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Unusual multiple insertion of diazo carbonyl compounds into (purin-6-yl)benzene derivative

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1. Synthetic procedures

1.1. A dried 10 ml Schlenk tube equipped with a magnetic stirrer was charged with methyl 3,3,3-trifluoro-2-[2-(9-isopropyl-9*H*-purin-6-yl)phenyl]propanoate **3** (0.145 g, 0.38 mmol), 1,2-dichloroethane (DCE, 6 ml), $[Cp^*RhCl_2]_2$ (5.9 mg, 9.5 μmol), $AgSbF_6$ (13.1 mg, 38 μmol), and diethyl diazomalonate (0.143 g, 0.76 mmol) under argon. After the reaction mixture was stirred at 85–95°C for 3–4 h, the reaction mixture was cooled to room temperature and concentrated under reduced pressure. The residue was purified by gradient column chromatography on silica gel (petroleum ether/ethyl acetate) to give the desired product.

Diethyl 2-[2-(9-isopropyl-9*H*-purin-6-yl)-3-(1,1,1-trifluoro-3-methoxy-3-oxopropan-2-yl)phenyl]malonate (1). A mixture of diastereomers (1:1), yield 23% as a white solid (eluent petroleum ether/ethyl acetate = 2:1 → 3:2); m.p. 159–160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07–1.27 (m, 6H, $2CH_3$), 1.73–1.76 (m, 6H, $2CH_3$), 3.65 and 3.78 (both s, 3H, OCH_3), 4.01–4.22 (m, 0.5H, CH + 0.5H, CH + 4H, $2OCH_2$), 4.30 (s, 0.5H, CH), 4.47 (q, *J* = 9.0 Hz, 0.5H, CH), 4.99–5.07 (m, 1H, CH), 7.62 (t *J* = 8.0 Hz, 1H, Ar), 7.77–7.86 (m, 2H, Ar), 8.16 and 8.19 (both s, 1H, CH), 9.13 and 9.15 (both s, 1H, CH); ^{19}F NMR (376 MHz, $CDCl_3$) δ −66.53 and −65.99 (both s, 3F, CF_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8 and 13.9, 22.5 and 22.6, 47.9, 50.9 (q, *J* =28.6 Hz, >CH) and 51.7 (q, *J* = 29.0 Hz, >CH), 52.9 and 53.1, 55.1 and 55.2, 61.6 and 61.7, 61.8 and 61.9, 123.4 (q, *J* =279.0 Hz, CF_3) and 123.6 (q, *J* = 279.0 Hz, CF_3), 128.1 and 128.2, 128.8 and 128.9, 129.73, 130.6, 132.7 and 132.8, 133.4, 133.8, 136.2 and 136.3, 143.2 and 143.6, 151.6 and 151.7, 151.9 and 152.3, 154.8 and 155.0, 166.2 and 166.5, 167.3 and 167.6; Calcd for $C_{25}H_{27}F_3N_4O_6$: C, 55.97; H, 5.07; N, 17.89; found: C, 55.73; H, 5.21; N, 17.97.

Tetraethyl 1-[2-(9-isopropyl-9*H*-purin-6-yl)-3-(1,1,1-trifluoro-3-methoxy-3-oxopropan-2-yl)phenyl]ethane-1,1,2,2-tetracarboxylate (2). A mixture of diastereomers (3:1), yield 22% as a white solid (eluent petroleum ether/ethyl acetate = 2:1 → 3:2); Melting point: 142–144 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92–1.00 (m, 5H, $2CH_3$), 1.09–1.12 (m, 1H, $2CH_3$), 1.16–1.22 (m, 1H, $2CH_3$), 1.24–1.28 (m, 5H, $2CH_3$), 1.68 and 1.73 (both d, *J* = 6.7 Hz, 6H, $2CH_3$), 3.60 and 3.68 (both s, 3H, OCH_3), 3.64–3.77 (m, 1.3H, OCH_2), 3.89-4.00 (m, 2H +0.7H, OCH_2), 4.04-4.15 (m, 2H, OCH_2 + 0.7H, CH), 4.23-4.38 (m, 2H + 0.5H, OCH_2), 4.99–5.06 (m, 1H, CH), 5.30 (br.s, 0.3H, CH), 7.43–7.49 (m, 1H, Ar), 7.53–7.58 (m, 1H, Ar), 7.83 and 7.92 (both d, *J* = 7.5 Hz, 1H, Ar), 8.18 (s, 1H, CH), 9.06 and 9.10 (both s, 1H, CH); ^{19}F NMR (376 MHz, $CDCl_3$) δ −66.29 and −64.38 (both s, 3F, CF_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.3 and 13.4, 13.5, 13.6 and 13.7, 22.2 and 22.6, 48.0 and 48.2, 51.8 (q, *J* =29.0 Hz, >CH), 52.8, 52.9, 60.9 and 61.0,

