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Aluminium trichloride-promoted tandem hydroarylation–ionic hydrogenation of 3-arylpropynoic acid derivatives and 4-phenylbut-3-yn-2-one

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Contents

1. Instruments and general remarks

The NMR spectra of solutions of compounds in $CDCl_3$ were recorded on Bruker AM-400 (at 400, 376 and 101 MHz for ^1H, ^{19}F and ^{13}C NMR spectra, respectively) spectrometer at 25°C, -75°C or -35°C, respectively. The residual proton-solvent peak $CDCl_3$ (δ_H 7.26 ppm) and CH_2Cl_2 (δ_H 5.32 ppm) for ^1H NMR spectra, the carbon signal of $CDCl_3$ (δ_C 77.0 ppm) and CH_2Cl_2 (δ_C 54.0 ppm) for ^{13}C NMR spectra were used as references. ^{19}F NMR spectra were indirectly referred to the signal of $CFCl_3$ (δ_F 0.0 ppm).

Chromato-mass-spectrometry data were obtained at Shimadzu QP-2010 Ultra with a SPB-1 SULFUR capillary column (30 m × 0.32 mm), thickness of the stationary phase 1.25 μm.

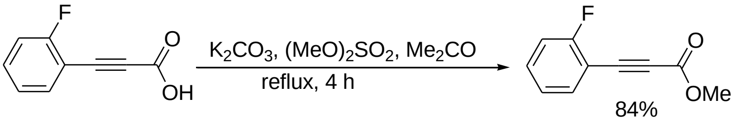
HRMS was carried out at instruments Bruker maXis HRMS-ESI-QTOF.

The reactions were monitored by thin-layer chromatography carried out on silica gel plates (Alugram SIL G/UV-254), using UV light for detection. Column chromatography was performed on silica gel Merck-60 with hexanes – ethyl acetate mixture eluation.

2. Synthesis and properties of starting compounds 1

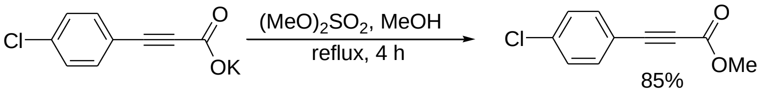
Synthesis and properties of *methyl 3-phenylpropynoate* **1d** were reported previously [S1].

Synthesis of *methyl 3-(2-fluorophenyl)propynoate* **1a** [S2].



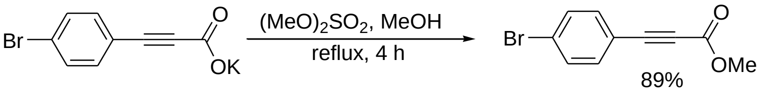
Freshly calcined potassium carbonate (25 mmol, 3.45 g) was added to a solution of 3-(2-fluorophenyl)propynoic acid (10 mmol, 1.64 g) in acetone (15 ml). The suspension was refluxed for 10 min, and dimethyl sulfate (11 mmol, 1.39 g) was introduced dropwise. The mixture was refluxed for 4 h. Volatile components were removed under reduced pressure. The residue was poured into water (100 ml) and extracted with benzene (30 ml). The organic layer was washed with water (2×100 ml) and dried over Na_2SO_4. The volatile components were removed under reduced pressure. Yield of **1a** was 1.5 g (84%). Yellowish oil. ^1H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.58-7.54 (m, 1H), 7.47-7.42 (m, 1H), 7.17 (td, J = 7.6 Hz, 1.4 Hz), 7.12 (t, J = 7.6 Hz, 1H), 3.85 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 165.0, 162.4, 154.1, 134.6, 132.7 (d, $^3J_{(C-F)}$ = 8.2 Hz), 124.3 (d, $^4J_{(C-F)}$ = 3.8 Hz), 115.9 (d, $^1J_{(C-F)}$ = 20.4 Hz), 108.5 (d, $^2J_{(C-F)}$ = 15.3 Hz), 84.9 (d, $^3J_{(C-F)}$ = 3.2 Hz), 79.9, 52.9. ^{19}F NMR (CDCl3, 376 MHz) δ, ppm: -107.25.

Synthesis of *methyl 3-(4-chlorophenyl)propynoate* **1b** [S3, S4].



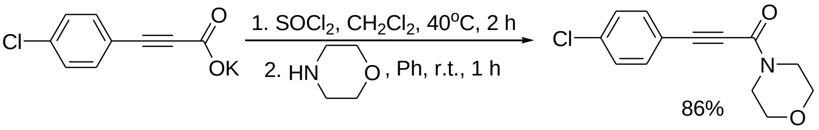
A mixture of potassium salt of 3-(4-chlorophenyl)propynoic acid (3 g, 13.8 mmol), dimethyl sulfate (1.95 ml, 21 mmol) in methanol (30 ml) was refluxed for 4 h in a 100 ml round bottom flask equipped with a reflux condenser with a calcium chloride tube. The reaction mixture was poured into water (300 ml), extracted with ethyl acetate (3×50 ml), washed with water (30 ml), saturated aqueous of solution $NaHCO_3$ (30 ml), again with water (20 ml), the combined extracts were dried with Na_2SO_4. The solvent was removed under reduced pressure. Yield of **1b** was 2.12 g (85%). Colorless solid, m.p. 95-97°C (lit. 93-94 °C [S3]). ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.51 (d, J =7.4 Hz, 2H), 7.36 (d, J = 7.4 Hz, 2H), 3.84 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 154.3, 137.1, 134.2, 129.0, 118.0, 85.2, 81.2, 52.9

Synthesis of *methyl 3-(4-bromophenyl)propynoate* **1c** [S3, S5].



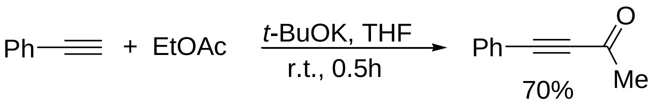
A mixture of potassium salt of 3-(4-bromophenyl)propynoic acid (3 g, 11.4 mmol), dimethyl sulfate (1.62 ml, 17 mmol) in methanol (30 ml) was refluxed for 4 h in a 100 ml round bottom flask equipped with a reflux condenser with a calcium chloride tube. The reaction mass was poured into water (300 ml), extracted with ethyl acetate (3×50 ml), washed with water (30 ml), saturated aqueous of solution $NaHCO_3$ (30 ml), again with water (20 ml), the combined extracts were dried with Na_2SO_4. The solvent was removed under reduced pressure. Yield of **1c** was 2.44 g (89%). Colorless solid, m.p. 104-106°C (lit. 105°C [S4]). ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.45 (d, *J* =7.4 Hz, 2H), 7.36 (d, *J* = 7.4 Hz, 2H), 3.78 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 154.1, 134.2, 132.0, 125.5, 118.4, 85.1, 81.3, 52.9.

Synthesis of *3-(4-chlorophenyl)-1-(morfolin-4-yl)prop-2-yn-2-one* **1e** [S6].



Potassium salt of 3-(4-chlorophenyl)propynoic acid (1 g, 4.6 mmol,) was added to a stirred mixture of thionyl chloride (3.76 g, 31mmol) in dichloromethane (6 ml). The mixture was stirred at 40 °C for 2 h. The volatile components were removed under reduced pressure. The residue was dissolved in benzene (8 ml). The resulting solution was cooled to 10°C, and a solution of morpholine cooled to 10°C (0.996 g, 11.4 mmol,) in benzene (8 ml) was added dropwise. The reaction mixture was stirred at room temperature for 1 h, then it was poured into water (80 ml). The organic layer was washed with aqueous solution of 3% H_3PO_4 (2×50 ml), aqueous 5% $NaHCO_3$ (30 ml), water (20 ml) and dried with Na_2SO_4. The volatile components were removed under reduced pressure. Yield of **1e** was 0.98 g (86%). Pale-yellow solid, m.p. 114-116°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.47 (d, *J* =8.5 Hz, 2H), 7.35 (d, *J* = 8.5 Hz, 2H), 3.81 (m, 2H), 3.75 (m, 2H), 3.70 (s, 4H) ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 153.0, 136.5, 133.6, 129.0, 118.8, 81.6, 66.5, 47.3, 42.0.

Synthesis of *4-phenylbut-3-yn-2one* **1f** [S7].



A mixture of phenylacetylene (7.36 g, 72 mmol) and potassium *tert*-butoxide (8.52 g, 72 mmol) was prepared in absolute THF (50 ml) under the argon atmosphere. Then ethyl acetate (7.04 ml, 72 mmol) was added, and the resulting mixture was stirred at room temperature for 30 min under the argon atmosphere. Then the mixture was poured into water (25 ml) and extracted with ethyl acetate (3×30 ml), the combined extracts were washed with water and dried with Na_2SO_4. The solvent was removed in vacuum, the product was isolated by column chromatography on silica gel (eluent – petroleum ether – ethyl acetate, 95:5, vol). Yield of **1f** was 7 g (70%). Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: δ 2.45 (s, 3H), 7.41 – 7.35 (m, 2H), 7.48 – 7.43 (m, 1H),7.59 – 7.55 (m, 2H).

3. Synthesis and properties of compounds 2

General procedure for the synthesis of compounds 2 by $AlCl_3$-promoted one-pot tandem hydroarylation-ionic hydrogenation of compounds 1. Compound **1** (0.3 mmol) was added to a stirred mixture of $AlCl_3$ (200 mg, 1.5 mmol), arene (2 ml), and cyclohexane (0.31 ml, 3 mmol). The mixture was stirred at room temperature for 15 h, then poured into iced water (150 ml), and extracted with CH_2Cl_2 (2×50 ml). The combined organic layers were washed with water (3×30 ml) and dried over Na_2SO_4. The solvents were removed under reduced pressure. The crude material was purified by column chromatography on silica gel using hexanes – ethyl acetate mixtures as eluents to obtain target compounds **2**.

Syntheses and properties of *methyl 3,3-diphenylpropanoate* **2d** and *3,3-diphenyl-1-(morfolin-4-yl)propan-1-one* **2h** were described previously [S1].

Methyl 3-(2-fluorophenyl)-3-phenylpropanoate **2a** [S8]. Yield 51%. ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.31 – 6.98 (m, 9H), 4.85 (t, *J* = 8.0 Hz, 1H), 3.59 (s, 3H), 3.09 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 172.0, 160.6 (d, *J* = 246.4 Hz), 142.2, 130.4 (d, *J* = 14.2 Hz), 128.6, 128.3 (d, *J* = 8.4 Hz), 128.0, 127.6, 126.7, 124.2 (d, *J* = 3.6 Hz), 115.7, 51.7, 40.4, 39.4. MS (GC-MS, EI), m/z: 258 $[M]^+$.

