Supporting Information

An Asymmetric Aromatic Finkelstein Reaction: A Platform for Remote Diarylmethane Desymmetrization

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1. General Information

Room temperature is defined as 21–23 °C. The following reagents, $Cu(MeCN)_4BF_4$ (>98%, TCI America), Cs_2CO_3 (99.995%, Acros), K_3PO_4 (>98%, Sigma Aldrich), were purchased from the corresponding commercial suppliers and used as received unless stated otherwise. All other reagents were purchased from commercial suppliers and used without further purification, unless otherwise noted. Acetonitrile, *N*,*N*-dimethylformamide, dichloromethane, tetrahydrofuran, and toluene were obtained from a Seca Solvent System by GlassContour, in which the solvent was dried over alumina and dispensed under an atmosphere of Ar. All other solvents were purchased from commercial suppliers and used without further purification, unless otherwise noted.

Analytical Methods:

Thin-layer chromatography: Analytical thin-layer chromatography (TLC) was performed using EMD Millipore silica gel 60 F254 precoated plates (0.25 mm thickness) and developed plates were visualized under a UV lamp. R_f values are reported.

Column chromatography: Normal phase flash column chromatography was conducted on an automated Biotage® IsoleraTM One purification system equipped with a 10, 25, 50 or 100 g SNAP Ultra (HP Sphere, 25 µm silica) cartridge or using 60 Å Silica Gel (32–62 micron) with an appropriate mobile phase composition and gradient. Reversed phase flash column chromatography was performed using an automated Biotage® IsoleraTM One purification system equipped with a 12, 30, 60 or 120 g SNAP Ultra C18 cartridge. The desired fractions were analyzed by TLC or UPLC/MS, collected, and concentrated under reduced pressure to afford the product.

NMR: Routine ^{1}H NMR spectra were recorded on Agilent 400, 500, or 600 MHz spectrometers at ambient temperature unless otherwise stated. All NMR solvents were purchased from Cambridge Isotope Laboratories and used without further purification. Deuterated solvents were stored at ambient temperature and were used immediately after opening. Spectra were processed using MestReNova 14.2.0 using the automatic phasing and polynomial baseline correction capabilities. Splitting was determined using the automatic multiplet analysis function with manual intervention as necessary. Spectral data are reported as follows: chemical shift (multiplicity [singlet (s), broad singlet (brs), doublet (d), triplet (t), quartet (q), pentet (p), multiplet (m), doublet of doublets (dd), doublet of doublet of doublets (ddd), doublet of triplet of doublets (dtd), doublet of doublet of doublet of doublets (dddd), doublet of triplets (dt), triplet of doublets (td), etc.], coupling constant, integration). Chemical shifts are reported in ppm (δ), and coupling constants are reported in Hz. ^{1}H Resonances are referenced to solvent residual peaks for $CDCl_3$ (7.26 ppm), D_2O (4.79 ppm), or CD_3OD (3.31 ppm).[1] Routine ^{13}C NMR spectra were recorded on Agilent 400, 500, or 600 MHz spectrometers with protons fully decoupled. ^{13}C Resonances are reported in ppm relative to solvent residual peaks for $CDCl_3$ (77.2 ppm) or CD_3OD (49.0 ppm).[1] ^{19}F NMR spectra were obtained on Agilent 400 (376) MHz or 500 (471) MHz spectrometers without proton decoupling. ^{19}F data are reported as chemical shift, multiplicity, coupling constant (Hz) and integration (where applicable). Note: Small deviations in chemical shifts may be observed depending on the concentration of NMR samples.

IR: Infrared spectra were recorded on a Nicolet 6700 ATR/FT-IR spectrometer, and ν_{max} are partially reported in cm^{-1}.

Mass spectrometry: Ultra high-performance liquid chromatography/mass spectrometry (UPLC/MS) and low-resolution mass spectrometry (LRMS) were performed on a Waters Acquity SQD2 instrument equipped with an Ultra BEH C18 column (1.7 µm, 2.1 x 50 mm), a dual atmospheric pressure chemical ionization (API)/electrospray ionization (ESI) mass spectrometry detector and a photodiode array detector. High-resolution mass spectrometry (HRMS) was conducted by the Chemical and Biophysical Instrumentation Center (CBIC) at Yale University and was performed on a Waters Xevo Q-TOF high-resolution mass spectrometer using ESI.

Optical rotation: Optical rotations were recorded on an Autopol VI Automatic Polarimeter at the sodium D-line (589 nm), using a Type 40T TempTrolTM cell of 0.50 dm path length at 20 °C and reported as follows: [α]λ temp, enantiomeric ratio, concentration (c, in g/100 mL), and solvent.

Analytical HPLC: Analytical normal phase highperformance liquid chromatography (HPLC) was performed using an Agilent 1100 series instrument equipped with a photodiode array detector (210, 230, 254, and 280 nm) and chiral columns (5 µm, 4.6 x 250 mm) from Daicel Chemical Industries.

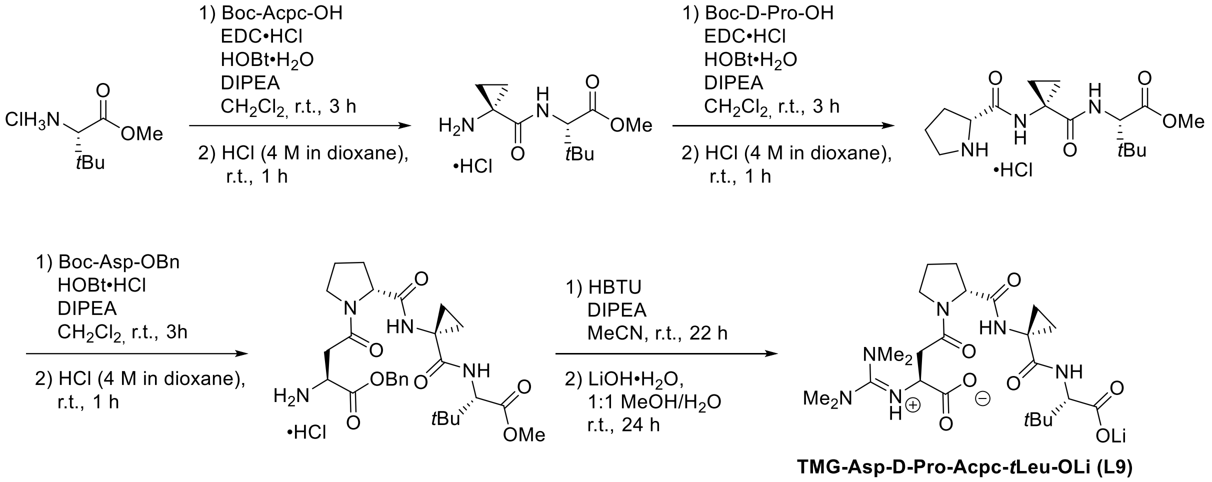
Abbreviations:

Acpc	1-Aminocyclopropane-1-carboxylic acid
Aib	*α*-Aminoisobutyric acid
Asp	Aspartic acid
Boc	*t*-Butoxycarbonyl
$CDCl_3$	Chloroform-*d*
CD_3CN	Acetonitrile-d_3
Chg	Cyclohexylglycine
CV	Column volume
DCM	Dichloromethane
DIPEA	*N*,*N*-Diisopropylethylamine
DMF	*N*,*N*’-dimethylformamide
EDC	*N*-(3-Dimethylaminopropyl)-*N′*-ethylcarbodiimide
er	Enantiomeric ratio
equiv.	Equivalents
EtOAc	Ethyl acetate
h	Hours
HATU	Hexafluorophosphate azabenzotriazole tetramethyl uronium
Hex	Hexanes
HOBt	1-Hydroxybenzotriazole
HPLC	High-performance liquid chromatography
HRMS	High-resolution mass spectrometry
IPA	Isopropyl alcohol
LCMS	Liquid chromatography mass spectrometry
Leu	Leucine
t-Leu	*t*-Leucine
NaI	1-Naphtylalanine

NBS	*N*-Bromosuccinimide
Neo	*Neo*-pentylalanine
NMR	Nuclear magnetic resonance
Phe	Phenylalanine
Pro	Proline
r.t.	Room temeperature
TFA	Trifluoroacetic acid, trifluoroacetate
THF	Tetrahydrofuran
TLC	Thin-layer chromatography
TMG	Tetramethylguanidine
Tol	Toluene
Val	Valine

2. Catalyst Synthesis and Characterization

2.1. Representative Synthetic Procedure for TMG-Peptides



Scheme S1: Representative synthetic route for the preparation of TMG-Asp-^{D}Pro-Acpc-*t*Leu-OLi (L9).

Peptide Coupling #1

A round bottom flask with stir bar was charged with H-*t*Leu-OMe • HCl (1.82 g. 10.0 mmol, 1.00 equiv.), Boc-Acpc-OH (2.01 g, 10.0 mmol, 1.00 equiv.), EDC • HCl (2.11 g, 11.0 mmol, 1.10 equiv.) and HOBt • H_2O (1.68 g, 11.0 mmol, 1.10 equiv.), before CH_2Cl_2 (50 mL) was added. After addition of DIPEA (3.74 mL, 22.0 mmol, 2.20 equiv.), the reaction mixture was stirred at r.t. for 3 h. The reaction was washed with 10% citric acid (aq.) (2x) and sat. $NaHCO_3$ (aq.) (2x). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo* and the crude peptide (Boc-Acpc-*t*Leu-OMe) was used in the next step without further purification.

Boc Deprotection #1

Crude Boc-Acpc-*t*Leu-OMe (assumed 10.0 mmol, 1.00 equiv.) was treated with HCl solution (4 M in 1,4-dioxane, 12.0 mL, 50.0 mmol, 5.00 equiv.) and the resulting mixture was stirred at r.t. for 1 h. Concentration *in vacuo* and co-evaporation with CH_2Cl_2 (3x) yielded an off-white foam, which was used in the next step without further purification.

Peptide Coupling #2

A round bottom flask with stir bar was charged with crude H-Acpc-*t*Leu-OMe (assumed 10.0 mmol, 1.00 equiv.), Boc-^{D}Pro-OH (2.37 g, 11.0 mmol, 1.10 equiv.), EDC • HCl (2.11 g, 11.0 mmol, 1.10 equiv.) and HOBt • H_2O (1.68 g, 11.0 mmol, 1.10 equiv.), before CH_2Cl_2 (50 mL) was added. After addition of DIPEA (3.74 mL, 22.0 mmol, 2.20 equiv.), the reaction mixture was stirred at r.t. for 3 h. The reaction was washed with 10% citric acid (aq.) (2x) and sat. $NaHCO_3$ (aq.) (2x). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo* and the crude peptide (Boc-D-Pro-Acpc-*t*Leu-OMe) was used in the next step without further purification.

Boc Deprotection #2

Crude Boc-^{D}Pro-Acpc-*t*Leu-OMe (assumed 10.0 mmol, 1.00 equiv.) was treated with HCl solution (4 M in 1,4-dioxane, 12.0 mL, 50.0 mmol, 5.00 equiv.) and the resulting mixture was stirred at r.t. for 1 h. Concentration *in vacuo* and co-evaporation with CH_2Cl_2 (3x) yielded an off-white foam, which was used in the next step without further purification.

Peptide Coupling #3

A round bottom flask with stir bar was charged with crude H-^{D}Pro-Acpc-*t*Leu-OMe (assumed 10.0 mmol, 1.00 equiv.), Boc-Asp-OBzl (3.56 g, 11.0 mmol, 1.10 equiv.), EDC • HCl (2.11 g, 11.0 mmol, 1.10 equiv.) and HOBt • H_2O (1.68 g, 11.0 mmol, 1.10 equiv.), before CH_2Cl_2 (50 mL) was added. After addition of DIPEA (3.74 mL, 22.0 mmol, 2.20 equiv.), the reaction mixture was stirred at r.t. for 3 h. The reaction was washed with 10% citric acid (aq.) (2x) and sat. $NaHCO_3$ (aq.) (2x). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo* and the crude material was purified by automated reverse phase chromatography (Biotage, SNAP Ultra C18 120 g, gradient MeCN in H_2O: 1 CV: 0-10%; 15 CV: 10-60% 1 CV: 60-100%) to give Boc-Asp(OBn)-^{D}Pro-Acpc-*t*Leu-OMe as a white foam (2.00 g).

Boc Deprotection #3

Boc-Asp(OBn)-^{D}Pro-Acpc-*t*Leu-OMe (2.00 g, 3.17 mmol, 1.00 equiv.) was treated with HCl solution (4 M in 1,4-dioxane, 3.98 mL, 15.9 mmol, 5.00 equiv.) and a minimal amount of CH_2Cl_2 and the resulting mixture was stirred at r.t. for 2 h. Concentration *in vacuo* and co-evaporation with CH_2Cl_2 (3x) yielded an off-white foam, which was used in the next step without further purification.

Guanidinylation

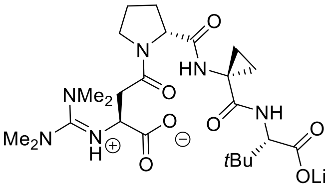
In a round bottom flask with stir bar crude H-Asp(OBn)-^{D}Pro-Acpc-*t*Leu-OMe (assumed 3.17 mmol, 1.00 equiv.) was dissolved in MeCN (32 mL). Following addition of HBTU (1.98 g, 5.22 mmol, 1.65 equiv.) and Et_3N (2.20 mL, 15.9 mmol, 5.00 equiv.), the reaction mixture was stirred at r.t. for 22 h. The reaction was diluted with CH_2Cl_2, washed with sat. $NaHCO_3$ (aq.) (2x) and 10% citric acid (aq.) (2x). The organic layer was dried over $NaSO_4$ and concentrated *in vacuo* and the crude material was purified by automated reverse phase chromatography (Biotage, SNAP Ultra C18 120 g, gradient MeCN in H_2O: 16 CV: 0-45%) to give TMG-Asp(OBn)-^{D}Pro-Acpc-*t*Leu-OMe • PF_6 as a white foam (1.10 g).

Ester Hydrolysis

TMG-Asp(OBn)-^{D}Pro-Acpc-*t*Leu-OMe (1.10 g, 1.42 mmol, 1.00 equiv.) was dissolved in 1:1 MeOH/H_2O (14 mL) and LiOH • H_2O (0.13 g, 3.12 mmol, 2.20 mmol) was added. The reaction mixture was stirred at r.t. for 24 h before being concentrated and purified by automated reverse phase chromatography (Biotage, SNAP Ultra C18 120 g, gradient MeCN in H_2O: 2 CV: 0%; 13 CV: 0-27%) to give TMG-Asp-^{D}Pro-Acpc-*t*Leu-OLi as a white foam.

2.2. Characterization of TMG-Peptides

The following TMG-peptides were reported previously: TMG-Asp-^{D}Pro-Aib-OLi (**L1**)[2], TMG-Gly-OLi (**L2**)[2], TMG-^{D}Asp-αMePro-OLi (**L6**)[3], TMG-Asp-^{D}Pro-Acpc-OLi (**L7**)[4], TMG-Asp-^{D}Pro-Aib-Val-OLi (**L14**)[5], TMG-Asp-^{D}Pro-Aib-^{D}Leu-OLi (**L15**)[4].



TMG-Asp-^{D}Pro-Acpc-*t*Leu-OLi (L10) was prepared according to the Representative Synthetic Procedure for TMG-Peptides and obtained as a white foam (0.53 g, 1.00 mmol, 10% over 8 steps).

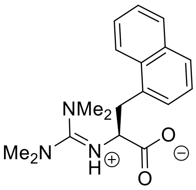
^{1}H NMR (400 MHz, CD_3OD) δ 4.35 (dd, *J* = 8.5, 4.5 Hz, 1H), 4.22 (dd, *J* = 9.4, 3.5 Hz, 1H), 4.09 (s, 1H), 3.75 – 3.67 (m, 1H), 3.64 – 3.54 (m, 1H), 3.06 – 2.79 (m, 14H), 2.41 – 2.26 (m, 1H), 2.18 – 1.89 (m, 3H), 1.55 (ddd, *J* = 11.1, 7.3, 3.8 Hz, 1H), 1.32 – 1.24 (m, 1H), 1.13 – 0.92 (m, 11H).

^{13}C NMR (101 MHz, CD_3OD) δ 177.2, 176.9, 176.0, 172.5, 171.4, 163.8, 64.7, 61.6, 57.9, 48.7, 40.1, 38.3, 35.8, 31.1, 27.7, 27. 7, 25.8, 17.3, 16.6.

HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{24}H_{40}N_6O_7 + H]^+$; requires m/z = 525.3031, found m/z = 525.3037.

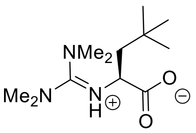
IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3397(bm), 3261(bm), 2965(w), 2910(bw), 1605(bs), 1526(m), 1405(s), 1309(m), 1234(w), 1206(w), 1168(w), 1069(w), 1035(w), 841(s), 557(s).

Optical: $[\alpha]_D^{20}$ = +49.9 (*c* = 1.0, MeOH).



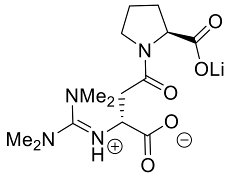
TMG-1NaI-OH (L3) was prepared according to the Representative Synthetic Procedure for TMG-Peptides and obtained as a white foam**.**

LRMS (ESI): Exact mass calculated for $[C_{18}H_{23}N_3O_2 + H]^+$; requires m/z = 314.19, found m/z = 314.82.



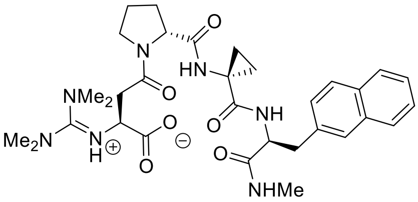
TMG-Neo-OH (L4) was prepared according to the Representative Synthetic Procedure for TMG-Peptides and obtained as a white foam**.**

LRMS (ESI): Exact mass calculated for $[C_{12}H_{25}N_3O_2 + H]^+$; requires m/z = 244.20, found m/z = 244.34.



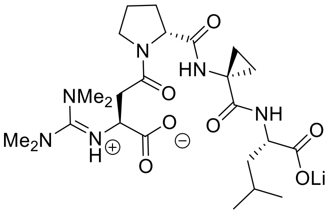
TMG-ᴰAsp-Pro-OLi (L5) was prepared according to the Representative Synthetic Procedure for TMG-Peptides and obtained as a white foam**.**

LRMS (ESI): Exact mass calculated for $[C_{14}H_{24}N_4O_5 + H]^+$; requires m/z = 329.18, found m/z = 329.41.



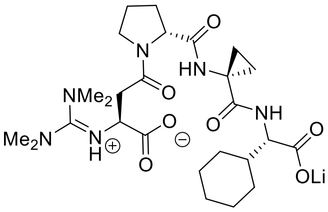
TMG-Asp-ᴰPro-Acpc-2NaI-NHMe (L8) was prepared according to the Representative Synthetic Procedure for TMG-Peptides and obtained as a white foam**.**

LRMS (ESI): Exact mass calculated for $[C_{32}H_{44}N_7O_6 + H]^+$; requires m/z = 622.33, found m/z = 622.71.



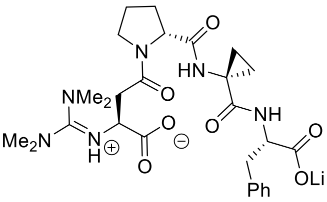
TMG-Asp-ᴰPro-Acpc-Leu-OLi (L9) was prepared according to the Representative Synthetic Procedure for TMG-Peptides and obtained as a white foam**.**

LRMS (ESI): Exact mass calculated for $[C_{24}H_{40}N_6O_7 + H]^+$; requires m/z = 525.30, found m/z = 525.51.



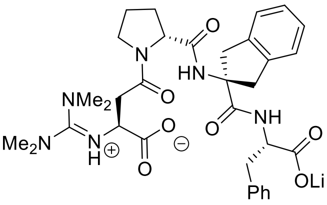
TMG-Asp-ᴰPro-Acpc-Chg-OLi (L11) was prepared according to the Representative Synthetic Procedure for TMG-Peptides and obtained as a white foam**.**

LRMS (ESI): Exact mass calculated for $[C_{26}H_{42}N_6O_7 + H]^+$; requires m/z = 551.32, found m/z = 551.50.



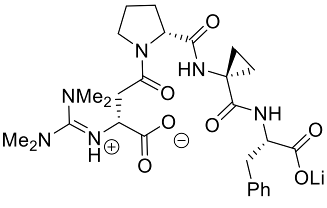
TMG-Asp-^{D}Pro-Acpc-Phe-OLi (L12) was prepared according to the Representative Synthetic Procedure for TMG-Peptides and obtained as a white foam**.**

LRMS (ESI): Exact mass calculated for $[C_{27}H_{38}N_6O_7 + H]^+$; requires m/z = 559.29, found m/z = 559.48.



TMG-Asp-^{D}Pro-Aic-Phe-OLi (L13) was prepared according to the Representative Synthetic Procedure for TMG-Peptides and obtained as a white foam**.**

LRMS (ESI): Exact mass calculated for $[C_{33}H_{42}N_6O_7 + H]^+$; requires m/z = 635.31, found m/z = 636.02.



TMG-^{D}Asp-^{D}Pro-Acpc-Phe-OLi (L16) was prepared according to the Representative Synthetic Procedure for TMG-Peptides and obtained as a white foam**.**

LRMS (ESI): Exact mass calculated for $[C_{27}H_{38}N_6O_7 + H]^+$; requires m/z = 559.29, found m/z = 559.48.

3. Synthesis and Characterization of Starting Materials

The following diarylmethines have been reported previously and were prepared according to literature procedures:

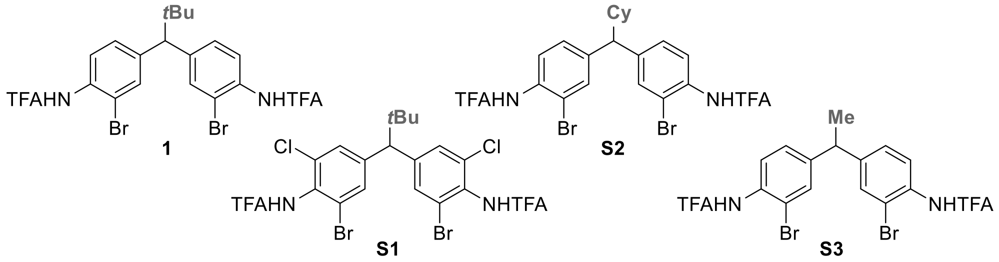
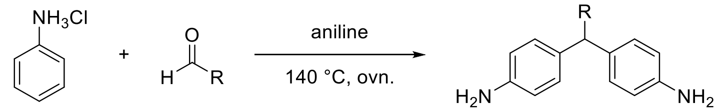
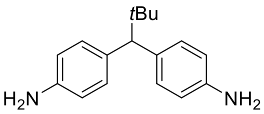


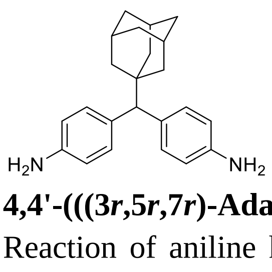
Figure S1: Previously prepared diarylmethines **1**[2], **S1**[2], **S2**[2], **S3**[2].



General Procedure A (GP A) for the synthesis of bis-amino diarylmethines:
A pressure tube equipped with a stir bar was charged with aniline hydrochloride (1.00 equiv.). Subsequently, aniline (3.00 equiv.) and the respective aldehyde (1.00 equiv.) were added, the tube was sealed and heated at 140 °C for 16-20 h. The reaction was cooled to r.t., diluted with CH_2Cl_2 and 5 M NaOH (aq.) was carefully added. The aqueous layer was extracted with CH_2Cl_2 (3x) and the combined organic layers were dried over $MgSO_4$, before being concentrated *in vacuo*. The crude material was purified by column chromatography (SiO_2, hexanes/EtOAc).



4,4'-(2,2-Dimethylpropane-1,1-diyl)dianiline (S4) was prepared following **GP A**. Reaction of aniline hydrochloride (2.59 g, 20.0 mmol, 1.00 equiv.) with aniline (5.43 mL, 60.0 mmol, 3.00 equiv.) and pivaldehyde (2.17 mL, 20.0 mmol, 1.00 equiv.) followed by purification via column chromatography (SiO_2, hexanes/EtOAc 1:1 → 0:1) yielded **S4** as a light-brown foam (3.32 g, 13.1 mmol, 65%). Analytical data are in agreement with literature.[2]
R_F: 0.60 (EtOAc)
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, J = 8.4 Hz, 4H), 6.59 (d, J = 8.4 Hz, 4H), 3.50 (s, 4H), 0.98 (s, 9H).
HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{17}H_{22}N_2 + H]^+$; requires m/z = 255.1864. Found 255.1861.



4,4'-(((3*r*,5*r*,7*r*)-Adamantan-1-yl)methylene)dianiline (S5) was prepared following **GP A**. Reaction of aniline hydrochloride (803 mg, 6.20 mmol, 1.00 equiv.) with aniline (1.69 mL, 18.6 mmol, 3.00 equiv.) and adamantane-1-carbaldehyde (1.02 mL, 6.20 mmol, 1.00 equiv.)

followed by purification via column chromatography (SiO_2, hexanes/EtOAc 8:2 → 6:4) yielded **S5** as a maroon solid (1.02 g, 3.07 mmol, 50%).

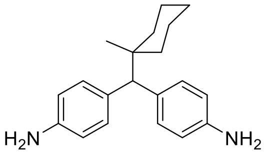
R$_F$: 0.34 (hexanes/EtOAc 6:4)

^{1}H NMR (400 MHz, d^6-DMSO) δ 7.02 (d, *J* = 8.2 Hz, 4H), 6.45 (d, *J* = 8.2 Hz, 4H), 4.80 (bs, 4H), 3.11 (s, 1H), 1.87 (bs, 3H), 1.66–1.38 (m, 12H).

^{13}C NMR (101 MHz, d^6-DMSO) δ 146.3, 130.2, 130.1, 113.4, 63.8, 40.6, 36.6, 36.2, 28.2.

HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{23}H_{28}N_2 + H]^+$; requires m/z = 333.2325. Found 333.2310 (ESI+).

IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3428(w), 3347(w), 2897(s), 2845(s), 1612(s), 1508(s), 1445(m), 1269(s), 1179(m), 1128(m), 1105(m), 978(w), 814(s), 518(s).



4,4'-((1-Methylcyclohexyl)methylene)dianiline (S6) was prepared following **GP A**. Reaction of aniline hydrochloride (972 mg, 7.50 mmol, 1.00 equiv.) with aniline (2.03 mL, 22.5 mmol, 3.00 equiv.) and 1-methylcyclohexyl carbaldehyde (1.04 mL, 7.50 mmol, 1.00 equiv.) followed by purification via automated column chromatography (Biotage, SNAP Ultra 100 g, gradient EtOAc in hexanes: 10 CV: 20-100%; 13 CV: 100%) yielded **S6** as a brown foam (996 mg, 3.36 mmol, 48%).

R$_F$: 0.64 (EtOAc)

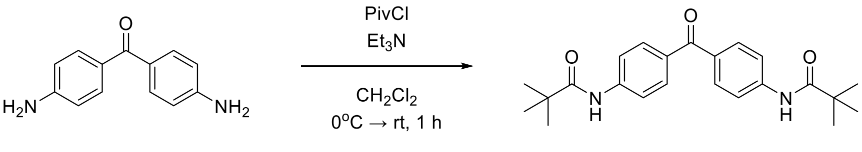
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (d, *J* = 8.4 Hz, 4H), 6.59 (d, *J* = 8.4 Hz, 4H), 3.59 (s, 1H), 3.49 (s, 4H), 1.52 (d, *J* = 10.6 Hz, 3H), 1.43 – 1.25 (m, 6H), 1.26 – 1.12 (m, 1H), 1.04 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 144.1, 133.5, 130.9, 114.9, 53.6, 37.5, 37.2, 26.3, 22.2, 21.5.

HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{20}H_{26}N_2 + H]^+$; requires m/z = 295.2169, found m/z = 295.2149.

IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3345(bw), 3214(w), 2973(w), 2922(m), 2859(m), 1734(m), 1617(s), 1510(s), 1449(m), 1376(w), 1273(s), 1215(m), 1180(bs), 1132(s), 1052(w), 902(w), 748(s), 667(s).

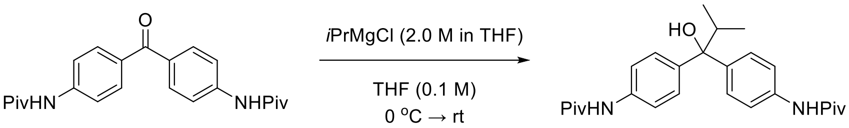
N,*N*'-(Carbonylbis(4,1-phenylene))bis(2,2-dimethylpropanamide) (S7)



A 500 mL round-bottom flask equipped with a stir bar was charged with 4,4’-diaminobenzophenone (5.31 g, 25.0 mmol, 1.00 equiv) and CH_2Cl_2 (125 mL, 0.20 M). The resulting tan suspension was immersed in an ice bath followed by the addition of triethylamine (10.5 mL, 75.0 mmol, 3.00 equiv) and dropwise addition of pivaloyl chloride (6.70 mL, 55.0 mmol, 2.20 equiv). The ice bath was removed, and the reaction mixture was vigorously stirred at room temperature for 1 h. Upon completion, the suspension was diluted with water

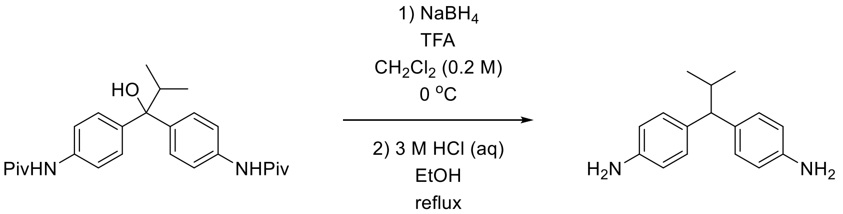
(125 mL) and filtered. The filter cake was washed with water and dried under reduced pressure to yield **S7** as a white solid (8.60 g, 22.6 mmol, 90% yield).
R$_F$: 0.41 (hexanes/EtOAc 6:4)
^{1}H NMR (400 MHz, *d$_6$*-DMSO) δ 9.55 (s, 2H), 7.86 (d, *J* = 8.7 Hz, 4H), 7.69 (d, *J* = 8.7 Hz, 4H), 1.25 (s, 18H).
^{13}C NMR (101 MHz, *d$_6$*-DMSO) δ 193.6, 177.0, 143.3, 131.8, 130.6, 119.1, 39.5, 27.1.
HRMS: Exact mass calculated for $[C_{23}H_{28}N_2O_3 + H]^+$; requires m/z = 381.2173. Found 381.2169 (ESI+).
IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3296(w), 2972(w), 1661(s), 1645(s), 1589(s), 1516(s), 1400(m), 1309(s), 1282(s), 1246(m), 1166(s), 937(s), 860(s), 762(s), 685(s), 637(s), 509(m).

***N,N'*-((1-Hydroxy-2-methylpropane-1,1-diyl)bis(4,1-phenylene))bis(2,2-dimethylpropanamide) (S8)**



A flame dried 250 mL round-bottom flask equipped with a stir bar was charged with **S7** (3.81 g, 10.0 mmol, 1.00 equiv). The flask was evacuated and backfilled with N_2 (3x) and THF (100 mL, 0.1 M) was added. The resulting white suspension was immersed in an ice bath followed by the dropwise addition of isopropylmagnesium chloride (2 M in THF, 20 mL, 40 mmol, 4.00 equiv.). The dark green reaction mixture was vigorously stirred and allowed to gradually warm to room temperature overnight. After 20 h, the light green suspension was quenched with 10% aqueous (w/v) citric acid solution (100 mL), diluted with EtOAc (100 mL) and transferred to a separatory funnel. The layers were partitioned, and the aqueous layer was extracted with EtOAc (2 x 100 mL). The combined organic layers were washed with Brine (100 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford crude **S5** as a neon yellow foam. The residue was purified by column chromatography (SiO_2, EtOAc/Hexanes 7:3 → 6:4) to afford **S8** as a yellow foam (2.50 g, 5.90 mmol, 59% yield).
R*$_f$*: 0.38 (hexanes/EtOAc 6:4)
^{1}H NMR (400 MHz, *d$_6$*-DMSO) δ 9.09 (s, 1H), 7.49 (d, *J* = 8.8 Hz, 4H), 7.38 (d, *J* = 8.8 Hz, 4H), 5.02 (s, 1H), 2.82 (hept, *J* = 6.6 Hz, 1H), 1.19 (s, 18H), 0.76 (d, *J* = 6.6 Hz, 6H).
^{13}C NMR (101 MHz, *d$_6$*-DMSO) δ 176.2, 143.0, 137.0, 125.7, 119.5, 78.9, 39.0, 34.6, 27.2, 17.2.
HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{26}H_{36}N_2O_3 + H]^+$; requires m/z = 425.2799, found m/z = 425.2806.
IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3331(w), 2965(w), 1657(s), 1599(s), 1523(s), 1402(s), 1319(m), 1175(m), 833(m), 735(m), 704(m).

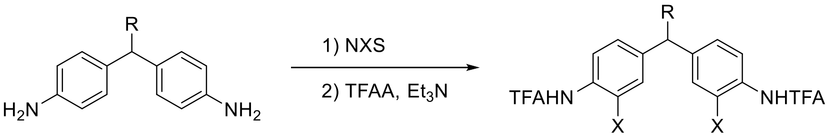
4,4'-(2-Methylpropane-1,1-diyl)dianiline (S9)

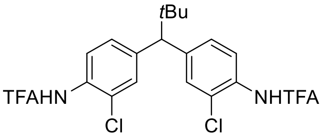


A 250 mL round-bottom flask equipped with a stir bar was charged with **S8** (2.55 g, 6.00 mmol, 1.00 equiv) and CH_2Cl_2 (30 mL, 0.2 M). The resulting yellow suspension was immersed in an ice bath followed by the addition of sodium hydride (2.27 g, 60.0 mmol, 10.0 equiv). To the reaction mixture was then added trifluoroacetic acid (60 mL) dropwise via an addition funnel over 40 min (Caution: Aggressive effervescence observed upon addition). The dark yellow suspension was vigorously stirred at 0 °C for 3 h after which, the reaction was diluted with CH_2Cl_2 (~170 mL), quenched with 5 M aqueous NaOH (~200 mL), and transferred to a separatory funnel. The layers were partitioned and the aqueous layer was extracted with CH_2Cl_2 (2 x 100 mL). The combined organic layers were washed with Brine (100 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford a white solid which was carried forward without further purification assuming 100% conversion.

A 1 L recovery flask was charged with the crude material (6.00 mmol), 3 M aqueous HCl (90.0 mL, 270 mmol, 24.0 equiv) and EtOH (150 mL). The resulting white suspension was immersed in a pre-heated 85 °C oil bath and vigorously stirred for 3 days. Upon completion, the light-yellow solution was diluted with CH_2Cl_2 (200 mL), quenched with 5 M aqueous NaOH (100 mL), and transferred to a separatory funnel. The layers were partitioned, and the aqueous layer was extracted with CH_2Cl_2 (2 x 100 mL). The combined organic layers were washed with Brine (100 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to afford crude CH_2Cl_2 as a brown solid, which was purified by automated reverse-phase column chromatography (Biotage, SNAP C18 Ultra 12 g, gradient MeCN in H_2O (with 0.1% formic acid buffer): 2 CV: 0%; 2 CV: 0-49%; 1 CV: 50%; 1 CV: 50-100%; 1.5 CV: 100%). The product was obtained as a tan solid (purity ~90%, 728 mg, 3.03 mmol, 51% yield over two steps) and used in the next step.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.02 (d, *J* = 8.4 Hz, 4H), 6.58 (d, *J* = 8.3, 4H), 3.51 (bs, 4H), 3.19 (d, *J* = 10.6 Hz, 1H), 2.41–2.25 (m, 1H), 0.85 (d, *J* = 6.5 Hz, 6H).





***N,N'*-((2,2-Dimethylpropane-1,1-diyl)bis(2-chloro-4,1-phenylene))bis(2,2,2-trifluoroacetamide) (10)**

In a round-bottom flask **S4** (1.48 g, 5.80 mmol, 1.00 equiv.) was dissolved in MeCN (30 mL). *N*-Chlorosuccinimide (1.55 g, 11.6 mmol, 2.00 equiv.) was added and the mixture was heated at 45 °C for 5 h. After cooling to r.t. the mixture was washed with sat. NaCl (aq.), dried over $MgSO_4$ and concentrated. The crude material was dissolved in CH_2Cl_2 (15 mL) and cooled to 0 °C. After slow addition of triethylamine (1.94 mL, 13.9 mmol, 2.40 equiv.) and TFAA (1.77 mL, 12.8 mmol, 2.20 equiv.), the mixture was stirred at r.t. for 3 h. The reaction was washed with sat. NaCl (aq.), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by automated column chromatography (Biotage, SNAP Ultra 100 g, gradient EtOAc in hexanes: 10 CV: 0-20%) yielded **10** as an orange foam (815 mg, 1.58 mmol, 27% over 2 steps).

R_F: 0.57 (hexanes/EtOAc 8:2)

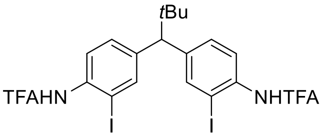
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 2H), 8.26 (d, *J* = 8.6 Hz, 2H), 7.42 (d, *J* = 2.1 Hz, 2H), 7.38 (dd, *J* = 8.6, 2.1 Hz, 2H), 3.67 (s, 1H), 1.03 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 141.1, 130.5, 130.3, 129.1, 123.4, 121.4, 62.7, 35.3, 29.0 (C_{CO} and C_{CF3} disguised).

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.86.

HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{21}H_{18}Cl_2F_6N_2O_2 - H]^-$; requires m/z = 513.0577, found m/z = 513.0604.

IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3401(w), 3304(bw), 2963(w), 2909(w), 2873(w), 1734(s), 1586(m), 1530(s), 1478(m), 1407(m), 1287(s), 1192(bs), 1136(bs), 1052(s), 902(s), 831(m), 736(s), 601(bm



_N,N'_-((2,2-Dimethylpropane-1,1-diyl)bis(2-iodo-4,1-phenylene))bis(2,2,2-trifluoroacetamide) (3)

In a round-bottom flask **S4** (254 mg, 1.00 mmol, 1.00 equiv.) was dissolved in MeCN (5 mL) and cooled to 0 °C. *N*-Iodosuccinimide (450 mg, 2.00 mmol, 2.00 equiv.) was added and the mixture was stirred at r.t. for 17 h. The mixture was washed with sat. NaCl (aq.), the aqueous layer extracted with CH_2Cl_2 (3x), dried over $MgSO_4$ and concentrated. The crude material was filtered through a plug of SiO_2, eluted with EtOAc and concentrated. The crude material was dissolved in CH_2Cl_2 (5 mL) and cooled to 0 °C. After slow addition of triethylamine (0.33 mL, 2.40 mmol, 2.40 equiv.) and TFAA (0.31 mL, 2.20 mmol, 2.20 equiv.), the mixture was stirred at r.t. for 3 h. The reaction was washed with sat. NaCl (aq.), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (SiO_2, hexanes/EtOAc 1:0 → 8:2) yielded **3** as a yellow solid (108 mg, 0.15 mmol, 15% over 2 steps).

R_F: 0.63 (hexanes/EtOAc 8:2)

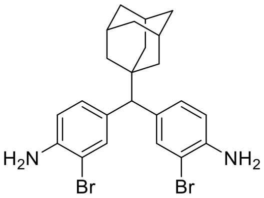
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 2H), 8.14 (d, *J* = 8.6 Hz, 2H), 7.79 (d, *J* = 2.1 Hz, 2H), 7.47 (dd, *J* = 8.6, 2.1 Hz, 2H), 3.61 (s, 1H), 1.02 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 154.9 (q, *J* = 37.7 Hz), 142.2, 140.3, 134.3, 130.5, 121.7, 115.7 (q, *J* = 288.8 Hz), 90.3, 62.4, 35.5, 29.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.83.

HRMS (ESI/Q-TOF): Exact mass calculated for [$C_{21}H_{18}I_2F_6N_2O_2$ – H]$^-$; requires m/z = 696.9289, found m/z = 696.9259.

IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3357(w), 3297(bw), 2964(w), 2905(w), 2870(w), 1728(s), 1574(m), 1525(s), 1285(s), 1188(bs), 1154(bs), 1036(m), 901(m), 831(m), 757(m), 734(m).



4,4'-(((3*r*,5*r*,7*r*)-Adamantan-1-yl)methylene)bis(2-bromoaniline) (S10)

In a round-bottom flask **S5** (831 mg, 2.50 mmol, 1.00 equiv.) was dissolved in CH_2Cl_2 (10 mL) and cooled to 0 °C. *N*-Bromosuccinimide (890 mg, 5.00 mmol, 2.00 equiv.) was added and the mixture was stirred at r.t. for 1 h. The mixture was washed with sat. NaCl (aq.), dried over $MgSO_4$ and concentrated. Purification by column chromatography (SiO_2, EtOAc/Hexanes 9:1 → 8:2) yielded **S10** as a brown foam (686 mg, 1.40 mmol, 56% yield).

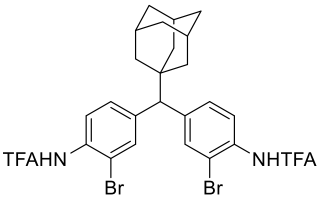
R$_F$: 0.43 (hexanes/EtOAc 8:2)

^{1}H NMR (400 MHz, *d$_6$*-DMSO) δ: 7.26 (d, *J* = 2.0 Hz, 2H), 7.13 (dd, *J* = 8.3, 2.1 Hz, 2H), 6.71 (d, *J* = 8.3, 2H), 5.10 (bs, 4H), 3.22 (s, 1H), 1.89 (bs, 3H), 1.66–1.38 (m, 12H).

^{13}C NMR (101 MHz, *d$_6$*-DMSO) δ: 143.6, 133.1, 131.5, 129.3, 115.0, 106.9, 62.1, 40.5, 36.5, 36.2, 28.1.

HRMS (ESI/Q-TOF): Exact mass calculated for [$C_{23}H_{26}Br_2N_2$ + H]$^+$; requires m/z = 489.0541, found m/z =489.0535.

IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3466(w), 3350(w), 2972(w), 2900(s), 2847(s), 1614(s), 1499(s), 1445(w), 1410(w), 1310(m), 1107(m), 1036(m), 822(m), 671(w), 586(w).



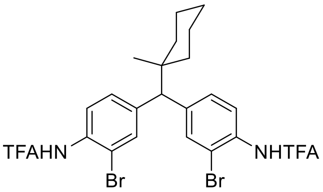
N,*N*'-((((3*r*,5*r*,7*r*)-Adamantan-1-yl)methylene)bis(2-bromo-4,1-phenylene))bis(2,2,2-trifluoroacetamide) (S11)

In a round-bottom flask **S10** (682 mg, 1.00 mmol, 1.00 equiv.) was dissolved in CH_2Cl_2 (5 mL) and cooled to 0 °C. After slow addition of triethylamine (0.33 mL, 2.40 mmol, 2.40 equiv.) and TFAA (0.28 mL, 2.20 mmol, 2.20 equiv.), the mixture was stirred at r.t. for 2.5 h. The reaction was washed with sat. NaCl (aq.), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by automated reverse-phase column chromatography (Biotage, SNAP C18 Ultra 60 g, gradient MeCN in H_2O (with 0.1% formic acid buffer): 2 CV: 0%; 16 CV: 0-100%; 2 CV: 100%) yielded **S11** as a white foam (590 mg, 0.87 mmol, 87%).

R$_F$: 0.59 (hexanes/EtOAc 8:2)

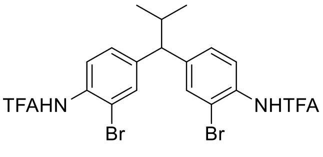
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 2H), 8.24 (d, *J* = 8.5 Hz, 2H), 7.57 (d, *J* = 2.1 Hz, 2H), 7.44 (dd, *J* = 8.6, 2.1 Hz, 2H), 3.43 (s, 1H), 2.00 – 1.93 (m, 4H), 1.69 – 1.63 (m, 4H), 1.60 – 1.51 (m, 10H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 154.7 (q, *J* = 37.7 Hz), 140.8, 133.9, 131.7, 129.9, 121.6, 115.69 (q, *J* = 288.7 Hz), 113.9, 64.7, 41.1, 37.3, 36.7, 28.7.
^{19}F NMR (376 MHz, $CDCl_3$) δ -75.86.
HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{27}H_{22}Br_2F_6N_2O_2 - H]^-$; requires m/z = 681.0015, found m/z = 681.0074.
IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3383(w), 2976(w), 2904(m), 2851(m), 1738(s), 1728(s), 1580(m), 1530(s), 1287(s), 1152(bs), 1042(s), 901(s), 733(s), 517(m), 440(m).



***N,N′*-(((1-Methylcyclohexyl)methylene)bis(2-bromo-4,1-phenylene))bis(2,2,2-trifluoroacetamide) (S12)**

In a round-bottom flask **S6** (950 mg, 3.23 mmol, 1.00 equiv.) was dissolved in CH_2Cl_2 (13 mL) and cooled to 0 °C. *N*-Bromosuccinimide (1.15 g, 6.45 mmol, 2.00 equiv.) was added and the mixture was stirred at r.r. for 1 h. The mixture was washed with sat. NaCl (aq.), dried over $MgSO_4$ and concentrated. The crude material was dissolved in CH_2Cl_2 (13 mL) and cooled to 0 °C. After slow addition of triethylamine (1.07 mL, 7.75 mmol, 2.40 equiv.) and TFAA (0.99 mL, 7.11 mmol, 2.20 equiv.), the mixture was stirred at r.t. for 2 h. The reaction was washed with sat. NaCl (aq.), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by automated column chromatography (Biotage, SNAP Ultra 100 g, gradient EtOAc in hexanes: 13 CV: 0-25%) yielded **S12** as a white foam (1.49 g, 2.31 mmol, 72% over 2 steps).
R_F: 0.58 (hexanes/EtOAc 8:2)
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 2H), 8.24 (d, *J* = 8.6 Hz, 2H), 7.58 (d, *J* = 2.1 Hz, 2H), 7.43 (dd, *J* = 8.6, 2.1 Hz, 2H), 3.74 (s, 1H), 1.53 (tt, *J* = 8.9, 4.7 Hz, 3H), 1.46 – 1.28 (m, 6H), 1.19 (ddt, *J* = 12.4, 8.1, 4.0 Hz, 1H), 1.06 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 154.8 (q, *J* = 37.9 Hz), 141.2, 134.0, 131.7, 130.2, 121.7, 115.7 (q, *J* = 288.7 Hz), 113.9, 62.7, 37.9, 37.1, 26.0, 22.0, 21.4.
^{19}F NMR (376 MHz, $CDCl_3$) δ -75.88.
HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{24}H_{22}Br_2F_6N_2O_2 - H]^-$; requires m/z = 642.9859, found m/z = 642.9929.
IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3384(w), 3304(bw), 2927(w), 2859(w), 1736(s), 1603(w), 1579(m), 1527(s), 1478(m), 1403(m), 1331(w), 1285(s), 1148(bs), 1041(s), 901(s), 819(m), 759 (m), 733(s), 715(m), 672(m), 594(bs), 516(s).



