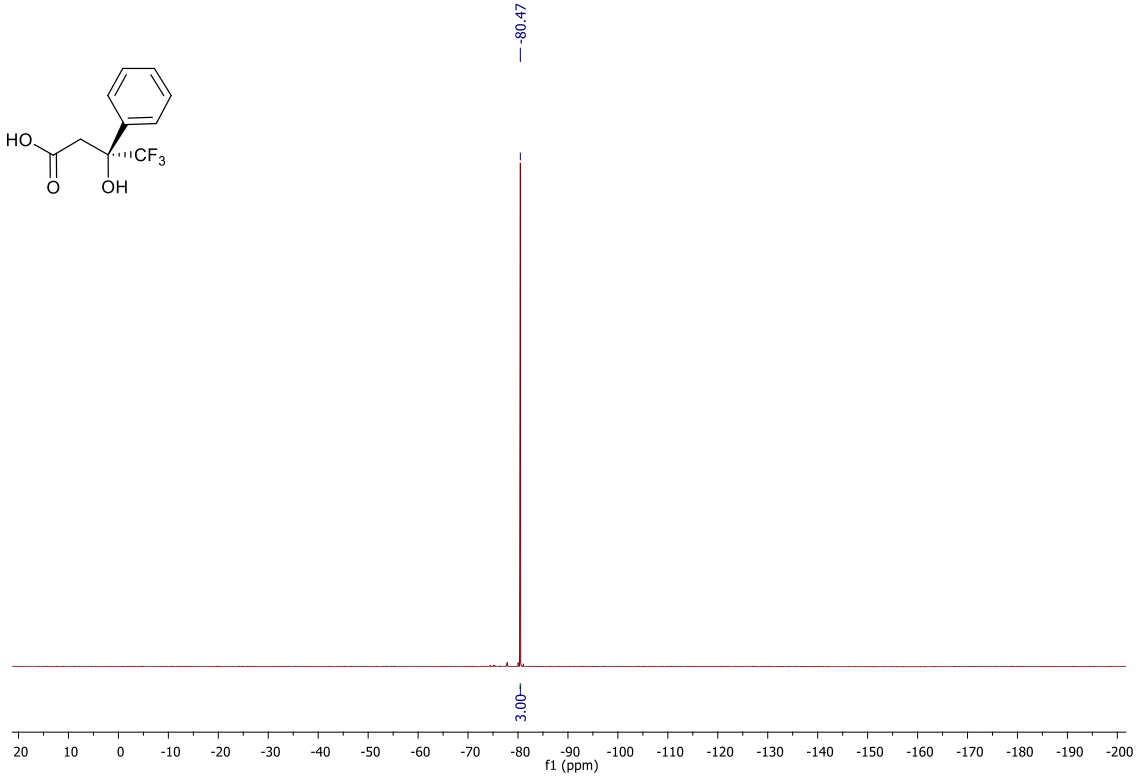
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)-**9Ea**



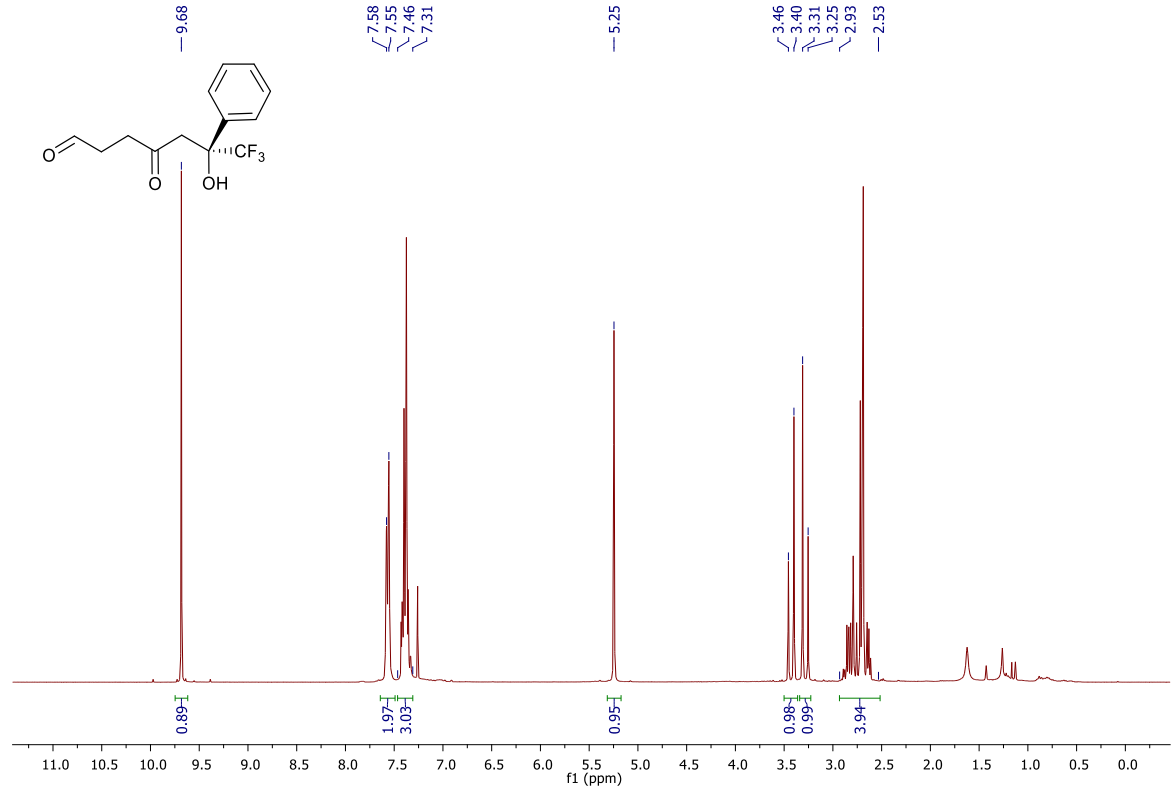
^{1}H NMR (300 MHz, $CDCl_3$) of (*S*)-**10**