Methyl 3-(4-chlorophenyl)-3-phenylpropanoate **2b** [S9] was obtained in yield of 20% as the oily mixture with compound **2d** (yield of 23%). ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm (selected signals from the spectrum of mixture with **2d**): 4.54 (t, *J* = 8.0 Hz, 1H), 3.593 (s, 3H), 3.04 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm (from the spectrum of mixture with **2d**): 172.0, 143.0, 142.0, 132.4, 129.0, 128.7, 127.5, 126.8, 51.7, 46.4, 40.4. MS (GC-MS, EI), m/z: 274 $[M]^+$.

Methyl 3-(4-bromophenyl)-3-phenylpropanoate **2c** [S10] was obtained in yield of 47% as the oily mixture with compound **2d** (yield of 32%). ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm (selected signals from the spectrum of mixture with **2d**): 7.40 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 4.52 (t, *J* = 8.0 Hz, 1H), 3.59 (s, 3H), 3.04 (d, *J* = 8.0 Hz, 2H) ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm (from the spectrum of mixture with **2d**): 172.0, 142.9, 142.5, 131.7, 129.4, 128.7, 127.5, 126.8, 120.5, 51.8, 46.4, 40.4. MS (GC-MS, EI), m/z: 318 $[M]^+$.

Methyl 3,3-bis(4-methylphenyl)propanoate **2e** [S11] and *methyl 3-(2-methylphenyl)-3-(4-methylphenyl)propanoate* **2f** were obtained as the oily mixture in the equal yields of 21% each. ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm (for mixture of isomers): 7.20 – 7.00 (m, 16H), 4.50 (t, *J* = 8.0 Hz, 2H), 3.59 (s, 6H), 3.06 (d, *J* = 8.0, 2H), 3.04 (d, *J* = 8.0, 2H), 2.32 (s, 6H), 2.31 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm (for mixture of isomers): 172.39, 172.37, 143.7, 143.6, 140.8, 140.7, 138.1, 136.00, 135.97, 129.3, 128.52, 128.47, 128.42, 127.50, 127.45, 127.30, 127.26, 124.54, 124.50, 51.6, 46.9, 46.6, 40.66, 40.61, 21.5, 21.0 MS (GC-MS, EI), m/z (for mixture of isomers): 268 $[M]^+$. HRMS (EI+) (for mixture of isomers): m/z calcd for $C_{18}H_{21}O_2$ $[M]^+$ 269.1536; found: 269.1538.

3-(4-Chlorophenyl)-1-(morpholin-4-yl)-3-phenylpropan-1-one **2g** [S12] was obtained in yield of 30% as the oily mixture with compound **2h** (yield of 16%). ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm (selected signals from the spectrum of mixture with **2h**): 4.65 (t, *J* = 7.5 Hz, 1H), 3.01 (d, *J* = 7.5 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm (from the spectrum of mixture with **2h**): 169.6, 143.5, 142.5, 132.3, 129.2, 128.68, 128.65, 127.8, 126.8, 66.80, 66.4, 46.68, 46.16, 42.07, 38.52. MS (GC-MS, EI), m/z: 329 $[M]^+$.

4,4-Diphenylbutan-2-one **2i** [S13] was obtained in yield of 98%. Yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ, ppm: 7.30-7.16 (m, 10H, 2Ph), 4.60 (t, *J* = 7.6 Hz, 1H, CH), 3.19 (d, *J* = 7.6 Hz, 2H, CH_2), 2.08 (s, 3H, Me) ^{13}C NMR (100 MHz, $CDCl_3$) δ, ppm: 206.9, 143.9, 128.6, 127.7, 126.5, 49.7, 46.1, 30.6. GC-MS (EI), m/z: 224 $[M]^+$.

4. Figures of ^{1}H and ^{13}C NMR spectra

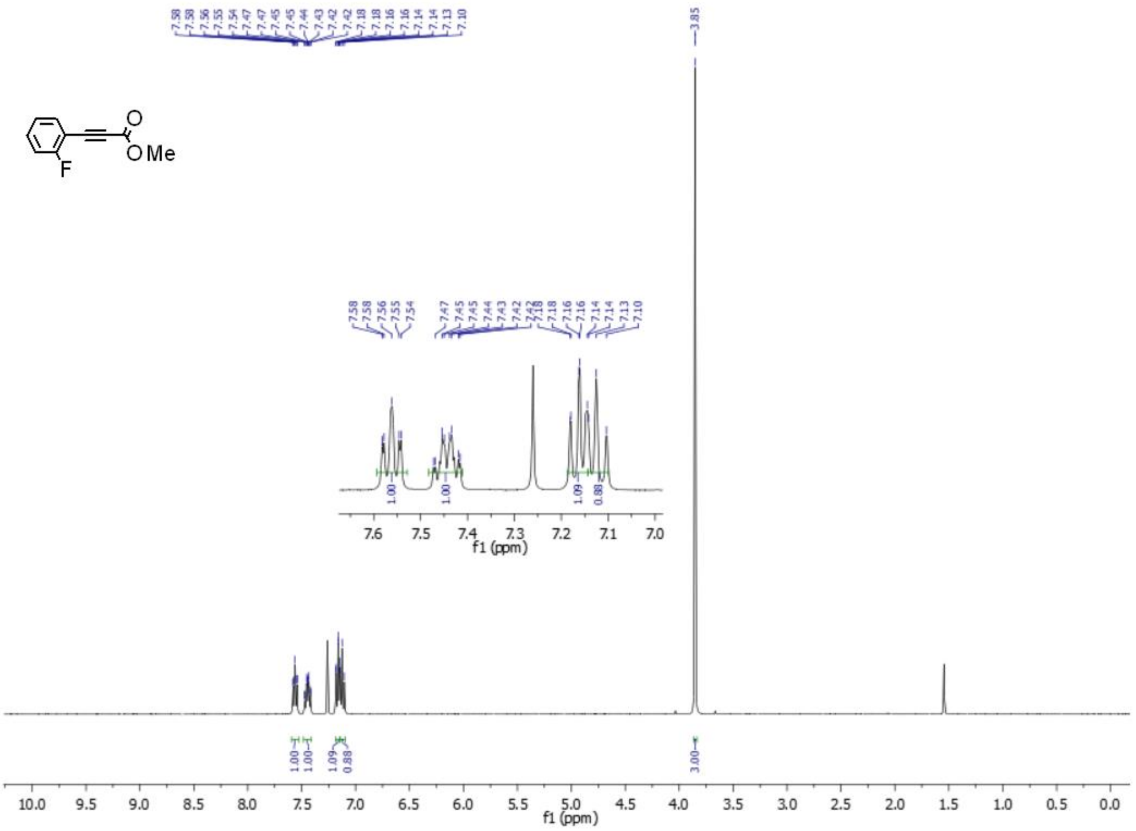


Figure S1. ^{1}H NMR spectrum of compound **1a** ($CDCl_3$, 400 MHz).

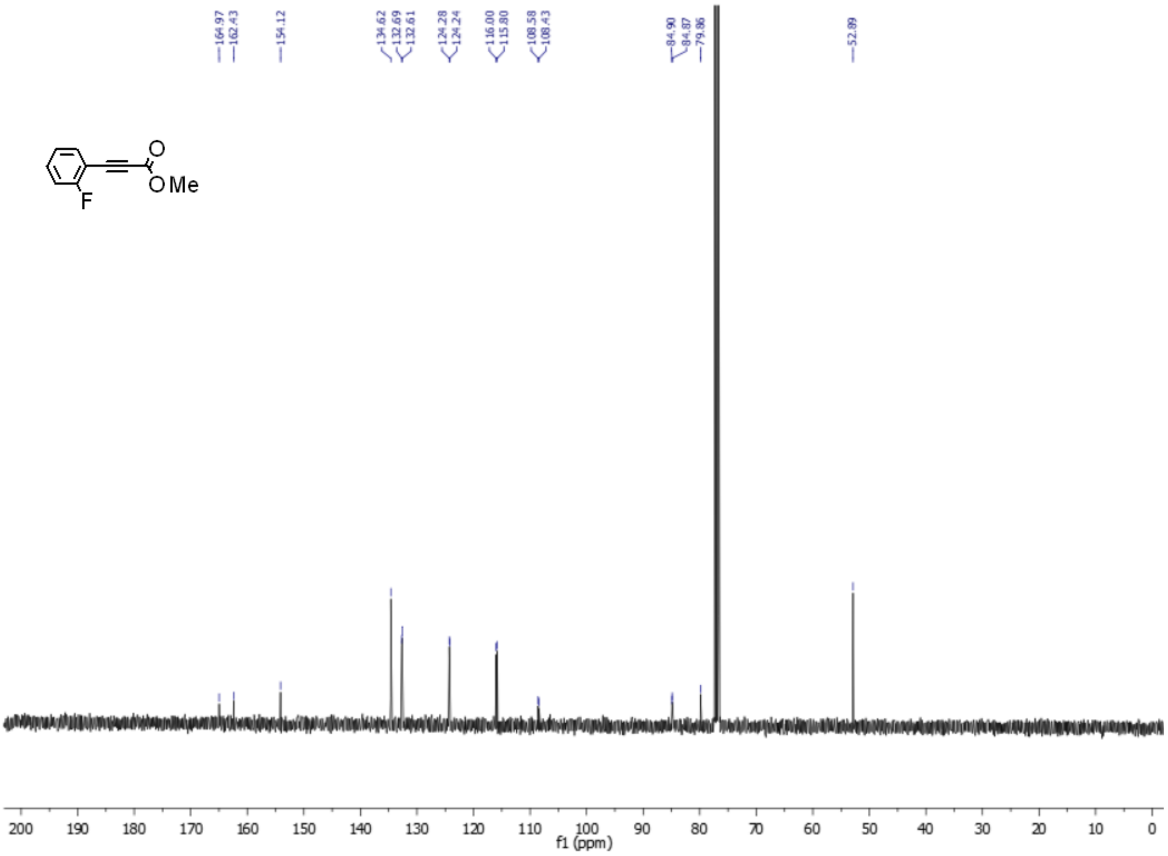


Figure S2. ^{13}C NMR spectrum of compound **1a** ($CDCl_3$, 100 MHz).