***N,N′*-((2-Methylpropane-1,1-diyl)bis(2-bromo-4,1-phenylene))bis(2,2,2-trifluoroacetamide) (S13)**

In a round-bottom flask **S9** (721 mg, 3.00 mmol, 1.00 equiv.) was dissolved in CH_2Cl_2 (12 mL) and cooled to 0 °C. *N*-Bromosuccinimide (1.07 g, 6.00 mmol, 2.00 equiv.) was added and the mixture was stirred at r.r. for 1.5 h. The mixture was washed with sat. NaCl (aq.), dried over $MgSO_4$ and concentrated. The crude material was dissolved in CH_2Cl_2 (13 mL) and cooled to 0 °C. After slow addition of triethylamine (1.00 mL, 7.20 mmol, 2.40 equiv.) and TFAA (0.92 mL, 6.60 mmol, 2.20 equiv.), the mixture was stirred at r.t. for 2 h. The reaction was washed with sat. NaCl (aq.), dried over $MgSO_4$ and concentrated *in vacuo*. Purification by automated reverse-phase column chromatography (Biotage, SNAP C18 Ultra 60 g, gradient MeCN in H_2O (with 0.1% formic acid buffer): 2 CV: 0%; 19 CV: 0-100%; 2 CV: 100%) yielded **S13** as a white foam (514 mg, 0.87 mmol, 29% over 2 steps).

R_F: 0.55 (hexanes/EtOAc 8:2)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 2H), 8.23 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 2.0 Hz, 2H), 7.28 (dd, *J* = 8.5, 2.0 Hz, 2H), 3.37 (d, *J* = 10.8 Hz, 1H), 2.41 (dsept, *J* = 10.7, 6.5 Hz, 1H), 0.89 (d, *J* = 6.5 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 154.7 (q, *J* = 37.8 Hz), 143.4, 132.0, 131.7, 128.2, 122.3, 115.7 (d, *J* = 288.7 Hz), 114.5, 59.2, 31.9, 21.7.

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.87.

HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{20}H_{14}Br_2F_6N_2O_2 - H]^-$; requires m/z = 588.9389, found m/z = 588.9452.

IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3383(w), 2974(w), 2874(w), 1738(s), 1730(s), 1582(m), 1530(s), 1406(m), 1285(s), 1152(bs), 1042(s), 903(s), 816(m), 733(s), 592(m), 440(m).

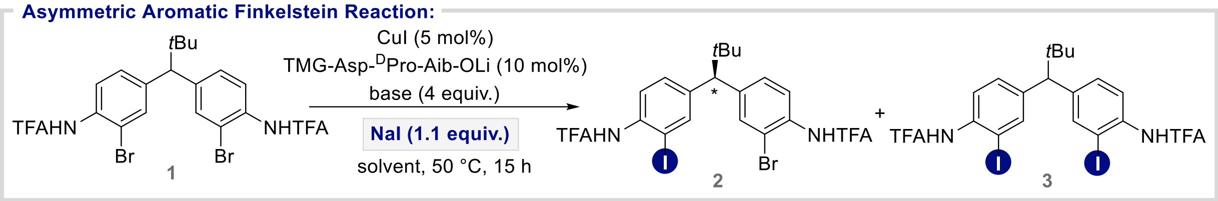
4. Reaction Optimization

General Procedure B (GP B) for reaction conditions optimization screening:

A 1-dram vial equipped with stir bar and septum cap was charged with **1** (60.4 mg, 0.10 mmol, 1.00 equiv.), Cu(I) source, TMG-Asp-^{D}Pro-Aib-OLi (**L1**), base (0.40 mmol, 4.00 equiv.) and NaI. The vial was evacuated and backfilled with N_2 (3x) before dry solvent was added. The reaction mixture was heated at the reported temperature for 15 h. After cooling to r.t., the mixture was filtered through a plug of SiO_2 (eluted with EtOAc) and concentrated *in vacuo*. The crude material was used for determination of NMR yield (CH_2Br_2 as internal standard; δ = 3.64 ppm) and chiral HPLC analysis.

Solvent and base screen:

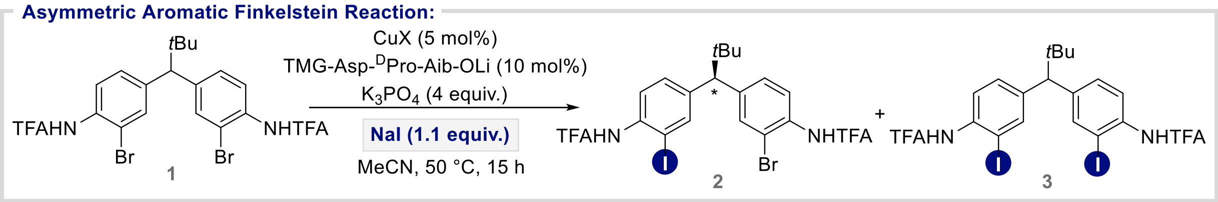
Table S1: Conditions optimization – solvent and base screen.



entry	base	solvent	*c* [M]	1 [%]	2 [%]	3 [%]	e.r. (2)
1	K_3PO_4	MeCN	0.5	24	**49**	10	**10 : 90**
2	K_3PO_4	DMF	0.5	26	**43**	19	**41 : 59**
3	K_3PO_4	THF	0.5	64	**16**	<5	**(~20 : 80)**
4	K_3PO_4	DMF/Tol 1:1	0.5	22	**55**	13	**9 : 91**
5	Cs_2CO_3	MeCN	0.5	38	**14**	<5	**35 : 65**

Copper source screen:

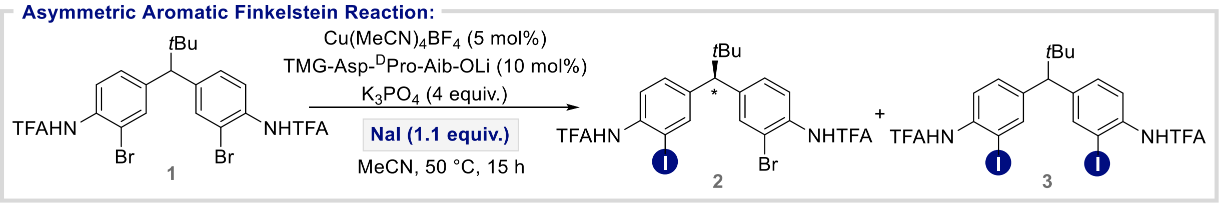
Table S2: Conditions optimization – Cu(I) screen.



entry	Cu source	*c* [M]	1 [%]	2 [%]	3 [%]	e.r. (2)
1	CuI (5 mol%)	0.5	24	**49**	10	**10 : 90**
2	$Cu(MeCN)_4OTf$ (5 mol%)	0.5	40	**45**	5	**9 : 91**
3	$Cu(MeCN)_4PF_6$ (5 mol%)	0.5	35	**46**	7	**9 : 91**
4	$Cu(MeCN)_4BF_4$ (5 mol%)	0.5	26	**52**	9	**8 : 92**

Concentration screen

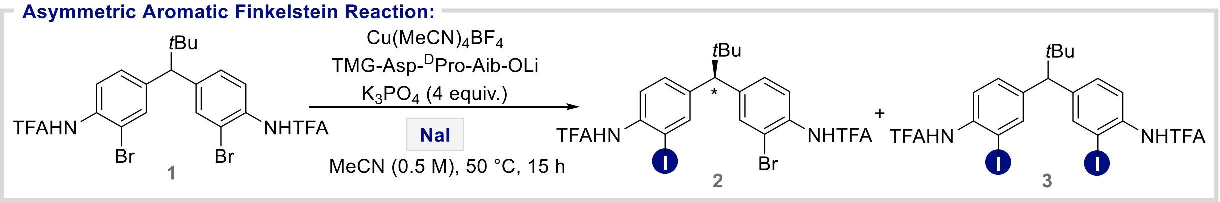
Table S3: Conditions optimization – concentration screen.



entry	*c* [M]	1 [%]	2 [%]	3 [%]	e.r. (2)
1	0.50	26	**52**	9	**8 : 92**
2	0.33	41	**46**	5	**9 : 91**
3	0.20	39	**48**	6	**9 : 91**
4	0.10	38	**47**	6	**9 : 91**

Loading screen

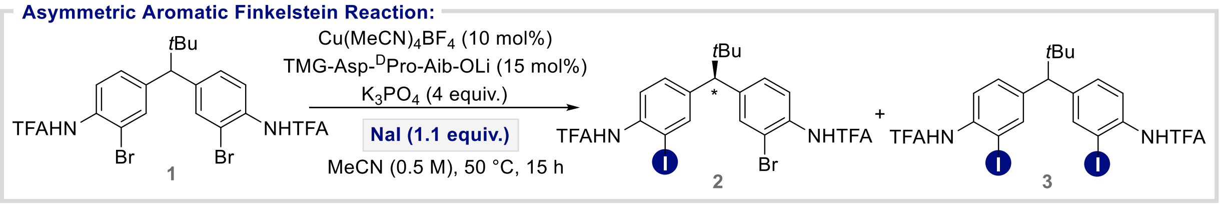
Table S4: Conditions optimization – loading screen.



entry	Cu loading	Ligand loading	NaI [equiv.]	1 [%]	2 [%]	3 [%]	e.r. (2)
1	5 mol%	10 mol%	1.1	26	**52**	9	**8 : 92**
2	10 mol%	20 mol%	1.1	17	**50**	12	**7 : 93**
3	10 mol%	15 mol%	1.1	17	**53**	14	**7 : 93**
4	10 mol%	15 mol%	1.2	15	**62**	20	**6 : 94**
5	10 mol%	15 mol%	1.3	17	**59**	16	**7 : 93**
6	10 mol%	15 mol%	1.5	16	**57**	14	**8 : 92**

Temperature screen

Table S5: Conditions optimization - temperature screen.

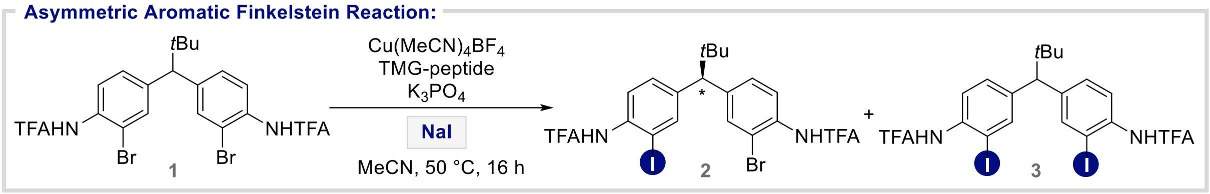


entry	Temperature	1 [%]	2 [%]	3 [%]	e.r. (2)
13	50 °C	17	**53**	14	**7 : 93**
14	45 °C	41	**52**	7	**8 : 92**
15	40 °C	48	**46**	5	**9 : 91**
16	30 °C	73	**25**	2	**10 : 90**
17	r.t.	89	**10**	0	**11 : 89**

General Procedure C (GP C) for catalyst optimization screening:

A 1-dram vial equipped with stir bar and septum cap was charged with **1** (60.4 mg, 0.10 mmol, 1.00 equiv.), $Cu(MeCN)_4BF_4$ (3.1 mg, 0.01 mmol, 0.10 equiv.), TMG-Asp-^{D}Pro-Aib-OLi (**L1**) (0.015 mmol, 0.15 equiv.), K_3PO_4 (84.9 mg, 0.40 mmol, 4.00 equiv.) and NaI (18.0 mg, 0.12 mmol, 1.20 equiv.). The vial was evacuated and backfilled with N_2 (3x) before dry MeCN (0.20 mL, 0.50 M) was added. The reaction mixture was heated at 50 °C for 15 h. After cooling to r.t., the mixture was filtered through a plug of SiO_2 (eluted with EtOAc) and concentrated *in vacuo*. The crude material was used for determination of NMR yield (CH_2Br_2 as internal standard; $\delta = 3.64$ ppm) and chiral HPLC analysis.

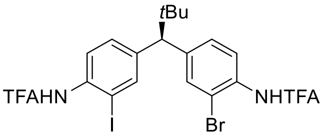
Table S6: Catalyst optimization screen.



entry	ligand	1 [%]	2 [%]	3 [%]	e.r. (2)
1	TMG-Asp-^{D}Pro-Aib-OLi	15	**62**	20	**6 : 94**
2	TMG-Gly-OLi	14	**37**	29	**50 : 50**
3	TMG-1Nal-OH	13	**38**	30	**58 : 42**
4	TMG-Neo-OH	25	**44**	18	**66 : 34**
5	TMG-^{D}Asp-Pro-OLi	23	**47**	7	**90 : 10**
6	TMG-^{D}Asp-αMePro-OLi	24	**52**	10	**91 : 9**
7	TMG-Asp-^{D}Pro-Acpc-OLi	51	**40**	4	**10 : 90**
8	TMG-Asp-^{D}Pro-Acpc-Leu-OLi	13	**62**	19	**5 : 95**
9	TMG-Asp-^{D}Pro-Acpc-^{t}Leu-OLi	8	**62**	22	**4 : 96**
10	TMG-Asp-^{D}Pro-Acpc-Phe-OLi	8	**55**	16	**4 : 96**
11	TMG-^{D}Asp-^{D}Pro-Acpc-Phe-OLi	45	**30**	4	**72 : 28**
12	TMG-Asp-^{D}Pro-Aic-Phe-OLi	8	**54**	17	**5 : 95**
13	TMG-Asp-^{D}Pro-Acpc-2Nal-NHMe	42	**48**	9	**19 : 81**
14	TMG-Asp-^{D}Pro-Acpc-Chg-OLi	14	**64**	14	**4 : 96**
15	TMG-Asp-^{D}Pro-Aib-^{D}Leu-OLi	31	**52**	8	**8 : 92**
16	TMG-Asp-^{D}Pro-Aib-Val-OLi	6	**56**	20	**4 : 96**

5. Preparation and Characterization of Products

5.1 Preparation and Characterization of 2



(*S*)-*N*-(2-Bromo-4-(1-(3-iodo-4-(2,2,2-trifluoroacetamido)phenyl)-2,2-dimethylpropyl)-phenyl)-2,2,2-trifluoroacetamide (2)

A 1-dram vial equipped with stir bar and septum cap was charged with **1** (120.8 mg, 0.20 mmol, 1.00 equiv.), $Cu(MeCN)_4BF_4$ (4.4 mg, 14.0 µmol, 0.07 equiv.), **L9** (15.9 mg, 0.03 mmol, 0.15 equiv.), K_3PO_4 (169.8 mg, 0.80 mmol, 4.00 equiv.) and NaI (36.0 mg, 0.24 mmol, 1.20 equiv.). The vial was evacuated and backfilled with N_2 (3x) before dry MeCN (0.3 mL, 0.66 M) was added. The reaction mixture was heated at 50 °C for 16 h. After cooling to r.t., the mixture was filtered through a plug of SiO_2 (eluted with EtOAc). The product is obtained as an inseparable mixture of **1**, **2** and **3**. NMR yield (64%; $\delta = 3.64$ ppm) was determined against CH_2Br_2 as internal standard and the enantiomeric ratio (e.r. 95:5) could be determined by chiral HPLC comparing against authentic samples of **1** and **3**.

A single crystal for x-ray crystallography was obtained by slow evaporation of the product mixture from EtOAc.

A racemic standard was obtained by using TMG-Gly-OLi (**L2**, Table S6, entry 2).

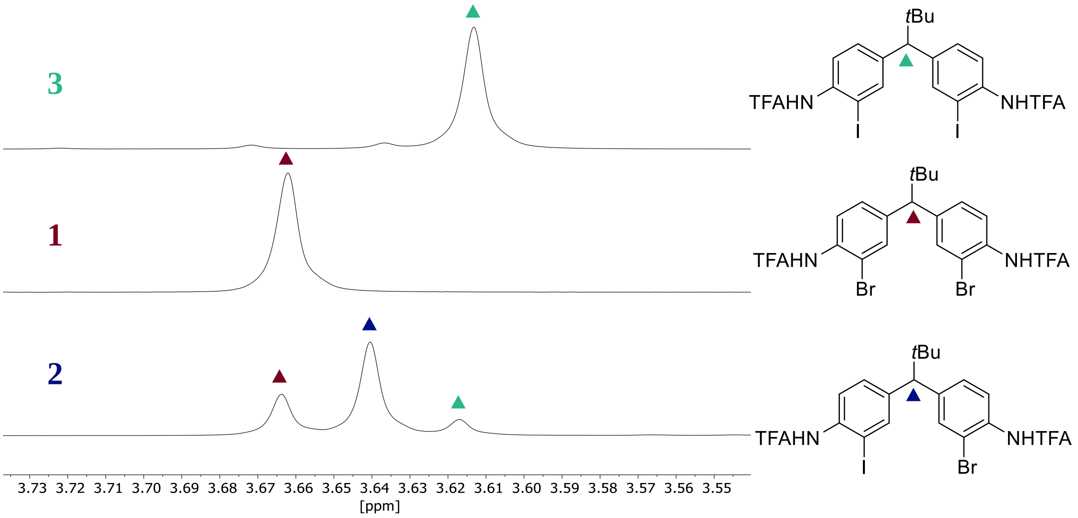
R_F: 0.57 (hexanes/EtOAc 8:2)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.27 – 8.21 (m, 2H), 8.14 (d, $J = 8.5$ Hz, 1H), 7.80 (s, 1H), 7.58 (t, $J = 2.2$ Hz, 1H), 7.51 – 7.46 (m, 1H), 7.45 – 7.40 (m, 1H), 3.64 (s, 1H), 1.03 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 154.8 (q, $J = 37.8$ Hz), 154.7 (q, $J = 37.8$ Hz), 142.2, 141.7, 140.3, 134.3, 133.7, 131.7, 130.5, 129.8, 121.8, 121.7, 115.7 (q, $J = 288.8$ Hz), 115.7 (q, $J = 288.8$ Hz), 114.0, 90.3, 62.6, 35.4, 29.1.

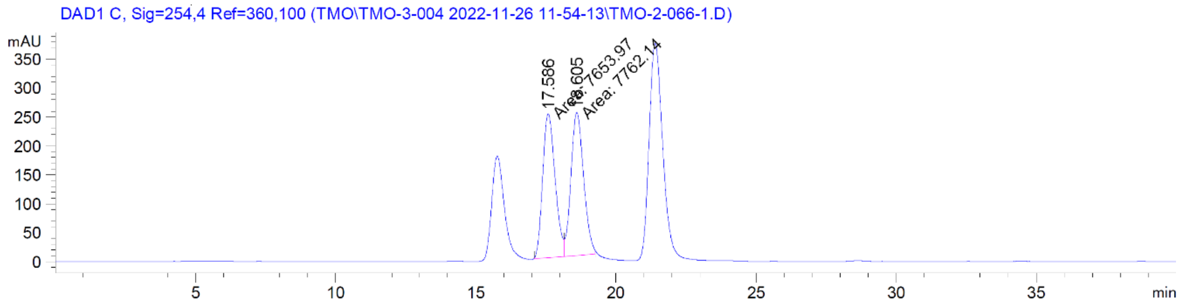
^{19}F NMR (376 MHz, $CDCl_3$) δ -75.84, -75.87.

HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{21}H_{18}BrF_6IN_2O_2 - H]^-$; requires m/z = 648.9428, found m/z = 648.9324.



HPLC (Chiralpak AD-H column, 2% *i*-PrOH in hexanes, 0.5 ml/min, 254 nm): t_R (minor enantiomer) = 17.5 min, t_R (major enantiomer) = 18.5 min.

racemic sample:

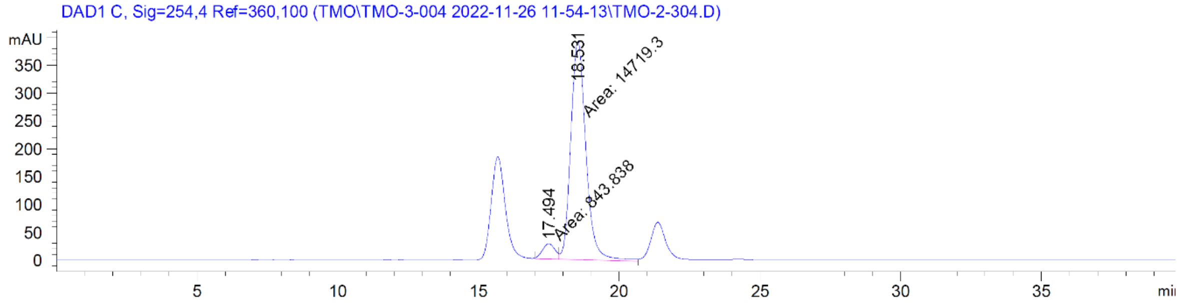


```
Signal 3: DAD1 C, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  17.586 MF    0.5130 7653.97021  248.65410  49.6492
   2  18.605 FM    0.5239 7762.13770  246.93634  50.3508

Totals :                  1.54161e4   495.59044
```

enantioselective sample:



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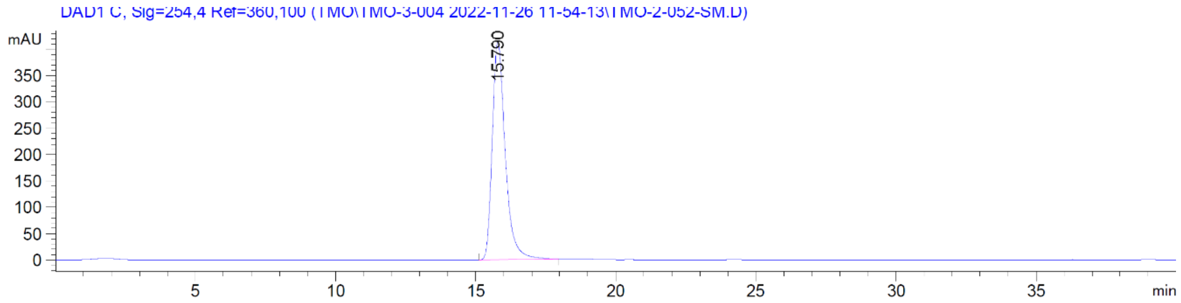
Signal 3: DAD1 C, Sig=254,4 Ref=360,100

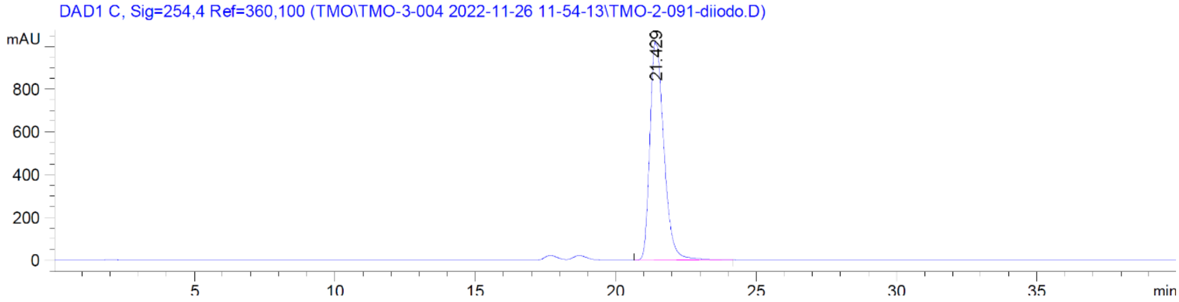
Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  17.494 MF    0.5124  843.83777   27.44887   5.4220
   2  18.531 FM    0.6251 1.47193e4   392.44827  94.5780

Totals :                  1.55632e4   419.89714
```

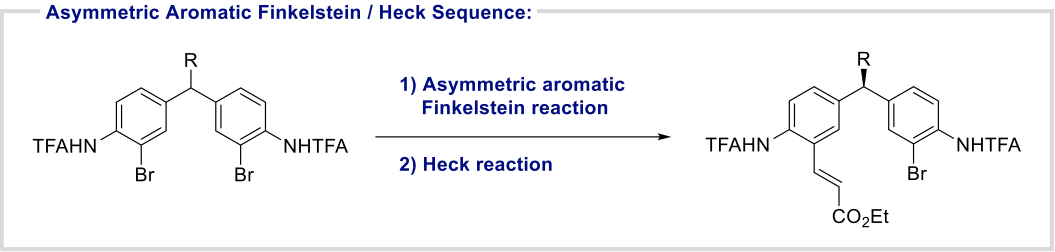
authentic sample of **1**:



authentic sample of **3**:



5.2 Preparation and Characterization of Asymmetric Aromatic Finkelstein / Heck Sequence Products



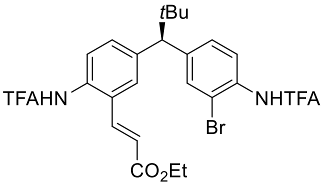
General Procedure D (GP D) for the asymmetric aromatic Finkelstein / Heck reaction sequence:

A 1-dram vial equipped with stir bar and septum cap was charged with corresponding diarylmethine (0.20 mmol, 1.00 equiv.), $Cu(MeCN)_4BF_4$ (4.4 mg, 14.0 µmol, 0.07 equiv.), **L9** (15.9 mg, 0.03 mmol, 0.15 equiv.), K_3PO_4 (169.8 mg, 0.80 mmol, 4.00 equiv.) and NaI (36.0 mg, 0.24 mmol, 1.20 equiv.). The vial was evacuated and backfilled with N_2 (3x) before dry MeCN (0.3 mL, 0.66 M) was added. The reaction mixture was heated at 50 °C for 16 h. After cooling to r.t., the mixture was filtered through a plug of SiO_2 (eluted with EtOAc), transferred into a scintillation vial and concentrated *in vacuo*.

To the vial containing the crude material was added a stir bar and $Pd(OAc)_2$ (4.5 mg, 0.02 mmol, 0.10 equiv.). Following evacuation and back-filling with N_2 (3x), dry DMF (1.0 mL, 0.2 M), ethyl acrylate (20.7 µL, 0.19 mmol, 0.95 equiv.) and Et_3N (38.8 µL, 0.28 mmol, 1.40 equiv.) was added. The vial was sealed and heated at 100 °C for 2 h. The reaction mixture was cooled to r.t. and the solvent was removed by airflow evaporation. Purification by automated column chromatography (Biotage, SNAP Ultra 10 g, gradient EtOAc in hexanes) yielded the desired products.

General Procedure E (GP E) for the synthesis of racemic Heck reaction products:

A 1-dram vial equipped with stir bar and septum cap was charged with corresponding diarylmethine (0.10 mmol, 1.00 equiv.), $Pd(PPh_3)_4$ (2.9 mg, 2.50 µmol, 0.025 equiv.) and K_3PO_4 (63.7 mg, 0.30 mmol, 3.00 equiv.) The vial was evacuated and backfilled with N_2 (3x) before dry toluene (0.5 mL, 0.2 M) and ethyl acrylate (12.0 µL, 0.11 mmol, 1.10 equiv.) was added. The reaction mixture was heated at 100 °C for 20 h. After cooling to r.t., the mixture was filtered through a plug of SiO_2 (eluted with EtOAc), concentrated *in vacuo* and purified by automated column chromatography (Biotage, SNAP Ultra 10 g, gradient EtOAc in hexanes).



Ethyl (*R*,*E*)-3-(5-(1-(3-bromo-4-(2,2,2-trifluoroacetamido)phenyl)-2,2-dimethylpropyl)-2-(2,2,2-trifluoroacetamido)phenyl)acrylate (4)

According to **GP D**, **1** (120.8 mg, 0.20 mmol, 1.00 equiv.) was converted to **4**. Purification by automated column chromatography (Biotage, SNAP Ultra 10 g, gradient EtOAc in hexanes: 15 CV: 0-25%) yielded **4** as a white foam (53.3 mg, 0.09 mmol, 43% over 2 steps / Finkelstein reaction: 64% NMR yield, Heck reaction: 67%).

R_F: 0.38 (hexanes/EtOAc 8:2)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.23 (d, *J* = 8.6 Hz, 2H), 7.76 – 7.67 (m, 2H), 7.59 (d, *J* = 2.0 Hz, 1H), 7.54 (d, *J* = 2.1 Hz, 1H), 7.50 (dd, *J* = 8.5, 2.1 Hz, 1H), 7.45 (dd, *J* = 8.6, 2.1 Hz, 1H), 6.38 (d, *J* = 15.8 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.71 (s, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.03 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 155.7 (q, *J* = 37.5 Hz), 154.8 (q, *J* = 37.9 Hz), 141.9, 141.7, 138.3, 133.8, 131. 9, 131.8, 131.4, 129.7, 129.1, 128.4, 125.0, 122.3, 121.8, 115.9 (q, *J* = 288.5 Hz), 115.5 (q, *J* = 288.5 Hz), 114.0, 63.1, 61.1, 35.4, 29.2, 14.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.50, -75.89.

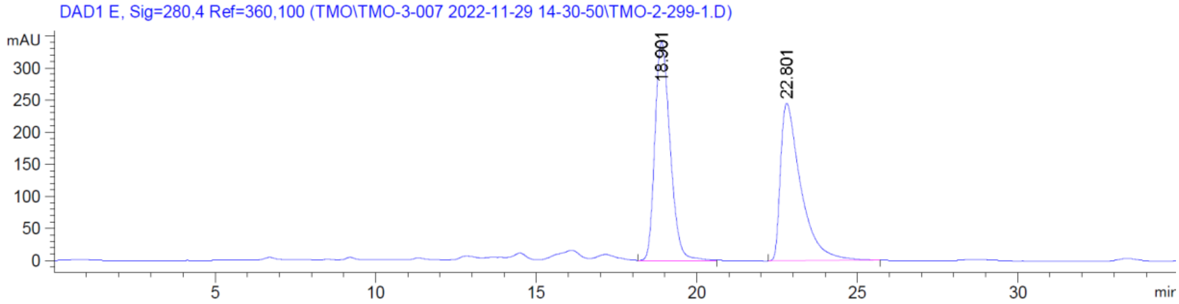
HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{26}H_{25}BrF_6N_2O_4 - H]^-$; requires m/z = 623.0809, found m/z = 623.0744.

IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3386(w), 3278(bw), 2966(w), 2909(w), 2869(w), 1700(bs), 1533(bs), 1285(m), 1258(m), 1194(bs), 1158(bs), 1043(w), 981(w), 903(w), 758(w), 736(w).

Optical: $[\alpha]^D_{20}$ = –27.6° (*er* = 94:6, *c* = 1.0, $CHCl_3$).

HPLC (Chiralpak AD-H column, 2% *i*-PrOH in hexanes, 0.5 ml/min, 254 nm): t_R (minor enantiomer) = 17.5 min, t_R (major enantiomer) = 18.5 min.

racemic sample:

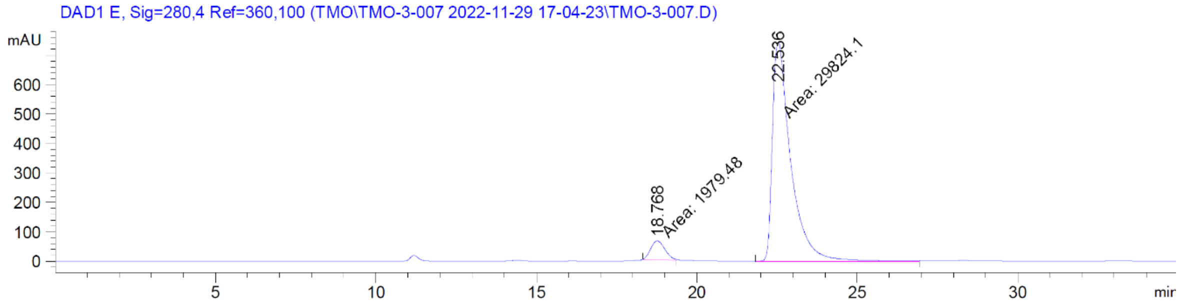


```
Signal 4: DAD1 E, Sig=280,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  18.901 VV    0.5052 1.12553e4  340.89792  51.0166
   2  22.801 BB    0.6437 1.08067e4  245.41492  48.9834

Totals :                  2.20620e4  586.31284
```

enantioselective sample:



```
Signal 4: DAD1 E, Sig=280,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  18.768 MM    0.5109 1979.47913   64.57323   6.2241
   2  22.536 MM    0.6663 2.98241e4   746.03143  93.7759

Totals :                  3.18036e4   810.60467
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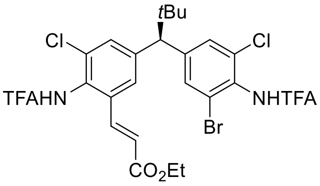


Ethyl (*R*,*E*)-3-(5-(1-(3-bromo-5-chloro-4-(2,2,2-trifluoroacetamido)phenyl)-2,2-dimethylpropyl)-3-chloro-2-(2,2,2-trifluoroacetamido)phenyl)acrylate (9)

According to **GP D**, **S1** (134.6 mg, 0.20 mmol, 1.00 equiv.) was converted to **9**. Purification by automated column chromatography (Biotage, SNAP Ultra 10 g, gradient EtOAc in hexanes: 18 CV: 0-25%) yielded **9** as a white foam (80.3 mg, 0.12 mmol, 58% over 2 steps)

R$_F$: 0.25 (hexanes/EtOAc 8:2)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.83 (s, 1H), 7.62 – 7.54 (m, 2H), 7.50 (d, *J* = 5.4 Hz, 2H), 7.45 (d, *J* = 1.9 Hz, 1H), 6.39 (d, *J* = 15.9 Hz, 1H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.70 (s, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 1.06 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.2, 156.1 (q, *J* = 38.2 Hz), 155.2 (q, *J* = 38.3 Hz), 144.8, 143.4 138.4, 134.1, 133.4, 132.9, 132.5, 131.8, 130.4, 129.0, 128.6, 127.2, 123.2, 122.7, 115.8 (q, *J* = 288.3 Hz), 115.8 (q, *J* = 288.3 Hz), 62.9, 61.2, 35.5, 29.1, 14.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.31, -75.48.

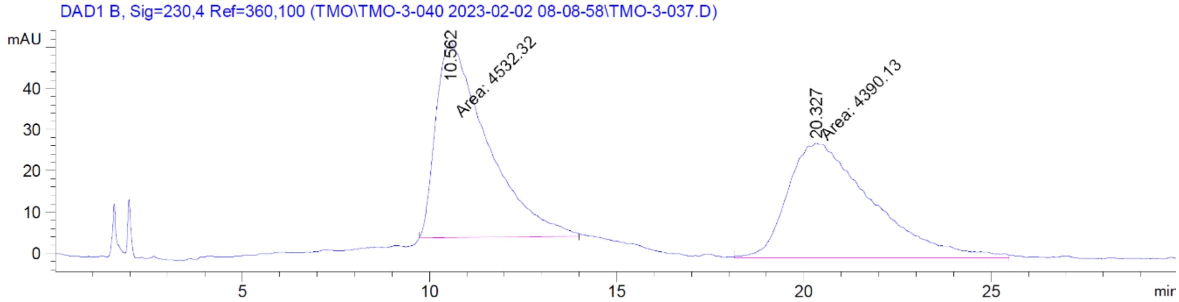
HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{26}H_{23}BrCl_2F_6N_2O_4 – H]^-$; requires m/z = 691.0029, found m/z = 691.0032.

IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3254(bm), 3039(bw), 2968(w), 2910(w), 2876(w), 1719(bs), 1636(w), 1536(m), 1465(m), 1369(w), 1318(m), 1269(m), 1201(bs), 1160(bs), 1039(w), 977(w), 919(w), 864(w), 758(m).

Optical: $[\alpha]_D^{20}$ = –16.2° (*er* = 93:7, *c* = 1.0, $CHCl_3$).

HPLC (Chiralpak IB column, 5% *i*-PrOH in hexanes, 1.0 ml/min, 230 nm): t_R (minor enantiomer) = 10.6 min, t_R (major enantiomer) = 20.3 min.

racemic sample:



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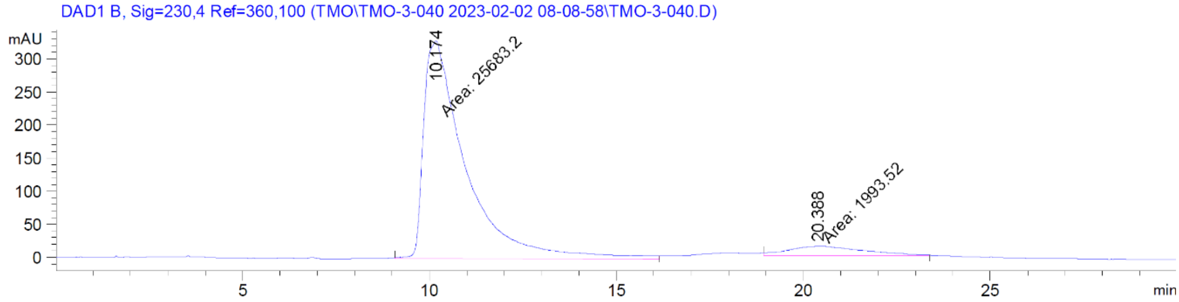
Signal 2: DAD1 B, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  10.562 MM     1.5819 4532.31592   47.75224  50.7968
   2  20.327 MM     2.6214 4390.13135   27.91212  49.2032

Totals :                   8922.44727   75.66436
```

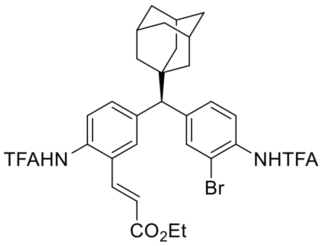
enantioselective sample:



```
Signal 2: DAD1 B, Sig=230,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  10.174 MM     1.3021 2.56832e4  328.75165  92.7971
   2  20.388 MM     2.3327 1993.51941  14.24329   7.2029

Totals :                   2.76767e4  342.99493
```



Ethyl (*E*)-3-(5-((1*R*)-((1*r*,3*R*)-adamantan-1-yl)(3-bromo-4-(2,2,2-trifluoroacetamido)-phenyl)methyl)-2-(2,2,2-trifluoroacetamido)phenyl)acrylate (11)

According to **GP D**, **S11** (136.4 mg, 0.20 mmol, 1.00 equiv.) was converted to **11**. Purification by automated column chromatography (Biotage, SNAP Ultra 10 g, gradient EtOAc in hexanes: 25 CV: 0-20%) yielded **11** as a white foam (49.6 mg, 0.07 mmol, 35% over 2 steps)

R$_F$: 0.42 (hexanes/EtOAc 8:2)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 8.23 (d, *J* = 8.6 Hz, 1H), 8.15 (s, 1H), 7.76 – 7.69 (m, 2H), 7.58 (d, *J* = 2.0 Hz, 1H), 7.54 – 7.49 (m, 2H), 7.46 (dd, *J* = 8.6, 2.0 Hz, 1H), 6.40 (d, *J* = 15.9 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.48 (s, 1H), 2.01 – 1.93 (m, 3H), 1.70 – 1.51 (m, 12H), 1.30 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 155.7 (q, *J* = 37.6 Hz), 154.7 (q, *J* = 37.7 Hz), 140.0, 140.8, 138.3, 133.9, 132.1, 131.7, 131.3, 129.9, 129.3, 128.2, 124.8, 122.3, 121.6, 115.9 (q, *J* = 288.7 Hz), 115.7 (q, *J* = 288.7 Hz), 113.9, 65.1, 61.1, 41.2, 37.2, 36.7, 28.7, 14.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.47, -75.86.

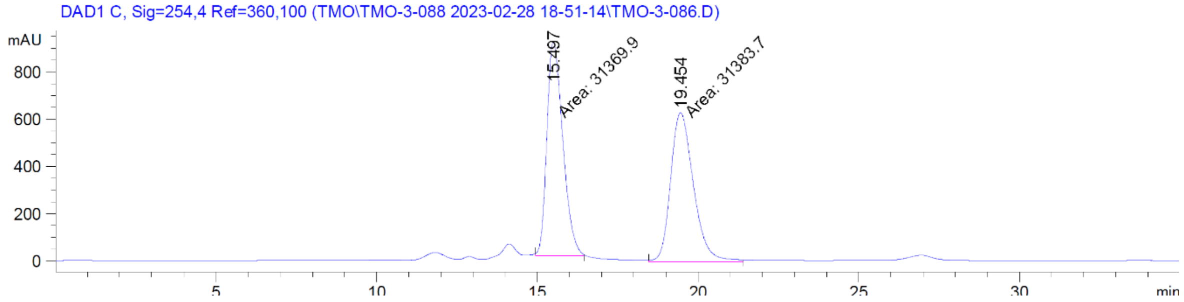
HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{32}H_{31}BrF_6N_2O_4 – H]^–$; requires m/z = 699.1298, found m/z = 699.1334.

IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3384(w), 3279(bw), 2905(m), 2850(w), 1718(s), 1636(m), 1533(s), 1311(m), 1284(m), 1255(m),1191(bs), 1157(bs), 1043(w), 979(w), 902(w), 758(m), 734(m).

Optical: $[\alpha]_D^{20}$ = –19.1° (*er* = 92:8, *c* = 1.0, $CHCl_3$)

HPLC (Chiralpak AD-H column, 5% *i*-PrOH in hexanes, 0.5 ml/min, 254 nm): t_R (major enantiomer) = 15.4 min, t_R (minor enantiomer) = 19.5 min.

racemic sample:

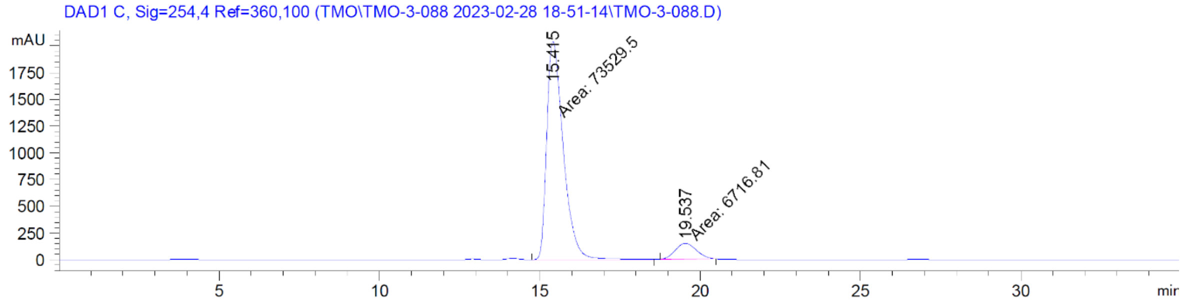


```
Signal 3: DAD1 C, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  15.497 MM    0.5757 3.13699e4  908.12622  49.9890
   2  19.454 MM    0.8280 3.13837e4  631.72595  50.0110

Totals :                  6.27536e4  1539.85217
```

enantioselective sample:



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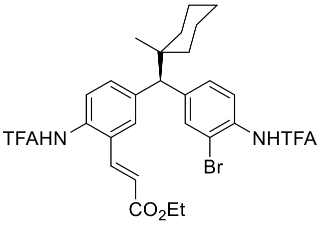
Signal 3: DAD1 C, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  15.415 MM    0.6003 7.35295e4 2041.44958  91.6298
   2  19.537 MM    0.7610 6716.81250  147.09999   8.3702

Totals :                  8.02463e4  2188.54958
```



Ethyl (*R*,*E*)-3-(5-((3-bromo-4-(2,2,2-trifluoroacetamido)phenyl)(1-methylcyclohexyl)-methyl)-2-(2,2,2-trifluoroacetamido)phenyl)acrylate (12)

According to **GP D**, **S12** (128.9 mg, 0.20 mmol, 1.00 equiv.) was converted to **12**. Purification by automated column chromatography (Biotage, SNAP Ultra 10 g, gradient EtOAc in hexanes: 30 CV: 0-25%) yielded **12** as a white foam (47.8 mg, 0.07 mmol, 36% over 2 steps).

R_F: 0.50 (hexanes/EtOAc 8:2)

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.39 (s, 1H), 8.33 (s, 1H), 8.22 (d, *J* = 8.6 Hz, 1H), 7.74 (d, *J* = 15.9 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 2.0 Hz, 1H), 7.54 (d, *J* = 2.0 Hz, 1H), 7.51 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.45 (dd, *J* = 8.6, 2.1 Hz, 1H), 6.38 (d, *J* = 15.8 Hz, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.79 (s, 1H), 1.57 – 1.47 (m, 3H), 1.48 – 1.37 (m, 2H), 1.36 – 1.29 (m, 4H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.23 – 1.13 (m, 1H), 1.07 (s, 3H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 166. 5, 155.8 (q, *J* = 37.7 Hz), 154.7 (q, *J* = 37.8 Hz), 141.4, 141.2, 138.5, 134.0, 132.3, 131.6, 131.4, 130.1, 129.3, 128.3, 125.0, 122.0, 121.7, 115.9 (q, *J* = 288.8 Hz), 115.7 (q, *J* = 288.8 Hz), 114.0, 61.1, 37.8, 37.1, 37.1, 26.0, 21.9, 21.4, 14.3.

^{19}F NMR (376 MHz, CDCl$_3$) δ -75.47, -75.86.

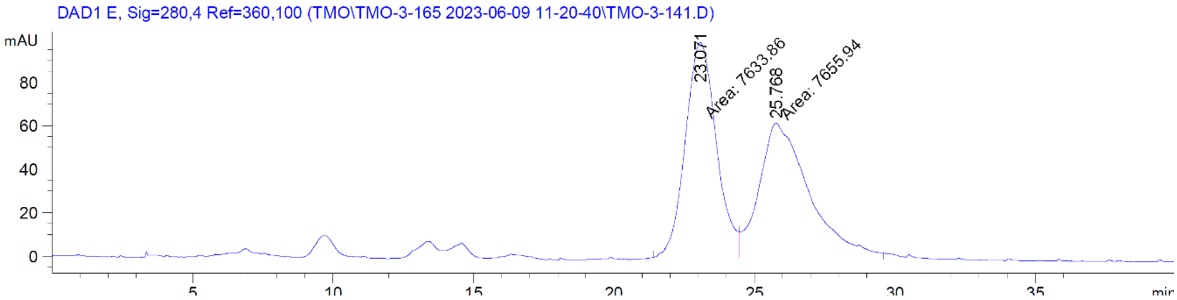
HRMS (ESI/Q-TOF): Exact mass calculated for [$C_{29}H_{29}BrF_6N_2O_4$ – H]$^-$; requires m/z = 663.1122, found m/z = 663.1281.

IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3384(w), 3281(bw), 2981(w), 2927(w), 2859(w), 1705(bs), 1529(bs), 1317(m), 1282(m), 1257(m), 1190(bs), 1155(bs), 1042(w), 980(w), 903(w), 867(w), 823(w), 758(m), 735(m).

Optical: $[\alpha]_D^{20}$ = –18.8° (*er* = 94:6, *c* = 1.0, CHCl$_3$)

HPLC (Chiralpak AD-H column, 2% *i*-PrOH in hexanes, 1.0 ml/min, 280 nm): t$_R$ (minor enantiomer) = 23.2 min, t$_R$ (major enantiomer) = 25.2 min.

racemic sample:

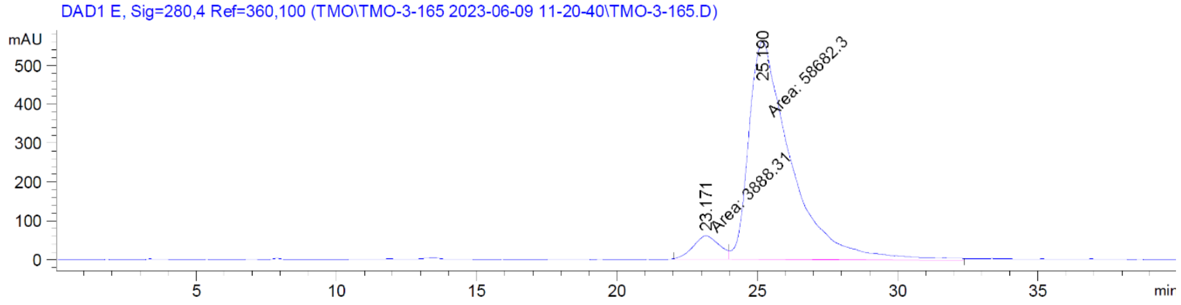


```
Signal 4: DAD1 E, Sig=280,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  23.071 MF     1.2830 7633.86377   99.16441  49.9278
   2  25.768 FM     2.0596 7655.93945   61.95399  50.0722

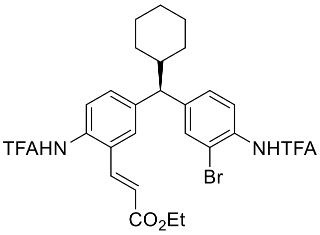
Totals :                  1.52898e4   161.11840
```

enantioselective sample:



```
Signal 4: DAD1 E, Sig=280,4 Ref=360,100

Peak RetTime Type  Width      Area       Height      Area
  #   [min]        [min]    [mAU*s]      [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  23.171 MF    1.0752 3888.30811   60.27350   6.2143
   2  25.190 FM    1.7402 5.86823e4   562.02362  93.7857
```



Ethyl (*R*,*E*)-3-(5-((3-bromo-4-(2,2,2-trifluoroacetamido)phenyl)(cyclohexyl)methyl)-2-(2,2,2-trifluoroacetamido)phenyl)acrylate (13)

According to **GP D**, **S2** (126.4 mg, 0.20 mmol, 1.00 equiv.) was converted to **13**. Purification by automated column chromatography (Biotage, SNAP Ultra 10 g, gradient EtOAc in hexanes: 17 CV: 0-30%) yielded **13** as a pale-yellow sticky oil (68.2 mg, 0.11 mmol, 53% over 2 steps)

R_F: 0.39 (hexanes/EtOAc 8:2)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 8.21 (d, *J* = 8.5 Hz, 1H), 8.07 (s, 1H), 7.71 (d, *J* = 9.3 Hz, 1H), 7.68 (d, *J* = 1.8 Hz, 1H), 7.45 (d, *J* = 2.0 Hz, 1H), 7.42 (d, *J* = 2.0 Hz, 1H), 7.34 (dd, *J* = 8.4, 2.0 Hz, 1H), 7.29 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.39 (d, *J* = 15.8 Hz, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.49 (d, *J* = 10.8 Hz, 1H), 2.12 – 2.00 (m, 1H), 1.73 – 1.53 (m, 4H), 1.34 – 1.12 (m, 7H), 0.93 – 0.82 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 155.7 (q, *J* = 37.8 Hz), 154.8 (q, *J* = 38.1 Hz), 143.3, 143.1, 138.1, 132.2, 131.6, 131.2, 130.4, 128.8, 128.2, 127.5, 125.5, 122.5, 122.4, 115.9 (q, *J* = 288.8 Hz), 115.7 (q, *J* = 288.8 Hz), 114.5, 61.1, 58.3, 41.1, 32.0, 26.4, 26.2, 14.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.51, -75.89.

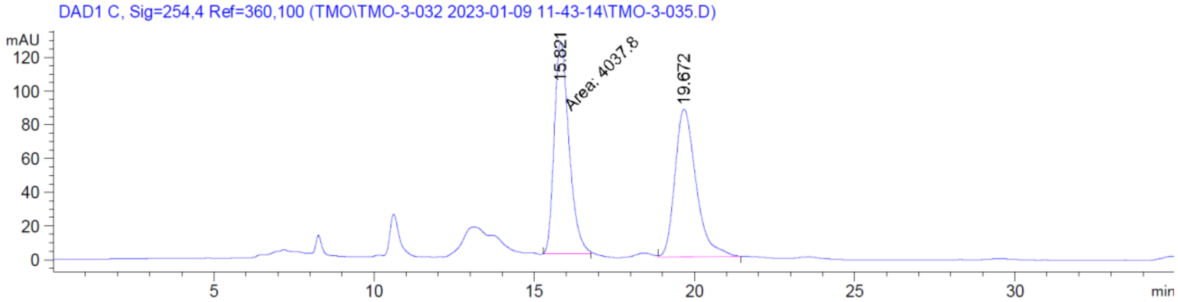
HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{28}H_{27}BrF_6N_2O_4 - H]^-$; requires m/z = 647.0986, found m/z = 647.1023.

IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3385(w), 3278(bw), 2931(m), 2853(w), 1718(bs), 1533(s), 1319(w), 1285(m), 1255(m), 1158(bs), 1043(w), 979(w), 904(w), 757(w), 734(w).

Optical: $[\alpha]_D^{20}$ = –13.4° (*er* = 84:16, *c* = 1.0, $CHCl_3$).

HPLC (Chiralpak AD-H column, 5% *i*-PrOH in hexanes, 0.5 ml/min, 254 nm): t_R (major enantiomer) = 15.7 min, t_R (minor enantiomer) = 19.7 min.

racemic sample:



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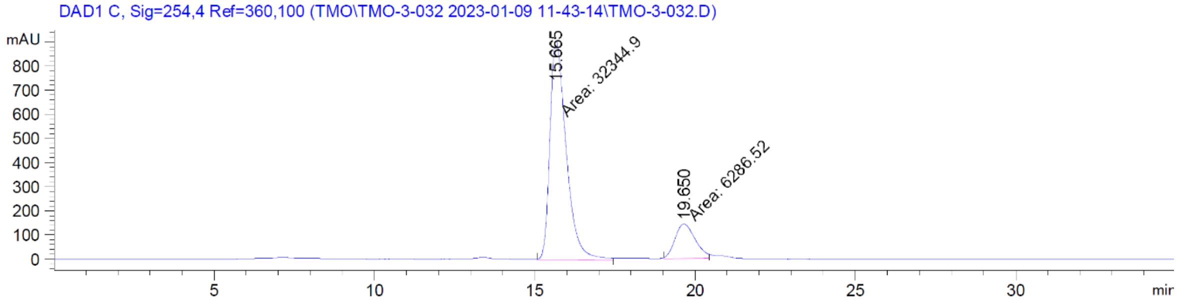
Signal 3: DAD1 C, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  15.821 MM    0.5344 4037.79932  125.92918  49.9942
   2  19.672 VB    0.7007 4038.73608   87.79043  50.0058

Totals :                  8076.53540  213.71960
```

enantioselective sample:



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Signal 3: DAD1 C, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  15.665 MM    0.5940 3.23449e4  907.48639  83.7269
   2  19.650 MM    0.7304 6286.52490 143.44273  16.2731

Totals :                  3.86314e4  1050.92912
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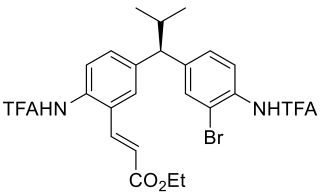


Ethyl (*R*,*E*)-3-(5-(1-(3-bromo-4-(2,2,2-trifluoroacetamido)phenyl)-2-methylpropyl)-2-(2,2,2-trifluoroacetamido)phenyl)acrylate (14)

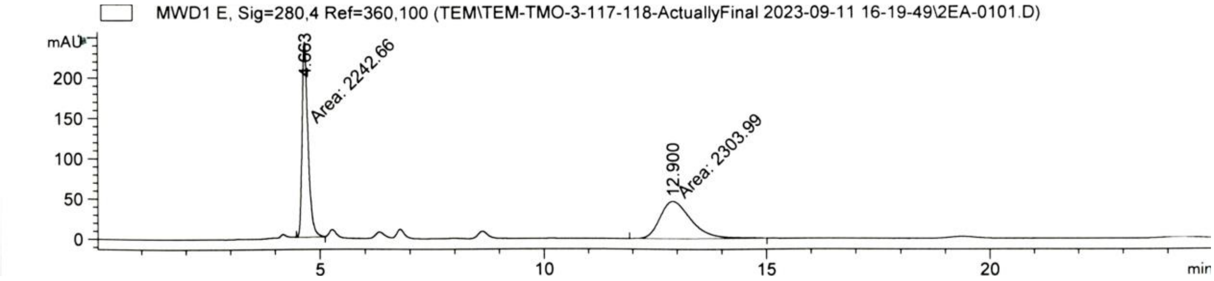
According to **GP D**, **S13** (118.0 mg, 0.20 mmol, 1.00 equiv.) was converted to **14**. Purification by automated column chromatography (Biotage, SNAP Ultra 10 g, gradient EtOAc in hexanes: 23 CV: 0-25%) yielded **14** as a white foam (52.5 mg, 0.09 mmol, 43% over 2 steps).

R$_F$: 0.35 (hexanes/EtOAc 8:2)

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.37 (s, 1H), 8.21 (d, *J* = 8.7 Hz, 2H), 7.76 – 7.64 (m, 2H), 7.45 (dd, *J* = 12.5, 2.0 Hz, 2H), 7.35 (dd, *J* = 8.4, 2.1 Hz, 1H), 7.29 (dd, *J* = 8.5, 2.0 Hz, 1H), 6.39 (d, *J* = 15.8 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 3.42 (d, *J* = 10.8 Hz, 1H), 2.44 (dsept, *J* = 10.7, 6.5 Hz, 1H), 1.29 (t, *J* = 7.1 Hz, 3H), 0.89 (t, *J* = 6.1 Hz, 6H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 155.8 (q, J = 37.7 Hz), 154.8 (q, J = 37.8 Hz), 143.6, 143.4, 138.2, 132.0, 131.6, 131.3, 130.3, 128.8, 128.1, 127.2, 125.6, 122.4, 122.3, 116.0 (q, J = 288.6 Hz), 115.7 (q, J = 288.6 Hz), 114.5, 61.1, 59.5, 31.8, 21.7, 14.3.
^{19}F NMR (376 MHz, $CDCl_3$) δ -75.48, -75.88.
HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{25}H_{23}BrF_6N_2O_4 – H]^–$; requires m/z = 607.0673, found m/z = 607.0677.
IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3385(w), 3268(bw), 2970(w), 2935(w), 2909(w), 2875(w), 1700(s), 1636(m), 1583(m), 1533(s), 1490(m), 1369(m), 1319(m), 1281(s), 1254(s), 1190(bs), 1152(bs), 1042(m), 979(m), 902(m), 827(w), 757(m), 734(m).
Optical: $[\alpha]_D^{20}$ = –14.0° (*er* = 82:18, *c* = 1.0, $CHCl_3$).
HPLC (Chiralpak IB column, 35% *i*-PrOH in hexanes, 1.0 ml/min, 254 nm): t_R (major enantiomer) = 4.7 min, t_R (minor enantiomer) = 12.9 min.

racemic sample:



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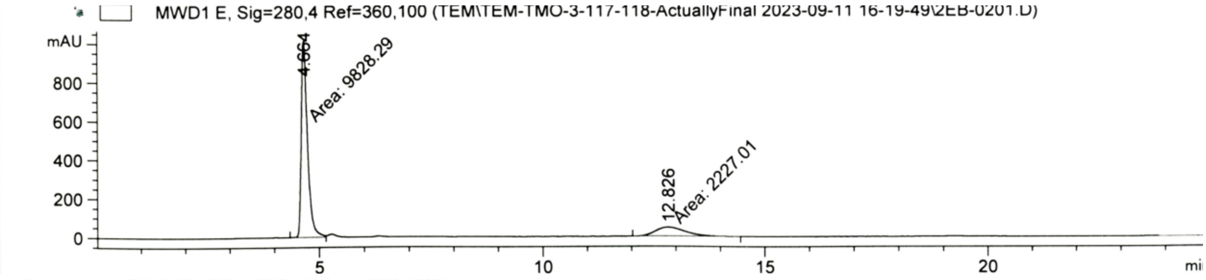
Signal 4: MWD1 E, Sig=280,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.663 MM    0.1540 2242.66040  242.71669  49.3255
   2  12.900 MM    0.8233 2303.99316   46.64045  50.6745

Totals :                  4546.65356  289.35714
```

enantioselective sample:



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Signal 4: MWD1 E, Sig=280,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   4.664 MM    0.1612 9828.29102 1016.29541  81.5267
   2  12.826 MM    0.7932 2227.01245   46.79409  18.4733

Totals :                  1.20553e4  1063.08950
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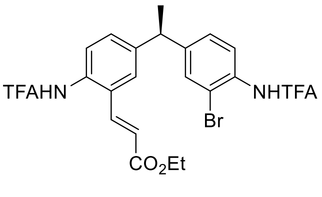


Ethyl (*R*,*E*)-3-(5-(1-(3-bromo-4-(2,2,2-trifluoroacetamido)phenyl)ethyl)-2-(2,2,2-trifluoroacetamido)phenyl)acrylate (15)

According to **GP D**, **S3** (112.4 mg, 0.20 mmol, 1.00 equiv.) was converted to **15**. Purification by automated column chromatography (Biotage, SNAP Ultra 10 g, gradient EtOAc in hexanes: 20 CV: 0-30%) yielded **15** as a white foam (24.0 mg, 0.04 mmol, 21% over 2 steps)

R_F: 0.33 (hexanes/EtOAc 8:2)

^{1}H NMR (400 MHz, CDCl$_3$) δ 8.39 (s, 1H), 8.22 (d, J = 8.5 Hz, 1H), 8.03 (s, 1H), 7.71 (d, J = 9.1 Hz, 1H), 7.68 (d, J = 1.6 Hz, 1H), 7.40 (dd, J = 8.1, 2.0 Hz, 2H), 7.29 – 7.26 (m, 1H), 7.22 (dd, J = 8.5, 2.1 Hz, 1H), 6.37 (d, J = 15.8 Hz, 1H), 4.24 (q, J = 7.1 Hz, 2H), 4.15 (q, J = 7.1 Hz, 1H), 1.64 (d, J = 7.3 Hz, 3H), 1.31 (t, J = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 166.3, 155.5 (d, J = 95.8 Hz), 145.0, 144.9, 138.0, 131.6, 131.2, 130.2, 128.9, 128.0, 126.8, 125.5, 122.6, 122.3, 115.9 (q, J = 288.6 Hz), 115.7 (q, J = 288.6 Hz), 114.6, 61.1, 43.8, 21.6, 14.3.

^{19}F NMR (376 MHz, CDCl$_3$) δ -75.47, -75.86.

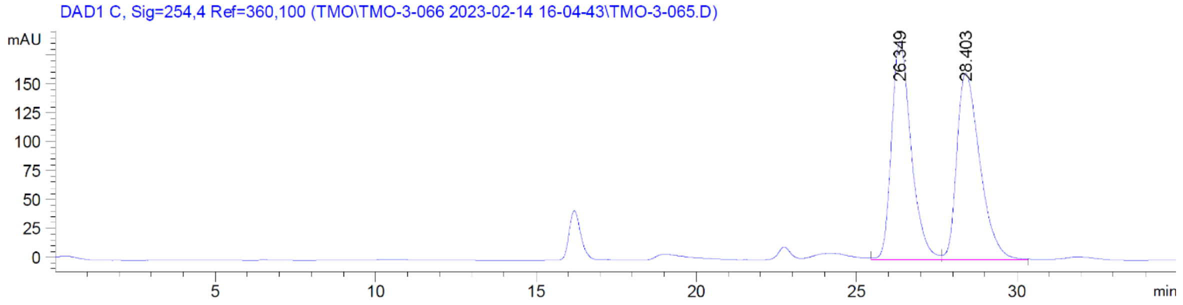
HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{23}H_{19}BrF_6N_2O_4 - H]^-$; requires m/z = 579.0360, found m/z = 579.0395.

IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3384(w), 3271(bm), 2977(w), 2925(w), 2851(w), 1715(s), 1636(w), 1584(w), 1533(m), 1320(w), 1283(m), 1253(m), 1194(bs), 1159(bs), 1043(w), 979(w), 915(w), 867(w), 829(w), 759(w), 727(w).

Optical: $[\alpha]_D^{20}$ = –0.8° (*er* = 55:45, *c* = 1.0, CHCl$_3$).

HPLC (Chiralpak AD-H column, 5% *i*-PrOH in hexanes, 0.5 mL/min, 254 nm): t_R (minor enantiomer) = 26.3 min, t_R (major enantiomer) = 28.4 min.

racemic sample:



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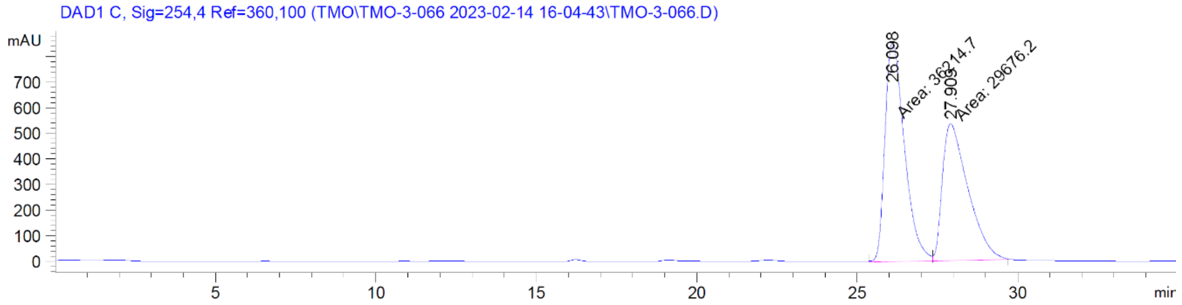
Signal 3: DAD1 C, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  26.349 VV    0.6395 8017.32373  188.75517  49.8669
   2  28.403 VB    0.7555 8060.12207  161.16119  50.1331

Totals :                  1.60774e4   349.91637
```

enantioselective sample:



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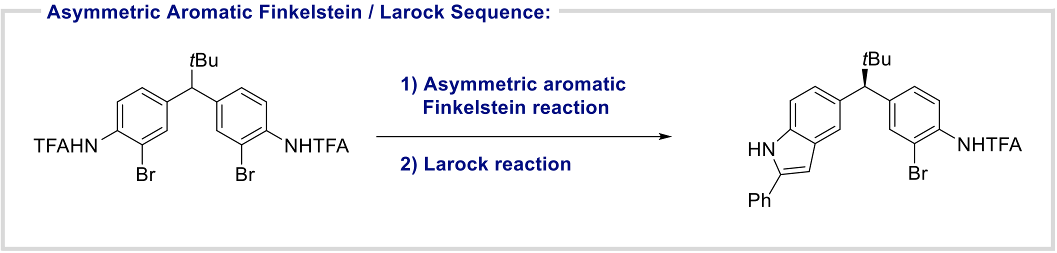
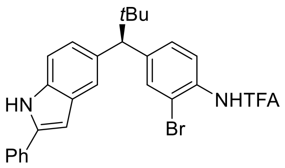
Signal 3: DAD1 C, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1  26.098 MF    0.7043 3.62147e4  856.92975  54.9616
   2  27.909 FM    0.9247 2.96762e4  534.90387  45.0384

Totals :                  6.58909e4  1391.83362
```

5.3 Preparation and Characterization of Asymmetric Aromatic Finkelstein / Larock Sequence Product





(*R*)-*N*-(2-Bromo-4-(2,2-dimethyl-1-(2-phenyl-1H-indol-5-yl)propyl)phenyl)-2,2,2-trifluoroacetamide (5)

A 1-dram vial equipped with stir bar and septum cap was charged with **1** (120.8 mg, 0.20 mmol, 1.00 equiv.), $Cu(MeCN)_4BF_4$ (4.4 mg, 14.0 μmol, 0.07 equiv.), **L9** (15.9 mg, 0.03 mmol, 0.15 equiv.), K_3PO_4 (169.8 mg, 0.80 mmol, 4.00 equiv.) and NaI (36.0 mg, 0.24 mmol, 1.20 equiv.). The vial was evacuated and backfilled with N_2 (3x) before dry MeCN (0.3 mL, 0.66 M) was added. The reaction mixture was heated at 50 °C for 16 h. After cooling to r.t., the mixture was filtered through a plug of SiO_2 (eluted with EtOAc), transferred into a scintillation vial and concentrated *in vacuo*.

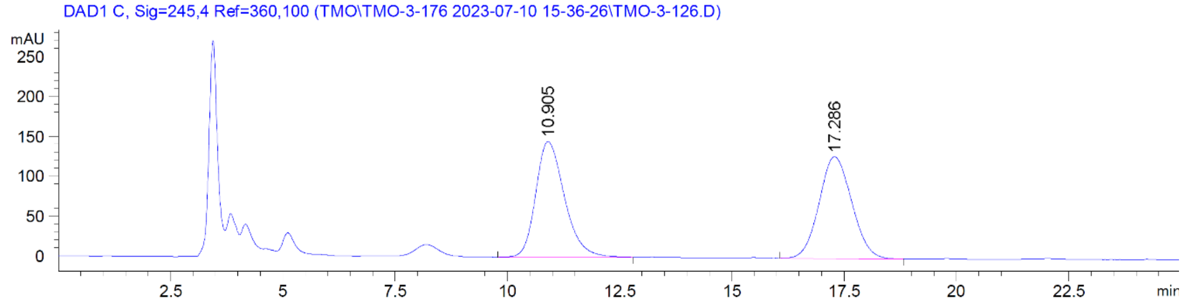
To the vial containing the crude material was added a stir bar, CuI (5.7 mg, 0.03 mmol, 0.15 equiv.), triphenylphosphine (15.7 mg, 0.06 mmol, 0.30 equiv.) and K_3PO_4 (84.9 mg, 0.40 mmol, 2.00 equiv.). Following evacuation and back-filling with N_2 (3x), degassed 1,4-dioxane (1.0 mL, 0.2 M) and phenylacetylene (20.4 μL, 0.20 mmol, 1.00 equiv.) was added. The vial was sealed and heated at 110 °C for 24 h. The reaction mixture was cooled to r.t. and filtered through a plug of SiO_2 (eluted with EtOAc). Purification by automated reverse-phase column chromatography (Biotage, SNAP C18 Ultra 12 g, gradient MeCN in H_2O (with 0.1%

formic acid buffer): 15 CV: 0-100%; 10 CV: 100%) yielded the desired product as a white foam (40.0 mg, 0.08 mmol, 38% over 2 steps).

Synthesis of racemic 5:

A 1-dram vial equipped with stir bar and septum cap was charged with **1** (60.4 mg, 0.10 mmol, 1.00 equiv.), $Pd(PPh_3)_4$ (2.9 mg, 2.50 µmol, 0.025 equiv.), CuI (1.9 mg, 0.01 mmol, 0.10 equiv.) and K_3PO_4 (63.7 mg, 0.30 mmol, 3.00 equiv.). The vial was evacuated and backfilled with N_2 (3x) before dry toluene (0.5 mL, 0.2 M) and phenylacetylene (12.1 µL, 0.11 mmol, 1.10 equiv.) was added. The reaction mixture was heated at 100 °C for 20 h. After cooling to r.t., the mixture was filtered through a plug of SiO_2 (eluted with EtOAc), concentrated *in vacuo* and purified by automated reverse-phase column chromatography (Biotage, SNAP C18 Ultra 12 g, gradient MeCN in H_2O (with 0.1% formic acid buffer): 15 CV: 0-100%; 10 CV: 100%).

R_F: 0.50 (hexanes/EtOAc 8:2)
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 – 8.31 (m, 2H), 8.21 (d, *J* = 8.5 Hz, 1H), 7.70 (d, *J* = 2.0 Hz, 1H), 7.66 – 7.61 (m, 3H), 7.55 (dd, *J* = 8.6, 2.1 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 7.36 – 7.28 (m, 2H), 7.20 (dd, *J* = 8.4, 1.7 Hz, 1H), 6.79 (s, 1H), 3.80 (s, 1H), 1.08 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 154.7 (q, *J* = 37.8 Hz), 144.1, 138.5, 135.7, 134.0, 133.8, 132.5, 131.0, 130.1, 129.4, 129.2, 127.9, 125.3, 124.7, 121.4, 121.4, 117.2 (d, *J* = 289.0 Hz), 113.7, 110.6, 100.1, 63.7, 35.5, 29.5.
^{19}F NMR (376 MHz, $CDCl_3$) δ -75.85.
HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{27}H_{24}BrF_3N_2O - H]^-$; requires m/z = 527.0951, found m/z = 527.0944.
IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3383(bw), 2952(w), 2906(w), 2869(w), 1734(s), 1539(s), 1364(m), 1286(s), 1190(bs), 1157(bs), 1041(m), 902(m), 875(m), 756(s), 745(s), 690(s).
Optical: $[\alpha]_D^{20}$ = +16.2° (*er* = 89:11, *c* = 1.0, $CHCl_3$).
HPLC (Chiralpak AD-H column, 20% EtOH in hexanes, 1.0 ml/min, 245 nm): t_R (minor enantiomer) = 10.9 min, t_R (major enantiomer) = 17.3 min.
racemic sample:



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Signal 3: DAD1 C, Sig=245,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
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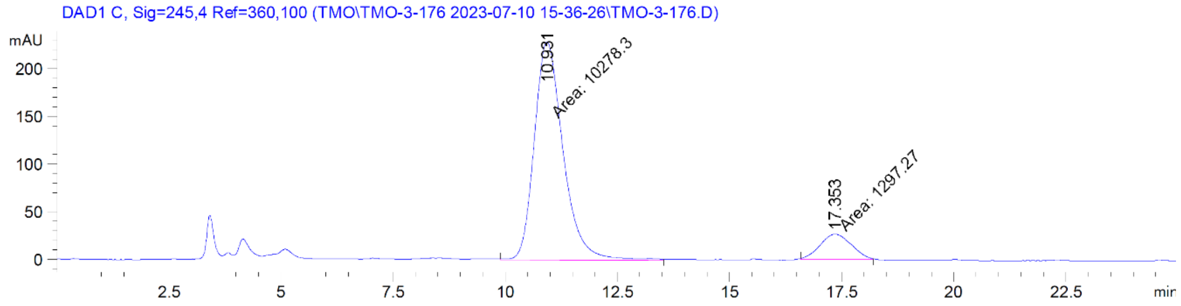
----|-------|----|-------|----------|----------|--------|
   1  10.905 BB     0.6879 6469.28076  145.16531  49.9640
   2  17.286 VB     0.7551 6478.61182  127.87296  50.0360

Totals :                   1.29479e4   273.03827
```

enantioselective sample:



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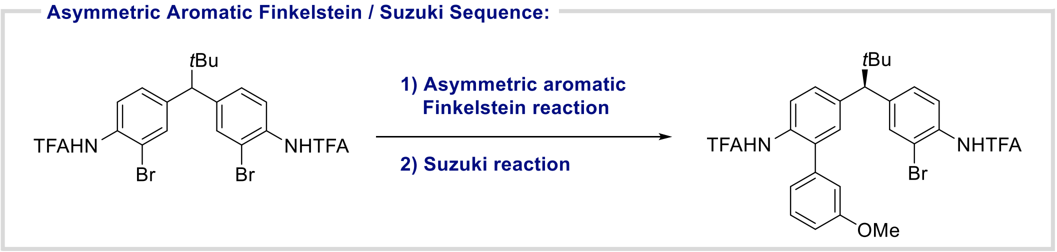
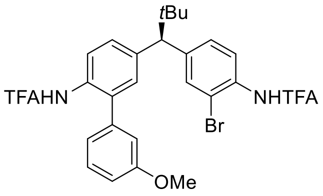
Signal 3: DAD1 C, Sig=245,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  10.931 MM    0.7478 1.02783e4  229.09161  88.7930
   2  17.353 MM    0.8150 1297.26660   26.53058  11.2070

Totals :                  1.15755e4  255.62220
```

5.4 Preparation and Characterization of Asymmetric Aromatic Finkelstein / Suzuki Sequence Product





(*R*)-*N*-(2-Bromo-4-(1-(3'-methoxy-6-(2,2,2-trifluoroacetamido)-[1,1'-biphenyl]-3-yl)-2,2-dimethylpropyl)phenyl)-2,2,2-trifluoroacetamide (6)

A 1-dram vial equipped with stir bar and septum cap was charged with **1** (120.8 mg, 0.20 mmol, 1.00 equiv.), Cu(MeCN)$_4$BF$_4$ (4.4 mg, 14.0 µmol, 0.07 equiv.), **L9** (15.9 mg, 0.03 mmol, 0.15 equiv.), K$_3$PO$_4$ (169.8 mg, 0.80 mmol, 4.00 equiv.) and NaI (36.0 mg, 0.24 mmol, 1.20 equiv.). The vial was evacuated and backfilled with N$_2$ (3x) before dry MeCN (0.3 mL, 0.66 M) was added. The reaction mixture was heated at 50 °C for 16 h. After cooling to r.t., the mixture was filtered through a plug of SiO$_2$ (eluted with EtOAc), transferred into a scintillation vial and concentrated *in vacuo*.

To the vial containing the crude material was added a stir bar and Pd(OAc)$_2$ (4.5 mg, 0.02 mmol, 0.10 equiv.) and 3-methoxyphenylboronic acid (42.5 mg, 0.28 mmol, 1.40 equiv.). Following evacuation and back-filling with N$_2$ (3x), dry toluene (1.0 mL, 0.2 M) and Et$_3$N (38.8 µL, 0.28 mmol, 1.40 equiv.) was added. The vial was sealed and heated at 100 °C for 24 h. The reaction mixture was cooled to r.t., filtered through a plug of SiO$_2$ (eluted with

EtOAc) and concentrated. Purification by automated column chromatography (Biotage, SNAP Ultra 10 g, gradient EtOAc in hexanes, 25 CV: 0-25%) yielded **6** as white solid (38.0 mg, 0.06 mmol, 30%).

Synthesis of racemic 6:

A 1-dram vial equipped with stir bar and septum cap was charged with **1** (60.4 mg, 0.10 mmol, 1.00 equiv.), $Pd(PPh_3)_4$ (2.9 mg, 2.50 µmol, 0.025 equiv.), CuI (1.9 mg, 0.01 mmol, 0.10 equiv.) and K_3PO_4 (63.7 mg, 0.30 mmol, 3.00 equiv.). The vial was evacuated and backfilled with N_2 (3x) before dry toluene (0.5 mL, 0.2 M) and phenylacetylene (12.1 µL, 0.11 mmol, 1.10 equiv.) was added. The reaction mixture was heated at 100 °C for 20 h. After cooling to r.t., the mixture was filtered through a plug of SiO_2 (eluted with EtOAc), concentrated *in vacuo* and purified by automated reverse-phase column chromatography (Biotage, SNAP C18 Ultra 12 g, gradient MeCN in H_2O (with 0.1% formic acid buffer): 15 CV: 0-100%; 10 CV: 100%).

R_F: 0.40 (hexanes/EtOAc 8:2)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (s, 1H), 8.24 (dd, *J* = 11.9, 8.5 Hz, 2H), 8.05 (s, 1H), 7.62 (d, *J* = 2.0 Hz, 1H), 7.49 – 7.41 (m, 3H), 7.30 (d, *J* = 2.2 Hz, 1H), 7.00 (ddd, *J* = 8.3, 2.5, 1.0 Hz, 1H), 6.94 – 6.88 (m, 1H), 6.88 – 6.82 (m, 1H), 3.85 (s, 3H), 3.72 (s, 1H), 1.04 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5, 155.1 (q, *J* = 37.5 Hz), 154.8 (q, *J* = 37.9 Hz), 142.4, 140.1, 138.1, 133.8, 132.8, 131.6, 131.6, 130.8, 130.8, 129.9, 129.8, 121.7, 121.2, 121.0, 115.9 (q, *J* = 288.5 Hz), 115.5 (q, *J* = 288.5 Hz), 114.7, 114.4, 113.9, 63.2, 55.5, 35.5, 29.3.

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.88, -76.03.

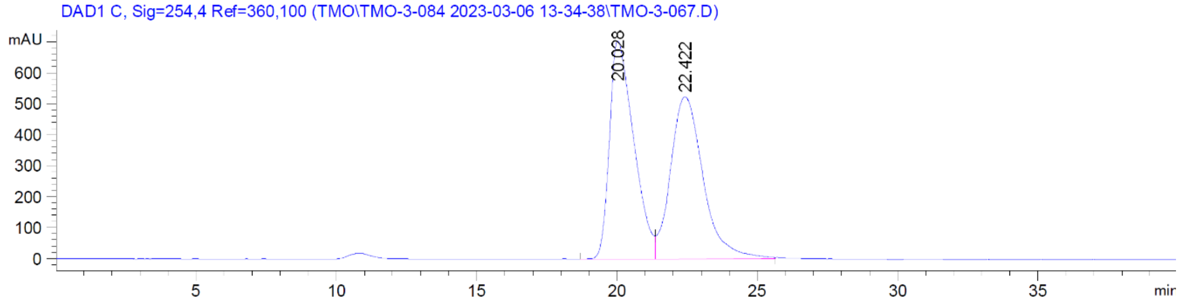
HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{28}H_{25}BrF_6N_2O_3 - H]^-$; requires m/z = 629.0880, found m/z = 629.0887.

IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3387(w), 3298(bw), 2963(bw), 2870(w), 1734(s), 1597(m), 1533(s), 1477(m), 1286(m), 1243(m), 1197(bs), 1159(s), 1039(w), 903(w), 833(w), 760(w), 735(w).

Optical: $[\alpha]_D^{20}$ = –4.2° (*er* = 91:9, *c* = 1.0, $CHCl_3$).

HPLC (Chiralpak AD-H column, 1% *i*-PrOH in hexanes, 1.0 ml/min, 254 nm): t_R (minor enantiomer) = 20.6 min, t_R (major enantiomer) = 22.4 min.

racemic sample:



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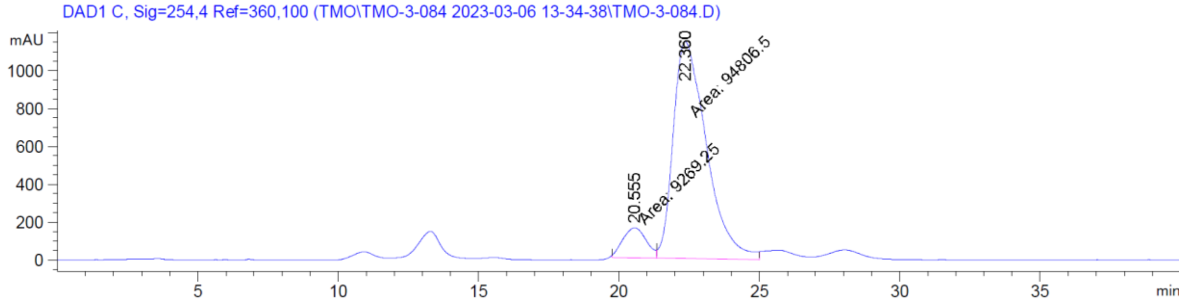
Signal 3: DAD1 C, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  20.028 BV     0.8987 4.23142e4  704.50958  49.8675
   2  22.422 VV     1.2121 4.25392e4  523.46753  50.1325

Totals :                   8.48534e4  1227.97711
```

enantioselective sample:



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Signal 3: DAD1 C, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height      Area
  #   [min]        [min]   [mAU*s]     [mAU]         %
----|-------|----|-------|----------|----------|--------|
   1  20.555 MF     0.9676 9269.24707  159.65927   8.9063
   2  22.360 FM     1.3777 9.48065e4  1146.93567  91.0937

Totals :                   1.04076e5  1306.59494
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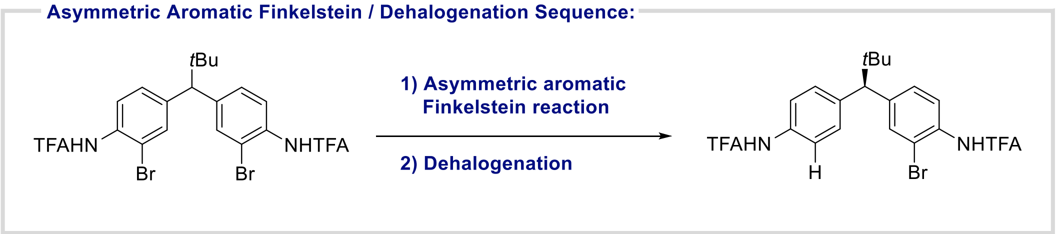
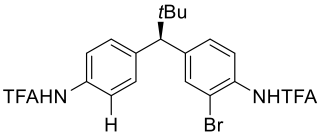
5.5 Preparation and Characterization of Asymmetric Aromatic Finkelstein / Dehalogenation Sequence Product





(*R*)-*N*-(4-(1-(3-Bromo-4-(2,2,2-trifluoroacetamido)phenyl)-2,2-dimethylpropyl)phenyl)-2,2,2-trifluoroacetamide (7)

A 1-dram vial equipped with stir bar and septum cap was charged with **1** (120.8 mg, 0.20 mmol, 1.00 equiv.), Cu(MeCN)$_4$BF$_4$ (4.4 mg, 14.0 µmol, 0.07 equiv.), **L9** (15.9 mg, 0.03 mmol, 0.15 equiv.), K$_3$PO$_4$ (169.8 mg, 0.80 mmol, 4.00 equiv.) and NaI (36.0 mg, 0.24 mmol, 1.20 equiv.). The vial was evacuated and backfilled with N$_2$ (3x) before dry MeCN (0.3 mL, 0.66 M) was added. The reaction mixture was heated at 50 °C for 16 h. After cooling to r.t., the mixture was filtered through a plug of SiO$_2$ (eluted with EtOAc), transferred into a scintillation vial and concentrated *in vacuo*.

To the vial containing the crude material was added a stir bar and $Pd(OAc)_2$ (4.5 mg, 0.02 mmol, 0.10 equiv.) and $NaBH_4$ (7.2 mg, 0.19 mmol, 0.95 equiv.). Following evacuation and back-filling with N_2 (3x), dry DMF (1.0 mL, 0.2 M) and TMEDA (39.2 µL, 0.26 mmol, 1.30 equiv.) was added. The vial was sealed and heated at 100 °C for 3 h. The reaction mixture was cooled to r.t., filtered through cotton (eluted with EtOAc) and concentrated by air stream evaporation. Purification by automated column chromatography (Biotage, SNAP Ultra 10 g, gradient EtOAc in hexanes, 20 CV: 0-25%) yielded **7** as white solid (42.1 mg, 0.08 mmol, 40%).

Synthesis of racemic 7:

A 1-dram vial equipped with stir bar and septum cap was charged with **1** (60.4 mg, 0.10 mmol, 1.00 equiv.), Pd_2dba_3 (4.6 mg, 5.00 µmol, 0.05 equiv.), SPhos (4.1 mg, 0.01 mmol, 0.10 equiv.), $NaBH_4$ (3.8 mg, 0.10 mmol, 1.00 equiv.) and K_3PO_4 (63.7 mg, 0.30 mmol, 3.00 equiv.). The vial was evacuated and backfilled with N_2 (3x) before dry toluene (0.5 mL, 0.2 M) and TMEDA (19.6 µL, 0.13 mmol, 1.30 equiv.) was added. The reaction mixture was heated at 100 °C for 18 h. After cooling to r.t., the mixture was filtered through a plug of SiO_2 (eluted with EtOAc), concentrated *in vacuo* and purified by automated column chromatography (Biotage, SNAP Ultra 10 g, gradient EtOAc in hexanes: 25 CV: 0-25%).

R_F: 0.25 (hexanes/EtOAc 8:2)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 8.21 (d, *J* = 8.6 Hz, 1H), 7.89 (s, 1H), 7.61 (d, *J* = 2.1 Hz, 1H), 7.51 (d, *J* = 8.6 Hz, 2H), 7.44 (dd, *J* = 8.6, 2.1 Hz, 1H), 7.39 (d, *J* = 8.6 Hz, 2H), 3.69 (s, 1H), 1.02 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 154.9 (q, *J* = 37.0 Hz), 154.8 (q, *J* = 37.0 Hz), 142.5, 140.4, 133.7, 131.5, 130.6, 129.9, 121.6, 120.4, 115.8 (q, *J* = 288.8 Hz), 115.7 (q, *J* = 288.8 Hz), 113.9, 63.1, 35.4, 29.2.

^{19}F NMR (376 MHz, $CDCl_3$) δ -75.72, -75.87.

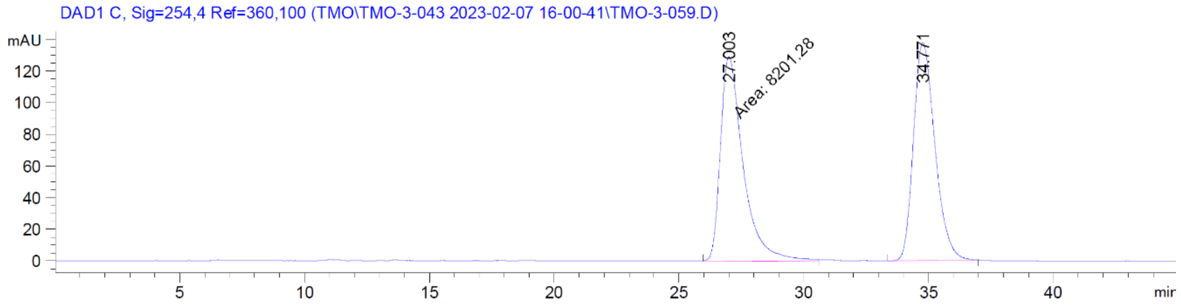
HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{21}H_{19}BrF_6N_2O_2 - H]^-$; requires m/z = 523.04613, found m/z = 523.0463.

IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3383(w), 3299(bw), 2964(w), 2925(w), 2874(w), 1715(s), 1605(w), 1533(m), 1285(m), 1247(m), 1189(bs), 1154(bs), 1044(w), 902(w), 837(w), 760(m), 733(m).

Optical: $[\alpha]_D^{20}$ = –5.9° (*er* = 92:8, *c* = 1.0, $CHCl_3$).

HPLC (Chiralpak AD-H column, 5% *i*-PrOH in hexanes, 0.5 ml/min, 254 nm): t_R (major enantiomer) = 26.9 min, t_R (minor enantiomer) = 35.1 min.

racemic sample:



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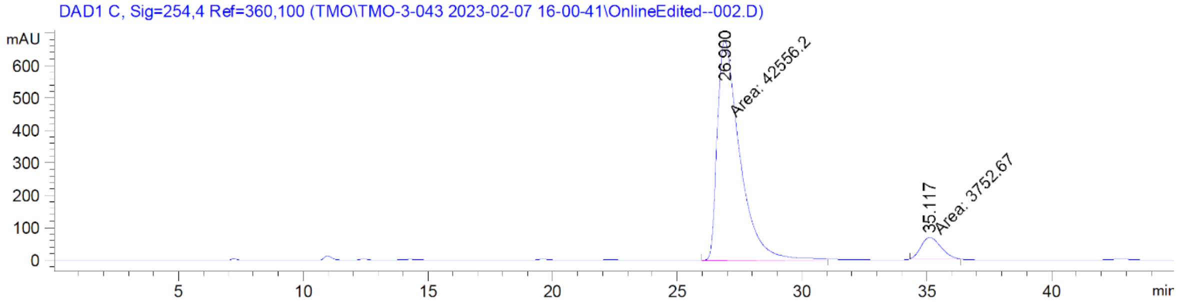
Signal 3: DAD1 C, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  27.003 MM    1.0582 8201.28418  129.17070  49.9062
   2  34.771 BB    0.9210 8232.10938  137.79858  50.0938

Totals :                  1.64334e4   266.96928
```

enantioselective sample:



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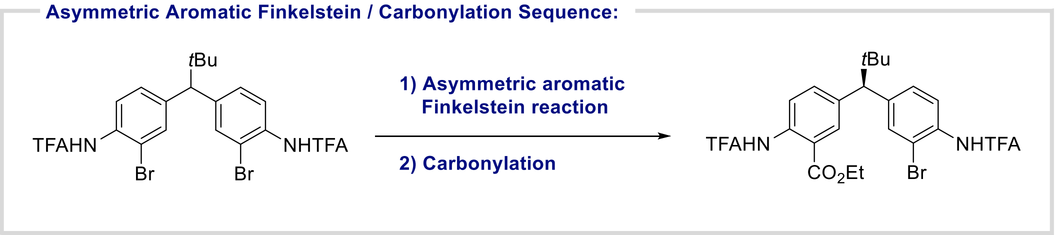
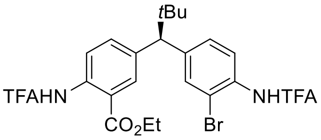
Signal 3: DAD1 C, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1  26.900 MM    1.0486 4.25562e4  676.38562  91.8964
   2  35.117 MM    0.9312 3752.67017  67.16611   8.1036

