SUPPORTING INFORMATION

An Unexpected Lewis Acid-Catalyzed Cascade Reaction of Bicyclo[1.1.0]butanes with Triazinanes to Biscyclobutenyl Amines

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Supporting Information

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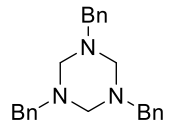
1. General Information

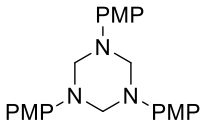
All available chemicals and solvents were purchased from chemical supplier and directly used without further purification. Thin layer chromatography (TLC) was carried out using precoated silica gel plates (0.25 mm, F254) and visualization was accomplished under UV light (254 nm). Flash column chromatography was performed on silica gel (200–300 mesh) or neutral alumina (400 mesh). Melting points were obtained uncorrected from an OptiMelt MPA100 melting point apparatus. ^{1}H NMR spectra were recorded in $CDCl_3$ on a Bruker Ascend 400 or 500 spectrometer (400 MHz or 500 MHz), and chemical shifts (δ values) were reported in parts per million (ppm) relative to internal tetramethylsilane standard (TMS, 0 ppm). Multiplicity was indicated as follows: s (singlet), d (doublet), dd (doublet of doublet), t (triplet), q (quartet) and m (multiple or unresolved). The number of protons (n) for a given resonance is reported as nH. Coupling constants (*J*) were given in Hertz (Hz). ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker Ascend 400 or 500 spectrometer (100 MHz or 125 HMz) relative to internal $CDCl_3$ standard (77.16 ppm). All high-resolution mass spectra (HRMS) were obtained on a Thermo Scientific Q Exactive UHMR Hybrid Quadrupole-Orbitrap mass spectrometer.

2. Preparation of Triazinane Substrates

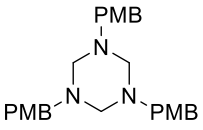
The triazinane substrates were all known compounds and synthesized according to related procedures.[1-3]



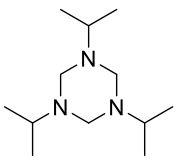
1a[1]



1b[2]



1c[3]



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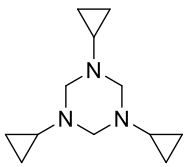
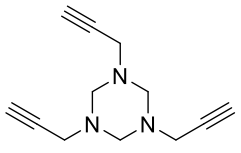


1e[3]



1f[3]

*General Procedure for **1a, 1c-f***

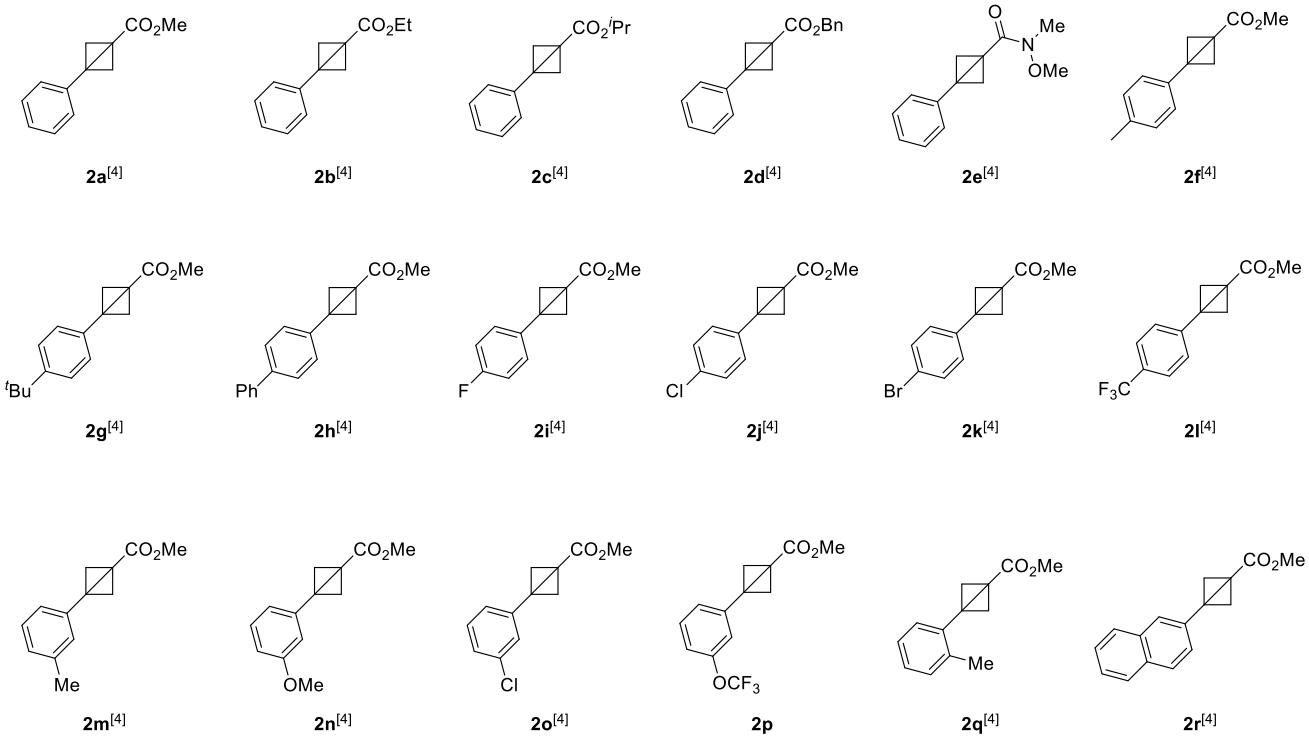
To a stirred suspension of anhydrous $MgSO_4$ in CH_2Cl_2 (25 mL), paraformaldehyde (18.7 mmol, 1.00 equiv) and freshly distilled benzylamine (18.7 mmol, 1.00 equiv) were added in sequence. The mixture was stirred at rt overnight. The $MgSO_4$ was filtered off, and the filtrate was concentrated in vacuo to give triazinane products **1a** and **1c-f**, which was used directly without further purification.

*General Procedure for **1b***

In a 100 mL round-bottomed flask equipped with a Dean-Stark apparatus, a mixture of *p*-anisidine (3.69 g, 30.0 mmol, 1.00 equiv) and paraformaldehyde (0.99 g, 33.0 mmol, 1.10 equiv) in toluene (50 mL) was heated to reflux in an oil bath for 2 h. Then the solvent was concentrated under reduced pressure, and a precipitate came out from the mixture. The precipitate was collected by filtration, washed with *n*-hexane several times, and dried to obtain triazinane product **1b** as a white solid.

3. Preparation of BCB Substrates

The BCB ester substrates (except **2p**) were known compounds and synthesized according to related procedures.[4, 5]

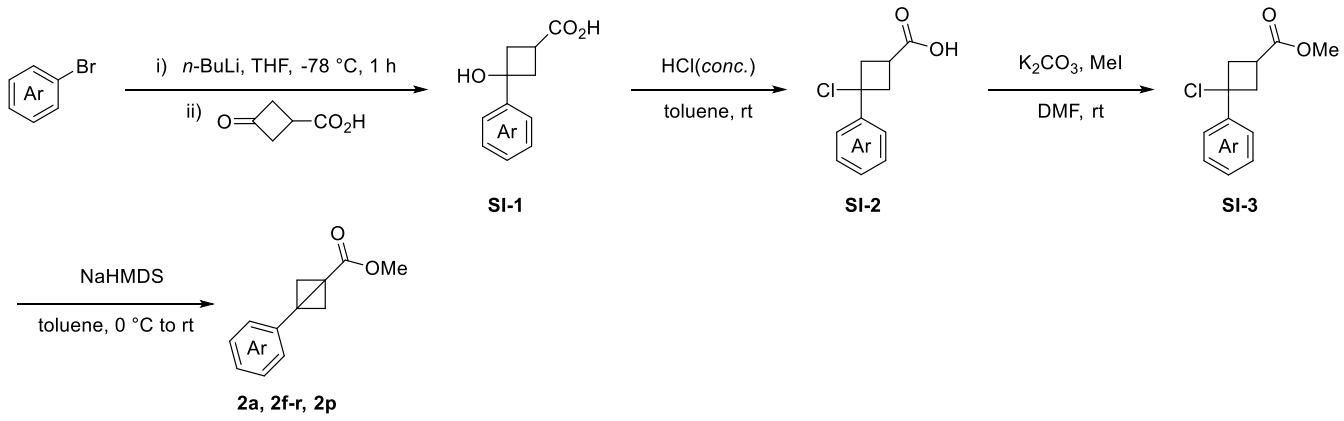


2a[4] **2b**[4] **2c**[4] **2d**[4] **2e**[4] **2f**[4]

2g[4] **2h**[4] **2i**[4] **2j**[4] **2k**[4] **2l**[4]

2m[4] **2n**[4] **2o**[4] **2p** **2q**[4] **2r**[4]

*General Procedure for **2a, 2f-r and 2p***



To a solution of ArBr (30.0 mmol, 2.00 equiv) in dry THF (40 mL) was added *n*-BuLi (20.0 ml, 30.0

mmol, 2.5 M in hexanes, 2.00 equiv) dropwise at -78 °C under argon. The mixture was stirred at -78 °C for 1 h and a solution of 3-oxocyclobutane-1-carboxylic acid (2.9 g, 15.0 mmol, 1.00 equiv) in dry THF (5 mL) was added in one-portion (reaction temperature became 25 °C). The mixture was stirred for 1 h, and quenched with saturated $NH_4Cl_{(aq)}$ (15 mL) and H_2O (10 mL). The organic layer was separated and washed with water (10 mL). The combined aqueous layers were acidified with HCl (2.0 M in H_2O) and extracted with EtOAc (30 mL). The organic layer was washed with brine (15 mL*2), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product **SI-1** was used for the next step without purification.

A round bottom flask equipped with a magnetic stir bar was charged with **SI-1** (15.0 mmol, 1.00 equiv), concentrated HCl (30 mL) and PhMe (30 mL). The reaction was vigorously stirred for 4 h at rt. The aqueous layer was extracted with EtOAc (50 ml*3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude acid **SI-2** was directly used in next step without further purification.

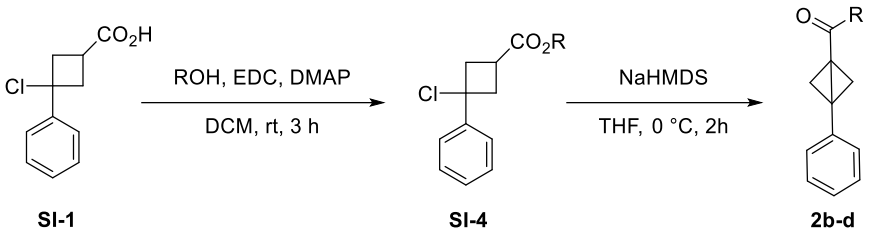
A round bottom flask equipped with a magnetic stir bar was charged with **SI-2** (15.0 mmol, 1.00 equiv) in DMF (75 mL). K_2CO_3 (4.15 g, 30.0 mmol, 2.00 equiv) and MeI (1.4 mL, 22.5 mmol, 1.50 equiv) were added sequentially. The reaction was stirred for 12 h at rt. The resulting mixture was diluted with H_2O (50 mL) and extracted with EtOAc (50 ml*3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc = 9:1) to afford ester **SI-3**.

An oven-dried round bottom flask equipped with a magnetic stir bar was evacuated and backfilled with argon three times. **SI-3** (5.0 mmol, 1.00 equiv) in THF (25 mL) was injected. The reaction was cooled to 0 ºC, and NaHMDS (3.0 ml, 6.0 mmol, 2.0 M in THF, 1.20 equiv) was injected to the solution. The reaction was continued for 0.5 h at 0 ºC and stirred at rt for another 2 h. The resulting mixture was quenched by aqueous NH_4Cl and extracted with EtOAc (50 ml*3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc = 20:1) to afford **2a, 2f-r** and **2p**.

Methyl 3-(3-(trifluoromethoxy)phenyl)bicyclo[1.1.0]butane-1-carboxylate: **2p**

2p was obtained as a yellow oil in 29% yield (1.9 g); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.34–7.29 (m, 1H), 7.24–7.19 (m, 1H), 7.14–7.11 (m, 1H), 7.11–7.07 (m, 1H), 3.49 (s, 3H), 2.94–2.89 (m, 2H), 1.65–1.61 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 169.6, 149.52, 149.50, 149.48, 149.46, 136.6, 130.0, 124.5, 120.5 (q, J = 257.0 Hz), 119.5, 118.5, 51.9, 36.1, 31.7, 24.0; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{13}H_{12}F_3O_3$ 273.0733; found 273.0728.

*General Procedure for **2b-d***



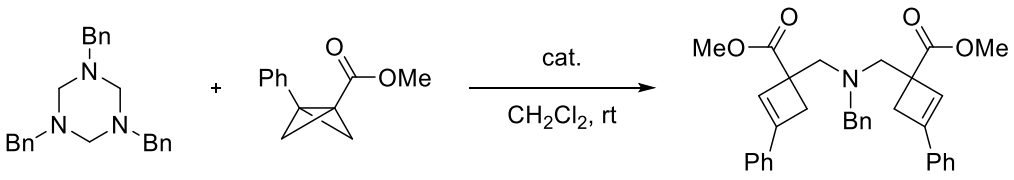
SI-1 **SI-4** **2b-d**

A magnetically stirred solution of **SI-1** (2.1 g, 10.0 mmol, 1.00 equiv) in CH_2Cl_2 (44 mL, 0.20 M) under argon was charged with 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide hydrochloride (EDC) (15.0 mmol, 1.50 equiv), alcohol (10.0 mmol, 1.00 equiv) and DMAP (2.0 mmol, 0.20 equiv). The mixture was stirred for 3 h. CH_2Cl_2 (20 mL) was added to the mixture, which was then quenched with saturated $NH_4Cl_{(aq)}$ (50 mL). The reaction was extracted with CH_2Cl_2 (50 mL*2), dried over Na_2SO_4, and concentrated under reduced pressure to give **SI-4**.

An oven-dried round bottom flask equipped with a magnetic stir bar was evacuated and backfilled with argon three times. **SI-4** (10.0 mmol, 1.00 equiv) in THF (25 mL) was injected. The reaction was cooled to 0 ºC, and NaHMDS (6.0 ml, 12.0 mmol, 2.0 M in THF, 1.20 equiv) was injected to the solution. The reaction was continued for 0.5 h at 0 ºC and stirred at rt for another 2 h. The resulting mixture was quenched by $NH_4Cl_{(aq)}$ and extracted with EtOAc (50 ml*3). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (hexanes/EtOAc) to afford **2b-d**.

4. Optimization of Reaction Conditions

Table S1 Screening catalysts.[a]



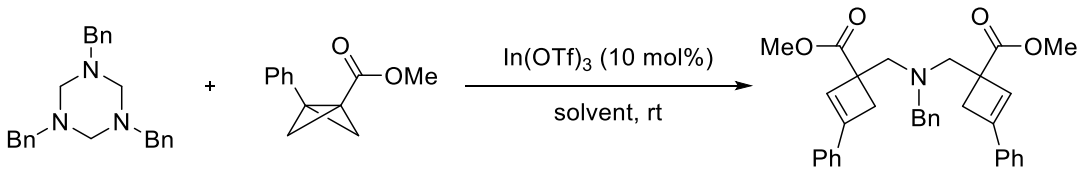
1a **2a** **3a**

entry	catalyst	yield (**3a**)[b]
1	-	-
2	$Cu(OTf)_2$	60
3	$FeCl_3•6H_2O$	28
4	$Co(OTf)_2$	54
5	$Mg(OTf)_2$	44
6	$Zn(OTf)_2$	62
7	$Ga(OTf)_3$	43

8	$Sc(OTf)_3$	58
9	$Yb(OTf)_3$	58
10	$Bi(OTf)_3$	53
11	$In(OTf)_3$	62
12	$BF_3•OEt_2$	50
13	$B(C_6F_5)_3$	58
14	TMSOTf	46
15[c]	$PtCl_2$	-
16[c,d]	$AuPPh_3Cl$	23
17[c]	$Rh_2(esp)_2$	-
18	$PdCl_2$	-

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), catalyst (10 mol%), CH_2Cl_2 (2.0 mL), rt, 24 h. [b] Isolated yield. [c] 5 mol% catalyst was added. [d] 5 mol% $NaBAr_F$ was added.

Table S6. Screening solvent.[a]



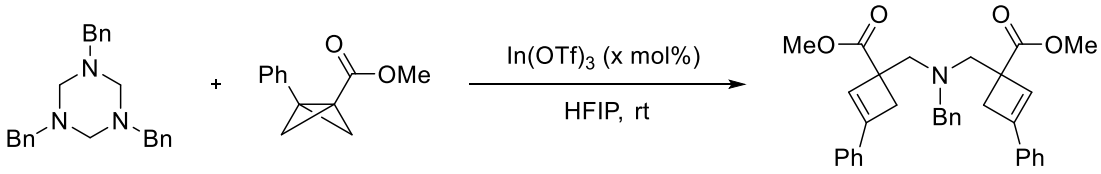
1a **2a** **3a**

entry	solvent	yield (**3a**)[b]
1	DCM	57
2	$CHCl_3$	41
3	DCE	59
4	PhCl	58
5	toluene	58
6	*p*-xylene	53
7	anisole	58
8	benzene	44
9	1,4-dioxane	42
10	DME	47
11	acetone	-
12	MeCN	43
13	THF	50

14	EtOAc	48
15	HFIP	63
16	DMF	-
17	DMSO	-

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), $In(OTf)_3$ (10 mol%), solvent (2.0 mL), rt, 24 h. [b] Isolated yield.

Table S7 Screening other parameters.[a]

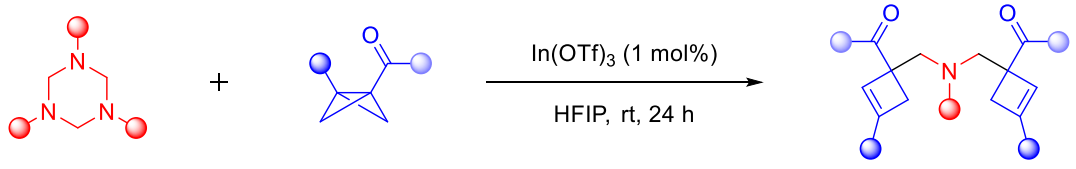


1a **2a** **3a**

entry	x	yield (**3a**)[b]
1	10	63
2[c]	10	99
3[c]	10	99
4[c]	5	99
5[c]	1	99
6[c,d]	1	49
7[e]	1	50
8[f]	10	83

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), $In(OTf)_3$ (10 mol%), HFIP (2.0 mL), rt, 24 h. [b] Isolated yield. [c] **2a** (0.5 mmol). [d] 4Å MS (100 mg) was added. [e] **2a** (0.2 mmol). [f] **2a** (0.4 mmol).

5. Substrate Scope

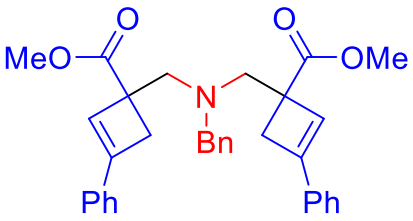


1 **2** **3** (dr = 1:1)

In an oven-dried reaction vial equipped with a magnetic stir bar, **1** (0.20 mmol, 1.00 equiv) and **2** (0.50 mmol, 2.50 equiv) were added into HFIP (2.0 mL). $In(OTf)_3$ (1.1 mg, 0.002 mmol, 1 mol%) was added. The reaction was stirred at rt for 24 h. The resulting mixture was concentrated under reduced pressure.

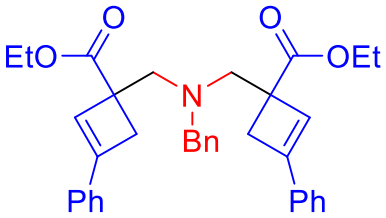
The residue was purified by flash column chromatography (hexanes/EtOAc) on silica gel to afford the corresponding products.

Dimethyl 1,1'-((benzylazanediyl)bis(methylene))bis(3-phenylcyclobut-2-ene-1-carboxylate): 3a



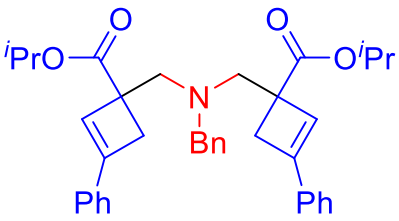
The title compound **3a** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a yellow oil in 99% yield (101.8 mg); **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.35–7.29 (m, 8H), 7.29–7.20 (m, 7H), 6.39 (d, *J* = 3.6 Hz, 2H), 3.72–3.58 (m, 8H), 3.19–3.07 (m, 4H), 2.97 (d, *J* = 13.3 Hz, 2H), 2.71 (dd, *J* = 13.0, 6.9 Hz, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.71, 174.69, 146.4, 146.3, 139.5, 133.8, 129.39, 129.37, 128.6, 128.54, 128.48, 128.46, 128.2, 127.06, 127.05, 125.0, 61.2, 60.0, 59.9, 51.94, 51.87, 51.8, 38.2, 38.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{33}H_{34}NO_4$ 508.2482; found 508.2473.

Diethyl 1,1'-((benzylazanediyl)bis(methylene))bis(3-phenylcyclobut-2-ene-1-carboxylate): 3b



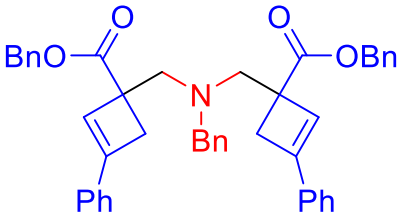
The title compound **3b** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a colorless oil in 96% yield (103.9 mg); **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.49–7.08 (m, 15H), 6.48–6.32 (m, 2H), 4.25–3.92 (m, 4H), 3.85–3.56 (m, 2H), 3.30–2.89 (m, 6H), 2.80–2.65 (m, 2H), 1.26–1.12 (m, 6H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.5, 174.4, 146.2, 146.1, 139.6, 133.9, 129.2, 128.82, 128.78, 128.5, 128.4, 128.2, 127.0, 125.0, 61.23, 61.21, 60.8, 59.9, 59.8, 52.0, 51.9, 38.2, 38.0, 14.3; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{35}H_{37}NO_4$ 536.2795; found 536.2791.

Diisopropyl 1,1'-((benzylazanediyl)bis(methylene))bis(3-phenylcyclobut-2-ene-1-carboxylate): 3c



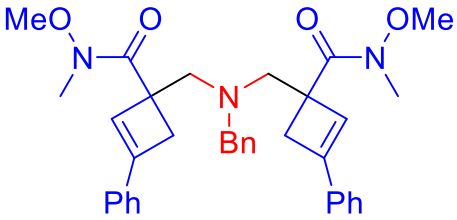
The title compound **3c** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a yellow oil in 99% yield (112.5 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.34–7.16 (m, 15H), 6.45–6.27 (m, 2H), 5.05–4.90 (m, 2H), δ 3.89–3.81 (m, 0.5H), 3.76 (s, 1H), 3.71–3.64 (m, 0.5H), 3.20 (t, *J* = 13.0 Hz, 2H), 3.08–2.97 (m, 4H), 2.77–2.66 (m, 2H), 1.28–1.21 (m, 6H), 1.21–1.15 (m, 6H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.2, 146.0, 145.9, 139.6, 134.0, 129.1, 128.93, 128.89, 128.4, 128.29, 128.28, 128.2, 127.0, 124.9, 68.1, 61.0, 60.9, 59.7, 59.6, 52.11, 52.05, 38.0, 37.9, 21.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{37}H_{42}NO_4$ 564.3108; found 564.3099.

Dibenzyl 1,1'-((benzylazanediyl)bis(methylene))bis(3-phenylcyclobut-2-ene-1-carboxylate): 3d



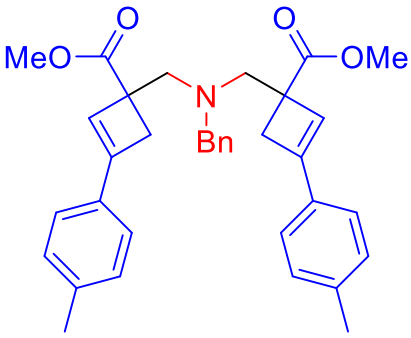
The title compound **3d** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a yellow oil in 83% yield (110.4 mg); **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.37–7.22 (m, 22H), 7.22–7.13 (m, 3H), 6.41 (s, 1H), 6.38 (s, 1H), 5.14–5.06 (m, 2H), 5.05–4.97 (m, 2H), 3.69 (s, 2H), 3.25–3.16 (m, 2H), 3.12–3.05 (m, 2H), 3.02–2.92 (m, 2H), 2.76–2.64 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.1, 146.2, 146.1, 139.4, 136.28, 136.26, 133.8, 129.2, 128.6, 128.54, 128.52, 128.43, 128.40, 128.24, 128.23, 128.2, 128.1, 127.0, 124.9, 66.4, 61.34, 61.28, 59.8, 52.1, 52.0, 38.1, 38.0; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{45}H_{42}NO_4$ 660.3108; found 660.3098.

1,1'-((Benzylazanediyl)bis(methylene))bis(N-methoxy-N-methyl-3-phenylcyclobut-2-ene-1-carboxamide): **3e**



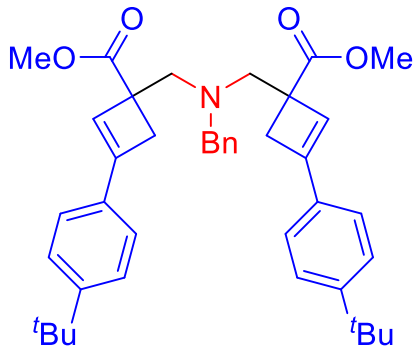
The title compound **3e** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a yellow oil in 53% yield (60.6 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.41–7.23 (m, 12H), 7.22–7.13 (m, 3H), 6.53–6.42 (m, 2H), 3.89 (d, *J* = 13.6 Hz, 0.5H), 3.78–3.76 (m, 1H), 3.68–3.62 (m, 1H), 3.57–3.51 (m, 5H), 3.29–2.98 (m, 12.5H), 2.88–2.74 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 144.9, 144.8, 134.0, 134.22, 134.18, 129.6, 129.54, 129.52, 129.2, 128.4, 128.1, 128.04, 128.01, 126.9, 126.8, 125.0, 124.9, 61.0, 60.7, 60.6, 60.5, 59.81, 59.75, 53.1, 53.0, 38.6, 38.5, 33.2; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{35}H_{40}N_3O_4$ 566.3013; found 566.3011.

Dimethyl 1,1'-((benzylazanediyl)bis(methylene))bis(3-(p-tolyl)cyclobut-2-ene-1-carboxylate): **3f**



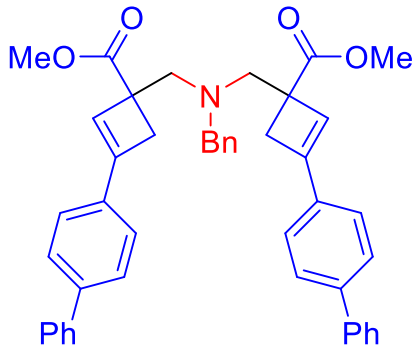
The title compound **3f** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a yellow oil in 97% yield (104.3 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.32–7.24 (m, 4H), 7.24–7.17 (m, 5H), 7.17–7.07 (m, 4H), 6.38–6.27 (m, 2H), 3.75–3.56 (m, 8H), 3.17–3.04 (m, 4H), 2.95 (d, *J* = 13.1 Hz, 2H), 2.75–2.63 (m, 2H), 2.34 (s, 6H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.73, 174.70, 146.2, 146.1, 139.4, 138.3, 131.1, 129.29, 129.26, 129.0, 128.0, 127.33, 127.28, 126.91, 126.89, 124.8, 61.11, 61.09, 59.8, 59.7, 51.81, 51.80, 51.70, 51.65, 38.2, 38.0, 21.4; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{35}H_{38}NO_4$ 536.2795; found 536.2791.

Dimethyl 1,1'-((benzylazanediyl)bis(methylene))bis(3-(4-(tert-butyl)phenyl)cyclobut-2-ene-1-carboxylate): **3g**



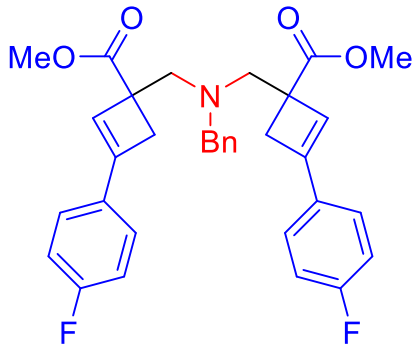
The title compound **3g** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a yellow oil in 73% yield (90.3 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.38–7.32 (m, 4H), 7.32–7.18 (m, 9H), 6.37–6.30 (m, 2H), 3.74–3.59 (m, 8H), 3.17–3.05 (m, 4H), 3.00–2.91 (m, 2H), 2.74–2.63 (m, 2H), 1.31 (s, 18H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.70, 174.67, 151.5, 146.1, 146.0, 139.4, 131.1, 129.3, 129.2, 128.0, 127.64, 127.59, 126.9, 125.3, 124.6, 61.1, 59.7, 59.6, 51.79, 51.77, 51.7, 38.2, 38.1, 34.7, 31.3; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{41}H_{50}NO_4$ 620.3734; found 620.3737.

Dimethyl 1,1'-((benzylazanediyl)bis(methylene))bis(3-([1,1'-biphenyl]-4-yl)cyclobut-2-ene-1-carboxylate): **3h**



The title compound **3h** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a white solid in 94% yield (124.7 mg); **mp:** 135–136 ^{o}C; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.65–7.50 (m, 8H), 7.49–7.32 (m, 10H), 7.32–7.19 (m, 5H), 6.51–6.35 (m, 2H), 3.82–3.54 (m, 8H), 3.24–3.08 m, 4H), 3.00 (d, *J* = 13.2 Hz, 2H), 2.85–2.67 (m, 2H); **^{13}C NMR (125MHz, $CDCl_3$):** δ 174.7, 146.0, 145.9, 141.2, 141.1, 140.7, 139.5, 132.8, 129.41, 129.39, 129.0, 128.8, 128.7, 128.2, 127.6, 127.2, 127.1, 125.5, 61.2, 60.0, 59.9, 52.0, 51.9, 38.3, 38.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{45}H_{42}NO_4$ 660.3108; found 660.3115.

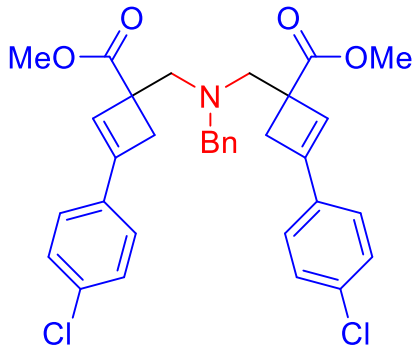
Dimethyl 1,1'-((benzylazanediyl)bis(methylene))bis(3-(4-fluorophenyl)cyclobut-2-ene-1-carboxylate): **3i**



The title compound **3i** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a yellow oil in 85% yield (92.8 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.36–7.17 (m, 9H), 7.08–6.93 (m, 4H), 6.36–6.27 (m, 2H), 3.75–3.56 (m, 8H), 3.17–3.03 (m, 4H), 2.95 (d, *J* = 13.2 Hz, 2H), 2.76–2.63 (m, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.64, 174.61, 162.9 (d, *J* = 248.1 Hz), 145.3, 145.2, 139.4, 130.2 (d, *J* = 3.3 Hz), 129.37, 129.35, 128.19, 128.18, 128.0 (d, *J* = 6.1 Hz), 127.9 (d, *J* = 6.1 Hz), 127.1 (d, *J*

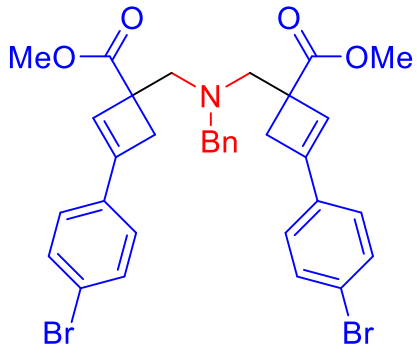
= 2.3 Hz), 126.8, 126.7, 115.6, 115.4, 61.13, 61.11, 60.1, 60.0, 52.0, 51.8, 51.7, 38.2, 38.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{33}H_{32}F_2NO_4$ 544.2294; found 544.2285.

Dimethyl 1,1'-((benzylazanediyl)bis(methylene))bis(3-(4-chlorophenyl)cyclobut-2-ene-1-carboxylate): 3j



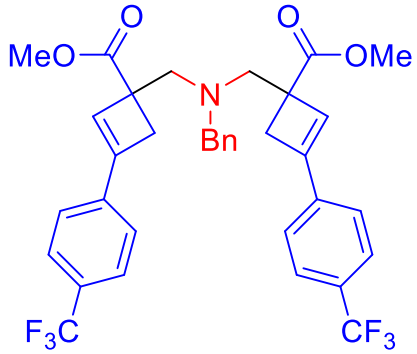
The title compound **3j** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a yellow oil in 97% yield (112.3 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.37–7.13 (m, 13H), 6.42–6.33 (m, 2H), 3.76–3.54 (m, 8H), 3.17–3.02 (m, 4H), 2.95 (d, *J* = 13.3 Hz, 2H), 2.75–2.64 (m, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.5, 174.4, 145.2, 145.1, 139.3, 134.20, 134.18, 132.2, 129.3, 129.19, 129.15, 128.7, 128.19, 128.17, 127.12, 127.10, 126.2, 61.1, 61.0, 60.1, 60.0, 52.0, 51.9, 51.8, 38.1, 37.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{33}H_{32}Cl_2NO_4$ 576.1703; found 576.1696.

Dimethyl 1,1'-((benzylazanediyl)bis(methylene))bis(3-(4-bromophenyl)cyclobut-2-ene-1-carboxylate): **3k**



The title compound **3k** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a yellow oil in 99% yield (132.2 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.52–7.37 (m, 4H), 7.35–7.19 (m, 5H), 7.19–7.08 (m, 4H), 6.47–6.32 (m, 2H), 3.79–3.52 (m, 8H), 3.19–3.01 (m, 4H), 2.95 (d, *J* = 13.2 Hz, 2H), 2.78–2.61 (m, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.41, 174.39, 145.3, 145.1, 139.3, 132.6, 131.6, 129.4, 129.34, 129.32, 128.18, 128.17, 127.12, 127.10, 126.5, 122.44, 122.42, 61.03, 61.00, 60.1, 60.0, 52.0, 51.9, 51.8, 38.0, 37.9; **HRMS (ESI):** calcd. for $[M + Na]^+$ $C_{33}H_3Br_2NNaO_4$ 686.0512; found 686.0521.

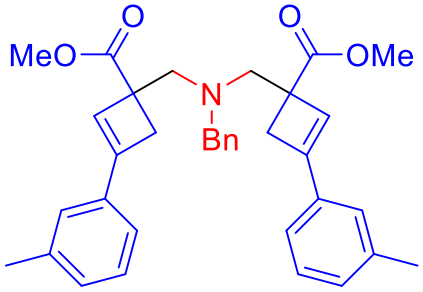
Dimethyl 1,1'-((benzylazanediyl)bis(methylene))bis(3-(4-(trifluoromethyl)phenyl)cyclobut-2-ene-1-carboxylate): **3l**



The title compound **3l** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a colorless oil in 98% yield (126.6 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.62–7.52 (m, 4H), 7.44–7.34 (m, 4H), 7.33–7.19 (m, 5H), 6.54–6.47 (m, 2H), 3.75–3.60 (m, 8H), 3.21–3.08 (m, 4H), 2.98 (d, *J* = 13.3 Hz, 2H), 2.81–2.68 (m, 2H); **^{13}C NMR (125**

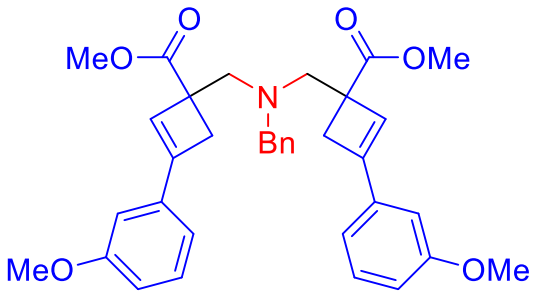
MHz, $CDCl_3$): δ 174.3, 145.1, 145.0, 139.2, 136.9, 131.5, 131.4, 130.2 (q, *J* = 32.4 Hz), 130.1 (q, *J* = 32.4 Hz), 129.3, 128.3, 128.2, 127.22, 127.20, 125.5 (q, *J* = 3.8 Hz), 125.2, 124.2 (q, *J* = 271.9 Hz), 61.10, 61.05, 60.2, 60.1, 52.12, 52.06, 38.1, 37.9; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{35}H_{32}F_6NO_4$ 644.2230; found 644.2220.