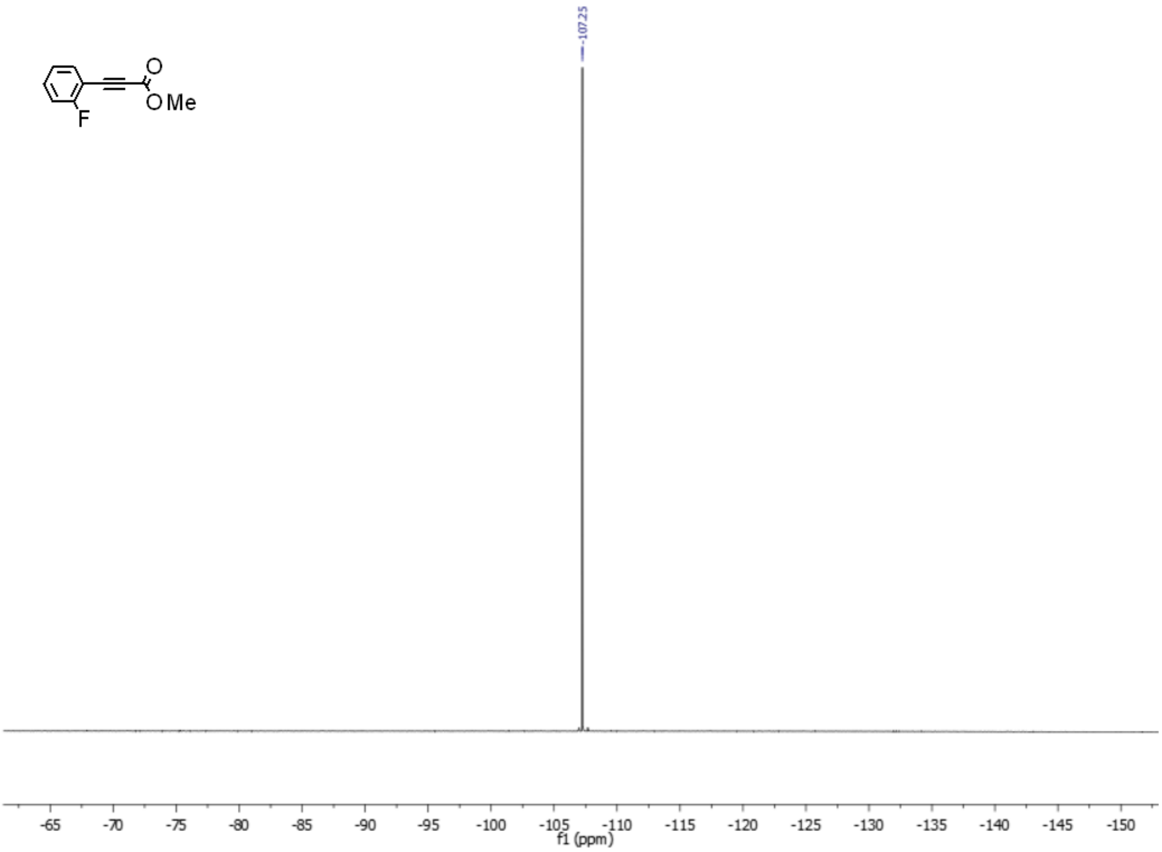


Figure S3. ^{19}F NMR spectrum of compound **1a** ($CDCl_3$, 376 MHz).

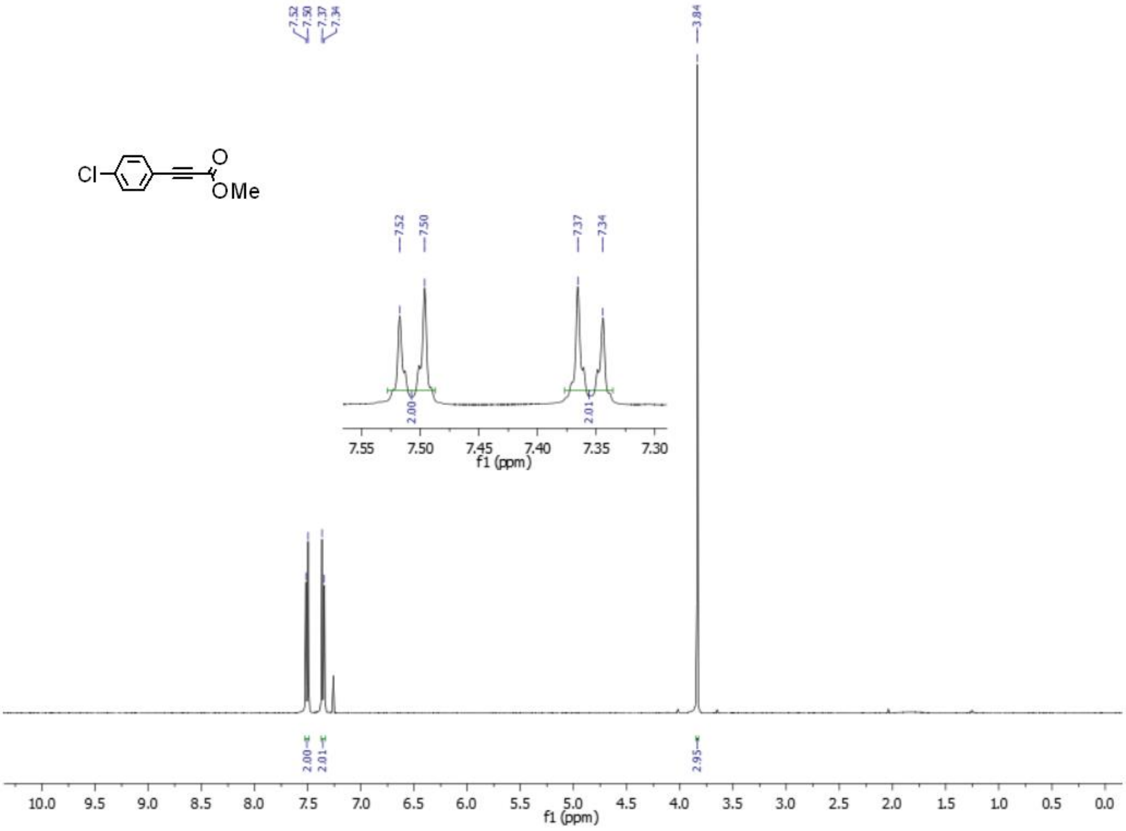


Figure S4. ^{1}H NMR spectrum of compound **1b** ($CDCl_3$, 400 MHz).

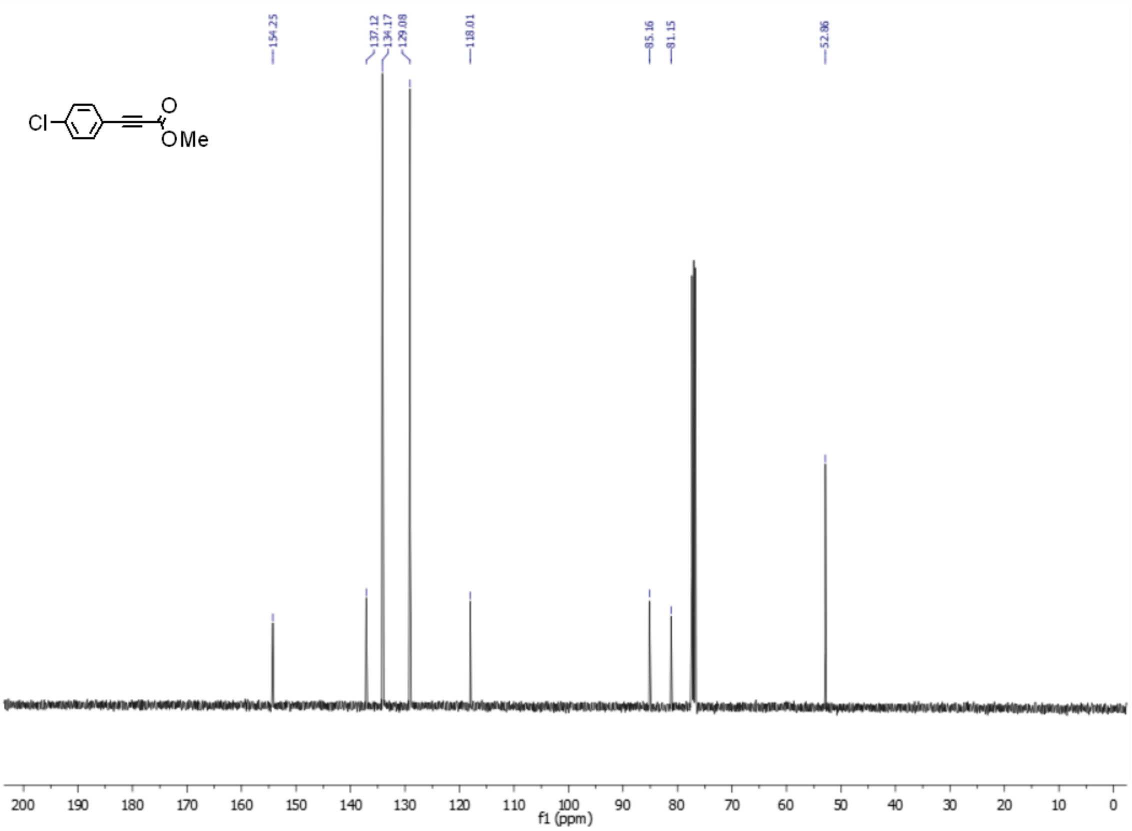


Figure S5. ^{13}C NMR spectrum of compound **1b** ($CDCl_3$, 100 MHz).

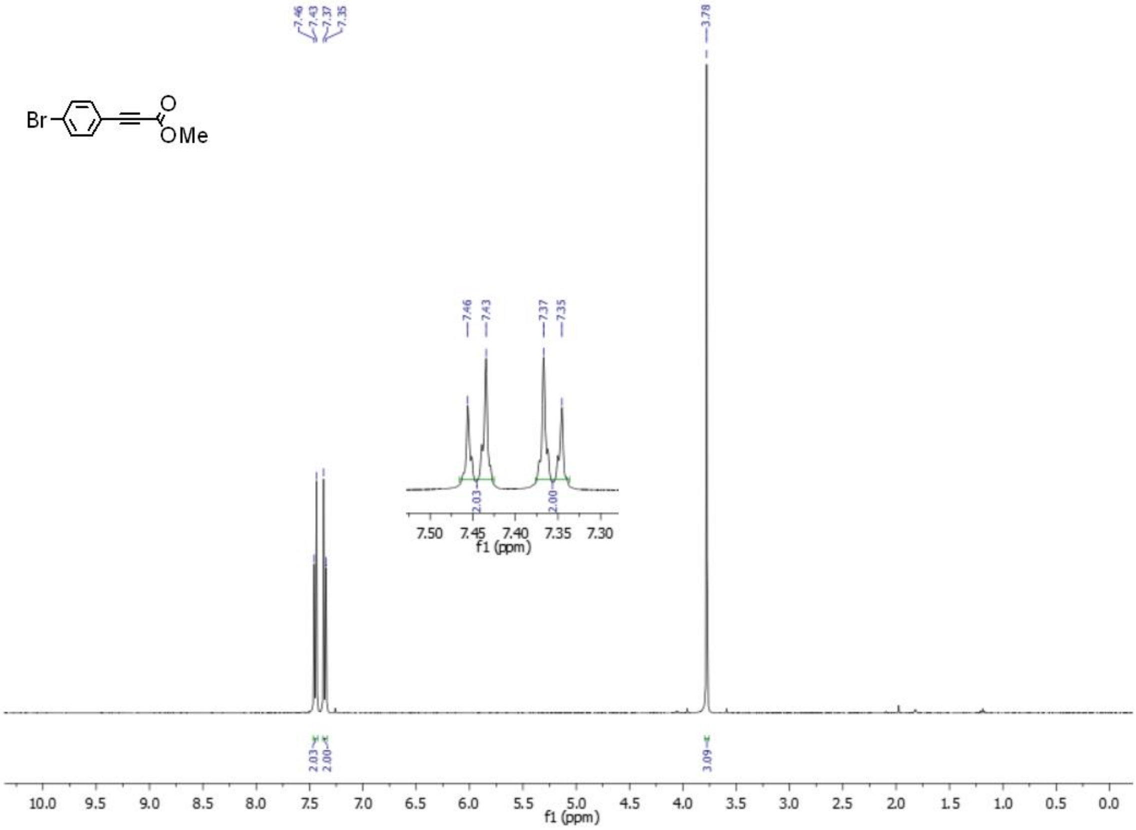


Figure S6. ^{1}H NMR spectrum of compound **1c** ($CDCl_3$, 400 MHz)