61.5, 62.5 and 62.6, 65.1, 123.3 (q, J =281.4 Hz, CF_3), 127.8, 128.8, 129.2 and 129.4, 130.1 and 130.2, 132.4-132.6 (m), 134.8, 136.1 and 136.2, 142.8 and 143.4, 150.8, 151.7 and 152.2, 155.1, 165.8 and 165.9, 167.7, 168.2 and 168.3; Calcd for $C_{32}H_{37}F_3N_4O_{10}\cdot 0.75CH_2Cl_2$: C, 51.87; H, 5.12; N, 7.39; found: C, 51.77; H, 5.61; N, 6.94.

1.2. ***O*^{1},*O*^{1}-Diethyl *O*^{2}-methyl 3,3,3-trifluoroprop-1-ene-1,1,2-tricarboxylate** was synthesized similarly to methyl 3,3-dicyano-2-chlorodifluoromethylacrylate [A. S. Golubev, P. V. Pasternak, A. F. Shidlovskii, L. N. Saveleva, B. B. Averkiev, V. N. Nesterov, M. Yu. Antipin, A. S. Peregudov, N. D. Chkanikov, *J. Fluorine Chem.* 2002, **114**, 63–74.]. A mixture of methyl 3,3,3-trifluoro-2-oxopropanoate (280 mg, 1.79 mmol), diethyl malonate (287 mg, 1.79 mmol) and pyridine (20 mg, 0.25 mmol) was heated at 100 °C for 4 h. Then $SOCl_2$ (1 g, 8.40 mmol) was added, and the mixture was refluxed for 5 h. The excess of thionyl chloride was distilled off under reduced pressure and the residue was chromatographed on SiO_2 in petroleum ether – ethyl acetate mixture (5:1). The yield was 363 mg of colorless liquid (68%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.40–4.30 (m, 4H, C(O)OC*H*$_2$CH$_3$), 3.92 (s, 3H, C(O)OCH$_3$), 1.39−1.31 (m, 6H, C(O)OCH$_2$C*H*$_3$). ^{19}F NMR (376 MHz, $CDCl_3$) δ –61.6. Calcd for $C_{11}H_{13}O_6F_3$: C, 44.30; H, 4.39; found: C, 43.95; H, 4.28.

2. X-ray diffraction study

Crystals of **2** were grown up by slow diffusion in two-layer system, petroleum ether and a solution of the compound in dichloromethane.