Dimethyl 1,1'-((benzylazanediyl)bis(methylene))bis(3-(m-tolyl)cyclobut-2-ene-1-carboxylate): **3m**



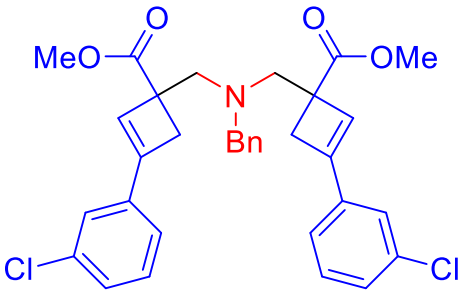
The title compound **3m** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a yellow oil in 93% yield (100.7 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.33–7.17 (m, 7H), 7.17–7.03 (m, 6H), 6.41–6.35 (m, 2H), 3.73–3.59 (m, 8H), 3.17–3.06 (m, 4H), 3.00–2.91 (m, 2H), 2.76–2.64 (m, 2H), 2.33 (s, 6H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.7, 174.6, 146.4, 146.2, 139.4, 138.0, 133.7, 129.28, 129.26, 129.2, 128.29, 128.26, 128.1, 126.93, 126.91, 125.5, 122.0, 61.13, 61.11, 59.8, 59.7, 51.8, 51.74, 51.69, 38.2, 38.1, 21.4; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{35}H_{38}NO_4$ 536.2795; found 536.2788.

Dimethyl 1,1'-((benzylazanediyl)bis(methylene))bis(3-(3-methoxyphenyl)cyclobut-2-ene-1-carboxylate): **3n**



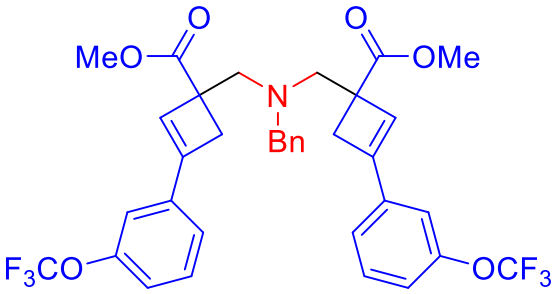
The title compound **3n** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a yellow oil in 89% yield (101.6 mg); **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.30–7.19 (m, 7H), 6.94–6.88 (m, 2H), 6.86–6.78 (m, 4H), 6.43–6.36 (m, 2H), 3.79 (s, 6H), 3.74–3.60 (m, 8H), 3.17–3.06 (m, 4H), 2.96 (d, *J* = 13.2 Hz, 2H), 2.76–2.64 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.62, 174.59, 159.8, 146.2, 146.1, 139.4, 135.2, 129.5, 129.4, 129.3, 128.94, 128.90, 128.2, 127.0, 117.5, 114.37, 114.35, 110.0, 61.2, 59.9, 59.8, 55.3, 51.9, 51.8, 51.7, 38.3, 38.2; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{35}H_{38}NO_6$ 568.2694; found 568.2687.

Dimethyl 1,1'-((benzylazanediyl)bis(methylene))bis(3-(3-chlorophenyl)cyclobut-2-ene-1-carboxylate): **3o**



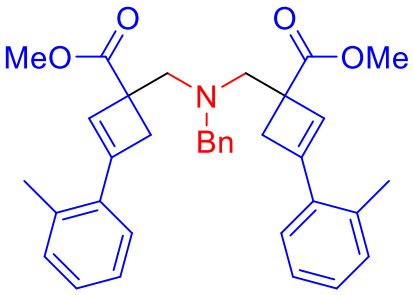
The title compound **3o** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a yellow oil in 95% yield (110.5 mg); **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.32–7.21 (m, 11H), 7.20–7.14 (m, 2H), 6.41 (s, 2H), 3.73–3.57 (m, 8H), 3.17–3.02 (m, 4H), 2.99–2.89 (m, 2H), 2.76–2.63 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.4, 145.1, 144.9, 139.2, 135.5, 134.6, 130.24, 130.18, 129.8, 129.3, 128.43, 128.41, 128.22, 128.20, 127.2, 127.1, 125.1, 123.1, 61.1, 61.0, 60.1, 60.0, 52.01, 51.96, 51.9, 38.1, 38.0; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{33}H_{32}Cl_2NO_4$ 576.1703; found 576.1696.

Dimethyl 1,1'-((benzylazanediyl)bis(methylene))bis(3-(3-(trifluoromethoxy)phenyl)cyclobut-2-ene-1-carboxylate): **3p**



The title compound **3p** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a yellow oil in 88% yield (119.3 mg); **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.38–7.31 (m, 2H), 7.30–7.19 (m, 7H), 7.17–7.08 (m, 4H), 6.47–6.40 (m, 2H), 3.76–3.57 (m, 8H), 3.20–3.05 (m, 4H), 2.97 (d, *J* = 13.2 Hz, 2H), 2.78–2.64 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.3, 149.6, 145.0, 144.9, 139.2, 135.8, 130.54, 130.50, 130.0, 129.4, 128.23, 128.21, 127.20, 127.18, 123.3, 120.8, 120.6 (q, *J* = 257.2 Hz), 117.4, 61.1, 61.1, 60.2, 60.1, 52.03, 51.98, 51.9, 38.1, 38.0; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{35}H_{32}F_6NO_6$ 676.2128; found 676.2136.

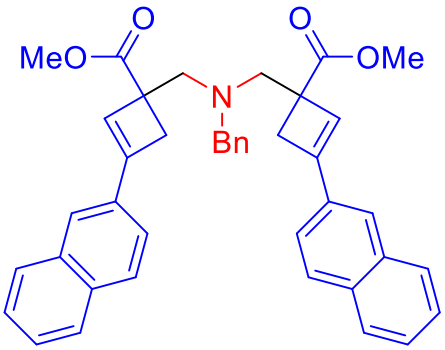
Dimethyl 1,1'-((benzylazanediyl)bis(methylene))bis(3-(o-tolyl)cyclobut-2-ene-1-carboxylate): **3q**



The title compound **3q** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a yellow oil in 93% yield (100.3 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.31–7.24 (m, 4H), 7.23–7.16 (m, 5H), 7.16–7.10 (m, 4H), 6.33 (s, 1H), 6.26 (s, 1H), 3.82 (d, *J* = 13.6 Hz, 0.5H), 3.71–3.60 (m, 7H), 3.58 (d, *J* = 13.6 Hz, 0.5H), 3.24 (s, 0.5H), 3.21 (d, *J* = 3.9 Hz, 1H), 3.18 (d, *J* = 3.9 Hz, 1H), 3.15 (s, 0.5H), 3.10–3.02 (m, 2H), 2.99 (d, *J* = 13.2 Hz, 1H), 2.81 (d, *J* = 3.3 Hz, 1H), 2.78 (d, *J* = 3.3 Hz, 1H), 2.35 (s, 6H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.8, 174.7, 146.2, 146.1, 139.5, 137.4, 132.4, 132.3, 132.1, 130.8, 129.34, 129.31, 128.3, 128.2, 127.1, 127.0, 126.81,

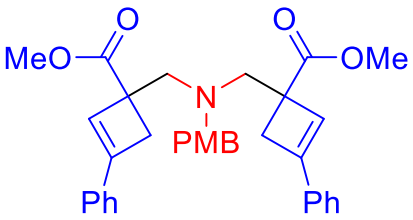
126.78, 125.9, 61.5, 61.2, 60.0, 59.8, 52.08, 52.06, 51.9, 39.8, 39.7, 21.89, 21.88; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{35}H_{38}NO_4$ 536.2795; found 536.2786.

Dimethyl 1,1'-((benzylazanediyl)bis(methylene))bis(3-(naphthalen-2-yl)cyclobut-2-ene-1-carboxylate): 3r



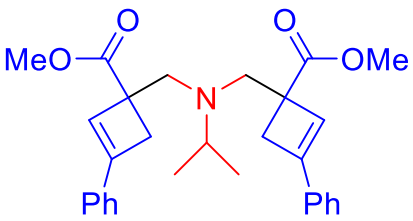
The title compound **3r** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a white solid in 97% yield (118.4 mg); **mp:** 144–145 °C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.85–7.68 (m, 6H), 7.66–7.59 (m, 2H), 7.54–7.42 (m, 6H), 7.34–7.19 (m, 5H), 6.55–6.47 (m, 2H), 3.82–3.60 (m, 8H), 3.27–3.13 (m, 4H), 3.08–3.00 (m, 2H), 2.91–2.79 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.6, 146.3, 146.2, 139.39, 139.37, 133.27, 133.25, 131.2, 129.3, 129.1, 128.2, 128.10, 128.06, 128.0, 127.8, 127.00, 126.97, 126.4, 126.3, 124.0, 122.7, 61.2, 61.1, 60.1, 60.0, 51.94, 51.90, 51.88, 38.1, 38.0; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{41}H_{38}NO_4$ 608.2795; found 608.2792.

Dimethyl 1,1'-(((4-methoxybenzyl)azanediyl)bis(methylene))bis(3-phenylcyclobut-2-ene-1-carboxylate): 3s



The title compound **3s** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a yellow oil in 95% yield (102.4 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.34–7.24 (m, 10H), 7.20–7.15 (m, 2H), 6.83–6.77 (m, 2H), 6.44–6.33 (m, 2H), 3.79–3.76 (m, 3H), 3.68–3.51 (m, 8H), 3.15–3.05 (m, 4H), 2.99–2.91 (m, 2H), 2.75–2.67 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.74, 174.72, 158.7, 146.3, 146.2, 133.8, 131.5, 130.5, 128.61, 128.58, 128.5, 128.4, 124.9, 113.5, 61.0, 59.2, 59.1, 55.3, 51.93, 51.85, 51.8, 38.2, 38.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{34}H_{36}NO_5$ 538.2588; found 538.2579.

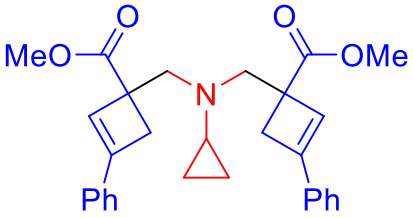
Dimethyl 1,1'-((isopropylazanediyl)bis(methylene))bis(3-phenylcyclobut-2-ene-1-carboxylate): 3t



The title compound **3t** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a yellow oil in 32% yield (29.6 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.39–7.30 (m, 8H), 7.29–7.25 (m, 2H), 6.49–6.41 (m, 2H), 3.74–3.61 (m, 6H), 3.15–3.04 (m, 4H), 2.84–2.70 (m, 4H), 0.99–

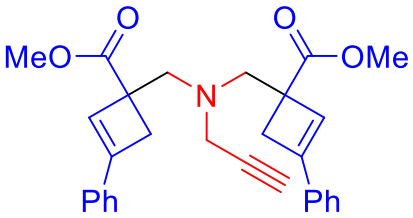
0.87 (m, 6H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.90, 174.88, 146.1, 134.0, 128.9, 128.8, 128.5, 128.4, 124.9, 56.7, 52.1, 52.0, 51.8, 50.0, 49.8, 38.04, 37.95, 17.6, 17.4, 17.3; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{29}H_{34}NO_4$ 460.2482; found 460.2477.

Dimethyl 1,1'-((cyclopropylazanediyl)bis(methylene))bis(3-phenylcyclobut-2-ene-1-carboxylate): 3u



The title compound **3u** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a yellow oil in 75% yield (69.6 mg); **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.46–7.29 (m, 8H), 7.29–7.17 (m, 2H), 6.54–6.34 (m, 2H), 3.86–3.50 (m, 6H), 3.36–3.03 (m, 6H), 2.82–2.68 (m, 2H), 1.94–1.79 (m, 1H), 0.63–0.33 (m, 4H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 175.1, 175.0, 146.4, 146.1, 133.9, 129.2, 129.0, 128.5, 128.44, 128.42, 124.9, 63.02, 62.98, 51.9, 51.83, 51.79, 38.3, 38.2, 37.8, 37.5, 8.6, 8.5, 8.4; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{29}H_{32}NO_4$ 458.2326; found 458.2320.

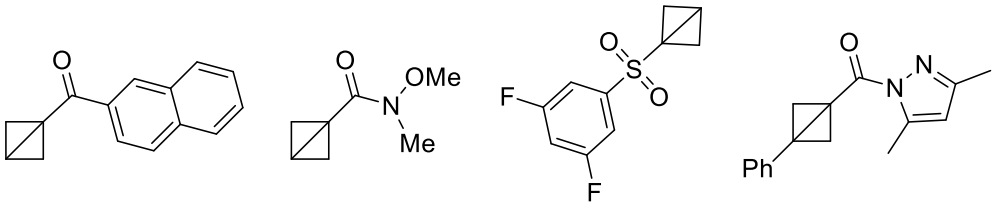
Dimethyl 1,1'-((prop-2-yn-1-ylazanediyl)bis(methylene))bis(3-phenylcyclobut-2-ene-1-carboxylate): 3v



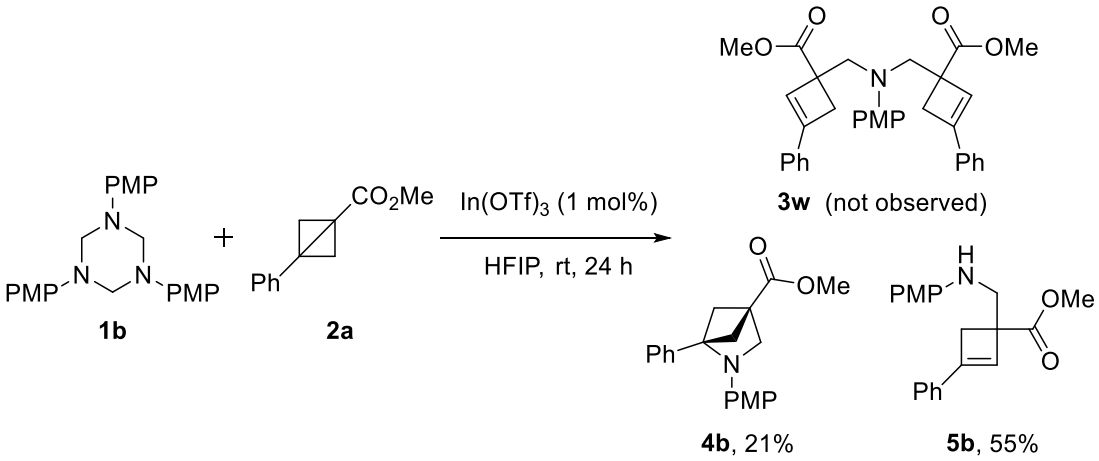
The title compound **3v** was prepared via general procedure, purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel and obtained as a white solid in 56% yield (51.8 mg); **mp:** 154–155 ^{o}C; **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.44–7.31 (m, 8H), 7.30–7.25 (m, 2H), 6.37 (dd, *J* = 5.1, 1.6 Hz, 2H), 3.74–3.61 (m, 6H), 3.58–3.50 (m, 2H), 3.25–3.09 (m, 4H), 3.03–2.93 (m, 2H), 2.85–2.74 (m, 2H), 2.26–2.11 (m, 1H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.51, 174.47, 147.1, 146.9, 133.8, 128.6, 128.7, 128.5, 128.0, 127.8, 125.0, 78.6, 78.5, 73.99, 73.95, 60.5, 60.3, 52.0, 51.9, 51.8, 42.6, 37.7, 37.6; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{29}H_{30}NO_4$ 456.2169; found 456.2160.

Unsuccessful Substrates

No target biscyclobutenyl amine product was observed when the following BCBs were used under standard conditions.



6. Mechanistic Studies



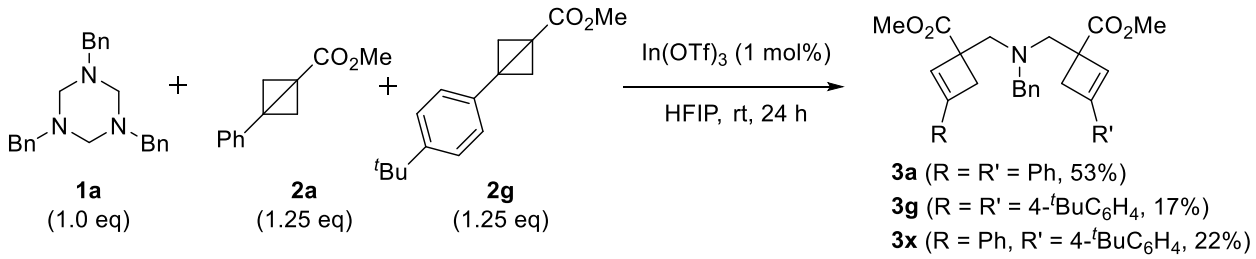
In an oven-dried reaction vial equipped with a magnetic stir bar, **1b** (81.1 mg, 0.20 mmol, 1.00 equiv) and **2a** (94.1 mg, 0.50 mmol, 2.50 equiv) were added into HFIP (2.0 mL). $In(OTf)_3$ (1.1 mg, 0.002 mmol, 1 mol%) was added. The reaction was stirred at rt for 24 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (hexanes/EtOAc = 20:1-10:1) on silica gel to afford two separable products **4b** (14.0 mg, 21 %, yellow oil) and **5b** (36.2 mg, 55 %, yellow oil). The product **3w** was not observed.

Methyl (1R,4R)-2-(4-methoxyphenyl)-1-phenyl-2-azabicyclo[2.1.1]hexane-4-carboxylate: 4b

Data of **4b**: **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.41–7.35 (m, 2H), 7.35–7.28 (m, 2H), 7.28–7.21 (m, 1H), 6.65–6.57 (m, 2H), 6.57–6.50 (m, 2H), 3.79–3.70 (m, 5H), 3.67 (s, 3H), 2.46–2.38 (m, 2H), 2.36–2.27 (m, 2H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 171.4, 153.4, 145.0, 139.6, 128.8, 127.4, 126.3, 120.6, 114.0, 72.1, 61.7, 55.5, 52.0, 49.5, 46.1; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{20}H_{22}NO_3$ 324.1594; found 324.1584.

Methyl 1-(((4-methoxyphenyl)amino)methyl)-3-phenylcyclobut-2-ene-1-carboxylate: 5b

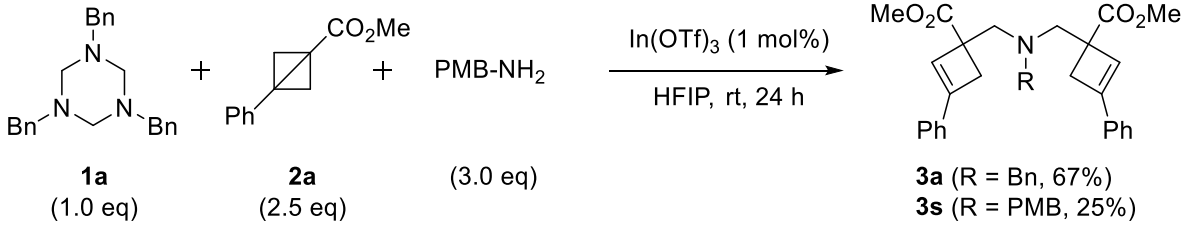
Data of **5b**: **^{1}H NMR (500 MHz, $CDCl_3$):** δ 7.40–7.32 (m, 4H), 7.32–7.28 (m, 1H), 6.80–6.74 (m, 2H), 6.66–6.59 (m, 2H), 6.40 (s, 1H), 3.74 (s, 3H), 3.71 (s, 3H), 3.61–3.55 (m, 1H), 3.54–3.49 (m, 1H), 3.18 (d, *J* = 13.1 Hz, 1H), 2.82 (d, *J* = 13.1 Hz, 1H); **^{13}C NMR (125 MHz, $CDCl_3$):** δ 174.9, 152.4, 147.8, 142.6, 133.6, 128.8, 128.6, 127.5, 125.0, 115.0, 114.7, 55.9, 52.3, 51.4, 50.8, 37.0; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{20}H_{22}NO_3$ 324.1594; found 324.1586.



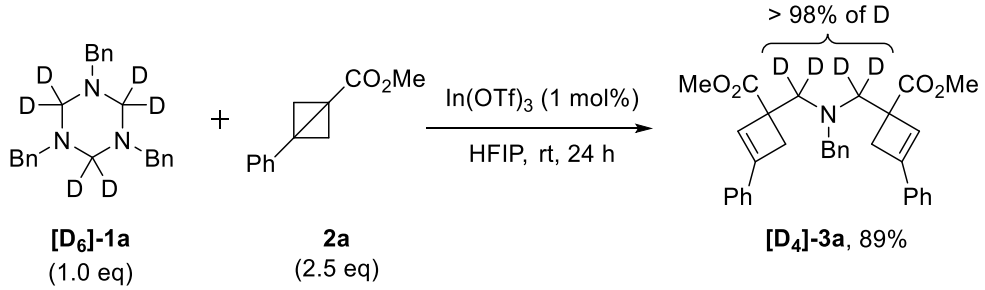
In an oven-dried reaction vial equipped with a magnetic stir bar, **1a** (71.5 mg, 0.20 mmol, 1.00 equiv), **2a** (47.1 mg, 0.25 mmol, 1.25 equiv) and **2g** (61.1 mg, 0.25 mmol, 1.25 equiv) were added into HFIP (2.0 mL). $In(OTf)_3$ (1.1 mg, 0.002 mmol, 1 mol%) was added. The reaction was stirred at rt for 24 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (hexanes/EtOAc = 35:1-20:1) on silica gel to afford three separable products **3a** (54.3 mg, 53 %, yellow oil), **3g** (21.1 mg, 17 %, yellow oil) and **3x** (25.4 mg, 22 %, dr = 1:1, yellow oil).

Methyl 1-((benzyl((1-(methoxycarbonyl)-3-phenylcyclobut-2-en-1-yl)methyl)amino)methyl)-3-(4-(tert-butyl)phenyl)cyclobut-2-ene-1-carboxylate: 3x

Data of **3x**: **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.43–7.13 (m, 14H), 6.43–6.30 (m, 2H), 3.81–3.53 (m, 8H), 3.22–3.03 (m, 4H), 3.02–2.89 (m, 2H), 2.78–2.61 (m, 2H), 1.31 (s, 9H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.8, 174.7, 151.7, 146.3, 146.2, 146.1, 139.5, 133.8, 131.2, 129.39, 129.37, 128.64, 128.58, 128.48, 128.45, 128.2, 127.71, 127.67, 127.0, 125.4, 125.0, 124.8, 61.3, 61.2, 61.1, 59.9, 59.8, 51.94, 51.90, 51.88, 51.8, 38.3, 38.2, 38.1, 34.9, 31.4; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{37}H_{42}NO_4$ 564.3108; found 564.3098.



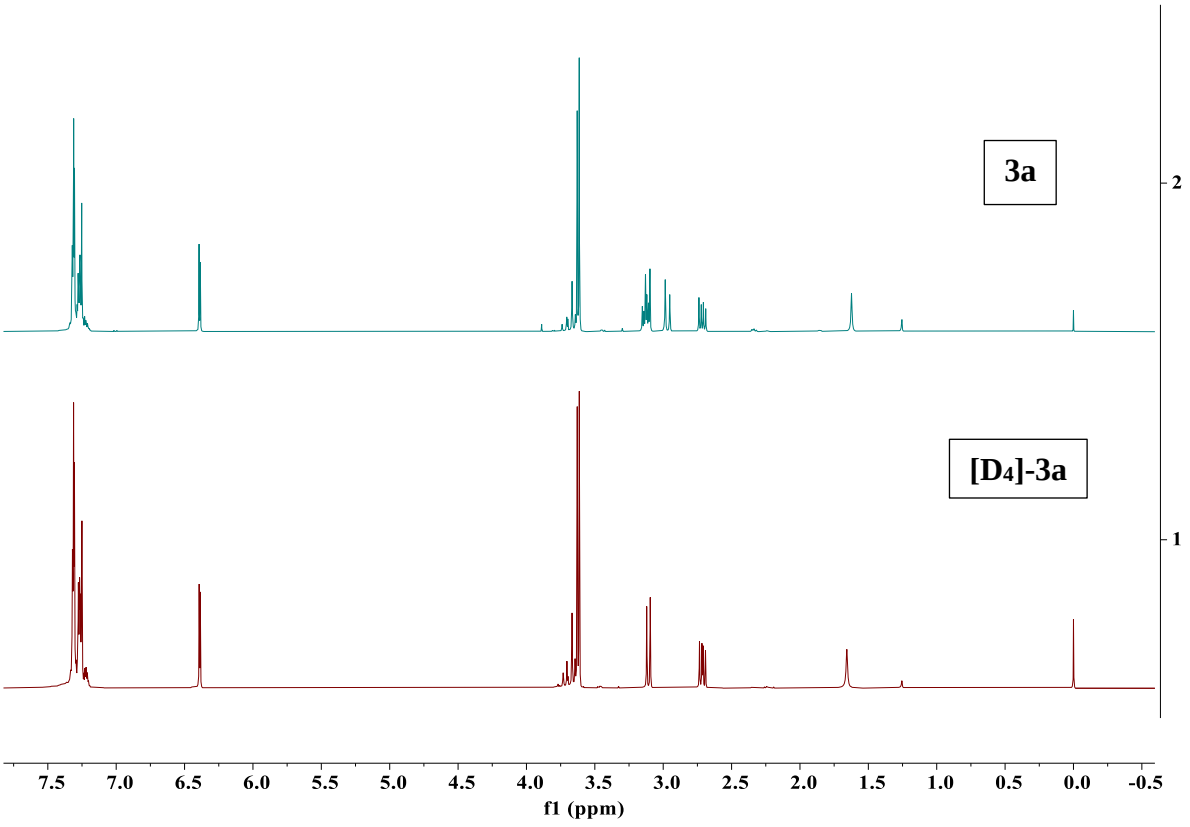
In an oven-dried reaction vial equipped with a magnetic stir bar, **1a** (71.5 mg, 0.20 mmol, 1.00 equiv), **2a** (94.1 mg, 0.50 mmol, 2.50 equiv) and PMB-NH_2 (82.3 mg, 0.60 mmol, 3.00 equiv) were added into HFIP (2.0 mL). $In(OTf)_3$ (1.1 mg, 0.002 mmol, 1 mol%) was added. The reaction was stirred at rt for 24 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (hexanes/EtOAc= 20:1) on silica gel to afford two separable products **3a** (68.5 mg, 67 %, yellow oil) and **3s** (27.2 mg, 55 %, yellow oil).

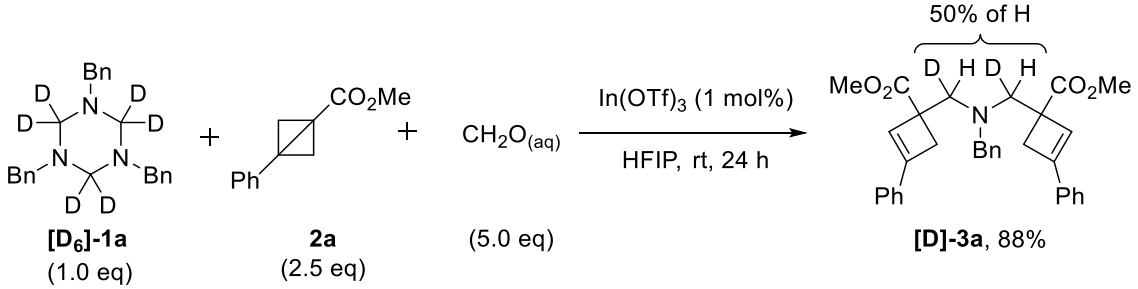


In an oven-dried reaction vial equipped with a magnetic stir bar, **[D$_6$]-1a** (72.7 mg, 0.20 mmol, 1.00 equiv) and **2a** (94.1 mg, 0.50 mmol, 2.50 equiv) were added into HFIP (2.0 mL). In(OTf)$_3$ (1.1 mg, 0.002 mmol, 1 mol%) was added. The reaction was stirred at rt for 24 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel to afford product **[D$_4$]-3a** (91.4 mg, 89 %) as a yellow oil. Based on the following ^{1}H NMR analysis, no deuterium loss was observed for product **[D$_4$]-3a**.

Dimethyl 1,1'-((benzylazanediyl)bis(methylene-d2))bis(3-phenylcyclobut-2-ene-1-carboxylate): [D$_4$]-3a

Data of **[D$_4$]-3a**:**^{1}H NMR (500 MHz, CDCl$_3$):** δ 7.35–7.18 (m, 15H), 6.43–6.36 (m, 2H), 3.75–3.58 (m, 8H), 3.11 (d, *J* = 13.0 Hz, 2H), 2.78–2.65 (m, 2H); **^{13}C NMR (125 MHz, CDCl$_3$):** δ 174.74, 174.7, 146.3, 146.2, 139.5, 133.8, 129.4, 129.3, 128.6, 128.5, 128.47, 128.4, 128.2, 127.04, 127.0, 124.9, 59.9, 59.7, 51.9, 51.7, 51.68, 38.2, 38.0; **HRMS (ESI):** calcd. for [M + H]$^+$ $C_{33}H_{30}D_4NO_4$ 512.2733; found 512.2726.



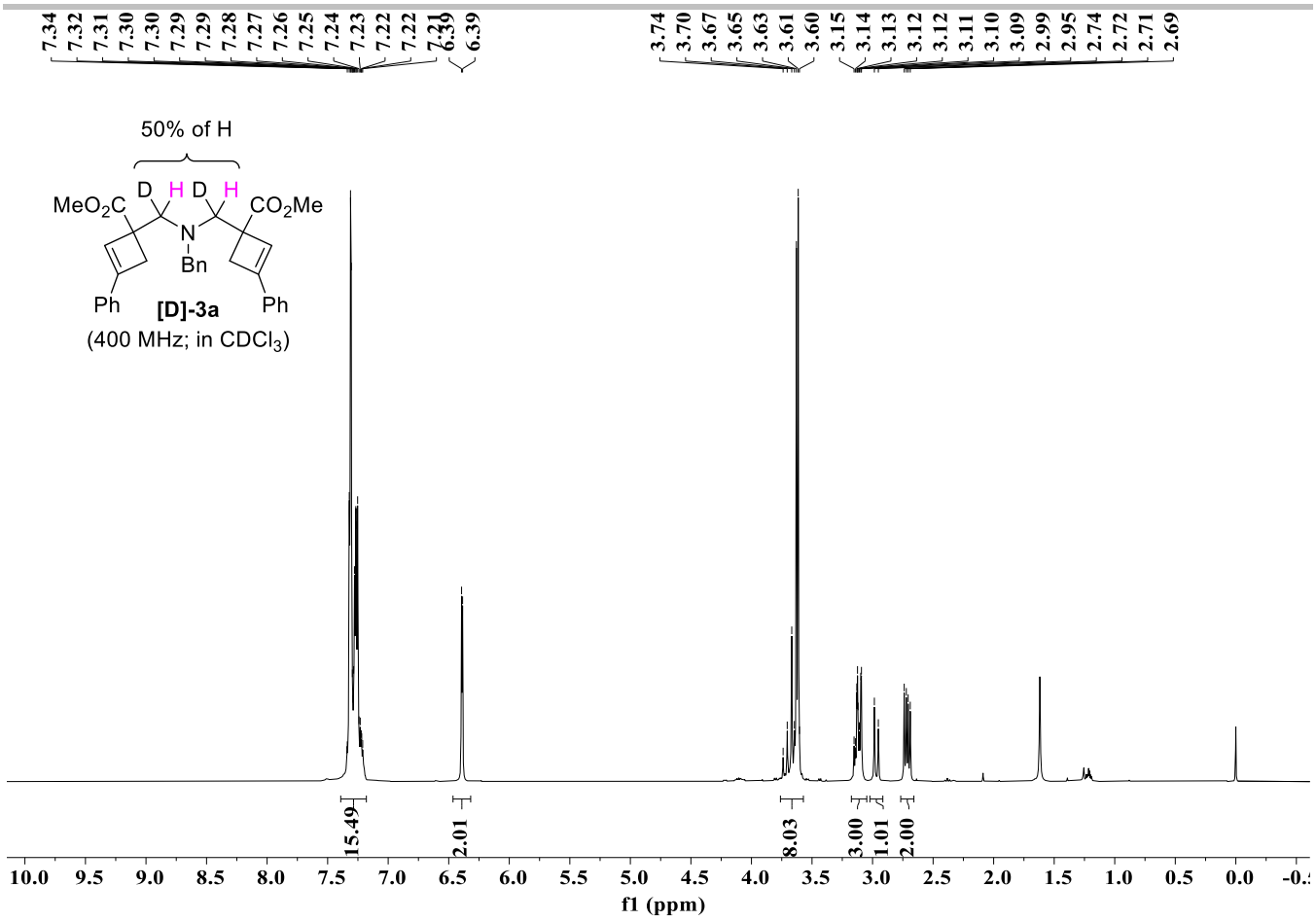


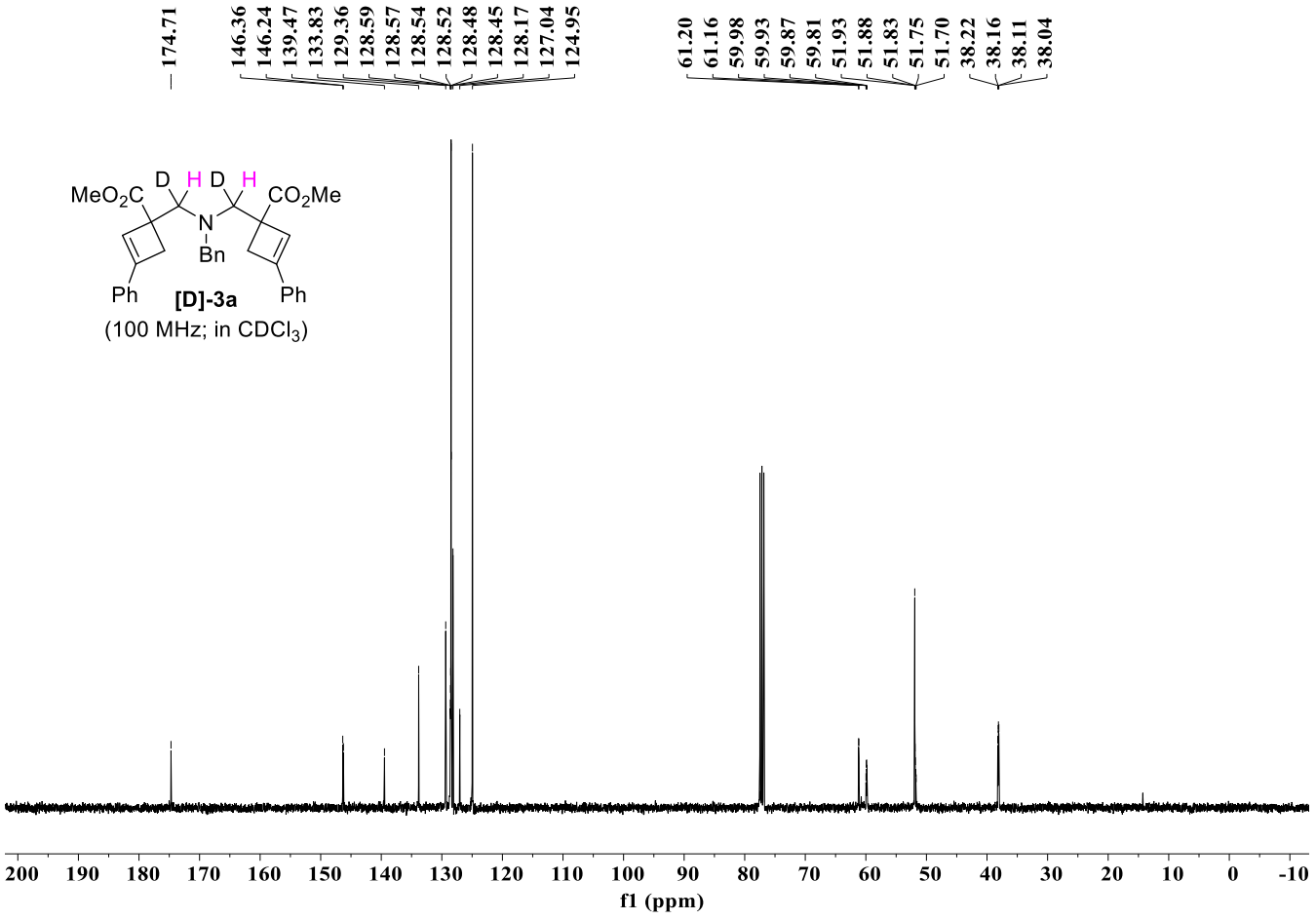
In an oven-dried reaction vial equipped with a magnetic stir bar, **[D$_6$]-1a** (72.7 mg, 0.20 mmol, 1.00 equiv), **2a** (94.1 mg, 0.50 mmol, 2.50 equiv) and $CH_2O_{(aq)}$ [81.2 mg, 1.00 mmol, 37.0-40.0% (with polymerization inhibitor) in H_2O, 5.00 equiv] were added into HFIP (2.0 mL). $In(OTf)_3$ (1.1 mg, 0.002 mmol, 1 mol%) was added. The reaction was stirred at rt for 24 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel to afford an inseparable mixture of **[D]-3a** (90.6 mg, 88 %) as a yellow oil. Based the analysis of the ^{1}H NMR of **3a**, **[D$_4$]-3a** and **[D]-3a**, the hydrogenation rate of **[D]-3a** is 50%.

