Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Access to Chiral Cyano-Containing Five-Membered Rings Through Enantioconvergent Rhodium-Catalyzed Cascade Cyclization of Diastereoisomeric *E*/*Z* Mixture of 1,6-Enynes

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Supporting Information

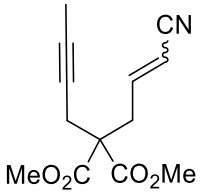
Table of contents

I. General information

All reactions were performed under an argon atmosphere. Reaction vessels were oven-dried, cooled under vacuum and flushed with argon before use. MeOH and 1,4-dioxane were distilled over sodium, water was distilled, DCM and THF was dried over alumina columns in an Innovative Technologies apparatus. All the solvents for catalysis were degassed prior to use. Reagents were obtained from commercial suppliers and used without further purification.
Reactions were monitored by thin layer chromatography (TLC) carried out on silica gel plates (Merck Kieselgel 60 F254); spots were detected with UV light and/or by staining with $KMnO_4$ solution. Flash column chromatography was performed on silica gel (Merck, spherical, neutral, 40-60 µm).
^{1}H NMR, ^{19}F NMR and $^{13}C\{^{1}H\}$ NMR were recorded on a Bruker Avance 400 instrument in $CDCl_3$. Chemical shifts are reported in delta (δ) units part per million (ppm). Residual $CHCl_3$ (δ 7.26) and $CDCl_3$ (δ 77.0) were used as internal standards for ^{1}H and ^{13}C NMR spectra respectively. Coupling constants (*J*) are reported in Hertz (Hz). The following abbreviations are used: s, singlet, d, doublet, t, triplet, q, quartet, m, multiplet, br, broad.
Enantiomeric excesses (ee) were determined by HPLC or SFC analyses using a Waters alliance e2695 system equipped with chiral stationary phase columns Daicel Chiralpak coupled with a dual wavelength (215/254 nm) Waters 2489 UV detector. Optical rotations were measured on a Perkin-Elmer 241 polarimeter (λ = 589 nm, Na lamp, 1 dm cell). High-resolution mass spectroscopic (HRMS) analyses were measured on LTQOrbitrap (Thermo Fisher Scientific) at Pierre et Marie Curie University. Melting points were measured with a Stuart Scientific melting point apparatus SMP1.
X-ray diffraction was made at Pierre et Marie Curie University. CCDC 1905851 contains the supplementary crystallographic data for compound **3ao**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

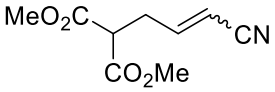
II. Synthesis of the starting materials

Dimethyl 2-(but-2-yn-1-yl)-2-(3-cyanoallyl)malonate (1a)



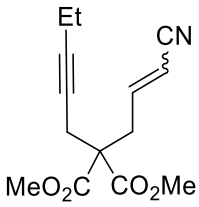
To a solution of dimethyl 2-(but-2-yn-1-yl)malonate (1.2 g, 6.5 mmol) in dry THF (25 mL) was added at 0 °C sodium hydride (1.15 g of a 60% suspension in mineral oil, 7.8 mmol) under argon. The mixture was stirred at room temperature for 0.5 h, then 4-bromobut-2-enenitrile (1.15 g, 7.8 mmol, mixture *E/Z* 1:2) was added and the reaction was stirred at room temperature for 3 h. The mixture was diluted with aq. HCl 1M and extracted with ethyl acetate. Combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude was purified by flash chromatography on silica gel (petroleum ether/EtOAc 9:1) to afford **1a** (1.02 g, 64 %) as a white oil in a *E*/*Z* 1.3:1 mixture.
R_f = 0.43 (petroleum ether/EtOAc 8:2).
^{1}H NMR (400 MHz, $CDCl_3$, δ): *E* isomer: 6.63 (dt, *J* = 16.2, 7.8 Hz, 1H), 5.45 (dt, *J* = 16.2, 1.5 Hz, 1H), 3.75 (s, 6H), 2.91 (dd, *J* = 7.8, 1.5 Hz, 2H), 2.74 (q, *J* = 2.6 Hz, 2H), 1.76 (t, *J* = 2.6 Hz, 3H). *Z* isomer: 6.47 (dt, *J* = 11.0, 7.8 Hz, 1H), 5.44 (dt, *J* = 11.0, 1.4 Hz, 1H), 3.76 (s, 6H), 3.14 (dd, *J* = 7.8, 1.4 Hz, 2H), 2.76 (q, *J* = 2.6 Hz, 2H), 1.79 (t, *J* = 2.6 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): *E* isomer: 169.6 (2C), 149.7, 116.8, 103.6, 80.1, 72.4, 56.7, 53.1 (2C), 36.4, 23.9, 3.5. *Z* isomer: 169.7 (2C), 148.6, 115.3, 102.9, 80.3, 72.3, 56.8, 53.1 (2C), 34.8, 24.0, 3.5.

Dimethyl 2-(3-cyanoallyl)malonate (S_1)



To a solution of dimethyl malonate (3.2 mL, 27.3 mmol) in dry THF (10 mL) was added at 0 °C sodium hydride (1.2 g of a 60% suspension in mineral oil, 30 mmol) under argon. The mixture was stirred at room temperature for 0.5 h, then 4-bromobut-2-enenitrile (4.3 g, 30 mmol, mixture *E/Z* 1:2) was added and the reaction was stirred at room temperature for 5 h. The mixture was diluted with aq. HCl 1M and extracted with ethyl acetate. Combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude was purified by flash chromatography on silica gel (petroleum ether/EtOAc 9:1) to afford **S_1** (2.7 g, 50 %) as a white oil in a *E*/*Z* 1:1.5 mixture.
R_f = 0.40 (petroleum ether/EtOAc 8:2).
^{1}H NMR (400 MHz, $CDCl_3$, δ): *E* isomer: 6.66 (dt, *J* = 16.3, 7.3 Hz, 1H), 5.45 (dt, *J* = 16.3, 1.6 Hz, 1H), 3.77 (s, 6H), 3.51 (t, *J* = 7.3 Hz, 1H), 2.80 (td, *J* = 7.3, 1.6 Hz, 2H). *Z* isomer: 6.53 (dt, *J* = 10.9, 7.3 Hz, 1H), 5.43 (dt, *J* = 10.9, 1.4 Hz, 1H), 3.78 (s, 6H), 3.55 (t, *J* = 7.3 Hz, 1H), 3.00 (td, *J* = 7.3, 1.4 Hz, 2H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): *E* isomer: 168.3 (2C), 150.5, 116.7, 102.8, 52.9 (2C), 49.9, 32.0. *Z* isomer: 168.3 (2C), 149.6, 115.2, 102.3, 52.9 (2C), 50.0, 30.5.

Dimethyl 2-(3-cyanoallyl)-2-(pent-2-yn-1-yl)malonate (1b)



To a solution of dimethyl 2-(3-cyanoallyl)malonate **S1** (600 mg, 3 mmol) in dry THF (10 mL) was added at 0 ºC sodium hydride (144 mg of a 60% suspension in mineral oil, 3.6 mmol) under argon. The mixture was stirred at room temperature for 0.5 h, then 1-bromopent-2-yne (522 mg, 3.6 mmol) was added and the reaction was stirred at room temperature for 3 h. The mixture was diluted with aq. HCl 1M and extracted with ethyl acetate. Combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude was purified by flash chromatography on silica gel (petroleum ether/EtOAc 9:1) to afford **1b** (629 mg, 79 %) as a white oil in a *E*/*Z* 1:1.5 mixture.

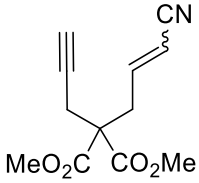
R_f = 0.54 (petroleum ether/EtOAc 8:2).

^{1}H NMR (400 MHz, $CDCl_3$, δ): *E* isomer: 6.64 (dt, *J* = 16.0, 7.7 Hz, 1H), 5.46 (dt, *J* = 16.0, 1.5 Hz, 1H), 3.76 (s, 6H), 2.92 (dd, *J* = 7.7, 1.5 Hz, 2H), 2.76 (t, *J* = 2.4 Hz, 2H), 2.20–2.09 (m, 2H), 1.10 (t, *J* = 7.7 Hz, 3H).

Z isomer: 6.49 (dt, *J* = 10.9, 7.7 Hz, 1H), 5.44 (dt, *J* = 10.9, 1.5 Hz, 1H), 3.77 (s, 6H), 3.15 (dd, *J* = 7.7, 1.5 Hz, 2H), 2.78 (t, *J* = 2.4 Hz, 2H), 2.20–2.09 (m, 2H), 1.10 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$, δ): *E* isomer: 169.6 (2C), 149.7, 116.8, 103.6, 86.2, 72.7, 56.8, 53.0 (2C), 36.5, 23.9, 14.1, 12.3. *Z* isomer: 169.7 (2C), 148.7, 115.3, 102.8, 86.3, 72.6, 56.9, 53.0 (2C), 34.8, 24.1, 14.0, 12.3.

Dimethyl 2-(3-cyanoallyl)-2-(prop-2-yn-1-yl)malonate (1c)



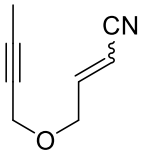
To a solution of dimethyl 2-(3-cyanoallyl)malonate **S1** (600 mg, 3 mmol) in dry THF (10 mL) was added at 0 ºC sodium hydride (144 mg of a 60% suspension in mineral oil, 3.6 mmol) under argon. The mixture was stirred at room temperature for 0.5 h, then propargyl bromide (0.4 mL of a 80 wt. % in toluene, 3.6 mmol) was added and the reaction was stirred at room temperature for 3 h. The mixture was diluted with aq. HCl 1M and extracted with ethyl acetate. Combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude was purified by flash chromatography on silica gel (petroleum ether/EtOAc 9:1) to afford **1c** (578 mg, 82 %) as a white oil in a *E*/*Z* 1:1.3 mixture.

R_f = 0.48 (petroleum ether/EtOAc 8:2).

^{1}H NMR (400 MHz, $CDCl_3$, δ): *E* isomer: 6.62 (dt, *J* = 16.2, 7.8 Hz, 1H), 5.49 (dt, *J* = 16.2, 1.7 Hz, 1H), 3.78 (s, 6H), 2.95 (dd, *J* = 7.8, 1.7 Hz, 2H), 2.81 (d, *J* = 2.7 Hz, 2H), 2.08 (t, *J* = 2.7 Hz, 1H). *Z* isomer: 6.50 (dt, *J* = 11.0, 7.8 Hz, 1H), 5.46 (dt, *J* = 11.0, 1.4 Hz, 1H), 3.79 (s, 6H), 3.17 (dd, *J* = 7.8, 1.4 Hz, 2H), 2.85 (d, *J* = 2.7 Hz, 2H), 2.10 (t, *J* = 2.7 Hz, 1H).

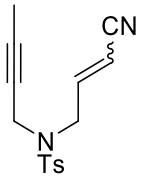
^{13}C NMR (101 MHz, $CDCl_3$, δ): *E* isomer: 169.2 (2C), 149.1, 116.7, 104.0, 77.7, 72.5, 56.3, 53.2 (2C), 36.3, 23.5. *Z* isomer: 169.4 (2C), 148.2, 115.2, 103.2, 77.8, 72.7, 56.5, 53.2 (2C), 34.8, 23.7.

***N*-(but-2-yn-1-yl)-*N*-(3-cyanoallyl)-4-methylbenzenesulfonamide (5a)**



In a round-bottom flask equipped with a reflux condenser was added IBX (3.6 g, 13 mmol) to a solution of 2-(but-2-yn-1-yloxy)ethan-1-ol[1] (988 mg, 8.7 mmol) dissolved in 35 mL of EtOAc. The resulting mixture was heated up to 80 °C for 5 h under vigorous stirring and filtered on a celite pad. The pad was washed with EtOAc and the filtrate was concentrated to dryness to afford the aldehyde. Under argon, the crude was dissolved in 20 mL of MeCN. Dry LiOH (314 mg, 13 mmol) was added and the mixture was cooled at 0 °C with an ice bath. Then, diethyl cyanomethylphosphonate (2.1 mL, 13 mmol) was added and the reaction was stirred at room temperature for 5 h. The mixture was diluted with aq. HCl 1M and extracted with ethyl acetate. Combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude was purified by flash chromatography on silica gel (petroleum ether/EtOAc 9:1) to afford **5a** (564 g, 48 %) as a colorless oil in a *E*/*Z* 2.4:1 mixture.
R_f = 0.35 (petroleum ether/EtOAc 8:2).
^{1}H NMR (400 MHz, $CDCl_3$, δ): *E* isomer: 6.74 (dt, *J* = 16.3, 3.8 Hz, 1H), 5.68 (dt, *J* = 16.3, 2.3 Hz, 1H), 4.19 (dd, *J* = 3.8, 2.3 Hz, 2H), 4.17 (q, *J* = 2.3 Hz, 2H), 1.86 (t, *J* = 2.3 Hz, 3H). *Z* isomer: 6.60 (dt, *J* = 11.2, 6.1 Hz, 1H), 5.47 (dt, *J* = 11.2, 1.8 Hz, 1H), 4.39 (dd, *J* = 6.1, 1.8 Hz, 2H), 4.16 (q, *J* = 2.4 Hz, 2H), 1.87 (t, *J* = 2.4 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): *E* isomer: 150.3, 117.2, 99.8, 83.6, 74.1, 67.7, 58.8, 3.5. *Z* isomer: 150.4, 115.0, 100.8, 83.8, 74.1, 67.4, 58.8, 3.5.

***N*-(but-2-yn-1-yl)-*N*-(3-cyanoallyl)-4-methylbenzenesulfonamide (5b)**

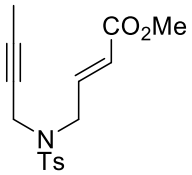


To a solution of *N*-(but-2-yn-1-yl)-4-methyl-*N*-(2-oxoethyl)benzenesulfonamide[2] (2.0 g, 7.5 mmol) in dry MeCN (45 mL) was added dry LiOH (237 mg, 9.75 mmol) under argon at room temperature. Then, diethyl cyanomethylphosphonate (1.46 mL, 9.0 mmol) was added and the reaction was stirred at room temperature for 5 hours. The mixture was diluted with aq. HCl 1M and extracted with ethyl acetate. Combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude was purified by flash chromatography on silica gel (petroleum ether/EtOAc 8:2) to afford **5b** (1.4 g, 64 %) as a yellow oil in a *E*/*Z* 3:1 mixture.
R_f = 0.24 (petroleum ether/EtOAc 8:2).
^{1}H NMR (400 MHz, $CDCl_3$, δ): *E* isomer: 7.78–7.68 (m, 2H), 7.41–7.29 (m, 2H), 6.62 (dt, *J* = 16.3, 5.4 Hz, 1H), 5.62 (dt, *J* = 16.3, 1.9 Hz, 1H), 4.00 (q, *J* = 2.5 Hz, 2H), 3.95 (dd, *J* = 5.4, 1.9 Hz, 2H), 2.44 (s, 3H), 1.58 (t, *J* = 2.5 Hz, 3H). *Z* isomer: 7.84–7.59 (m, 2H), 7.40–7.27 (m, 2H), 6.53 (dt, *J* = 11.0, 6.8 Hz, 1H), 5.50 (dt, *J* = 11.0, 1.7 Hz, 1H), 4.12 (dd, *J* = 6.8, 1.7 Hz, 2H), 4.00 (q, *J* = 2.4 Hz, 2H), 2.44 (s, 3H), 1.58 (t, *J* = 2.5 Hz, 3H).

[1] Zhao, L.; Lu, X.; Xu, W. *J. Org. Chem.* **2005**, *70*, 4059-4063.
[2] Tsukamoto, H.; Ueno, T.; Kondo, Y., *J. Am. Chem. Soc.* **2006**, *128*, 1406.

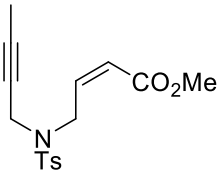
^{13}C NMR (101 MHz, $CDCl_3$, δ): *E* isomer: 148.8, 144.0, 135.4, 129.6 (2C), 127.8 (2C), 116.5, 102.7, 82.7, 71.1, 47.8, 37.9, 21.6, 3.3. *Z* isomer: 149.3, 144.0, 135.4, 129.6 (2C), 127.9 (2C), 116.5, 102.4, 82.7, 71.1, 47.0, 38.2, 21.6, 3.3.

Methyl (*E*)-4-((*N*-(but-2-yn-1-yl)-4-methylphenyl)sulfonamido)but-2-enoate ((*E*)-5c)



To a solution of *N*-(but-2-yn-1-yl)-4-methyl-*N*-(2-oxoethyl)benzenesulfonamide[2] (2.0 g, 7.5 mmol) in dry MeCN (45 mL) was added dry LiOH (237 mg, 9.75 mmol) under argon at room temperature. Then, trimethyl phosphonoacetate (1.45 mL, 9.0 mmol) was added and the reaction was stirred at room temperature overnight. The mixture was diluted with aq. HCl 1M and extracted with EtOAc. Combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude was purified by flash chromatography on silica gel (petroleum ether/EtOAc 8:2) to afford **(*E*)-5c** (1.9 g, 79 %) as an orange oil. Spectroscopic data were identical to those reported in literature.[3]

Methyl (*Z*)-4-((*N*-(but-2-yn-1-yl)-4-methylphenyl)sulfonamido)but-2-enoate ((*Z*)-5c)



To a solution of methyl *P*,*P*-bis(2,2,2-trifluoroethyl)phosphonoacetate (0.95 mL, 4.5 mmol) in dry THF (25 mL) was added 18-crown-6 (4.95 g, 18.75 mmol). The mixture was cooled to -78 °C and a KHMDS solution (1M in THF, 4.5 mL, 4.5 mmol) was added dropwise under argon at -78 °C. After 30 min, a solution of *N*-(but-2-yn-1-yl)-4-methyl-*N*-(2-oxoethyl) benzenesulfonamide[2] (1.0 g, 3.75 mmol) in THF (20 mL) was added dropwise and the reaction mixture was allowed to gradually reach 0 °C. The mixture was quenched with aq. NH_4Cl and extracted with EtOAc several times. Combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The crude was purified by flash chromatography on silica gel (petroleum ether/EtOAc 8:2) to afford **(*Z*)-5c** (262 mg, 22 %) as a yellow oil.

R_f = 0.29 (petroleum ether/EtOAc 8:2).

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.89–7.61 (m, 2H), 7.34–7.28 (m, 2H), 6.31 (dt, *J* = 11.5, 5.8 Hz, 1H), 5.89 (dt, *J* = 11.5, 2.2 Hz, 1H), 4.42 (dd, *J* = 5.8, 2.2 Hz, 2H), 4.02 (t, *J* = 2.5 Hz, 2H), 3.71 (s, 3H), 2.43 (s, 3H), 1.57 (t, *J* = 2.5 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$, δ): 166.3, 146.3, 143.5, 135.8, 129.4 (2C), 127.8 (2C), 121.0, 81.9, 71.7, 51.4, 46.0, 38.4, 21.5, 3.3.

[3] Takimoto, M.; Mizuno, T.; Mori, M.; Sato, Y. *Tetrahedron* **2006**, *62*, 7589-7597.

III. Access to cyclopentane derivatives

A. General procedure (1) for the preparation of racemic cyclopentane derivatives

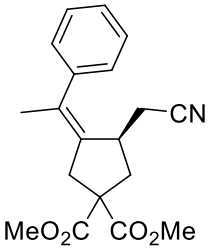
In a septum-capped vial, equipped with a magnetic stirring bar, were introduced $[Rh(cod)OH]_2$ 1.5 mol%, 2.25 µmol, 1.1 mg), the corresponding boronic acid (0.375 mmol) and the enyne **1** or **5** (0.15 mmol). The vial was closed, evacuated under vacuum and placed under argon atmosphere. Degassed MeOH was added and the resulting mixture was heated at 60 °C (preheated oil bath) until full consumption of the starting material. Solvents were removed under vacuum and the crude was purified by silica gel chromatography.

B. General procedure (2) for the preparation of chiral cyclopentane derivatives

In a septum-capped vial, equipped with a magnetic stirring bar, were introduced the chiral diene 2-Me-4-$MeOC_6H_3$-MSBod (3.3 mol%, 10.0 µmol, 2.9 mg) and $[Rh(C_2H_4)_2Cl]_2$ (1.5 mol%, 4.5 µmol, 1.8 mg). The vial was closed, evacuated under vacuum and placed under argon atmosphere. Degassed dichloromethane (0.2 mL) was added and the mixture was stirred for 15 min at room temperature. Then, a degassed solution of KOH in MeOH (50 µL, c = 0.22 M) was added, the solution was stirred for 15 min and solvents were removed under vacuum. The corresponding boronic acid (0.75 mmol) and the enyne **1** or **5** (0.30 mmol) were added to the dry residue, followed by degassed methanol (1 mL) and the resulting mixture was heated at 60 °C (preheated oil bath) until full conversion of the starting material. Solvents were removed under vacuum and the crude was purified by silica gel chromatography.

C. Characterization

Dimethyl (*R,Z*)-3-(cyanomethyl)-4-(1-phenylethylidene)cyclopentane-1,1-dicarboxylate 3aa



Colorless oil (86 mg, 88 %) obtained from the general procedure (2) using substrate **1a** (76 mg, 0.30 mmol) and phenylboronic acid (92 mg, 0.75 mmol).

R_f = 0.19 (petroleum ether/EtOAc 9:1).

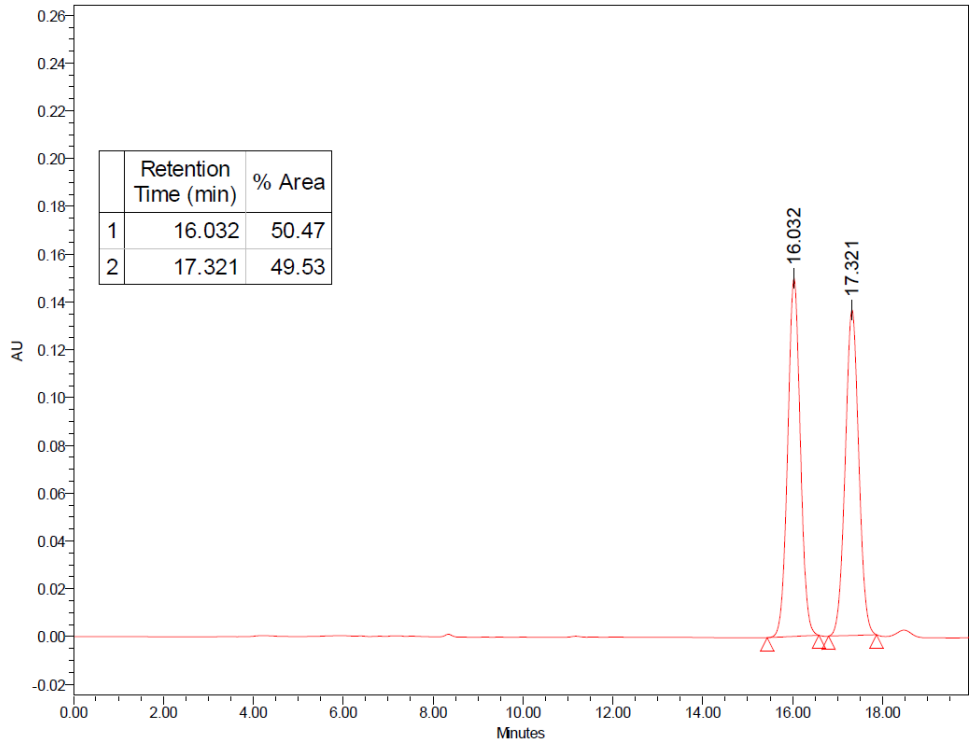
HPLC (Chiralpak IA, hexane/*i*PrOH 95:5, 0.5 mL/min): Rt = 15.9 min (major), 17.2 min (minor).

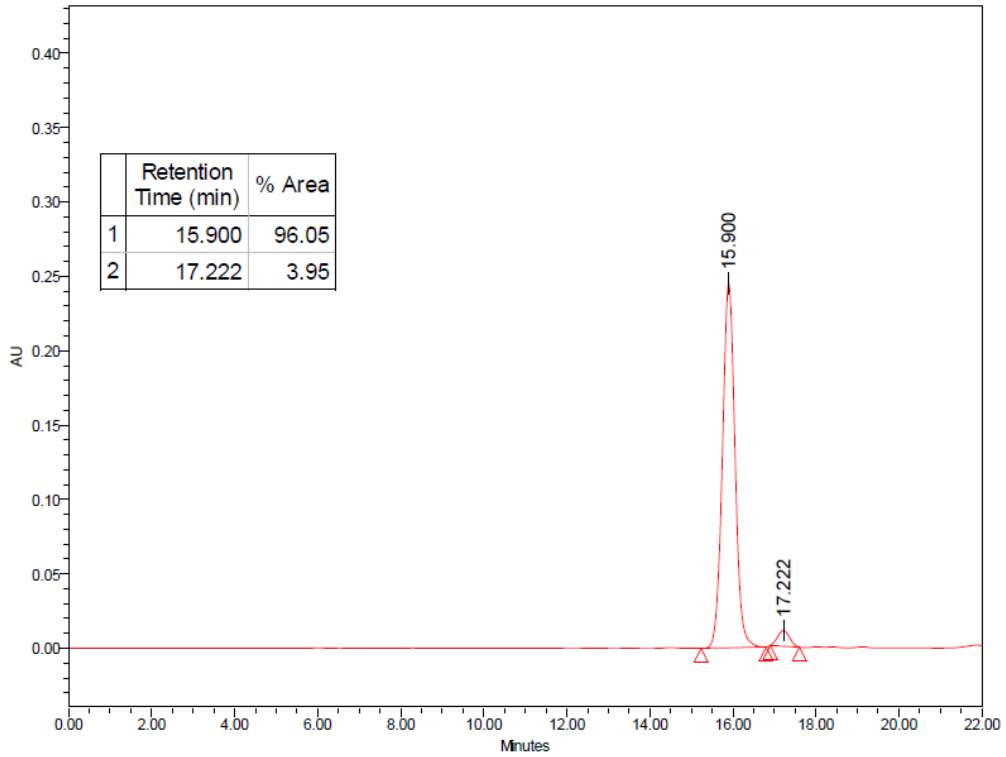
$[\alpha]_D^{20}$ = -53 (c = 0.68, $CHCl_3$) for an enantiomeric excess of 92 %.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.37–7.31 (m, 2H), 7.29–7.25 (m, 1H), 7.19–7.11 (m, 2H), 3.79 (s, 3H), 3.78 (s, 3H), 3.25–3.15 (m, 1H), 3.14 (d, *J* = 16.8 Hz, 1H), 3.05 (dt, *J* = 16.8, 2.0 Hz, 1H), 2.69 (ddd, *J* = 13.4, 8.5, 1.6 Hz, 1H), 2.11 (dd, *J* = 13.4, 8.5 Hz, 1H), 2.01–1.94 (m, 4H), 1.81 (dd, *J* = 16.8, 8.5 Hz, 1H).

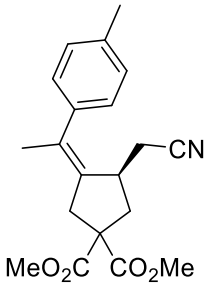
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.9, 171.6, 142.6, 134.5, 133.5, 128.8 (2C), 127.3 (2C), 127.2, 118.4, 58.4, 53.00, 52.96, 39.4, 39.3, 37.1, 22.7, 21.3.

HRMS (ESI): Calculated for $C_{19}H_{21}NO_4Na$ $(M+Na)^+$ 350.1368, found 350.1364.

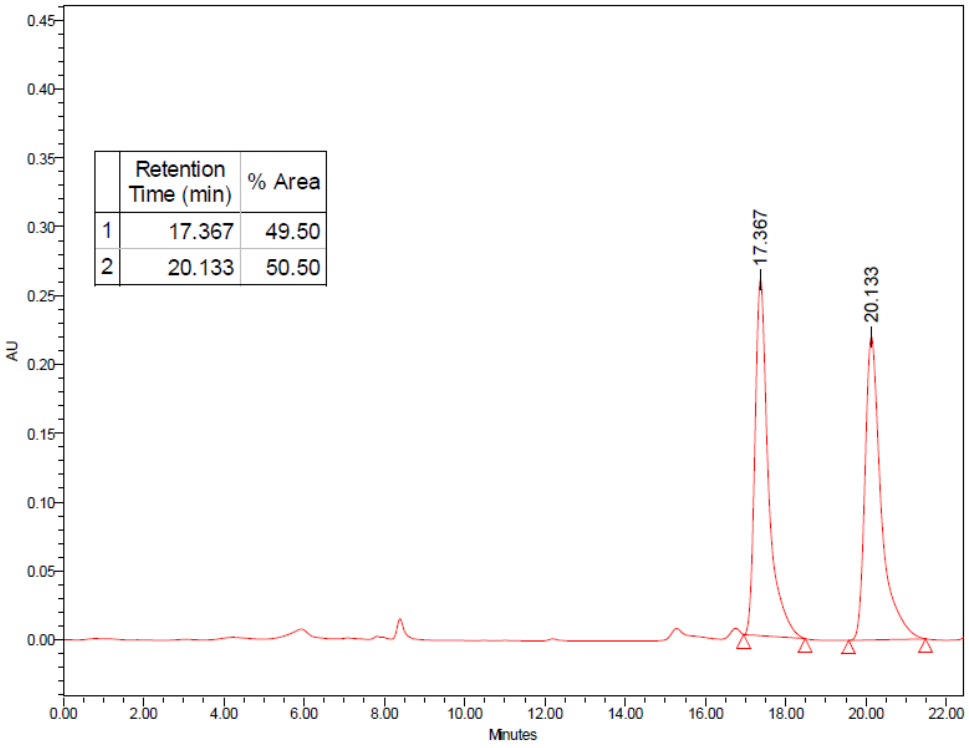


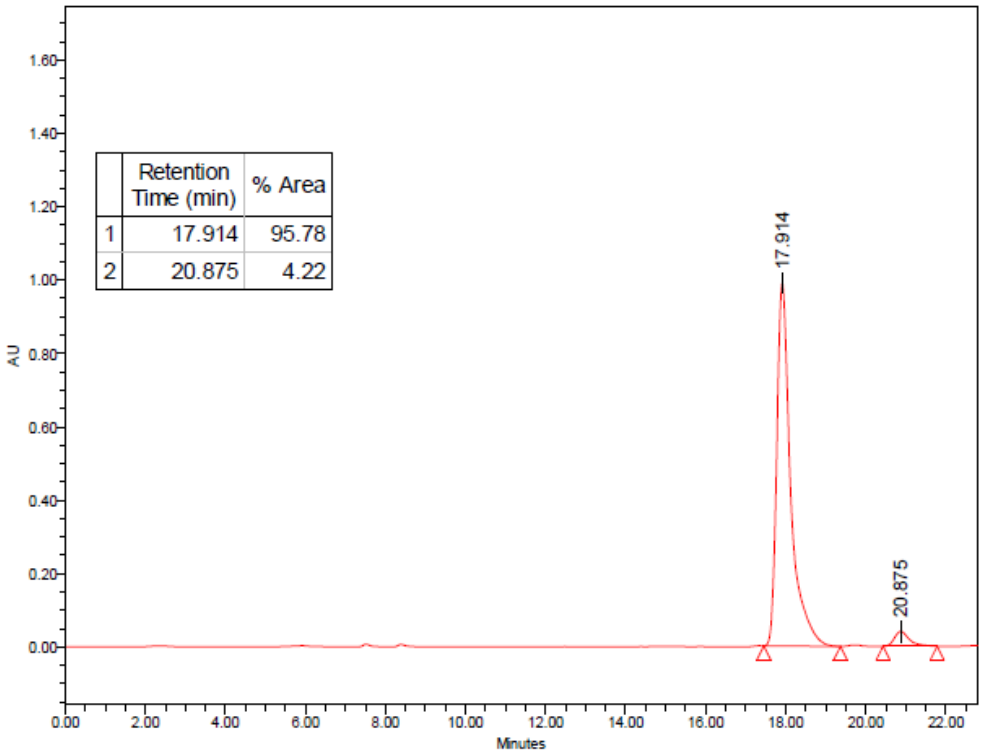


Dimethyl (*R*,*Z*)-3-(cyanomethyl)-4-(1-(*p*-tolyl)ethylidene)cyclopentane-1,1-dicarboxylate 3ab

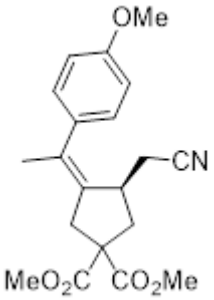


Colorless oil (81 mg, 79 %) obtained from the general procedure (2) using substrate **1a** (76 mg, 0.30 mmol) and *p*-tolylboronic acid (103 mg, 0.75 mmol).
R_f = 0.25 (petroleum ether/EtOAc 9:1).
HPLC (Chiralpak IA, hexane/*i*PrOH 97/3, 0.5 mL/min): Rt = 17.9 min (major), 20.9 min (minor).
$[\alpha]_D^{20}$ = -82 (c = 0.46, $CHCl_3$) for an enantiomeric excess of 92 %.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.17–7.11 (m, 2H), 7.05–6.98 (m, 2H), 3.79 (s, 3H), 3.77 (s, 3H), 3.28–3.16 (m, 1H), 3.12 (d, *J* = 16.8 Hz, 1H), 3.04 (dt, *J* = 16.8, 2.0 Hz, 1H), 2.69 (ddd, *J* = 13.4, 8.5, 1.6 Hz, 1H), 2.34 (s, 3H), 2.10 (dd, *J* = 13.4, 8.5 Hz, 1H), 2.04–1.94 (m, 4H), 1.84 (dd, *J* = 16.8, 8.5 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.8, 171.6, 139.6, 136.9, 134.2, 133.3, 129.5 (2C), 127.2 (2C), 118.5, 58.4, 52.99, 52.95, 39.38, 39.36, 37.2, 22.7, 21.3, 21.2.
HRMS (ESI): Calculated for $C_{20}H_{23}NO_4Na$ $(M+Na)^+$ 364.1525, found 364.1520.

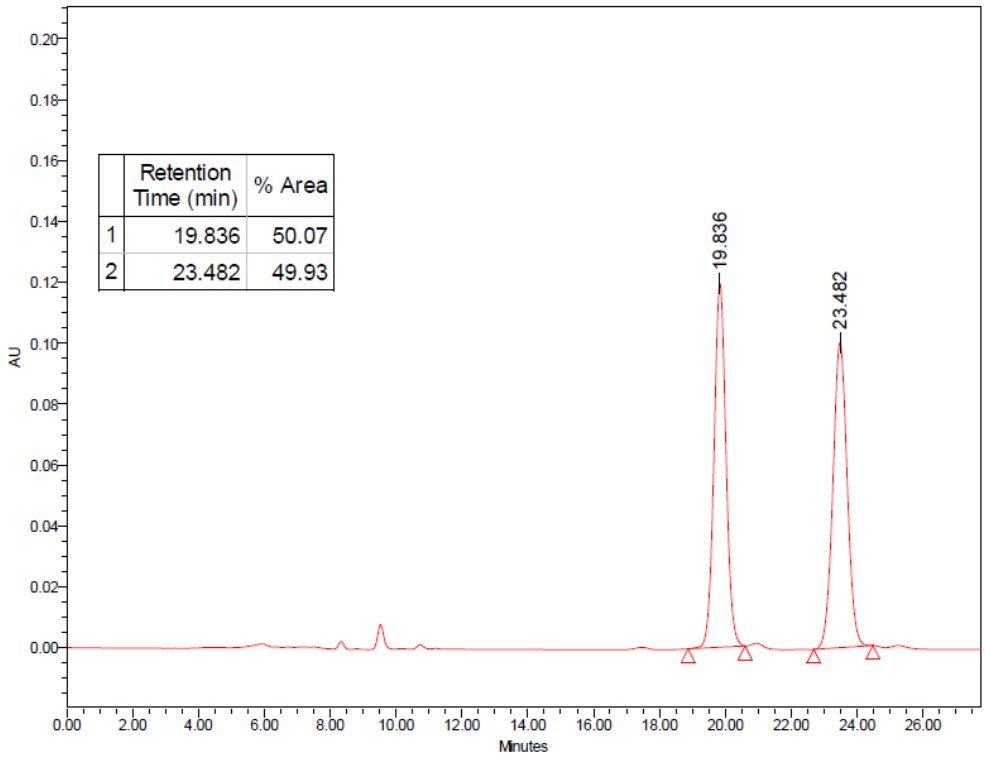


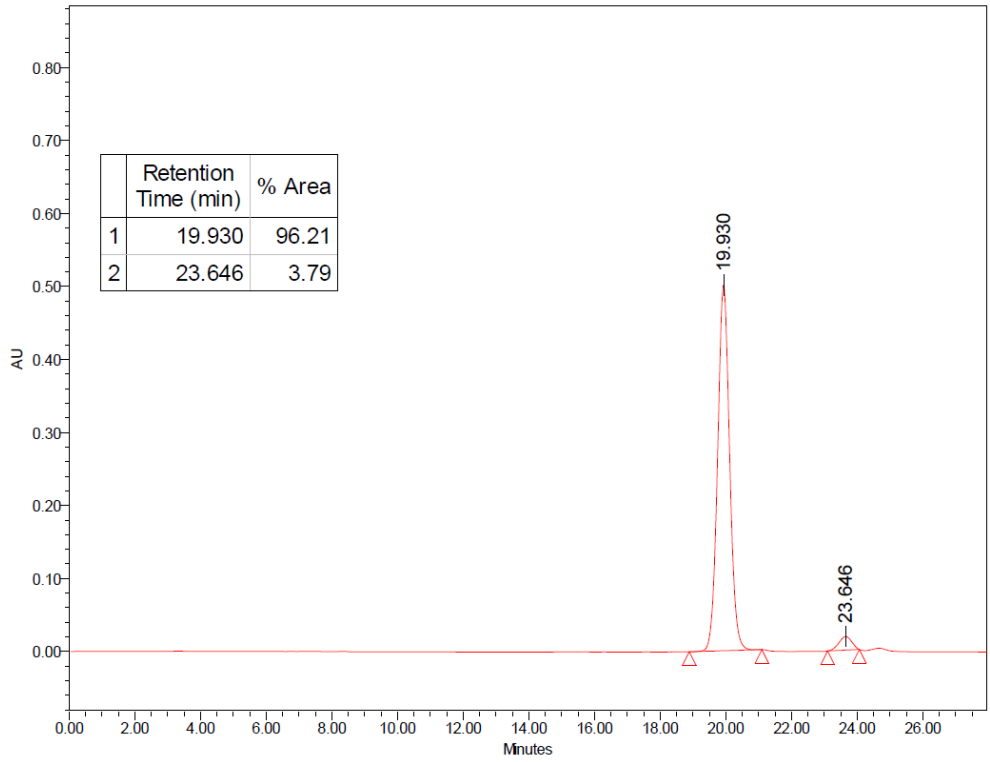


Dimethyl (*R*,*Z*)-3-(cyanomethyl)-4-(1-(4-methoxyphenyl)ethylidene)cyclopentane-1,1-dicarboxylate 3ac

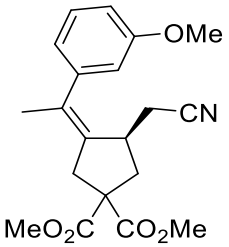


Colorless oil (98 mg, 92 %) obtained from the general procedure (2) using substrate **1a** (76 mg, 0.30 mmol) and 4-methoxyphenylboronic acid (114 mg, 0.75 mmol).
R_f = 0.13 (petroleum ether/EtOAc 9:1).
HPLC (Chiralpak IA, hexane/*i*PrOH 95:5, 0.5 mL/min): Rt = 19.9 min (major), 23.6 min (minor).
$[\alpha]_D^{20}$ = -91 (c = 0.57, $CHCl_3$) for an enantiomeric excess of 92 %.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.10–7.03 (m, 2H), 6.92–6.83 (m, 2H), 3.81 (s, 3H), 3.79 (s, 3H), 3.77 (s, 3H), 3.27–3.15 (m, 1H), 3.12 (d, *J* = 16.8 Hz, 1H), 3.03 (dt, *J* = 16.8, 2.0 Hz, 1H), 2.69 (ddd, *J* = 13.3, 8.3, 1.6 Hz, 1H), 2.10 (dd, *J* = 13.3, 8.3 Hz, 1H), 2.01 (dd, *J* = 16.8, 3.9 Hz, 1H), 1.98–1.93 (m, 3H), 1.85 (dd, *J* = 16.8, 8.3 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.8, 171.6, 158.6, 134.8, 134.2, 133.0, 128.4 (2C), 118.4, 114.1 (2C), 58.4, 55.2, 52.98, 52.94, 39.4, 39.4, 37.2, 22.8, 21.2.
HRMS (ESI): Calculated for $C_{20}H_{23}NO_5Na$ $(M+Na)^+$ 380.1474, found 380.1469.

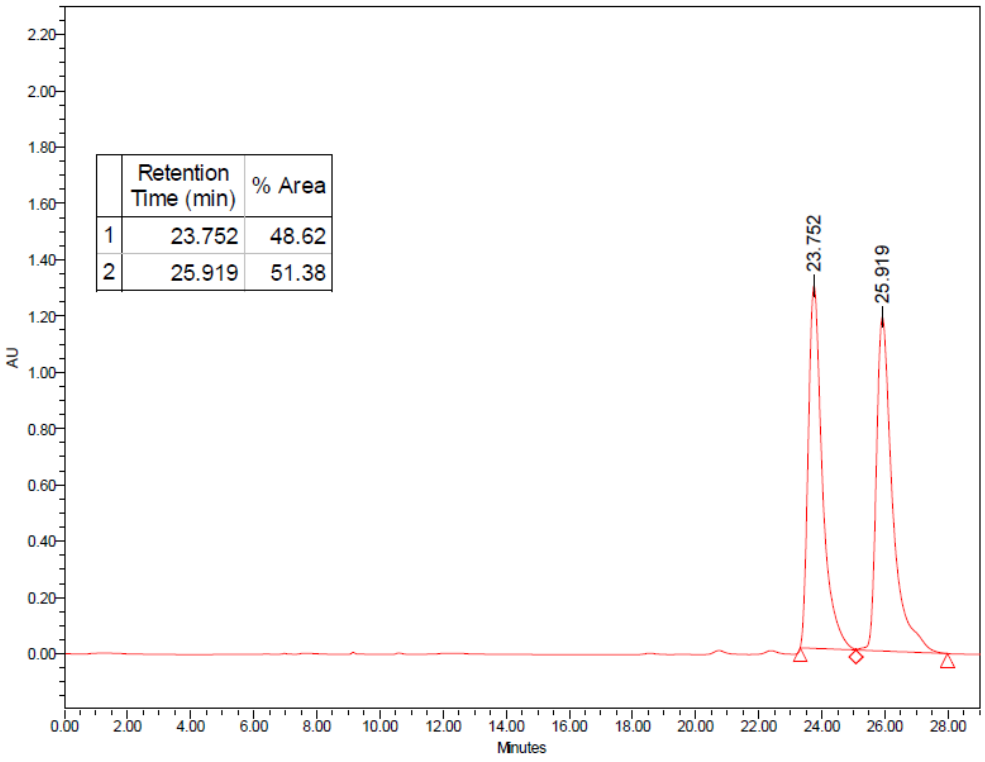

Retention Time (min) | % Area
1 | 19.836 | 50.07
2 | 23.482 | 49.93
19.836
23.482
AU
Minutes

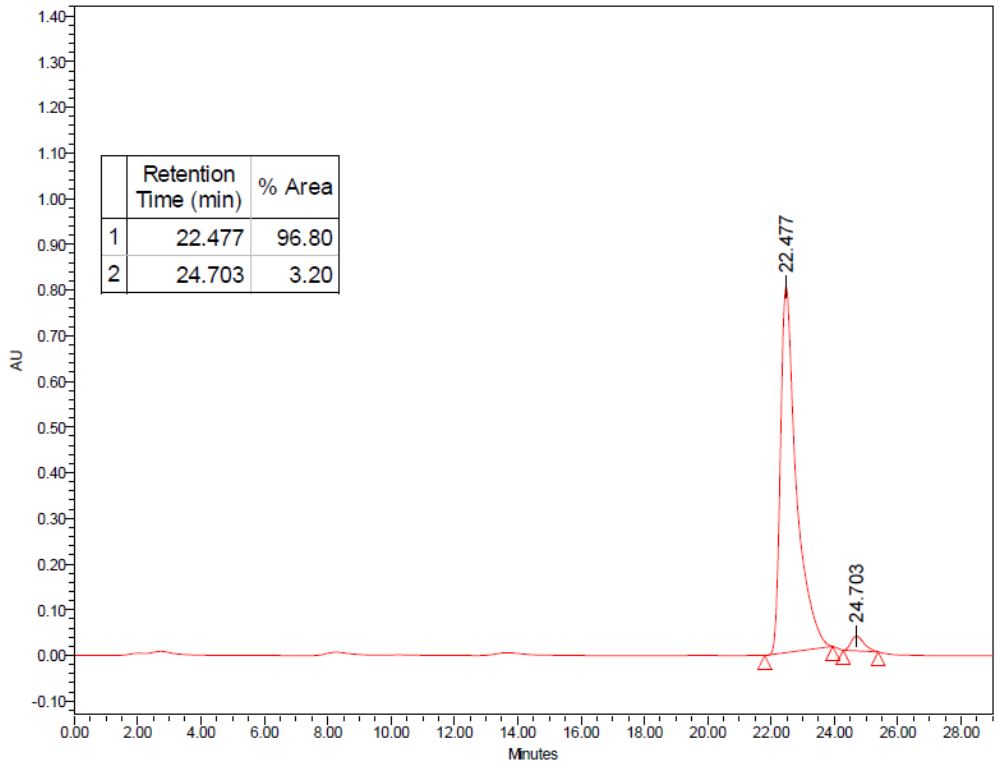

Retention Time (min) | % Area
1 | 19.930 | 96.21
2 | 23.646 | 3.79
19.930
23.646
AU
Minutes

Dimethyl (*R*,*Z*)-3-(cyanomethyl)-4-(1-(3-methoxyphenyl)ethylidene)cyclopentane-1,1-dicarboxylate 3ad

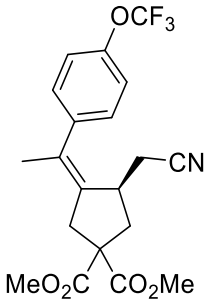


Colorless oil (101 mg, 94 %) obtained from the general procedure (2) using substrate **1a** (76 mg, 0.30 mmol) and 3-methoxyphenylboronic acid (114 mg, 0.75 mmol).
R_f = 0.14 (petroleum ether/EtOAc 9:1).
HPLC (Chiralpak IA, hexane/*i*PrOH 97:3, 0.5 mL/min): Rt = 22.5 min (major), 24.7 min (minor).
$[\alpha]_D^{20}$ = -78 (c = 0.52, $CHCl_3$) for an enantiomeric excess of 94 %.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.27–7.24 (m, 1H), 6.86–6.77 (m, 1H), 6.75–6.70 (m, 1H), 6.69–6.65 (m, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.77 (s, 3H), 3.25–3.17 (m, 1H), 3.13 (d, *J* = 16.8 Hz, 1H), 3.04 (dt, *J* = 16.8, 2.1 Hz, 1H), 2.69 (dd, *J* = 13.4, 8.0 Hz, 1H), 2.12 (dd, *J* = 13.4, 8.0 Hz, 1H), 2.02 (dd, *J* = 16.8, 3.9 Hz, 1H), 1.98 (s, 3H), 1.86 (dd, *J* = 16.8, 8.0 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.7, 171.6, 159.8, 144.1, 134.5, 133.2, 129.9, 119.7, 118.4, 113.2, 112.3, 58.4, 55.2, 52.99, 52.96, 39.3 (2C), 37.2, 22.6, 21.3.
HRMS (ESI): Calculated for $C_{20}H_{23}NO_5Na$ $(M+Na)^+$ 380.1474, found 380.1470.

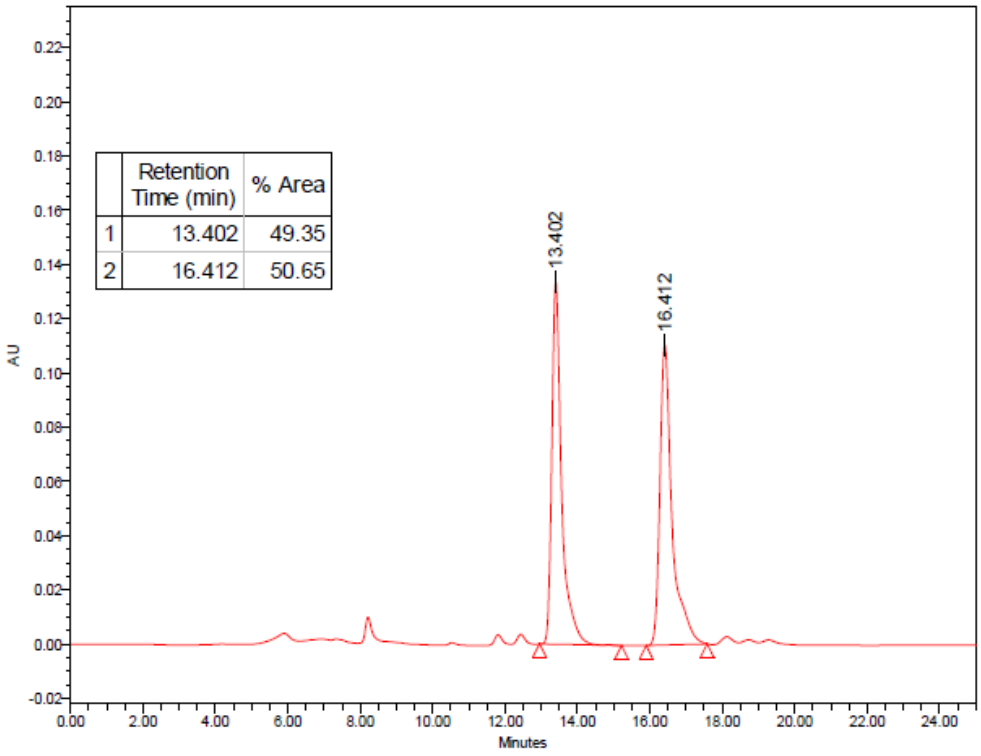


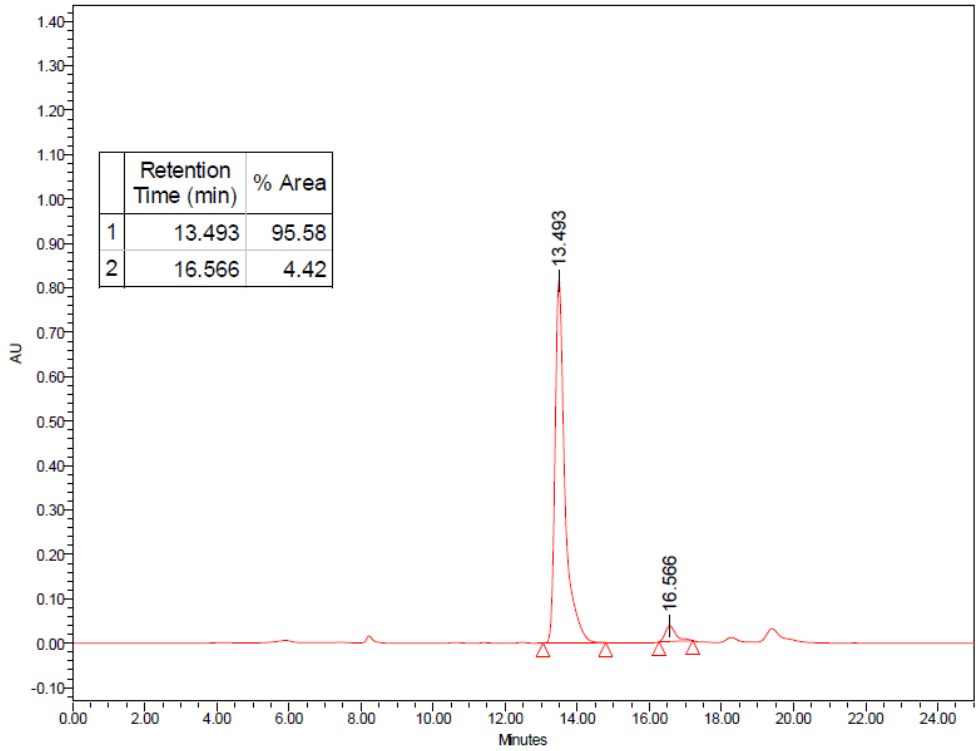


Dimethyl (*R*,*Z*)-3-(cyanomethyl)-4-(1-(4-(trifluoromethoxy)phenyl)ethylidene) cyclopentane-1,1-dicarboxylate 3ae

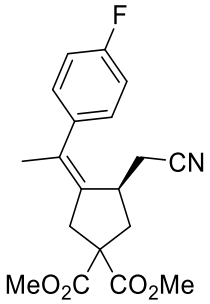


Colorless oil (101 mg, 82%) obtained from the general procedure (2) using substrate **1a** (76 mg, 0.30 mmol) and 4-trifluoromethoxyphenylboronic acid (155 mg, 0.75 mmol).
R_f = 0.21 (petroleum ether/EtOAc 9:1).
HPLC (Chiralpak IA, hexane/*i*PrOH 93:7, 0.5 mL/min): Rt = 13.5 min (major), 16.6 min (minor).
$[\alpha]_D^{20}$ = -45 (c = 0.83, $CHCl_3$) for an enantiomeric excess of 91%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.21–7.15 (m, 4H), 3.79 (s, 3H), 3.78 (s, 3H), 3.24–3.17 (m, 1H), 3.14 (d, *J* = 16.8 Hz, 1H), 3.05 (dt, *J* = 16.8, 2.0 Hz, 1H), 2.69 (ddd, *J* = 13.4, 8.3, 1.5 Hz, 1H), 2.13 (dd, *J* = 13.4, 8.3 Hz, 1H), 2.08–1.96 (m, 4H), 1.84 (dd, *J* = 16.8, 8.3 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.7, 171.4, 148.2, 141.2, 135.6, 132.1, 128.9 (2C), 121.3 (2C), 120.4 (q, *J* = 256.1 Hz), 118.0, 58.4, 53.02, 53.00, 39.4, 39.2, 37.1, 22.7, 21.4.
^{19}F NMR (376 MHz, $CDCl_3$, δ): -57.9.
HRMS (ESI): Calculated for $C_{20}H_{20}F_3NO_5Na$ $(M+Na)^+$ 434.1191, found 434.1184.

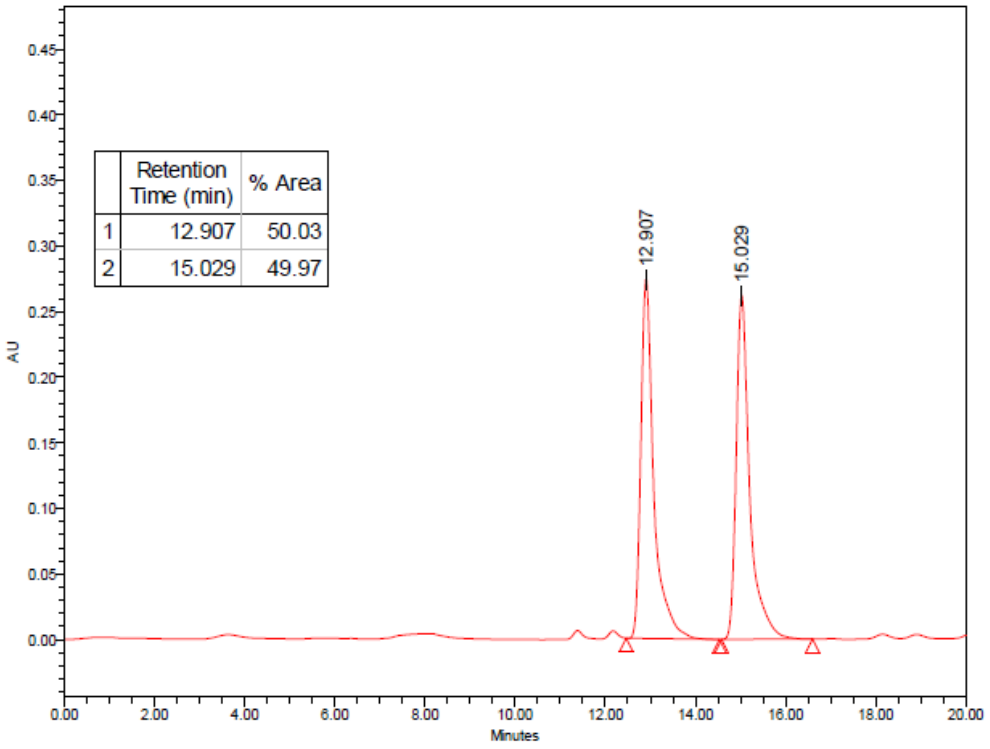

Retention Time (min) | % Area
1 | 13.402 | 49.35
2 | 16.412 | 50.65
13.402
16.412
AU
Minutes

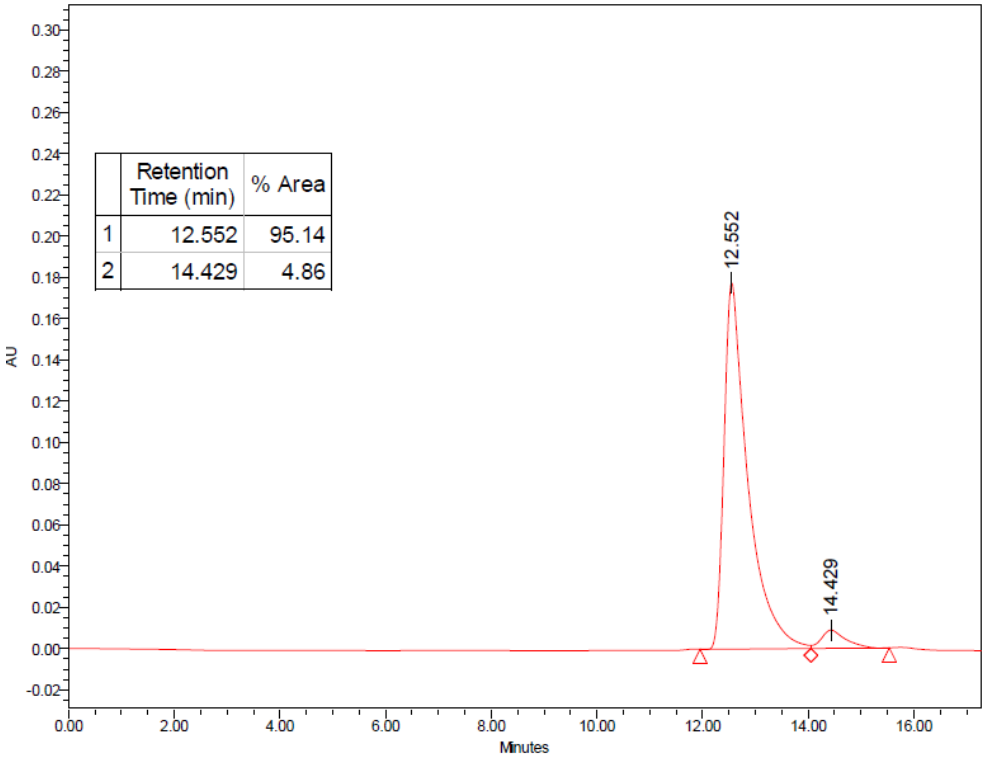

Retention Time (min) | % Area
1 | 13.493 | 95.58
2 | 16.566 | 4.42
13.493
16.566
AU
Minutes

Dimethyl (*R,Z*)-3-(cyanomethyl)-4-(1-(4-fluorophenyl)ethylidene)cyclopentane-1,1-dicarboxylate 3af

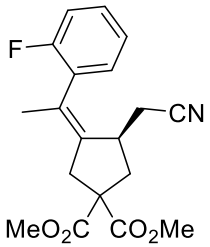


Colorless oil (79 mg, 76%) obtained from the general procedure (2) using substrate **1a** (76 mg, 0.30 mmol) and 4-fluorophenylboronic acid (105 mg, 0.75 mmol).
Scale-up reaction: colorless oil (320 mg, 77%) obtained from the general procedure (2) using substrate **1a** (304 mg, 1.2 mmol) and 4-fluorophenylboronic acid (420 mg, 3 mmol).
R_f = 0.22 (petroleum ether/EtOAc 9:1).
HPLC (Chiralpak IA, hexane/*i*PrOH 90:10, 0.5 mL/min): Rt = 12.5 min (major), 14.4 min (minor).
$[\alpha]_D^{20}$ = -37 (c = 0.64, $CHCl_3$) for an enantiomeric excess of 90%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.15–7.09 (m, 2H), 7.07–7.00 (m, 2H), 3.79 (s, 3H), 3.78 (s, 3H), 3.23–3.14 (m, 1H), 3.13 (d, *J* = 17.0 Hz, 1H), 3.04 (dt, *J* = 17.0, 2.0 Hz, 1H), 2.69 (ddd, *J* = 13.4, 8.3, 1.6 Hz, 1H), 2.11 (dd, *J* = 13.4, 8.3 Hz, 1H), 2.05–1.95 (m, 4H), 1.84 (dd, *J* = 17.0, 8.3 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.7, 171.5, 161.8 (d, *J* = 246.7 Hz), 138.5 (d, *J* = 3.2 Hz), 135.1, 132.4, 129.0 (d, *J* = 7.8 Hz, 2C), 118.1, 115.8 (d, *J* = 21.3 Hz, 2C), 58.4, 53.01, 52.98, 39.4, 39.3, 37.1, 22.8, 21.3.
^{19}F NMR (376 MHz, $CDCl_3$, δ): -114.6.
HRMS (ESI): Calculated for $C_{19}H_{20}FNO_4Na$ $(M+Na)^+$ 368.1274, found 368.1270.