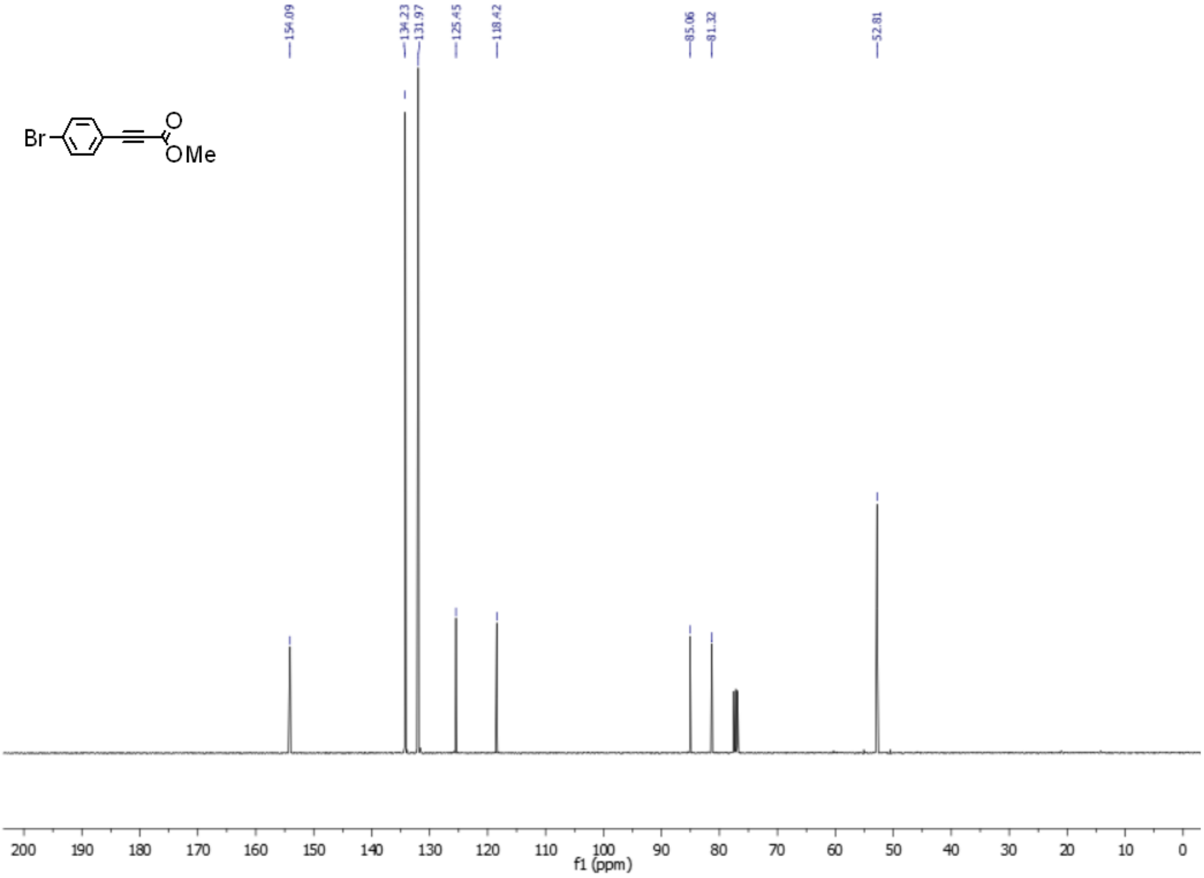


Figure S7. ^{13}C NMR spectrum of compound **1c** ($CDCl_3$, 100 MHz)

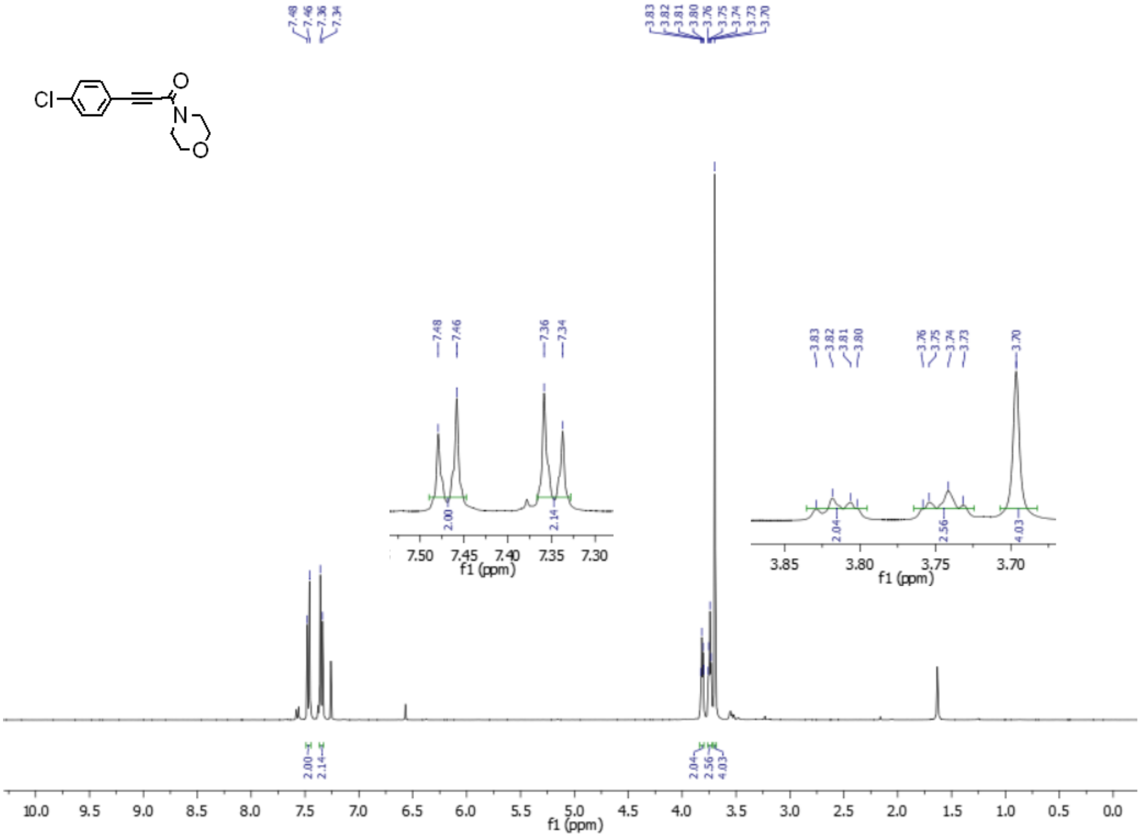


Figure S8. ^{1}H NMR spectrum of compound **1e** ($CDCl_3$, 400 MHz).

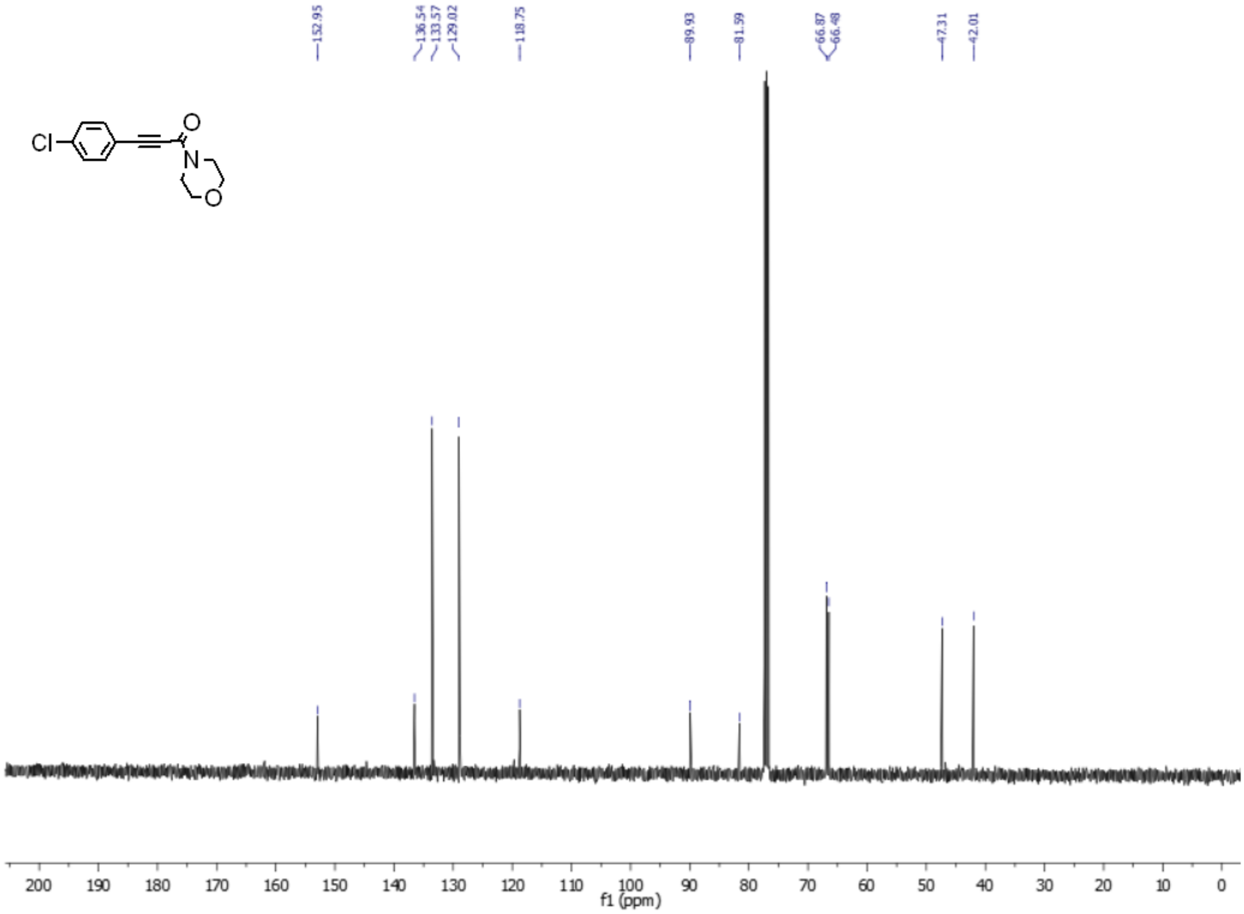


Figure S9. ^{13}C NMR spectrum of compound **1e** ($CDCl_3$, 100 MHz).

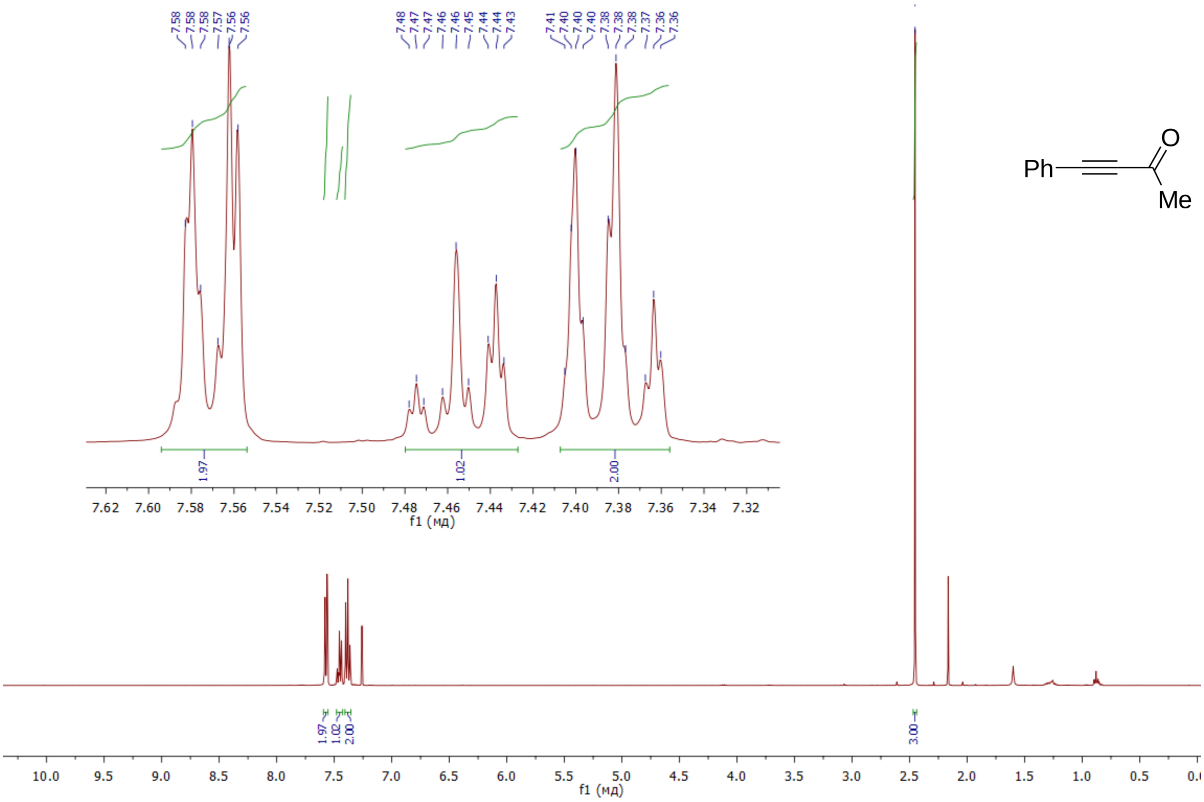


Figure S10. ^{1}H NMR spectrum of compound **1f** ($CDCl_3$, 400 MHz).

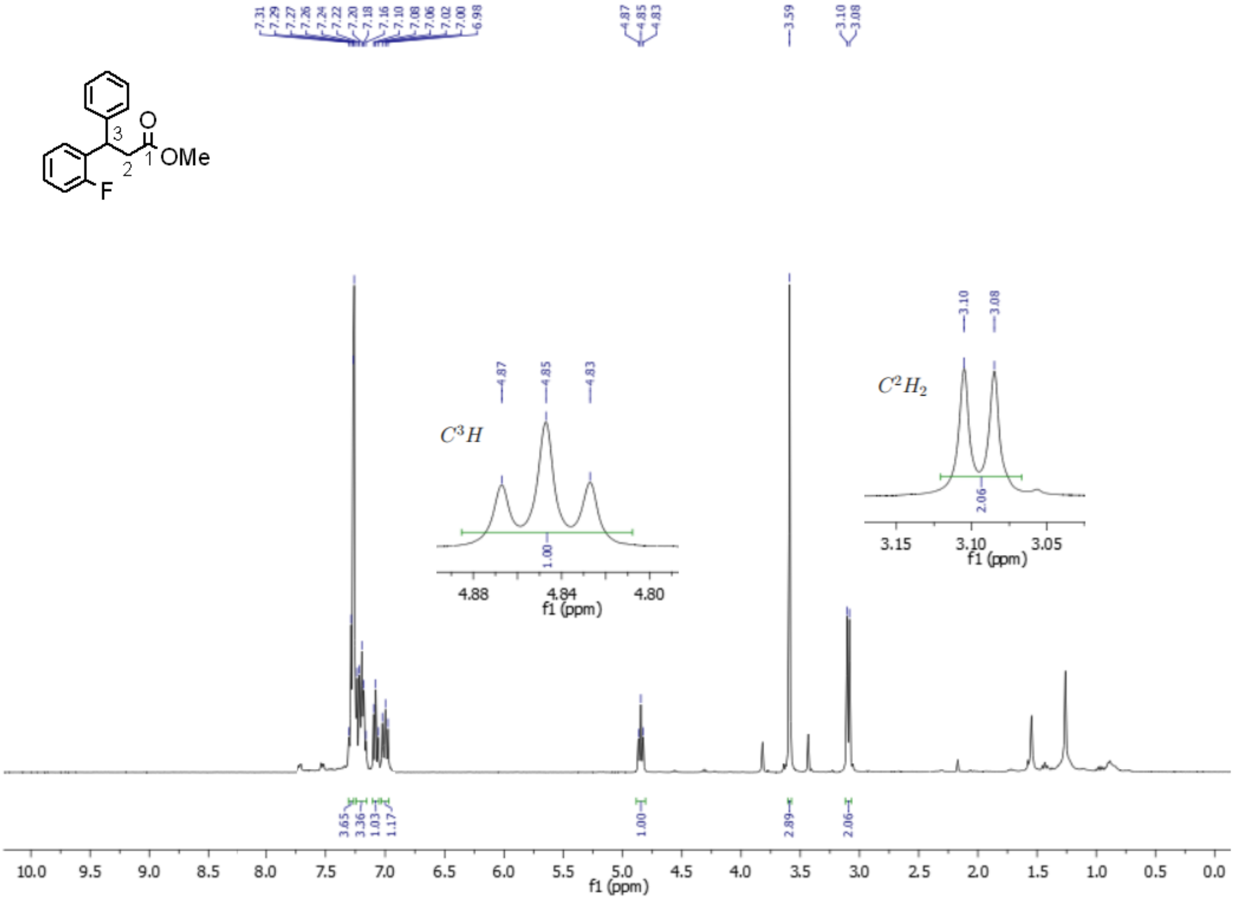


Figure S11. ^{1}H NMR spectrum of compound **2a** ($CDCl_3$, 400 MHz).

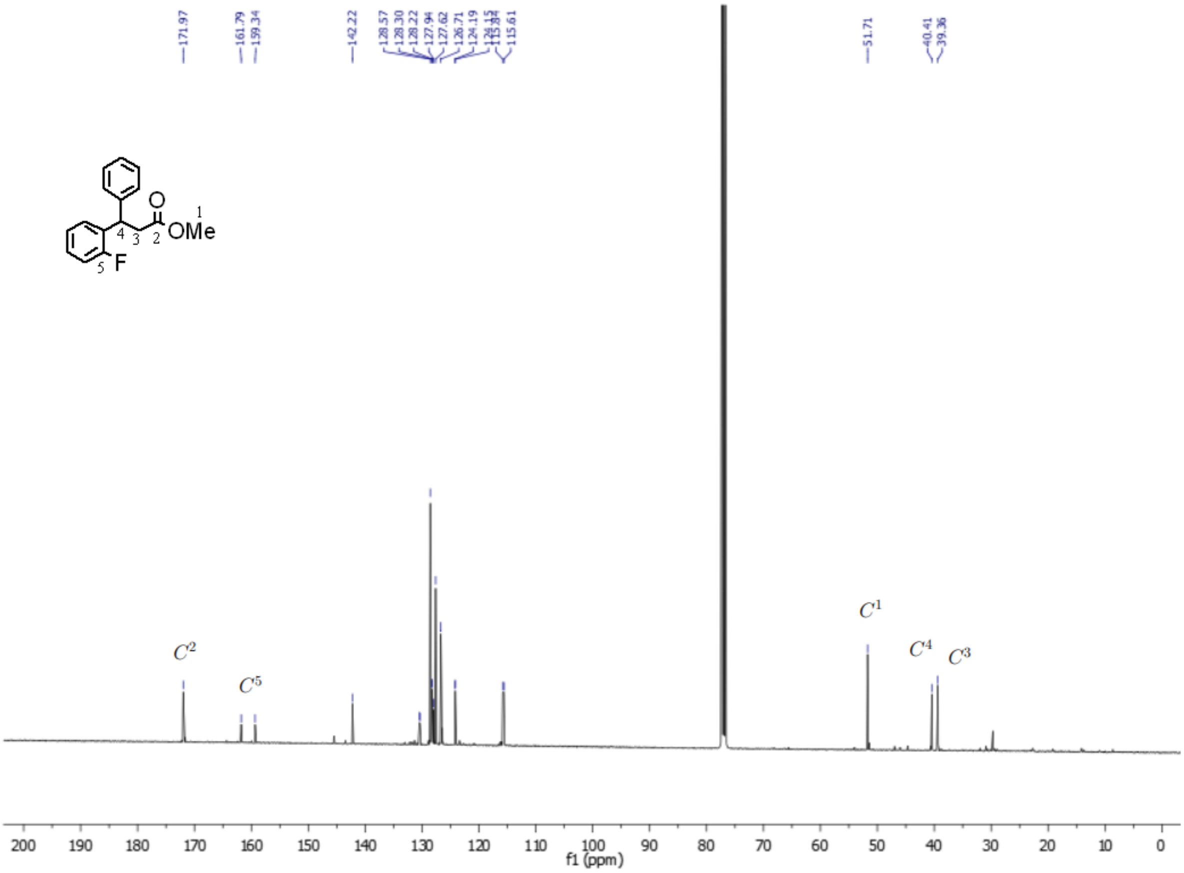


Figure S12. ^{13}C NMR spectrum of compound **2a** ($CDCl_3$, 100 MHz).

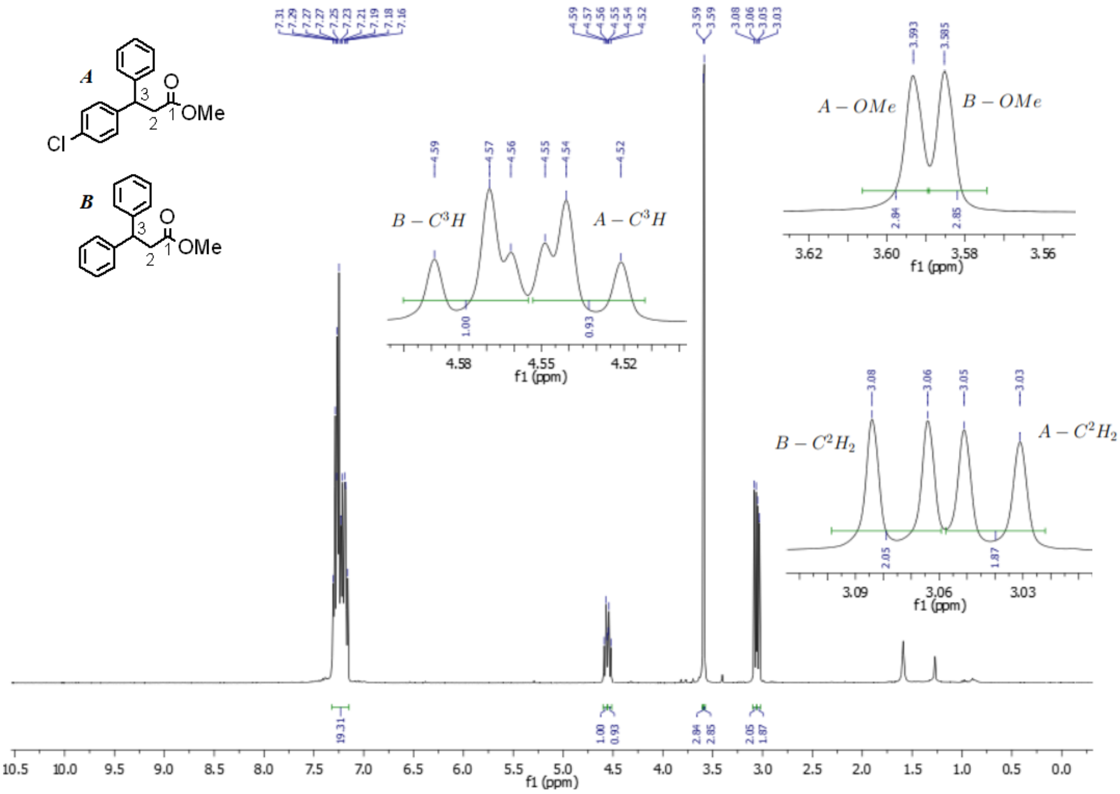


Figure S13. ^{1}H NMR spectrum of the mixture **2b** (A) and **2d** (B) (CDCl$_3$, 400 MHz)

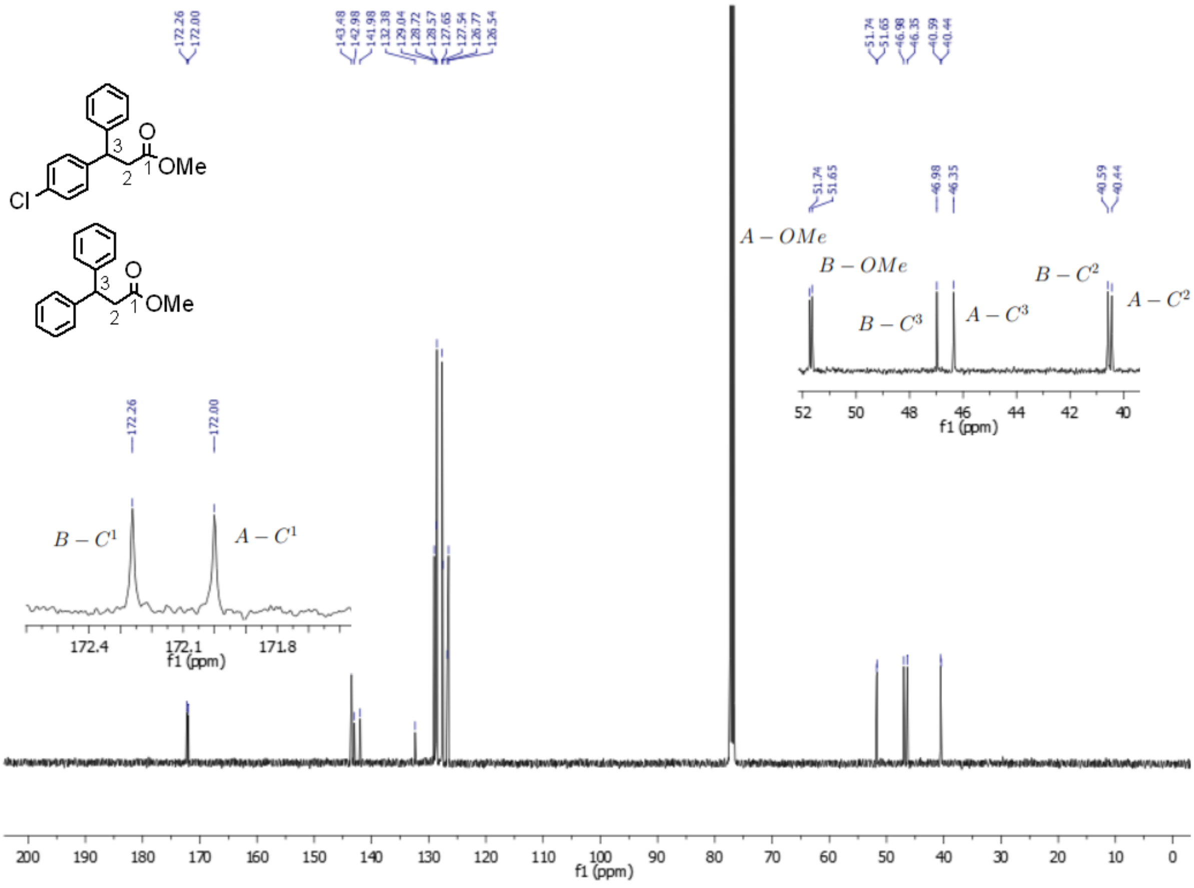


Figure S14. ^{13}C NMR spectrum of the mixture **2b** (A) and **2d** (B) (CDCl$_3$, 100 MHz)

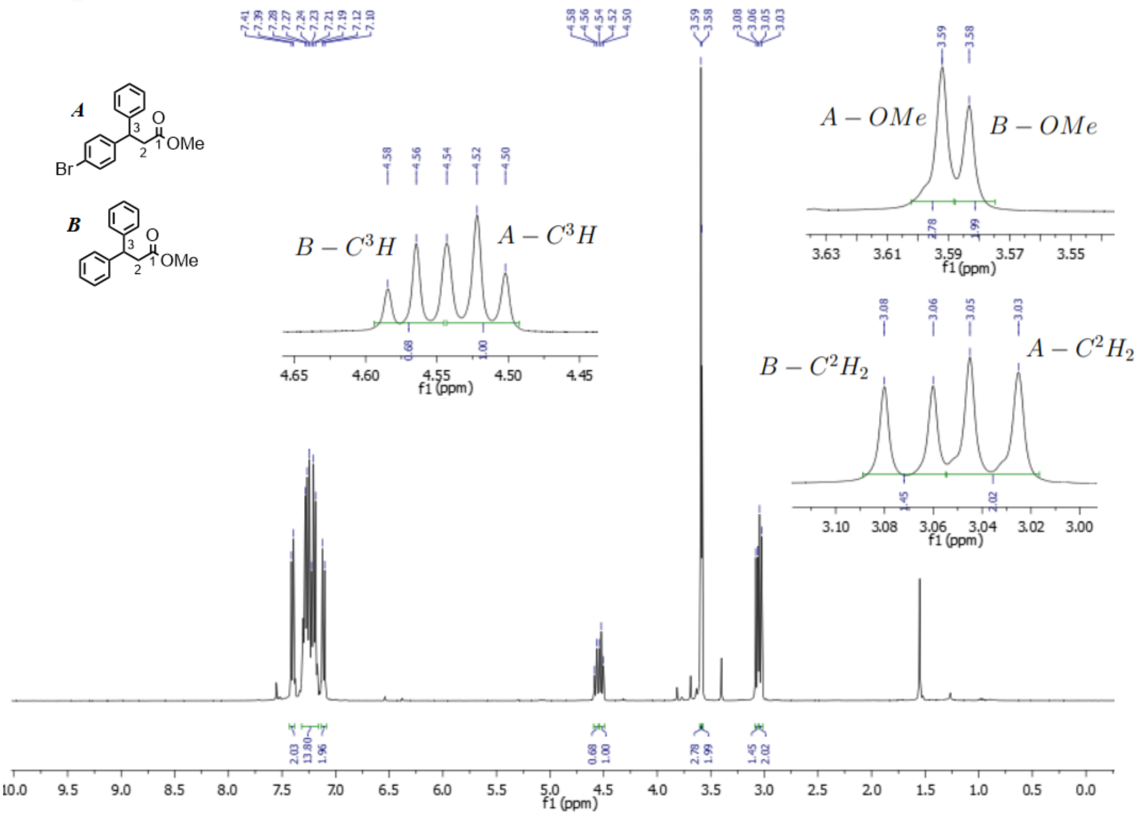


Figure S15. ^{1}H NMR spectrum of the mixture **2c** (A) and **2d** (B) (CDCl$_3$, 400 MHz).

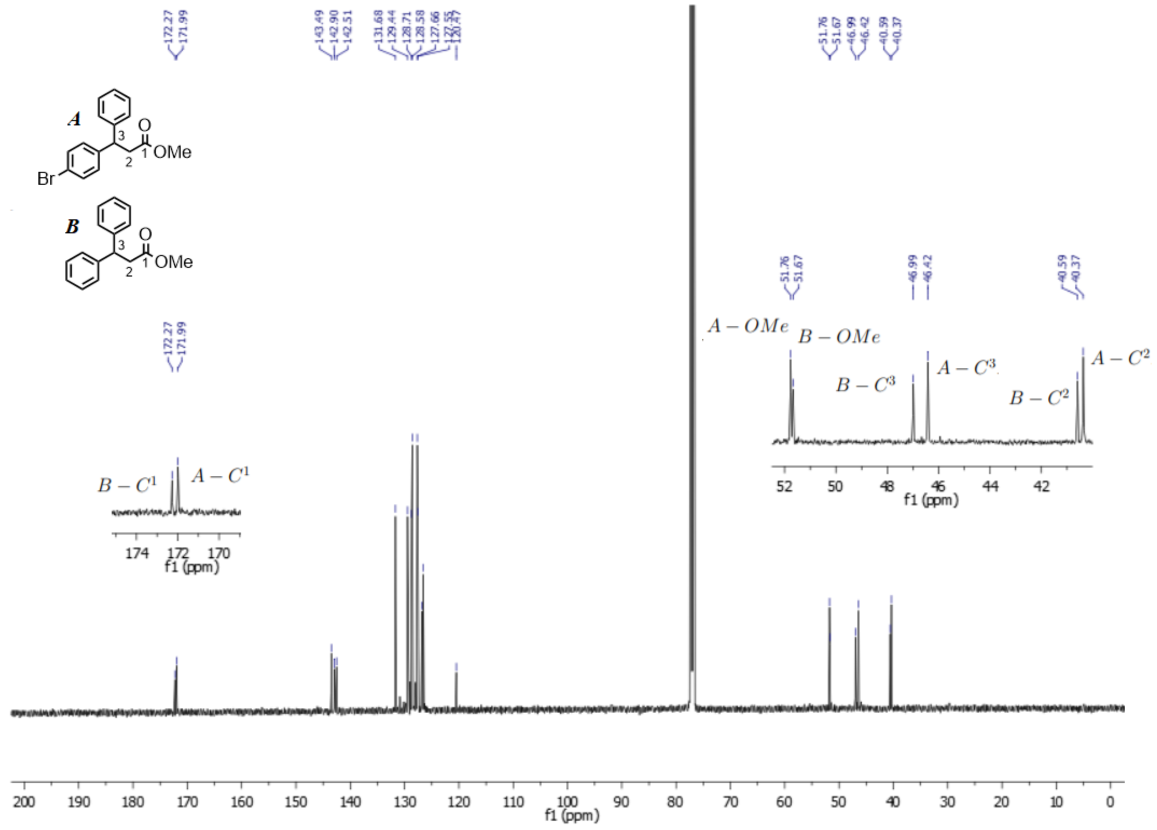


Figure S16. ^{13}C NMR spectrum of the mixture **2c** (A) and **2d** (B) (CDCl$_3$, 100 MHz).

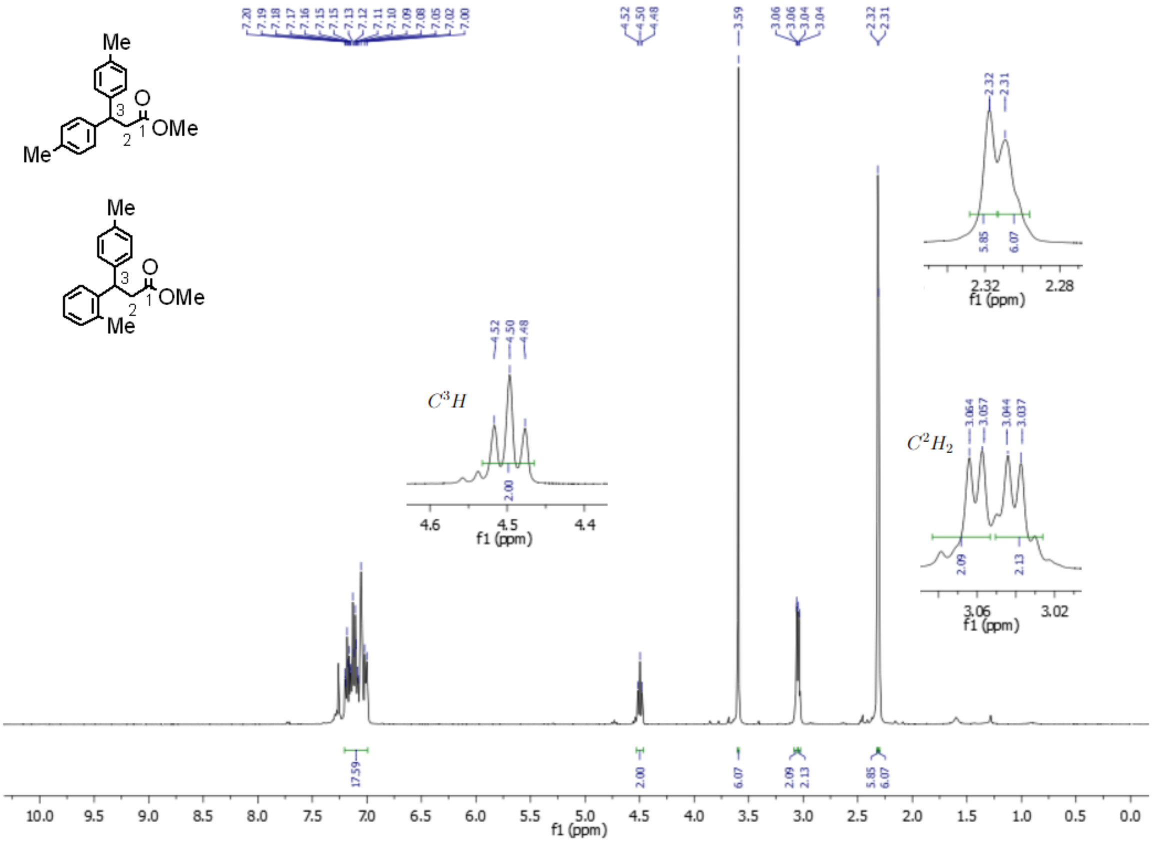


Figure S17. ^{1}H NMR spectrum of the mixture **2e** and **2f** ($CDCl_3$, 400 MHz).

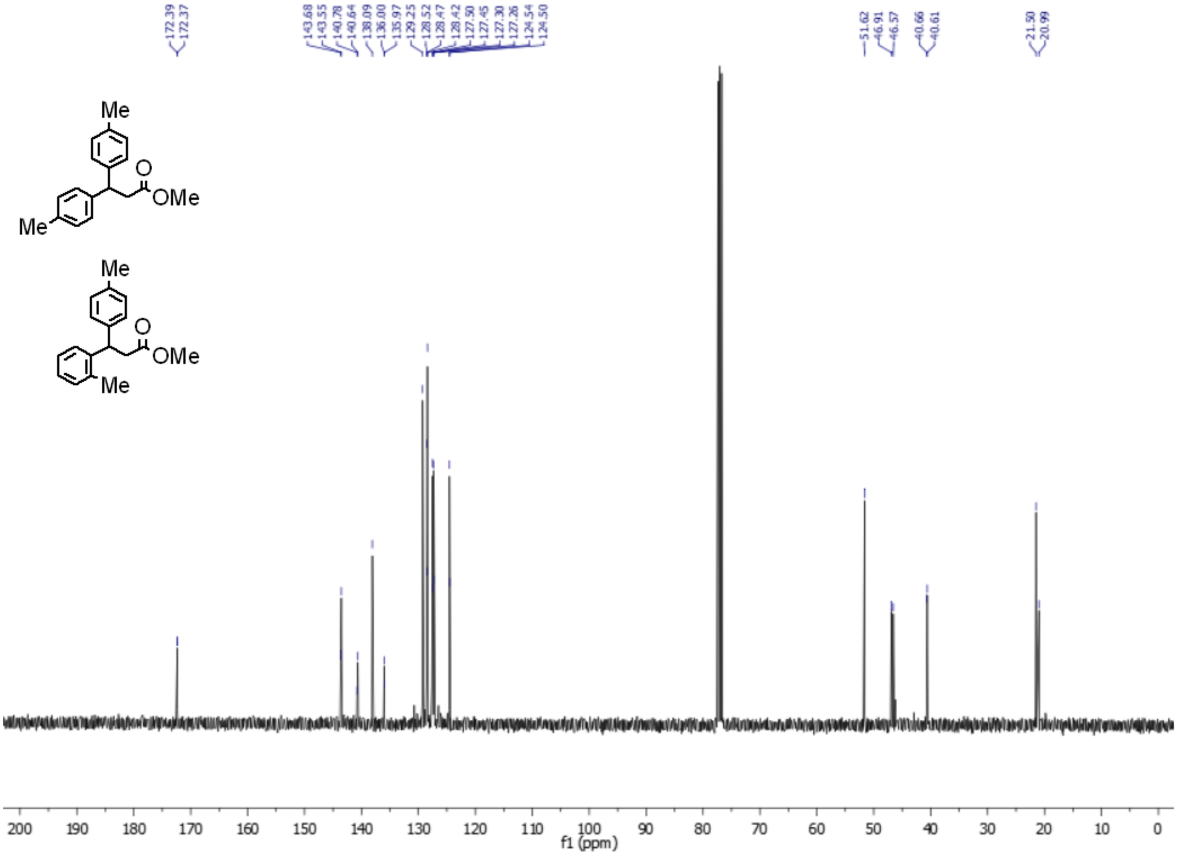


Figure S18. ^{13}C NMR spectrum of the mixture **2e** and **2f** ($CDCl_3$, 100 MHz).

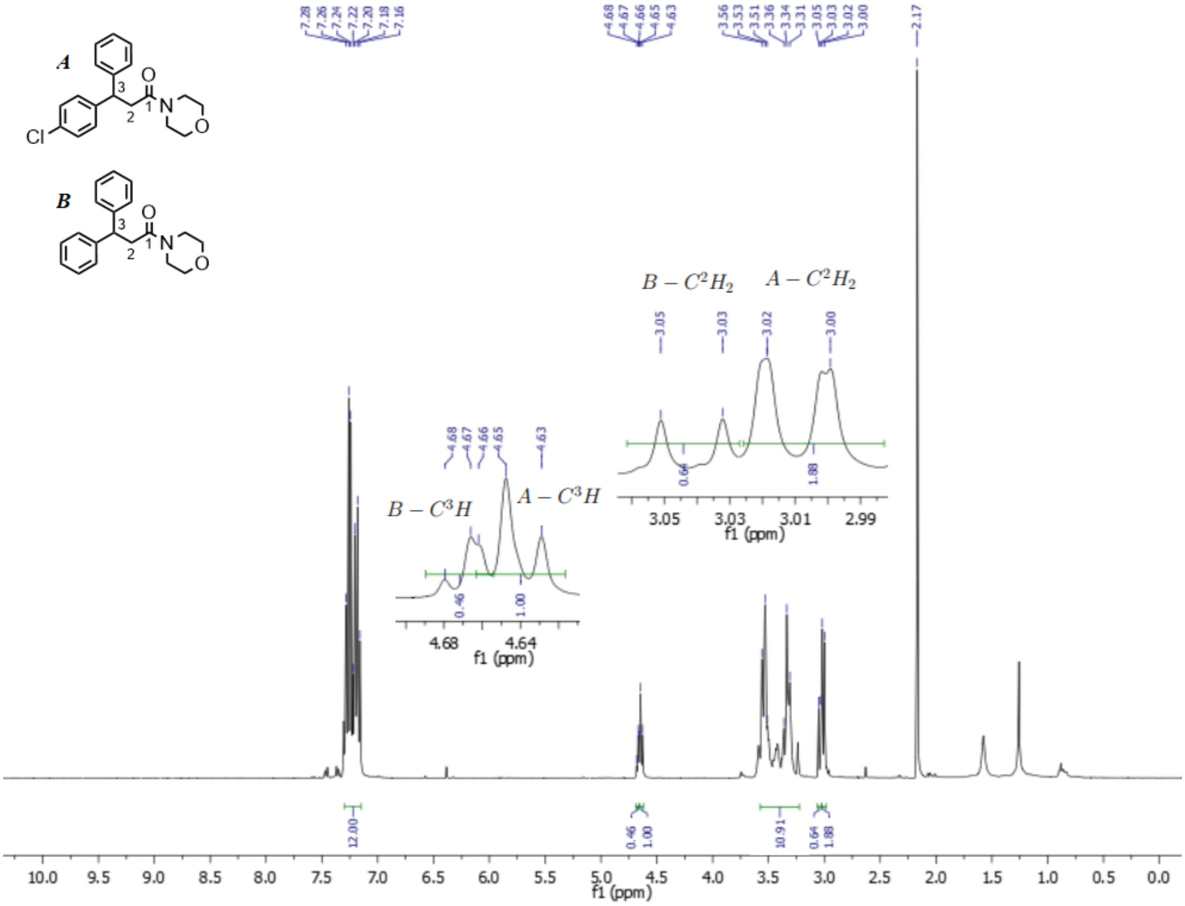


Figure S19. ^{1}H NMR spectrum of the mixture **2g** (A) and **2h** (B) ($CDCl_3$, 400 MHz).

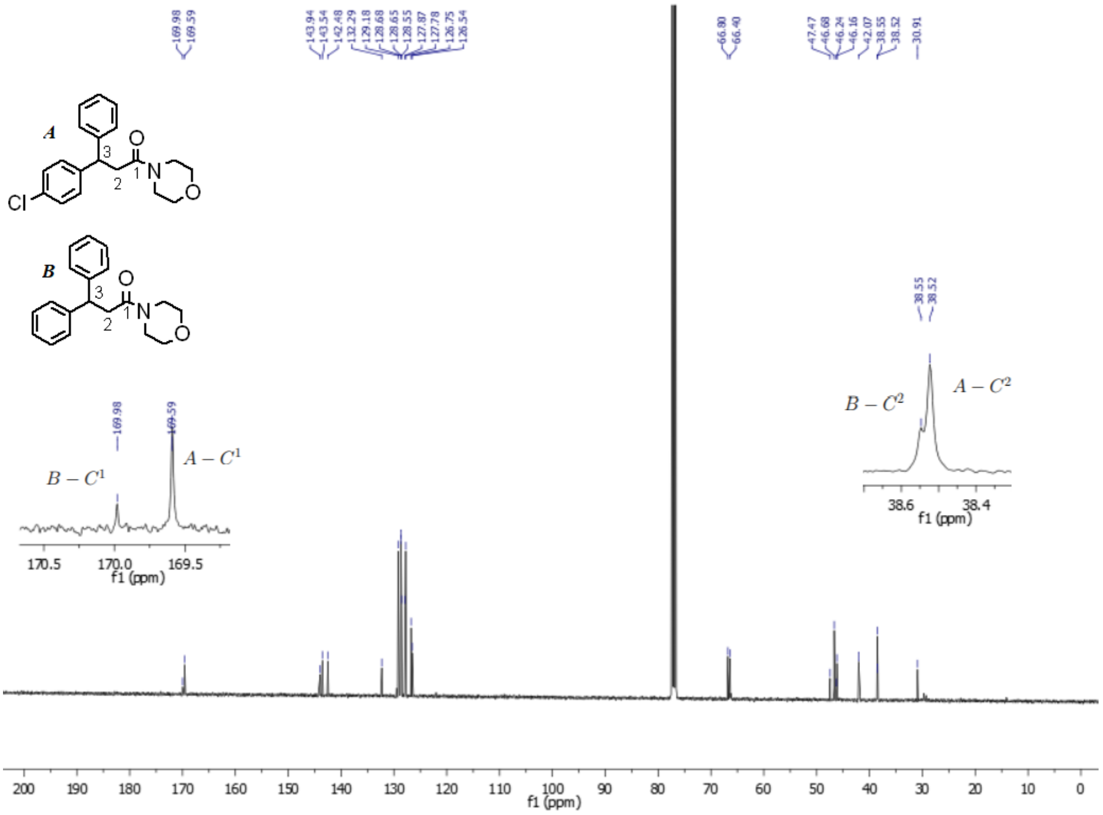


Figure S20. ^{13}C NMR spectrum of the mixture **2g** (A) and **2h** (B) ($CDCl_3$, 100 MHz).

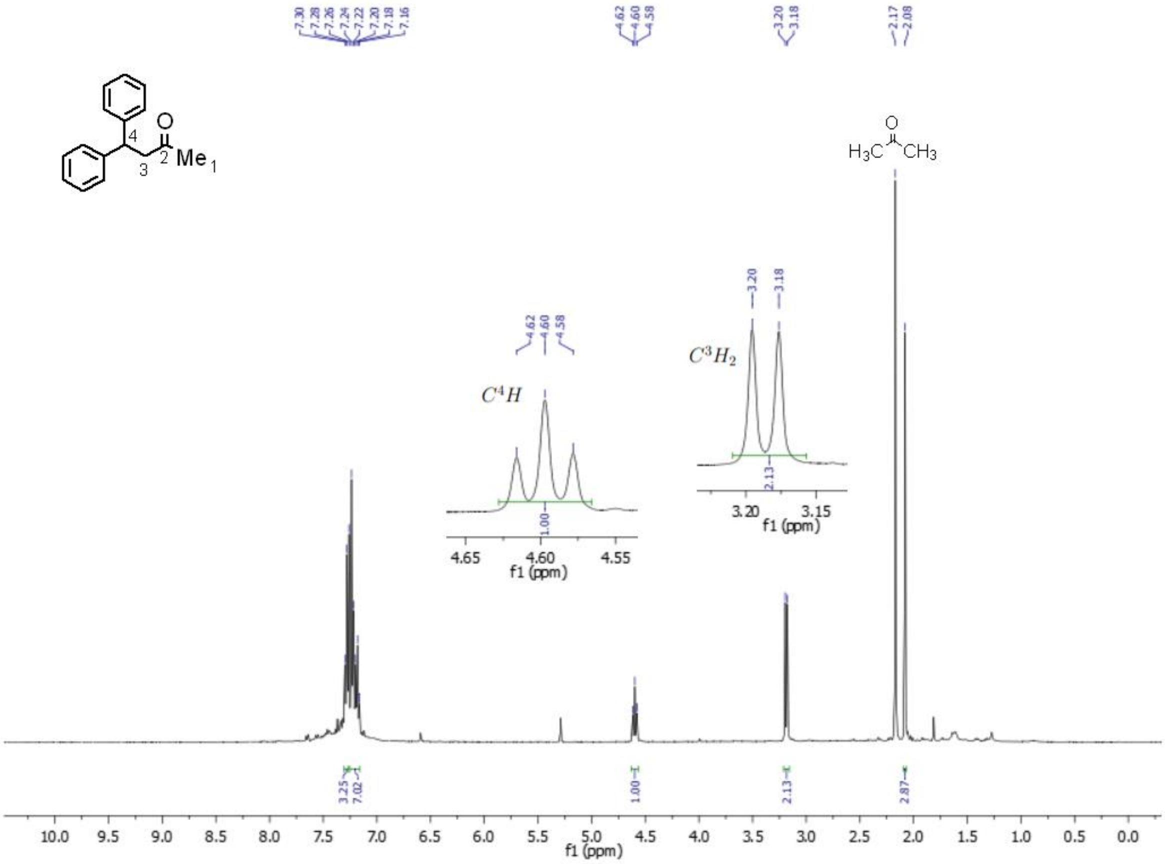


Figure S21. ^{1}H NMR spectrum of compound **2i** ($CDCl_3$, 400 MHz).

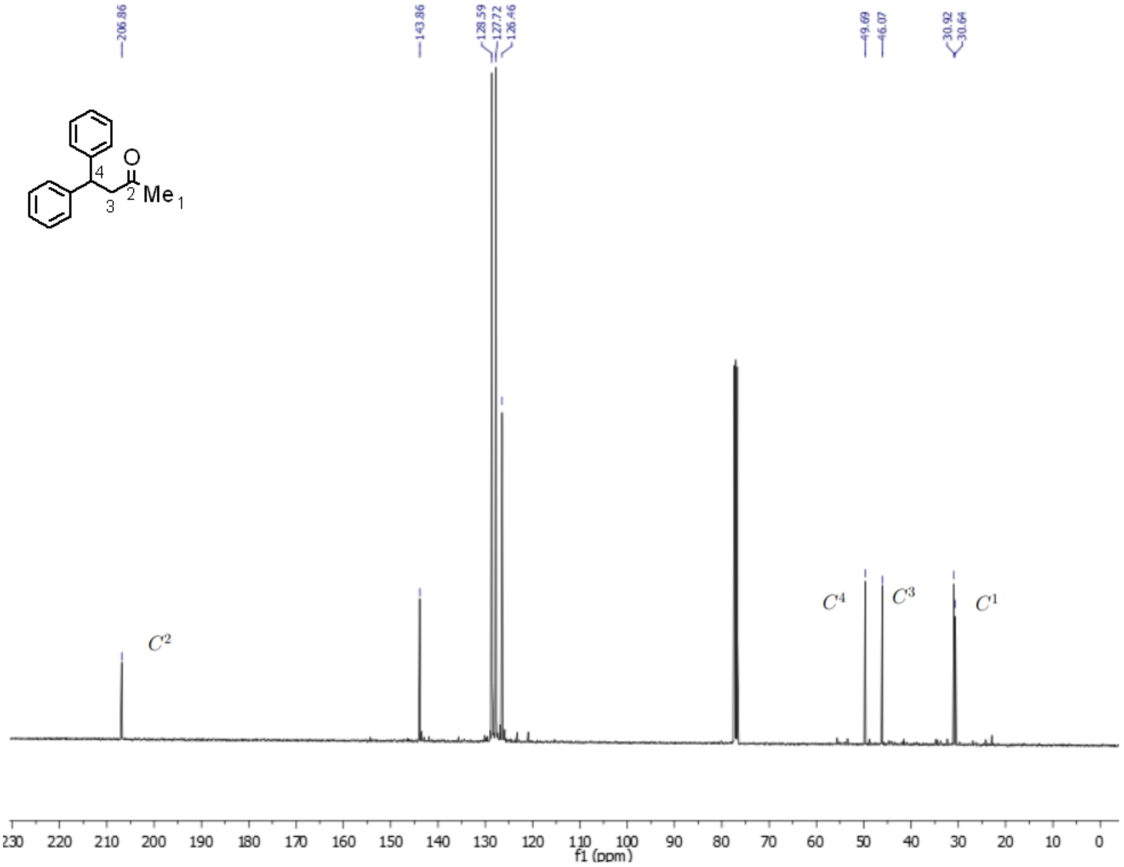


Figure S22. ^{13}C NMR spectrum of compound **2i** ($CDCl_3$, 100 MHz).

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