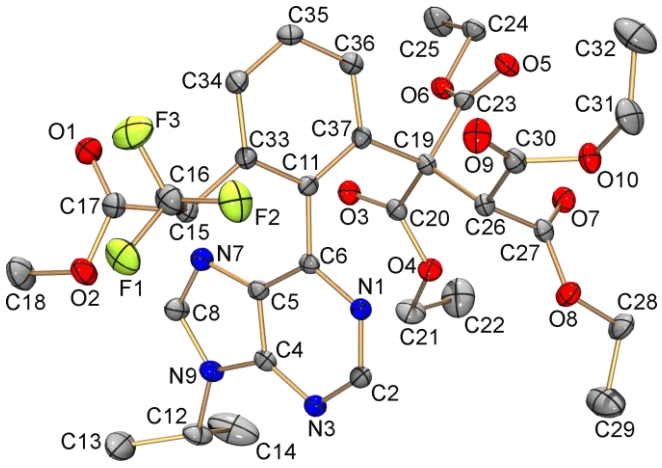

Figure S1. Compound **2** with atoms shown as thermal ellipsoids at 50% probability level. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (º): N1−C2 1.348(2), N1−C6 1.345(2), N3−C2 1.336(2), N3−C4 1.332(3), N7−C5 1.379(2), N7−C8 1.312(3), N9−C4 1.374(2), N9−C8 1.375(3), C4−C5 1.406(3), C5−C6 1.392(3), C6−C11 1.495(2), C11−C33 1.411(3), C11−C37 1.414(3), C15−C33 1.526(3), C19−C37 1.556(2), C19−C26 1.560(3), C16−C15−C17 108.63(16), C20−C19−C23 109.07(15), C27−C26−C30 112.07(15).

3. NMR spectroscopy

^{1}H, $^{13}C\{^{1}H\}$ and ^{19}F NMR spectra were recorded on a Bruker Avance-400 spectrometer operating at 400, 100 and 376 MHz, respectively. The $^{13}C\{^{1}H\}$ NMR spectrum of compound **1** was recorded on a Bruker Avance-500 spectrometer operating at 125 MHz.