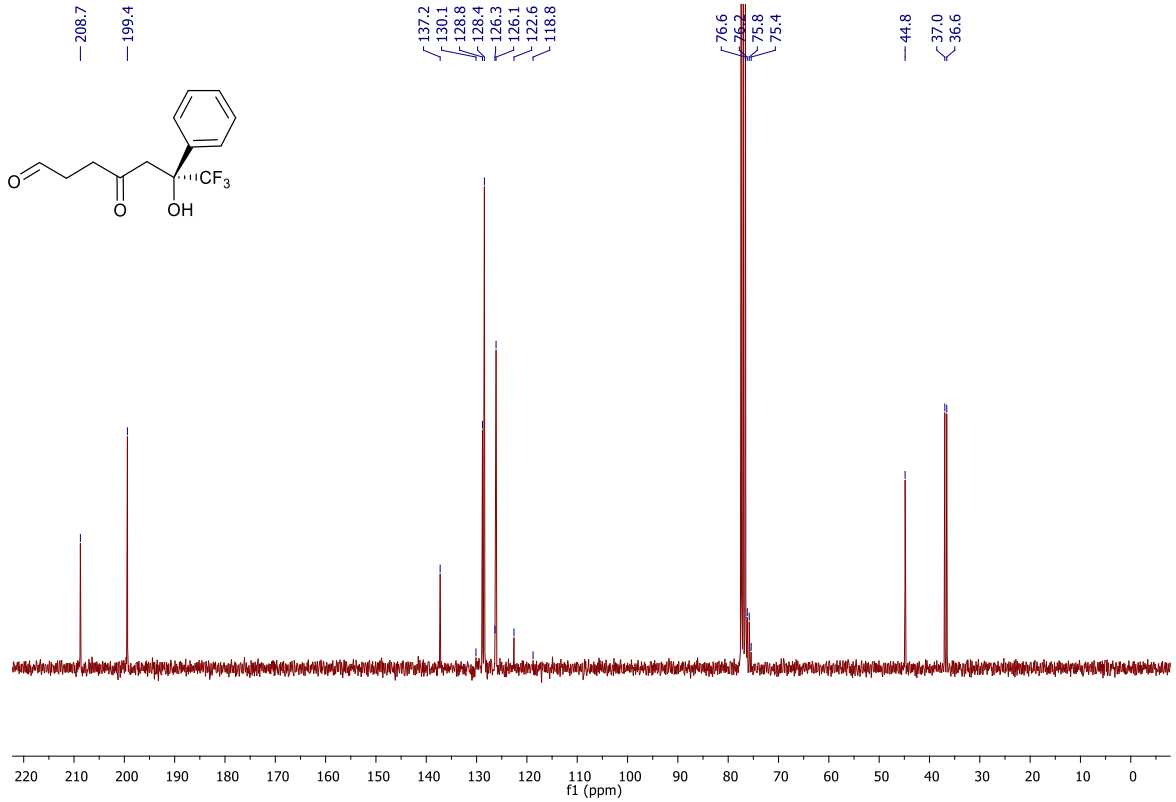
^{19}F NMR (282.5 MHz, CDCl3) of (*S*)-**10**



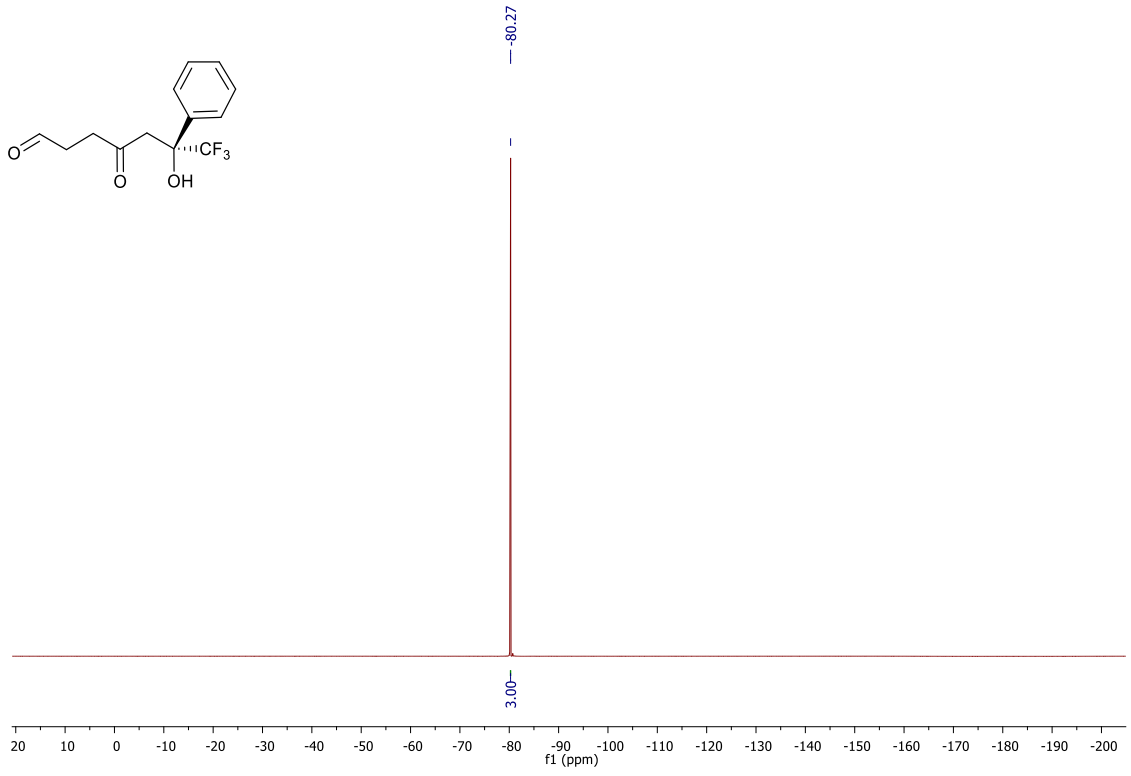
^{1}H NMR (300 MHz, $CDCl_3$) of (*S*)-**11**