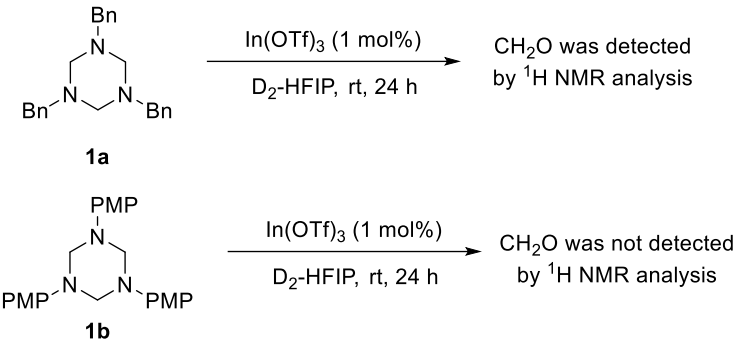
Dimethyl 1,1'-((benzylazanediyl)bis(methylene-d))bis(3-phenylcyclobut-2-ene-1-carboxylate):

[D]-3a

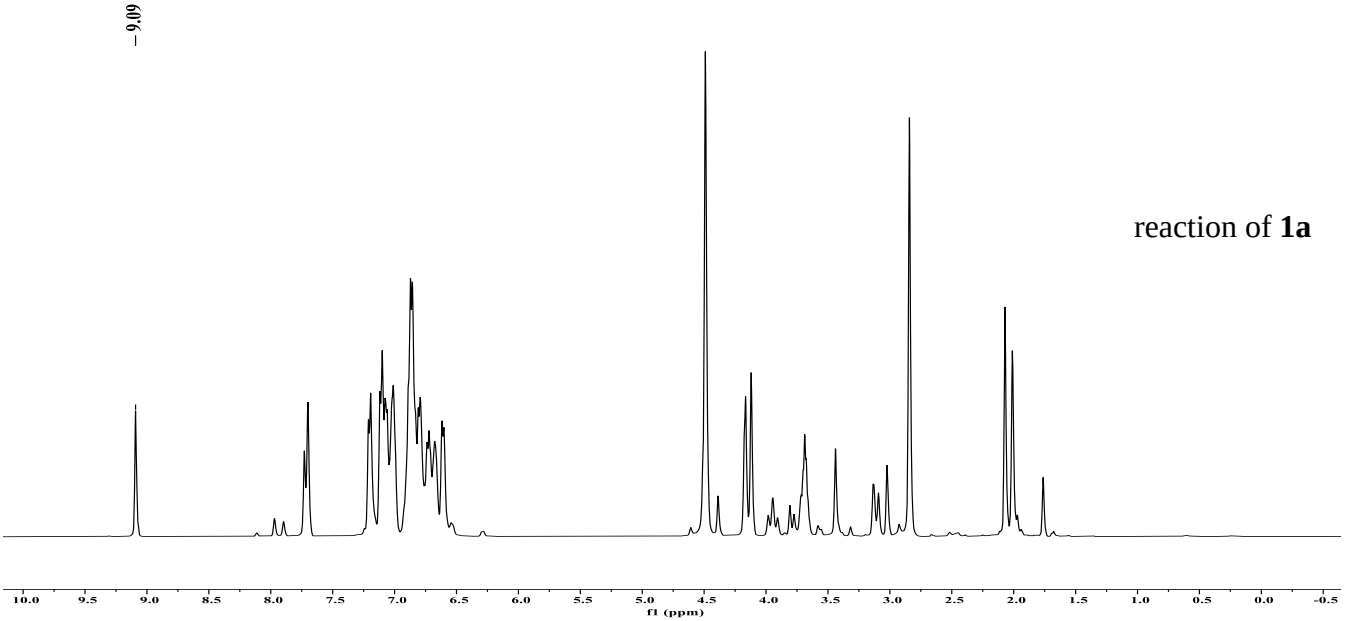
Data of **[D]-3a: ^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.39–7.18 (m, 15H), 6.47–6.32 (m, 2H), 3.76–3.57 (m, 8H), 3.18–3.05 (m, 3H), 2.97 (d, *J* = 13.1 Hz, 1H), 2.77–2.66 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.7, 146.4, 146.2, 139.5, 133.8, 129.4, 128.6, 128.57, 128.54, 128.5, 128.48, 128.45, 128.2, 127.0, 125.0, 61.2, 61.16, 60.0, 59.9, 59.87, 59.8, 51.9, 51.88, 51.8, 51.75, 51.7, 38.2, 38.16, 38.1, 38.0; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{33}H_{32}D_2NO_4$ 510.2608; found 510.2600.

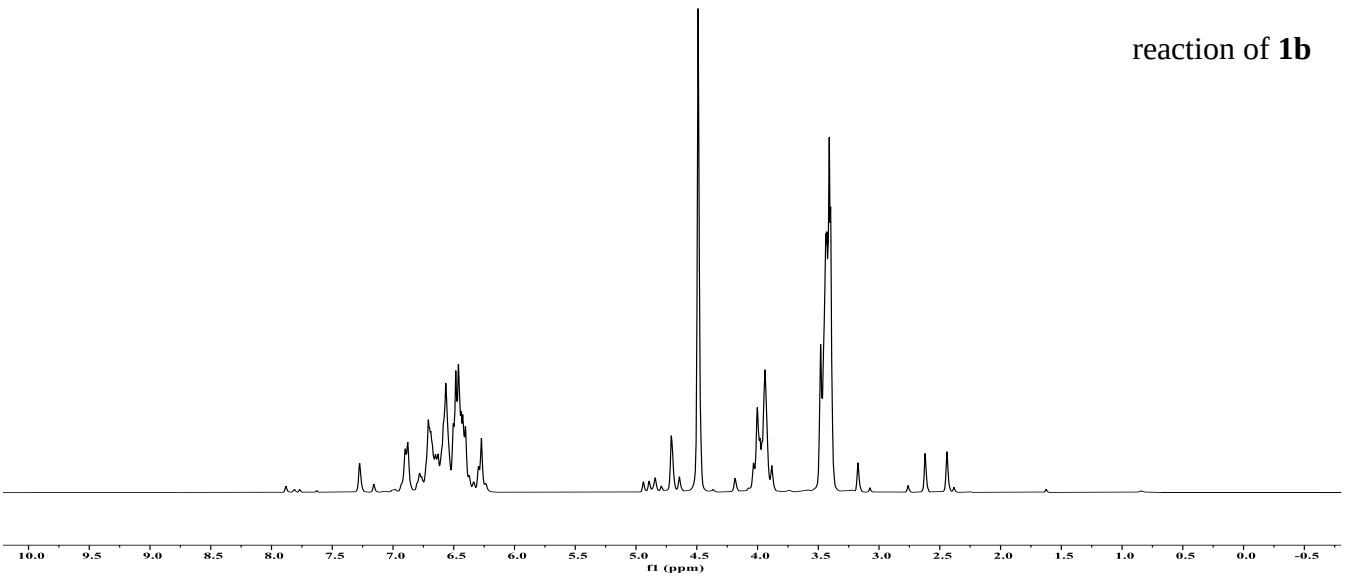

7.34 7.32 7.31 7.30 7.30 7.29 7.29 7.28 7.27 7.26 7.25 7.24 7.23 7.22 7.22 7.21 6.39 6.39
3.74 3.70 3.67 3.65 3.63 3.61 3.60 3.15 3.14 3.13 3.12 3.12 3.11 3.10 3.09 2.99 2.95 2.74 2.72 2.71 2.69
50% of H
MeO2C D H D H CO2Me
N
Bn
Ph Ph
[D]-3a
(400 MHz; in CDCl3)
15.49 2.01 8.03 3.00 1.01 2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

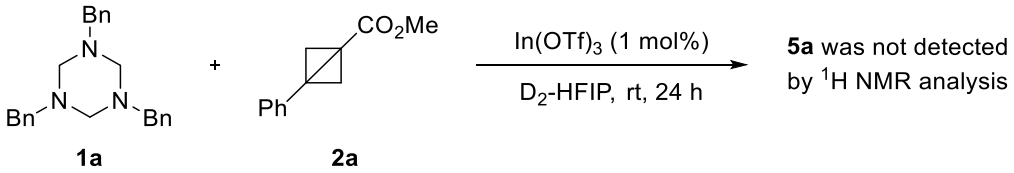

174.71
146.36 146.24 139.47 133.83 129.36 128.59 128.57 128.54 128.52 128.48 128.45 128.17 127.04 124.95
61.20 61.16 59.98 59.93 59.87 59.81 51.93 51.88 51.83 51.75 51.70 38.22 38.16 38.11 38.04
MeO2C D H D H CO2Me
N
Bn
Ph Ph
[D]-3a
(100 MHz; in CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



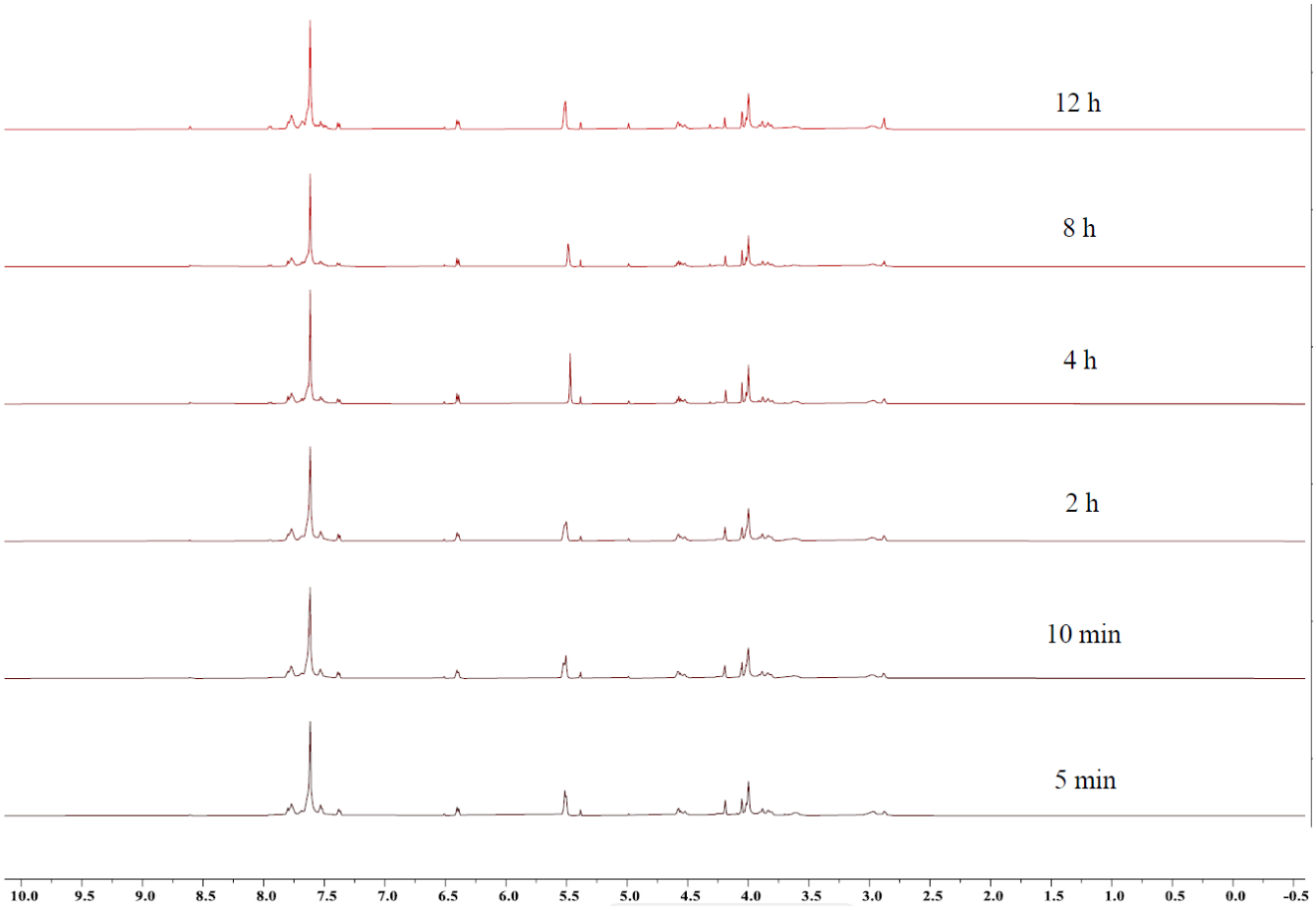
In an oven-dried nuclear magnetic tube, **1a** or **1b** (0.10 mmol, 1.00 equiv) was added into D_2-HFIP (1.0 mL). $In(OTf)_3$ (0.6 mg, 0.001 mmol, 1 mol%) was added. The reaction system was shaken well and ^1H NMR analysis was performed directly after 24 hours. CH_2O was observed by ^1H NMR analysis in the reaction of **1a**, but not detected in the reaction of **1b**.

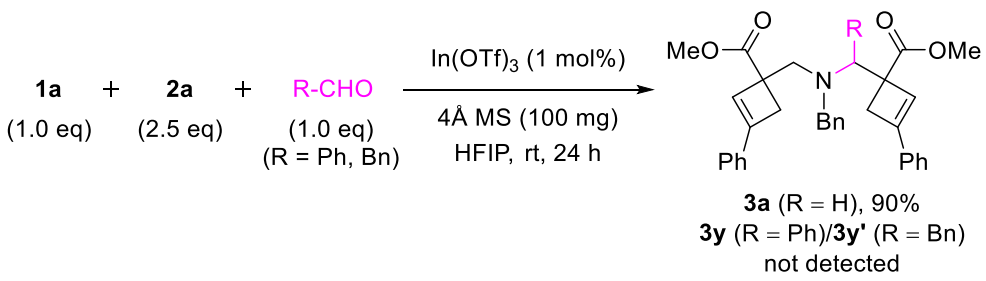






In an oven-dried nuclear magnetic tube, **1a** (17.9 mg, 0.05 mmol, 1.00 equiv) and **2a** (23.5 mg, 0.125 mmol, 2.50 equiv) were added into D_2-HFIP (0.5 mL). $In(OTf)_3$ (0.3 mg 0.0005 mmol, 1 mol%) was added. The reaction system was shaken well. Then, ^1H NMR analysis was performed directly at 5 min, 10 min, 2 h, 4 h, 8 h, and 12 h of the reaction respectively. The results are as follows. Unfortunately, we did not detect the existence of the intermediate **5a**.



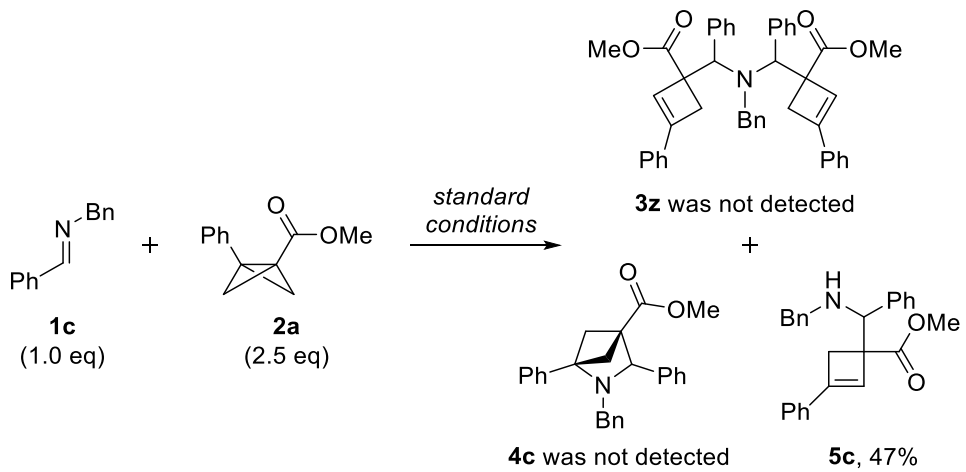


3a (R = H), 90%
3y (R = Ph)/**3y'** (R = Bn)
not detected

In an oven-dried reaction vial equipped with a magnetic stir bar, **1a** (71.5 mg, 0.20 mmol, 1.00 equiv) and 4Å MS (100 mg) were added into HFIP (2.0 mL), the mixture was stirred at rt for 1 h. Then **2a** (94.1 mg, 0.50 mmol, 2.50 equiv) and benzaldehyde or phenylacetaldehyde (0.20 mmol, 1.00 equiv) and $In(OTf)_3$ (1.1 mg, 0.002 mmol, 1 mol%) was added. The reaction was stirred at rt for 24 h. The resulting mixture was filtrated and concentrated under reduced pressure. Then carried out the separation and purification of the reaction by PTLC (Preparative Thin-Layer Chromatography). It was found that regardless of whether benzaldehyde or phenylacetaldehyde was added to the system, only the product **3a** could be generated in 90% yield, while **3y** or **3y'** could not be produced.

7. Further Investigations

7.1 Exploration of other imines

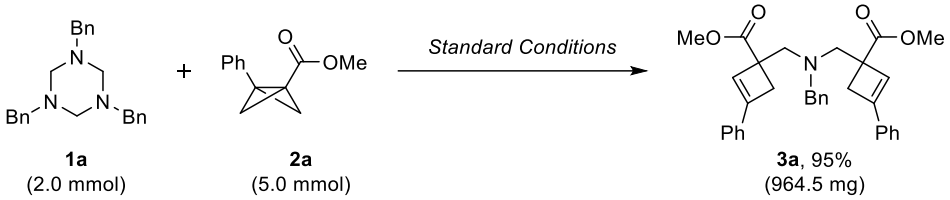


In an oven-dried reaction vial equipped with a magnetic stir bar, **1c** (39.1 mg, 0.2 mmol, 1.00 equiv) and **2a** (94.1 mg, 0.5 mmol, 2.50 equiv) were added into HFIP (2.0 mL). $In(OTf)_3$ (1.1 mg, 0.02 mmol, 1 mol%) was added. The reaction was stirred at rt for 24 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel to afford **5c** as a yellow oil in 47% yield (36.0 mg). But we did not detect **3z** and **4c**.

Methyl 1-((benzylamino)(phenyl)methyl)-3-phenylcyclobut-2-ene-1-carboxylate: 5c

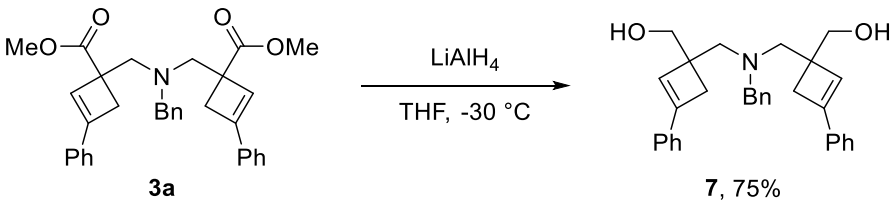
Data of **5c**: **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.37–7.21 (m, 15H), 6.37 (s, 1H), 4.16 (s, 1H), 3.74 (d, *J* = 13.5 Hz, 1H), 3.54 (s, 4H), 3.11–2.98 (m, 2H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 174.5, 147.7, 140.6, 140.2, 133.7, 128.51, 128.45, 128.4, 128.31, 128.28, 128.0, 127.5, 127.0, 126.4, 125.0, 64.7, 56.3, 51.9, 51.2, 35.4; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{26}H_{26}NO_2$ 384.1964; found 384.1960.

7.2 Scale-up Synthesis



In an oven-dried reaction vial equipped with a magnetic stir bar, **1a** (2.0 mmol, 1.00 equiv) and **2a** (5.0 mmol, 2.50 equiv) were added into HFIP (20.0 mL). $In(OTf)_3$ (11.2 mg, 0.02 mmol, 1 mol%) was added. The reaction was stirred at rt for 24 h. The resulting mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography (hexanes/EtOAc = 20:1) on silica gel to afford **3a** as a yellow oil in 95% yield (964.5 mg).

7.3 Transformation



A solution of **3a** (50.7 mg, 0.10 mmol, 1.0 equiv) in THF (0.5 mL) was added dropwise over 5 min to a suspension of $LiAlH_4$ (15.2 mg, 0.20 mmol, 2.0 equiv) in THF (1 mL) at -30 °C. After the addition was complete, the mixture was then stirred at -30 °C overnight. The mixture was aqueous NH_4Cl (3 mL). The mixture was then extracted with EtOAc. After the removal of solvent by rotate evaporation, the residue was purified by column chromatography (hexanes/EtOAc = 10:1) to give the desired product **7** as a colorless oil in 75% yield (33.9 mg).

(((Benzylazanediyl)bis(methylene))bis(3-phenylcyclobut-2-ene-1,1-diyl))dimethanol: 7

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.20 (m, 15H), 6.60 (s, 1H), 6.49 (s, 1H), 4.49 (s, 2H), 3.91 (d, *J* = 12.9 Hz, 1H), 3.82–3.68 (m, 4H), 3.63 (s, 1H), 3.35 (d, *J* = 12.9 Hz, 1H), 3.08 (d, *J* = 13.1 Hz, 1H), 2.92–2.80 (m, 2H), 2.67–2.48 (m, 4H), 2.42 (d, *J* = 13.1 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 145.6, 145.5, 138.5, 134.3, 131.2, 131.0, 129.59, 129.56, 128.90, 128.86, 128.5, 128.3, 128.2, 127.80, 127.76, 124.71, 69.1, 69.0, 62.0, 61.6, 60.8, 60.7, 46.9, 46.8, 37.4, 37.3; **HRMS (ESI):** calcd. for $[M + H]^+$ $C_{31}H_{34}NO_2$ 452.2584; found 452.2579.

8. X-Ray Structure

The suitable crystals were obtained by interlayer diffusion of hexanes into $CHCl_3$ solution at ambient temperature. A colorless crystal of the corresponding compound was mounted on a glass fiber at a random orientation. The data were collected at 100 K by a diffractometer Rigaku Oxford Diffraction Supernova Dual Source, Cu at Zero equipped with an AtlasS2 CCD using Cu Kα radiation (1.54178 Å) by using a w scan mode.

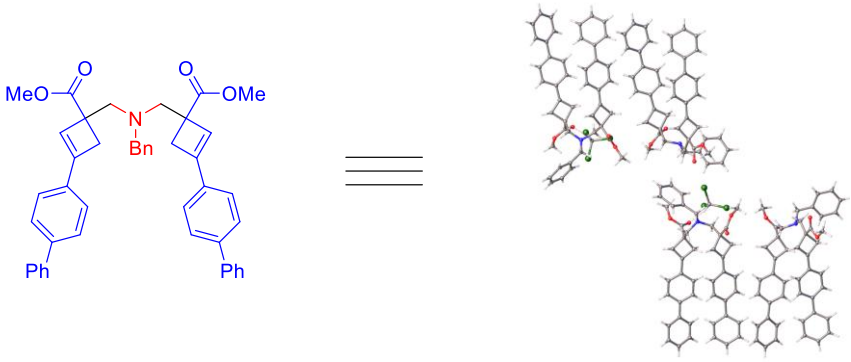


Table S9 Crystal data and structure refinement for 3h.

CCDC	2363143
Empirical formula	$C_{182}H_{166}Cl_6N_4O_{16}$
Formula weight	2877.88
Temperature/K	264(50)
Crystal system	monoclinic
Space group	Cc
a/Å	18.3009(3)
b/Å	19.4720(2)
c/Å	43.4558(8)
α/°	90
β/°	90.201(2)
γ/°	90
Volume/$Å^3$	15485.6(4)
Z	4
$\rho_{calc}g/cm^3$	1.234
μ/mm^{-1}	1.536
F(000)	6064.0
Crystal size/mm^3	? × ? × ?
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	6.928 to 133.198
Index ranges	$-21 \le h \le 21$, $-20 \le k \le 23$, $-51 \le l \le 51$
Reflections collected	94806
Independent reflections	25804 [R_{int} = 0.0527, R_{sigma} = 0.0465]
Data/restraints/parameters	25804/176/1870
Goodness-of-fit on F^2	1.039
Final R indexes [I>=2σ (I)]	R_1 = 0.0853, wR_2 = 0.2504
Final R indexes [all data]	R_1 = 0.0912, wR_2 = 0.2569

Largest diff. peak/hole / e Å^{-3}	0.68/-0.43
Flack parameter	0.11(3)

9. References

[1] S. Duan, H. Meng, S. T. Jablasone Jr., H. Luo, Z.-F. Xu and C.-Y. Li, Rhodium(II)-Catalyzed [4+2] Annulation of Ester-Tethered 1-Sulfonyl-1,2,3-Triazoles and Hexahydro-1,3,5-Triazines. *Asian J. Org. Chem.*, 2021, **10**, 1076-1080.

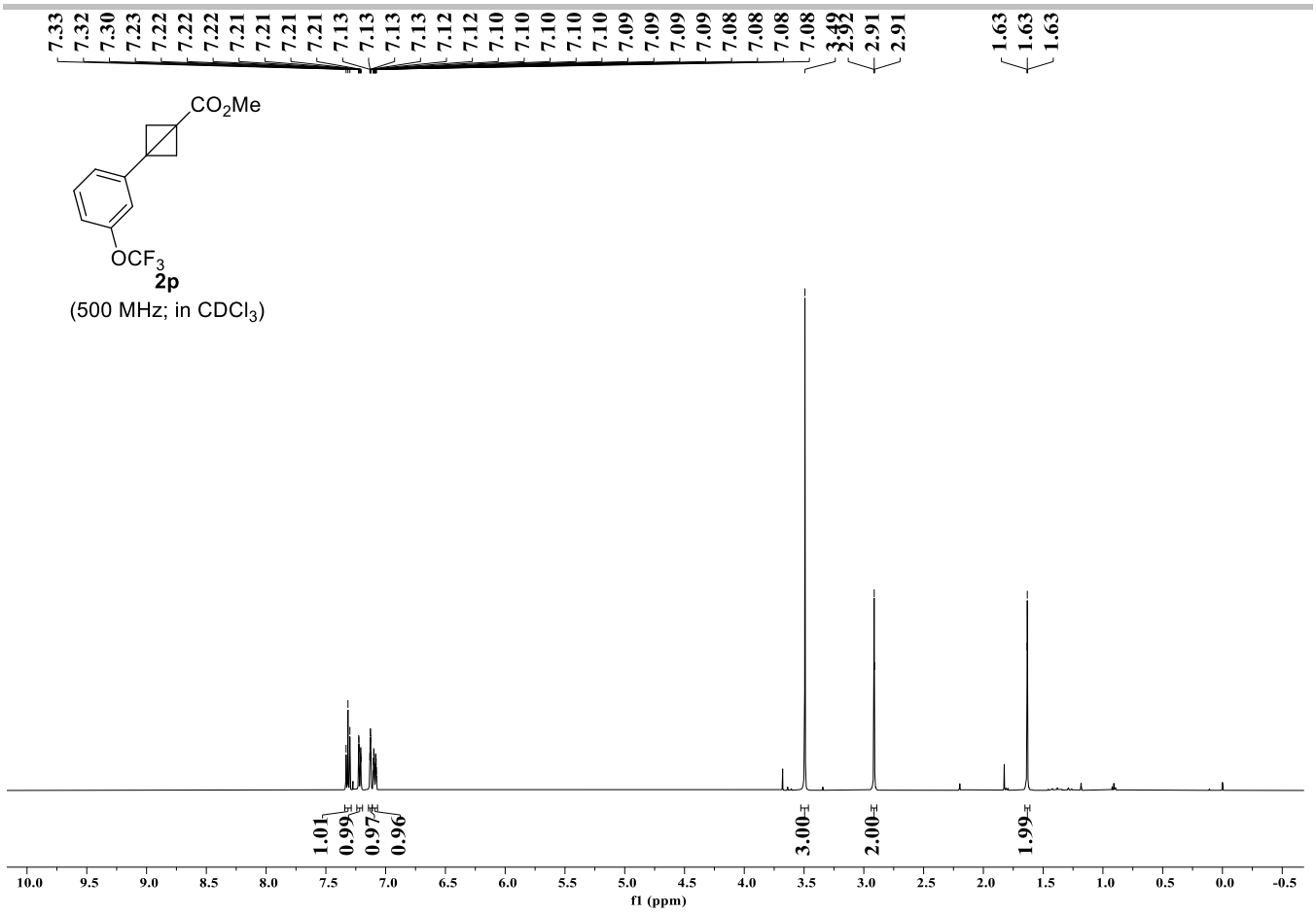
[2] C. Zhu, G. Xu and J. Sun, Gold-Catalyzed Formal [4+1]/[4+3] Cycloadditions of Diazo Esters with Triazines. *Angew. Chem. Int. Ed.*, 2016, **55**, 11867-11871.

[3] N. Guranova, D. Dar'in and M. Krasavin, Facile Access to 3-Unsubstituted Tetrahydroisoquinolonic Acids via the Castagnoli–Cushman Reaction. *Synthesis*, 2018, **50**, 2001-2008.

[4] S.-L. Lin, Y.-H. Chen, H.-H. Liu, S.-H. Xiang and B. Tan, Enantioselective Synthesis of Chiral Cyclobutenes Enabled by Brønsted Acid-Catalyzed Isomerization of BCBs. *J. Am. Chem. Soc.*, 2023, **145**, 21152-21158.

[5] Y. Liang, F. Paulus, C. G. Daniliuc and F. Glorius, Catalytic Formal [2π+2σ] Cycloaddition of Aldehydes with Bicyclobutanes: Expedient Access to Polysubstituted 2-Oxabicyclo[2.1.1]hexanes. *Angew. Chem. Int. Ed.*, 2023, **62**, e202305043.

10. NMR Spectra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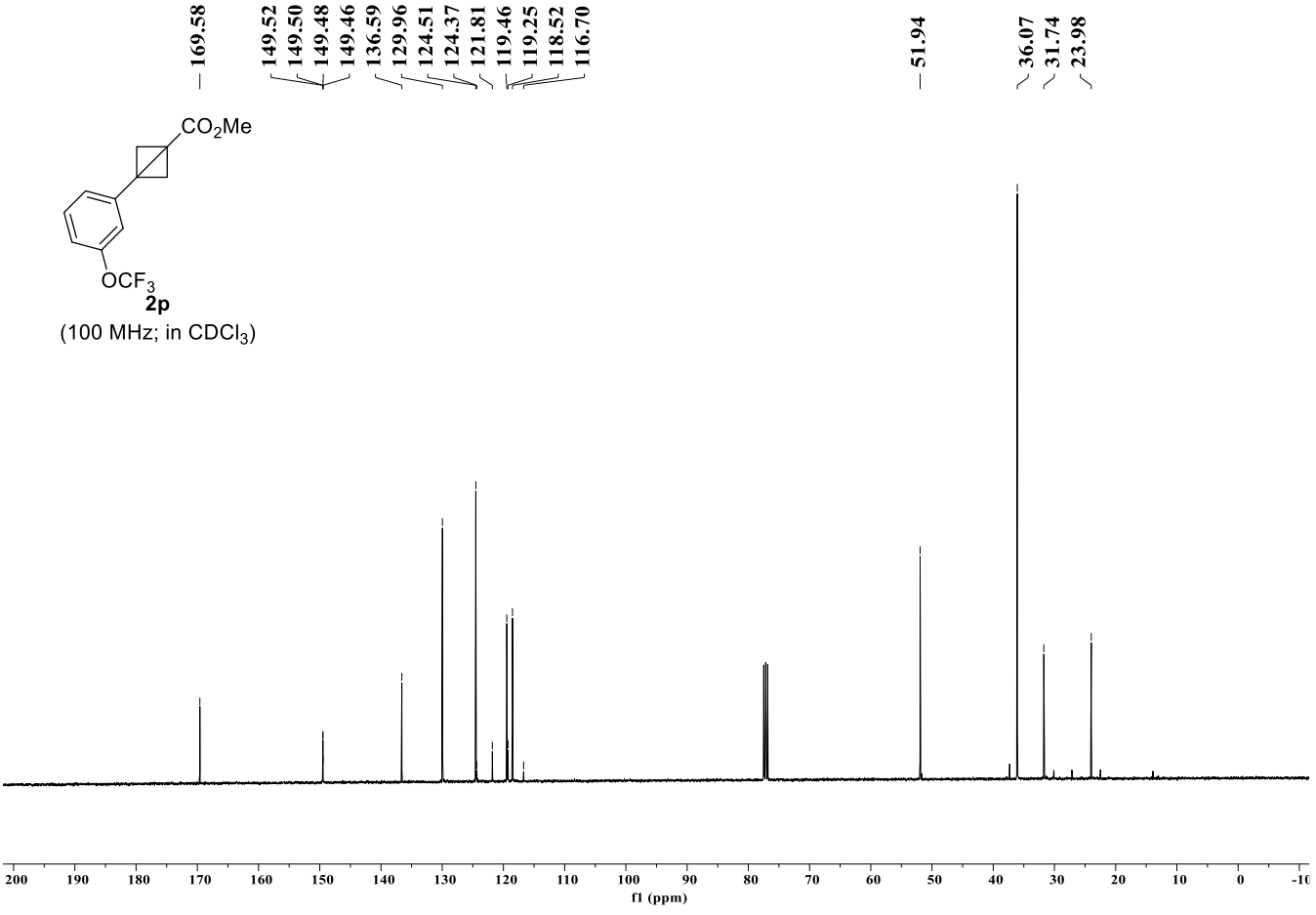
CO2Me
OCF3
2p
(500 MHz; in CDCl3)
1.01 0.99 0.97 0.96 3.00 2.00 1.99
f1 (ppm)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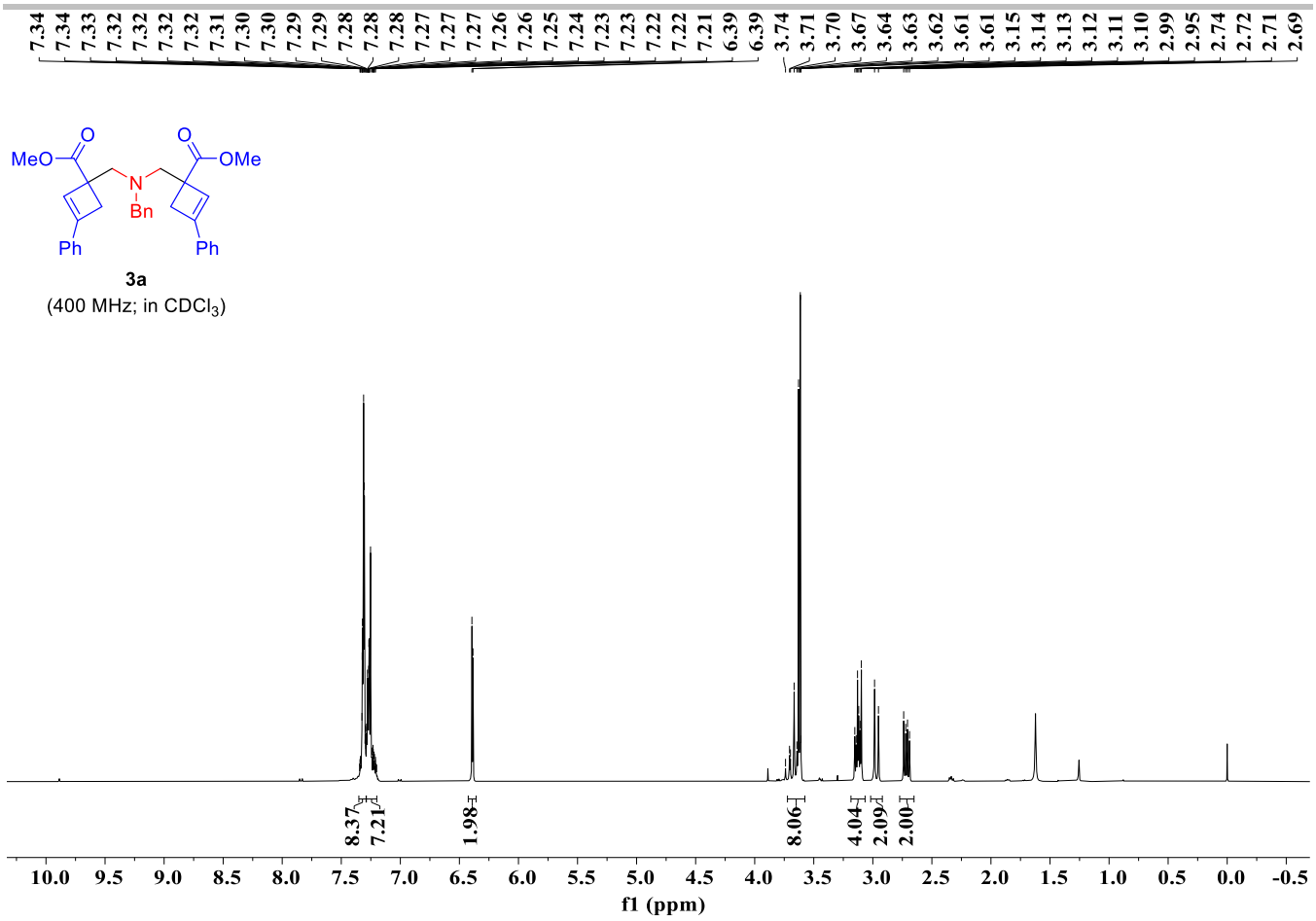
CO2Me
OCF3
2p
(100 MHz; in CDCl3)
f1 (ppm)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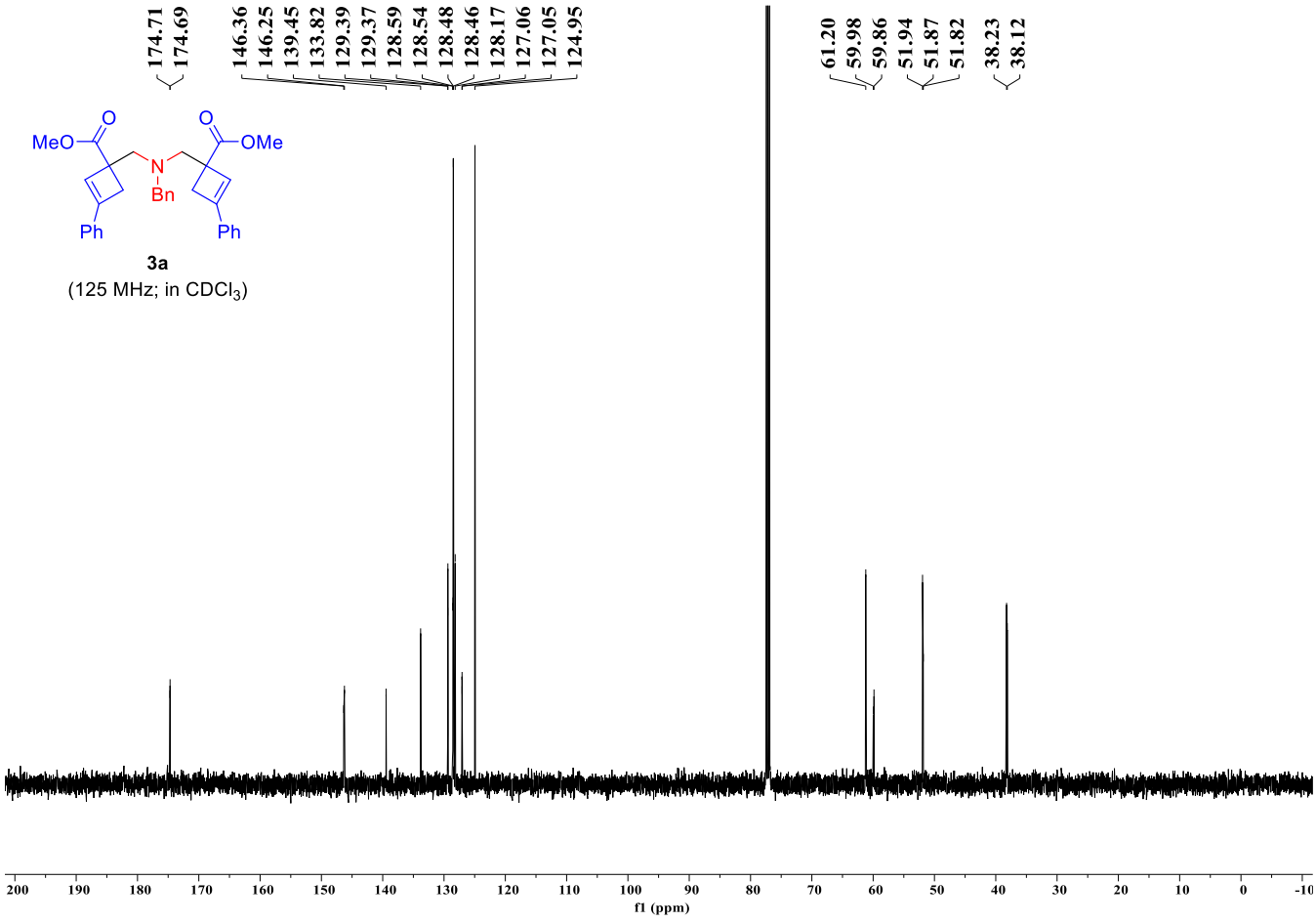
3.74 3.71 3.70 3.67 3.64 3.63 3.62 3.61 3.61 3.15 3.14 3.13 3.12 3.11 3.10 2.99 2.95 2.74 2.72 2.71 2.69
MeO
O
O
OMe
N
Bn
Ph
Ph
3a
(400 MHz; in CDCl3)
8.37
7.21
1.98
8.06
4.04
2.09
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