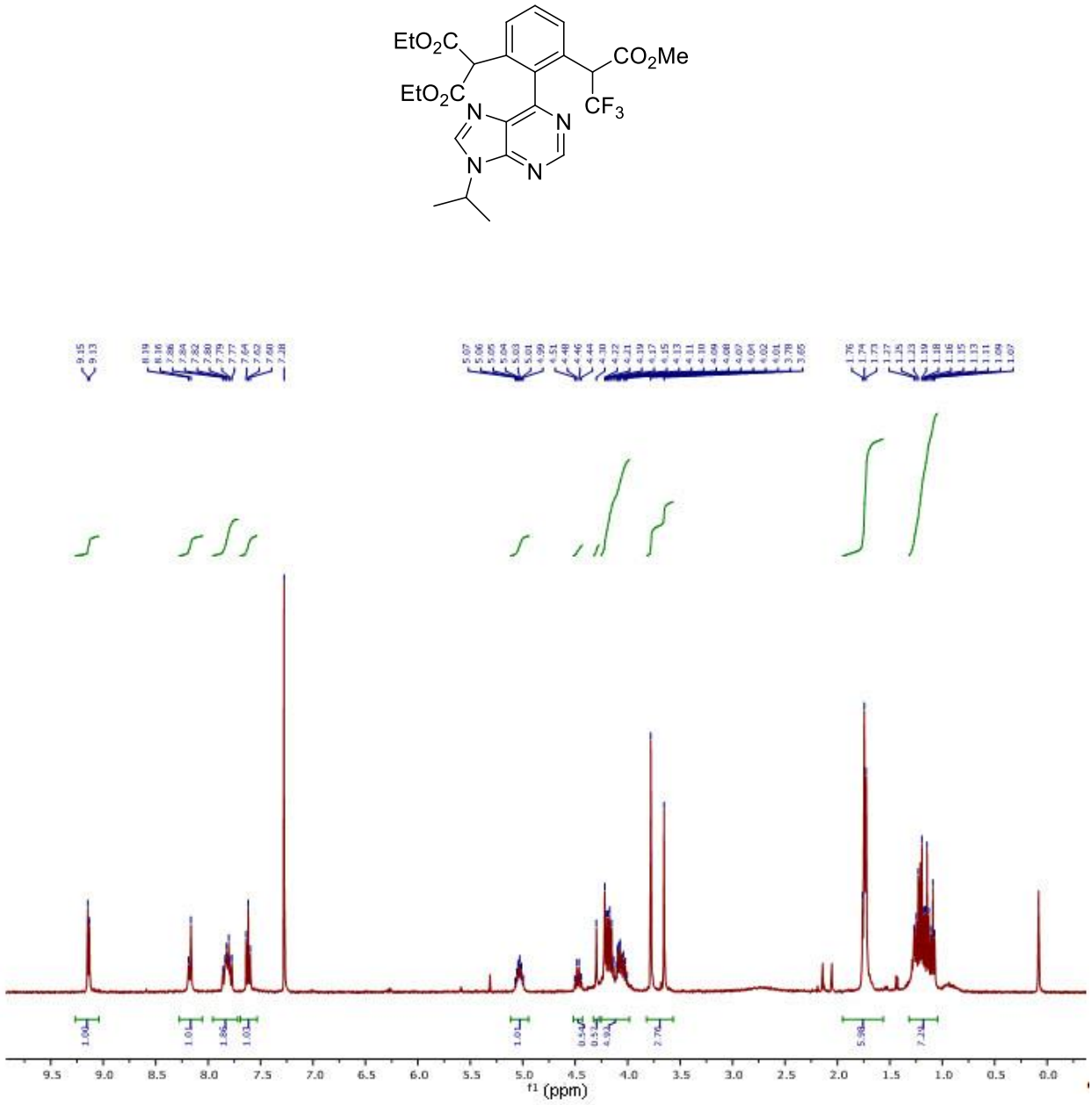

Figure S2. ^{1}H NMR spectra of compound **1** in $CDCl_3$

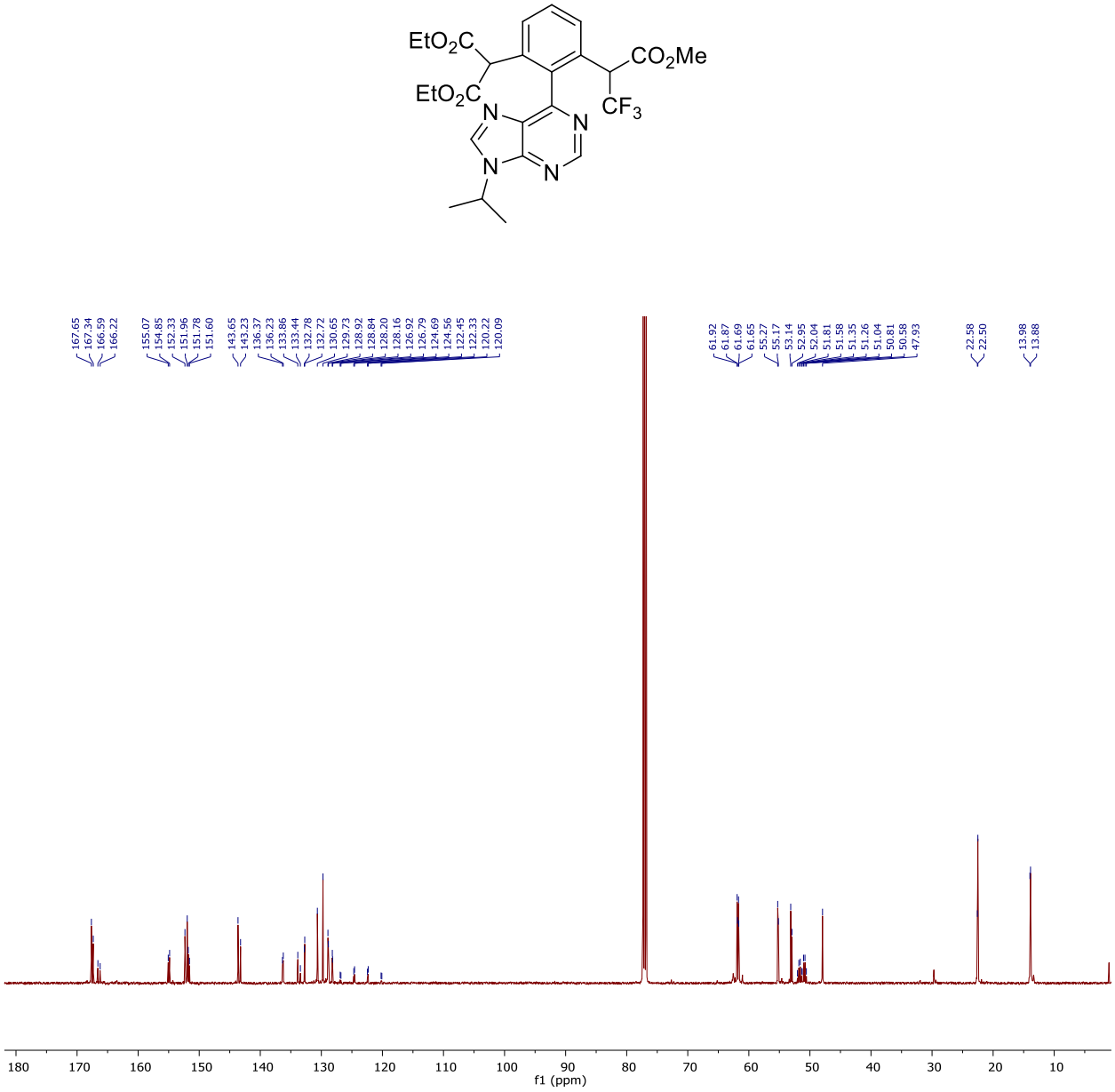