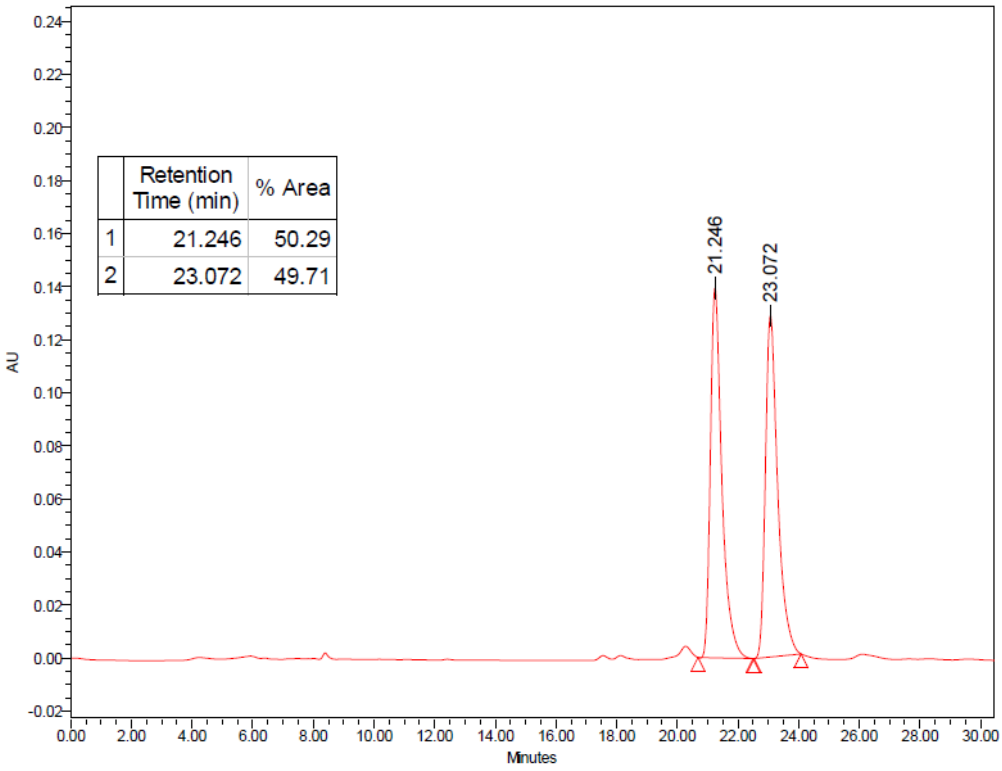


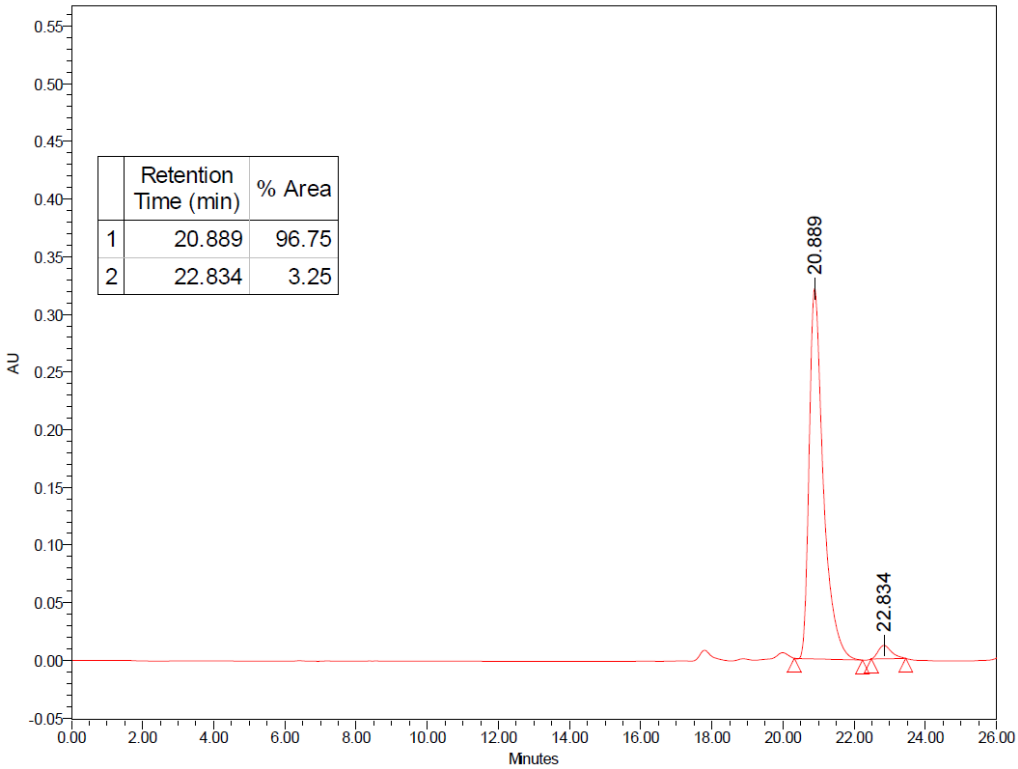


Dimethyl (*R,Z*)-3-(cyanomethyl)-4-(1-(2-fluorophenyl)ethylidene)cyclopentane-1,1-dicarboxylate 3ag

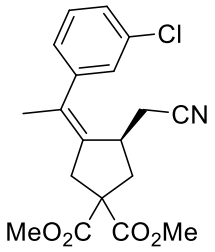


Colorless oil (79 mg, 76%) obtained from the general procedure (2) using substrate **1a** (76 mg, 0.30 mmol) and 2-fluorophenylboronic acid (105 mg, 0.75 mmol).
R_f = 0.21 (petroleum ether/EtOAc 9:1).
HPLC (Chiralpak IA, hexane/*i*PrOH 97:3, 0.5 mL/min): Rt = 20.9 min (major), 22.8 min (minor).
$[\alpha]_D^{20}$ = -44 (c = 0.84, $CHCl_3$) for an enantiomeric excess of 94%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.32–7.22 (m, 1H), 7.16–7.03 (m, 3H), 3.78 (s, 3H), 3.77 (s, 3H), 3.18 (d, *J* = 16.8 Hz, 1H), 3.07 (dt, *J* = 16.8, 1.9 Hz, 3H), 3.06–2.97 (m, 1H), 2.72 (ddd, *J* = 13.5, 8.0, 1.6 Hz, 1H), 2.15 (dd, *J* = 13.5, 8.0 Hz, 1H), 2.05–1.96 (m, 4H), 1.92 (dd, *J* = 16.8, 8.0 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.7, 171.6, 159.0 (d, *J* = 246.1 Hz), 158.0, 137.3, 129.8 (d, *J* = 3.0 Hz), 129.6 (d, *J* = 17.0 Hz), 129.3 (d, *J* = 7.9 Hz), 124.6 (d, *J* = 2.6 Hz), 118.25, 116.1 (d, *J* = 22.2 Hz), 58.6, 53.1 (2C), 39.3, 39.1, 37.5, 22.0, 21.4.
^{19}F NMR (376 MHz, $CDCl_3$, δ): -115.3.
HRMS (ESI): Calculated for $C_{19}H_{20}FNO_4Na$ $(M+Na)^+$ 368.1274, found 368.1270.

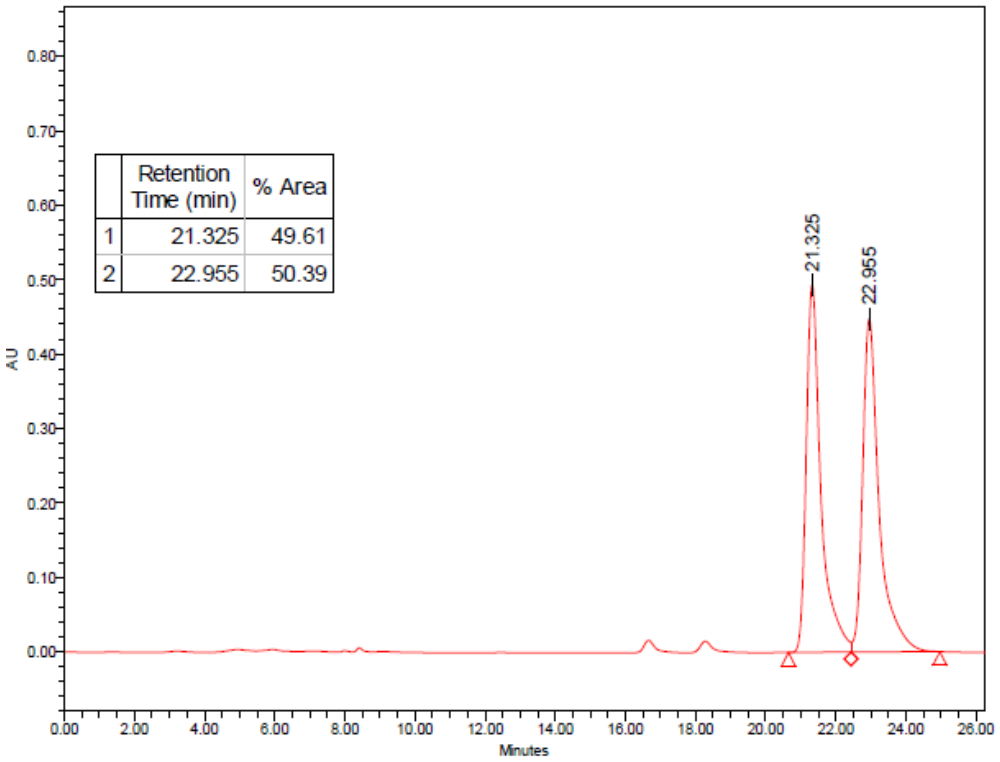

Retention Time (min) | % Area
1 | 21.246 | 50.29
2 | 23.072 | 49.71
21.246
23.072
AU
Minutes

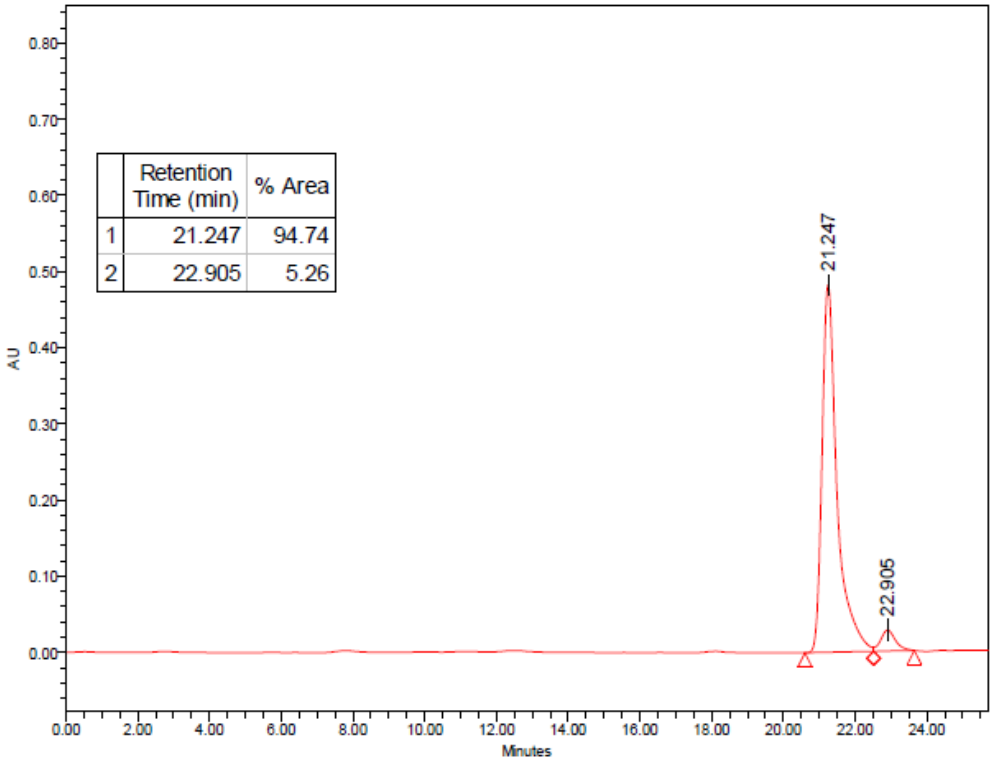

Retention Time (min) | % Area
1 | 20.889 | 96.75
2 | 22.834 | 3.25
20.889
22.834
AU
Minutes

Dimethyl (*R*,*Z*)-3-(1-(3-chlorophenyl)ethylidene)-4-(cyanomethyl)cyclopentane-1,1-dicarboxylate 3ah

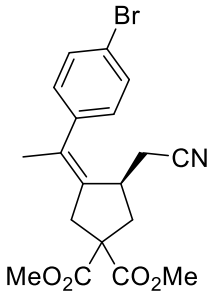


Colorless oil (105 mg, 97%) obtained from the general procedure (2) using substrate **1a** (76 mg, 0.30 mmol) and 3-chlorophenylboronic acid (118 mg, 0.75 mmol).
R_f = 0.21 (petroleum ether/EtOAc 9:1).
HPLC (Chiralpak IA, hexane/*i*PrOH 97:3, 0.5 mL/min): Rt = 21.2 min (major), 22.9 min (minor).
$[\alpha]_D^{20}$ = -57 (c = 0.80, $CHCl_3$) for an enantiomeric excess of 90%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.33–7.24 (m, 2H), 7.13 (t, *J* = 1.5 Hz, 1H), 7.04 (dt, *J* = 7.0, 1.5 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.25–3.16 (m, 1H), 3.13 (d, *J* = 16.8 Hz, 1H), 3.05 (dt, *J* = 16.8, 2.0 Hz, 1H), 2.70 (ddd, *J* = 13.5, 8.3, 1.5 Hz, 1H), 2.14 (dd, *J* = 13.5, 8.3 Hz, 1H), 2.02 (dd, *J* = 16.8, 3.9 Hz, 1H), 1.99–1.96 (m, 3H), 1.87 (dd, *J* = 16.8, 8.3 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): δ 171.7, 171.5, 144.4, 135.6, 134.7, 132.1, 130.2, 127.4 (2C), 125.6, 118.1, 58.4, 53.06, 53.01, 39.3, 39.2, 37.1, 22.6, 21.4.
HRMS (ESI): Calculated for $C_{19}H_{20}ClNO_4Na$ $(M+Na)^+$ 384.0979, found 384.0975.

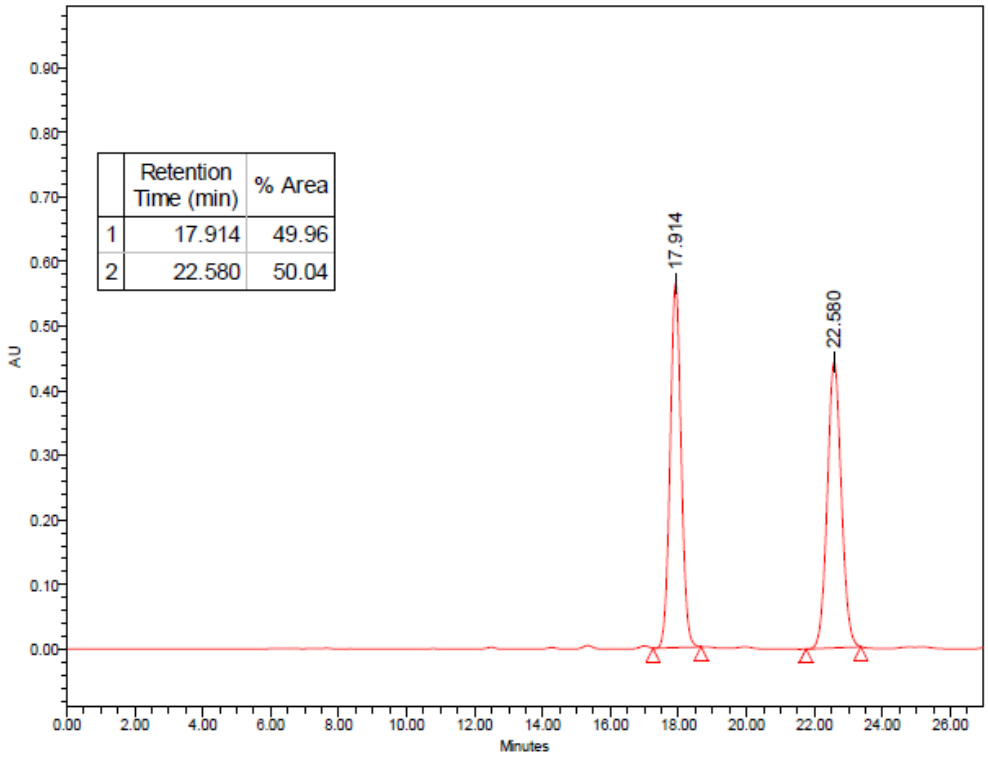


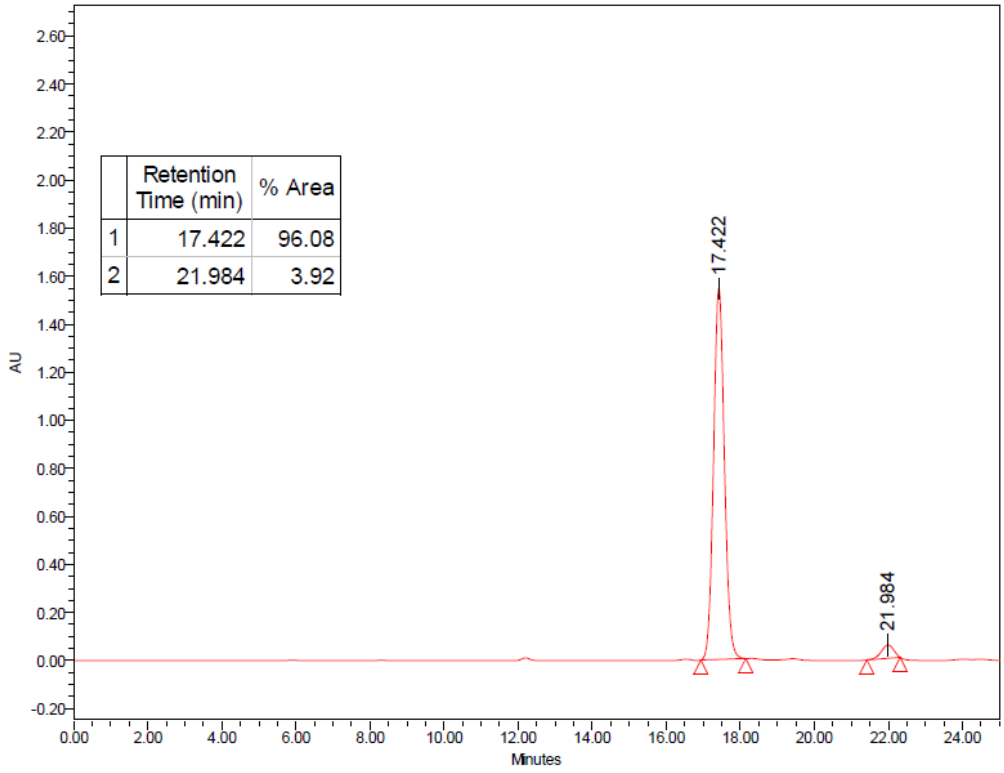


Dimethyl (*R*,*Z*)-3-(1-(4-bromophenyl)ethylidene)-4-(cyanomethyl)cyclopentane-1,1-dicarboxylate 3ai

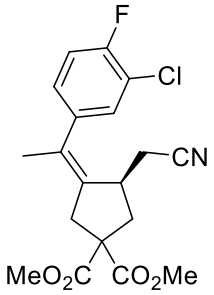


Colorless oil (111 mg, 91%) obtained from the general procedure (2) using substrate **1a** (76 mg, 0.30 mmol) and 4-bromophenylboronic acid (151 mg, 0.75 mmol).
R_f = 0.23 (petroleum ether/EtOAc 9:1).
HPLC (Chiralpak IA, hexane/*i*PrOH 95:5, 0.5 mL/min): Rt = 17.4 min (major), 22.0 min (minor).
$[\alpha]_D^{20}$ = -49 (c = 0.72, $CHCl_3$) for an enantiomeric excess of 92%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.50–7.45 (m, 2H), 7.07–7.01 (m, 2H), 3.79 (s, 3H), 3.78 (s, 3H), 3.22–3.15 (m, 1H), 3.12 (d, *J* = 17.0 Hz, 1H), 3.04 (dt, *J* = 17.0, 2.0 Hz, 1H), 2.69 (ddd, *J* = 13.4, 8.0, 1.6 Hz, 1H), 2.12 (dd, *J* = 13.4, 8.0 Hz, 1H), 2.02 (dd, *J* = 17.0, 3.9 Hz, 1H), 1.98–1.96 (m, 3H), 1.86 (dd, *J* = 17.0, 8.0 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.7, 171.5, 141.5, 135.3, 132.2, 132.0 (2C), 129.1 (2C), 121.1, 118.1, 58.3, 53.04, 53.01, 39.4, 39.3, 37.1, 22.6, 21.4.
HRMS (ESI): Calculated for $C_{19}H_{20}BrNO_4Na$ $(M+Na)^+$ 428.0473, found 428.0468.

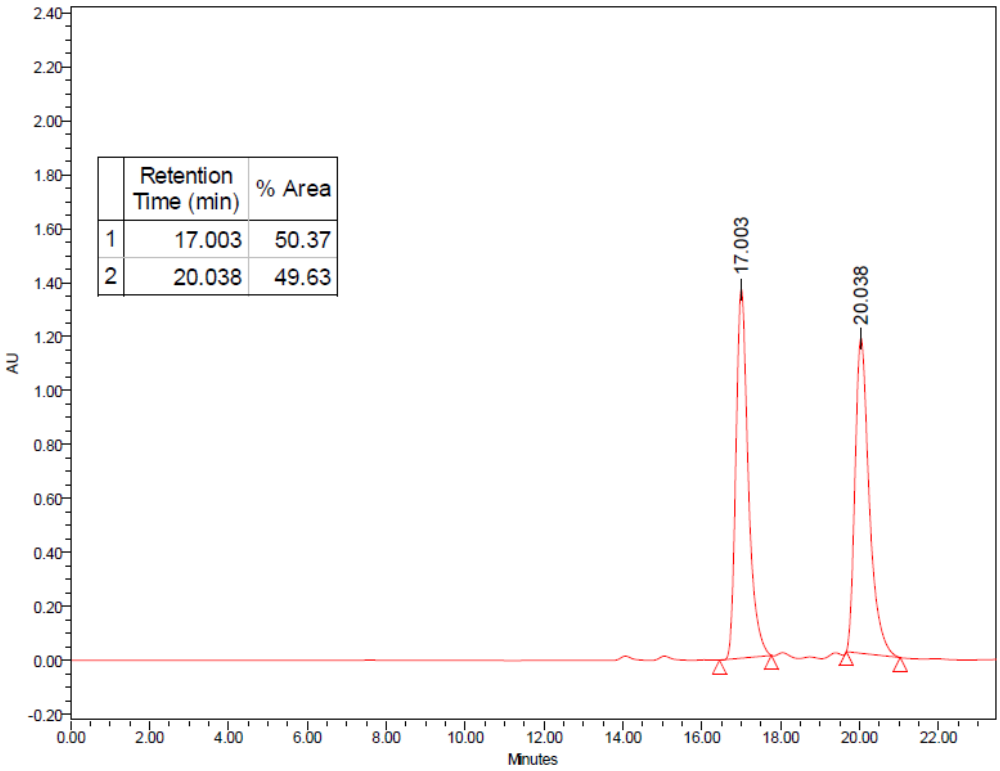

Retention Time (min) | % Area
1 | 17.914 | 49.96
2 | 22.580 | 50.04
17.914
22.580
AU
Minutes

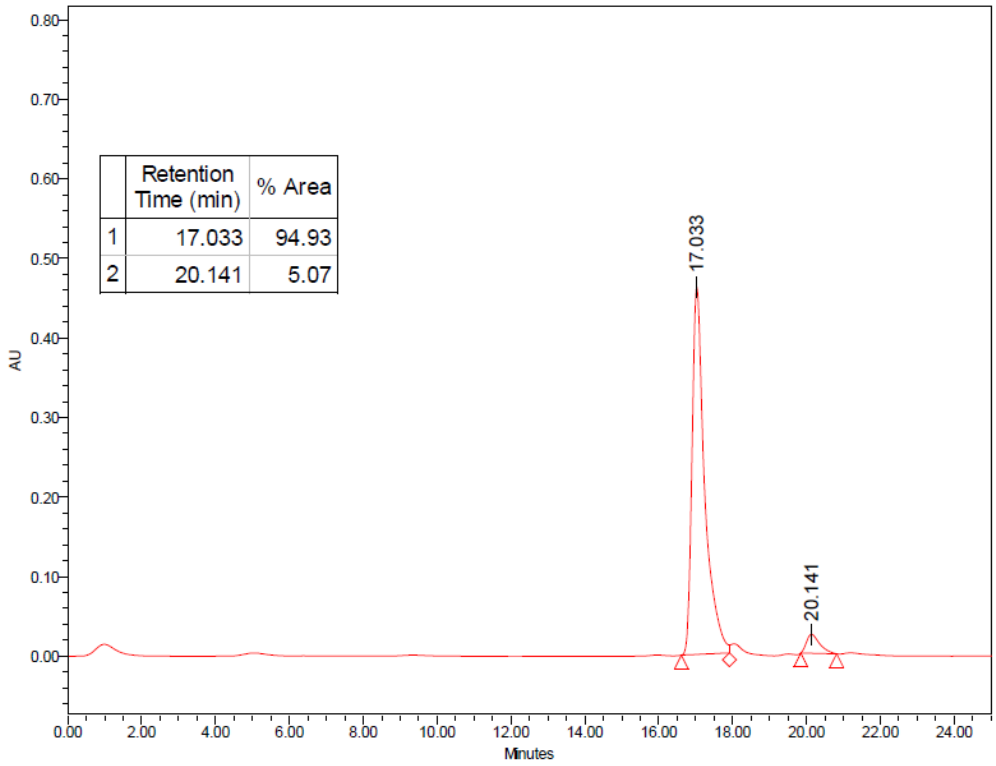

Retention Time (min) | % Area
1 | 17.422 | 96.08
2 | 21.984 | 3.92
17.422
21.984
AU
Minutes

Dimethyl (*R*,*Z*)-3-(1-(3-chloro-4-fluorophenyl)ethylidene)-4-(cyanomethyl)cyclopentane-1,1-dicarboxylate 3aj

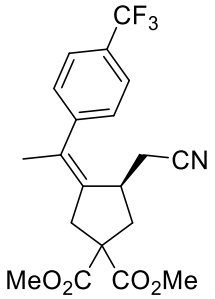


Yellow oil (98 mg, 86%) obtained from the general procedure (2) using substrate **1a** (76 mg, 0.30 mmol) and 3-chloro-4-fluorophenylboronic acid (132 mg, 0.75 mmol).
R_f = 0.17 (petroleum ether/EtOAc 9:1).
HPLC (Chiralpak IE, hexane/*i*PrOH 90:10, 0.5 mL/min): Rt = 27.4 min (major), 29.4 min (minor).
$[\alpha]_D^{20}$ = -50 (c = 0.43, $CHCl_3$) for an enantiomeric excess of 87%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.18 (dd, *J* = 7.0, 2.1 Hz, 1H), 7.12 (t, *J* = 8.6 Hz, 1H), 7.03 (ddd, *J* = 8.4, 4.6, 2.1 Hz, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 3.23–3.14 (m, 1H), 3.12 (d, *J* = 16.9 Hz, 1H), 3.03 (dt, *J* = 16.9, 2.0 Hz, 1H), 2.69 (ddd, *J* = 13.5, 8.3, 1.5 Hz, 1H), 2.13 (dd, *J* = 13.5, 8.3 Hz, 1H), 2.04 (dd, *J* = 16.9, 3.9 Hz, 1H), 1.99–1.95 (m, 3H), 1.89 (dd, *J* = 16.9, 8.3 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.7, 171.4, 157.1 (d, *J* = 249.6 Hz), 139.6 (d, *J* = 4.1 Hz), 136.1, 131.3, 129.5, 127.3 (d, *J* = 6.9 Hz), 121.4 (d, *J* = 17.8 Hz), 117.9, 117.1 (d, *J* = 20.9 Hz), 58.3, 53.07, 53.03, 39.4, 39.2, 37.1, 22.7, 21.5.
^{19}F NMR (376 MHz, $CDCl_3$, δ): -116.8.
HRMS (ESI): Calculated for $C_{19}H_{19}ClFNO_4Na$ $(M+Na)^+$ 402.0884, found 402.0880.

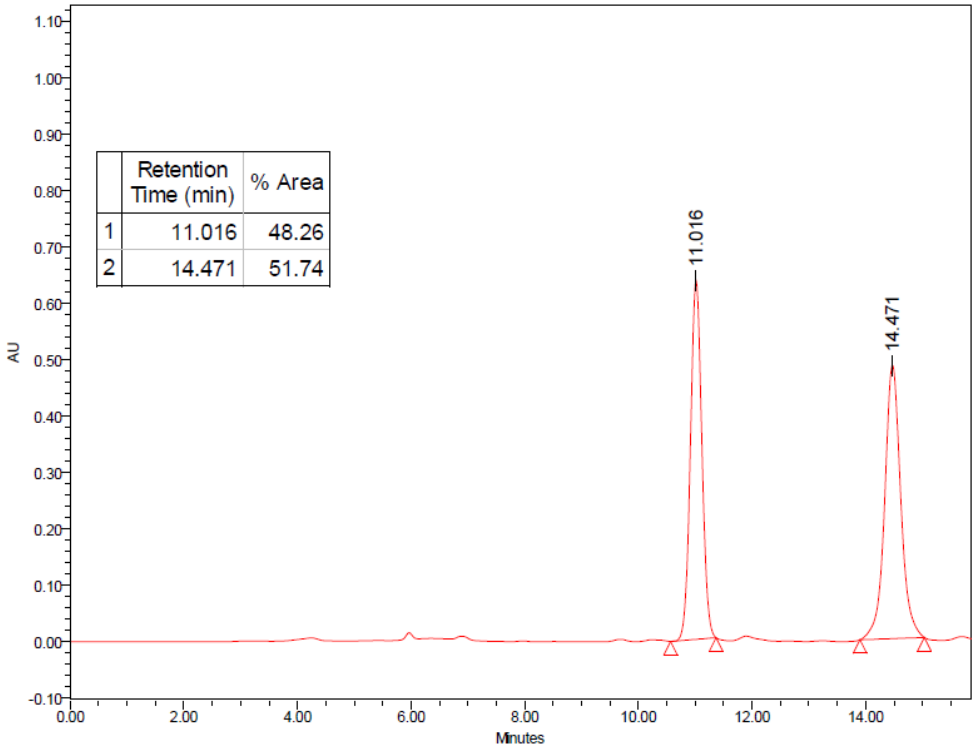


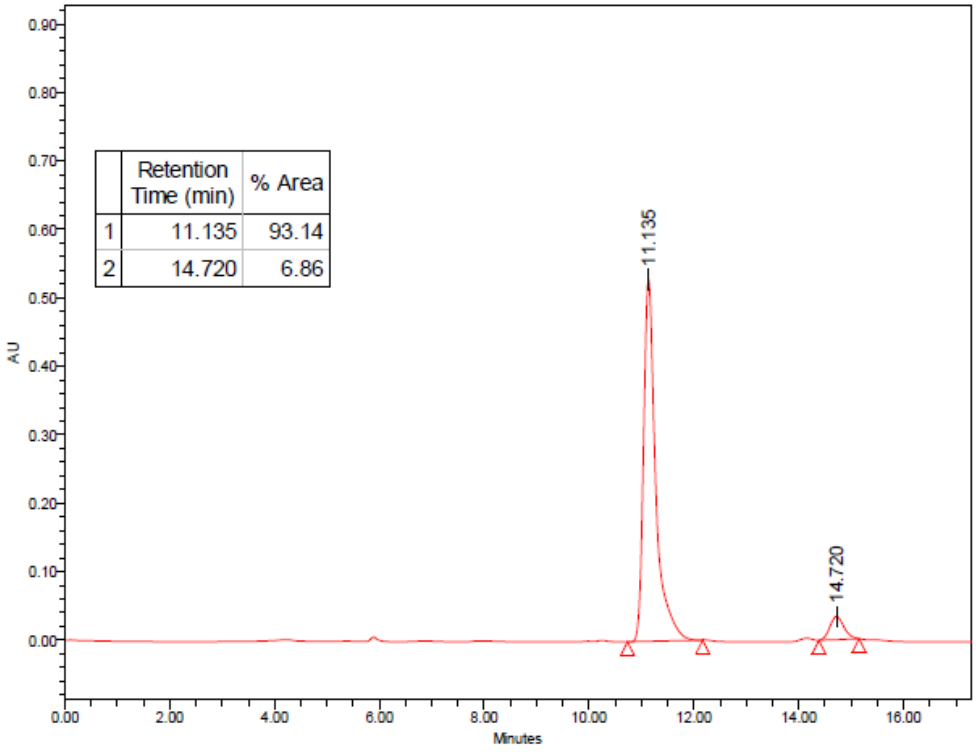


Dimethyl (*R*,*Z*)-3-(cyanomethyl)-4-(1-(4-(trifluoromethyl)phenyl)ethylidene) cyclopentane-1,1-dicarboxylate 3ak

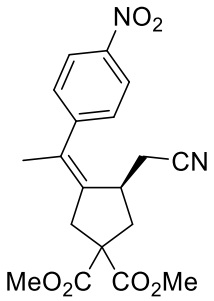


Colorless oil (102 mg, 86%) obtained from the general procedure (2) using substrate **1a** (76 mg, 0.30 mmol) and 4-trifluoromethylphenylboronic acid (142 mg, 0.75 mmol).
R_f = 0.15 (petroleum ether/EtOAc 9:1).
HPLC (Chiralpak IA, hexane/*i*PrOH 95:5, 0.7 mL/min): Rt = 11.1 min (major), 14.7 min (minor).
$[\alpha]_D^{20}$ = -53 (c = 0.36, $CHCl_3$) for an enantiomeric excess of 86%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.61 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 3.80 (s, 3H), 3.79 (s, 3H), 3.22–3.12 (m, 2H), 3.07 (dt, *J* = 16.9, 2.0 Hz, 1H), 2.70 (ddd, *J* = 13.5, 8.3, 1.5 Hz, 1H), 2.14 (dd, *J* = 13.5, 8.3 Hz, 1H), 2.03–1.95 (m, 4H), 1.83 (dd, *J* = 16.9, 8.3 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.7, 171.4, 146.4, 136.0, 132.2, 129.4 (q, *J* = 32.6 Hz), 127.8 (2C), 125.9 (q, *J* = 3.9 Hz, 2C), 124.0 (q, *J* = 272.1 Hz), 117.9, 58.3, 53.06, 53.03, 39.4, 39.2, 37.1, 22.6, 21.5.
^{19}F NMR (376 MHz, $CDCl_3$, δ): -62.5.
HRMS (ESI): Calculated for $C_{20}H_{20}F_3NO_4Na$ $(M+Na)^+$ 418.1242, found 418.1236.

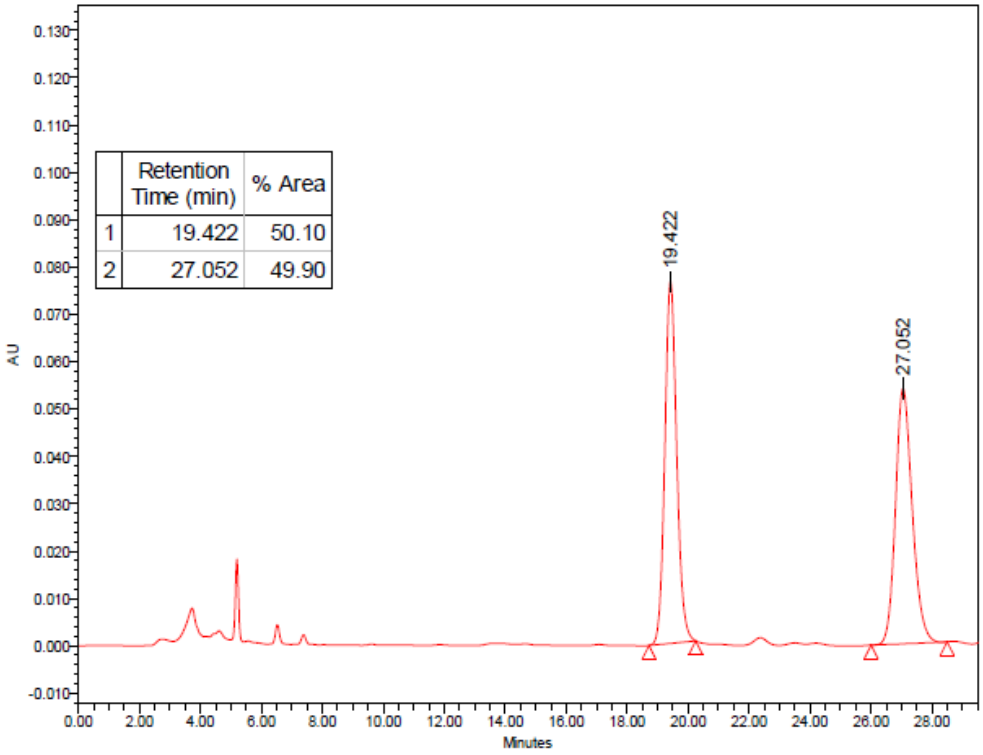

Retention Time (min)
% Area
1
11.016
48.26
2
14.471
51.74
11.016
14.471
AU
Minutes

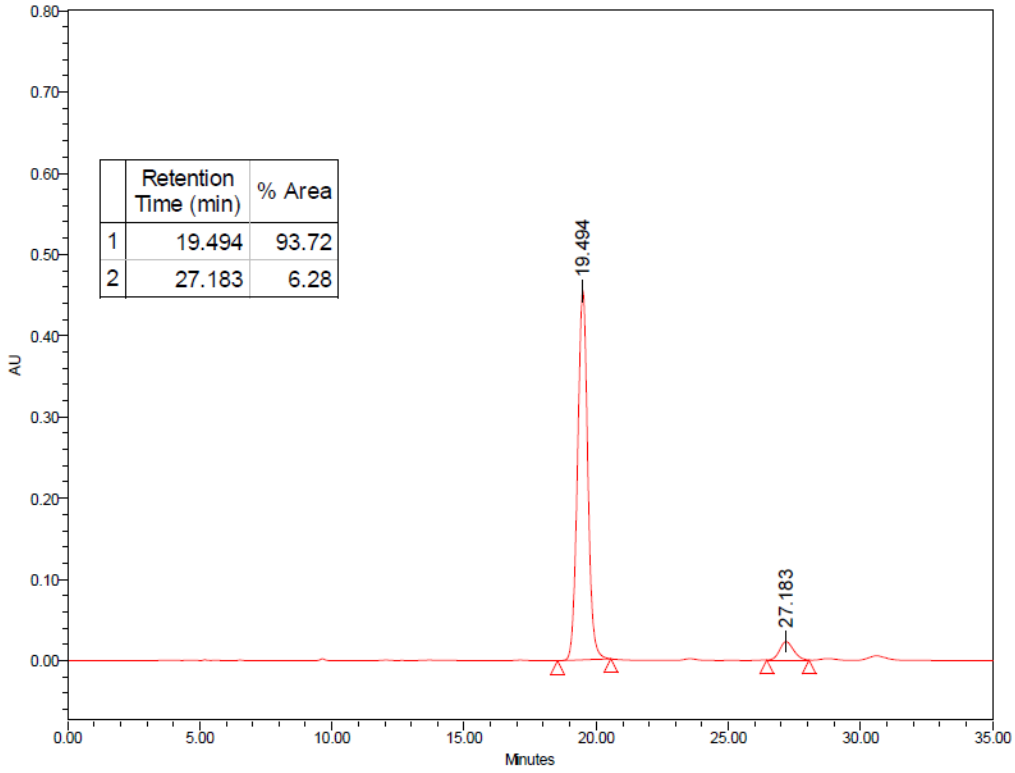

Retention Time (min)
% Area
1
11.135
93.14
2
14.720
6.86
11.135
14.720
AU
Minutes

Dimethyl (*R*,*Z*)-3-(cyanomethyl)-4-(1-(4-nitrophenyl)ethylidene)cyclopentane-1,1-dicarboxylate 3al

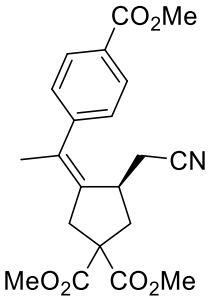


Yellow oil (94 mg, 84%) obtained from the general procedure (2) using substrate **1a** (76 mg, 0.30 mmol) and 4-nitrophenylboronic acid (125 mg, 0.75 mmol).
R_f = 0.11 (petroleum ether/EtOAc 8:2).
HPLC (Chiralpak IA, hexane/*i*PrOH 93:7, 0.8 mL/min): Rt = 19.5 min (major), 27.2 min (minor).
$[\alpha]_D^{20}$ = -88 (c = 0.56, $CHCl_3$) for an enantiomeric excess of 88%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.27–8.19 (m, 2H), 7.40–7.33 (m, 2H), 3.80 (s, 3H), 3.79 (s, 3H), 3.26–3.17 (m, 1H), 3.17 (d, *J* = 17.2 Hz, 1H), 3.08 (dt, *J* = 17.2, 2.0 Hz, 1H), 2.71 (ddd, *J* = 13.5, 8.0, 1.5 Hz, 1H), 2.16 (dd, *J* = 13.5, 8.0 Hz, 1H), 2.07–1.96 (m, 4H), 1.85 (dd, *J* = 17.2, 8.0 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.6, 171.3, 149.5, 146.9, 137.1, 131.5, 128.5 (2C), 124.2 (2C), 117.6, 58.3, 53.13, 53.10, 39.5, 39.2, 37.1, 22.5, 21.5.
HRMS (ESI): Calculated for $C_{19}H_{20}N_2O_6Na$ $(M+Na)^+$ 395.1219, found 395.1215.

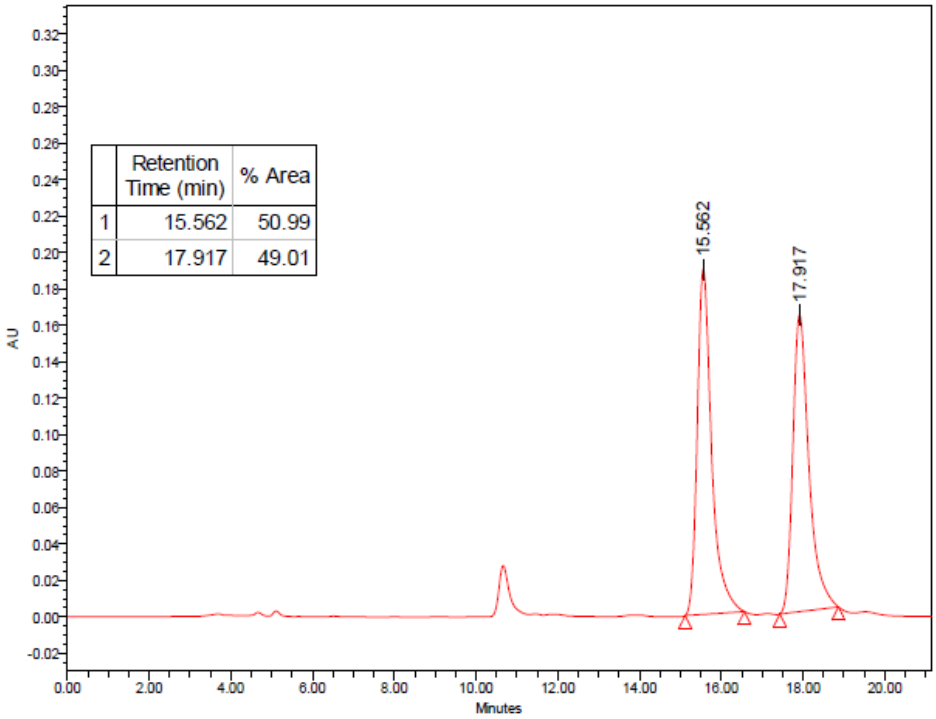


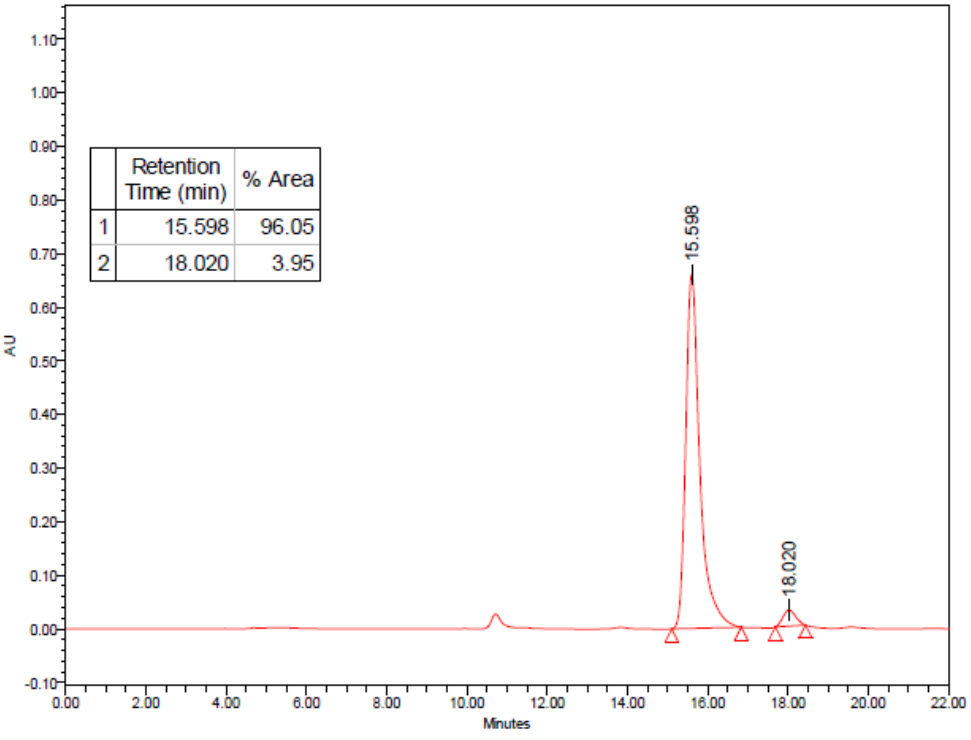


Dimethyl (*R*,*Z*)-3-(cyanomethyl)-4-(1-(4-(methoxycarbonyl)phenyl)ethylidene) cyclopentane-1,1-dicarboxylate 3am

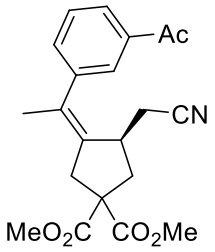


Colorless oil (105 mg, 91%) obtained from the general procedure (2) using substrate **1a** (76 mg, 0.30 mmol) and 4-methoxycarbonylphenylboronic acid (136 mg, 0.75 mmol).
R_f = 0.10 (petroleum ether/EtOAc 9:1).
HPLC (Chiralpak IA, hexane/*i*PrOH 93:7, 0.8 mL/min): Rt = 15.6 min (major), 18.0 min (minor).
$[\alpha]_D^{20}$ = -140 (c = 0.75, $CHCl_3$) for an enantiomeric excess of 92%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.00–7.91 (m, 2H), 7.19–7.14 (m, 2H), 3.86 (s, 3H), 3.73 (s, 3H), 3.71 (s, 3H), 3.16–3.11 (m, 1H), 3.08 (d, *J* = 16.9 Hz, 1H), 2.99 (dt, *J* = 16.9, 2.0 Hz, 1H), 2.63 (ddd, *J* = 13.4, 8.0, 1.5 Hz, 1H), 2.06 (dd, *J* = 13.4, 8.0 Hz, 1H), 1.95–1.93 (m, 3H), 1.90 (dd, *J* = 16.9, 3.9 Hz, 1H), 1.75 (dd, *J* = 16.9, 8.0 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.7, 171.4, 166.7, 147.5, 135.7, 132.6, 130.2 (2C), 129.1, 127.5 (2C), 118.0, 58.3, 53.06, 53.02, 52.2, 39.5, 39.3, 37.1, 22.5, 21.5.
HRMS (ESI): Calculated for $C_{21}H_{23}NO_6Na$ $(M+Na)^+$ 408.1423, found 408.1418.

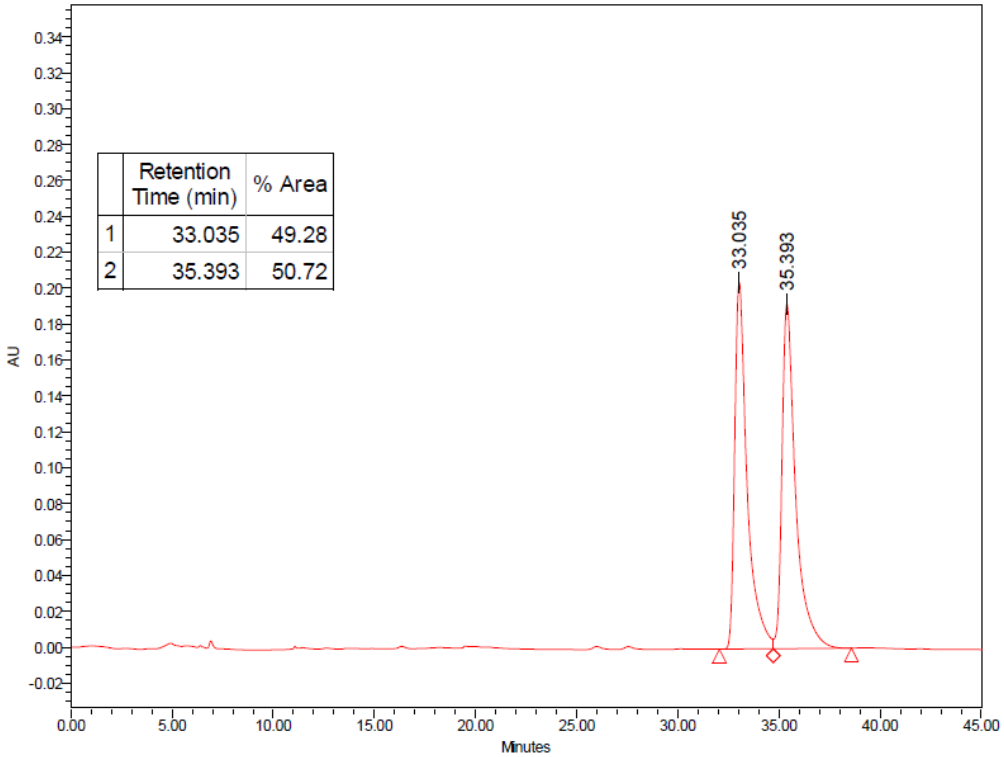

Retention Time (min) | % Area
1 | 15.562 | 50.99
2 | 17.917 | 49.01
15.562
17.917
AU
Minutes

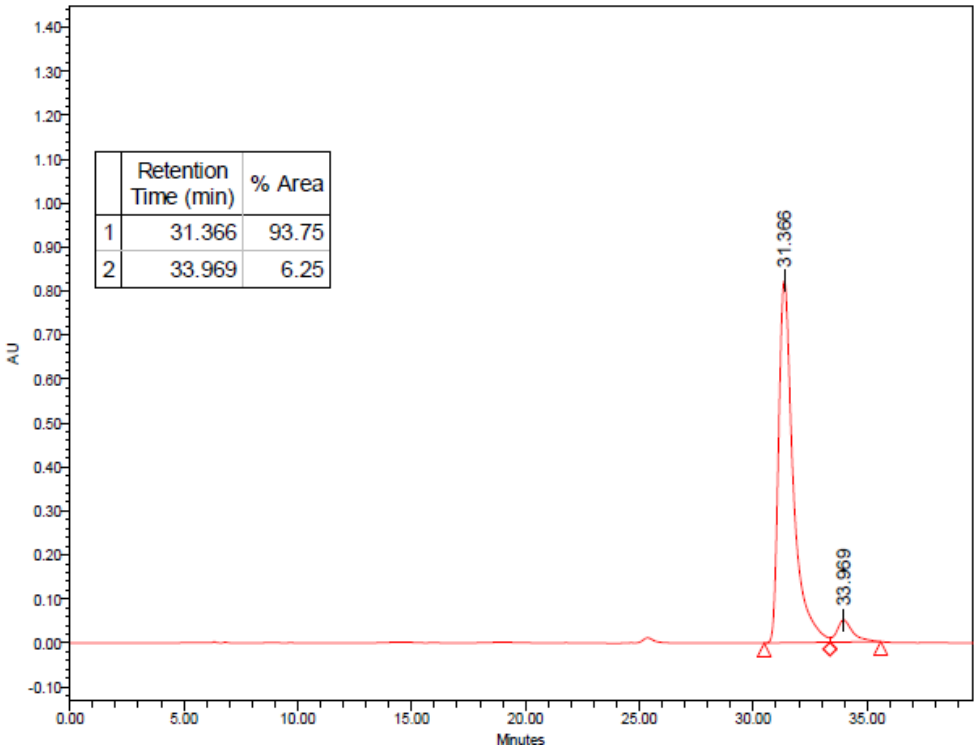

Retention Time (min) | % Area
1 | 15.598 | 96.05
2 | 18.020 | 3.95
15.598
18.020
AU
Minutes

Dimethyl (*R*,*Z*)-3-(1-(3-acetylphenyl)ethylidene)-4-(cyanomethyl)cyclopentane-1,1-dicarboxylate 3an

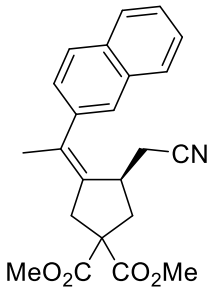


Yellow oil (84 mg, 76%) obtained from the general procedure (2) using substrate **1a** (76 mg, 0.30 mmol) and 3-acetylphenylboronic acid (124 mg, 0.75 mmol).
R_f = 0.15 (petroleum ether/EtOAc 8:2).
HPLC (Chiralpak IA, hexane/*i*PrOH 95:5, 0.6 mL/min): Rt = 31.4 min (major), 34.0 min (minor).
$[\alpha]_D^{20}$ = -102 (c = 0.71, $CHCl_3$) for an enantiomeric excess of 88%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.86 (dt, *J* = 7.7, 1.6 Hz, 1H), 7.74 (t, *J* = 1.6 Hz, 1H), 7.46 (t, *J* = 7.7 Hz, 1H), 7.37 (dt, *J* = 7.7, 1.6 Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.20–3.13 (m, 1H), 3.16 (d, *J* = 17.0 Hz, 1H), 3.07 (dt, *J* = 17.0, 2.0 Hz, 1H), 2.70 (ddd, *J* = 13.5, 8.5, 1.4 Hz, 1H), 2.62 (s, 3H), 2.15 (dd, *J* = 13.5, 8.5 Hz, 1H), 2.05–2.01 (m, 3H), 1.97 (dd, *J* = 17.0, 4.0 Hz, 1H), 1.82 (dd, *J* = 17.0, 8.5 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 197.8, 171.7, 171.6, 143.2, 137.6, 135.7, 132.5, 132.1, 129.2, 127.3, 127.0, 118.0, 58.4, 53.08, 53.03, 39.3, 39.3, 37.2, 26.7, 22.7, 21.4.
HRMS (ESI): Calculated for $C_{21}H_{23}NO_5Na$ $(M+Na)^+$ 392.1474, found 392.1470.

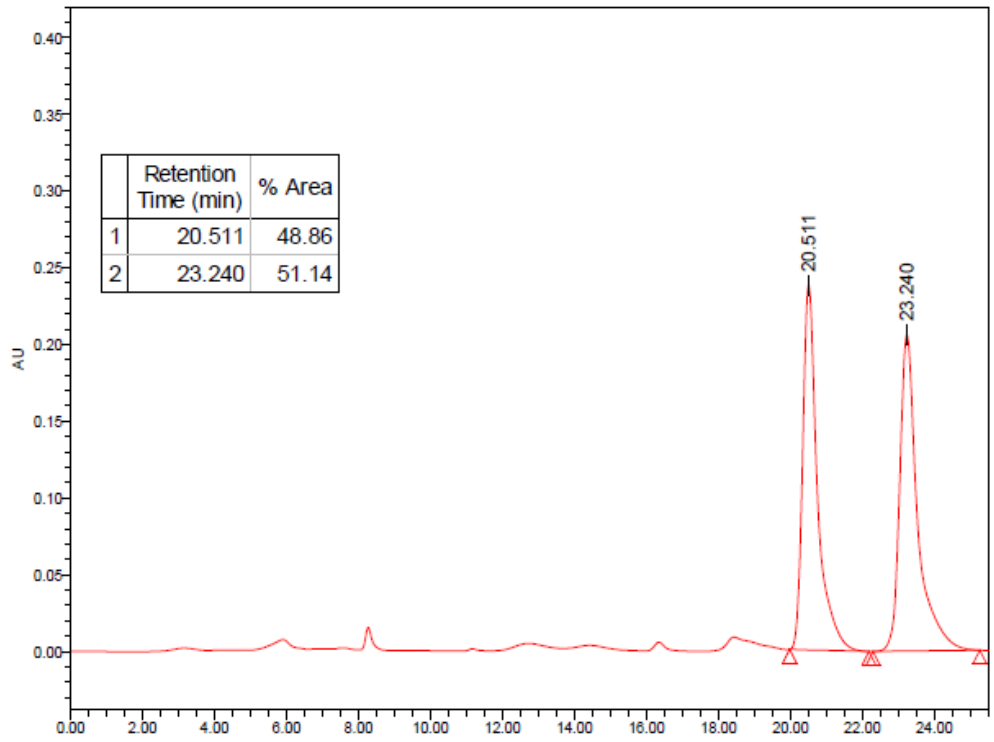


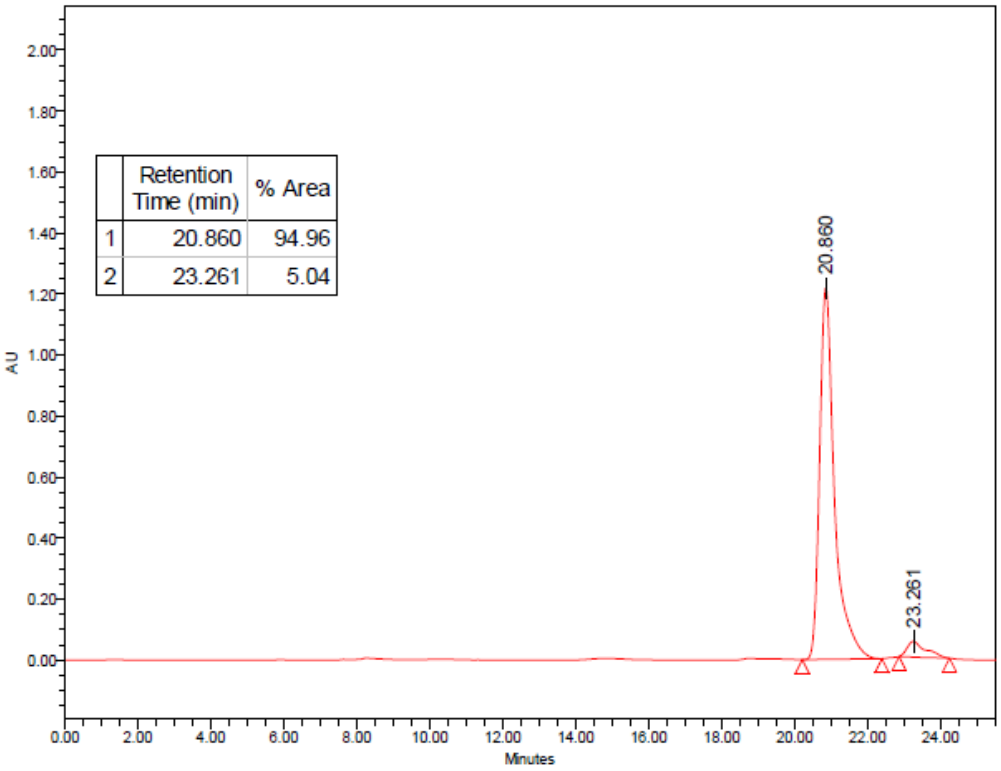


Dimethyl (*R*,*Z*)-3-(cyanomethyl)-4-(1-(naphthalen-2-yl)ethylidene)cyclopentane-1,1-dicarboxylate 3ao

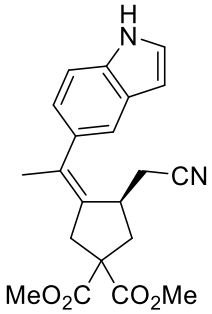


Colorless oil (110 mg, 97%) obtained from the general procedure (2) using substrate **1a** (76 mg, 0.30 mmol) and 2-naphthylboronic acid (130 mg, 0.75 mmol).
R$_f$ = 0.40 (petroleum ether/EtOAc 8:2).
HPLC (Chiralpak IA, hexane/*i*PrOH 95:5, 0.5 mL/min): Rt = 20.9 min (major), 23.3 min (minor).
$[\alpha]_D^{20}$ = -46 (c = 0.37, $CHCl_3$) for an enantiomeric excess of 90%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.88–7.77 (m, 3H), 7.59 (s, 1H), 7.57–7.46 (m, 2H), 7.28 (dd, *J* = 8.5, 1.8 Hz, 1H), 3.83 (s, 3H), 3.79 (s, 3H), 3.32–3.26 (m, 1H), 3.20 (d, *J* = 16.9 Hz, 1H), 3.11 (dt, *J* = 16.9, 2.0 Hz, 1H), 2.72 (ddd, *J* = 13.4, 8.2, 1.6 Hz, 1H), 2.13 (dd, *J* = 13.4, 8.2 Hz, 1H), 2.09–2.05 (m, 3H), 1.95 (dd, *J* = 16.9, 3.9 Hz, 1H), 1.82 (dd, *J* = 16.9, 8.2 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.8, 171.6, 140.1, 135.0, 133.4, 133.3, 132.4, 128.6, 127.8, 127.8, 126.4, 126.1, 125.8, 125.7, 118.3, 58.5, 53.1, 53.0, 39.5, 39.4, 37.2, 22.8, 21.4.
HRMS (ESI): Calculated for $C_{23}H_{23}NO_4Na$ $(M+Na)^+$ 400.1525, found 400.1519.