Totals :                  4.63089e4   743.55173
```

5.6 Preparation and Characterization of Asymmetric Aromatic Finkelstein / Carbonylation Sequence Product





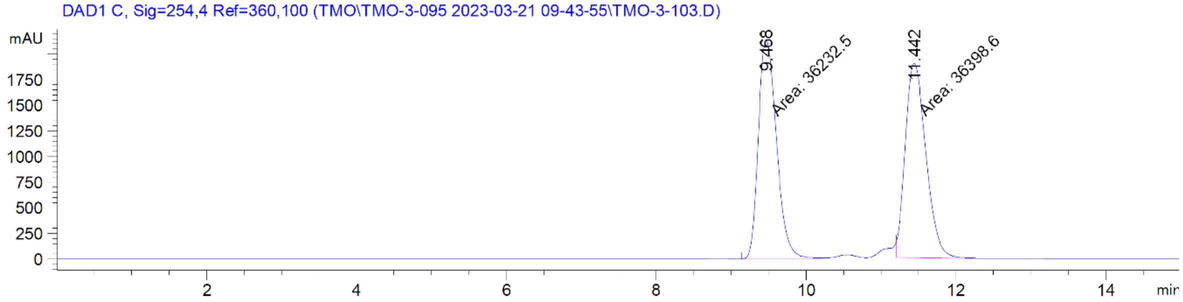
Ethyl (*R*)-5-(1-(3-bromo-4-(2,2,2-trifluoroacetamido)phenyl)-2,2-dimethylpropyl)-2-(2,2,2-trifluoroacetamido)benzoate (8)

A 1-dram vial equipped with stir bar and septum cap was charged with **1** (120.8 mg, 0.20 mmol, 1.00 equiv.), $Cu(MeCN)_4BF_4$ (4.4 mg, 14.0 µmol, 0.07 equiv.), **L9** (15.9 mg, 0.03 mmol, 0.15 equiv.), K_3PO_4 (169.8 mg, 0.80 mmol, 4.00 equiv.) and NaI (36.0 mg, 0.24 mmol, 1.20 equiv.). The vial was evacuated and backfilled with N_2 (3x) before dry MeCN (0.3 mL, 0.66 M) was added. The reaction mixture was heated at 50 °C for 16 h. After cooling to r.t., the mixture was filtered through a plug of SiO_2 (eluted with EtOAc), transferred into a scintillation vial and concentrated *in vacuo*.

To the vial containing the crude material was added a stir bar and $Pd(OAc)_2$ (4.5 mg, 0.02 mmol, 0.10 equiv.). Following evacuation and back-filling with N_2 (3x), dry DMF (2.0 mL, 0.1 M), Et_3N (0.28 mL, 2.00 mL, 10.0 equiv.) and EtOH (0.25 mL) was added. The mixture was purged with CO (balloon) for 5 min, and the mixture was heated at 90 °C for 16 h under an atmosphere of CO. The reaction mixture was cooled to r.t., filtered through a plug SiO_2 (eluted with EtOAc) and concentrated by air stream evaporation. Purification by automated reverse-phase column chromatography (Biotage, SNAP C-18 Ultra 12 g, gradient MeCN in water (0.1% formic acid buffer), 3 CV: 0-60%, 10 CV: 60-100%, 5 CV: 100%) yielded **8** as white solid (59.8 mg, 0.10 mmol, 50%).

Synthesis of racemic 8: Prepared according to the procedure for enantioenriched **8**, using TMG-Gly-OLi as ligand for the aromatic Finkelstein reaction.

R_F: 0.55 (hexanes/EtOAc 8:2)
^{1}H NMR (400 MHz, $CDCl_3$) δ 12.23 (s, 1H), 8.60 (d, *J* = 8.7 Hz, 1H), 8.39 (s, 1H), 8.24 (d, *J* = 8.5 Hz, 1H), 8.09 (d, *J* = 2.3 Hz, 1H), 7.67 (dd, *J* = 8.7, 2.3 Hz, 1H), 7.62 (d, *J* = 2.1 Hz, 1H), 7.45 (dd, *J* = 8.6, 2.1 Hz, 1H), 4.44 (q, *J* = 7.1 Hz, 2H), 3.73 (s, 1H), 1.46 (t, *J* = 7.1 Hz, 3H), 1.03 (s, 9H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 155.3 (q, *J* = 37.4 Hz), 154.8 (q, *J* = 37.8 Hz), 141.9, 138.7, 137.5, 135.7, 133.7, 132.2, 131.7, 129.9, 121.7, 120.7, 116.4, 115.8 (q, *J* = 288.6 Hz), 115.7 (q, *J* = 288.5 Hz), 113.9, 62.8, 62.4, 35.5, 29.1, 14.3.
^{19}F NMR (376 MHz, $CDCl_3$) δ -75.87, -76.24.
HRMS (ESI/Q-TOF): Exact mass calculated for $[C_{23}H_{21}BrF_6N_2O_4 - H]^-$; requires m/z = 595.0673, found m/z = 595.0682.
IR (FT-ATR, cm^{-1}, thin film) ν_{max} = 3389(w), 2967(bw), 2874(w), 1734(s), 1695(m), 1603(m), 1530(s), 1371(m), 1289(s), 1266(s), 1192(bs), 1159(bs), 1086(m), 1018(w), 903(w), 838(w), 734(m), 600(w).
Optical: $[\alpha]_D^{20}$ = +9.8° (*er* = 93:7, *c* = 1.0, $CHCl_3$).
HPLC (Chiralpak AD-H column, 5% *i*-PrOH in hexanes, 0.5 ml/min, 254 nm): t_R (major enantiomer) = 9.5 min, t_R (minor enantiomer) = 11.5 min.
racemic sample:



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Signal 3: DAD1 C, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]        %
----|-------|----|-------|----------|----------|--------|
   1   9.468 MM    0.2825 3.62325e4  2137.33325  49.8857
   2  11.442 MM    0.3197 3.63986e4  1897.69580  50.1143

Totals :                  7.26311e4  4035.02905
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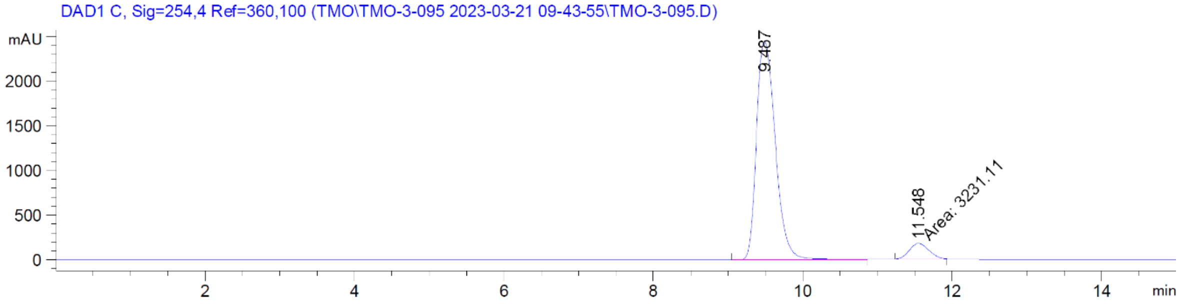
enantioselective sample:



```
Signal 3: DAD1 C, Sig=254,4 Ref=360,100

Peak RetTime Type  Width     Area      Height     Area
  #   [min]        [min]   [mAU*s]     [mAU]       %
----|-------|----|-------|----------|----------|--------|
   1   9.487 VV    0.2747 4.29832e4  2450.28442  93.0084
   2  11.548 MM    0.3027 3231.11060  177.87854   6.9916