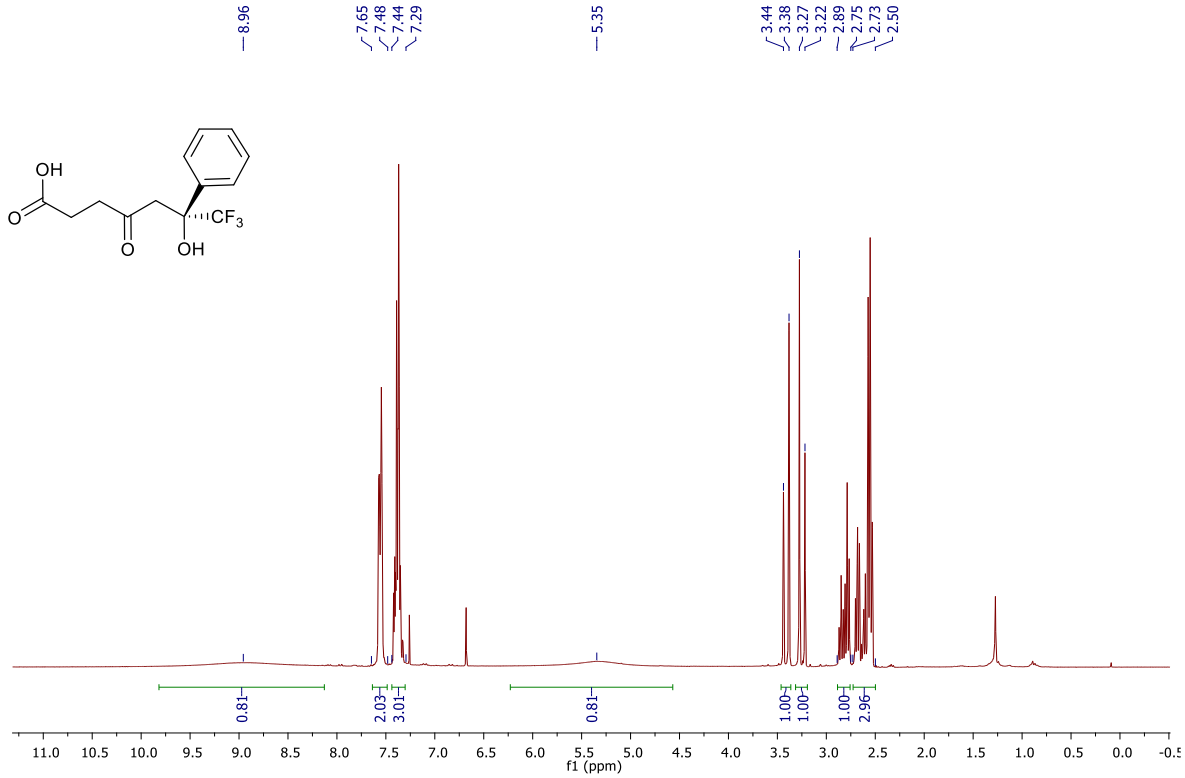
^{13}C NMR (75.5 MHz, $CDCl_3$) of (*S*)-**11**



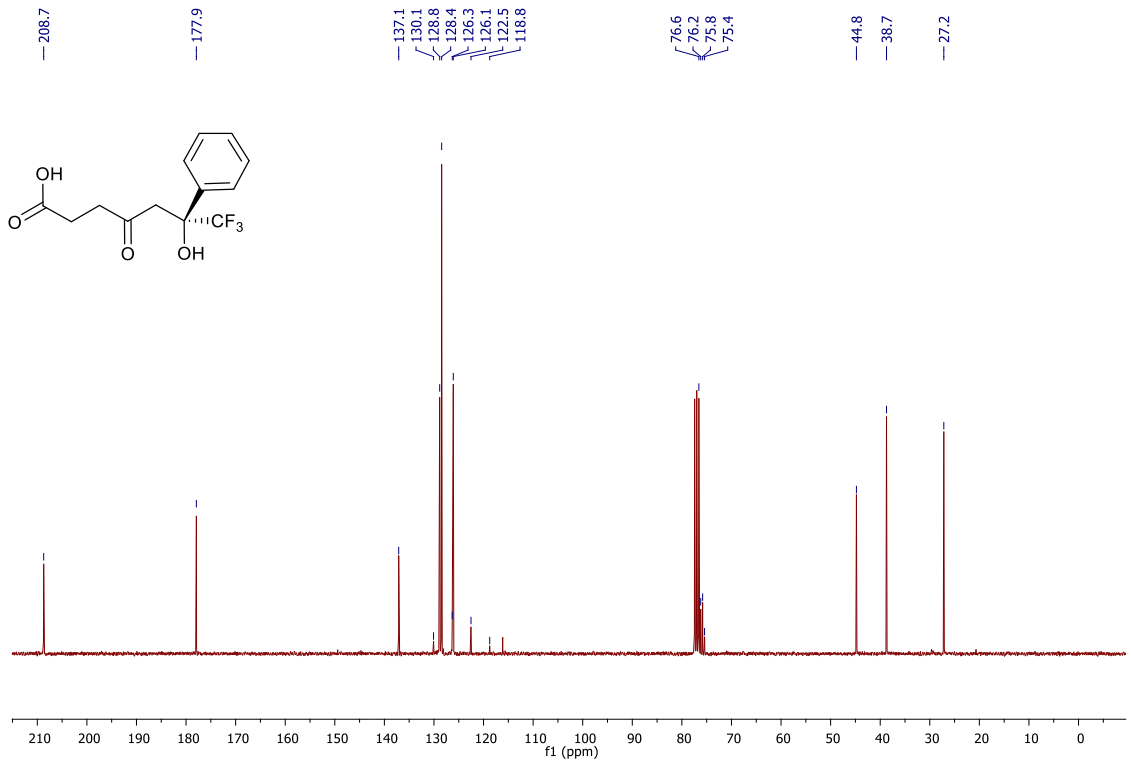
^{19}F NMR (471 MHz, $CDCl_3$) of (*S*)-**11**



