

Pd-Catalyzed Aldehyde to Ester Conversion: A Hydrogen Transfer Approach

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General Considerations:

Aldehydes were purchased and used without further purification. Acetone was purchased extra dry and degassed. Alcohols were degassed and dried over sieves. The base, K_2CO_3 , was ground up using a mortar and pestle and dried in the oven at 180 °C overnight and stored at 80 °C until used. ^1H , ^{13}C , and ^{19}F spectra were recorded at 500.39, 125.75, 471 MHz, respectively. Analytical thin-layer chromatography (TLC) was performed on TLC silica gel plates (0.25 mm) precoated with a fluorescent indicator. Standard flash chromatography procedures were followed using 40–63 μm silica gel. Visualization was effected with ultraviolet light.

General Procedure A: To a Biotage microwave, vial $\text{Pd}(\text{OAc})_2$ (5.6 mg, 0.025 mmol, 2.5 mol %), XPhos (23.8 mg, 0.050 mmol, 5 mol %) were added. The vial was then sealed and subsequently evacuated and purged with N_2 (3x). Next anhyd acetone (2.8 mL, 0.36 M) was added to the vial. The mixture was allowed to stir for 20 min at rt under N_2 . A second vial was charged with the aldehyde (1 mmol, 1 equiv) and oven dried K_2CO_3 (24.8 mg, 0.18 mmol, 18 mol %) in a glovebox. This microwave vial was taken out of the glovebox, and degassed alcohol, ROH (2.2 mL) was added. After 20 min, the contents of the first microwave vial were added to the second microwave vial *via* syringe. The reaction was allowed to run for the specified reaction time at rt or 50 °C as specified for the substrate. The crude reaction mixture was filtered through a silica plug and concentrated *in vacuo*. The concentrated crude reaction mixture was purified by flash column chromatography on silica gel (hexanes or pentanes and Et_2O).

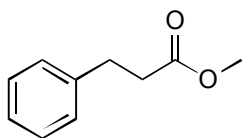
General Procedure B:

To a Biotage microwave vial Pd(OAc)₂ (5.6 mg, 0.025 mmol, 2.5 mol %) , XPhos (23.8 mg, 0.050 mmol, 5 mol %) were added, then the vial was sealed and subsequently evacuated and purged with N₂. Next anhyd acetone (2.8 mL, 0.36 M) was added to the vial. The mixture was allowed to stir for 20 min at rt under N₂. A second vial was charged with oven dried K₂CO₃ (24.8 mg, 0.18 mmol, 18 mol %), and the aldehyde (1mmol) if a solid. This microwave vial was purged and evacuated with N₂ and degassed alcohol, ROH, (2.2 mL) and the aldehyde (1 mmol) was added if a liquid. After 20 min, the contents of the first microwave vial were added to the second microwave vial *via* syringe. The reaction was allowed to run for the specified reaction time at rt or 50 °C as specified for the substrate. The crude reaction mixture was filtered through a silica plug and concentrated *in vacuo*. The concentrated crude reaction mixture was purified using flash column chromatography(hexanes or pentanes and Et₂O).

Scale Up Procedure. Preparation of Ethyl 3-Phenylpropanoate.

To a Biotage microwave vial Pd(OAc)₂ (7.84 mg, 0.035 mmol, 0.5 mol %), XPhos (33.3 mg, 0.07 mmol, 1 mol %) were added. The vial was then sealed and subsequently evacuated and purged with N₂ (3x). Next anhyd acetone (19.6 mL, 0.36 M) was added to the vial. The mixture was allowed to stir for 20 min at rt under N₂. A 50 mL round bottom flask with a septa was charged with oven dried K₂CO₃ (24.8 mg, 0.18 mmol, 18 mol %). This flask was purged and evacuated with N₂, and degassed EtOH (15 mL) and 3-phenylpropanal (939.4 mg, 7 mmol) was added. After 20 min, the contents of the first

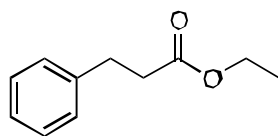
microwave vial were added to the second microwave vial via syringe. The reaction was allowed to run for 24 h at rt. The crude reaction mixture was filtered through a silica plug and concentrated *in vacuo*. The concentrated crude reaction mixture was purified using flash column chromatography(hexanes or pentanes and Et₂O). The desired ester was isolated as a yellow oil (1.23 g, 99% yield).



Methyl 3-phenylpropanoate (1a).¹

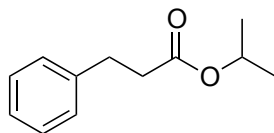
General procedure A was used at rt for 2 h with 3-phenylpropanal (134.2 mg, 1 mmol) to yield the desired ester as a yellow oil (127.7 mg, 77% yield).

¹H NMR (500 MHz, CDCl₃): δ = 7.32 – 7.25 (m, 2H), 7.20 (dd, J = 7.3, 5.4 Hz, 3H), 3.66 (s, 3H), 2.99-2.91(m, 2H), 2.63 (dd, J = 9.3, 6.4 Hz, 2H). ¹³C NMR (125.8 MHz, CDCl₃): δ = 173.5, 140.7, 128.7, 128.4, 126.4, 51.8, 35.9, 31.1 ppm.



Ethyl 3-phenylpropanoate (1b).²

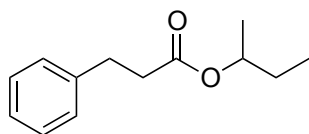
General procedure A was used at rt for 2 h with 3-phenylpropanal (134.2 mg, 1 mmol) to yield the desired ester as a yellow oil (141.5 mg, 79%). ¹H NMR (500 MHz, CDCl₃) δ 7.28 (m, 2H), 7.23 – 7.16 (m, 3H), 4.13 (q, J = 7.1 Hz, 2H), 3.14 – 2.86 (m, 2H), 2.78 – 2.40 (m, 2H), 1.24 (dd, J = 12.4, 5.2 Hz, 3H). ¹³C NMR (500 MHz, CDCl₃) δ 172.85, 140.60, 128.5, 128.3, 126.2, 60.4, 35.9, 31.0, 14.2.



Isopropyl 3-phenylpropanoate (1c).³

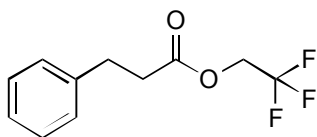
General procedure B was used at rt for 8 h with 3-phenylpropanal (134.2 mg, 1 mmol) to yield the desired ester as a colorless oil (115.6 mg, 60%).

¹H NMR (360 MHz, CDCl₃) δ 7.31 – 7.24 (m, 2H), 7.19 (dd, *J* = 10.1, 4.4 Hz, 3H), 5.00 (m, 1H), 2.94 (t, *J* = 7.8 Hz, 2H), 2.62 – 2.54 (m, 2H), 1.20 (d, *J* = 6.3 Hz, 6H). ¹³C NMR (126 MHz, CDCl₃) δ 172.4, 140.6, 128.4, 128.3, 128.3, 126.2, 67.7, 36.2, 31.0, 21.8.



sec-Butyl 3-phenylpropanoate (1e).

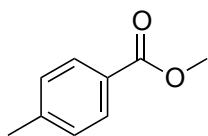
General procedure B was used at 50 °C for 24 h with 3-phenyl propanal (134.2 mg, 1 mmol) to yield the desired ester as a colorless oil (112.9 mg, 55%). ¹H NMR (500 MHz, CDCl₃) δ 7.30 – 7.23 (m, 2H), 7.22 – 7.16 (m, 3H), 4.84 (m, 1H), 2.94 (t, *J* = 7.7 Hz, 2H), 2.60 (td, *J* = 7.9, 1.9 Hz, 2H), 1.61 – 1.43 (m, 2H), 1.20 – 1.13 (m, 3H), 0.85 (td, *J* = 7.4, 1.9 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 172.5, 140.5, 128.4, 128.2, 126.1, 72.2, 36.1, 31.0, 28.7, 19.3, 9.5. HRMS calcd. for C₁₃H₁₈O₂Na (M+Na)⁺ 277.1052, found 277.1041.



2,2,2-Trifluoroethyl 3-phenylpropanoate (1f).

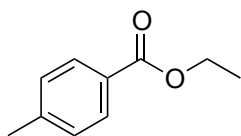
General procedure B was used at 50 °C for 24 h with 3-phenyl propanal (134.2 mg, 1 mmol) to yield the desired ester as a colorless oil (118.6 mg, 51%). ¹H NMR (500 MHz, CDCl₃) δ 7.34 – 7.27 (m, 2H), 7.23 (dd, *J* = 12.5, 7.2 Hz, 3H), 4.47 (q, *J* = 8.5 Hz, 2H), 3.06 – 2.95 (m, 2H), 2.76 (t, *J* = 7.8 Hz, 2H). ¹³C NMR (126 MHz, CDCl₃) δ 171.4,

139.9, 128.8, 128.7, 128.5, 128.4, 126.7, 124.2, 122.0, 60.6, 60.3, 35.4, 30.8. HRMS calcd. for $C_{11}H_{11}F_3O_2$ (M+) 277.1052, found 277.1041. ^{19}F NMR (471 MHz, C_6D_6) δ - 73.8 Hz.



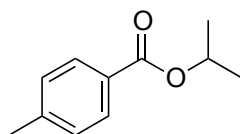
Methyl 4-methylbenzoate (2a).⁴

General procedure A was used at 50 °C overnight with 4-methyl benzaldehyde (120.2 mg, 1 mmol) to yield the desired ester as a colorless oil (94.1 mg, 62%). 1H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, J = 8.1 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 3.90 (d, J = 2.5 Hz, 3H), 2.40 (s, 3H). ^{13}C NMR (500 MHz, $CDCl_3$) δ 167.1, 143.4, 129.5, 129.0, 127.4, 51.8, 21.5.



Ethyl 4-methylbenzoate (2b).⁵

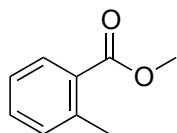
General procedure A was used at 50 °C overnight with 4-methyl benzaldehyde (120.2 mg, 1 mmol) to yield the desired ester as a colorless oil (79.6 mg, 49%). 1H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, J = 8.2 Hz, 2H), 7.24 – 7.20 (m, 2H), 4.35 (q, J = 7.1 Hz, 2H), 2.39 (s, 3H), 1.38 (t, J = 7.1 Hz, 3H). ^{13}C NMR (500 MHz, $CDCl_3$) δ 166.8, 166.8, 143.5, 143.5, 129.7, 129.1, 128.0, 60.9, 21.7, 14.5.



Isopropyl 4-methylbenzoate (2c).⁶

General procedure A was used at 50 °C overnight with 4-methyl benzaldehyde (120.2 mg, 1 mmol) to yield the desired ester as a pale yellow oil (13.8 mg, 8%).

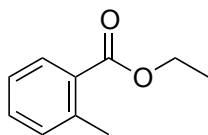
¹H NMR (500 MHz, CDCl₃) δ 7.97 – 7.93 (m, 2H), 7.25 (d, *J* = 8.5 Hz, 2H), 5.26 (m, 1H), 2.43 (s, 3H), 1.38 (d, *J* = 6.3 Hz, 6H). ¹³C NMR (126 MHz, CDCl₃) δ 166.3, 143.4, 129.7, 129.2, 129.1, 128.4, 68.2, 22.1, 21.7.



Methyl 2-methylbenzoate (3a).⁷

General procedure A was used at 50 °C overnight with 2-methyl benzaldehyde (120.2 mg, 1 mmol) to yield the desired ester as a colorless oil (93 mg, 62%).

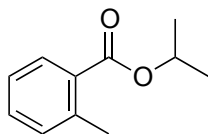
¹H NMR (500 MHz, CDCl₃) δ 7.93 (t, *J* = 8.1 Hz, 1H), 7.41 (dd, *J* = 14.2, 6.7 Hz, 1H), 7.28 – 7.22 (m, 2H), 3.90 (s, 3H), 2.62 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 168.0, 140.1, 131.9, 131.6, 130.5, 129.5, 125.6, 51.7, 21.6.



Ethyl 2-methylbenzoate (3b).⁵

General procedure A was used at 50 °C overnight with 2-methylbenzaldehyde (120.2 mg, 1 mmol) to yield the desired ester as a colorless oil (122.8 mg, 75%).

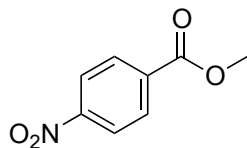
¹H NMR (500 MHz, CDCl₃) δ 7.92 (m, 1H), 7.40 (m, 1H), 7.28 – 7.23 (m, 2H), 4.37 (q, *J* = 7.1 Hz, 2H), 2.61 (s, 3H), 1.41 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 167.6, 139.9, 131.7, 131.5, 130.4, 129.9, 125.6, 60.6, 21.6, 14.2.



Isopropyl 2-methylbenzoate (3c).⁸

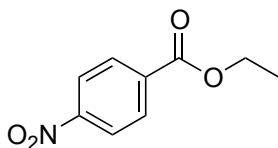
General procedure A was used at 50 °C overnight with 2-methylbenzaldehyde (120.2 mg, 1 mmol) to yield the desired ester as a colorless oil (26.8 mg, 22%).

¹H NMR (500 MHz, CDCl₃) δ 7.89 – 7.86 (m, 1H), 7.38 (m, 1H), 7.24 (m, 2H), 5.25 (m, 1H), 2.60 (s, 3H), 1.37 (d, *J* = 6.3 Hz, 6H). ¹³C NMR (126 MHz, CDCl₃) δ 167.5, 139.9, 131.8, 131.7, 130.7, 130.5, 125.8, 68.3, 22.1, 21.8.



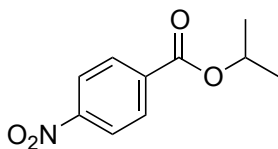
Methyl 4-nitrobenzoate (4a).⁷

General procedure A was used at 50 °C overnight with 4-nitrobenzaldehyde (151.1 mg, 1 mmol) to yield the desired ester as an off-white solid (81.3 mg, 50%), mp. 93-95°C(lit. 94-95°C)⁹. ¹H NMR (500 MHz, CDCl₃) δ 8.30 (d, *J* = 8.9 Hz, 2H), 8.22 (d, *J* = 8.9 Hz, 2H), 3.99 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 165.3, 150.7, 135.6, 130.9, 123.7, 53.0.



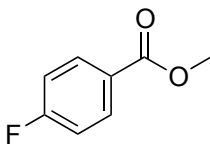
Ethyl 4-nitrobenzoate (4b).⁵

General procedure A was used at 50 °C overnight with 4-nitrobenzaldehyde (151.1 mg, 1 mmol) to yield the desired ester as a tan solid (92 mg, 47%), mp 55-56°C (lit. 56-57 °C)¹⁰. ¹H NMR (500 MHz, CDCl₃) δ 8.30 (d, *J* = 8.9 Hz, 2H), 8.22 (d, *J* = 8.9 Hz, 2H), 3.99 (s, 2H), 1.46 – 1.37 (m, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 165.3, 150.7, 135.6, 130.9, 123.7, 53.0.



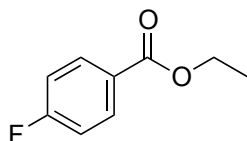
Isopropyl 4-nitrobenzoate (4c).¹¹

General procedure A was used at 50 °C overnight with 4-nitrobenzaldehyde (151.1 mg, 1 mmol) to yield the desired ester as a white solid (107.2 mg, 51%), mp 107 °C (lit. 104-106 °C). ¹H NMR (500 MHz, CDCl₃) δ 8.32 – 8.25 (m, 2H), 8.24 – 8.17 (m, 2H), 5.29 (dt, *J* = 12.5, 6.3 Hz, 1H), 1.40 (d, *J* = 6.3 Hz, 6H). ¹³C NMR (126 MHz, CDCl₃) δ 164.3, 150.6, 136.4, 130.8, 123.6, 69.9, 22.0.



Methyl 4-fluorobenzoate (5a).¹²

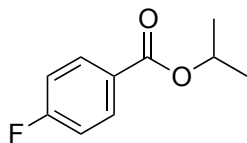
General procedure A was used at 50 °C overnight with 4-fluorobenzaldehyde (124.1 mg, 1 mmol) to yield the desired ester as a colorless oil (79.5 mg, 52%). ¹H NMR (500 MHz, CDCl₃) δ 8.13 – 7.97 (m, 2H), 7.18 – 7.02 (m, 2H), 3.91 (d, *J* = 3.1 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 166.0, 165.7 (d, *J* = 259 Hz), 132.0, (d, *J* = 8.8 Hz), 126.4(d, *J* = 2.5 Hz), 115.4 (d, *J* = 21.4 Hz), 52.1.



Ethyl 4-fluorobenzoate (5b).¹³

General procedure A was used at 50 °C overnight with 4-fluorobenzaldehyde (124.1 mg, 1 mmol) to yield the desired ester as a pale yellow oil (135.0 mg, 80%).

¹H NMR (500 MHz, CDCl₃) δ 8.12 – 8.03 (m, 2H), 7.16 – 7.07 (m, 2H), 4.38 (q, *J* = 7.1 Hz, 2H), 1.43 – 1.37 (m, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 165.7 (d, *J* = 254 Hz), 165.6, 132.0 (d, *J* = 8.8 Hz), 126.7 (d, *J* = 259 Hz), 115.3 (d, *J* = 22.6 Hz), 61.0, 14.2.

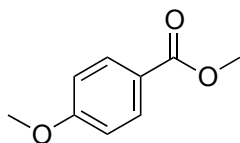


Isopropyl 4-fluorobenzoate (5c).

General procedure A was used at 50 °C overnight with 4-fluorobenzaldehyde (124.1 mg, 1 mmol) to yield the desired ester as a colorless oil (30.8 mg, 17%).

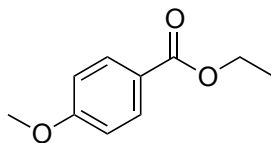
¹H NMR (500 MHz, CDCl₃) δ 8.34 – 7.67 (m, 2H), 7.09 (dd, *J* = 18.4, 9.7 Hz, 2H), 5.23 (dq, *J* = 12.5, 6.3 Hz, 1H), 1.46 – 1.25 (m, 6H).

¹³C NMR (126 MHz, CDCl₃) δ 165.3 (d, *J* = 254 Hz), 165.3, 132.2 (d, *J* = 10.1 Hz), 127.3 (d, *J* = 3.8 Hz), 115.5 (d, *J* = 21.4 Hz), 68.7, 22.1.



Methyl 4-methoxybenzoate (6a).¹⁴

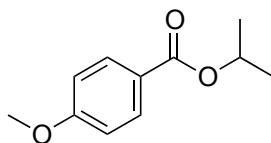
General procedure A was used at 50 °C overnight with 4-methoxybenzaldehyde (136.2 mg, 1 mmol) to yield the desired ester as a tan solid (142.6 mg, 86%), mp 47-49 °C(lit 48- 49°C). ¹H NMR (500 MHz, CDCl₃) δ 7.99 (d, *J* = 8.7 Hz, 2H), 6.92 (d, *J* = 8.7 Hz, 2H), 3.88 (s, 3H), 3.86 (s, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 166.9, 163.3, 131.6, 122.6, 113.6, 55.4, 51.8.



Ethyl 4-methoxybenzoate (6b).⁸

General procedure A was used at 50 °C overnight with 4-methoxybenzaldehyde (136.2 mg, 1 mmol) to yield the desired ester as a yellow oil (130.5 mg, 72%).

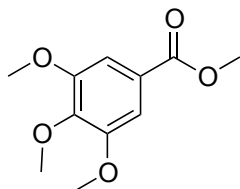
¹H NMR (500 MHz, CDCl₃) δ 7.99 (d, *J* = 8.9 Hz, 2H), 6.90 (d, *J* = 8.9 Hz, 2H), 4.33 (q, *J* = 7.1 Hz, 2H), 3.84 (d, *J* = 6.6 Hz, 3H), 1.37 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 166.5, 163.4, 131.7, 123.1, 113.7, 60.8, 55.5, 14.5.



Isopropyl 4-methoxybenzoate (6c).⁶

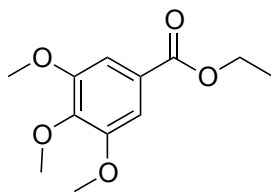
General procedure A was used at 50 °C overnight with 4-methoxybenzaldehyde (136.2 mg, 1 mmol) to yield the desired ester as a yellow oil (12.9 mg, 7%).

¹H NMR (500 MHz, CDCl₃) δ 8.00 (t, *J* = 9.1 Hz, 2H), 6.92 (t, *J* = 9.0 Hz, 2H), 5.22 (dt, *J* = 12.5, 6.2 Hz, 1H), 3.93 – 3.82 (m, 3H), 1.45 – 1.31 (m, 6H). ¹³C NMR (126 MHz, CDCl₃) δ 166.5, 163.4, 131.7, 123.1, 113.7, 60.8, 55.5, 14.5.



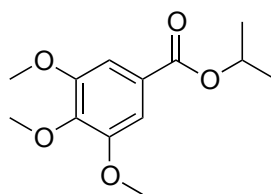
Methyl 3,4,5-trimethoxybenzoate (7a).¹⁵

General procedure A was used at 50 °C overnight with 3,4,5-trimethoxybenzaldehyde (196.2 mg, 1 mmol) to yield the desired ester as a white solid (160 mg, 71%), mp 82°C(lit. 81-82°C)¹⁶. ¹H NMR (500 MHz, CDCl₃) δ 7.30 (s, 2H), 3.91 (m, 12H). ¹³C NMR (126 MHz, CDCl₃) δ 166.9, 153.1, 142.3, 125.3, 106.9, 61.1, 56.4, 52.4.



Ethyl 3,4,5-trimethoxybenzoate (7b).⁷

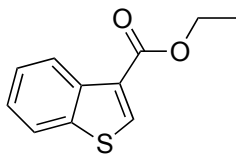
General procedure A was used at 50 °C overnight with 3,4,5-trimethoxybenzaldehyde (196.2 mg, 1 mmol) to yield the desired ester as a tan solid (167 mg, 70%), mp 59-60°C(lit. 52°C)¹⁶. ¹H NMR (500 MHz, CDCl₃) δ 7.28 (s, 2H), 4.35 (q, *J* = 7.1 Hz, 2H), 3.89 (d, *J* = 3.6 Hz, 9H), 1.38 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 166.1, 152.8, 142.0, 125.42, 106.7, 61.0, 60.8, 56.1, 14.3.



Isopropyl 3,4,5-trimethoxybenzoate (7c).

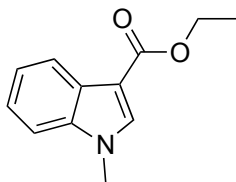
General procedure A was used at 50 °C overnight with 3,4,5-trimethoxybenzaldehyde (196.2 mg, 1 mmol) to yield the desired ester as a yellow oil (44 mg, 17%).

¹H NMR (500 MHz, CDCl₃) δ 7.29 (s, 2H), 5.24 (hept, *J* = 6.3 Hz, 1H), 3.91 (d, *J* = 7.3 Hz, 9H), 1.38 (d, *J* = 6.3 Hz, 6H). ¹³C NMR (126 MHz, CDCl₃) δ 165.9, 153.0, 126.1, 106.9, 68.7, 61.1, 56.4, 22.1.



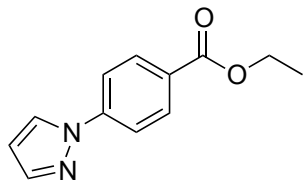
Ethyl benzo[*b*]thiophene-3-carboxylate (8b).

General procedure B was used at 50 °C overnight with benzo[*b*]thiophene-3-carbaldehyde (162.2 mg, 1 mmol) to yield the desired ester as a colorless oil (150 mg, 73%). ¹H NMR (500 MHz, CDCl₃) δ 8.60 (d, *J* = 8.2 Hz, 1H), 8.34 (s, 1H), 7.83 (d, *J* = 8.1 Hz, 1H), 7.46 (dd, *J* = 8.1, 7.2 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 1.41 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 163.0, 140.2, 136.9, 136.6, 127.6, 125.5, 125.1, 124.9, 122.6, 60.8, 14.6. HRMS calcd. for C₁₁H₁₁O₂S (MH⁺) 207.0480, found 207.0472.



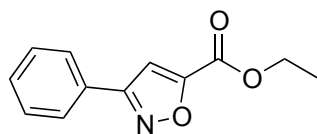
Ethyl 1-methyl-1*H*-indole-3-carboxylate (9b).¹⁸

General procedure B was used at 50 °C overnight with benzo[*b*]thiophene-3-carbaldehyde (159.2 mg, 1 mmol) to yield the desired ester as an off-white solid (78.1 mg, 38%), mp. 71-74°C (lit. 73-75°C)¹⁹. ¹H NMR (500 MHz, CDCl₃) δ 8.18 (dd, *J* = 6.4, 2.2 Hz, 1H), 7.79 (s, 1H), 7.37 – 7.33 (m, 1H), 7.32 – 7.26 (m, 2H), 4.38 (q, *J* = 7.1 Hz, 2H), 3.84 (s, 3H), 1.42 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 165.0, 137.1, 135.1, 126.6, 122.6, 121.7, 121.6, 109.7, 59.5, 33.2, 14.5.



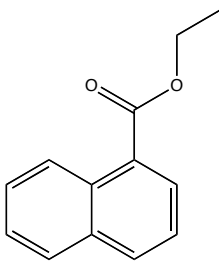
Ethyl 4-(1*H*-pyrazol-1-yl)benzoate (10b).

General procedure B was used at 50 °C overnight with 4-(1*H*-pyrazol-1-yl)benzaldehyde (172.2 mg, 1 mmol) to yield the desired ester as a white solid (26.1 mg, 12%), mp 62–64 °C. ¹H NMR (500 MHz, CDCl₃) δ 8.14 (d, *J* = 8.8 Hz, 2H), 8.01 (d, *J* = 2.4 Hz, 1H), 7.78 (dd, *J* = 10.5, 5.1 Hz, 3H), 6.57 – 6.47 (m, 1H), 4.40 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 166.1, 143.4, 142.10, 131.3, 128.3, 127.0, 118.4, 108.6, 61.3, 14.5. HRMS calcd. for C₁₂H₁₃N₂O₂ (M+H) 217.0977, found 217.0968.



Ethyl 3-phenylisoxazole-5-carboxylate (11b).

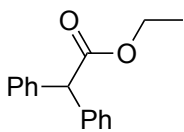
General procedure B was used at 50 °C overnight with 3-phenylisoxazole-5-carbaldehyde (173.2 mg, 1 mmol) to yield the desired ester as a white solid (134.5 mg, 63%), mp. 49–50 °C. ¹H NMR (500 MHz, CDCl₃) δ 7.92 – 7.73 (m, 2H), 7.48 (dd, *J* = 3.8, 2.6 Hz, 3H), 7.25 (s, 1H), 4.46 (q, *J* = 7.1 Hz, 2H), 1.43 (q, *J* = 6.9 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 163.1, 161.1, 157.0, 130.7, 129.2, 128.1, 127.0, 107.5, 62.5, 14.3. HRMS calcd. for C₁₂H₁₂NO₃ (M+H) 218.0817, found 218.0820.



Ethyl 1-naphthoate (12b).²⁰

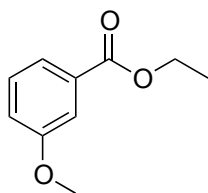
General procedure B was used at 50 °C overnight with 1-naphthaldehyde (156.2 mg, 1 mmol) to yield the desired ester as a yellow oil (160.9 mg, 80%).

¹H NMR (500 MHz, CDCl₃) δ 8.90 (d, *J* = 8.7 Hz, 1H), 8.17 (d, *J* = 7.2 Hz, 1H), 8.00 (d, *J* = 8.1 Hz, 1H), 7.87 (d, *J* = 8.1 Hz, 1H), 7.65 – 7.58 (m, 1H), 7.50 (m, 2H), 4.47 (q, *J* = 7.1 Hz, 2H), 1.45 (t, *J* = 7.1 Hz, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 167.8, 134.0, 133.4, 131.5, 130.2, 128.7, 127.9, 127.7, 126.3, 126.0, 124.7, 61.2, 14.6.



Ethyl 2,2-diphenylacetate (13b).²¹

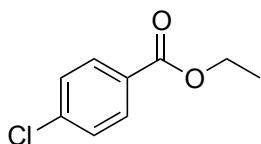
General procedure B was used at 50 °C overnight with 4-(trifluoromethyl)benzaldehyde (240.3 mg, 1 mmol, 93% pure) to yield the desired ester as a colorless oil (80.6 mg, 33% yield, 89% pure). ¹H NMR (500 MHz, CDCl₃) δ 7.31 (t, *J* = 4.2, 8H), 7.28 – 7.23 (m, 2H), 5.01 (s, 1H), 4.21 (q, *J* = 7.1, 2H), 1.25 (t, *J* = 7.1, 3H). ¹³C NMR (126 MHz, CDCl₃) δ 172.68, 138.97, 128.79, 128.77, 127.41, 61.38, 57.31, 14.33.



Ethyl 3-methoxybenzoate(14b).⁵

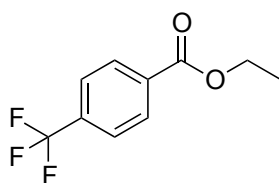
General procedure B was used at 50 °C overnight with 3-methoxybenzaldehyde (136.2 mg, 1 mmol) to yield the desired ester as a colorless oil (129.2 mg, 53%).