Totals :                  4.62143e4  2628.16296
```

6. Mechanistic Studies

6.1. Reaction Progress Monitoring

Eight 1-dram vials were equipped with a stir bar and septum cap and were charged with **1** (60.4 mg, 0.10 mmol, 1.00 equiv.), Cu(MeCN)$_4$BF$_4$ (3.1 mg, 10.0 µmol, 0.01 equiv.), **L9** (8.0 mg, 0.015 mmol, 0.15 equiv.), K$_3$PO$_4$ (84.9 mg, 0.40 mmol, 4.00 equiv.) and NaI (18.0 mg, 0.12 mmol, 1.20 equiv.). The vials were evacuated and backfilled with N$_2$ (3x) before dry MeCN (0.2 mL, 0.5 M) was added. The reaction mixtures were heated at 50 °C for 0, 2, 4, 7, 10, 11.5, 13, 16 h. After cooling to r.t., each mixture was filtered through a plug of SiO$_2$ (eluted with EtOAc), concentrated and analyzed by ^{1}H NMR and chiral HPLC. NMR yield ($\delta = 3.64$ ppm) was determined against CH$_2$Br$_2$ as internal standard and the enantiomeric ratio could be determined by chiral HPLC comparing against authentic samples of **1** and **3**.

Table S7: Reaction progress monitoring.

	Molar Fraction [%]					
Time [h]	**1**	**2**	**3**	***er***		***ee***
0	100	0	0			
2	100	0	0			
4	100	0	0			
7	97	5	0	12	88	76
10	83	21	0	10	90	80
11.5	27	57	14	8	92	84
13	24	63	13	6	94	88
16	22	61	12	5	95	90

6.2. Origin of Induction Period

Pre-stirring Substrate and Base: Two 1-dram vials were equipped with a stir bar and septum cap and were charged with **1** (60.4 mg, 0.10 mmol, 1.00 equiv.) and K$_3$PO$_4$ (84.9 mg, 0.40 mmol, 4.00 equiv.). The vials were evacuated and backfilled with N$_2$ (3x) before dry MeCN (0.2 mL, 0.5 M) was added. The reaction mixtures were heated at 50 °C for 6 h. After cooling to r.t., Cu(MeCN)$_4$BF$_4$ (3.1 mg, 10.0 µmol, 0.01 equiv.), **L9** (8.0 mg, 0.015 mmol, 0.15 equiv.), and NaI (18.0 mg, 0.12 mmol, 1.20 equiv.) were added before heating at 50 °C was continued for 30 min and 60 min, respectively. Each mixture was filtered through a plug of SiO$_2$ (eluted with EtOAc), concentrated and analyzed by ^{1}H NMR. NMR yield ($\delta = 3.64$ ppm) was determined against CH$_2$Br$_2$ as internal standard.

Table S8: Identifying the origin of the induction period.

	Molar Fraction [%]			
Time [min]	**1**	**2**	**3**	
0	100	0	0	*assumed*
30	88	13	0	
60	46	48	6	

Pre-stirring Catalyst: Two 1-dram vials were equipped with a stir bar and septum cap and were charged with $Cu(MeCN)_4BF_4$ (3.1 mg, 10.0 µmol, 0.01 equiv.), **L9** (8.0 mg, 0.015 mmol, 0.15 equiv.), NaI (18.0 mg, 0.12 mmol, 1.20 equiv.) and K_3PO_4 (84.9 mg, 0.40 mmol, 4.00 equiv.). The vials were evacuated and backfilled with N_2 (3x) before dry MeCN (0.2 mL, 0.5 M) was added. The reaction mixtures were heated at 50 °C for 6 h. After cooling to r.t., **1** (60.4 mg, 0.10 mmol, 1.00 equiv.) was added before heating at 50 °C was continued for 30 min and 60 min, respectively. Each mixture was filtered through a plug of SiO_2 (eluted with EtOAc), concentrated and analyzed by ^1H NMR. NMR yield ($\delta = 3.64$ ppm) was determined against CH_2Br_2 as internal standard.

Table S9: Identifying the origin of the induction period.

	Molar Fraction [%]			
Time [min]	**1**	**2**	**3**	
0	100	0	0	*assumed*
30	92	6	0	
60	96	6	0	

6.3. Correlation of ^{13}C NMR Shift with Enantioselectivity

Table S10: NMR correlation of central methine carbon.

Compound	Substituent	*er*		*ee* [%]	ln(*er*)	^{13}C NMR shift [ppm]	V_{Bur} ($r = 3.0$ Å) LEC [%]
15	Me	55	45	10	0.2006707	43.5	60.7
14	*i*Pr	82	18	64	1.51634749	59.2	85.7
13	Cy	84	16	68	1.65822808	58	90.5
12	CyMe	94	6	88	2.75153531	62.7	96.6
11	Ad	92	8	84	2.44234704	64.7	94.1
4	*t*Bu	94	6	88	2.75153531	62.8	94.2

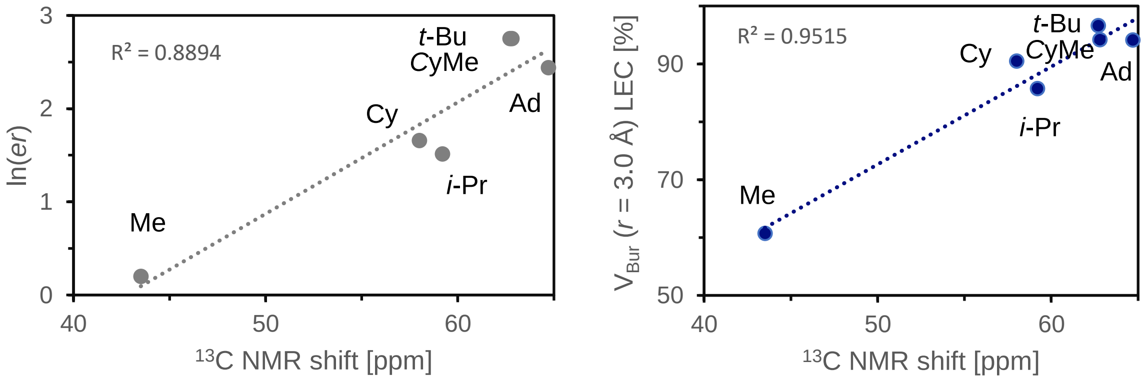


Figure S2: Correlation between 13C NMR shift of central methylene carbon and enantioselectivty/computed V_{Bur}.

7. Computational Details

Conformational Search and DFT Geometry Optimization:

Molecular mechanics conformational search employing Schrödinger MacroModel and the OPLS4 force field was performed for each diarylmethine.[6,7] The conformational searches were performed in gas phase with a maximum of 10,000 interactions and convergence threshold of 0.001 au. The conformer window was restricted to 5.02 kcal/mol of the lowest energy conformer, excluding mirror-image conformers. Density Functional Theory (DFT) geometry optimizations for all conformers were then performed at the ωB97X-D/def2-SVP level employing Gaussian16 version C.01.[8] Frequency calculations confirmed the minima nature of each conformer. Energies and molecular features were computed at the ωB97X-D/def2-TZVP level. Natural bond orbital analysis was performed using NBO 7.0.[9]