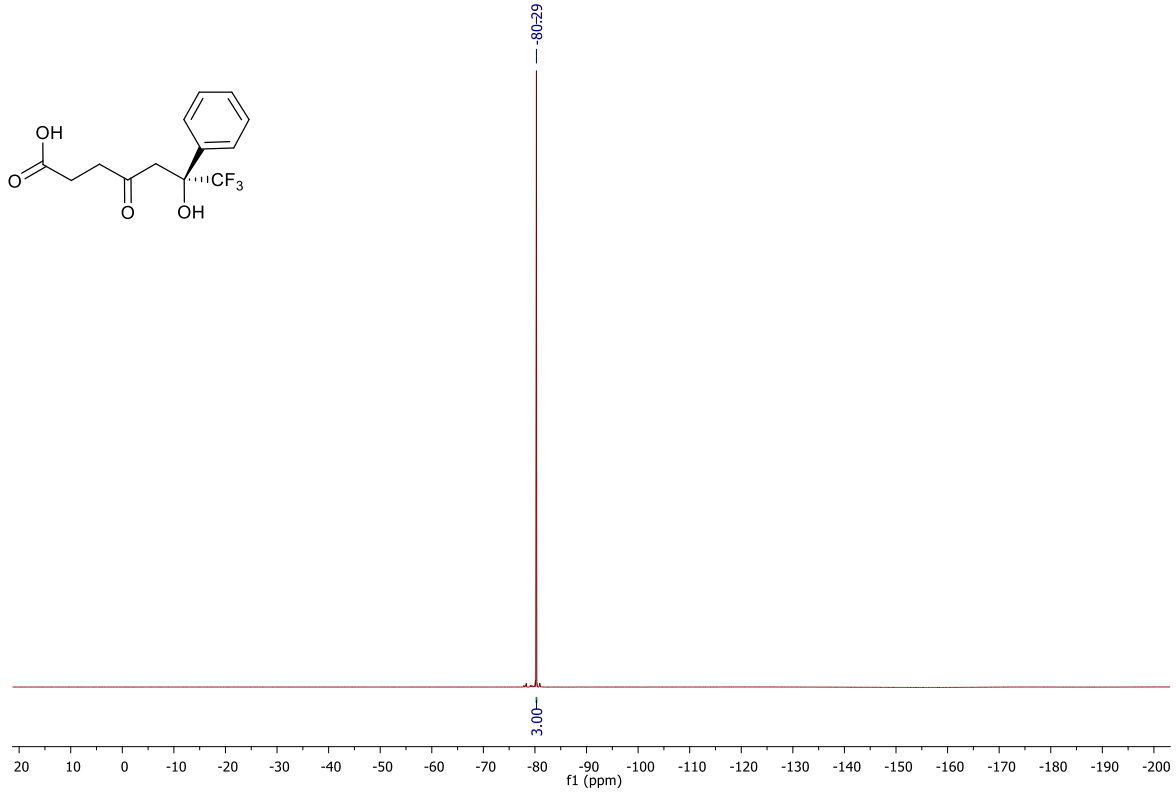
^{1}H NMR (300 MHz, $CDCl_3$) of (*S*)-**12**