Figure S3. ^{13}C NMR spectra of compound **1** in $CDCl_3$

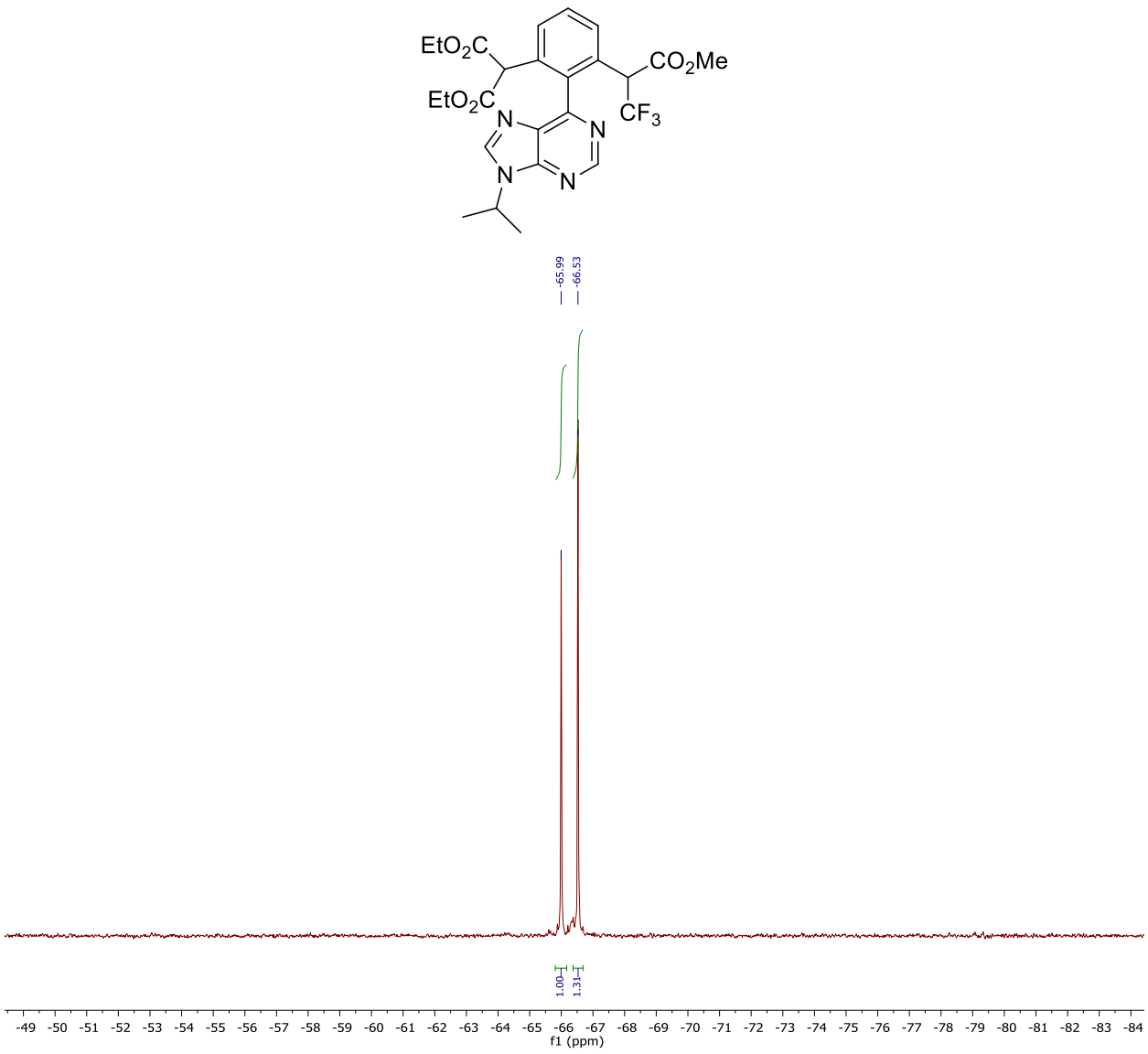