Featurization and Molecular Descriptors Collection:

Global and atom-specific (Figure S3) molecular descriptors were collected from Gaussian output files or computed with the Morfeus python package[10] and the DBSTEP python package.[11] For each molecular descriptor, the minimum, maximum, and Boltzmann-weighted average values of the descriptor as well as the descriptor value for lowest energy conformer in the conformational ensemble were collected. Boltzmann-weighted properties were calculated using the Gibbs corrected energies computed using GoodVibes.[12] A complete list of these descriptors is available as supporting information as “Computed_Properties.xlsx.”

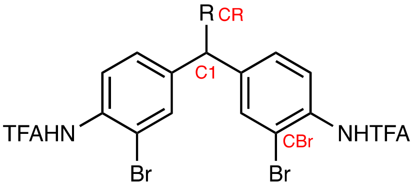


Figure S3: Atom numbering used to collect atom-specific descriptors.

Global descriptors:

- HOMO and LUMO energies
- dipole moment
- molar volume.

Atom-specific descriptors:

- Natural Population Analysis charges for C1, CR, and CBr.{keyword: POP=NBO7]
- NMR shielding for C1, CR, and CBr. {keyword: NMR}
- V_{Bur} for C1 and CR calculated from 2 to 5 Å at 0.5 Å steps, computed with Morfeus.
- Sterimol Bmin and Bmax values (C1 to CR) from 0 to 3 Å at 0.5 Å steps, computed with DBSTEP.

Linear Regression:

Univariate linear regressions were generated to search for correlations between the computed molecular descriptors and the measured enantioselectivities. The linear models were trained on compounds **4**, **11**, **13**, **14**, and **15** and tested to predict the enantioselectivity of compound **12**. We identified the two best fit univariate linear models which show correlation between the measure enantioselectivities with variations of the computed buried volume (V_{Bur}) at the substituent carbon. Each model has an R^2 value of 0.89 and error in the predicted $\Delta\Delta G^{\ddagger}$ for **12** lower than 0.03 kcal/mol, Table S11. Since both models exhibit similar metric, we focused the discussion centered on the V_{Bur} (r = 3.0 Å) computed for the lowest energy conformer (LEC) in the manuscript, Table S12. The advantage of using this descriptor lies in its reliance on the calculation of V_{Bur} for only one conformer, as opposed to minimum value V_{Bur}, which require calculations for multiple conformers. Given previous studies,[13] we also evaluated the correlation between observed enantioselectivity and Charton values (Figure S4A). Notably, this led to similar overall statistics ($R^2 = 0.90$) but is limited to substituents for which the Charton value has been empirically determined. Charton values are modestly correlated, but not perfectly co-linear with the V_{Bur} parameter employed in our model, Figure S4B.

Table S11: Linear regression models.

Molecular Descriptor	Equation	R^2	Q^2	Predicted $\Delta\Delta G^{\ddagger}$ 12 [kcal/mol]	Error $\Delta\Delta G^{\ddagger}$ 12 [kcal/mol]
V_{Bur} (R = 2.5 Å) min value	y = 0.07*x – 5.01	0.89	0.91	1.54 [*e.r.* 92:8]	–0.022
V_{Bur} (R = 3.0 Å) LEC	y = 0.04*x – 2.53	0.89	0.89	1.59 [*e.r.* 92:8]	+0.025

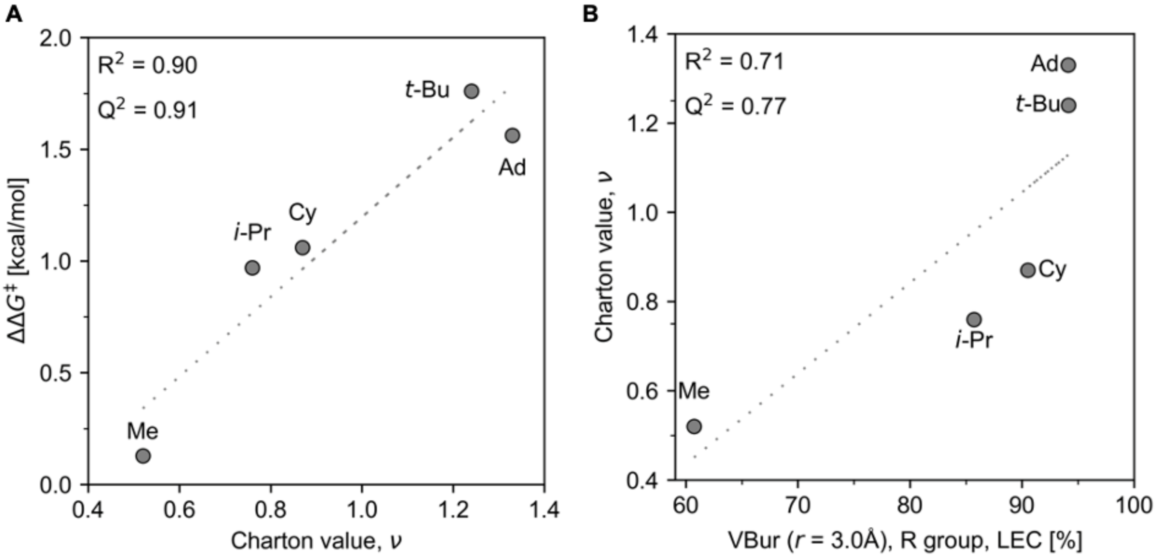


Figure S4: Correlation between empirically derived Charton values and computed V_{Bur}.

Computed buried volume and plane angle for each diarylmethine:

Table S12: Gibbs corrected energy range within the conformational ensemble, computed buried volume for the lowest energy conformer (LEC), and plane angle for the LEC, Boltzmann averaged, and the range within the conformational ensemble of each diarylmethine.

Name	**Energy range (kcal/mol)**	**V_{Bur} (*r* = 3.0 Å) LEC [%]**	**Plane Angle LEC [°]**	**Plane Angle Boltzmann [°]**	**Plane Angle Range [°]**
4	0.72	94.2	57.9	59.7	3.4
11	0.52	94.1	72.8	72.5	1.1
13	2.61	90.5	74.3	74.6	2.5
14	2.13	85.7	75.5	75.0	3.2
12	0.84	96.6	67.9	68.1	1.6
15	1.53	60.7	87.8	87.4	1.9

8. X-Ray Crystallography

Experimental

Low-temperature diffraction data (ω-scans) were collected on a Rigaku Synergy-S diffractometer coupled to a HyPix-Arc 100 detector with Cu Kα (λ = 1.54178 Å) for the structure of syn-23123. The diffraction images were processed and scaled using Rigaku Oxford Diffraction software (CrysAlisPro; Rigaku OD: The Woodlands, TX, 2015). The structure was solved with SHELXT and was refined against F^2 on all data by full-matrix least squares with SHELXL.[14] All non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included in the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the U value of the atoms to which they are linked (1.5 times for methyl groups). This data was refined as a 2-component inversion twin.