^1H NMR (500 MHz, CDCl_3) δ 7.65 – 7.62 (m, 1H), 7.56 (dd, J = 2.5, 1.5 Hz, 1H), 7.33 (t, J = 7.9 Hz, 1H), 7.08 (m, 1H), 4.37 (q, J = 7.1 Hz, 2H), 3.84 (s, 3H), 1.39 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 166.6, 159.7, 131.9, 129.5, 122.0, 119.4, 114.1, 61.2, 55.5, 14.4.



Ethyl 4-chlorobenzoate (15b).⁸

General procedure B was used at 50 °C overnight with 4-chlorobenzaldehyde (136.2 mg, 1 mmol) to yield the desired ester as a colorless oil (9.1 mg, 5%). ^1H NMR (500 MHz, CDCl_3) δ 8.04 – 7.94 (m, 2H), 7.45 – 7.38 (m, 2H), 4.39 (m, 2H), 1.45 – 1.36 (m, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 165.9, 139.4, 131.1, 129.1, 128.8, 61.4, 14.4.

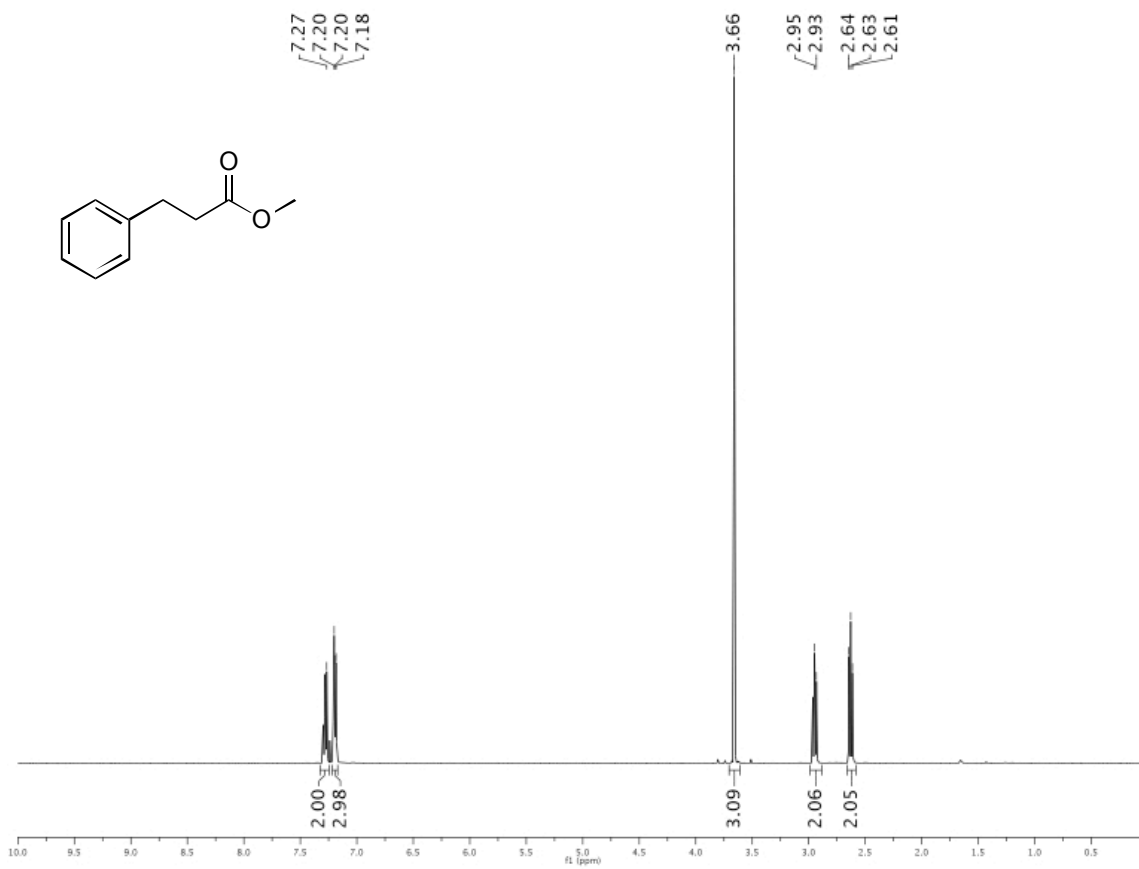


Ethyl 4-(trifluoromethyl)benzoate (16b).²²

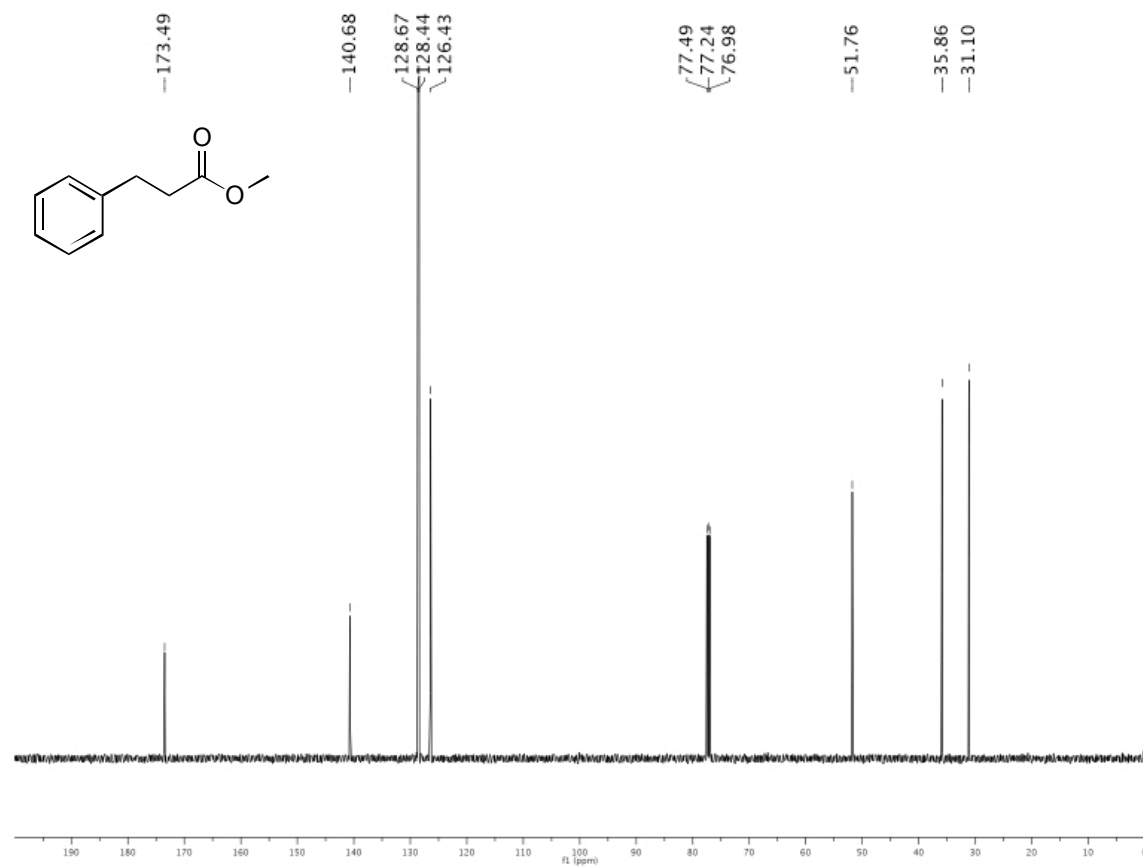
General procedure B was used at 50 °C overnight with 4-(trifluoromethyl)benzaldehyde (174.1 mg, 1 mmol) to yield the desired ester as a colorless oil (123 mg, 69%). ^1H NMR (500 MHz, CDCl_3) δ 8.16 (d, J = 8.1 Hz, 2H), 7.70 (d, J = 8.2 Hz, 2H), 4.42 (q, J = 7.1 Hz, 2H), 1.42 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 165.2, 133.6, 129.8, 125.2, 125.16, 125.13, 125.10, 61.3, 14.0.

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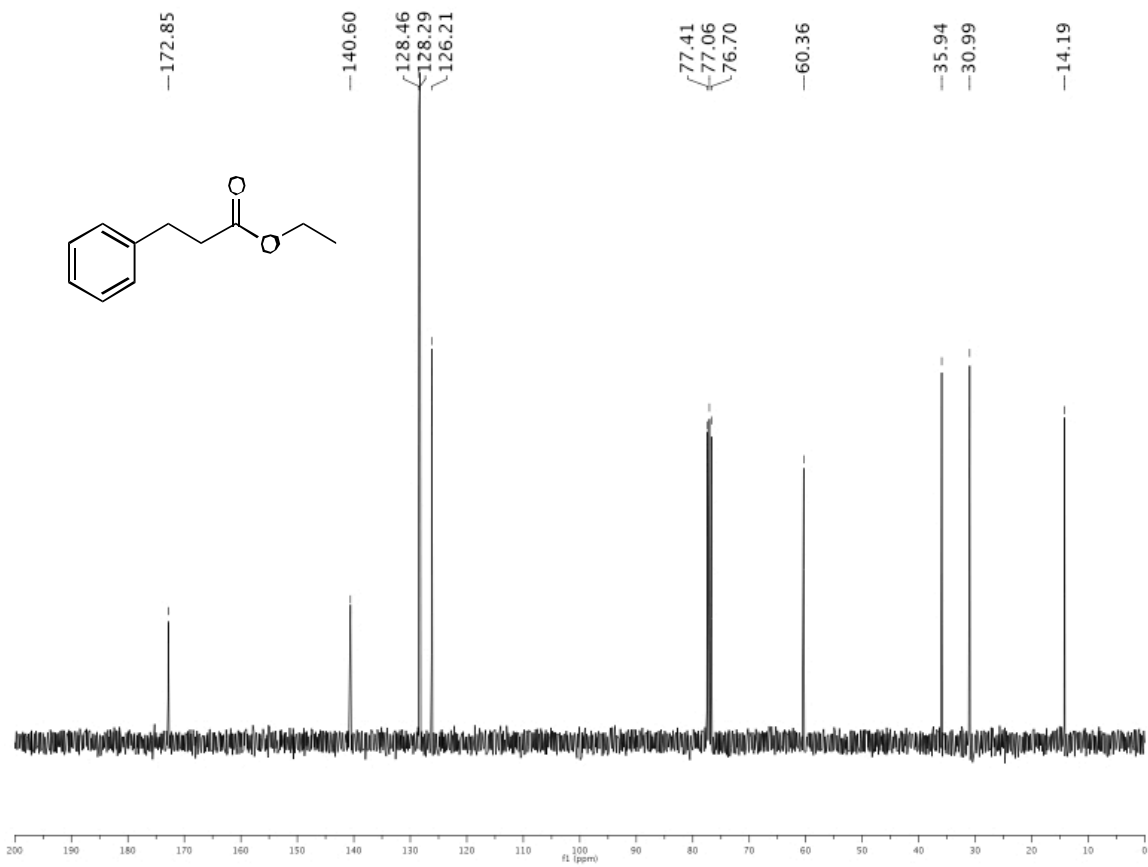
¹H NMR (500 MHz, CDCl₃) of methyl 3-phenylpropanoate (Table 1, entry 1a).



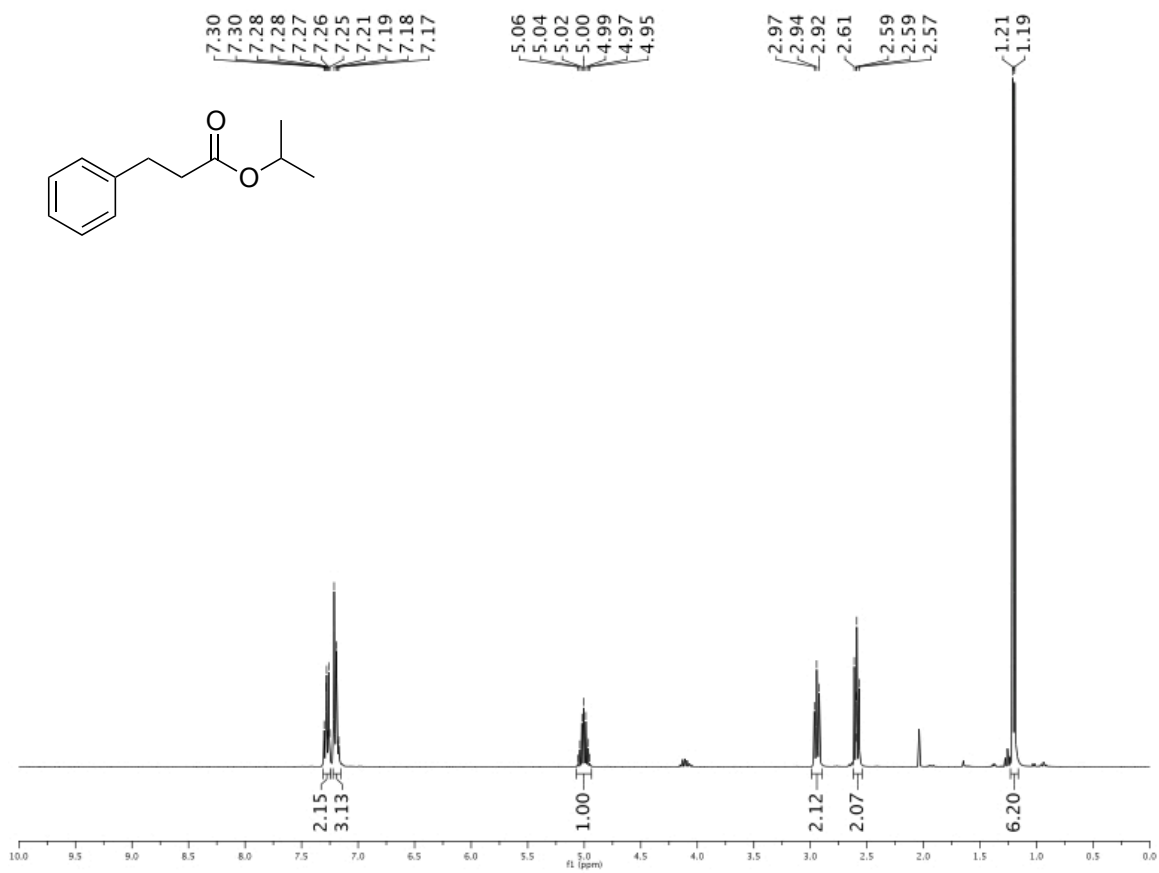
¹³C NMR (126 MHz, CDCl₃) of methyl 3-phenylpropanoate (Table 1, entry 1a).



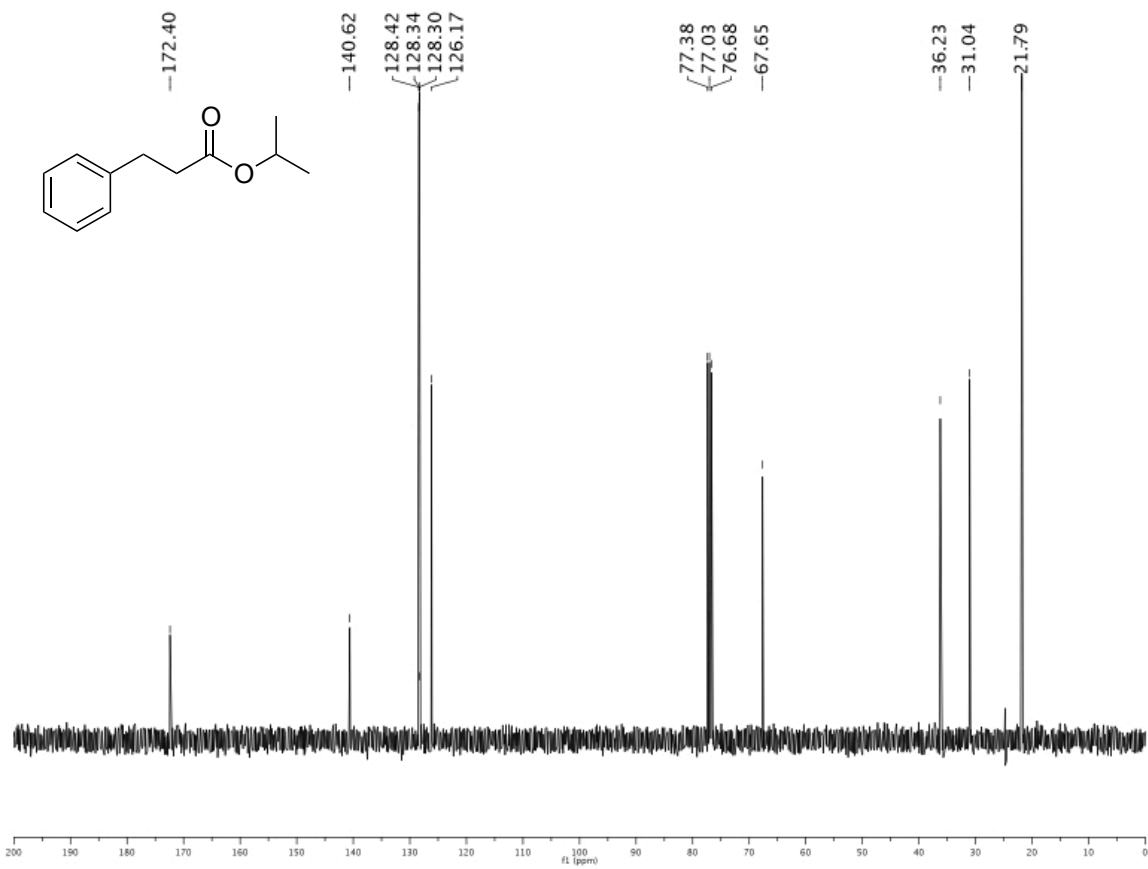
¹H NMR (500 MHz, CDCl₃) of ethyl 3-phenylpropanoate (Table 1, entry 1b).



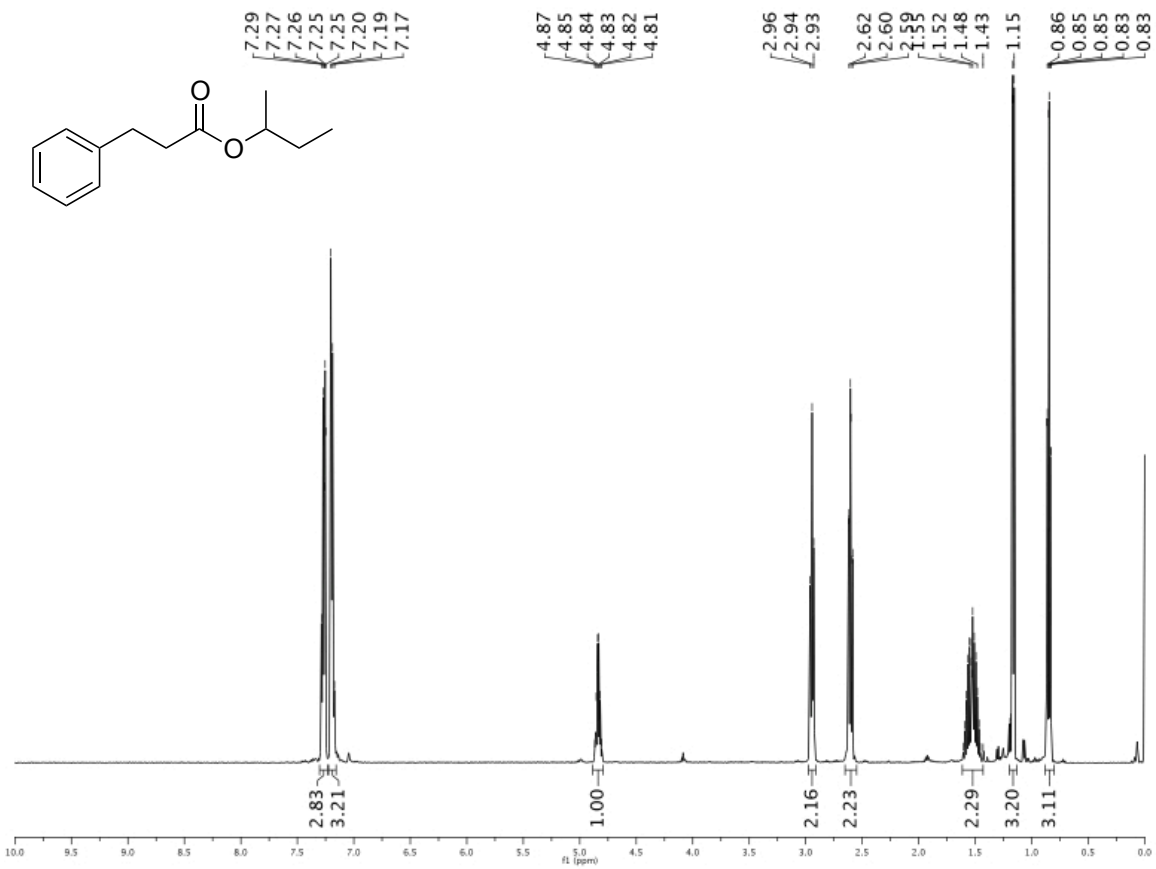
¹³C NMR (126 MHz, CDCl₃) of ethyl 3-phenylpropanoate (Table 1, entry 1b).



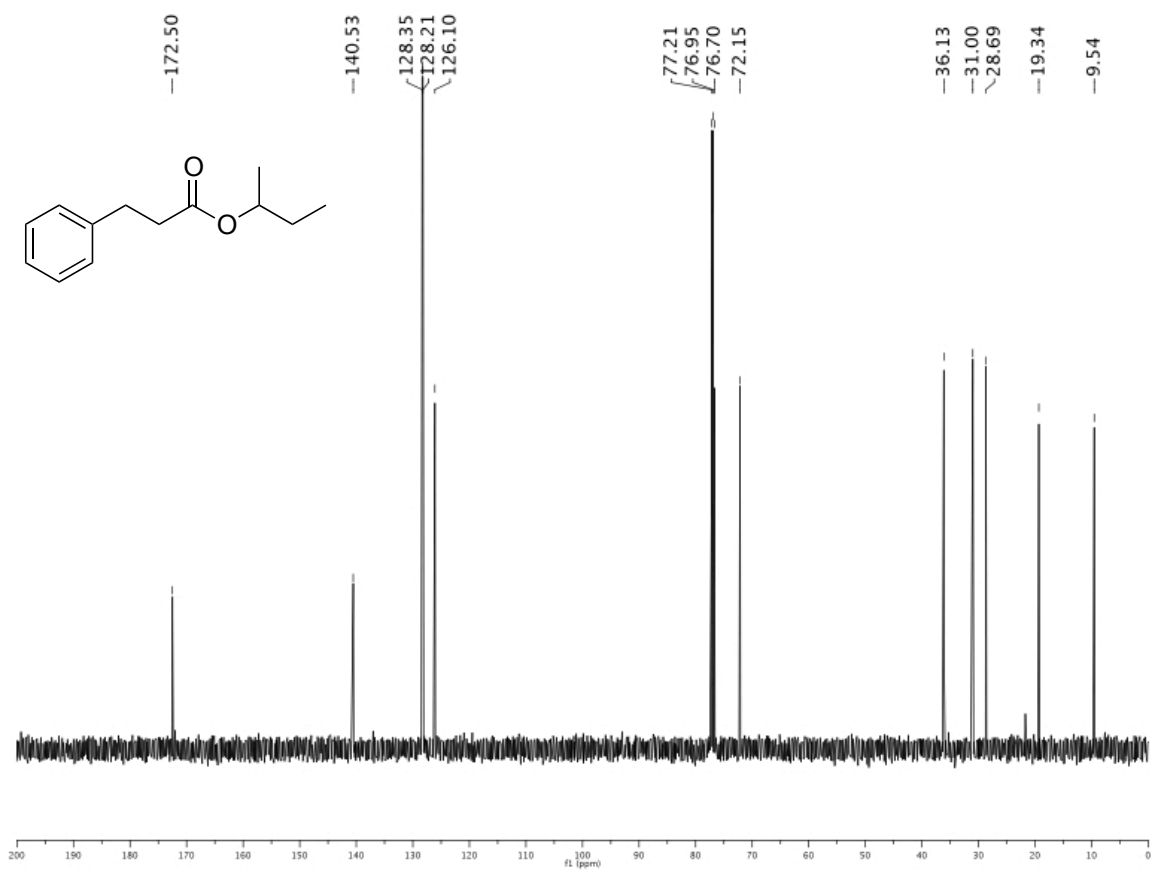
^1H NMR (500 MHz, CDCl_3) of isopropyl 3-phenylpropanoate (Table 1, entry 1c).



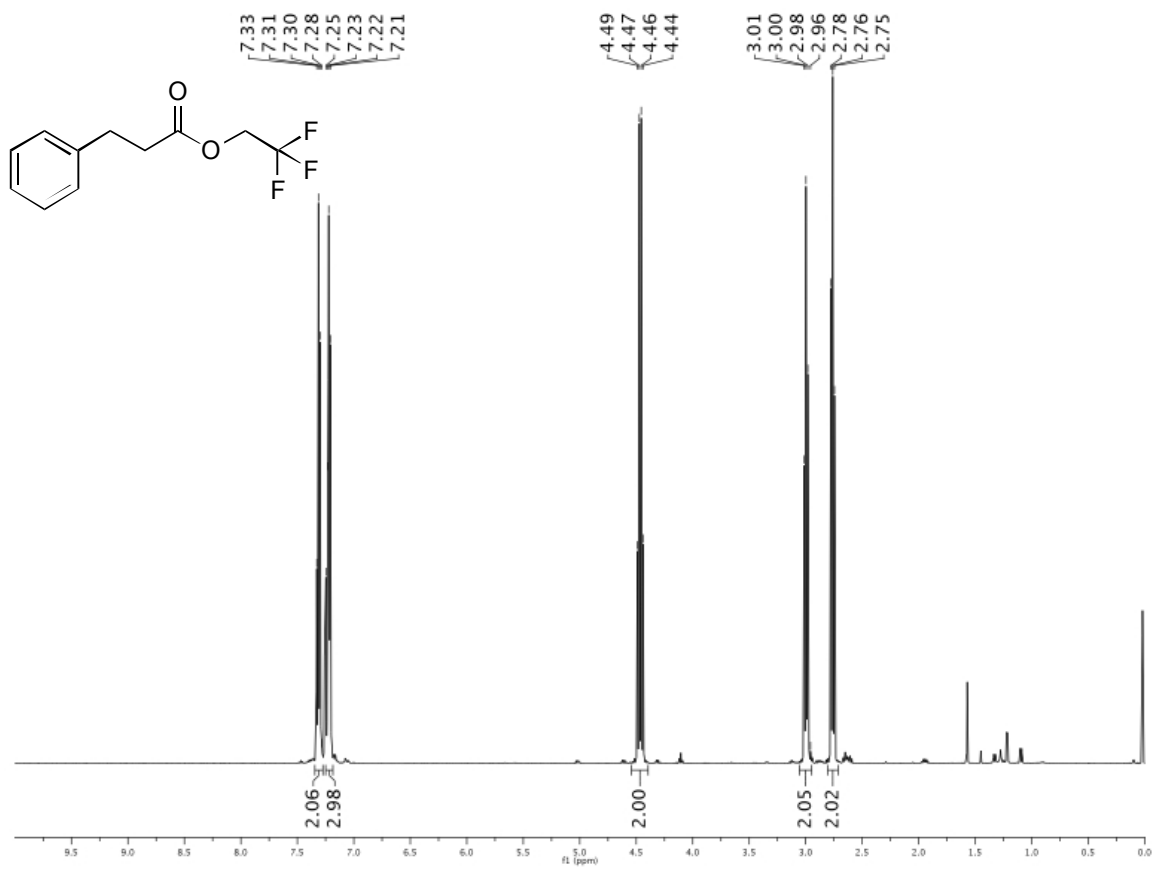
¹³C NMR (126 MHz, CDCl₃) of isopropyl 3-phenylpropanoate (Table 1, entry 1c).



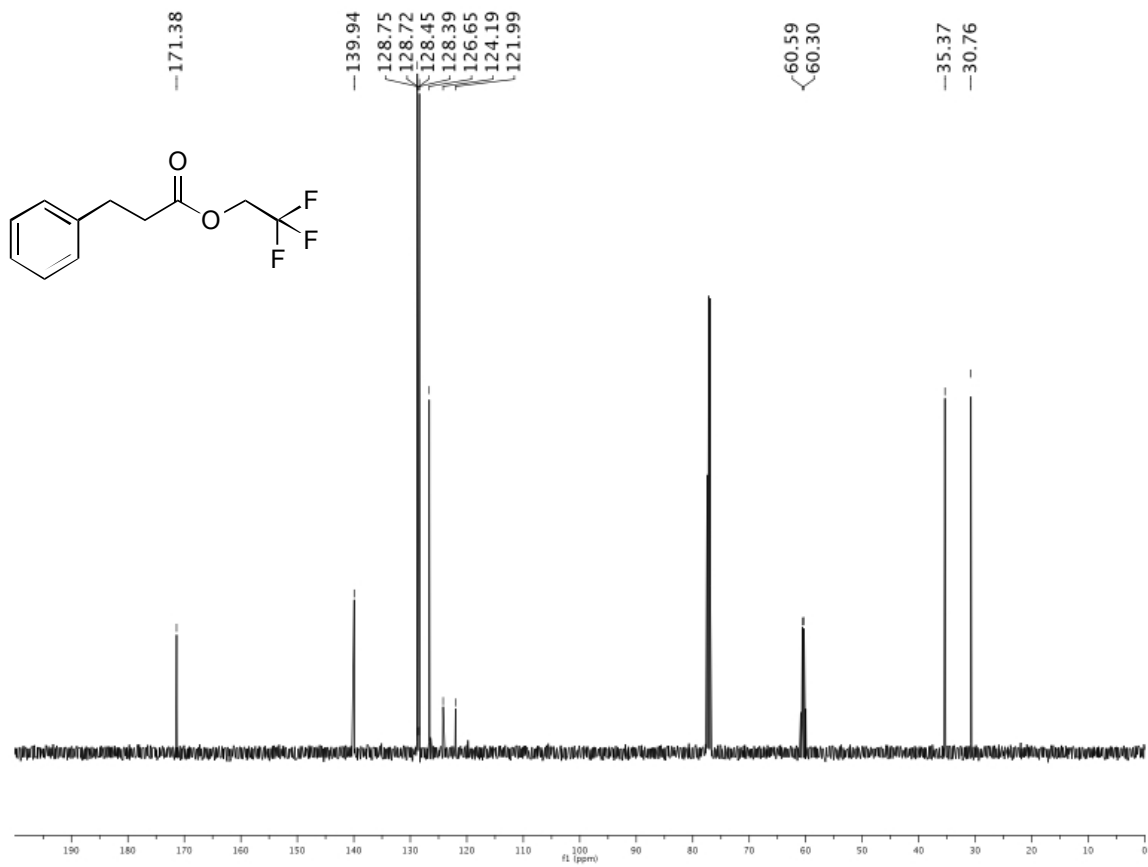
^1H NMR (500 MHz, CDCl_3) of sec-butyl 3-phenylpropanoate (Table 1, entry 1e).