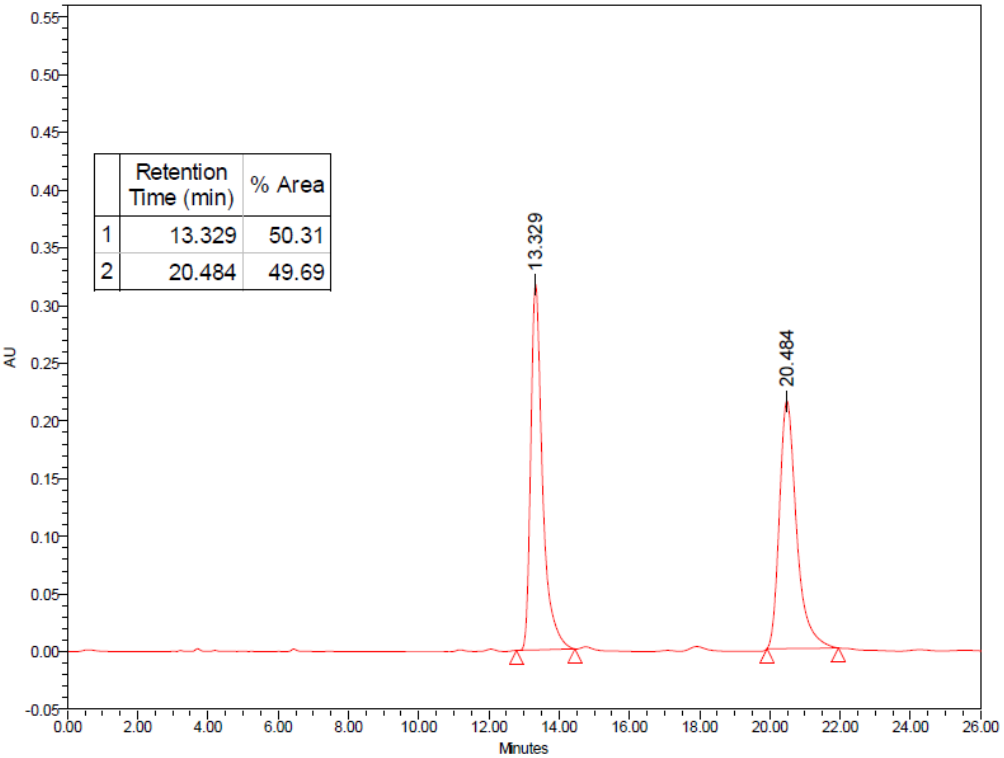

Retention Time (min) | % Area
1 | 20.511 | 48.86
2 | 23.240 | 51.14
20.511
23.240
AU
0.00
0.05
0.10
0.15
0.20
0.25
0.30
0.35
0.40
0.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00
20.00
22.00
24.00

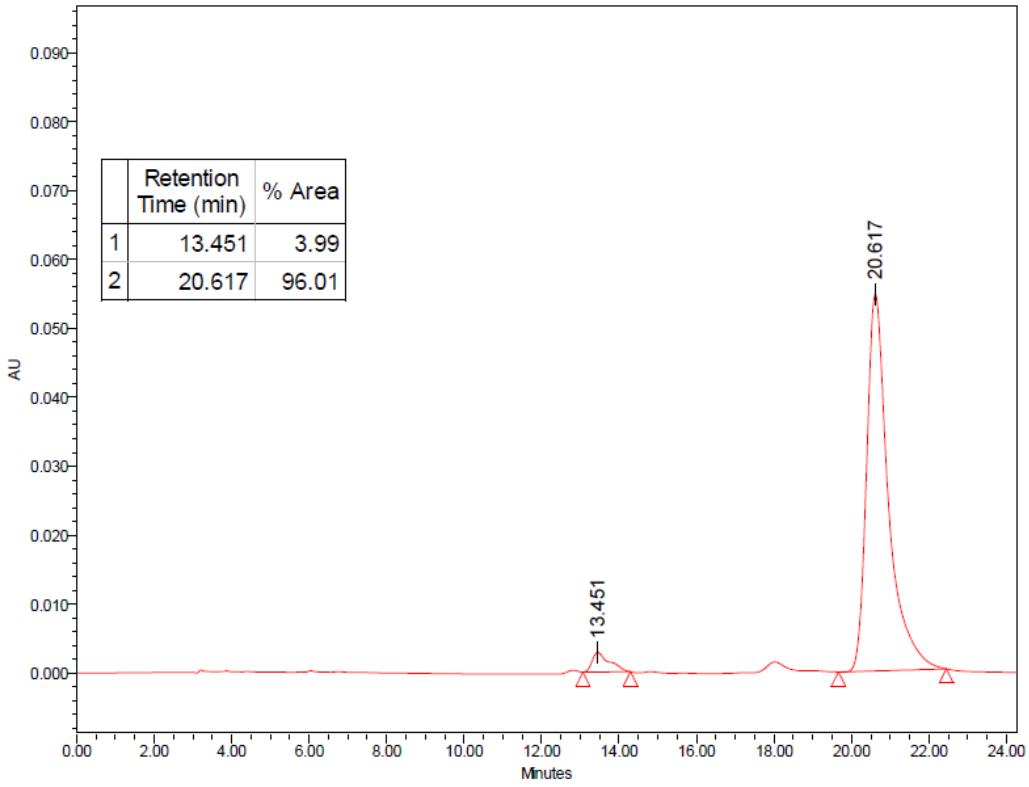

Retention Time (min) | % Area
1 | 20.860 | 94.96
2 | 23.261 | 5.04
20.860
23.261
AU
0.00
0.20
0.40
0.60
0.80
1.00
1.20
1.40
1.60
1.80
2.00
0.00
2.00
4.00
6.00
8.00
10.00
12.00
14.00
16.00
18.00
20.00
22.00
24.00
Minutes

Dimethyl (*R*,*Z*)-3-(1-(1*H*-indol-5-yl)ethylidene)-4-(cyanomethyl)cyclopentane-1,1-dicarboxylate 3ap

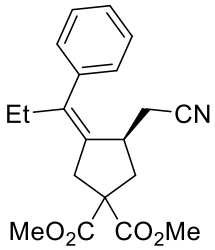


Yellow oil (94 mg, 86%) obtained from the general procedure (2) using substrate **1a** (76 mg, 0.30 mmol) and (1*H*-indol-5-yl)boronic acid (122 mg, 0.75 mmol).
R_f = 0.18 (petroleum ether/EtOAc 8:2).
HPLC (Chiralpak IA, hexane/*i*PrOH 90:10, 1 mL/min): Rt = 13.4 min (minor), 20.6 min (major).
$[\alpha]_D^{20}$ = -98 (c = 0.59, $CHCl_3$) for an enantiomeric excess of 92%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 8.18 (s, 1H), 7.39–7.38 (m, 1H), 7.37–7.34 (m, 1H), 7.25–7.21 (m, 1H), 6.97 (dd, *J* = 8.3, 1.6 Hz, 1H), 6.67–6.48 (m, 1H), 3.81 (s, 3H), 3.78 (s, 3H), 3.33–3.23 (m, 1H), 3.17 (d, *J* = 16.6 Hz, 1H), 3.07 (dt, *J* = 16.6, 2.1 Hz, 1H), 2.70 (ddd, *J* = 13.3, 8.4, 1.6 Hz, 1H), 2.09 (dd, *J* = 13.3, 8.4 Hz, 1H), 2.06–2.03 (m, 3H), 1.95 (dd, *J* = 16.9, 3.9 Hz, 1H), 1.80 (dd, *J* = 16.9, 8.4 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.9, 171.7, 134.8, 134.4, 134.2, 133.6, 128.0, 124.9, 121.6, 119.1, 118.7, 111.4, 102.7, 58.5, 53.00, 52.93, 39.5, 39.4, 37.2, 23.3, 21.3.
HRMS (ESI): Calculated for $C_{21}H_{22}N_2O_4Na$ $(M+Na)^+$ 389.1477, found 389.1473.

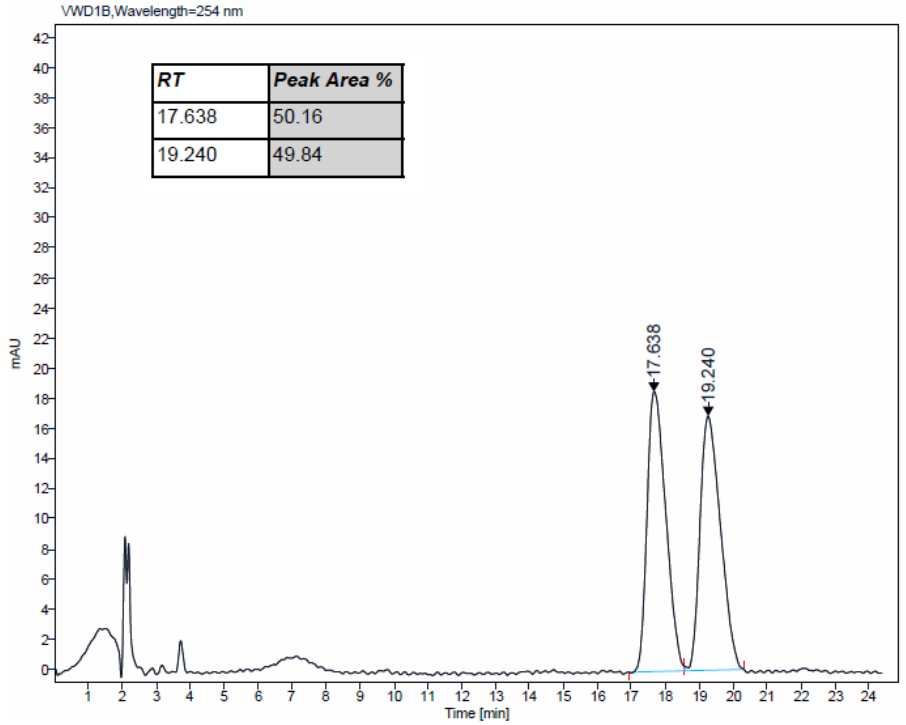




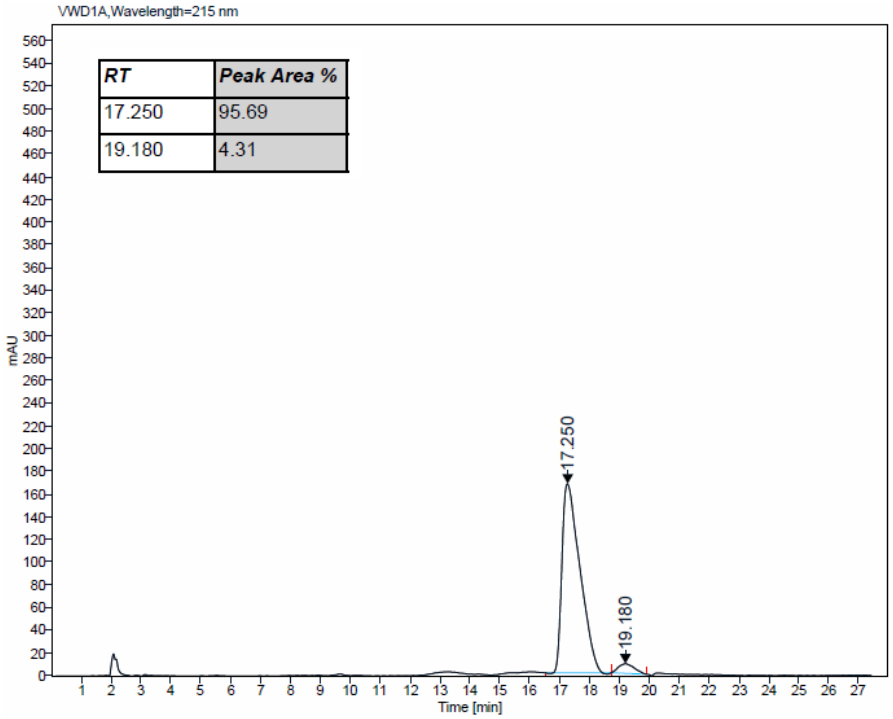
Dimethyl (*R*,*Z*)-3-(cyanomethyl)-4-(1-phenylpropylidene)cyclopentane-1,1-dicarboxylate 3ba



Colorless oil (93 mg, 91%) obtained from the general procedure (2) using substrate **1b** (79 mg, 0.30 mmol) and phenylboronic acid (92 mg, 0.75 mmol).
R_f = 0.22 (petroleum ether/EtOAc 9:1).
SFC (Chiralpak IE *s*CO_2/MeOH 98:2, 2 mL/min, P = 100 bar): Rt = 17.2 min (major), 19.2 min (minor).
$[\alpha]_D^{20}$ = -48 (c = 0.59, $CHCl_3$) for an enantiomeric excess of 91%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.36–7.30 (m, 2H), 7.29–7.24 (m, 1H), 7.12–7.06 (m, 2H), 3.79 (s, 3H), 3.78 (s, 3H), 3.16 (dd, *J* = 16.1, 2.0 Hz, 1H), 3.15–3.06 (m, 1H), 3.03 (dt, *J* = 16.1, 2.0 Hz, 1H), 2.69 (ddd, *J* = 13.4, 8.3, 1.8 Hz, 1H), 2.50–2.36 (m, 1H), 2.33–2.18 (m, 1H), 2.07 (dd, *J* = 13.4, 8.3 Hz, 1H), 1.96 (dd, *J* = 16.9, 3.8 Hz, 1H), 1.81 (dd, *J* = 16.9, 8.3 Hz, 1H), 0.89 (t, *J* = 7.5 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.7, 171.5, 141.1, 140.0, 133.8, 128.7 (2C), 127.9 (2C), 127.2, 118.4, 58.6, 53.0 (2C), 39.0, 38.6, 36.9, 29.5, 21.4, 12.1.
HRMS (ESI): Calculated for $C_{20}H_{23}NO_4Na$ $(M+Na)^+$ 364.1525, found 364.1520.

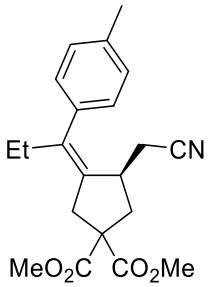


RT	Peak Area %
17.638	50.16
19.240	49.84

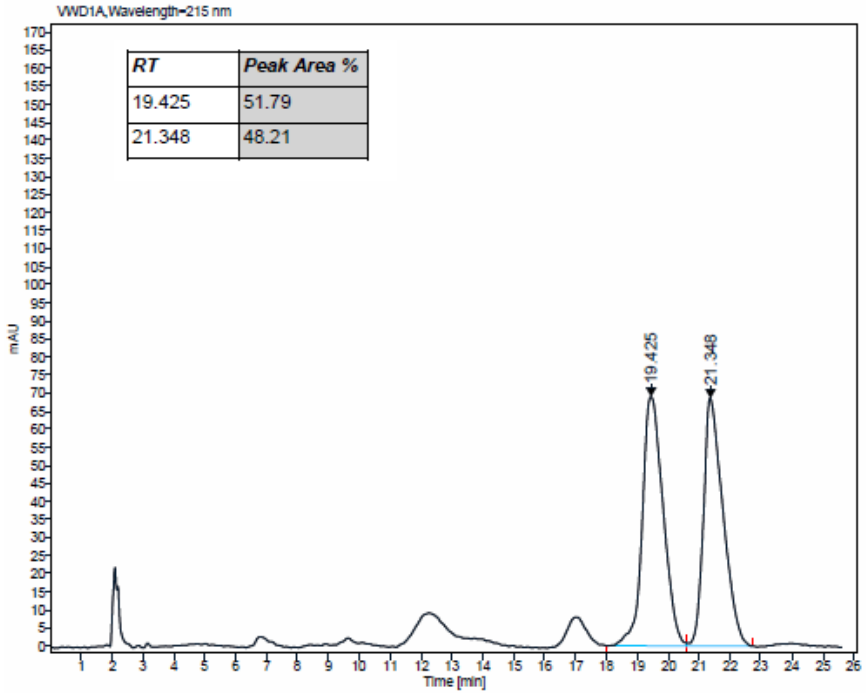


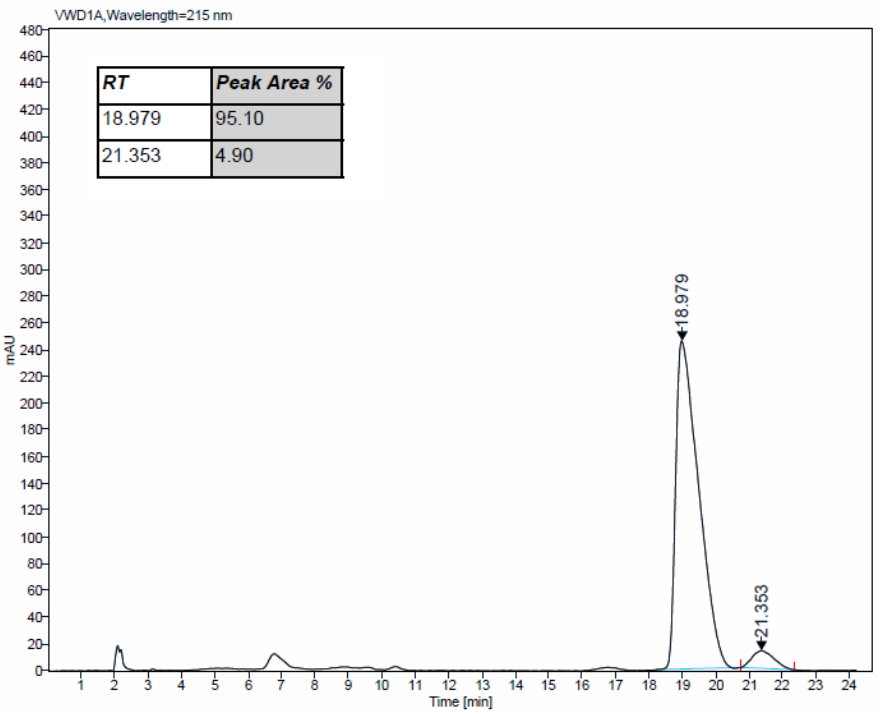
RT	Peak Area %
17.250	95.69
19.180	4.31

Dimethyl (*R*,*Z*)-3-(cyanomethyl)-4-(1-(p-tolyl)propylidene)cyclopentane-1,1-dicarboxylate 3bb

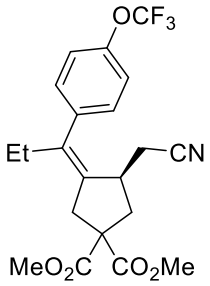


Colorless oil (91 mg, 86%) obtained from the general procedure (2) using substrate **1b** (79 mg, 0.30 mmol) and 4-tolylboronic acid (102 mg, 0.75 mmol).
R_f = 0.28 (petroleum ether/EtOAc 9:1).
SFC (Chiralpak IE *s*CO_2/MeOH 98:2, 2 mL/min, P = 100 bar): Rt = 19.0 min (major), 21.3 min (minor).
$[\alpha]_D^{20}$ = -73 (c = 0.54, $CHCl_3$) for an enantiomeric excess of 90%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.13 (d, *J* = 8.0 Hz, 2H), 6.98 (d, *J* = 8.0 Hz, 2H), 3.78 (s, 3H), 3.77 (s, 3H), 3.14 (dd, *J* = 16.3, 1.8 Hz, 1H), 3.13–3.05 (m, 1H), 3.02 (dt, *J* = 16.3, 1.8 Hz, 1H), 2.69 (ddd, *J* = 13.3, 8.1, 1.8 Hz, 1H), 2.48–2.36 (m, 1H), 2.35 (s, 3H), 2.26–2.16 (m, 1H), 2.07 (dd, *J* = 13.3, 8.5 Hz, 1H), 1.98 (dd, *J* = 16.9, 3.9 Hz, 1H), 1.83 (dd, *J* = 16.9, 8.5 Hz, 1H), 0.88 (t, *J* = 7.5 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.7, 171.5, 139.9, 138.0, 136.8, 133.6, 129.4 (2C), 127.8 (2C), 118.5, 58.6, 52.9 (2C), 39.0, 38.6, 36.9, 29.5, 21.4, 21.2, 12.1.
HRMS (ESI): Calculated for $C_{21}H_{25}NO_4Na$ $(M+Na)^+$ 378.1681, found 378.1677.

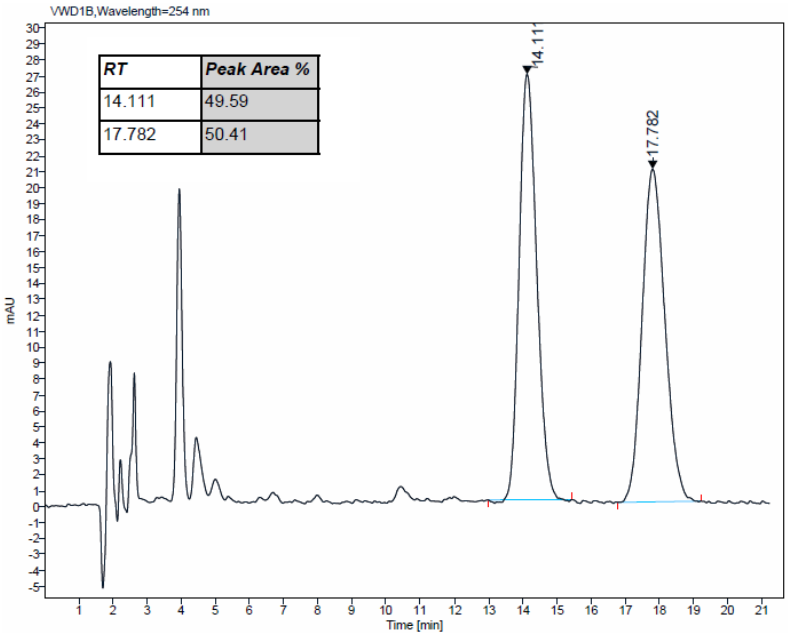


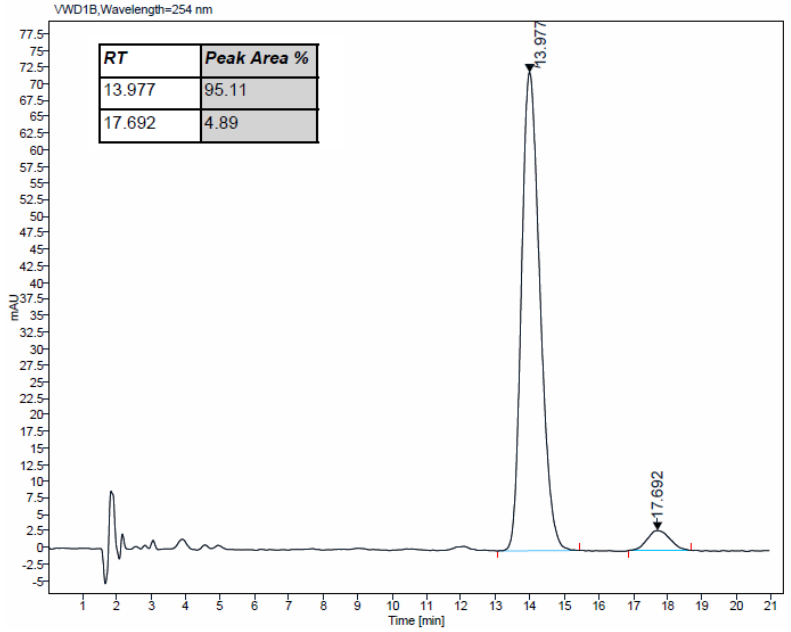


Dimethyl (*R*,*Z*)-3-(cyanomethyl)-4-(1-(4-(trifluoromethoxy)phenyl)propylidene) cyclopentane-1,1-dicarboxylate 3be

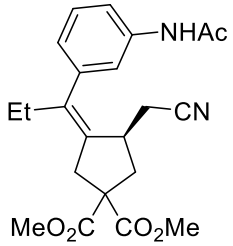


Yellow oil (111 mg, 87%) obtained from the general procedure (2) using substrate **1b** (79 mg, 0.30 mmol) and 4-trifluoromethoxyphenylboronic acid (152 mg, 0.75 mmol).
R_f = 0.24 (petroleum ether/EtOAc 9:1).
SFC (Chiralpak IE *s*CO_2/MeOH 98:2, 2 mL/min, P = 100 bar): Rt = 14.0 min (major), 17.7 min (minor).
$[\alpha]_D^{20}$ = -55 (c = 0.77, $CHCl_3$) for an enantiomeric excess of 90%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.23–7.16 (m, 2H), 7.16–7.10 (m, 2H), 3.78 (s, 3H), 3.77 (s, 3H), 3.15 (dd, *J* = 16.3, 1.8 Hz, 1H), 3.10–3.06 (m, 1H), 3.03 (dt, *J* = 16.3, 1.8 Hz, 1H), 2.68 (ddd, *J* = 13.4, 8.0, 1.8 Hz, 1H), 2.50–2.36 (m, 1H), 2.27–2.15 (m, 1H), 2.09 (dd, *J* = 13.4, 8.4 Hz, 1H), 1.99 (dd, *J* = 16.9, 3.8 Hz, 1H), 1.82 (dd, *J* = 16.9, 8.0 Hz, 1H), 0.89 (t, *J* = 7.5 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.6, 171.3, 148.2, 139.7, 138.7, 134.9, 129.5 (2C), 121.2 (2C), 120.4 (q, *J* = 257.5 Hz), 118.0, 58.5, 53.0 (2C), 38.9, 38.6, 36.8, 29.5, 21.5, 12.0.
^{19}F NMR (376 MHz, $CDCl_3$, δ): -57.9.
HRMS (ESI): Calculated for $C_{21}H_{22}NO_5F_3Na$ $(M+Na)^+$ 448.1348, found 448.1341.



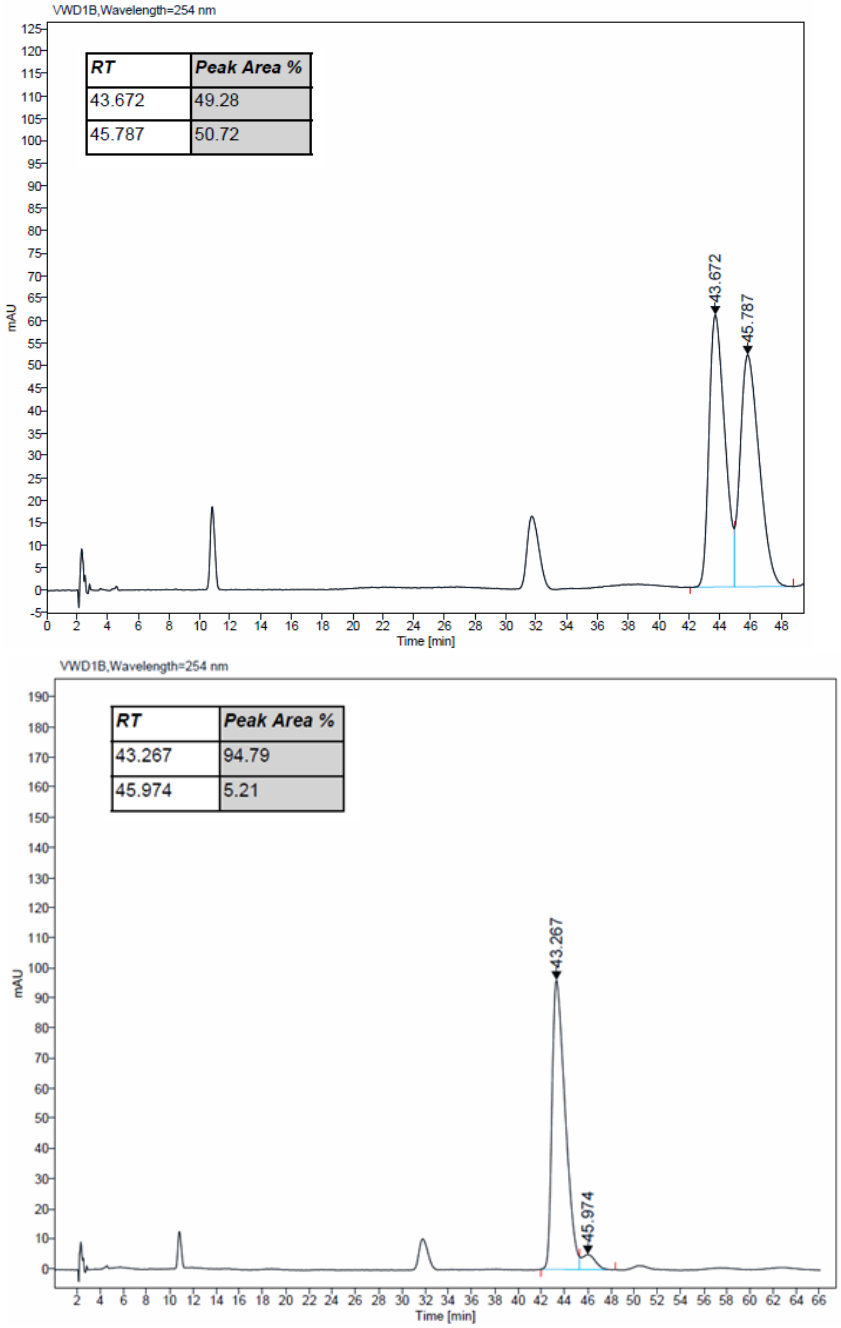


Dimethyl (*R*,*Z*)-3-(1-(3-acetamidophenyl)propylidene)-4-(cyanomethyl)cyclopentane-1,1-dicarboxylate 3bq

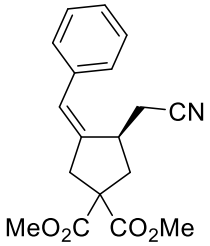


Yellow oil (107 mg, 90%) obtained from the general procedure (2) using substrate **1b** (79 mg, 0.30 mmol) and 3-acetamidophenylboronic acid (135 mg, 0.75 mmol).
R_f = 0.33 (petroleum ether/EtOAc 4:6).
SFC (Chiralpak IE *s*CO_2/MeOH 95:5, 2 mL/min, P = 100 bar): Rt = 43.2 min (major), 46.0 min (minor).
$[\alpha]_D^{20}$ = -46 (c = 0.79, $CHCl_3$) for an enantiomeric excess of 90%.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.50–7.43 (m, 2H), 7.32–7.24 (m, 1H), 7.23 (s, 1H), 6.88–6.75 (m, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 3.20–3.05 (m, 2H), 3.01 (dt, *J* = 16.4, 2.0 Hz, 1H), 2.67 (ddd, *J* = 13.4, 8.1, 1.7 Hz, 1H), 2.45–2.33 (m, 1H), 2.27–2.18 (m, 1H), 2.16 (s, 3H), 2.07 (dd, *J* = 13.4, 8.1 Hz, 1H), 2.02 (dd, *J* = 16.9, 3.9 Hz, 1H), 1.88 (dd, *J* = 16.9, 8.4 Hz, 1H), 0.88 (t, *J* = 7.5 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.7, 171.5, 168.5, 141.8, 139.5, 138.3, 134.2, 129.4, 123.8, 119.2, 118.6, 118.4, 58.6, 53.0 (2C), 39.0, 38.6, 36.9, 29.4, 24.6, 21.5, 12.1.
HRMS (ESI): Calculated for $C_{22}H_{26}N_2O_5Na$ $(M+Na)^+$ 421.1739, found 421.1732.



Dimethyl (*R*,*Z*)-3-benzylidene-4-(cyanomethyl)cyclopentane-1,1-dicarboxylate 3ca



Colorless oil (64 mg, 68%) obtained from the general procedure (2), with slight modifications, using substrate **1c** (70 mg, 0.30 mmol), phenylboronic acid (92 mg, 0.75 mmol) and potassium fluoride (35 mg, 0.6 mmol).

R_f = 0.22 (petroleum ether/EtOAc 9:1).

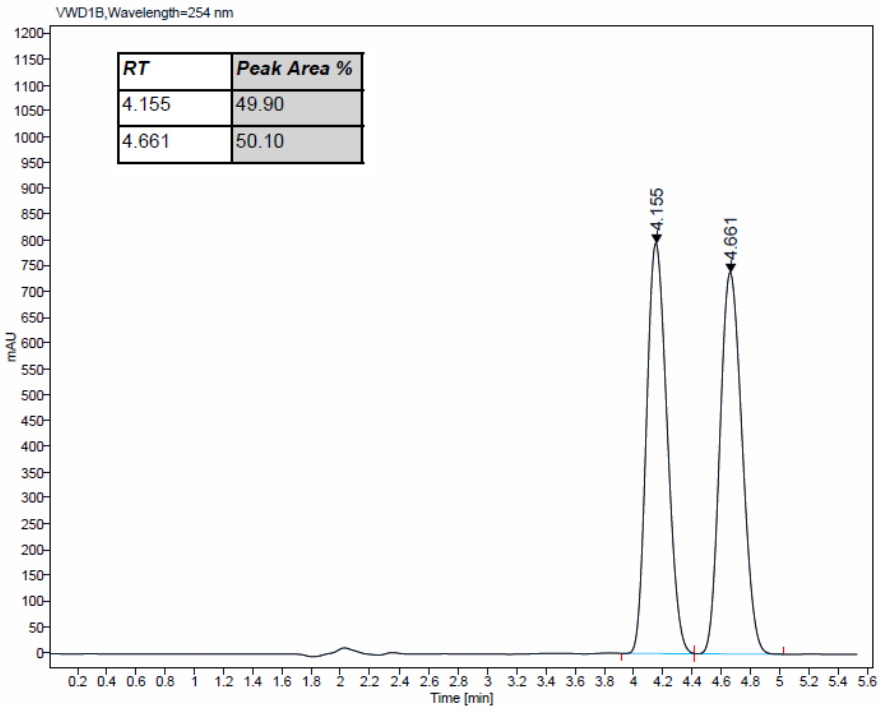
SFC (Chiralpak ADH *s*CO_2/MeOH 90:10, 2 mL/min, P = 100 bar): Rt = 4.2 min (minor), 4.7 min (major).

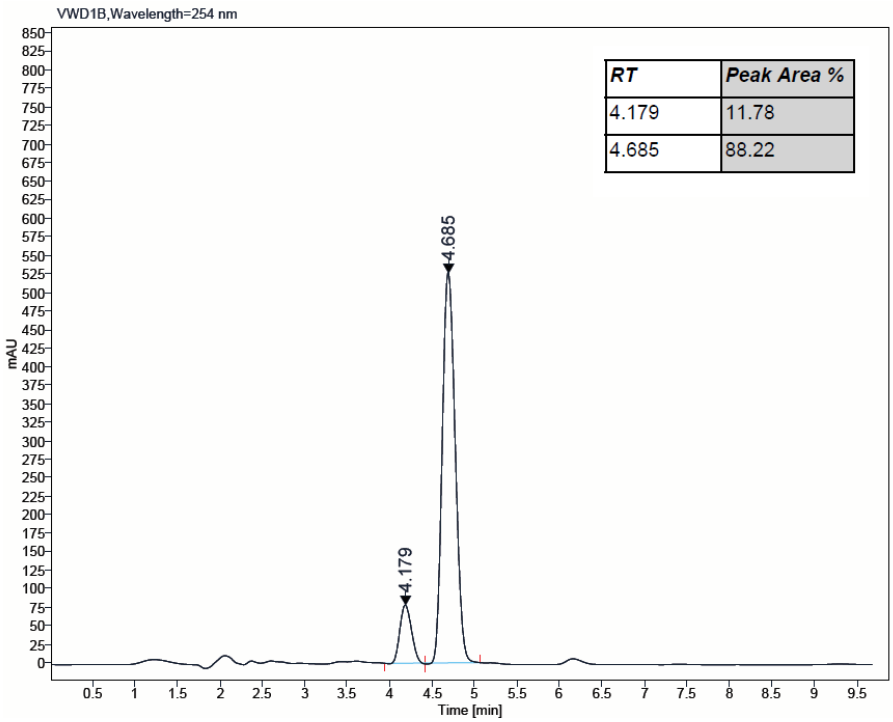
$[\alpha]_D^{20}$ = -62 (c = 0.88, $CHCl_3$) for an enantiomeric excess of 77%.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.34–7.31 (m, 2H), 7.27–7.21 (m, 1H), 7.24–7.18 (m, 2H), 6.55 (s, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 3.61–3.51 (m, 1H), 3.24 (dt, *J* = 16.5, 2.6 Hz, 1H), 3.08 (dt, *J* = 16.5, 1.7 Hz, 1H), 2.84 (ddd, *J* = 13.6, 8.3, 1.7 Hz, 1H), 2.43 (dd, *J* = 17.0, 3.9 Hz, 1H), 2.24 (dd, *J* = 17.0, 9.2 Hz, 1H), 2.21 (dd, *J* = 13.8, 7.4 Hz, 1H).

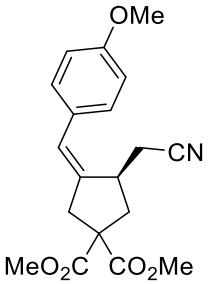
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.5, 171.4, 141.2, 136.4, 128.7 (2C), 127.9 (2C), 127.3, 125.6, 118.2, 58.2, 53.0 (2C), 42.8, 39.6, 36.3, 20.8.

HRMS (ESI): Calculated for $C_{18}H_{19}NO_4Na$ $(M+Na)^+$ 336.1212, found 336.1205.





Dimethyl (*R*,*Z*)-3-(cyanomethyl)-4-(4-methoxybenzylidene)cyclopentane-1,1-dicarboxylate 3cc



Colorless oil (66 mg, 64%) obtained from the general procedure (2) with slight modifications using substrate **1c** (70 mg, 0.30 mmol), 4-methoxyphenylboronic acid (115 mg, 0.75 mmol) and potassium fluoride (35 mg, 0.6 mmol).

R_f = 0.18 (petroleum ether/EtOAc 9:1).

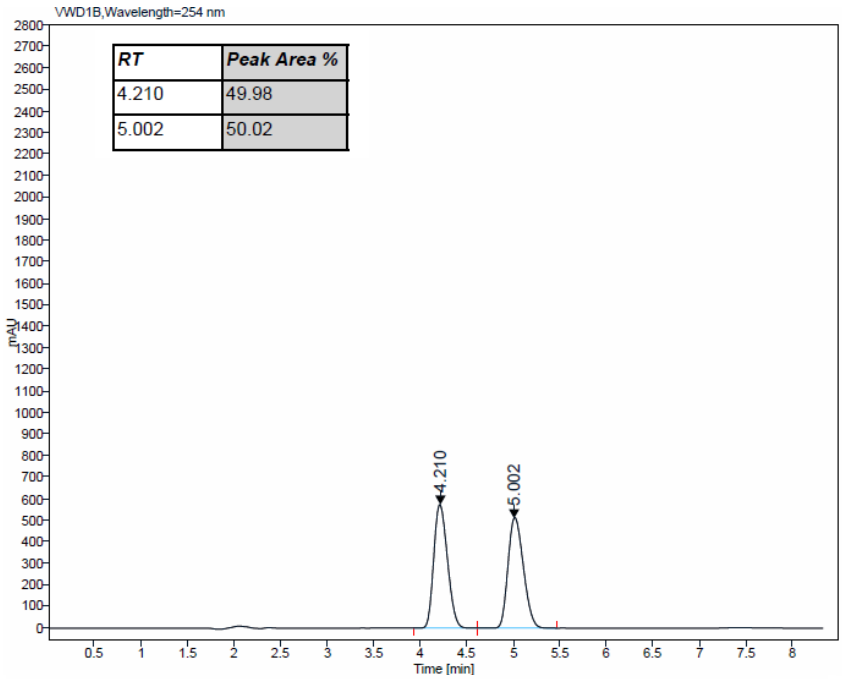
SFC (Chiralpak ADH *s*CO_2/MeOH 90:10, 2 mL/min, P = 100 bar): Rt = 4.1 min (major), 4.9 min (minor).

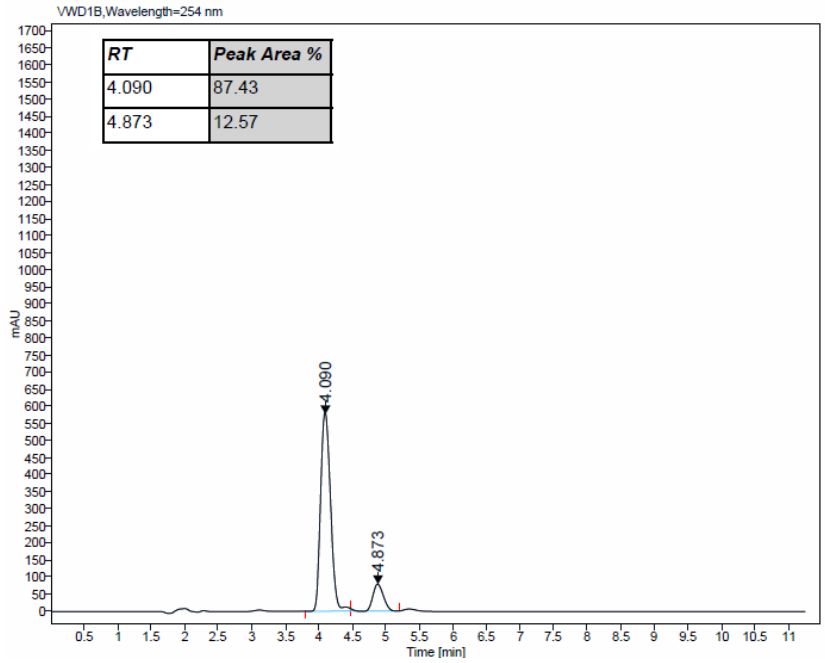
$[\alpha]_D^{20}$ = -49 (c = 0.81, $CHCl_3$) for an enantiomeric excess of 75%.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.17–7.10 (m, 2H), 6.89–6.84 (m, 2H), 6.47 (s, 1H), 3.81 (s, 3H), 3.77 (s, 3H), 3.76 (s, 3H), 3.58–3.48 (m, 1H), 3.21 (dt, *J* = 16.4, 2.5 Hz, 1H), 3.06 (dt, *J* = 16.4, 1.7 Hz, 1H), 2.84 (ddd, *J* = 13.6, 8.4, 1.7 Hz, 1H), 2.48 (dd, *J* = 17.0, 3.9 Hz, 1H), 2.26 (dd, *J* = 17.1, 9.2 Hz, 1H), 2.21 (dd, *J* = 13.6, 7.2 Hz, 1H).

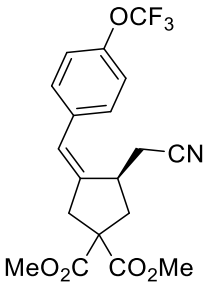
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.5 (2C), 158.7, 139.5, 129.1 (2C), 128.9, 125.1, 118.4, 114.1 (2C), 58.2, 55.3, 53.0 (2C), 42.8, 39.6, 36.4, 20.7.

HRMS (ESI): Calculated for $C_{19}H_{21}NO_5Na$ $(M+Na)^+$ 366.1317, found 366.1313.



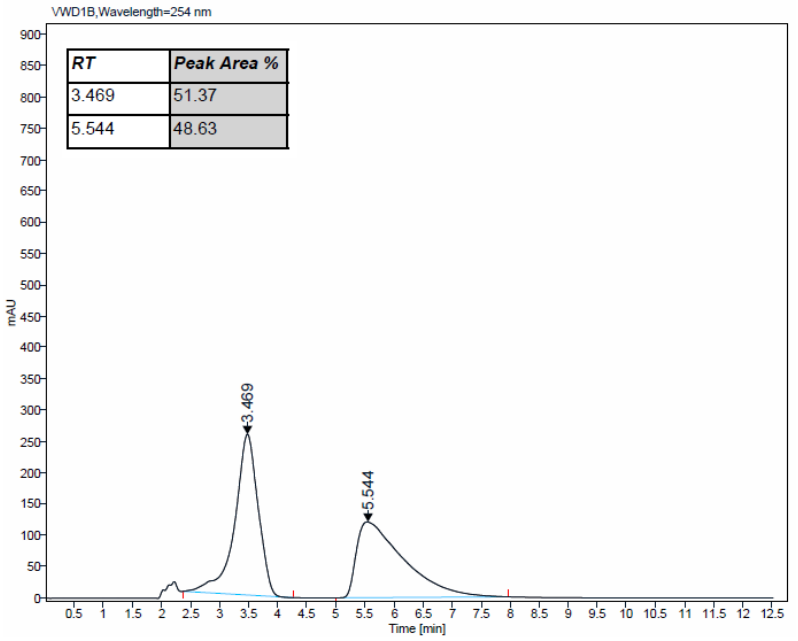


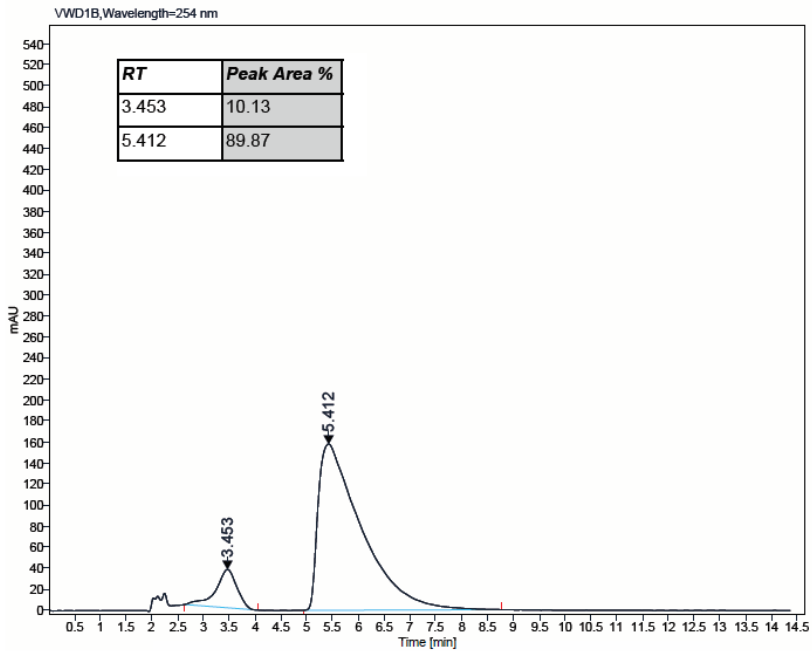
Dimethyl (*R*,*Z*)-3-(cyanomethyl)-4-(4-(trifluoromethoxy)benzylidene)cyclopentane-1,1-dicarboxylate 3ce



Yellow oil (84 mg, 71%) obtained from the general procedure (2) with slight modifications using substrate **1c** (70 mg, 0.30 mmol), 4-trifluoromethoxyphenylboronic acid (152 mg, 0.75 mmol) and potassium fluoride (35 mg, 0.6 mmol).

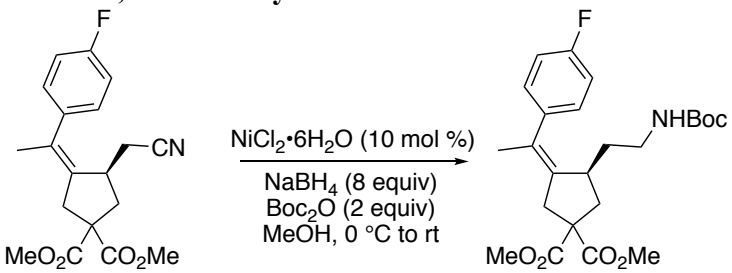
R_f = 0.24 (petroleum ether/EtOAc 9:1).
SFC (Chiralpak ID *s*CO_2/MeOH 98:2, 2 mL/min, P = 100 bar): Rt = 3.5 min (minor), 5.5 min (major).
$[\alpha]_D^{20}$ = -54 (c = 0.71, $CHCl_3$) for an enantiomeric excess of 80%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.25–7.22 (m, 2H), 7.20–7.16 (m, 2H), 6.52 (s, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 3.57–3.47 (m, 1H), 3.24 (dt, *J* = 16.5, 2.5 Hz, 1H), 3.08 (dt, *J* = 16.5, 1.7 Hz, 1H), 2.84 (ddd, *J* = 13.6, 8.3, 1.7 Hz, 1H), 2.41 (dd, *J* = 17.0, 4.0 Hz, 1H), 2.25 (dd, *J* = 17.0, 8.8 Hz, 1H), 2.21 (dd, *J* = 13.6, 7.3 Hz, 1H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 171.4, 171.3, 148.1, 142.4, 135.1, 129.3 (2C), 124.3, 121.2 (2C), 120.4 (q, *J* = 257.4 Hz), 117.9, 58.1, 53.1 (2C), 42.8, 39.5, 36.3, 20.9.
^{19}F NMR (376 MHz, $CDCl_3$, δ): -57.8.
HRMS (ESI): Calculated for $C_{19}H_{18}NO_5F_3Na$ $(M+Na)^+$ 420.1035, found 420.1029.





D. Post-functionalization

Dimethyl (*R*,*Z*)-3-(2-((tert-butoxycarbonyl)amino)ethyl)-4-(1-(4-fluorophenyl) ethylidene)cyclopentane-1,1-dicarboxylate 4af



To a solution of **3af** (50 mg, 0.145 mmol) in MeOH (3.5 mL), cooled at 0 °C, was added Boc_2O (64 mg, 0.29 mmol) and $NiCl_2$•$6H_2O$ (3.5 mg, 14.5 μmol). To this solution was added $NaBH_4$ (45 mg, 1.16 mmol) in portions with stirring and the mixture was stirred vigorously overnight. After total consumption of the starting material, monitored by TLC, the reaction mixture was concentrated under vacuum. The residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc 80:20) to afford **4af** (41 mg, 63%) as a colorless oil.

R_f = 0.35 (petroleum ether/EtOAc 8:2).

HPLC (Chiralpak ID, hexane/*i*PrOH 90:10, 1 mL/min): Rt = 12.6 min (major), 15.2 min (minor).

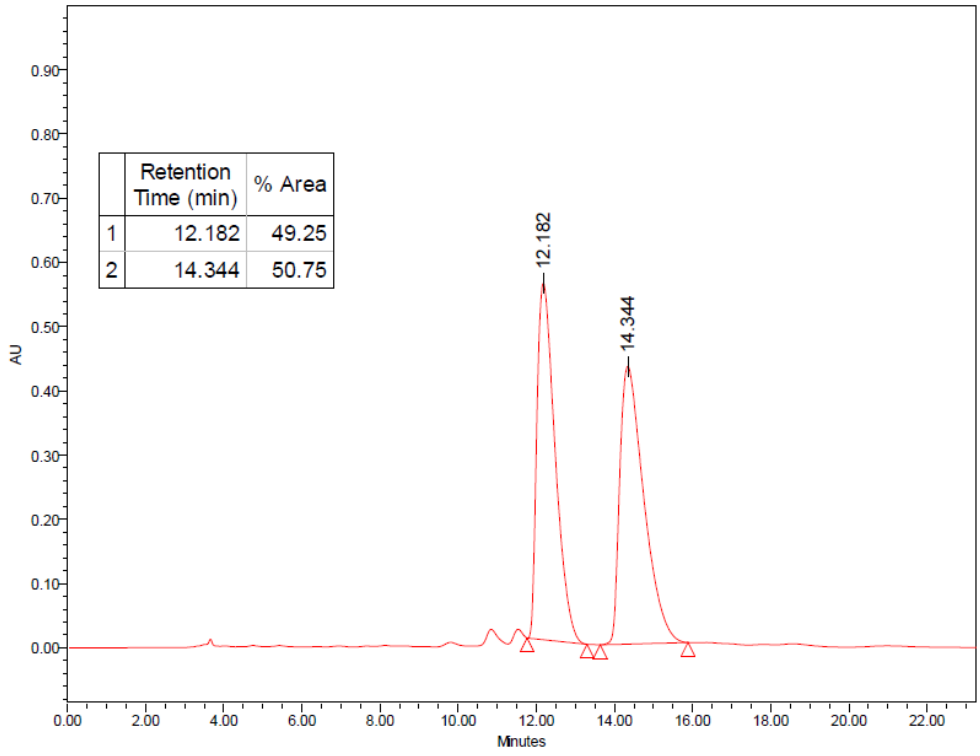
$[\alpha]_D^{20}$ = -82 (c = 0.36, $CHCl_3$) for an enantiomeric excess of 90%.

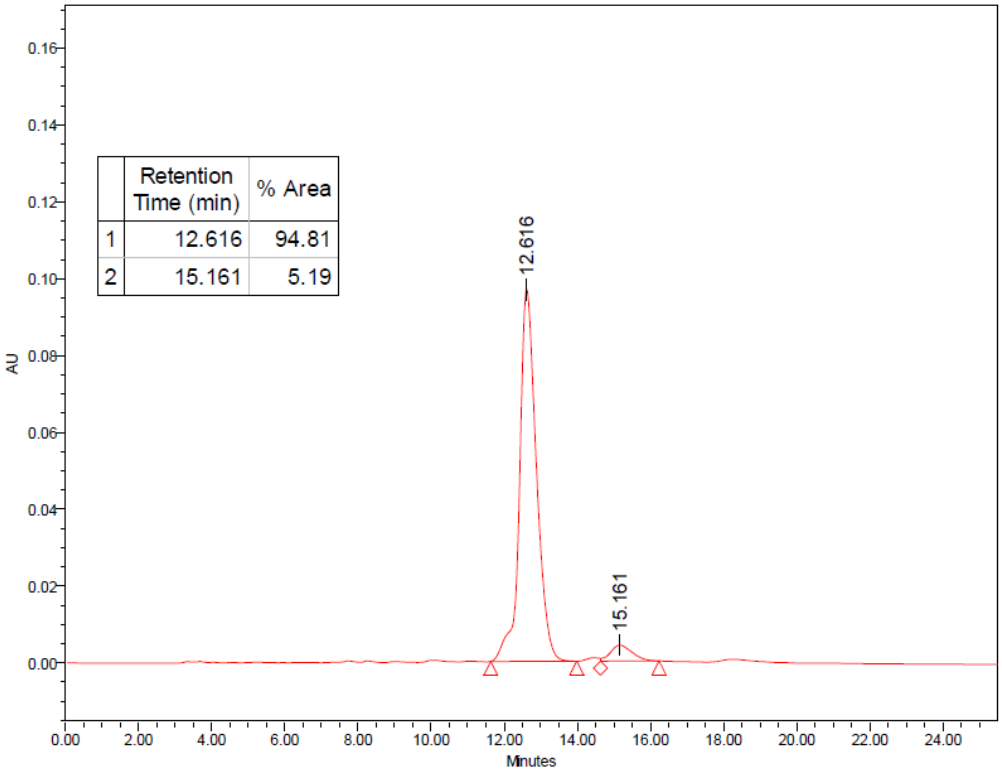
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.14–7.06 (m, 2H), 7.04–6.96 (m, 2H), 3.88 (br s, 1H), 3.76 (s, 3H), 3.74 (s, 3H), 3.06 (d, *J* = 16.6 Hz, 1H), 2.98 (d, *J* = 16.8 Hz, 1H), 2.93–2.76 (m, 3H), 2.59 (dd, *J* = 13.1, 8.1 Hz, 1H), 1.98–1.92 (m, 4H), 1.39 (s, 9H), 1.21–1.01 (m, 2H).

^{13}C NMR (101 MHz, $CDCl_3$, δ): 172.3 (2C), 161.4 (d, *J* = 245.8 Hz), 155.7, 139.6 (d, *J* = 3.2 Hz), 138.4, 129.4, 129.3 (d, *J* = 8.2 Hz, 2C), 115.3 (d, *J* = 21.1 Hz, 2C), 79.0, 58.9, 52.8, 52.7, 39.2, 38.9, 38.2, 37.9, 34.3, 28.3 (3C), 22.4.

^{19}F NMR (376 MHz, $CDCl_3$, δ): -115.7.

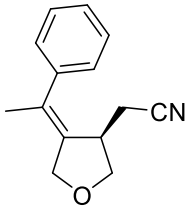
HRMS (ESI): Calculated for $C_{24}H_{33}FNO_6$ $(M+H)^+$ 450.2292, found 450.2285.


Retention Time (min) | % Area
1 | 12.182 | 49.25
2 | 14.344 | 50.75
12.182
14.344
AU
Minutes

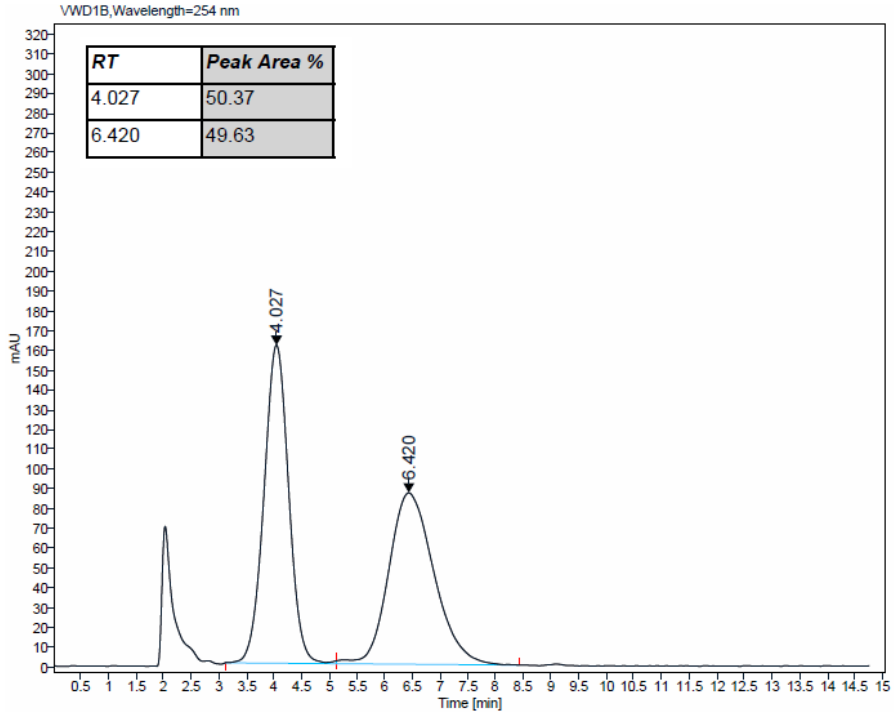

Retention Time (min) | % Area
1 | 12.616 | 94.81
2 | 15.161 | 5.19
12.616
15.161
AU
Minutes

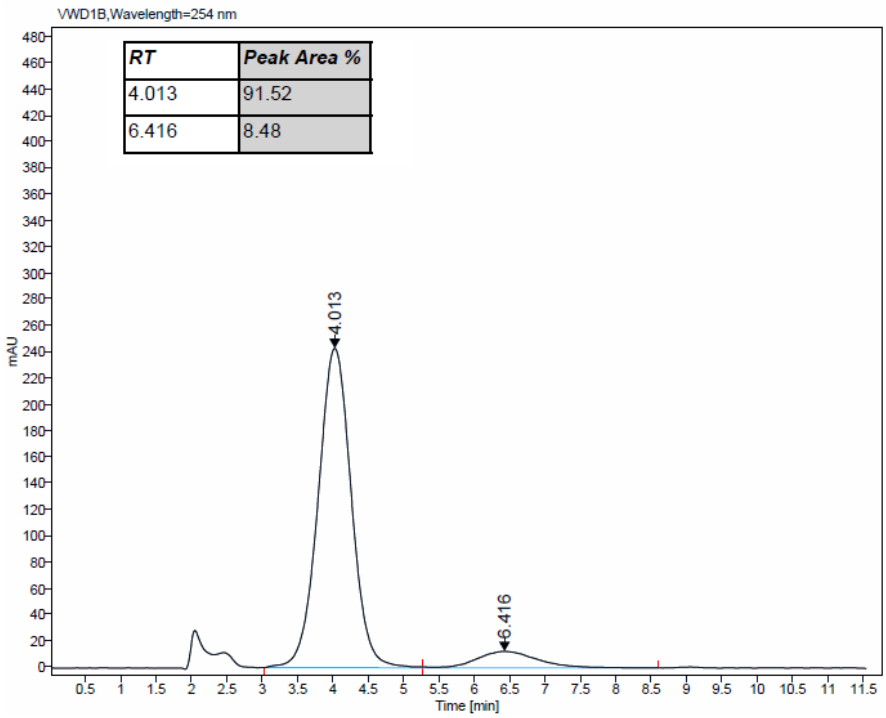
IV. Access to heterocyclic derivatives

(*R*,*E*)-2-(4-(1-phenylethylidene)tetrahydrofuran-3-yl)acetonitrile 6aa

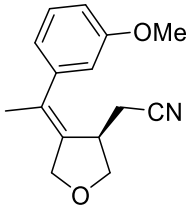


Yellow oil (29 mg, 45%) obtained from the general procedure (2), with slight modifications, using substrate **5a** (41 mg, 0.30 mmol), phenylboronic acid (111 mg, 0.90 mmol) and potassium fluoride (35 mg, 0.60 mmol) in a mixture of dioxane/water 10:1 at 80 °C.
R_f = 0.28 (petroleum ether/EtOAc 85:15).
SFC (Chiralpak ADH *s*CO_2/MeOH 98:2, 2 mL/min, P = 100 bar): Rt = 4.0 min (major), 6.4 min (minor).
$[\alpha]_D^{20}$ = -72 (c = 0.59, $CHCl_3$) for an enantiomeric excess of 83%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.43–7.15 (m, 5H), 4.52 (dt, *J* = 13.4, 1.6 Hz, 1H), 4.42 (d, *J* = 13.9 Hz, 1H), 4.00 (dd, *J* = 9.3, 5.9 Hz, 1H), 3.90 (dd, *J* = 9.3, 3.3 Hz, 1H), 3.24–3.12 (m, 1H), 2.13 (dd, *J* = 16.8, 9.3 Hz, 1H), 2.02 (ddd, *J* = 16.8, 4.0, 0.8 Hz, 1H), 1.95–1.89 (m, 3H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 142.3, 135.6, 131.0, 128.9 (2C), 127.4, 127.1 (2C), 118.4, 73.1, 70.5, 38.8, 22.0, 19.8.
HRMS (ESI): Calculated for $C_{14}H_{15}NONa$ $(M+Na)^+$ 236.1051, found 236.1047.