Figure S4. ^{19}F NMR spectra of compound **1** in $CDCl_3$

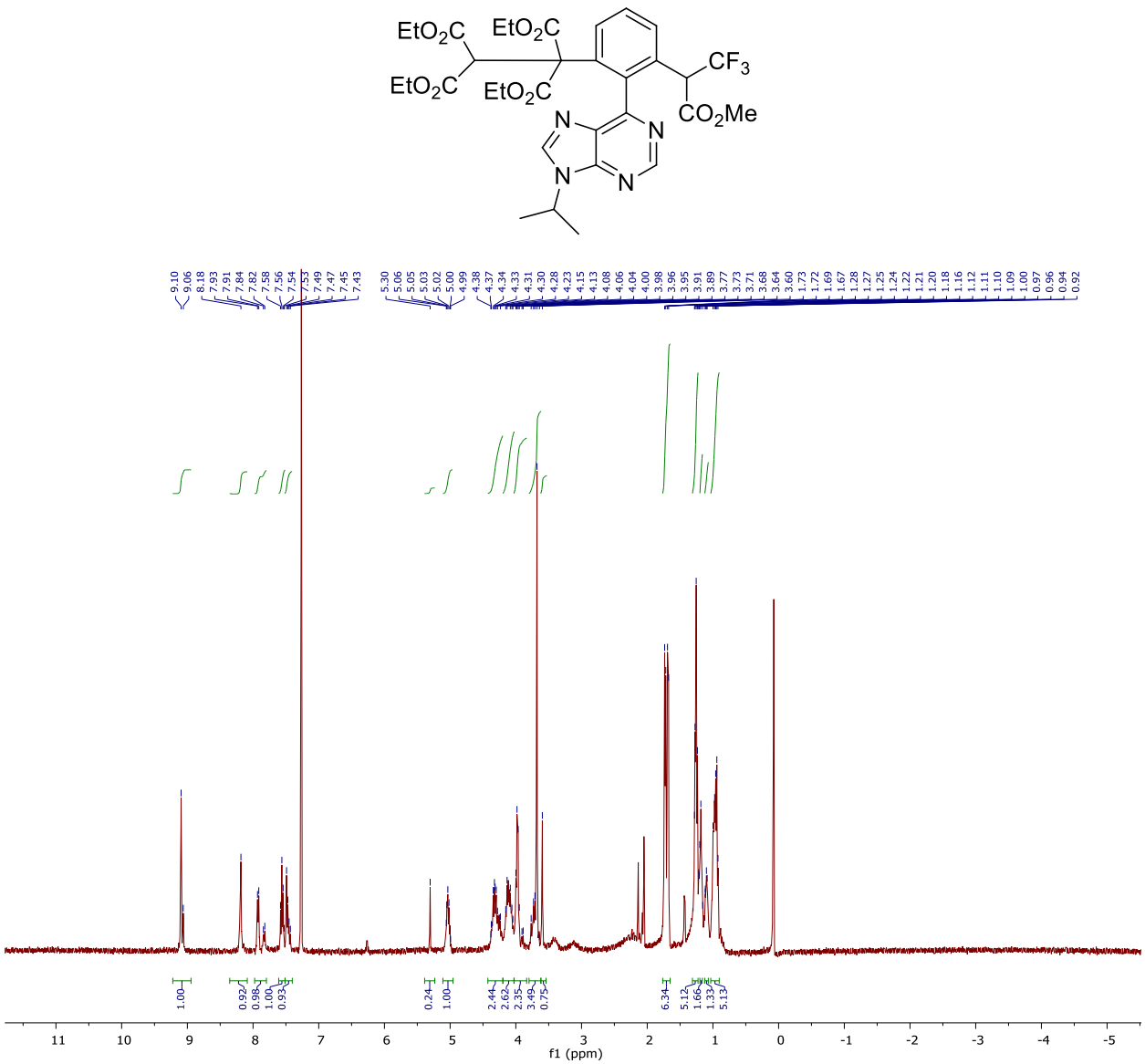