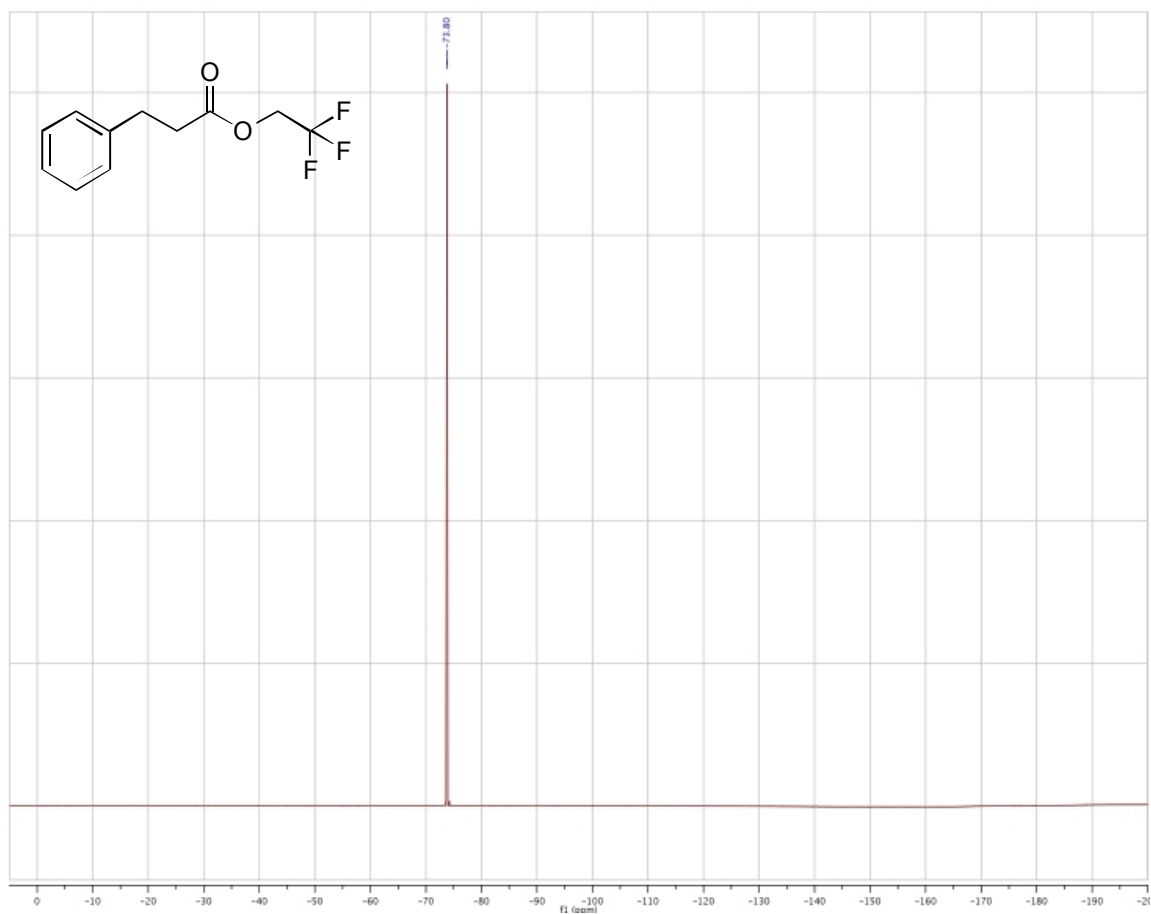
¹³C NMR (126 MHz, CDCl₃) of sec-butyl 3-phenylpropanoate (Table 1, entry 1e).



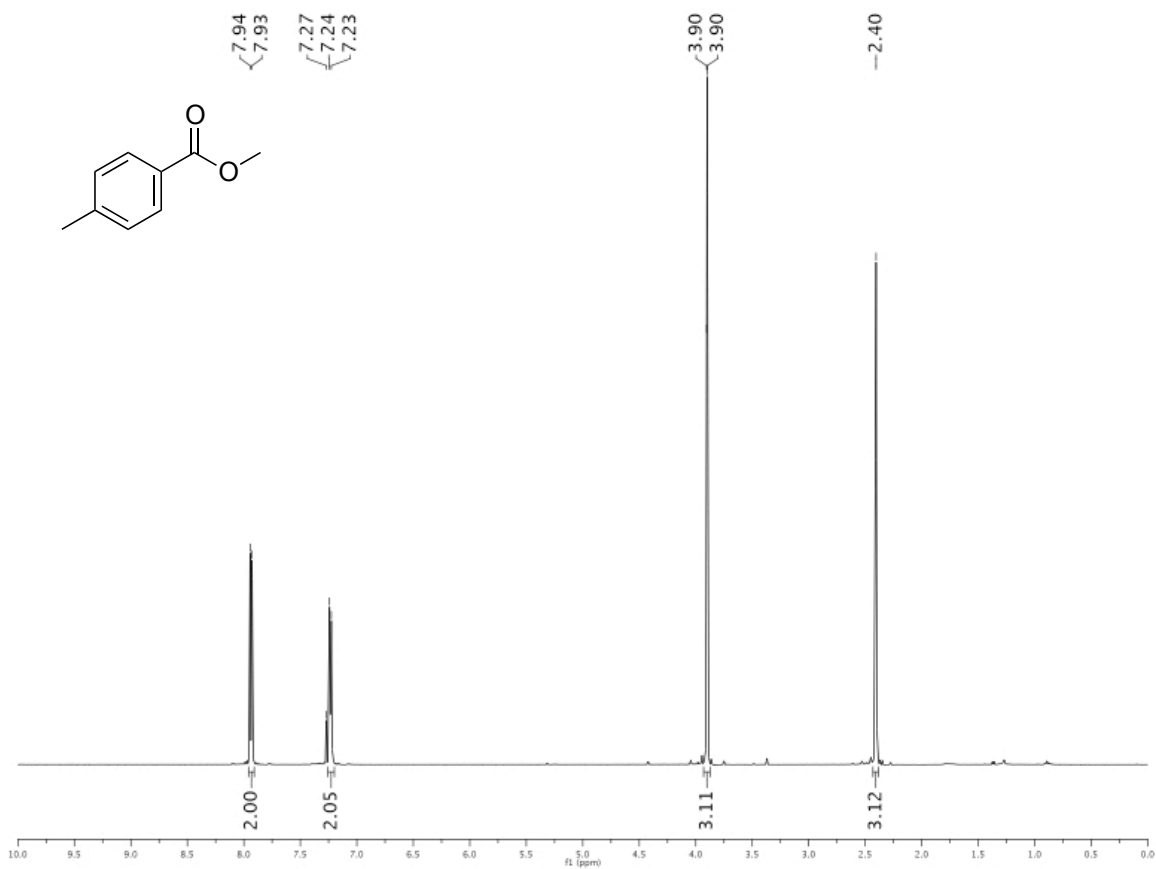
¹H NMR (500 MHz, CDCl₃) of 2,2,2-Trifluoroethyl 3-phenylpropanoate (Table 1, entry 1f).



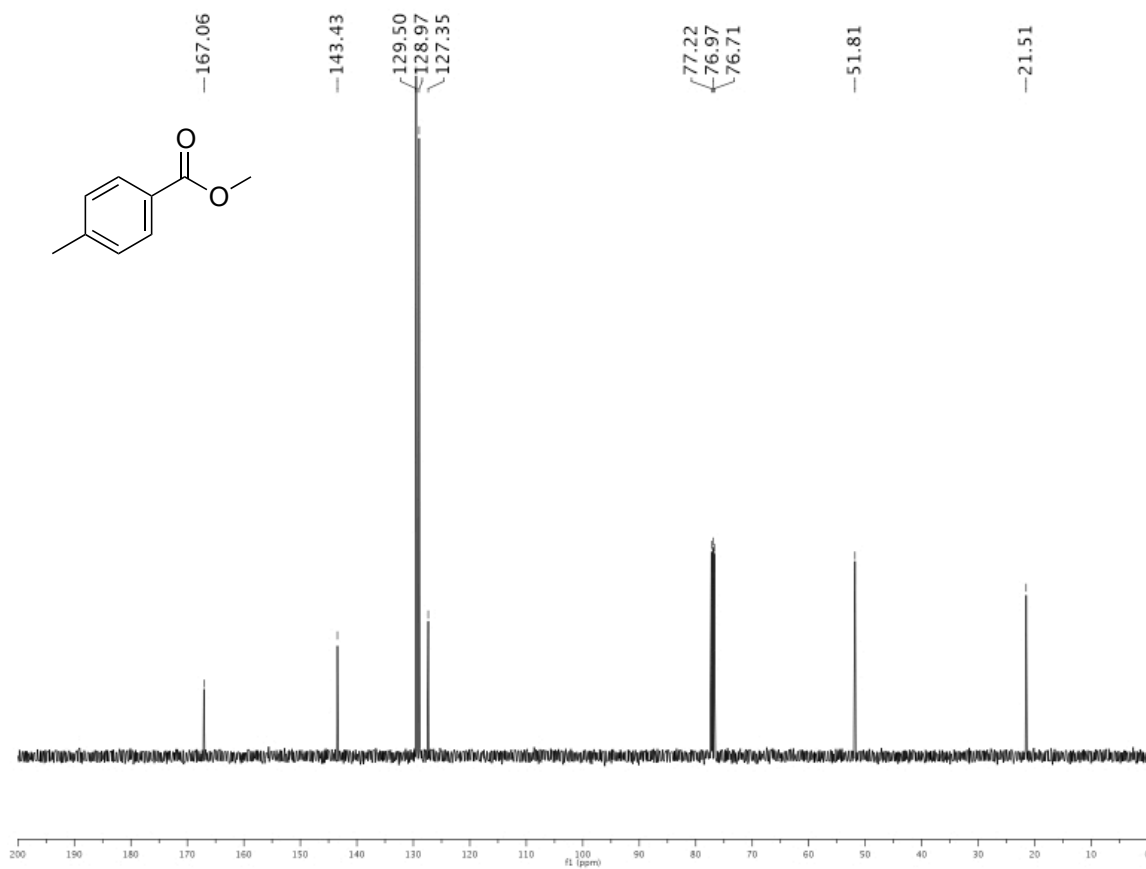
¹³C NMR (126 MHz, CDCl₃) of 2,2,2-Trifluoroethyl 3-phenylpropanoate (Table 1, entry 1f).



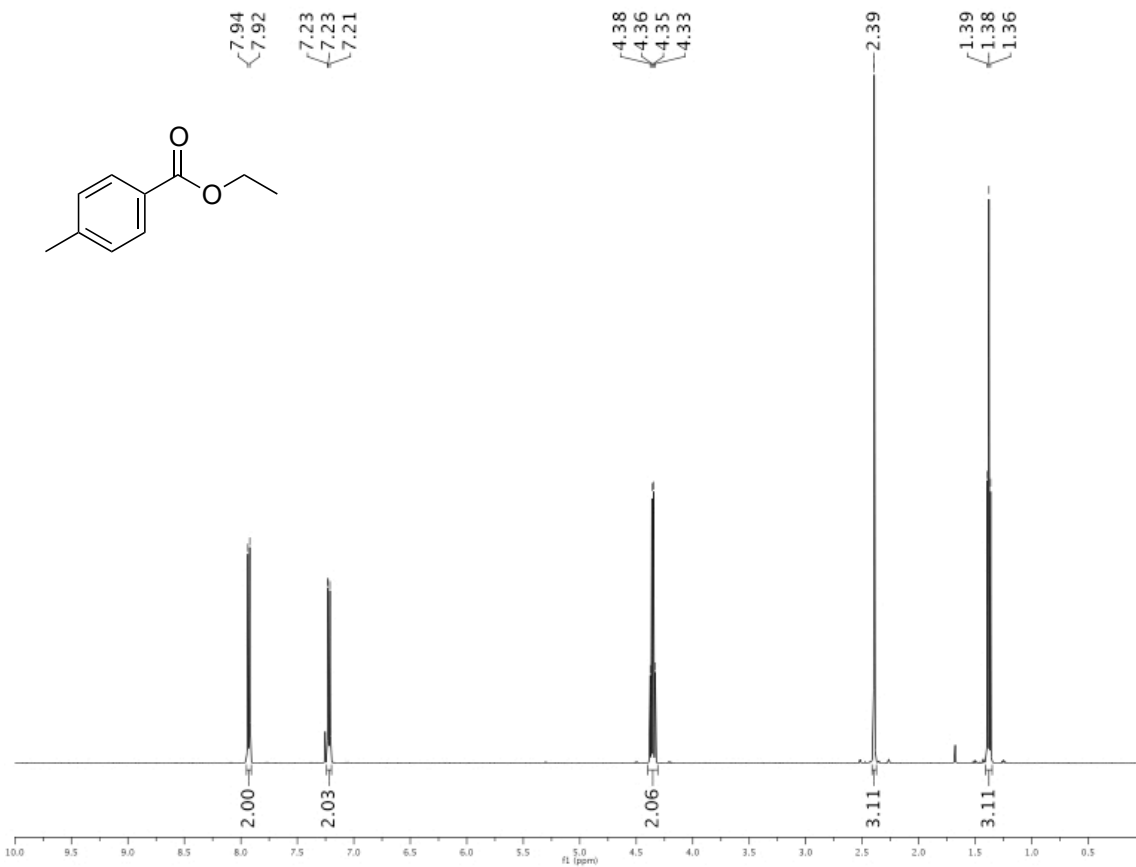
^{19}F NMR (471 MHz, CDCl_3) of 2,2,2-Trifluoroethyl 3-phenylpropanoate (Table 1, entry 1f).



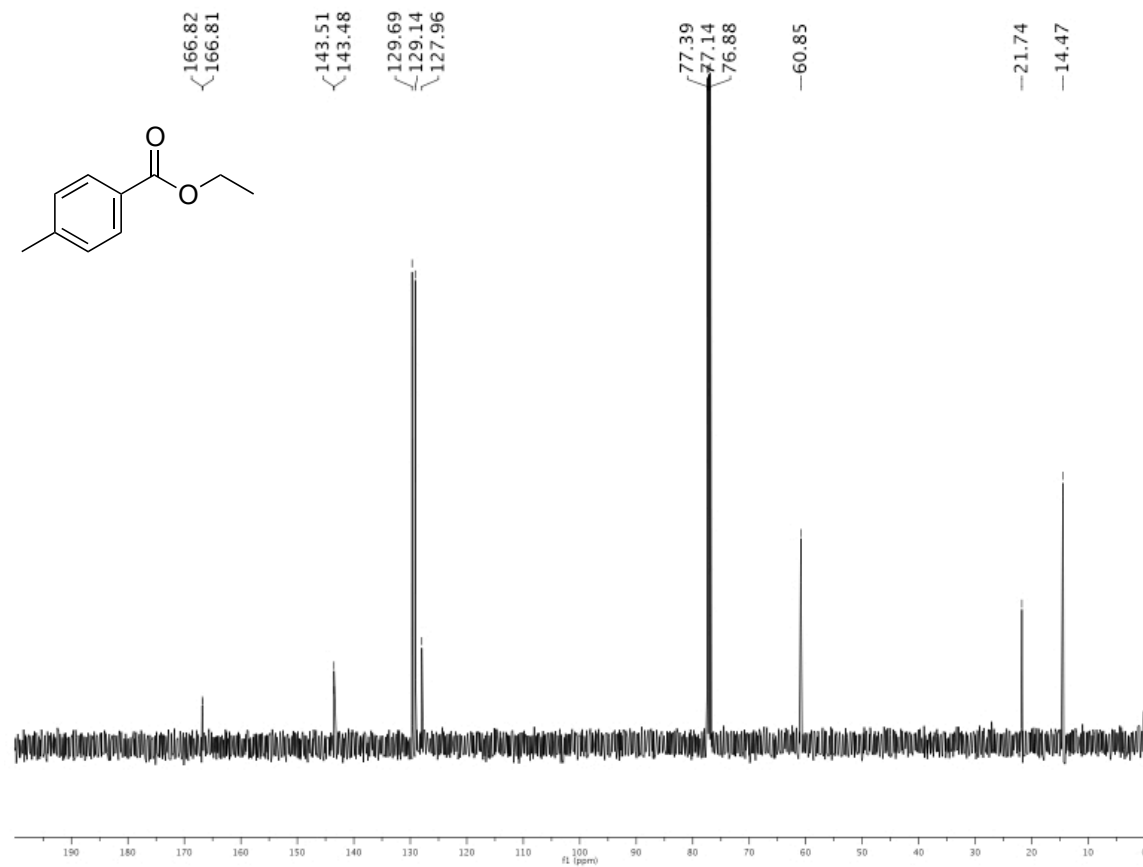
¹H NMR (500 MHz, CDCl₃) of methyl 4-methylbenzoate (Table 2, entry 2a).



¹³C NMR (126 MHz, CDCl₃) of methyl 4-methylbenzoate (Table 2, entry 2a).



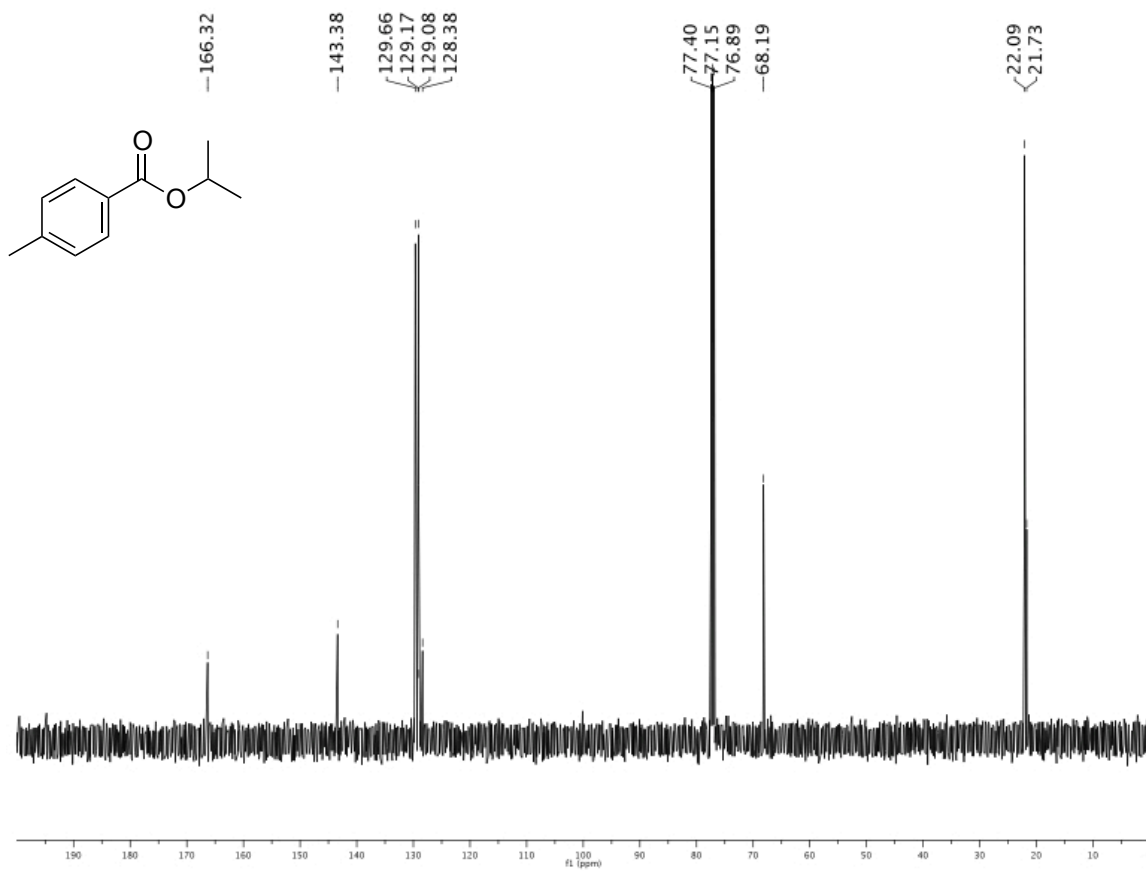
¹H NMR (500 MHz, CDCl₃) of ethyl 4-methylbenzoate (Table 2, entry 2b).



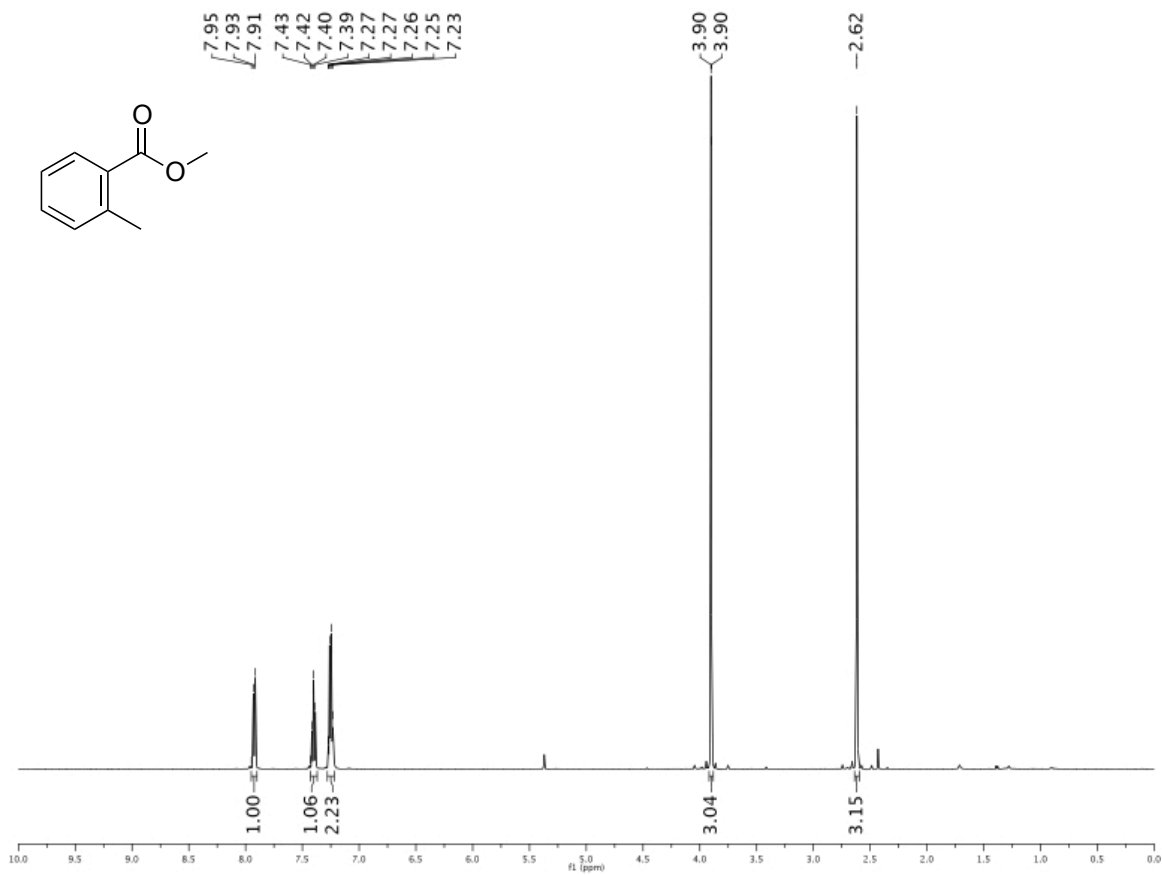
¹³C NMR (126 MHz, CDCl₃) of ethyl 4-methylbenzoate (Table 2, entry 2b).



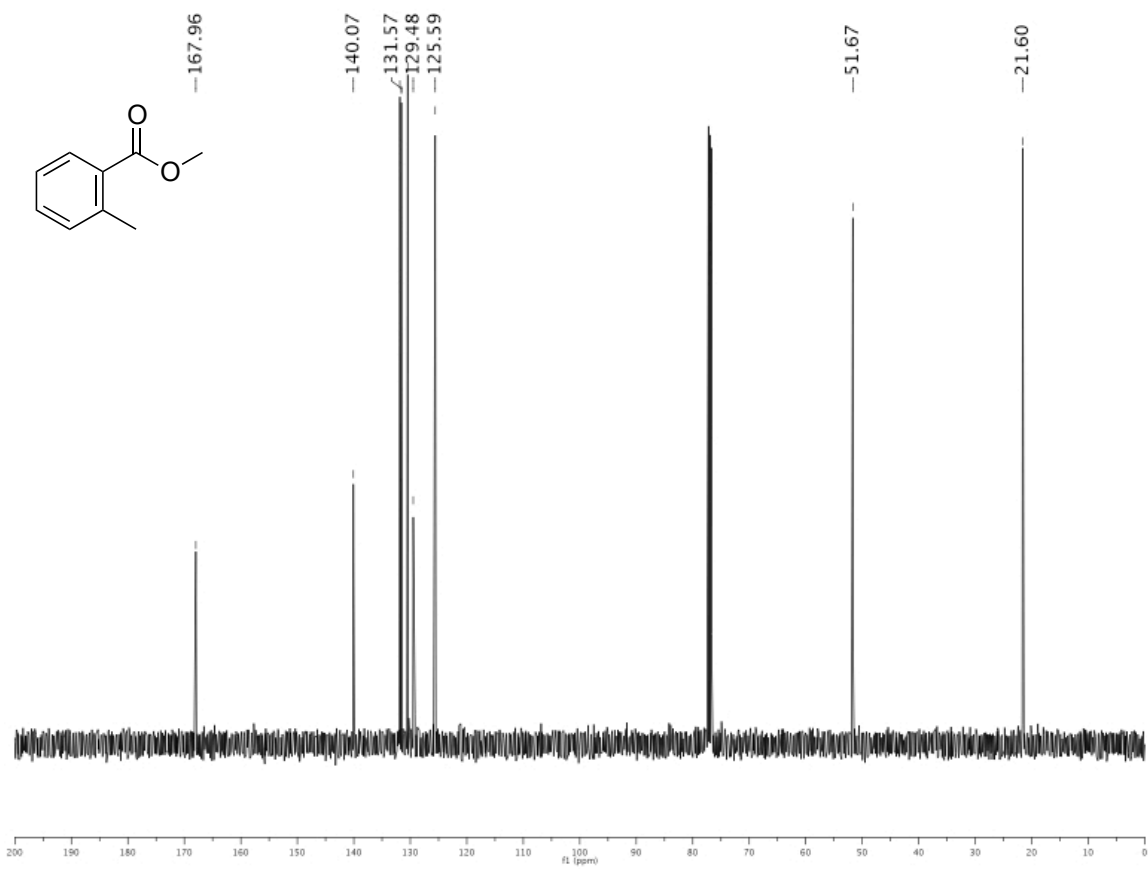
¹H NMR (500 MHz, CDCl₃) of isopropyl 4-methylbenzoate (Table 2, entry 2c).