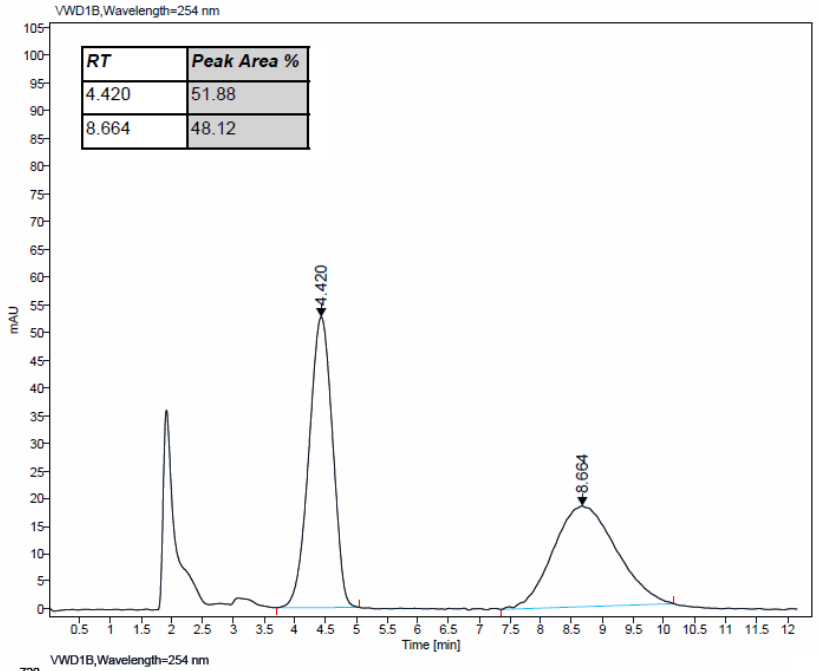


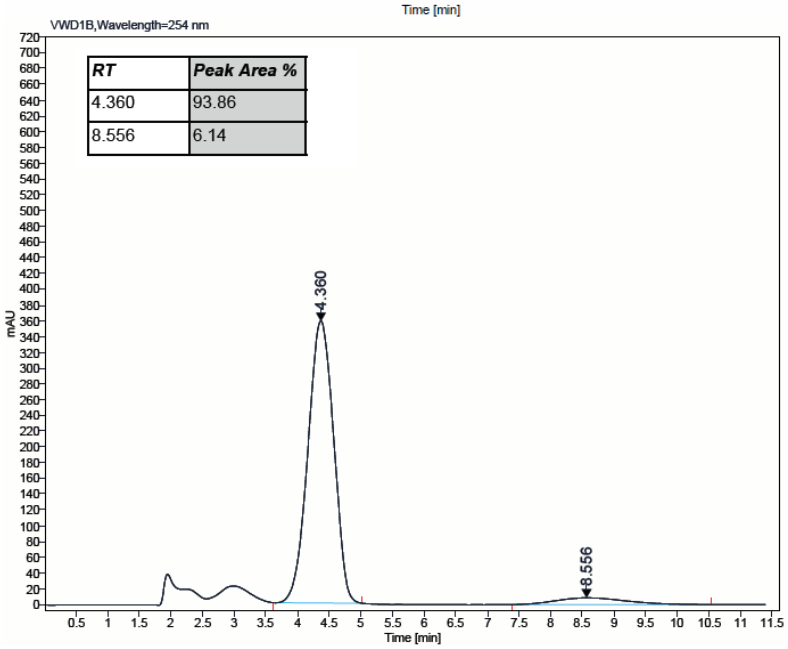


(*R*,*E*)-2-(4-(1-(3-methoxyphenyl)ethylidene)tetrahydrofuran-3-yl)acetonitrile 6ad

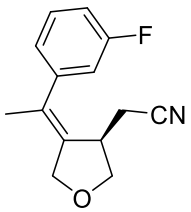


Yellow oil (41 mg, 56%) obtained from the general procedure (2), with slight modifications, using substrate **5a** (41 mg, 0.30 mmol), 3-methoxyphenylboronic acid (138 mg, 0.90 mmol) and potassium fluoride (35 mg, 0.60 mmol) in a mixture of dioxane/water 10:1 at 80 °C.
R_f = 0.23 (petroleum ether/EtOAc 85:15).
SFC (Chiralpak ADH *s*CO_2/MeOH 98:2, 2 mL/min, P = 100 bar): Rt = 4.4 min (major), 8.6 min (minor).
$[\alpha]_D^{20}$ = -57 (c = 0.72, $CHCl_3$) for an enantiomeric excess of 88%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.33–7.26 (m, 1H), 6.83 (ddd, *J* = 8.3, 2.6, 1.0 Hz, 1H), 6.77 (ddd, *J* = 7.5, 1.6, 1.0 Hz, 1H), 6.72 (dd, *J* = 2.6, 1.5 Hz, 1H), 4.51 (dt, *J* = 13.4, 1.6 Hz, 1H), 4.41 (d, *J* = 13.4 Hz, 1H), 3.99 (dd, *J* = 9.4, 5.8 Hz, 1H), 3.90 (dd, *J* = 9.4, 3.3 Hz, 1H), 3.82 (s, 3H), 3.33–3.13 (m, 1H), 2.15 (dd, *J* = 16.9, 9.4 Hz, 1H), 2.06 (ddd, *J* = 16.9, 4.1, 0.8 Hz, 1H), 1.92 (q, *J* = 1.4 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 159.8, 143.8, 135.6, 130.9, 130.0, 119.5, 118.4, 113.2, 112.4, 73.1, 70.5, 55.3, 38.8, 21.9, 19.8.
HRMS (ESI): Calculated for $C_{15}H_{17}NO_2Na$ $(M+Na)^+$ 266.1157, found 266.1152.



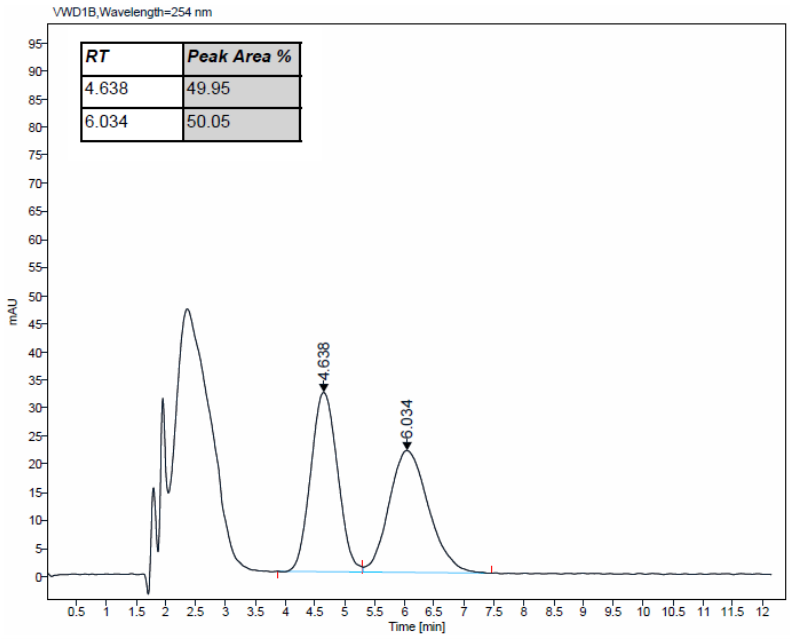


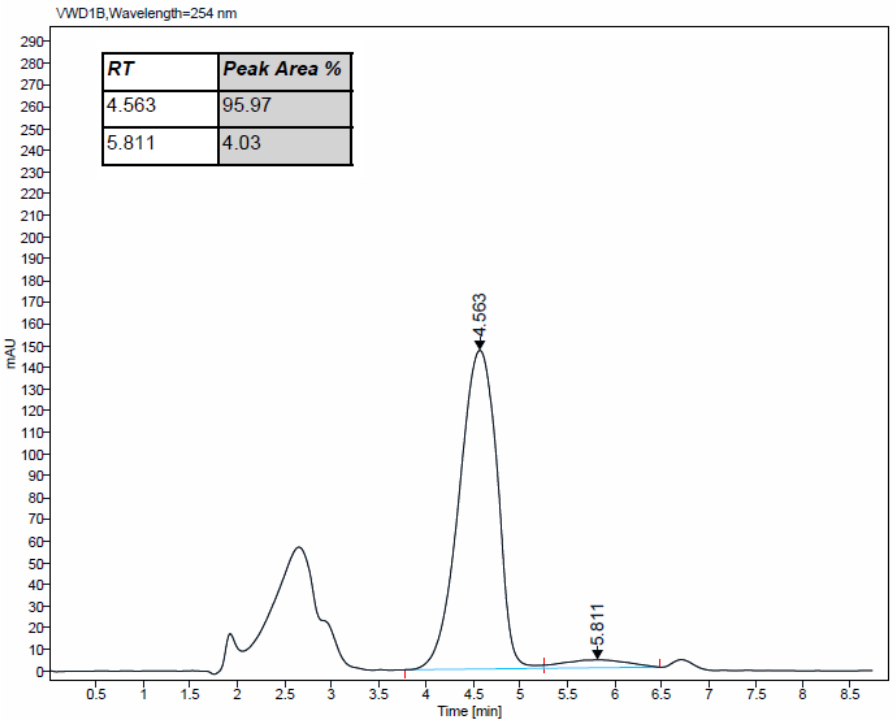
(*R*,*E*)-2-(4-(1-(3-fluorophenyl)ethylidene)tetrahydrofuran-3-yl)acetonitrileacetonitrile 6ar



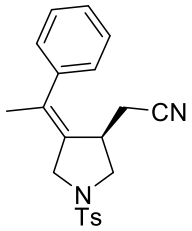
Yellow oil (35 mg, 51%) obtained from the general procedure (2), with slight modifications, using substrate **5a** (41 mg, 0.30 mmol), 3-fluorophenylboronic acid (126 mg, 0.90 mmol) and potassium fluoride (35 mg, 0.60 mmol) in a mixture of dioxane/water 10:1 at 80 °C.
R_f = 0.29 (petroleum ether/EtOAc 85:15).
SFC (Chiralpak ADH *s*CO_2/MeOH 98:2, 2 mL/min, P = 100 bar): Rt = 4.5 min (major), 5.8 min (minor).
$[\alpha]_D^{20}$ = -35 (c = 0.88, $CHCl_3$) for an enantiomeric excess of 92%.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.45–7.29 (m, 1H), 7.06–6.94 (m, 2H), 6.90 (ddd, *J* = 9.6, 2.6, 1.5 Hz, 1H), 4.52 (dt, *J* = 13.6, 1.6 Hz, 1H), 4.41 (d, *J* = 14.2 Hz, 1H), 3.99 (dd, *J* = 9.4, 5.8 Hz, 1H), 3.92 (ddd, *J* = 9.4, 3.2, 0.6 Hz, 1H), 3.19–3.14 (m, 1H), 2.16 (dd, *J* = 16.9, 9.5 Hz, 1H), 2.04 (ddd, *J* = 16.9, 4.0, 0.9 Hz, 1H), 1.92 (q, *J* = 1.4 Hz, 3H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 163.0 (d, *J* = 247.7 Hz), 144.6 (d, *J* = 7.3 Hz), 136.6, 130.6 (d, *J* = 8.5 Hz), 130.0, 123.0 (d, *J* = 3.1 Hz), 118.2, 114.5 (d, *J* = 15.1 Hz), 114.3 (d, *J* = 15.3 Hz), 73.1, 70.5, 38.8, 21.9, 20.0.
^{19}F NMR (376 MHz, $CDCl_3$, δ): -112.0.
HRMS (ESI): Calculated for $C_{14}H_{14}FNONa$ $(M+Na)^+$ 254.0957, found 254.0952.





(*R*,*E*)-2-(4-(1-phenylethylidene)-1-tosylpyrrolidin-3-yl)acetonitrile 6ba



Colorless oil (70 mg, 64%) obtained from the general procedure (2), with slight modifications, using substrate **5b** (86 mg, 0.30 mmol), phenylboronic acid (111 mg, 0.90 mmol) and potassium fluoride (35 mg, 0.60 mmol) in a mixture of dioxane/water 10:1 at 80 °C.

R_f = 0.15 (petroleum ether/EtOAc 85:15).

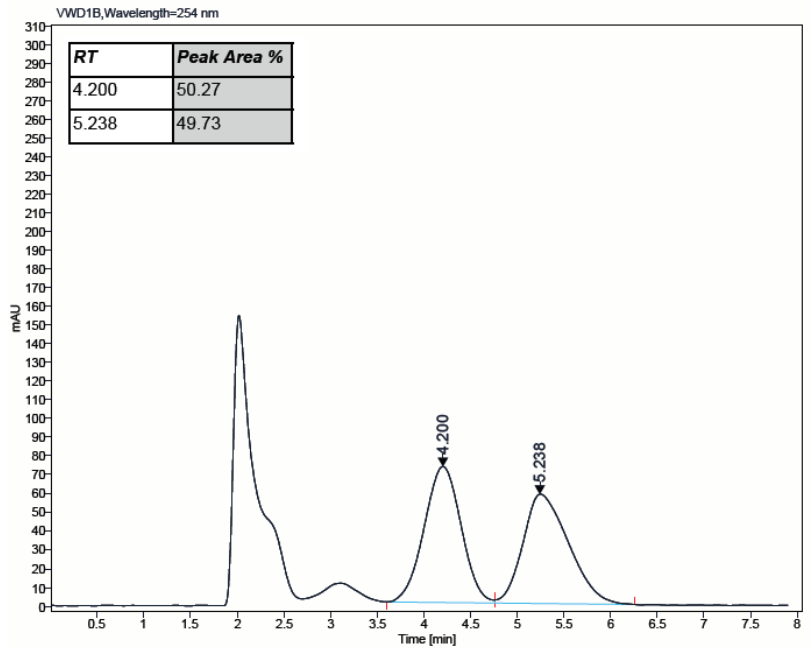
SFC (Chiralpak ADH *s*CO_2/MeOH 98:2, 2 mL/min, P = 100 bar): Rt = 4.1 min (major), 5.2 min (minor).

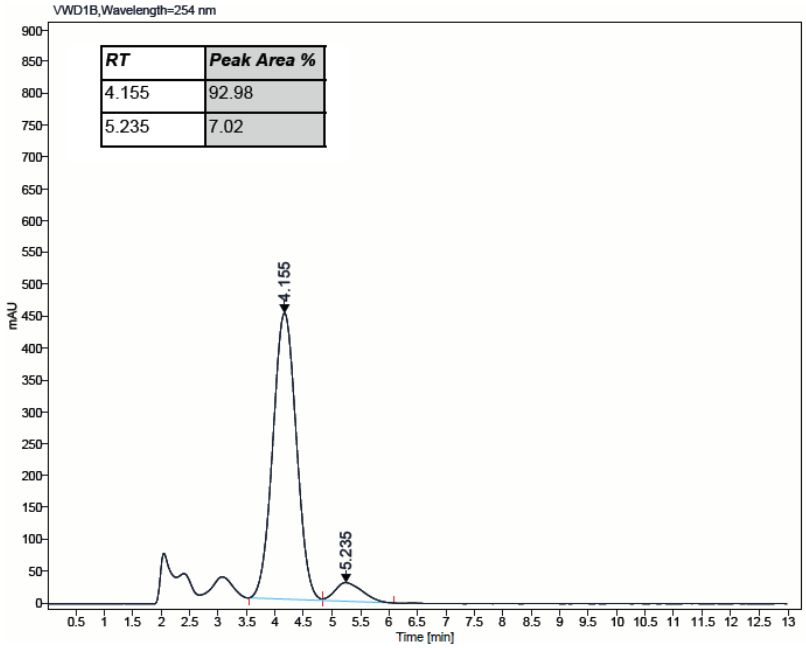
$[\alpha]_D^{20}$ = -26 (c = 0.34, $CHCl_3$) for an enantiomeric excess of 86%.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.82–7.71 (m, 2H), 7.45–7.23 (m, 5H), 7.12–6.98 (m, 2H), 3.99 (dt, *J* = 14.1, 1.6 Hz, 1H), 3.81 (dd, *J* = 14.6, 1.6 Hz, 1H), 3.36 (dd, *J* = 10.1, 3.4 Hz, 1H), 3.29 (dd, *J* = 10.1, 6.4 Hz, 1H), 3.18–3.07 (m, 1H), 2.47 (s, 3H), 2.08 (dd, *J* = 16.9, 9.6 Hz, 1H), 1.98 (dd, *J* = 12.7, 4.2 Hz, 1H), 1.91–1.87 (m, 3H).

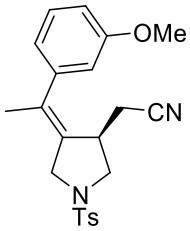
^{13}C NMR (101 MHz, $CDCl_3$, δ): 144.2, 141.5, 134.1, 132.1, 131.6, 129.9 (2C), 129.0 (2C), 128.0 (2C), 127.6, 127.0 (2C), 117.8, 52.7, 50.7, 37.9, 22.3, 21.6, 20.5.

HRMS (ESI): Calculated for $C_{21}H_{22}N_2O_2SNa$ $(M+Na)^+$ 389.1300, found 389.1294.

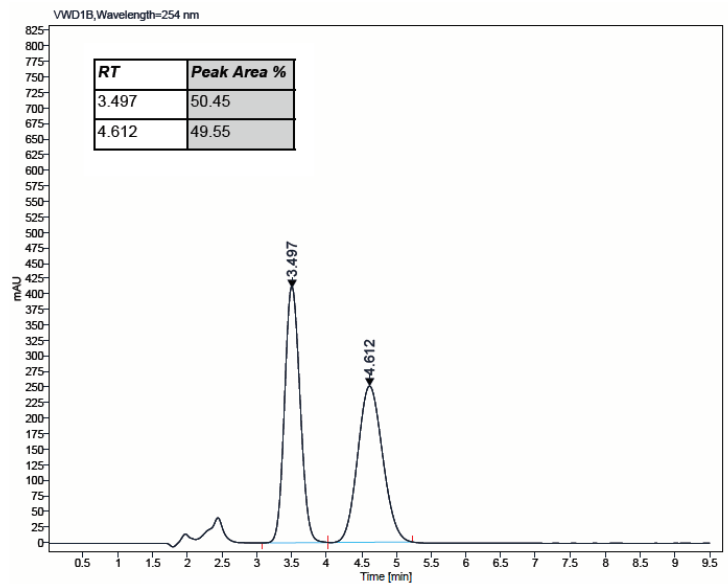


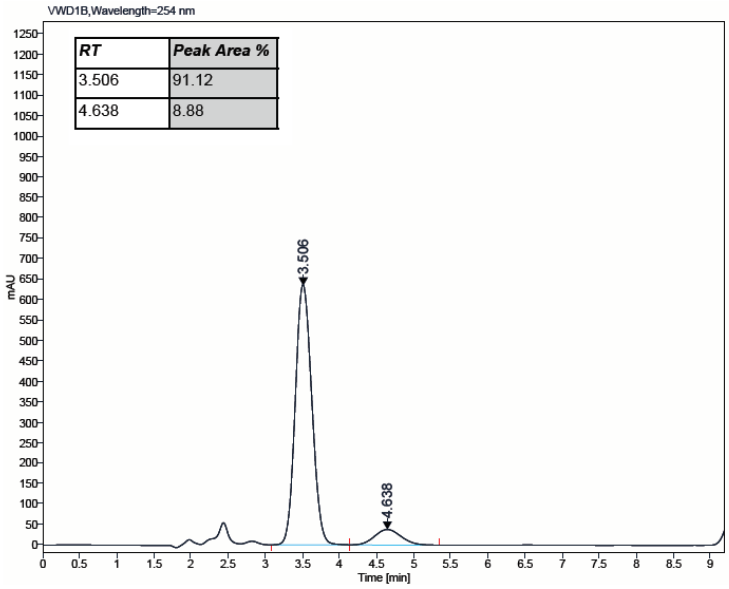


(*R*,*E*)-2-(4-(1-(3-methoxyphenyl)ethylidene)-1-tosylpyrrolidin-3-yl)acetonitrile 6bd

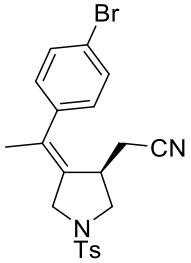


Colorless oil (72 mg, 61%) obtained from the general procedure (2), with slight modifications, using substrate **5b** (86 mg, 0.30 mmol), 4-methoxyphenylboronic acid (135 mg, 0.90 mmol) and potassium fluoride (35 mg, 0.60 mmol) in a mixture of dioxane/water 10:1 at 80 °C.
R_f = 0.12 (petroleum ether/EtOAc 85:15).
SFC (Chiralpak ADH *s*CO_2/MeOH 95:5, 2 mL/min, P = 100 bar): Rt = 3.5 min (major), 4.6 min (minor).
$[\alpha]_D^{20}$ = -64 (c = 0.94, $CHCl_3$) for an enantiomeric excess of 82%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.76 (d, *J* = 8.0 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.25 (t, *J* = 8.0 Hz, 1H), 6.89–6.76 (m, 1H), 6.67–6.60 (m, 1H), 6.57 (t, *J* = 2.1 Hz, 1H), 3.98 (dt, *J* = 14.1, 1.8 Hz, 1H), 3.83–3.79 (m, 1H), 3.79 (s, 3H), 3.35 (dd, *J* = 10.1, 3.5 Hz, 1H), 3.29 (dd, *J* = 10.1, 6.4 Hz, 1H), 3.20–3.06 (m, 1H), 2.47 (s, 3H), 2.10 (ddd, *J* = 16.9, 9.4, 0.7 Hz, 1H), 2.02 (dd, *J* = 16.9, 4.3 Hz, 1H), 1.88 (s, 3H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 159.9, 144.2, 142.9, 133.9, 132.1, 131.6, 130.1, 129.9 (2C), 128.0 (2C), 119.3, 117.9, 113.1, 112.5, 55.2, 52.7, 50.7, 37.9, 22.2, 21.6, 20.5.
HRMS (ESI): Calculated for $C_{22}H_{24}N_2O_3SNa$ $(M+Na)^+$ 419.1405, found 419.1398.





(*R*,*E*)-2-(4-(1-(4-bromophenyl)ethylidene)-1-tosylpyrrolidin-3-yl)acetonitrile 6bi



Yellow oil (82 mg, 62%) obtained from the general procedure (2), with slight modifications, using substrate **4b** (88 mg, 0.30 mmol), 4-bromophenylboronic acid (181 mg, 0.90 mmol) and potassium fluoride (35 mg, 0.60 mmol) in a mixture of dioxane/water 10:1 at 80ºC.

R_f = 0.38 (petroleum ether/EtOAc 7:3).

HPLC (Chiralpak IE, *i*PrOH/CH_2Cl_2 95:5, 0.5 mL/min): Rt = 19.4 min (major), 22.4 min (minor).

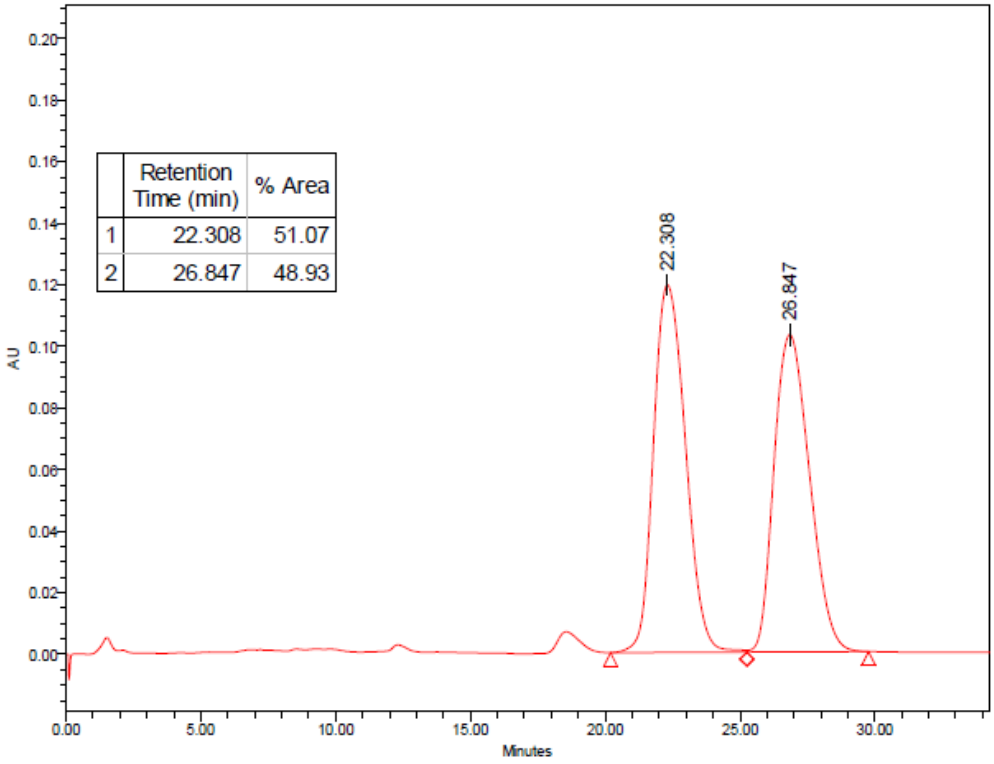
$[\alpha]_D^{20}$ = -63 (c = 0.94, $CHCl_3$) for an enantiomeric excess of 80%.

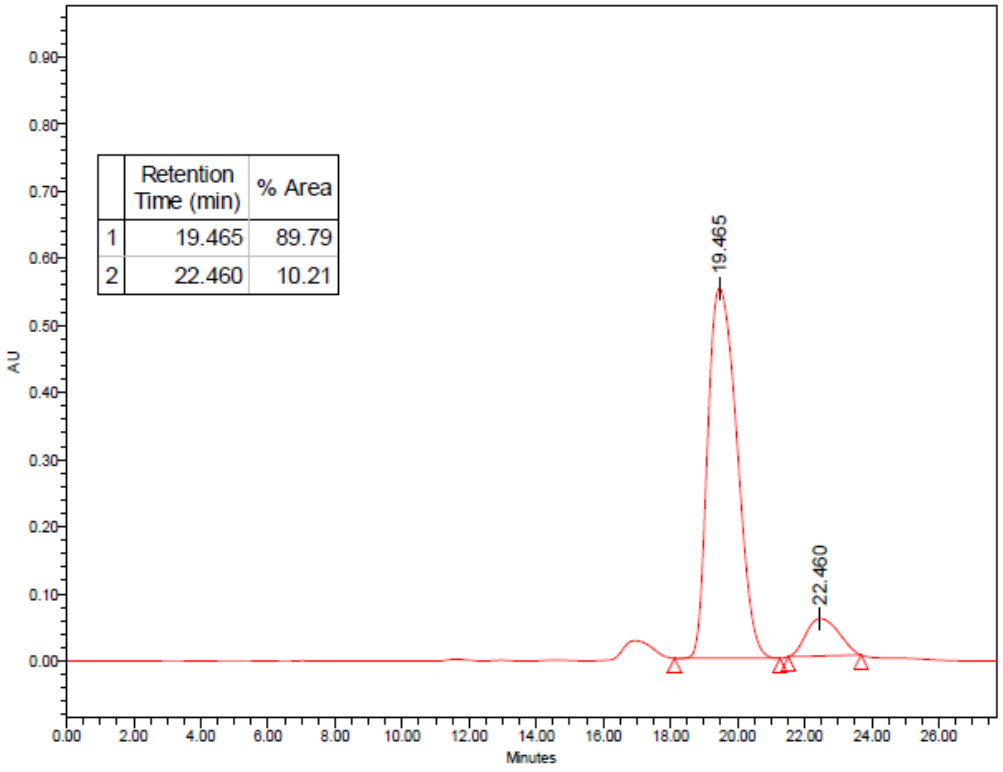
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.83–7.69 (m, 2H), 7.50–7.44 (m, 2H), 7.42–7.33 (m, 2H), 7.08–6.89 (m, 2H), 3.98 (dt, *J* = 14.3, 1.6 Hz, 1H), 3.88–3.74 (m, 1H), 3.36 (dd, *J* = 10.2, 3.3

Hz, 1H), 3.29 (dd, J = 10.2, 6.3 Hz, 1H), 3.16–3.03 (m, 1H), 2.47 (s, 3H), 2.11 (dd, J = 16.9, 9.4 Hz, 1H), 2.00 (dd, J = 16.9, 4.2 Hz, 1H), 1.88 (d, J = 1.3 Hz, 3H).

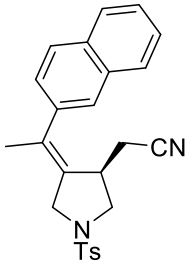
^{13}C NMR (101 MHz, $CDCl_3$, δ): 144.2, 140.3, 132.9, 132.4, 132.2 (2C), 132.1, 129.9 (2C), 128.8 (2C), 128.0 (2C), 121.7, 117.6, 52.6, 50.6, 37.8, 22.1, 21.6, 20.6.

HRMS (ESI): Calculated for $C_{21}H_{21}BrN_2O_2SNa$ $(M+Na)^+$ 467.0405, found 467.0397.

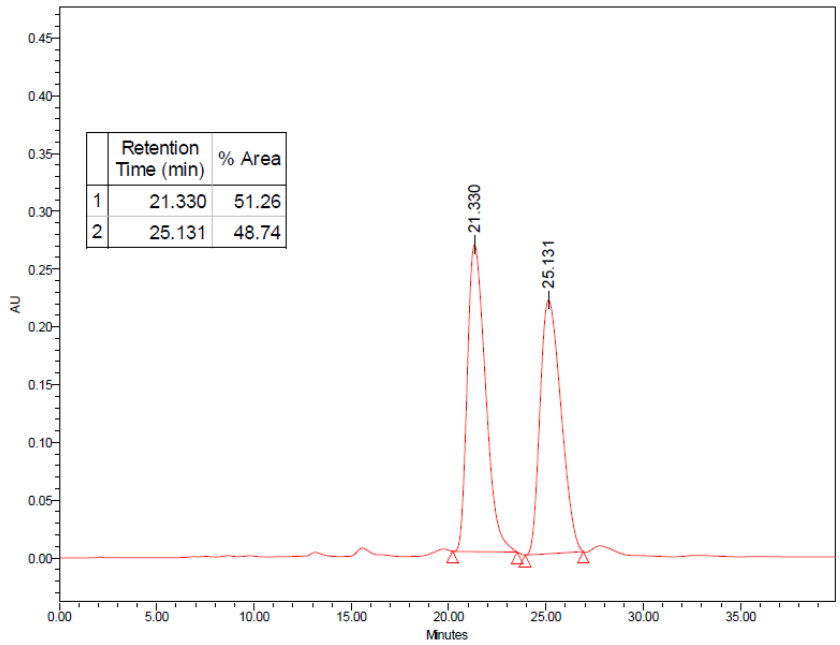


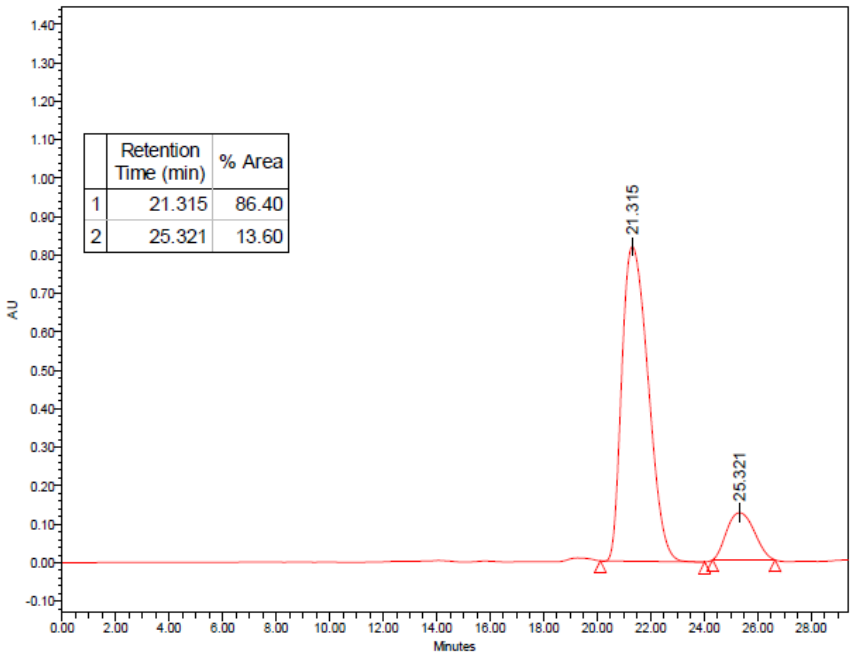


(*R*,*E*)-2-(4-(1-(naphthalen-2-yl)ethylidene)-1-tosylpyrrolidin-3-yl)acetonitrile 6bo

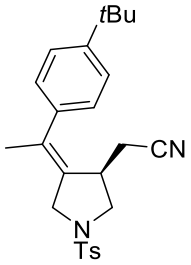


Colorless oil (75 mg, 60%) obtained from the general procedure (2), with slight modifications, using substrate **5b** (86 mg, 0.30 mmol), 2-naphthylboronic acid (155 mg, 0.90 mmol) and potassium fluoride (35 mg, 0.60 mmol) in a mixture of dioxane/water 10:1 at 80 ºC.
R_f = 0.17 (petroleum ether/EtOAc 85:15).
HPLC (Chiralpak IE, *i*PrOH/CH_2Cl_2 95:5, 0.5 mL/min): Rt = 21.3 min (major), 25.3 min (minor).
$[\alpha]_D^{20}$ = -41 (c = 0.75, $CHCl_3$) for an enantiomeric excess of 74%.
^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.93–7.73 (m, 5H), 7.55–7.47 (m, 3H), 7.41 (dt, *J* = 8.0, 0.7 Hz, 2H), 7.18 (dd, *J* = 8.5, 1.7 Hz, 1H), 4.04 (dt, *J* = 14.2, 1.6 Hz, 1H), 3.89 (d, *J* = 14.3 Hz, 1H), 3.37-3.34 (m, 2H), 3.28–3.14 (m, 1H), 2.48 (s, 3H), 2.08 (dd, *J* = 16.9, 9.5 Hz, 1H), 1.99–1.98 (m, 3H), 2.02–1.93 (m, 1H).
^{13}C NMR (101 MHz, $CDCl_3$, δ): 144.2, 138.9, 134.0, 133.3, 132.5, 132.2, 132.1, 129.9 (2C), 128.8, 128.1 (2C), 127.8 (2C), 126.7, 126.4, 125.7, 125.1, 117.7, 52.7, 50.8, 37.9, 22.4, 21.6, 20.6.
HRMS (ESI): Calculated for $C_{25}H_{24}N_2O_2SNa$ $(M+Na)^+$ 439.1456, found 439.1448.





(*R*,*E*)-2-(4-(1-(4-(tert-butyl)phenyl)ethylidene)-1-tosylpyrrolidin-3-yl)acetonitrile 6bs



Colorless oil (77 mg, 61%) obtained from the general procedure (2), with slight modifications, using substrate **5b** (86 mg, 0.30 mmol), phenylboronic acid (160 mg, 0.90 mmol) and potassium fluoride (35 mg, 0.60 mmol) in a mixture of dioxane/water 10:1 at 80 °C.

R_f = 0.22 (petroleum ether/EtOAc 85:15).

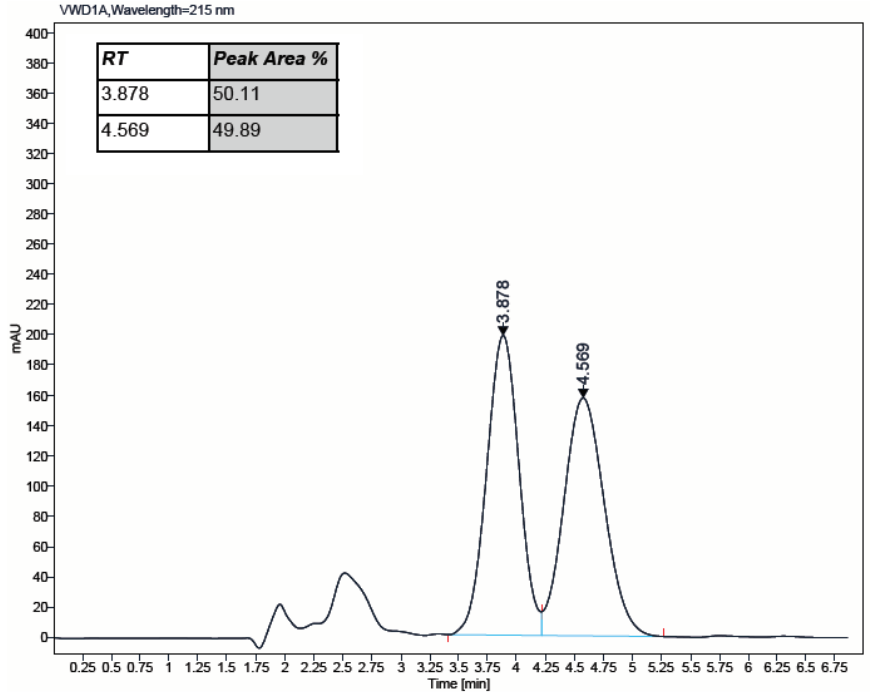
SFC (Chiralpak ADH *s*CO_2/MeOH 95:5, 2 mL/min, P = 100 bar): Rt = 3.9 min (major), 4.6 min (minor).

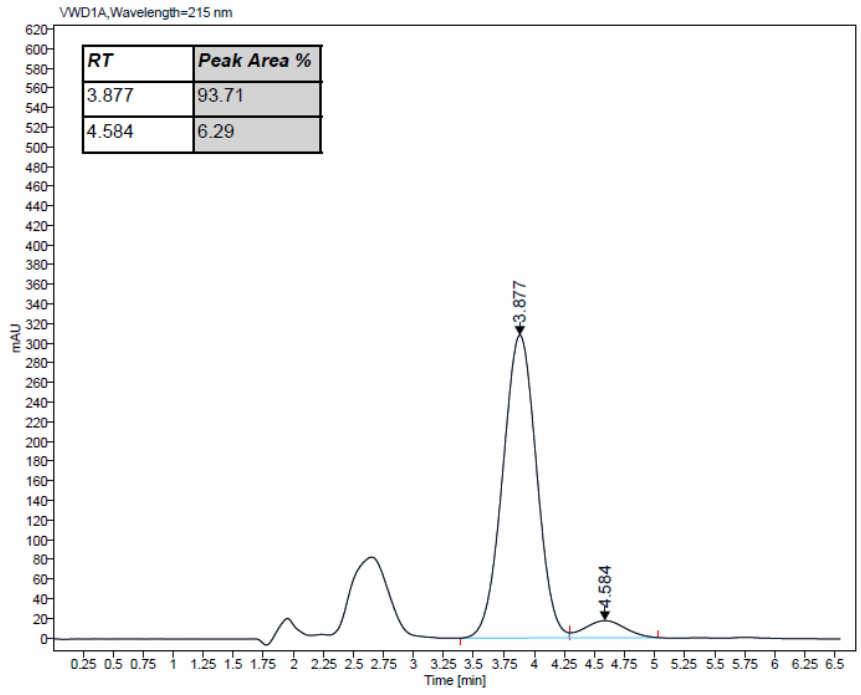
$[\alpha]_D^{20}$ = -38 (c = 0.86 $CHCl_3$) for an enantiomeric excess of 87%.

^{1}H NMR (400 MHz, $CDCl_3$, δ): 7.87–7.71 (m, 2H), 7.43–7.36 (m, 2H), 7.36–7.31 (m, 2H), 7.10–6.93 (m, 2H), 3.99 (dt, *J* = 14.0, 1.6 Hz, 1H), 3.80 (d, *J* = 14.0 Hz, 1H), 3.36 (dd, *J* = 10.1, 3.2 Hz, 1H), 3.28 (dd, *J* = 10.1, 6.5 Hz, 1H), 3.21–3.06 (m, 1H), 2.47 (s, 3H), 2.09 (dd, *J* = 16.8, 9.6 Hz, 1H), 2.00 (dd, *J* = 16.8, 4.2 Hz, 1H), 1.91–1.86 (m, 3H), 1.31 (s, 9H).

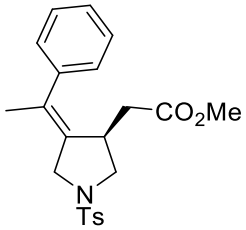
^{13}C NMR (101 MHz, $CDCl_3$, δ): 150.6, 144.1, 138.4, 134.0, 132.2, 131.3, 129.9 (2C), 128.0 (2C), 126.6 (2C), 125.8 (2C), 118.0, 52.6, 50.7, 37.9, 34.6, 31.3 (3C), 22.3, 21.6, 20.5.

HRMS (ESI): Calculated for $C_{25}H_{30}N_2O_2SNa$ $(M+Na)^+$ 445.1926, found 445.1920.



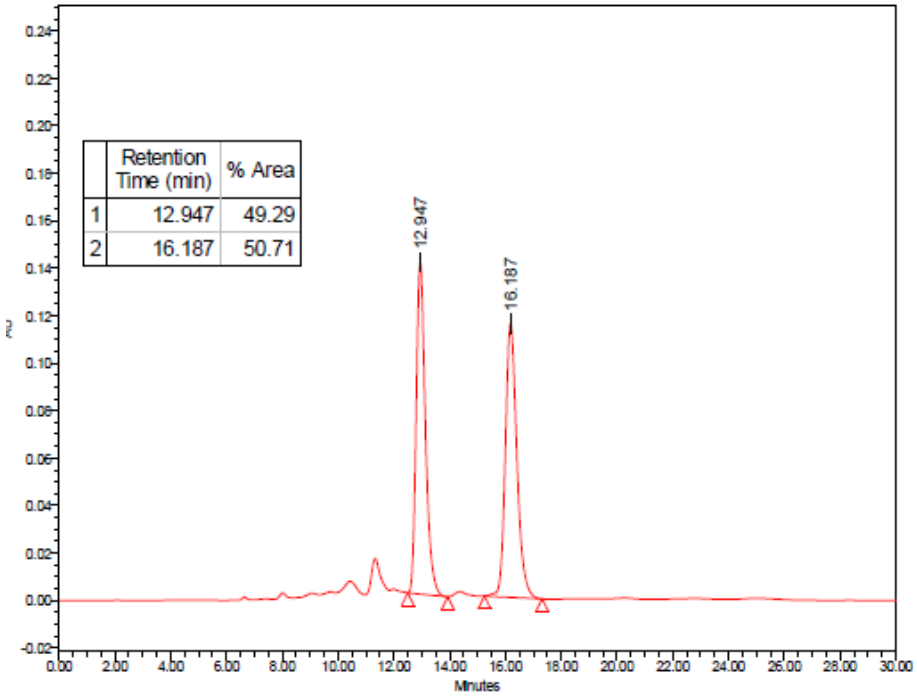


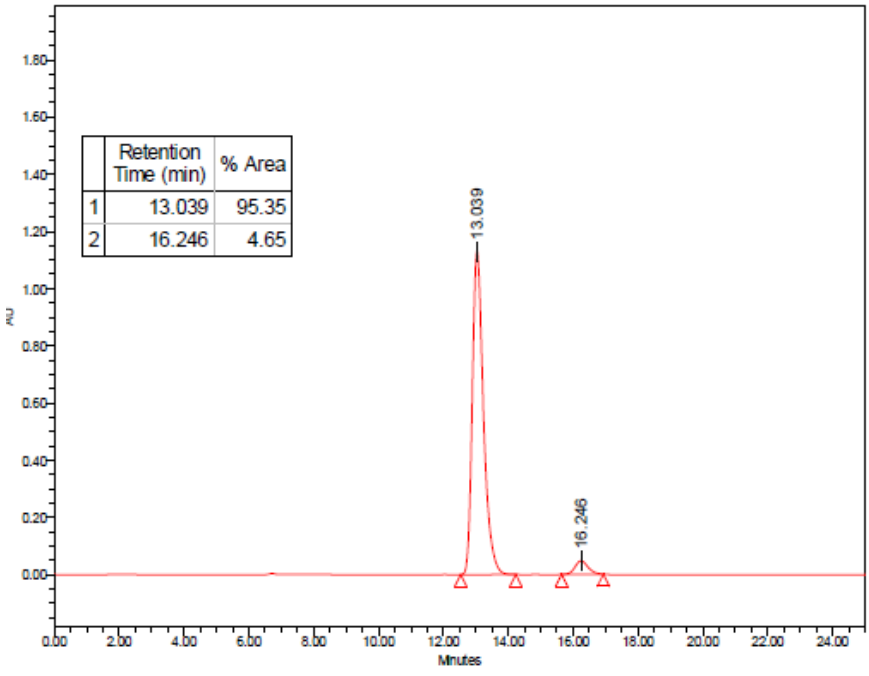
Methyl (*R*,*E*)-2-(4-(1-phenylethylidene)-1-tosylpyrrolidin-3-yl)acetate 6ca



White solid (66 mg, 55%) obtained from the general procedure (2) using substrate **(*Z*)-5c** (96 mg, 0.30 mmol) and phenylboronic acid (74 mg, 0.60 mmol). Spectroscopic data were identical to those reported in literature.[4]

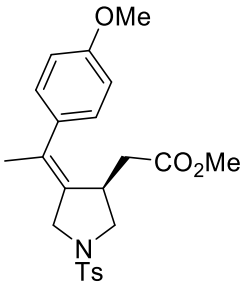
HPLC (Chiralpak ID, *i*PrOH/DCM 90:10, 0.5 mL/min): Rt = 13.0 min (major), 16.2 min (minor).





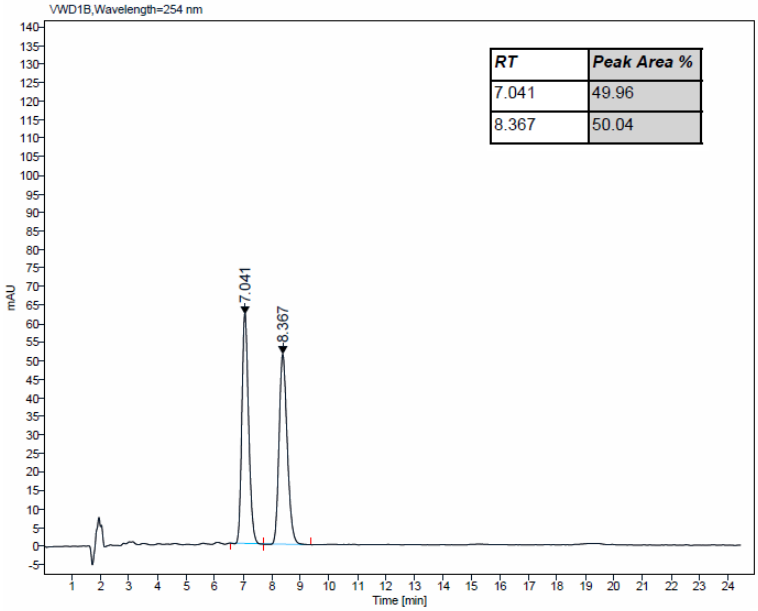
[4] Serpier, F.; Flamme, B.; Brayer, J.-L.; Folléas, B.; Darses, S., *Org. Lett.* **2015**, *17*, 1720.

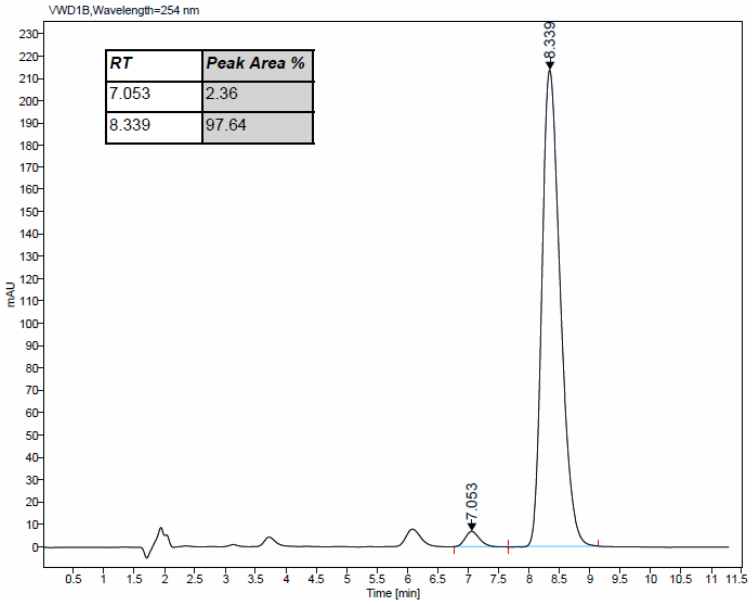
Methyl (*R*,*E*)-2-(4-(1-(4-methoxyphenyl)ethylidene)-1-tosylpyrrolidin-3-yl)acetate 6cc



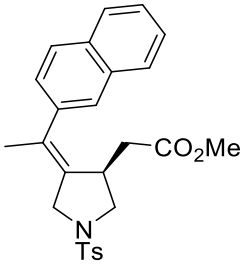
Orange oil (84 mg, 63%) obtained from the general procedure (2) using substrate **(*Z*)-5c** (96 mg, 0.30 mmol) and 4-methoxyphenylboronic acid (92 mg, 0.60 mmol). Spectroscopic data were identical to those reported in literature.[4]

SFC (Chiralpak ASH sCO_2/MeOH 90:10, 2 mL/min, P = 100 bar): Rt = 7.0 min (minor), 8.3 min (major).

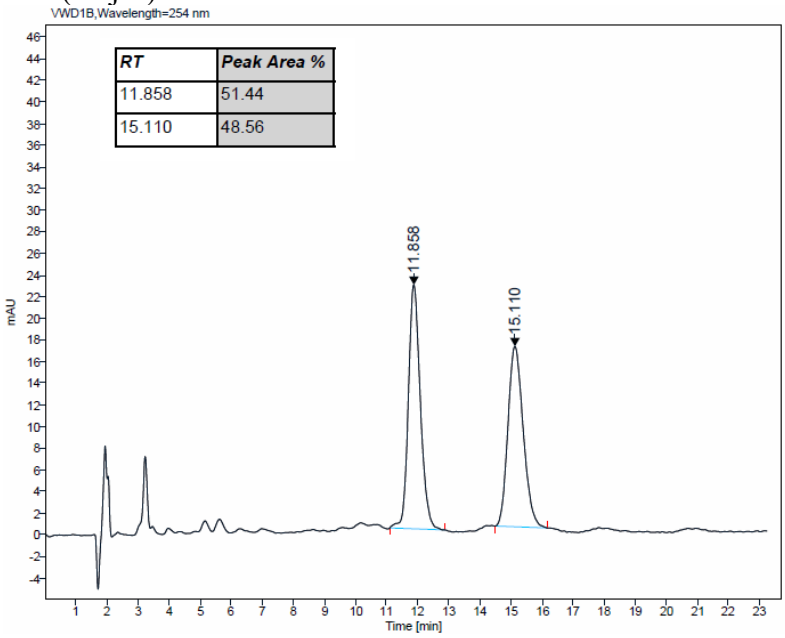


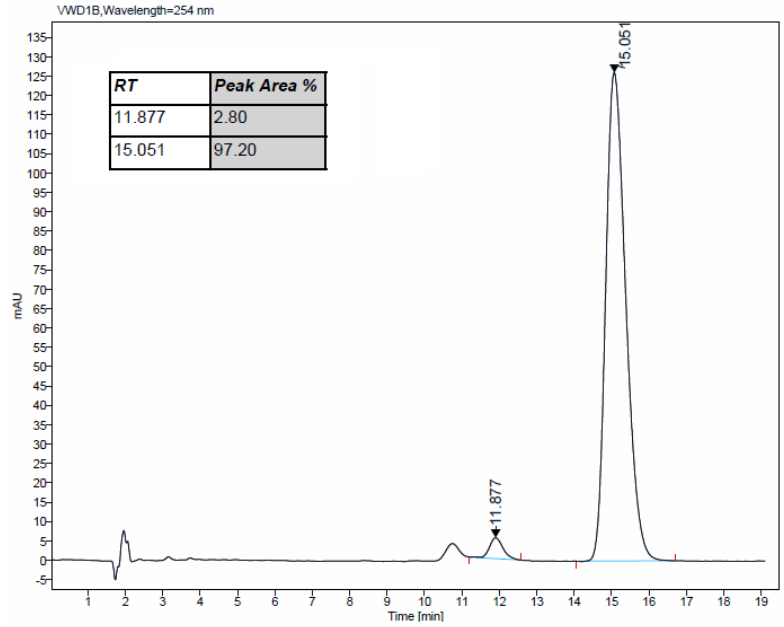


Methyl (*R*,*E*)-2-(4-(1-(4-methoxyphenyl)ethylidene)-1-tosylpyrrolidin-3-yl)acetate 6co



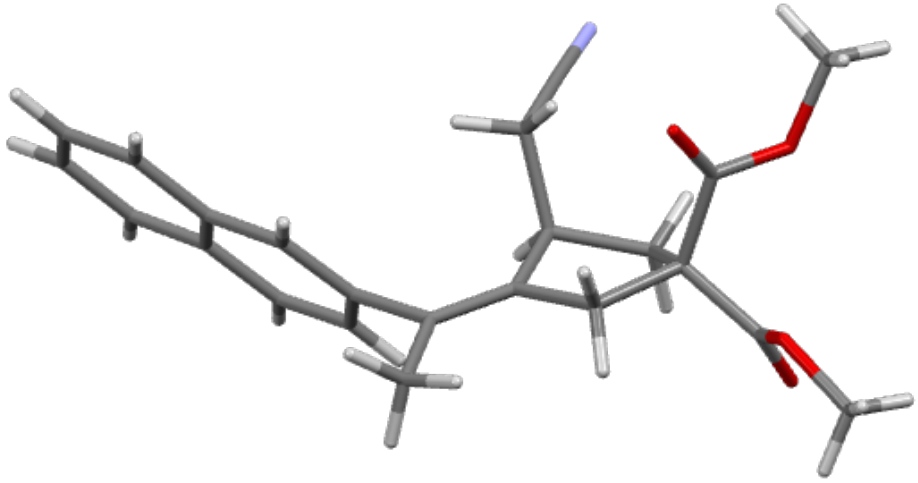
White solid (94 mg, 67%) obtained from the general procedure (2) using substrate **(*Z*)-5c** (96 mg, 0.30 mmol) and 2-naphthylboronic acid (107 mg, 0.60 mmol).
White solid (98 mg, 70%) obtained from the general procedure (2) using substrates **(*E*)-5c** (48 mg, 0.15 mmol) and **(*Z*)-5c** (48 mg, 0.15 mmol) and 2-naphthylboronic acid (107 mg, 0.60 mmol). Spectroscopic data were identical to those reported in literature.[4]
SFC (Chiralpak ADH *s*CO_2/MeOH 90:10, 2 mL/min, P = 100 bar): Rt = 11.9 min (minor), 15.1 min (major).





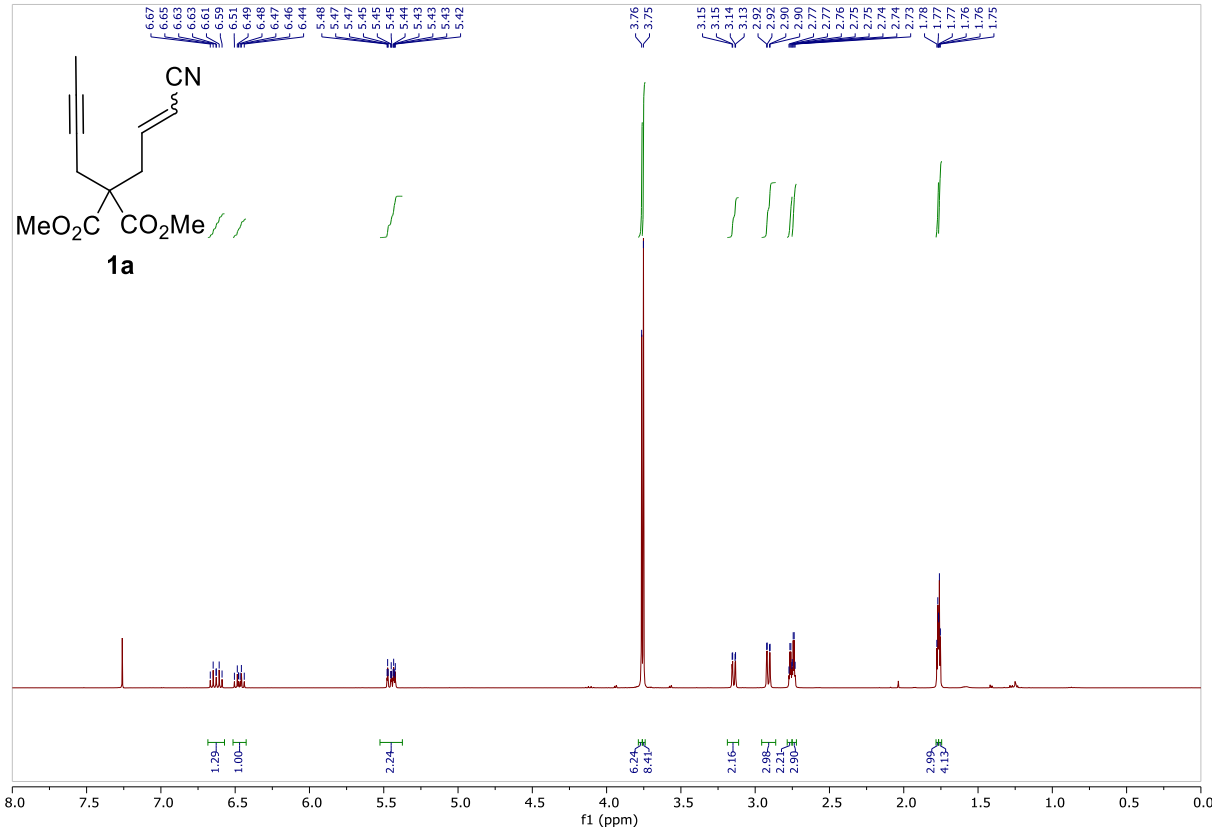
V. X-ray diffraction of 3ao

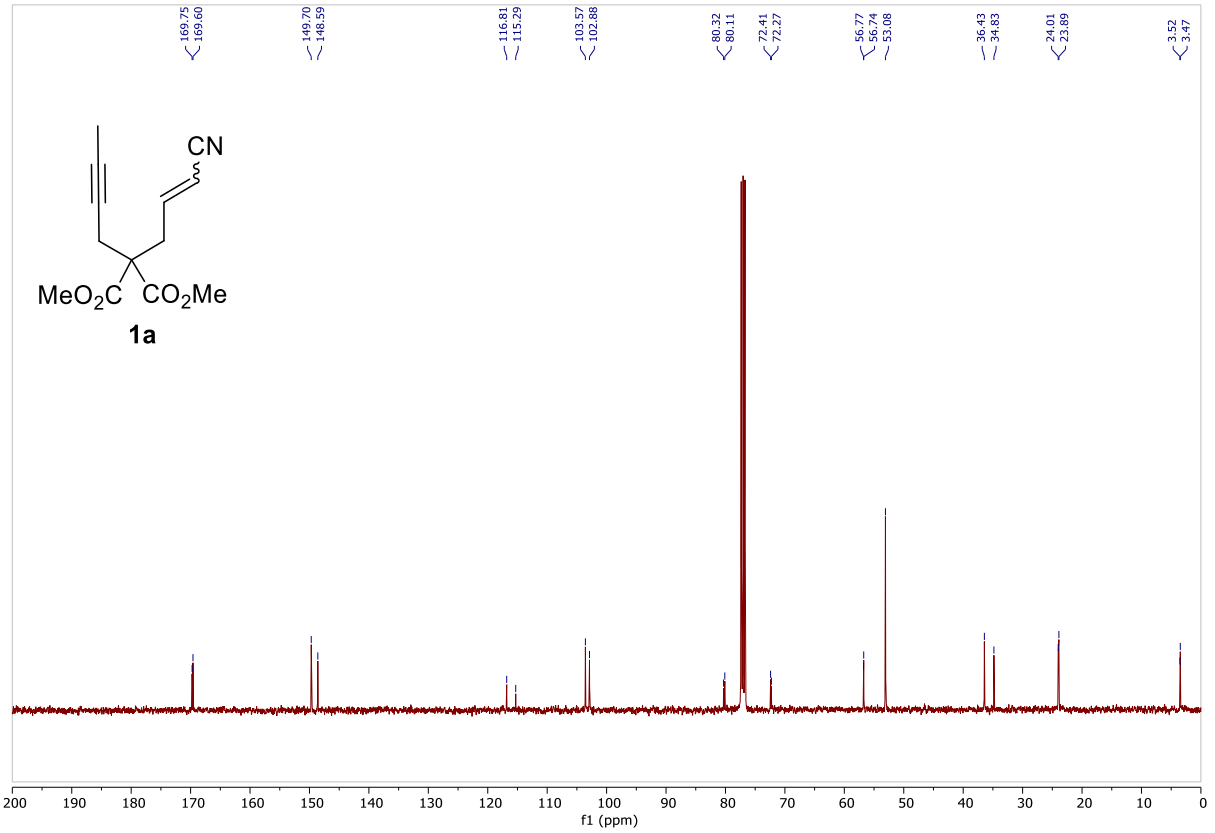
Single crystals were selected, mounted and transferred into a cold nitrogen gas stream. Intensity data was collected with a Bruker Kappa-APEX2 system using micro-source Cu-Kα radiation. Unit-cell parameters determination, data collection strategy, integration and absorption correction were carried out with the Bruker APEX2 suite of programs. The structures were solved with SHELXT-2014[5] and refined anisotropically by full-matrix least-squares methods with SHELXL-2014[5] using the WinGX suite.[6] Absolute structures were determined by anomalous scattering effects analysis and chemical absolute configurations were then deduced.[7] Crystal data for **3ao**, colorless needles: $C_{23}H_{23}NO_4$, monoclinic, *P* $2_1/c$, a = 10.9543(3), b = 7.5524(2), c = 24.3467(6)Å, β = 101.5450(10)°, V = 1973.48(9) $Å^3$, Z = 4, T = 200(2) K, μ = 0.704 mm^{-1}, 27498 reflections measured, 6805 independent (R_{int}= 0.0400), 6610 observed [I≥2σ(I)], 598 parameters, 97 restraints, final R indices R_1 [I≥2σ(I)] = 0.0341 and wR_2 (all data)= 0.0921, GOF on F^2 = 1.031, max/min residual electron density = 0.19/-0.17 e.$Å^{-3}$.

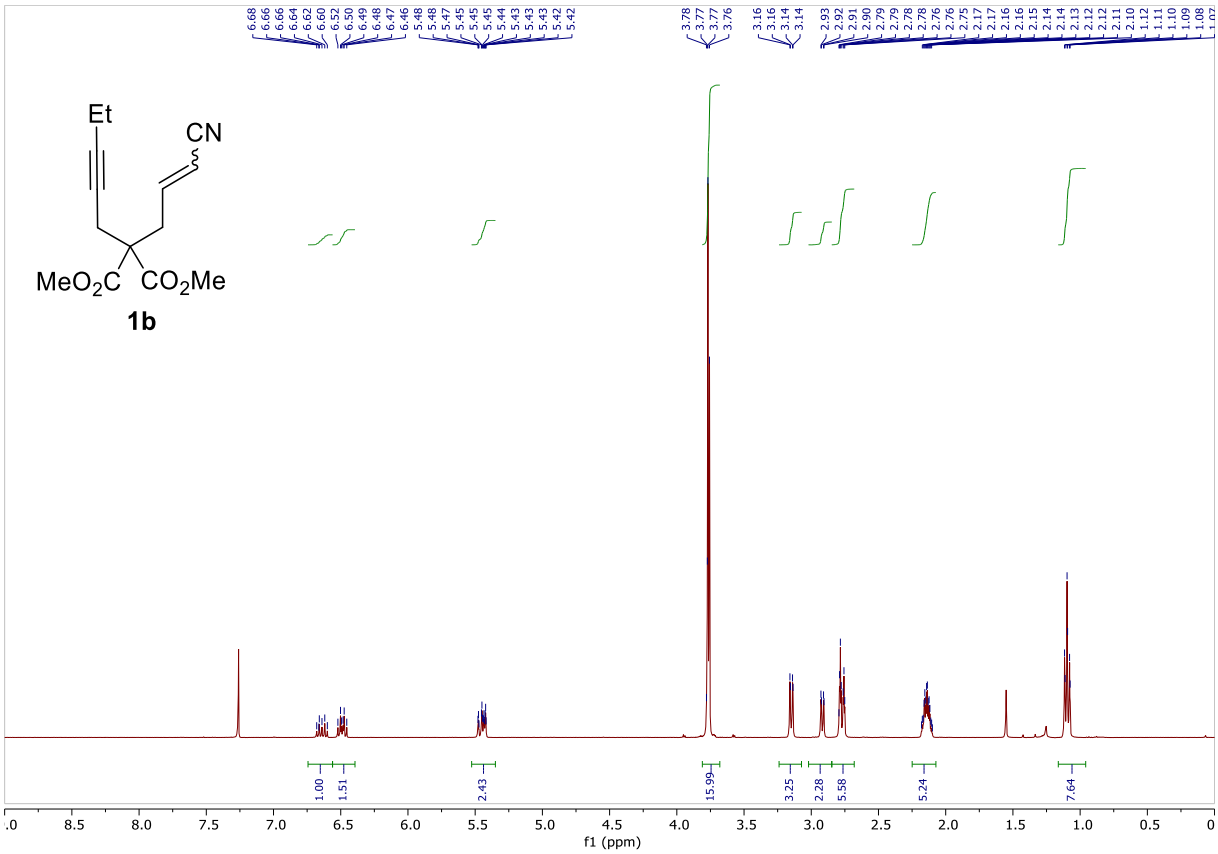


[5] Sheldrick, G. M., *Acta Crystallogr. C Struct. Chem.* **2015**, *71*, 3.
[6] Farrugia, L. J., *J. Appl. Crystallogr.* **1999**, *32*, 837.
[7] Flack, H. D.; Bernardinelli, G., *J. Appl. Crystallogr.* **2000**, *33*, 1143.