The fractional volume contribution of the minor twin component was freely refined to a converged value of 0.184(5). After accounting for the inversion twin, the major volume of the crystal produced a model with the S enantiomer and a Hooft parameter of 0.0176(11), calculated by the program OLEX2.[15] A centrosymmetric solution of $P2_1/c$ was investigated. There is a 100% fit of the data to a *c*-glide which would imply a racemic mixture within the crystal. However, the *c*-glide is a pseudosymmetry element in this case. The glide plane would require the I and Br to occupy the same space. The $P2_1/c$ model was tested and the distributions of I and Br did indeed converge near 50/50. However, the refinement metrics of $P2_1/c$ are much worse than $P2_1$, implying the polar space group is correct. The I and Br atoms are not related by crystallographic symmetry. The inversion twin does suggest a small amount of the crystal could contain the R enantiomer, but not at a racemic population. This is corroborated by the distributions seen in the chiral HPLC separation. The full numbering scheme of compound syn-23123 can be found in the full details of the X-ray structure determination (CIF), which is included as Supporting Information. CCDC number 2286887 (syn-23123) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

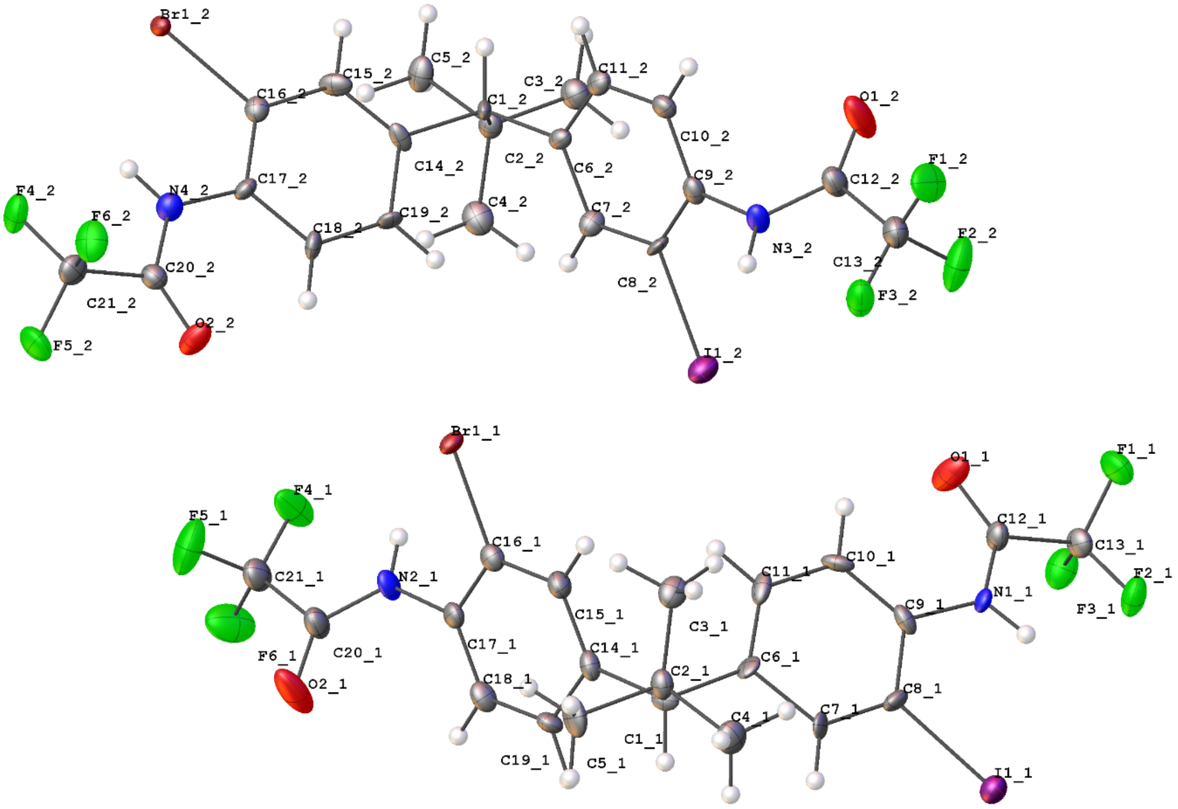


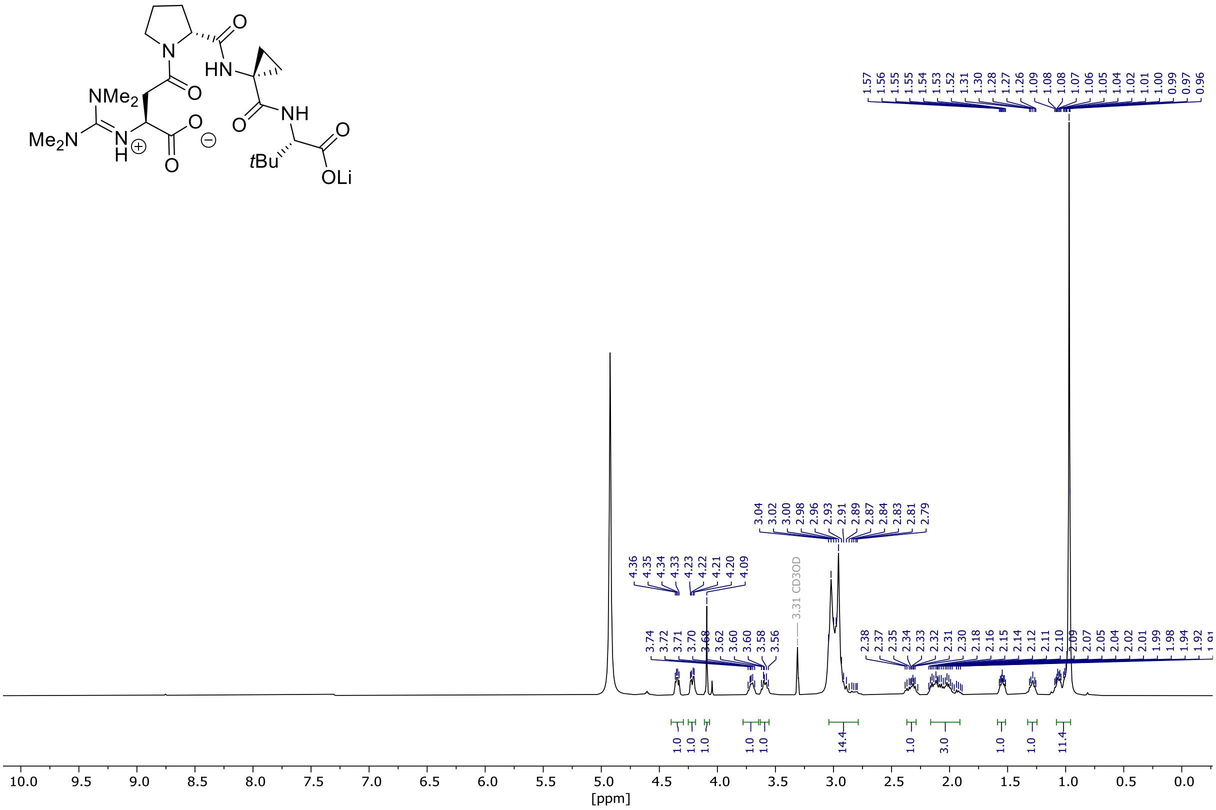
Figure S5: The complete numbering scheme of **2** with 50% thermal ellipsoid probability levels. The models have the same numbers for chemically identical atoms that are crystallographically distinct. These two models are distinguished with the suffixes _1 and _2. The hydrogen atoms are shown as circles for clarity.

Table S13: Crystal data and structure refinement for syn-23123.

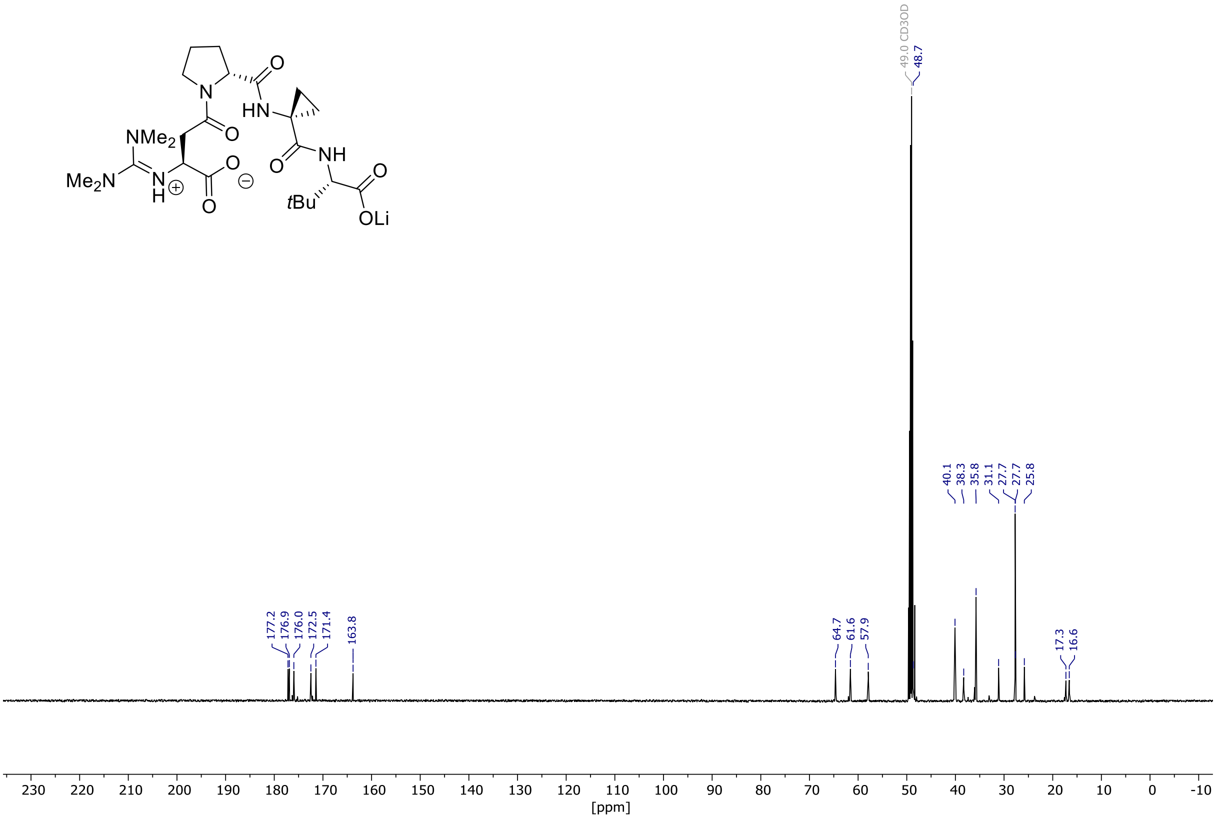
Identification code	syn-23123	
Empirical formula	C21 H18 Br F6 I N2 O2	
Formula weight	651.18	
Temperature	93(2) K	
Wavelength	1.54184 Å	
Crystal system	Monoclinic	
Space group	$P2_1$	
Unit cell dimensions	a = 12.38796(9) Å	α= 90°.
	b = 14.12473(10) Å	β= 100.3448(7)°.
	c = 13.32450(10) Å	γ = 90°.
Volume	2293.58(3) Å^3	
Z	4	
Density (calculated)	1.886 Mg/m^3	
Absorption coefficient	13.663 mm^{-1}	
F(000)	1264	
Crystal size	0.050 x 0.050 x 0.010 mm^3	
Crystal color and habit	Colorless Plate	
Diffractometer	XtaLAB Synergy, Dualflex, HyPix-Arc 100	
Theta range for data collection	3.372 to 79.806°.	
Index ranges	-15<=h<=15, -17<=k<=17, -16<=l<=16	
Reflections collected	68100	
Independent reflections	9705 [R(int) = 0.0566]	
Observed reflections (I > 2sigma(I))	9470	
Completeness to theta = 67.684°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.26536	
Solution method	SHELXT-2014/5 (Sheldrick, 2014)	
Refinement method	SHELXL-2014/7 (Sheldrick, 2014)	
Data / restraints / parameters	9705 / 1 / 602	
Goodness-of-fit on F^2	1.083	
Final R indices [I>2sigma(I)]	R1 = 0.0349, wR2 = 0.0909	
R indices (all data)	R1 = 0.0357, wR2 = 0.0916	
Absolute structure parameter	0.184(5)	
Extinction coefficient	n/a	
Largest diff. peak and hole	1.915 and -0.904 e.Å^{-3}	

9. NMR Spectra

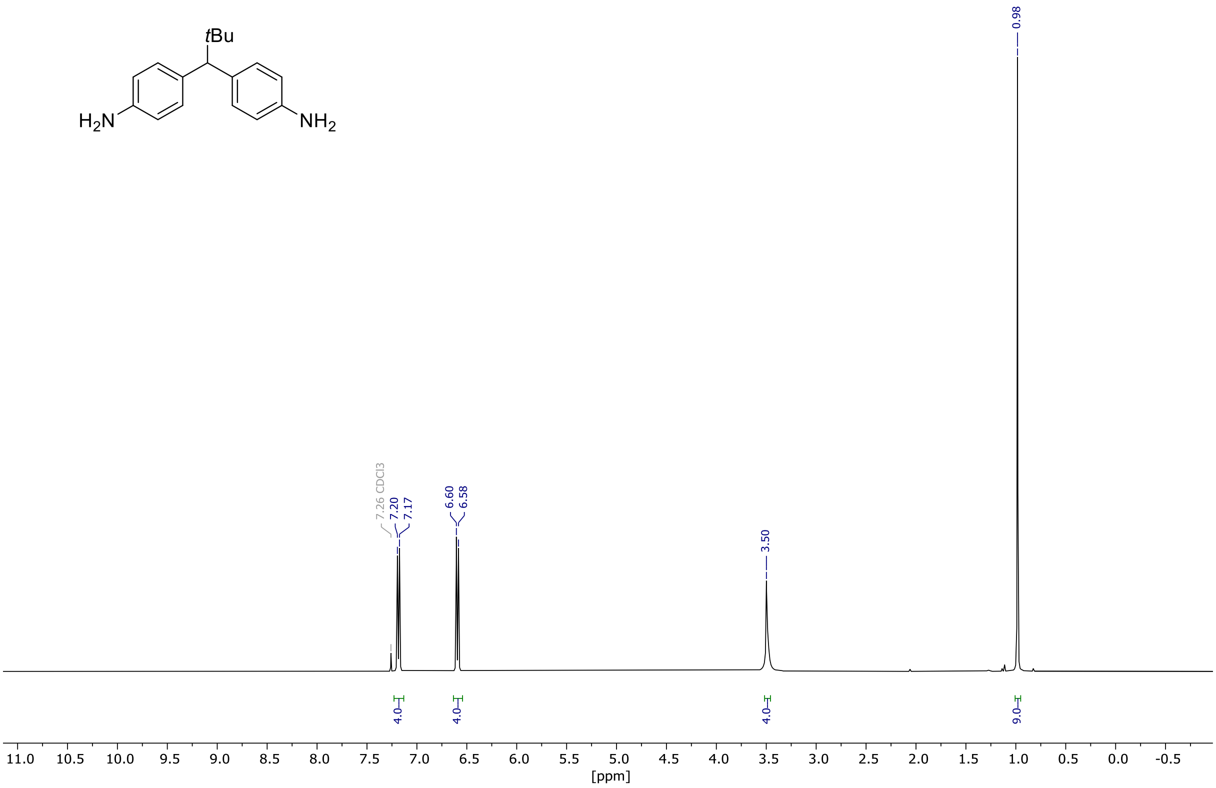
^{1}H NMR (400 MHz, CD_3OD): **L10**



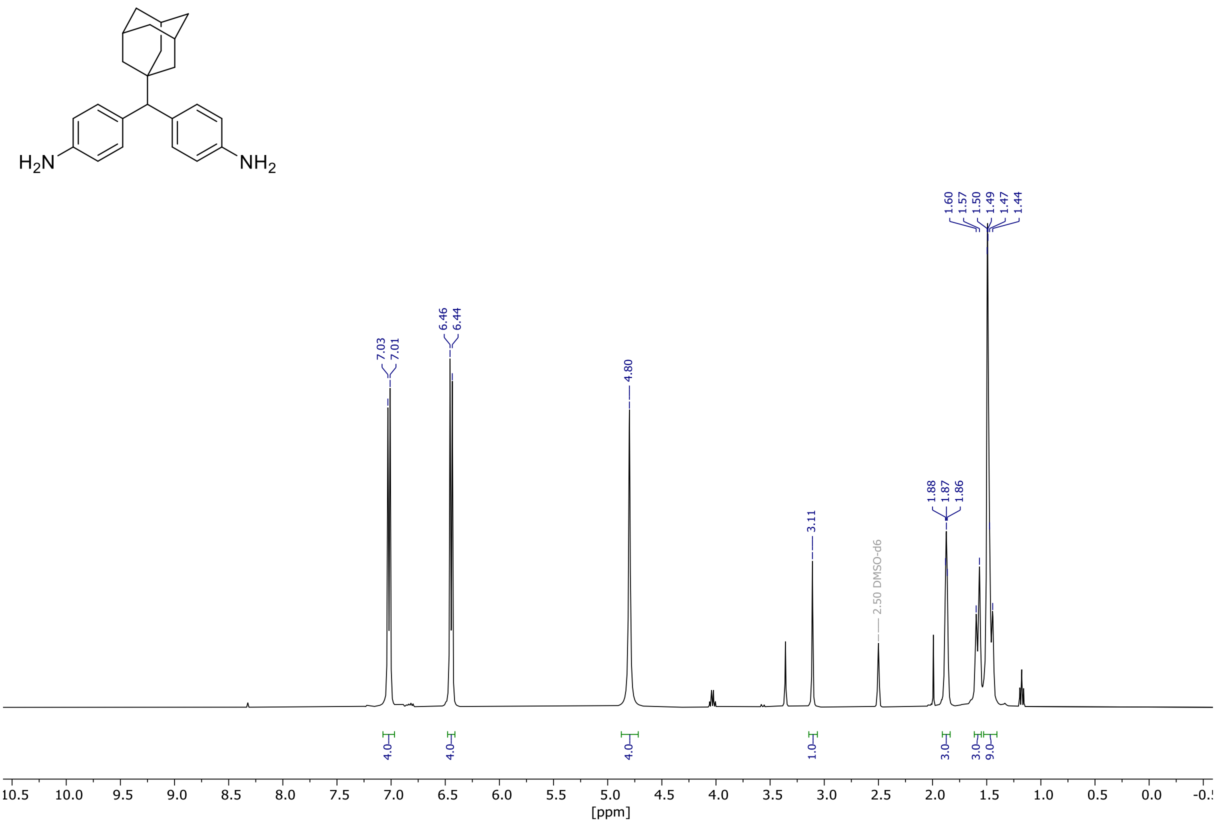
^{13}C NMR (101 MHz, CD_3OD): **L10**



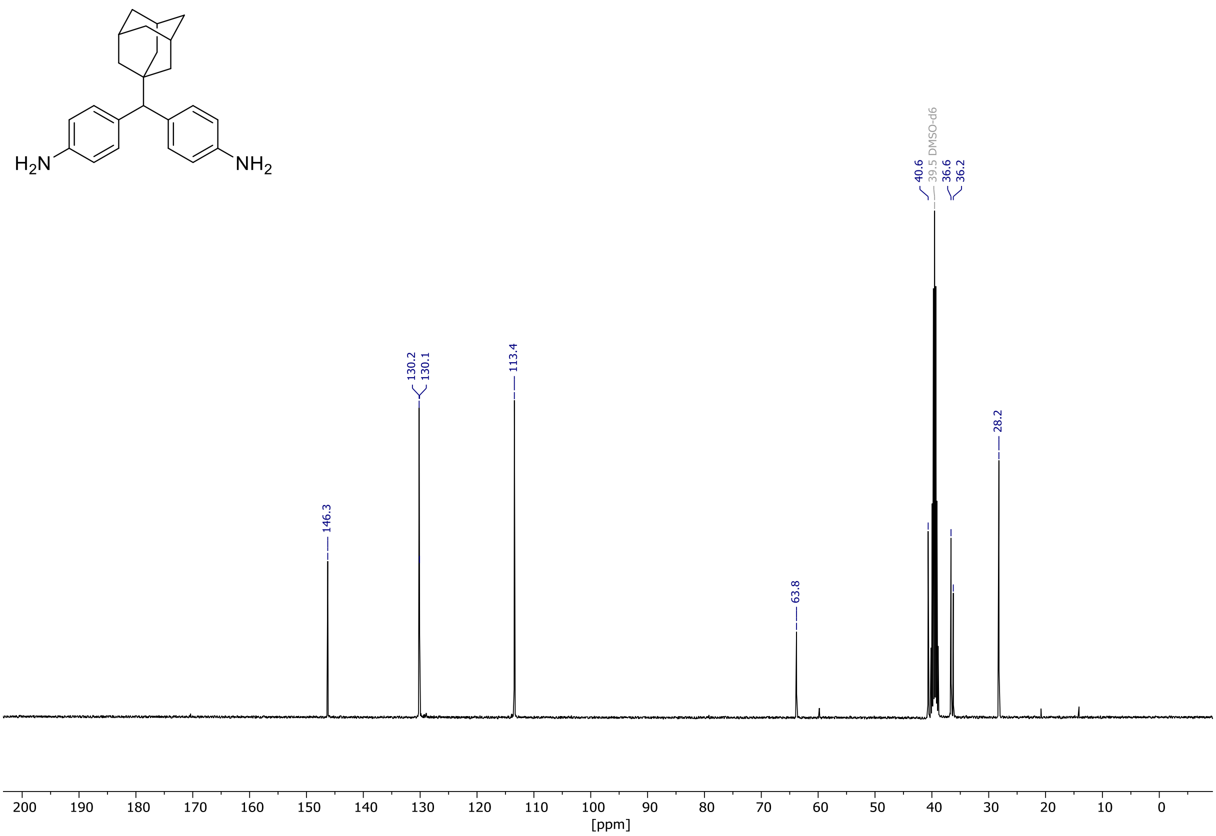
^{1}H NMR (400 MHz, $CDCl_3$): **S4**



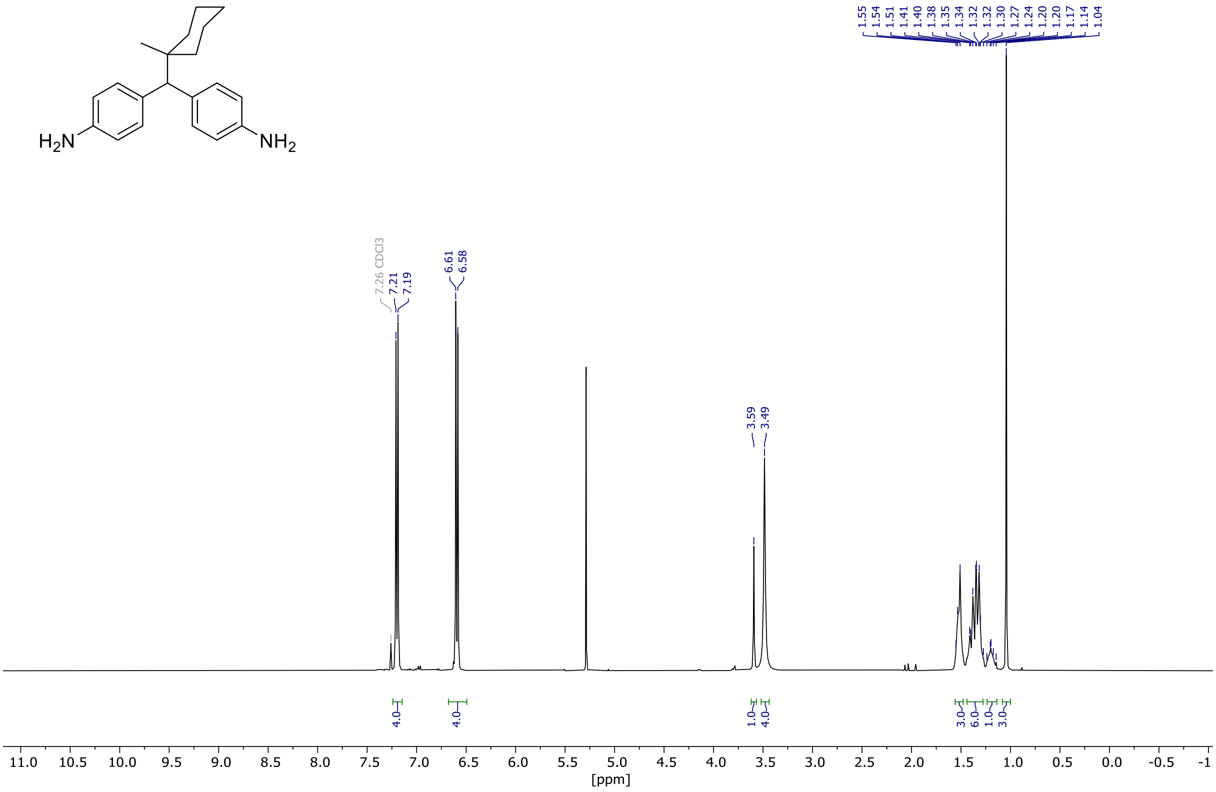
^{1}H NMR (400 MHz, *d_6*-DMSO): **S5**



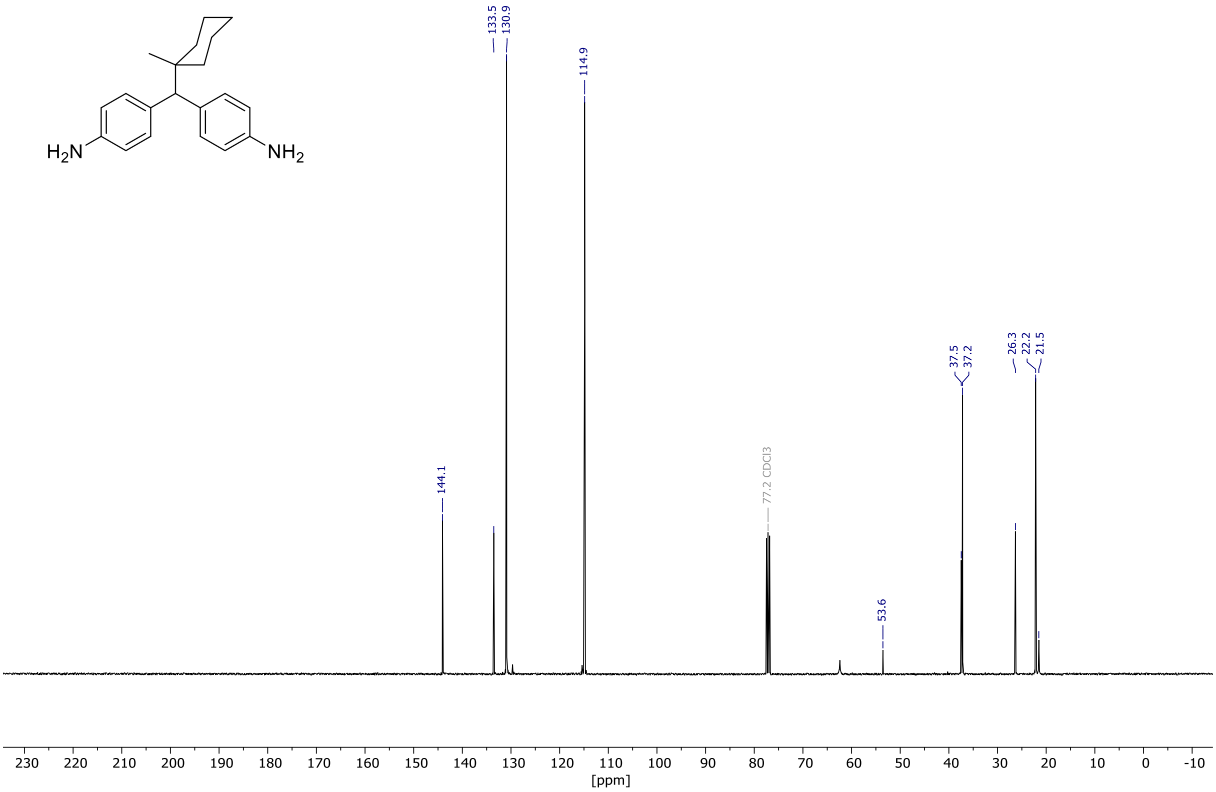
^{13}C NMR (101 MHz, *d*$_6$-DMSO): S5



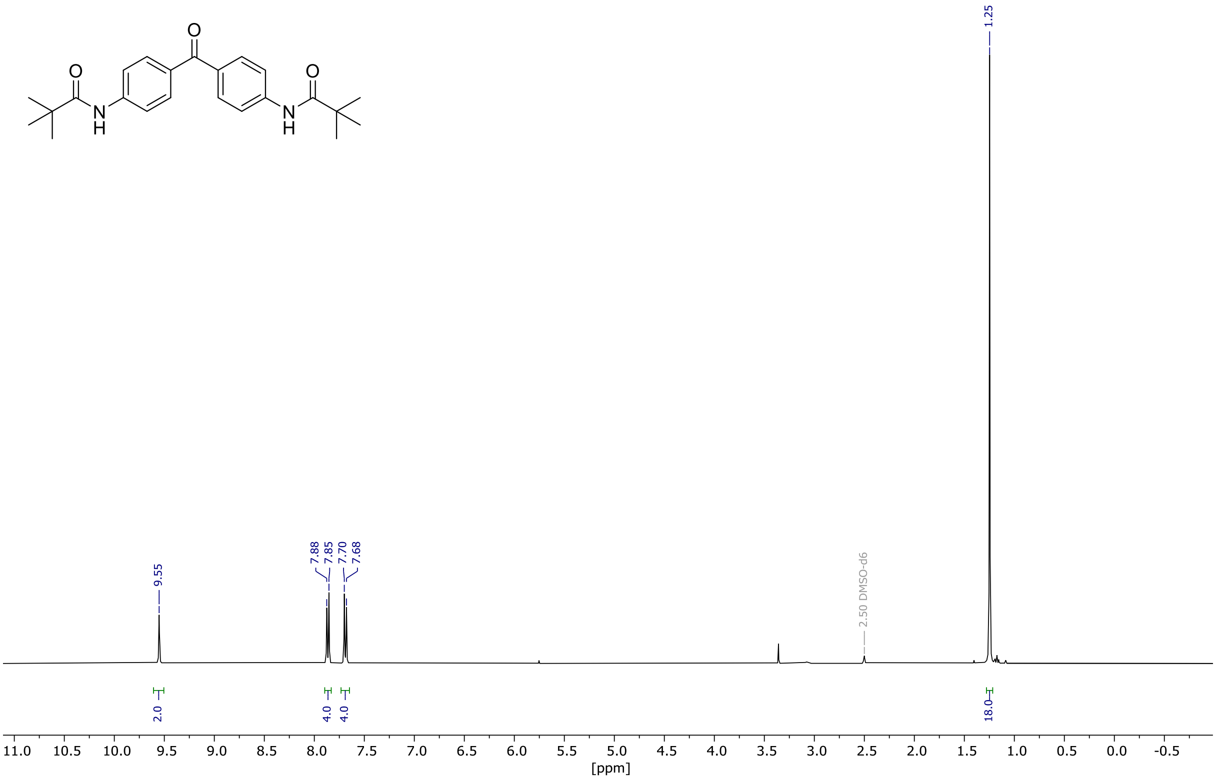
^{1}H NMR (400 MHz, CDCl$_3$): S6



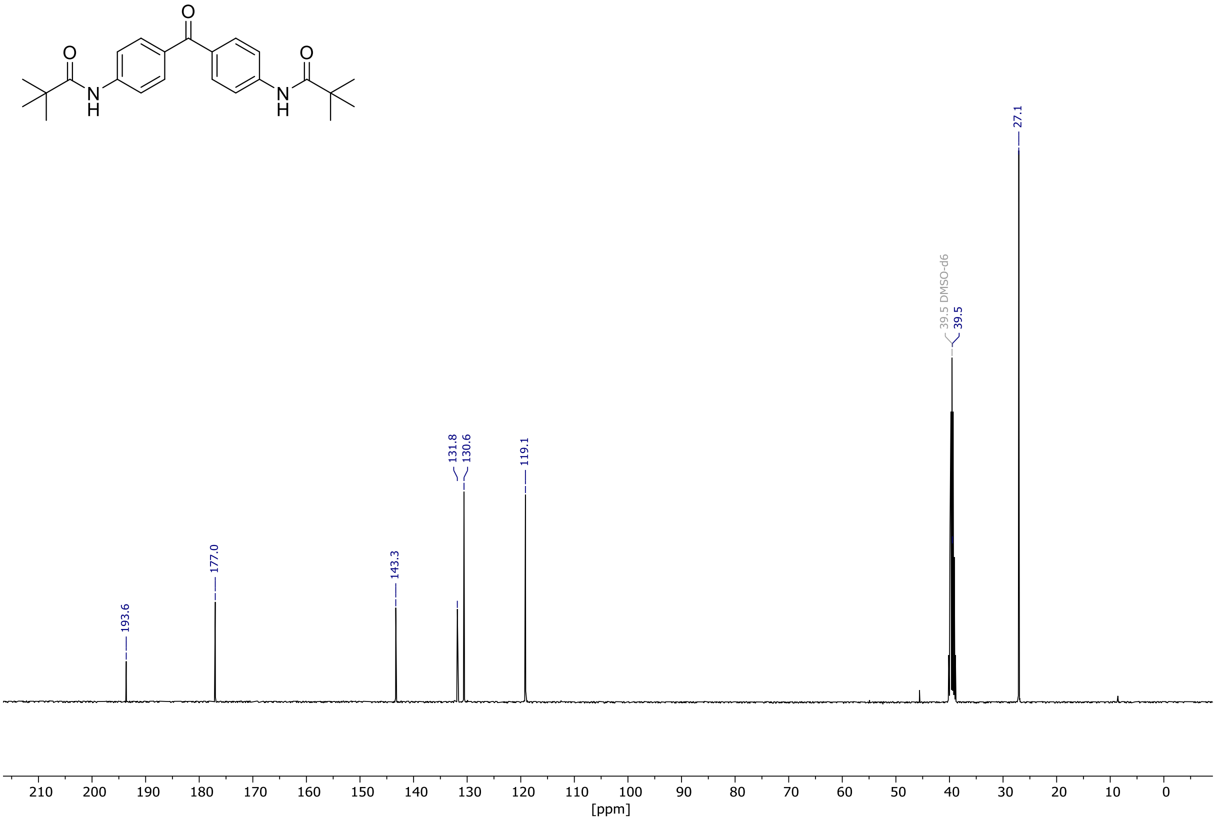
^{13}C NMR (101 MHz, $CDCl_3$): **S6**



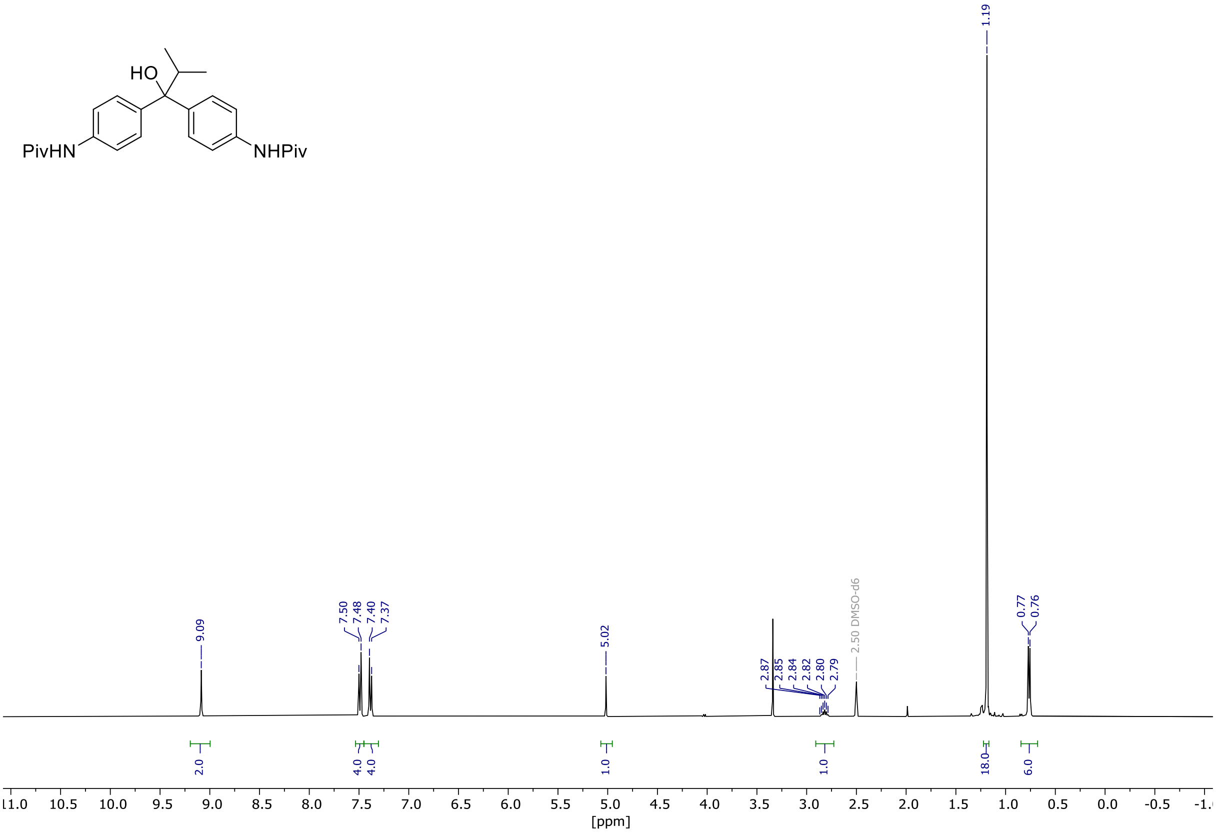
^{1}H NMR (400 MHz, d_6-DMSO): **S7**



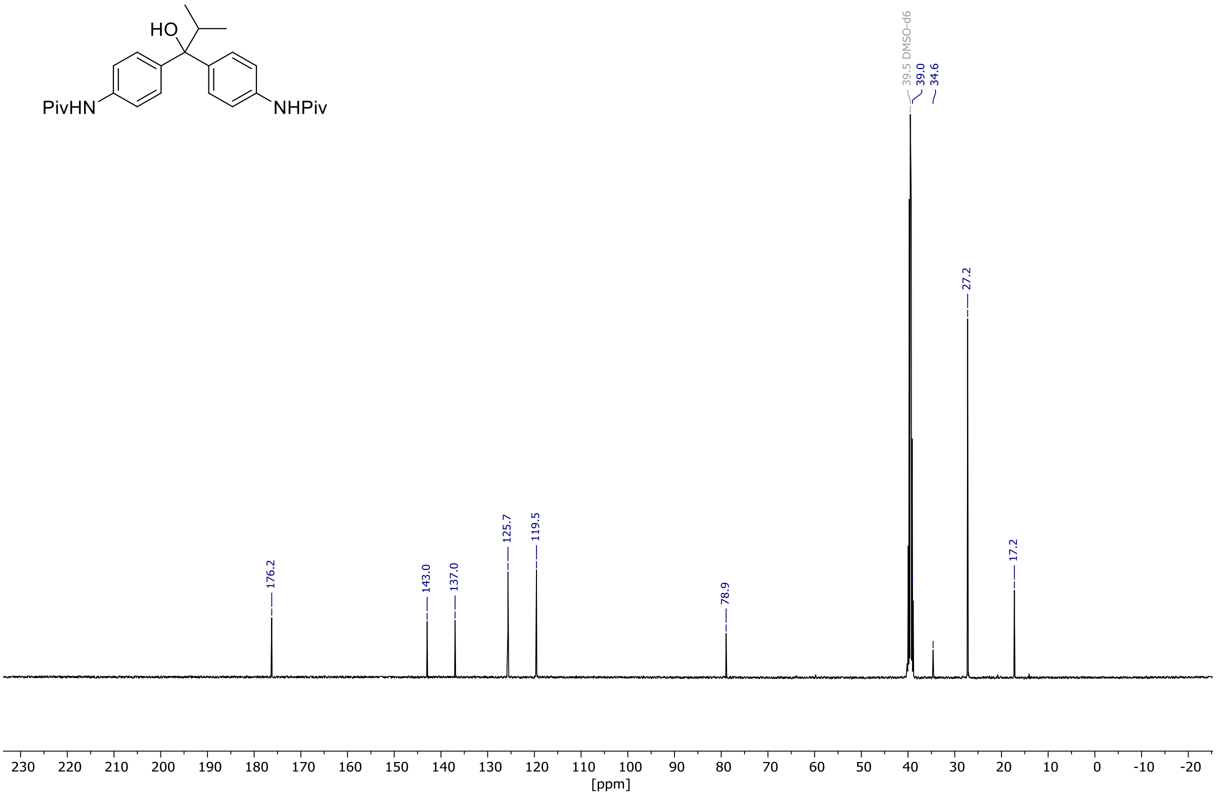
^{13}**C NMR** (101 MHz, *d*$_6$-DMSO): **S7**



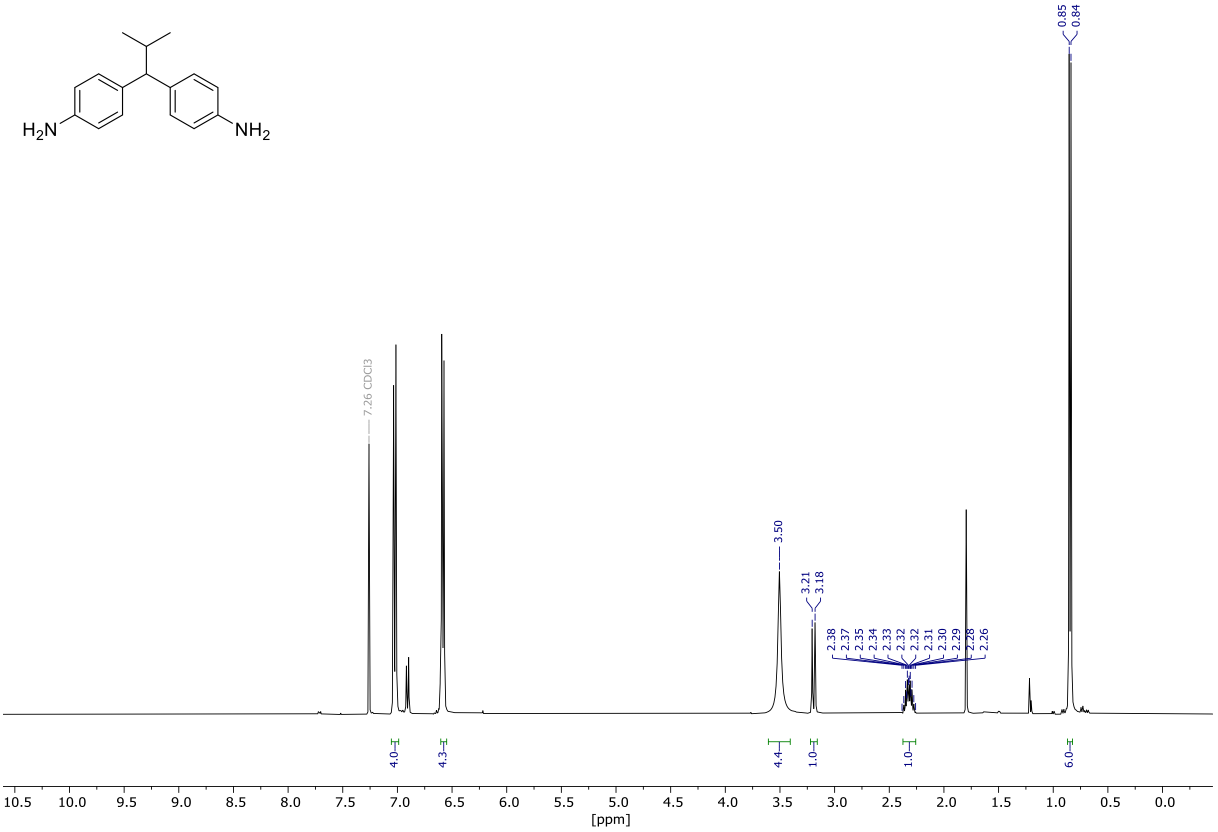
^{1}**H NMR** (400 MHz, *d*$_6$-DMSO): **S8**



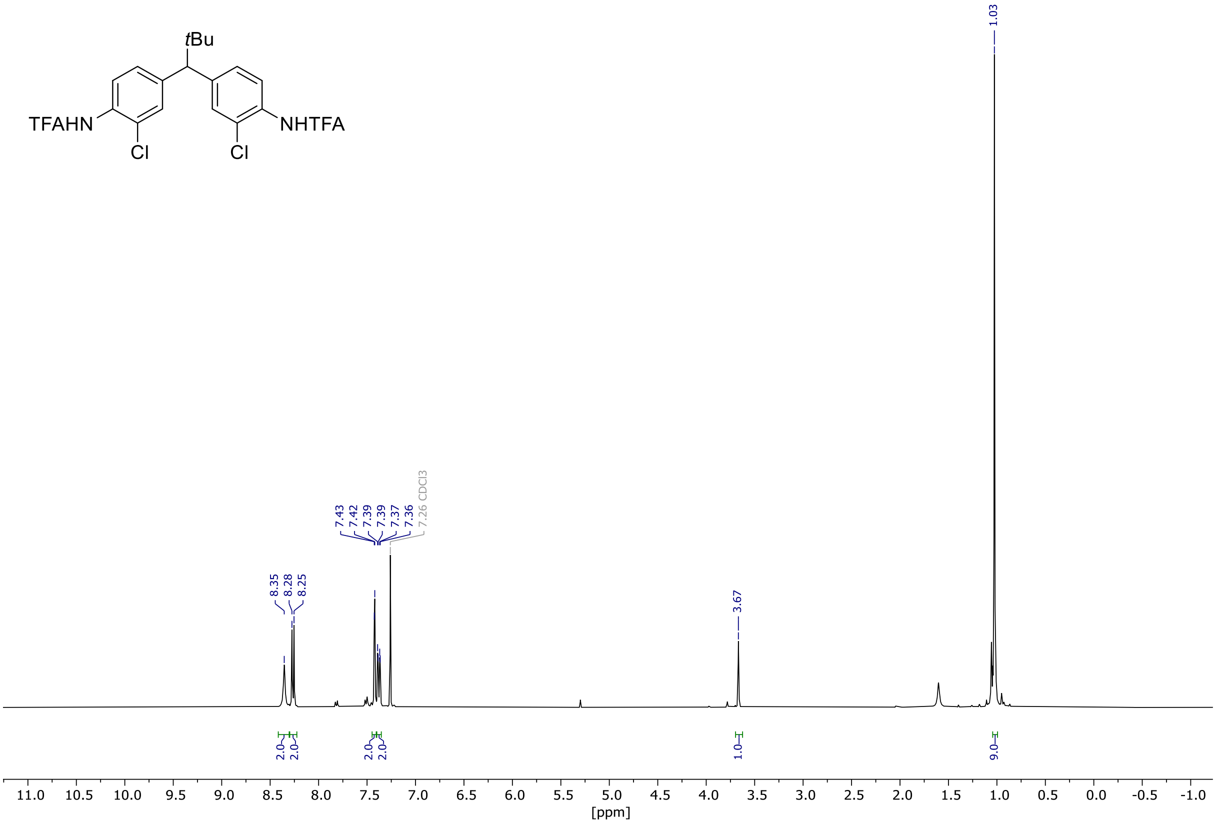
^{13}C NMR (101 MHz, *d*$_6$-DMSO): **S8**



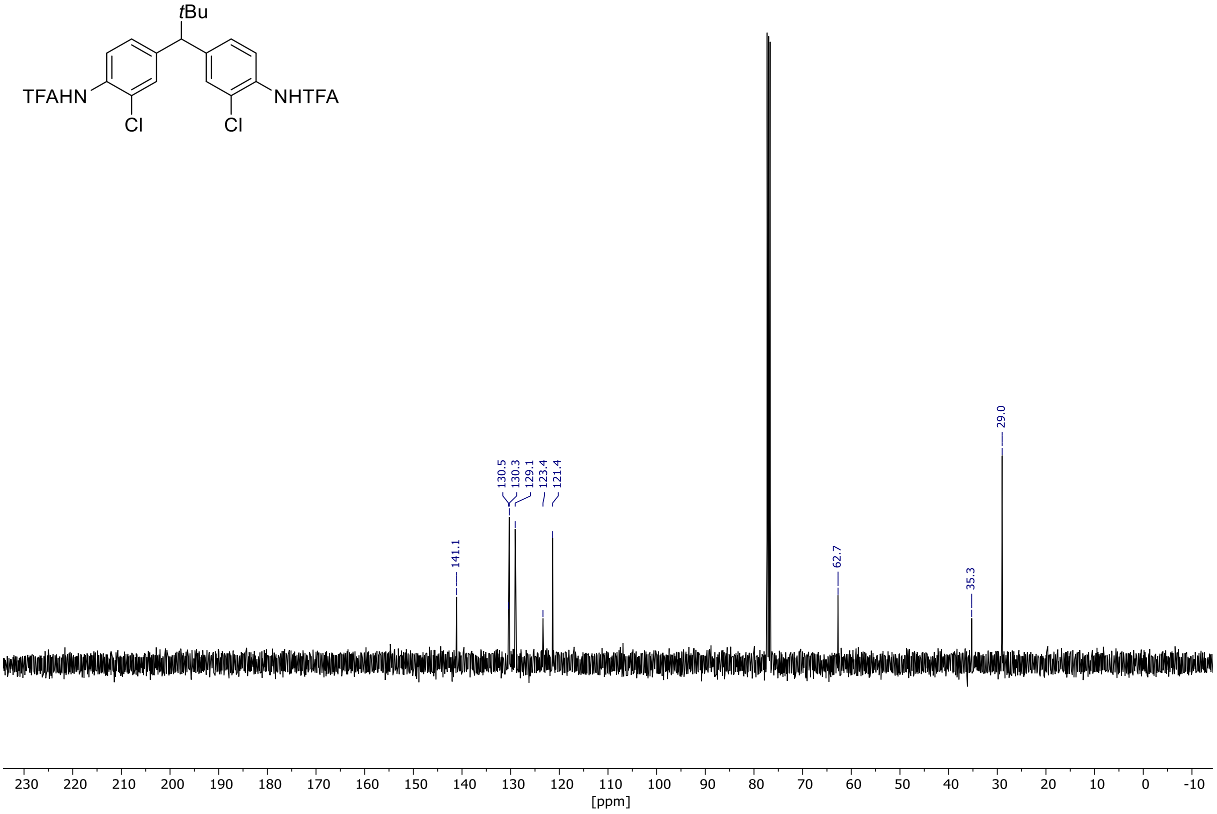
^{1}H NMR (400 MHz, CDCl$_3$): **S9**



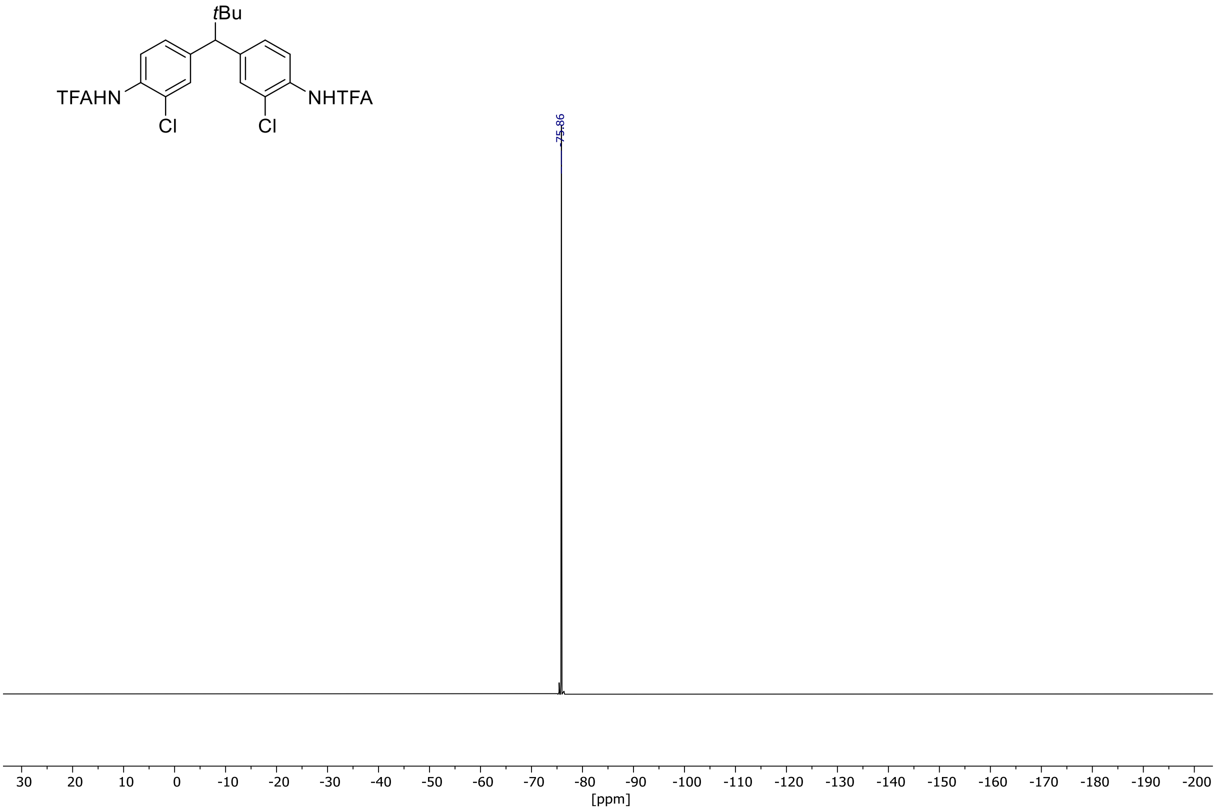