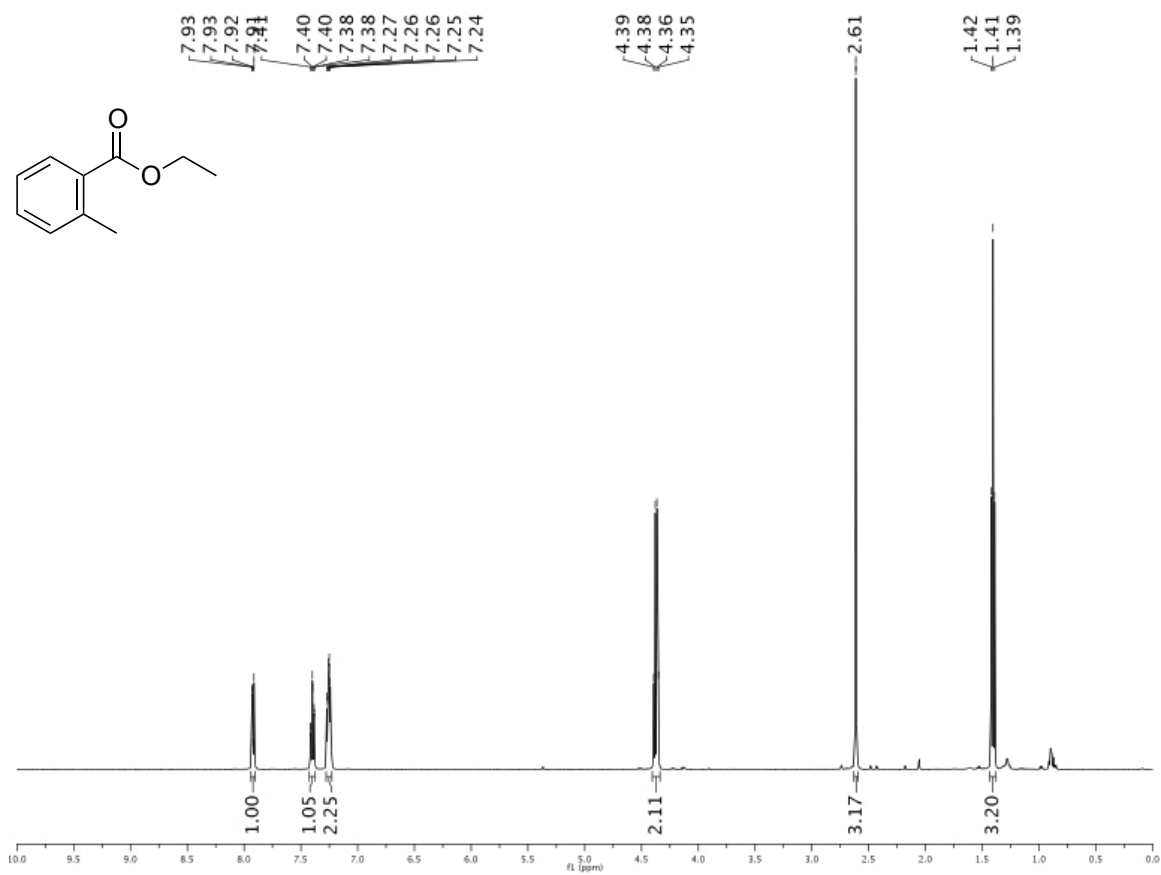
^{13}C NMR (126 MHz, CDCl_3) of isopropyl 4-methylbenzoate (Table 2, entry 2c).



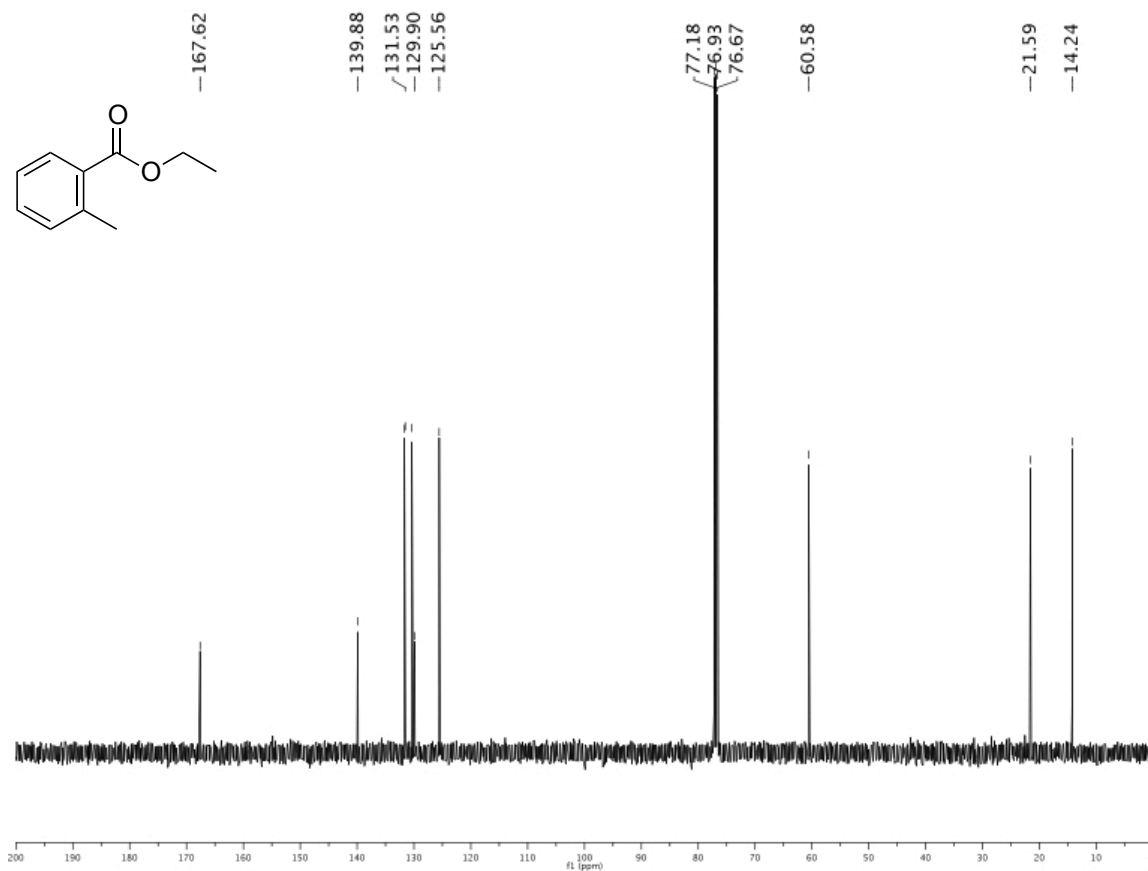
¹H NMR (500 MHz, CDCl₃) of methyl 2-methylbenzoate (Table 2, entry 3a).



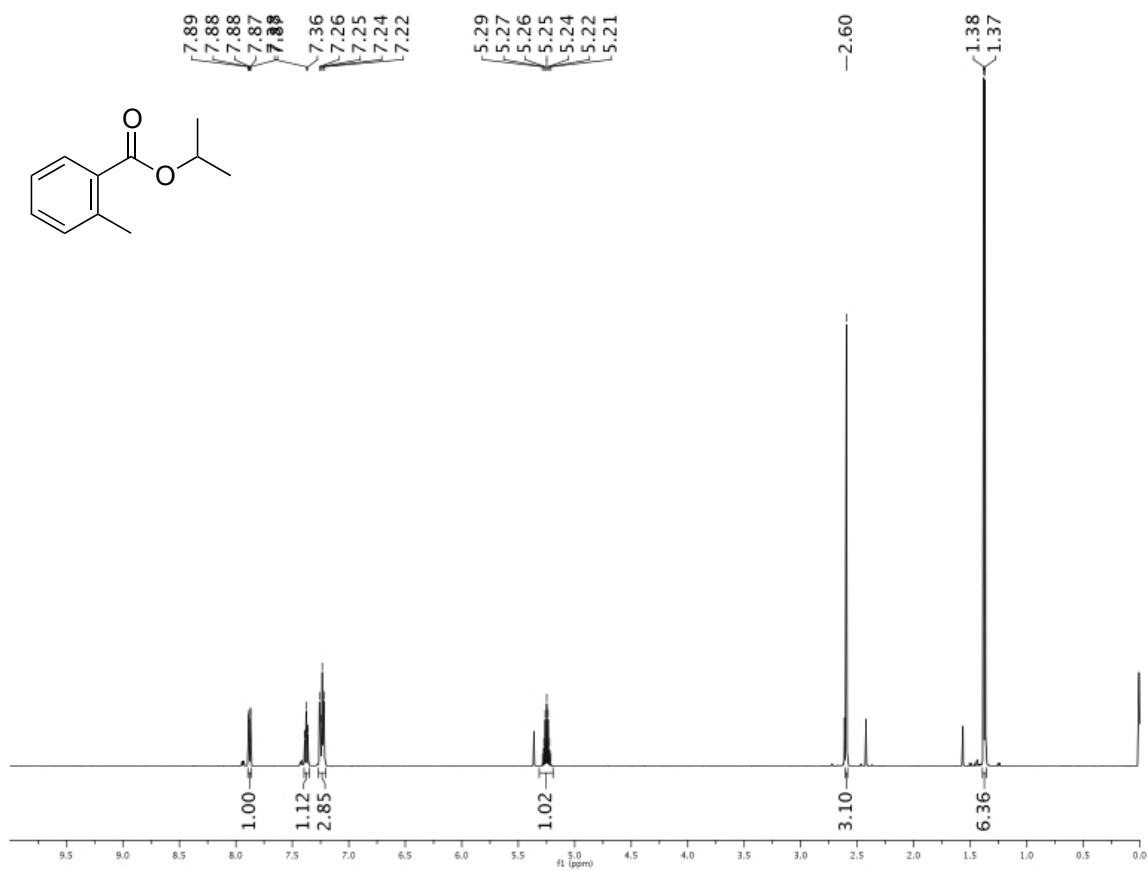
¹³C NMR (126 MHz, CDCl₃) of methyl 2-methylbenzoate (Table 2, entry 3a).



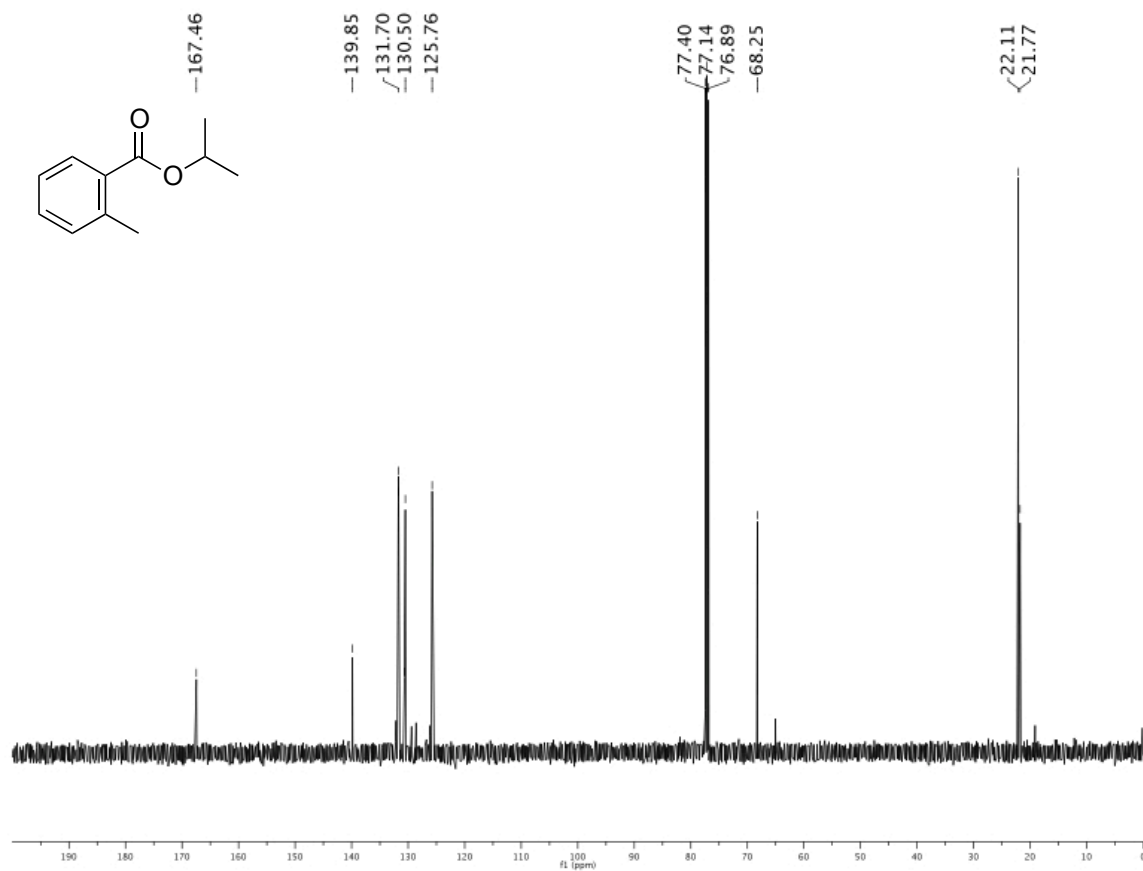
¹H NMR (500 MHz, CDCl₃) of ethyl 2-methylbenzoate (Table 2, entry 3b).



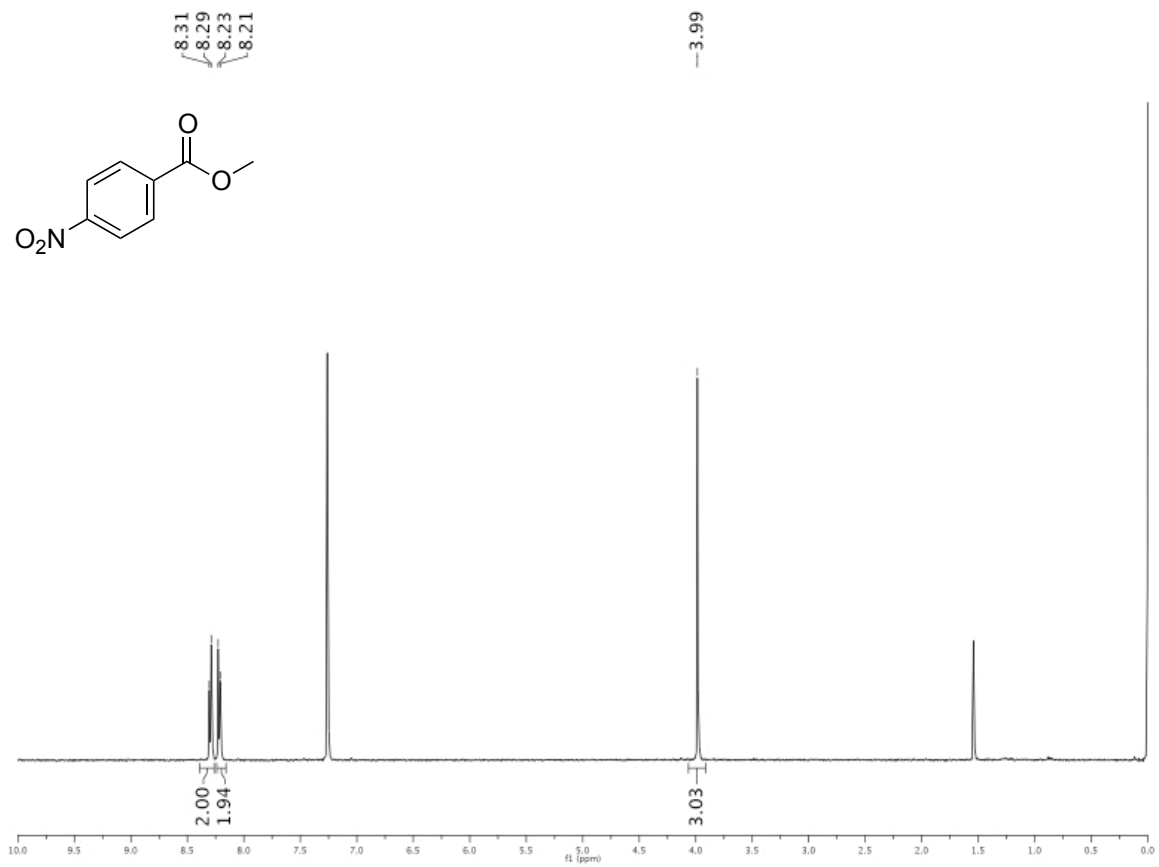
¹³C NMR (126 MHz, CDCl₃) of ethyl 2-methylbenzoate (Table 2, entry 3b).



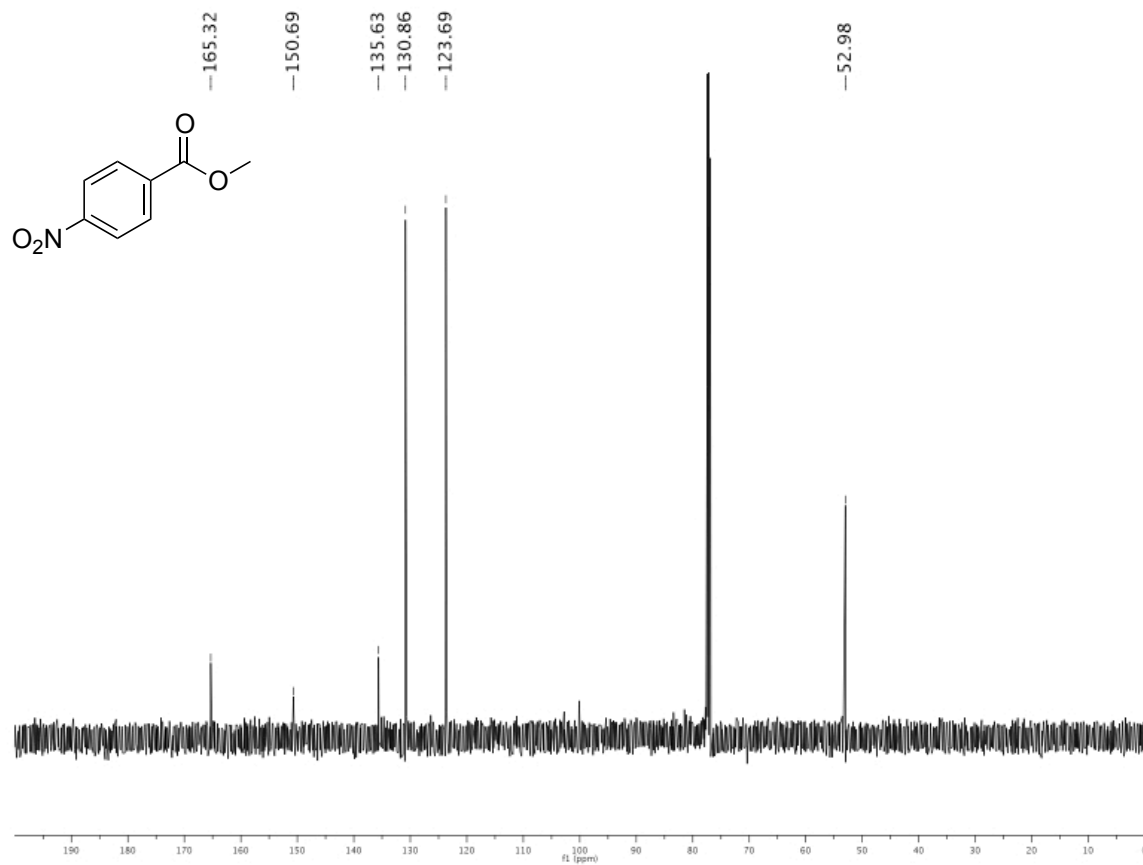
^1H NMR (500 MHz, CDCl_3) of isopropyl 2-methylbenzoate (Table 2, entry 3c).



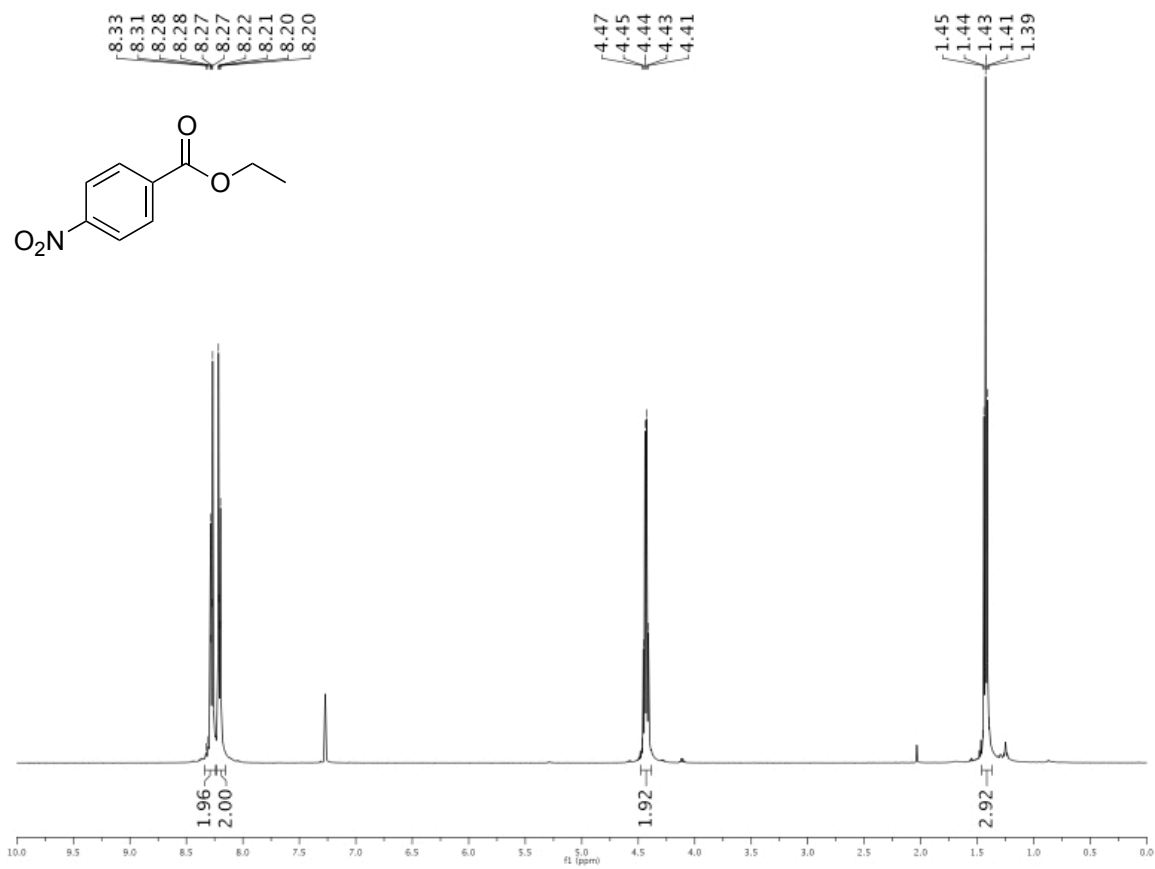
¹³C NMR (126 MHz, CDCl₃) of isopropyl 2-methylbenzoate (Table 2, entry 3c).



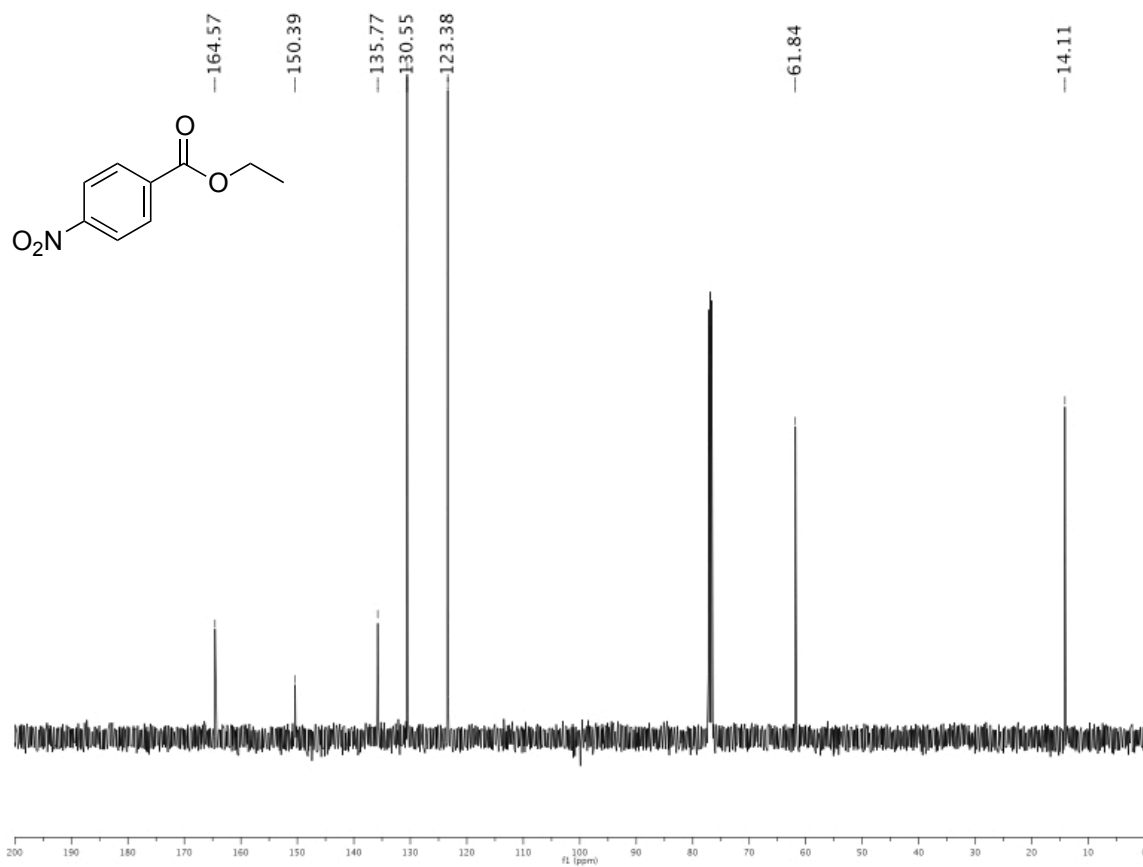
¹H NMR (500 MHz, CDCl₃) of methyl 4-nitrobenzoate (Table 2, entry 4a).



¹³C NMR (126 MHz, CDCl₃) of methyl 4-nitrobenzoate (Table 2, entry 4a).



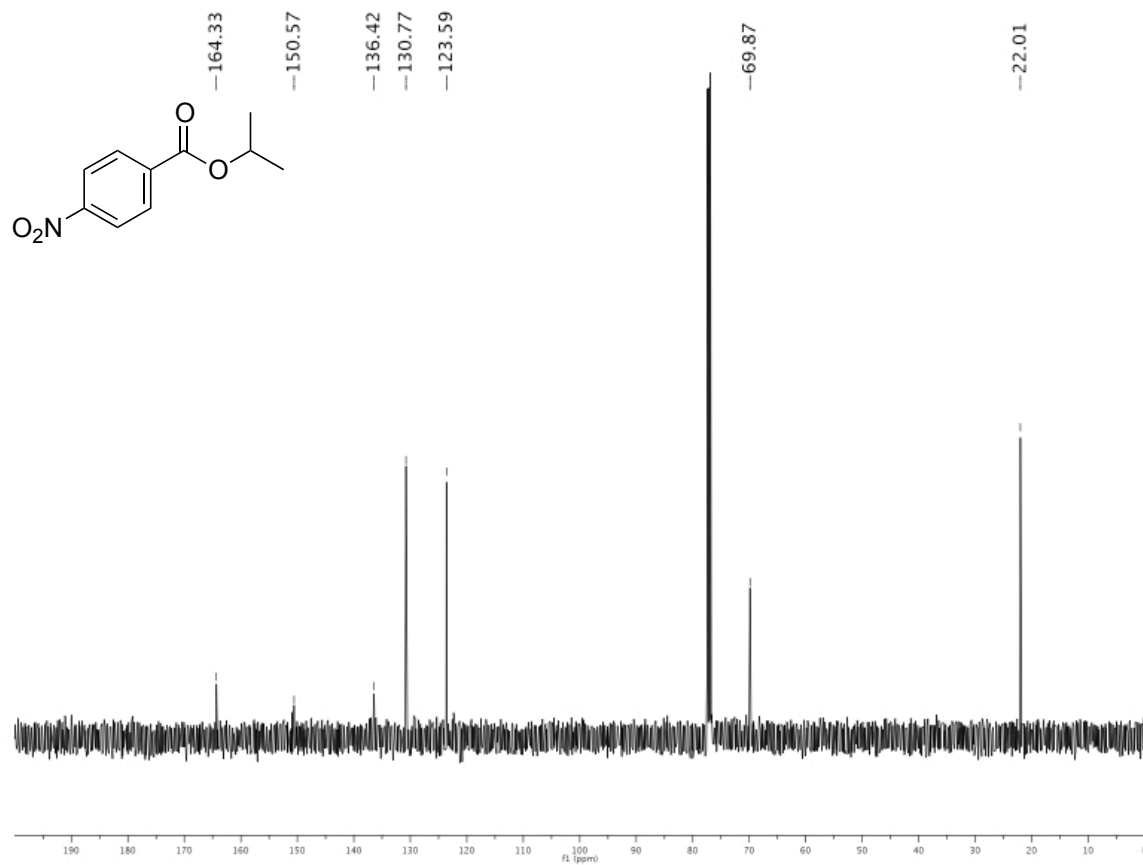
¹H NMR (500 MHz, CDCl₃) of ethyl 4-nitrobenzoate (Table 2, entry 4b).