VI. NMR spectra



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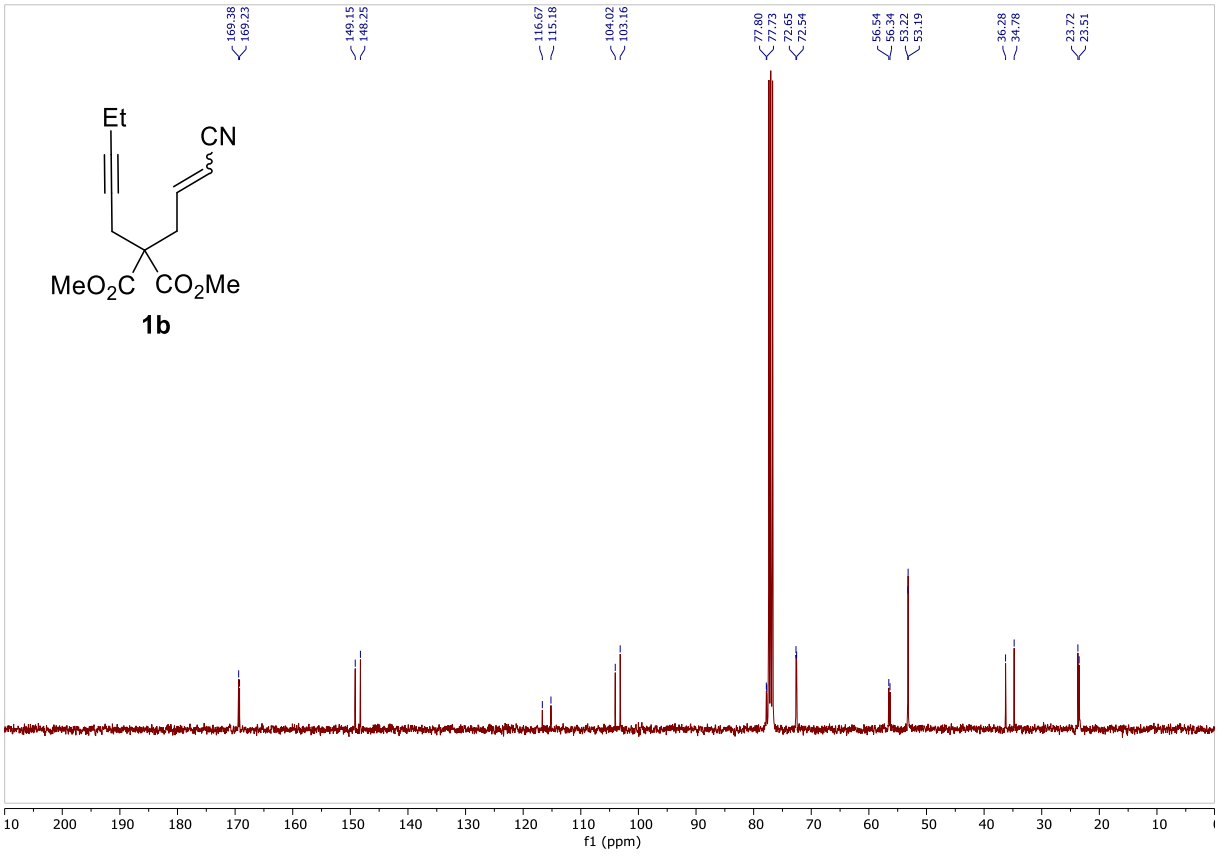
MeO2C
CO2Me
1b
f1 (ppm)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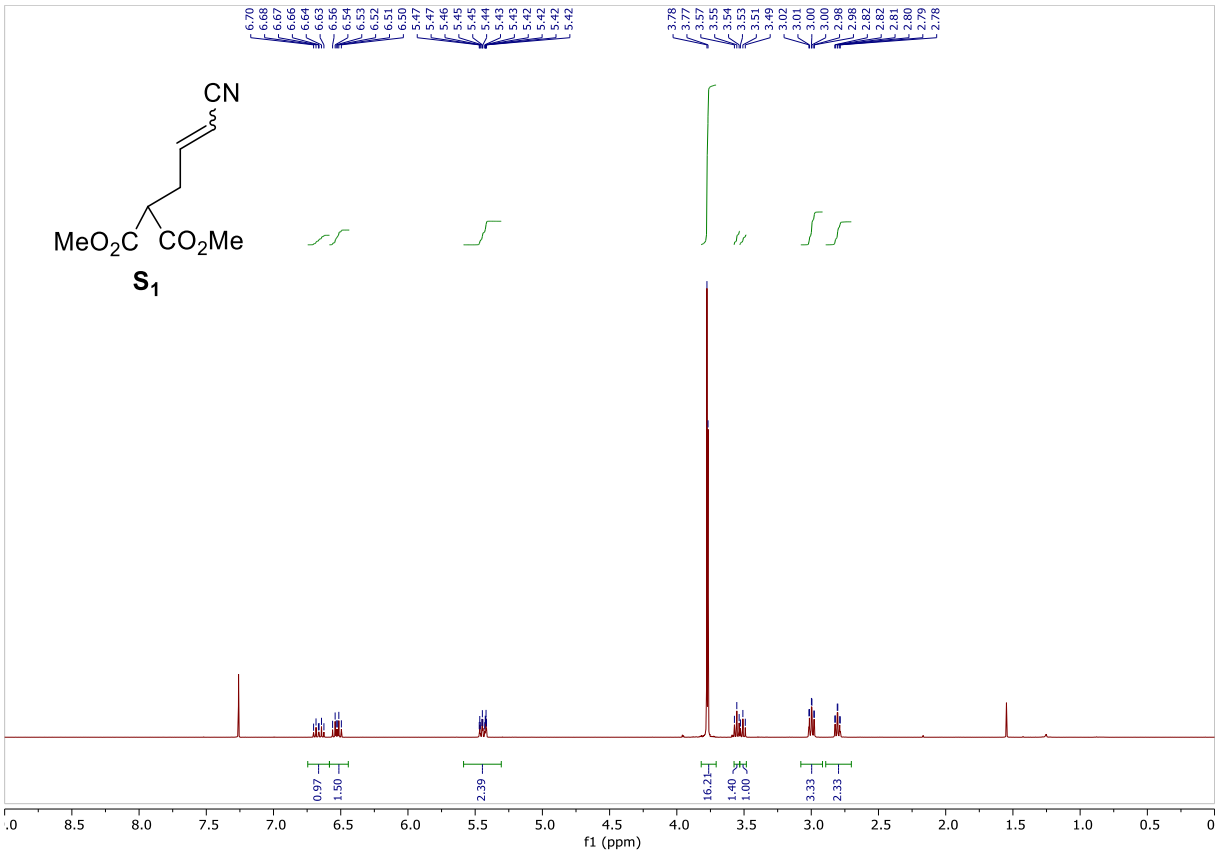
CN
MeO2C
CO2Me
1b
f1 (ppm)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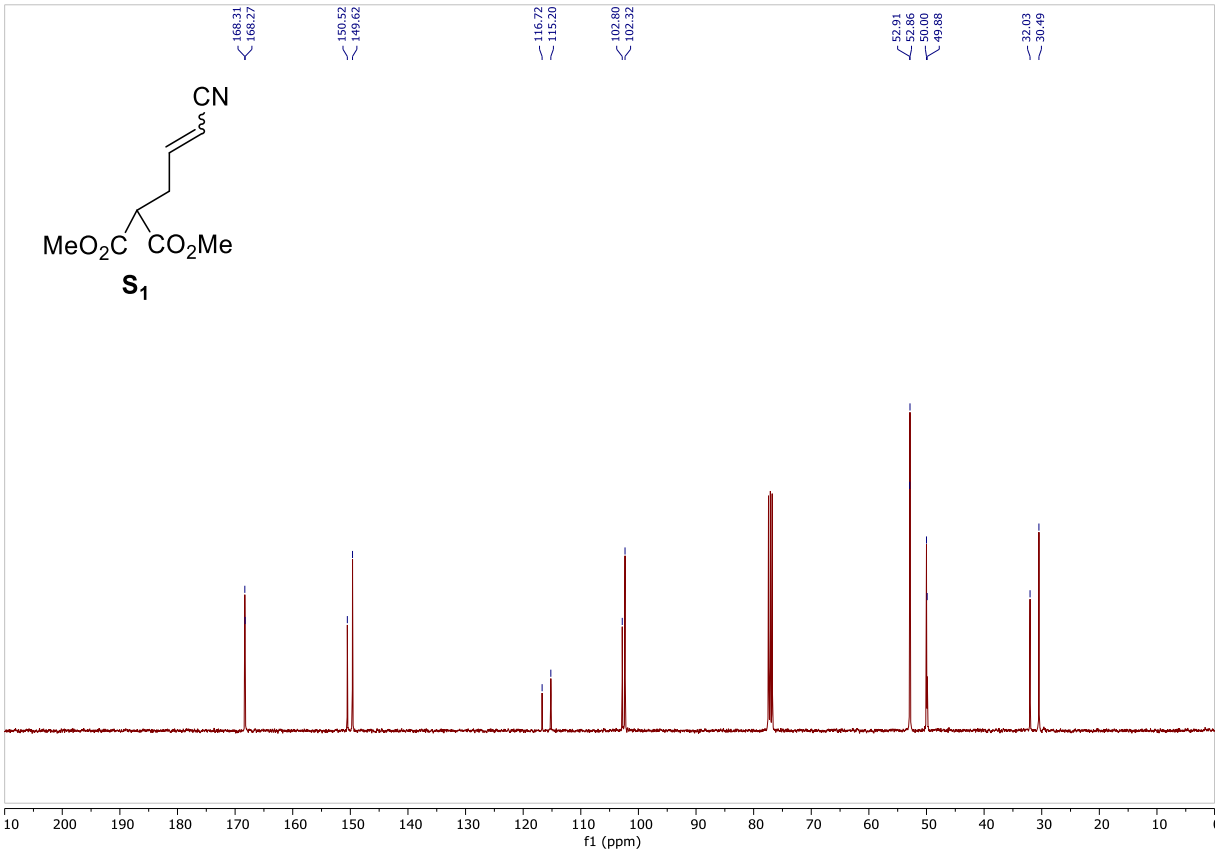
S1
f1 (ppm)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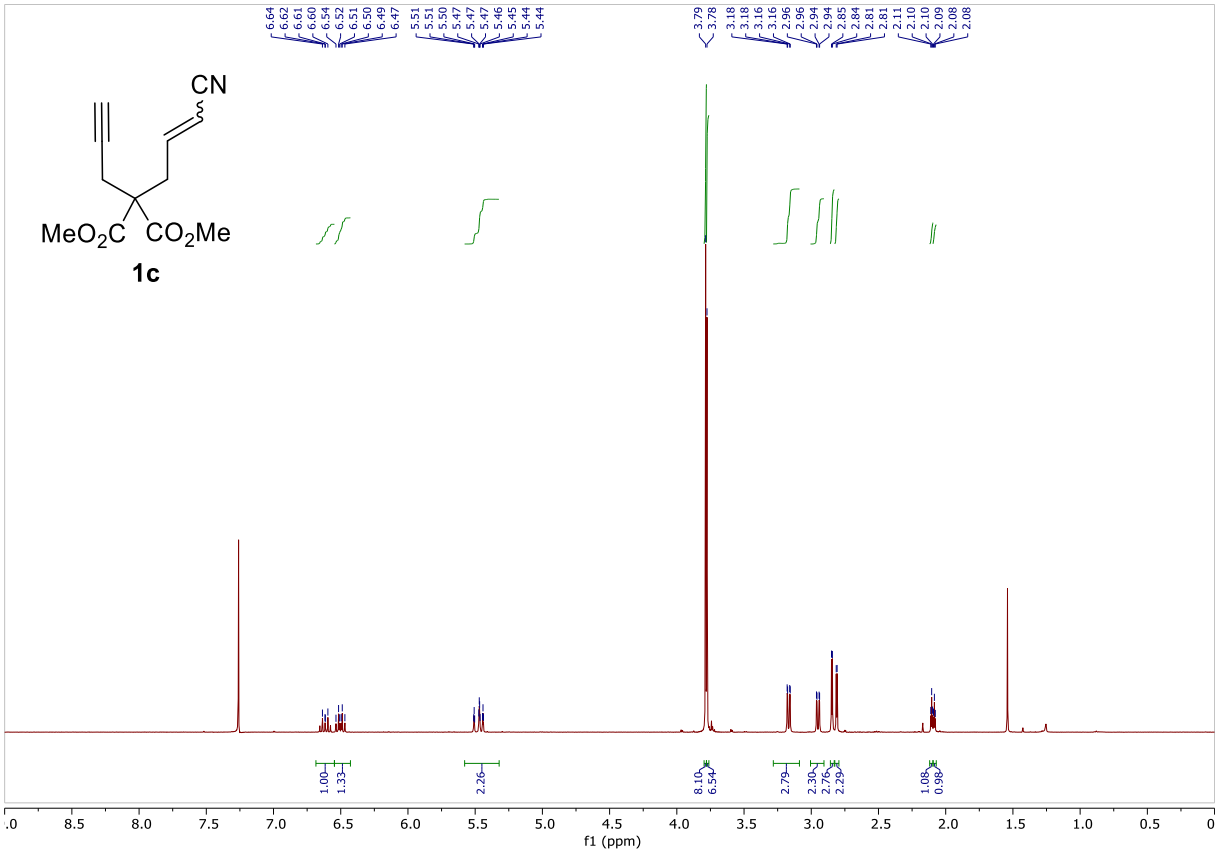
S1
f1 (ppm)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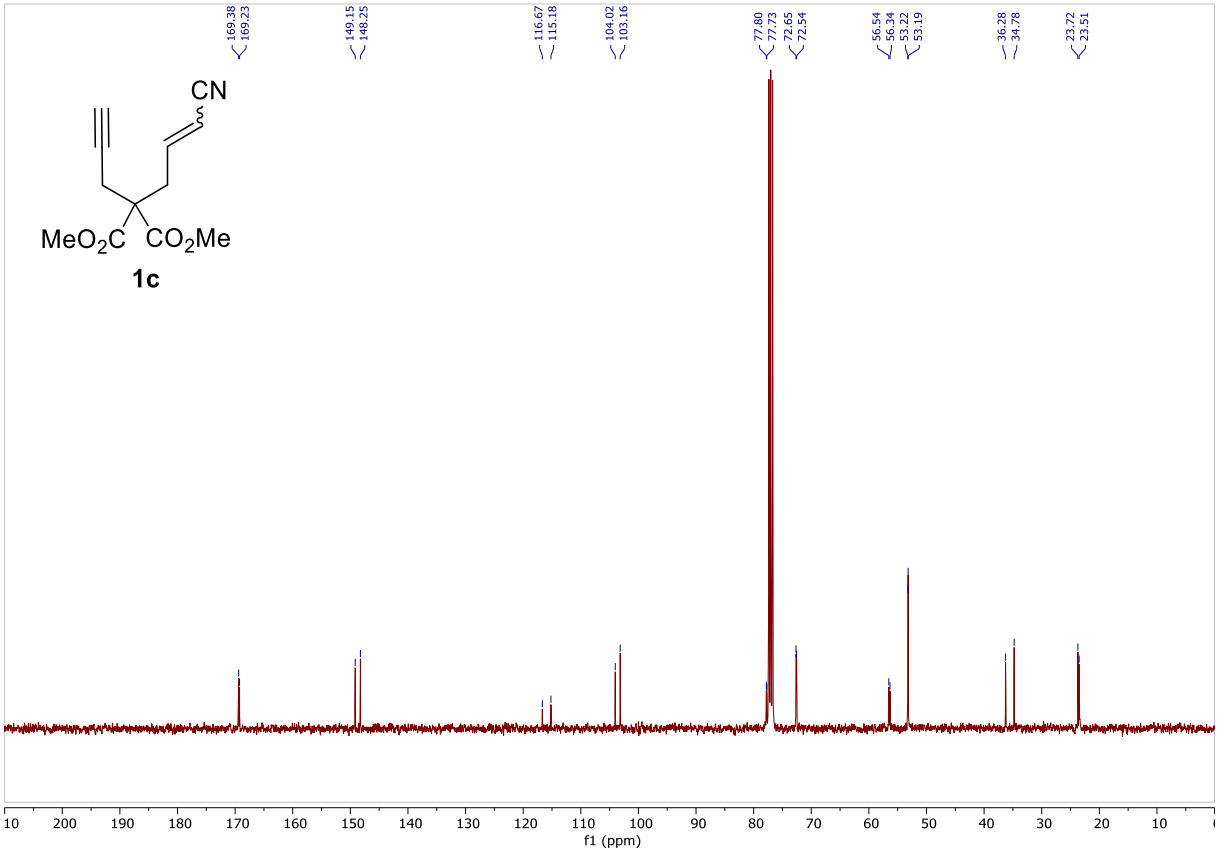
1c
f1 (ppm)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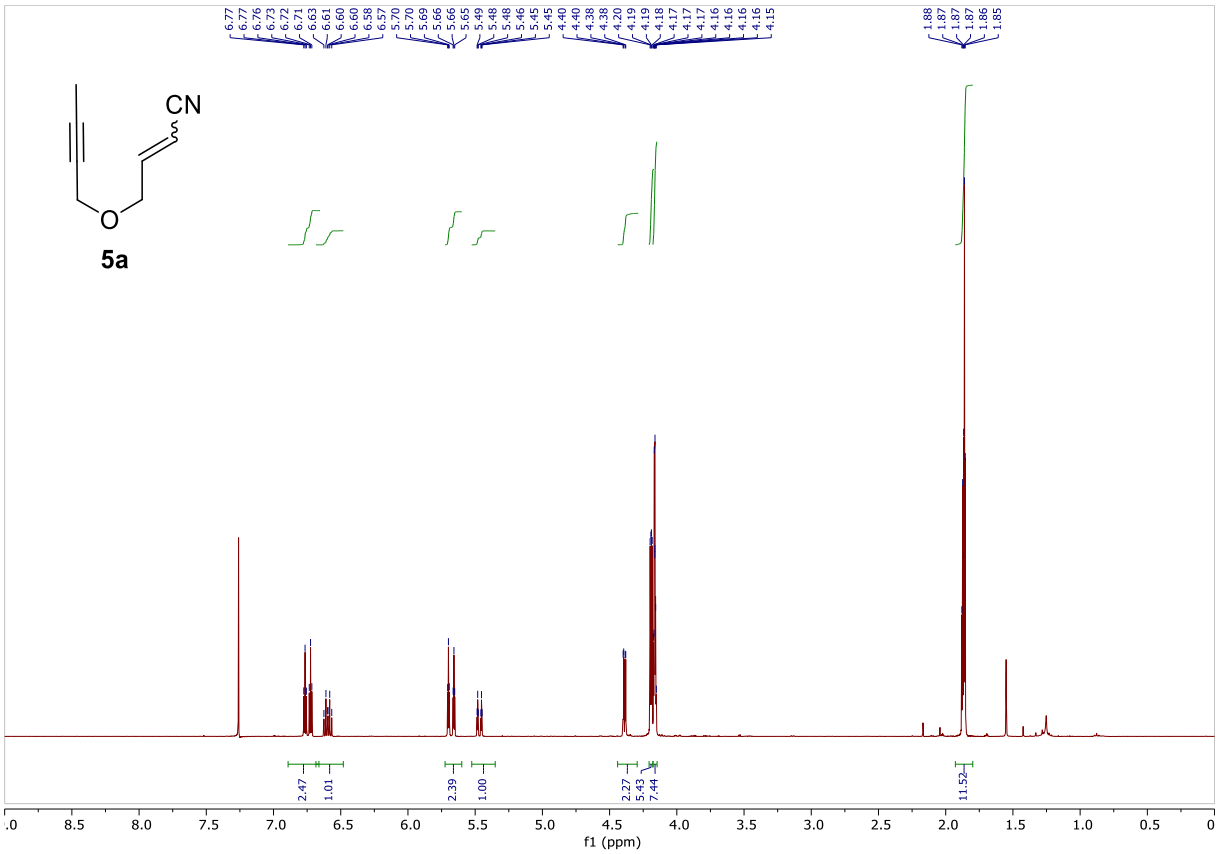
MeO2C CO2Me
1c
f1 (ppm)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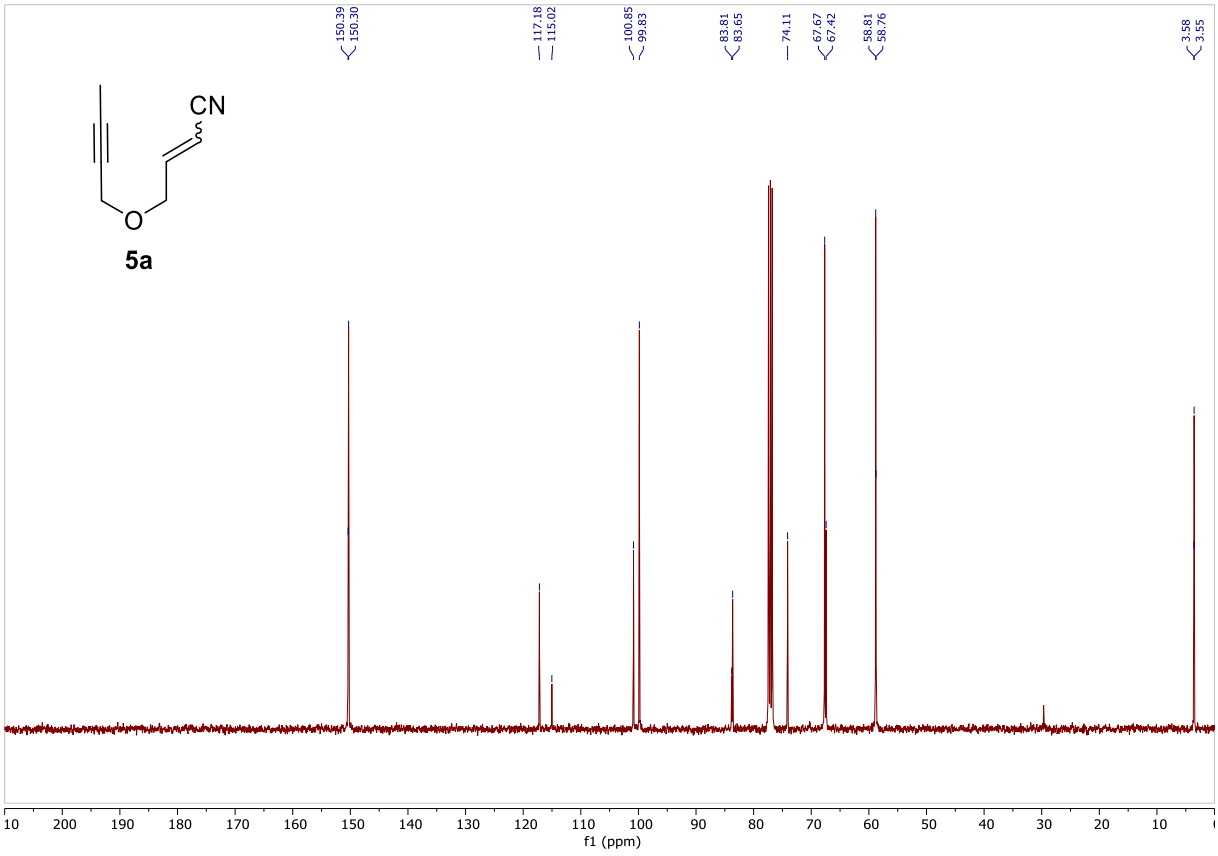
O
5a
f1 (ppm)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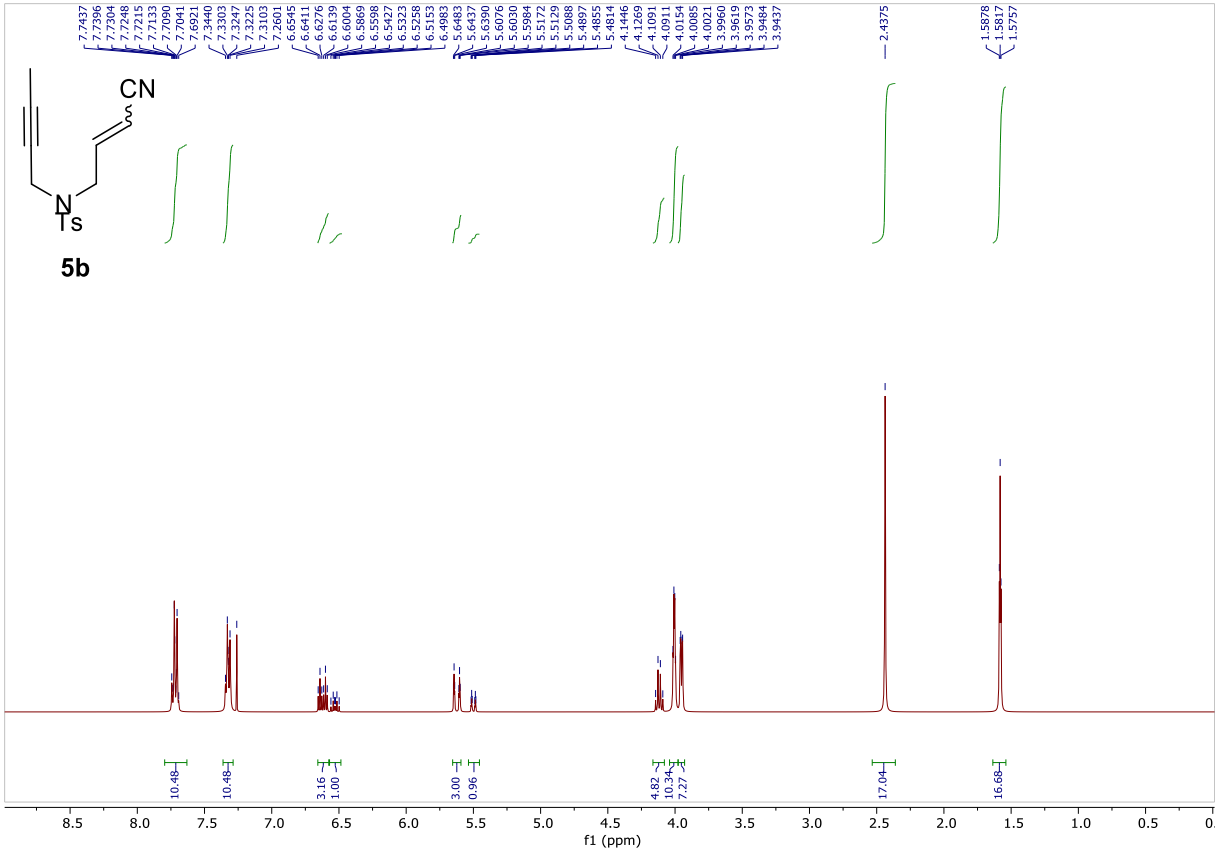
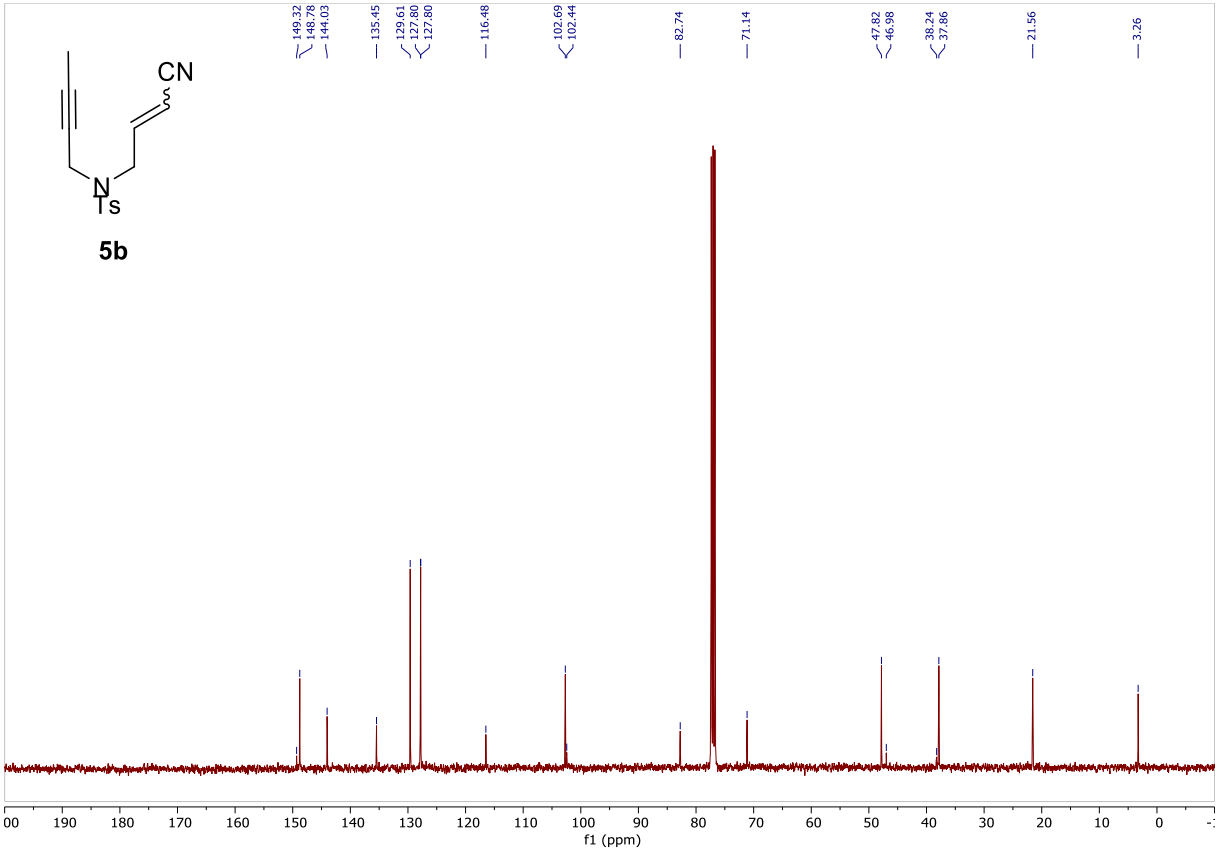
O
5a
f1 (ppm)


CN
N
Ts
5b
f1 (ppm)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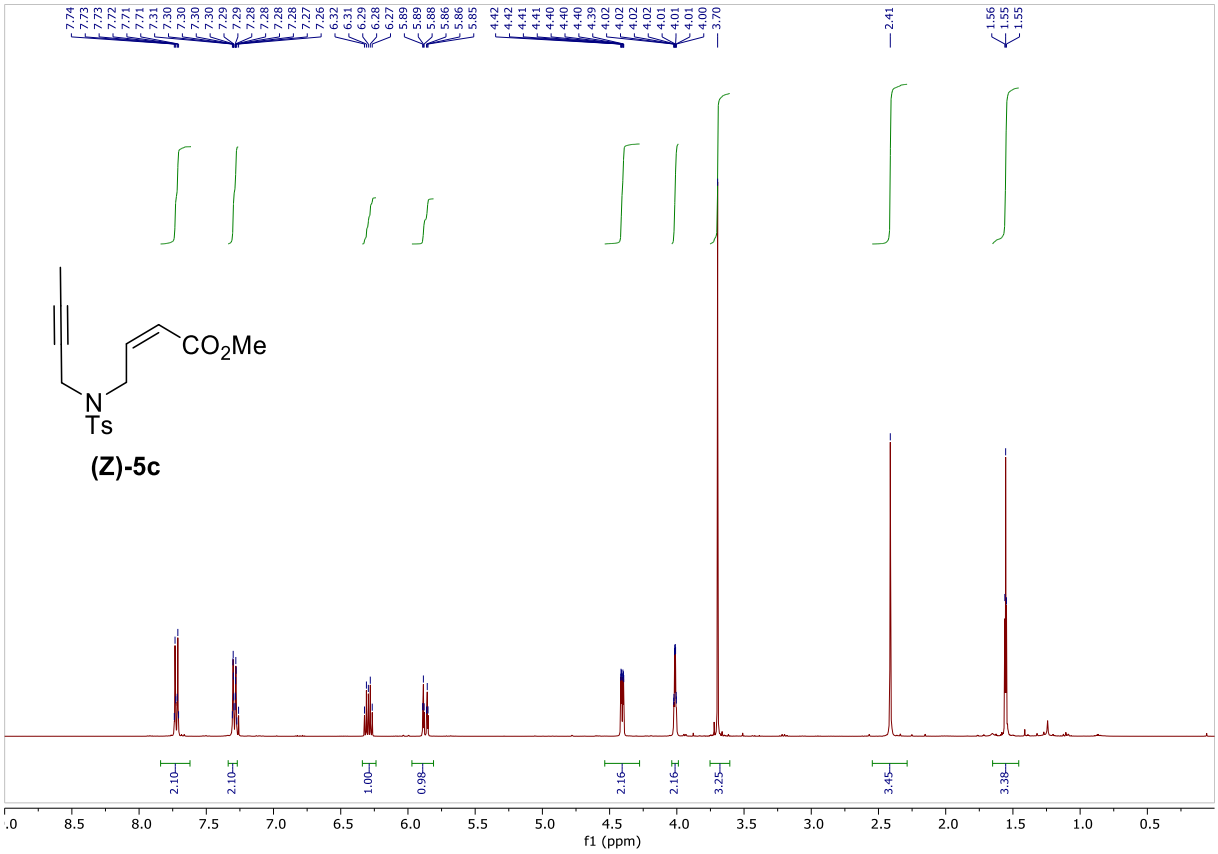
N
Ts
5b
f1 (ppm)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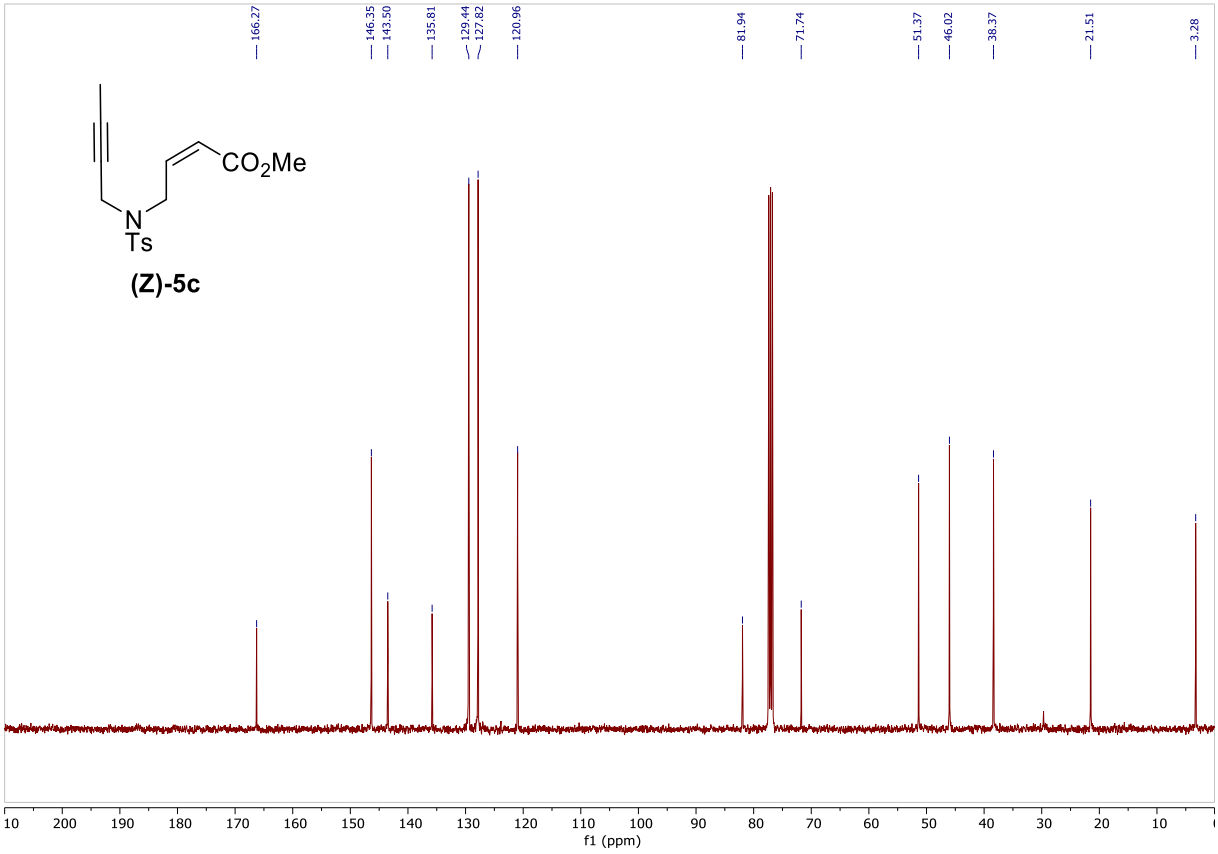
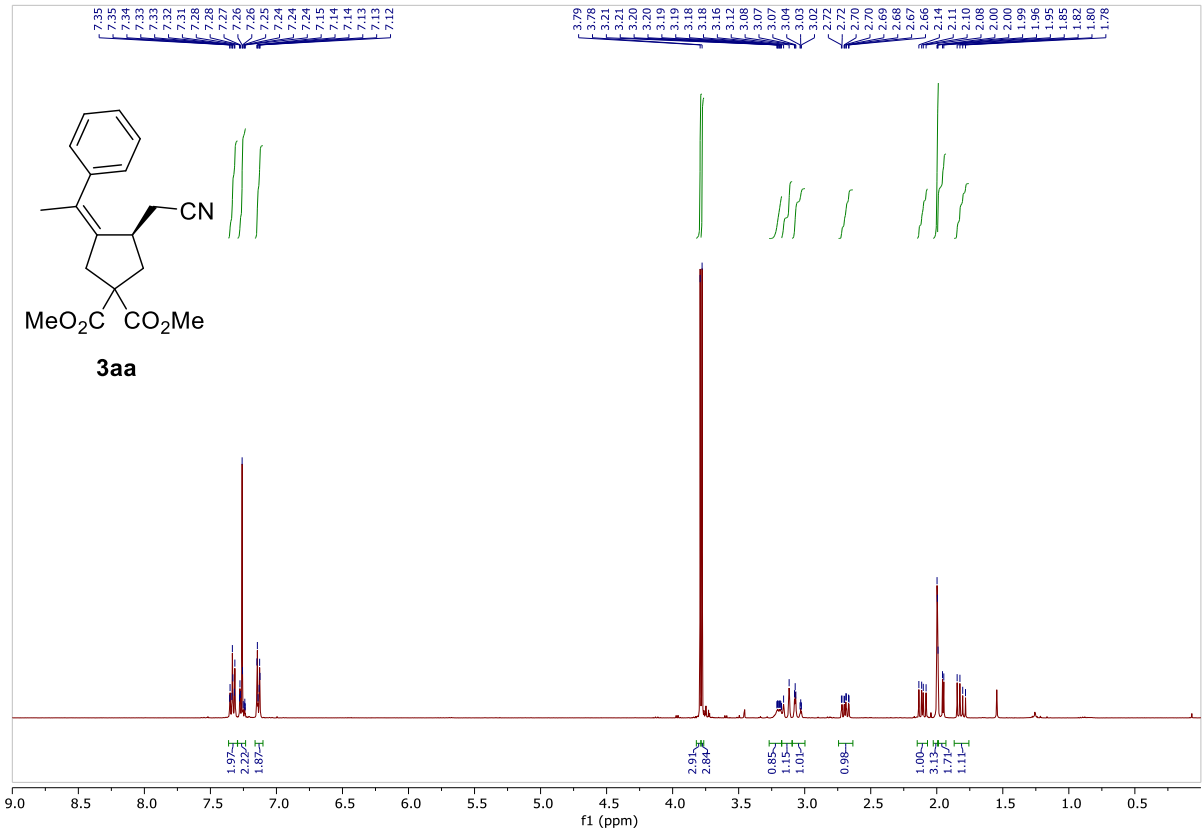
N
Ts
(Z)-5c
f1 (ppm)