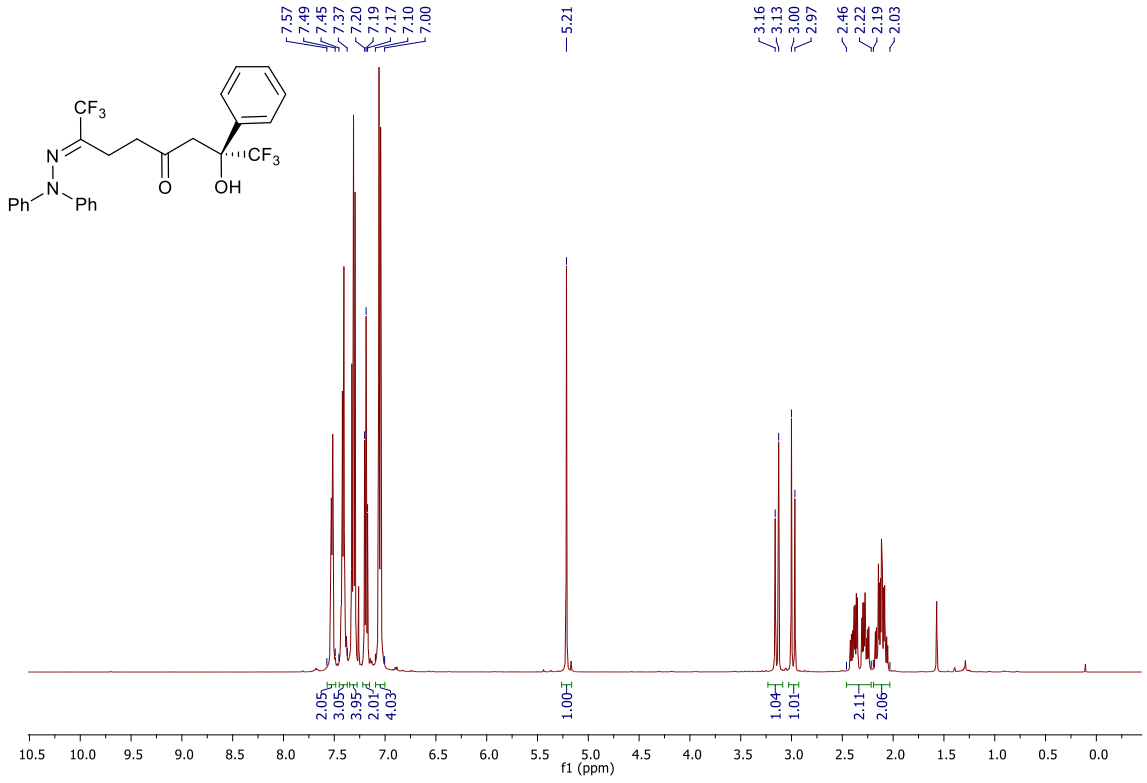
^{13}C NMR (75.5 MHz, $CDCl_3$) of (*S*)-**12**



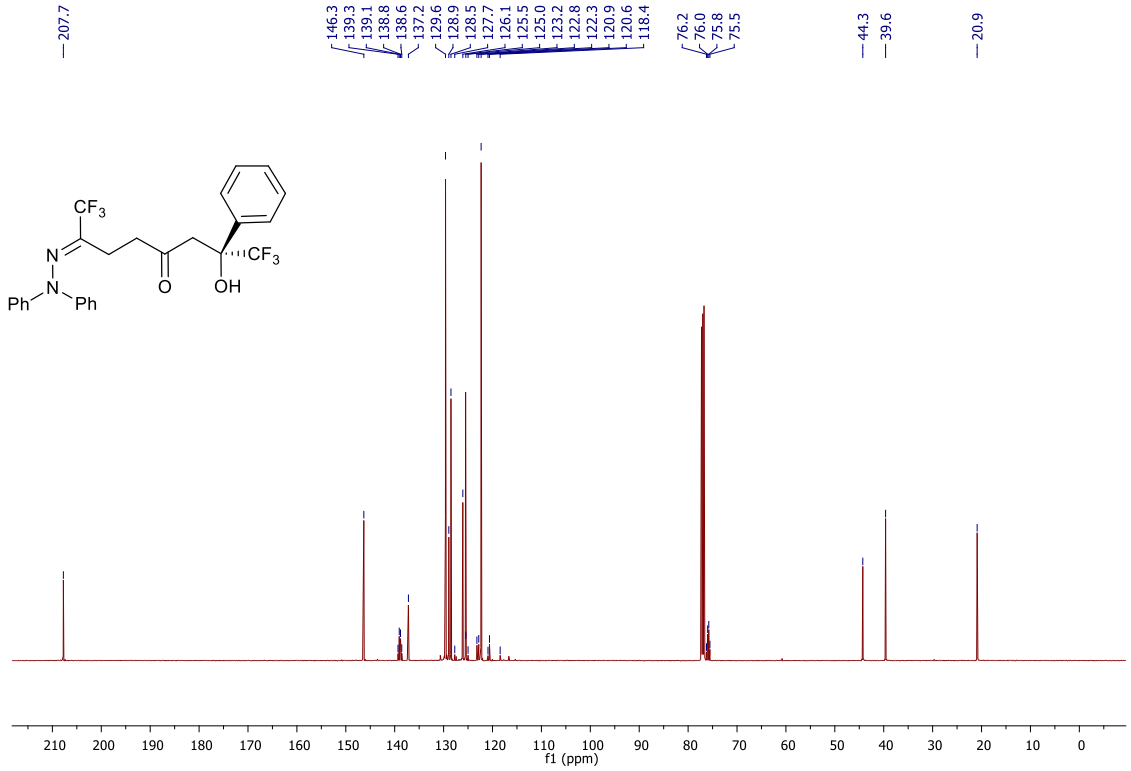
^{19}F NMR (282.5 MHz, $CDCl_3$) of (*S*)-**12**