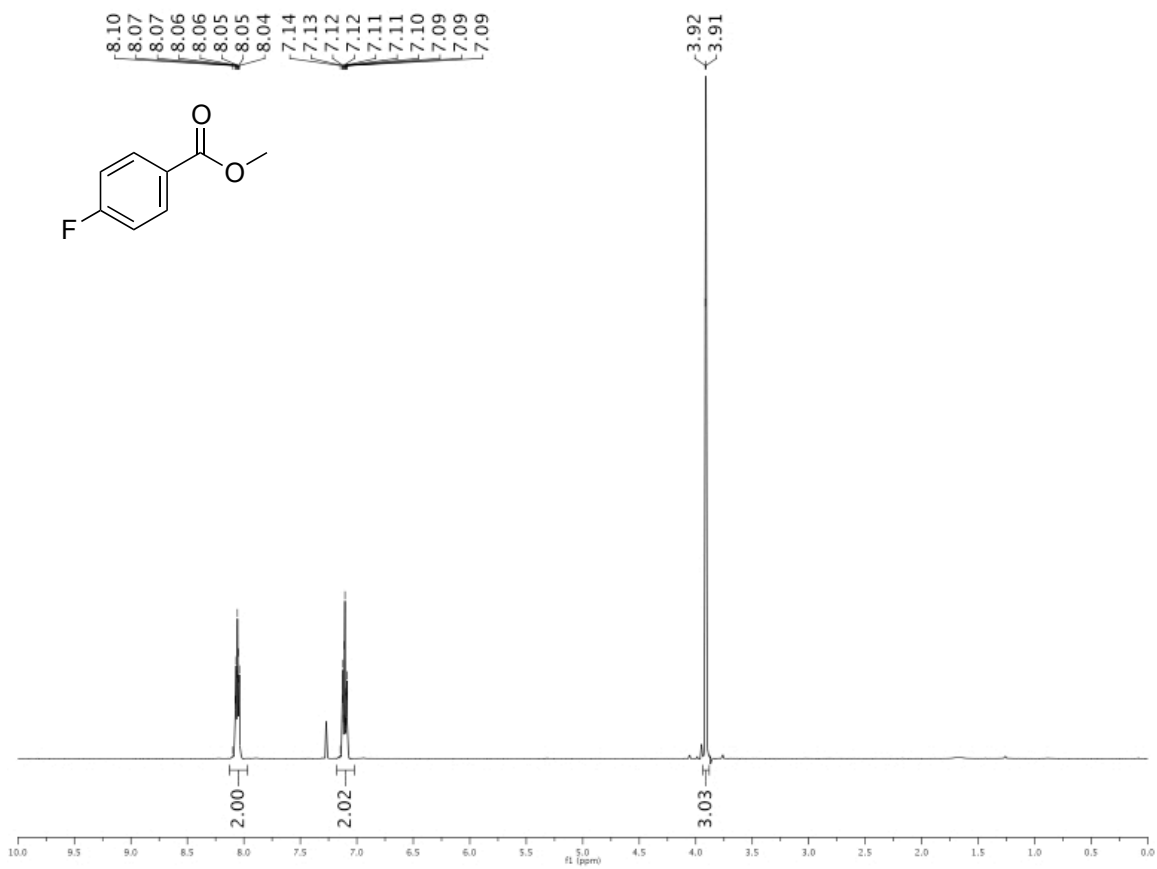
¹³C NMR (126 MHz, CDCl₃) of ethyl 4-nitrobenzoate (Table 2, entry 4b).



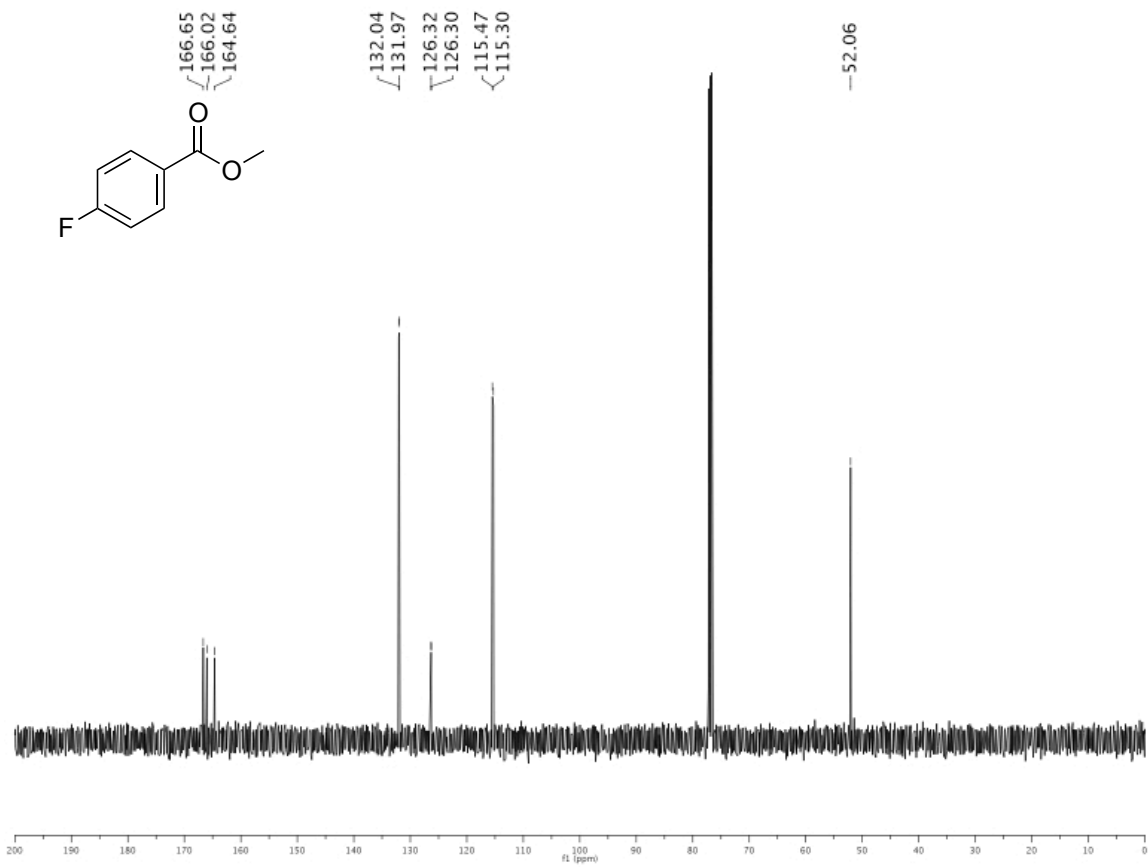
¹H NMR (500 MHz, CDCl₃) of isopropyl 4-nitrobenzoate (Table 2, entry 4c).



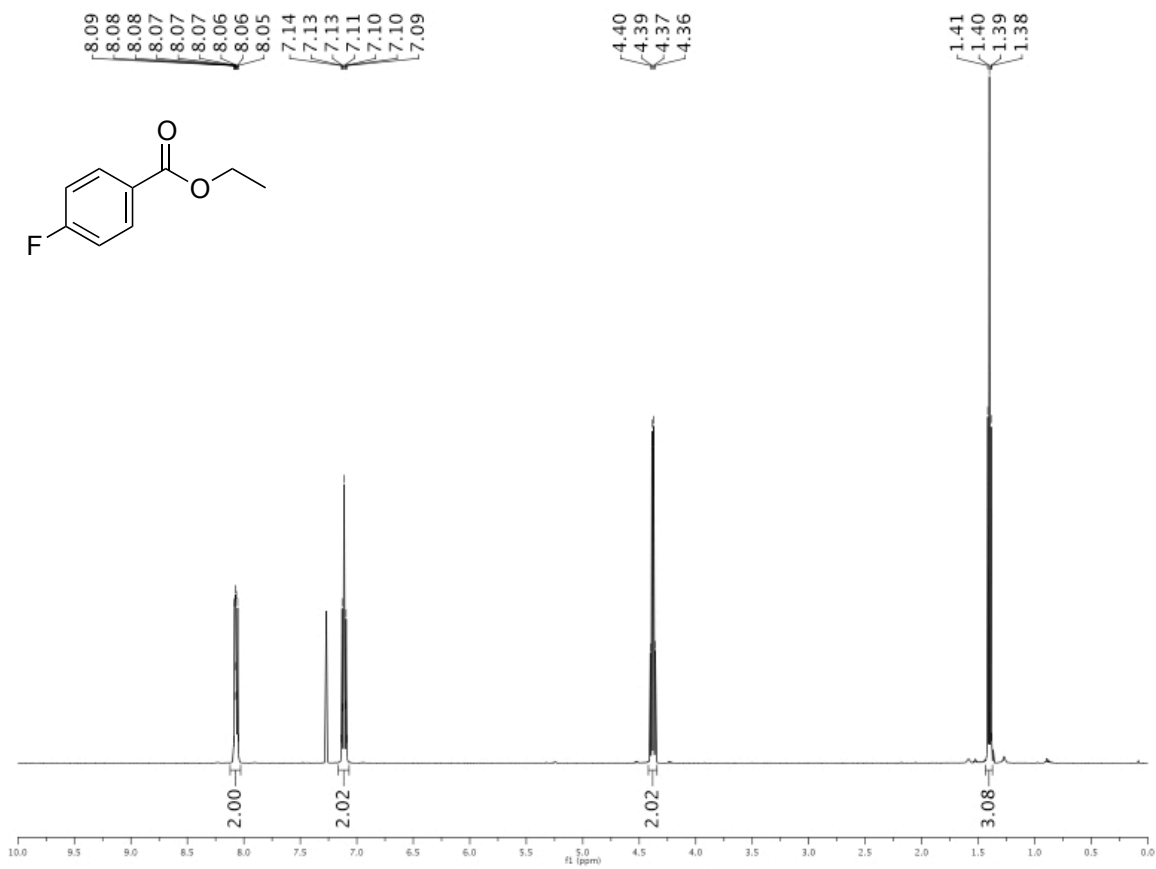
¹³C NMR (126 MHz, CDCl₃) of isopropyl 4-nitrobenzoate (Table 2, entry 4c).



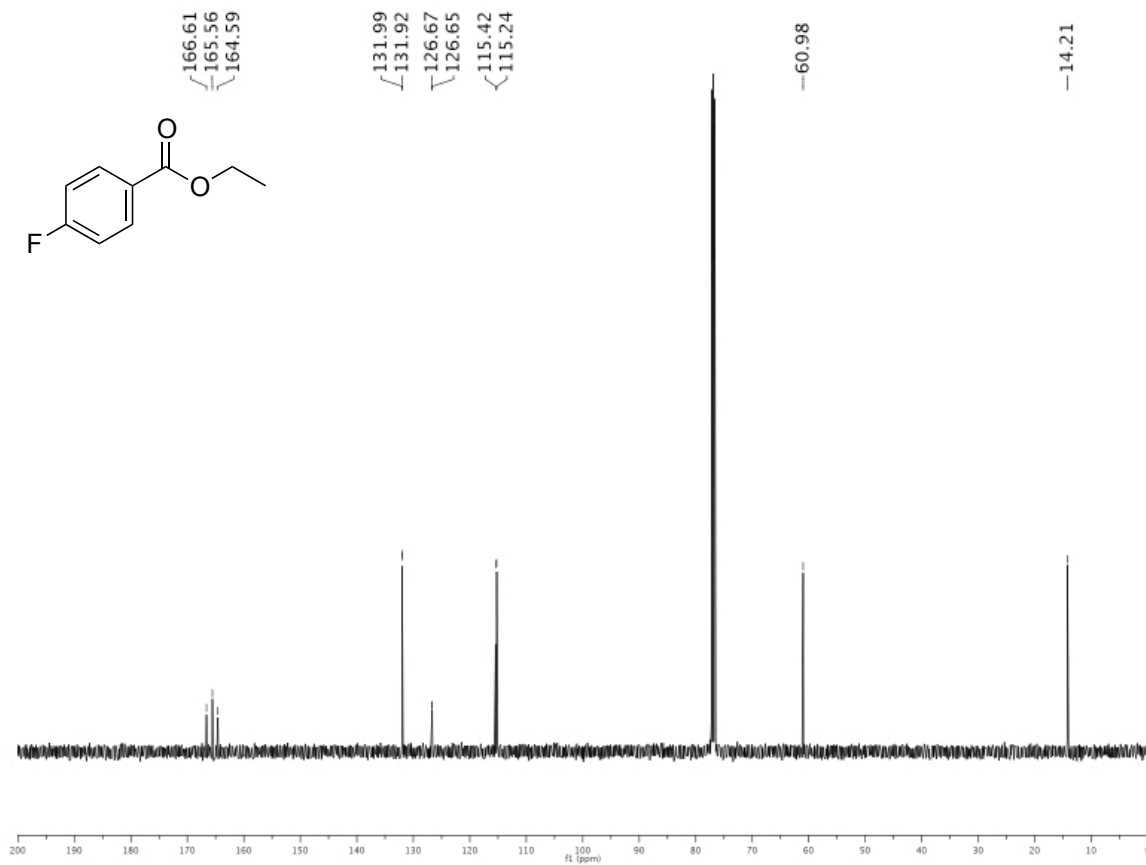
¹H NMR (500 MHz, CDCl₃) of methyl 4-fluorobenzoate (Table 2, entry 5a).



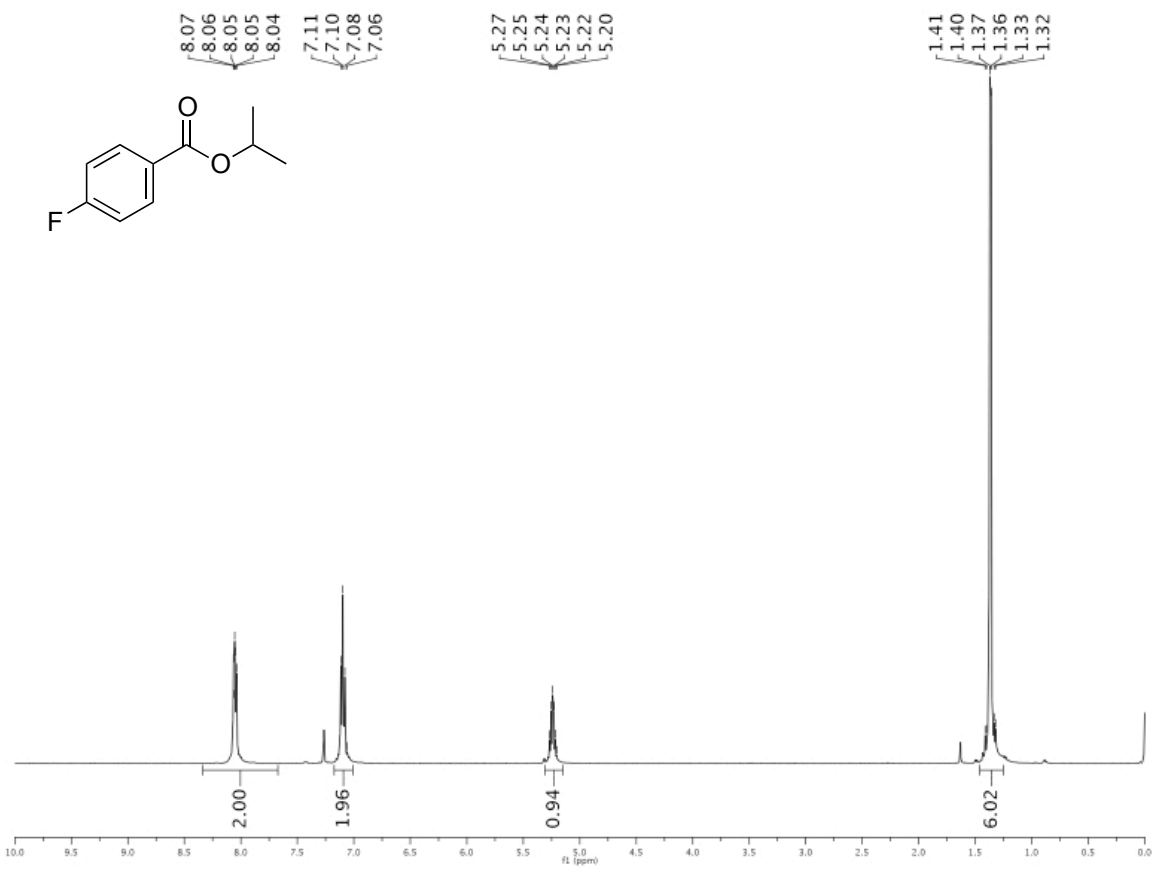
¹³C NMR (126 MHz, CDCl₃) of methyl 4-fluorobenzoate (Table 2, entry 5a).



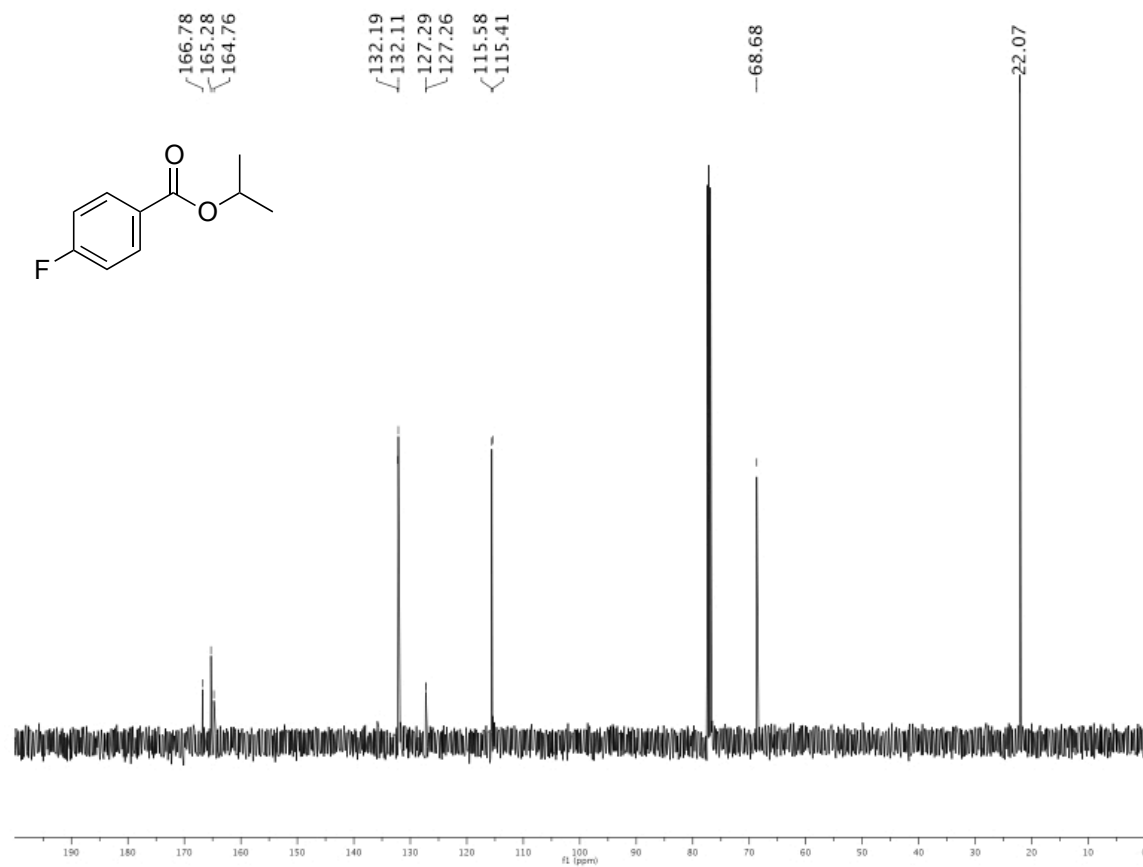
^1H NMR (500 MHz, CDCl_3) of ethyl 4-fluorobenzoate (Table 2, entry 5b).



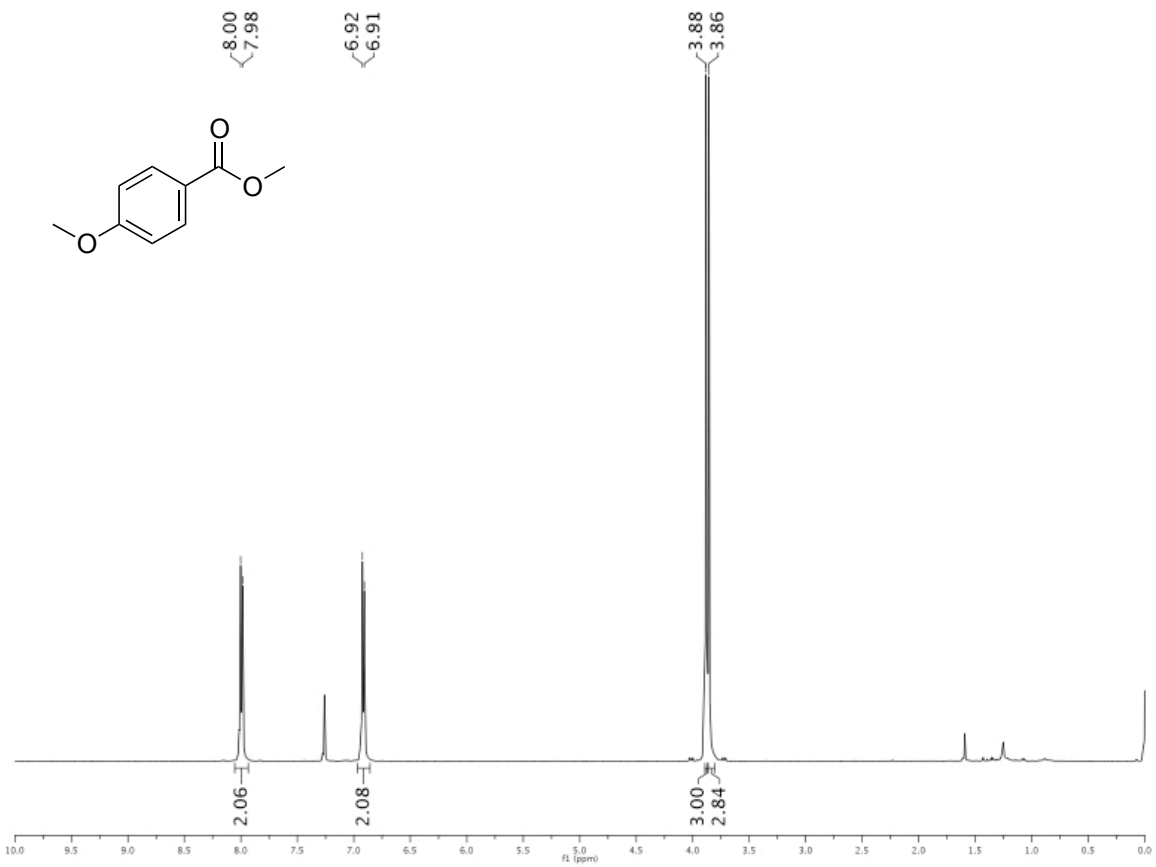
¹³C NMR (126 MHz, CDCl₃) of ethyl 4-fluorobenzoate (Table 2, entry 5b).



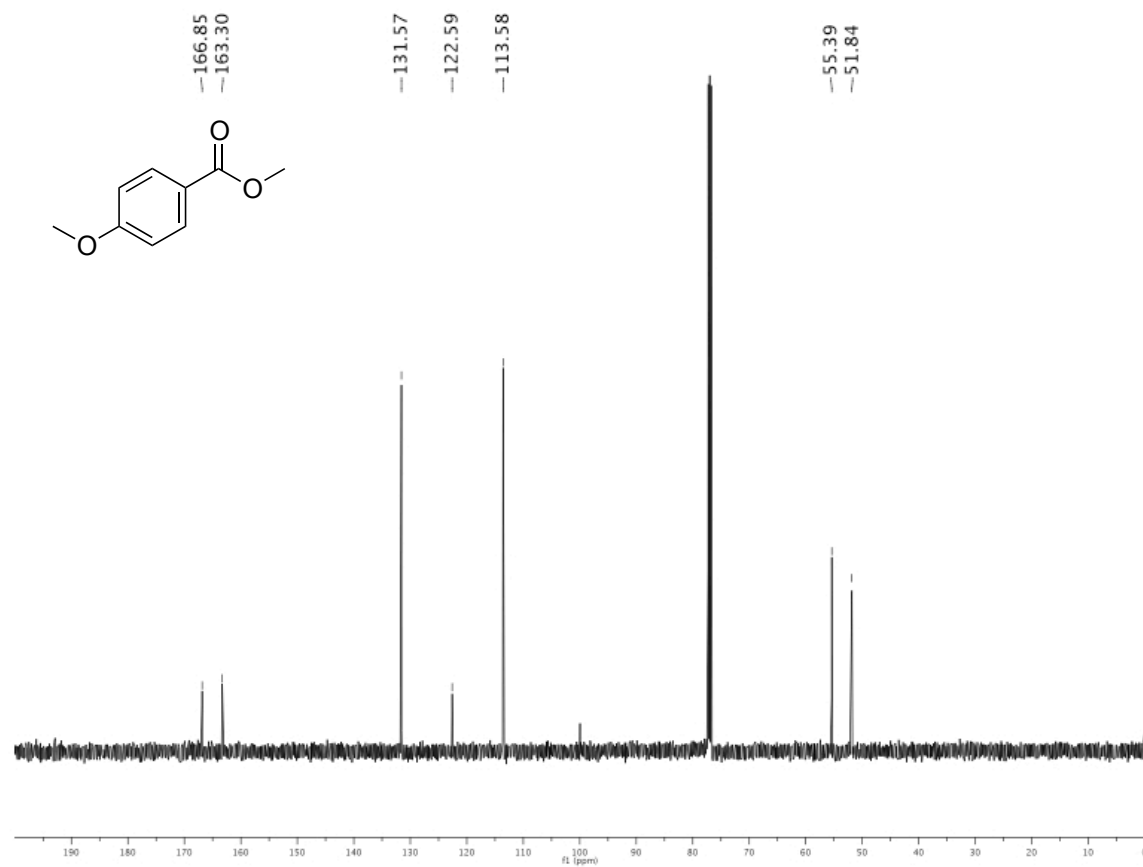
¹H NMR (500 MHz, CDCl₃) of isopropyl 4-fluorobenzoate (Table 2, entry 5c).



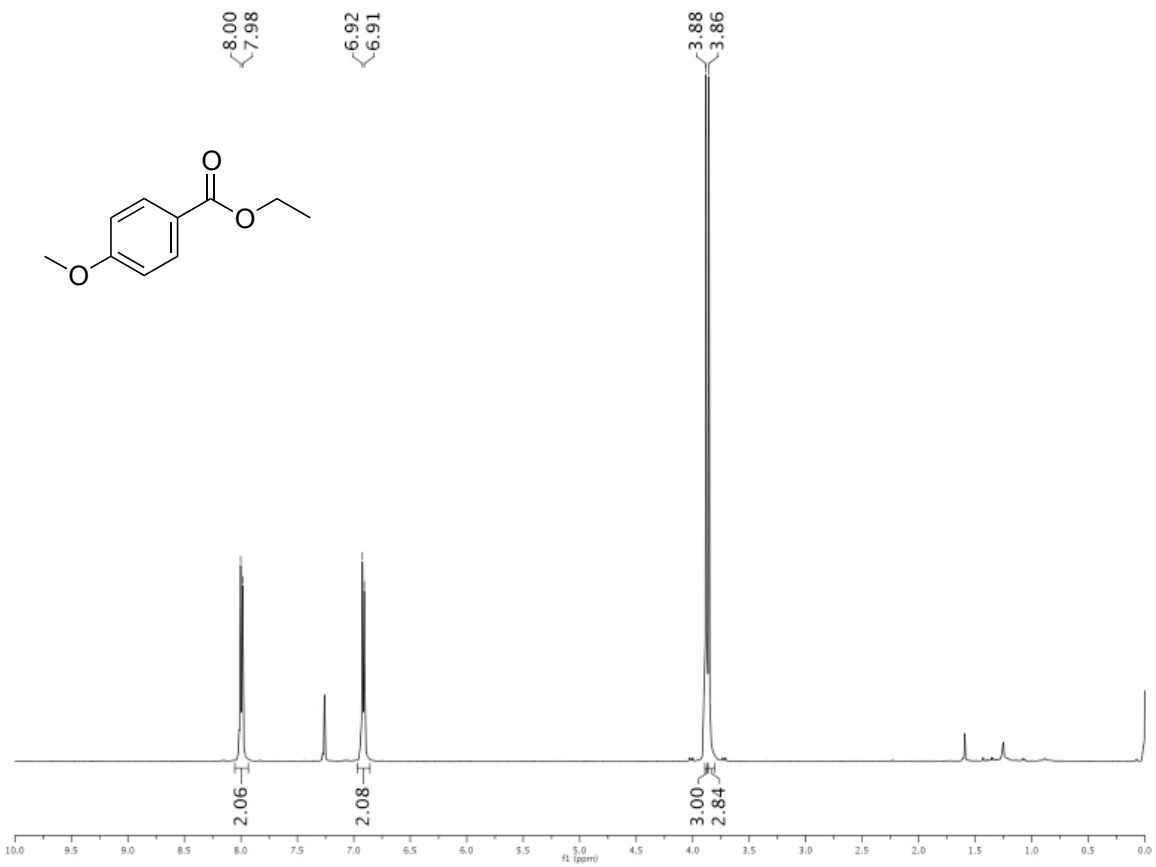
¹³C NMR (126 MHz, CDCl₃) of isopropyl 4-fluorobenzoate (Table 2, entry 5c).