CO2Me
N
Ts
(Z)-5c
f1 (ppm)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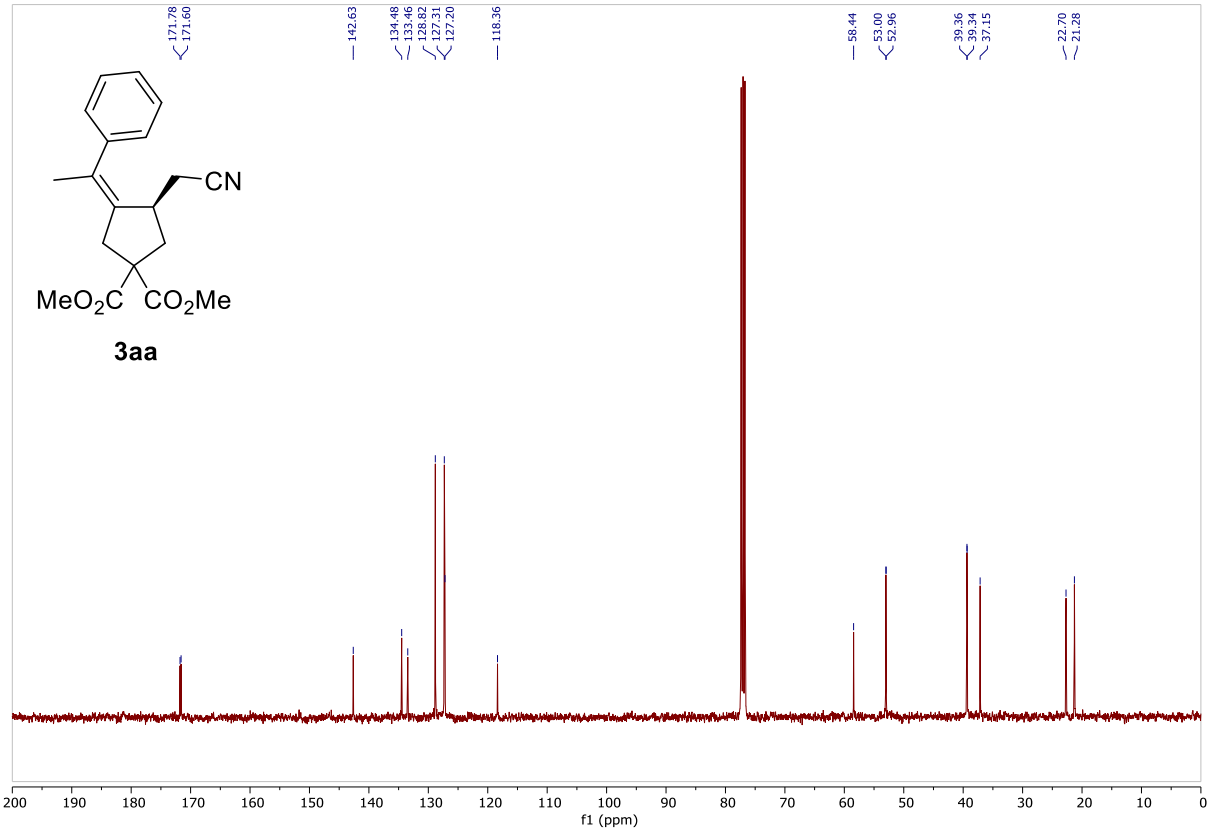
3aa
f1 (ppm)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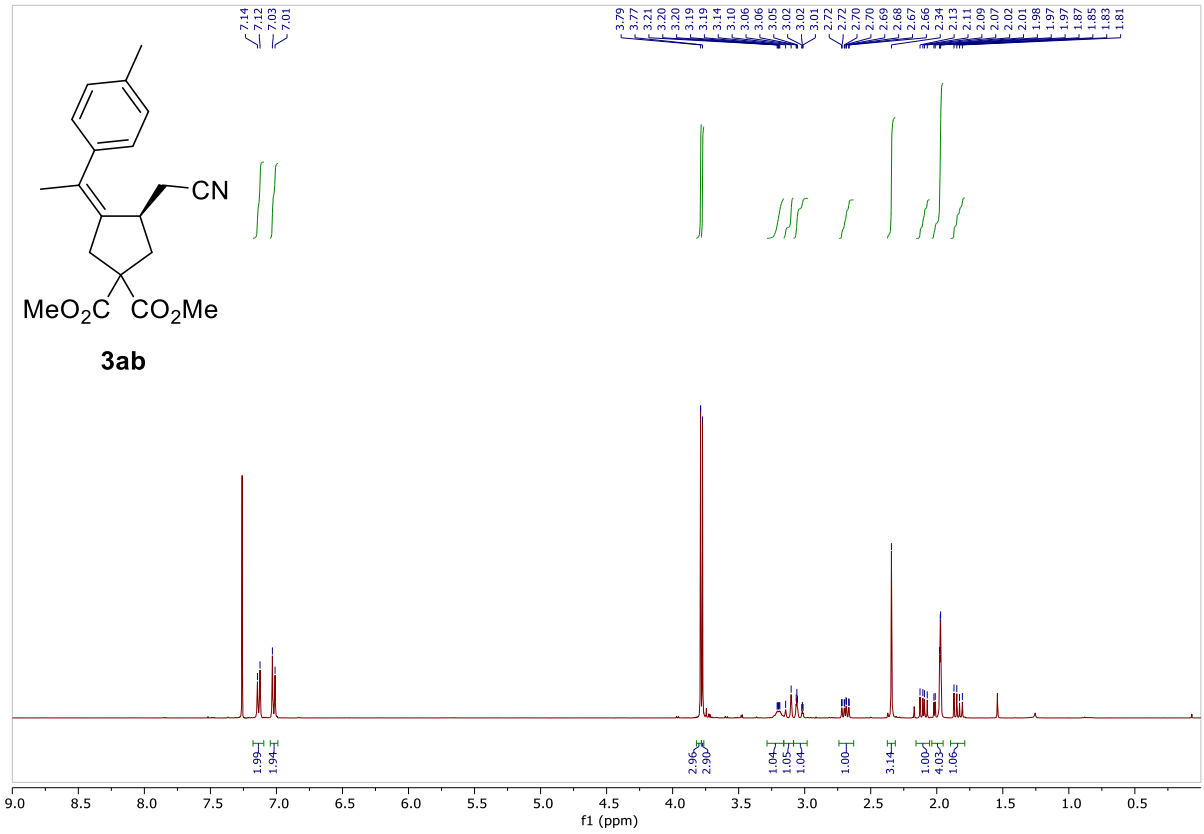
MeO2C CO2Me
3aa
f1 (ppm)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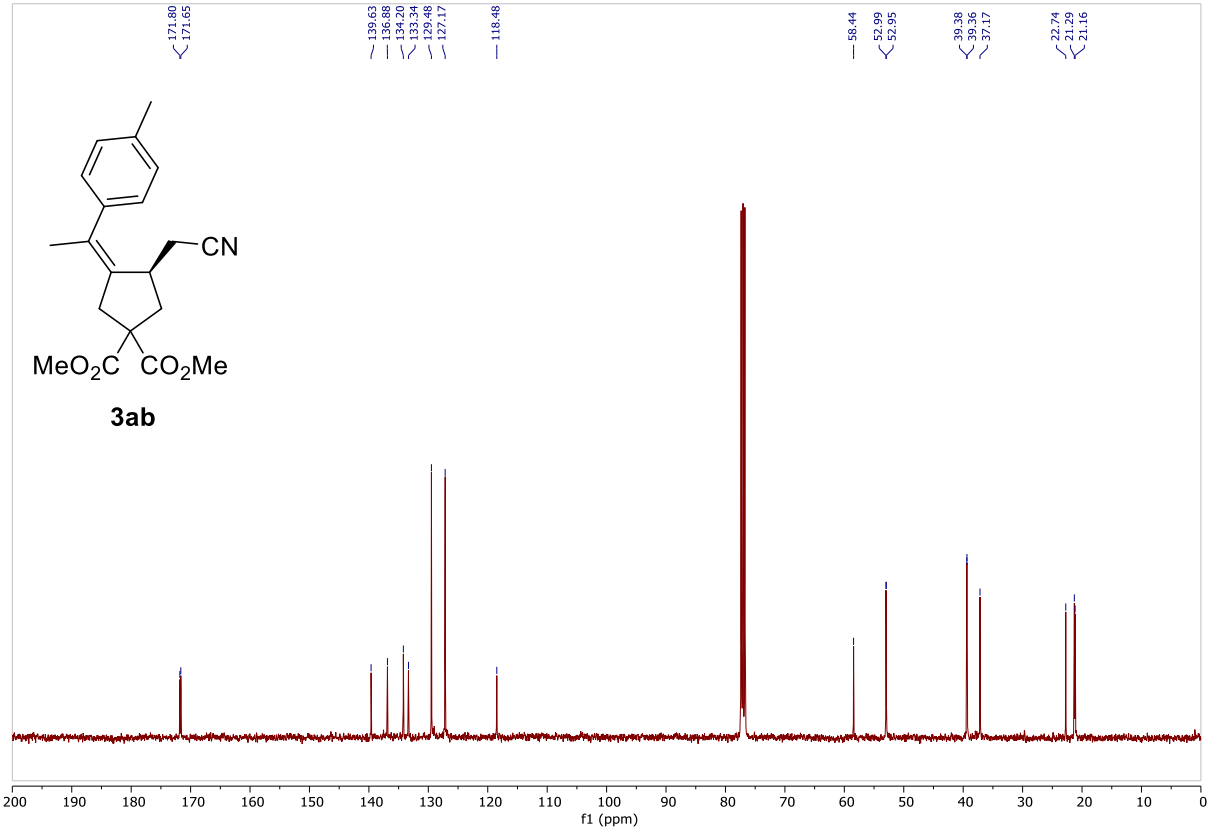
3ab
f1 (ppm)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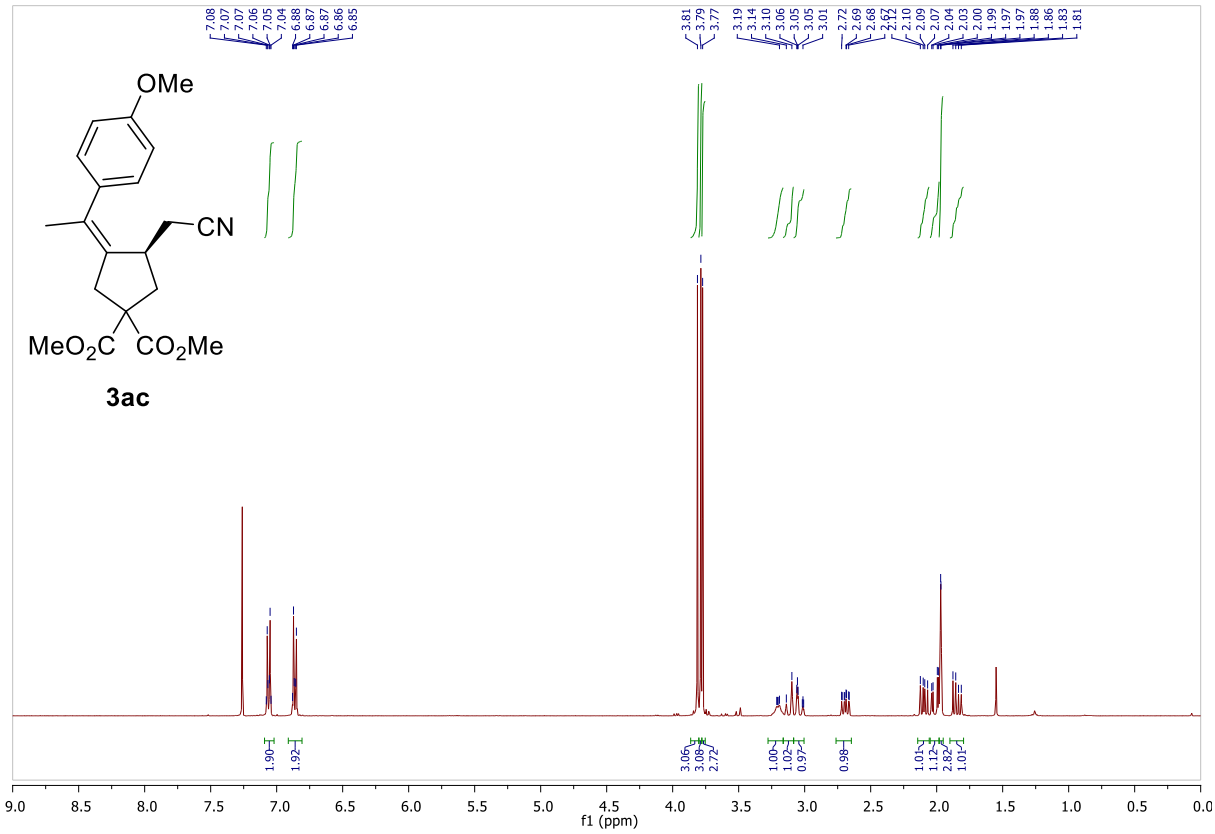
3ab
f1 (ppm)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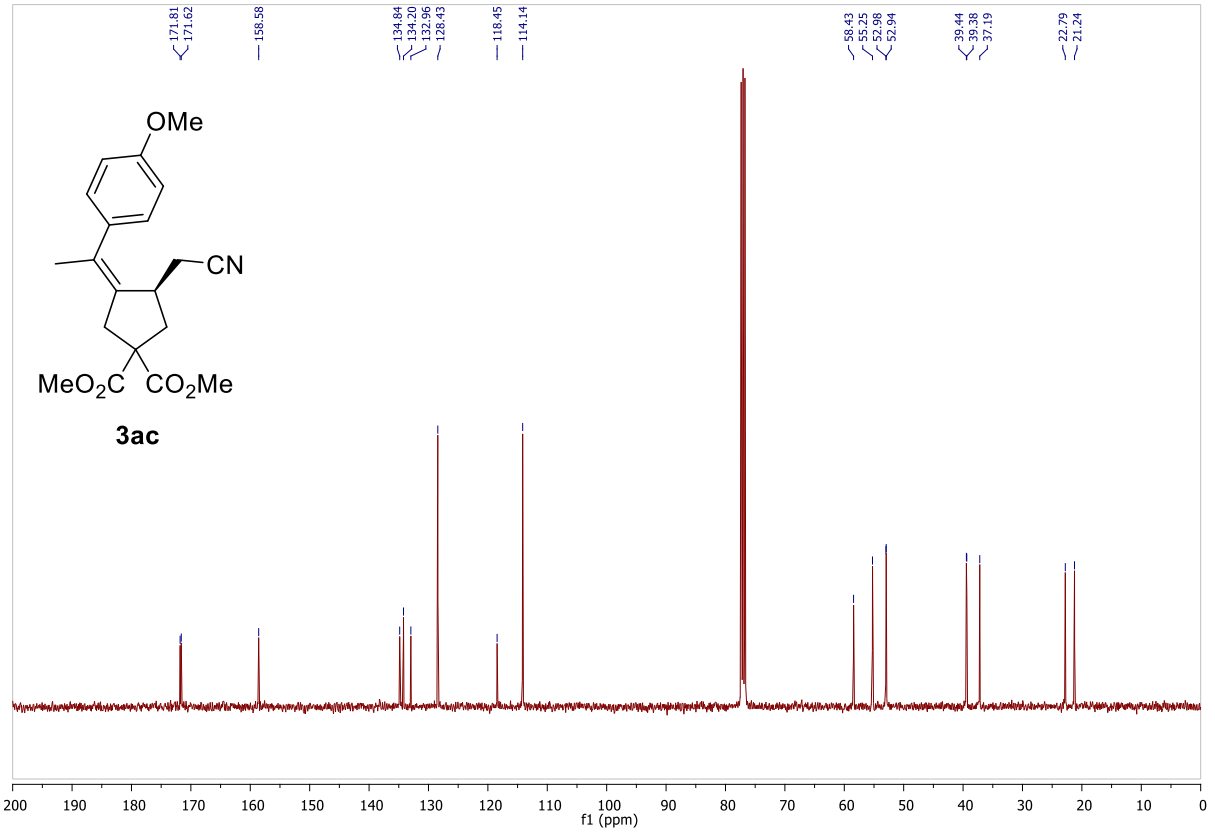
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CN
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CO2Me
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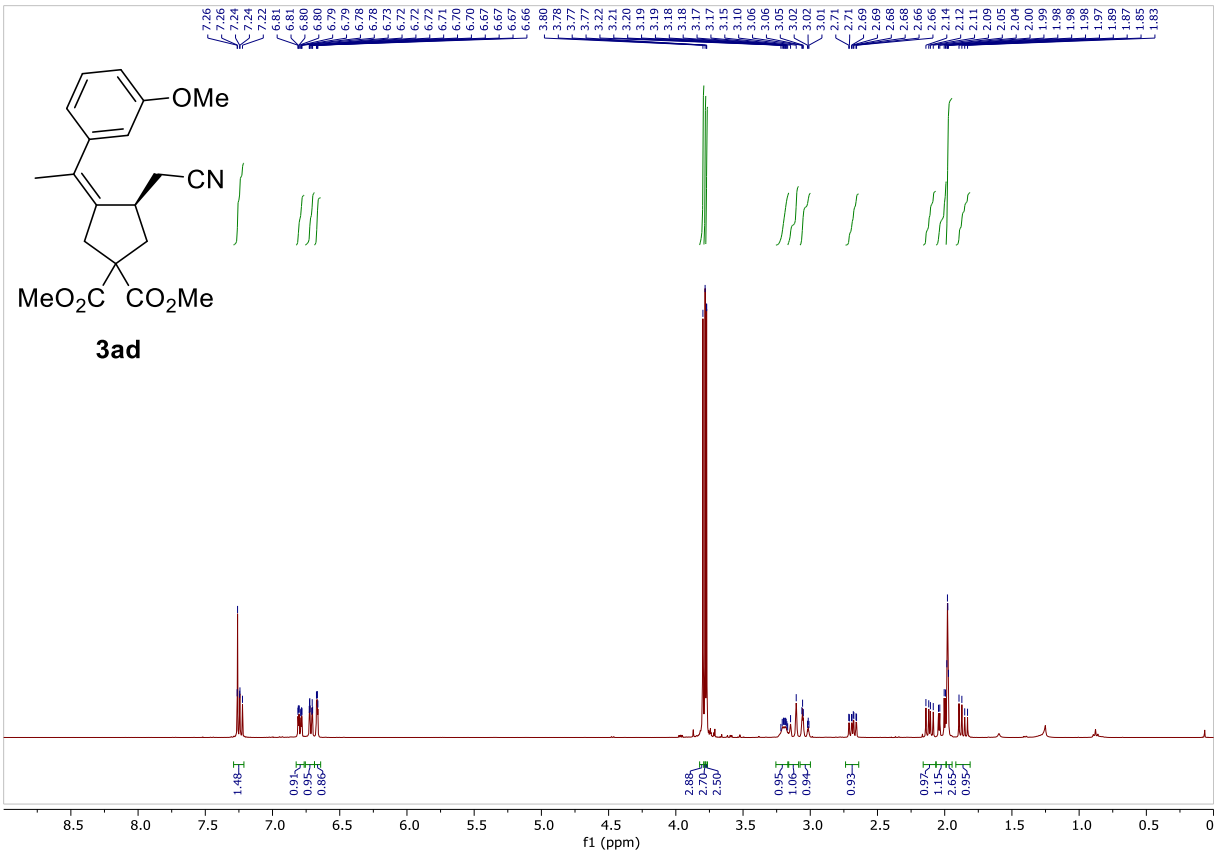
f1 (ppm)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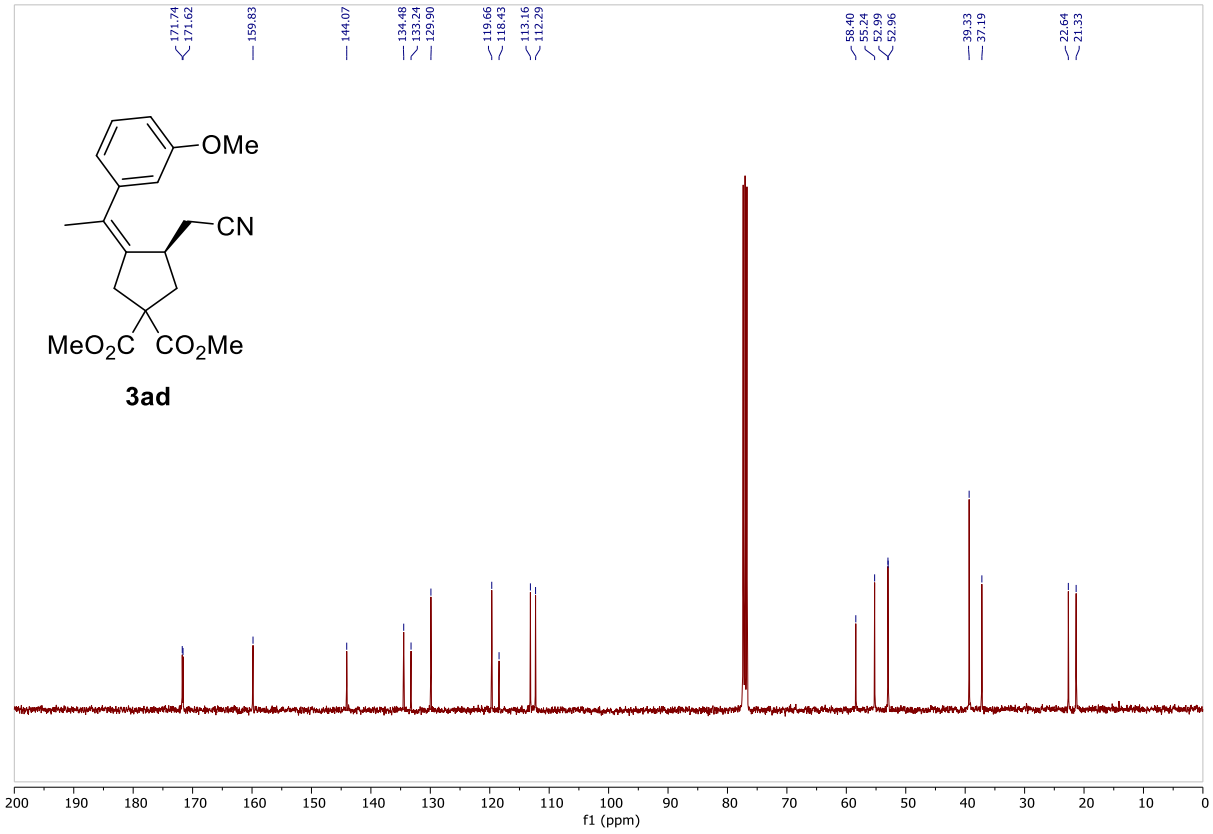
f1 (ppm)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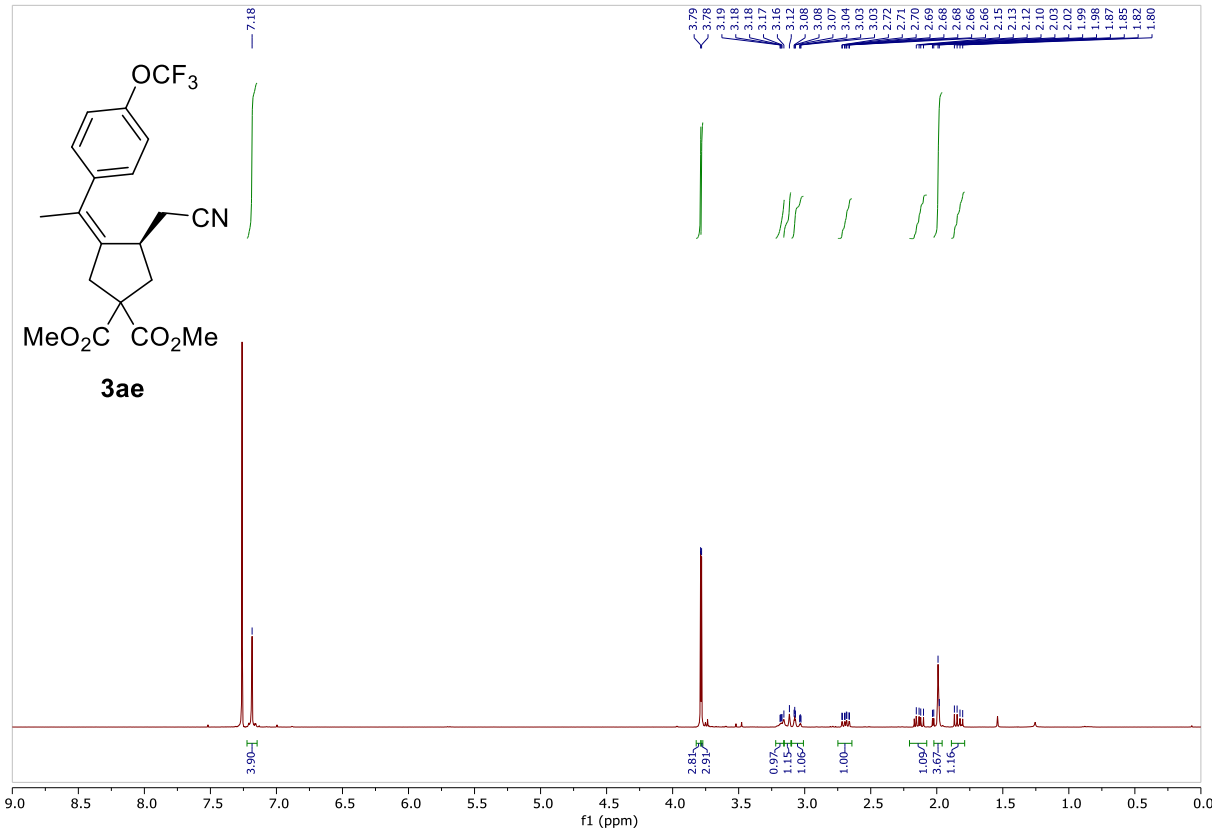
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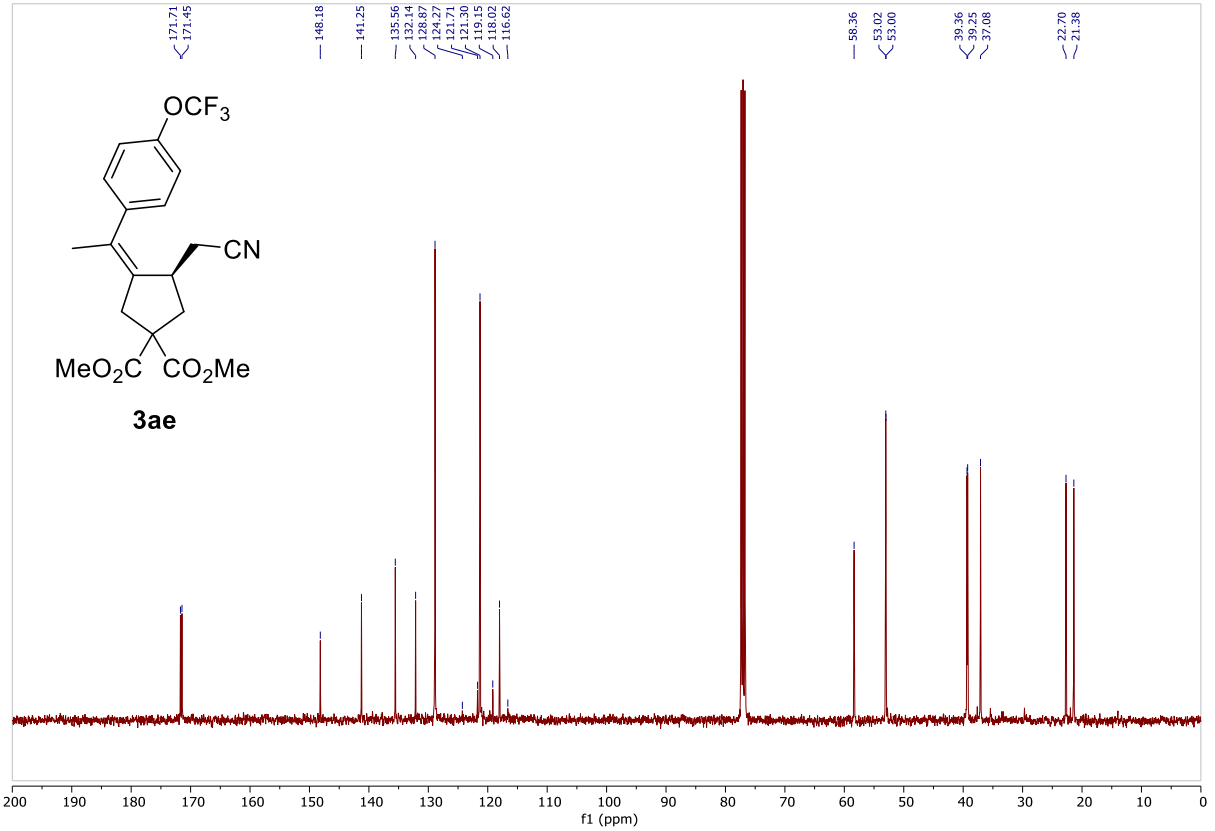
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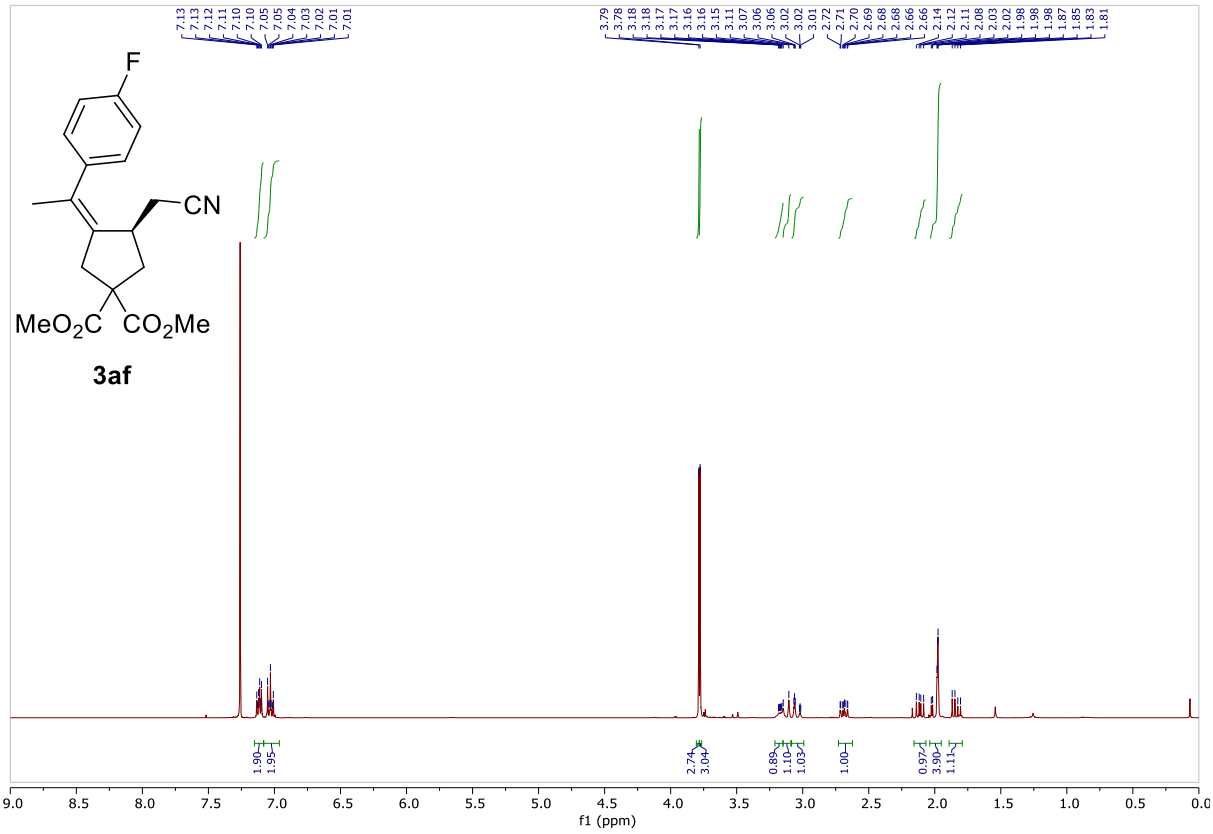
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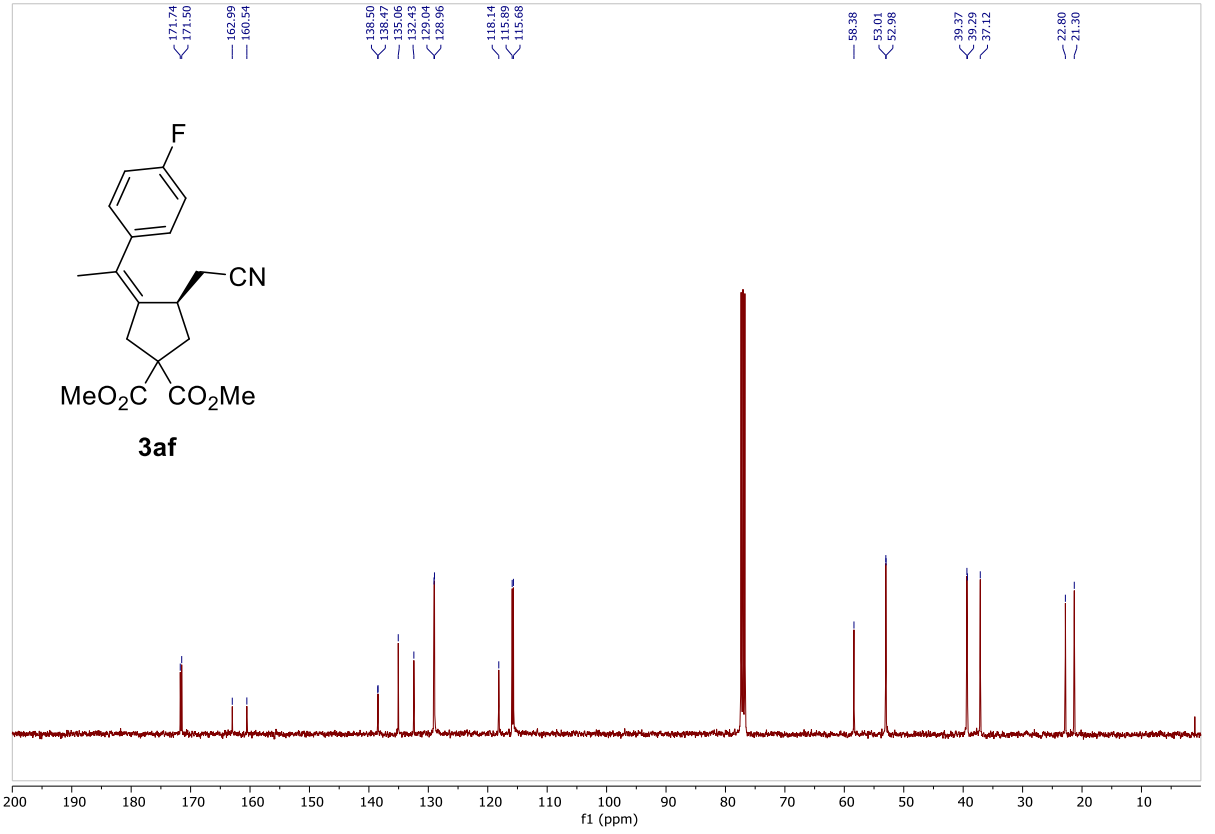
3af
f1 (ppm)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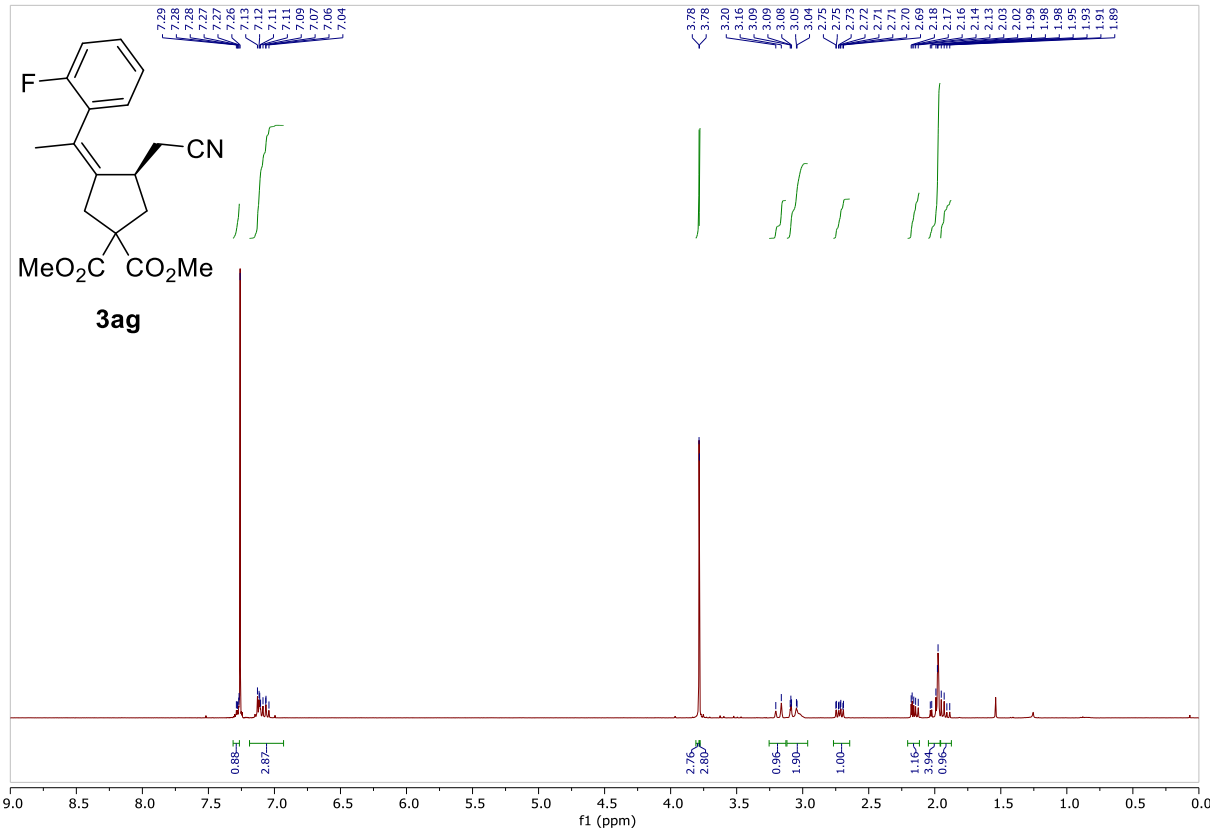
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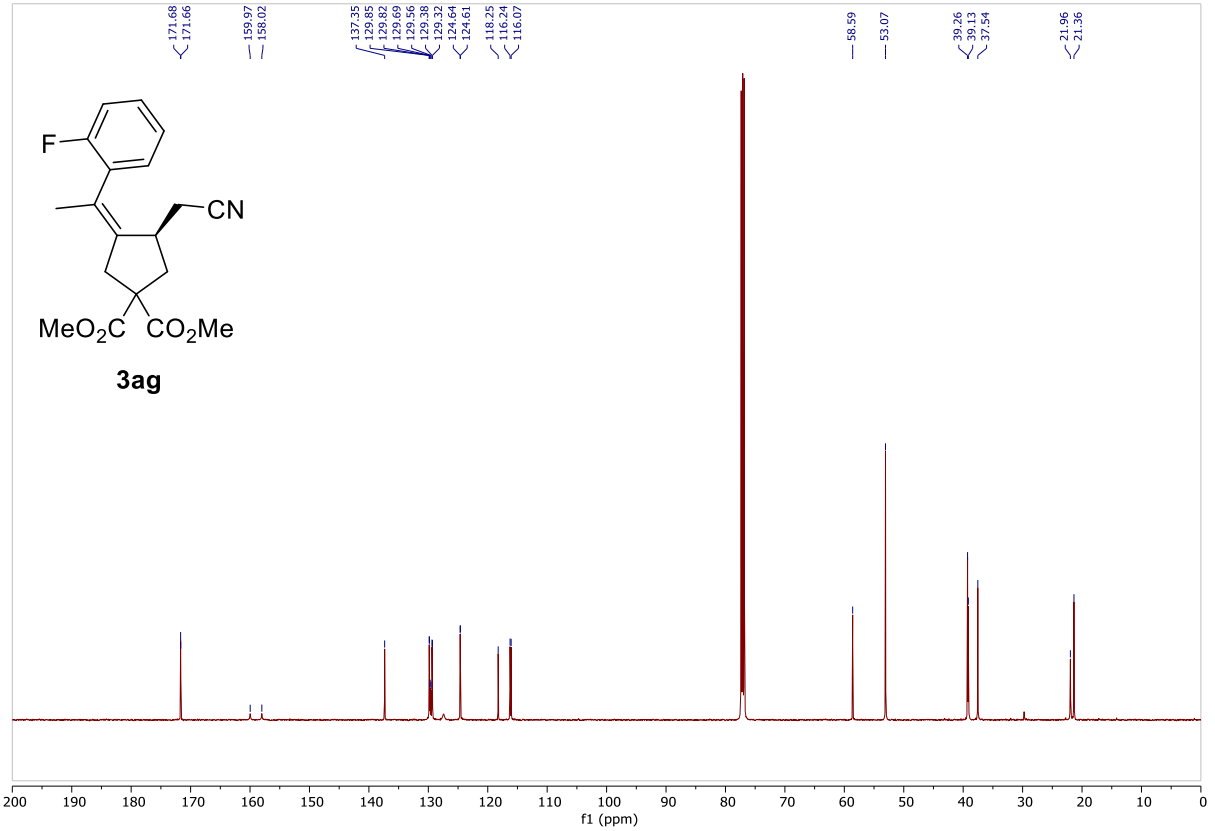
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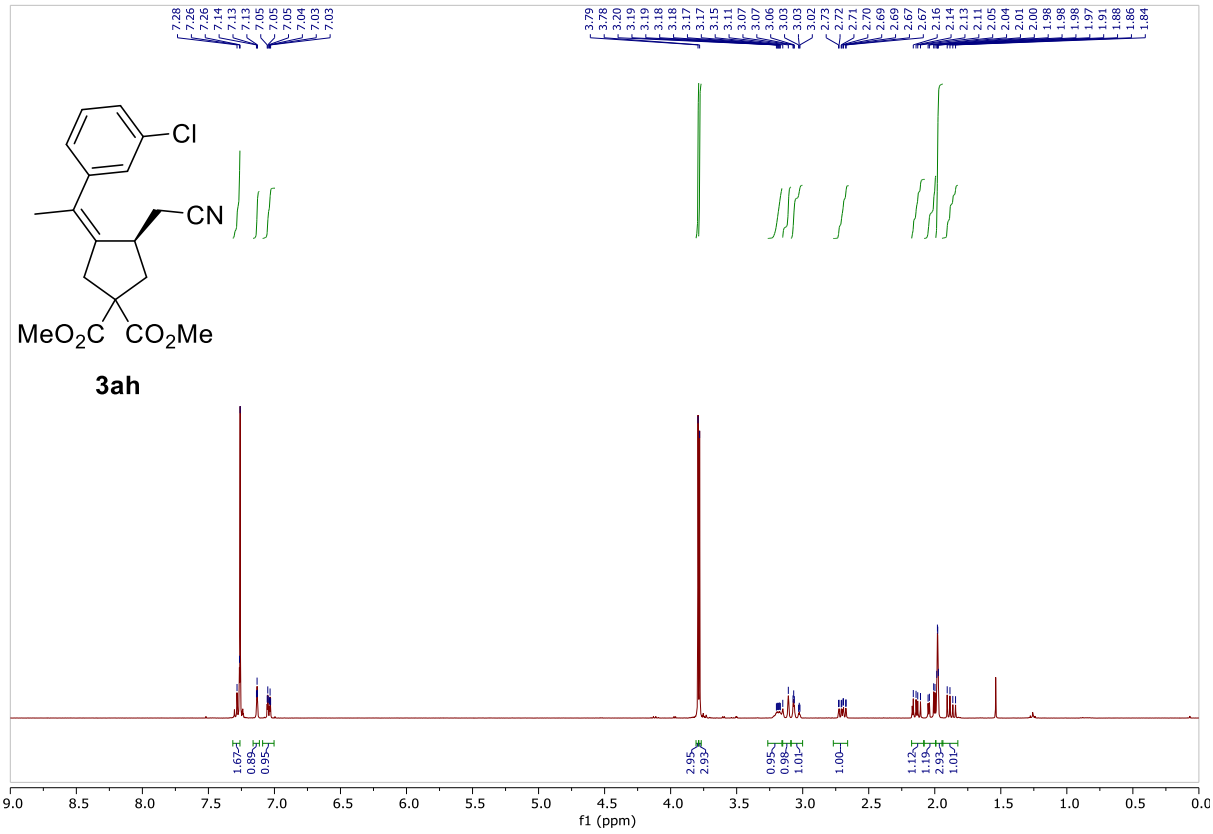
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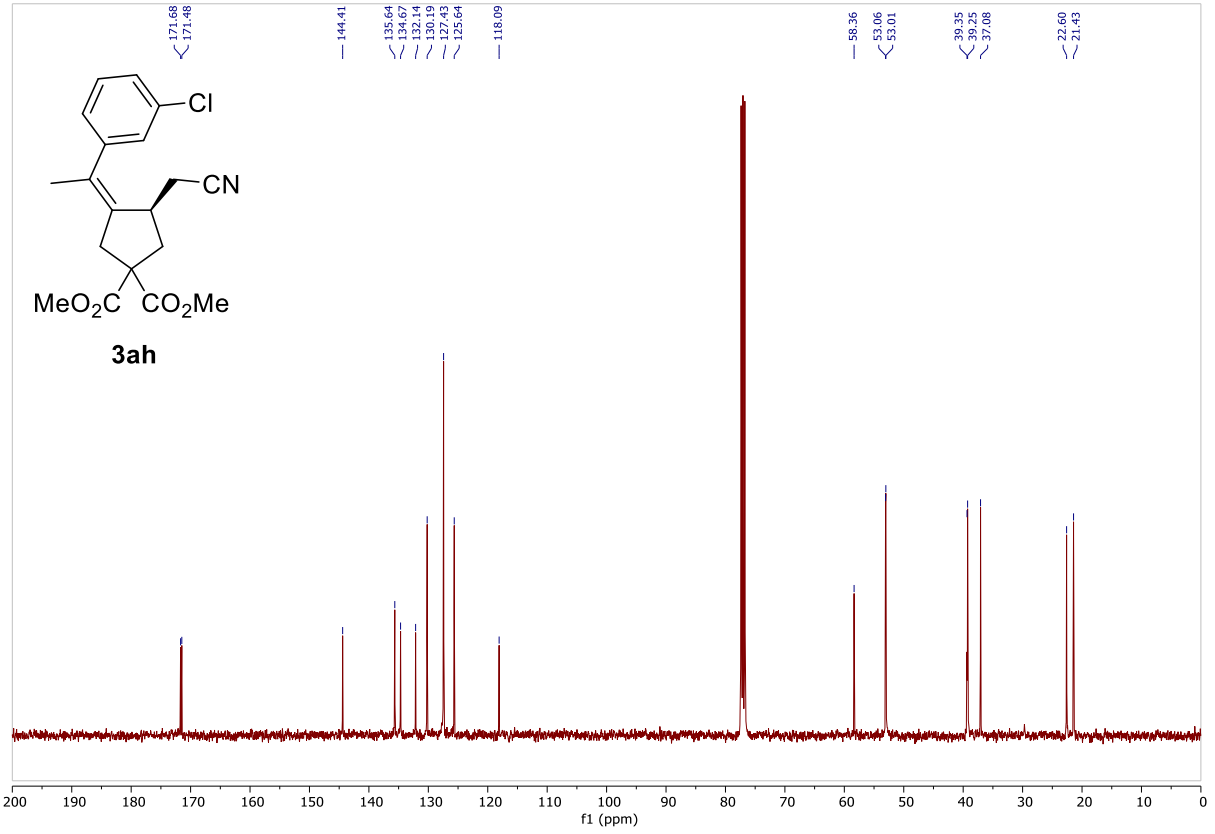
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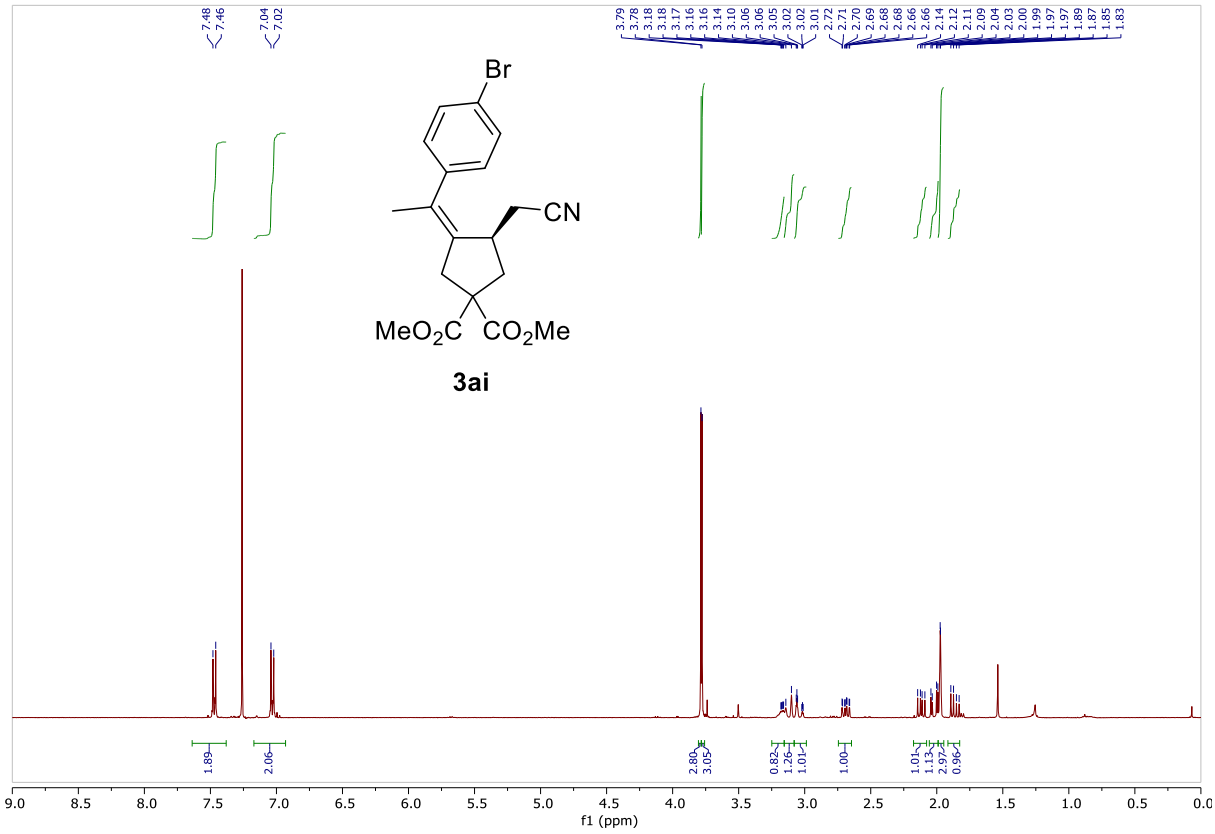
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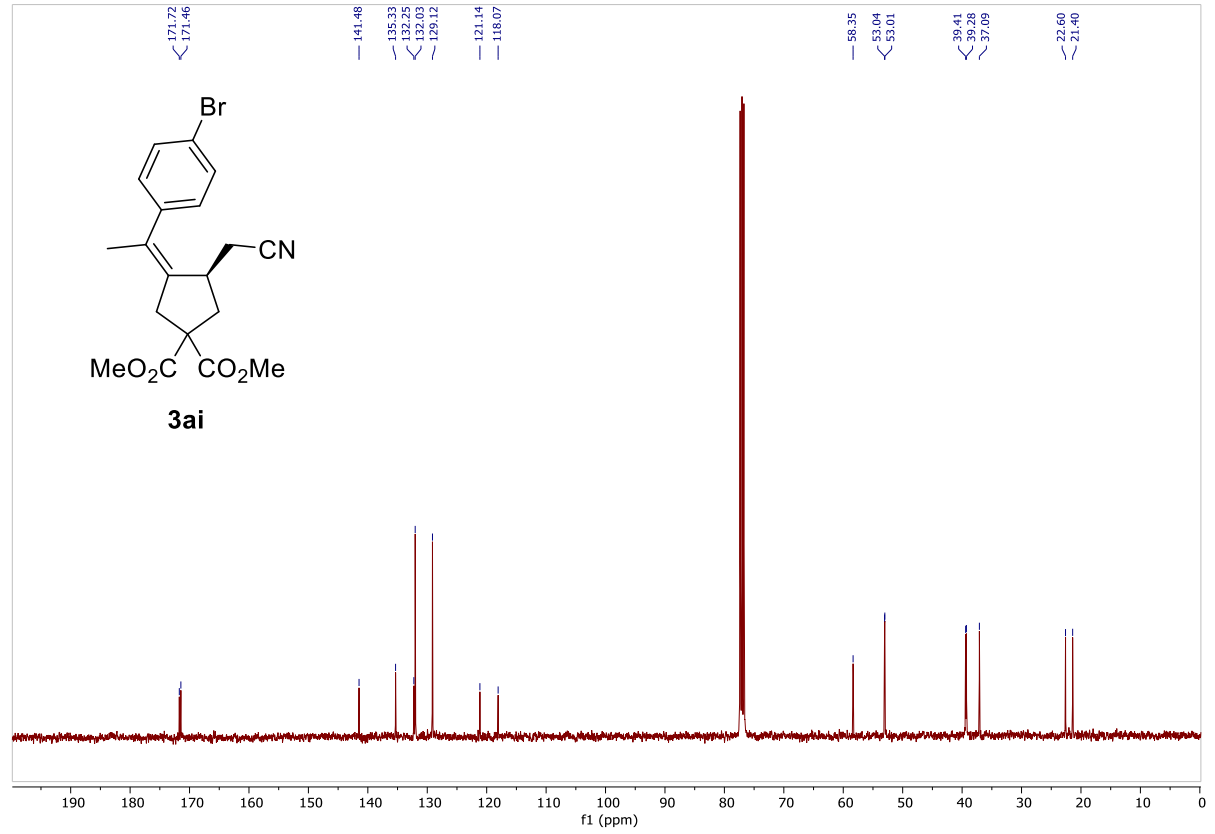
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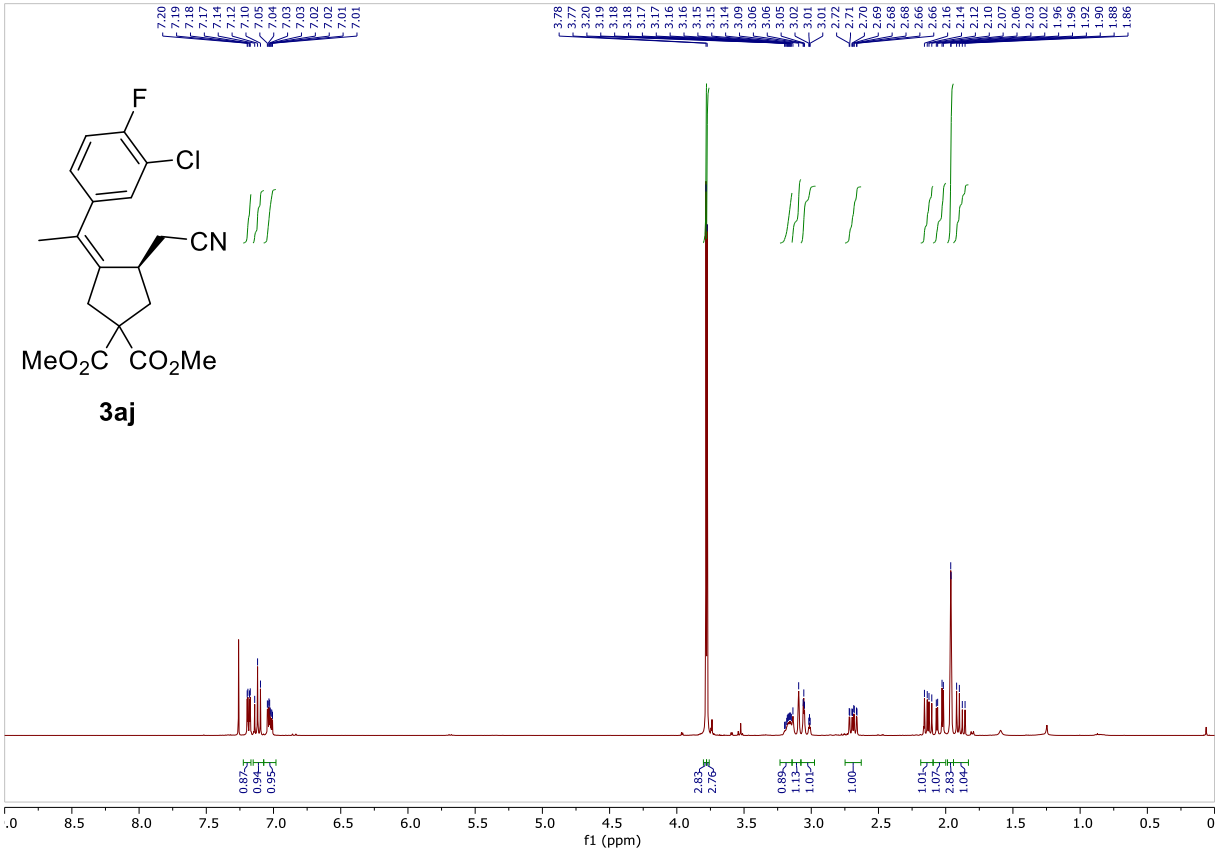
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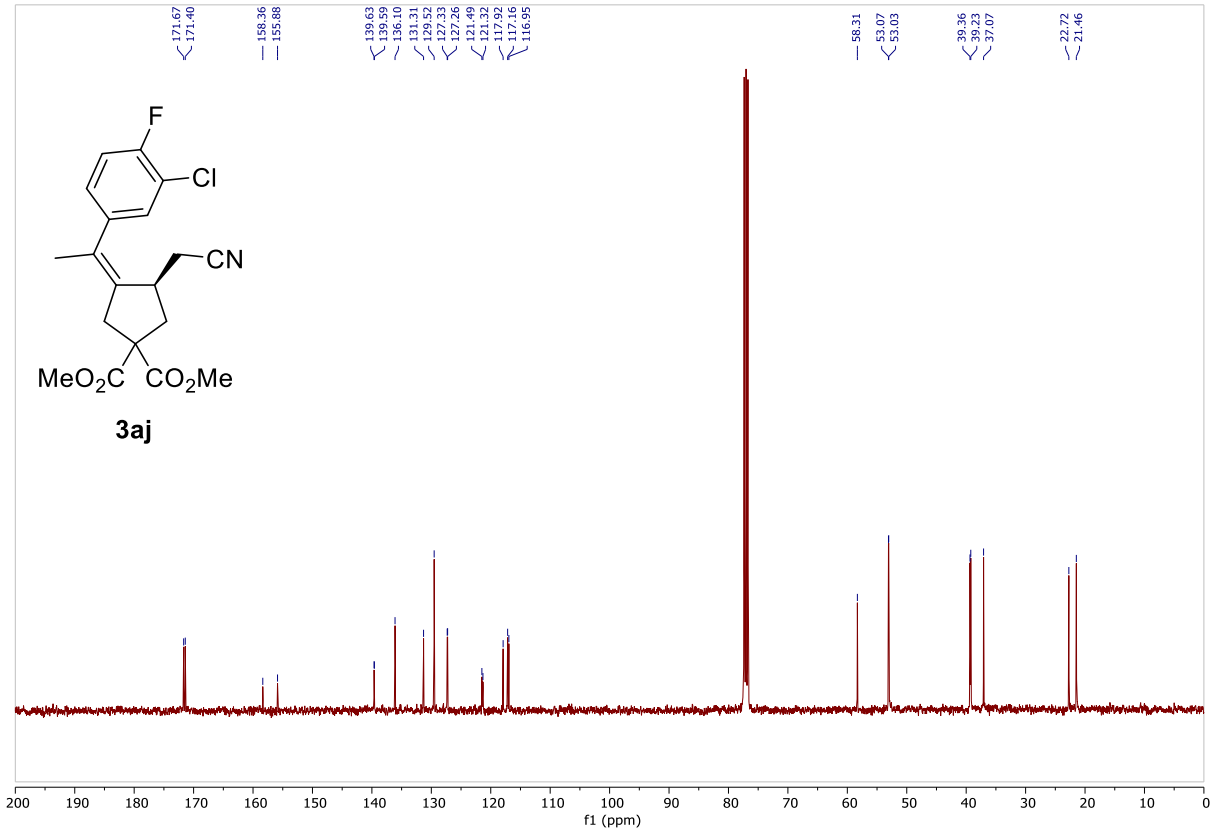
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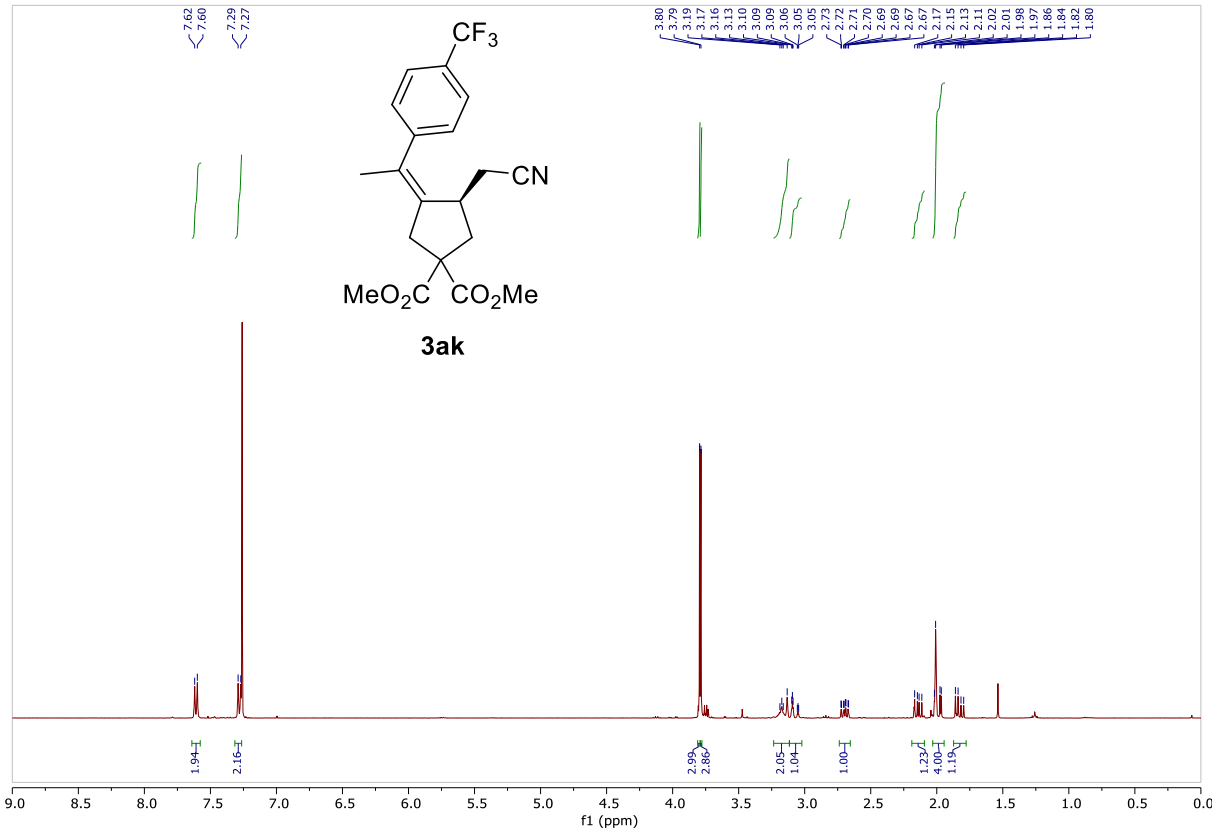
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2.15
2.13
2.11
2.02
2.01
1.98
1.97
1.86
1.84
1.82
1.80
CF3
CN
MeO2C
CO2Me
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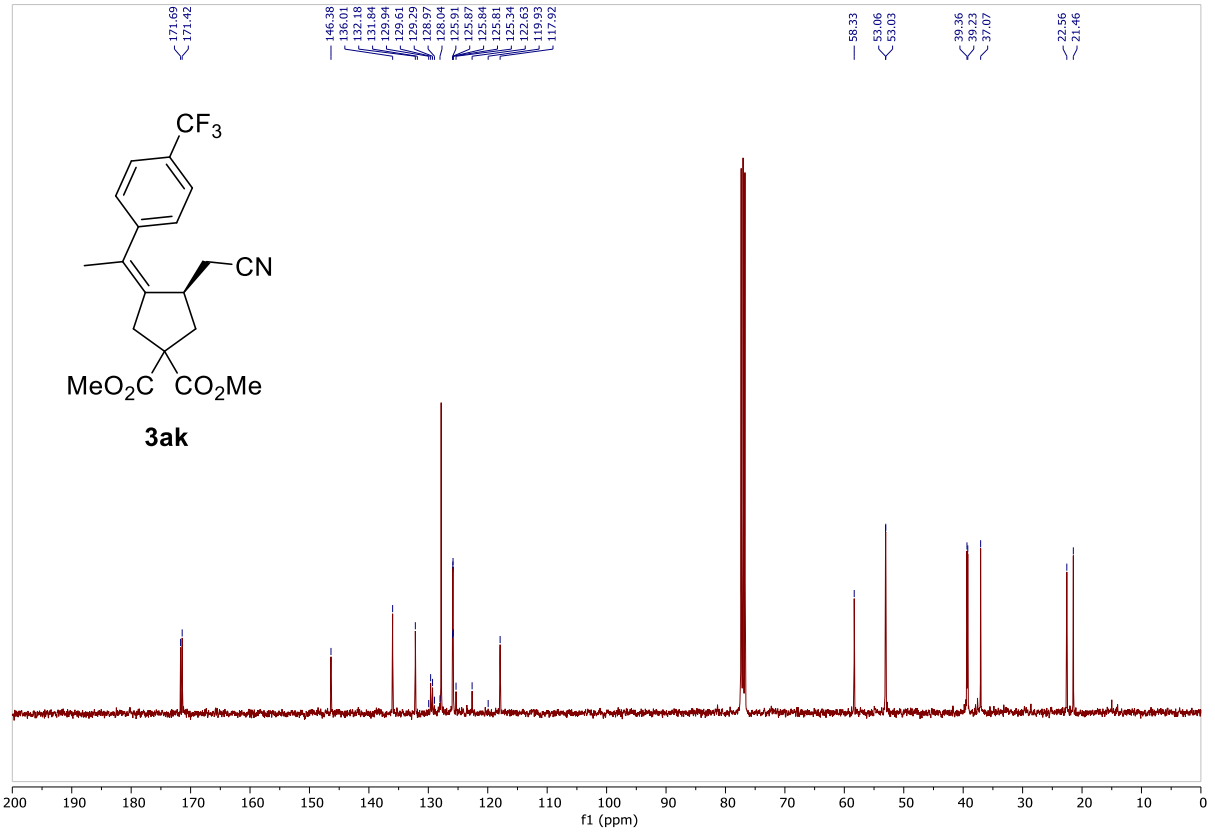
1.19
f1 (ppm)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171.42
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136.01
132.18
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129.94
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129.29
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128.04
125.91
125.87
125.84
125.81
123.34
122.63
119.93
117.92
58.33
53.06
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37.07
22.56
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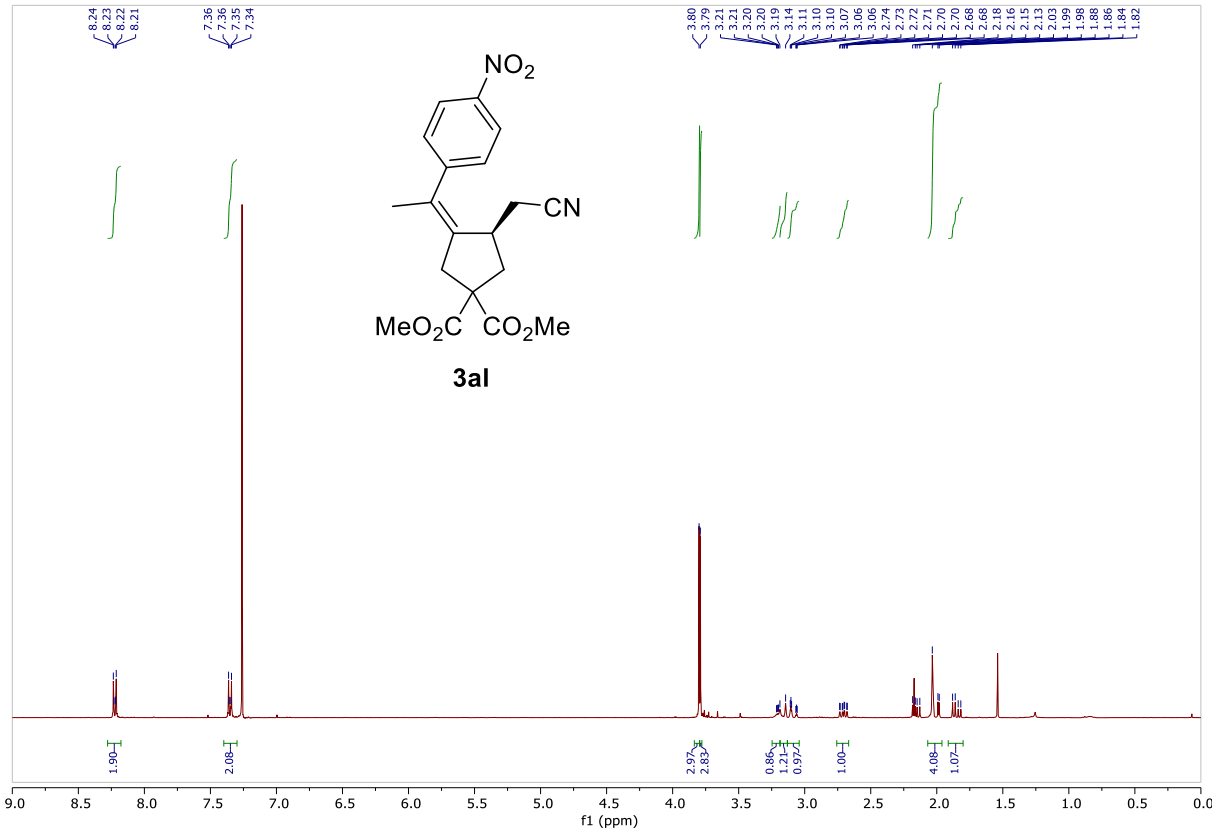
CF3
CN
MeO2C
CO2Me
3ak
f1 (ppm)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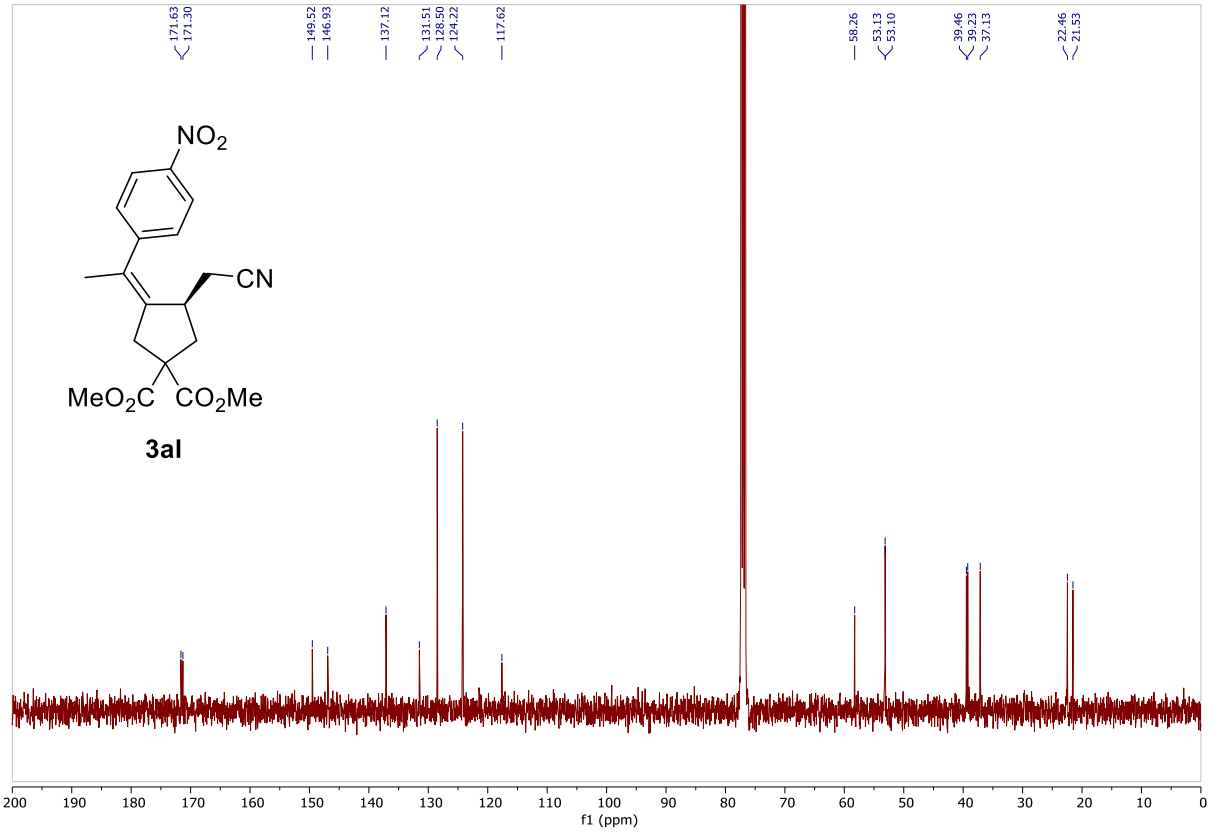
CO2Me
3aI
f1 (ppm)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CN
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CO2Me
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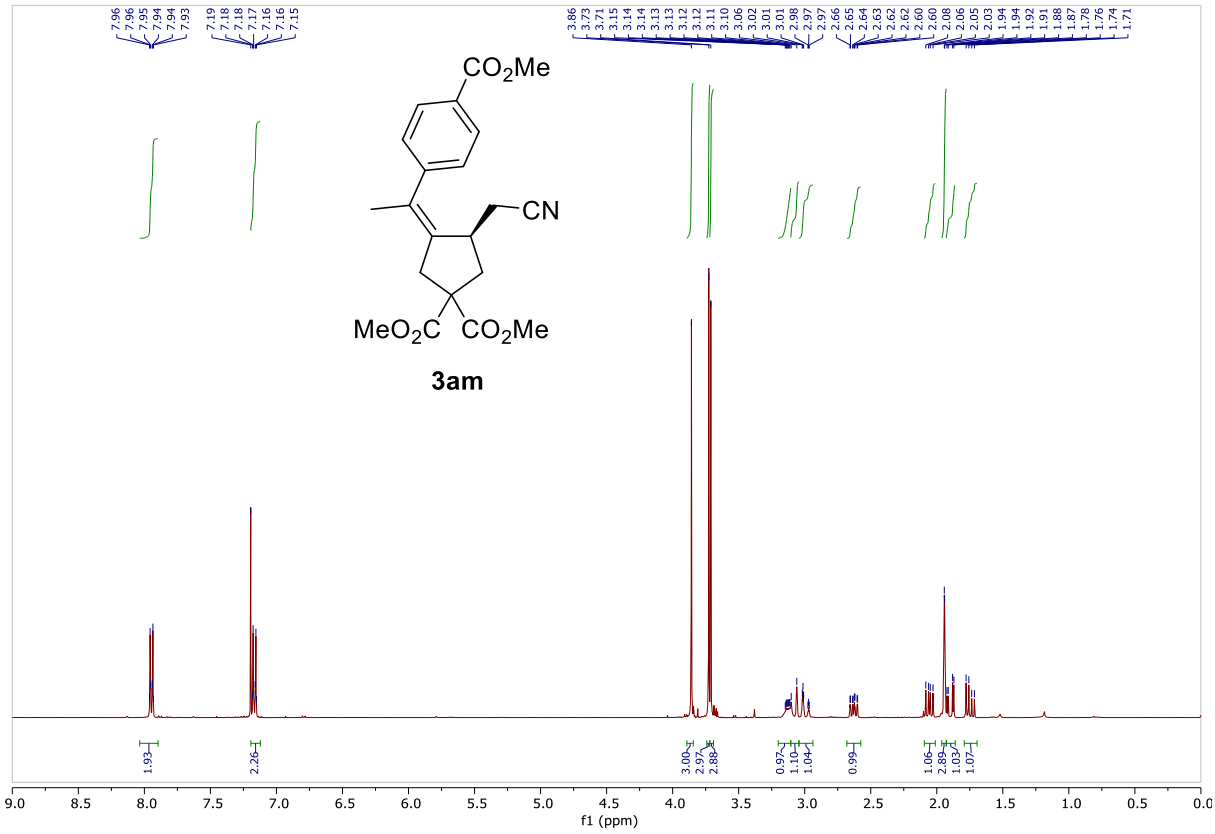
f1 (ppm)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7.15
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3.73
3.71
3.15
3.14
3.14
3.13
3.13
3.12
3.12
3.11
3.10
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3.02
3.01
3.01
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2.05
2.03
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1.94
1.92
1.91
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1.87
1.78
1.76
1.74
1.71
CO2Me
CN
MeO2C
CO2Me
3am
1.93
2.26
3.00
2.97
2.88
0.97
1.10
1.04
0.99
1.06
2.85
1.03
1.07
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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3.0
2.5
2.0
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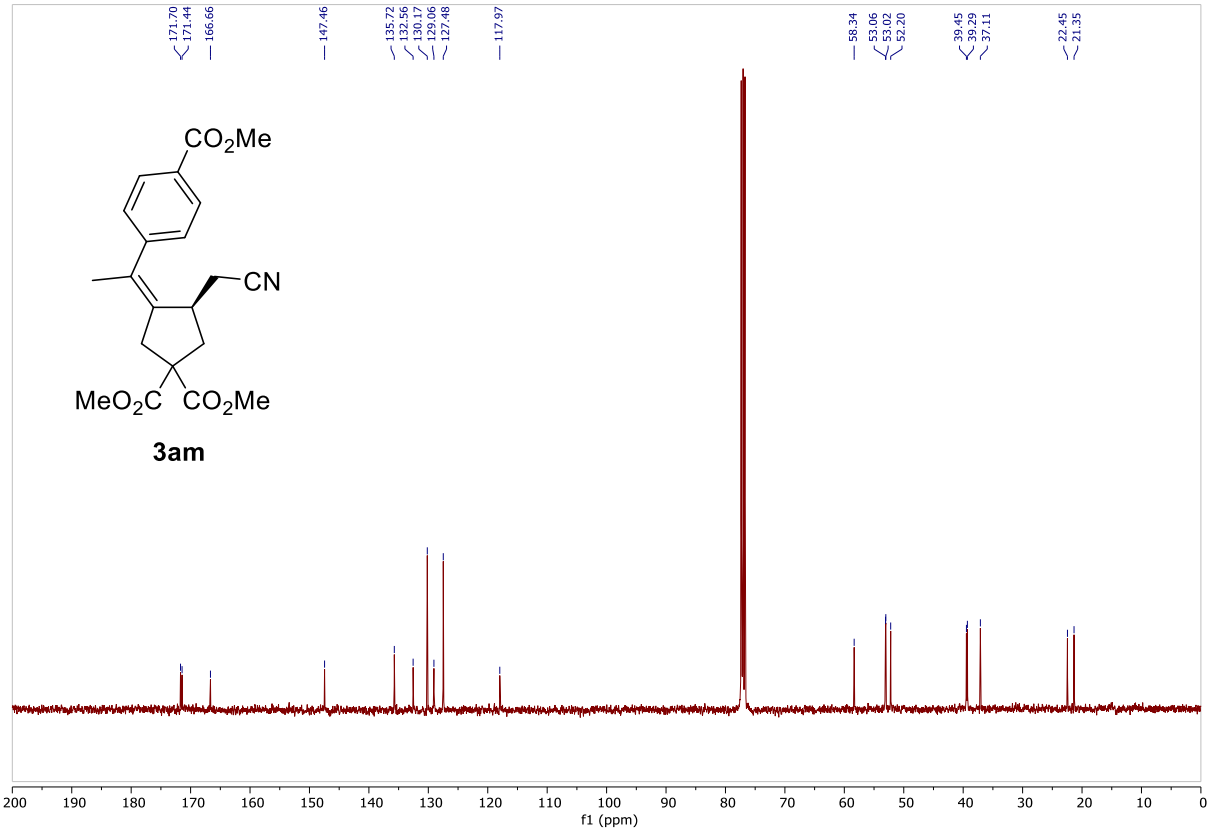
1.0
0.5
0.0
f1 (ppm)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129.06
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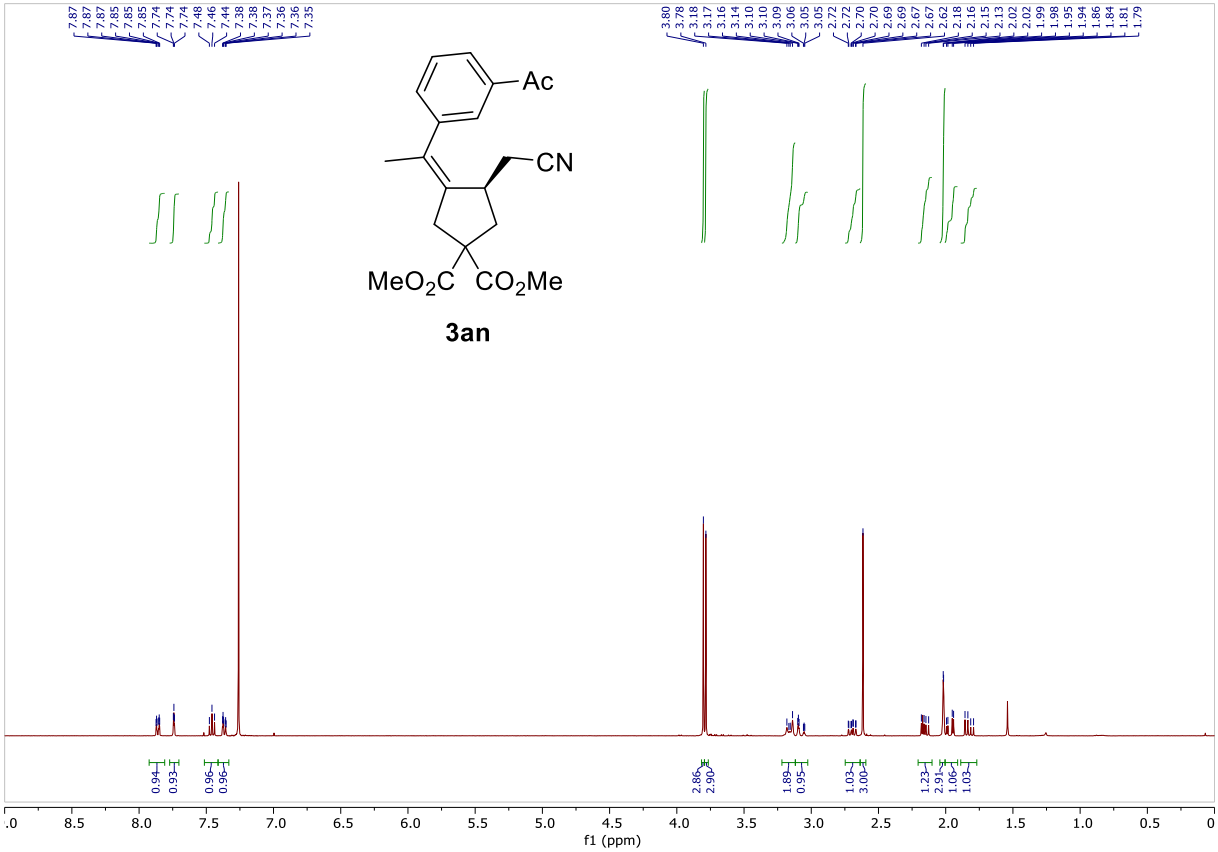
117.97
58.34
53.06
53.02
52.20
39.45
39.29
37.11
22.45
21.35
CO2Me
CN
MeO2C
CO2Me
3am
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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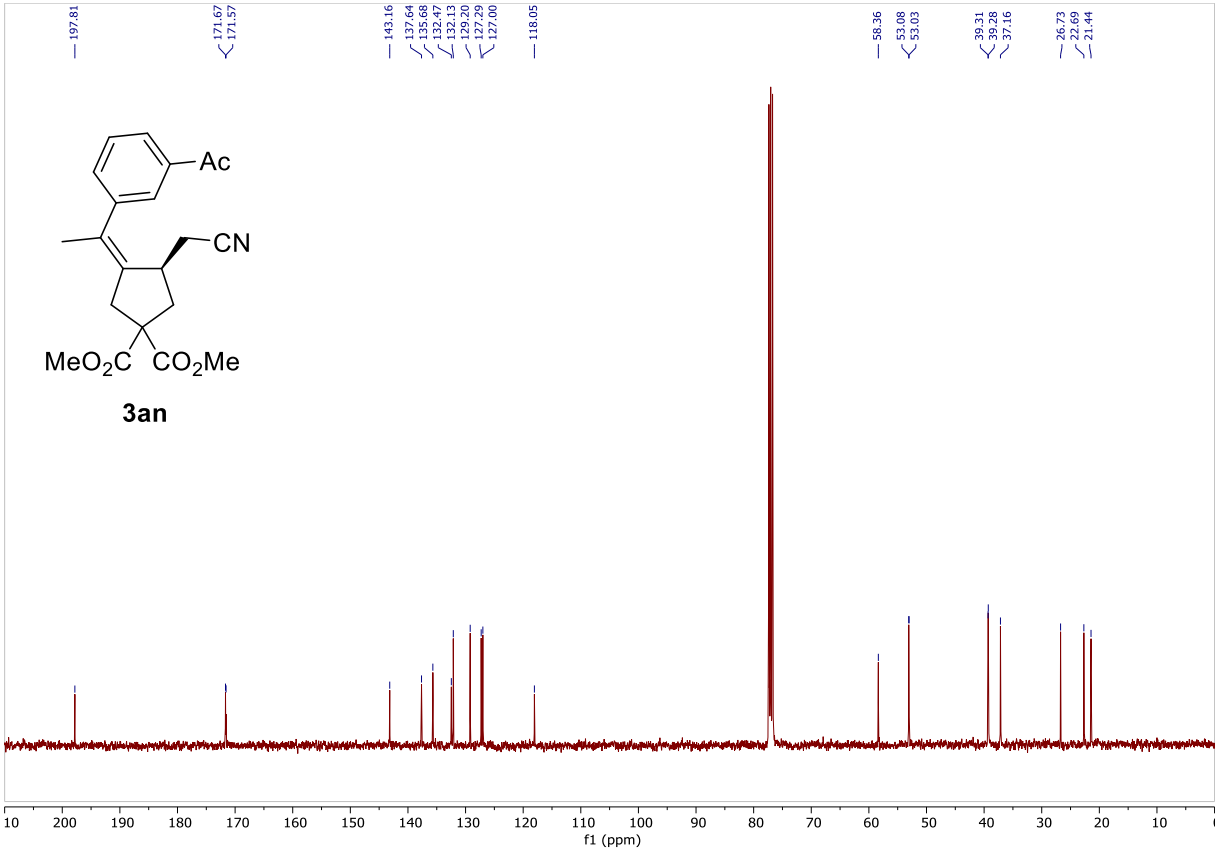
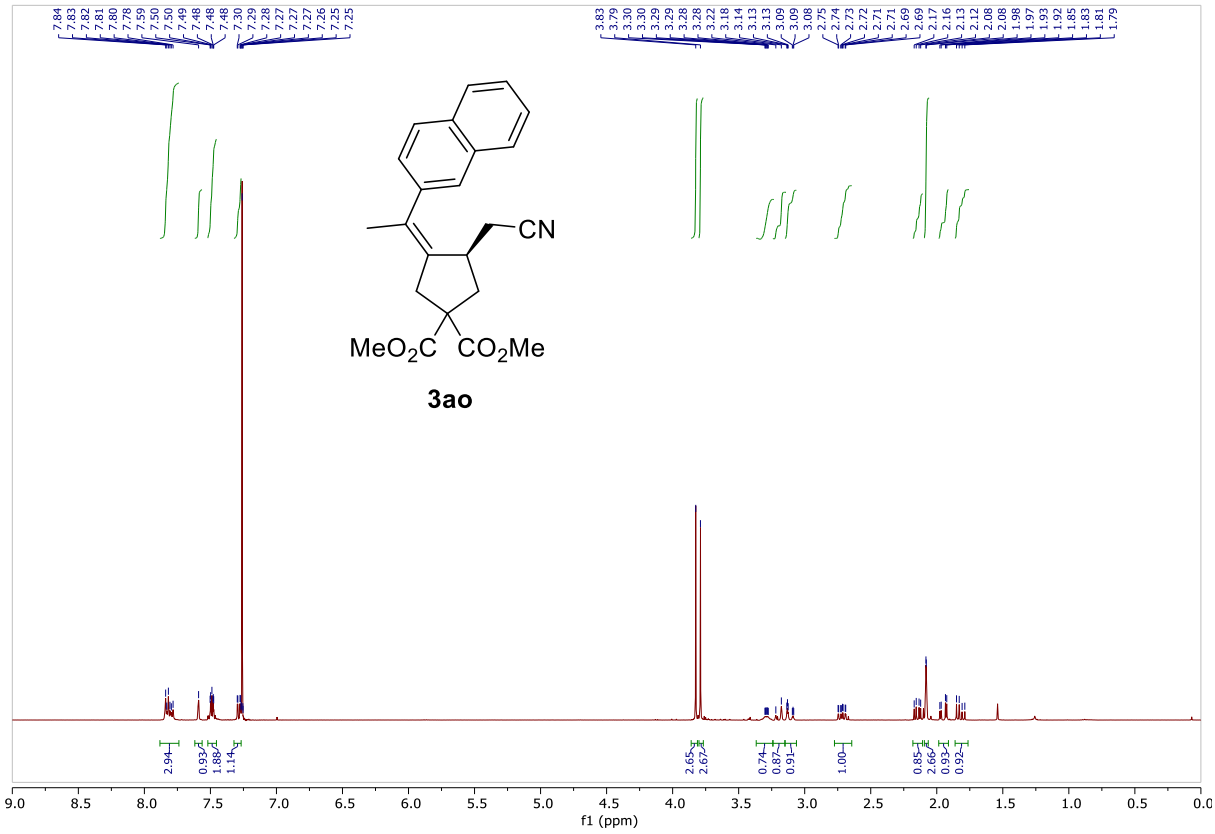
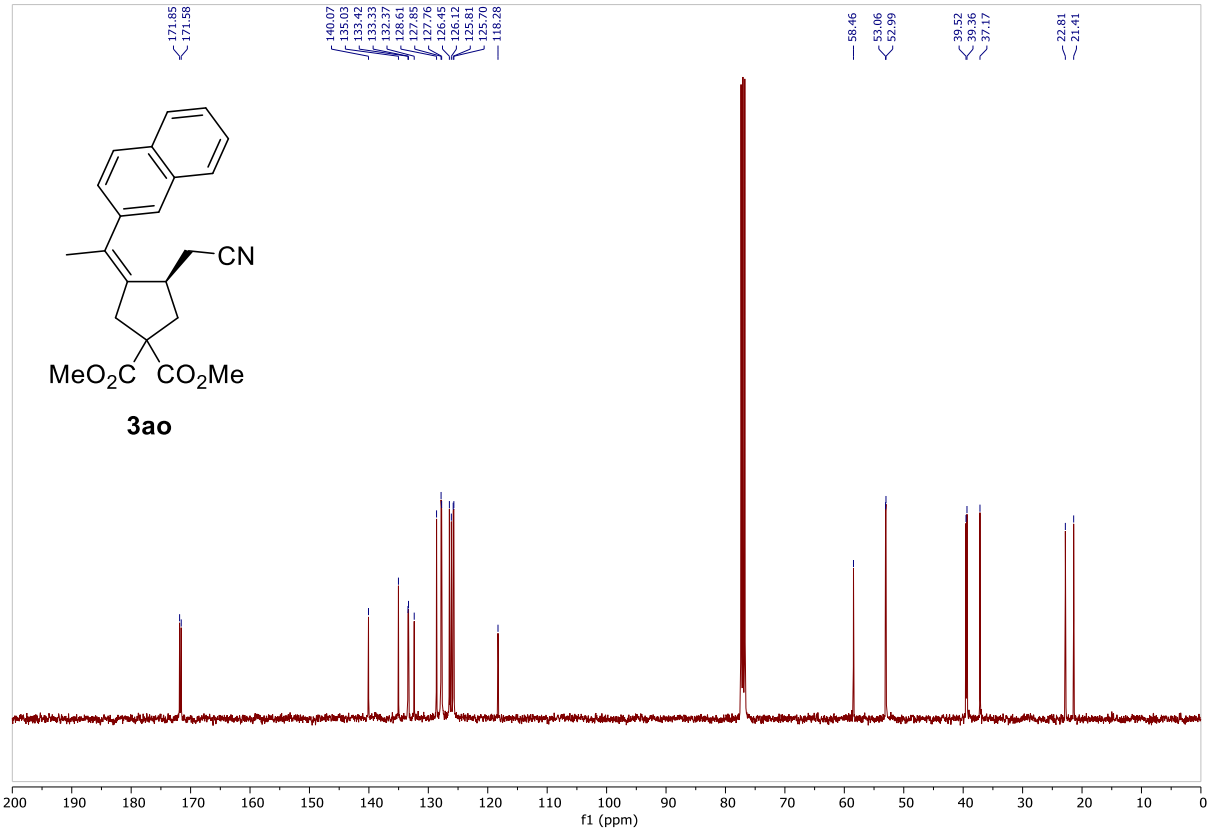
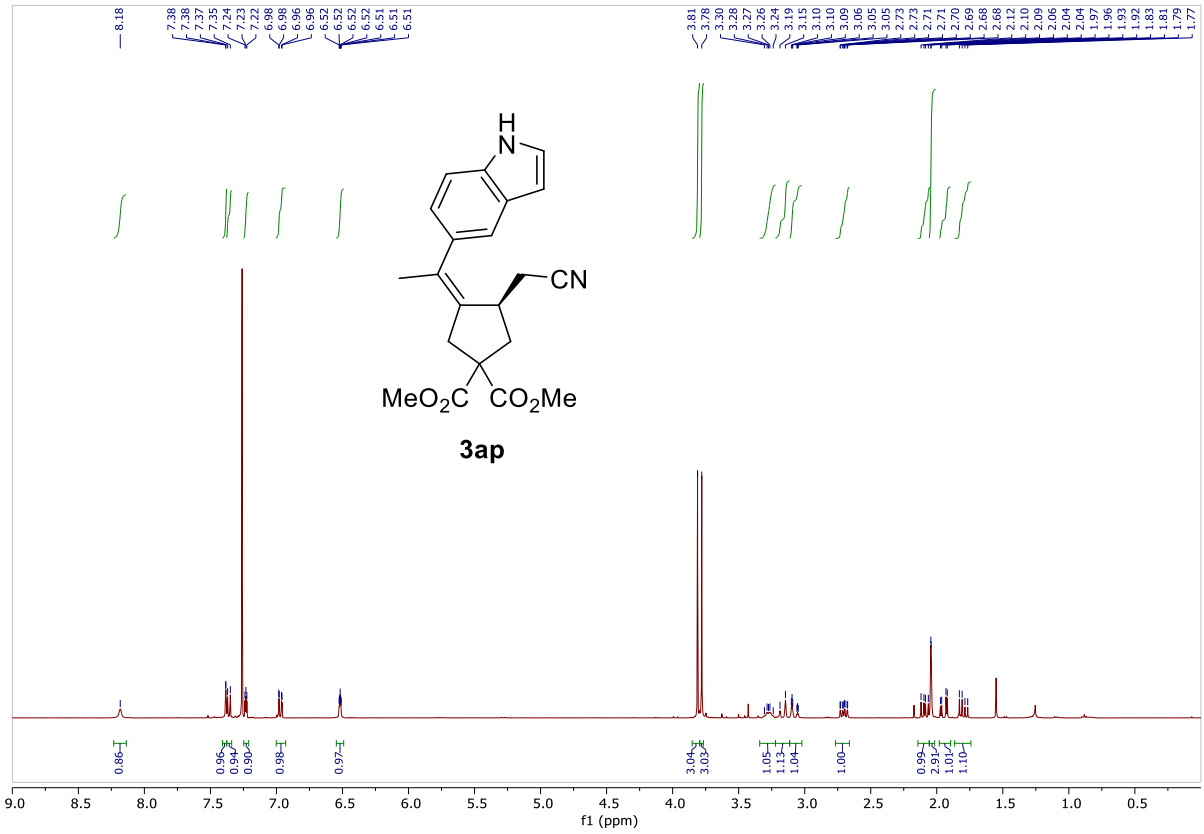
CN
MeO2C CO2Me
3an
f1 (ppm)