Figure S5. ^{1}H NMR spectra of compound **2** in $CDCl_3$

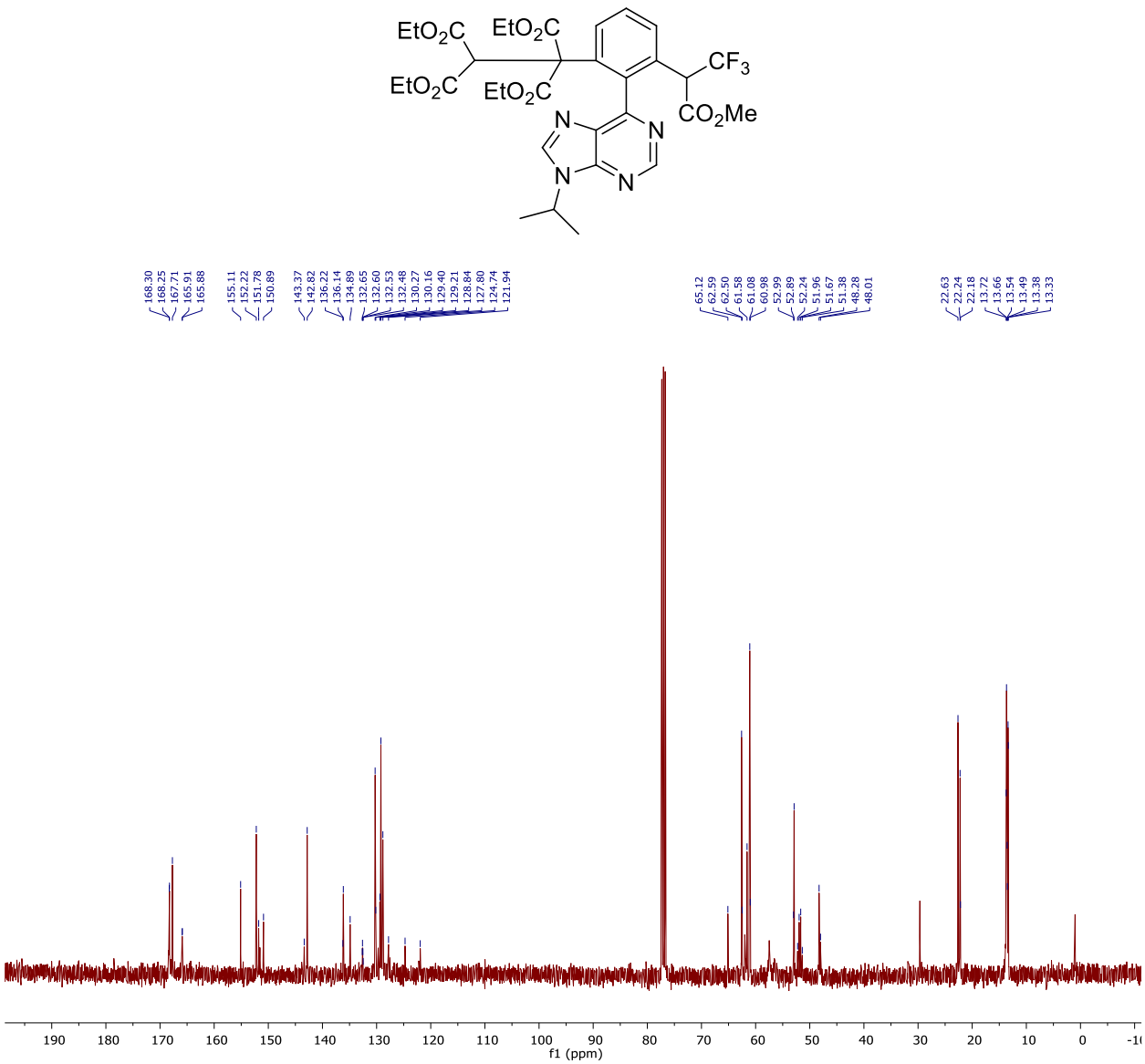

Figure S6. ^{13}C NMR spectra of compound **2** in $CDCl_3$

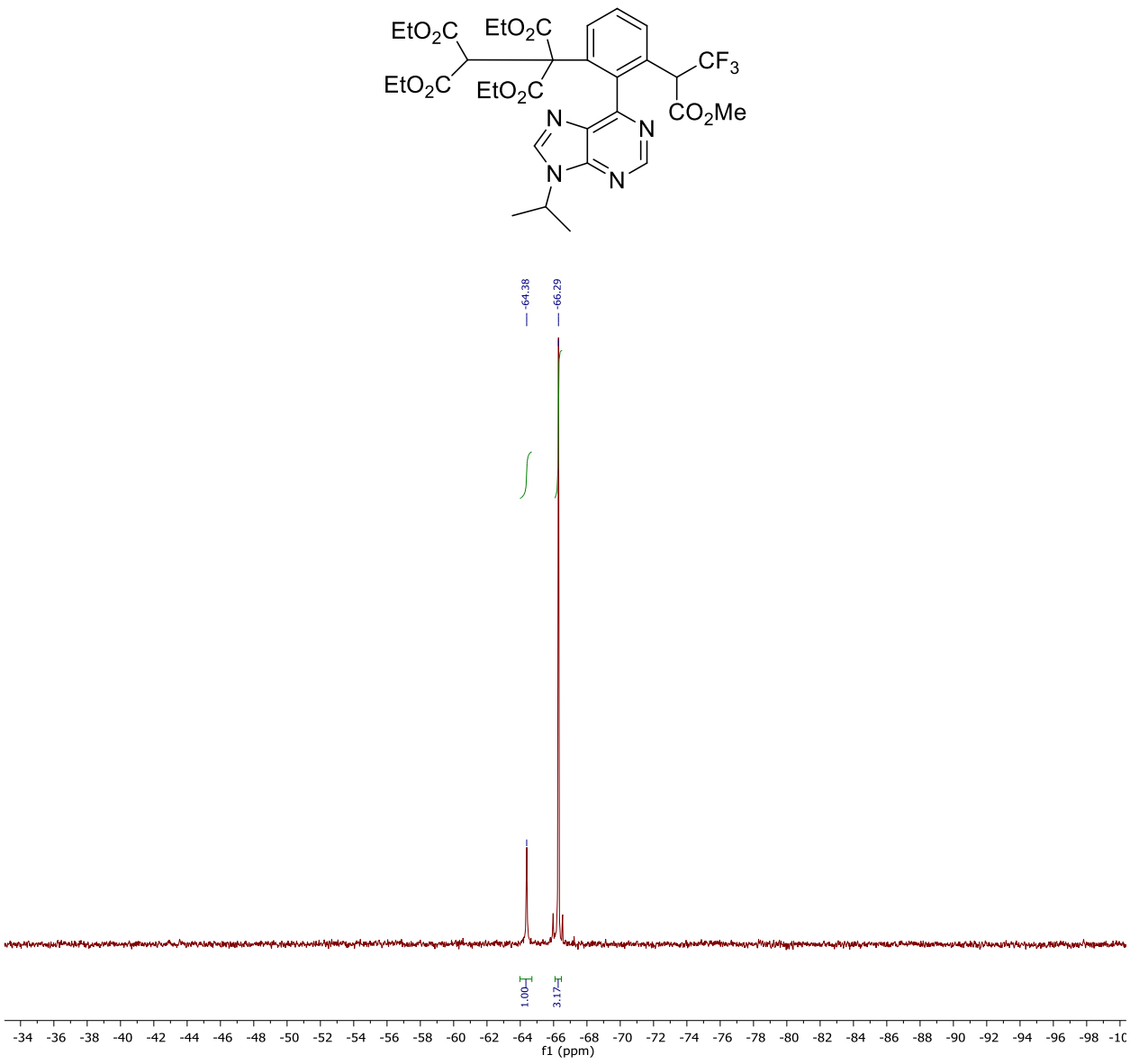

Figure S7. ^{19}F NMR spectra of compound **2** in $CDCl_3$