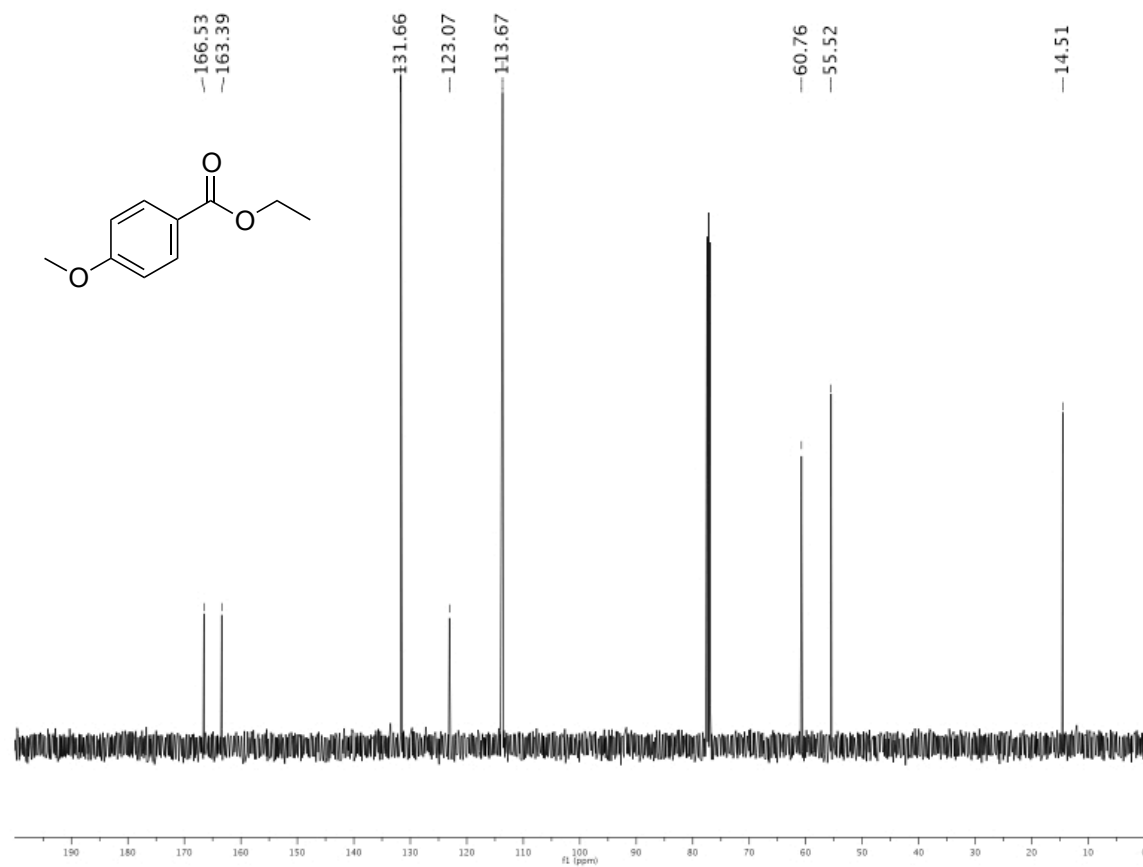
¹H NMR (500 MHz, CDCl₃) of methyl 4-methoxybenzoate (Table 2, entry 6a).



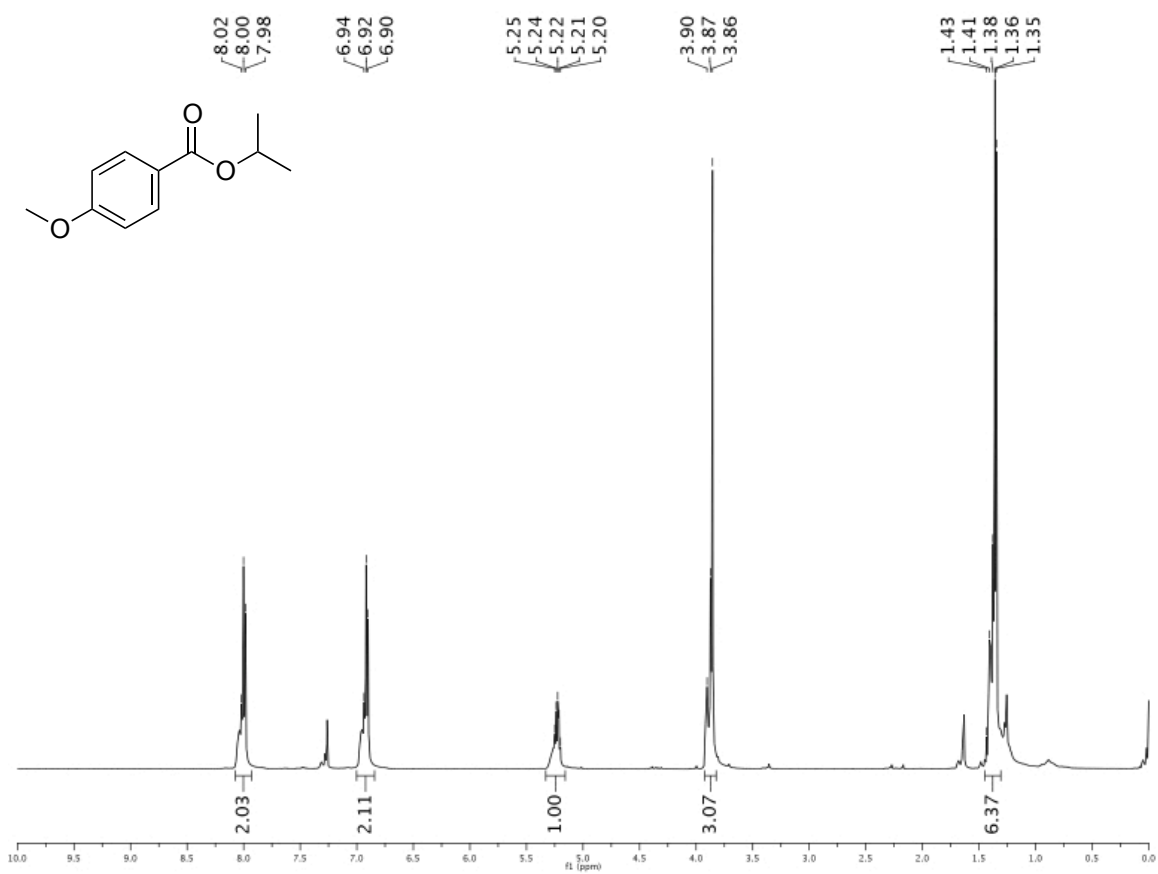
¹³C NMR (126 MHz, CDCl₃) of methyl 4-methoxybenzoate (Table 2, entry 6a).



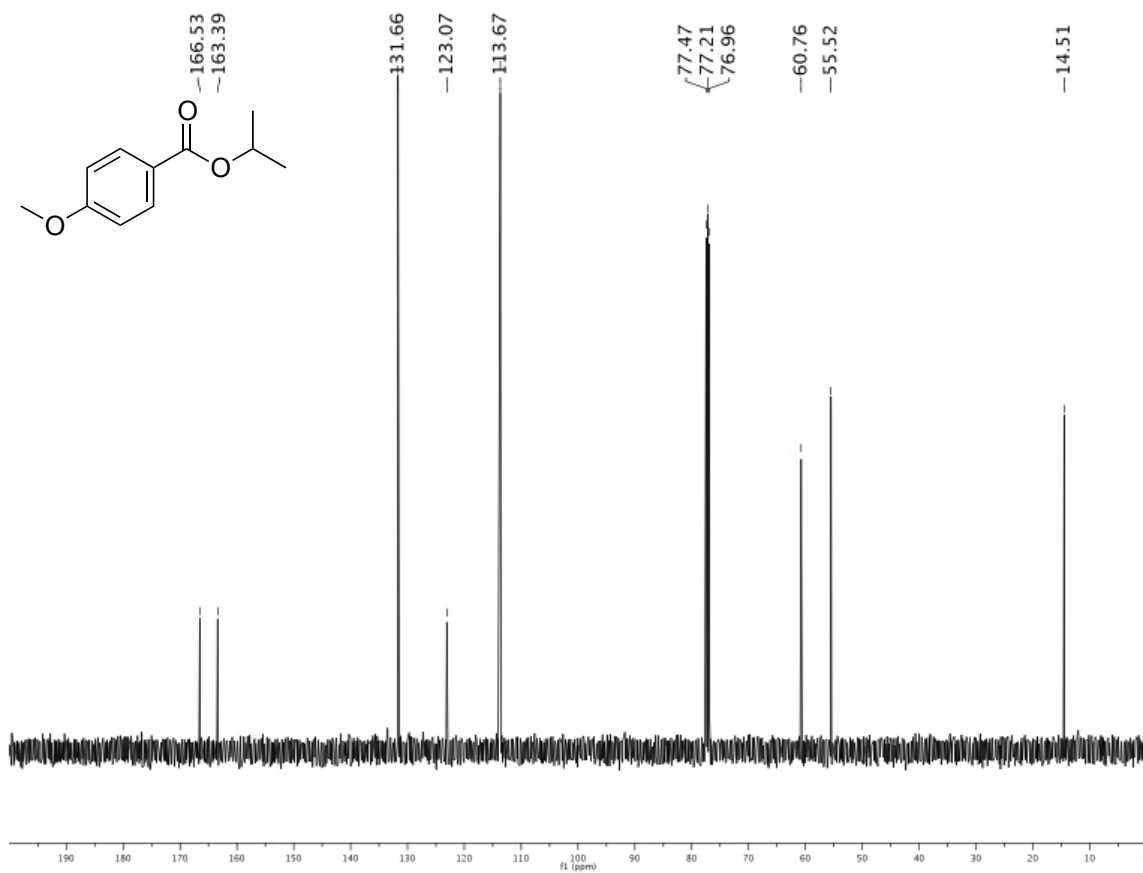
^1H NMR (500 MHz, CDCl_3) of ethyl 4-methoxybenzoate (Table 2, entry 6b).



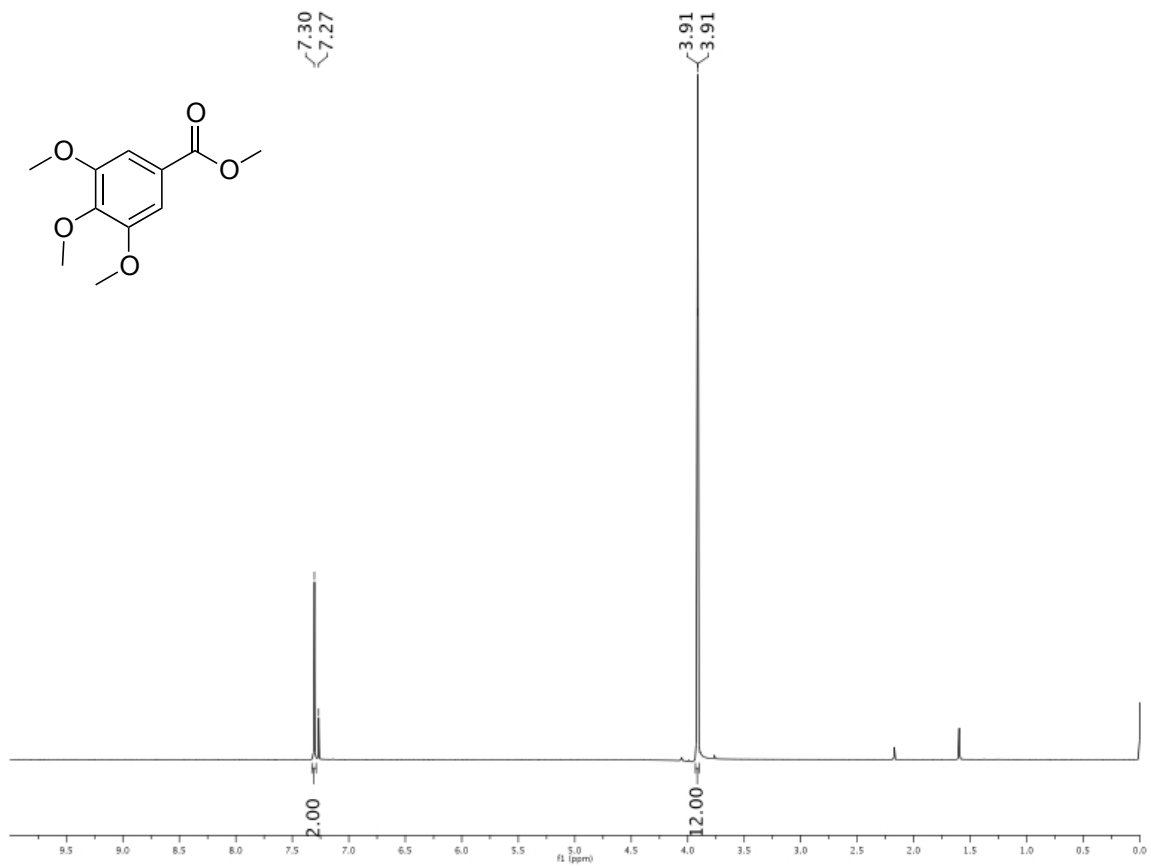
^{13}C NMR (126 MHz, CDCl_3) of ethyl 4-methoxybenzoate (Table 2, entry 6b).



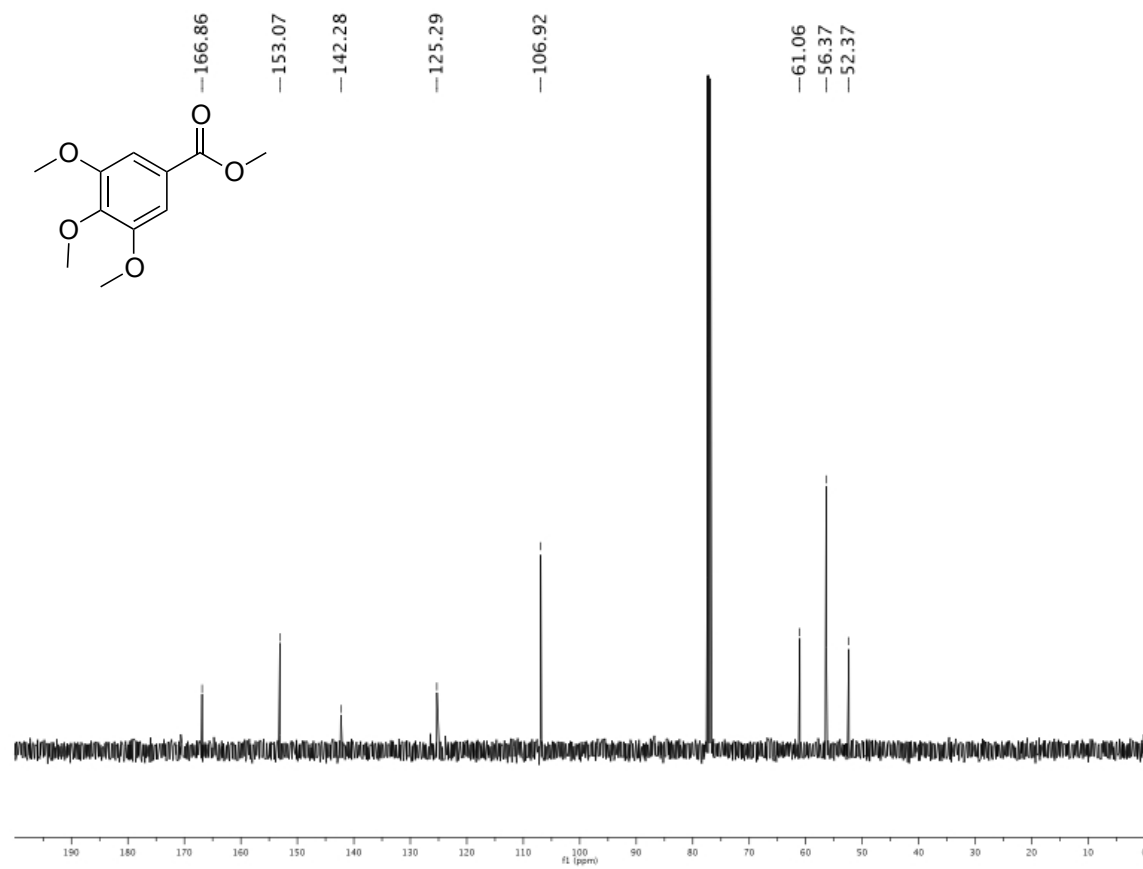
^1H NMR (500 MHz, CDCl_3) of isopropyl 4-methoxybenzoate (Table 2, entry 6c).



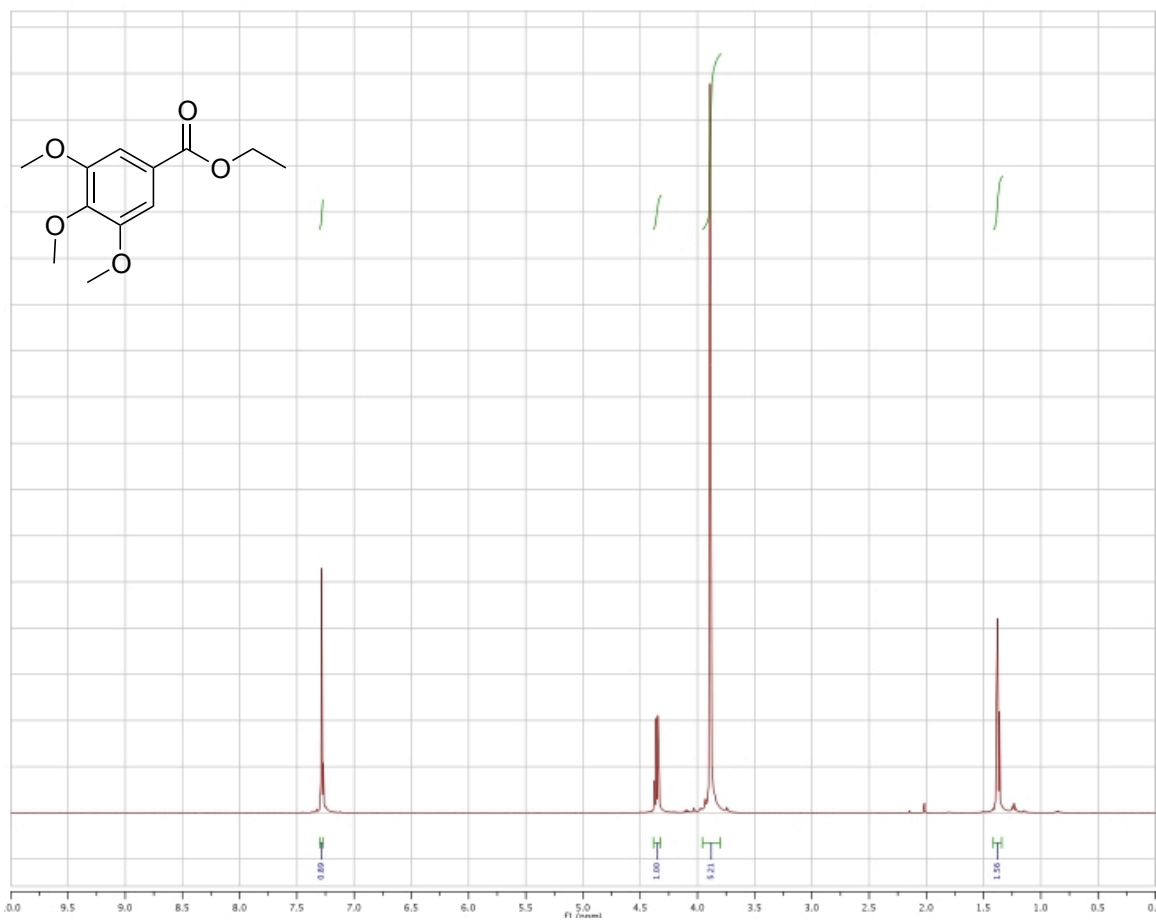
¹³C NMR (126 MHz, CDCl₃) of isopropyl 4-methoxybenzoate (Table 2, entry 6c).



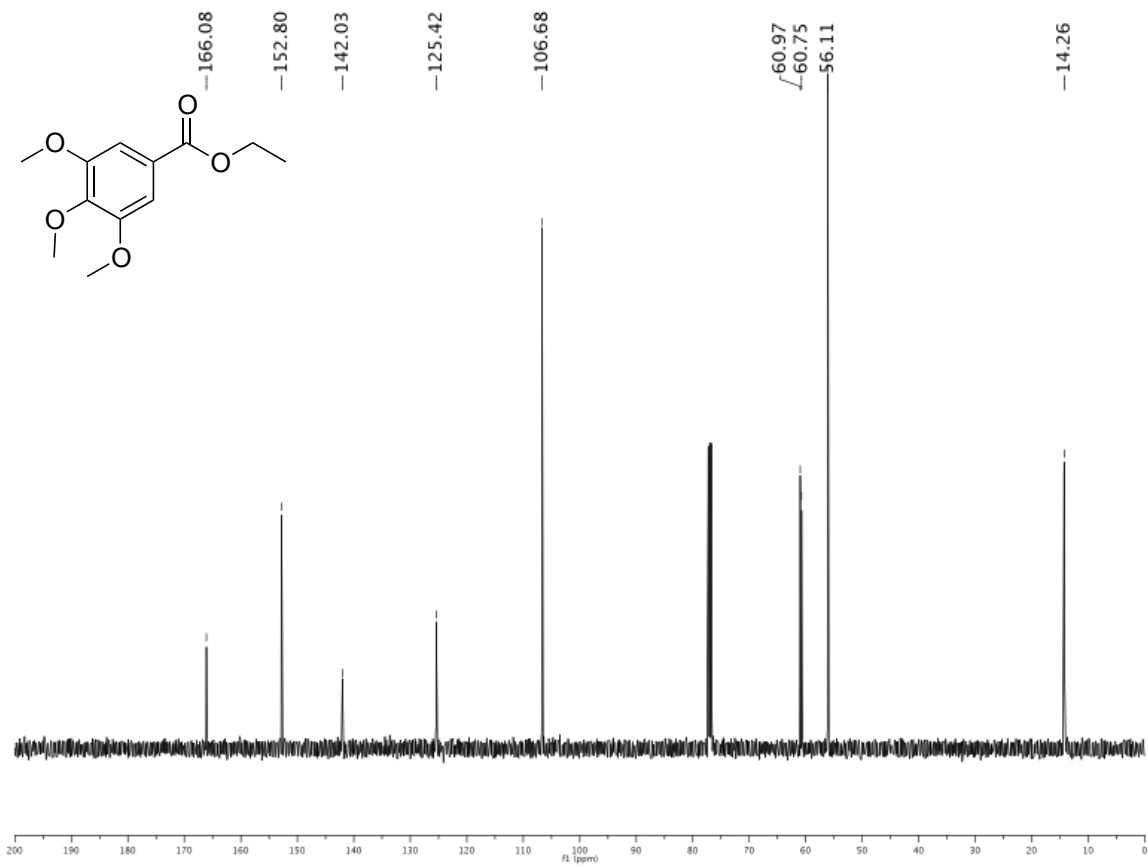
¹H NMR (500 MHz, CDCl₃) of methyl 3,4,5-trimethoxybenzoate (Table 2, entry 7a).



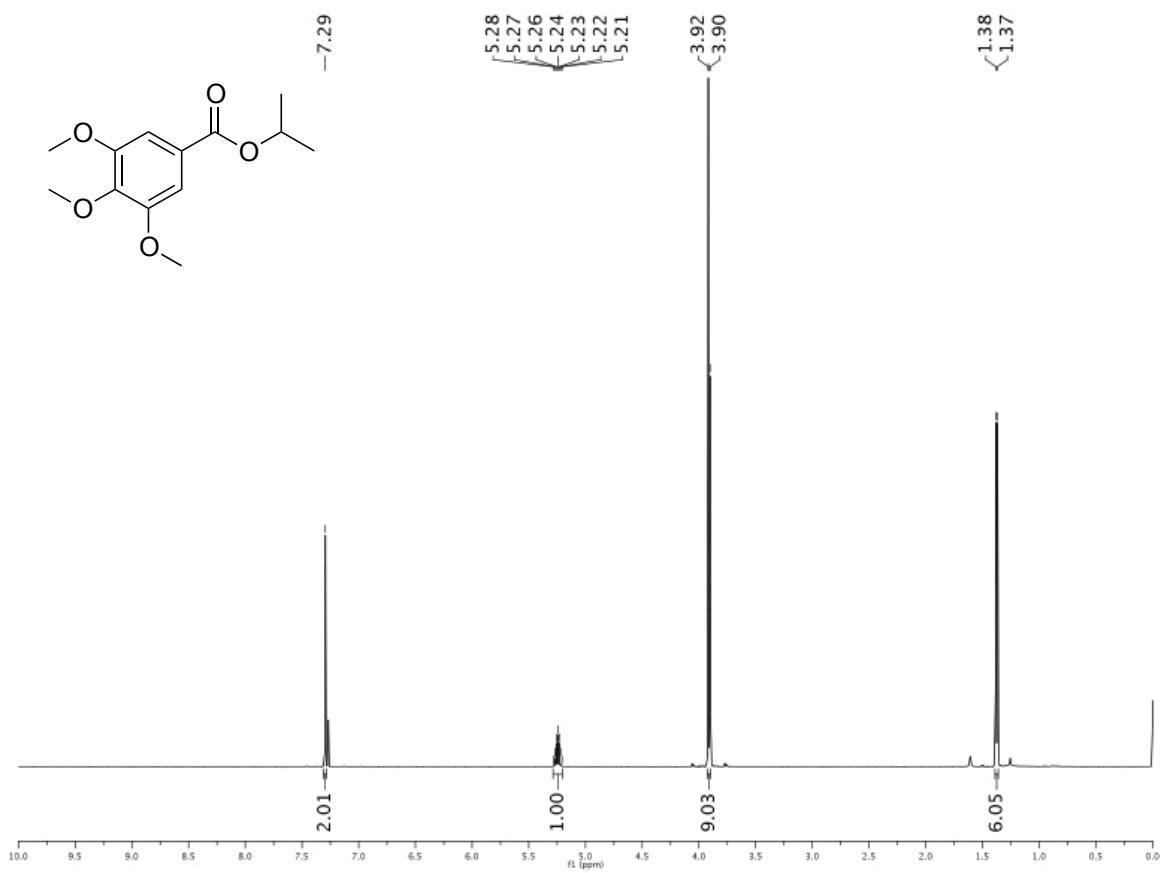
¹³C NMR (126 MHz, CDCl₃) of methyl 3,4,5-trimethoxybenzoate (Table 2, entry 7a).



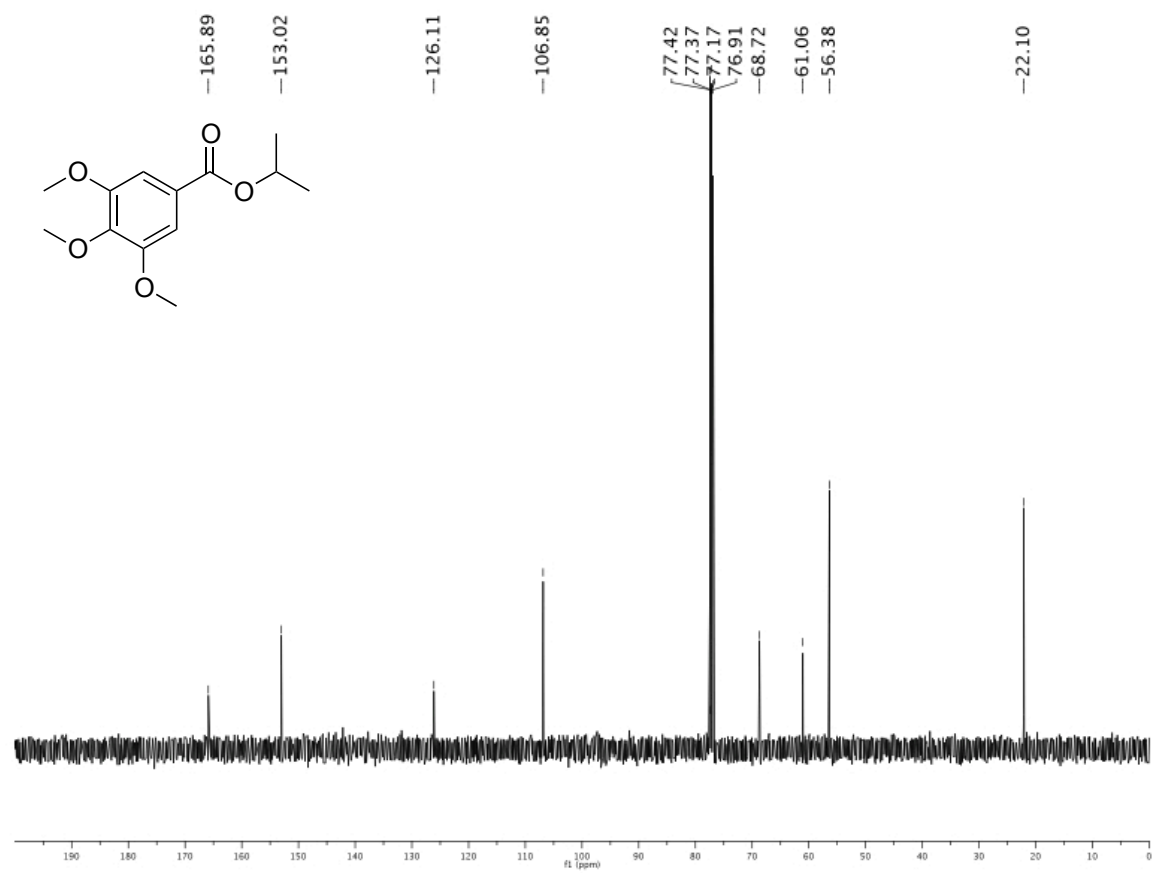
¹H NMR (500 MHz, CDCl₃) of ethyl 3,4,5-trimethoxybenzoate (Table 2, entry 7b).