Ac
CN
MeO2C CO2Me
3an
f1 (ppm)


CN
MeO2C CO2Me
3ao
f1 (ppm)


CN
MeO2C CO2Me
3ao
f1 (ppm)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6.96
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6.52
6.51
6.51
6.51
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3.78
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3.10
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3.06
3.05
3.05
2.73
2.73
2.71
2.71
2.70
2.69
2.68
2.68
2.12
2.10
2.09
2.06
2.04
2.04
1.97
1.96
1.93
1.92
1.83
1.81
1.79
1.77
H
N
CN
MeO2C
CO2Me
3ap
0.86
0.96
0.94
0.90
0.98
0.97
3.04
3.03
1.05
1.13
1.04
1.00
0.99
2.91
1.01
1.10
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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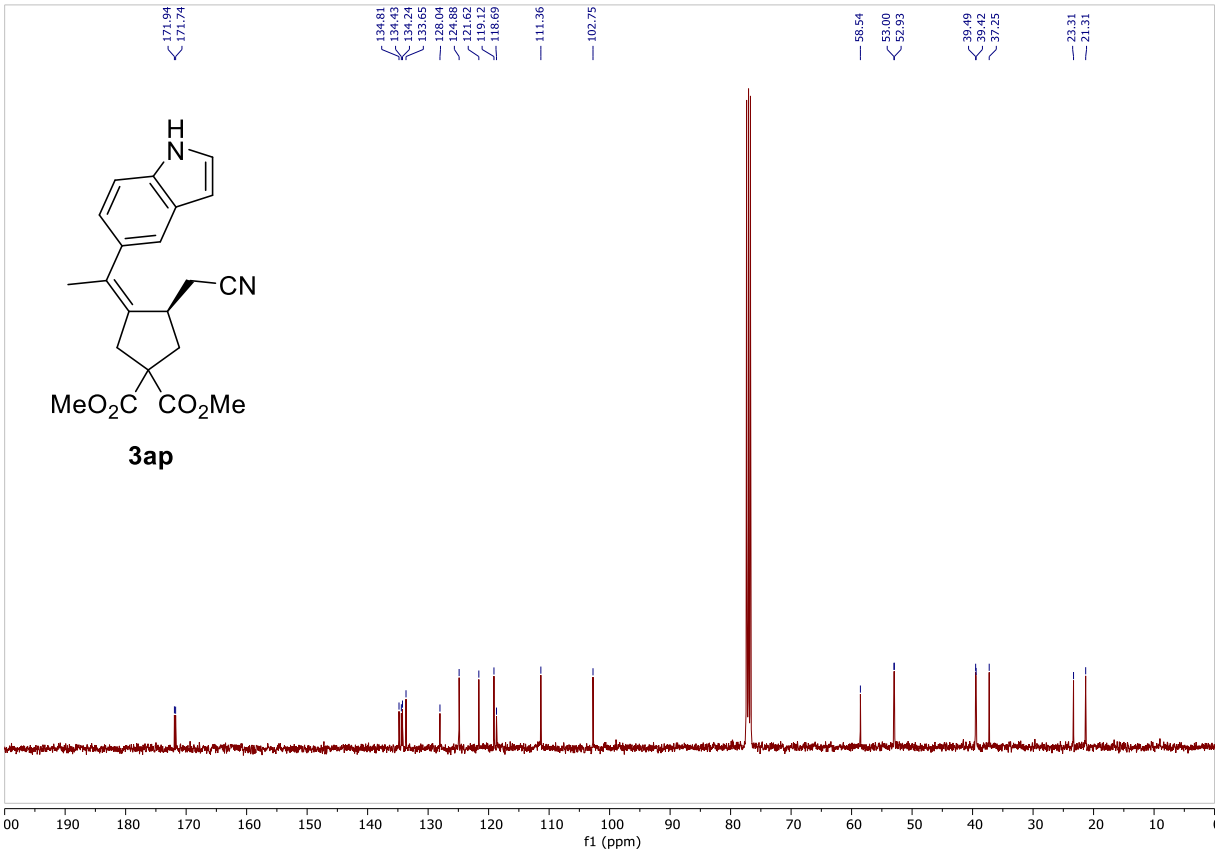
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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133.65
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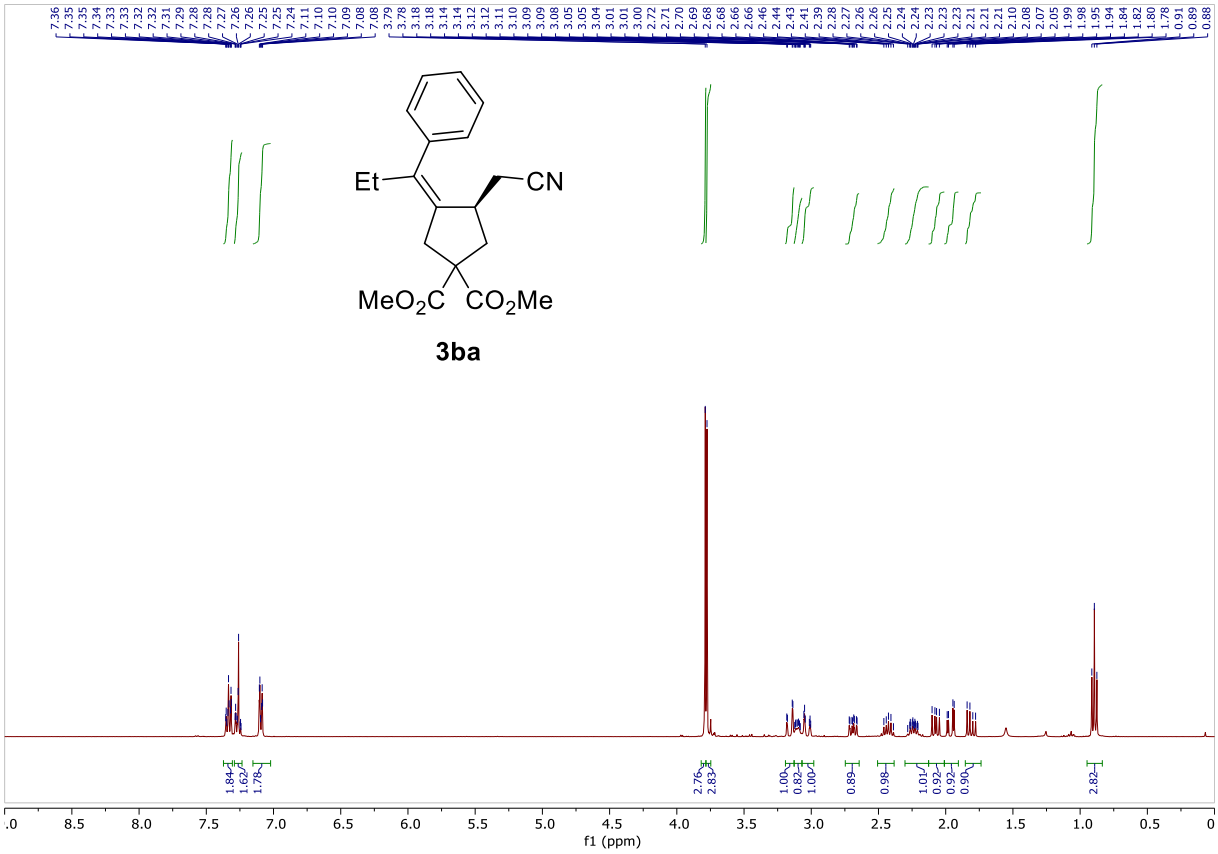
124.88
121.62
119.12
118.69
111.36
102.75
58.54
53.00
52.93
39.49
39.42
37.25
23.31
21.31
H
N
CN
MeO2C
CO2Me
3ap
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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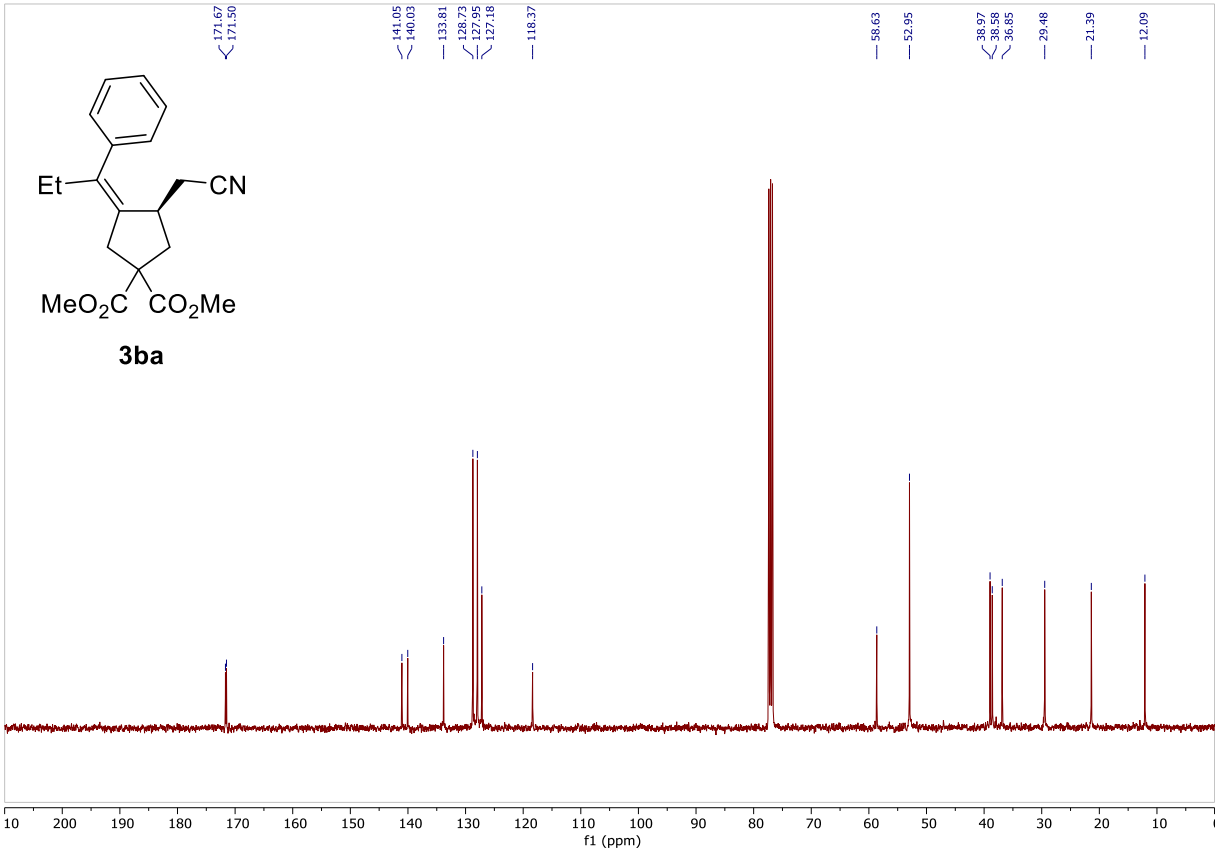
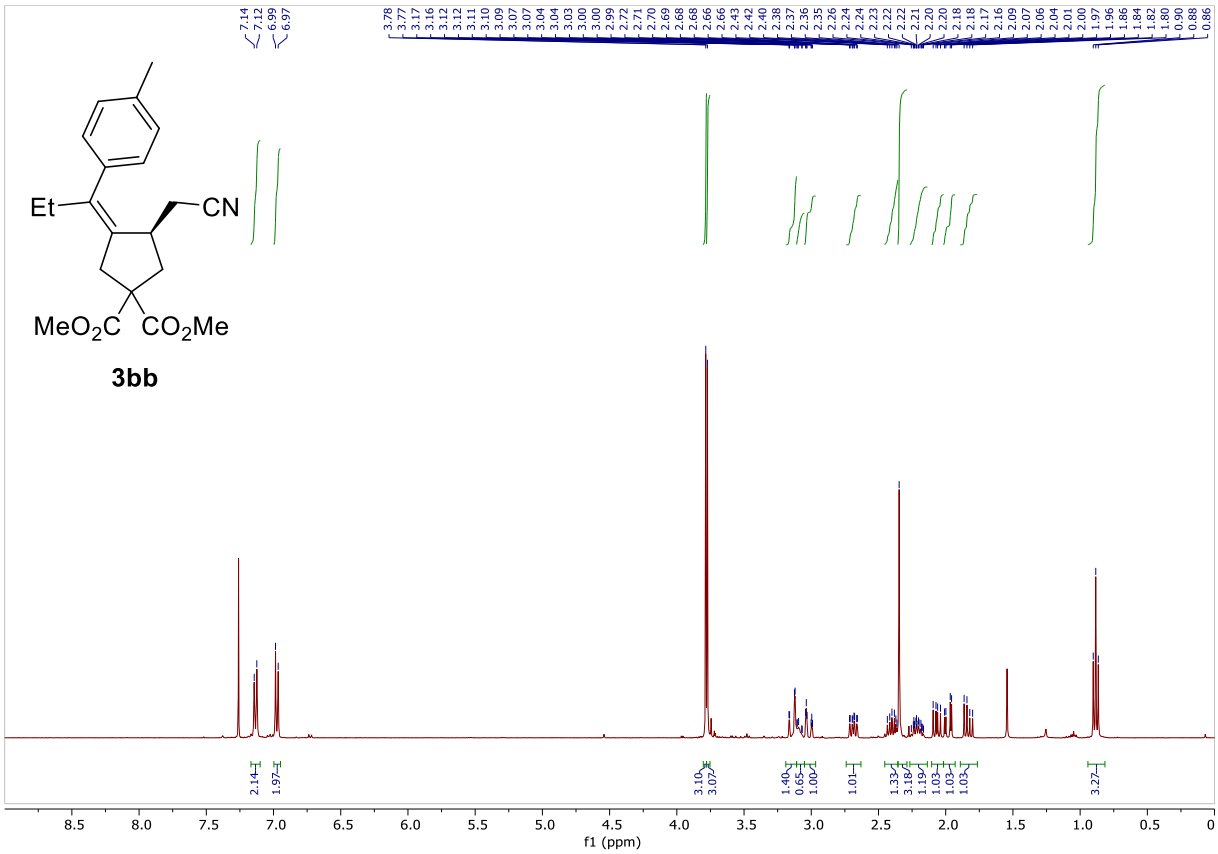
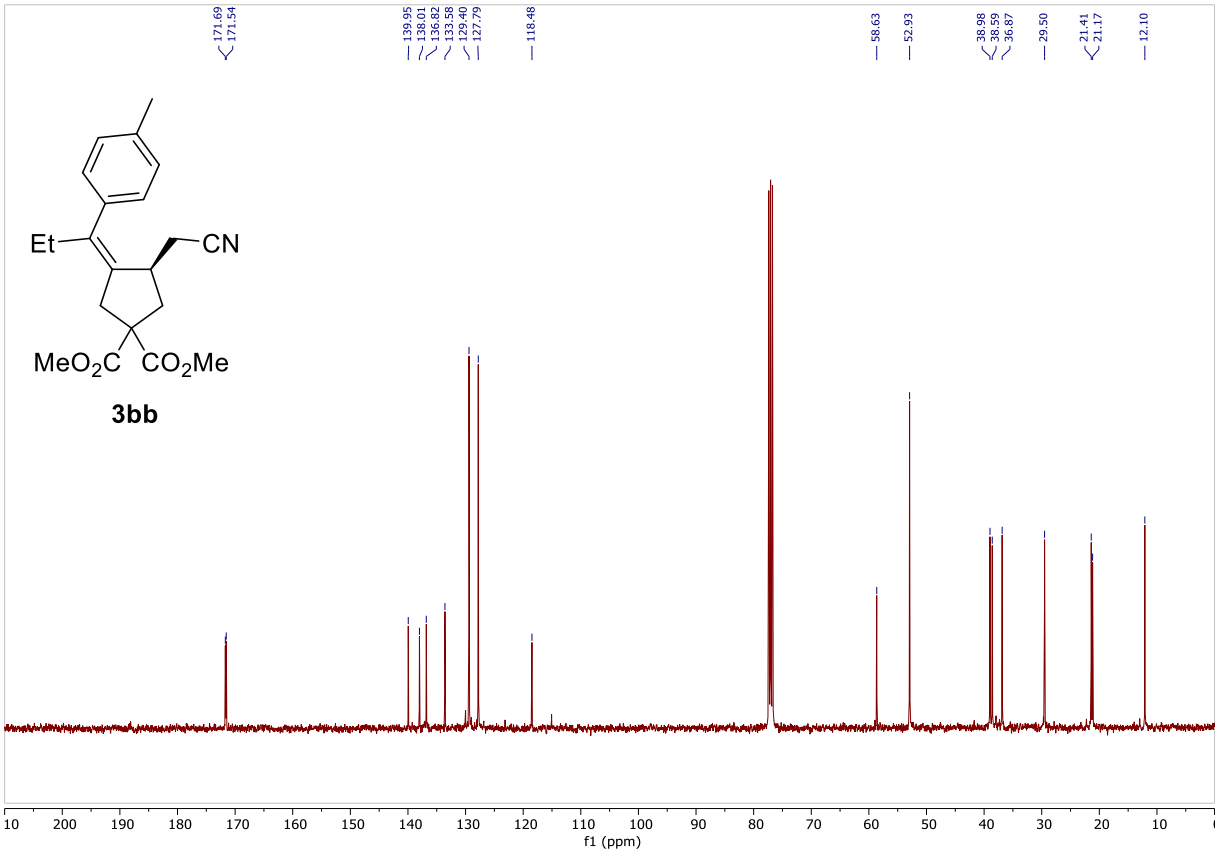
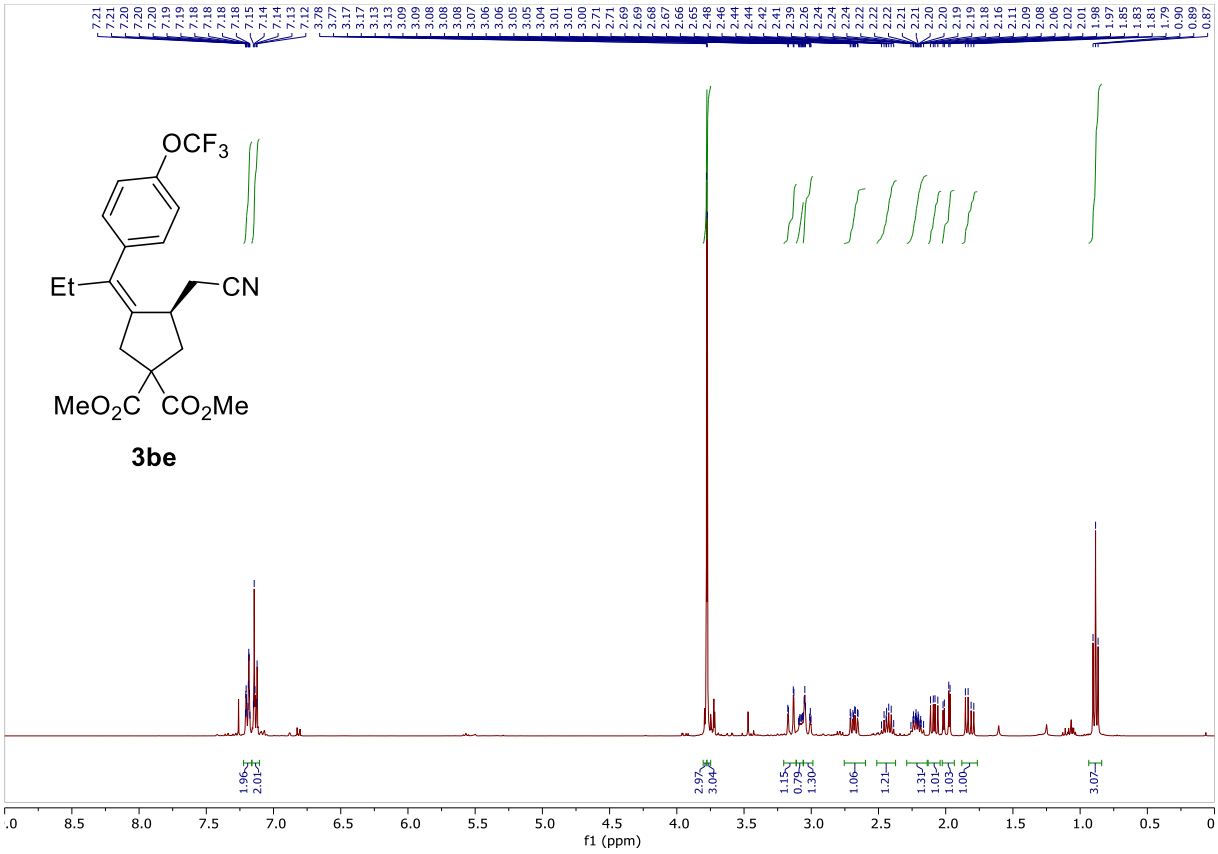
CN
MeO2C
CO2Me
3ba
f1 (ppm)


Et
CN
MeO2C
CO2Me
3ba
f1 (ppm)


Et
CN
MeO2C
CO2Me
3bb
f1 (ppm)


Et
CN
MeO2C
CO2Me
3bb
f1 (ppm)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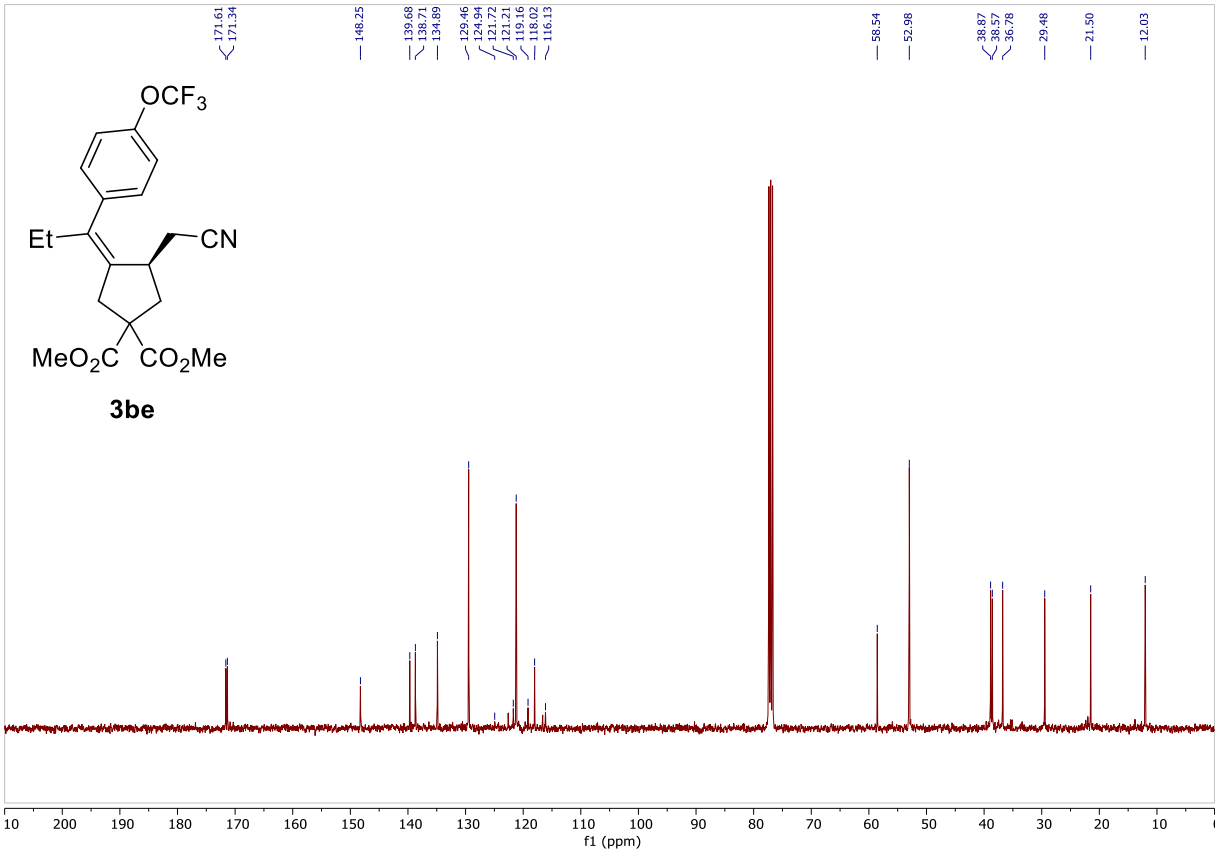
Et
CN
MeO2C
CO2Me
3be
f1 (ppm)


OCF3
Et
CN
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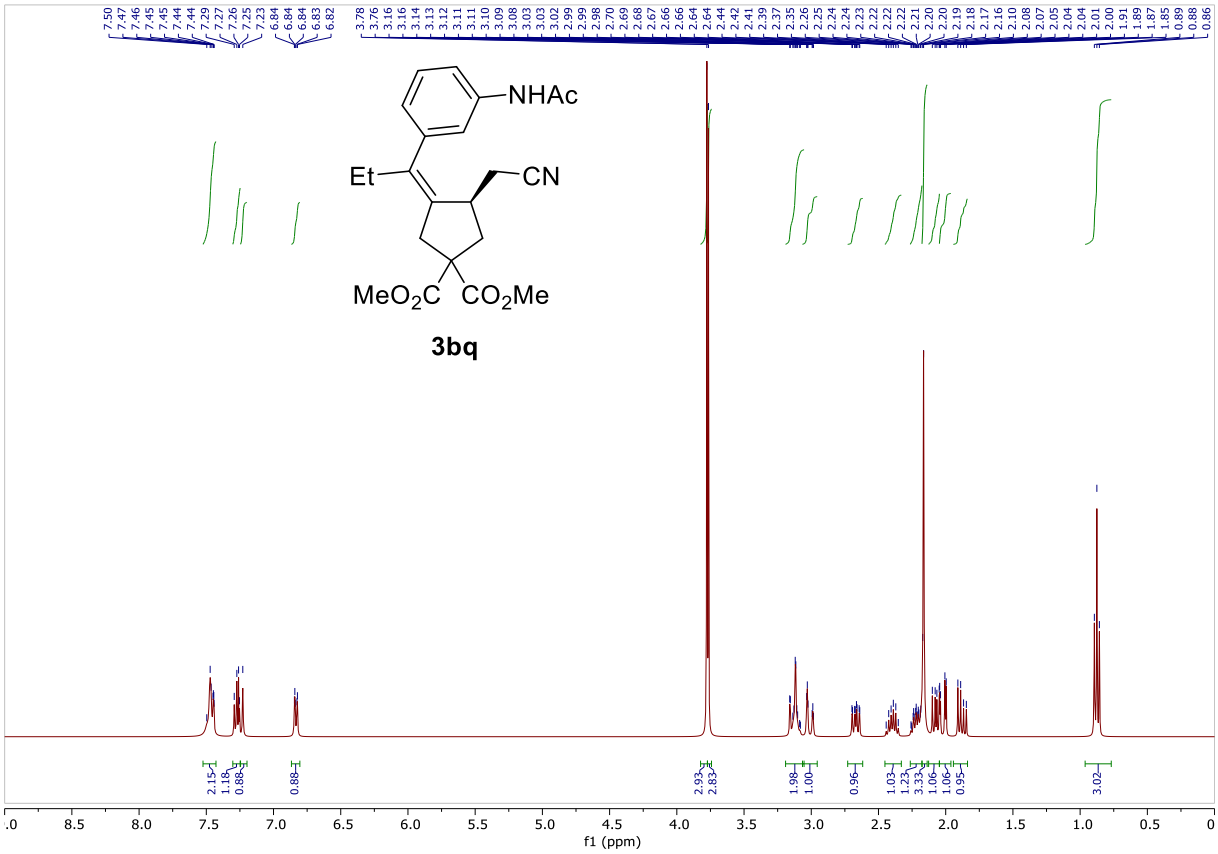
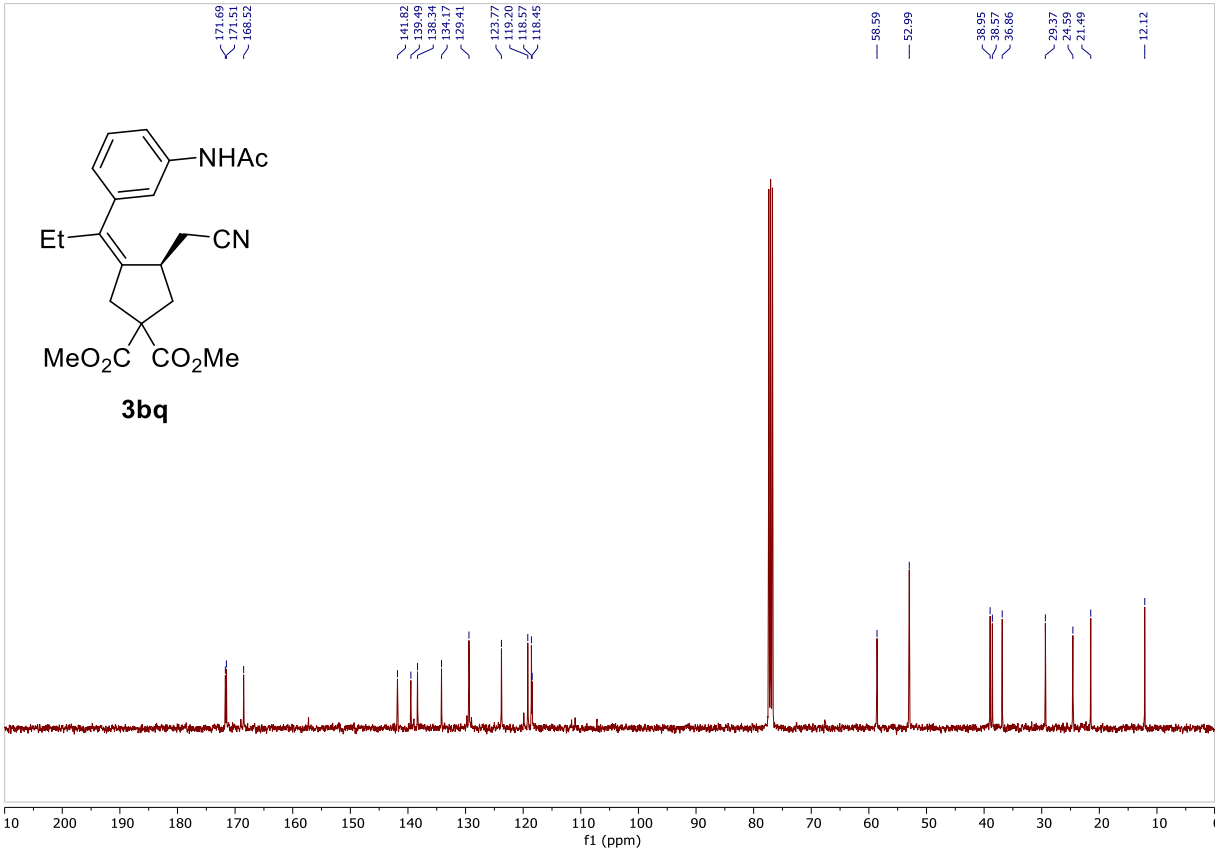
CO2Me
3be
f1 (ppm)


NHAc
Et
CN
MeO2C
CO2Me
3bq
f1 (ppm)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138.34
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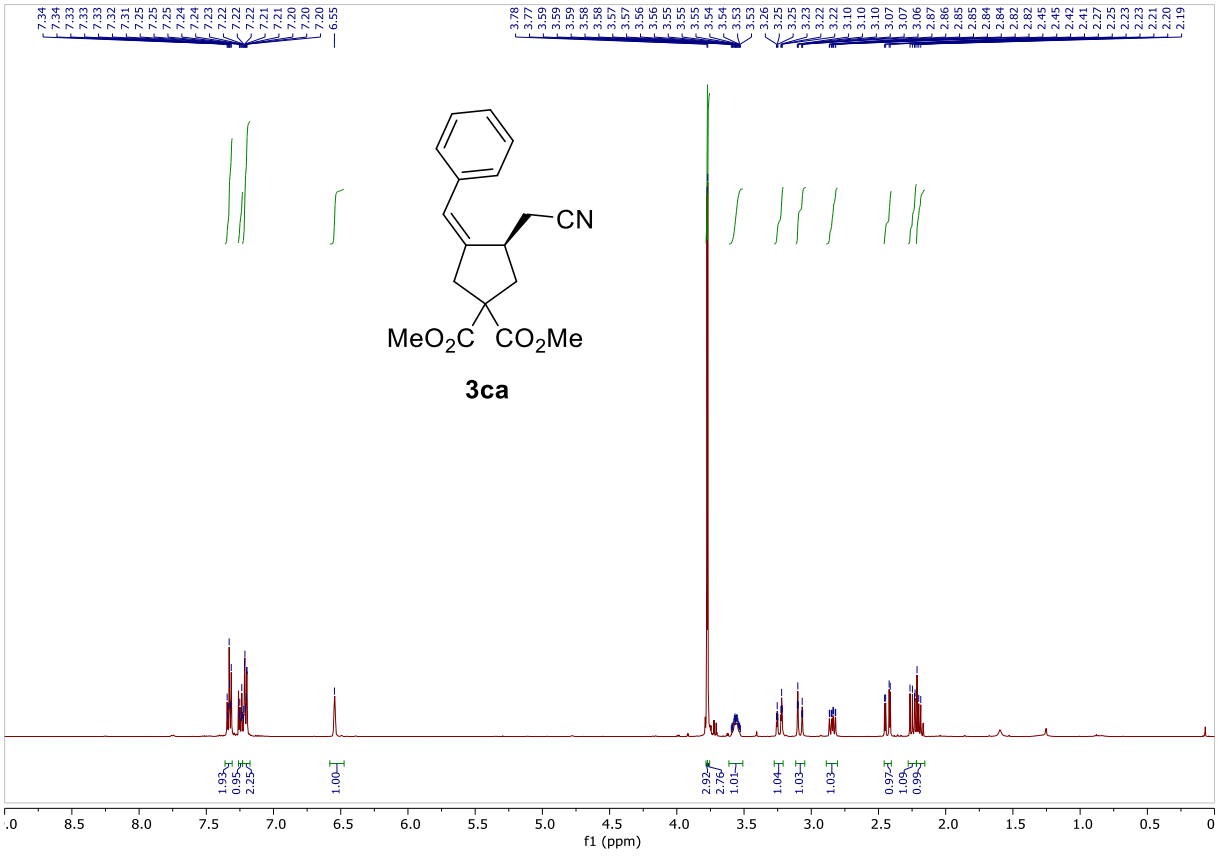
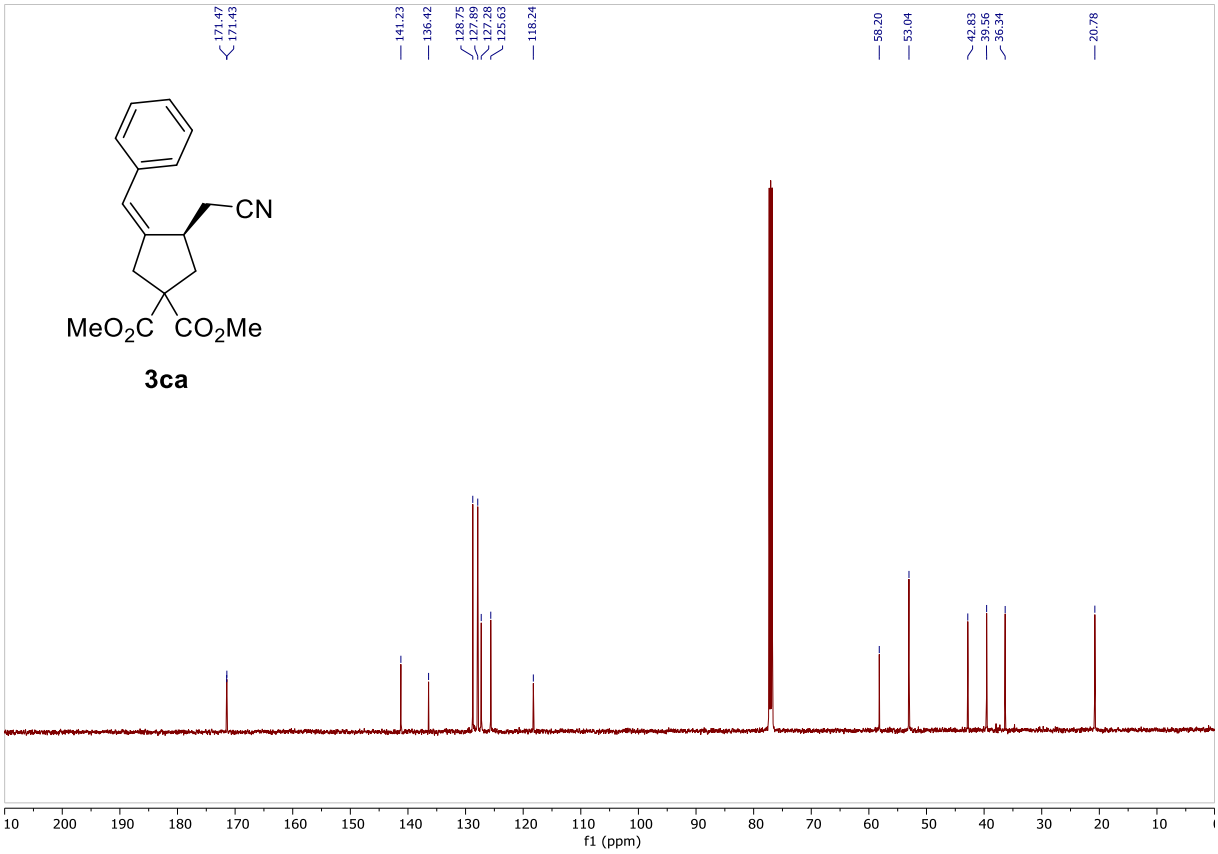
129.41
123.77
119.20
118.57
118.45
58.59
52.99
38.95
38.57
36.86
29.37
24.59
21.49
12.12
NHAc
Et
CN
MeO2C
CO2Me
3bq
f1 (ppm)

.


CN
MeO2C
CO2Me
3ca
f1 (ppm)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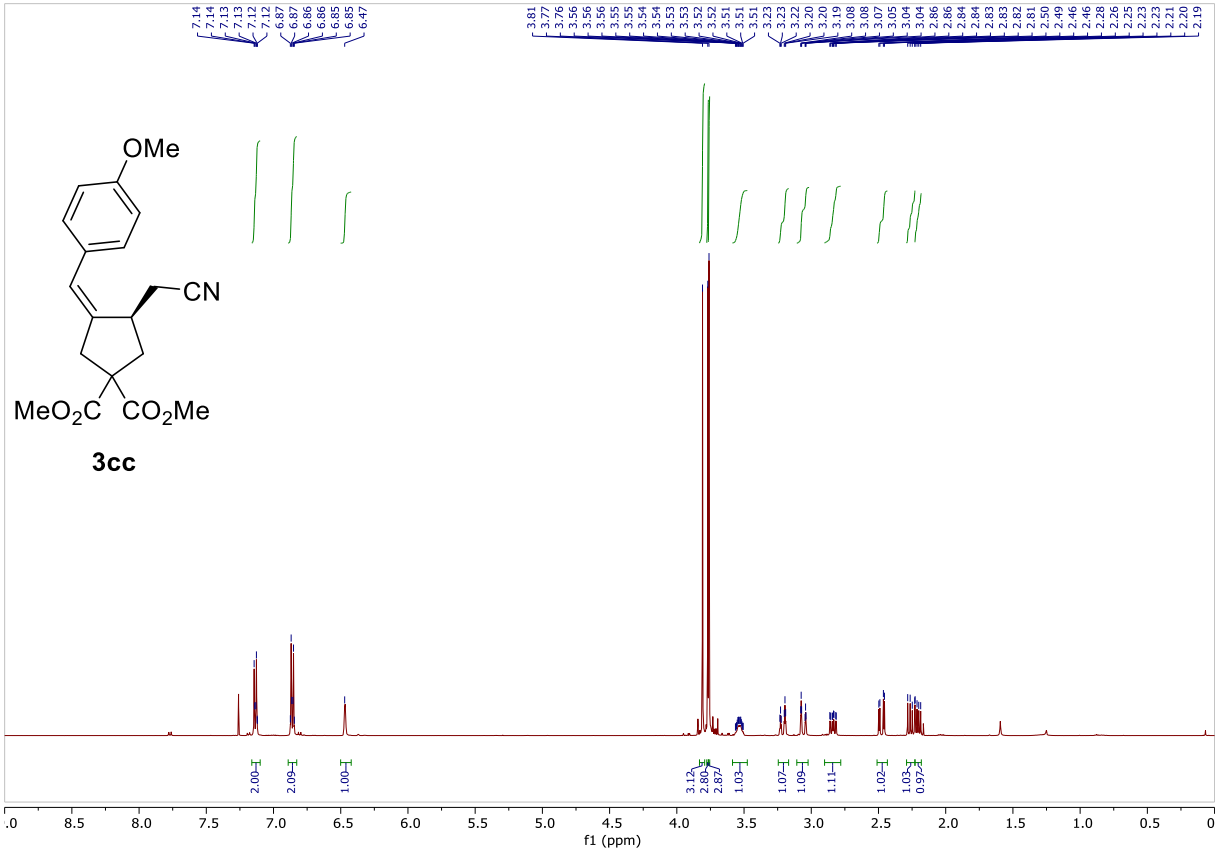
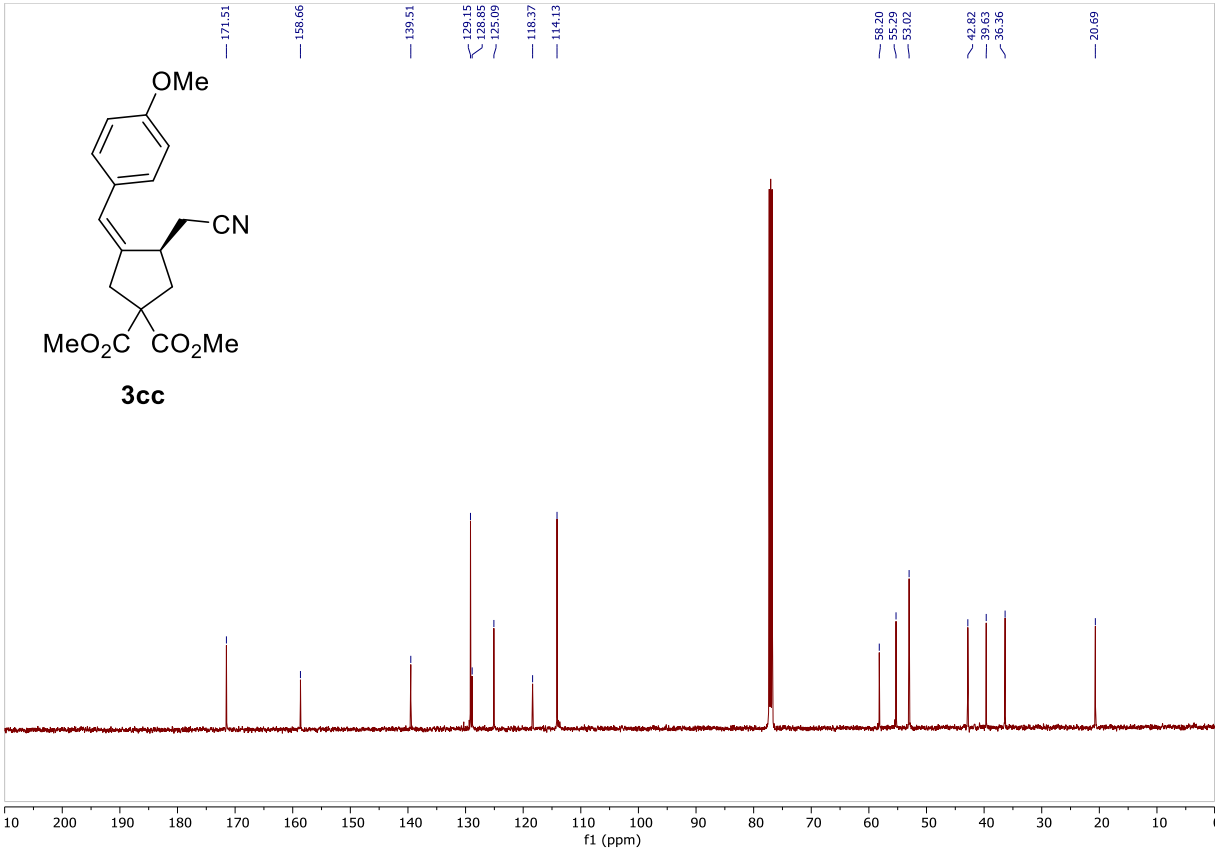
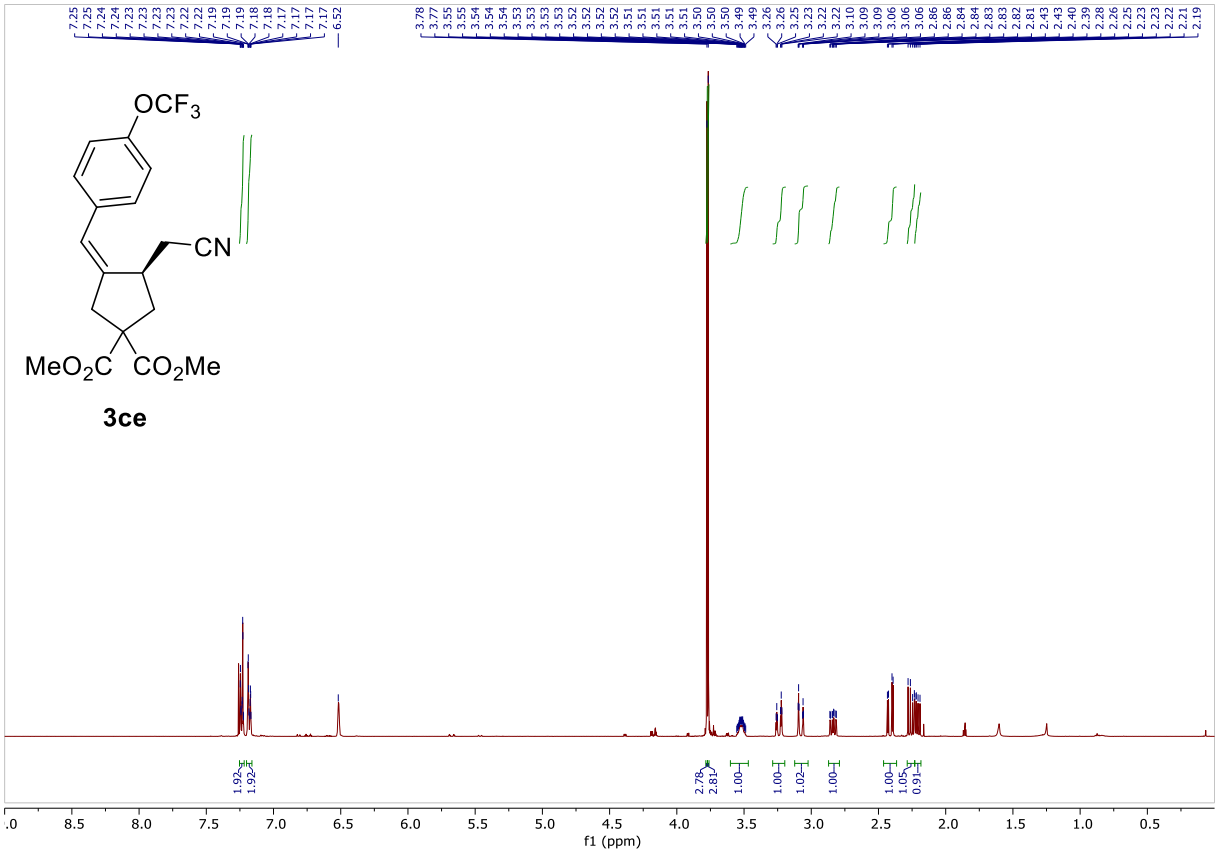
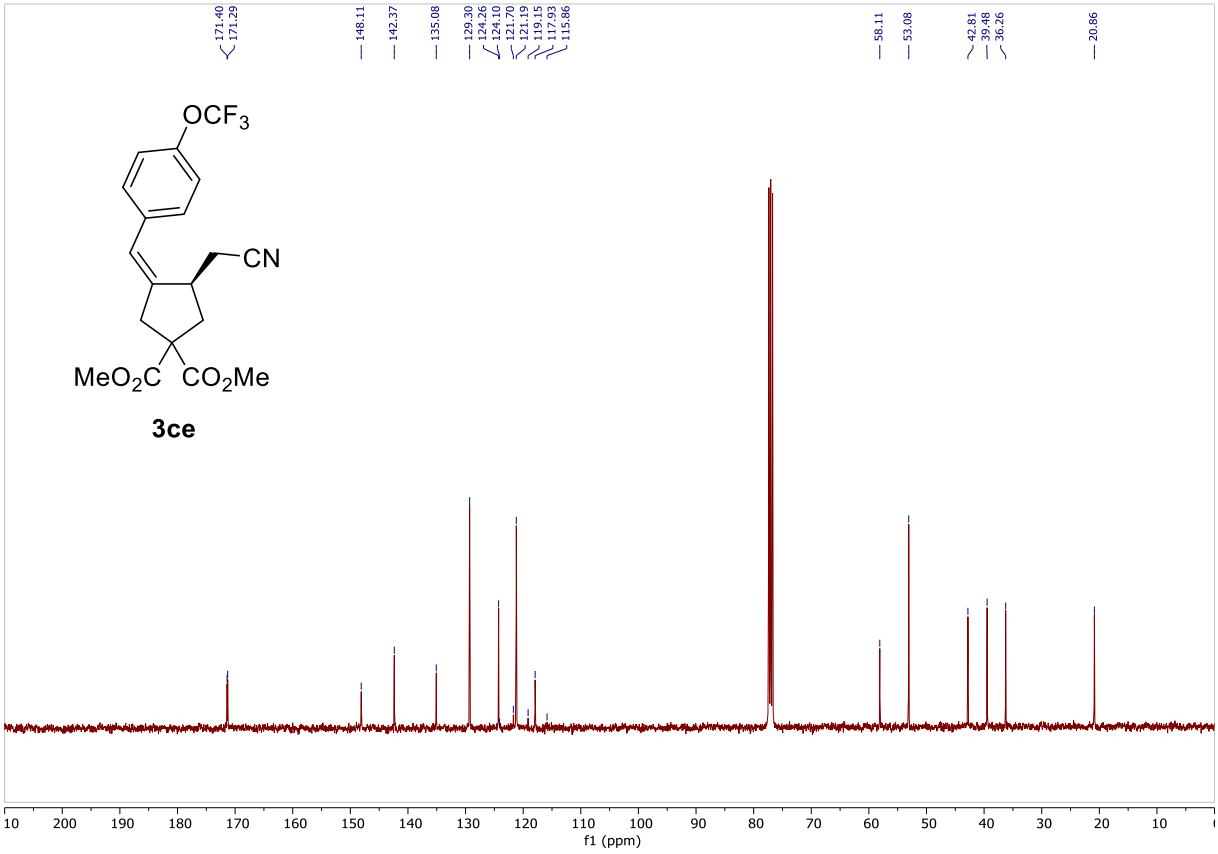
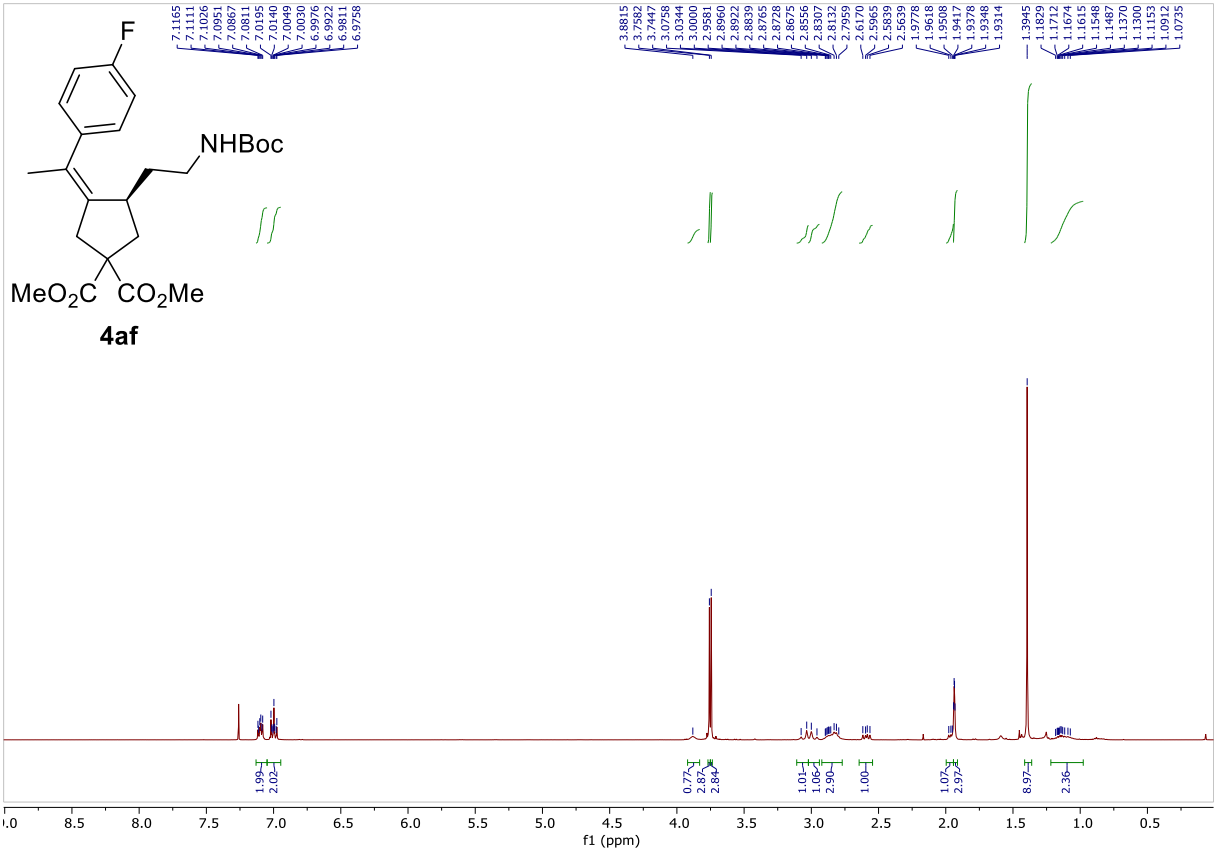
127.89
127.28
125.63
118.24
58.20
53.04
42.83
39.56
36.34
20.78
CN
MeO2C
CO2Me
3ca
f1 (ppm)

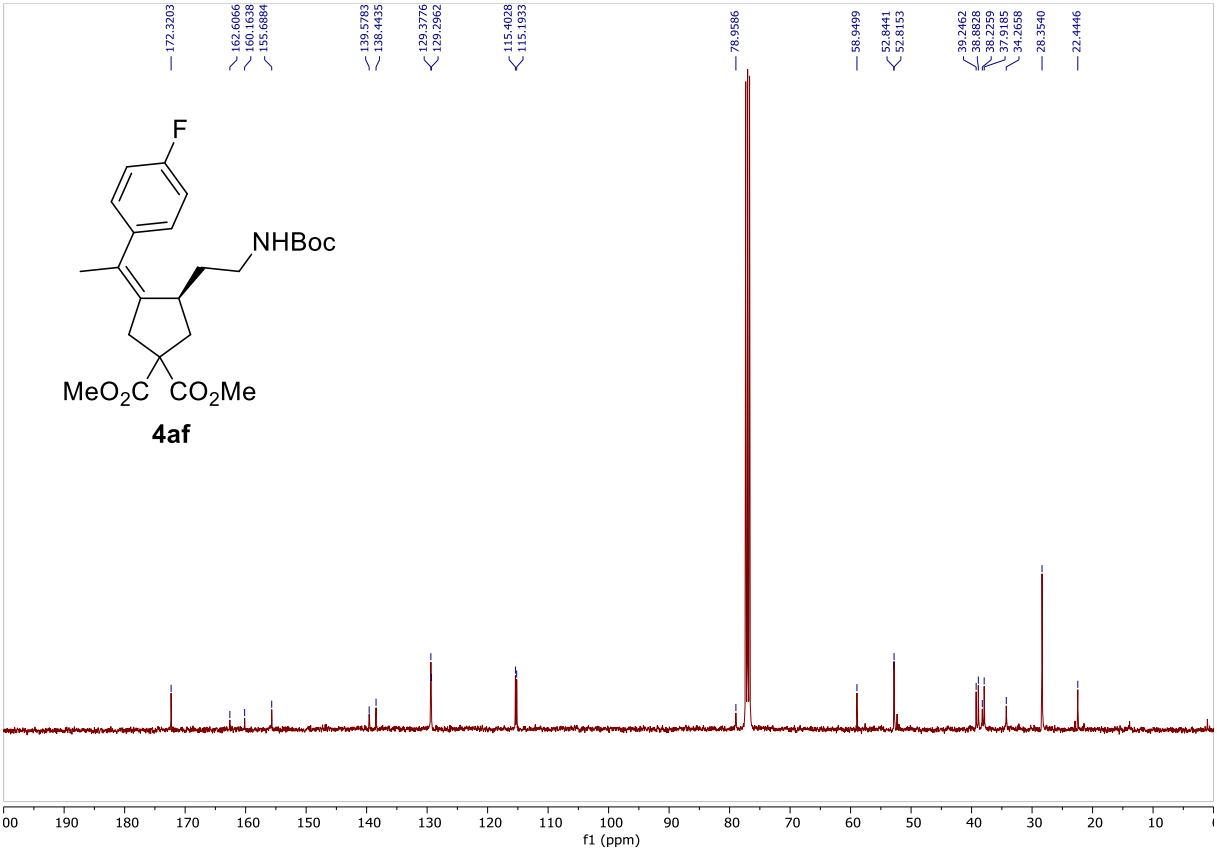

OMe
CN
MeO2C CO2Me
3cc
f1 (ppm)

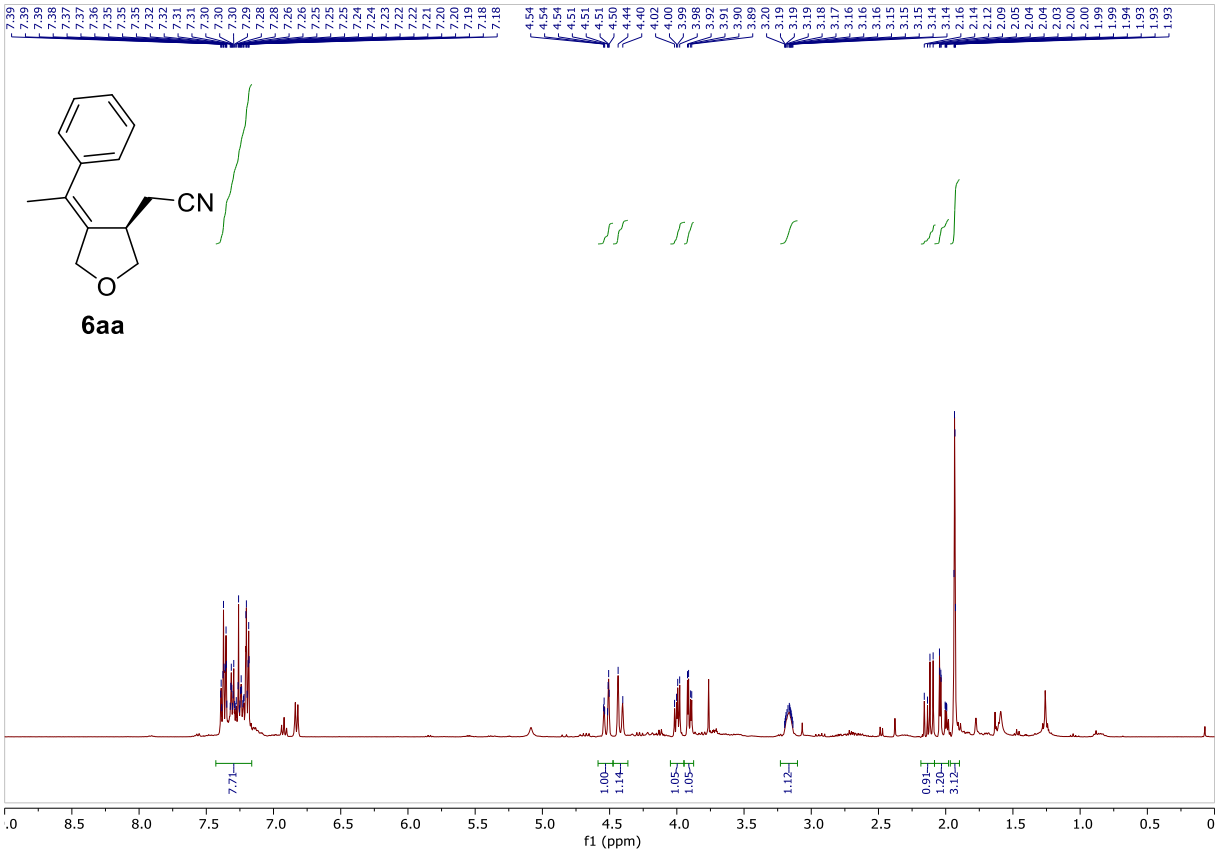

OMe
CN
MeO2C CO2Me
3cc
f1 (ppm)

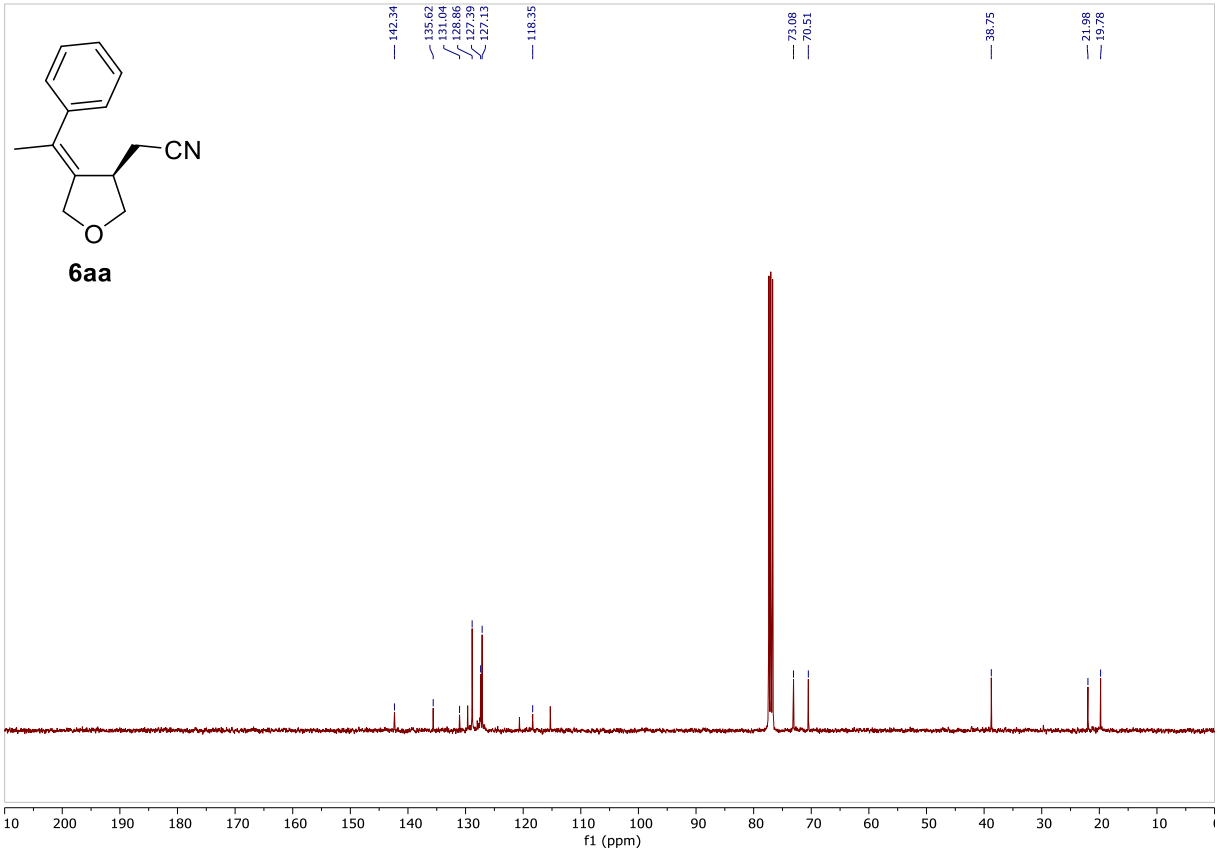

OCF3
CN
MeO2C CO2Me
3ce
f1 (ppm)

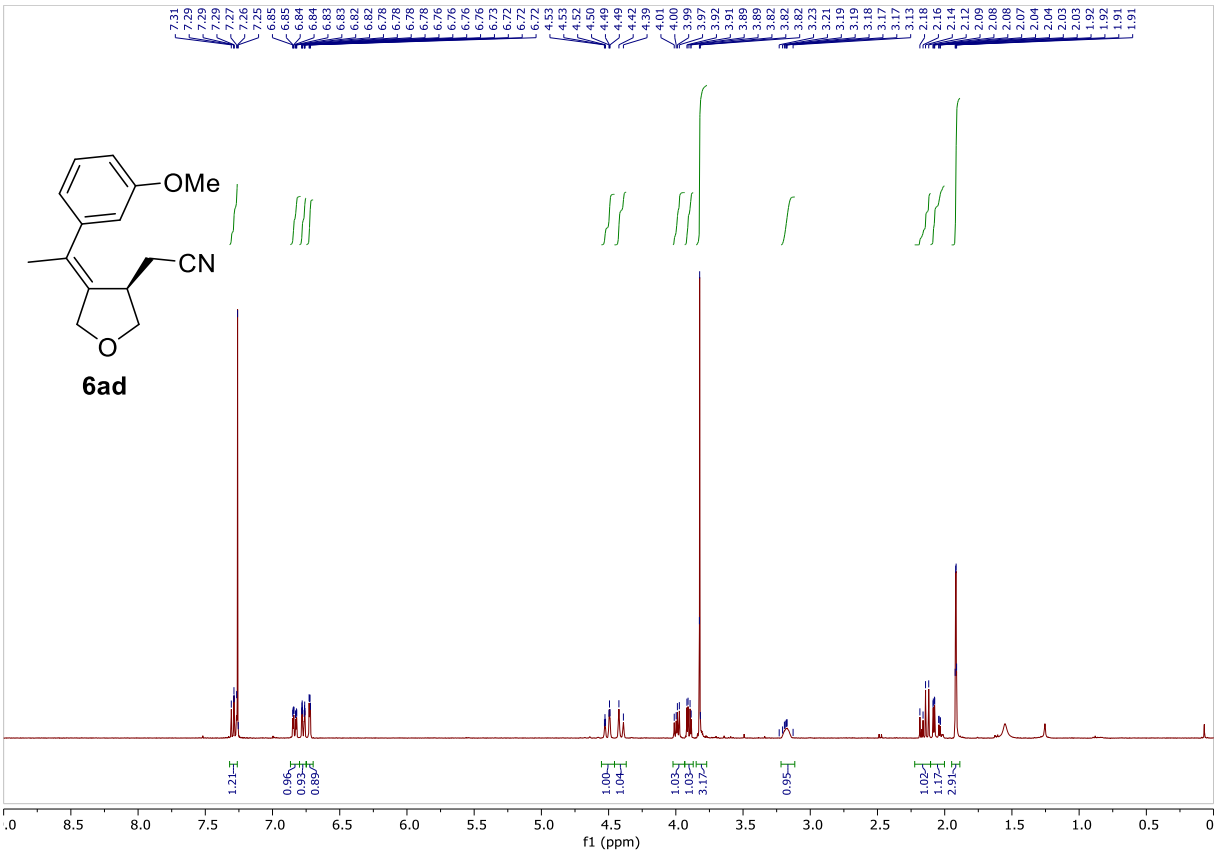

OCF3
CN
MeO2C CO2Me
3ce
f1 (ppm)

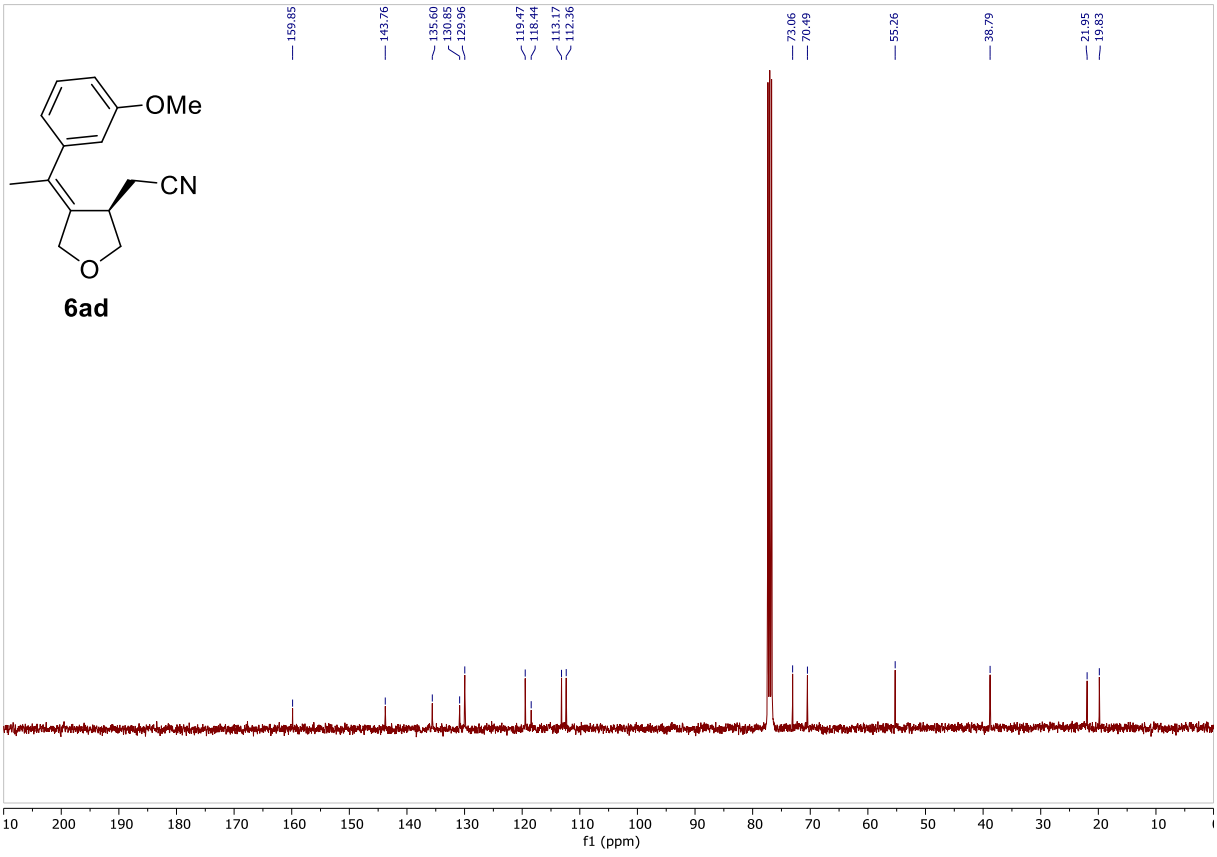

F
NHBoc
MeO2C CO2Me
4af
f1 (ppm)

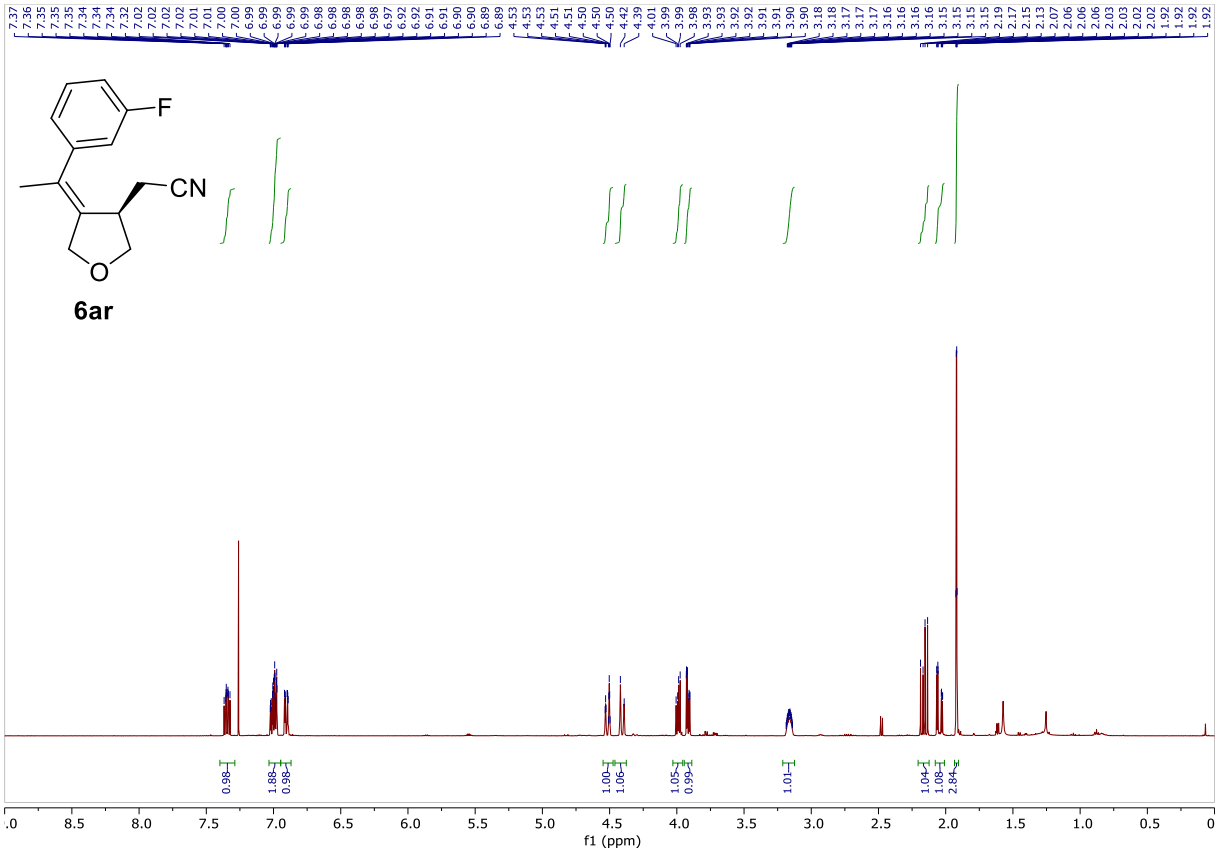

F
NHBoc
MeO2C CO2Me
4af
f1 (ppm)

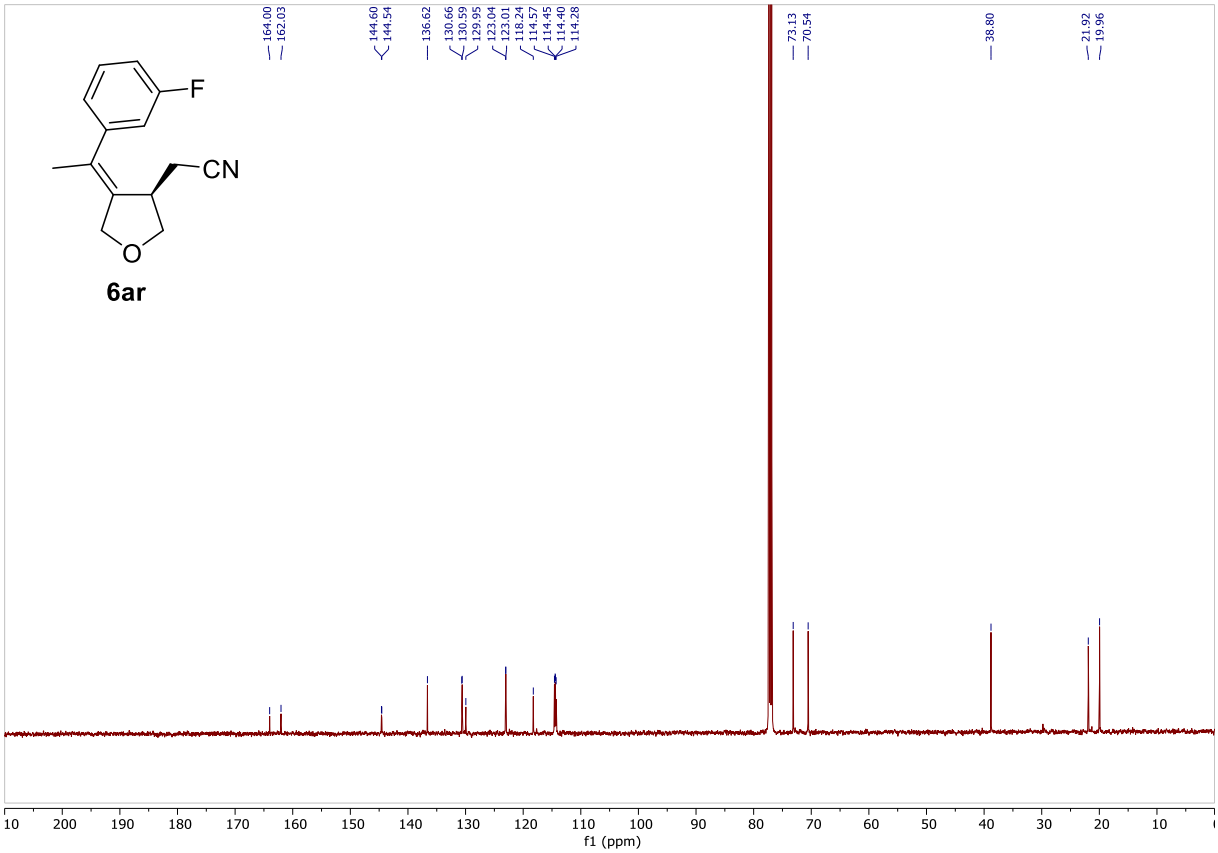

CN
O
6aa
f1 (ppm)


CN
O
6aa
f1 (ppm)


OMe
CN
O
6ad
f1 (ppm)


OMe
CN
O
6ad
f1 (ppm)


F
CN
O
6ar
f1 (ppm)


F
CN
O
6ar
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136.62
130.66
130.59
129.95
123.04
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118.24
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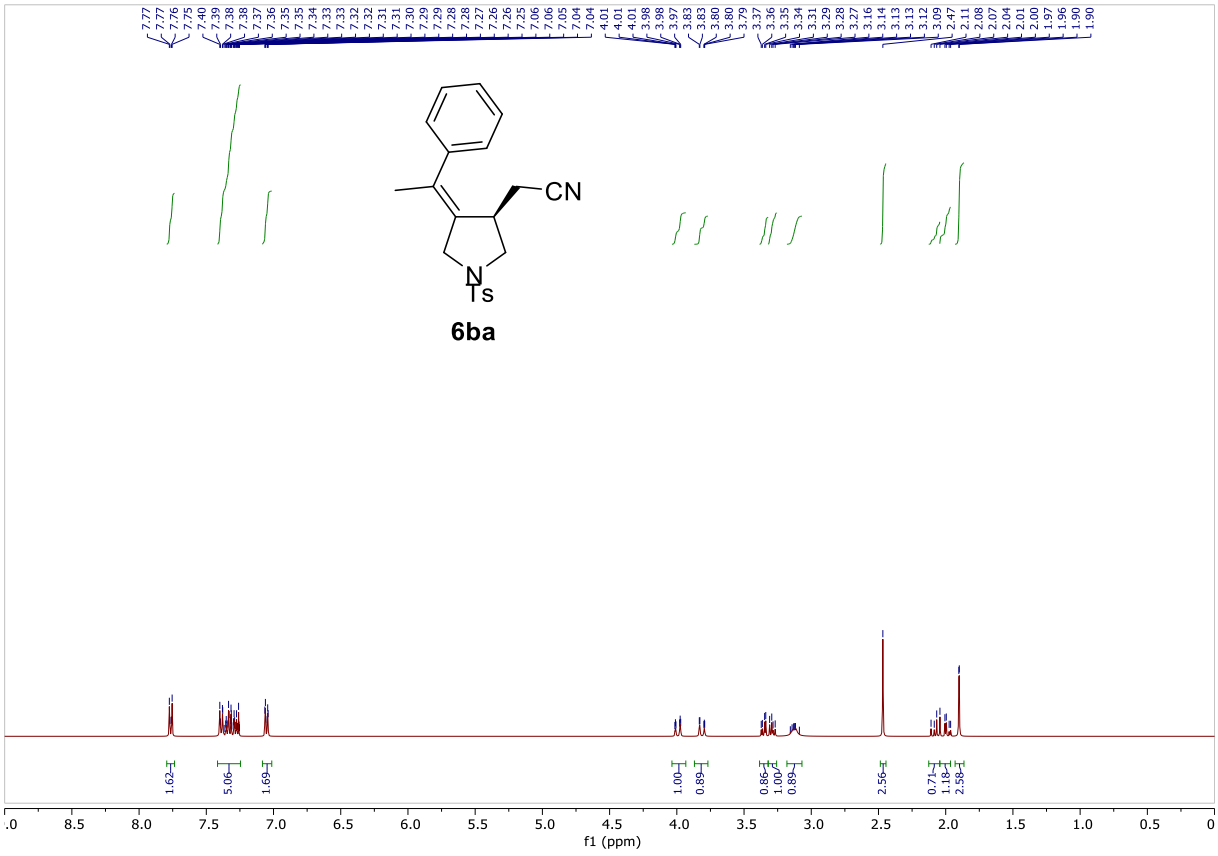
114.45
114.40
114.28
73.13
70.54
38.80
21.92
19.96
f1 (ppm)


CN
N
Ts
6ba
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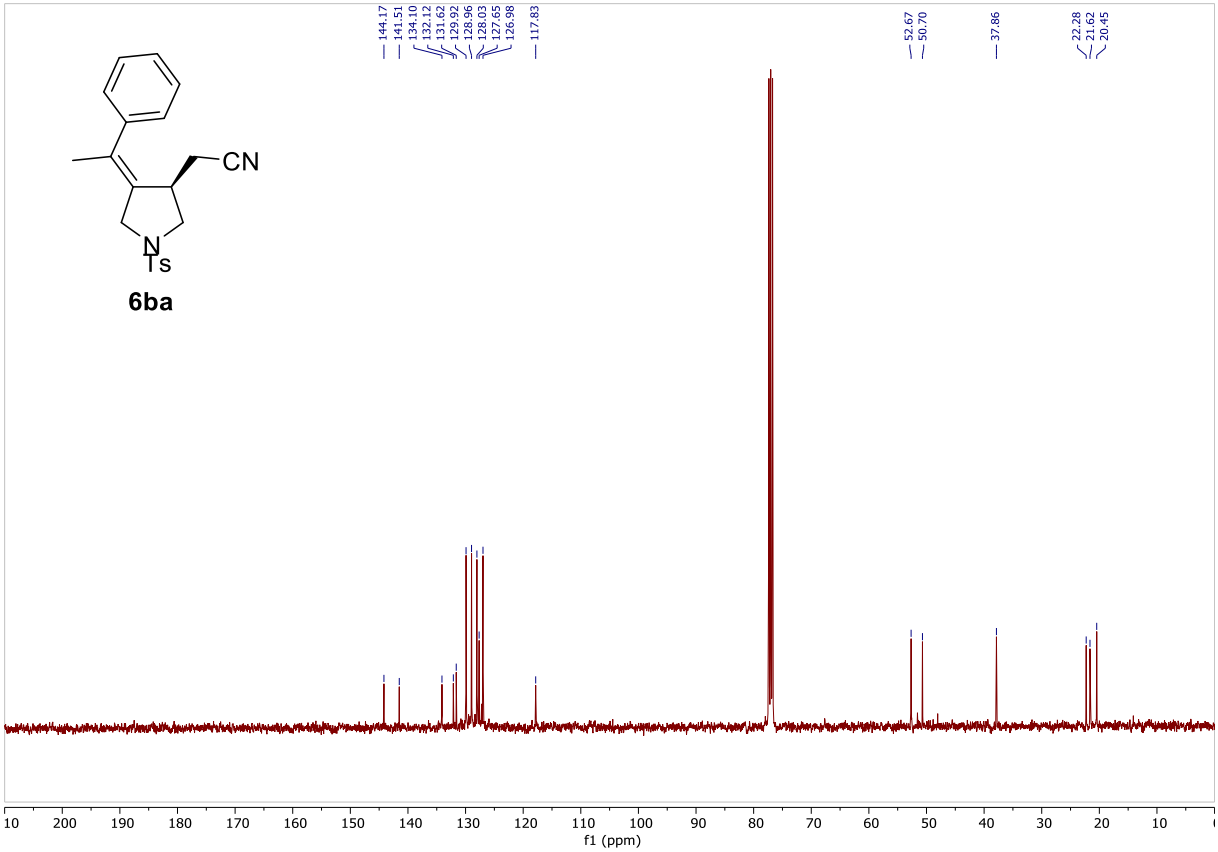
0.86
1.00
0.89
2.56
0.71
1.18
2.58
f1 (ppm)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131.62
129.92
128.96
128.03
127.65
126.98
117.83
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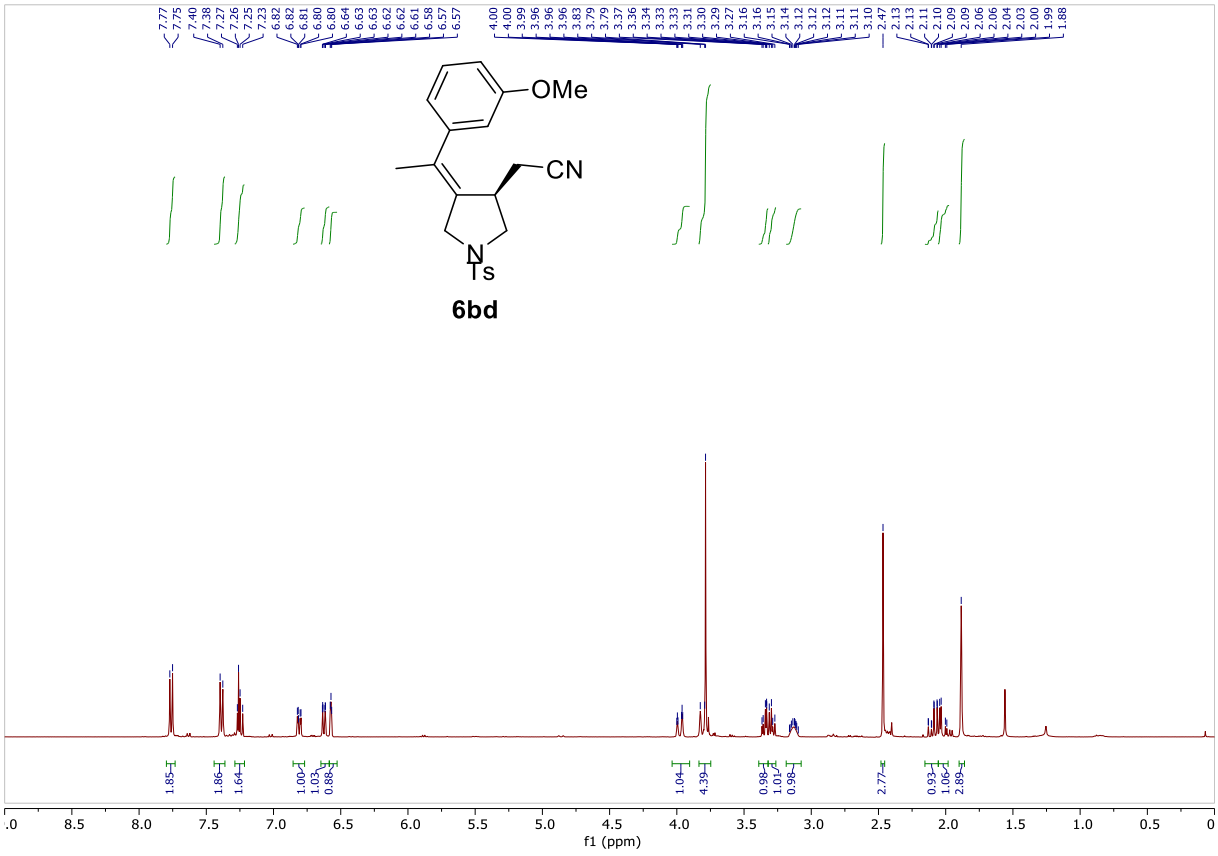
50.70
37.86
22.28
21.62
20.45
CN
N
Ts
6ba
f1 (ppm)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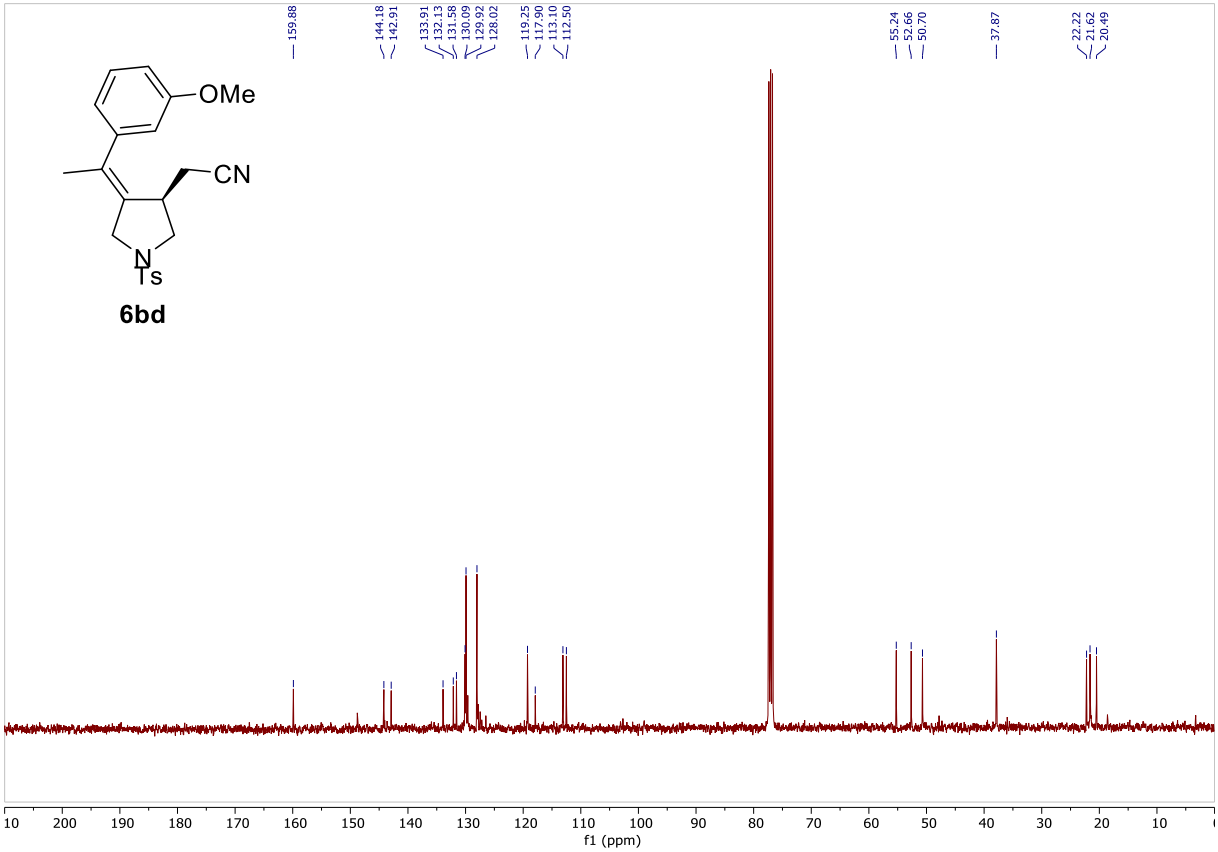
CN
N
Ts
6bd
f1 (ppm)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131.58
130.09
129.92
128.02
119.25
117.90
113.10
112.50
55.24
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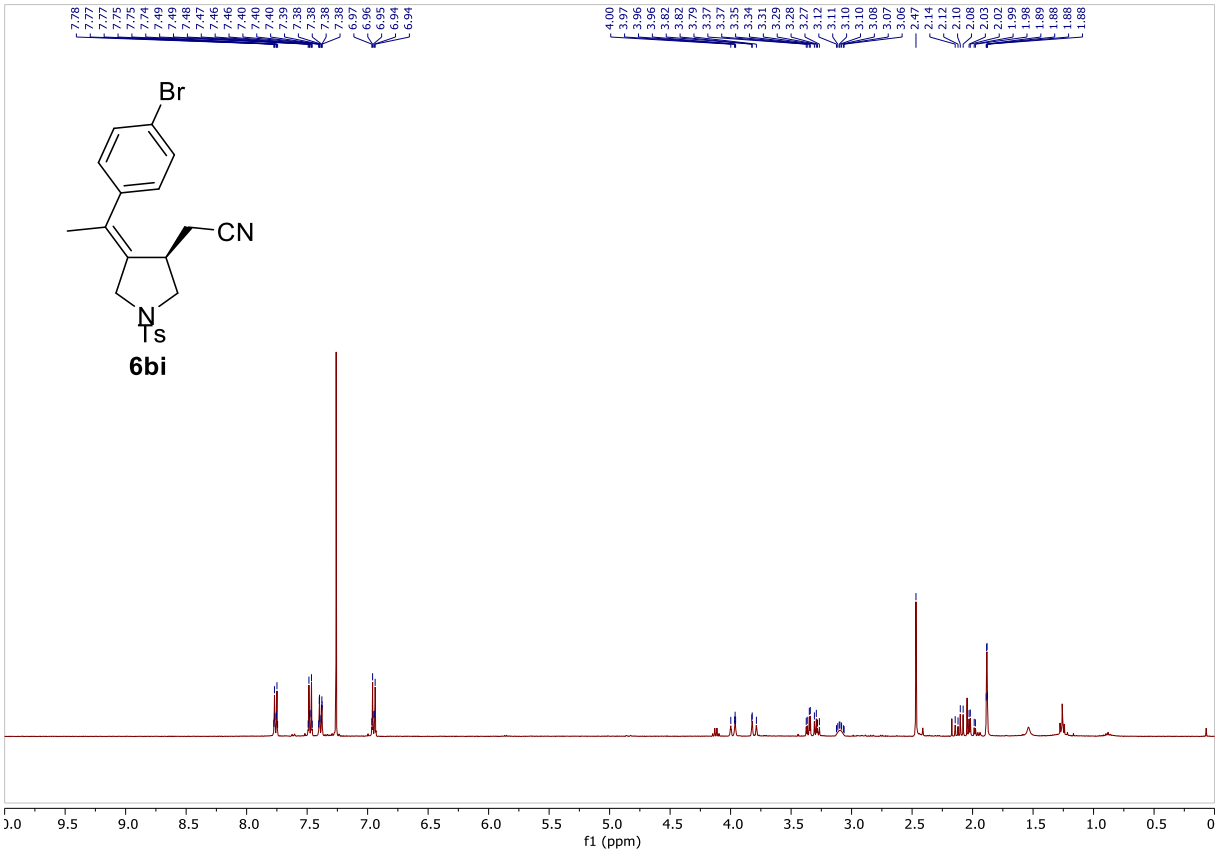
50.70
37.87
22.22
21.62
20.49
OMe
CN
N
Ts
6bd
f1 (ppm)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2.12
2.10
2.08
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1.88
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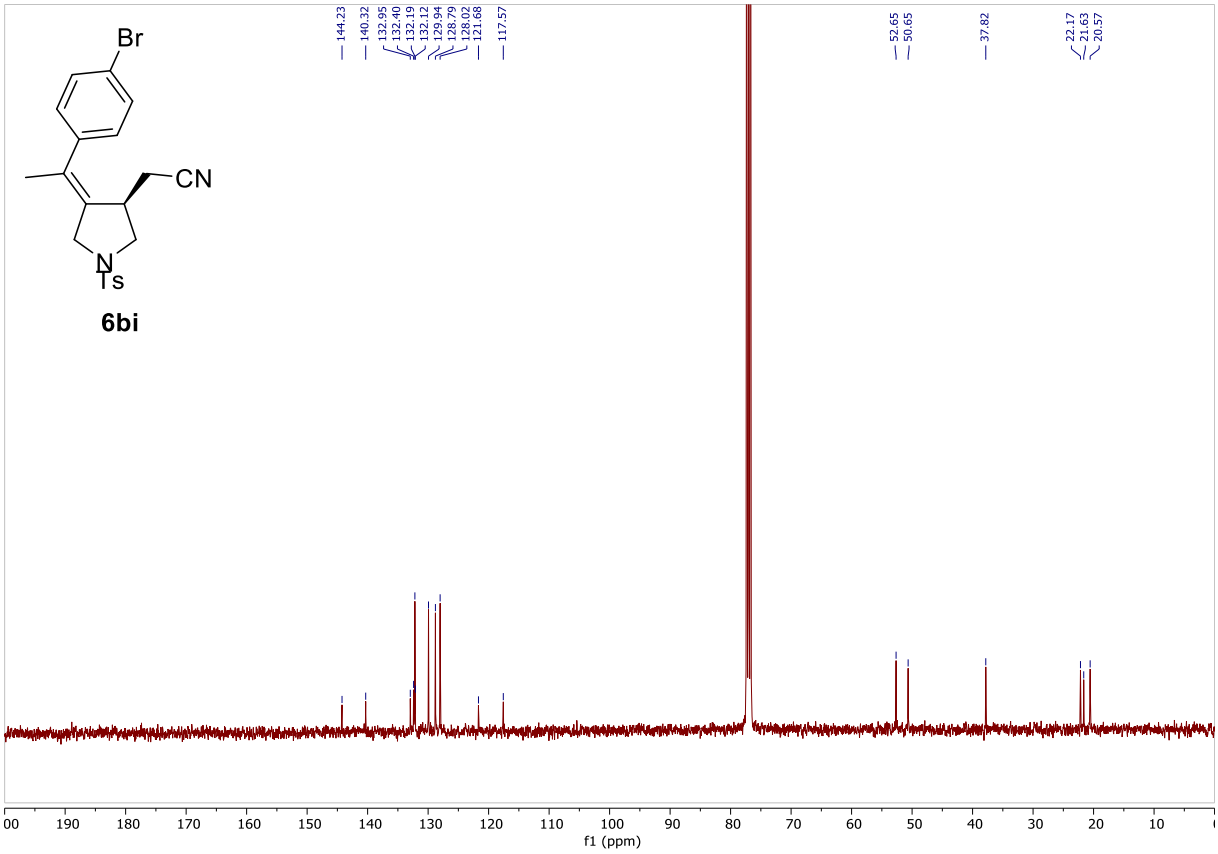
Br
CN
N
Ts
6bi
f1 (ppm)


Br
CN
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Ts
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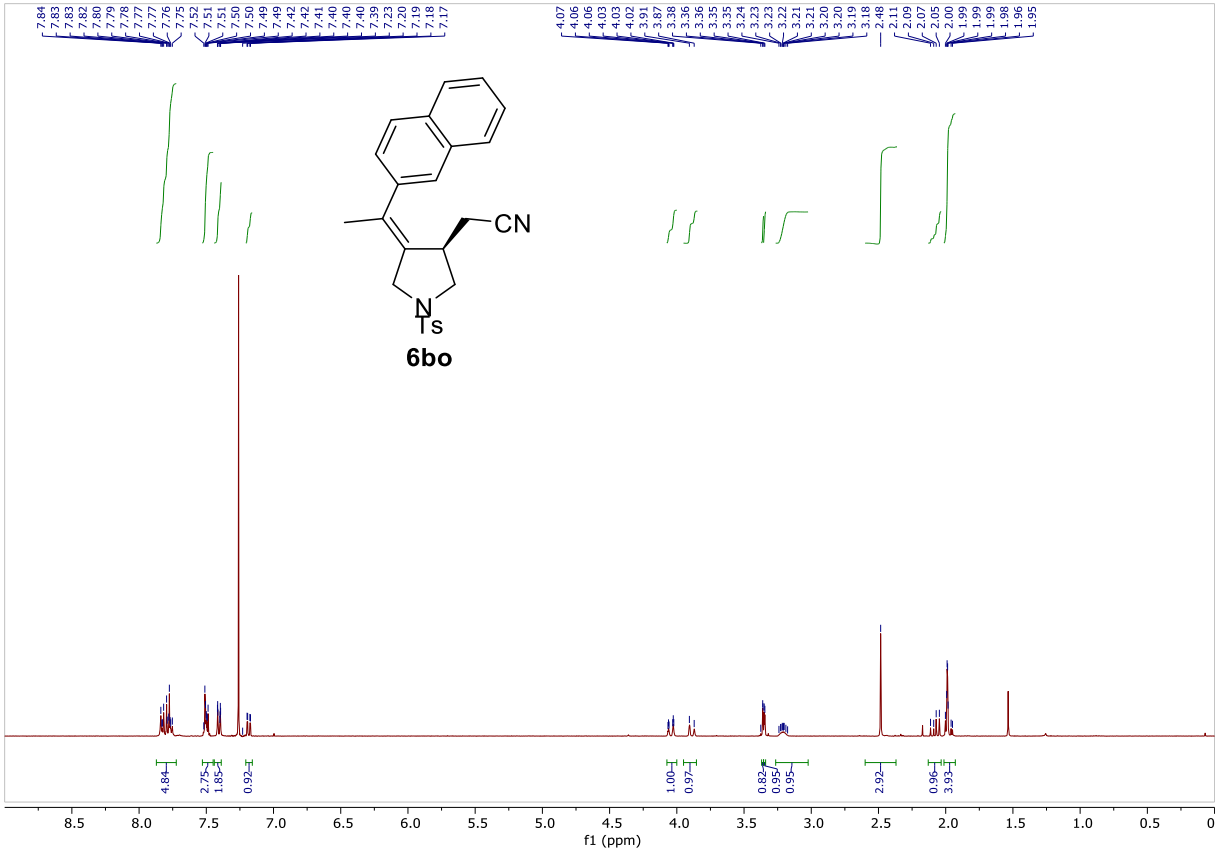
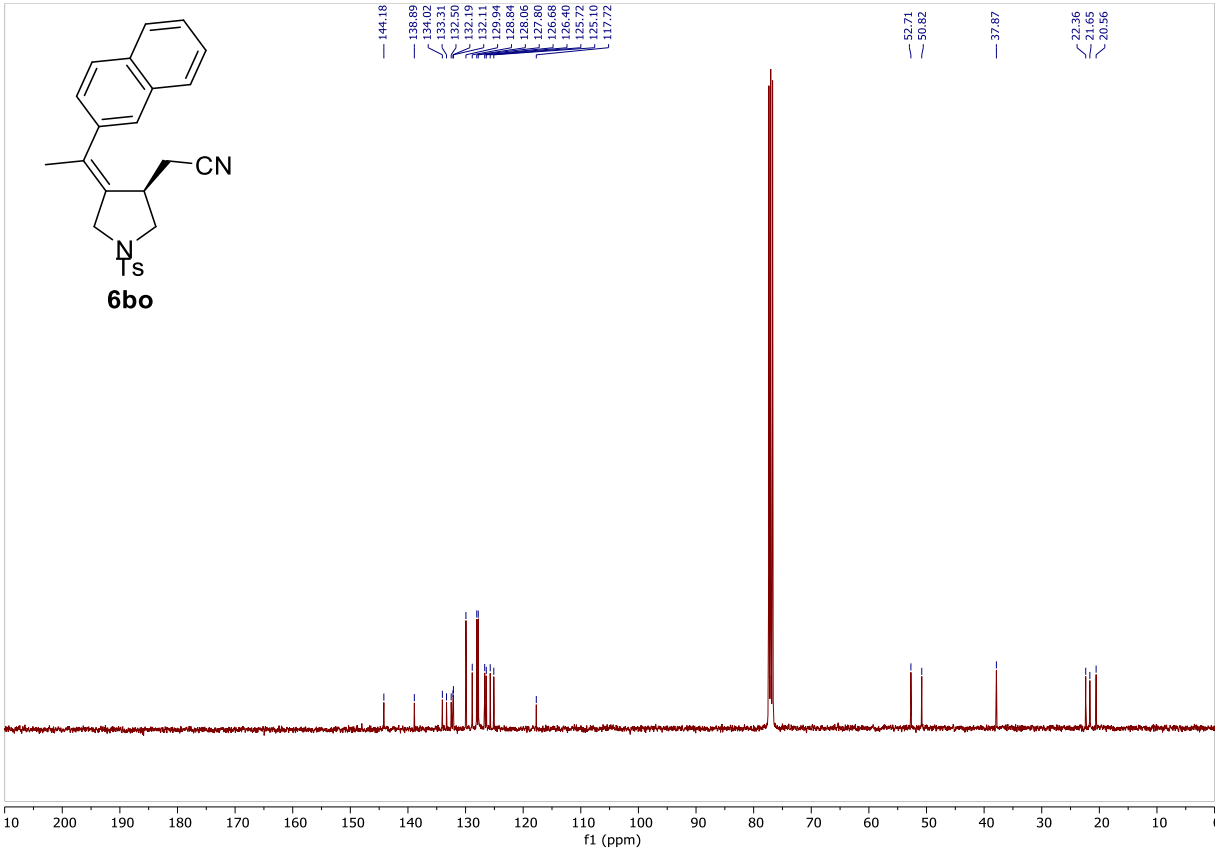
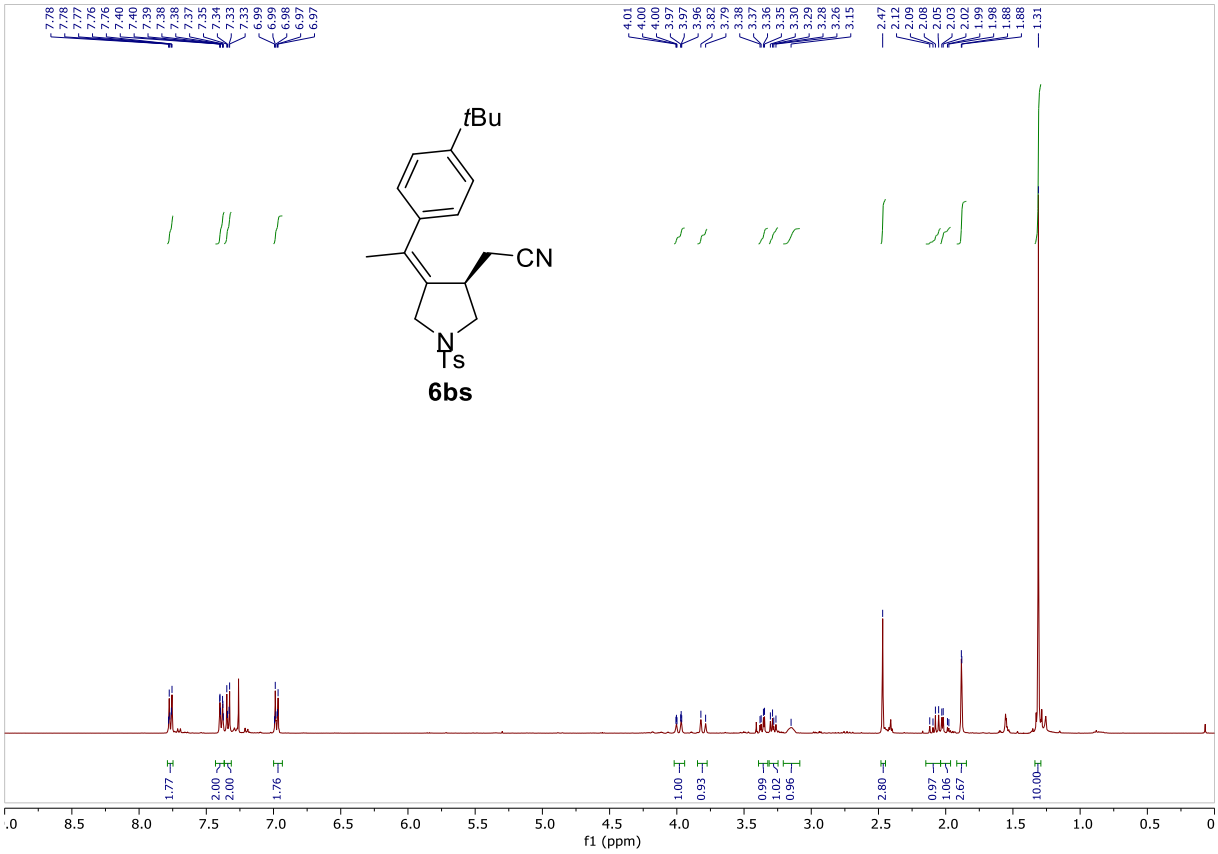
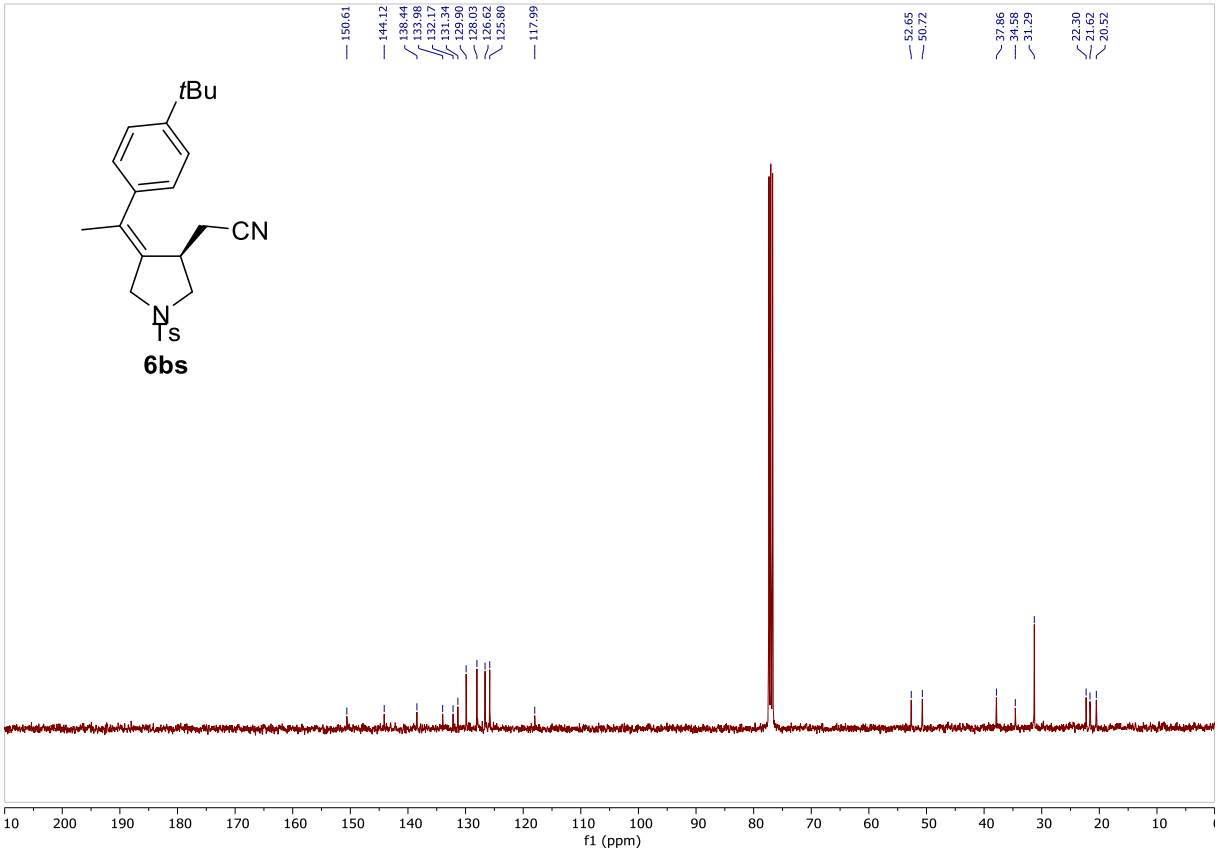
132.95
132.40
132.19
132.12
129.94
128.79
128.02
121.68
117.57
52.65
50.65
37.82
22.17
21.63
20.57
f1 (ppm)


CN
N
Ts
6bo
f1 (ppm)


CN
N
Ts
6bo
f1 (ppm)


tBu
CN
N
Ts
6bs
f1 (ppm)


tBu
CN
N
Ts
6bs
f1 (ppm)