^{1}H NMR (400 MHz, CDCl$_3$): **10**



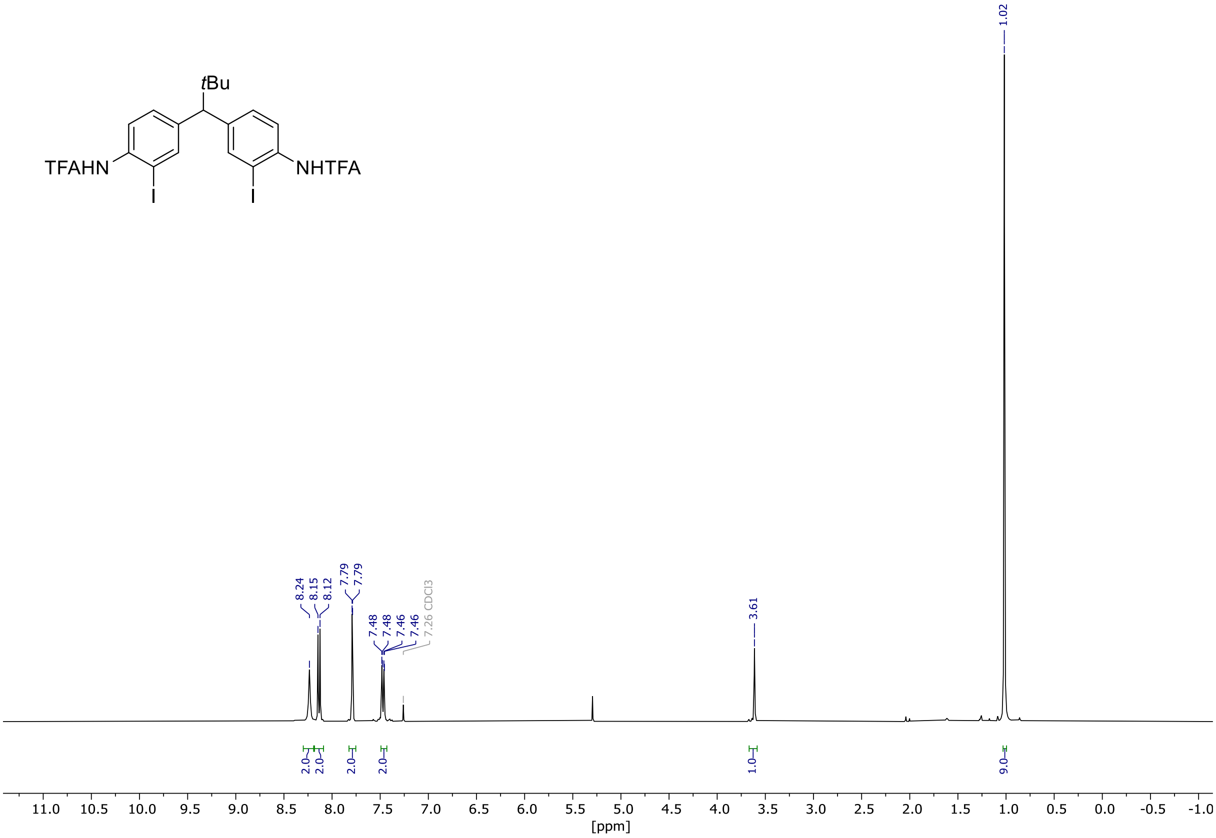
^{13}C NMR (101 MHz, CDCl$_3$): **10**



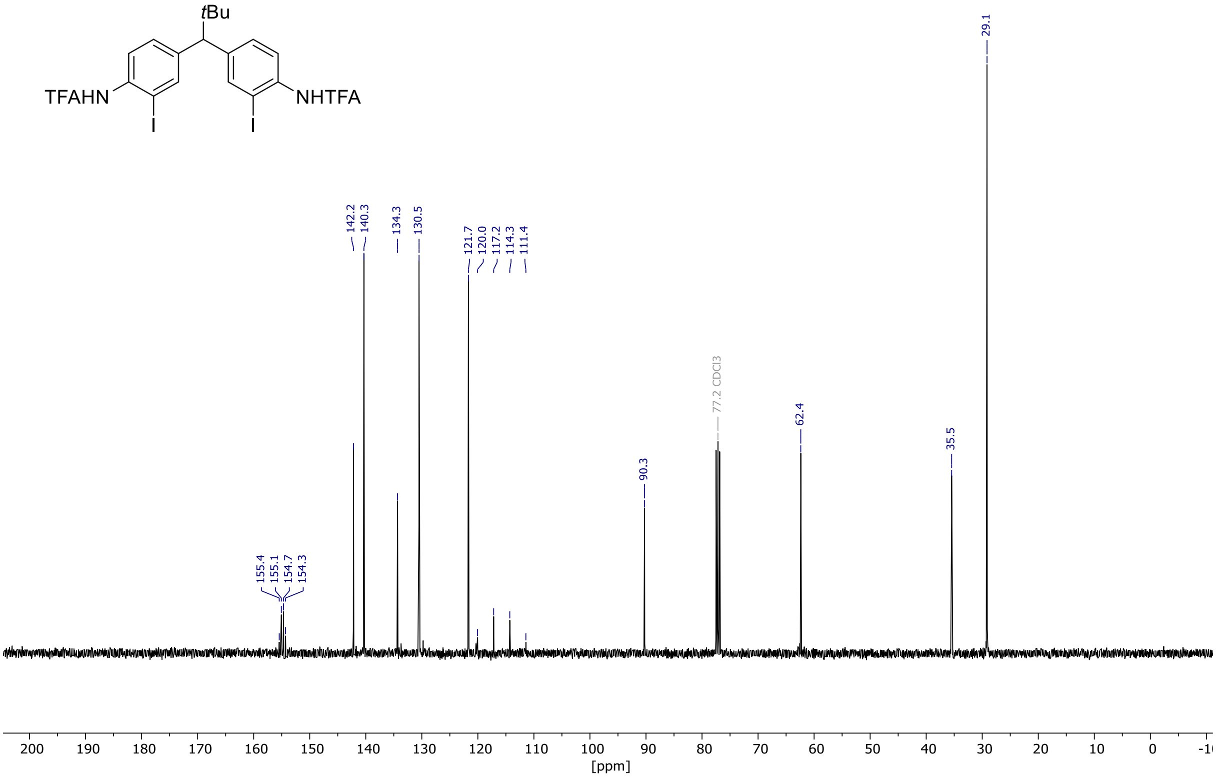
^{19}F NMR (376 MHz, CDCl$_3$): **10**



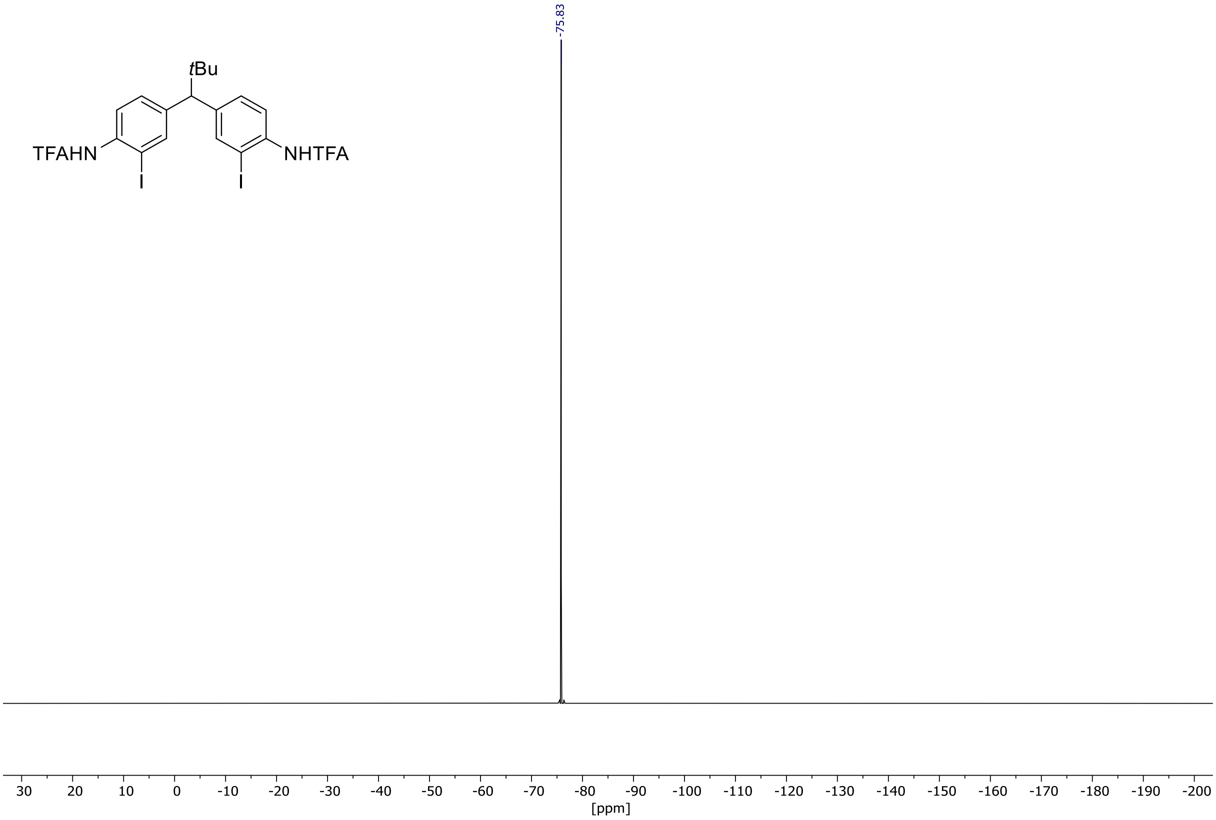
^{1}H NMR (400 MHz, CDCl$_3$): **3**



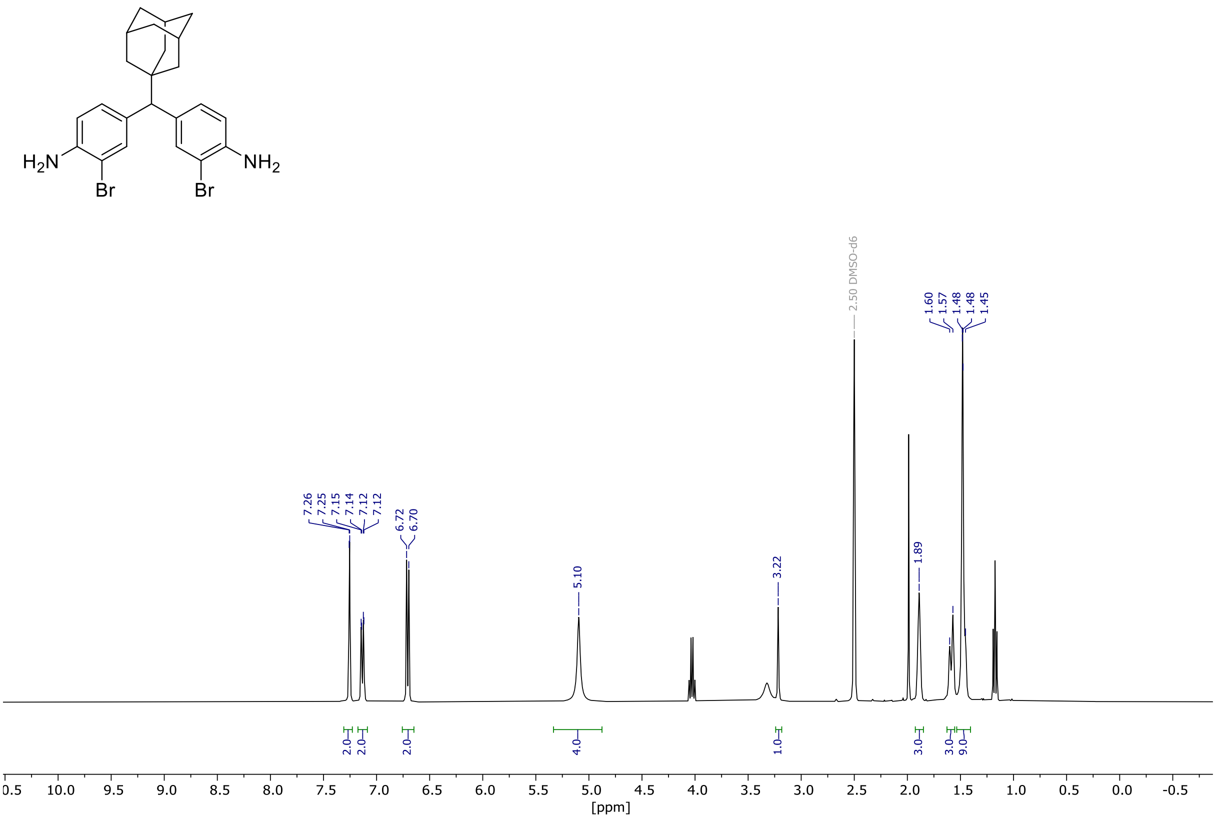
^{13}**C NMR** (101 MHz, CDCl$_3$): **3**



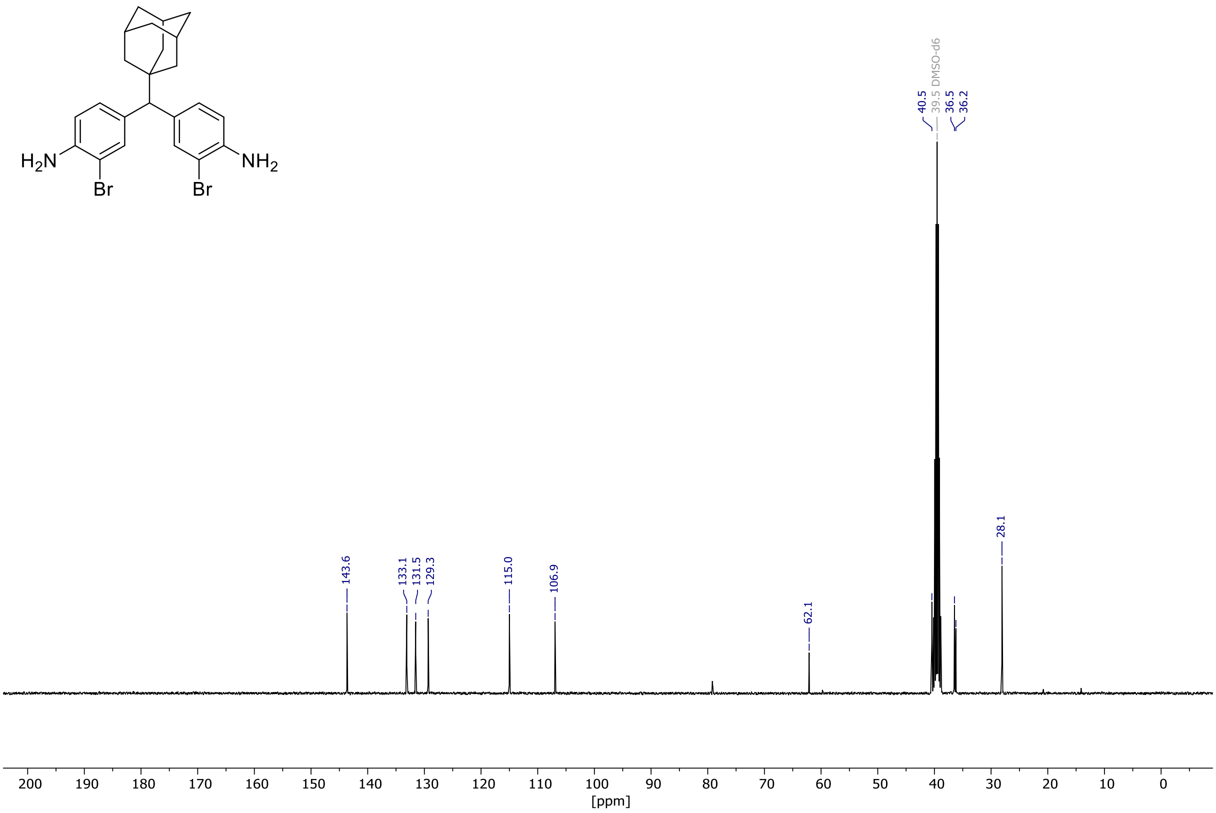
^{19}**F NMR** (376 MHz, CDCl$_3$): **3**



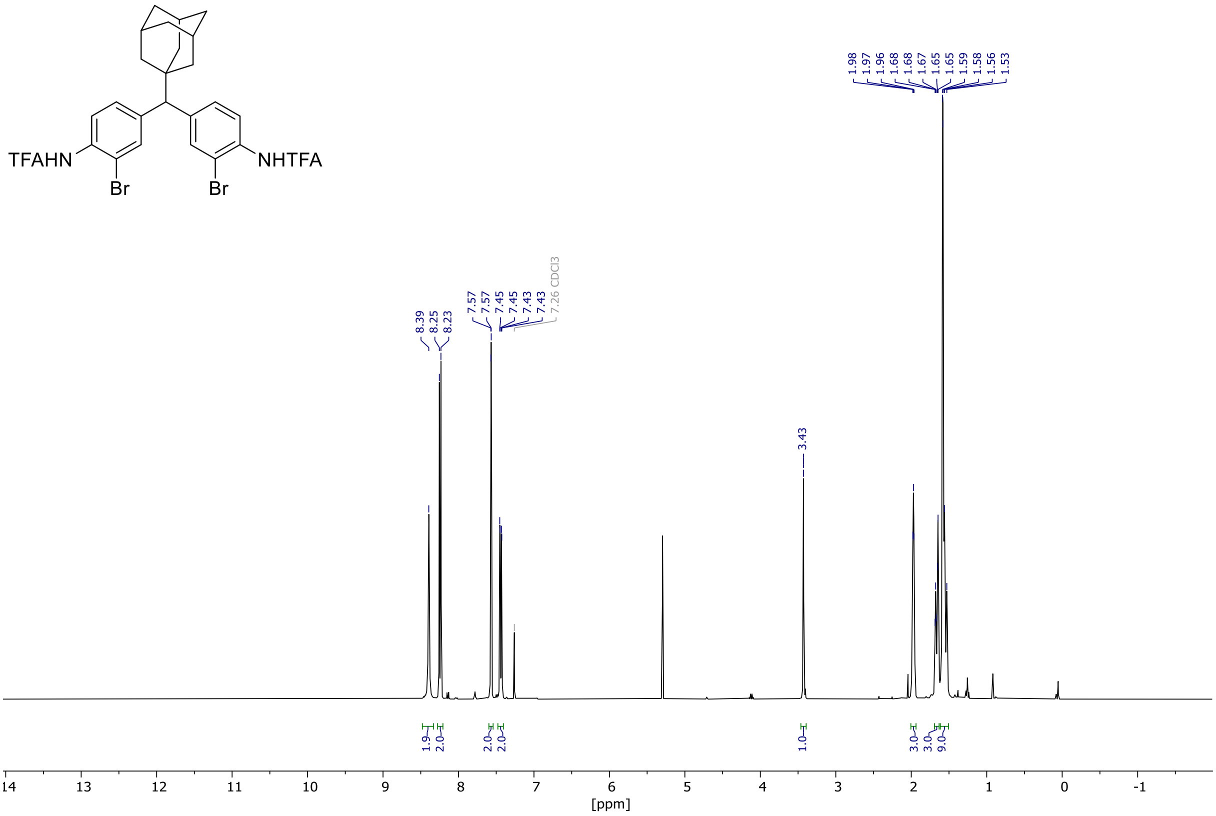
^{1}H NMR (400 MHz, d_6-DMSO): S10



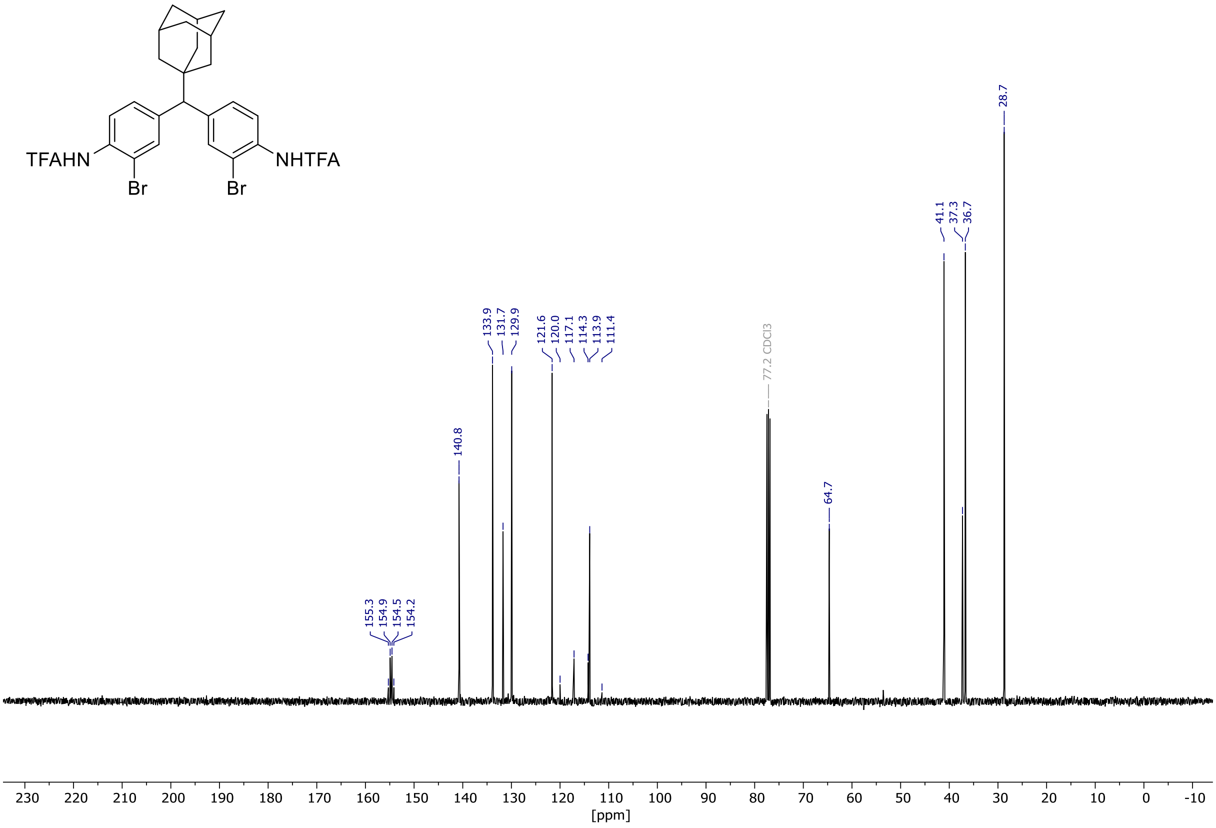
^{13}C NMR (101 MHz, d_6-DMSO): S10



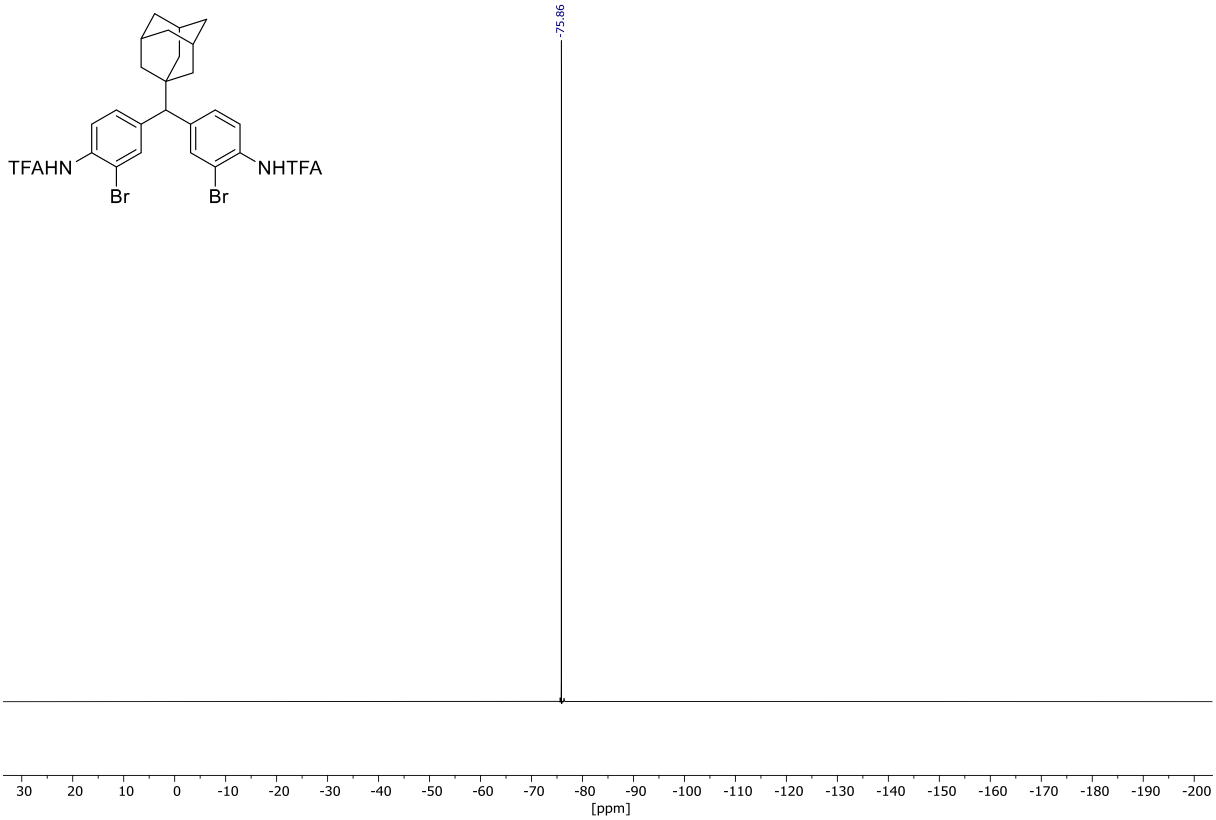
^{1}H NMR (400 MHz, CDCl$_3$): S11



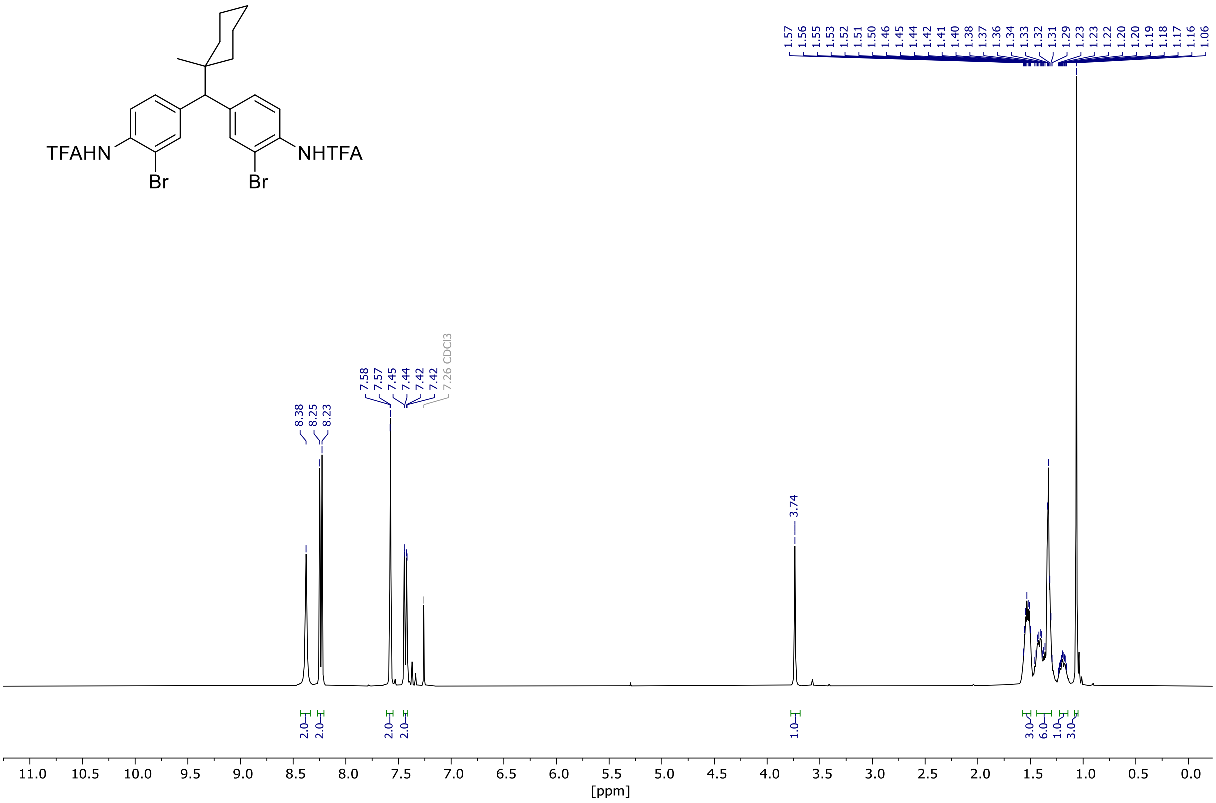
^{13}C NMR (101 MHz, CDCl$_3$): S11



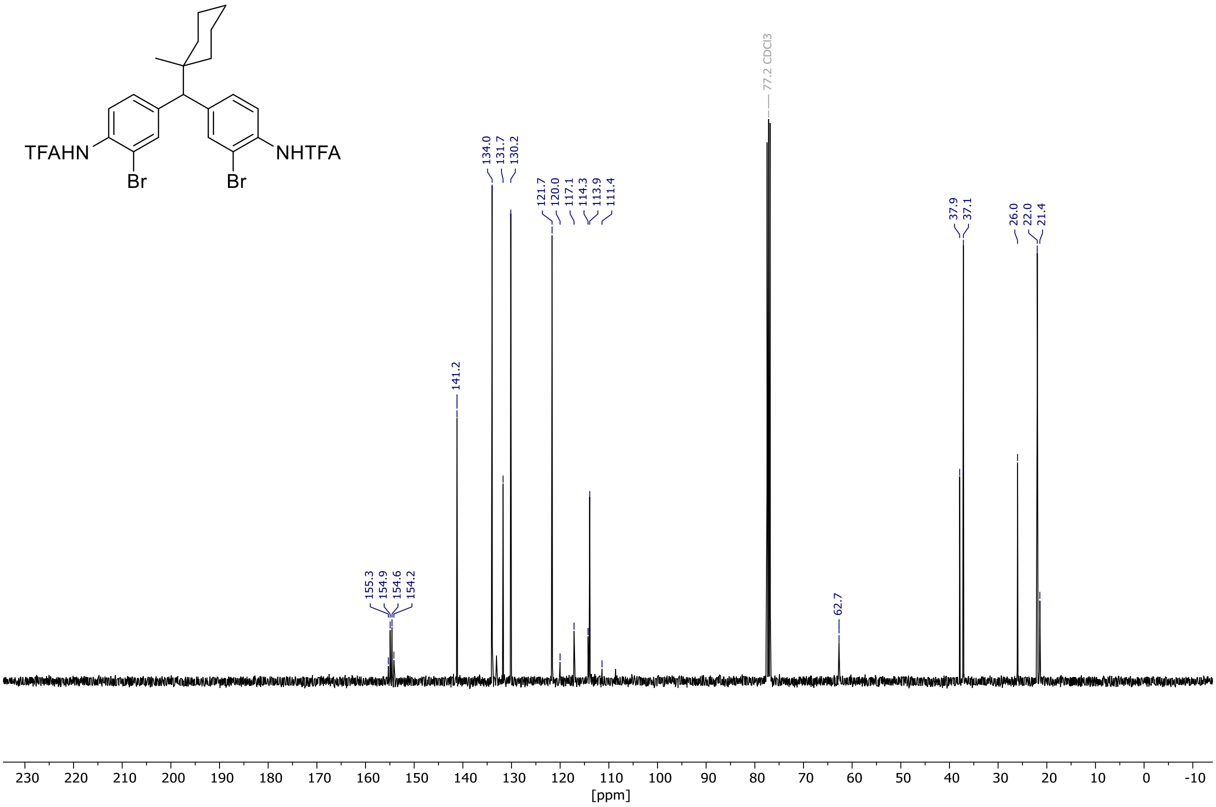
^{19}F NMR (376 MHz, CDCl$_3$): **S11**



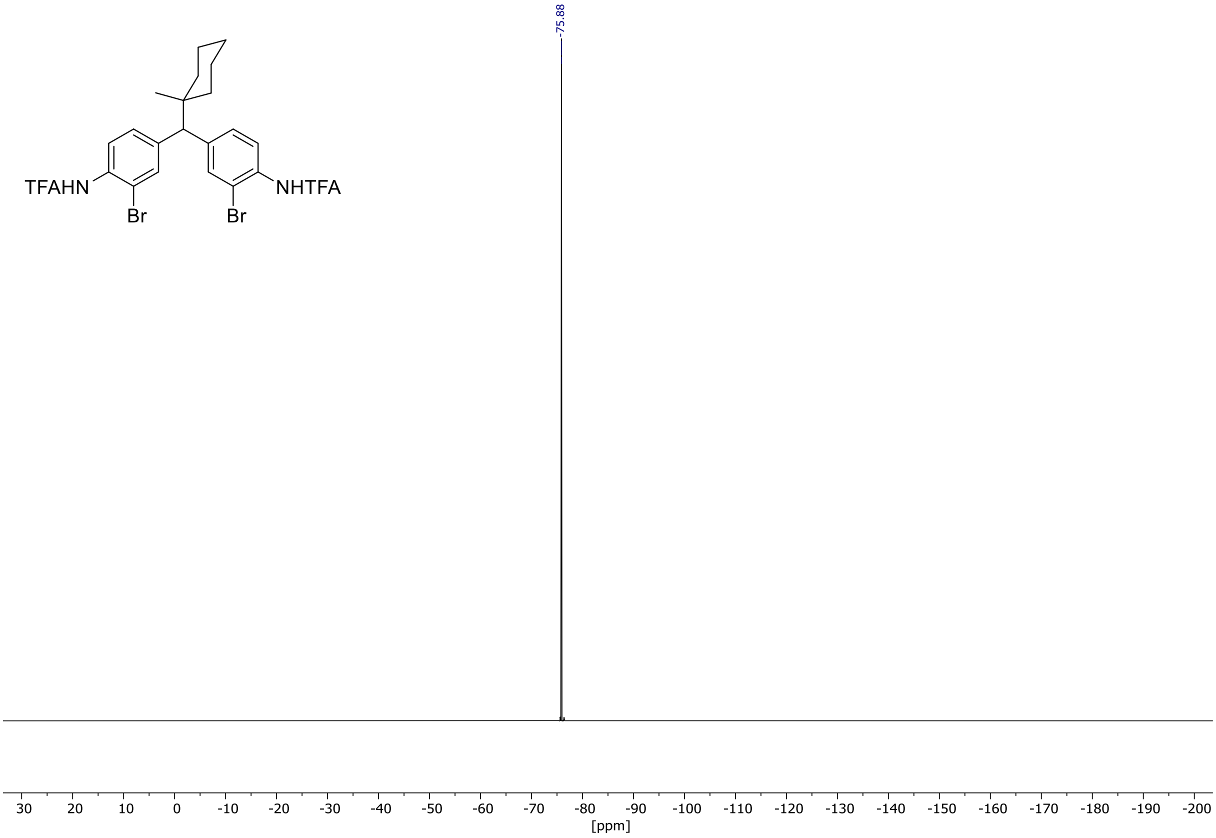
^{1}H NMR (400 MHz, CDCl$_3$): **S12**



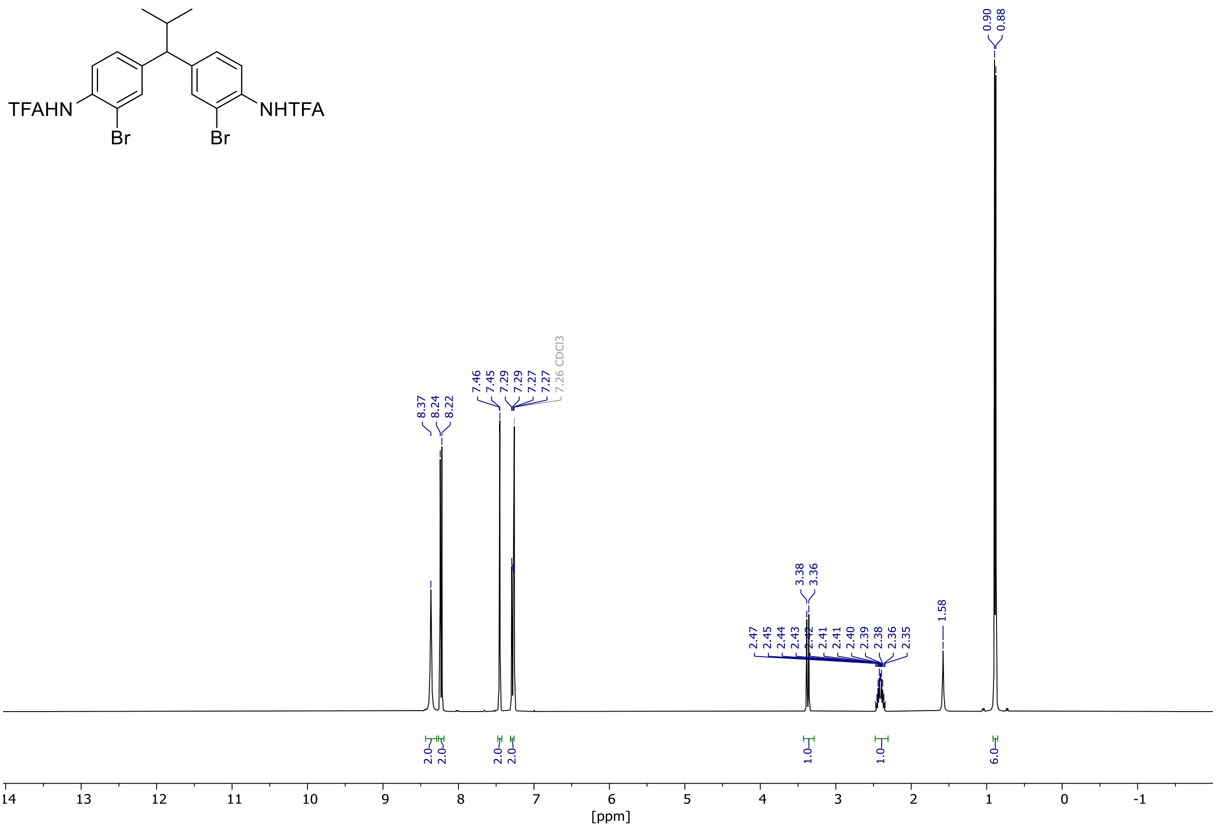
^{13}C NMR (101 MHz, CDCl$_3$): S12



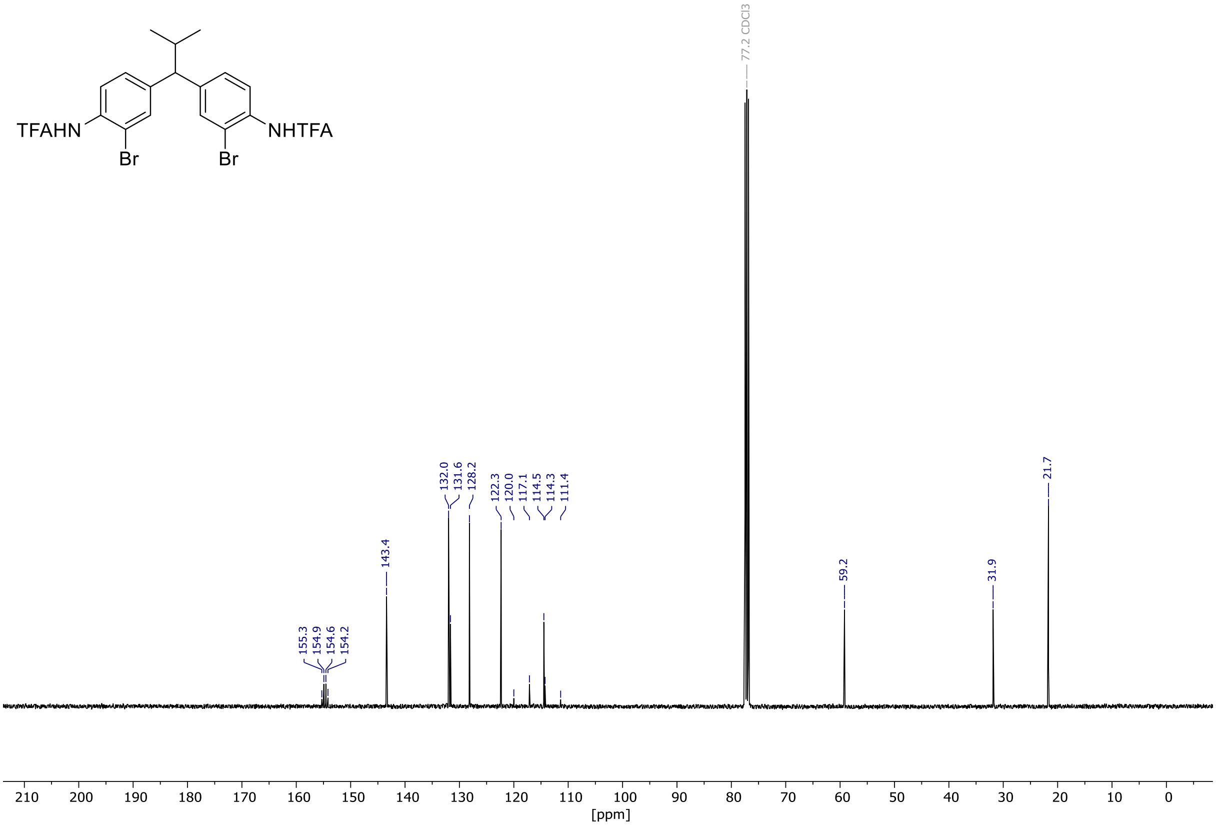
^{19}F NMR (376 MHz, CDCl$_3$): S12



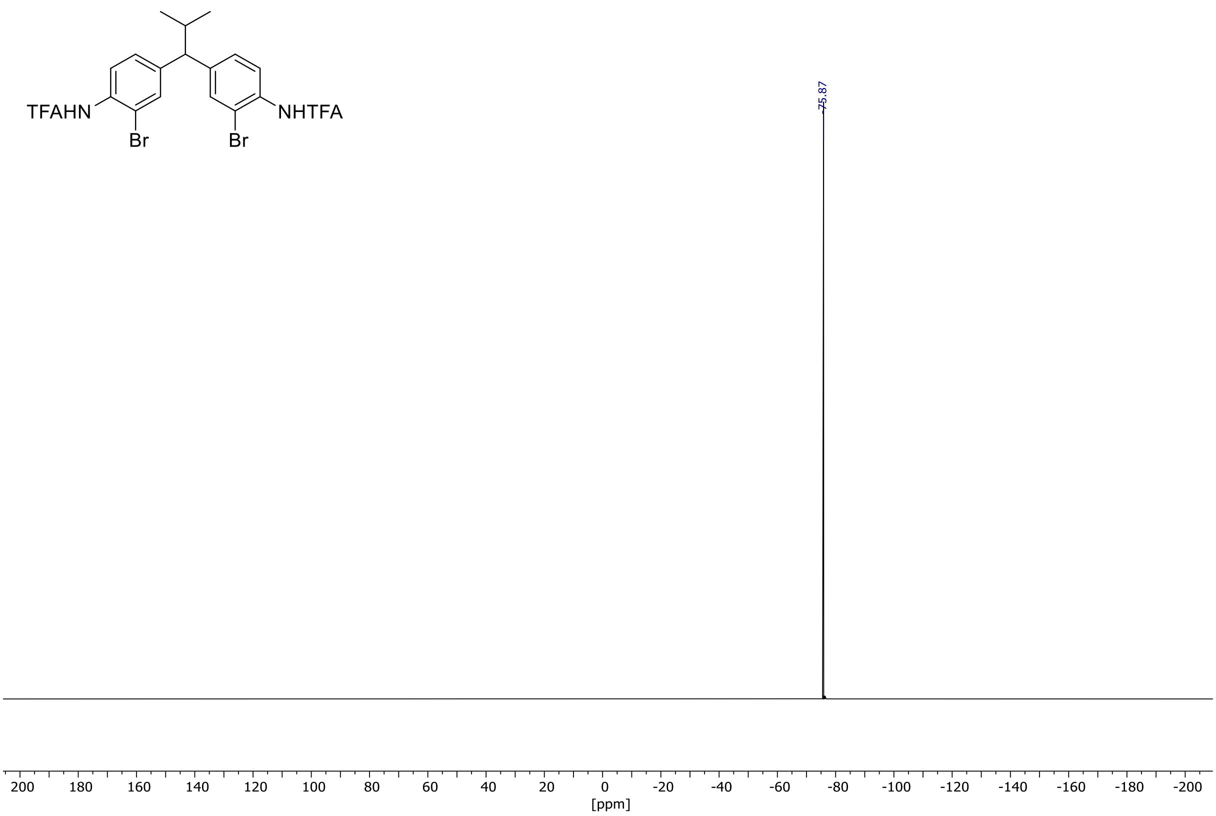
^{1}H NMR (400 MHz, $CDCl_3$): **S13**



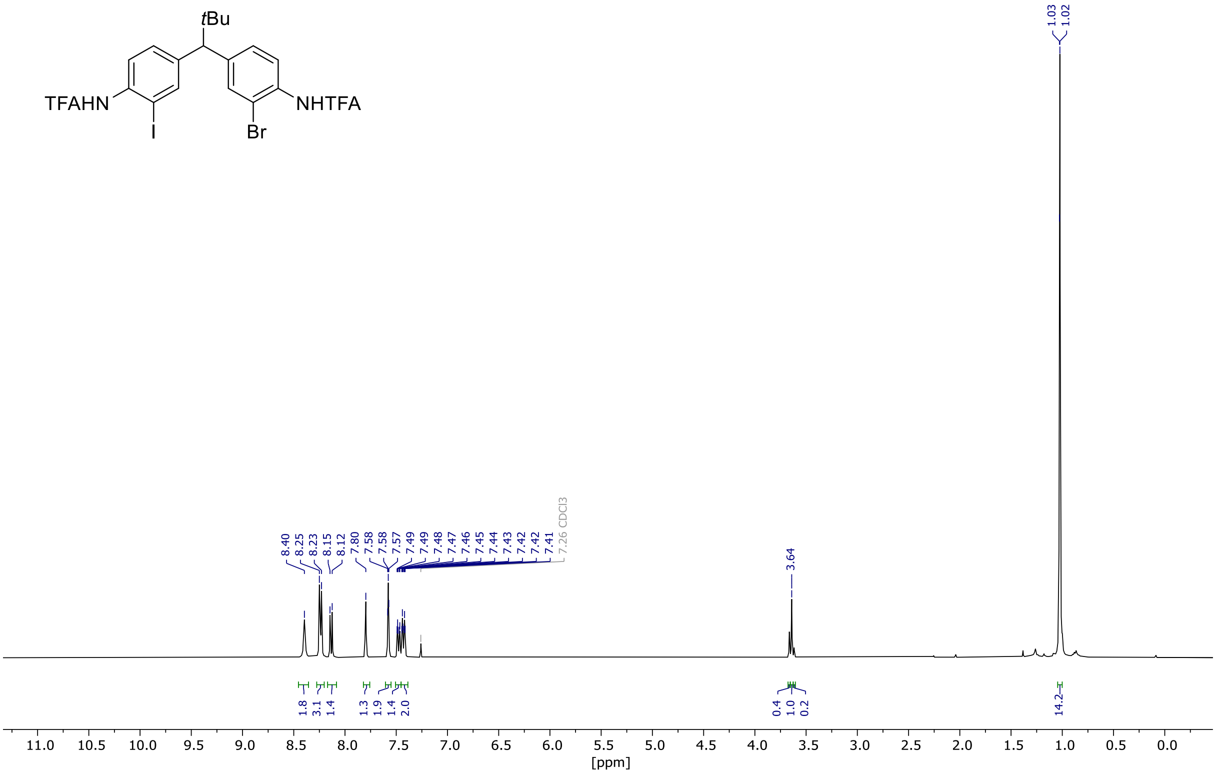
^{13}C NMR (101 MHz, $CDCl_3$): **S13**



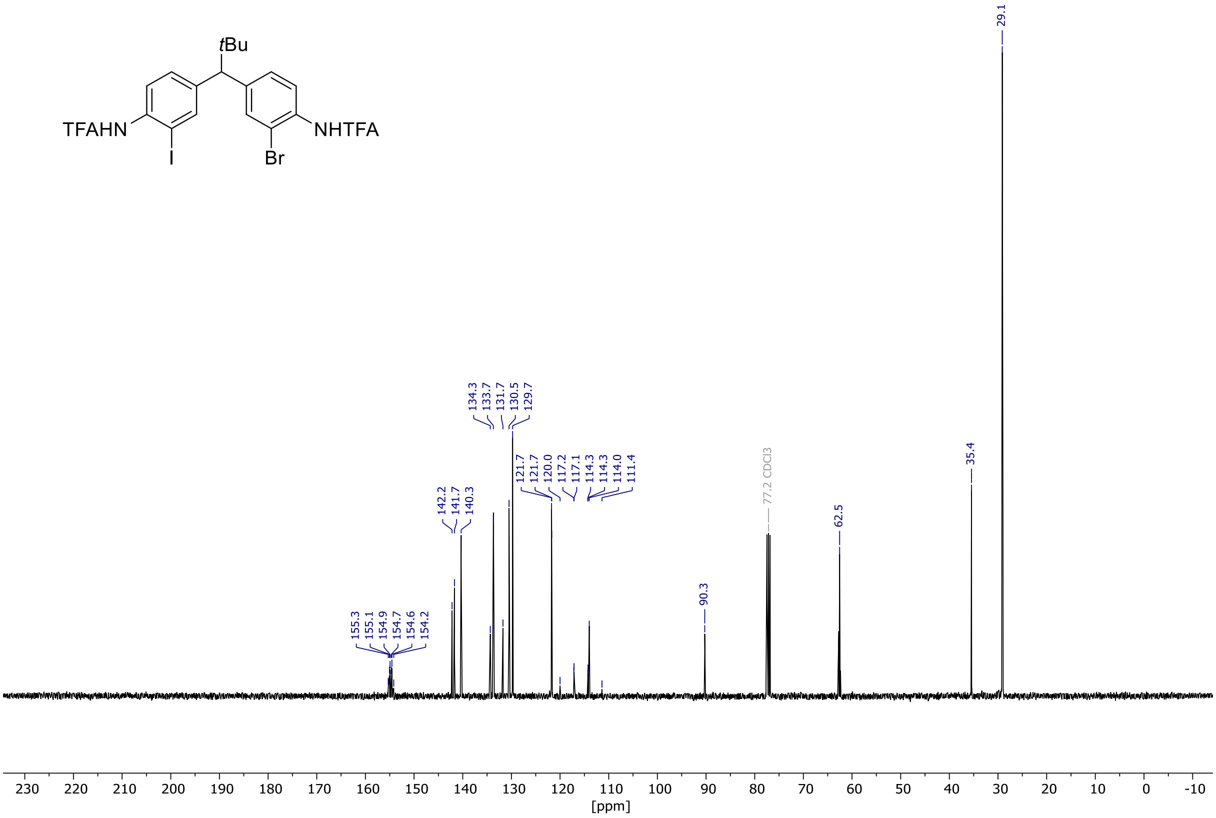
^{19}F NMR (376 MHz, CDCl$_3$): **S13**



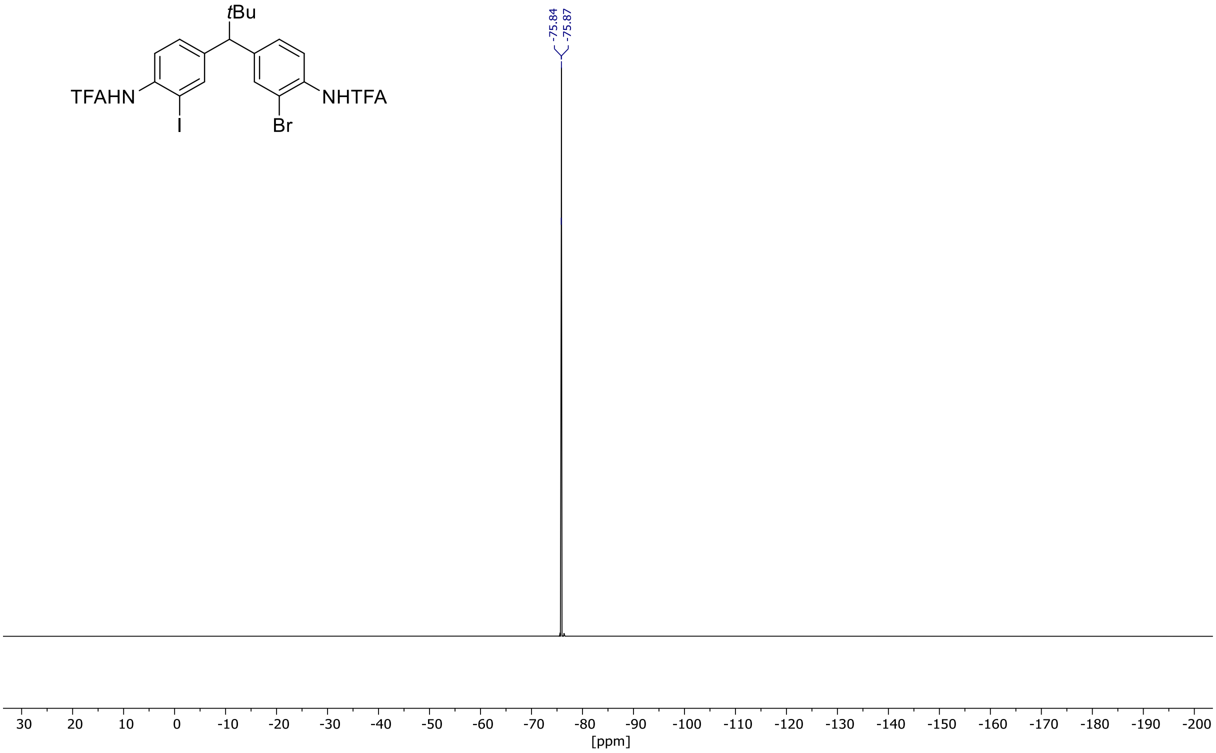
^{1}H NMR (400 MHz, CDCl$_3$): **2** (obtained as inseparable mixture, containing **1** and **3**)



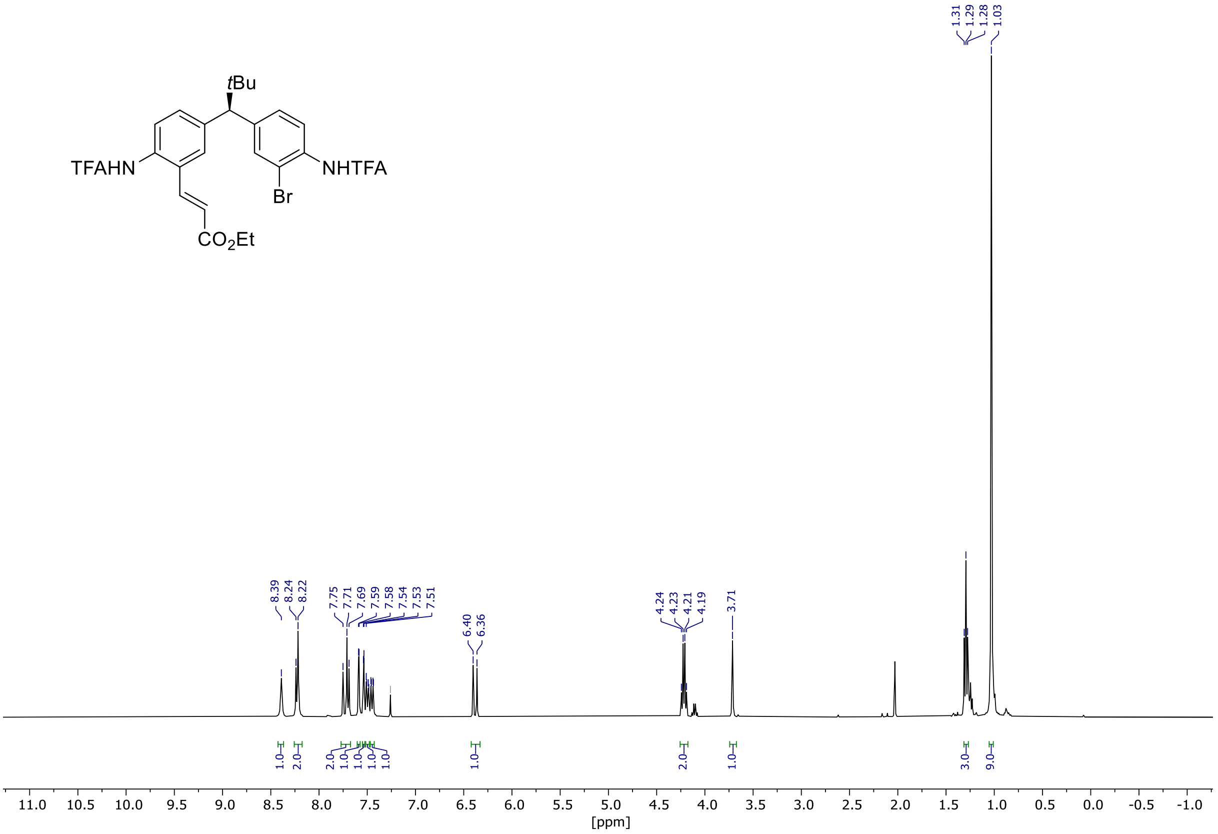
^{13}C NMR (101 MHz, CDCl$_3$): **2**



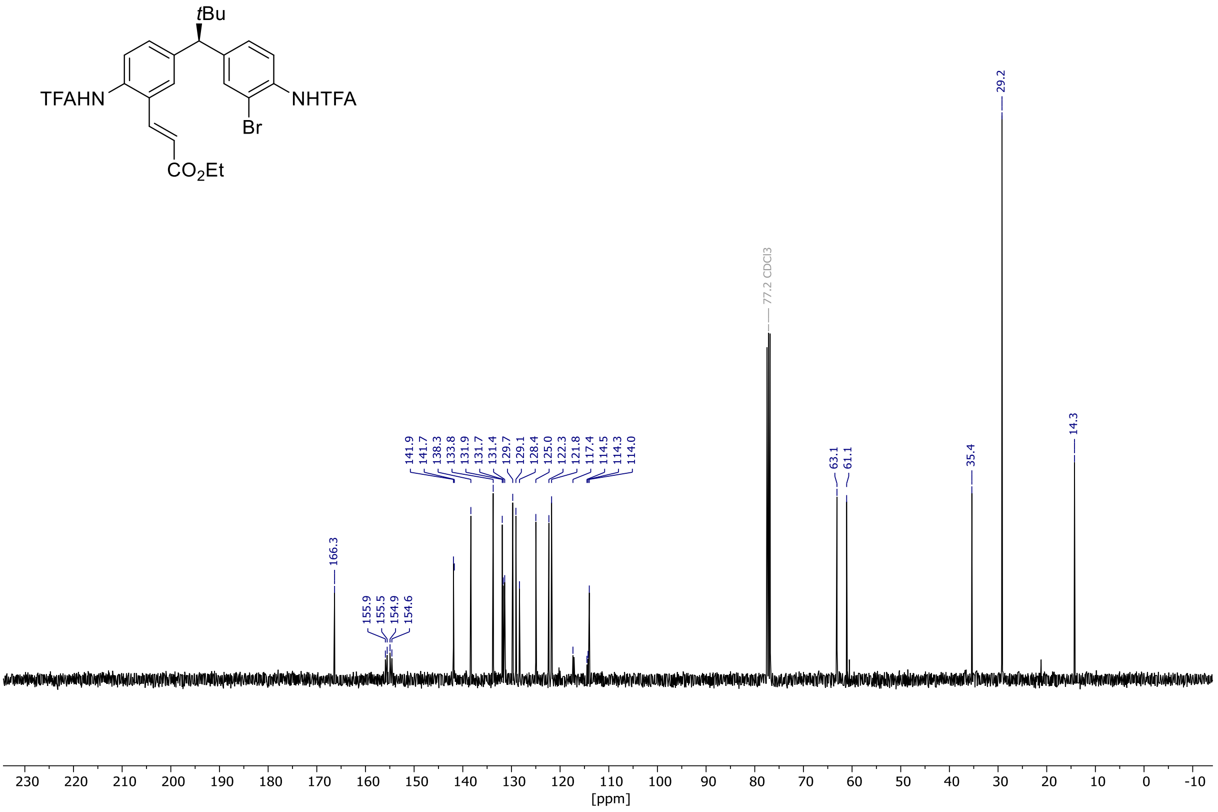
^{19}F NMR (376 MHz, CDCl$_3$): **2**



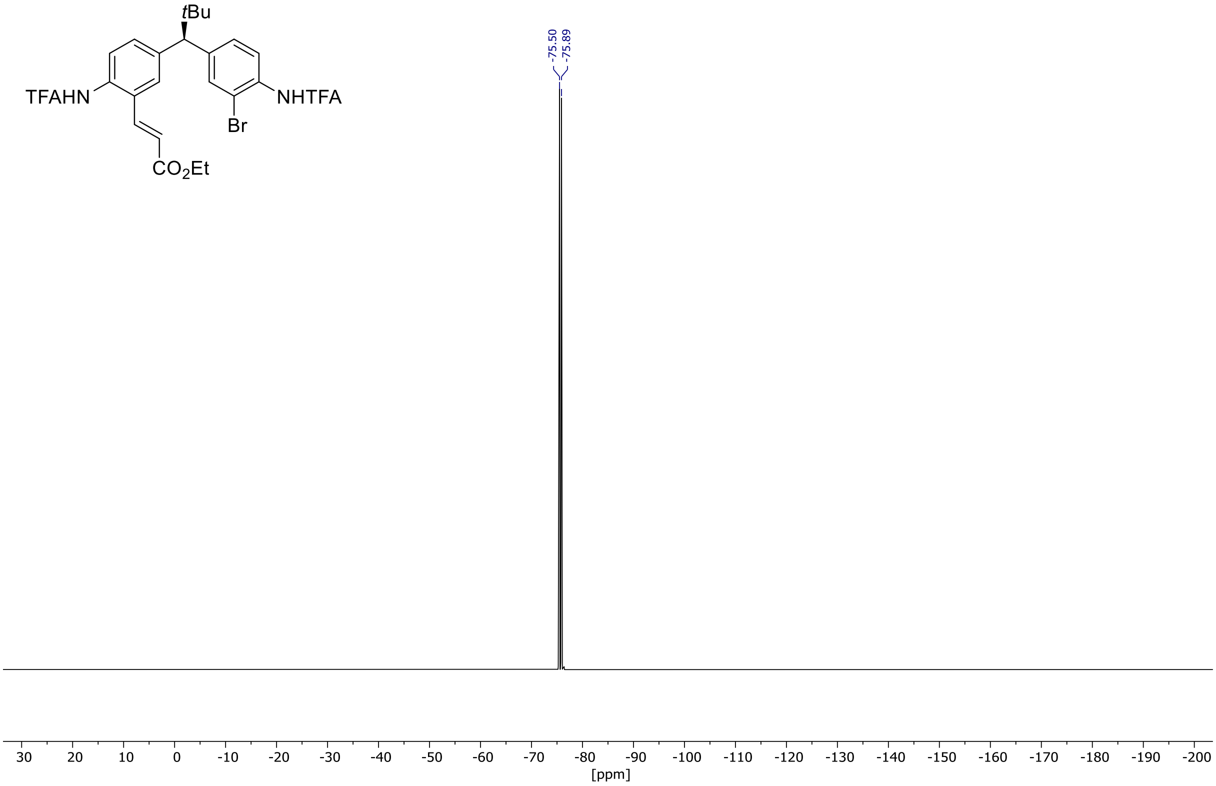
^{1}H NMR (400 MHz, CDCl$_3$): **4**



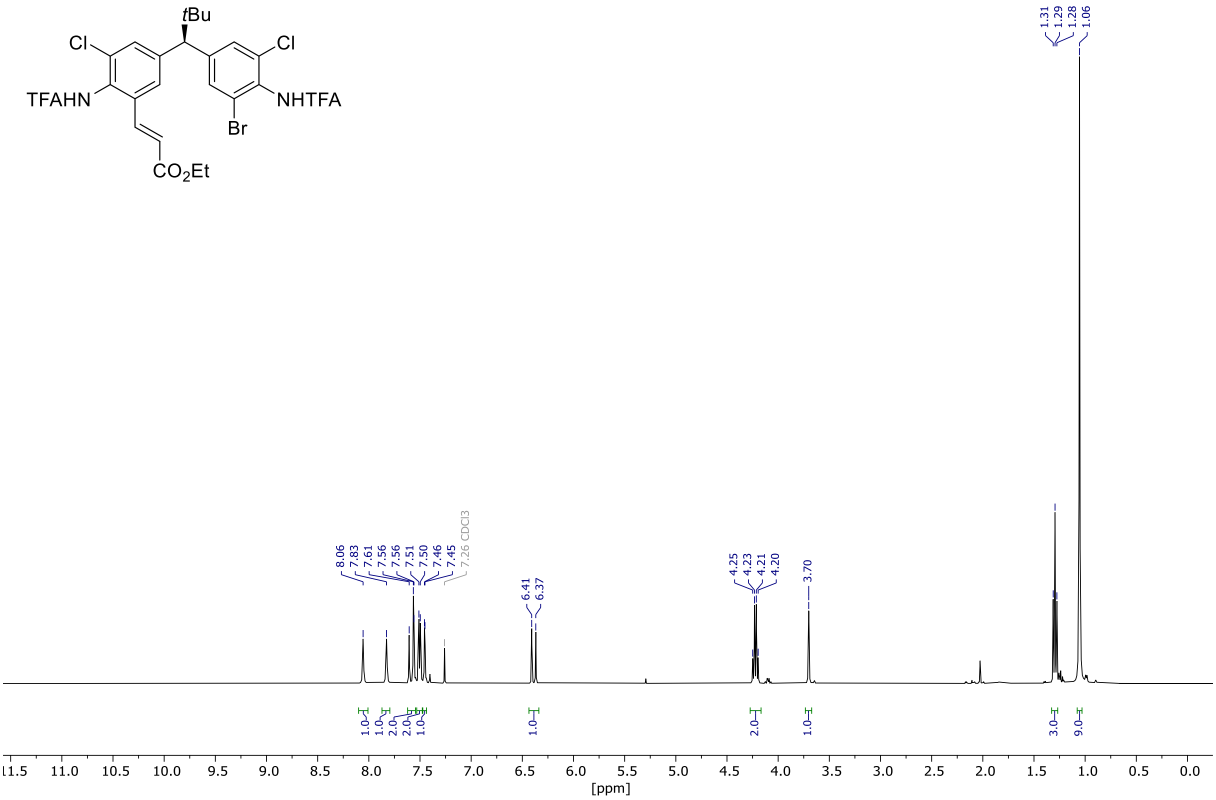
^{13}C NMR (101 MHz, CDCl$_3$): **4**



^{19}F NMR (376 MHz, $CDCl_3$): **4**



^{1}H NMR (400 MHz, $CDCl_3$): **9**



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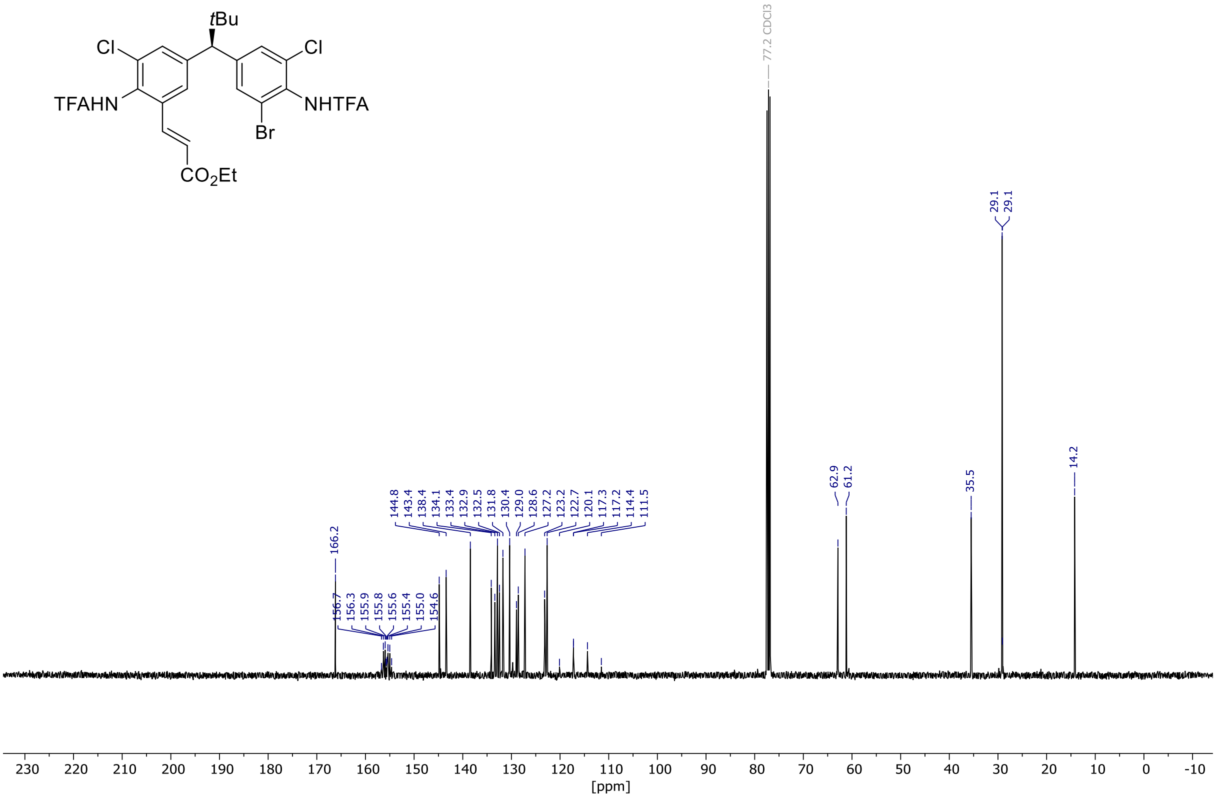
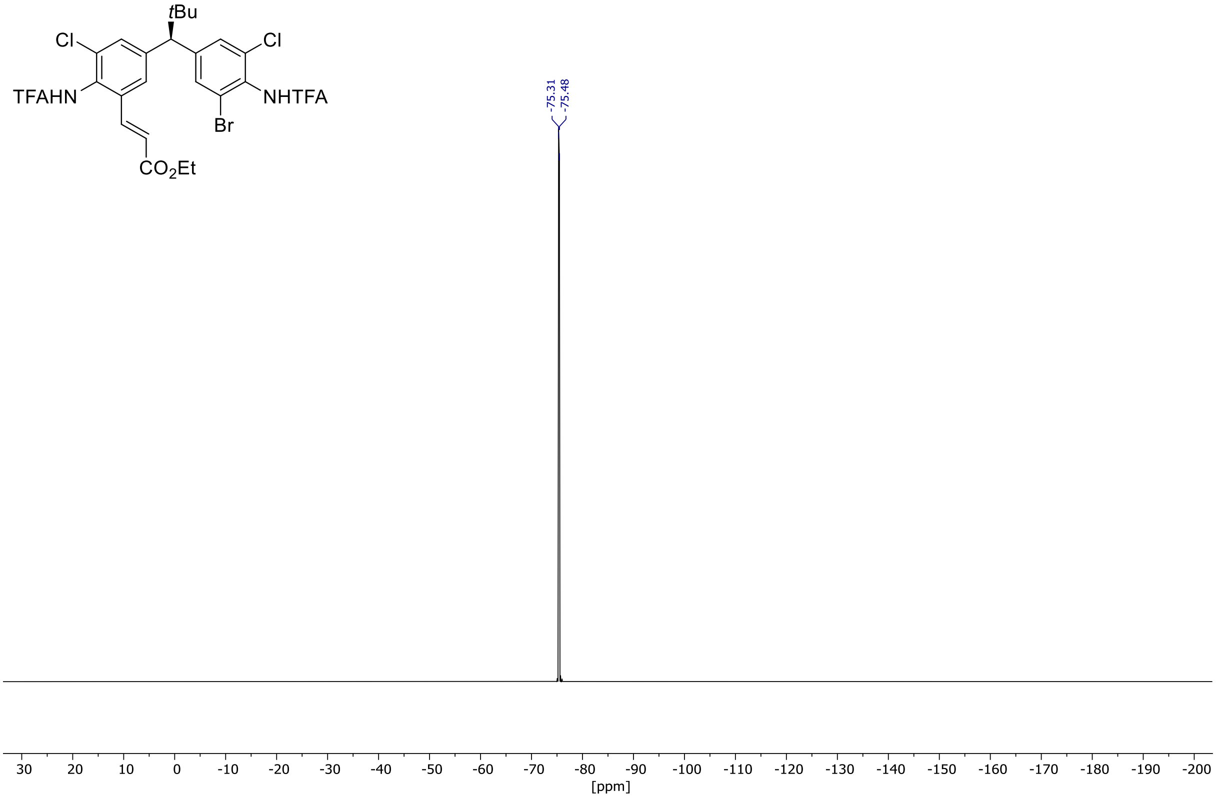
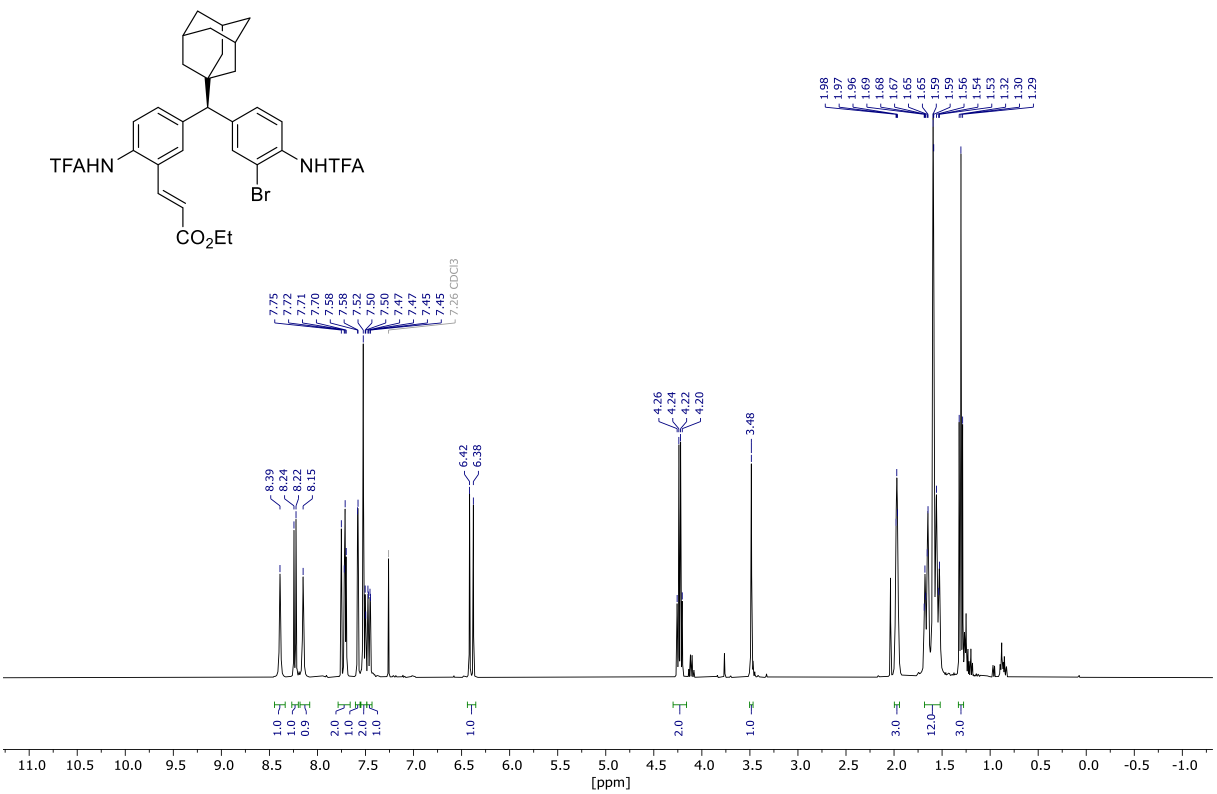


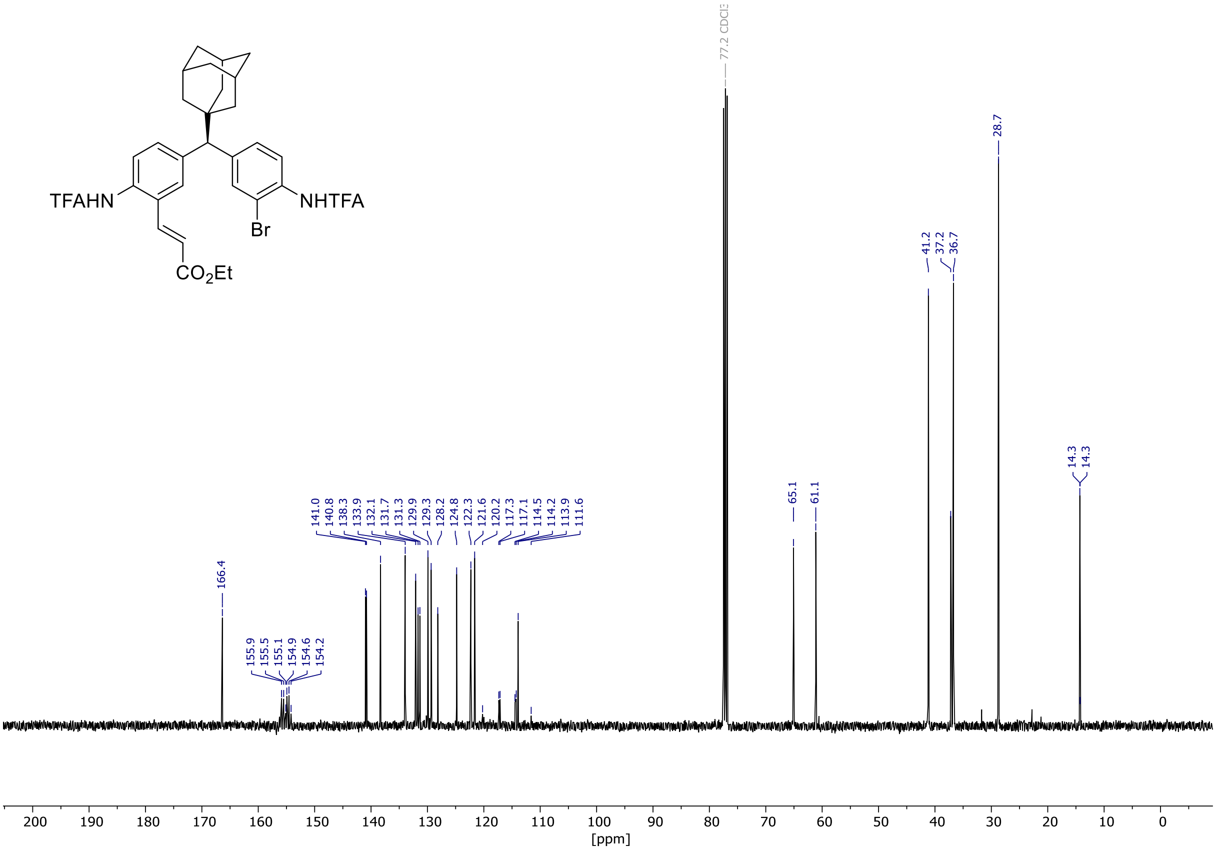
^{19}F NMR (376 MHz, $CDCl_3$): **9**



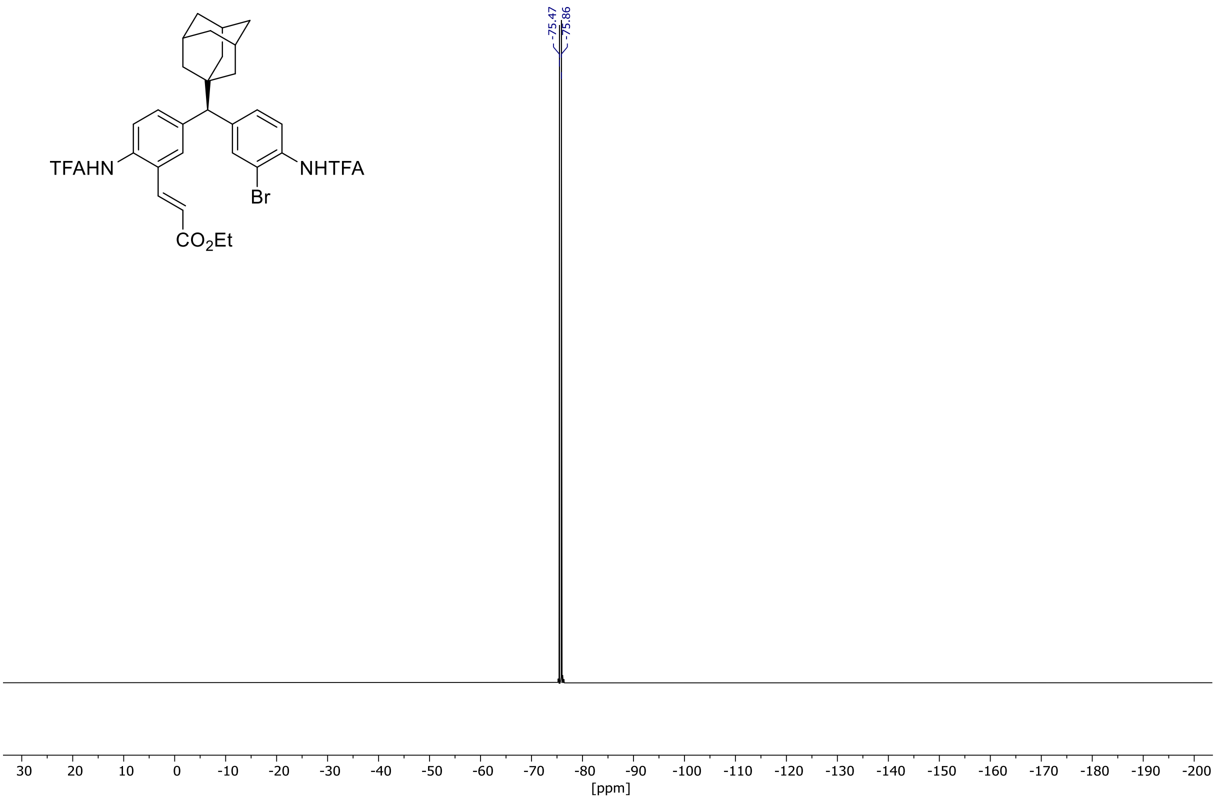
^{1}**H NMR** (400 MHz, CDCl$_3$): **11**



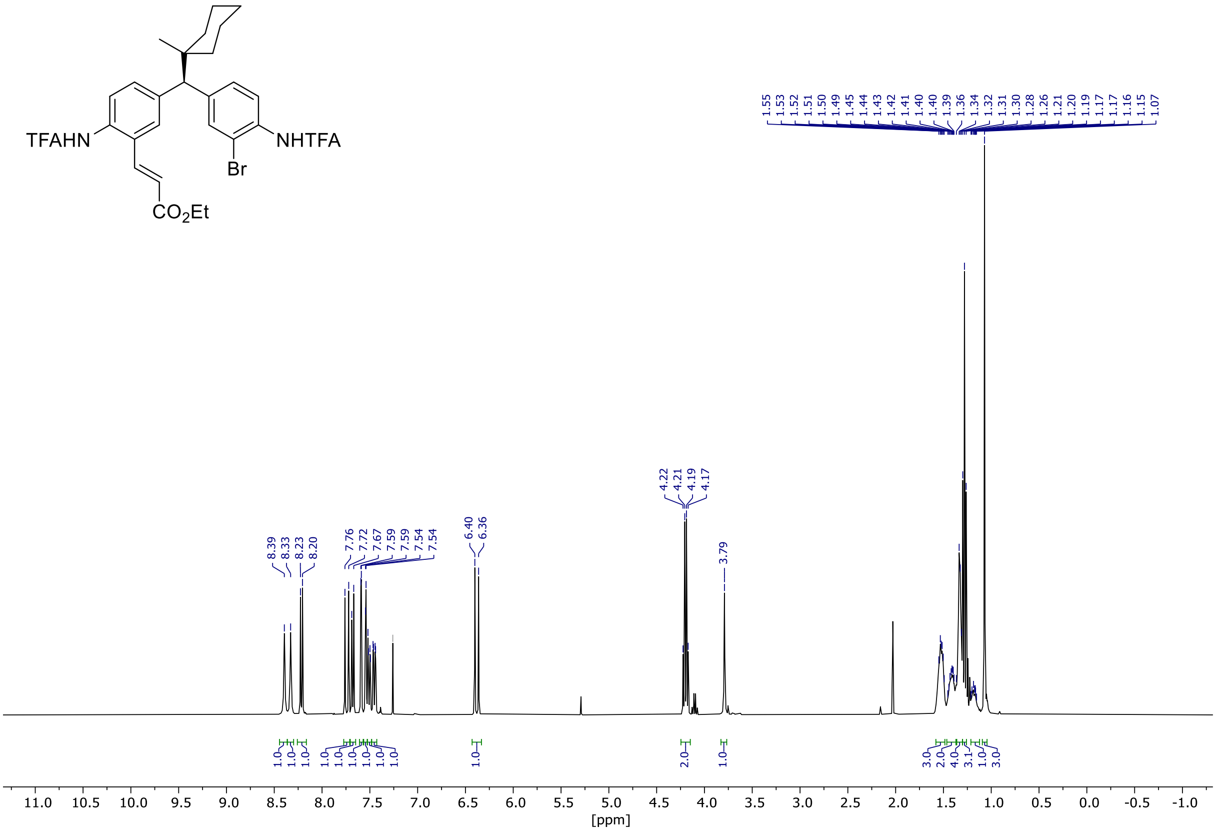
^{13}**C NMR** (101 MHz, CDCl$_3$): **11**



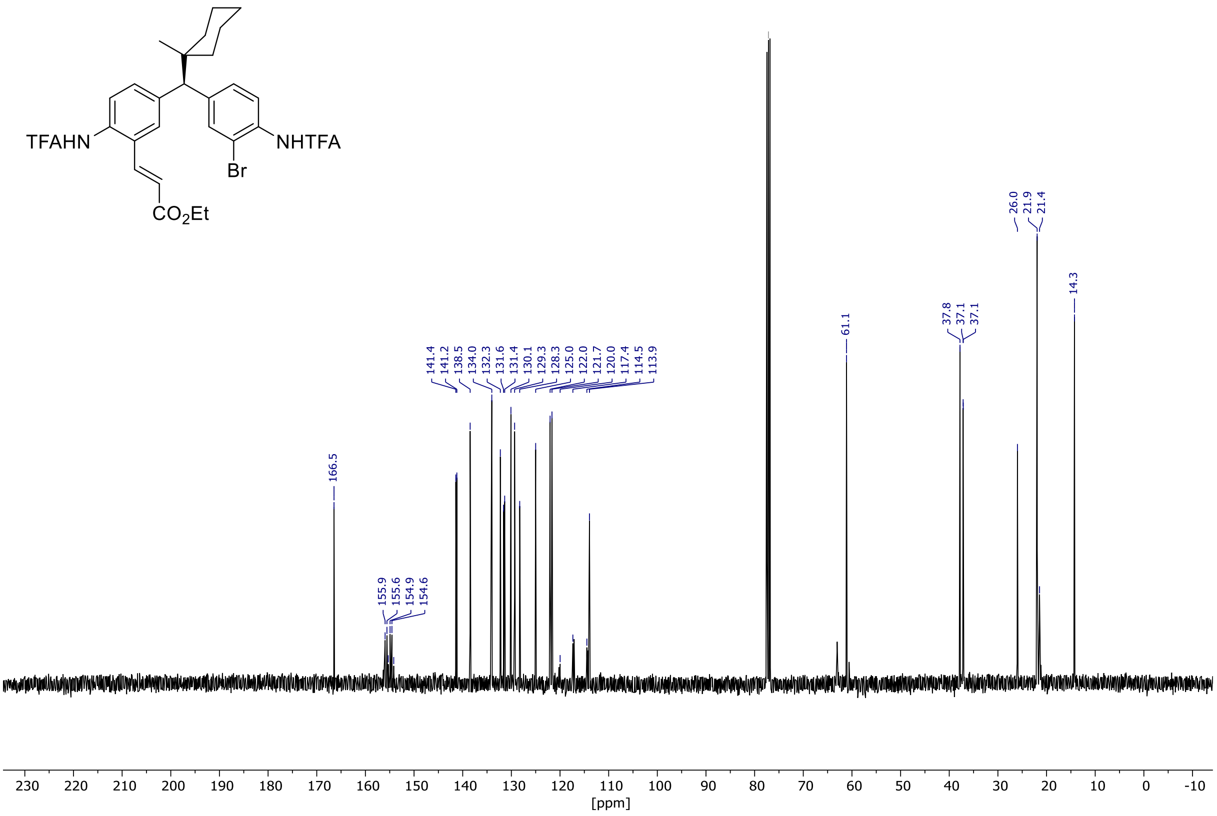
^{19}F NMR (376 MHz, CDCl$_3$): **11**



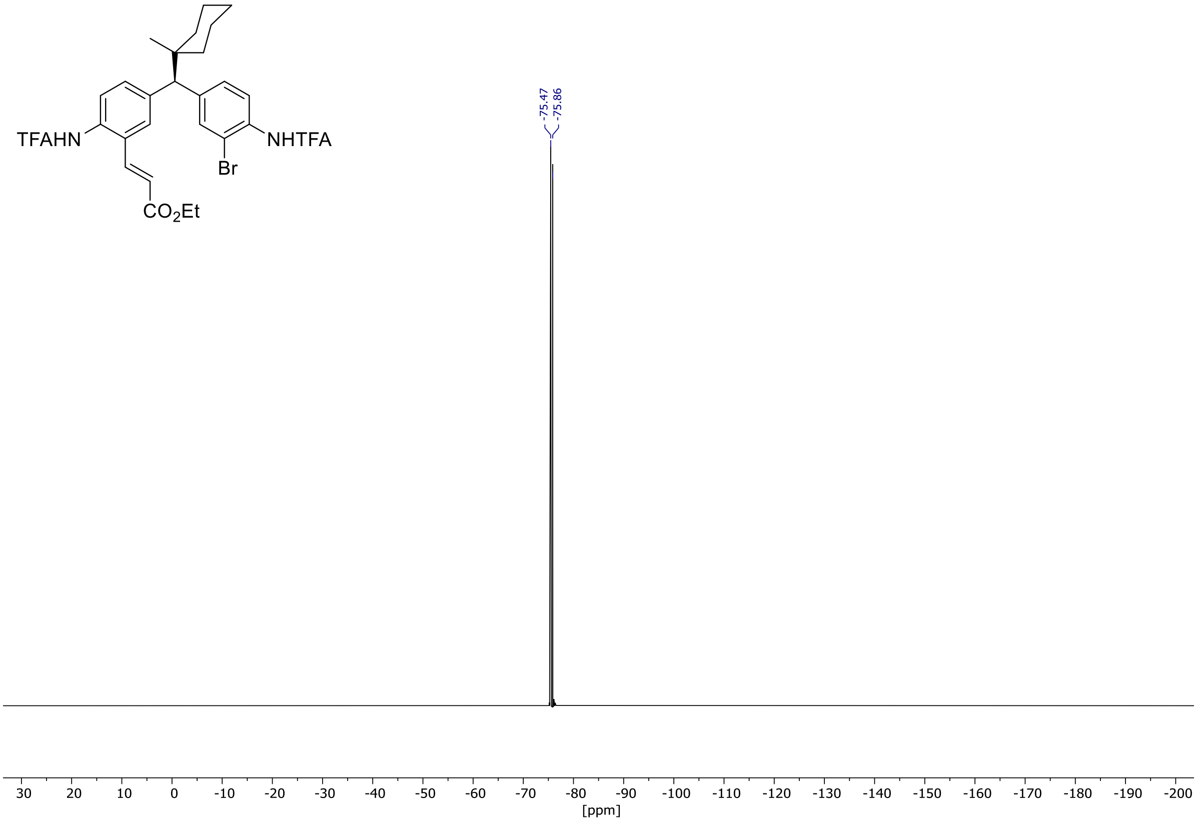
^{1}H NMR (400 MHz, CDCl$_3$): **12**



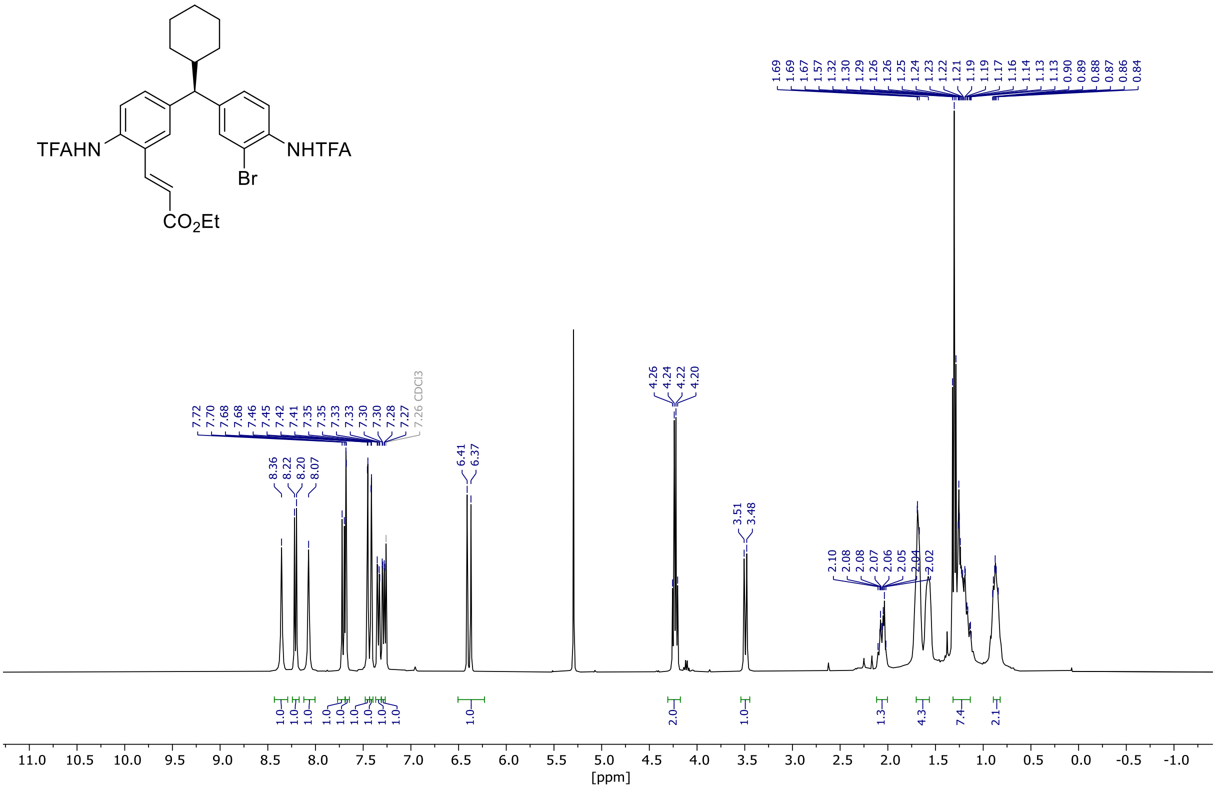
^{13}C NMR (101 MHz, $CDCl_3$): **12**



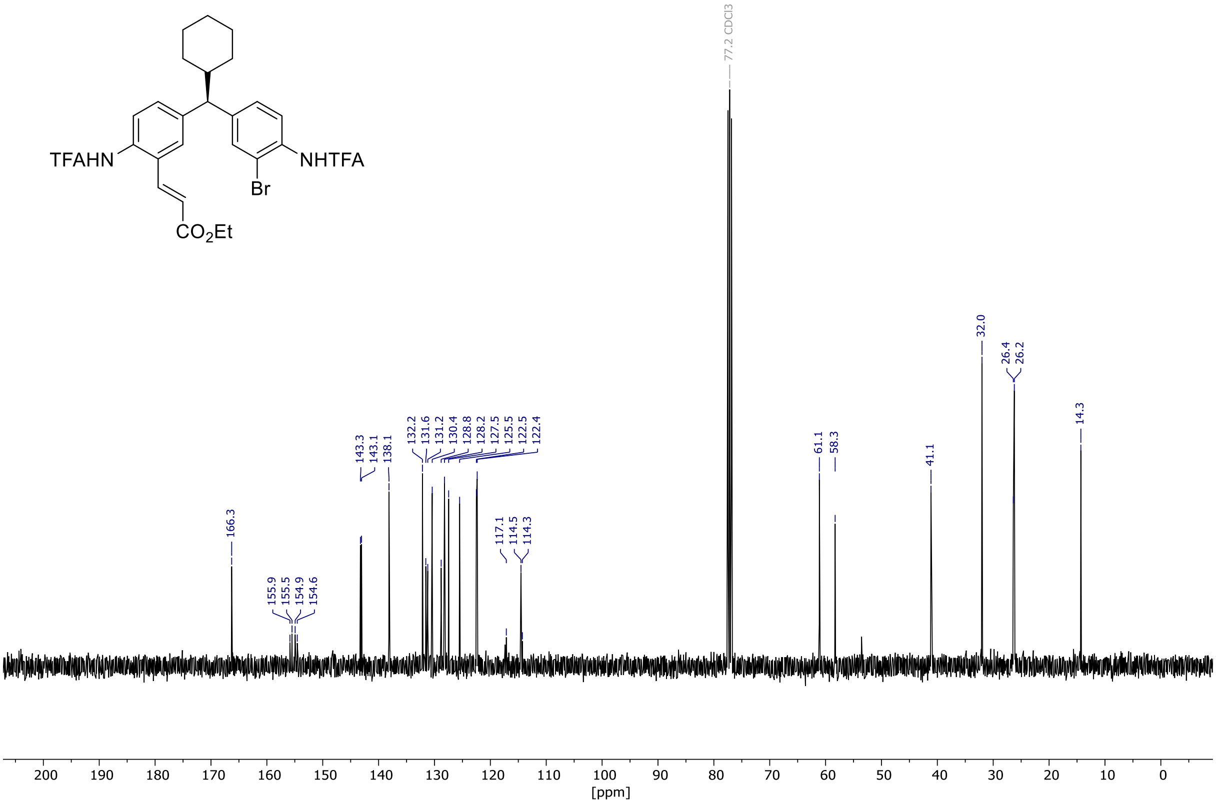
^{19}F NMR (376 MHz, $CDCl_3$): **12**



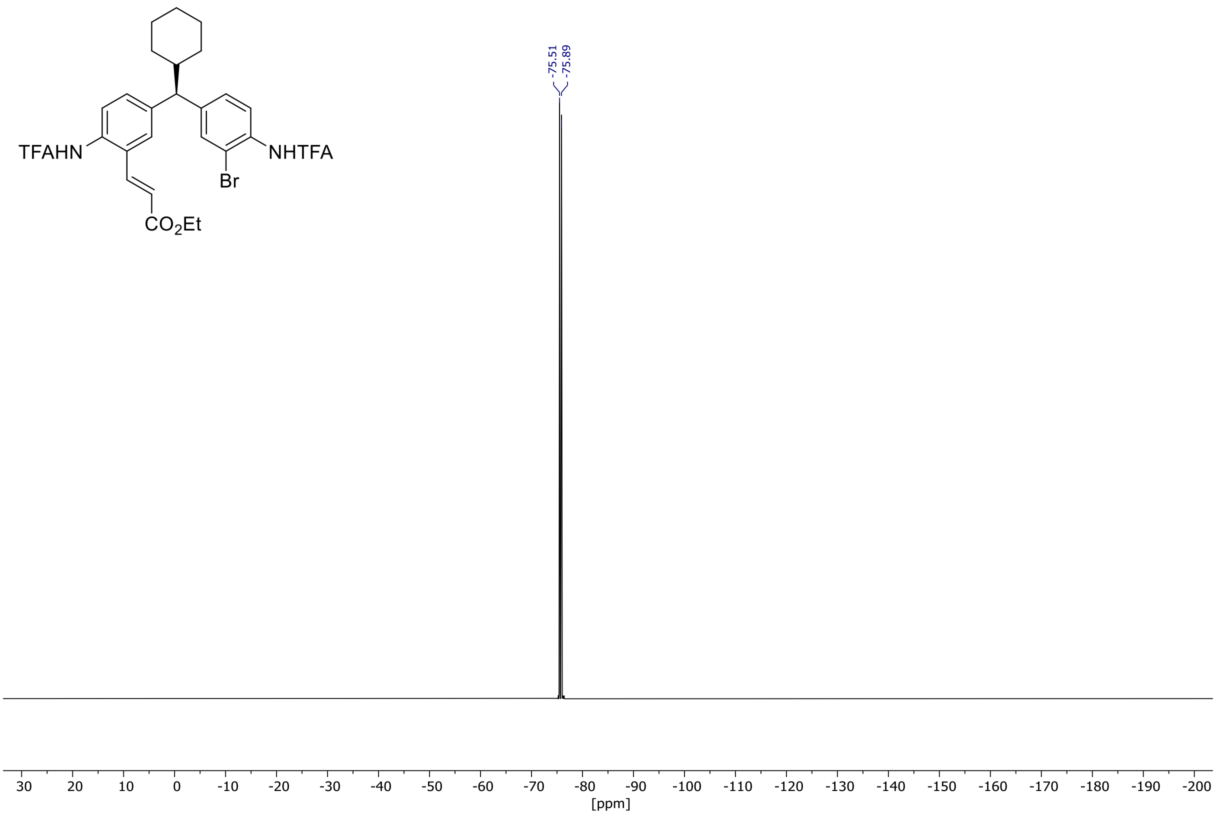
^{1}**H NMR** (400 MHz, CDCl$_3$): **13**



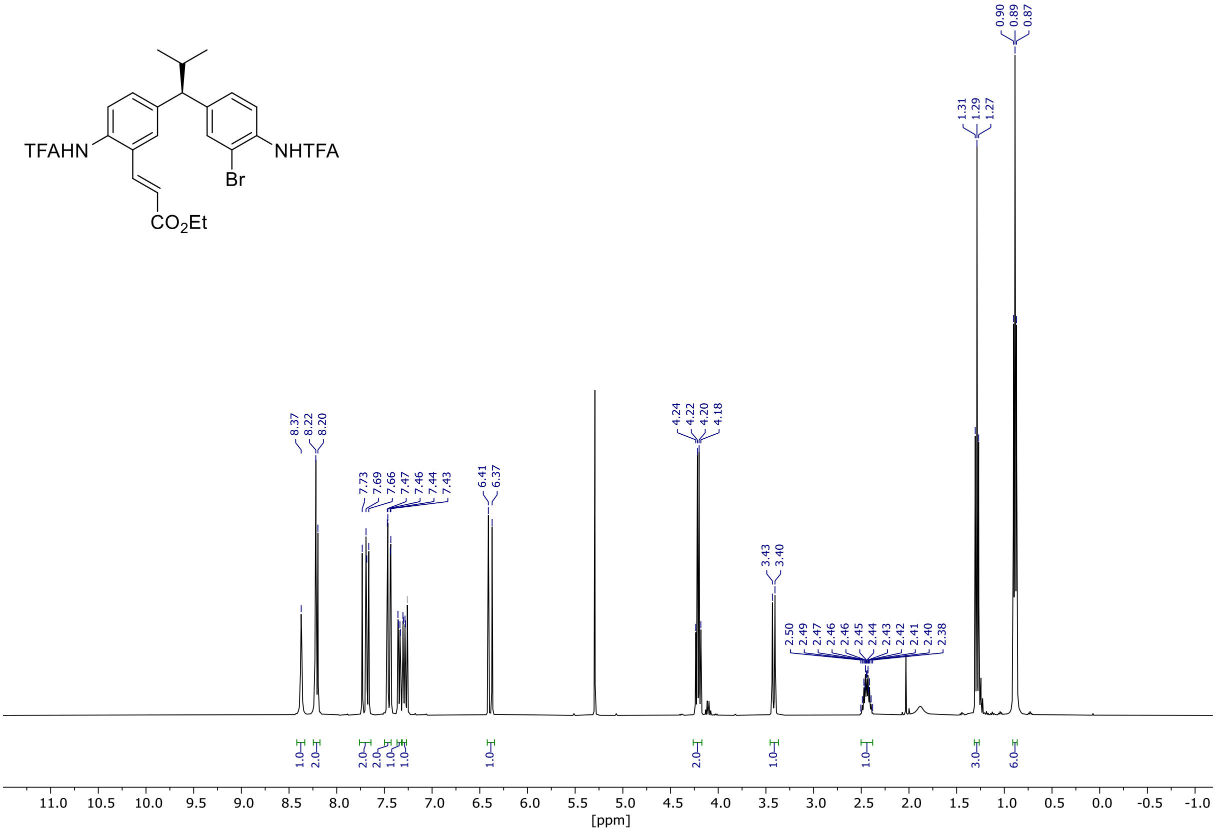
^{13}**C NMR** (101 MHz, CDCl$_3$): **13**



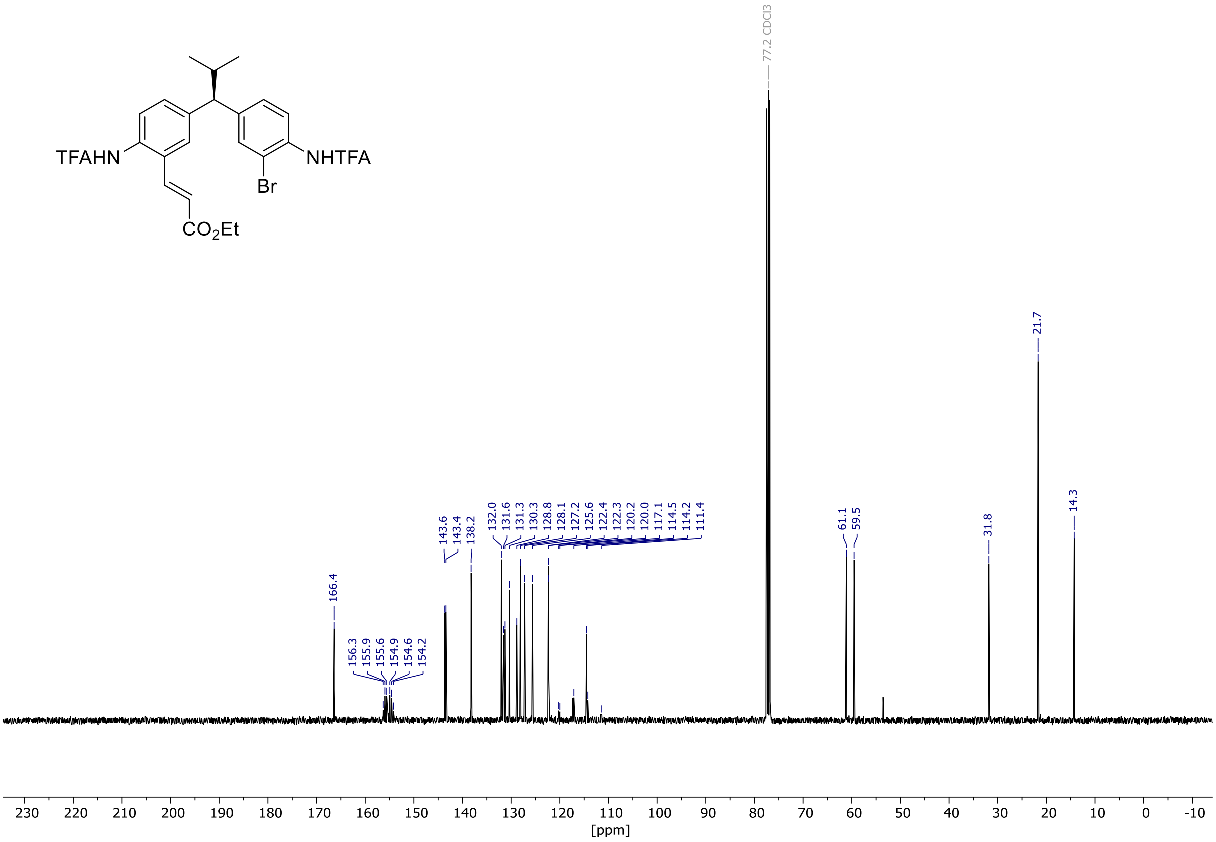
^{19}F NMR (376 MHz, CDCl$_3$): **13**



^{1}H NMR (400 MHz, CDCl$_3$): **14**

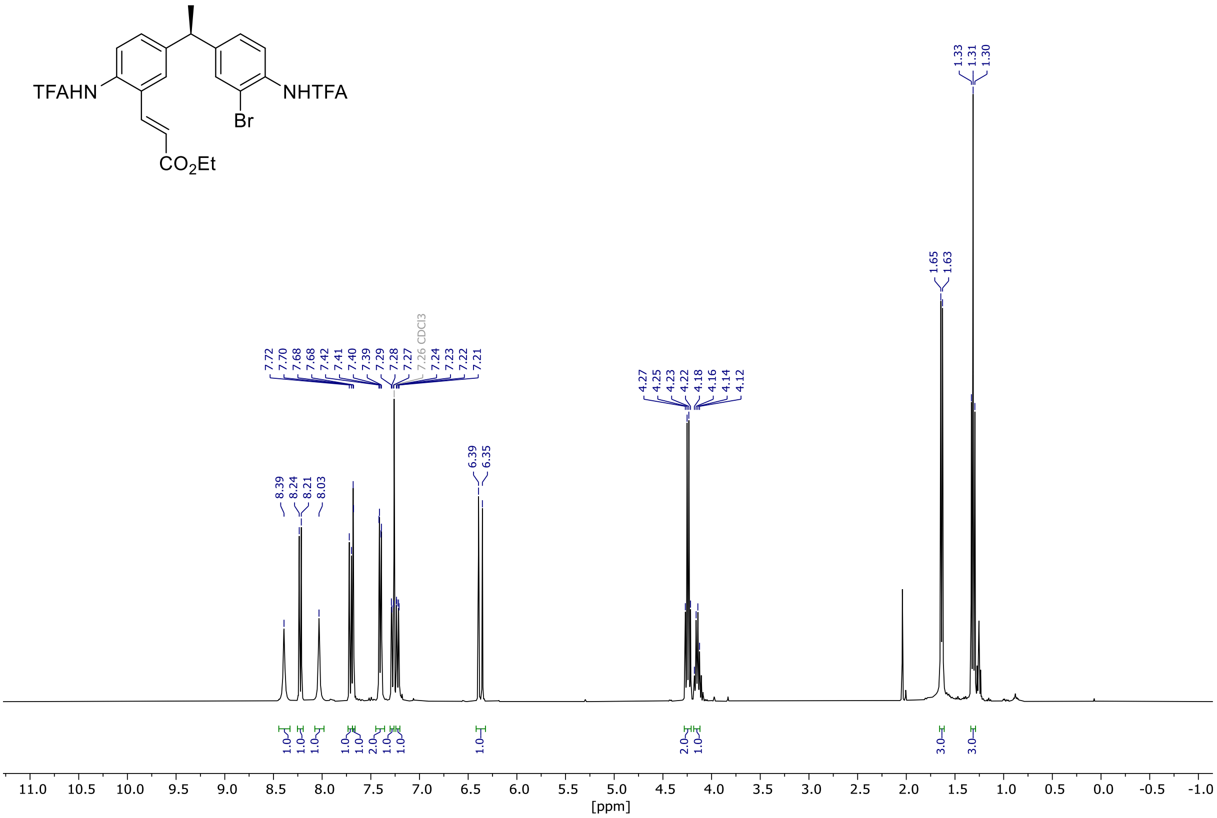


^{13}C NMR (101 MHz, CDCl$_3$): **14**



^{19}F NMR (376 MHz, CDCl$_3$): **14**

^{1}H NMR (400 MHz, $CDCl_3$): **15**



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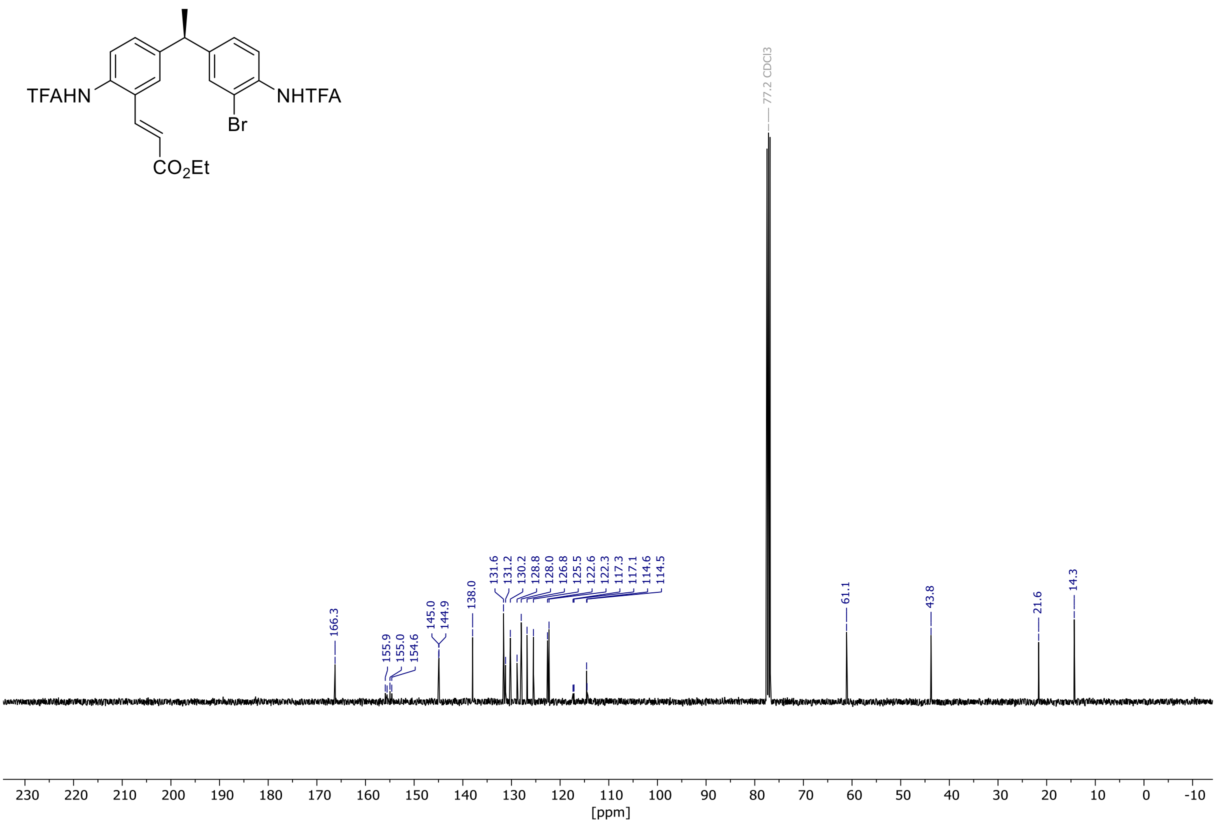

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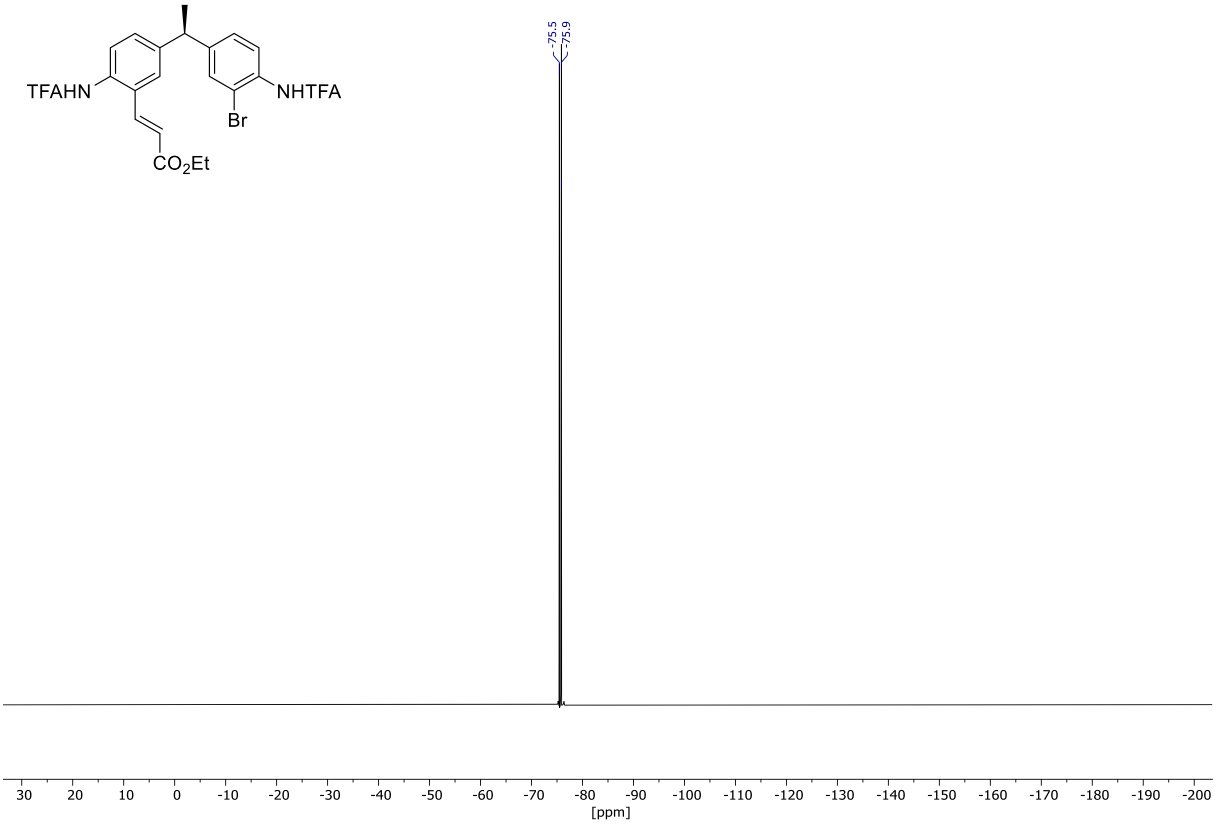

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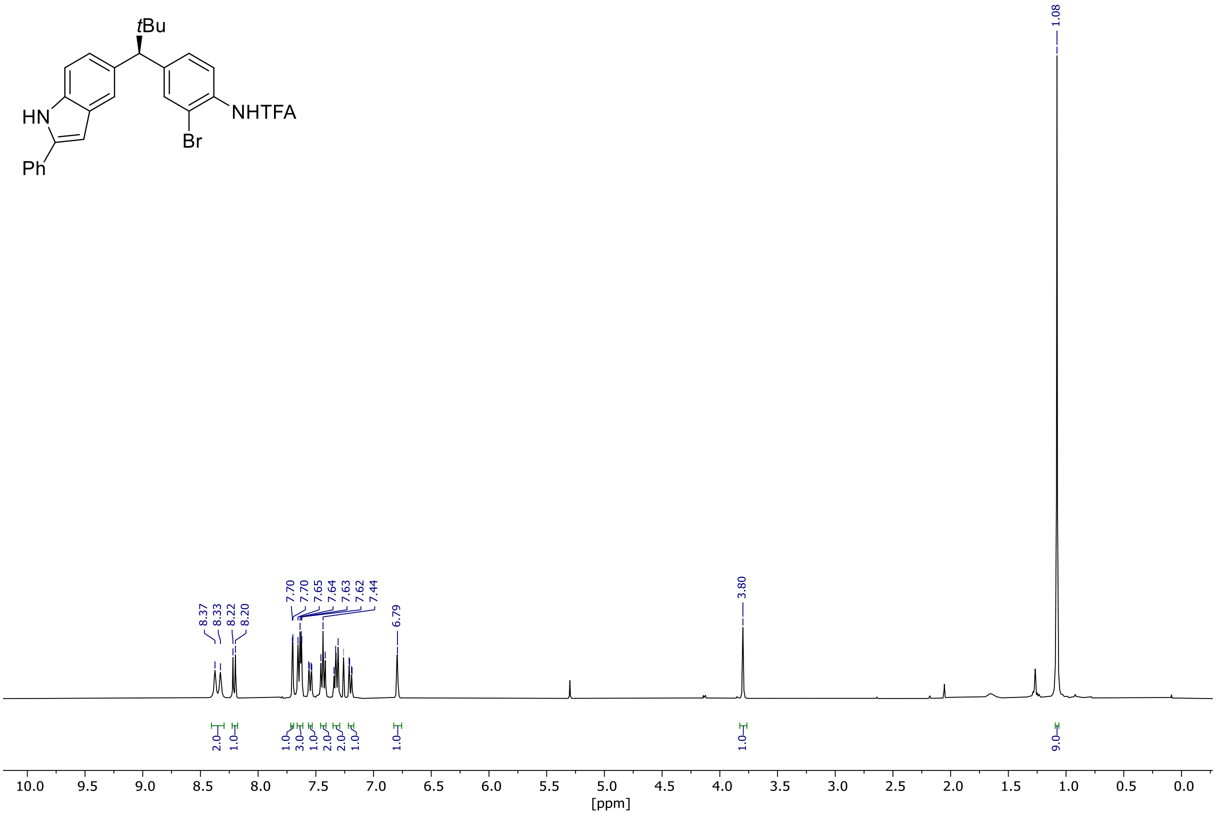
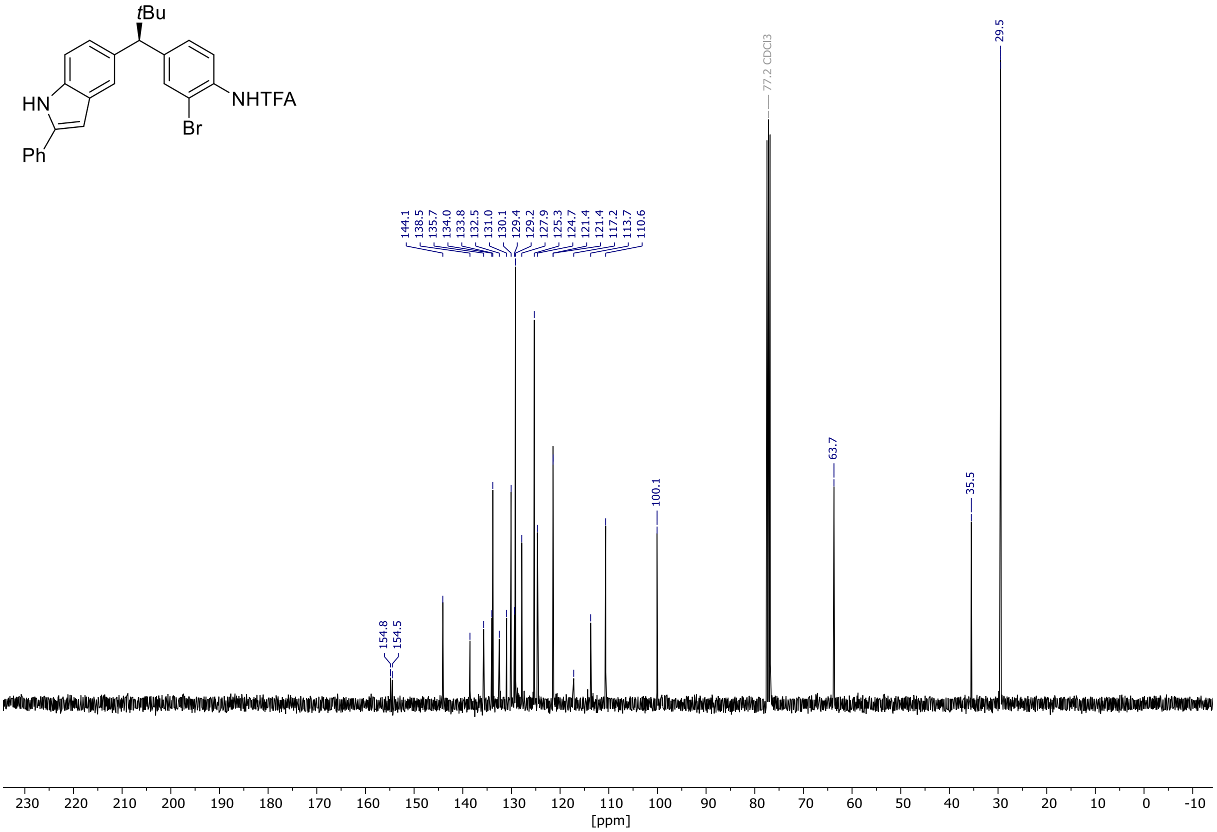


^{13}C NMR (101 MHz, CDCl$_3$): **5**



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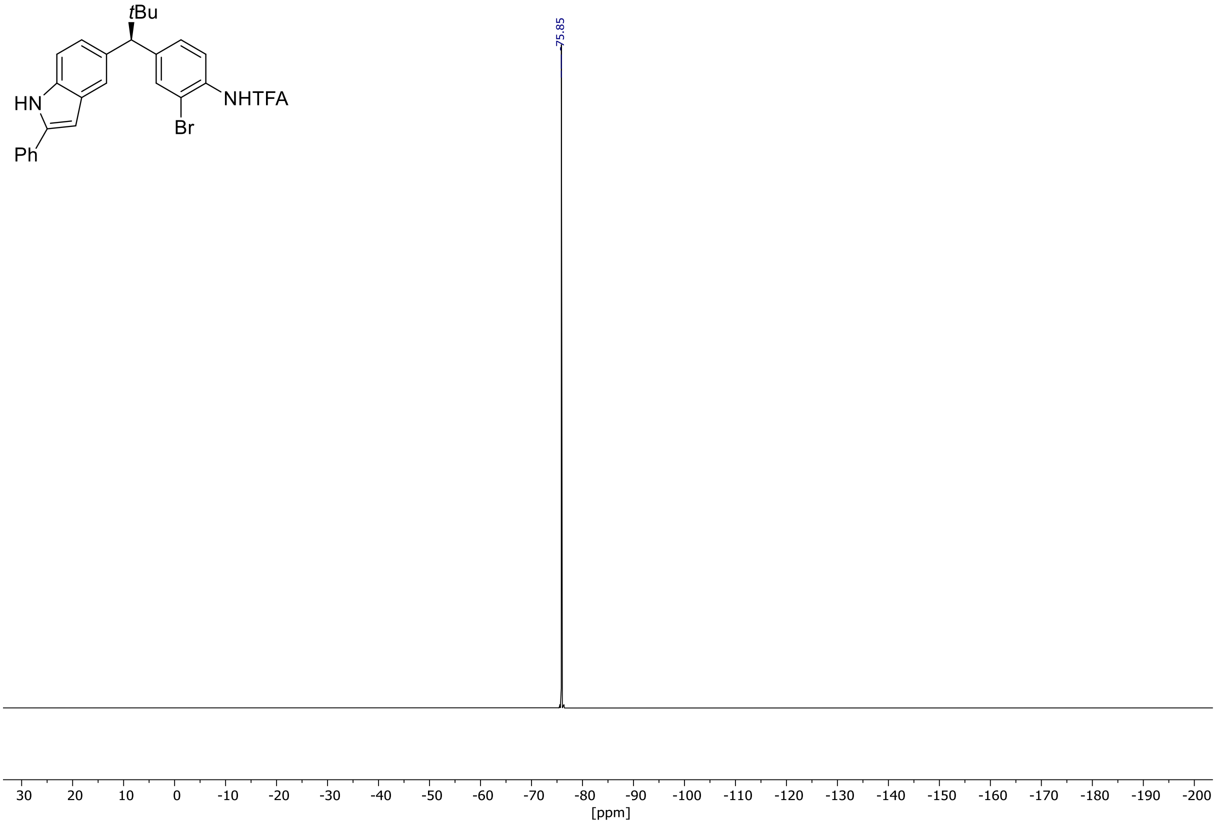

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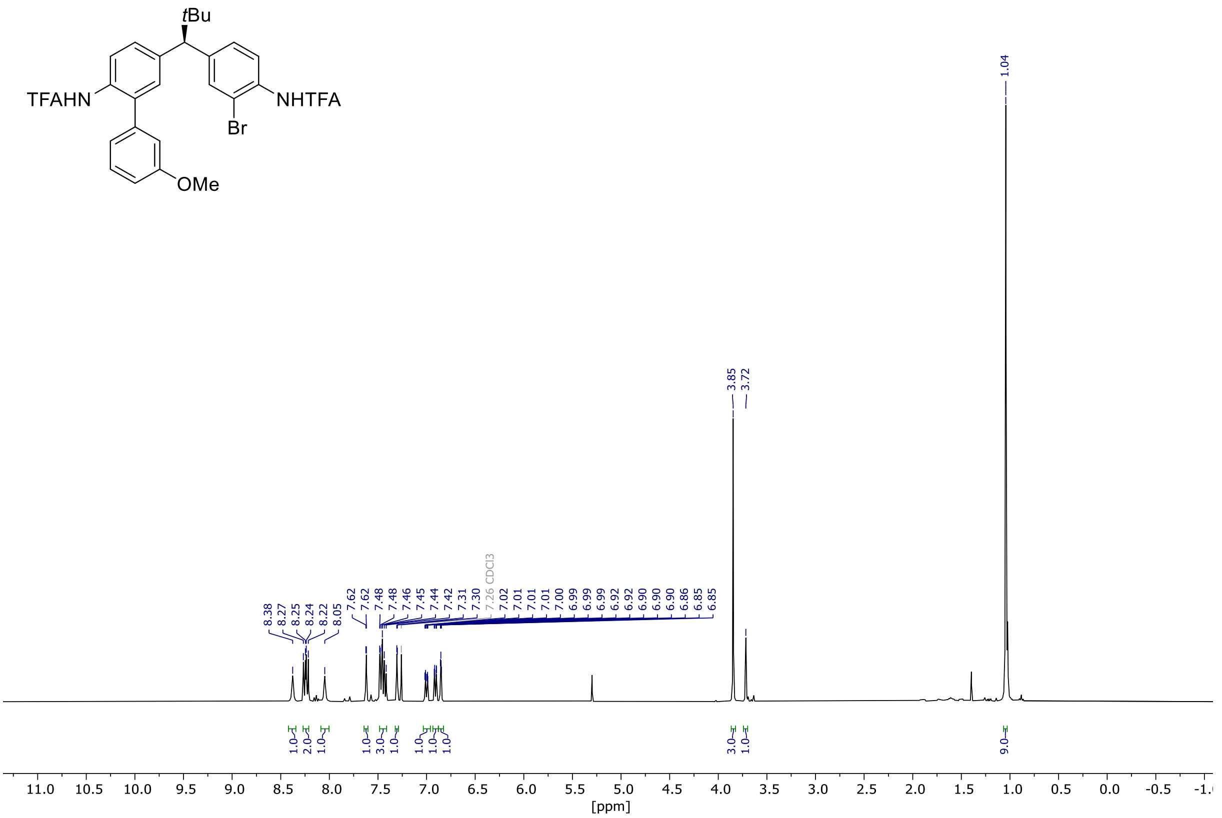
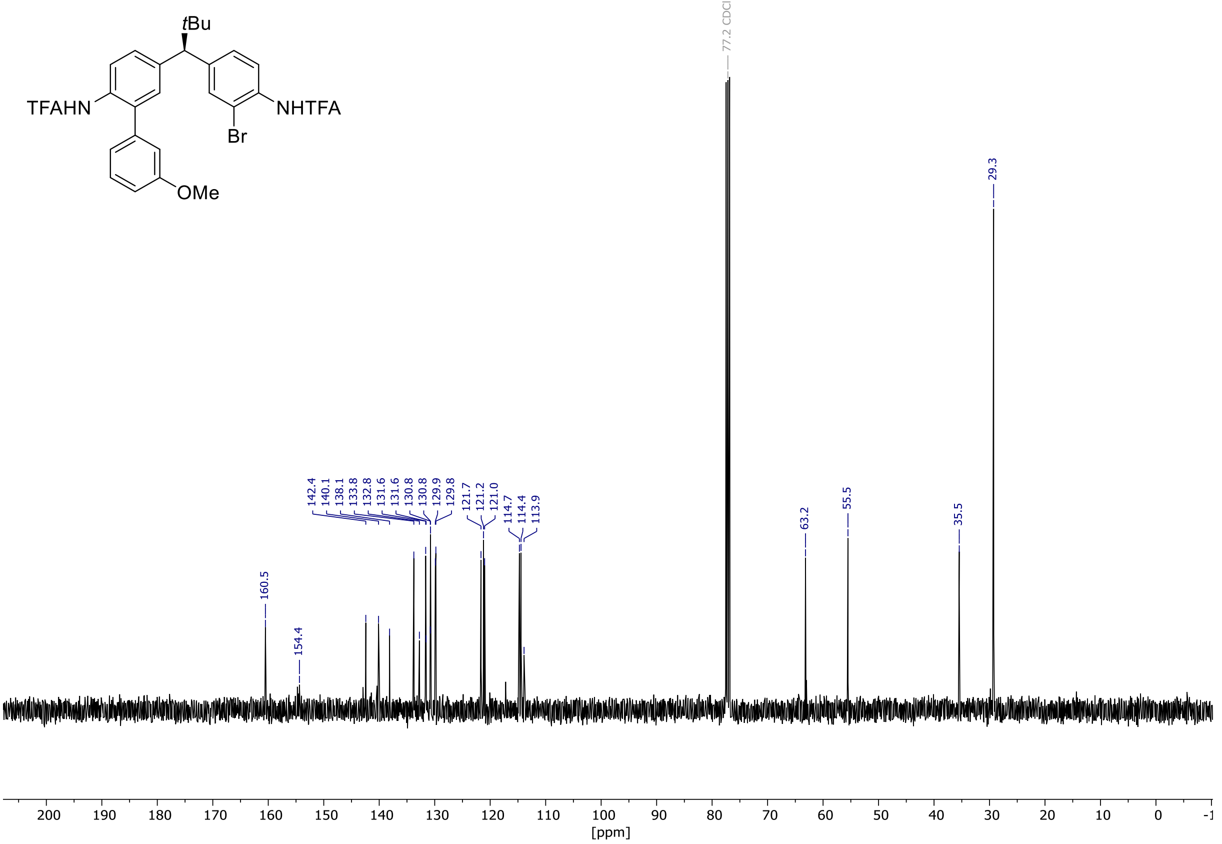
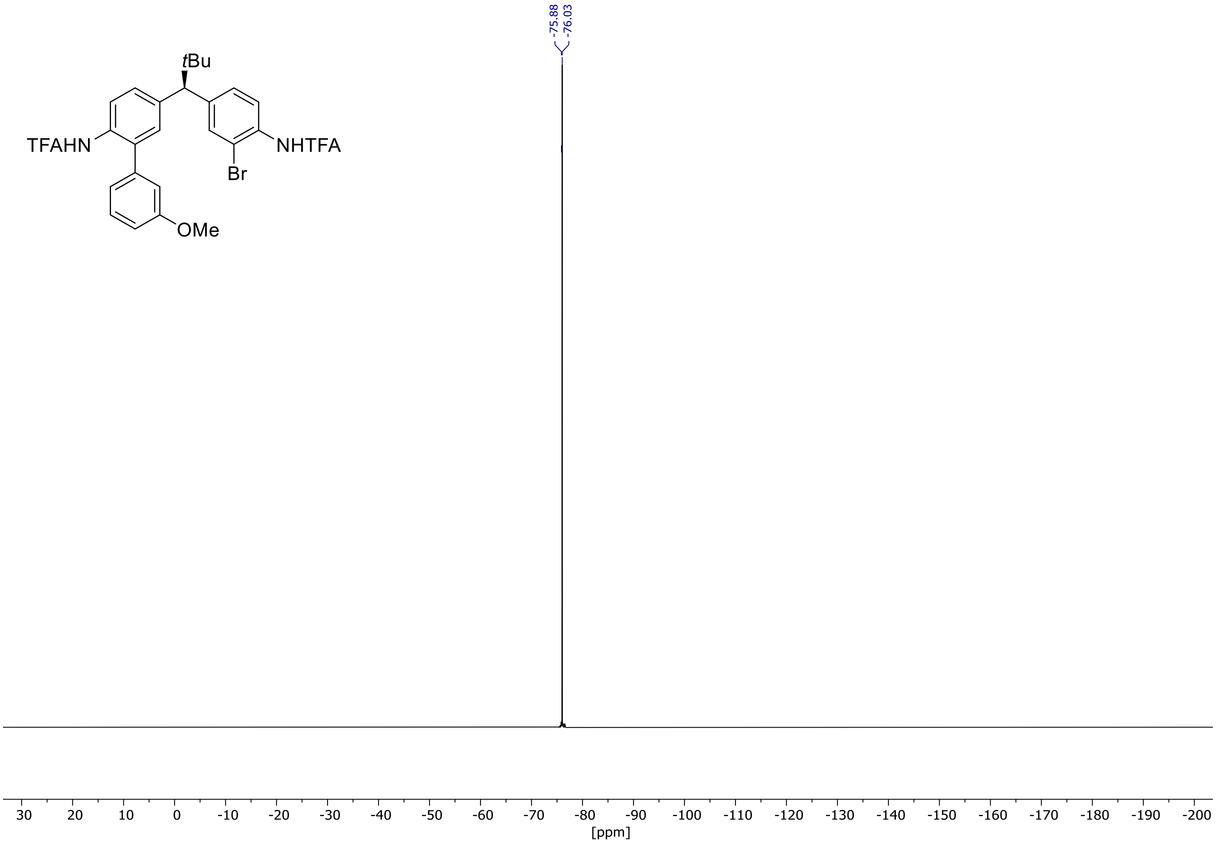


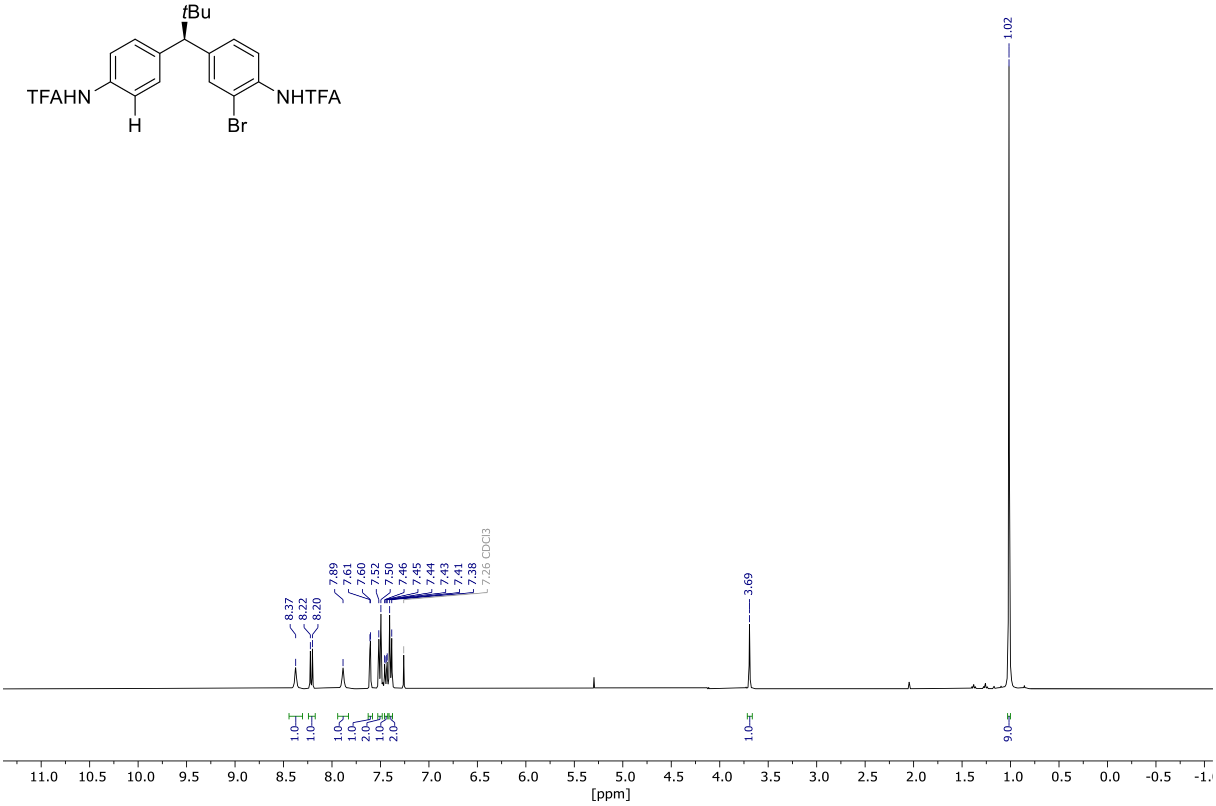
^{13}C NMR (101 MHz, CDCl$_3$): **6**



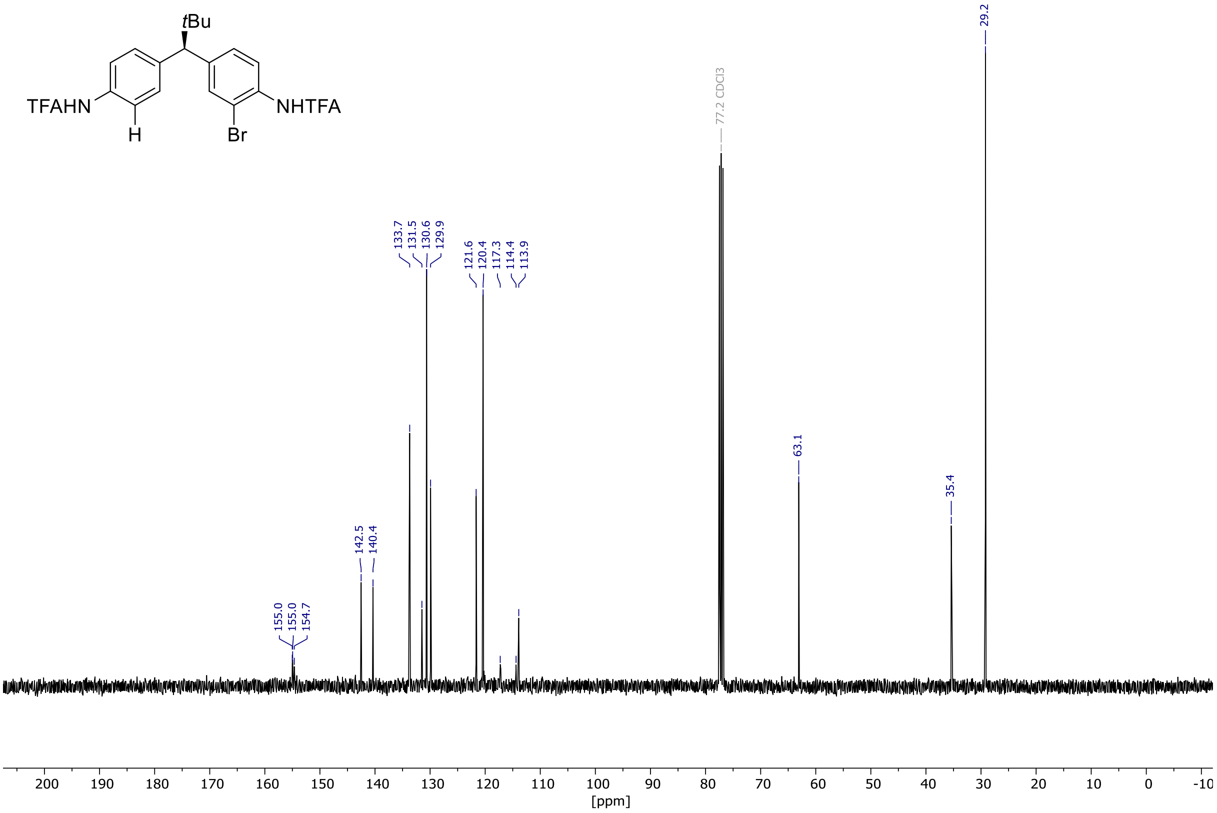
^{19}F NMR (376 MHz, $CDCl_3$): **6**



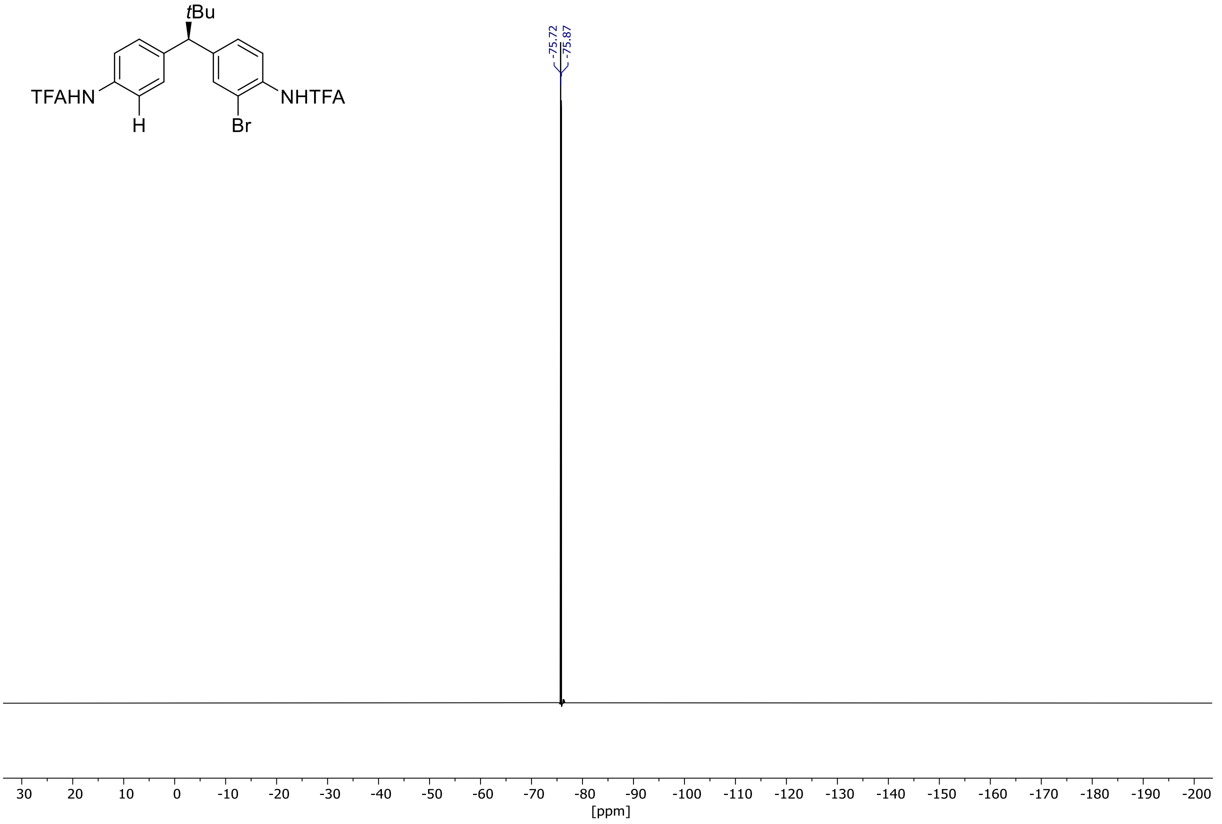
^{1}H NMR (400 MHz, $CDCl_3$): **7**



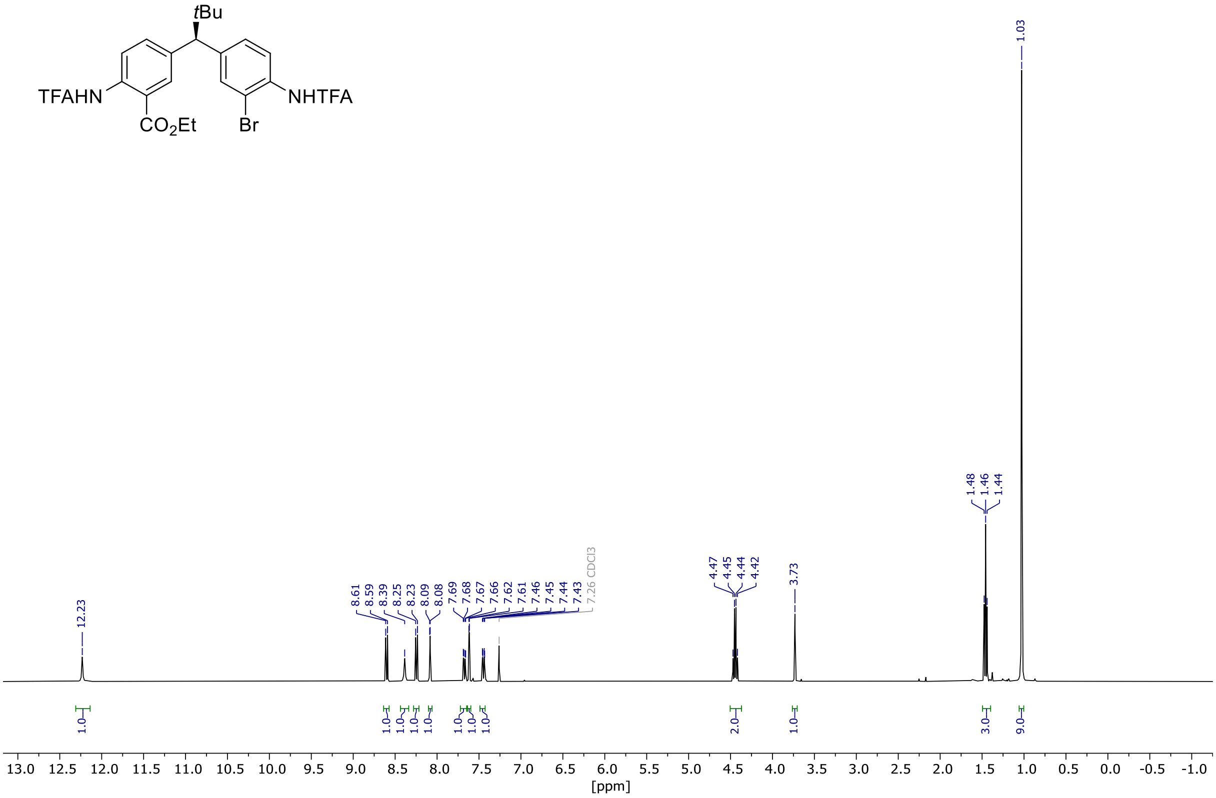
^{13}**C NMR** (101 MHz, $CDCl_3$): **7**



^{19}**F NMR** (376 MHz, $CDCl_3$): **7**



^{1}H NMR (400 MHz, $CDCl_3$): **8**



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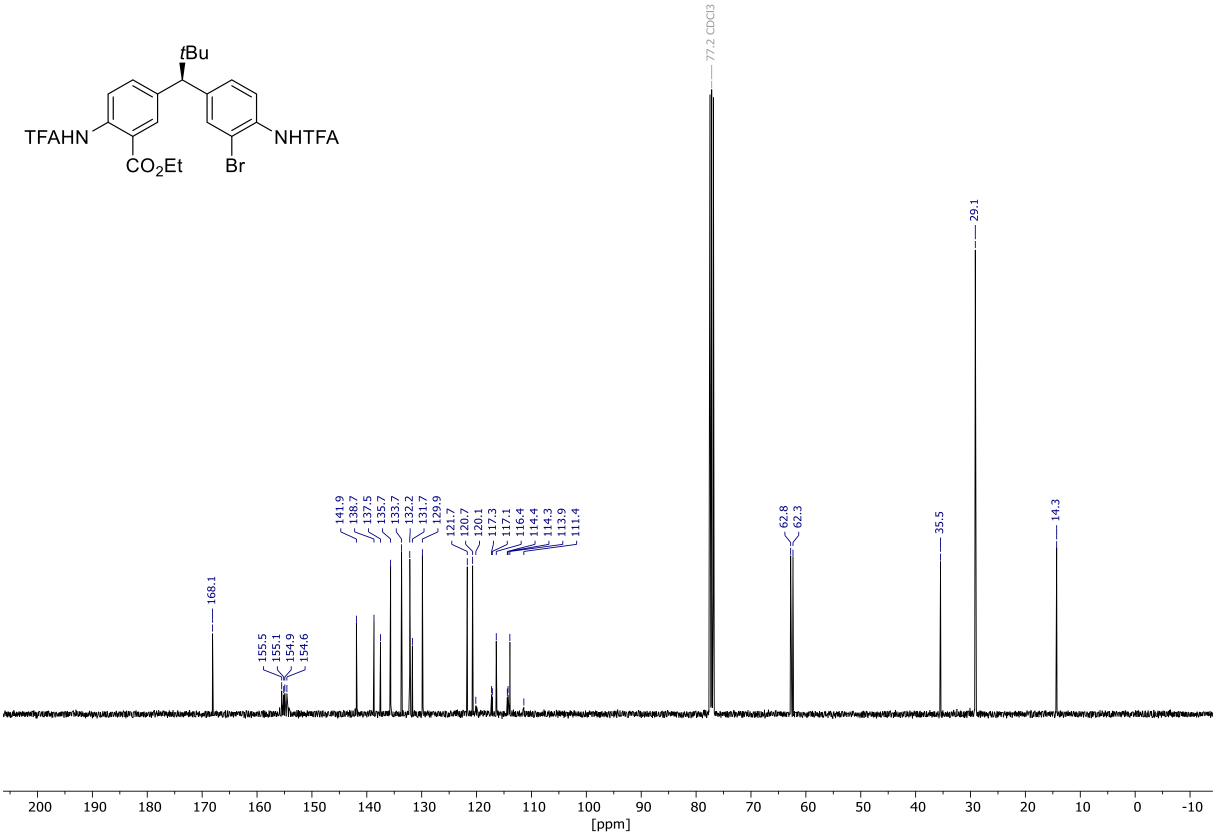

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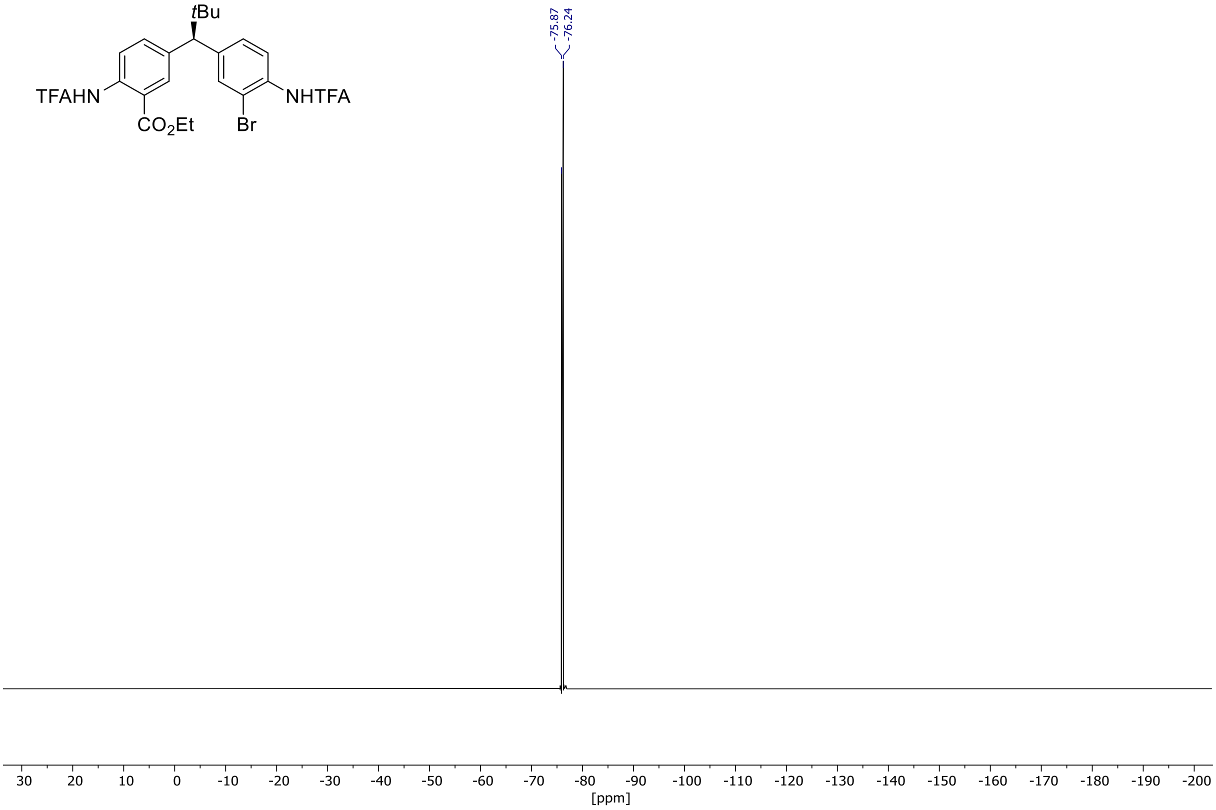

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