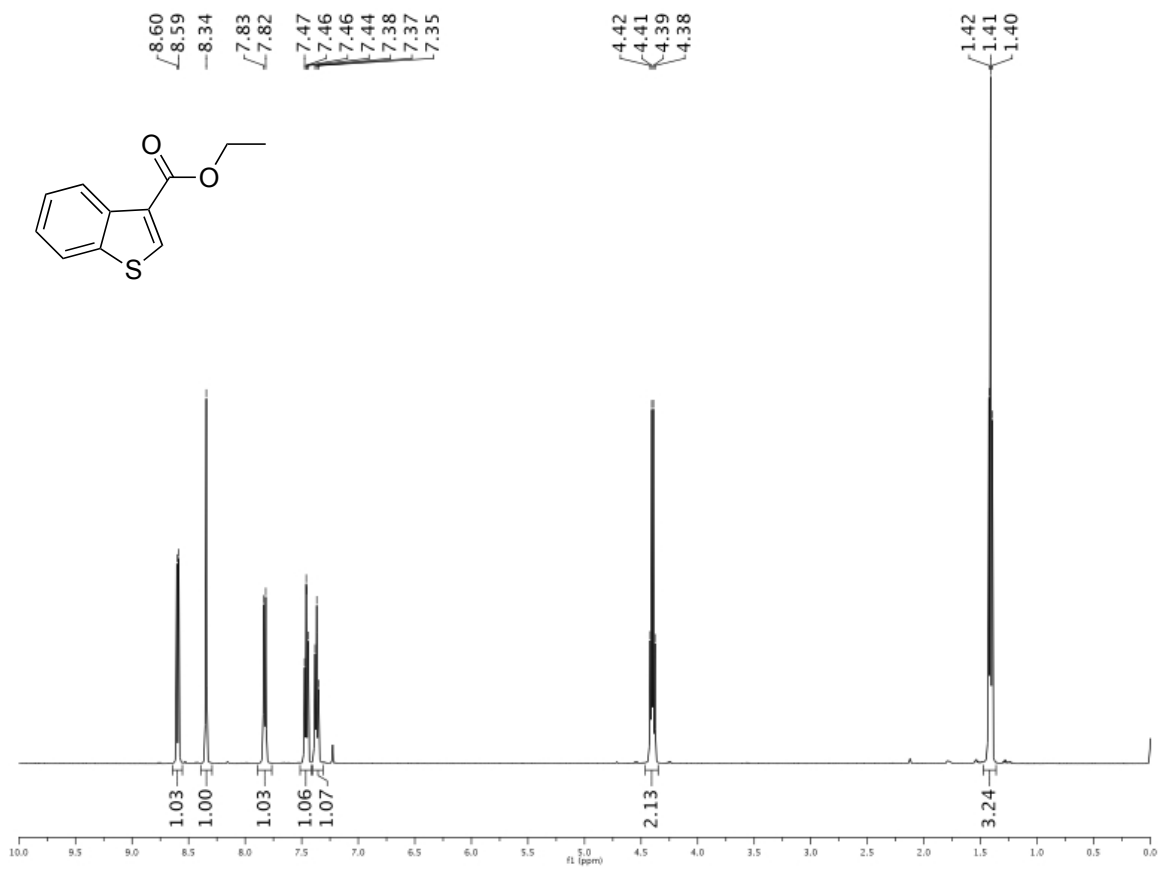
¹³C NMR (126 MHz, CDCl₃) of ethyl 3,4,5-trimethoxybenzoate (Table 2, entry 7b).



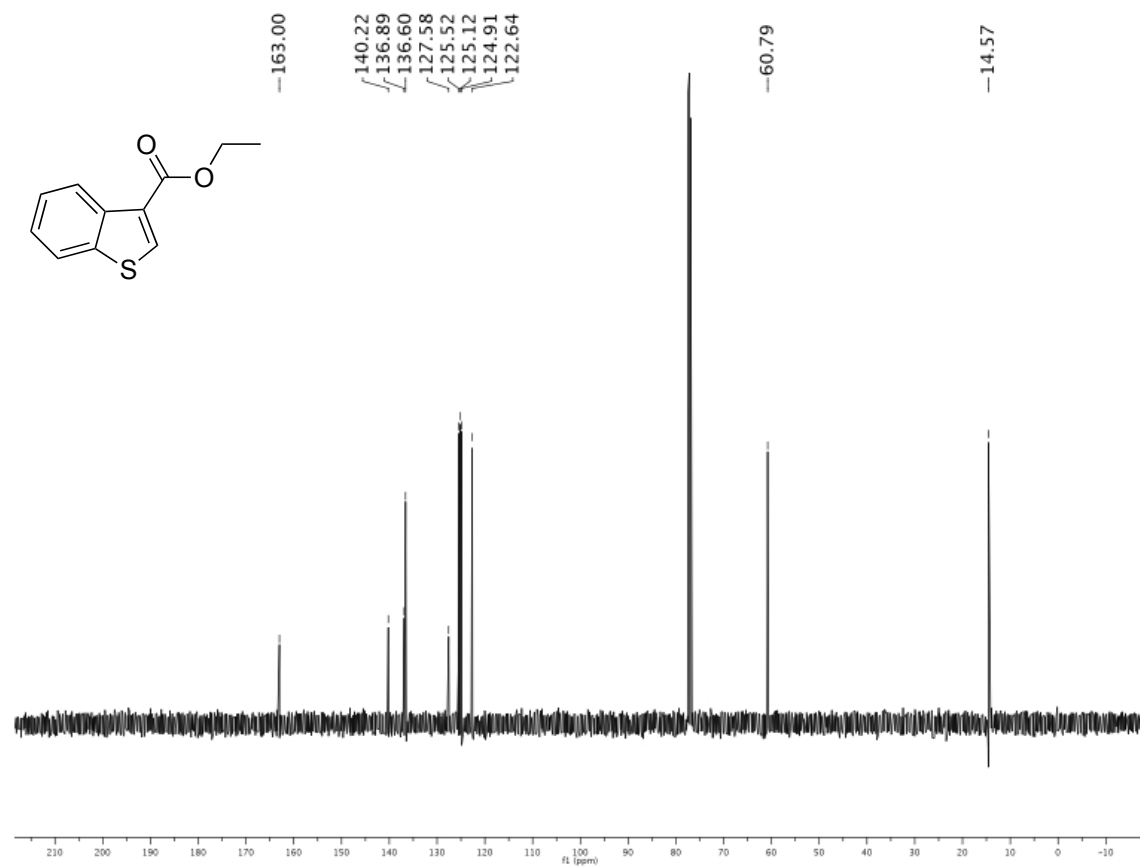
¹H NMR (500 MHz, CDCl₃) of isopropyl 3,4,5-trimethoxybenzoate (Table 2, entry 7c).



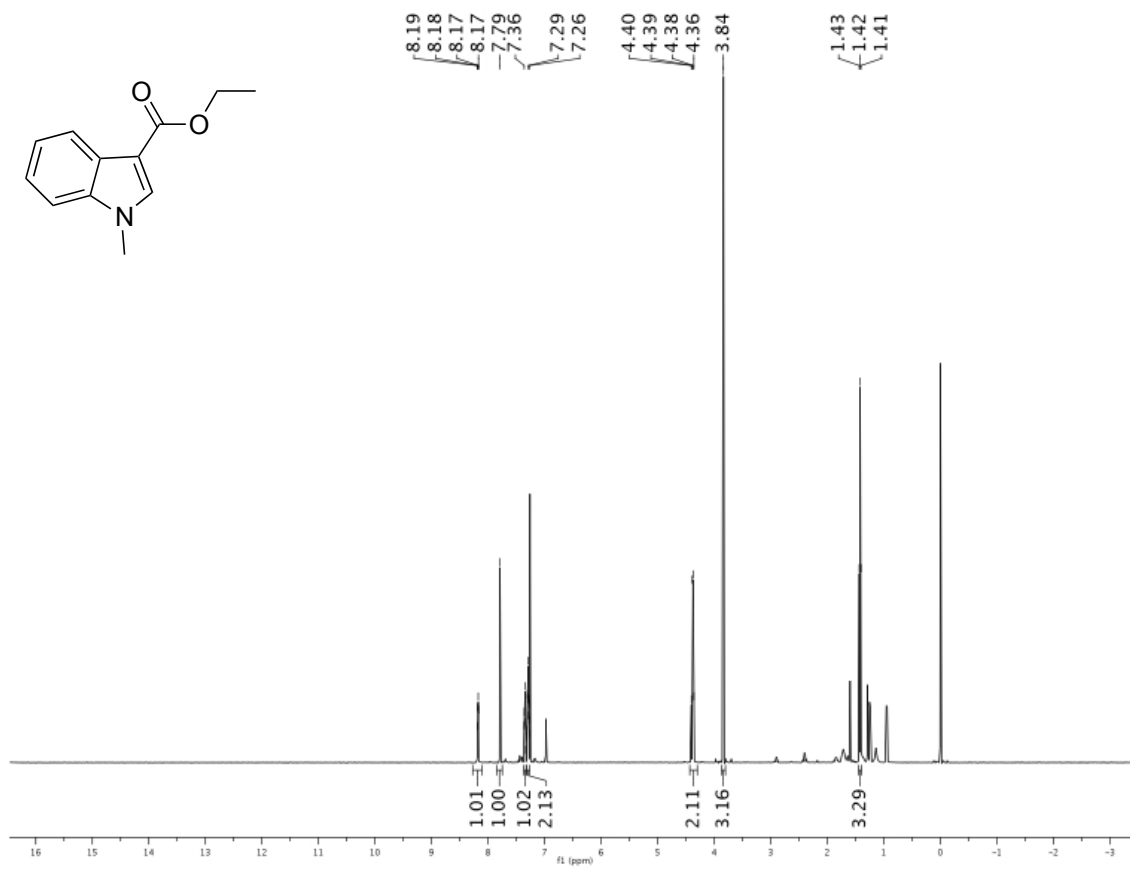
¹³C NMR (126 MHz, CDCl₃) of isopropyl 3,4,5-trimethoxybenzoate (Table 2, entry 7c).



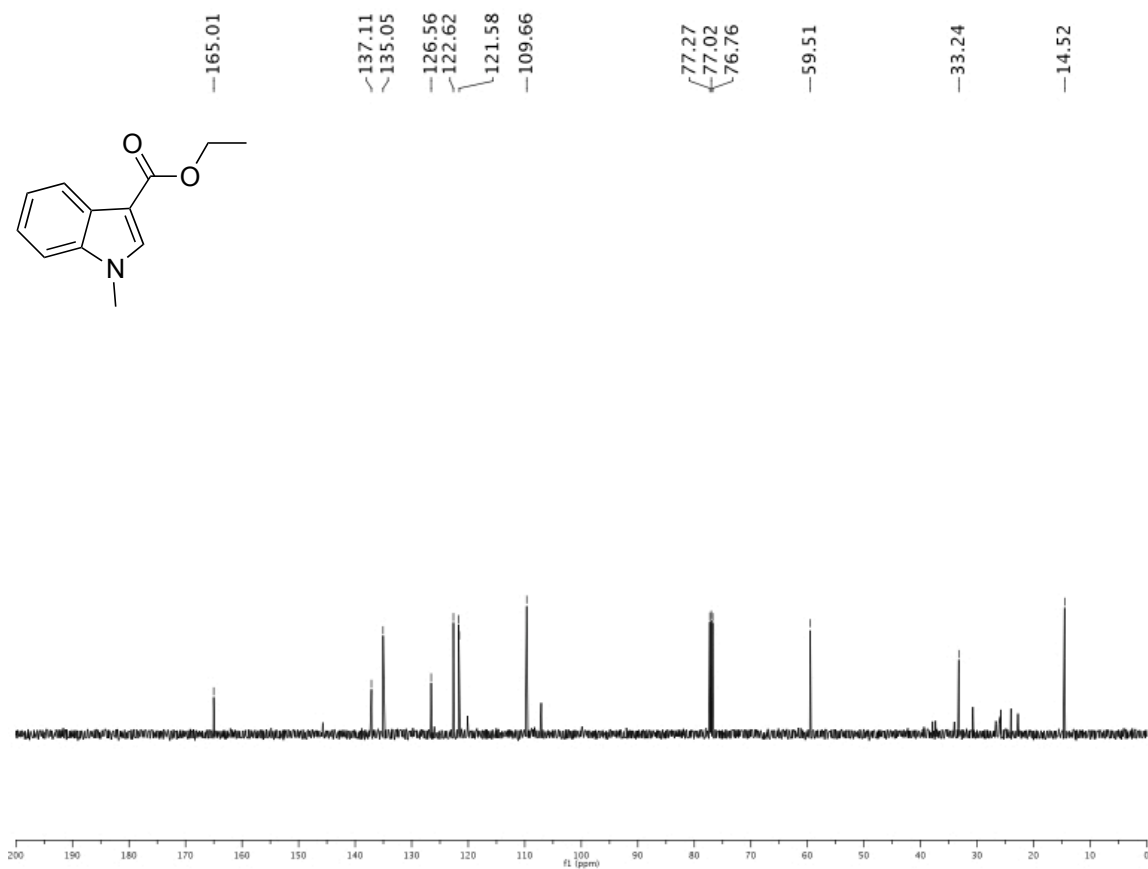
¹H NMR (500 MHz, CDCl₃) of Ethyl benzo[*b*]thiophene-3-carboxylate (Table 3, entry 8b).



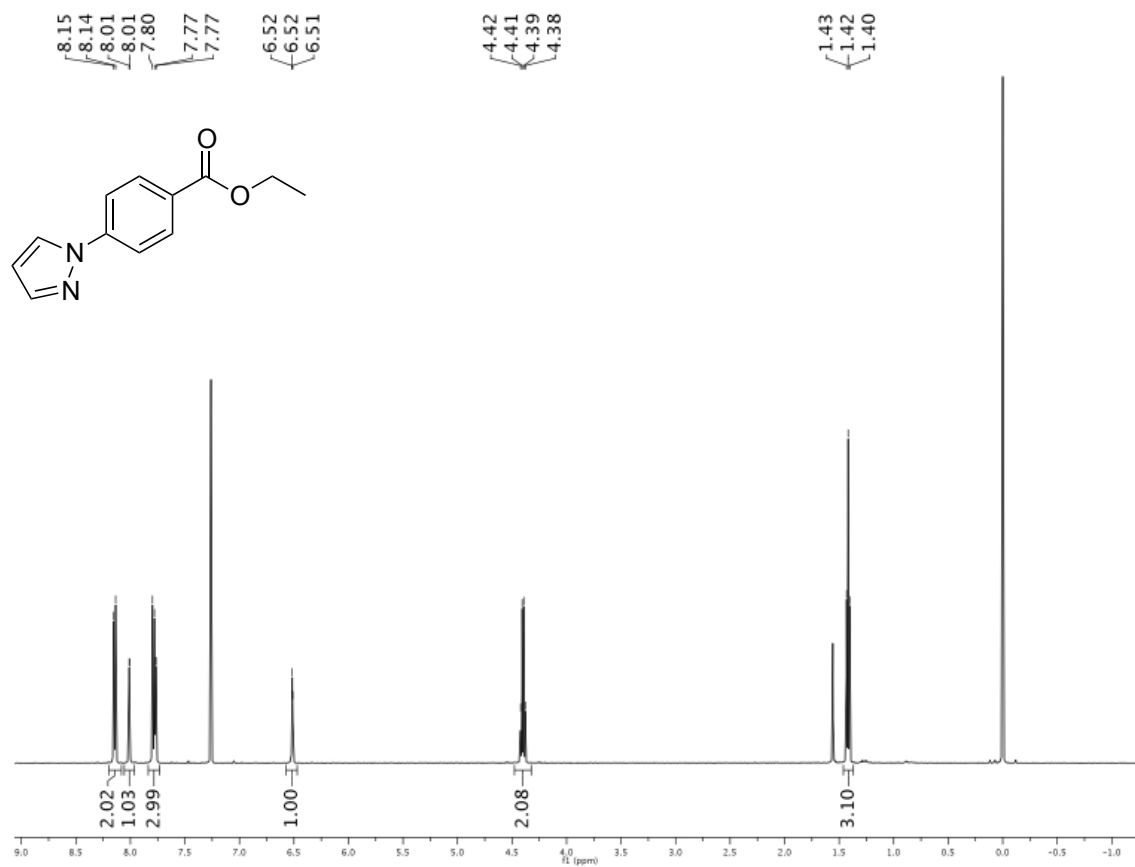
¹³C NMR (126 MHz, CDCl₃) of Ethyl benzo[*b*]thiophene-3-carboxylate (Table 3, entry 8b).



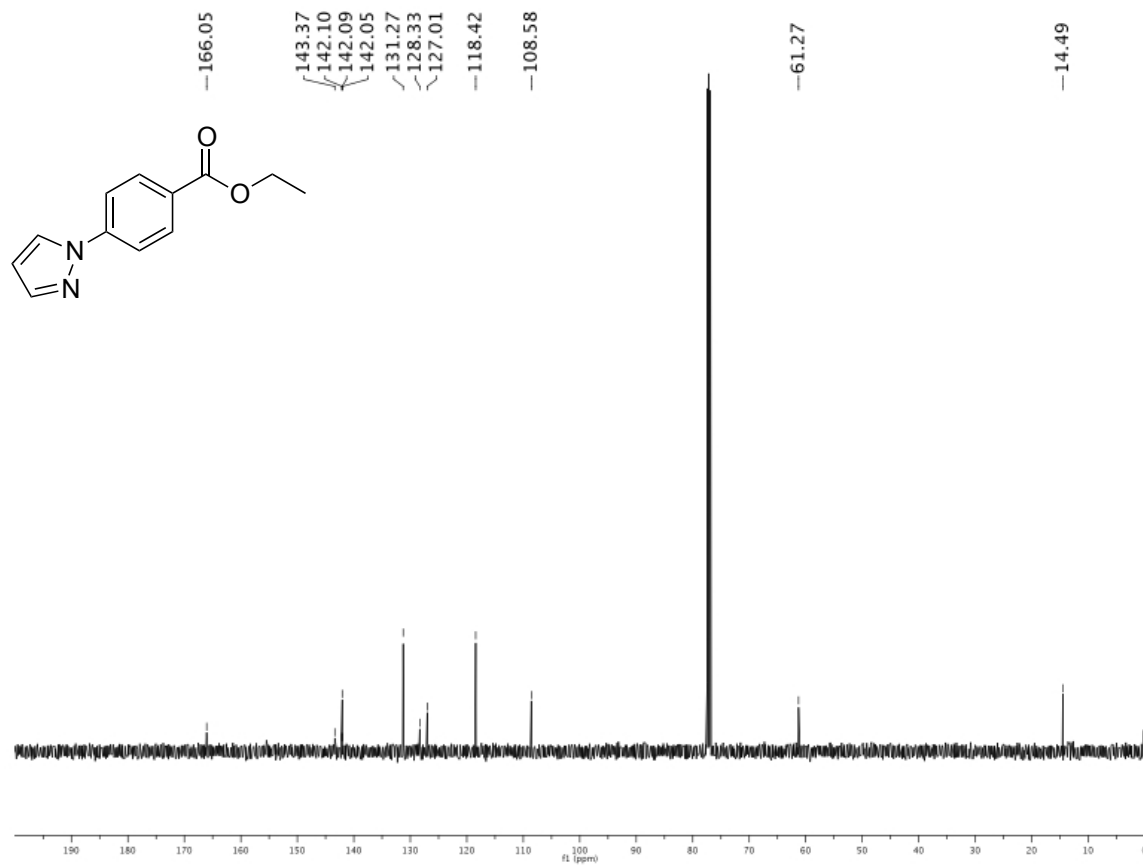
¹H NMR (500 MHz, CDCl₃) of ethyl 1-methyl-1*H*-indole-3-carboxylate (Table 3, entry 9b).



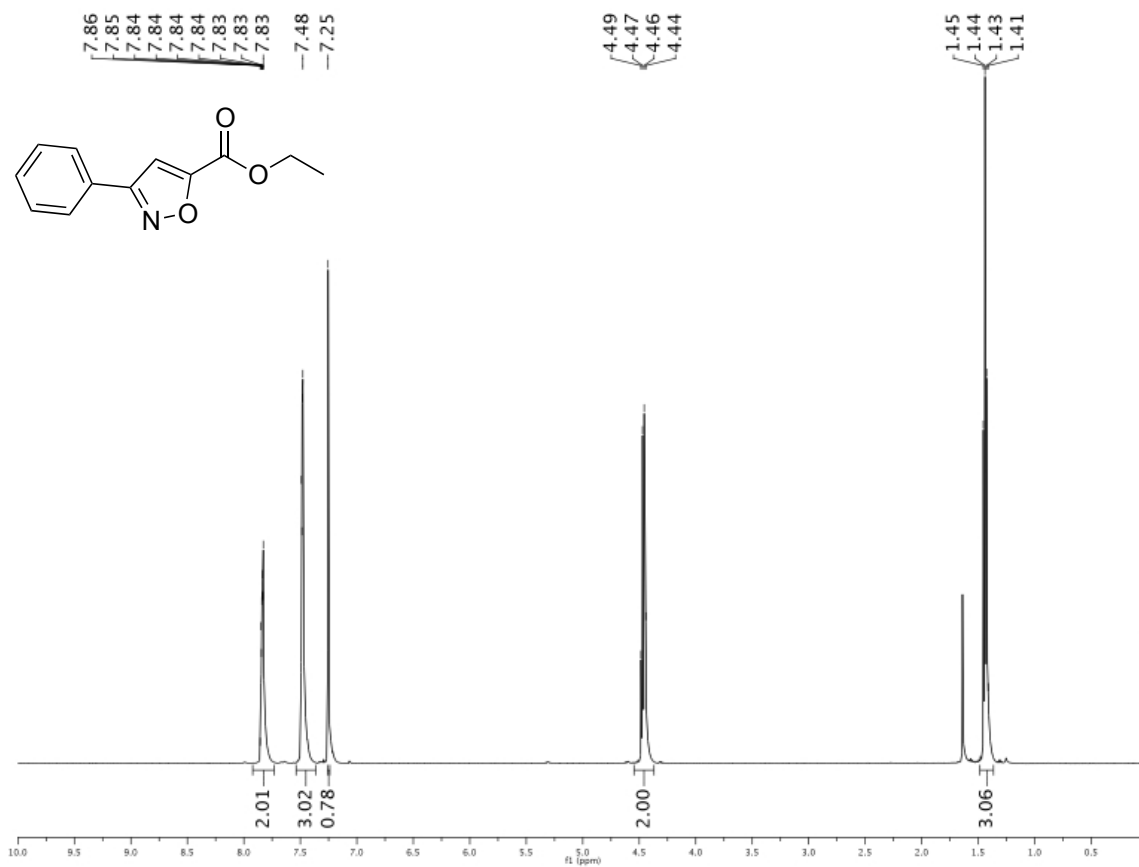
¹³C NMR (126 MHz, CDCl₃) of ethyl 1-methyl-1*H*-indole-3-carboxylate (Table 3, entry 9b).



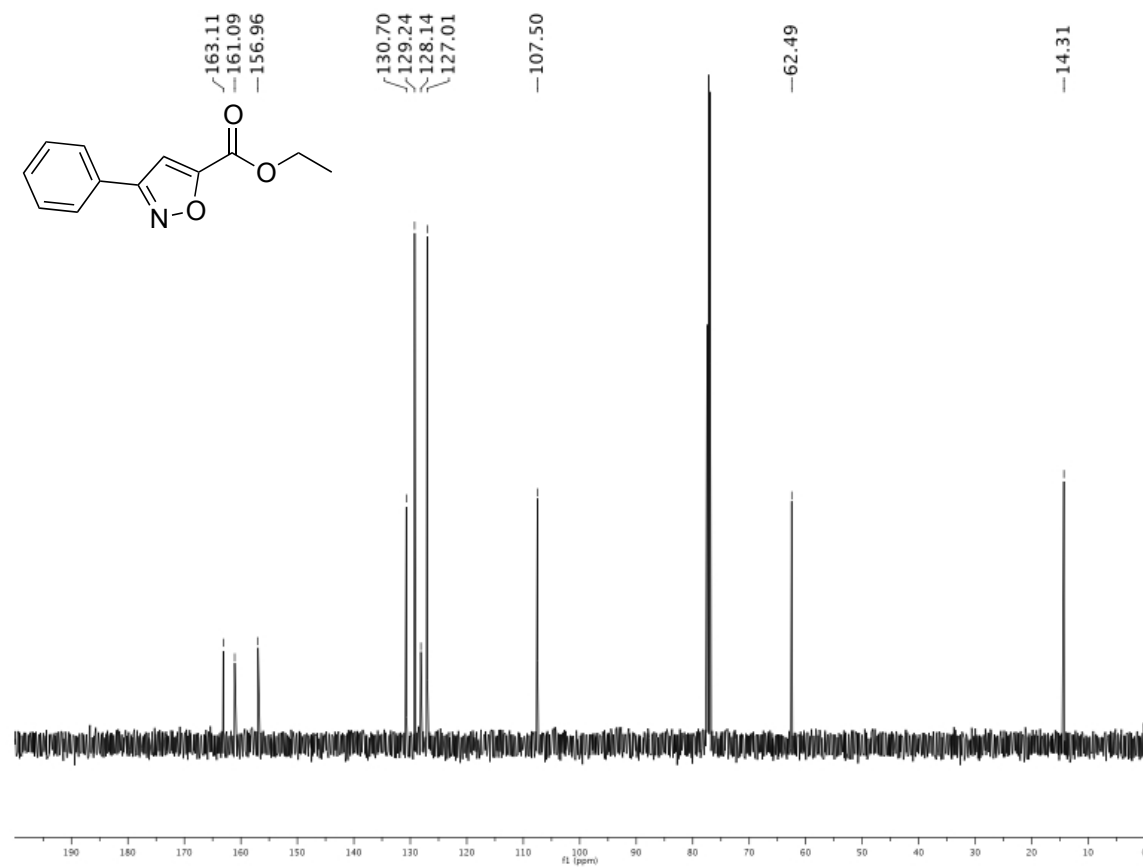
¹H NMR (500 MHz, CDCl₃) of ethyl 4-(1*H*-pyrazol-1-yl) benzoate (Table 3, entry 10b).



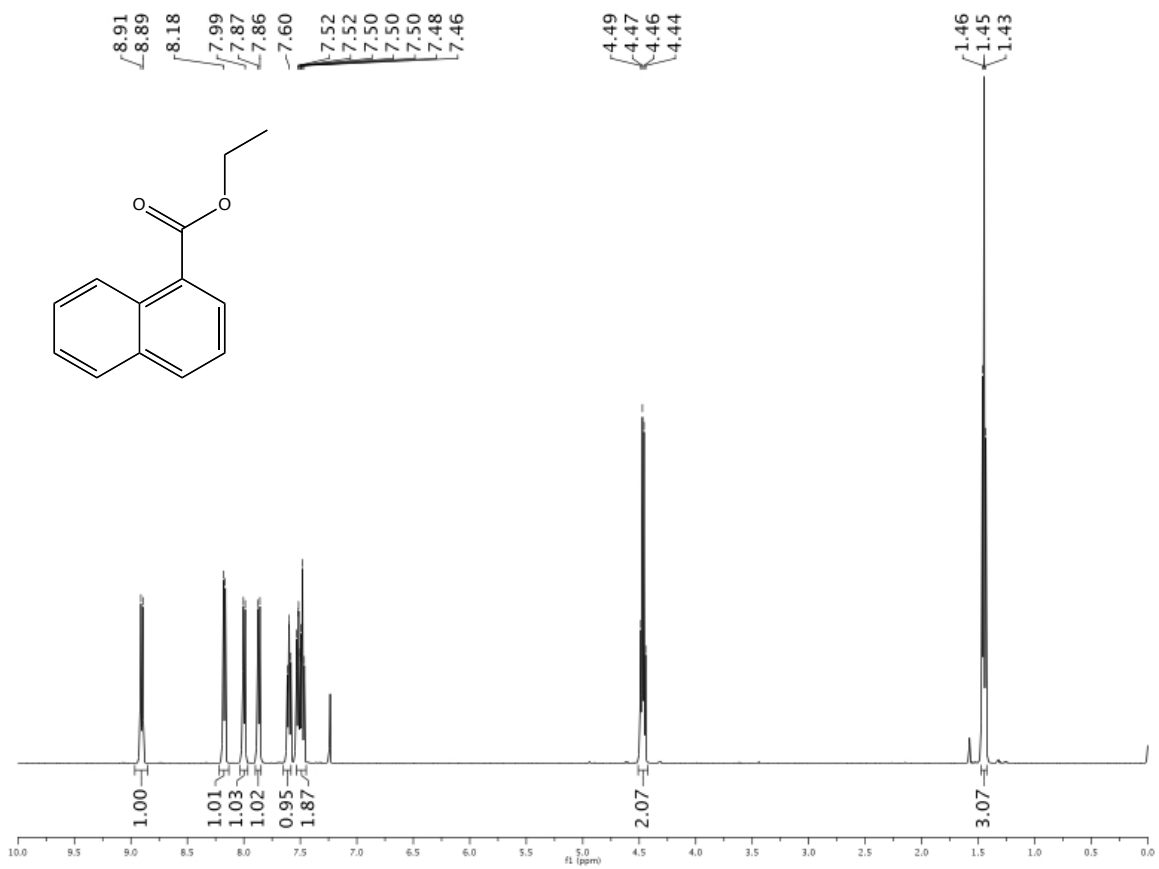
¹³C NMR (126 MHz, CDCl₃) of ethyl 4-(1*H*-pyrazol-1-yl) benzoate (Table 3, entry 10b).