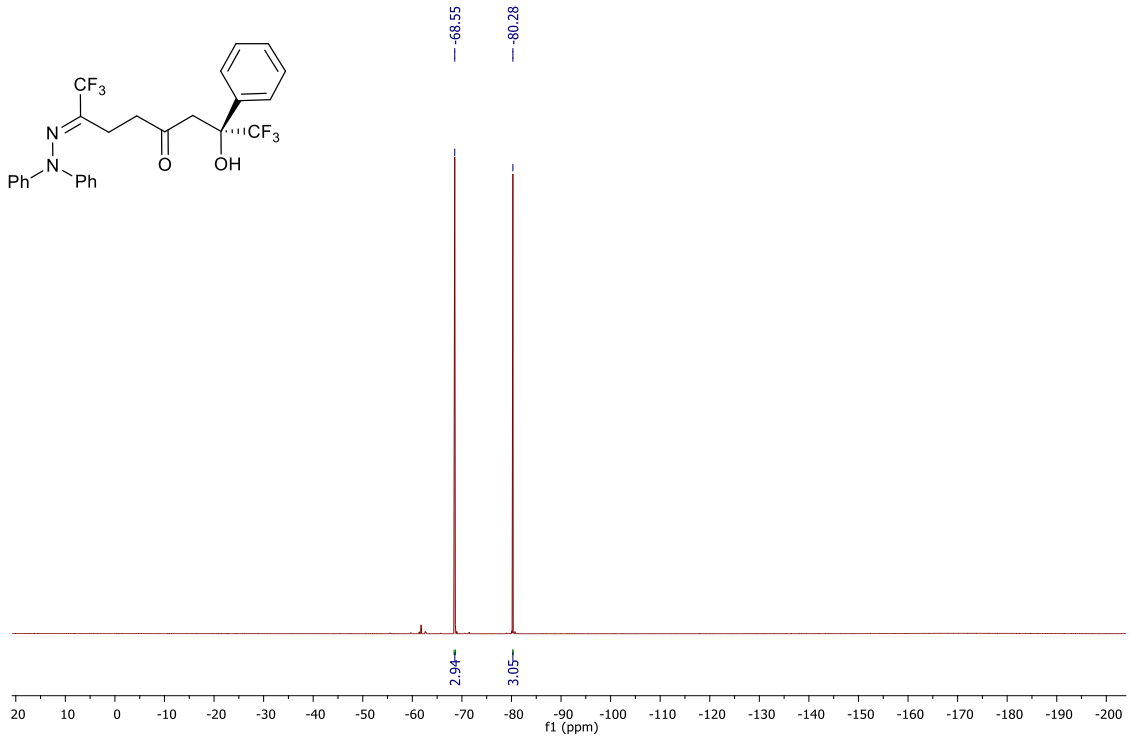
^{1}H NMR (500 MHz, $CDCl_3$) of (*E*)-(*S*)-**13**



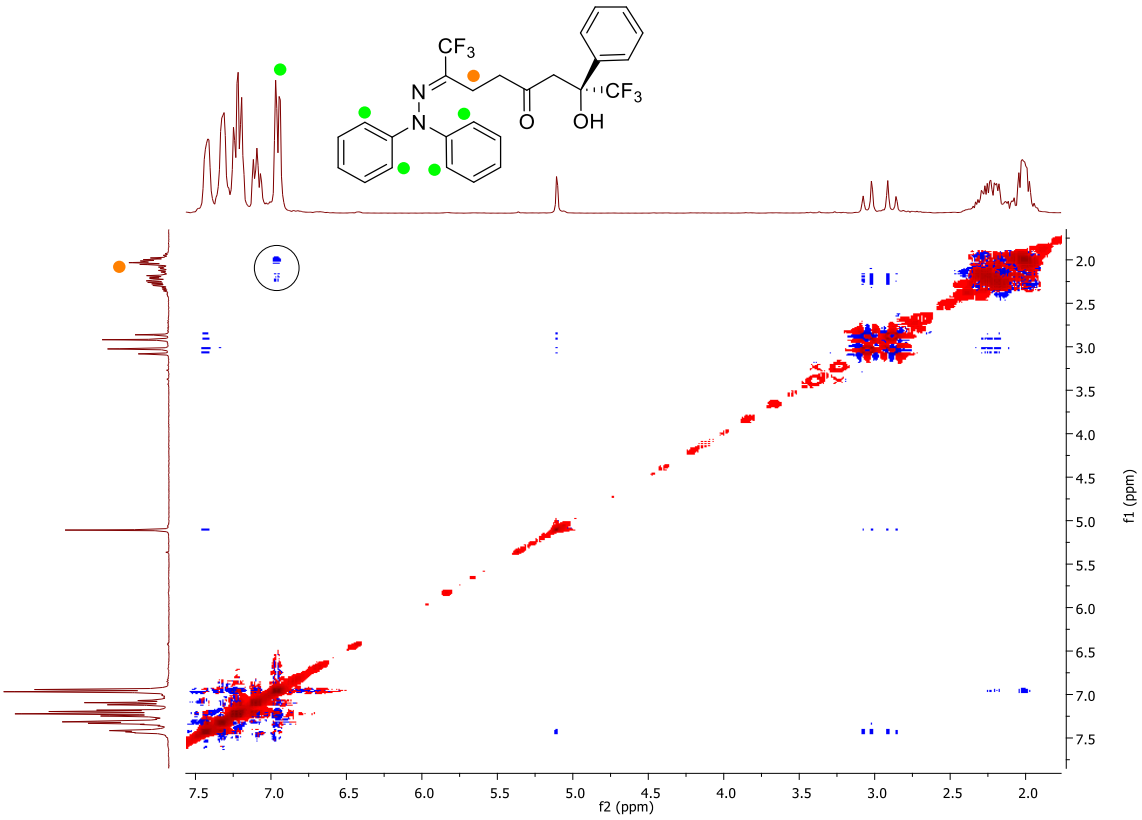
^{13}C NMR (126 MHz, $CDCl_3$) of (*E*)-(*S*)-**13**



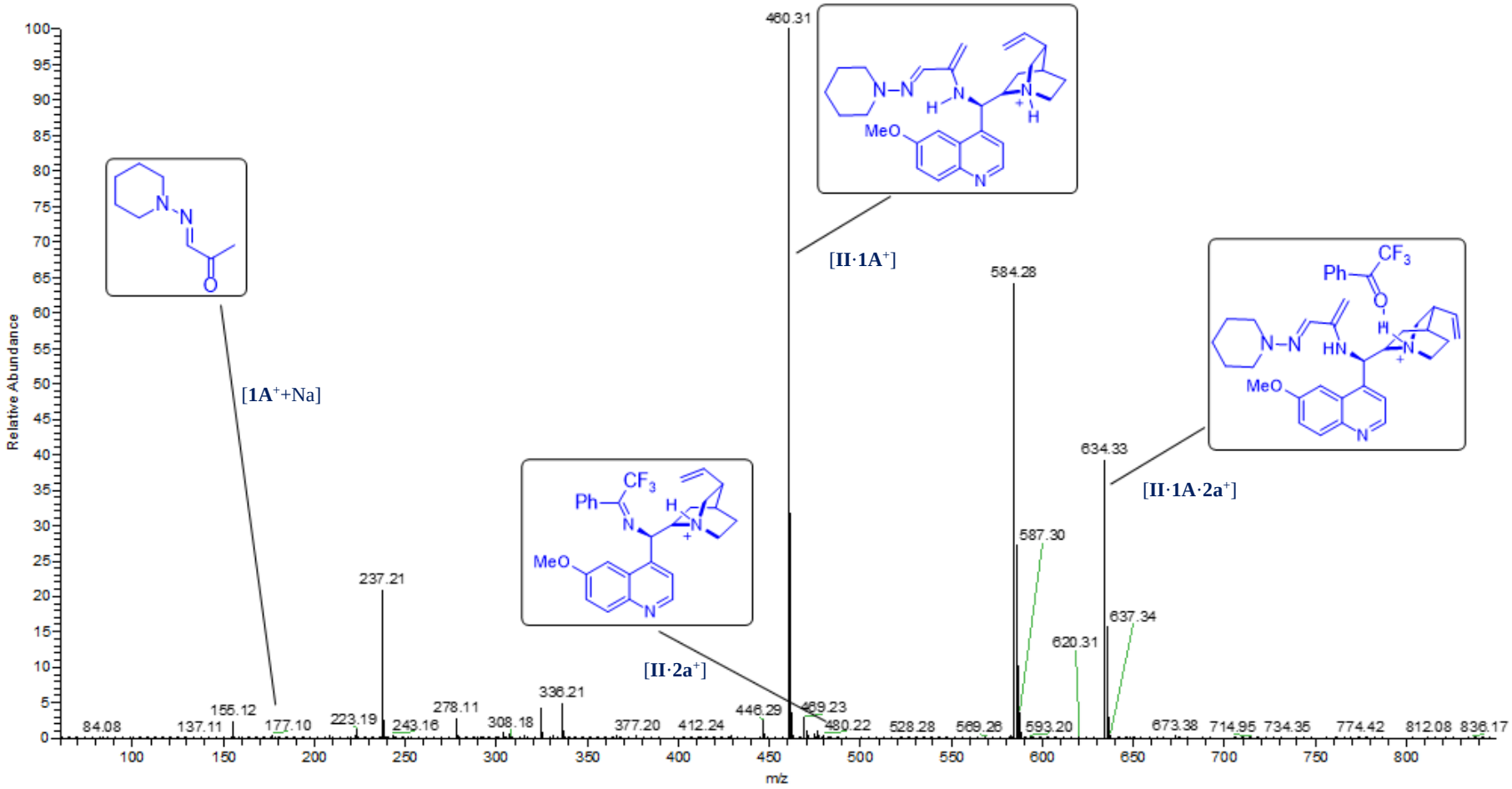
^{19}F NMR (471 MHz, $CDCl_3$) of (*E*)-(*S*)-**13**



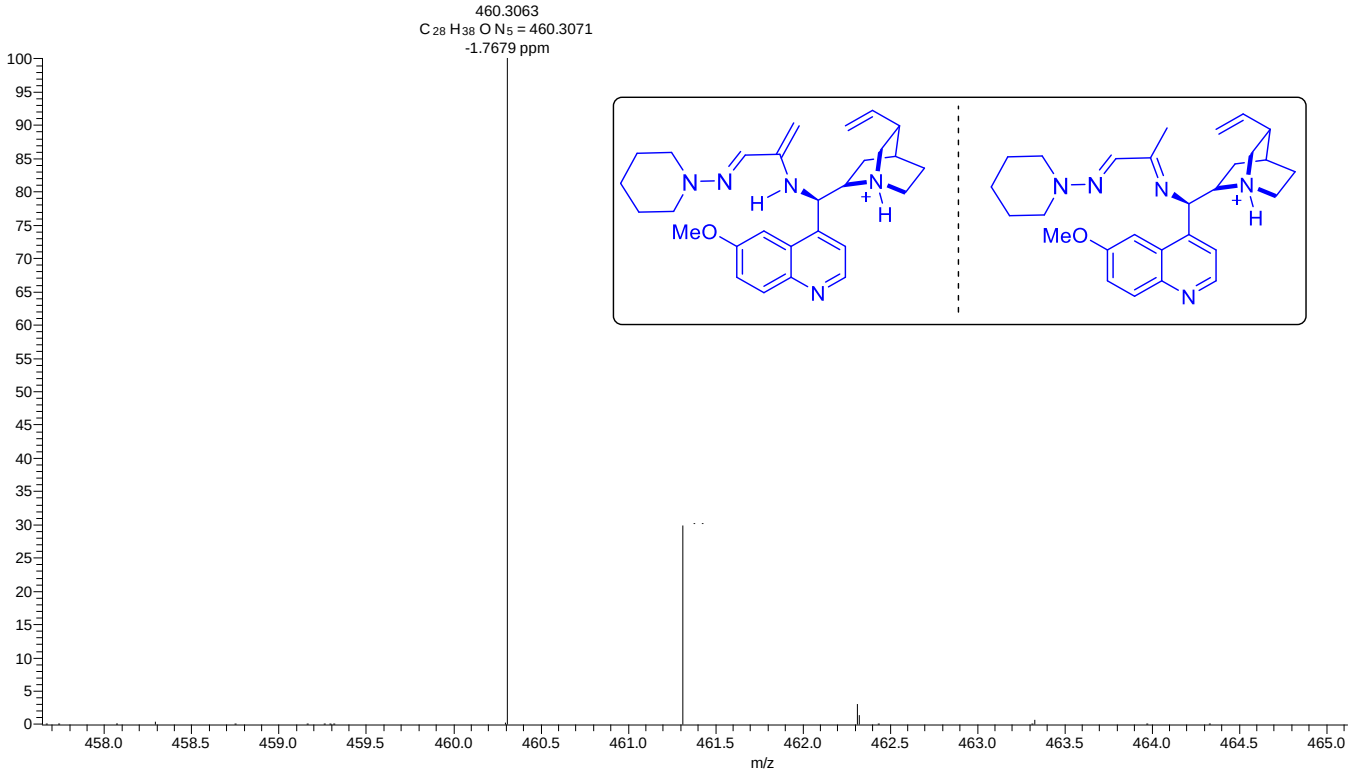
NOESY of (*E*)-(*S*)-**13**



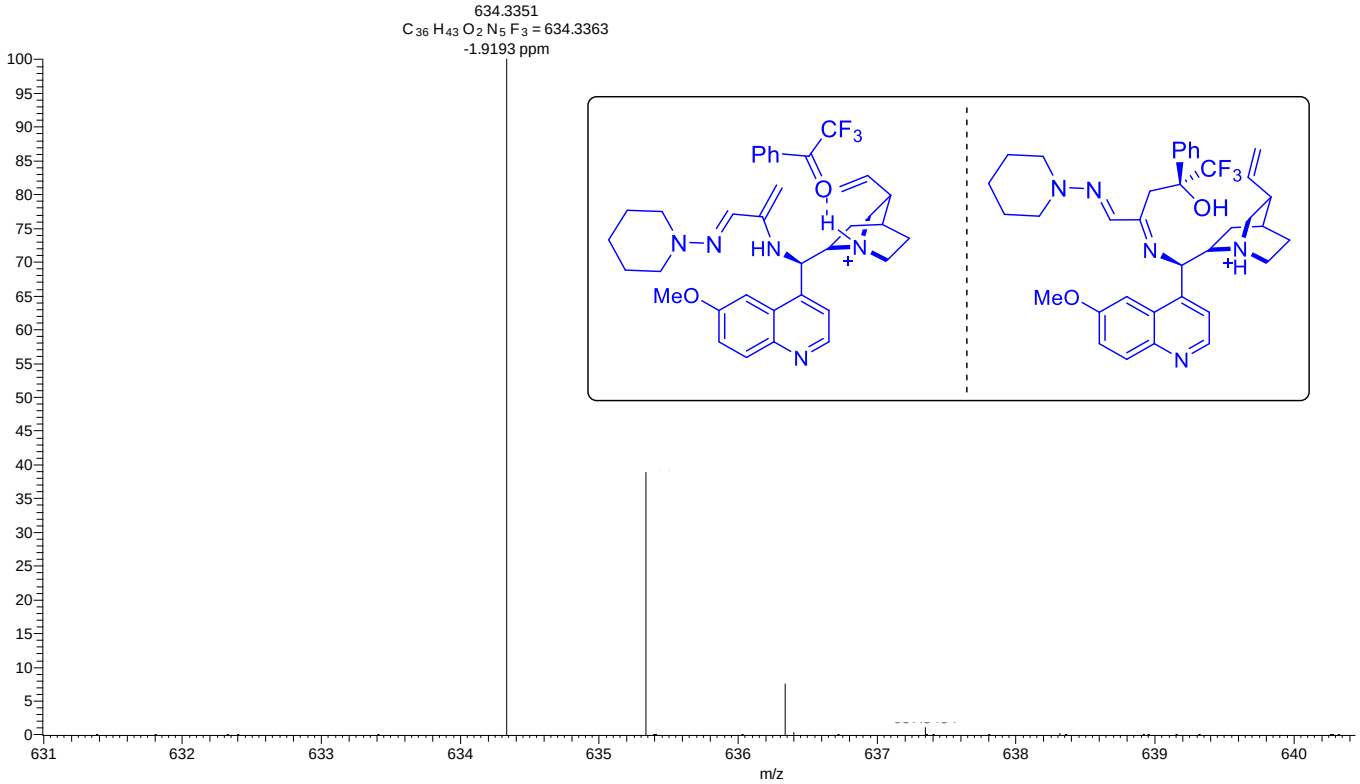
14. Mass spectra analysis



(+)-ESI-MS scan of the reaction between **1A** (0.2 mmol) and **2a** (0.1 mmol) in the presence of **II(SA)$_2$** (0.02 mmol) in toluene/H_2O 8:1 (1.0 M) at room temperature.



(+)-ESI-HRMS of [**II**·**1A**$^{+}$]



(+)-ESI-HRMS of [**II**·**1A**·**2a**$^{+}$]/[**II**·**3Aa**$^{+}$]