174.71 174.69
146.36 146.25 139.45 133.82 129.39 129.37 128.59 128.54 128.48 128.46 128.17 127.06 127.05 124.95
61.20 59.98 59.86 51.94 51.87 51.82 38.23 38.12
MeO
O
O
OMe
N
Bn
Ph
Ph
3a
(125 MHz; in CDCl3)
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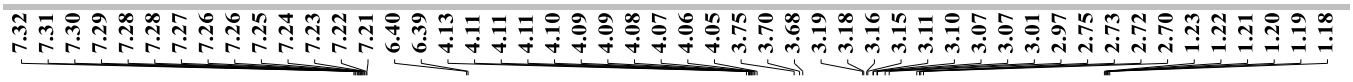
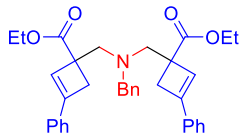
f1 (ppm)





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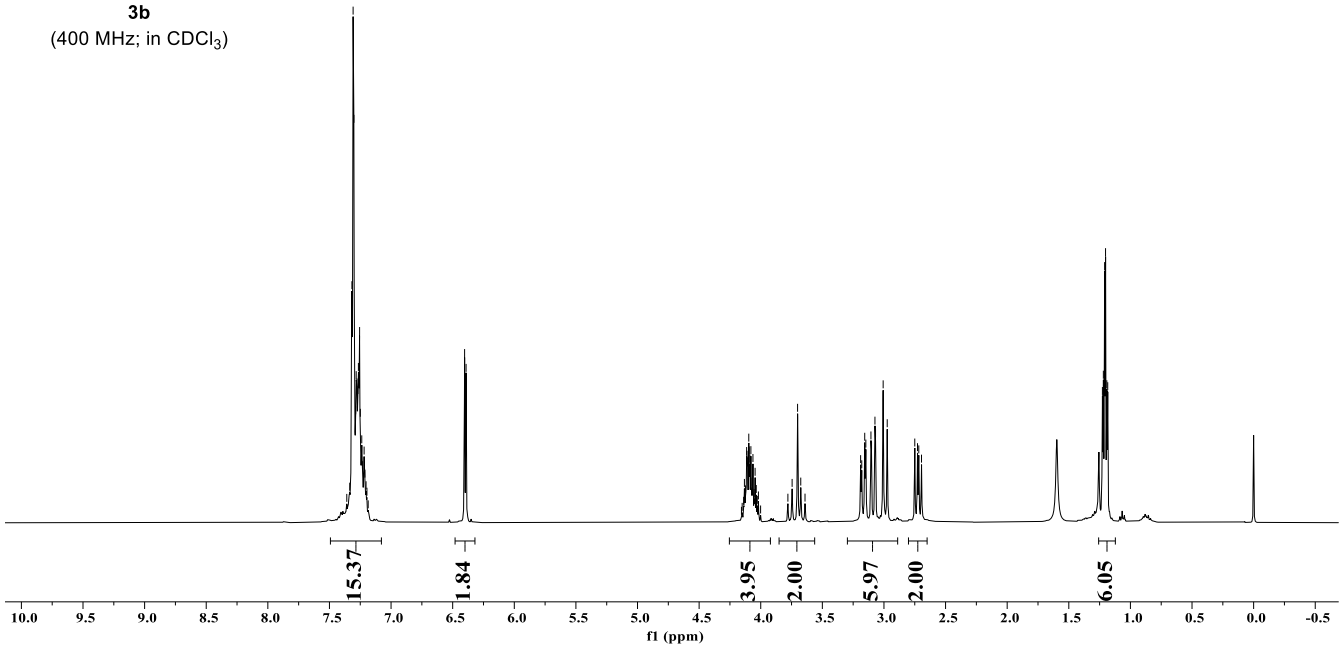
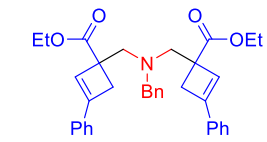
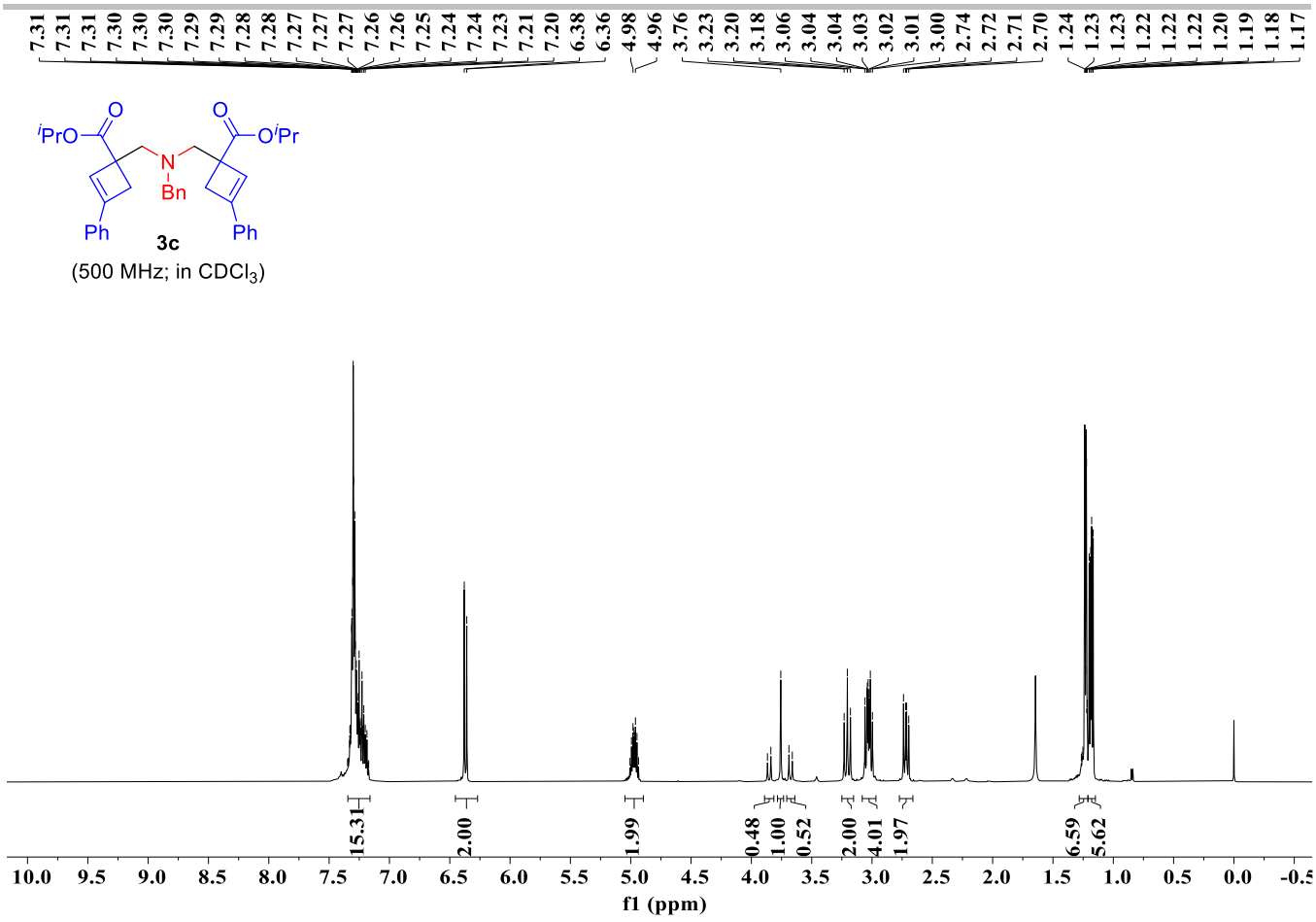




3b
(100 MHz; in $CDCl_3$)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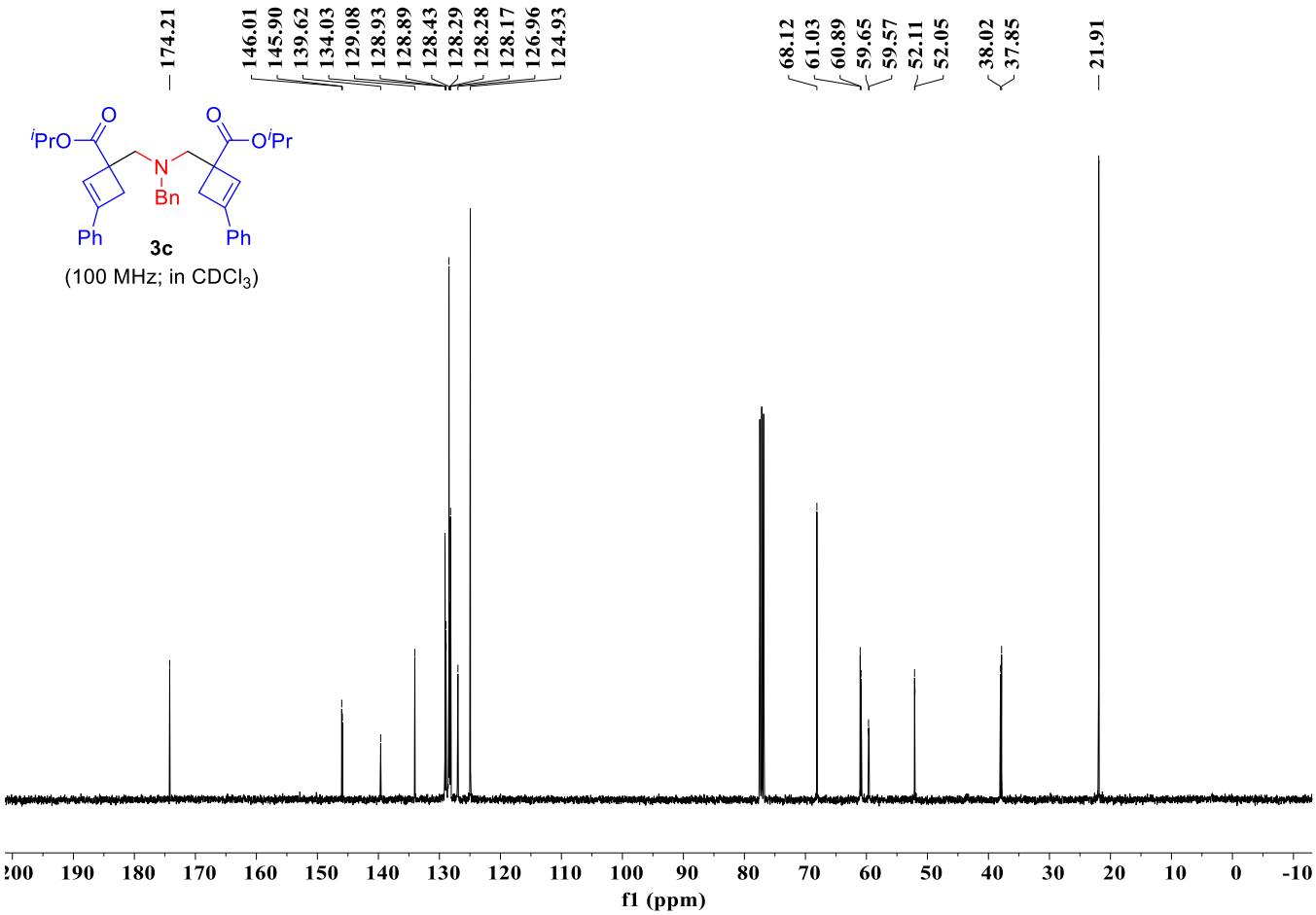
iPrO
O
O
OiPr
N
Bn
Ph
Ph
3c
(500 MHz; in CDCl3)
15.31
2.00
1.99
0.48
1.00
0.52
2.00
4.01
1.97
6.59
5.62
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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68.12 61.03 60.89 59.65 59.57 52.11 52.05 38.02 37.85 21.91
iPrO
O
O
OiPr
N
Bn
Ph
Ph
3c
(100 MHz; in CDCl3)
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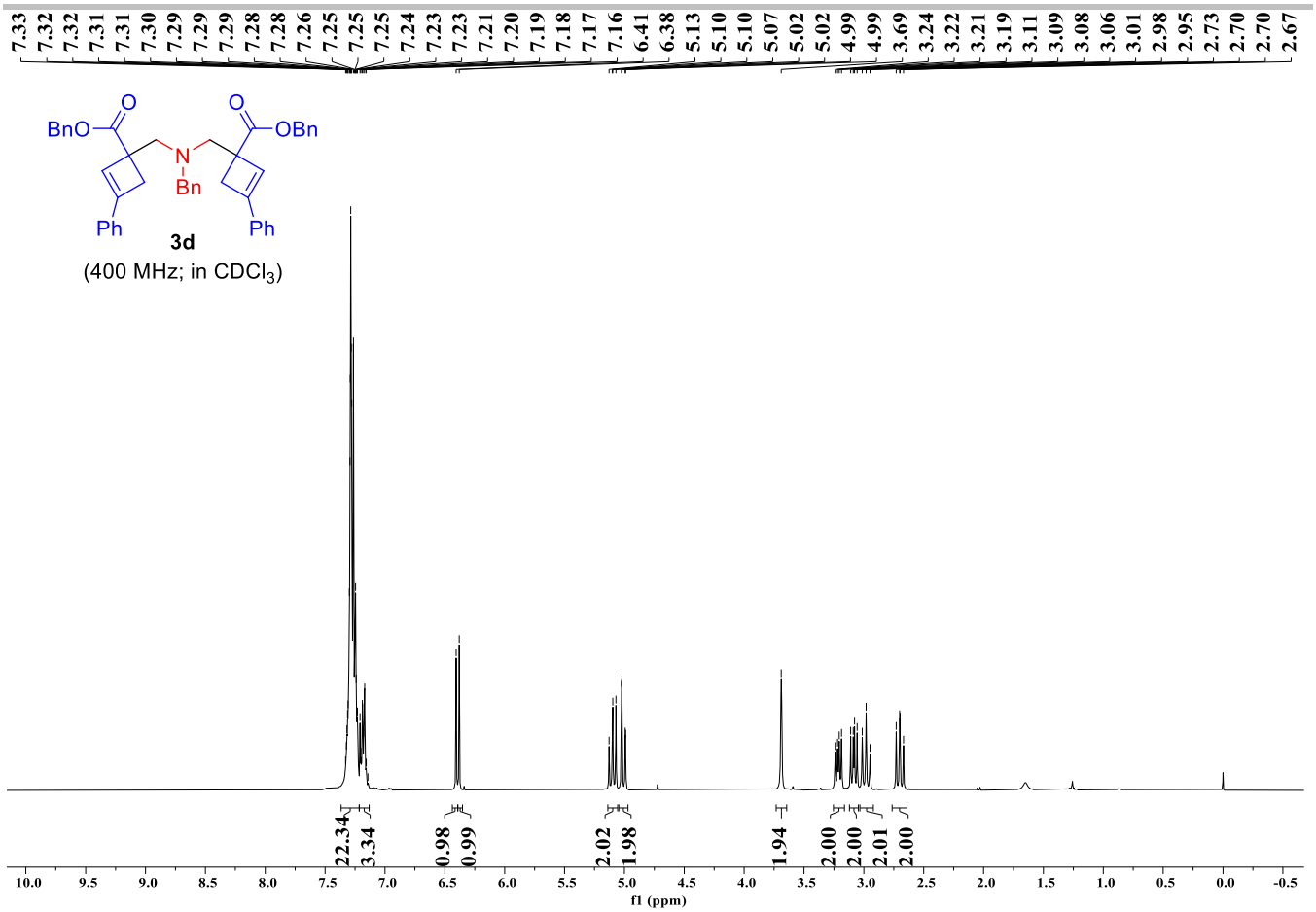
f1 (ppm)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BnO
O
O
OBn
N
Bn
Ph
Ph
3d
(400 MHz; in CDCl3)
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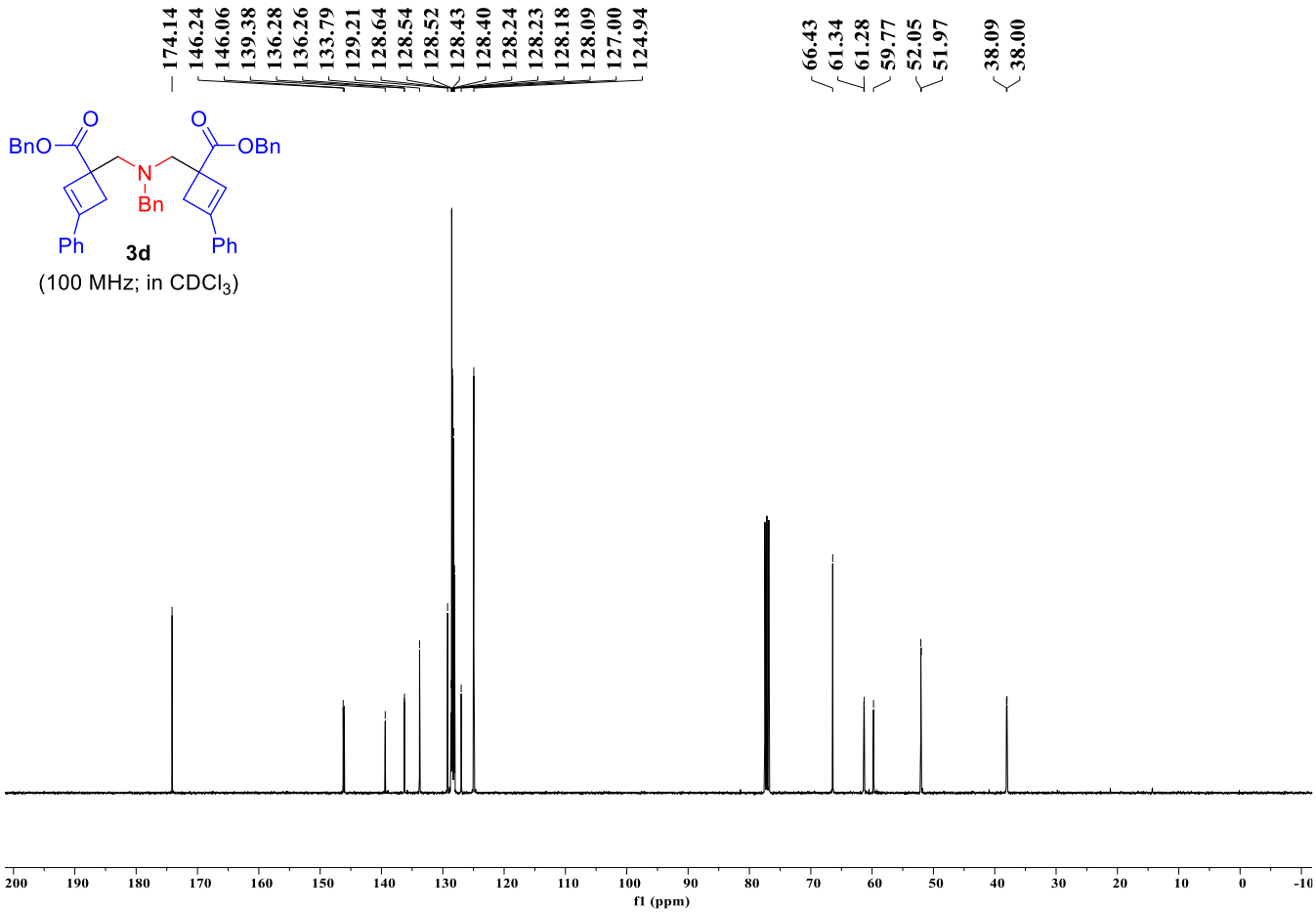
f1 (ppm)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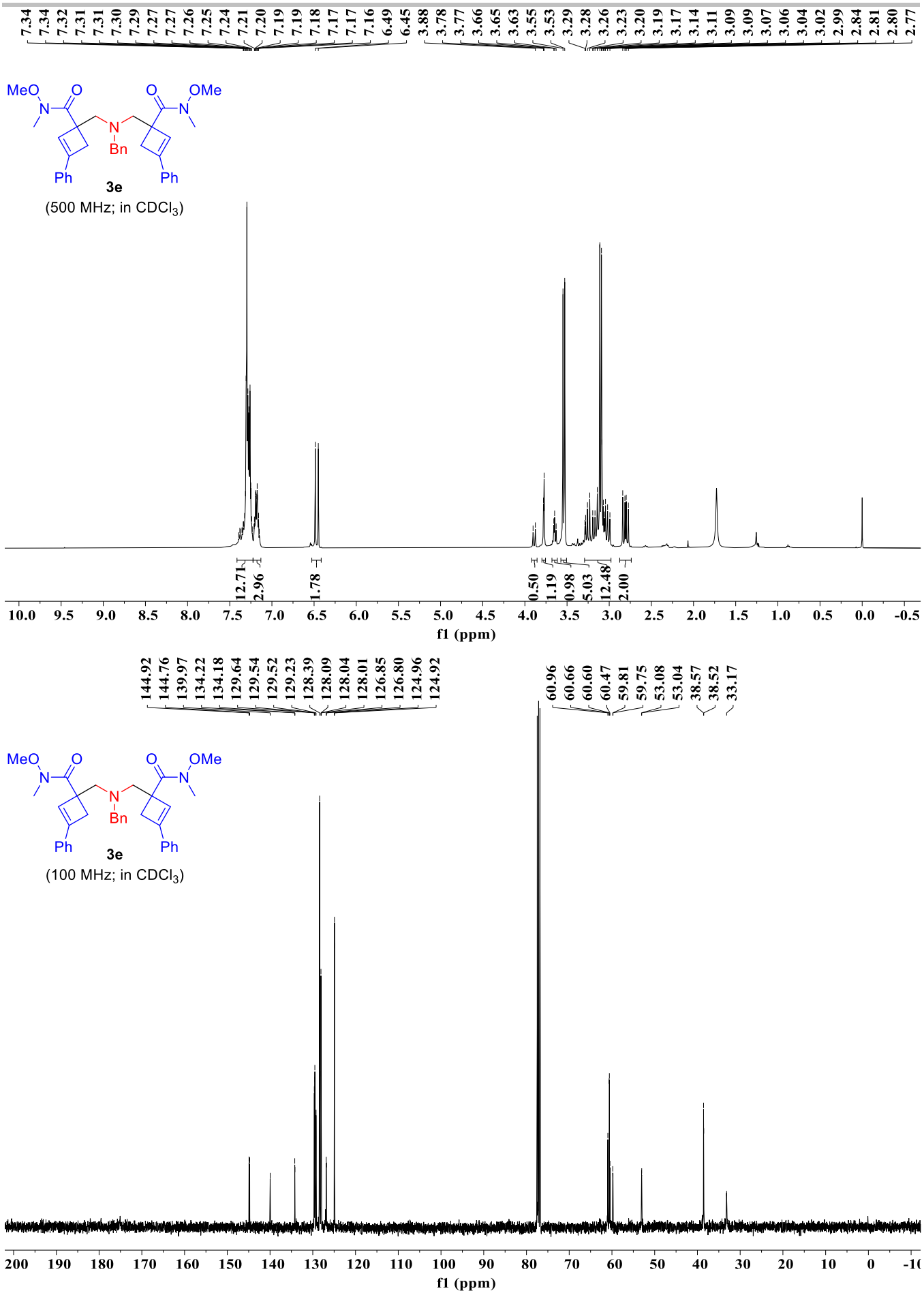
66.43 61.34 61.28 59.77 52.05 51.97 38.09 38.00
BnO
O
O
OBn
N
Bn
Ph
Ph
3d
(100 MHz; in CDCl3)
f1 (ppm)


7.34 7.34 7.32 7.31 7.31 7.30 7.29 7.27 7.27 7.26 7.25 7.24 7.21 7.20 7.19 7.19 7.18 7.17 7.17 7.16 6.49 6.45
3.88 3.78 3.77 3.66 3.65 3.63 3.55 3.53 3.29 3.28 3.26 3.23 3.20 3.19 3.17 3.14 3.11 3.09 3.09 3.07 3.06 3.04 3.02 2.99 2.84 2.81 2.80 2.77
MeO N O O N OMe
N Bn
Ph Ph
3e
(500 MHz; in CDCl3)
12.71 2.96 1.78 0.50 1.19 0.98 5.03 12.48 2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
144.92 144.76 139.97 134.22 134.18 129.64 129.54 129.52 129.23 128.39 128.09 128.04 128.01 126.85 126.80 124.96 124.92
60.96 60.66 60.60 60.47 59.81 59.75 53.08 53.04 38.57 38.52 33.17
MeO N O O N OMe
N Bn
Ph Ph
3e
(100 MHz; in CDCl3)
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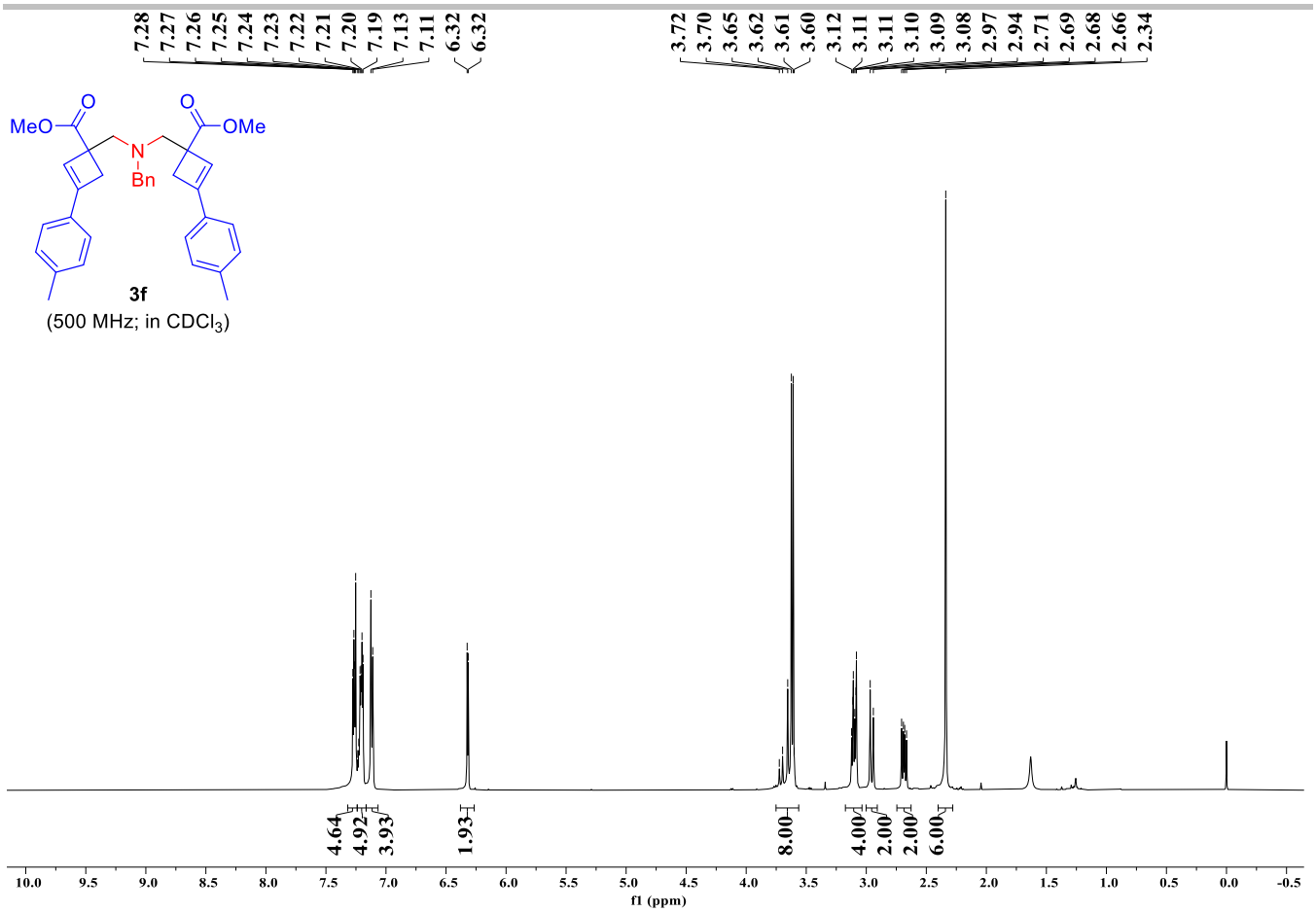
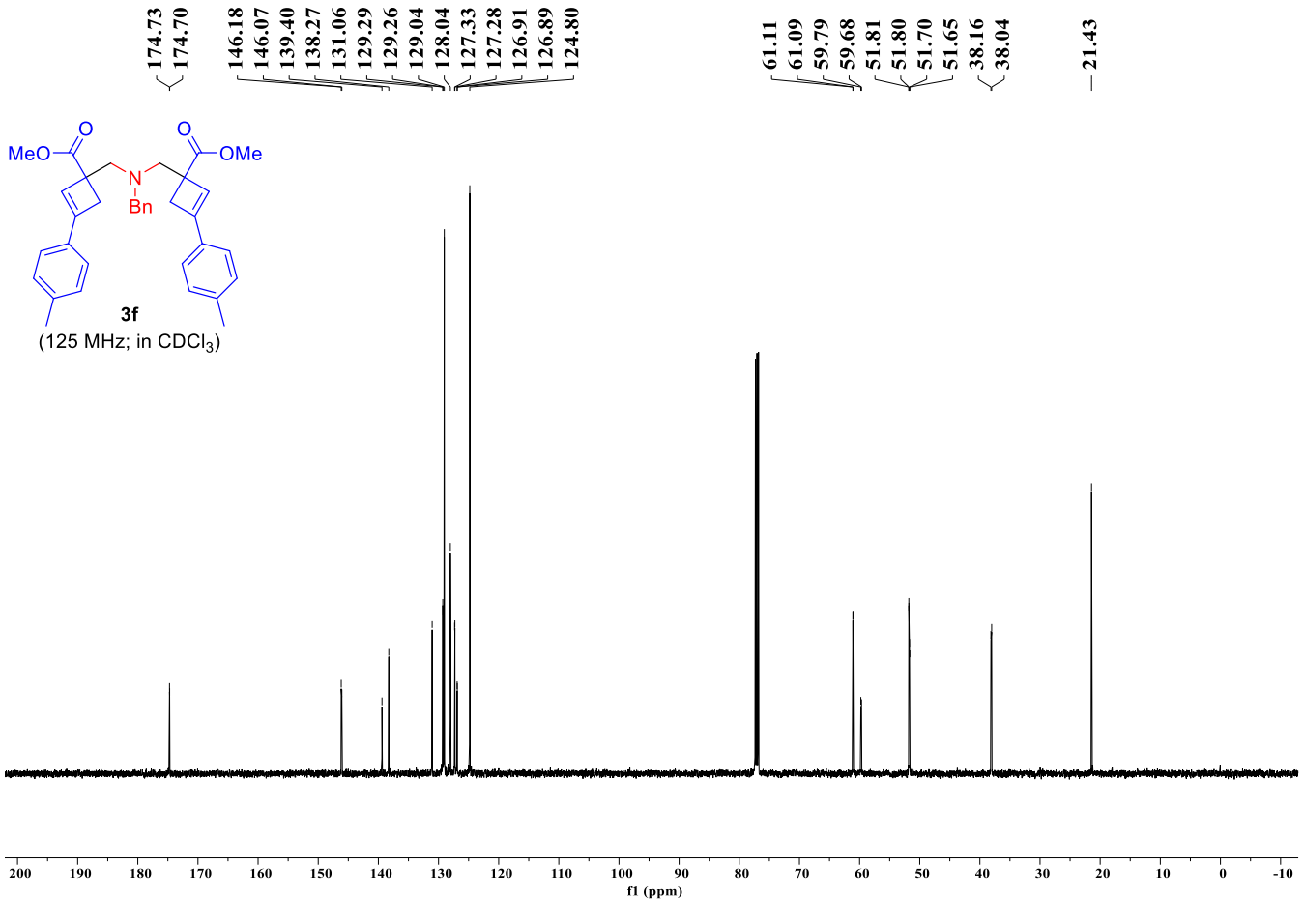
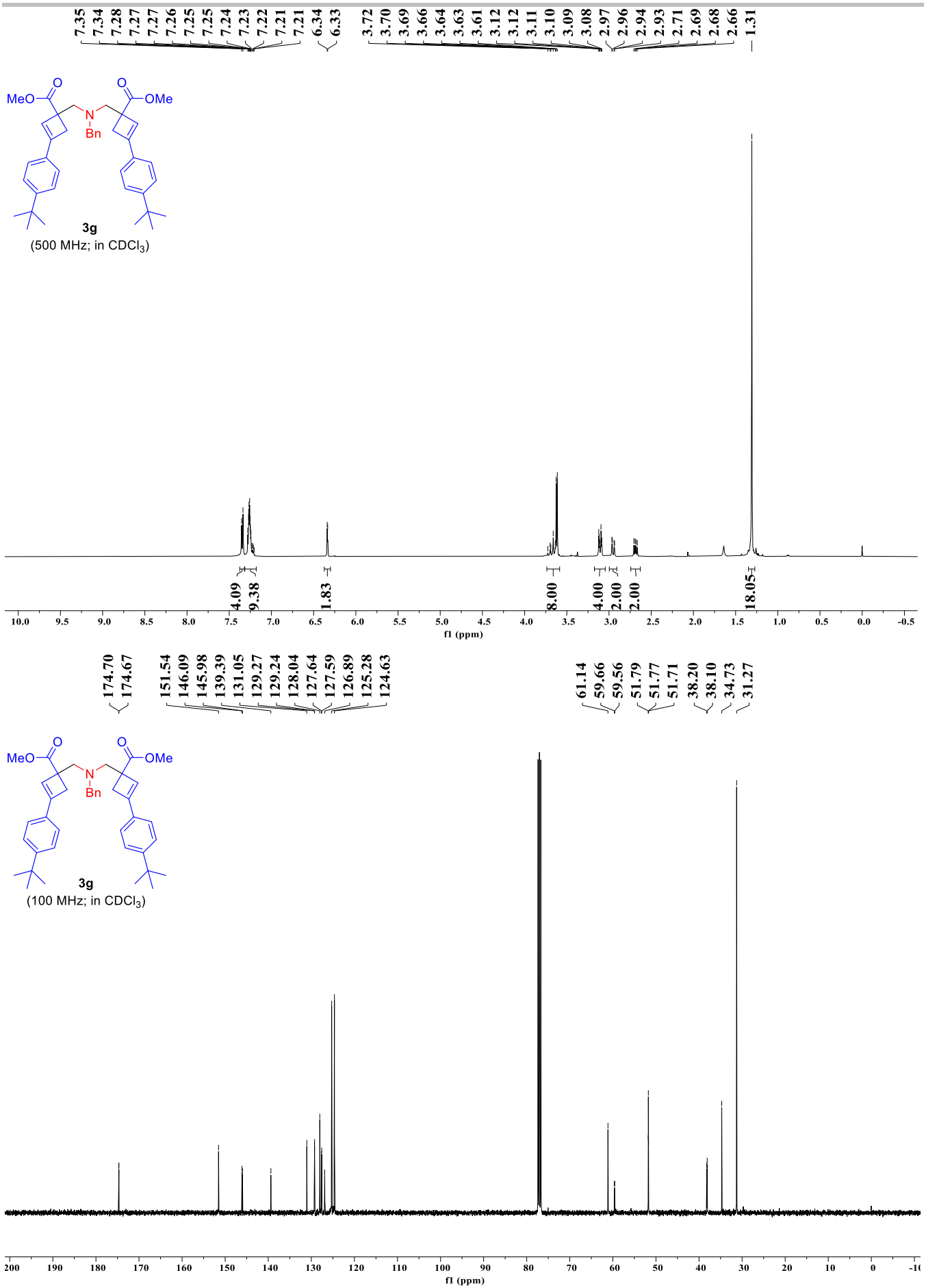
f1 (ppm)



3f
(500 MHz; in $CDCl_3$)



3f
(125 MHz; in $CDCl_3$)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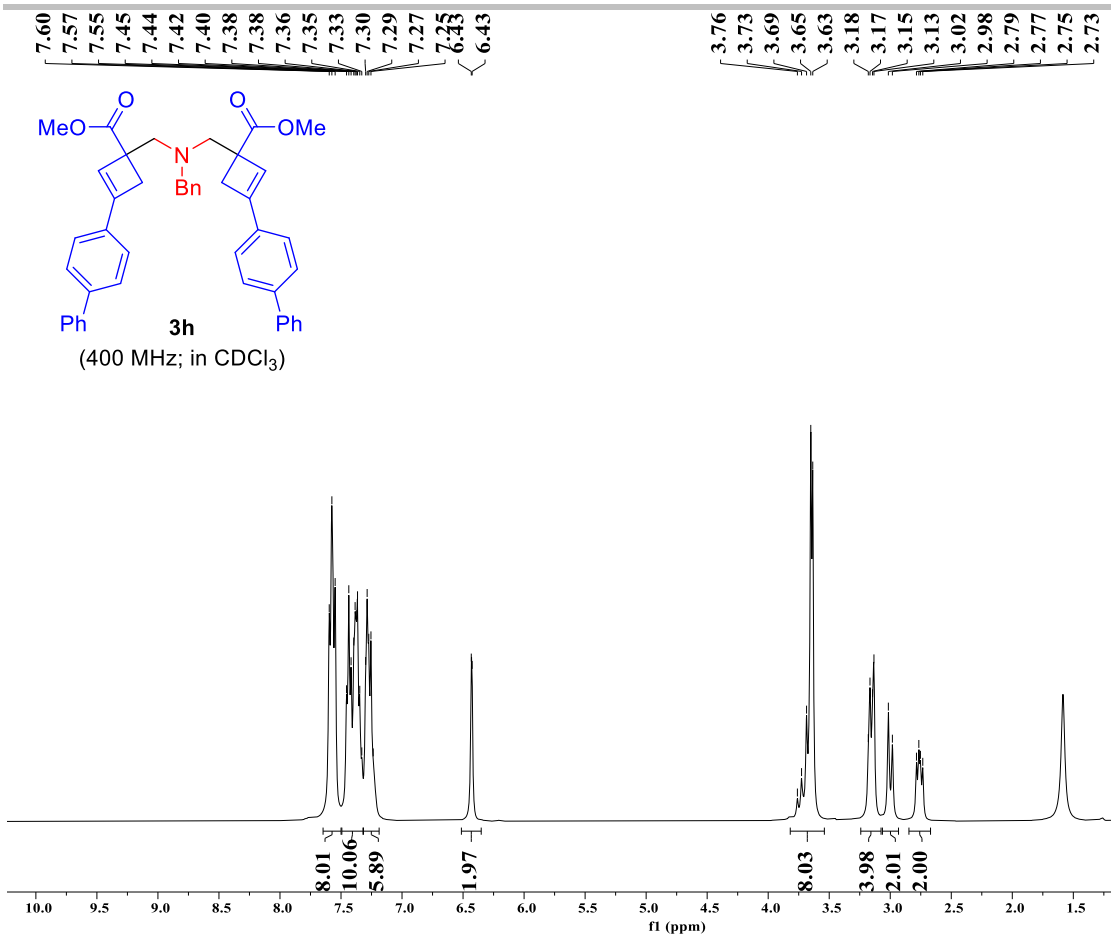
MeO
O
N
Bn
O
OMe
3g
(500 MHz; in CDCl3)
4.09 9.38 1.83 8.00 4.00 2.00 2.00 18.05
f1 (ppm)
174.70 174.67 151.54 146.09 145.98 139.39 131.05 129.27 129.24 128.04 127.64 127.59 126.89 125.28 124.63 61.14 59.66 59.56 51.79 51.77 51.71 38.20 38.10 34.73 31.27
MeO
O
N
Bn
O
OMe
3g
(100 MHz; in CDCl3)
f1 (ppm)



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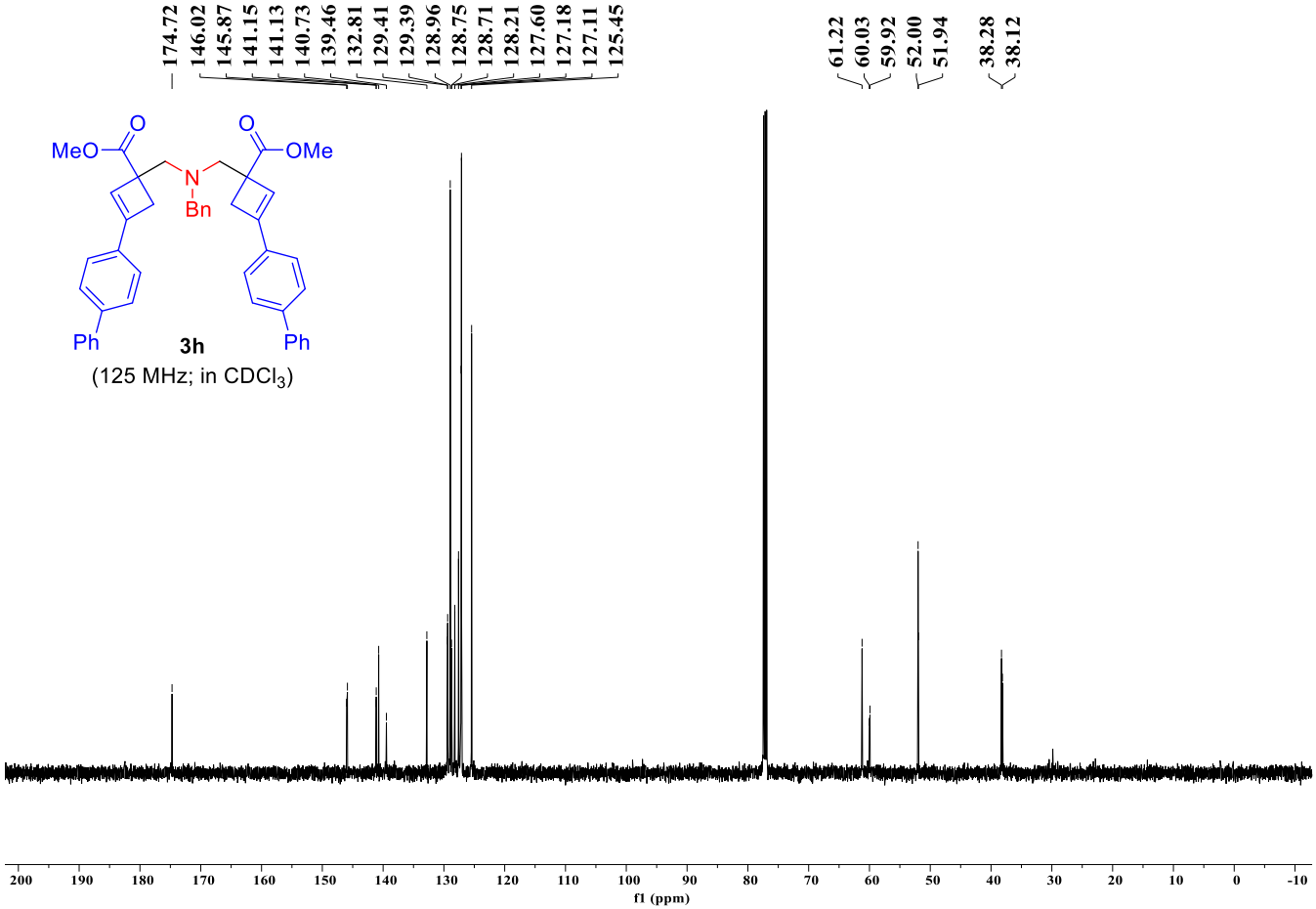
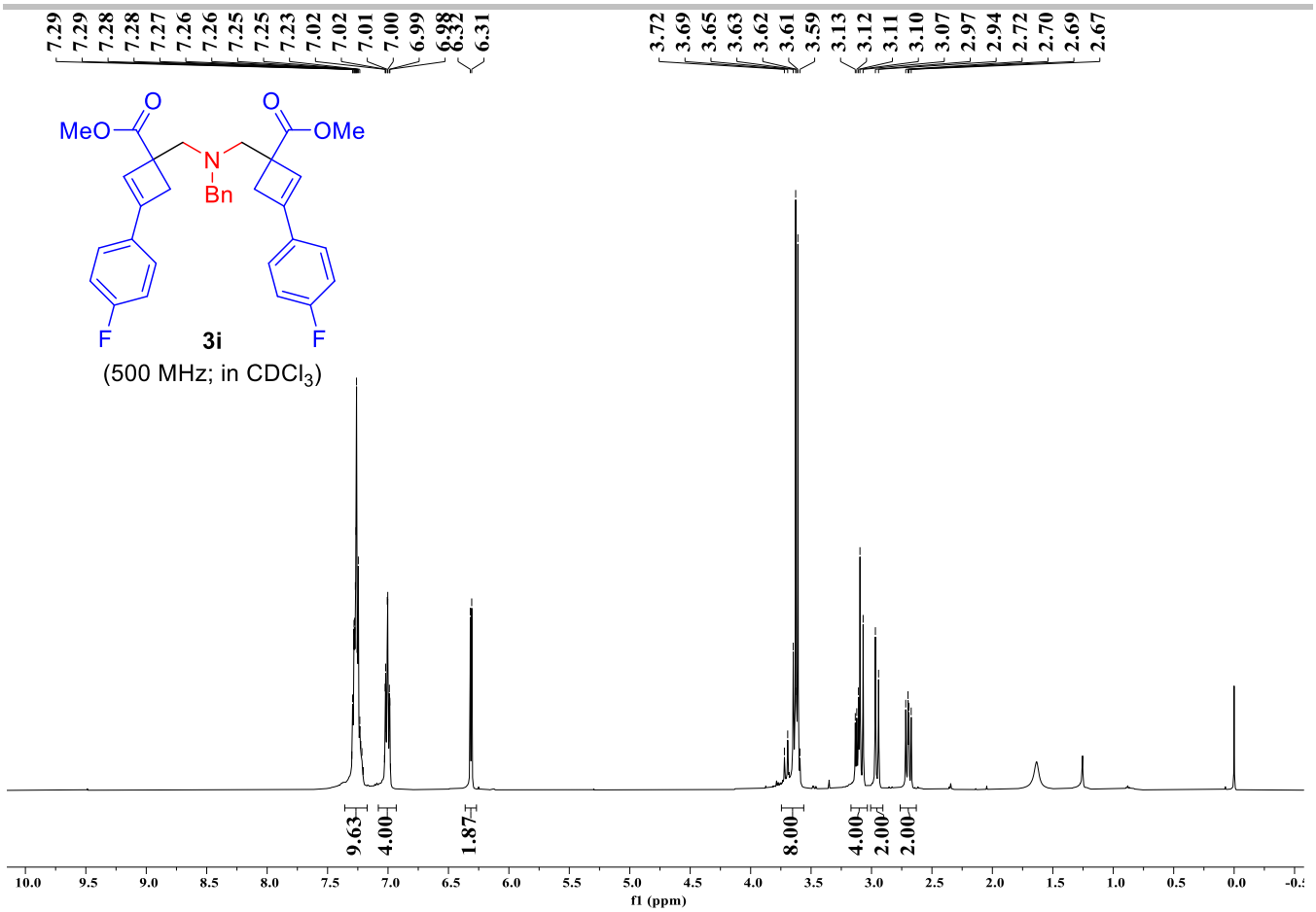
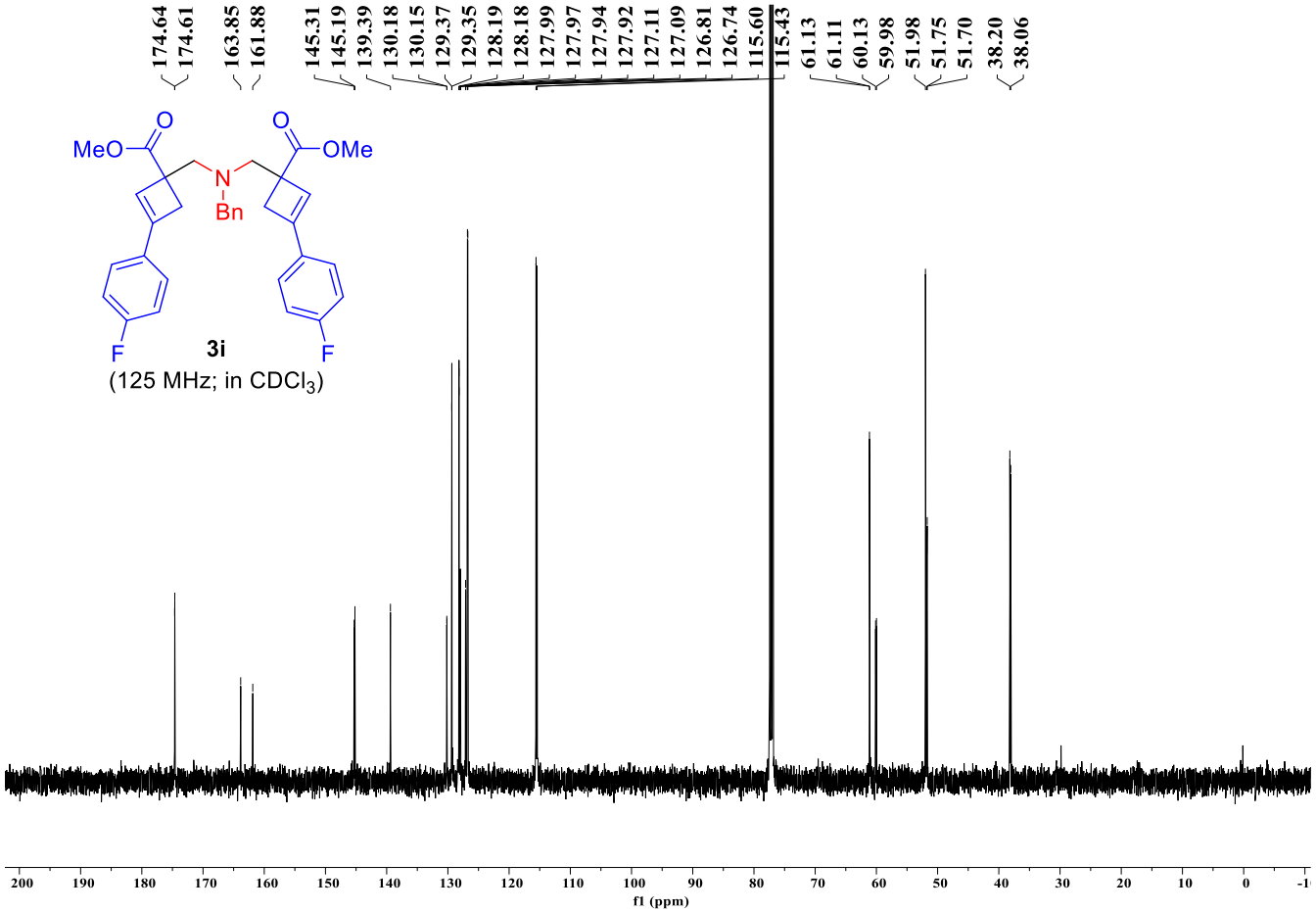


(125 MHz; in $CDCl_3$)


7.29
7.29
7.28
7.28
7.27
7.26
7.26
7.25
7.25
7.23
7.02
7.02
7.01
7.00
6.99
6.32
6.31
3.72
3.69
3.65
3.63
3.62
3.61
3.59
3.13
3.12
3.11
3.10
3.07
2.97
2.94
2.72
2.70
2.69
2.67
MeO
OMe
N
Bn
F
F
3i
(500 MHz; in CDCl3)
9.63
4.00
1.87
8.00
4.00
2.00
2.00
f1 (ppm)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174.61
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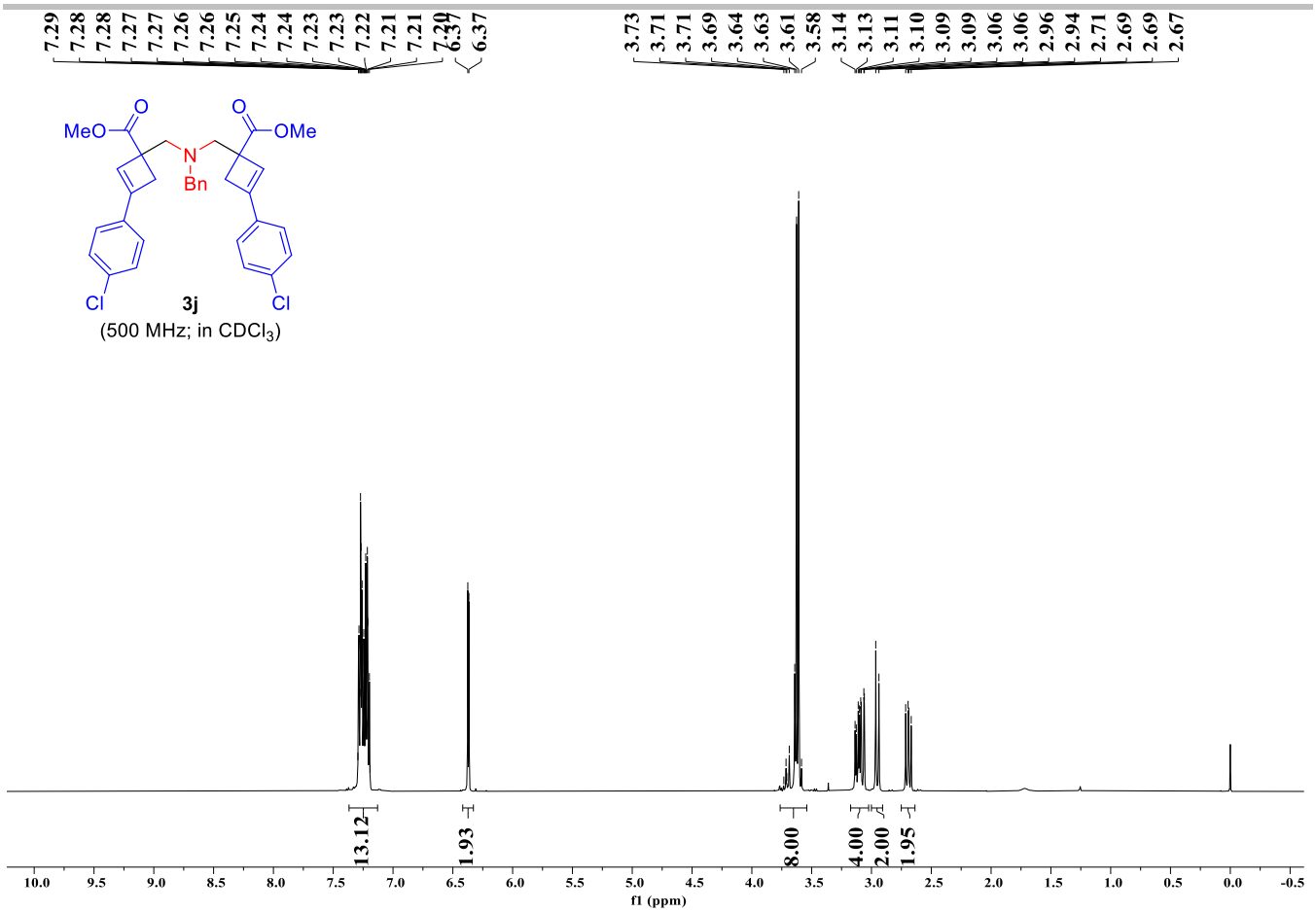
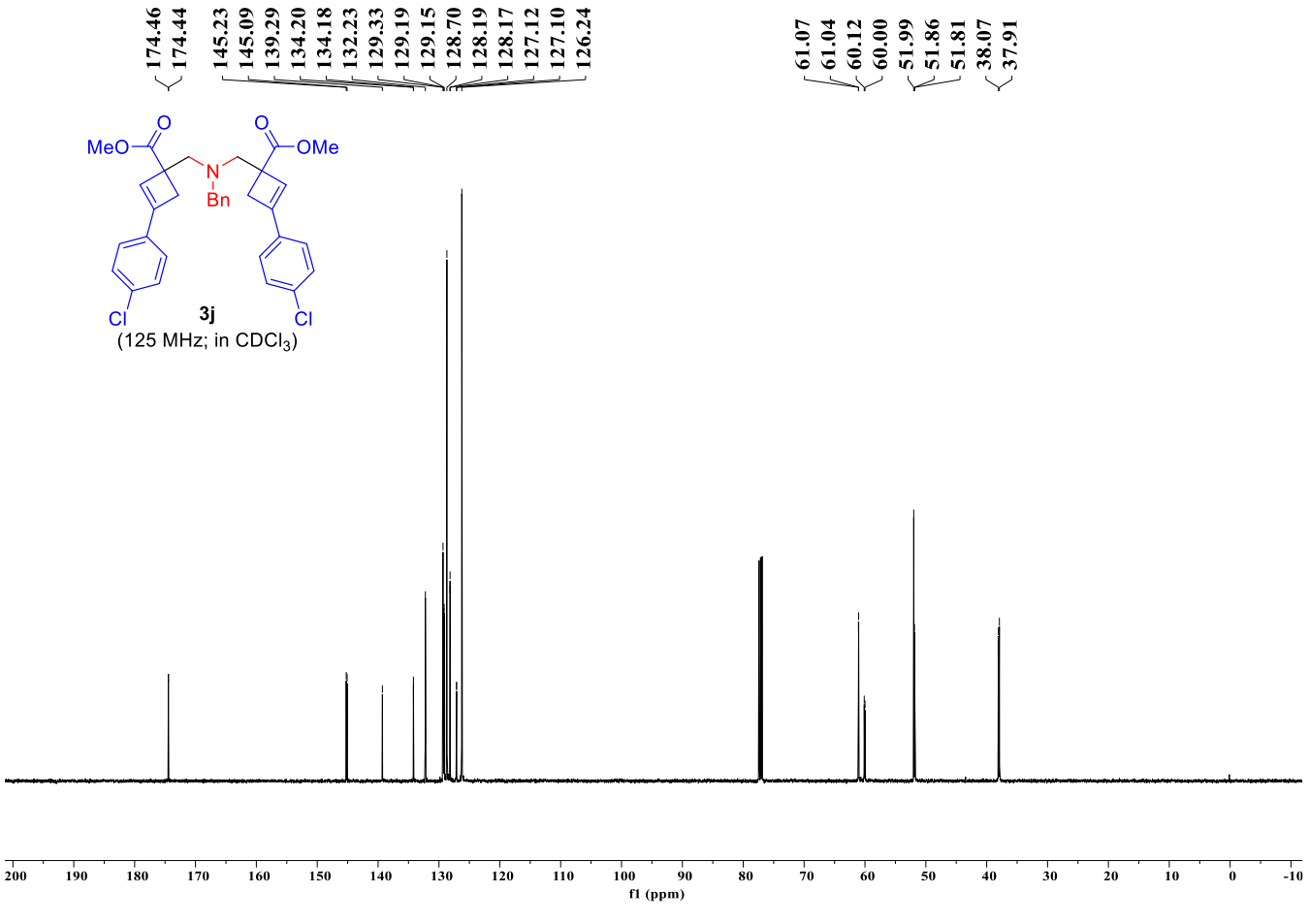
161.88
145.31
145.19
139.39
130.18
130.15
129.37
129.35
128.19
128.18
127.99
127.97
127.94
127.92
127.11
127.09
126.81
126.74
115.60
115.43
61.13
61.11
60.13
59.98
51.98
51.75
51.70
38.20
38.06
MeO
OMe
N
Bn
F
F
3i
(125 MHz; in CDCl3)
f1 (ppm)


7.29 7.28 7.28 7.27 7.27 7.26 7.26 7.25 7.24 7.24 7.23 7.23 7.22 7.21 7.21 7.20 6.37 6.37
3.73 3.71 3.71 3.69 3.64 3.63 3.61 3.58 3.14 3.13 3.11 3.10 3.09 3.09 3.06 3.06 2.96 2.94 2.71 2.69 2.69 2.67
MeO
O
N
Bn
O
OMe
Cl
Cl
3j
(500 MHz; in CDCl3)
13.12
1.93
8.00
4.00
2.00
1.95
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


174.46 174.44 145.23 145.09 139.29 134.20 134.18 132.23 129.33 129.19 129.15 128.70 128.19 128.17 127.12 127.10 126.24
61.07 61.04 60.12 60.00 51.99 51.86 51.81 38.07 37.91
MeO
O
N
Bn
O
OMe
Cl
Cl
3j
(125 MHz; in CDCl3)
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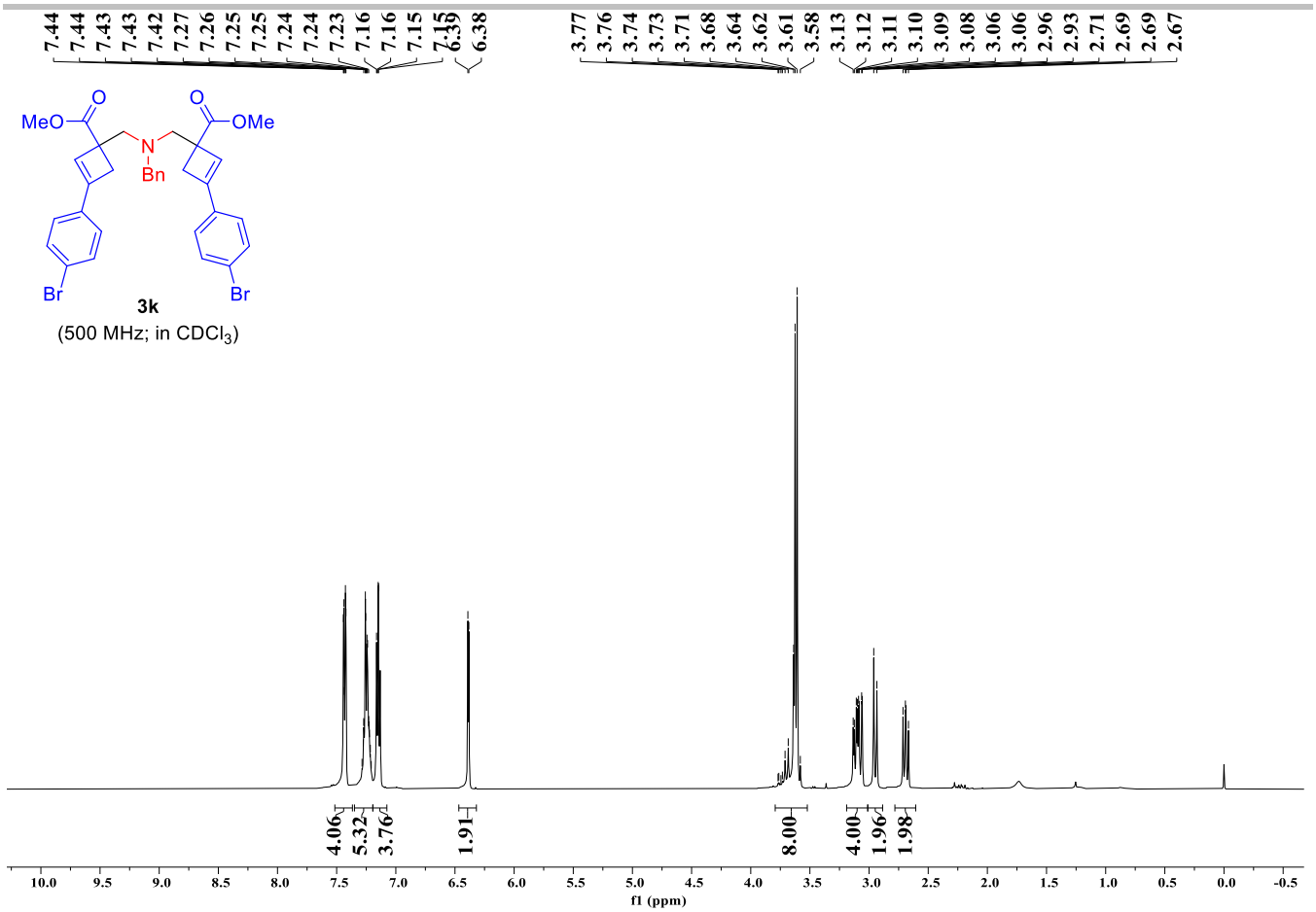
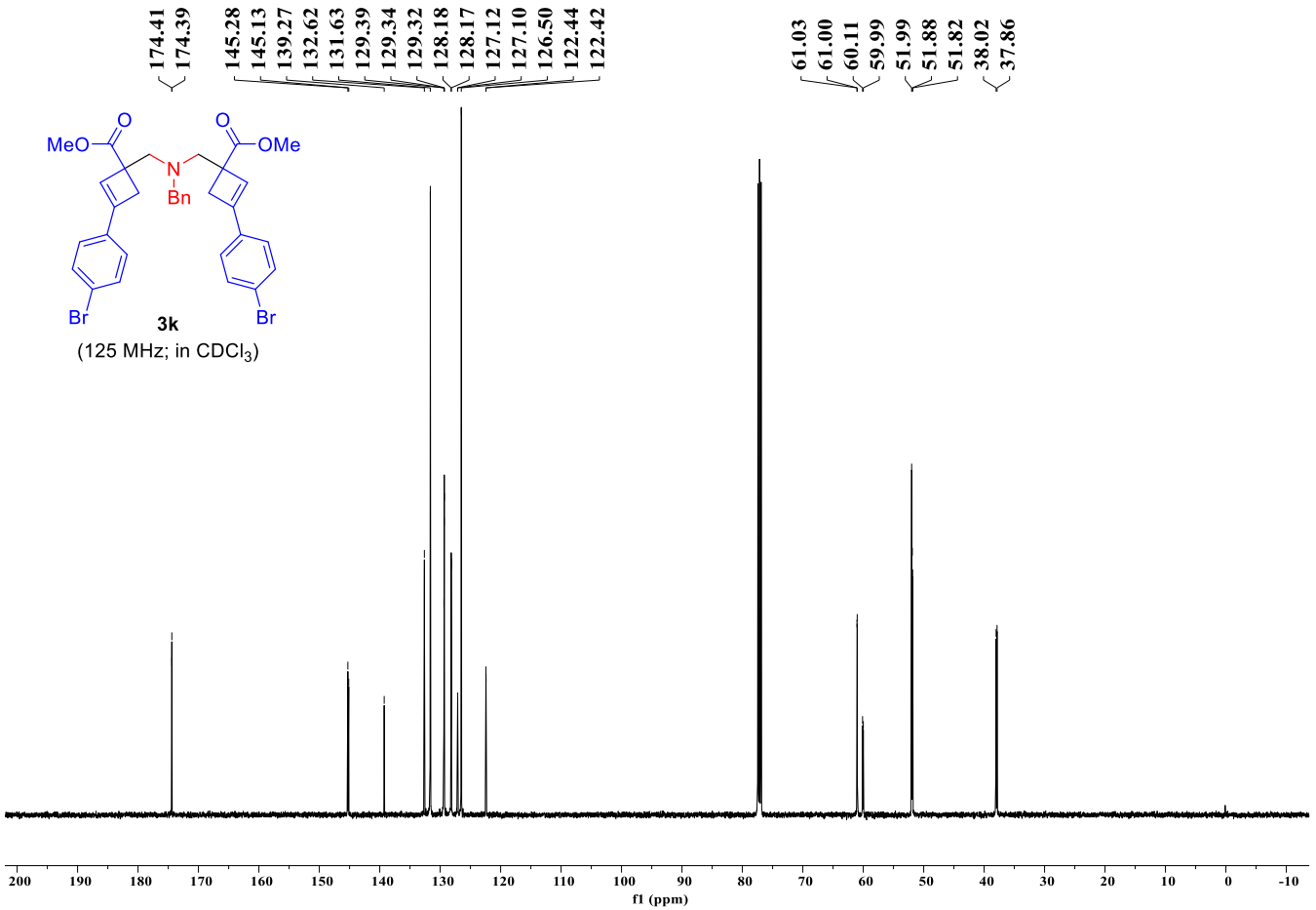
f1 (ppm)



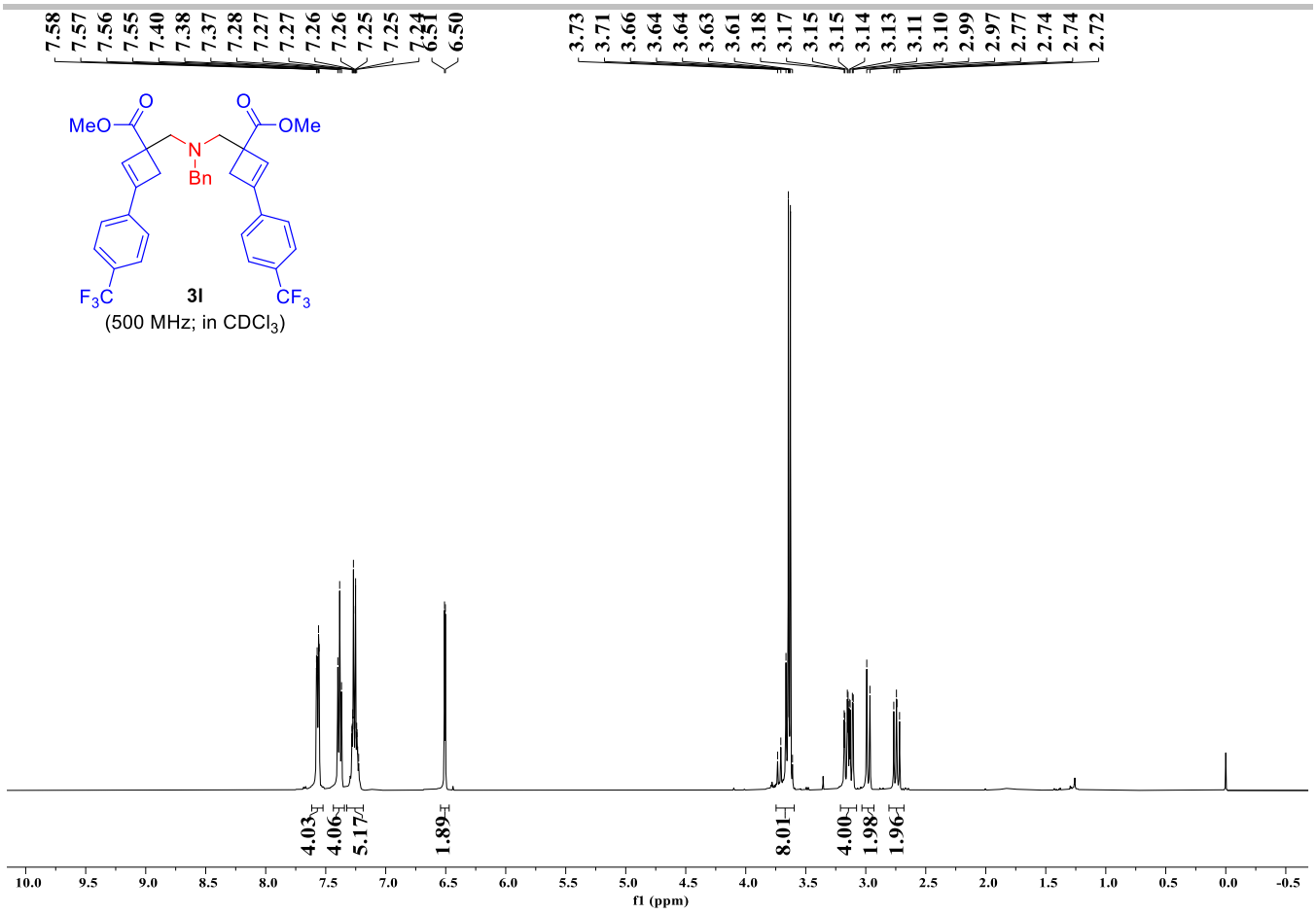
3k

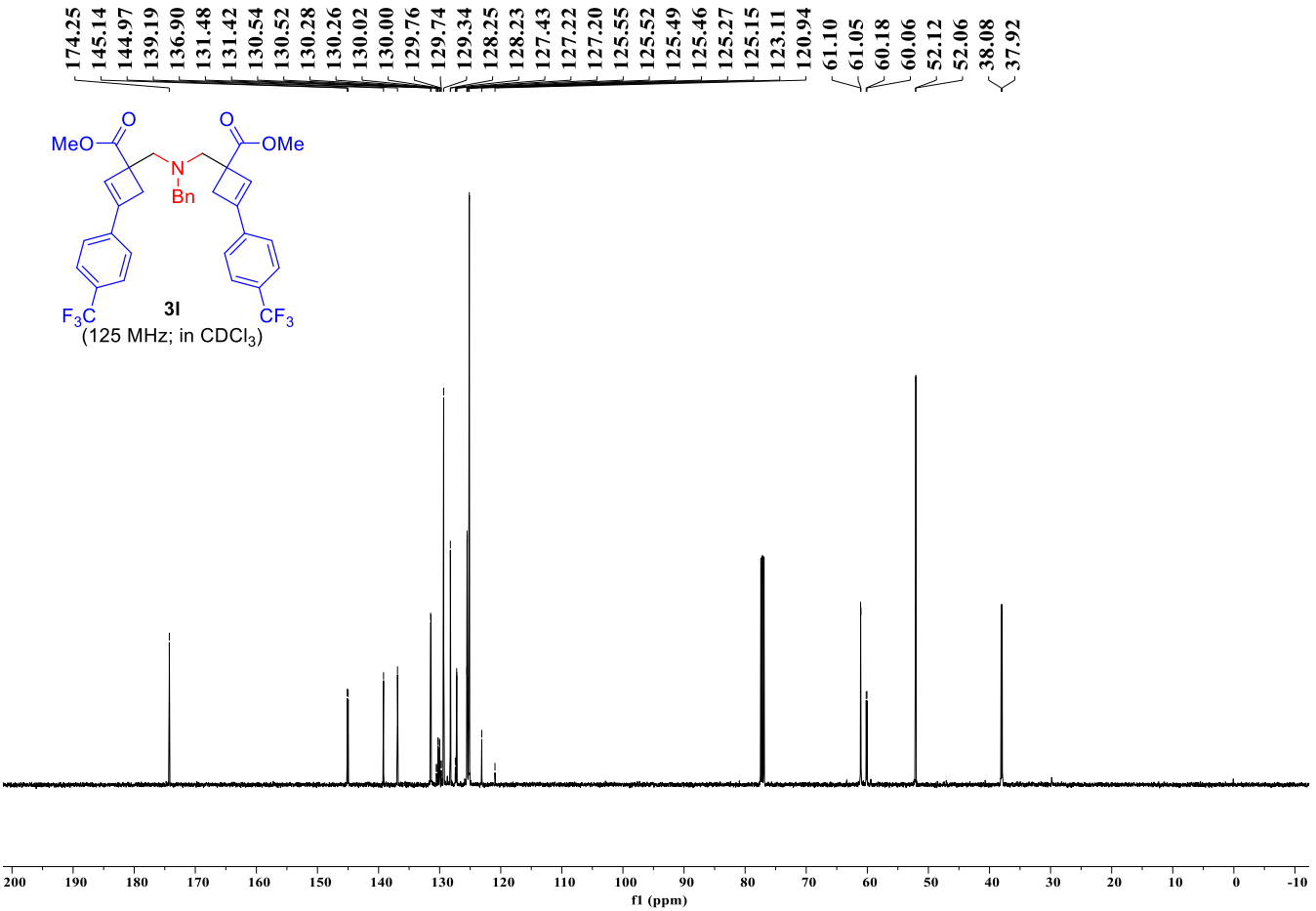
(500 MHz; in $CDCl_3$)

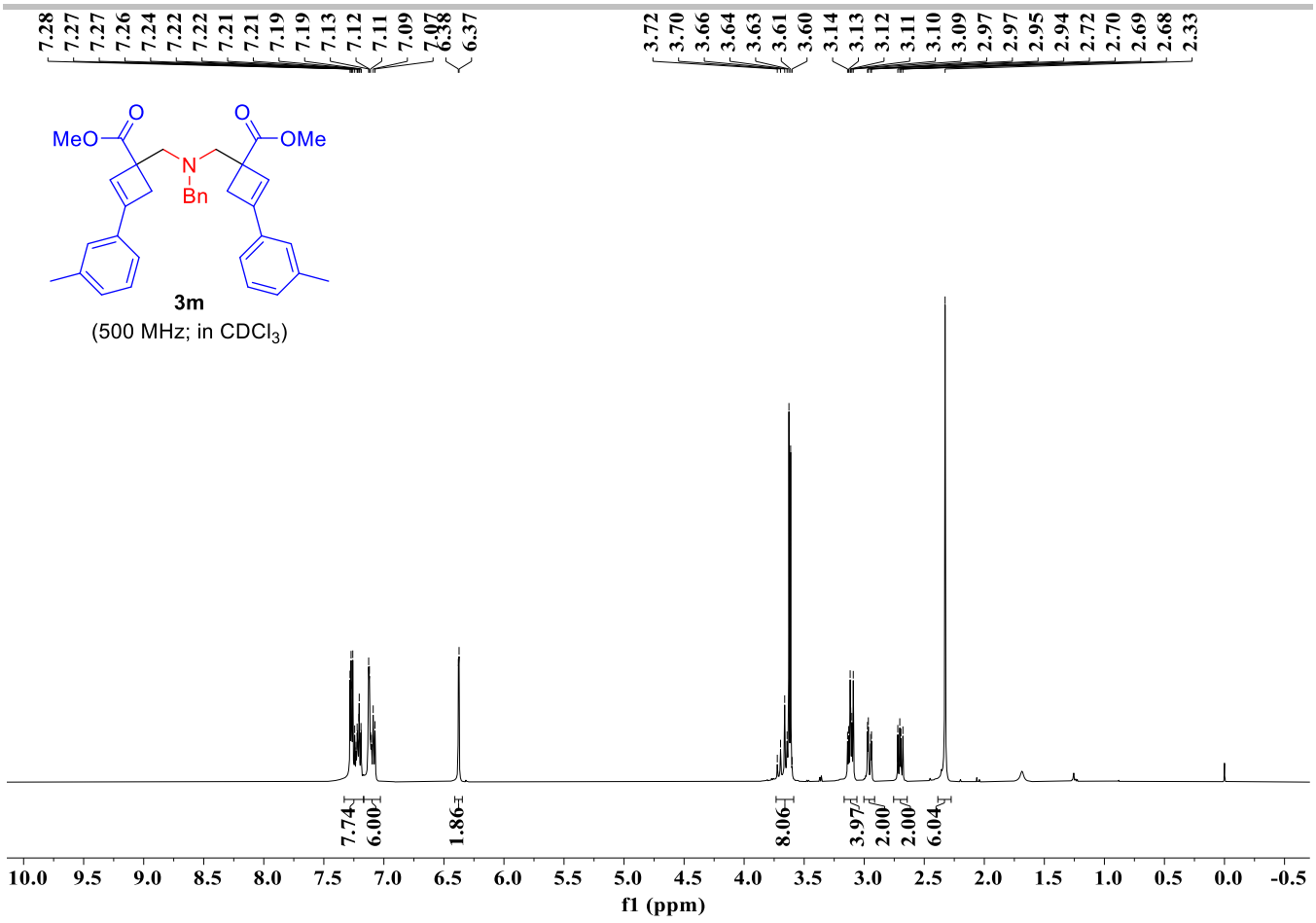


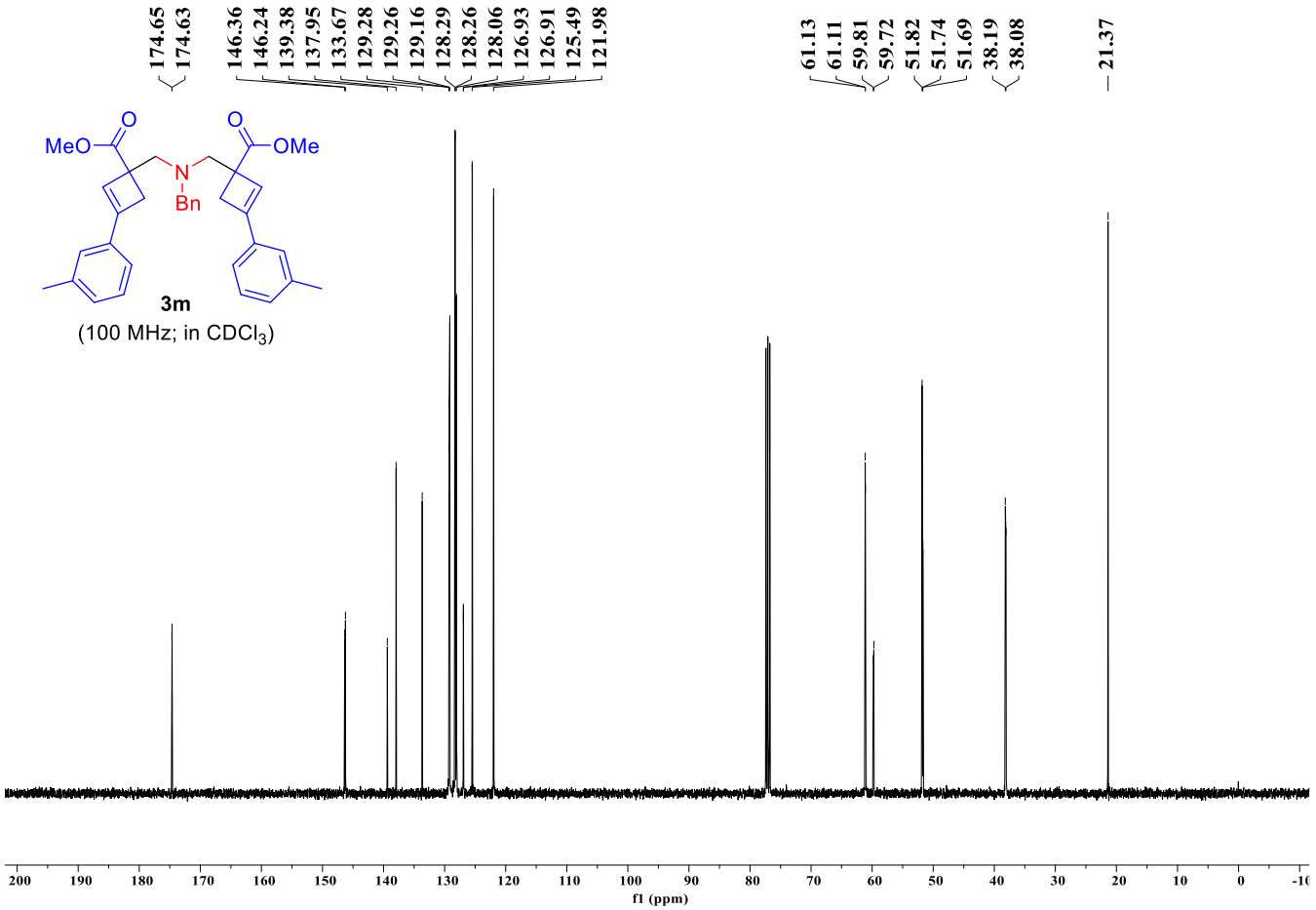
3k

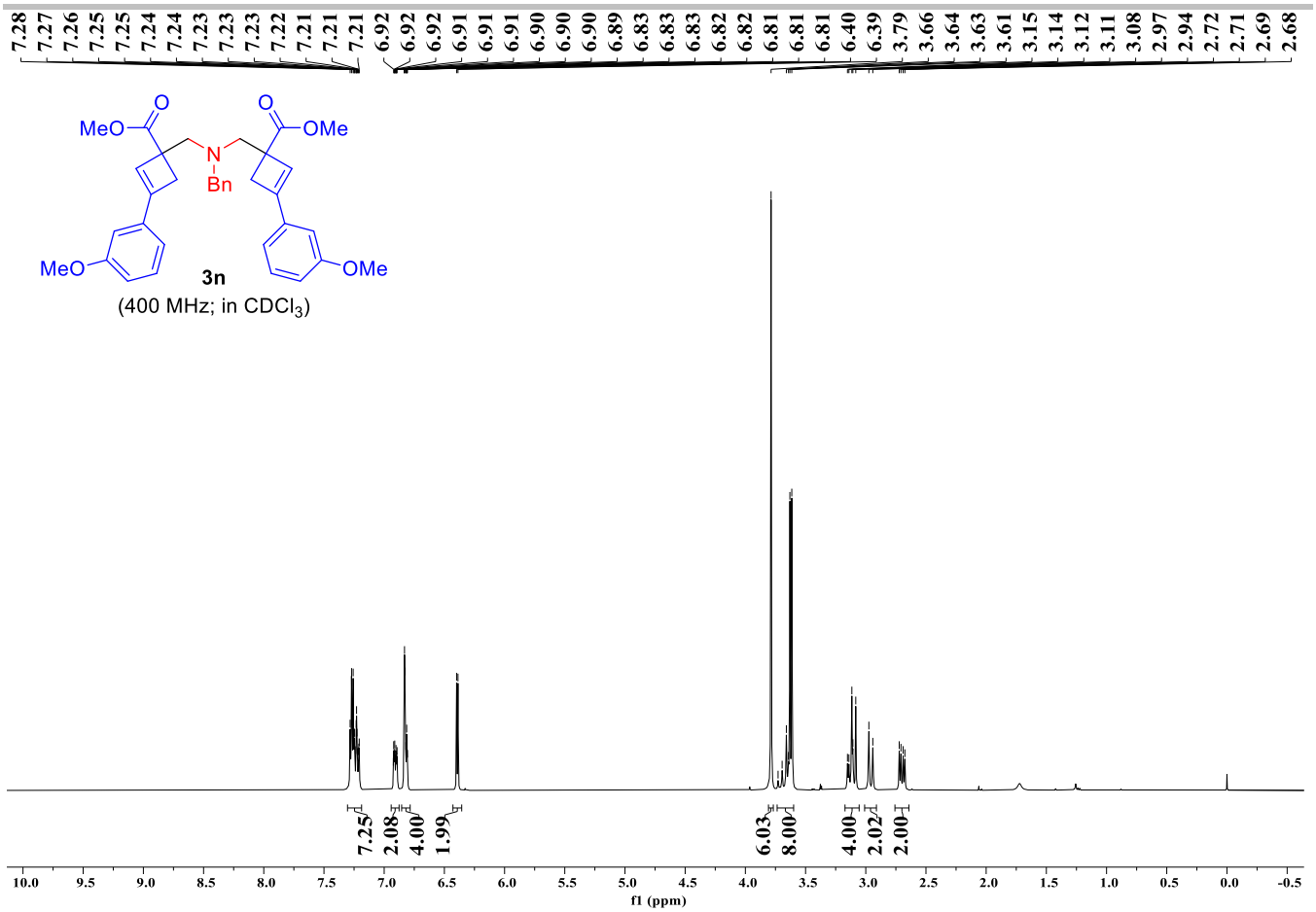
(125 MHz; in $CDCl_3$)

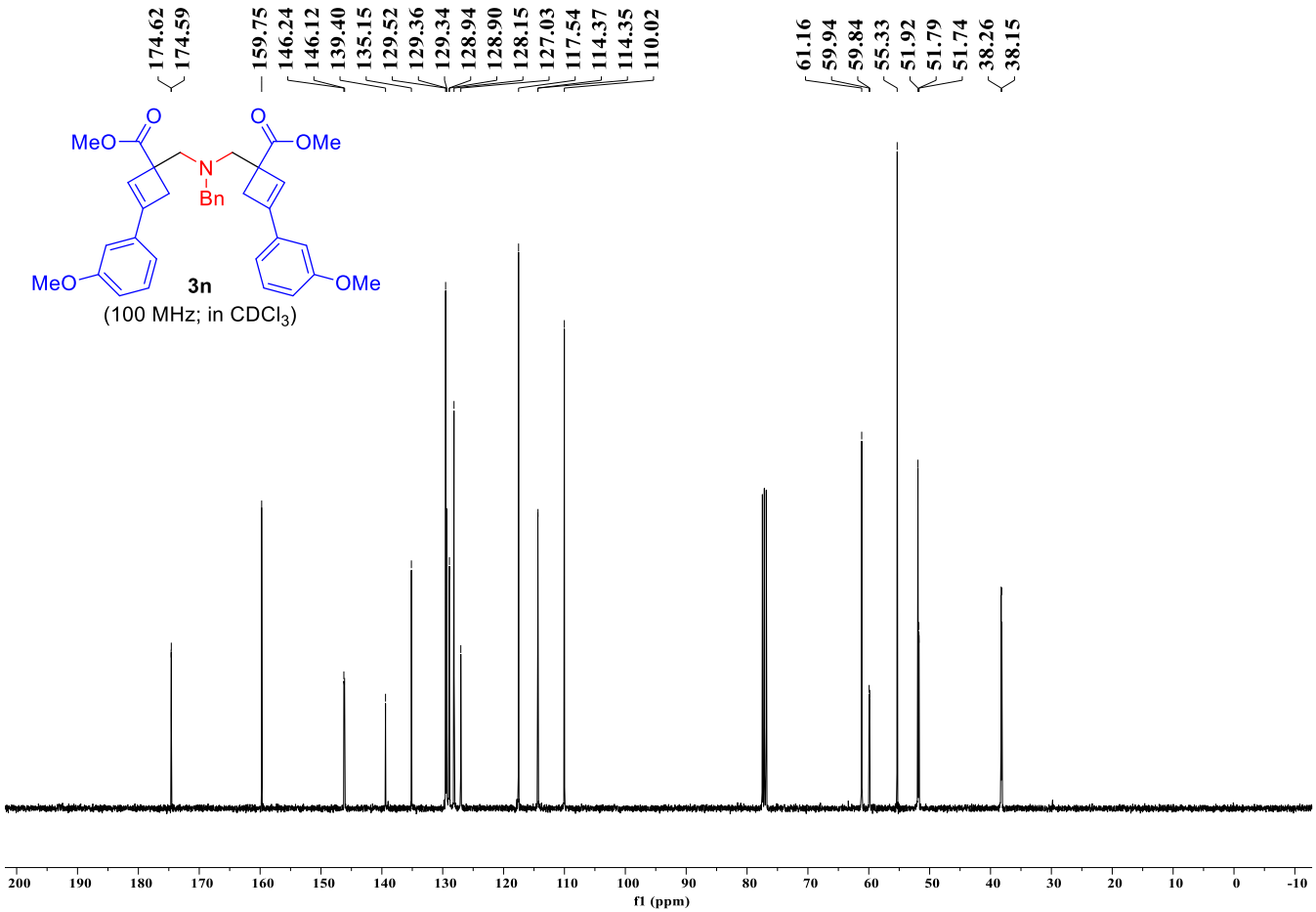

7.58 7.57 7.56 7.55 7.40 7.38 7.37 7.28 7.27 7.27 7.26 7.26 7.25 7.25 7.24 6.51 6.50
3.73 3.71 3.66 3.64 3.64 3.63 3.61 3.18 3.17 3.15 3.15 3.14 3.13 3.11 3.10 2.99 2.97 2.77 2.74 2.74 2.72
MeO
O
N
Bn
OMe
F3C
CF3
3l
(500 MHz; in CDCl3)
4.03 4.06 5.17 1.89 8.01 4.00 1.98 1.96
f1 (ppm)

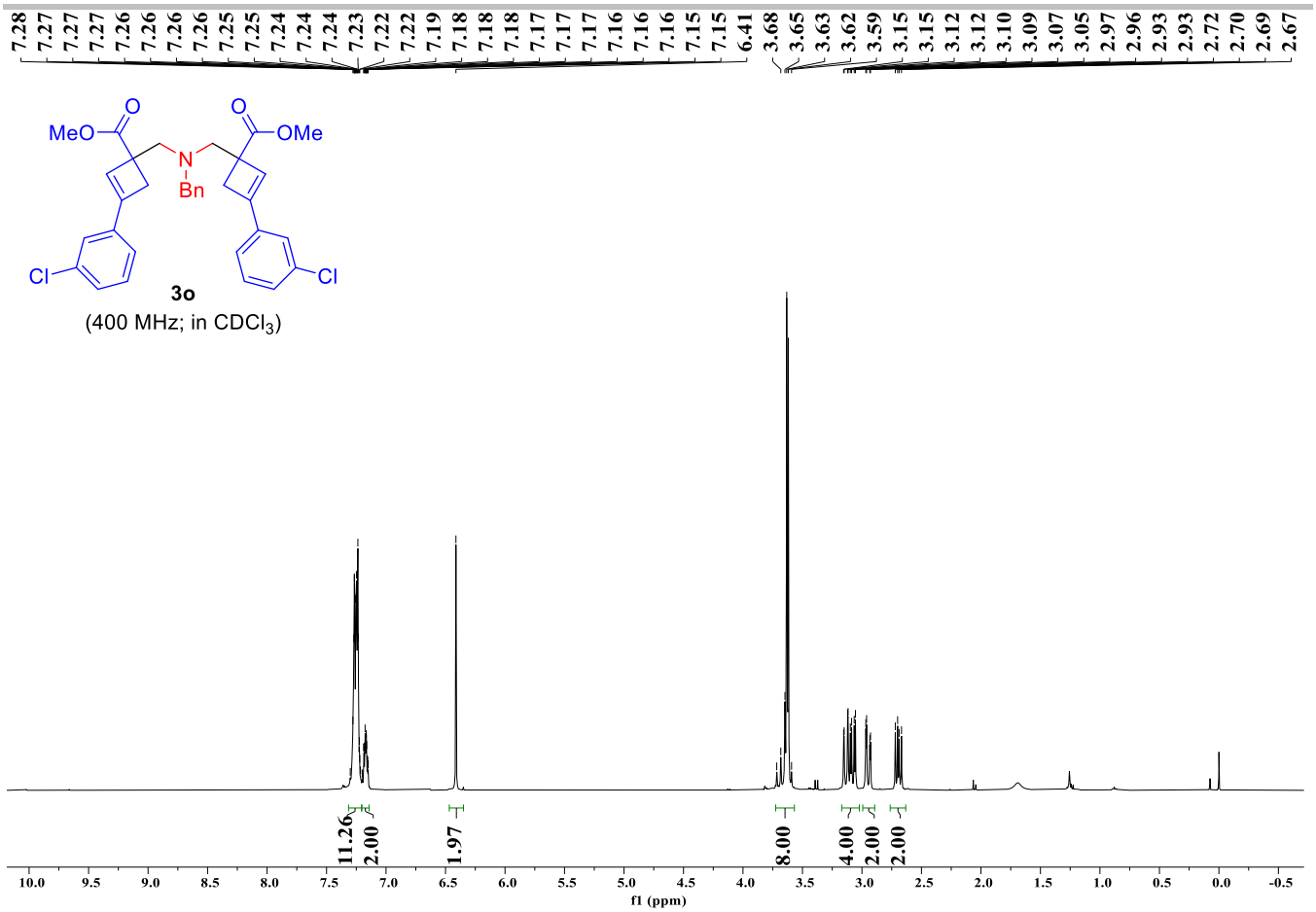

174.25 145.14 144.97 139.19 136.90 131.48 131.42 130.54 130.52 130.28 130.26 130.02 130.00 129.76 129.74 129.34 128.25 128.23 127.43 127.22 127.20 125.55 125.52 125.49 125.46 125.27 125.15 123.11 120.94 61.10 61.05 60.18 60.06 52.12 52.06 38.08 37.92
MeO
O
N
Bn
OMe
F3C
CF3
3l
(125 MHz; in CDCl3)
f1 (ppm)

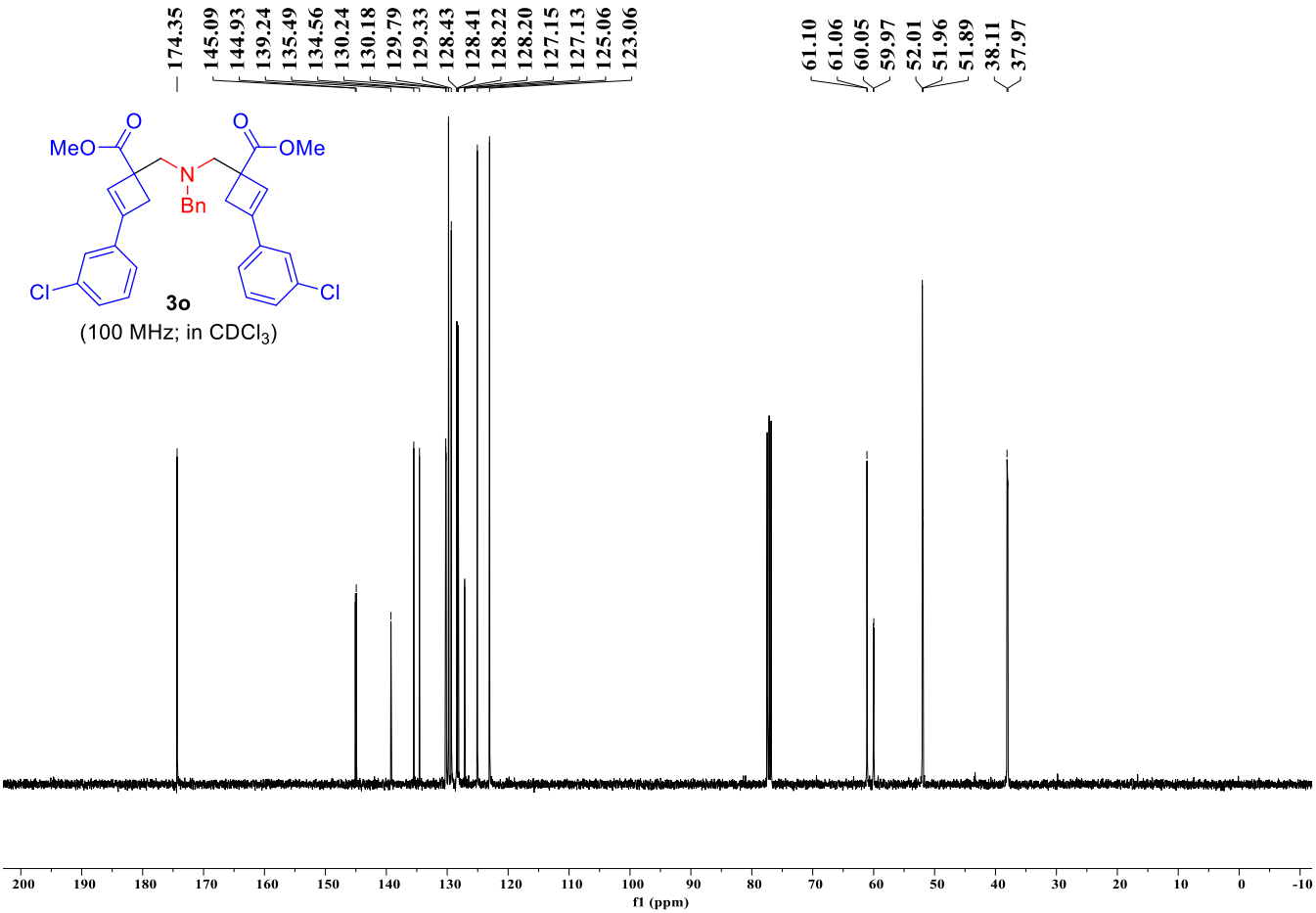

7.28 7.27 7.27 7.26 7.24 7.22 7.22 7.21 7.21 7.19 7.19 7.13 7.12 7.11 7.09 7.07 6.38 6.37
3.72 3.70 3.66 3.64 3.63 3.61 3.60 3.14 3.13 3.12 3.11 3.10 3.09 2.97 2.97 2.95 2.94 2.72 2.70 2.69 2.68 2.33
MeO
O
N
Bn
O
OMe
3m
(500 MHz; in CDCl3)
7.74 6.00 1.86 8.06 3.97 2.00 2.00 6.04
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

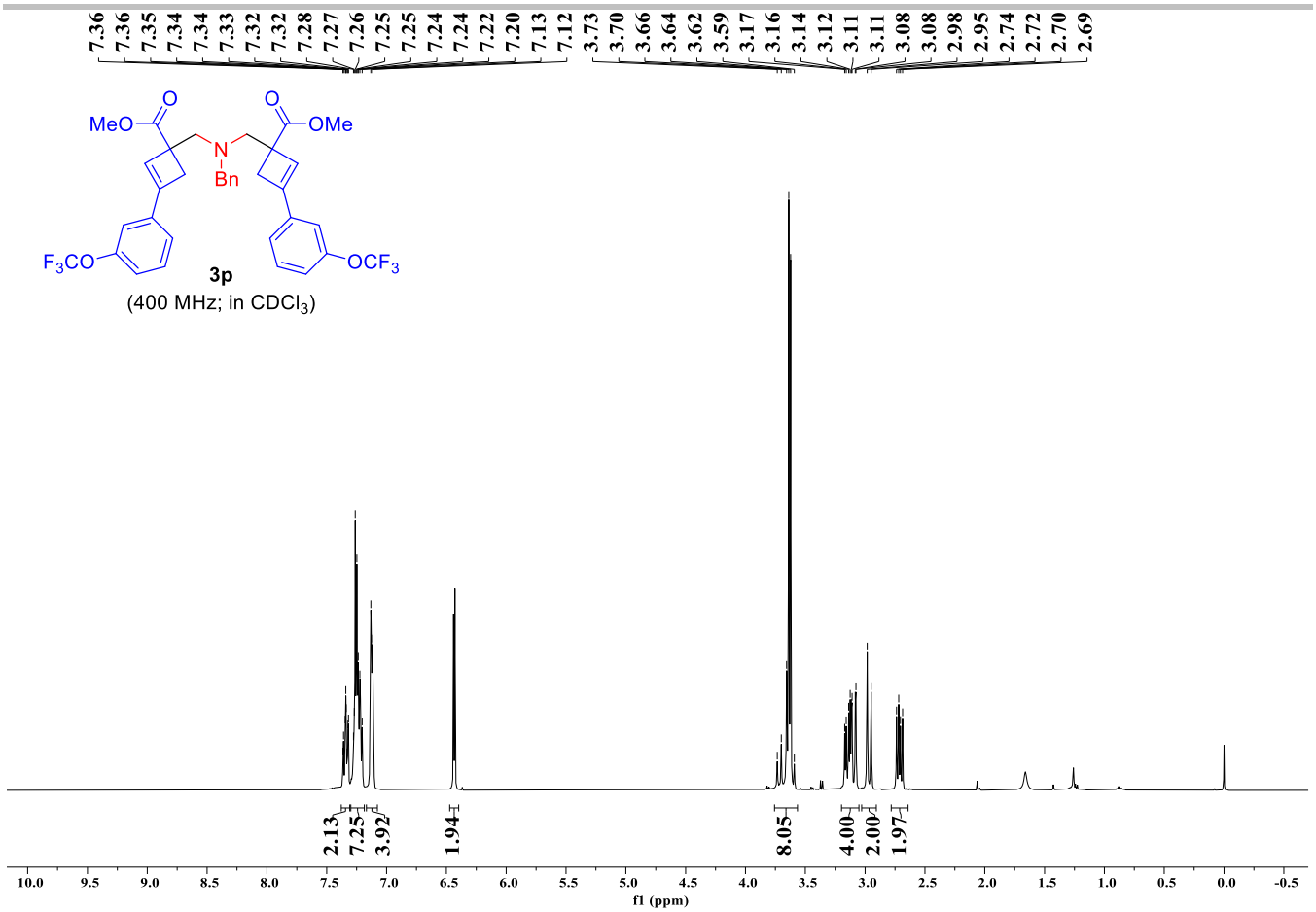

174.65 174.63 146.36 146.24 139.38 137.95 133.67 129.28 129.26 129.16 128.29 128.26 128.06 126.93 126.91 125.49 121.98
61.13 61.11 59.81 59.72 51.82 51.74 51.69 38.19 38.08 21.37
MeO
O
N
Bn
O
OMe
3m
(100 MHz; in CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

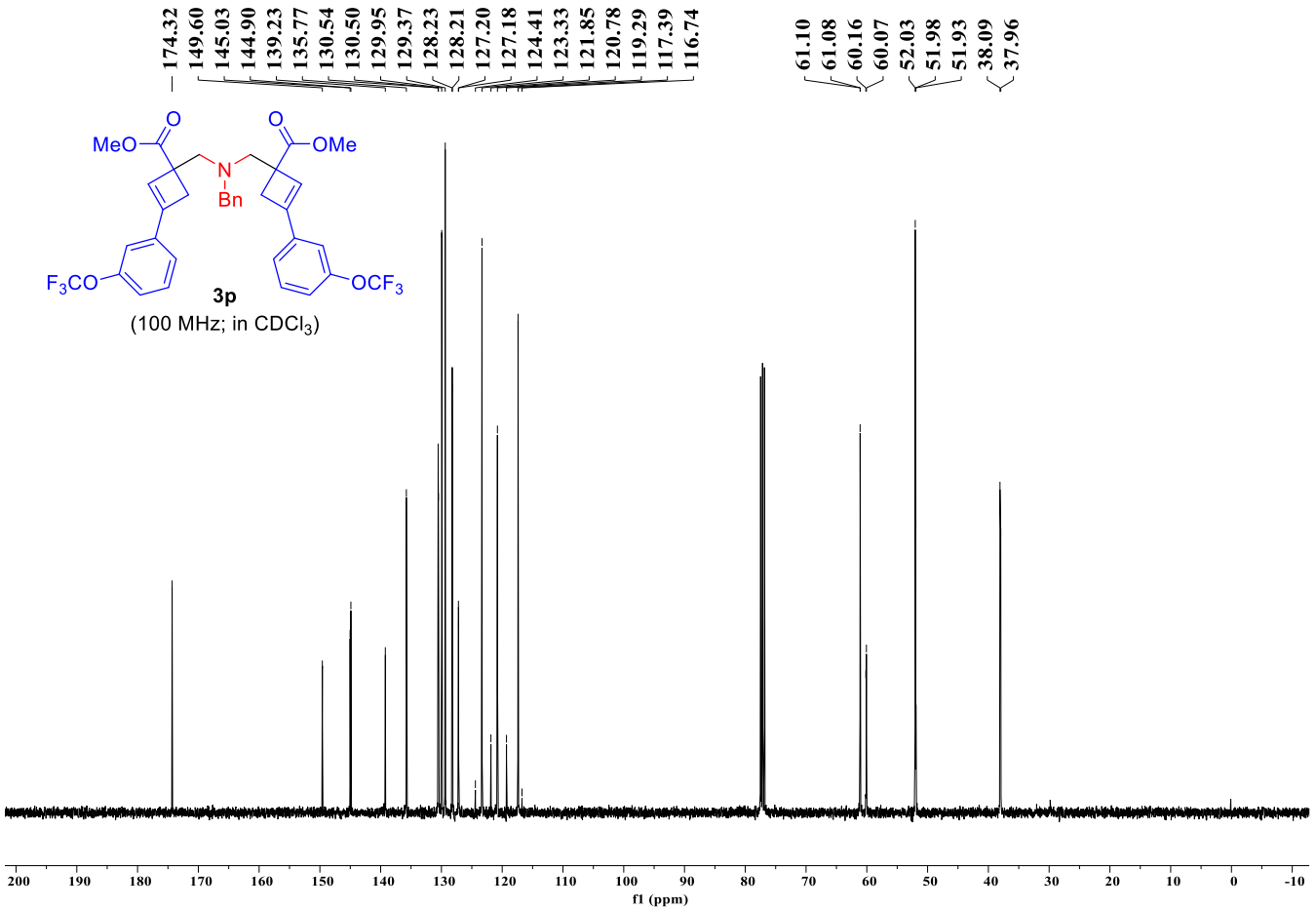

7.28 7.27 7.26 7.25 7.25 7.24 7.24 7.23 7.23 7.23 7.22 7.21 7.21 7.21
6.92 6.92 6.92 6.91 6.91 6.91 6.90 6.90 6.90 6.89 6.83 6.83 6.83 6.82 6.82 6.81 6.81 6.81 6.40 6.39 3.79 3.66 3.64 3.63 3.61 3.15 3.14 3.12 3.11 3.08 2.97 2.94 2.72 2.71 2.69 2.68
MeO
O
O
OMe
N
Bn
MeO
OMe
3n
(400 MHz; in CDCl3)
7.25
2.08
4.00
1.99
6.03
8.00
4.00
2.02
2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

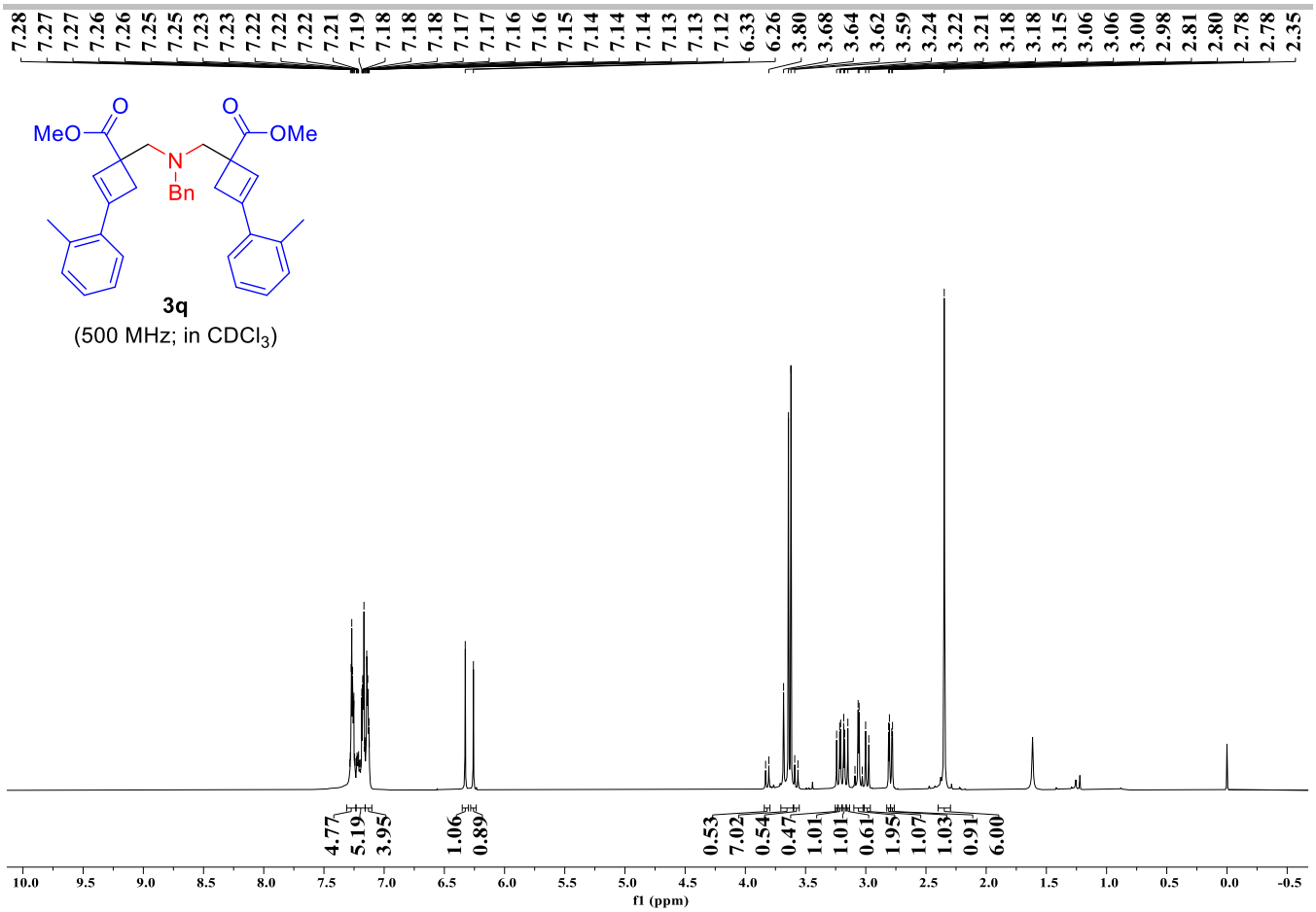

174.62 174.59
159.75
146.24 146.12 139.40 135.15 129.52 129.36 129.34 128.94 128.90 128.15 127.03 117.54 114.37 114.35 110.02
61.16 59.94 59.84 55.33 51.92 51.79 51.74 38.26 38.15
MeO
O
O
OMe
N
Bn
MeO
OMe
3n
(100 MHz; in CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.28 7.27 7.27 7.27 7.26 7.26 7.26 7.26 7.25 7.25 7.24 7.24 7.24 7.23 7.22 7.22 7.19 7.18 7.18 7.18 7.17 7.17 7.17 7.16 7.16 7.16 7.15 7.15 6.41
3.68 3.65 3.63 3.62 3.59 3.15 3.15 3.12 3.12 3.10 3.09 3.07 3.05 2.97 2.96 2.93 2.93 2.72 2.70 2.69 2.67
MeO
O
O
OMe
N
Bn
Cl
Cl
3o
(400 MHz; in CDCl3)
11.26
2.00
1.97
8.00
4.00
2.00
2.00
f1 (ppm)

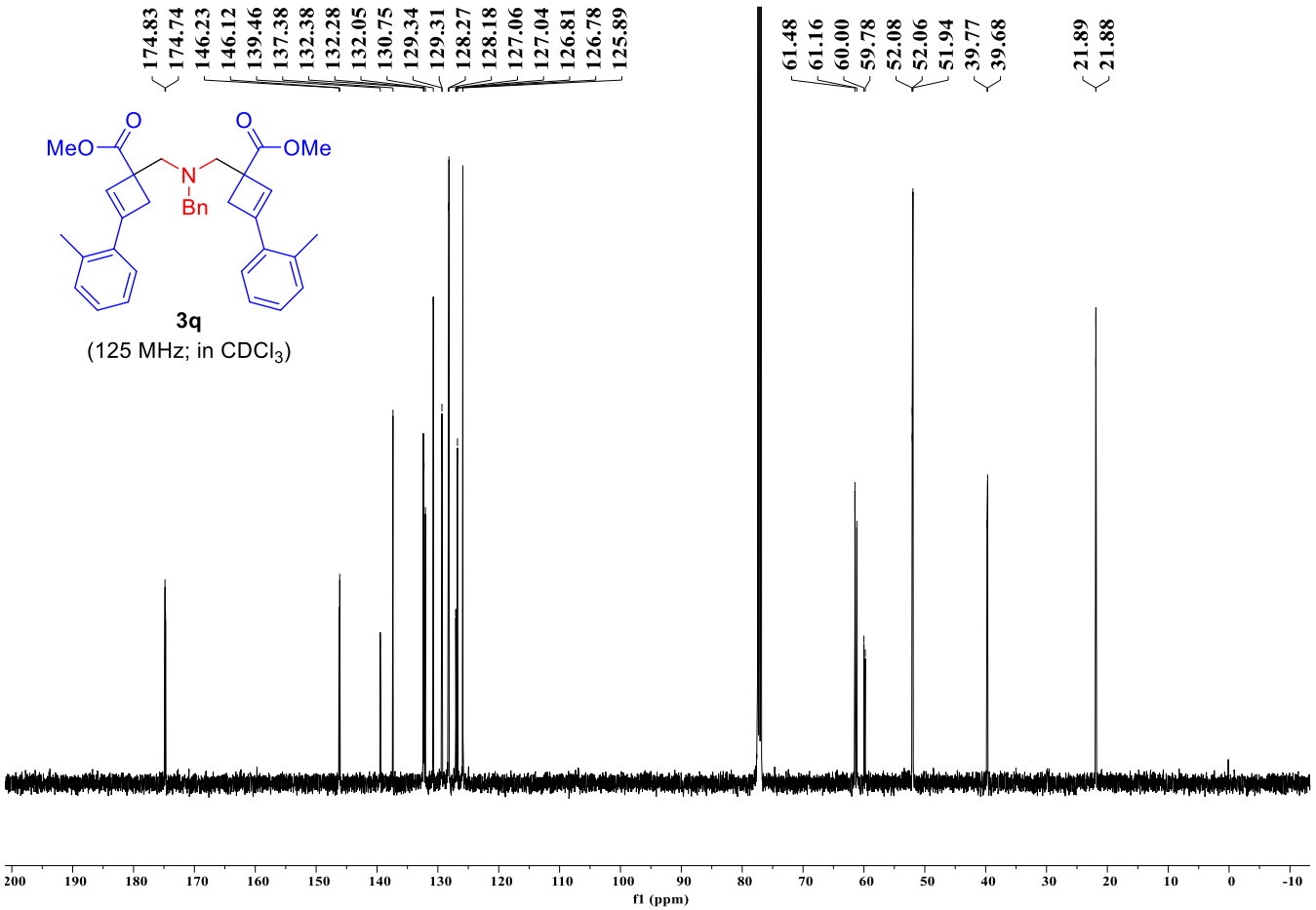

174.35
145.09 144.93 139.24 135.49 134.56 130.24 130.18 129.79 129.33 128.43 128.41 128.22 128.20 127.15 127.13 125.06 123.06
61.10 61.06 60.05 59.97 52.01 51.96 51.89 38.11 37.97
MeO
O
O
OMe
N
Bn
Cl
Cl
3o
(100 MHz; in CDCl3)
f1 (ppm)


7.36 7.36 7.35 7.34 7.34 7.33 7.32 7.32 7.28 7.27 7.26 7.25 7.25 7.24 7.24 7.22 7.20 7.13 7.12
3.73 3.70 3.66 3.64 3.62 3.59 3.17 3.16 3.14 3.12 3.11 3.11 3.08 3.08 2.98 2.95 2.74 2.72 2.70 2.69
MeO
O
O
OMe
N
Bn
F3CO
OCF3
3p
(400 MHz; in CDCl3)
2.13 7.25 3.92 1.94 8.05 4.00 2.00 1.97
f1 (ppm)

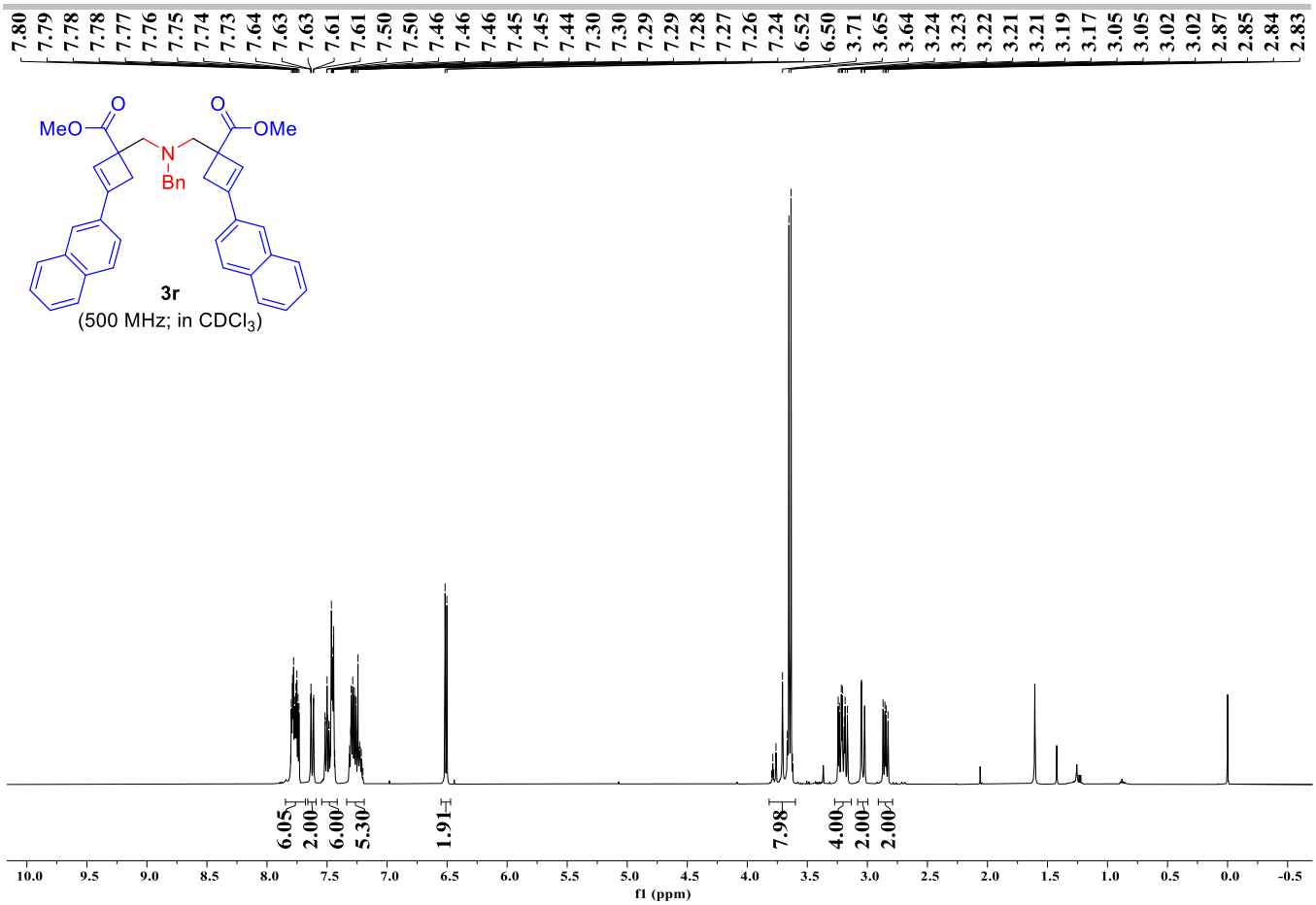

174.32 149.60 145.03 144.90 139.23 135.77 130.54 130.50 129.95 129.37 128.23 128.21 127.20 127.18 124.41 123.33 121.85 120.78 119.29 117.39 116.74
61.10 61.08 60.16 60.07 52.03 51.98 51.93 38.09 37.96
MeO
O
O
OMe
N
Bn
F3CO
OCF3
3p
(100 MHz; in CDCl3)
f1 (ppm)

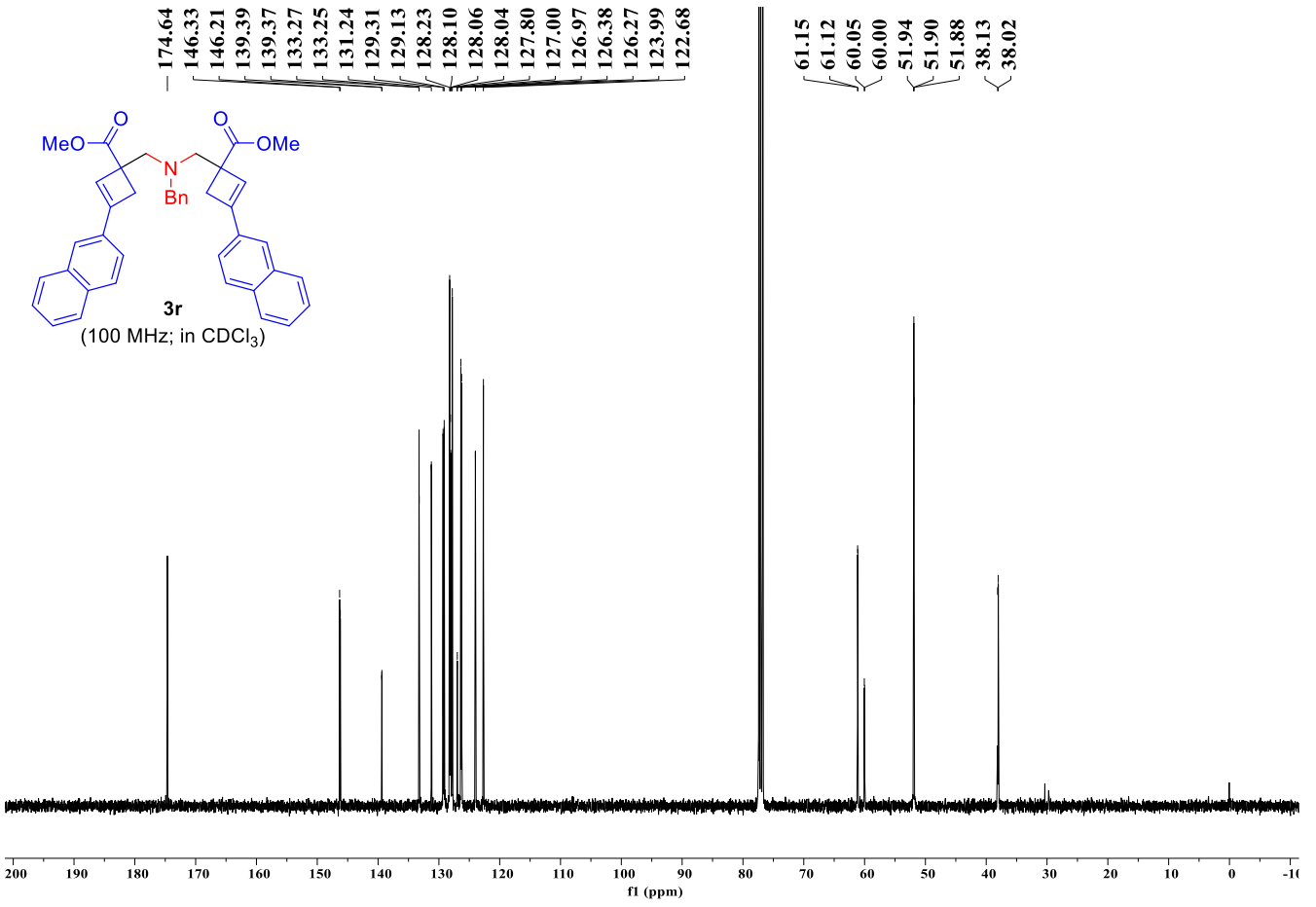


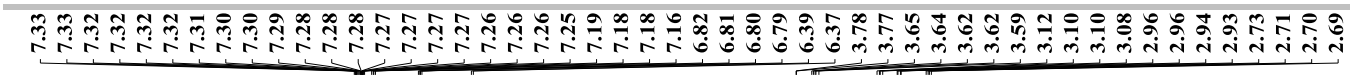
3q
(500 MHz; in $CDCl_3$)

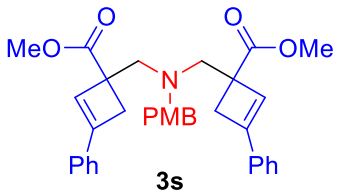


3q
(125 MHz; in $CDCl_3$)


7.80 7.79 7.78 7.78 7.77 7.76 7.75 7.74 7.73 7.64 7.63 7.63 7.61 7.61 7.50 7.50 7.46 7.46 7.46 7.45 7.45 7.44 7.30 7.30 7.29 7.29 7.28 7.27 7.26 7.24 6.52 6.50 3.71 3.65 3.64 3.24 3.23 3.22 3.21 3.21 3.19 3.17 3.05 3.05 3.02 3.02 2.87 2.85 2.84 2.83
MeO
O
O
OMe
N
Bn
3r
(500 MHz; in CDCl3)
6.05 2.00 6.00 5.30 1.91 7.98 4.00 2.00 2.00
f1 (ppm)

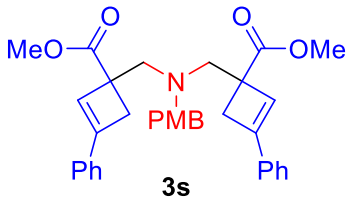

174.64 146.33 146.21 139.39 139.37 133.27 133.25 131.24 129.31 129.13 128.23 128.10 128.06 128.04 127.80 127.00 126.97 126.38 126.27 123.99 122.68
61.15 61.12 60.05 60.00 51.94 51.90 51.88 38.13 38.02
MeO
O
O
OMe
N
Bn
3r
(100 MHz; in CDCl3)
f1 (ppm)





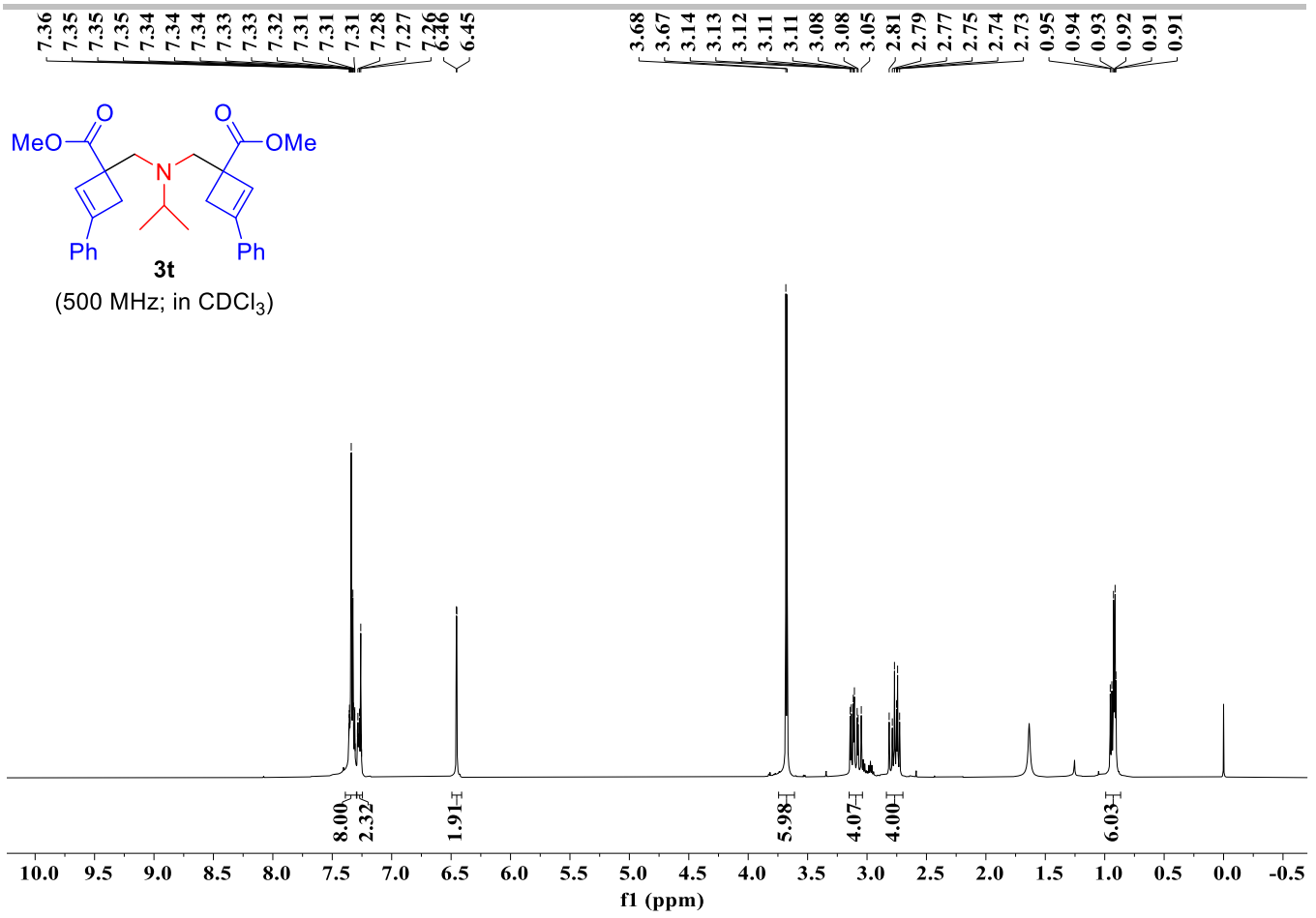
3s

(500 MHz; in $CDCl_3$)



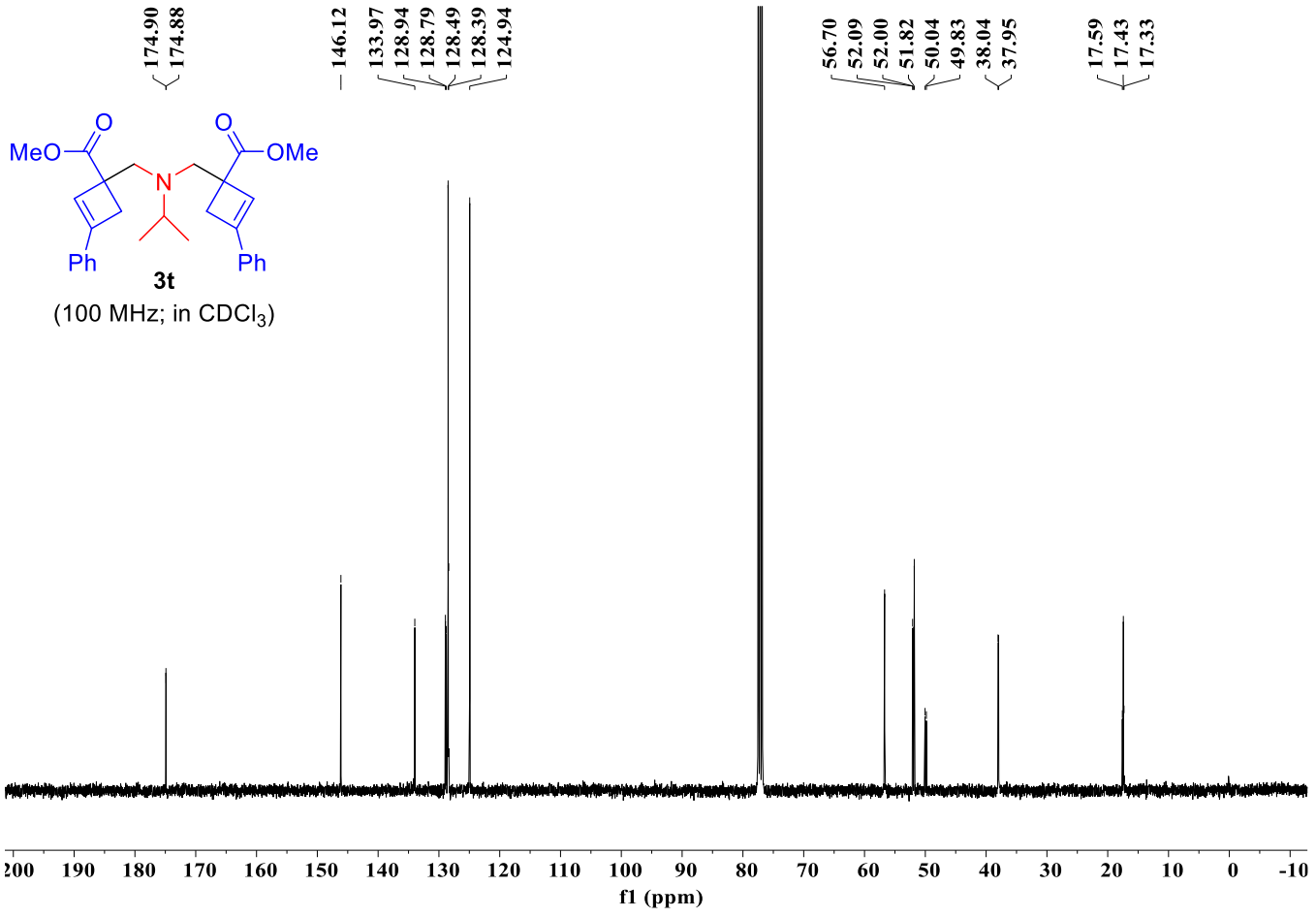
3s

(100 MHz; in $CDCl_3$)



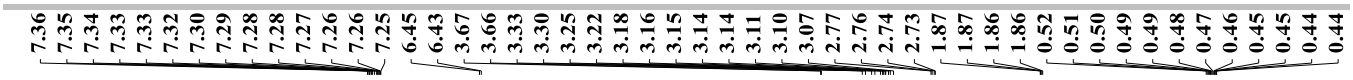
3t

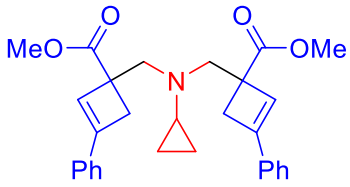
(500 MHz; in $CDCl_3$)



3t

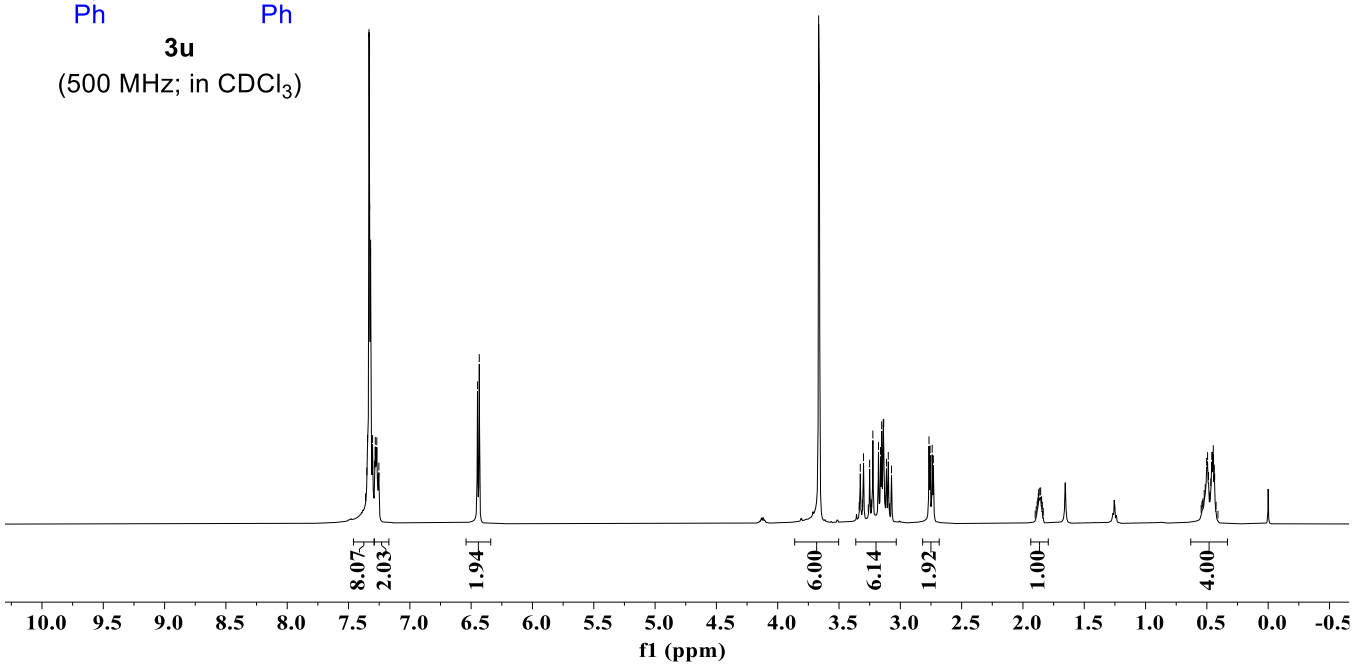
(100 MHz; in $CDCl_3$)

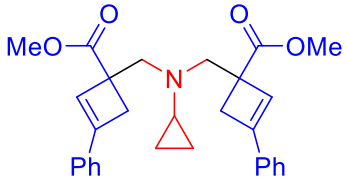




3u

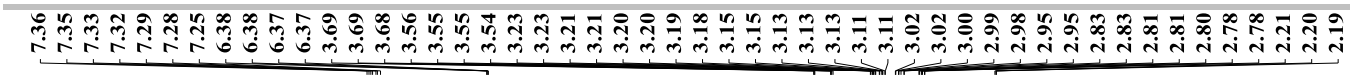
(500 MHz; in $CDCl_3$)

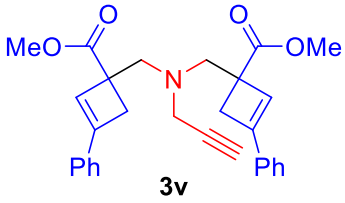




3u

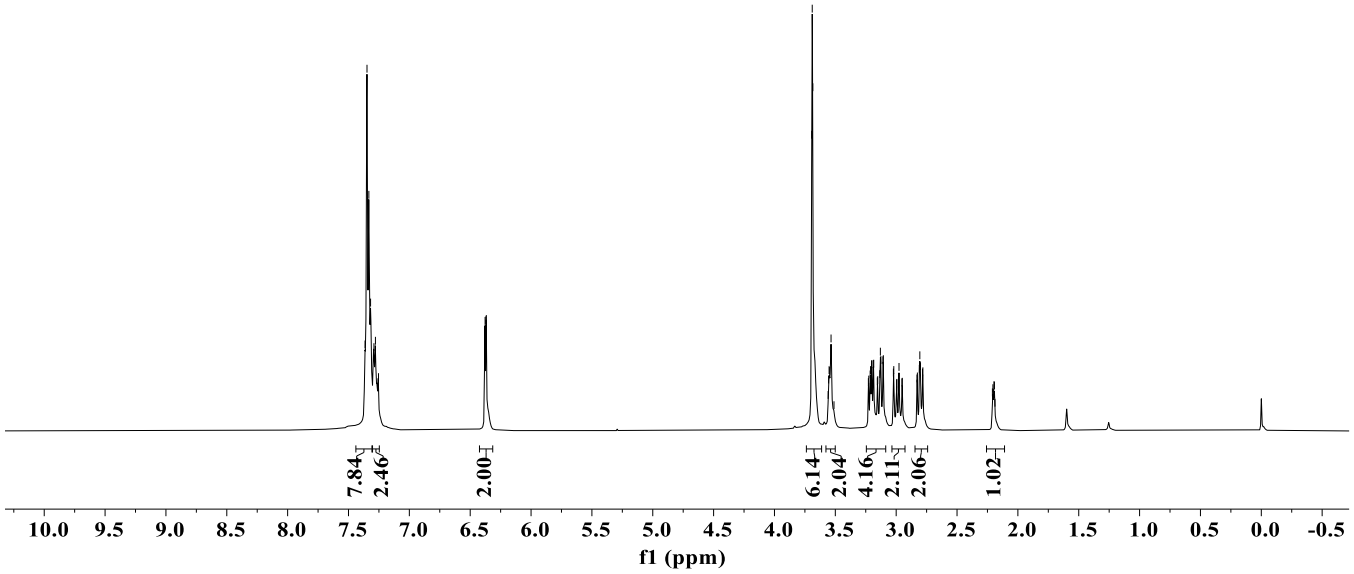
(125 MHz; in $CDCl_3$)

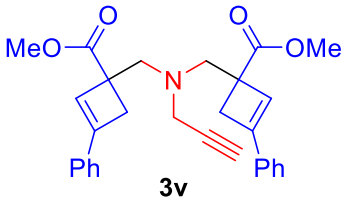




3v

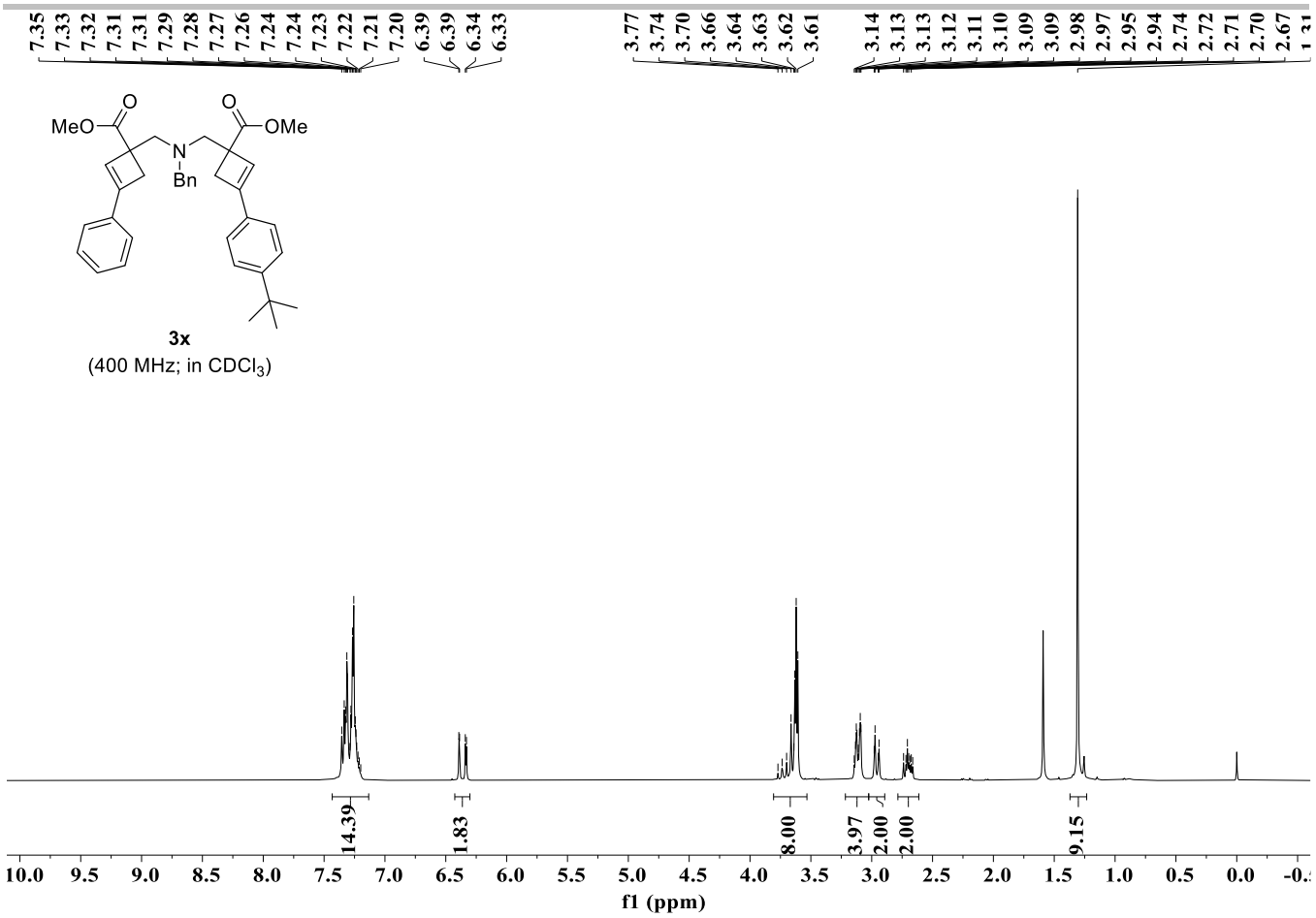
(500 MHz; in $CDCl_3$)



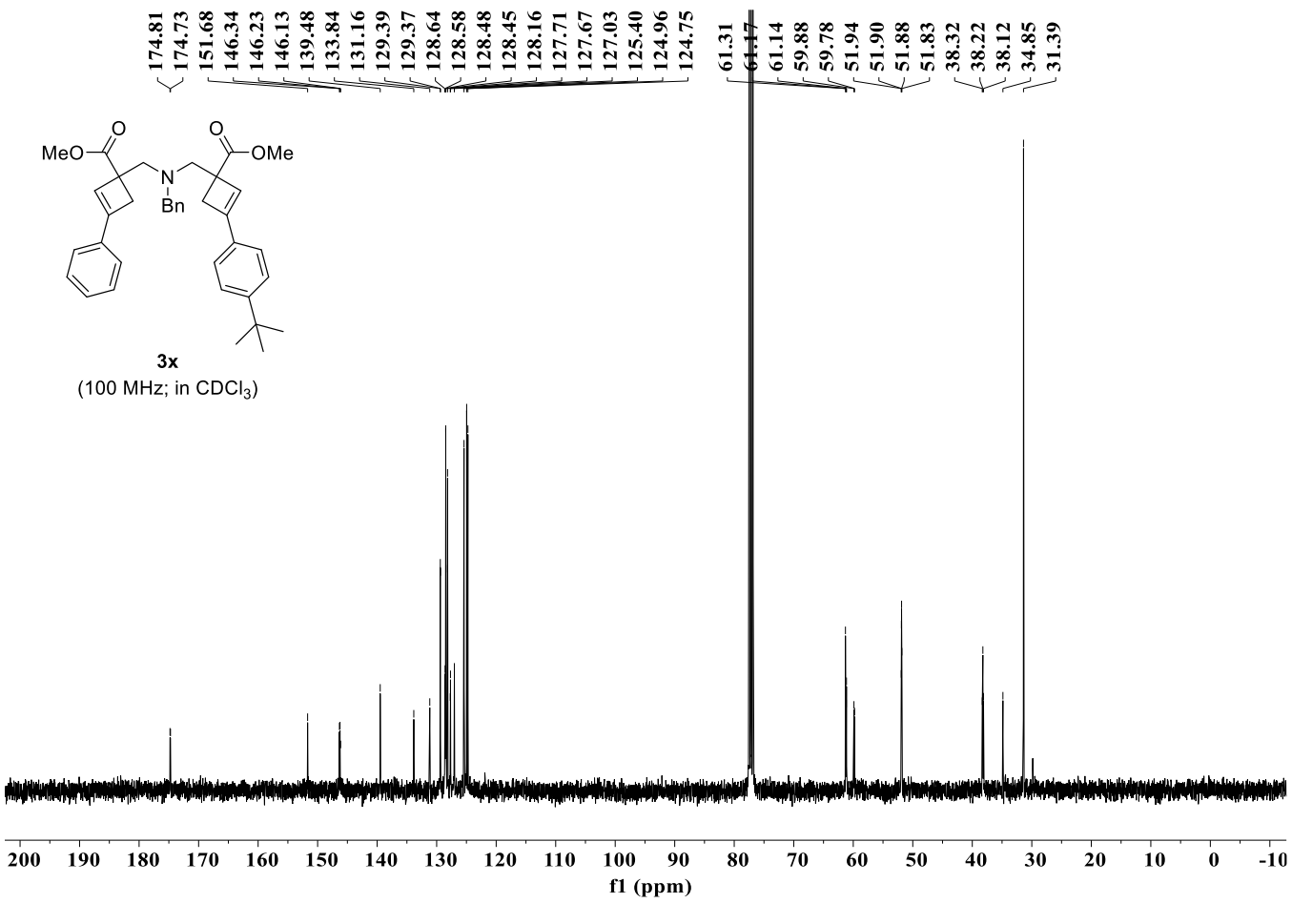


3v

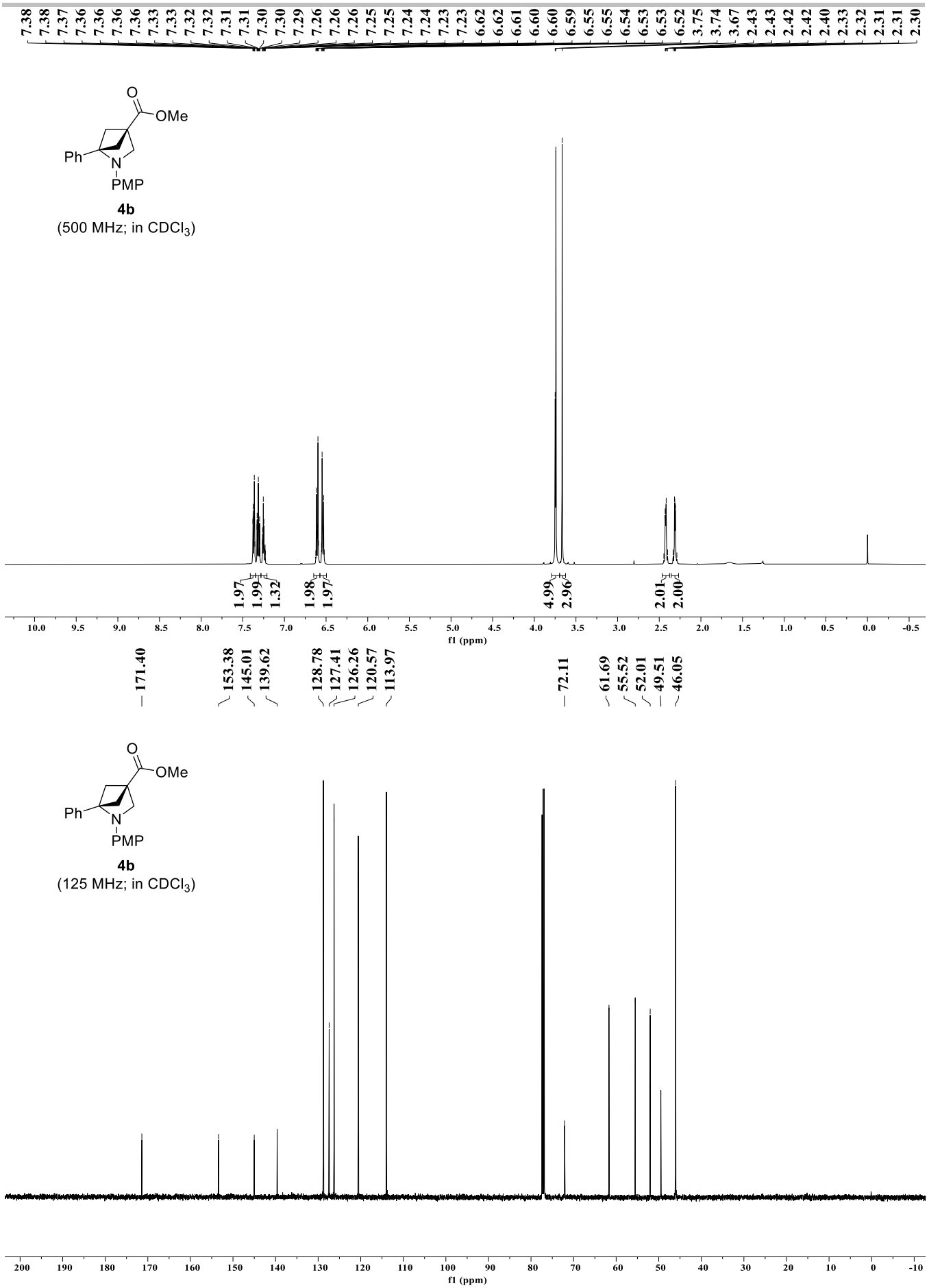
(125 MHz; in $CDCl_3$)

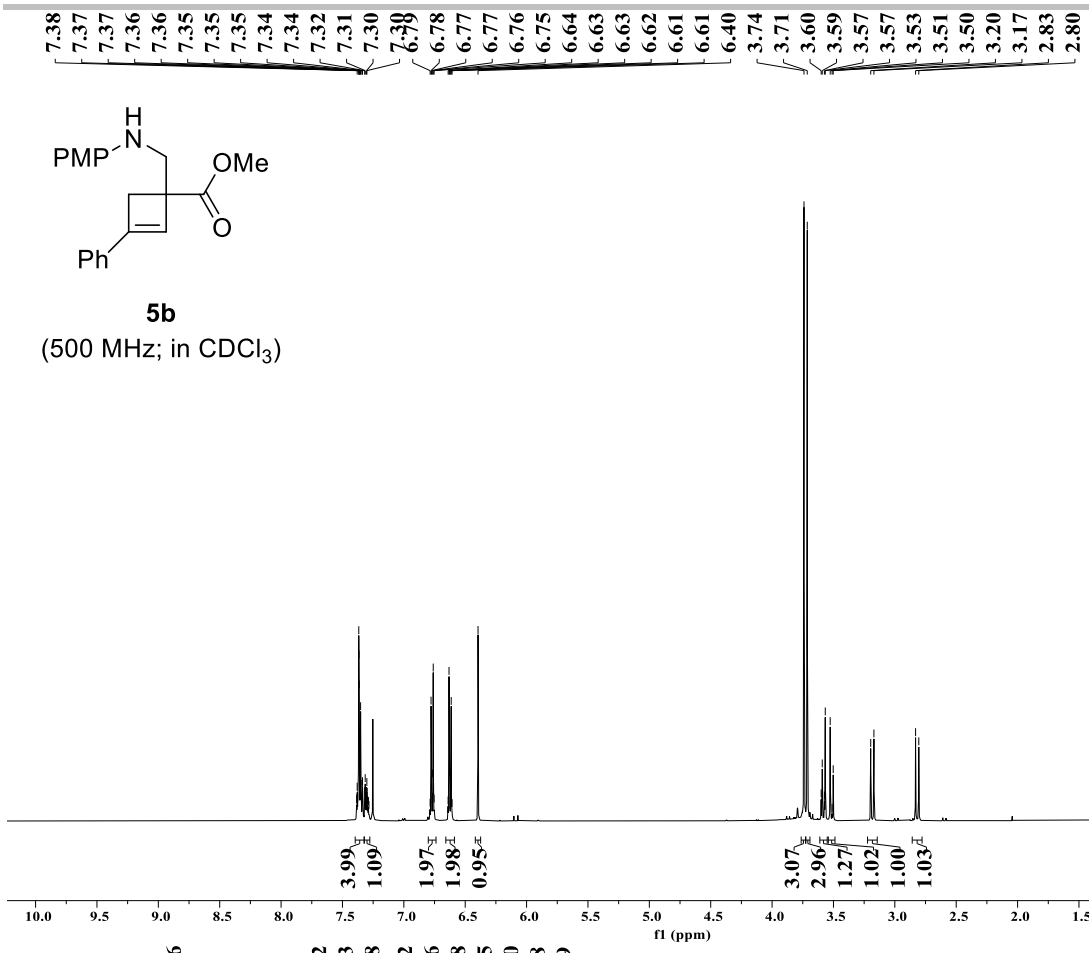


3x
(400 MHz; in $CDCl_3$)

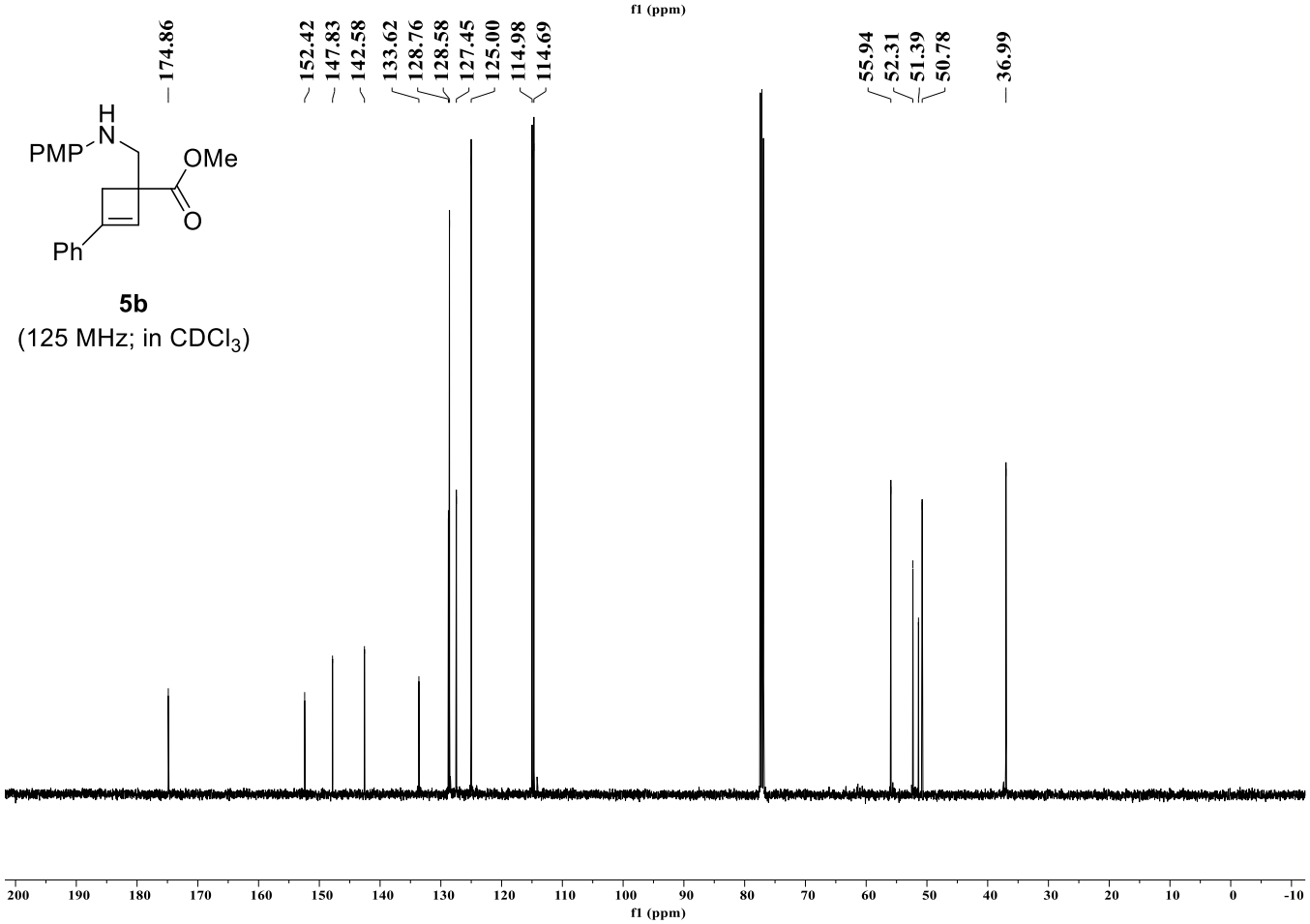


3x
(100 MHz; in $CDCl_3$)

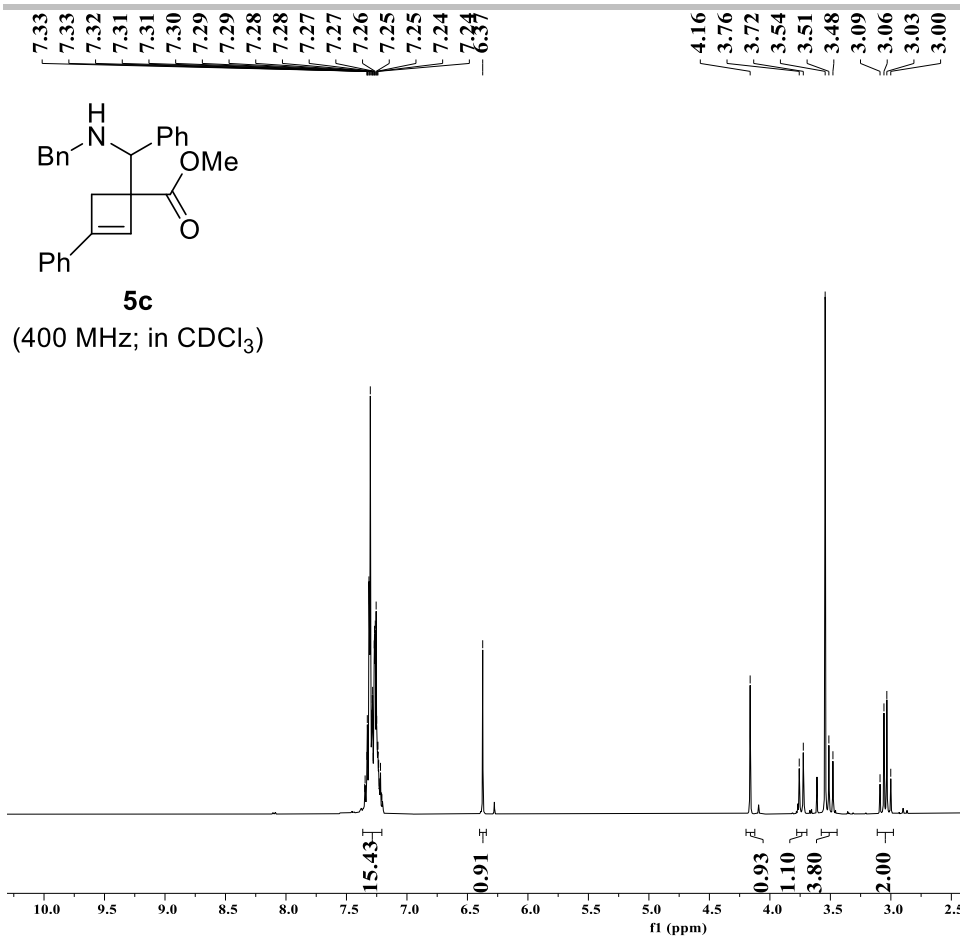

7.38 7.38 7.37 7.36 7.36 7.36 7.36 7.33 7.33 7.32 7.32 7.31 7.31 7.30 7.30 7.29 7.26 7.26 7.26 7.25 7.25 7.24 7.24 7.23 7.23 6.62 6.62 6.61 6.60 6.60 6.59 6.55 6.55 6.54 6.53 6.53 6.52 3.75 3.74 3.67 2.43 2.43 2.42 2.42 2.40 2.33 2.32 2.31 2.31 2.30
O
OMe
Ph
N
PMP
4b
(500 MHz; in CDCl3)
1.97 1.99 1.32 1.98 1.97 4.99 2.96 2.01 2.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
171.40 153.38 145.01 139.62 128.78 127.41 126.26 120.57 113.97 72.11 61.69 55.52 52.01 49.51 46.05
O
OMe
Ph
N
PMP
4b
(125 MHz; in CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



5b
(500 MHz; in $CDCl_3$)

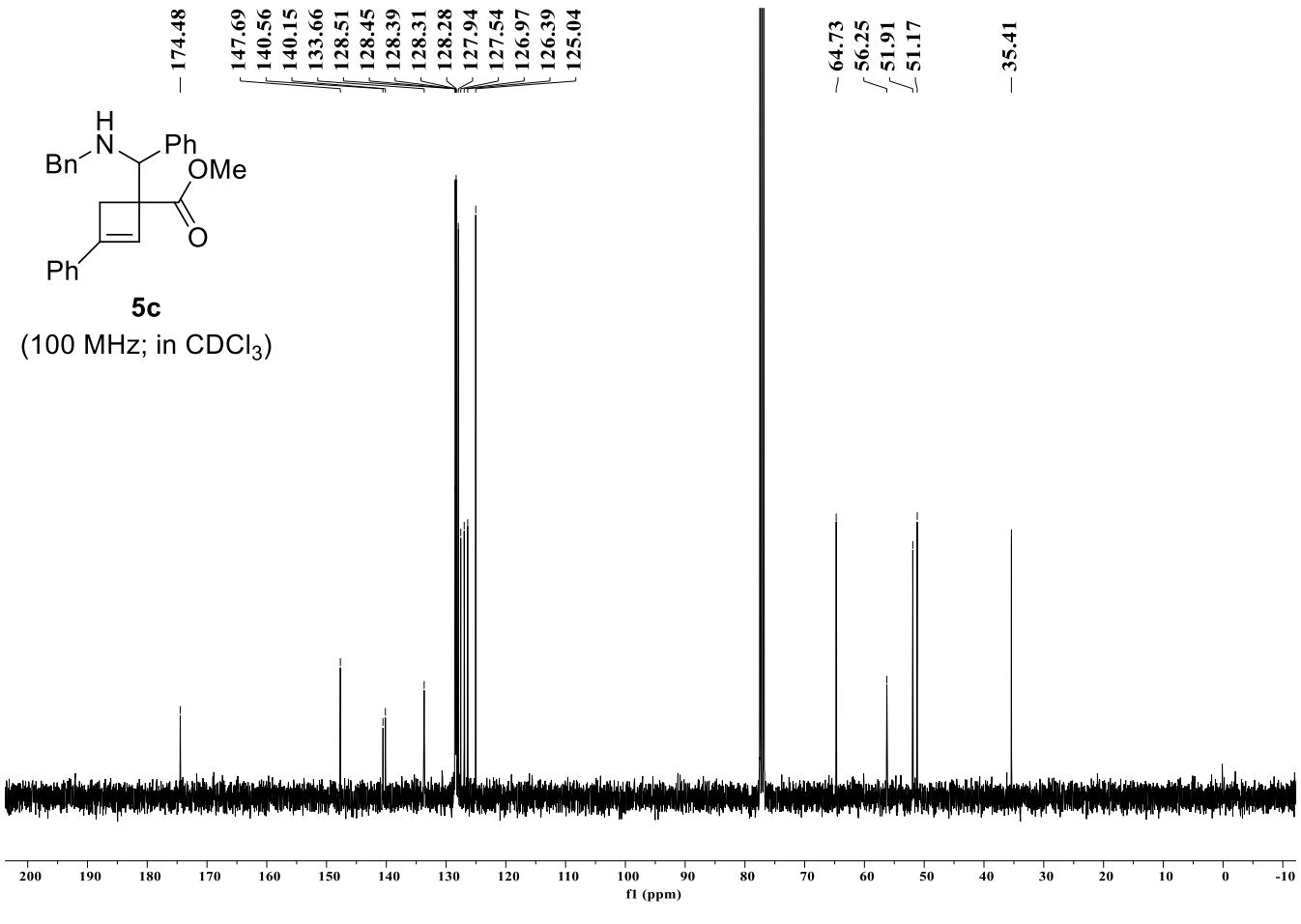


5b
(125 MHz; in $CDCl_3$)



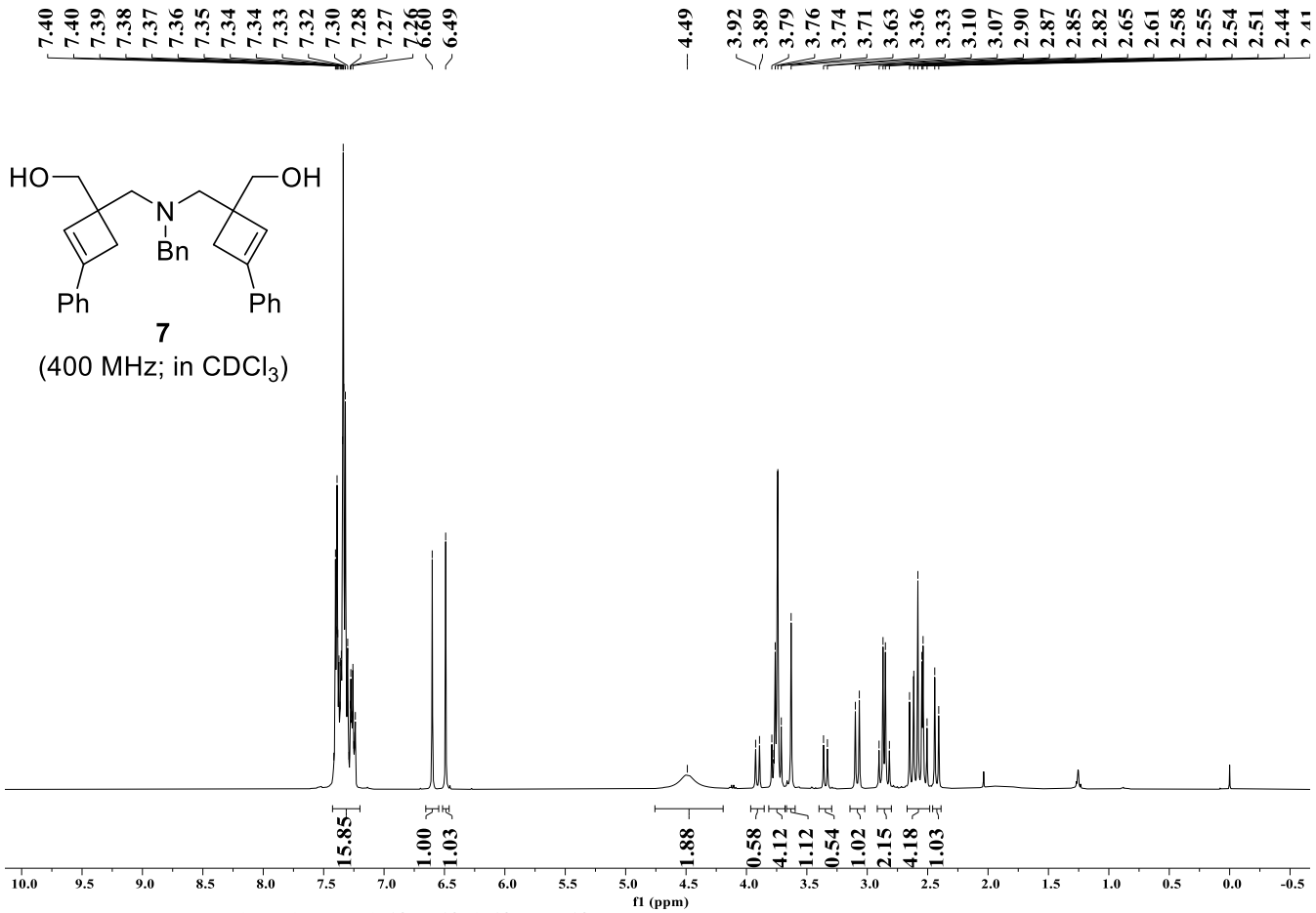
5c

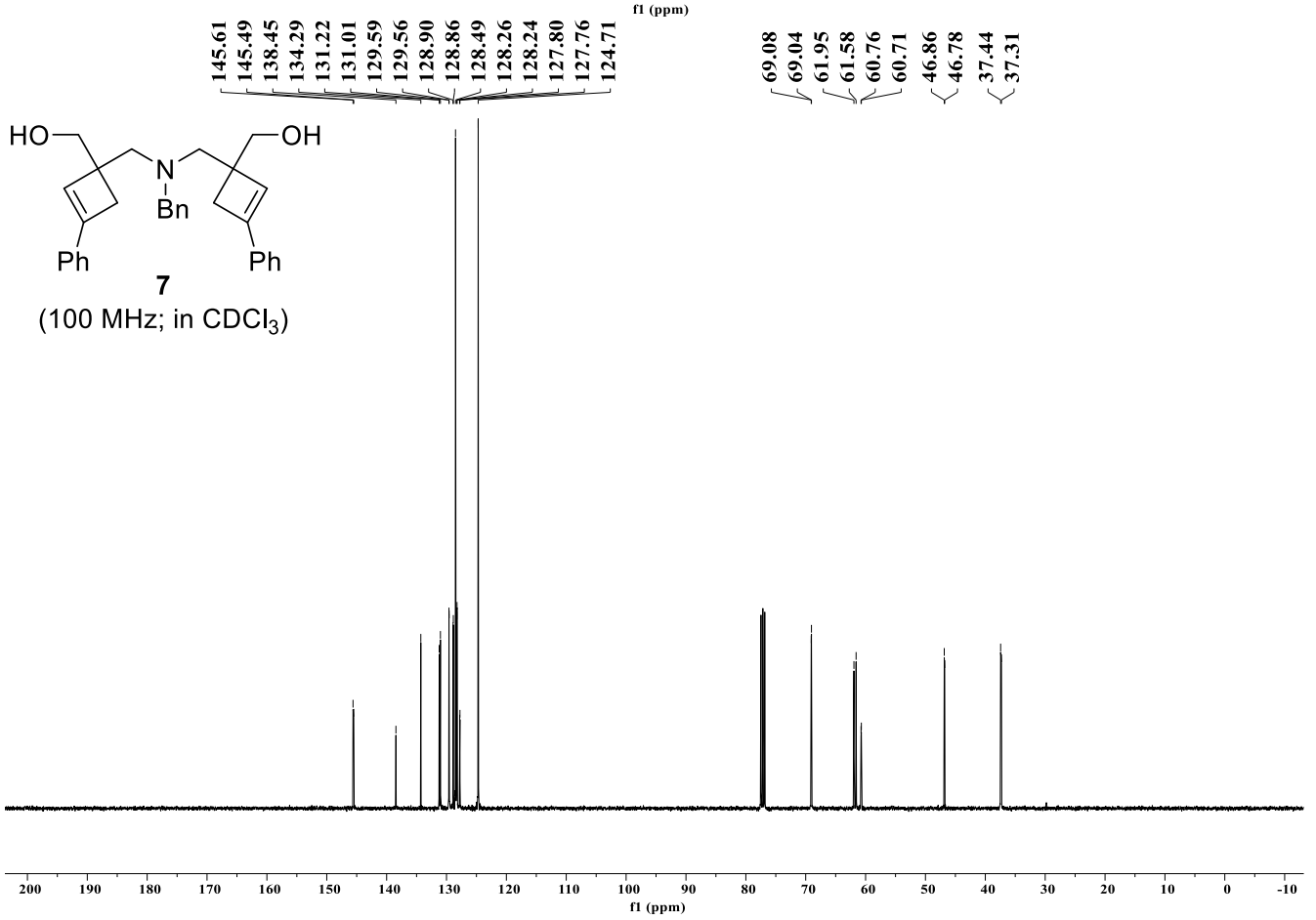
(400 MHz; in $CDCl_3$)



5c

(100 MHz; in $CDCl_3$)


7.40
7.40
7.39
7.38
7.37
7.36
7.35
7.34
7.34
7.33
7.32
7.30
7.28
7.27
7.26
6.60
6.49
4.49
3.92
3.89
3.79
3.76
3.74
3.71
3.63
3.36
3.33
3.10
3.07
2.90
2.87
2.85
2.82
2.65
2.61
2.58
2.55
2.54
2.51
2.44
HO
OH
N
Bn
Ph
Ph
7
(400 MHz; in CDCl3)
15.85
1.00
1.03
1.88
0.58
4.12
1.12
0.54
1.02
2.15
4.18
1.03
f1 (ppm)


145.61
145.49
138.45
134.29
131.22
131.01
129.59
129.56
128.90
128.86
128.49
128.26
128.24
127.80
127.76
124.71
69.08
69.04
61.95
61.58
60.76
60.71
46.86
46.78
37.44
37.31
HO
OH
N
Bn
Ph
Ph
7
(100 MHz; in CDCl3)
f1 (ppm)