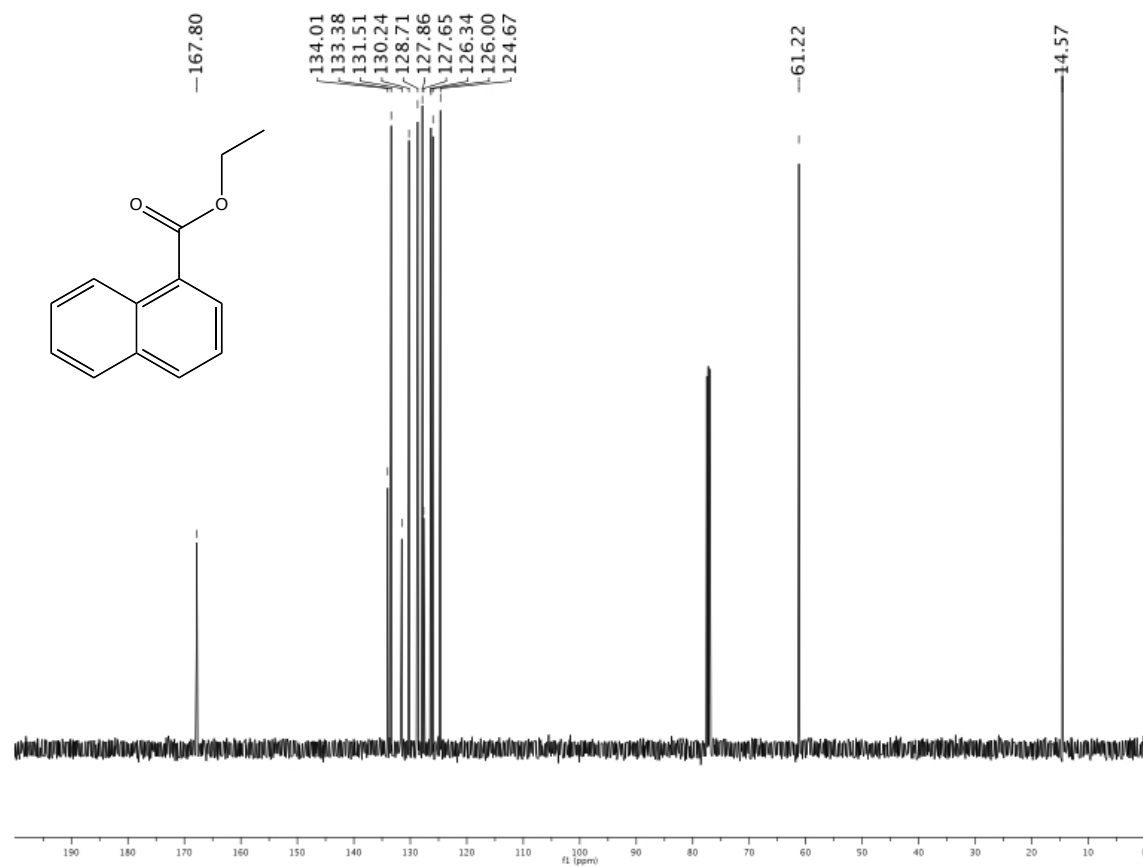
¹H NMR (500 MHz, CDCl₃) of Ethyl 3-phenylisoxazole-5-carboxylate (Table 3, entry 11b).



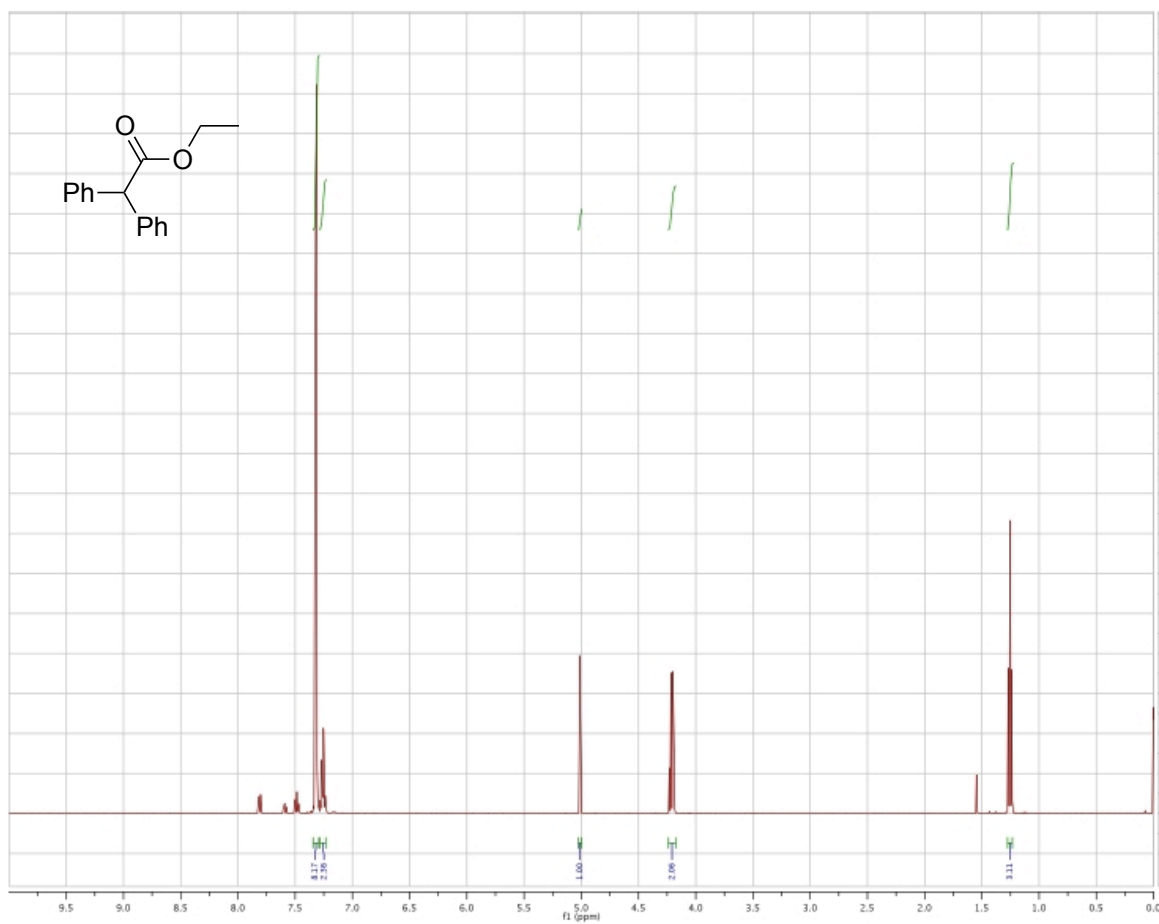
¹³C NMR (126 MHz, CDCl₃) of Ethyl 3-phenylisoxazole-5-carboxylate (Table 3, entry 11b).



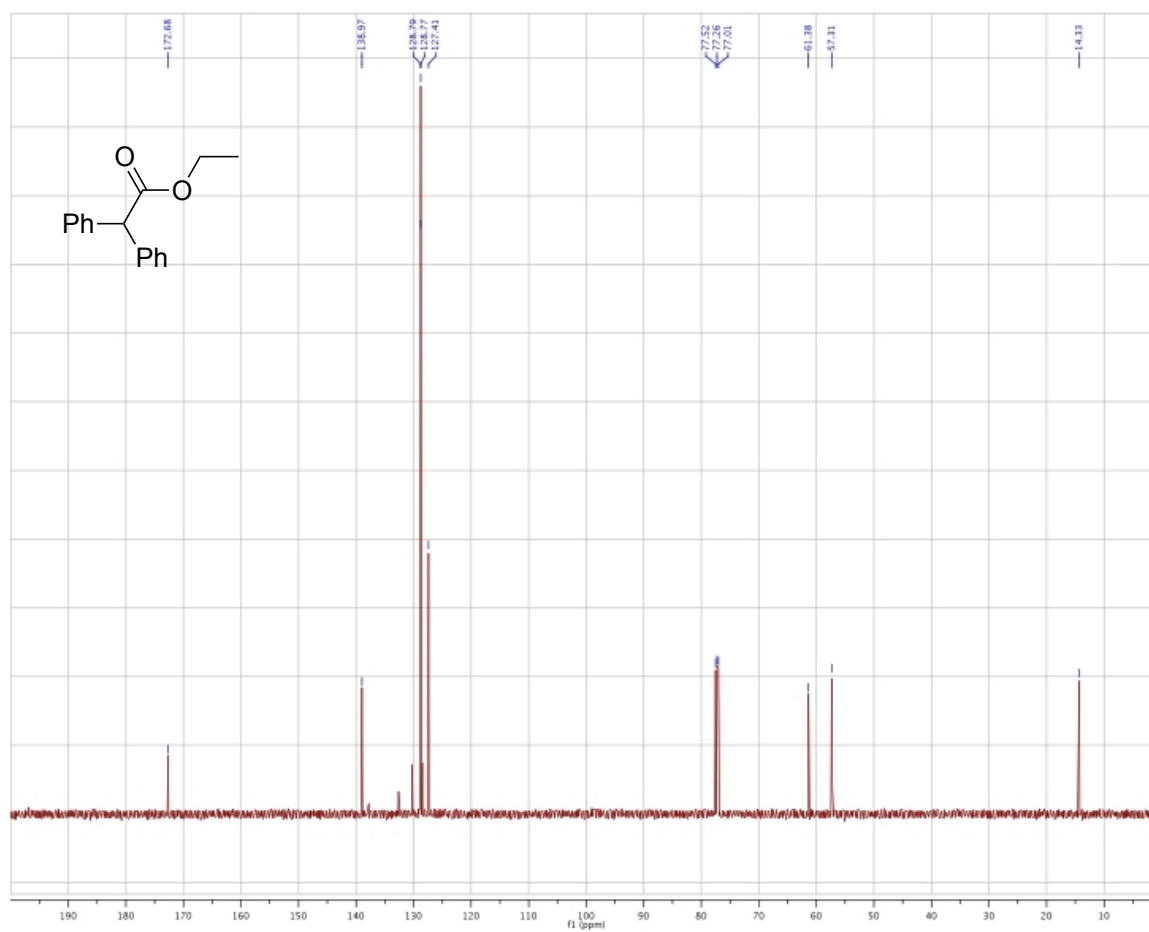
¹H NMR (500 MHz, CDCl₃) of Ethyl 1-naphthoate (Table 3, entry 12b).



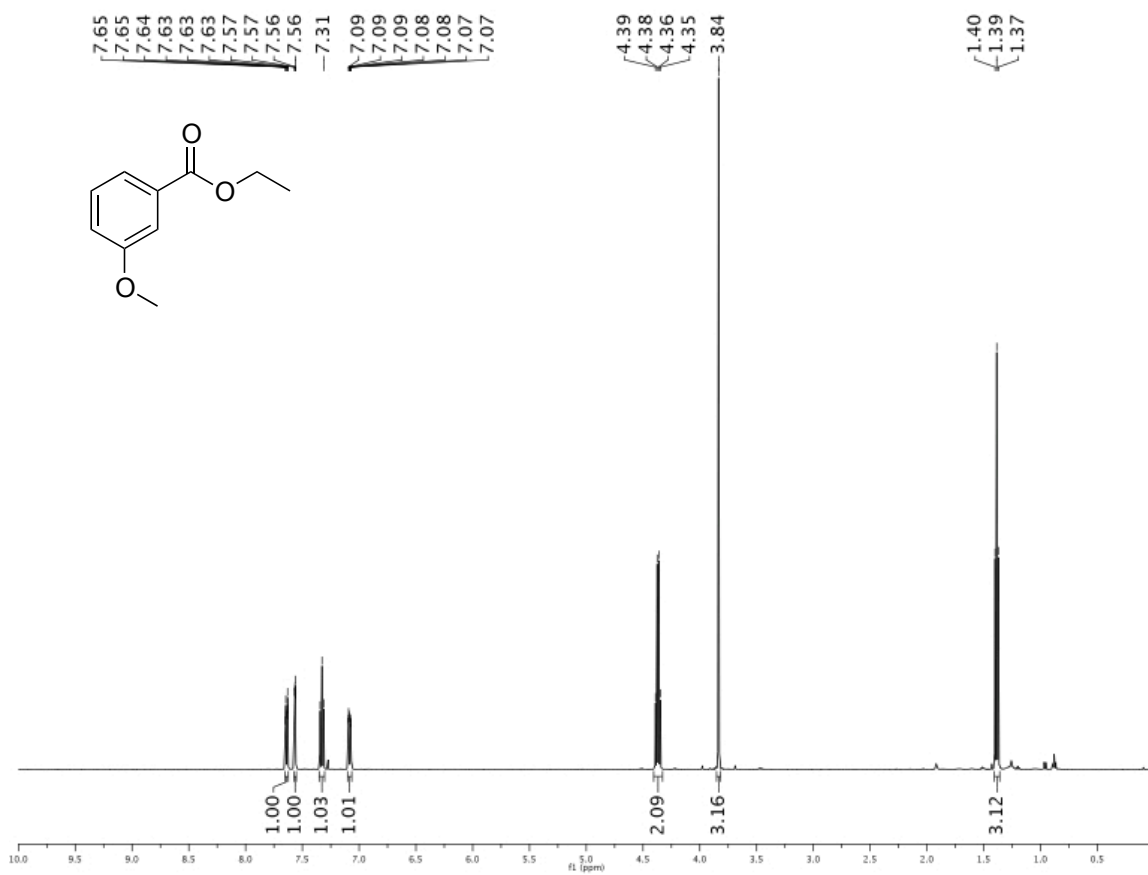
^{13}C NMR (126 MHz, CDCl_3) of Ethyl 1-naphthoate (Table 3, entry 12b).



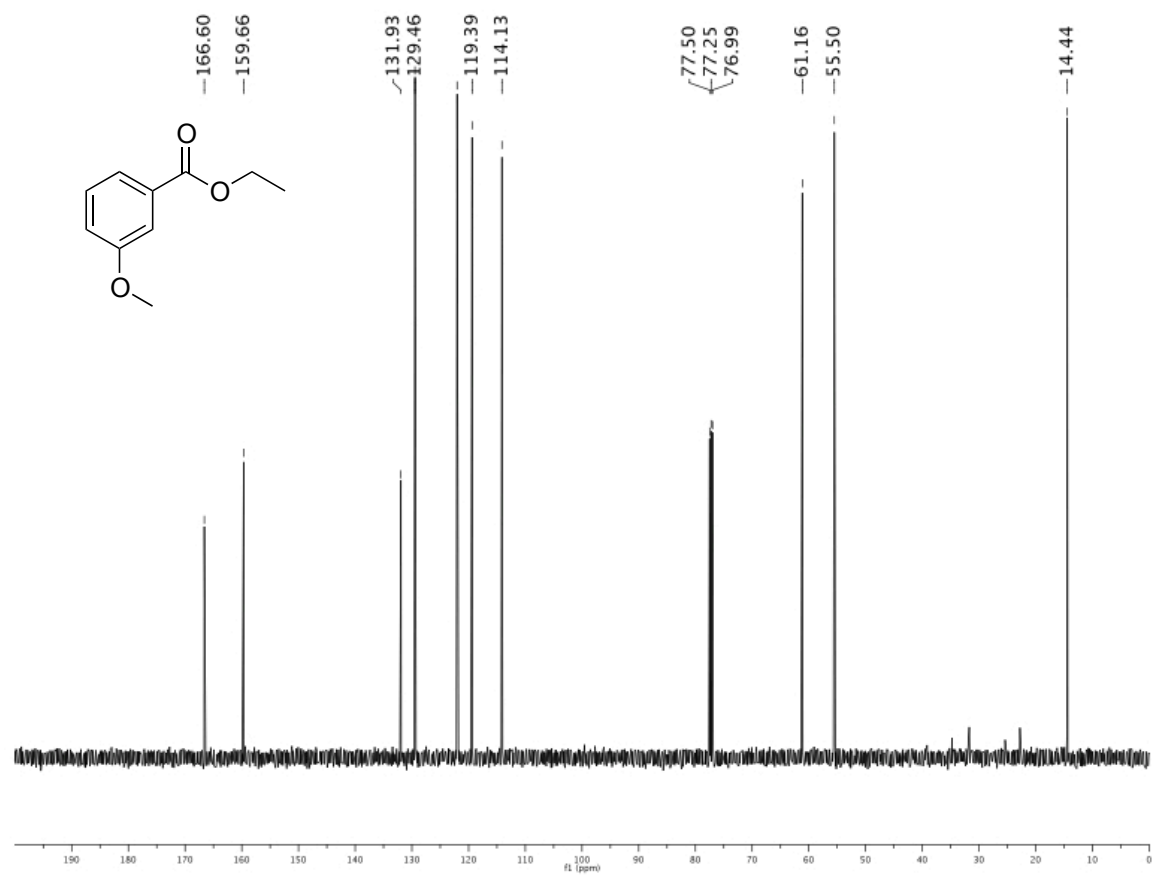
¹H NMR (500 MHz, CDCl₃) of ethyl 2,2-diphenylacetate (Table 3, entry 13b).



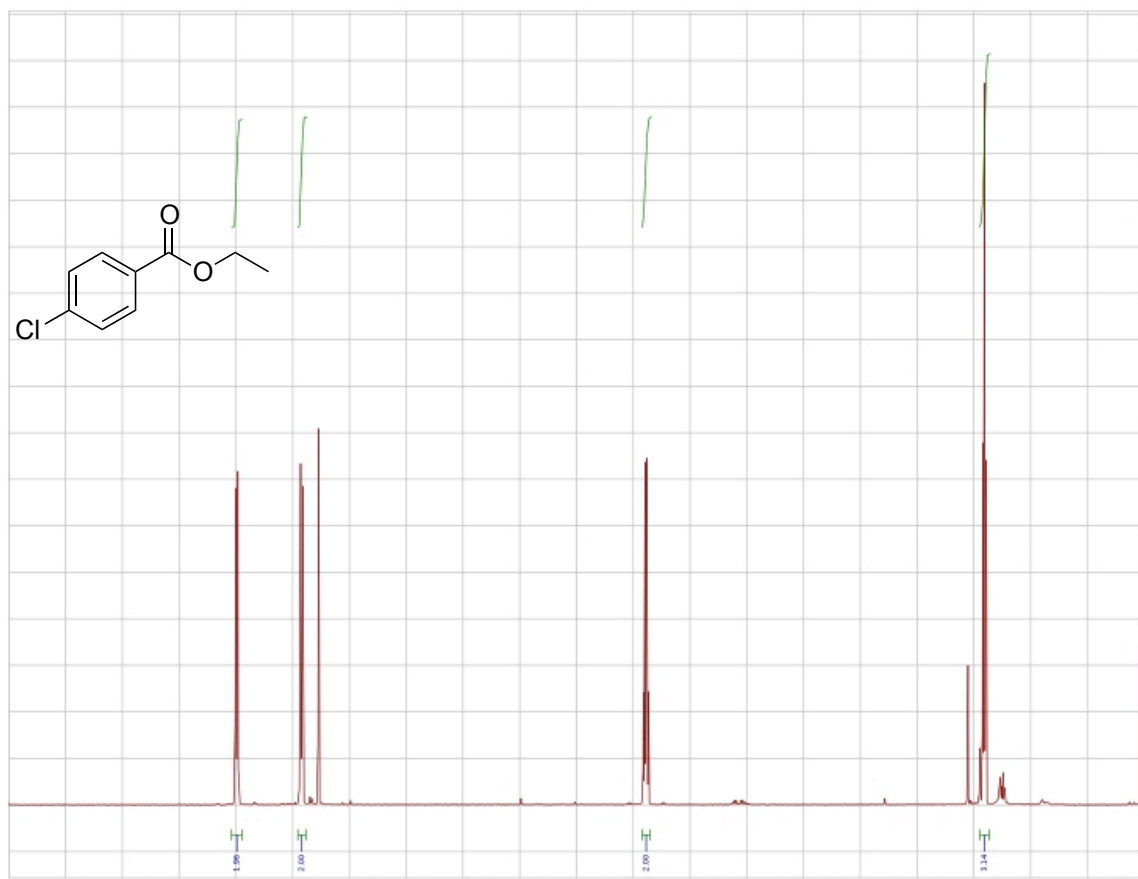
¹³C NMR (126 MHz, CDCl₃) of ethyl 2,2-diphenylacetate (Table 3, entry 13b).



¹H NMR (500 MHz, CDCl₃) of ethyl 3-methoxybenzoate (Table 3, entry 14b).



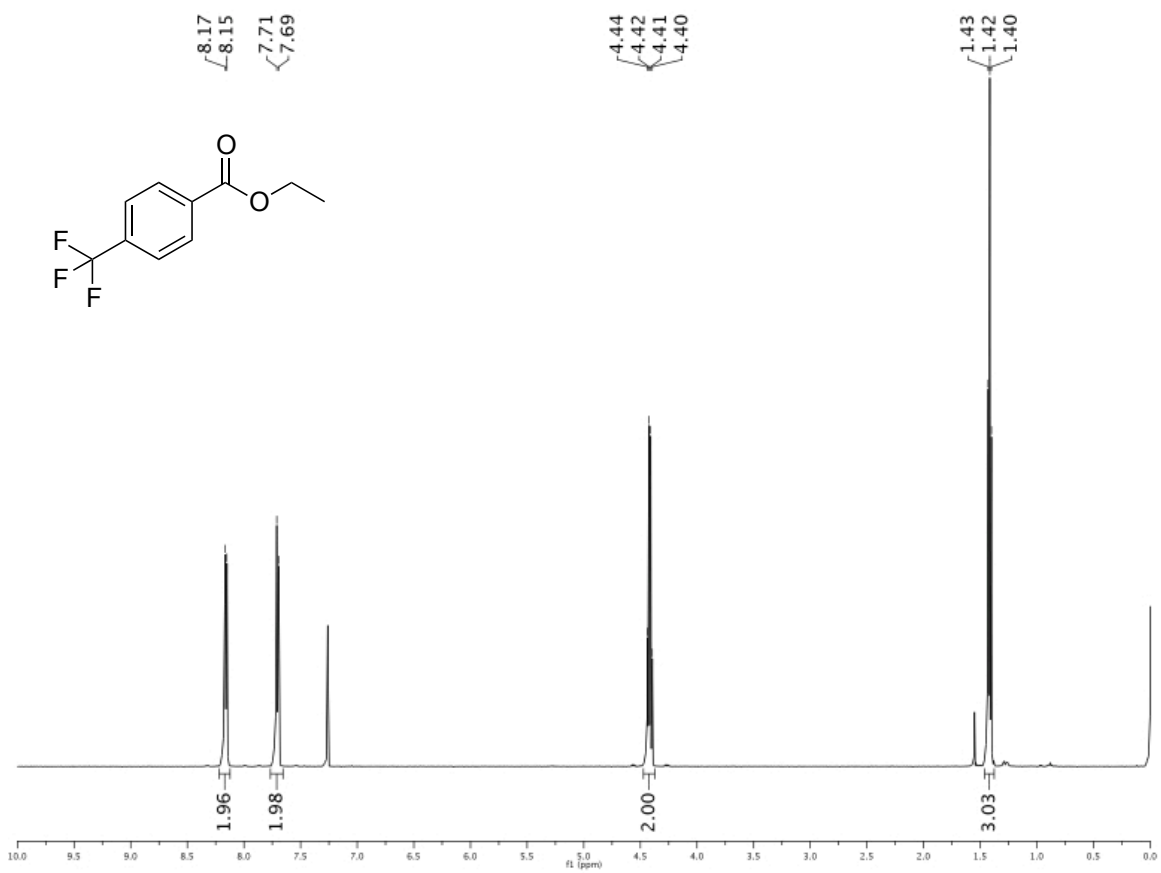
¹³C NMR (126 MHz, CDCl₃) of ethyl 3-methoxybenzoate (Table 3, entry 14b).



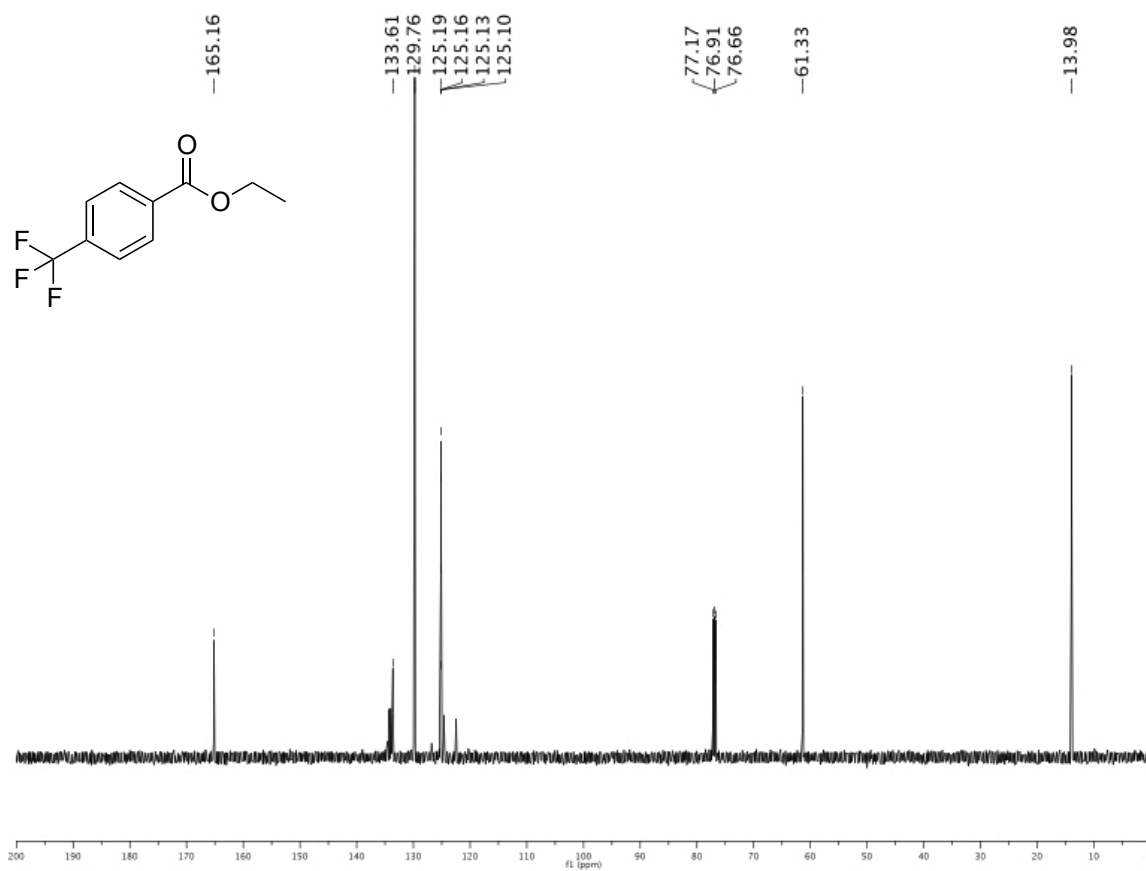
¹H NMR (500 MHz, CDCl₃) of ethyl 4-chlorobenzoate (Table 3, entry 15b).



^{13}C NMR (126 MHz, CDCl_3) of Ethyl 4-chlorobenzoate (Table 3, entry 15b).

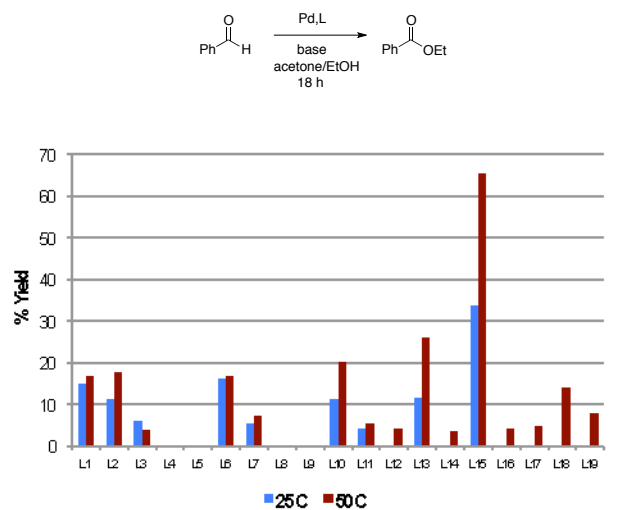


¹H NMR (500 MHz, CDCl₃) of ethyl 4-(trifluoromethyl)benzoate (Table 3, entry 16b).



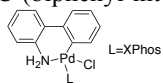
¹³C NMR (126 MHz, CDCl₃) of ethyl 4-(trifluoromethyl)benzoate (Table 3, entry 16b).

Figure 3. Comparison of Alternative Catalysts.^a



- L1-L15 Pd(OAc)₂ + indicated ligand
- L1 DavePhos: 2-Dicyclohexylphosphino-2'-(*N,N*-dimethylamino)biphenyl
- L2 JohnPhos: (2-Biphenyl)-di-*tert*-butylphosphine
- L3 XantPhos: 4,5-Bis(diphenylphosphino)-9,9-dimethylxanthene
- L4 *t*-BuXPhos: 2-Di-*tert*-butylphosphino-2',4',6'-tri-*iso*-propylbiphenyl
- L5 Me₄*t*-BuXPhos: 2-Di-*tert*-butylphosphino-3,4,5,6-tetramethyl-2',4',6'-tri-*iso*-propyl-1,1'-biphenyl
- L6 SPhos: 2-Dicyclohexylphosphino-2',6'-dimethoxybiphenyl
- L7 RuPhos: 2-Dicyclohexylphosphino-2',6'-di-*iso*-propoxybiphenyl
- L8 BrettPhos: 2-(Dicyclohexylphosphino)-3,6-dimethoxy-2',4',6'-tri-*iso*-propyl-1,1'-biphenyl
- L9 Binap: 2,2'-Bis(diphenylphosphino)-1,1'-binaphthalene
- L10 P(*o*-Tol)₃
- L11 CataCXium A: Di(1-adamantyl)-*n*-butylphosphine
- L12 dppf: 1,1'-Bis(diphenylphosphino)ferrocene
- L13 dtbpf: 1,1'-Bis(di-*tert*-butylphosphino)ferrocene
- L14 PPh₃
- L15 XPhos: 2-Dicyclohexylphosphino-2',4',6'-tri-*iso*-propylbiphenyl
- L16 XPhos w/ [(allyl)PdCl]₂ instead of Pd(OAc)₂
- L17 XPhos w/ PdCl₂(MeCN)₂ instead of Pd(OAc)₂
- L18 XPhos-Pd-G2^b precatalyst instead of Pd(OAc)₂
- L19 XPhos-Pd-G2^b precatalyst + 1 additional equiv XPhos ligand

^a Yield determined by HPLC (biphenyl internal standard).



^b XPhos-Pd-G2 precatalyst: