Supporting Information for

Lateral Lithiation in Deep Eutectic Solvents: Regioselective Functionalization of Substituted Toluene Derivatives

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Experimental Details

Materials and methods. Unless specified, all reagents were used as received without further purifications. Ethyl benzoate and benzaldehyde were distilled under vacuum prior to use. Reactions were monitored by GC-MS analysis or by thin-layer chromatography (TLC) carried out on 0.25 mm silica gel coated aluminum plates (60 Merck F254) with UV light (254 nm) as visualizing agent. Chromatographic separations were carried out under pressure on silica gel (40-63 μm, 230-400 mesh) using flash-column techniques. The following solutions of organolithium reagents were furnished by Sigma-Aldrich and used with the following concentration: *n*-BuLi 2.5 M in hexanes, *s*-BuLi 1.4 M in cyclohexane, *t*-BuLi 1.7 M in pentane. The exact concentration of the organolithium solutions was determined by titration with diphenylacetic acid in anhydrous THF prior to use.[1] *N*,*N*-diisopropylbenzamides **1a-c**[2] and **1k**,[3] oxazoline **1d**,[4] *N*,*N*-diethylbenzenesulfonamides **1e-f**,[5] and OMOM-substituted toluenes **1g-h**[6] were synthesized according to the procedures reported in the literature. *Deep Eutectic Solvents* [choline chloride (ChCl)/urea (1:2 mol/mol); ChCl/glycerol (Gly) (1:2 mol/mol), ChCl/H_2O (1:2 mol/mol)] were prepared by heating under stirring at 60–80 °C for 10–30 min the corresponding individual components until a clear solution was obtained.[7] Full characterization data, including copies of ^{1}H and ^{13}C NMR spectra, have been reported for both the newly synthesized compounds and the known compounds.

Instrumentation. ^{1}H NMR (600 MHz) and ^{13}C{1H} (150 MHz) NMR spectra were recorded on a Jeol ECZR600 spectrometer at room temperature using residual solvent peak as an internal reference. ^{2}H NMR (92.07 MHz) spectra were obtained in CH_2Cl_2 using residual CD_2Cl_2 as an internal reference. Chemical shifts (δ) are given in parts per million (ppm) and coupling constants (*J*) in Hertz (Hz). Multiplicities are reported as follows: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), sext (sextet), sept (septet), m (multiplet), br (broad). Low-resolution MS spectra were recorded at an ionizing voltage of 70 eV on a HP 5989B mass selective detector connected to an HP 5890 GC with a methyl silicone capillary column (EI). GC analyses were performed on a PerkinElmer Autosystem XL chromatographic system equipped with a methyl silicone capillary column. The MS flow-injection analyses were run on a high resolving power hybrid mass spectrometer (HRMS) Orbitrap Fusion (Thermo Scientific, Rodano, Italy), equipped with an a ESI ion source. The samples were analyzed in acetonitrile solution using a syringe pump at a flow rate of 5 μL/min. The tuning parameters adopted for the ESI source were: source voltage 4.0 kV. The heated capillary temperature was maintained at 275 °C. The mass accuracy of the recorded ions (vs. the calculated ones) was ± 2.5 mmu (milli-mass units). Analyses were run using both full MS (150-2000 m/z range) and MS/MS acquisition, at 500000 resolutions (200 m/z).

Nitromethane was used as internal standard for quantitative NMR analyses on crude reaction mixtures.

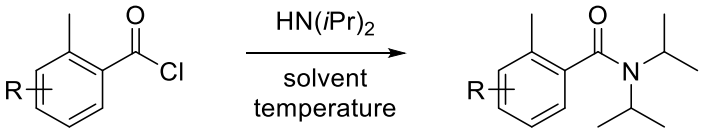
For each ^{1}H NMR the amount of product was determined by applying the following equation (Eq. 1):

$$yield\ (\%) = \frac{x\ (product) \cdot n\ (CH_3NO_2)}{n(starting\ material)} \cdot f \cdot 100$$

where:

- *x* is the value of integral/number of protons;
- *n* is the amount of starting material or CH_3NO_2 in mmol;
- *f* the diluting factor used for the preparation of the sample.

Synthesis and analysis of compounds **1i** and **1j**.



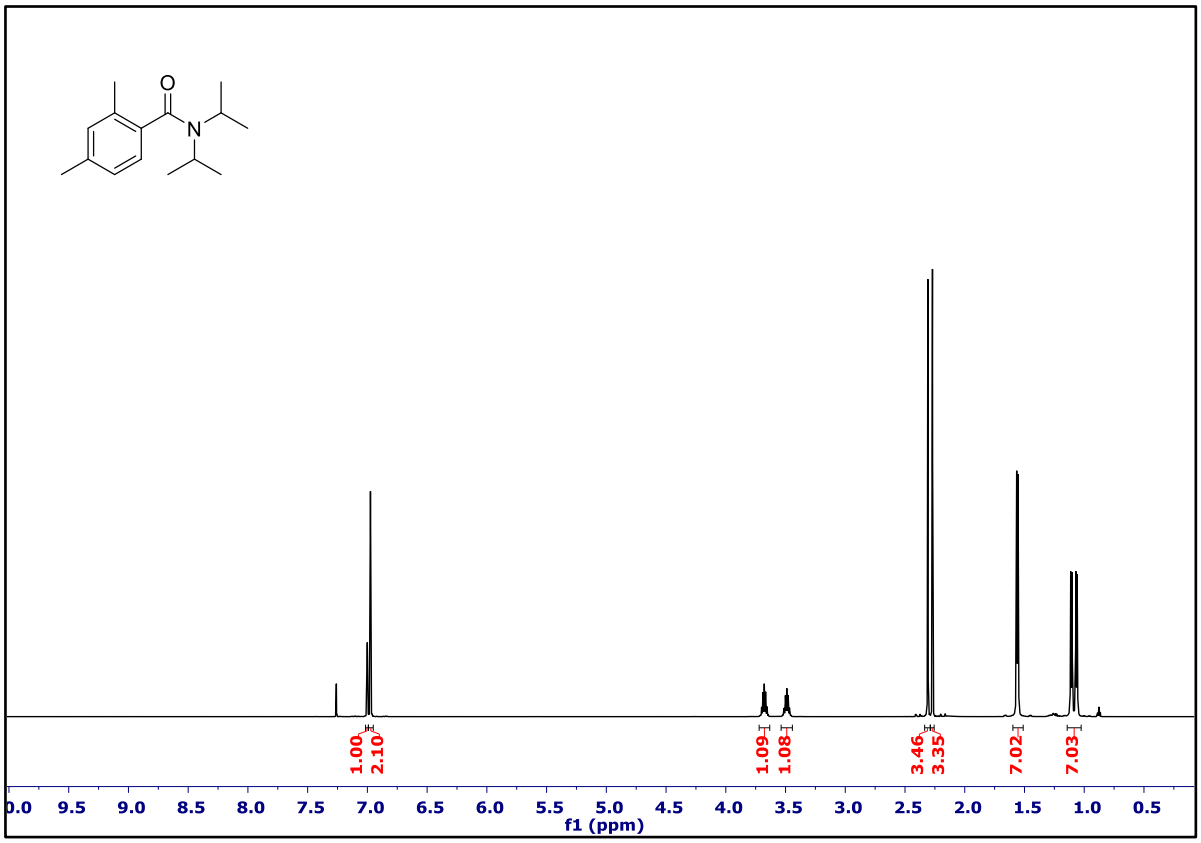
1i: R = 4-Me
1j: R = 6-Me

***N,N*-diisopropyl-2,4-dimethylbenzamide** (**1i**): 2,4-Dimethylbenzoyl chloride (1.5 g, 10 mmol) was added dropwise to a solution of *N,N*-diisopropylamine (7.3 ml, 50 mmol) in dichloromethane (20 mL) at 0 °C. The reaction mixture was warmed to room temperature and stirred until completion as monitored by TLC analysis (6 h). Water (15 mL) was added and the organic layer was washed with 1 M aq. HCl (3 x 15 mL) followed by saturated $NaHCO_3$ aq. solution (3 x 15 mL), dried over $NaSO_4$ and concentrated to under reduced pressure. Purification by crystallization from heptane gave **1i** as a white crystalline solid (1.67 g, 71%, R_f = 0.38 PE/EtOAc 9/1 v/v), mp 81-83 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.00-6.97 (m, 3H), 3.68 (sept, *J* = 6.7 Hz, 1H), 3.49 (sept, *J* = 6.8 Hz, 1H), 2.31 (s, 3H), 2.27 (s, 3H), 1.56 (d, *J* = 6.2 Hz, 6H), 1.11 (d, *J* = 6.9 Hz, 3H), 1.06 (d, *J* = 6.9 Hz, 3H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 171.2, 137.9, 135.8, 133.6, 131.2, 126.5, 124.7, 50.9, 45.9, 21.3, 21.0, 20.9, 20.8, 20.7, 18.9. EI-MS *m/z* (%): 233 (M^+, 16), 218 (12), 190 (17), 133 (100). ESI-HRMS $[M+Na]^+$: *m/z* 256.1675, $C_{15}H_{23}NONa^+$ requires 256.1672.

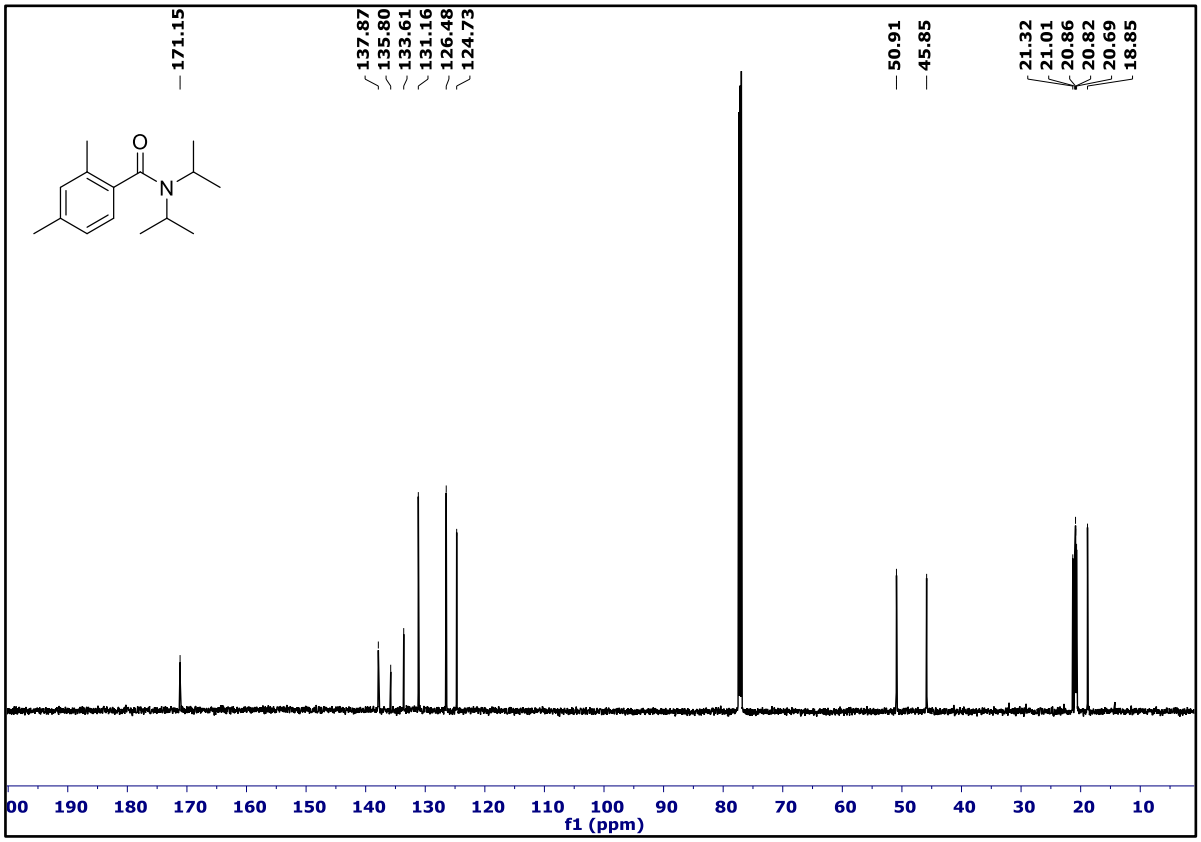
***N,N*-diisopropyl-2,6-dimethylbenzamide (1j)**: 2,6-Dimethylbenzoyl chloride (1.5 g, 10 mmol) was added dropwise to a solution of *N,N*-diisopropylamine (7.3 mL, 50 mmol) in dichloroethane (20 mL) at 0 °C. The mixture was heated to reflux and stirred until completion as monitored by TLC analysis (12 h). Water (15 mL) was added and the organic layer was washed with 1 M aq. HCl (3 x 15 mL) followed by saturated $NaHCO_3$ aq. solution (3 x 15 mL), dried over $NaSO_4$ and concentrated to under reduced pressure. Purification by flash column chromatography (PE/EtOAc 9/1 v/v) gave the amide **1j** as a white solid (1.47 g, 67%, R_f = 0.38 PE/EtOAc 9/1 v/v), mp 130-132. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.09 (t, *J* = 7.6 Hz, 1H), 6.98 (d, *J* = 7.6 Hz, 2H), 3.61 (sept, *J* = 6.7 Hz, 1H), 3.51 (sept, *J* = 6.9 Hz, 1H), 2.27 (s, 6H), 1.59 (d, *J* = 6.9 Hz, 6H), 1.10 (d, *J* = 6.5 Hz, 6H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 170.4, 138.2, 133.4, 127.6, 127.6, 50.9, 46.0, 21.2, 20.7, 19.1. EI-MS *m/z* (%): 233 (M^+, 6), 218 (13), 190 (12), 133 (100). ESI-HRMS $[M+Na]^+$: *m/z* 256.1677, $C_{15}H_{23}NONa^+$ requires 256.1672.

***N*,*N*-diisopropyl-2,4-dimethylbenzamide (1i)**

^{1}H NMR (600 MHz, $CDCl_3$)

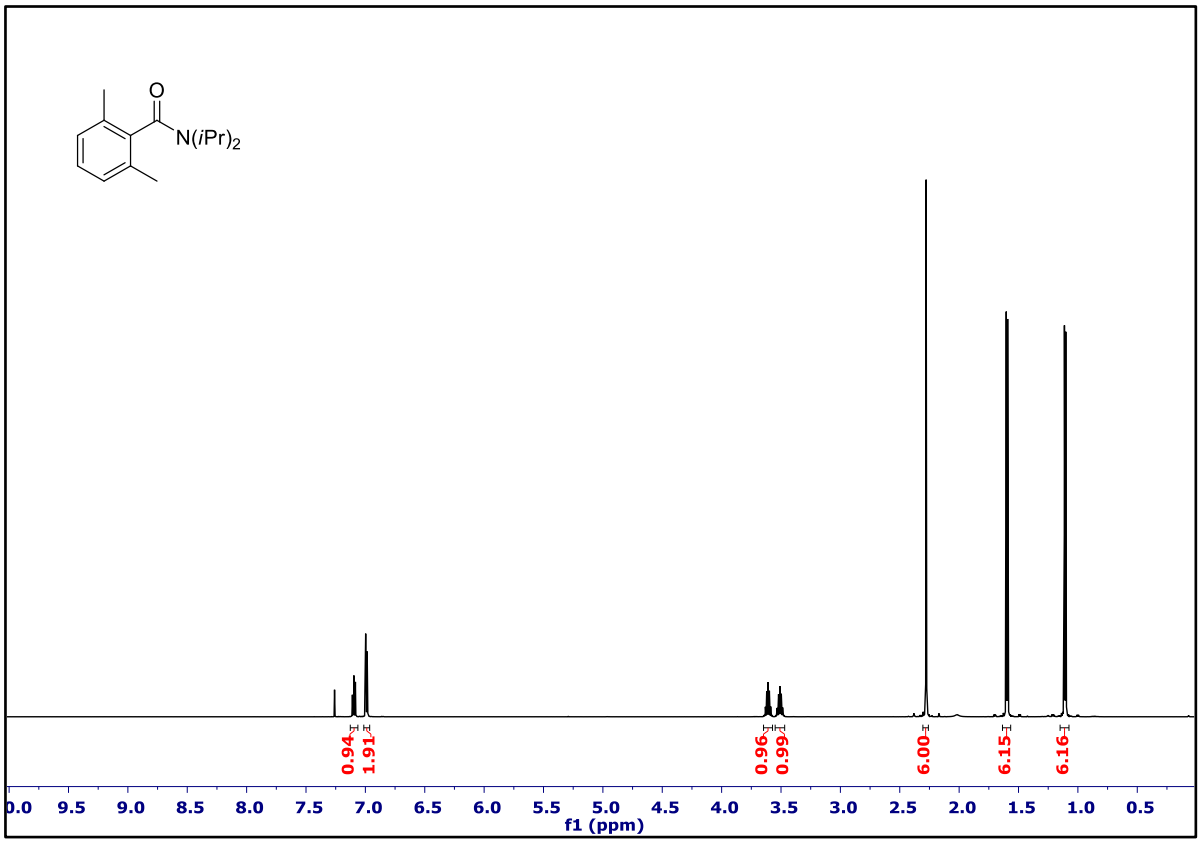


^{13}C NMR (150 MHz, $CDCl_3$)

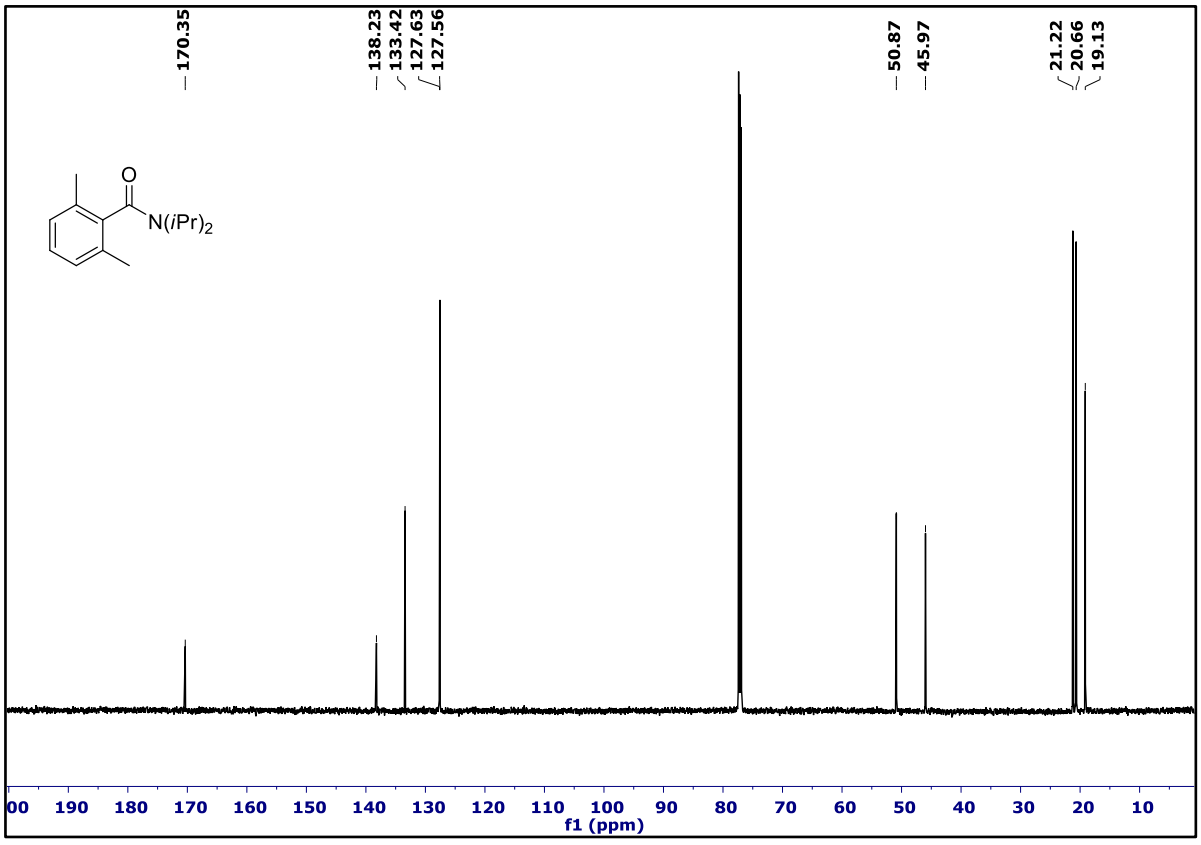


***N,N*-diisopropyl-2,6-dimethylbenzamide (1j)**

^{1}H NMR (600 MHz, $CDCl_3$)



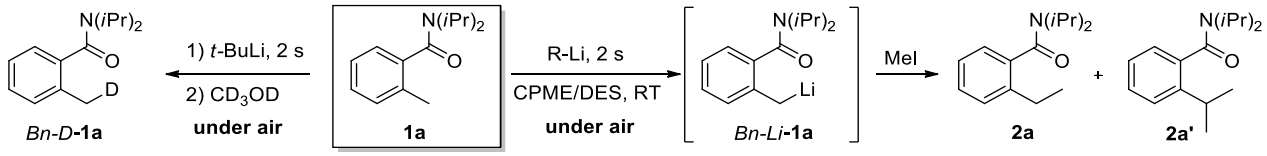
^{13}C NMR (150 MHz, $CDCl_3$)



Lateral metalation of *N*,*N*-diisopropyl-2-methylbenzamide **1a** under different reaction conditions

All reactions were performed under air. In an open screw cap vial, *N*,*N*-diisopropyl-2-methylbenzamide **1a** (43.8 mg, 0.2 mmol, 1 eq.) was dissolved in the selected unconventional solvent and the resulting mixture was vigorously stirred for 5 min. A selected amount of organolithium base was rapidly spread over the heterogeneous mixture, which was kept under vigorous stirring and quenched by addition of iodomethane or deuterated methanol after 2 seconds (experimental details are reported in each Figure caption). The mixture was diluted with water (5 mL) and extracted with Et_2O (3 x 5 mL). The combined organic layers were dried over Na_2SO_4 and the solvent removed under reduced pressure. Yields of **1a** were determined by quantitative ^{1}H NMR analysis of the crude reaction mixtures using nitromethane (0.074 mmol, 4 μL) as internal standard and a diluting factor 2 for the preparation of the sample (see Eq. 1). A sample of **2a** was synthesized according to the procedure reported in the literature[2a] and used as reference for qNMR analyses (^{1}H NMR reported in Figure S1).

Table S1. Metalation reaction of *N*,*N*-diisopropyl-2-methylbenzamide **1a** under different conditions.[a]



Entry	DES	R-Li (eq.)	E^+ (eq.)	Product (yield %)[b]	**2a'** (%)[b]
1	ChCl/Gly	*t*-Bu (2)	MeI (5)	**2a** (62)	6
2	ChCl/Gly[c]	*t*-Bu (2)	MeI (5)	-	-
3	ChCl/Gly[d]	*t*-Bu (2)	MeI (5)	**2a** (52)	9
4	ChCl/urea	*t*-Bu (2)	MeI (5)	**2a** (59)	7
5	ChCl/H_2O	*t*-Bu (2)	MeI (5)	-	-
6	ChCl/Gly	*t*-Bu (2)	MeI (3)	**2a** (41)	6
7	ChCl/Gly	*t*-Bu (1)	MeI (5)	**2a** (50)	-
8	ChCl/Gly	*t*-Bu (1.2)	MeI (5)	**2a** (58)	-
9	ChCl/Gly	*t*-Bu (1.5)	MeI (5)	**2a** (70)	2
10	ChCl/Gly	*t*-Bu (1.5)	CD_3OD (5)	*Bn-D*-**1a**[e]	-
11	ChCl/Gly	*n*-Bu (1.5)	MeI (5)	**2a** (26)	-
12	ChCl/Gly	*s*-Bu (1.5)	MeI (5)	**2a** (38)	-

[a] Reaction conditions: 1.0 g DES per 0.2 mmol of **1a,** CPME (0.2 mL); DES: ChCl/Gly (1:2 mol mol^{-1}); ChCl/urea (1:2 mol mol^{-1}); ChCl/H_2O (1:2 mol mol^{-1}). [b] Determined by ^{1}H NMR using CH_3NO_2 as the internal standard. [c] No CPME was added. [d] T = 0 °C. [e] *Bn-D*-**1a**: 80% isolated yield (80% D incorporation).

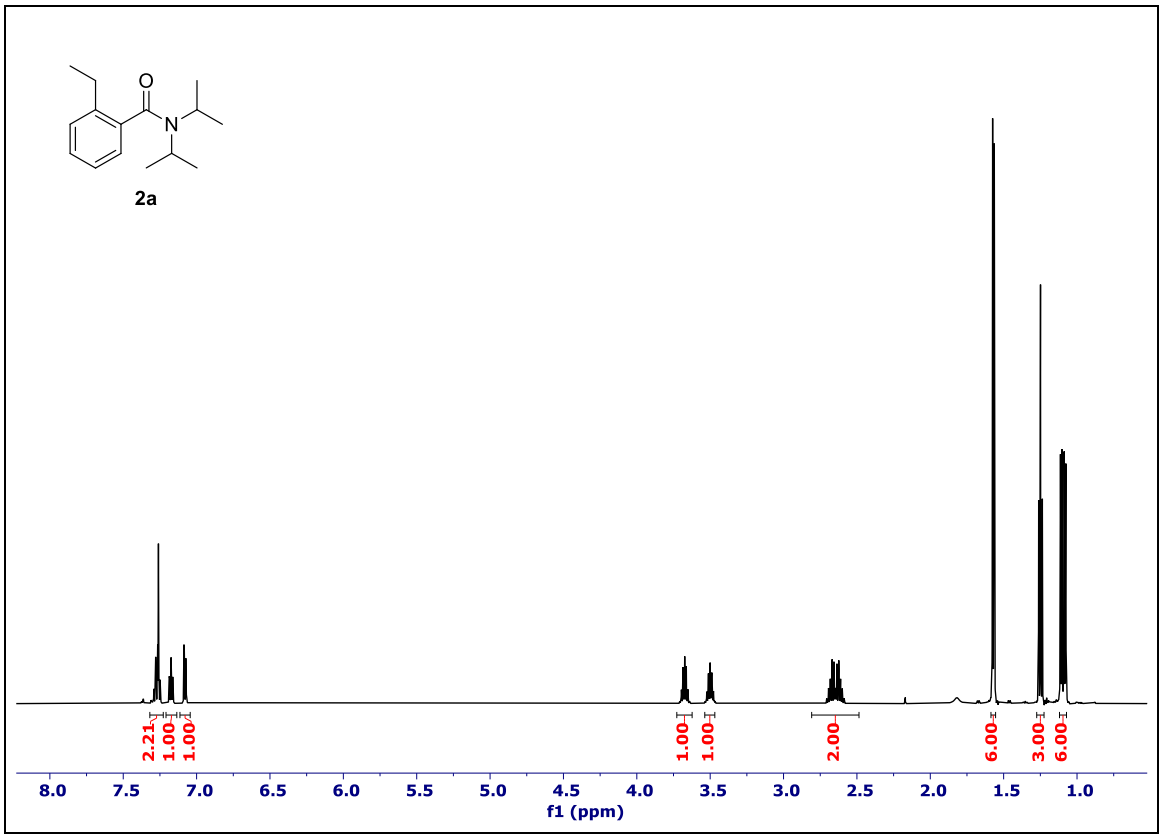


Figure S1. ^{1}H NMR spectrum of *N*,*N*-diisopropyl-2-ethylbenzamide **2a**.

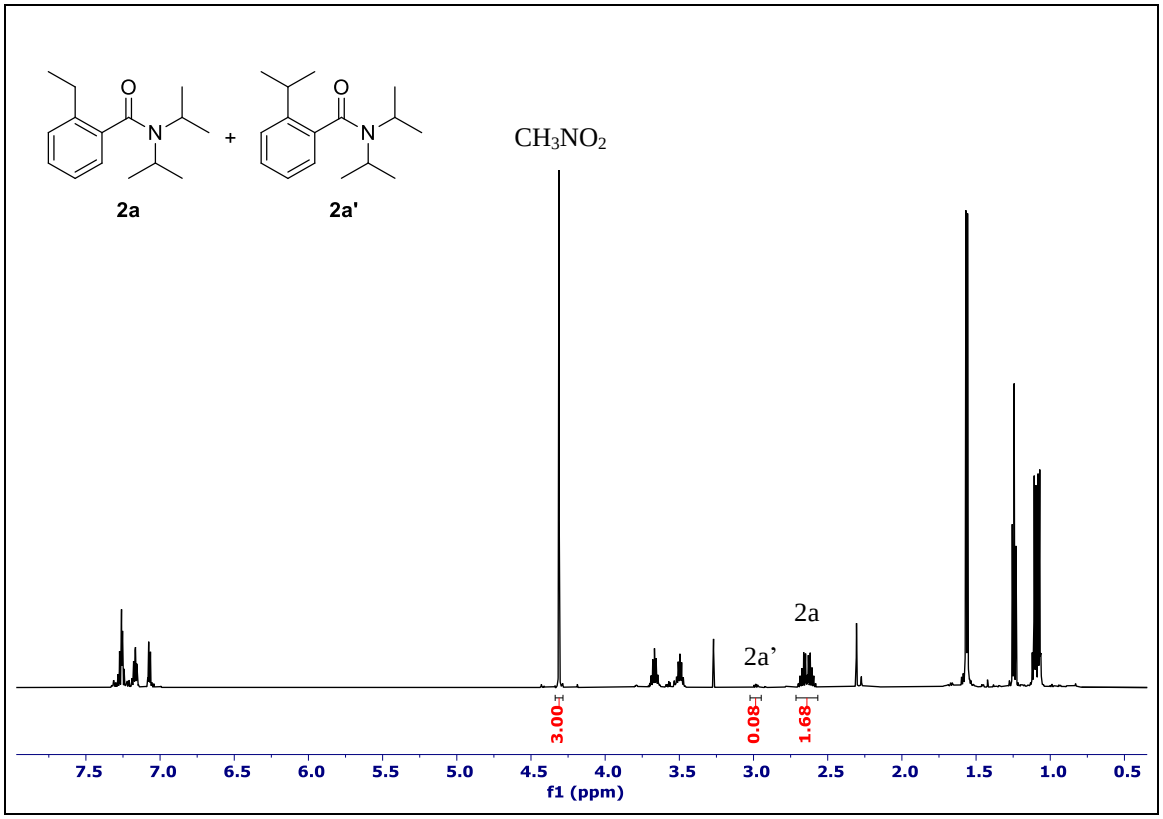


Figure S2. Table S1 entry 1: crude ^{1}H NMR spectrum of the reaction performed in CPME (0.2 mL) - *ChCl/Gly 1:2* (1 g), 2 eq. of *t*-BuLi, 5 eq. of CH_3I. Room temperature. Yield of **2a**: 62%. Yield of **2a'**: 6%.

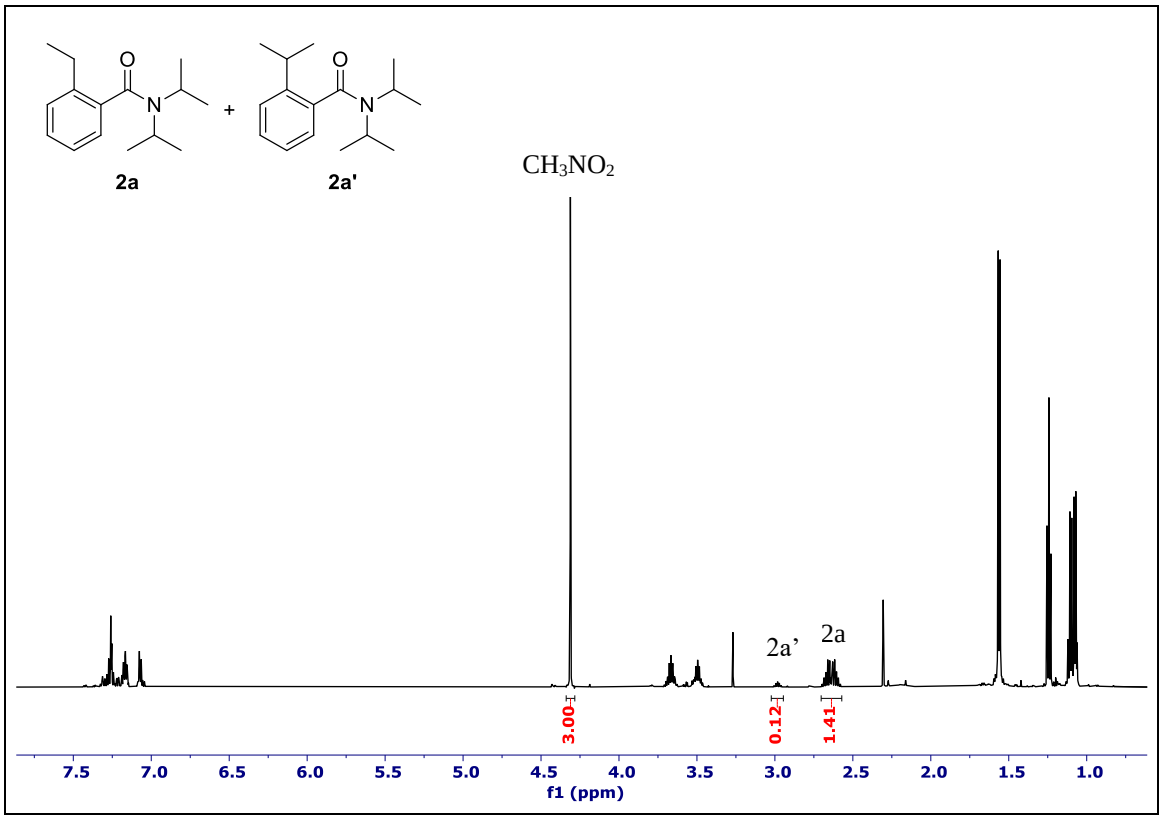


Figure S3. Table S1 entry 3: crude ^{1}H NMR spectrum of the reaction performed in CPME (0.2 mL) - *ChCl/Gly 1:2* (1 g), 2 eq. of *t*-BuLi, 5 eq. of CH_3I. 0 °C. Yield of **2a**: 52%. Yield of **2a'**: 9%.

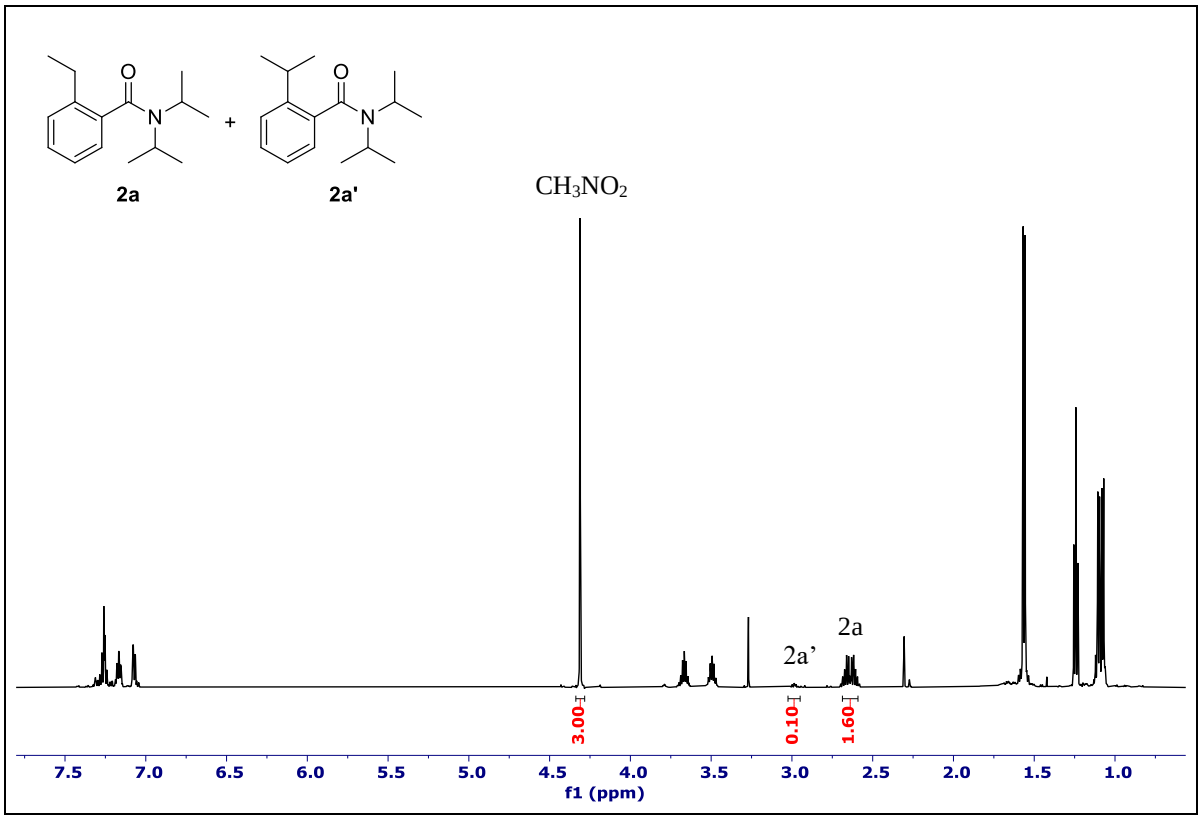


Figure S4. Table S1 entry 4: crude ^{1}H NMR spectrum of the reaction performed in CPME (0.2 mL) - *ChCl/urea 1:2* (1 g), 2 eq. of *t*-BuLi, 5 eq. of CH_3I. Room temperature. Yield of **2a**: 59%. Yield of **2a'**: 7%.

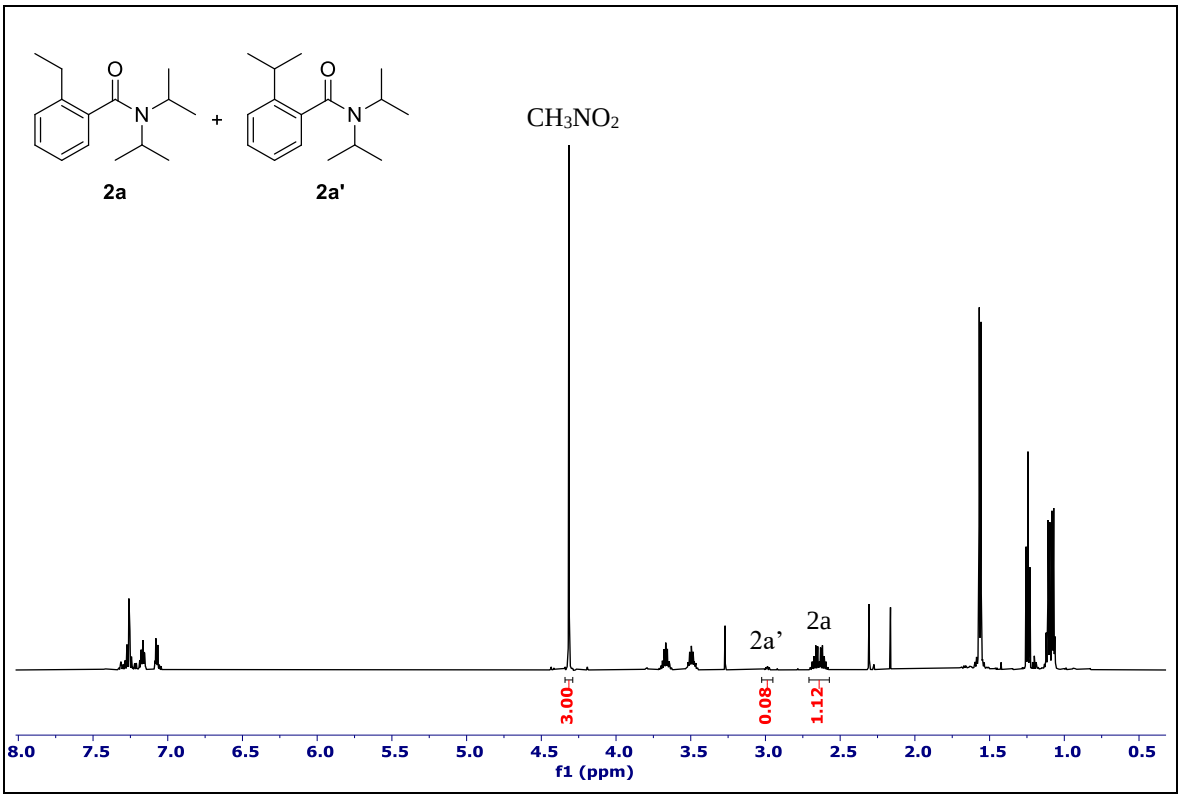


Figure S6. Table S1 entry 6: crude ^{1}H NMR spectrum of the reaction performed in CPME (0.2 mL) - *ChCl/Gly 1:2* (1 g), 2 eq. of *t*-BuLi, 3 eq. of CH_3I. Room temperature. Yield of **2a**: 41%. Yield of **2a'**: 6%.

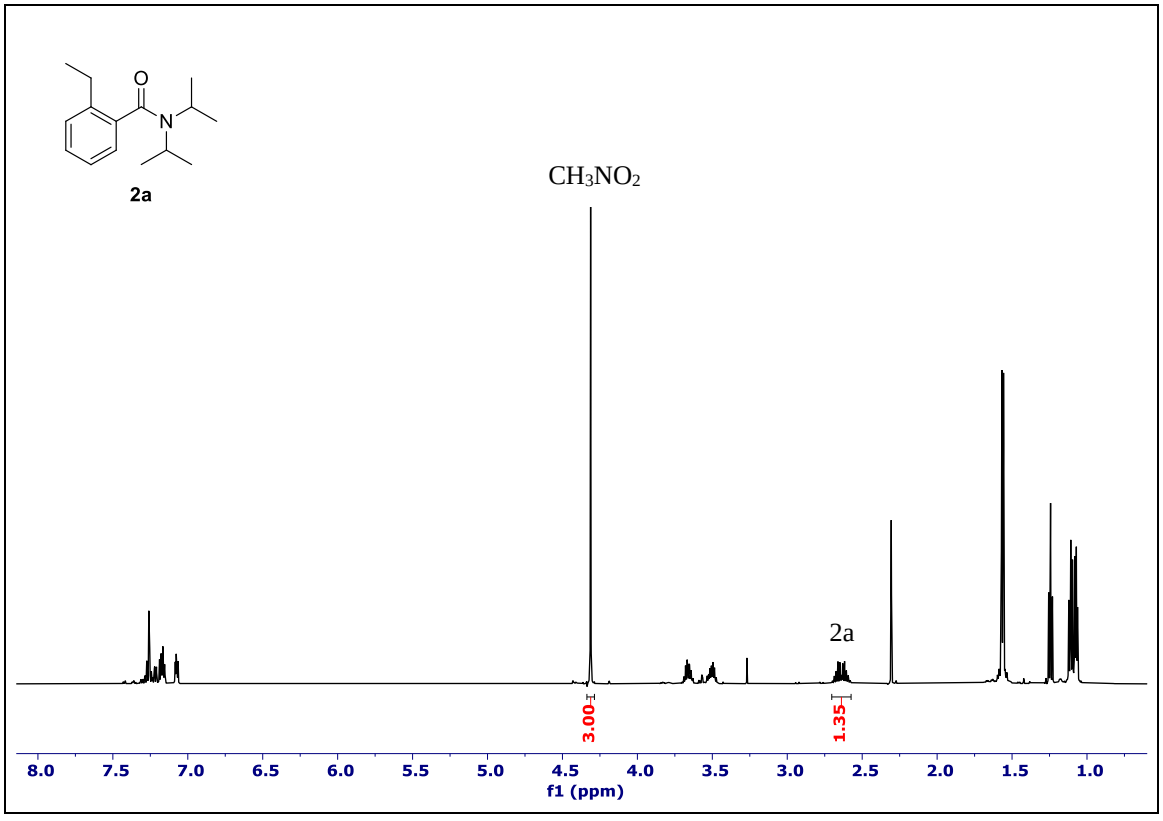


Figure S7. Table S1 entry 7: crude ^{1}H NMR spectrum of the reaction performed in CPME (0.2 mL) - *ChCl/Gly 1:2* (1 g), 1 eq. of *t*-BuLi, 5 eq. of CH_3I. Room temperature. Yield of **2a**: 50%.

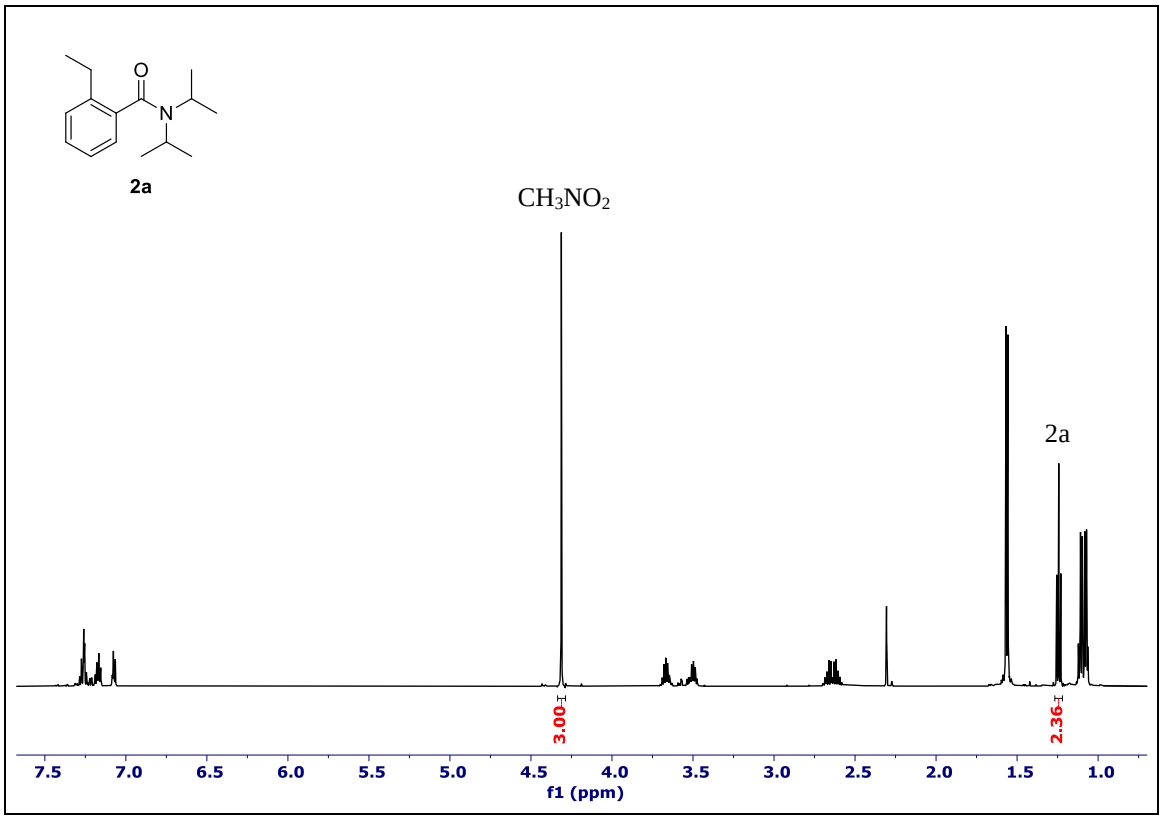


Figure S8. Table S1 entry 8: crude ^{1}H NMR spectrum of the reaction performed in CPME (0.2 mL) - *ChCl/Gly 1:2* (1 g), 1.2 eq. of *t*-BuLi, 5 eq. of CH_3I. Room temperature. Yield of **2a**: 58%.

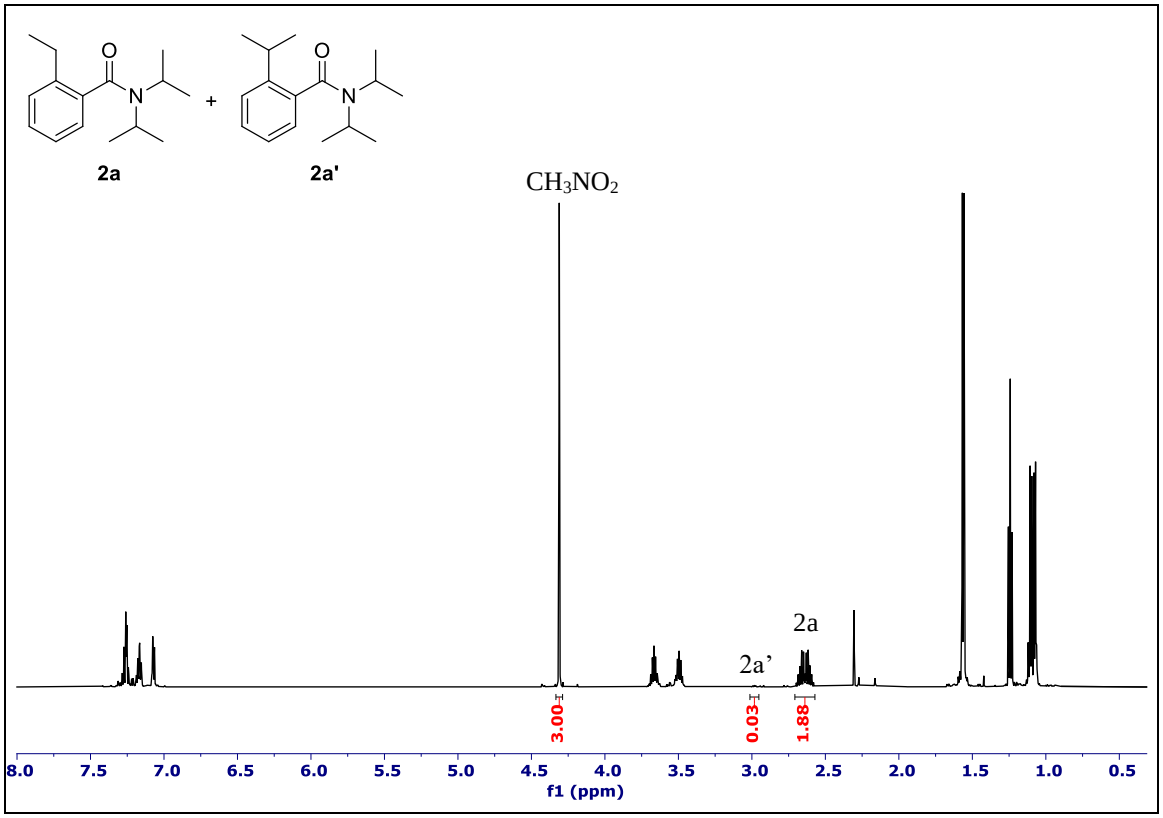


Figure S9. Table S1 entry 9: crude ^{1}H NMR spectrum of the reaction performed in CPME (0.2 mL) - *ChCl/Gly 1:2* (1 g), 1.5 eq. of *t*-BuLi, 5 eq. of CH_3I. Room temperature. Yield of **2a**: 70%. Yield of **2a'**: 2%.

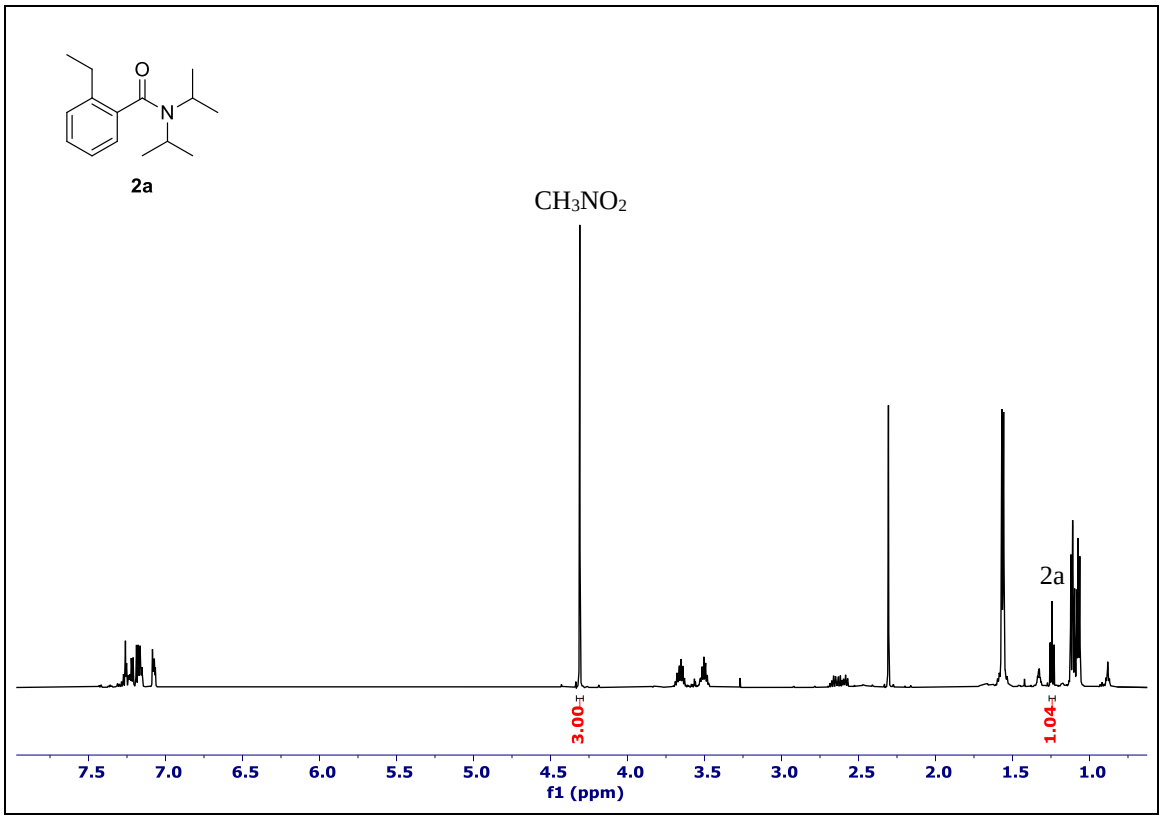


Figure S10. Table S1 entry 11: crude ^{1}H NMR spectrum of the reaction performed in CPME (0.2 mL) - *ChCl/Gly 1:2* (1 g), 1.5 eq. of *n*-BuLi, 5 eq. of CH_3I. Room temperature. Yield of **2a**: 26%.

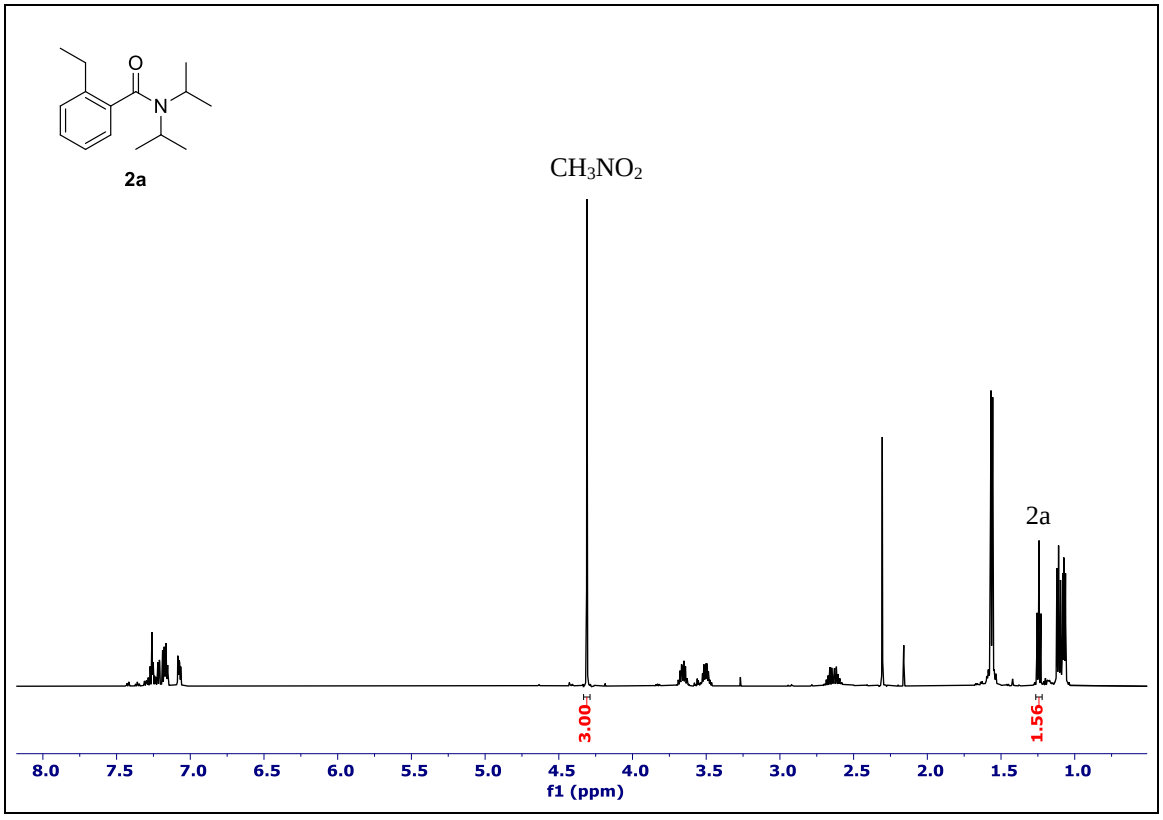


Figure S11. Table S1 entry 12: crude ^{1}H NMR spectrum of the reaction performed in CPME (0.2 mL) - *ChCl/Gly 1:2* (1 g), 1.5 eq. of *s*-BuLi, 5 eq. of CH_3I. Room temperature. Yield of **2a**: 38%.

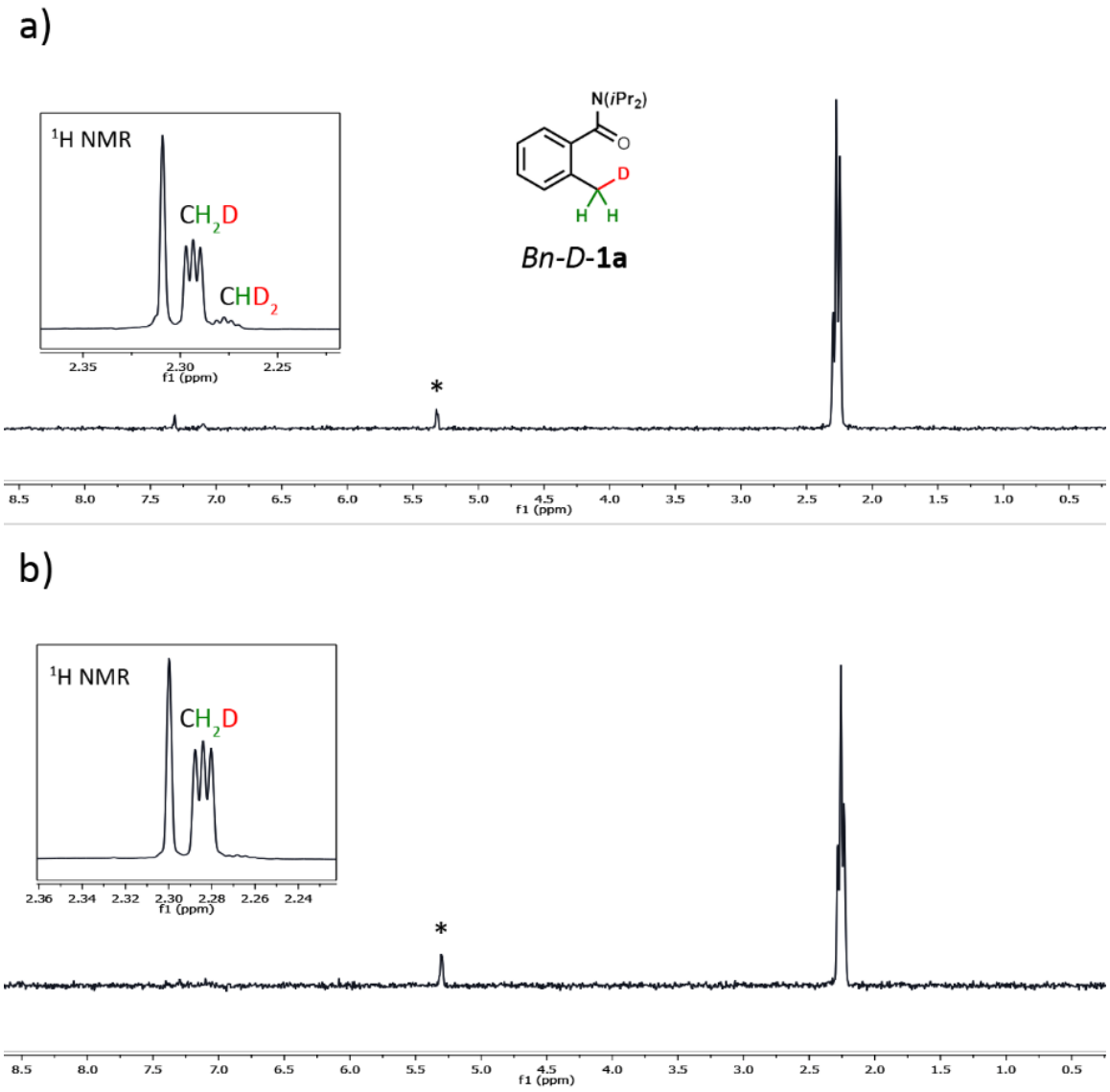
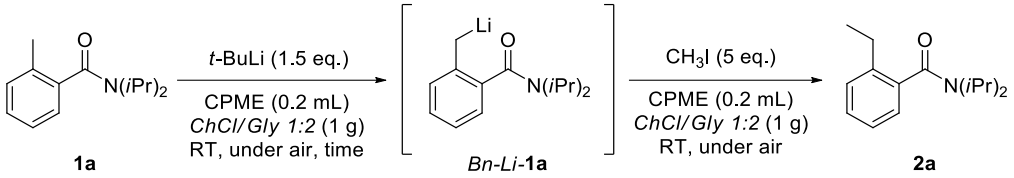


Figure S12. ^{2}H NMR spectra of products from lithiation of **1a** in CPME/DES with a) 2 equiv. and b) 1.5 equiv. of *t*-BuLi. Inset: ^{1}H NMR spectra expansion of benzylic CH_3 region. *: residual CD_2Cl_2 solvent peak.

Kinetic analysis of *Bn-Li*-**1a** in CPME-*ChCl/Gly (1:2 mol mol^{-1})*

All reactions were performed under air at room temperature. In an open screw cap vial, *N*,*N*-diisopropyl-2-methylbenzamide **1a** (43.8 mg, 0.2 mmol, 1 eq.) was dissolved in CPME (0.2 mL, 1 M), then *ChCl/Gly (1:2 mol mol^{-1})* (1 g) was added and the resulting mixture was vigorously stirred for 5 min. *t*-BuLi (0.3 mmol, 1.5 eq.) was rapidly spread over the heterogeneous mixture, which was kept under vigorous stirring then quenched by addition of iodomethane (62 µL, 1 mmol, 5 eq.) after different times. The mixture was diluted with water (5 mL) and extracted with Et_2O (3 x 5 mL). The combined organic layers were dried over Na_2SO_4 and the solvent removed under reduced pressure. Yields were determined by quantitative ^{1}H NMR analysis of the crude reaction mixtures using nitromethane (0.074 mmol, 4 µL) as internal standard and a diluting factor 2 for the preparation of the sample (see Eq. 1).

Table S2. Study of half-life of organolithium species *Bn-Li*-**1a**



Entry	CH_3I addition time (s)	Yield %
1	2	70
2	5	58
3	7	52
4	10	31
5	15	4
6	20	0

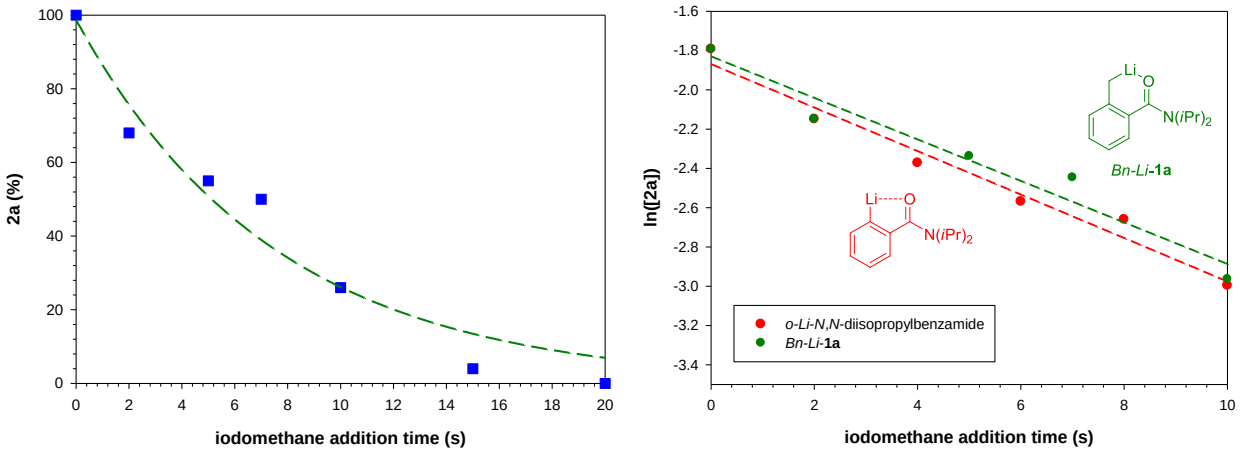


Figure S13. Kinetic analysis of lateral metalation of **1a**. First-order kinetic plot of *ortho*-lithiated *N*,*N*-diisopropylbenzamide under the same reaction conditions was added for comparison.[8]

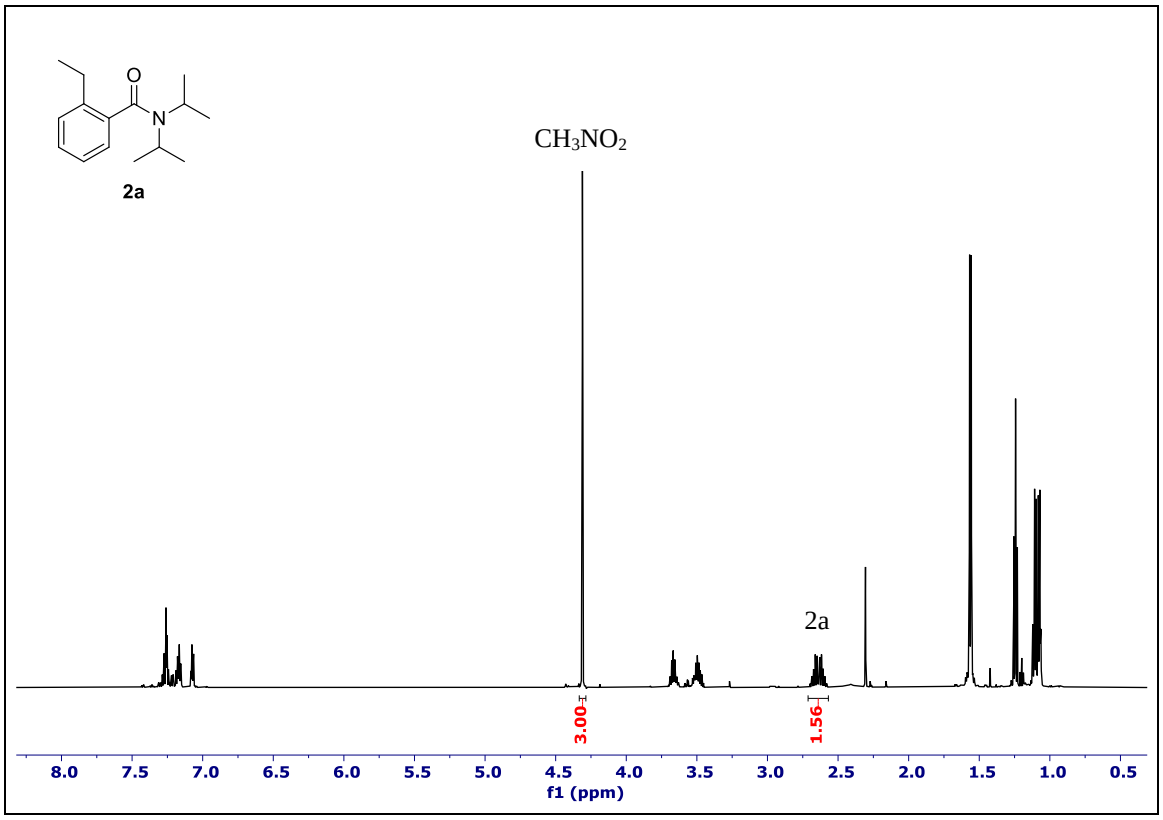


Figure S14. Table S2 entry 2: crude ^{1}H NMR spectrum of the reaction, quench after 5 s. Yield of **2a**: 58%

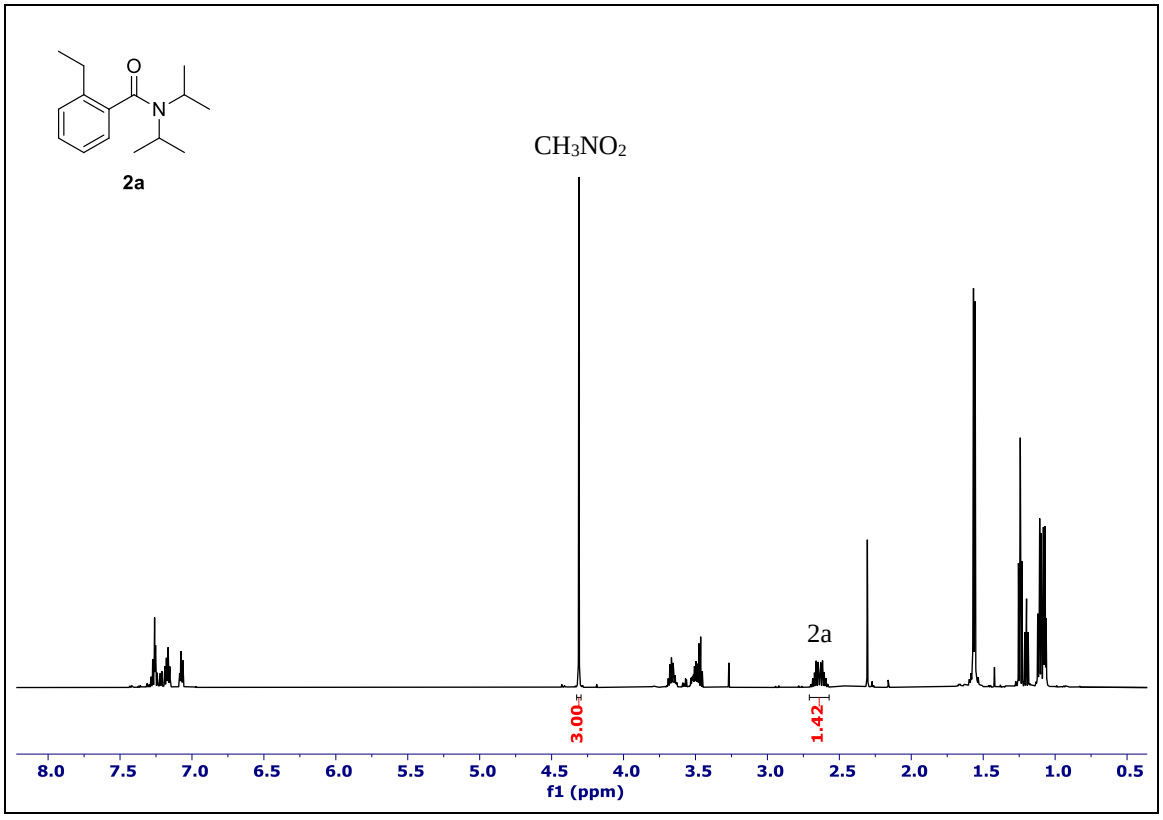


Figure S15. Table S2 entry 3: crude ^{1}H NMR spectrum of the reaction, quench after 7 s. Yield of **2a**: 52%

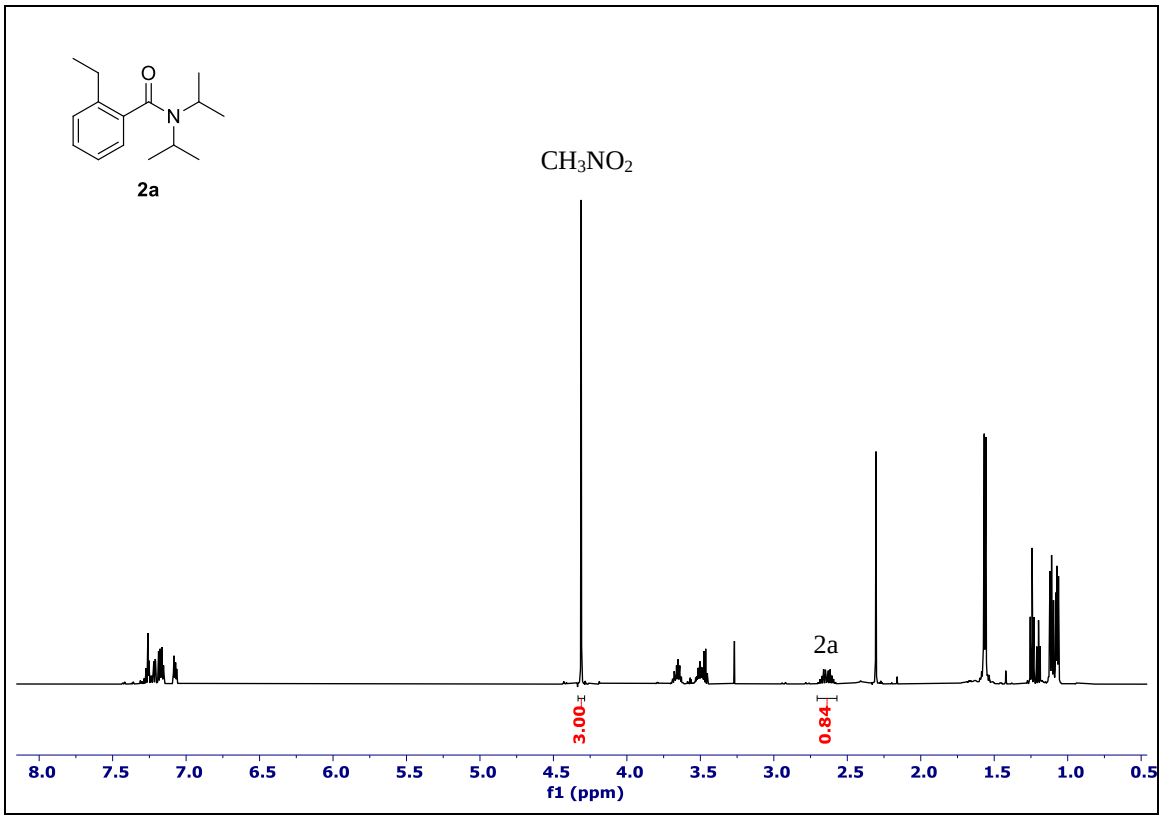
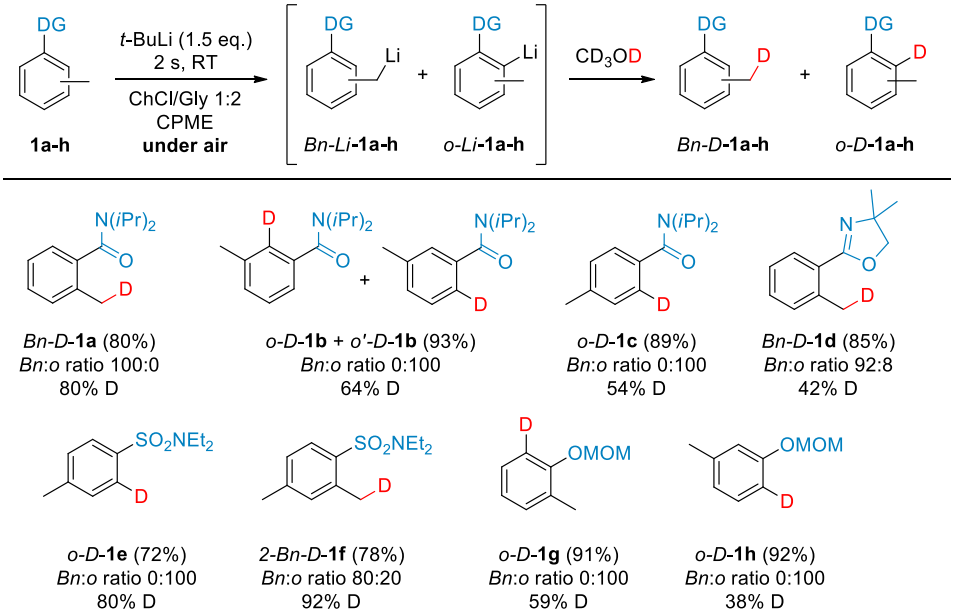


Figure S16. Table S2 entry 4: crude ^{1}H NMR spectrum of the reaction, quench after 10 s. Yield of **2a**: 31%

Deuteration labelling experiments of substituted toluenes **1a-h**.

General procedure. Reactions were performed under air at room temperature. In an open screw cap vial, substrates **1a-h** (0.2 mmol, 1 eq.) were dissolved in CPME (0.2 mL, 1 M), then *ChCl/Gly (1:2 mol mol^{-1})* (1 g) was added and the resulting mixture was vigorously stirred for 5 min. *t*-BuLi (0.3 mmol, 1.5 eq.) was rapidly spread over the heterogeneous mixture, which was kept under vigorous stirring and quenched by addition of CD_3OD (5 eq.) after 2 seconds. The mixture was diluted with water (5 mL) and extracted with Et_2O (3 x 5 mL). The combined organic extracts were dried over Na_2SO_4 and the solvent removed under reduced pressure. The crude products were purified by flash column chromatography on silica gel.



Scheme S1. Metalation reaction of substituted toluenes **1a-h** using *t*-BuLi in CPME/DES at RT under air. Reaction conditions: **1a-h** (0.2 mmol), CPME (0.2 mL), DES (1.0 g), CD_3OD (5 equiv). DES: ChCl/Gly (1:2 mol mol^{-1}). Ratios and D incorporation are based on ^{1}H NMR integration and confirmed with ^{2}H NMR. Yields in brackets refer to products isolated after flash column chromatography.

2-(Deuteriomethyl)-*N*,*N*-diisopropylbenzamide (*Bn-D*-1a): general procedure starting from **1a**. Purification by flash column chromatography (PE/EtOAc 9/1 v/v) gave *Bn-D*-**1a** (80% D incorporation) as a white solid (35 mg, 80%, R_f = 0.16 PE/EtOAc 9/1 v/v), mp 98.6-99.5 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.22 (td, *J* = 7.4, 1.5 Hz, 1H), 7.20-7.14 (m, 2H), 7.08 (dd, *J* = 7.7, 1.4 Hz, 1H), 3.66 (sept, *J* = 6.7 Hz, 1H), 3.51 (sept, *J* = 6.9 Hz, 1H), 2.30 (m, 2H), 1.57 (dd, *J* = 6.6, 1.6 Hz, 6H), 1.12 (d, *J* = 6.7 Hz, 3H), 1.07 (d, *J* = 6.7 Hz, 3H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 170.8, 138.7, 133.7, 130.5, 128.2, 125.9, 124.8, 50.9, 45.9, 21.0, 20.9, 20.8, 20.7, 18.6 (t, *J* = 19.5 Hz, 1C). ^{2}H NMR (92.07 MHz, CH_2Cl_2): δ 2.28 (t, *J* = 2.44 Hz). EI-MS *m/z* (%): 220 (M^+, 12), 120 (100), 119 (43), 92 (27). ESI-HRMS $[M+Na]^+$: *m/z* 243.1572, $C_{14}H_{20}DNONa^+$ requires 243.1578.

2-Deuterio-*N,N*-diisopropyl-3-methylbenzamide (*o-D*-1b) and **6-Deuterio-*N,N*-diisopropyl-3-methylbenzamide (*o'-D*-1b)**: general procedure starting from **1b**. Purification by flash column chromatography (PE/EtOAc 9/1 v/v) gave an inseparable mixture of *o-D*-**1b** (30% D incorporation) and *o'-D*-**1b** (34% D incorporation) as a white solid (41 mg, 93%, R_f = 0.20 PE/EtOAc 9/1 v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.26-7.23 (m, 1H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.11 (s, 1H, 30%D), 7.08 (d, *J* = 7.6 Hz, 1H, 34%D), 3.95-3.38 (br m, 2H), 2.35 (s, 3H), 1.77-0.94 (br m, 12H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 171.3, 139.1, 139.0, 138.4, 138.3, 129.4, 128.4, 128.3, 126.4, 122.3 (t, *J* = 23.8 Hz, 1C), 50.9, 45.9, 21.5, 21.5, 20.8. ^{2}H NMR (92.07 MHz, CH_2Cl_2): δ 7.11 (s). EI-MS *m/z* (%): 220 (M^+, 17), 176 (24), 177 (22), 120 (86), 119 (100), 91 (27).[8]

2-Deuterio-*N,N*-diisopropyl-4-methylbenzamide (*o-D*-1c): general procedure starting from **1c**. Purification by flash column chromatography (PE/EtOAc 85/15 v/v) gave *o-D*-**1c** (54% D incorporation) as a white solid (39 mg, 89%, R_f = 0.38 PE/EtOAc 85/15 v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.22-7.19 (m, 2H), 7.19-7.16 (m, 2H), 4.10-3.31 (m, 2H), 2.36 (s, 3H), 1.67-0.95 (m, 12H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 171.4, 138.6, 136.2, 136.1, 129.1, 129.0, 125.8, 125.5 (t, *J* = 24.3 Hz, 1C), 50.9, 45.9, 21.4, 20.9. ^{2}H NMR (92.07 MHz, CH_2Cl_2): δ 7.19 (s). EI-MS *m/z* (%): 220 (M^+, 14), 219 (17), 177 (21), 176 (23), 120 (90), 119 (100), 92 (17), 91 (20).[9]

2-(Deuteriomethyl)-4,4-dimethyl-2-phenyl-4,5-dihydrooxazole (*Bn-D*-1d): General procedure starting from **1d**. Purification by flash column chromatography (9/1 PE/EtOAc v/v) gave *Bn-D*-**1d** (42% D incorporation) as yellow oil (32.3 mg, 85%, R_f = 0.45 9/1 PE/EtOAc v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.74 (d, *J* = 7.6 Hz, 1H), 7.31 (td, *J* = 7.6, 1.4 Hz, 1H), 7.22-7.19 (m, 2H), 4.07 (s, 2H), 2.56-2.54 (m, 2H), 1.39 (s, 6H).^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 162.9, 138.6, 131.2, 130.5, 129.9, 127.8, 125.6, 78.8, 67.9, 28.6, 21.2 (t, *J* = 19.5 Hz, 1C). ^{2}H NMR (92.07 MHz, CH_2Cl_2): δ 2.55 (t, *J* = 2.3 Hz). EI-MS *m/z* (%): 190 (M^+, 51), 189 (100), 174 (78), 158 (25), 146 (38), 118 (65). ESI-HRMS $[M+Na]^+$: *m/z* 213.1105, $C_{12}H_{14}DNONa^+$ requires 213.1109.

2-Deuterio-*N,N*-diethyl-4-methylbenzenesulfonamide (*o-D*-1e): general procedure starting from **1e**. Purification by flash column chromatography (PE/EtOAc 9/1 v/v) gave *o-D*-**1e** (80% D incorporation) as a white solid (33 mg, 72%, R_f = 0.23 PE/EtOAc 9/1 v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.70-7.66 (m, 1H), 7.30-7.24 (m, 2H), 3.21 (q, *J* = 7.2 Hz, 4H), 2.40 (s, 3H), 1.11 (t, *J* = 7.2 Hz, 6H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 143.0, 137.5, 137.4, 129.7, 129.6, 126.9 (t, *J* = 25.3 Hz, 1C), 42.1, 21.6, 14.2. ^{2}H NMR (92.07 MHz, CH_2Cl_2): δ 7.69 (s). EI-MS *m/z* (%): 228 (M^+, 14), 213 (100), 212 (47), 156 (90), 92 (81).[5b]

2-(Deuteriomethyl)-*N,N*-diethyl-4-methylbenzenesulfonamide (2-*Bn-D*-1f): general procedure starting from **1f**. Purification by flash column chromatography (PE/EtOAc 9/1 v/v) gave 2-*Bn-D*-**1f** (92% D incorporation, 4:1 mixture of 2-*Bn*-D-**1f** and *o*-D-**1f**) as a colourless oil (38 mg, 78%, R_f = 0.32 PE/EtOAc 9/1 v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.78 (d, *J* = 7.9 Hz, 1H), 7.10-7.04 (m, 2H), 3.28 (q, *J* = 7.1 Hz, 4H), 2.53-2.51 (m, 2H), 2.35 (s, 3H), 1.10 (t, *J* = 7.1 Hz, 6H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 143.1, 137.6,

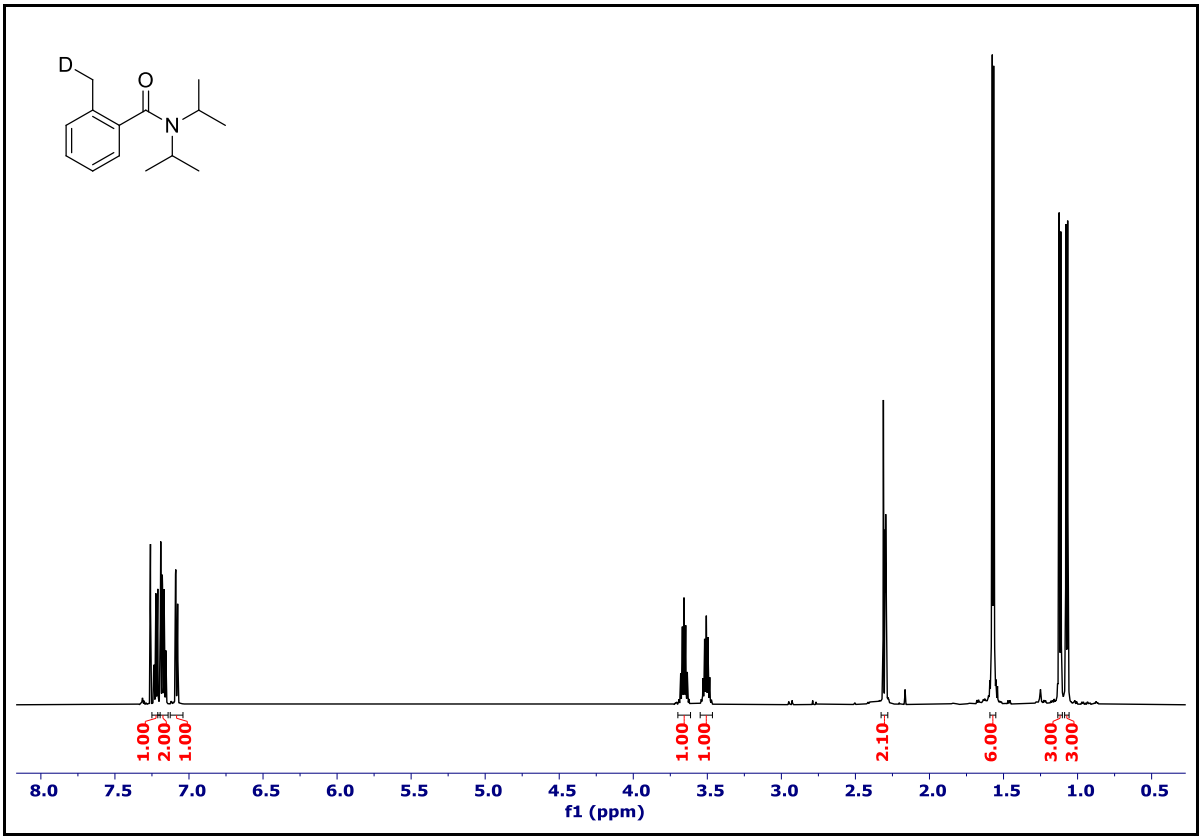
135.6, 133.4, 129.9, 126.6, 40.7, 21.3, 20.0 (t, *J* = 19.7 Hz, 1C), 13.7. ^{2}H NMR (92.07 MHz, CH_2Cl_2): δ 2.53 (t, *J* = 2.3 Hz). EI-MS *m/z* (%): 242 (M^+, 24), 227 (73), 170 (78), 106 (100), 105 (40). ESI-HRMS $[M+Na]^+$: *m/z* 265.1086, $C_{12}H_{18}DNO_2SNa^+$ requires 265.1091.

6-Deuterio-1-(methoxymethoxy)-2-methylbenzene (*o*-*D*-1g): general procedure starting from **1g**. Purification by flash column chromatography (PE/EtOAc 95/5 v/v) gave *o*-*D*-**1g** (59% D incorporation) as a colourless oil (28 mg, 91%, R_f = 0.54 PE/EtOAc 95/5 v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.18-7.14 (m, 2H), 7.06 (d, *J* = 8.2 Hz, 1H), 6.93 (t, *J* = 7.4 Hz, 1H), 5.22 (s, 2H), 3.51 (s, 3H), 2.28 (s, 3H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 155.5, 155.5, 130.9, 127.5, 127.0, 126.9, 121.7, 121.7, 114.0, 113.7 (t, *J* = 24.4 Hz, 1C), 94.6, 56.1, 16.4. ^{2}H NMR (92.07 MHz, CH_2Cl_2): δ 7.03 (s). EI-MS *m/z* (%): 153 (M^+, 34), 152 (20), 123 (11), 122 (12), 92 (14), 91 (10), 45 (100).[10]

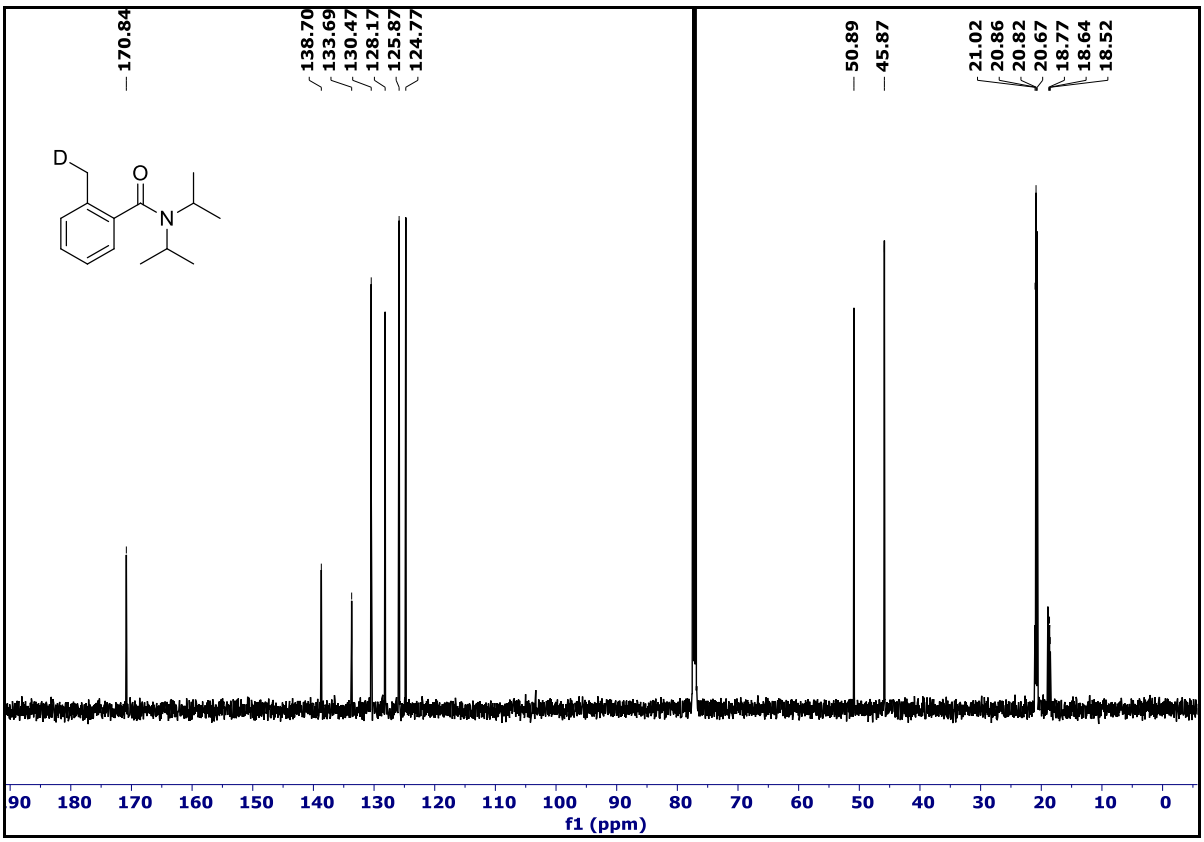
6-Deuterio-1-(methoxymethoxy)-3-methylbenzene (*o*-*D*-1h): general procedure starting from **1h**. Purification by flash column chromatography (PE/EtOAc 95/5 v/v) gave *o*-*D*-**1h** (38% D incorporation) as a colourless oil (28 mg, 92%, R_f = 0.58 PE/EtOAc 95/5 v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.19-7.16 (m, 1H), 6.87 (s, 1H), 6.86-6.92 (m, 2H), 5.17 (s, 2H), 3.48 (s, 3H), 2.34 (s, 3H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 157.4, 139.7, 129.4, 129.3, 122.9, 117.1, 113.4, 113.1 (t, *J* = 24.6 Hz, 1C), 94.5, 56.1, 26.4. ^{2}H NMR (92.07 MHz, CH_2Cl_2): δ 6.84 (s). EI-MS *m/z* (%): 153 (M^+, 32), 152 (40), 123 (17), 122 (26), 92 (15), 91 (19), 45 (100).[10]

2-(Deuteriomethyl)-*N*,*N*-diisopropylbenzamide (*Bn-D*-1a)

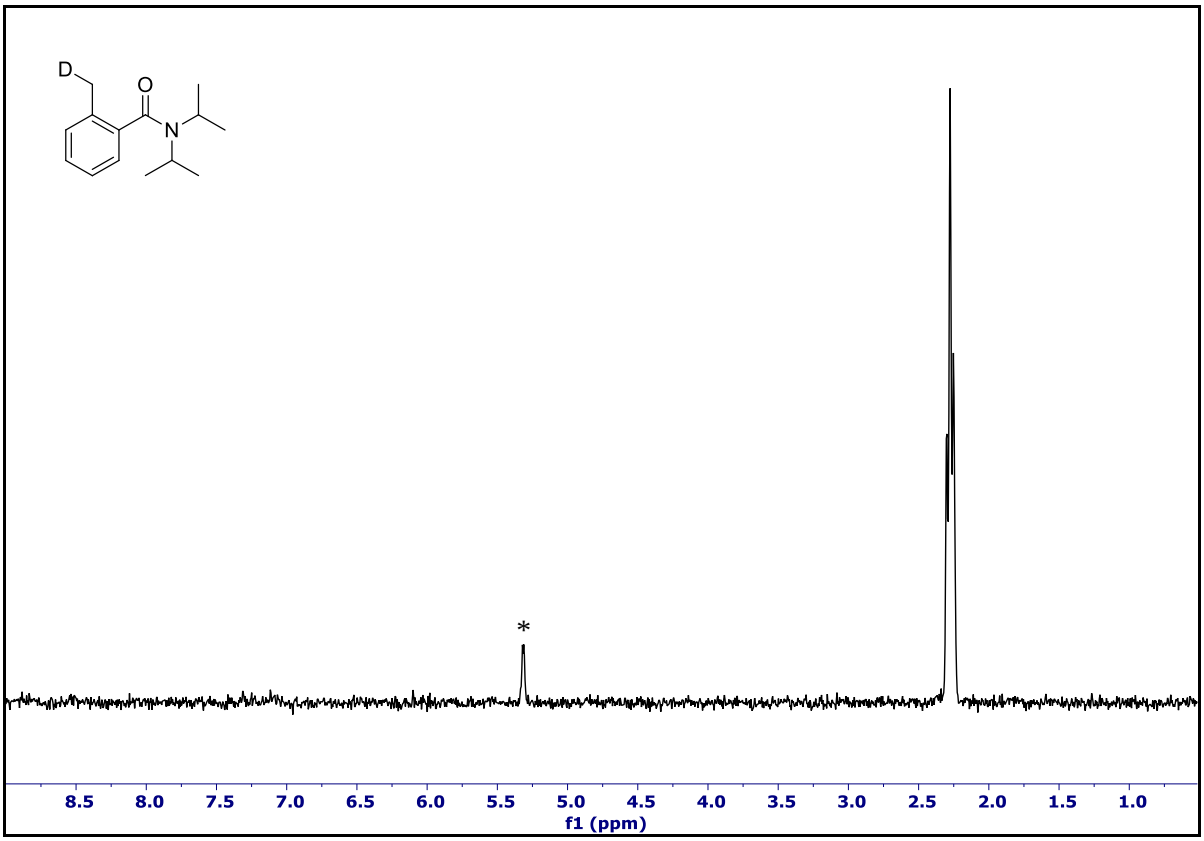
^{1}H NMR (600 MHz, $CDCl_3$)



^{13}C NMR (150 MHz, $CDCl_3$)



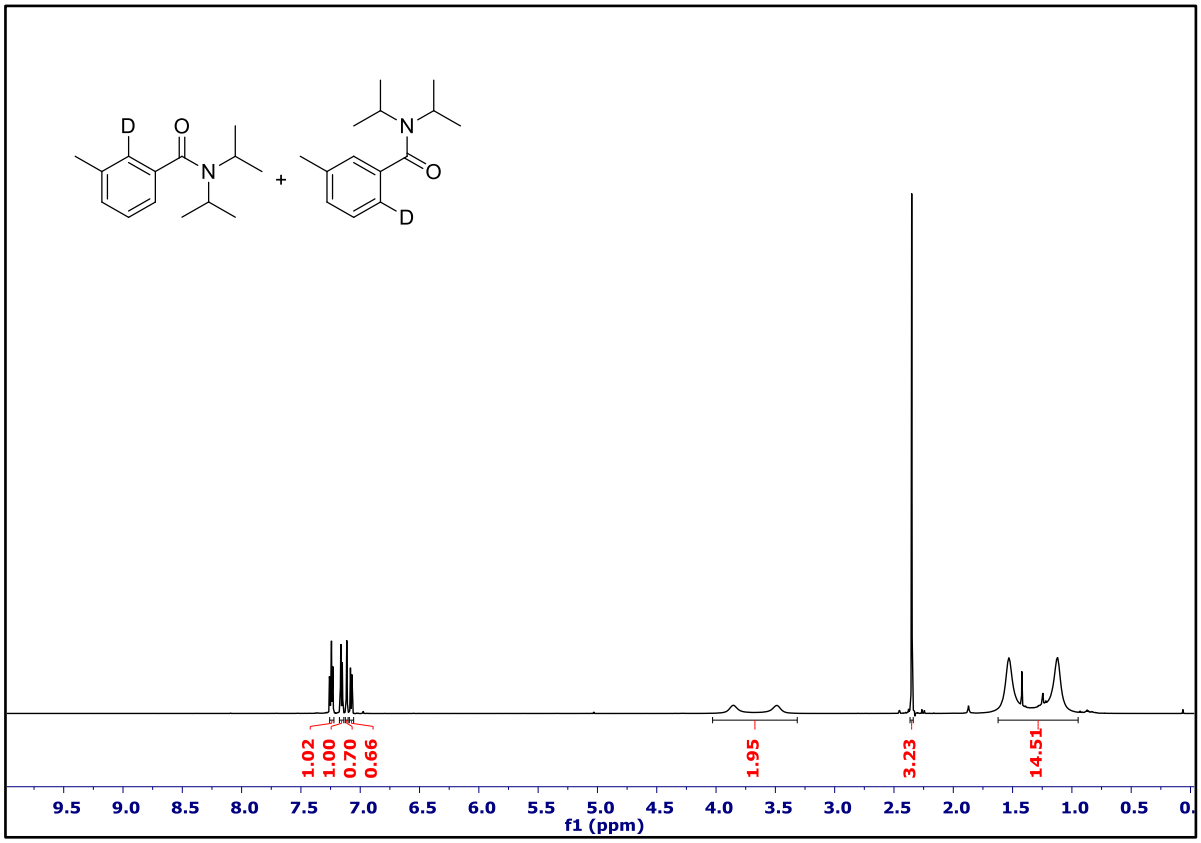
^{2}H NMR (92.07 MHz, CH_2Cl_2)



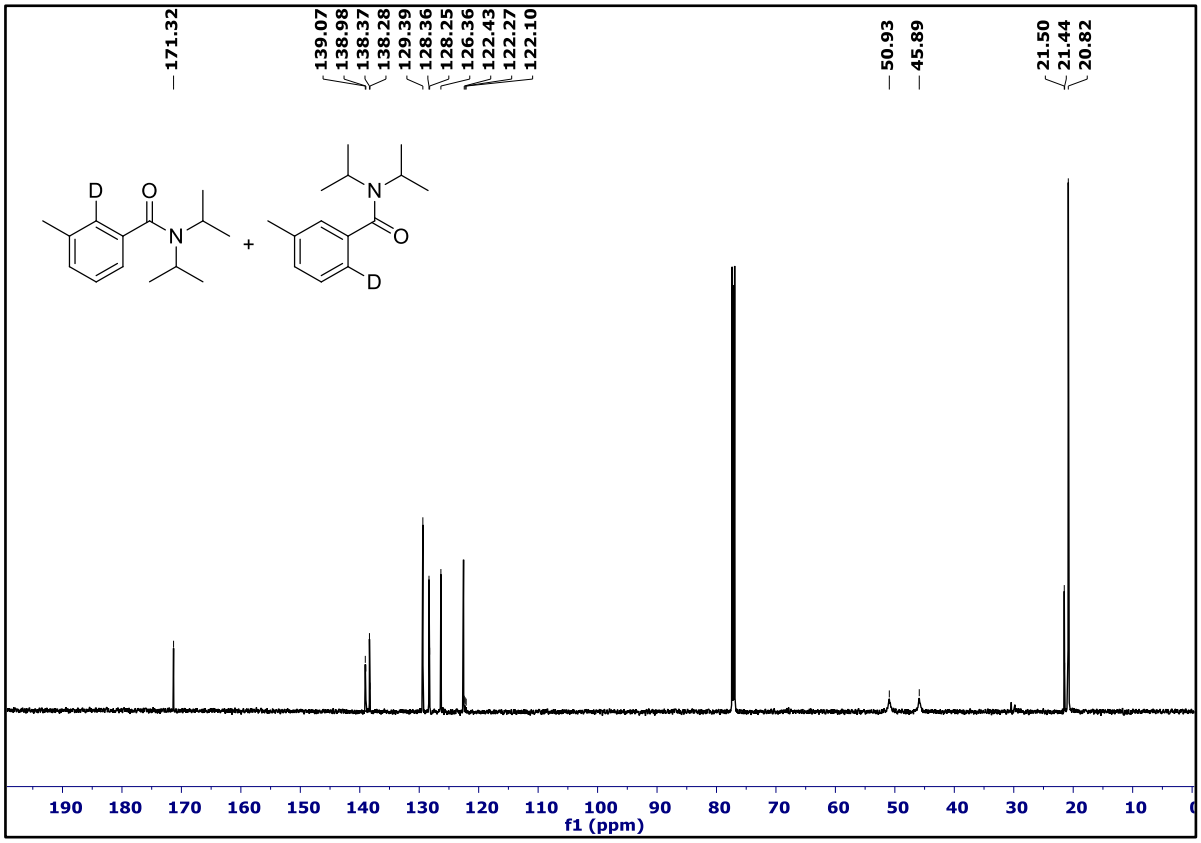
* residual CD_2Cl_2 solvent peak

2-Deuterio- and 6-deuterio-*N*,*N*-diisopropyl-3-methylbenzamide (*o*-*D*-1b and *o'*-*D*-1b)

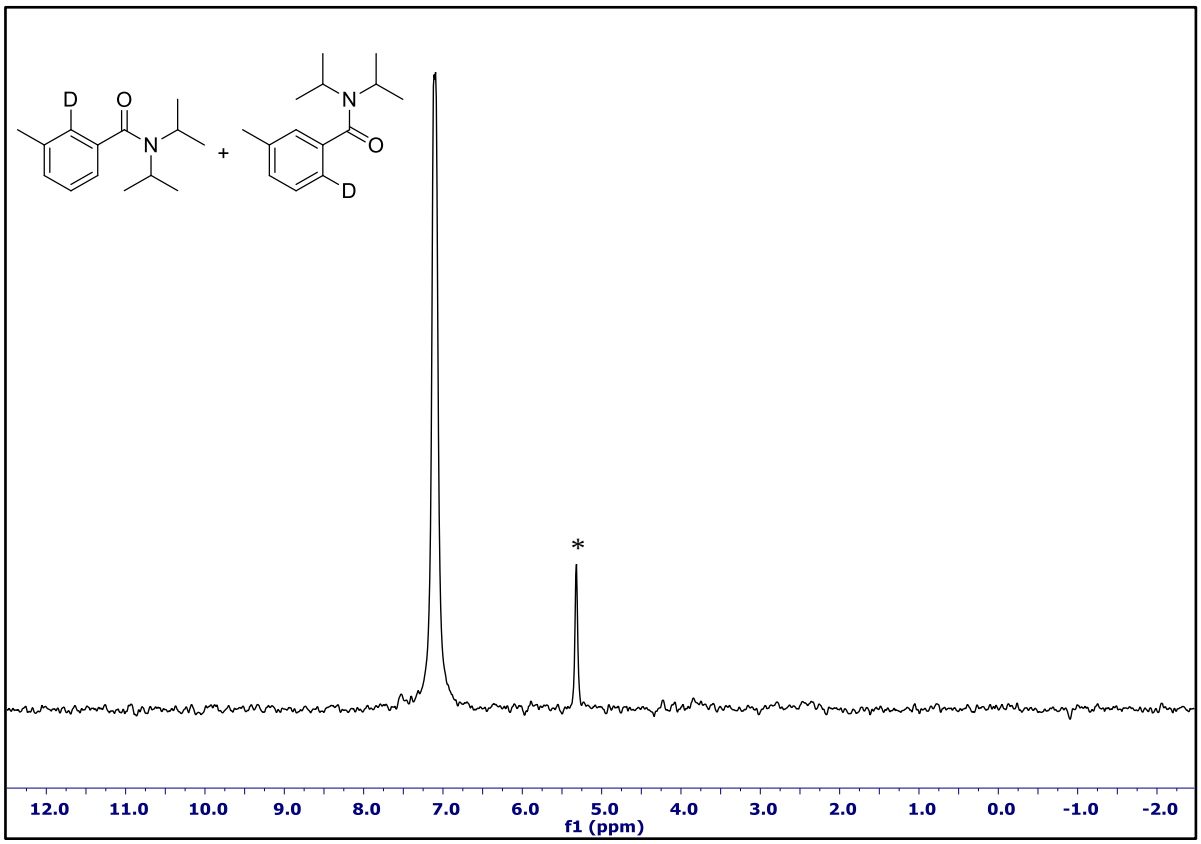
^{1}H NMR (600 MHz, $CDCl_3$)



^{13}C NMR (150 MHz, $CDCl_3$)



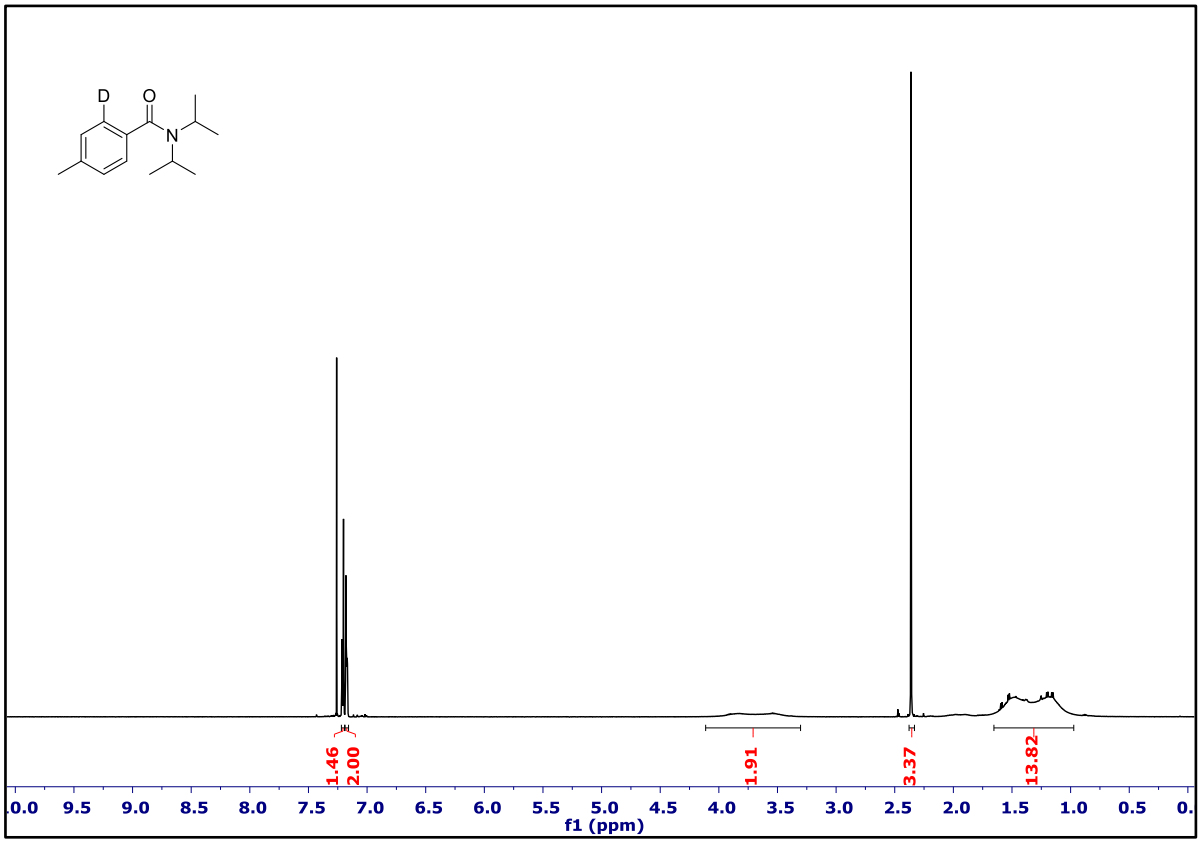
^{2}H NMR (92.07 MHz, CH_2Cl_2)



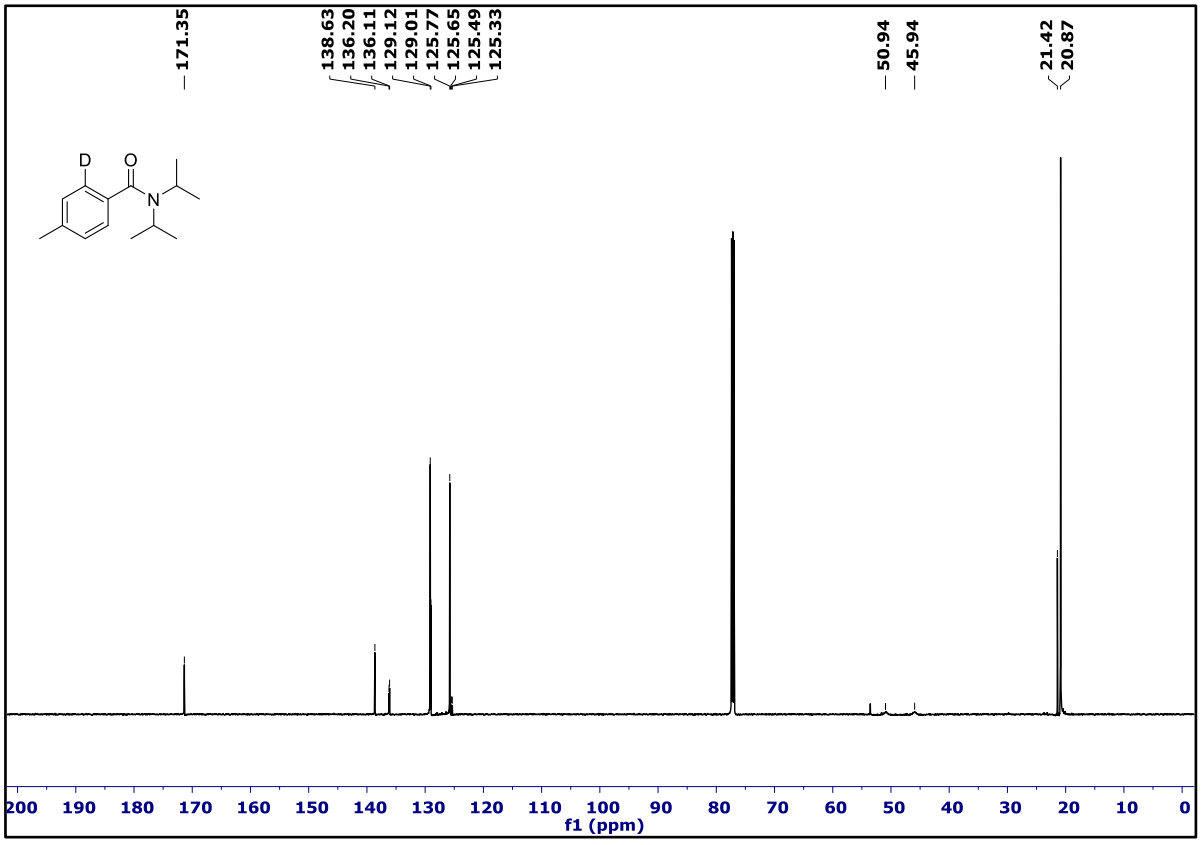
* residual CD_2Cl_2 solvent peak

2-Deuterio-*N*,*N*-diisopropyl-4-methylbenzamide (*o*-*D*-1c)

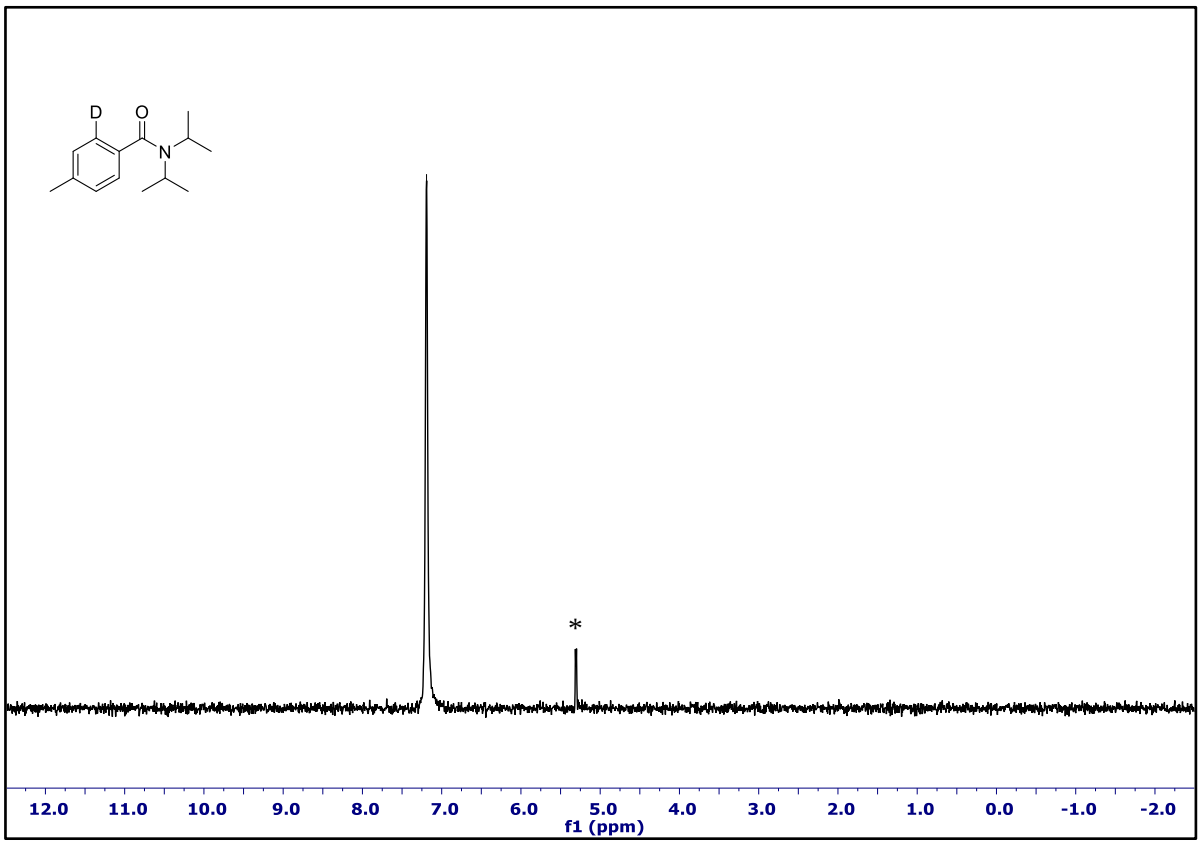
^{1}H NMR (600 MHz, $CDCl_3$)



^{13}C NMR (150 MHz, $CDCl_3$)



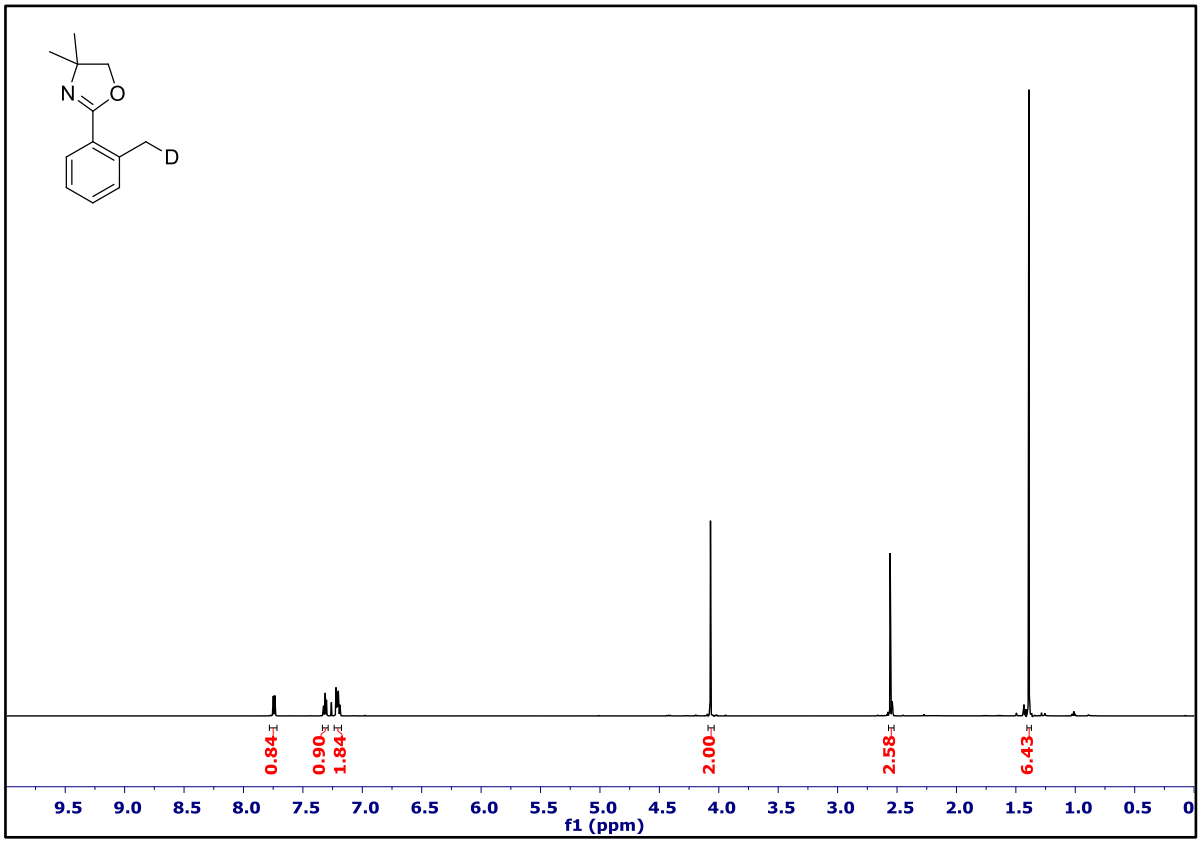
^{2}H NMR (92.07 MHz, CH_2Cl_2)



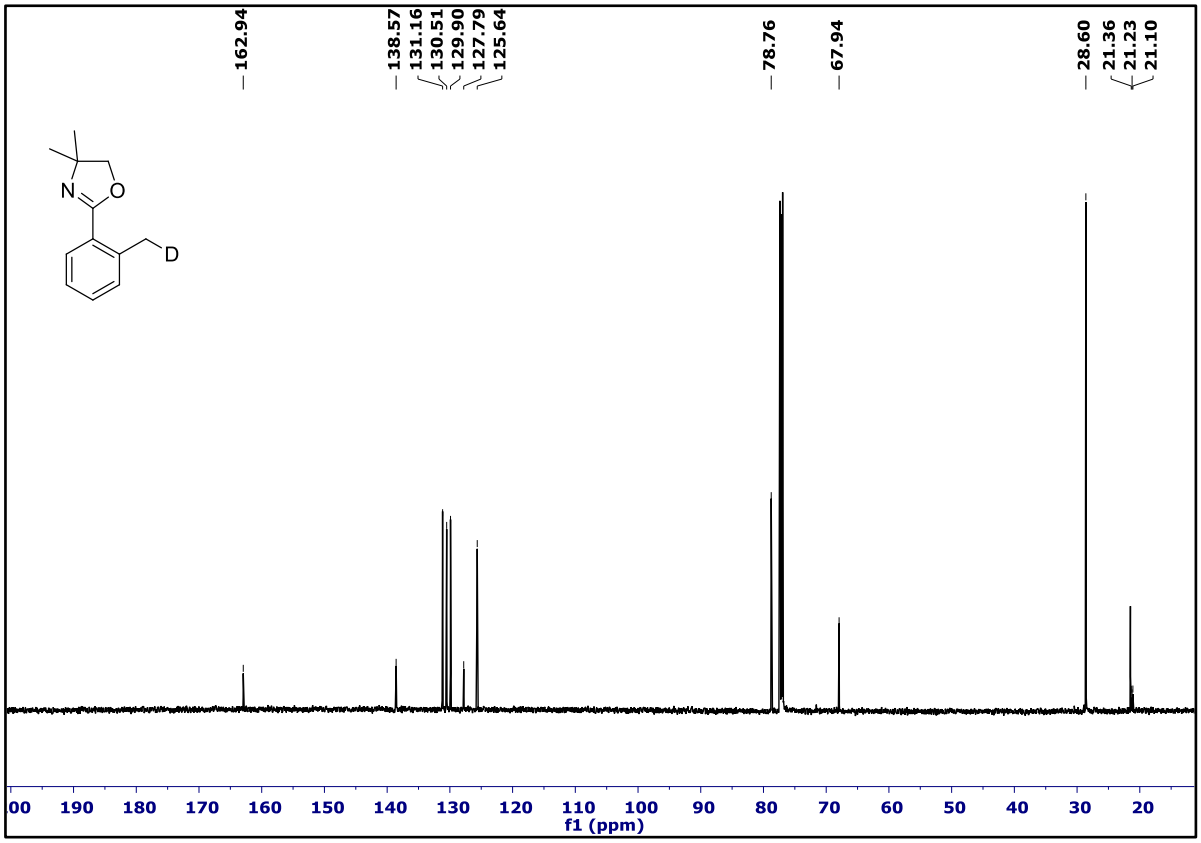
* residual CD_2Cl_2 solvent peak

2-(Deuteriomethyl)-4,4-dimethyl-2-phenyl-4,5-dihydrooxazole (*Bn-D*-1d)

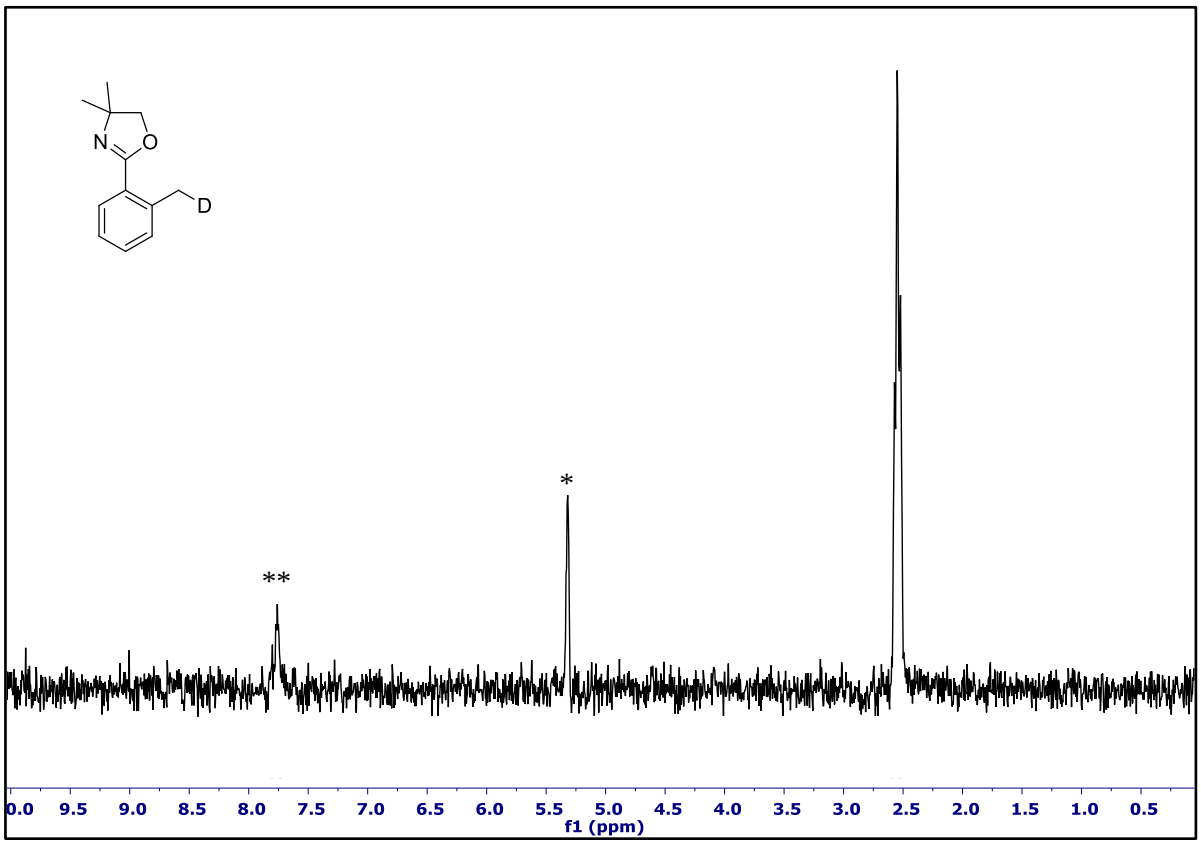
^{1}H NMR (600 MHz, $CDCl_3$)



^{13}C NMR (150 MHz, $CDCl_3$)



^{2}H NMR (92.07 MHz, CH_2Cl_2)

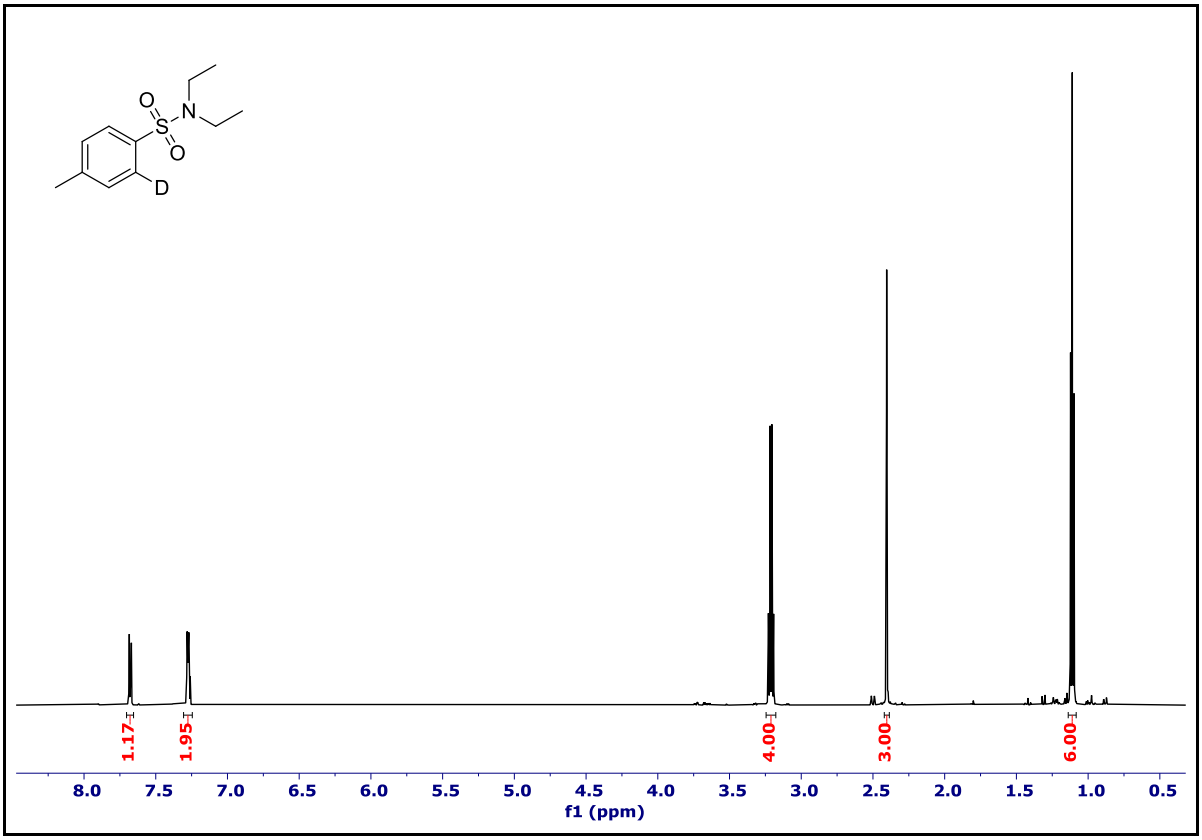


* residual CD_2Cl_2 solvent peak

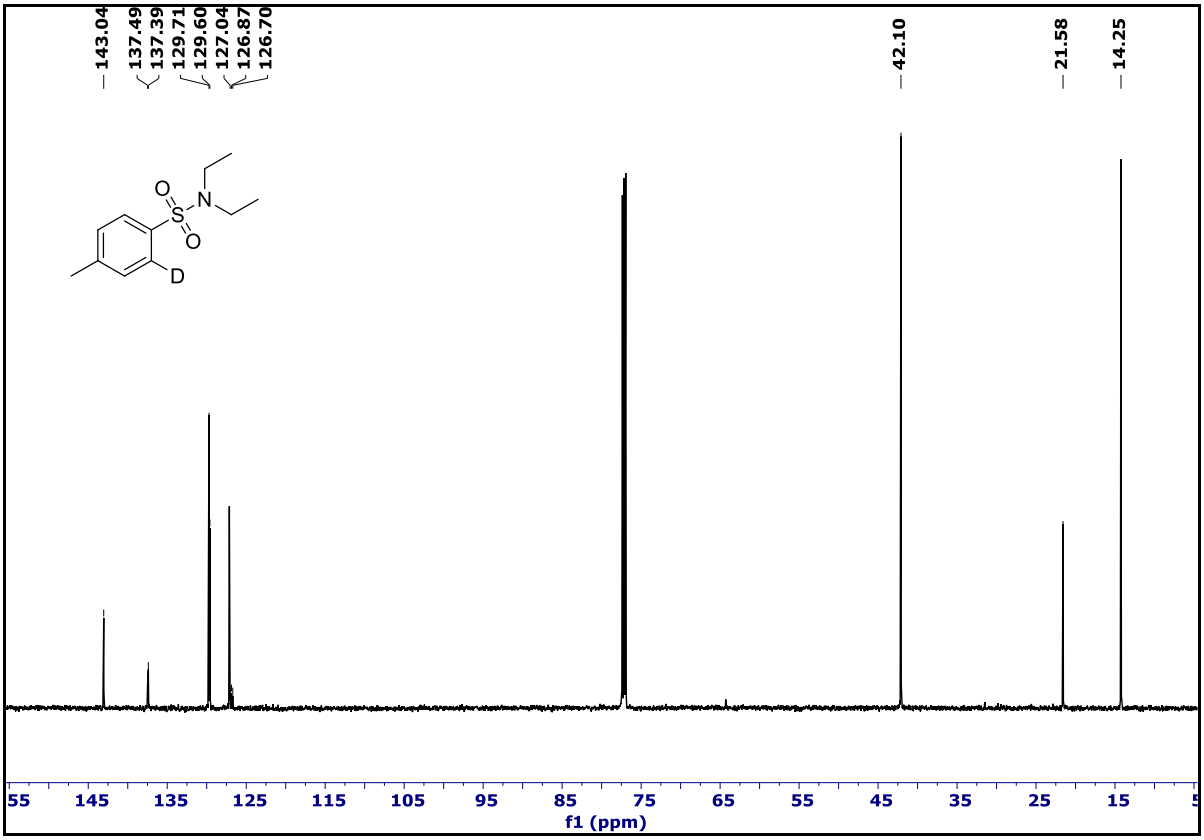
** *o-D*-**1d**

2-Deuterio-*N*,*N*-diethyl-4-methylbenzenesulfonamide (*o*-*D*-1e)

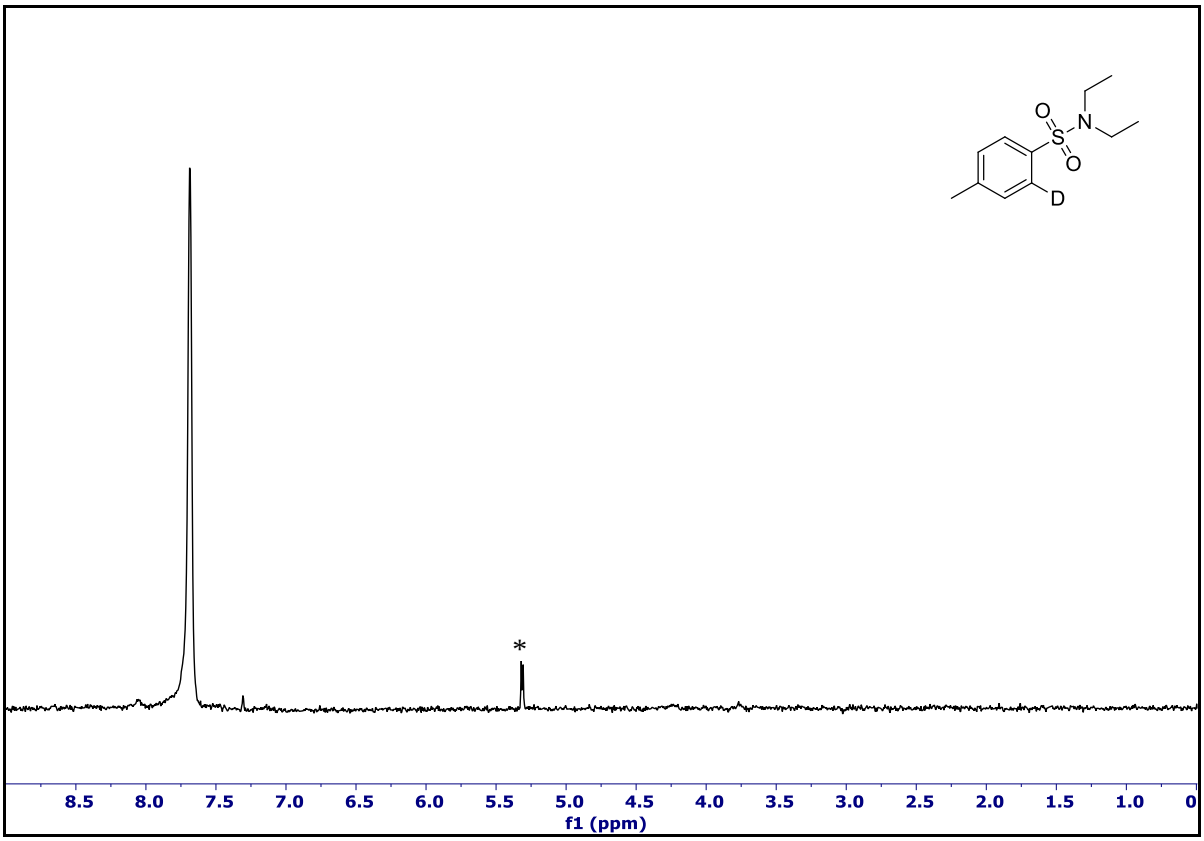
^{1}H NMR (600 MHz, $CDCl_3$)



^{13}C NMR (150 MHz, $CDCl_3$)



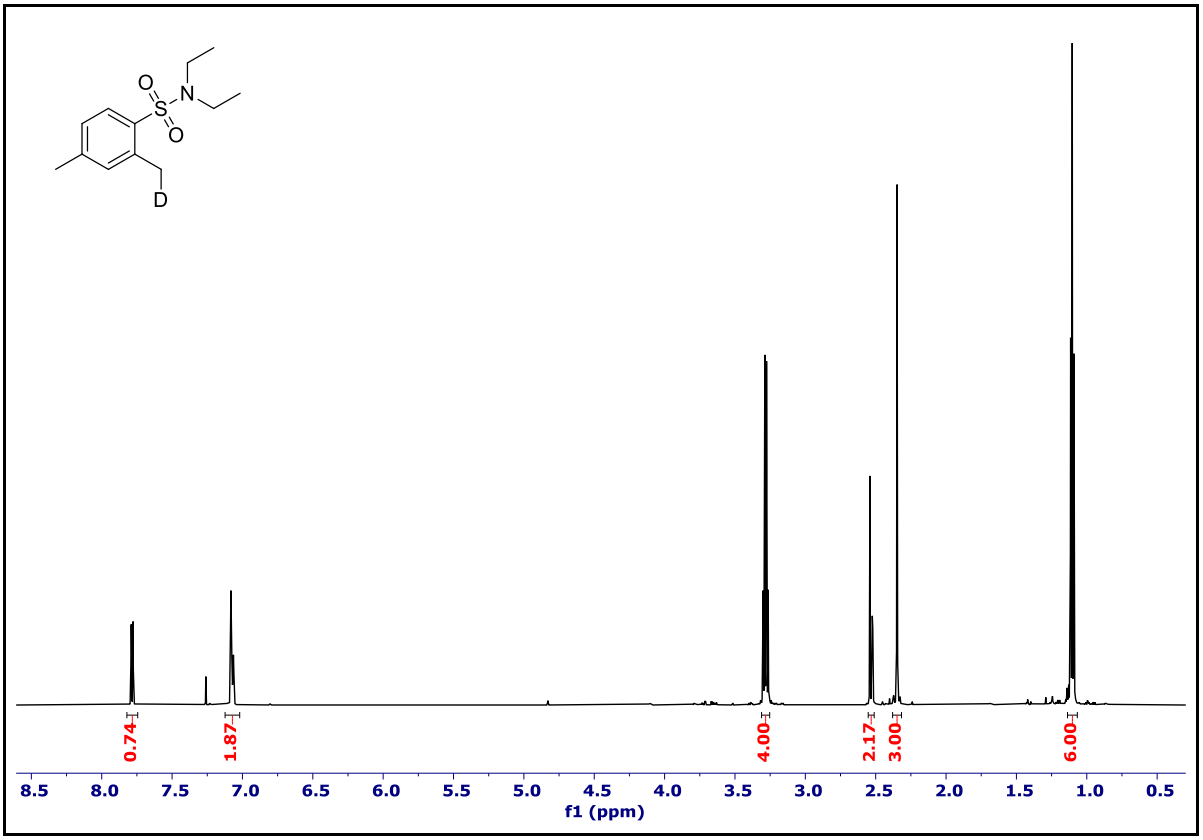
^{2}H NMR (92.07 MHz, CH_2Cl_2)



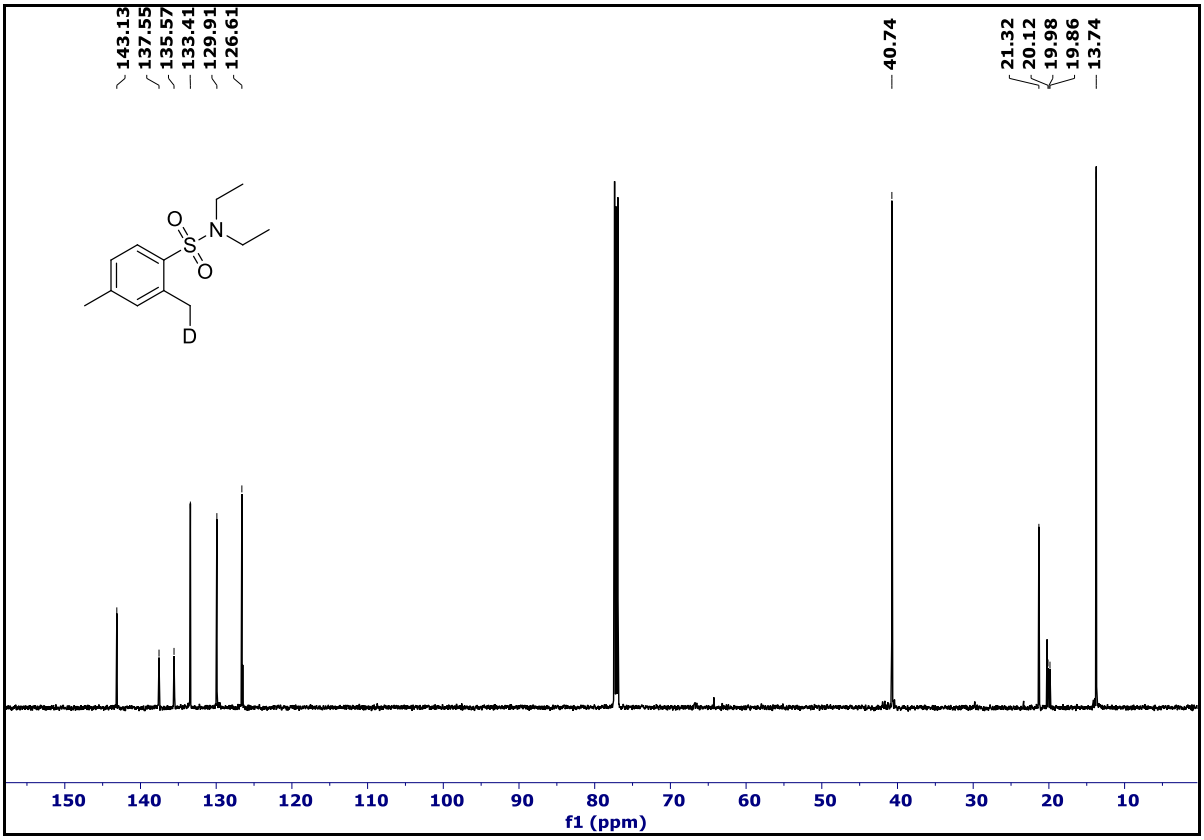
* residual CD_2Cl_2 solvent peak

2-(Deuteriomethyl)-*N*,*N*-diethyl-4-methylbenzenesulfonamide (2-*Bn*-*D*-1f)

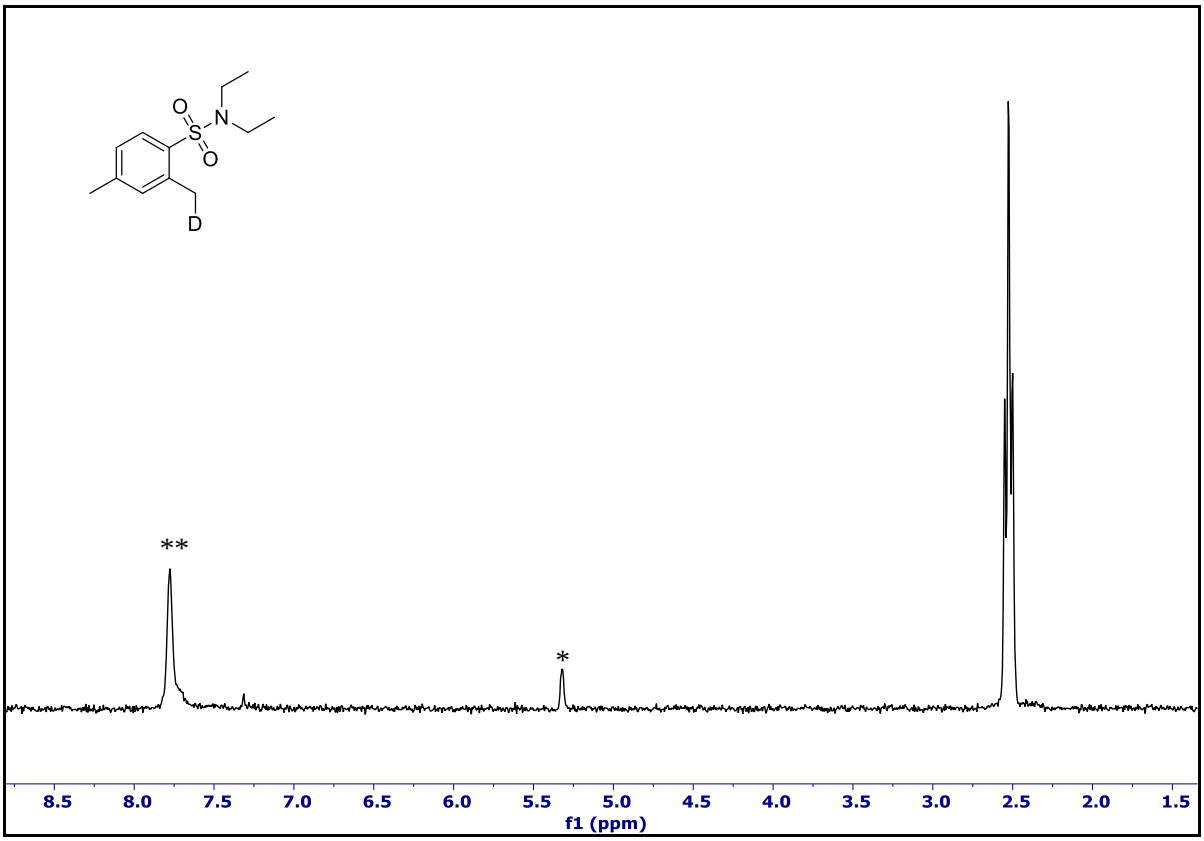
^{1}H NMR (600 MHz, $CDCl_3$)



^{13}C NMR (150 MHz, $CDCl_3$)



^{2}H NMR (92.07 MHz, CH_2Cl_2)

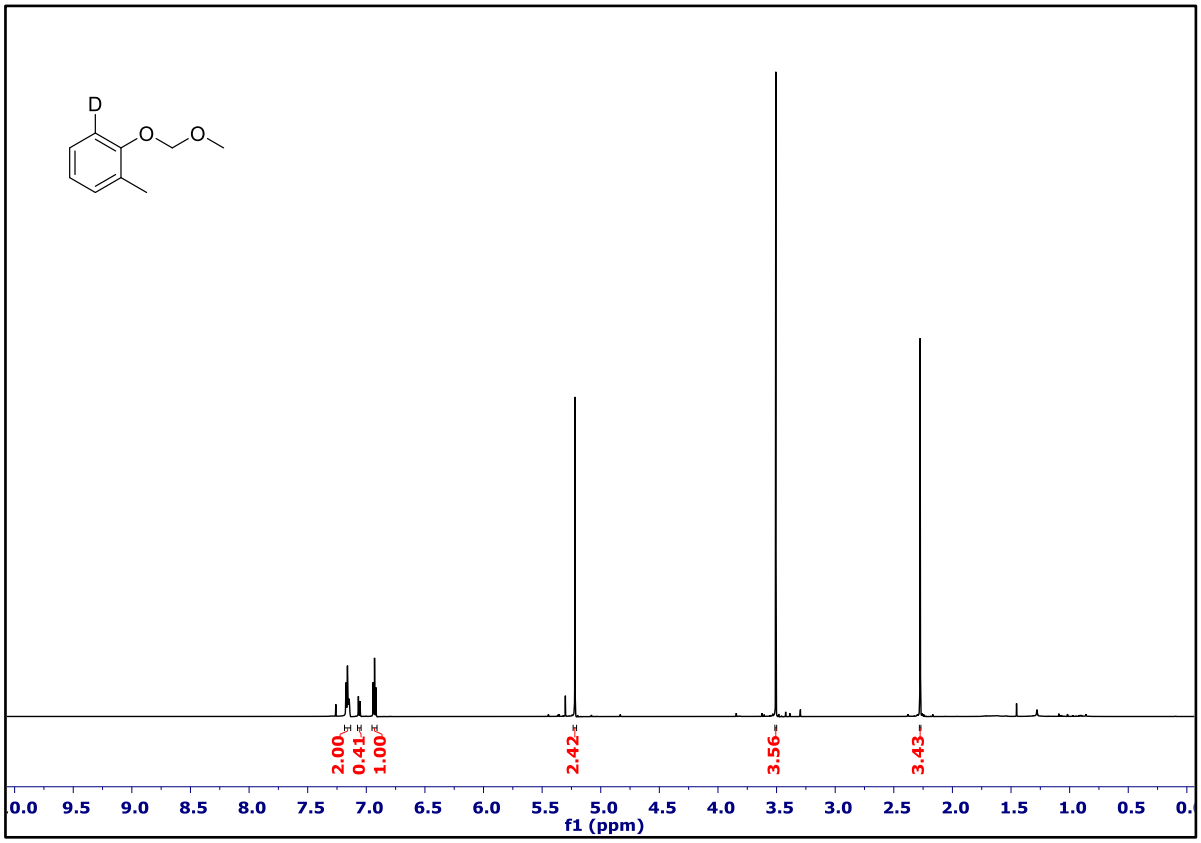


* residual CD_2Cl_2 solvent peak

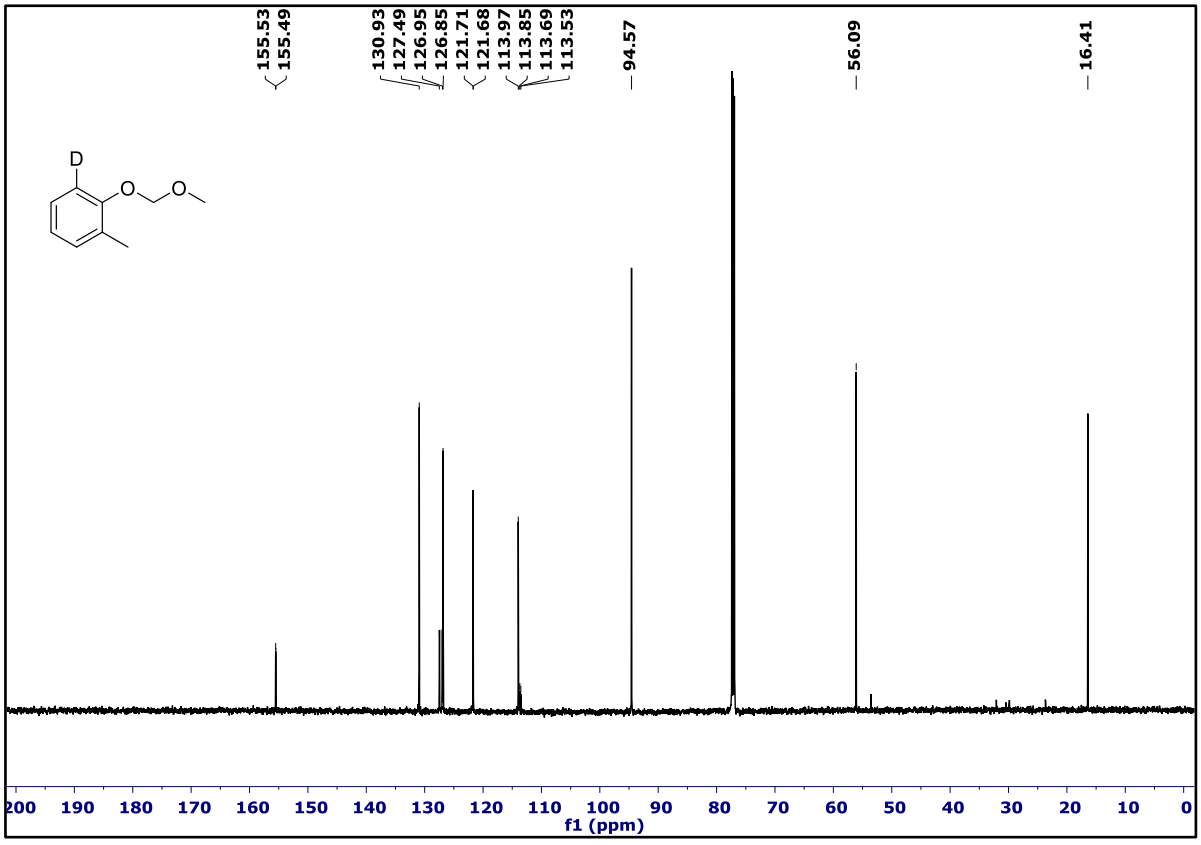
** *o-D*-**1f**

6-Deuterio-1-(methoxymethoxy)-2-methylbenzene (*o*-*D*-1g)

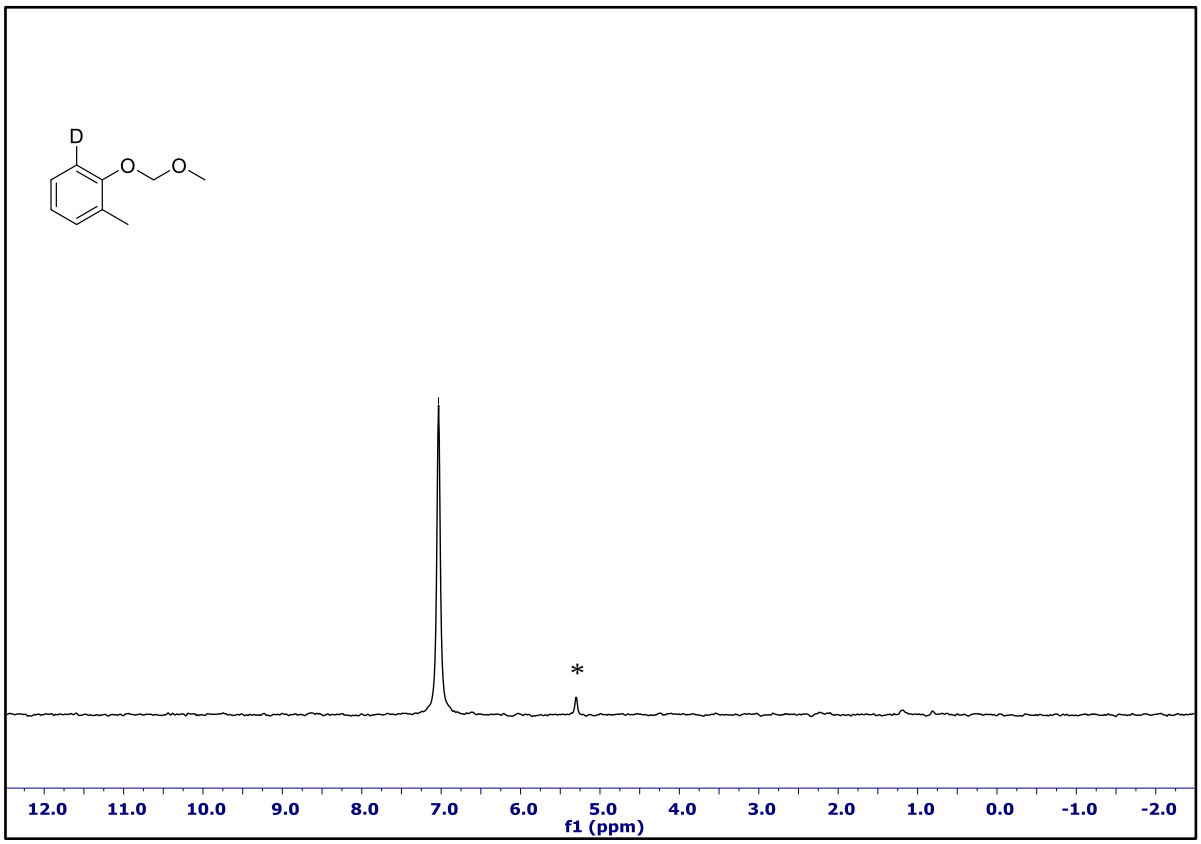
^{1}H NMR (600 MHz, $CDCl_3$)



^{13}C NMR (150 MHz, $CDCl_3$)



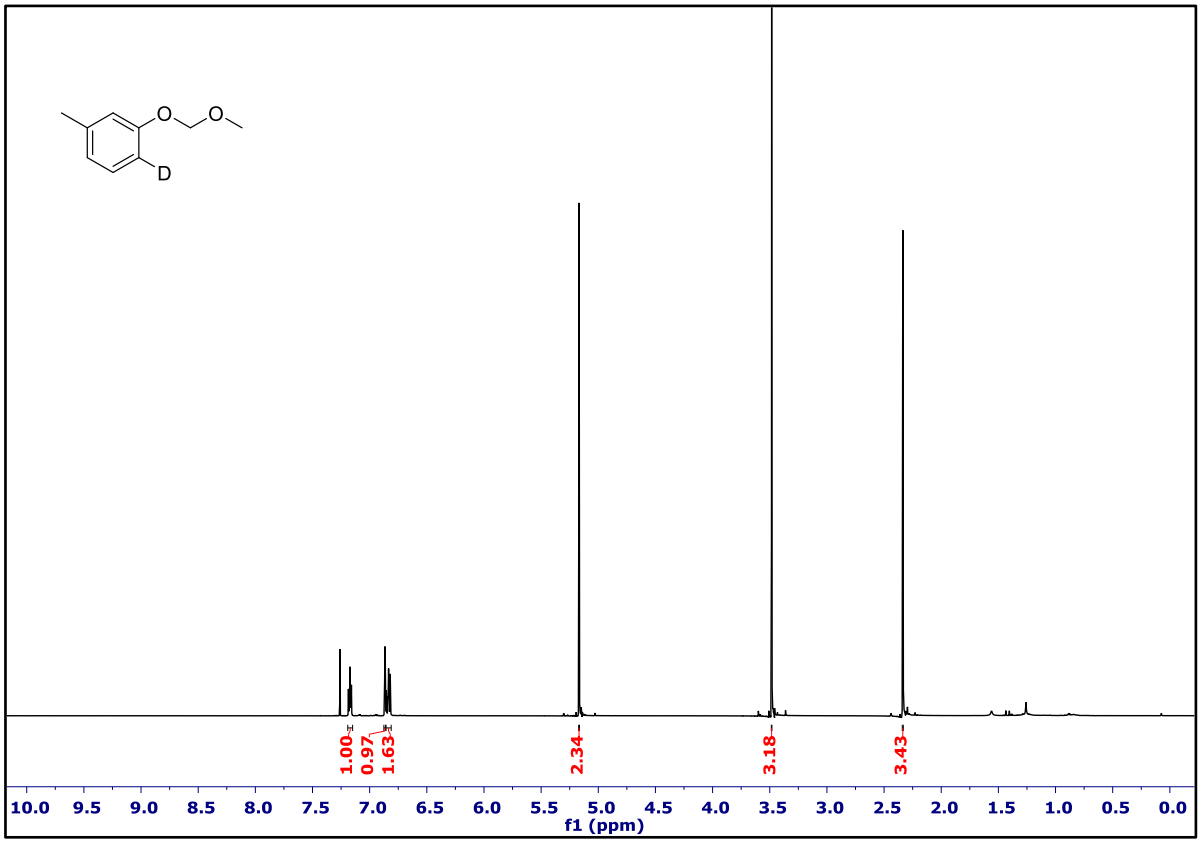
^{2}H NMR (92.07 MHz, CH_2Cl_2)



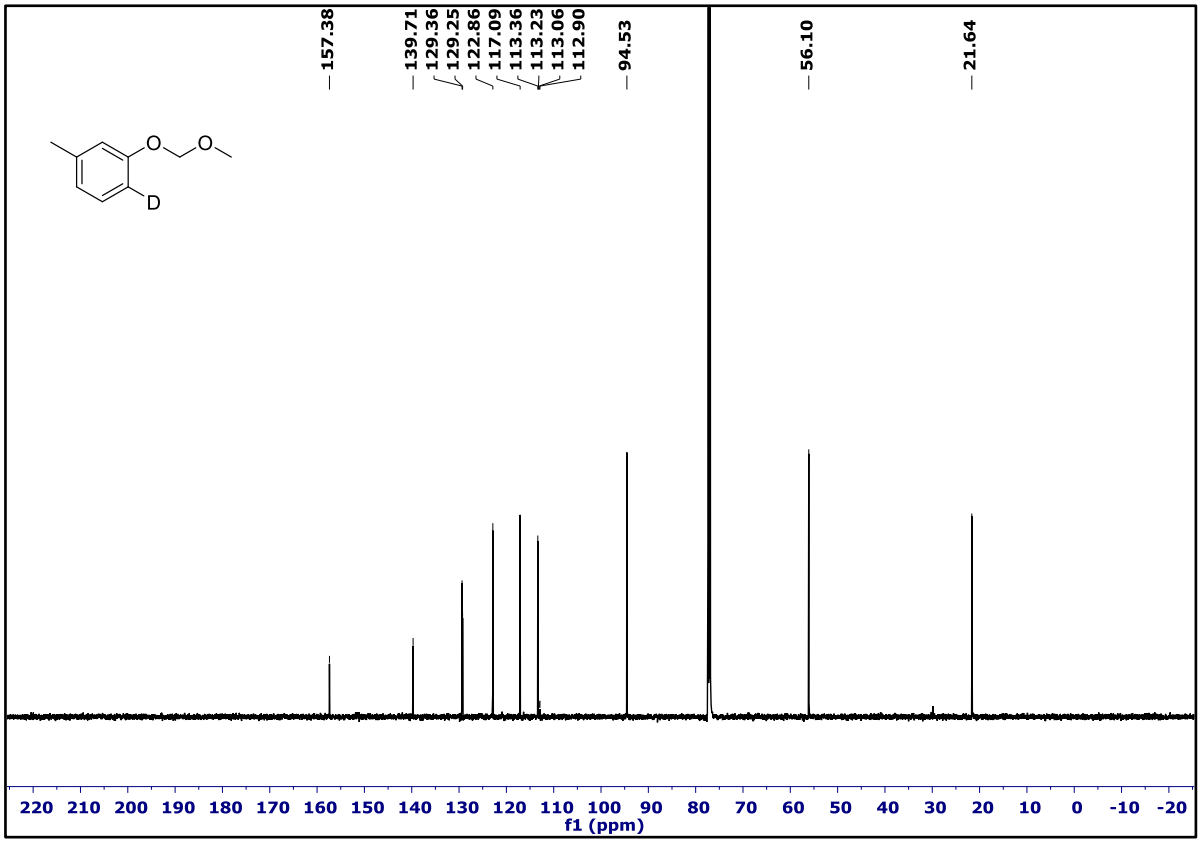
* residual CD_2Cl_2 solvent peak

6-Deuterio-1-(methoxymethoxy)-3-methylbenzene (*o*-*D*-1h)

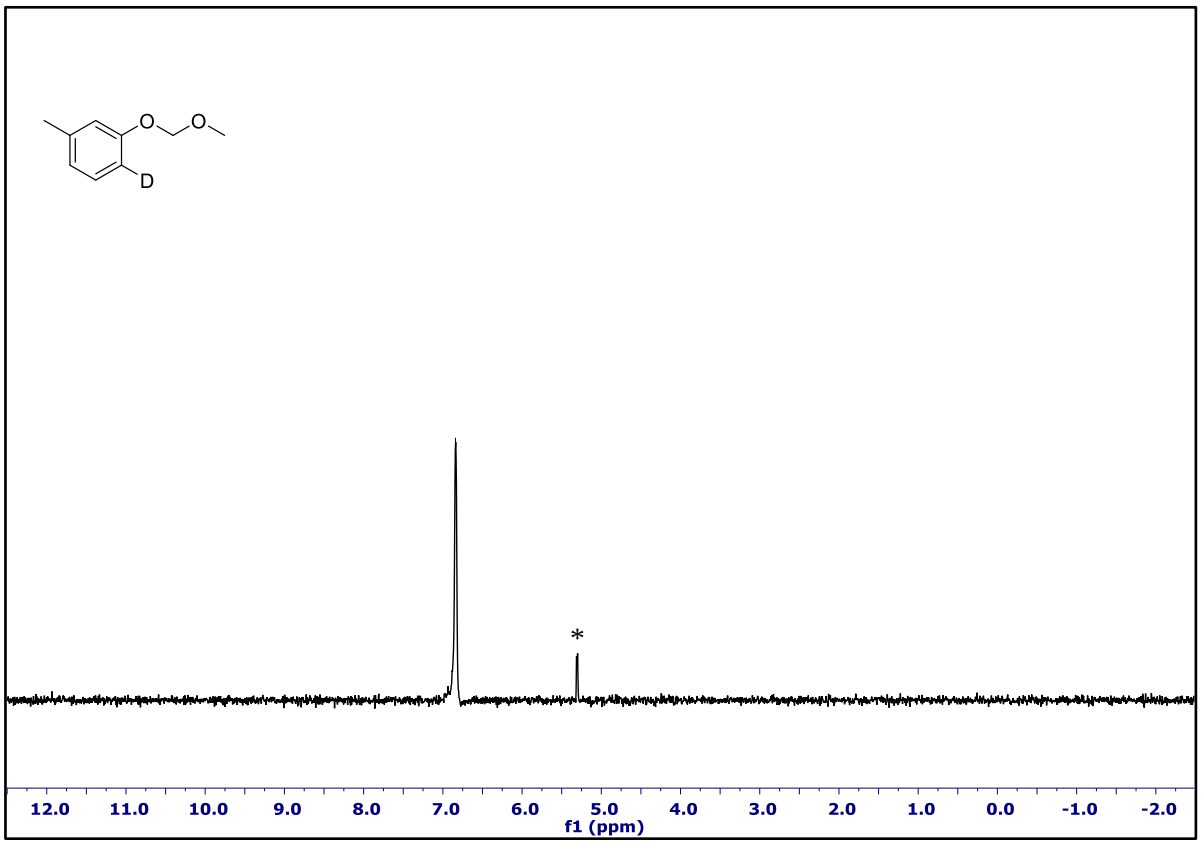
^{1}H NMR (600 MHz, $CDCl_3$)



^{13}C NMR (150 MHz, $CDCl_3$)



^{2}H NMR (92.07 MHz, CH_2Cl_2)



* residual CD_2Cl_2 solvent peak

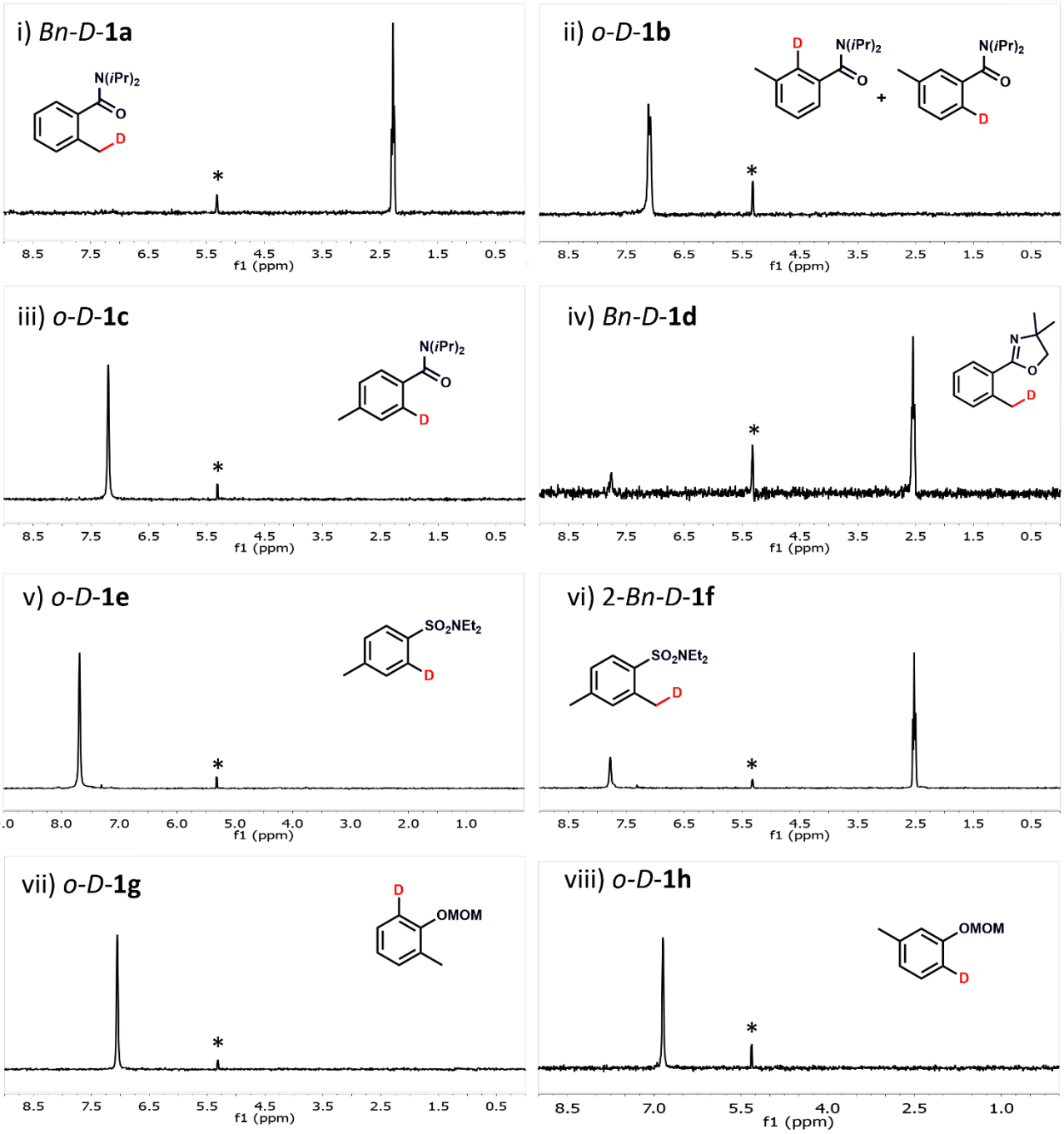
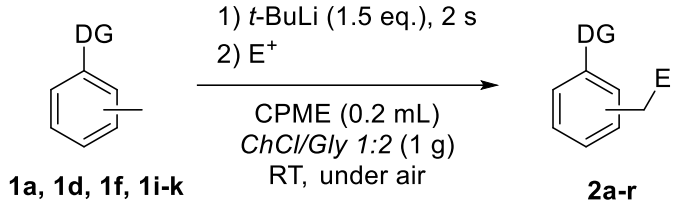


Figure S17. ^{2}H NMR spectra of deuteration labelling experiments: lithiation/deuteration of substituted toluenes **1a-h** using *t*-BuLi in CPME/DES at RT under air. *: residual CD_2Cl_2 solvent peak.

Synthesis and analysis of compounds **2a-r**.

General procedure. Reactions were performed under air at room temperature. In an open screw cap vial, substrates **1a**, **1d**, **1f** or **1i-k** (0.2 mmol, 1 eq.) were dissolved in CPME (0.2 mL, 1 M), then *ChCl/Gly (1:2 mol mol^{-1})* (1 g) was added and the resulting mixture was vigorously stirred for 5 min. *t*-BuLi (0.3 mmol, 1.5 eq.) was rapidly spread over the heterogeneous mixture, which was kept under vigorous stirring and quenched by addition of a selected electrophile (1 mmol, 5 eq.) after 2 seconds. The mixture was diluted with water (5 mL) and extracted with Et_2O (3 x 5 mL). The combined organic extracts were dried over Na_2SO_4 and the solvent removed under reduced pressure. The crude products were purified by flash column chromatography on silica gel.



***N,N*-diisopropyl-2-ethylbenzamide (2a):** general procedure starting from **1a** and iodomethane. Purification by flash column chromatography (PE/EtOAc 9/1 v/v) gave **2a** as a white solid (30 mg, 64%, R_f = 0.21 PE/EtOAc 9/1 v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.30-7.23 (m, 2H), 7.17 (td, *J* = 7.2, 1.7 Hz, 1H), 7.10-7.08 (dd, *J* = 7.1, 1.2 Hz, 1H), 3.67 (sept, *J* = 6.8 Hz, 1H), 3.50 (sept, *J* = 6.8 Hz, 1H), 2.65 (m, 2H), 1.57 (d, *J* = 6.8 Hz , 6H), 1.25 (t, *J* = 7.6 Hz, 3H), 1.11 (d, *J* = 6.7 Hz, 3H), 1.08 (d, *J* = 6.7 Hz, 3H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 170.8, 140.0, 138.1, 128.7, 128.4, 125.8, 124.9, 50.8, 45.8, 25.8, 20.9, 20.8, 20.8, 20.7, 15.3. EI-MS *m/z* (%): 233 (M^+, 20), 190 (17), 133 (100), 132 (26), 105 (11).[11]

2-(2-hydroxy-2-phenylethyl)-*N,N*-diisopropylbenzamide (2b): general procedure starting from **1a** and benzaldehyde. Purification by flash column chromatography (PE/EtOAc 8/2 v/v) gave **2b** as a white semi-solid (43 mg, 66%, R_f = 0.22 PE/EtOAc 8/2 v/v). Minor and major diastereoisomers (d_r = 5:1) were not separated by chromatography. ^{1}H NMR (600 MHz, $CDCl_3$, mixture of diastereoisomers): δ 7.52-6.71 (m, 9H, major + 9H, minor), 5.19 (dd, *J* = 6.4, 4.0 Hz, 1H, minor), 4.81 (dd, *J* = 11.0, 3.5 Hz, 1H, major), 4.31 (br s, 1H, major + 1H, minor), 3.81 (sept, *J* = 6.7 Hz, 1H, major), 3.71 (sept, *J* = 6.8 Hz, 1H, minor), 3.56 (m, 1H, major + 1H, minor), 3.11 (dd, *J* = 13.8, 4.0 Hz, 1H, minor), 2.99 (dd, *J* = 13.8, 3.5 Hz, 1H, major), 2.92 (dd, *J* = 13.9, 6.4 Hz, 1H, minor), 2.77 (dd, *J* = 13.8, 11.0 Hz, 1H, major), 1.64 (d, *J* = 6.7 Hz, 3H, major) superimposed to 1.63 (d, *J* = 6.8 Hz, 3H, minor), 1.59 (d, *J* = 6.8 Hz, 3H, major) superimposed to 1.59 (d, *J* = 6.9 Hz, 3H, minor), 1.18 (d, *J* = 6.7 Hz, 3H, major), 1.13 (d, *J* = 6.6 Hz, 3H, minor), 1.08 (d, *J* = 6.7 Hz, 3H, minor), 1.03 (d, *J* = 6.8 Hz, 3H, major). ^{13}C{1H} NMR (150 MHz, $CDCl_3$, mixture of diastereoisomers): δ 172.2 (major), 171.7 (minor), 146.6, 144.6, 138.5, 138.0, 136.2, 133.9, 131.9, 130.5, 129.4, 128.5, 128.1, 128.0, 127.1, 127.0, 126.6, 126.5, 126.2, 125.7, 124.9, 124.8, 75.7 (major), 72.9 (minor), 51.6 (major), 51.3

(minor), 46.5 (major), 46.2 (minor), 44.3 (major), 43.0 (minor), 21.3 (major), 21.2 (minor), 20.9 (minor), 20.8 (major), 20.6, 20.5. EI-MS *m/z* (%): 325 (M^+, 4), 219 (70), 207 (62), 178 (41), 176 (100), 119 (86).[12]

***N*,*N*-diisopropyl-2-(2-phenyl-2-(phenylamino)ethyl)benzamide (2c):** general procedure starting from **1a** and *N*-benzylidene aniline. Purification by flash column chromatography (hexane/EtOAc 9/1 v/v) gave **2c** as a white solid (43 mg, 53%, R_f = 0.24 hexane/EtOAc 9/1 v/v), mp 168-169 °C (MeOH). Minor and major diastereoisomers (d_r = 8:1) were not separated by chromatography. ^{1}H NMR (600 MHz, $CDCl_3$, mixture of diastereoisomers): δ 7.52 (d, *J* = 7.4 Hz, 2H, major), 7.45 (d, *J* = 7.6 Hz, 1H, major), 7.39-7.14 (m, 6H, major + 7H, minor), 7.07-7.02 (m, 4H, minor), 6.97 (t, *J* = 7.8 Hz, 2H, major), 6.60 (t, *J* = 7.3 Hz, 1H, minor), 6.56 (d, *J* = 8.0 Hz, 2H, minor), 6.50 (t, *J* = 7.3 Hz, 1H, major) superimposed to 6.47 (d, *J* = 8.0 Hz, 2H, major), 4.78 (dd, *J* = 6.3, 4.1 Hz, 1H, minor), 4.46 (dd, *J* = 11.4, 3.6 Hz, 1H, major), 3.71-3.61 (m, 1H, major + 1H, minor), 3.54 (sept, *J* = 6.6 Hz, 1H, major + 1H, minor), 3.19 (dd, *J* = 14.0, 4.1 Hz, 1H, minor), 3.08 (dd, *J* = 14.0, 6.2 Hz, 1H, minor), 3.01 (dd, *J* = 13.9, 3.6 Hz, 1H, major), 2.82 (dd, *J* = 13.9, 11.2 Hz, 1H, major), 1.65 (dd, *J* = 6.8, 1.5 Hz, 6H, major), 1.61 (dd, *J* = 9.5, 6.8 Hz, 6H, minor), 1.14-1.09 (m, 3H, major + 6H, minor), 0.99 (d, *J* = 6.7 Hz, 3H, major). ^{13}C{1H} NMR (150 MHz, $CDCl_3$, mixture of diastereoisomers): δ 171.5 (major), 171.4 (minor), 148.0 (major), 145.2 (major), 139.0 (minor), 138.6 (major), 135.4 (minor), 135.2 (major), 133.1 (minor), 133.0 (minor), 131.5 (minor), 129.8 (major), 129.4 (minor), 129.0 (major), 128.9 (minor), 128.9 (major), 128.8 (major), 128.5 (minor), 127.7 (minor), 127.2 (minor), 127.0 (major), 126.8 (minor), 126.8 (major), 126.3 (major), 125.9 (minor), 124.7 (major), 115.9 (major), 115.7 (minor), 113.7 (minor), 113.0 (major), 60.8 (major), 60.5 (minor), 51.2 (major), 51.1 (minor), 46.2 (major), 46.2 (minor), 42.6 (major), 41.3 (minor), 21.1 (minor), 21.0 (major + minor), 20.8 (major), 20.6 (major + minor + minor), 20.5 (major). EI-MS *m/z* (%): 400 (M^+, 7), 182 (100). ESI-HRMS $[M+Na]^+$: *m/z* 423.2412, $C_{27}H_{32}NO_2Na^+$ requires 423.2407.

2-(3-hydroxybutyl)-*N*,*N*-diisopropylbenzamide (2d): general procedure starting from **1a** and propylene oxide. Purification by flash column chromatography (PE/EtOAc 8/2 v/v) gave **2d** as a colourless oil (31 mg, 56%, R_f = 0.15 PE/EtOAc 8/2 v/v). Minor and major diastereoisomers (d_r = 4:1) were not separated by chromatography. ^{1}H NMR (600 MHz, $CDCl_3$, mixture of diastereoisomers): δ 7.33-7.25 (m, 2H, major + 2H, minor), 7.21-7.15 (m, 1H, major + 1H, minor), 7.08-7.04 (m, 1H, major + 1H, minor), 3.86-3.80 (m, 1H, minor), 3.71 (sept, *J* = 6.6 Hz, 1H, minor) superimposed to 3.66 (sept, *J* = 6.7 Hz, 1H, major), 3.52 (sept, *J* = 6.8 Hz, 1H, minor) superimposed to 3.51 (sept, *J* = 7.0 Hz, 1H, major), 3.46 (dqd, *J* = 12.6, 6.3, 2.5 Hz, 1H major), 3.27 (br s, 1H, major + 1H, minor), 2.74-2.60 (m, 2H, major + 2H, minor), 1.85-1.67 (m, 2H, major + 2H, minor), 1.60-1.52 (m, 6H, major + 6H, minor), 1.16-1.06 (m, 9H, major + 9H, minor). ^{13}C{1H} NMR (150 MHz, $CDCl_3$, mixture of diastereoisomers): δ 172.2 (major), 171.5 (minor), 139.0 (minor), 138.4 (major), 137.9 (major), 137.4 (minor), 129.8 (minor), 129.7 (major), 128.7 (major), 128.7 (minor), 126.1 (major), 125.9 (minor), 124.8 (minor), 124.6 (major), 68.3 (minor), 63.7 (major), 51.4 (major), 51.1 (minor), 46.3 (major), 46.0 (minor), 41.0 (minor), 40.8 (major), 29.9 (minor), 28.1 (major), 23.7 (minor), 23.2 (major), 20.9 (minor), 20.8 (major), 20.8 (major), 20.7 (minor), 20.7 (minor), 20.6 (minor), 20.5 (major), 20.4 (major). EI-MS *m/z*

(%): 277 (M^+, 5), 159 (54), 135 (55), 133 (39), 131, (100), 86 (72). ESI-HRMS $[M+Na]^+$: *m/z* 300.1936, $C_{17}H_{27}NO_2Na^+$ requires 300.1934.

2-(2-(diisopropylcarbamoyl)phenyl)acetic acid (2e): general procedure starting from **1a** and CO_2 (bubbled for 15 seconds). The crude acid was dissolved in 1 N NaOH (5 mL) and washed with Et_2O (2 x 5 mL). The aqueous layer was then acidified with 1M hydrochloric acid (6 mL) and extracted with EtOAc (3 x 5 mL). The organic extracts were washed with water (2 x 5 mL), dried over Na_2SO_4, and concentrated under reduced pressure to give **2e** as a white solid (26 mg, 50%, R_f = 0.14 PE/EtOAc 7/3 v/v + HCOOH 1%) mp 147.3-148.5 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.47 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.40 (td, *J* = 7.7, 1.5 Hz, 1H), 7.32 (td, *J* = 7.5, 1.3 Hz, 1H), 7.22 (dd, *J* = 7.8, 1.5 Hz, 1H), 3.95 (sept, *J* = 6.8 Hz, 1H), 3.65-3.52 (m, 3H), 1.61 (d, *J* = 6.8 Hz, 3H), 1.55 (d, *J* = 6.8 Hz, 3H), 1.27 (d, *J* = 6.7 Hz, 3H), 1.11 (d, *J* = 6.7 Hz, 3H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 172.5, 171.1, 136.0, 132.2, 131.3, 130.4, 127.5, 125.8, 52.1, 47.2, 41.9, 21.5, 21.0, 20.4, 20.2. ESI-HRMS $[M+Na]^+$: *m/z* 286.1422, $C_{15}H_{21}NNaO_3^+$ requires 286.1414.

2-(2-(Benzylamino)-2-thioxoethyl)-*N,N*-diisopropylbenzamide (2f): General procedure starting from **1a** and benzyl isothiocyanate. Purification by flash column chromatography (95/5 Toluene/EtOAc v/v) gave **2f** as yellow oil (25 mg, 34%, R_f = 0.45 95/5 Toluene/EtOAc v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 10.51 (br s, 1H), 7.68 (d, *J* = 8.3 Hz, 1H), 7.36 (td, *J* = 7.6 Hz, 1.4 Hz, 1H), 7.28 (td, *J* = 7.6 Hz, 1.5 Hz, 1H), 7.24-7.17 (m, 3H), 7.14 (dd, *J* = 7.6 Hz, 1.4 Hz, 1H), 7.11-7.10 (m, 2H), 4.86 (dd, *J* = 15.1, 5.5 Hz, 1H), 4.72 (dd, *J* = 15.1, 5.5 Hz, 1H), 4.18 (d, *J* = 13.1 Hz, 1H), 3.89 (d, *J* = 13.8 Hz, 1H), 3.80 (sept, *J* = 6.8 Hz, 1H), 3.55 (sept, *J* = 6.8 Hz, 1H), 1.55 (d, *J* = 6.9 Hz, 3H), 1.52 (d, *J* = 6.9 Hz, 3H), 1.17 (d, *J* = 6.9 Hz, 3H), 1.08 (d, *J* = 6.9 Hz, 3H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 201.2, 171.8, 137.1, 136.8, 133.9, 130.3, 129.5, 128.5, 127.4, 127.3, 127.2, 124.9, 51.7, 50.0, 49.9, 46.5, 21.3, 20.8, 20.5. EI-MS *m/z* (%): 368 (M^+, 60), 335 (3), 291 (12), 268 (16), 234 (20), 176 (28), 91 (100). ESI-HRMS $[M+H]^+$: *m/z* 369.1986, $C_{22}H_{29}N_2OS^+$ requires 369.1995.

***N,N*-diisopropyl-2-(2-oxo-2-phenylethyl)benzamide (2g):** general procedure starting from **1a** and *N*-methoxy-*N*-methylbenzamide. Purification by flash column chromatography (PE/EtOAc 8/2 v/v) gave **2g** as a white solid (38 mg, 59%, R_f = 0.14 PE/EtOAc 8/2 v/v), mp 101.2-102.1 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.04 (dd, *J* = 8.3, 1.2, 2H), 7.58-7.53 (m, 1H), 7.48-7.43 (m, 2H), 7.32 (td, *J* = 7.5, 1.4 Hz, 1H), 7.29-7.25 (m, 1H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.19 (dd, *J* = 7.5, 1.3 Hz, 1H), 4.61 (d, *J* = 17.2 Hz, 1H), 4.25 (d, *J* = 17.2 Hz, 1H), 3.82 (sept, *J* = 6.6 Hz, 1H), 3.41 (sept, *J* = 6.8 Hz, 1H), 1.52 (d, *J* = 6.7 Hz, 3H), 1.34 (d, *J* = 6.7 Hz, 3H), 1.12 (d, *J* = 6.7 Hz, 3H), 1.01 (d, *J* = 6.5 Hz, 3H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 197.7, 170.4, 138.6, 136.6, 133.4, 131.8, 131.5, 128.8, 128.6 (2C), 126.9, 125.1, 51.1, 45.9, 42.6, 21.0, 20.7, 20.6, 20.5. EI-MS *m/z* (%): 323 (M^+, 35), 322 (50), 223 (86), 195 (99), 105 (100), 86 (47), 77 (52). ESI-HRMS $[M+Na]^+$: *m/z* 346.1783, $C_{21}H_{25}NO_2Na^+$ requires 346.1778.

Diphenyl (2-(diisopropylcarbamoyl)benzyl)phosphonate (2h): general procedure starting from **1a** and diphenyl phosphoryl chloride. Purification by flash column chromatography (PE/EtOAc 8/2 v/v) gave **2h** as a white solid (23.5 mg, 26% yield, R_f = 0.08 PE/EtOAc 8/2 v/v), mp 105-107 °C. ^{1}H NMR (600 MHz, $CDCl_3$):

δ 7.71 (dd, *J* = 7.8, 2.5 Hz, 1H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.31-7.25 (m, 5H), 7.20 (d, *J* = 7.5 Hz, 1H), 7.16 (d, *J* = 7.0 Hz, 1H), 7.13 (d, *J* = 7.1 Hz, 1H), 7.10 (d, *J* = 8.1 Hz, 2H), 7.07 (d, *J* = 8.1 Hz, 2H), 3.81 (sept, *J* = 6.6 Hz, 1H), 3.73 (dd, *J* = 20.4, 15.7 Hz, 1H), 3.56 (dd, *J* = 22.8, 15.7 Hz, 1H), 3.48 (sept, *J* = 6.7 Hz, 1H), 1.55 (d, *J* = 6.8 Hz, 3H), 1.50 (d, *J* = 6.8 Hz, 3H), 1.12 (d, *J* = 6.6 Hz, 3H), 1.04 (dd, *J* = 6.6 Hz, 1H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 169.8, 150.4 (d, *J* = 9.7 Hz, 1C), 150.3 (d, *J* = 8.9 Hz, 1C), 131.1 (d, *J* = 5.2 Hz, 1C), 129.9, 129.8, 128.8, 127.7 (d, *J* = 8.5 Hz, 1C), 127.2, 125.7, 125.4, 125.3, 120.9 (d, *J* = 4.0 Hz, 1C), 120.8 (d, *J* = 4.6 Hz, 1C), 51.2, 46.1, 30.1 (d, *J* = 140.6 Hz, 1C), 21.0, 20.9, 20.8, 20.5. ^{31}P NMR (242 MHz, $CDCl_3$): δ 20.60 (t, *J* = 21.8 Hz). ESI-HRMS $[M+Na]^+$: *m/z* 474.1816, $C_{26}H_{30}NO_4PNa^+$ requires 474.1805.

2-(Deuteriomethyl)-*N*,*N*-diisopropyl-4-methylbenzamide (*Bn-D*-1i): General procedure starting from **1i** and CD_3OD. Purification by flash column chromatography (9/1 PE/EtOAc v/v) gave *Bn-D*-**1i** (86% D incorporation) as white solid (42 mg, 90%, R_f = 0.25 9/1 PE/EtOAc v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.00-6.94 (m, 3H), 3.68 (sept, *J* = 6.7 Hz, 1H), 3.49 (sept, *J* = 6.8 Hz, 1H), 2.31 (s, 3H), 2.27-2.23 (m, 2H), 1.56 (d, *J* = 6.9 Hz, 6H), 1.10 (d, *J* = 6.9 Hz, 3H), 1.06 (d, *J* = 6.5 Hz, 3H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 171.1, 137.8, 135.9, 133.5, 131.1, 126.5, 124.7, 50.9, 45.8, 21.3, 21.0, 20.9, 20.8, 20.7, 18.6 (t, *J* = 18.9 Hz, 1C). ^{2}H NMR (92.07 MHz, CH_2Cl_2): 2.24 (t, *J* = 2.4 Hz). EI-MS *m/z* (%): 234 (M^+, 13), 218 (12), 191 (13), 134 (100), 133 (41), 233 (10). ESI-HRMS $[M+H]^+$: *m/z* 235.1908, $C_{15}H_{23}DNO^+$ requires 235.1915.

2-(2-(Diisopropylcarbamoyl)-5-methylphenyl)acetic acid (2i): general procedure starting from **1i** and CO_2 (bubbled for 15 seconds). The crude acid was dissolved in 1 N NaOH (5 mL) and washed with Et_2O (2 x 5 mL). The aqueous layer was then acidified with 1M hydrochloric acid (6 mL) and extracted with EtOAc (3 x 5 mL). The organic extracts were washed with water (2 x 5 mL), dried over Na_2SO_4, and concentrated under reduced pressure to give **2i** (20.5 mg, 37% yield) as a white semi-solid. ^{1}H NMR (600 MHz, $CDCl_3$): δ 13.31 (br s, 1H), 7.27 (br s, 1H), 7.12-7.09 (m, 2H), 3.98 (sept, *J* = 6.7 Hz, 1H), 3.60 (sept, *J* = 6.7 Hz, 1H) superimposed to 3.56 (d, *J* = 12.7 Hz, 1H), 3.53 (d, *J* = 12.7 Hz, 1H), 2.35 (s, 3H), 1.60 (d, *J* = 6.8 Hz, 3H), 1.54 (d, *J* = 6.8 Hz, 3H), 1.26 (d, *J* = 6.7 Hz, 3H), 1.10 (d, *J* = 6.7 Hz, 3H). EI-MS *m/z* (%): 277 (M^+, 13), 276 (22), 177 (21), 149 (100), 133 (38), 86 (37). ^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 172.8, 171.4, 140.7, 133.1, 132.3, 131.9, 128.2, 125.8, 52.1, 47.1, 41.9, 21.5, 21.3, 21.0, 20.5, 20.1. EI-MS *m/z* (%): 277 (M^+, 14), 276 (23), 177 (21), 149 (100), 133 (39), 86 (3). ESI-HRMS $[M+Na]^+$: *m/z* 300.1573, $C_{16}H_{23}NO_3Na^+$ requires 300.1570.

***N*,*N*-Diisopropyl-4-methyl-2-(2-oxo-2-phenylethyl)benzamide (2j):** general procedure starting from **1i** and *N*-methoxy-*N*-methylbenzamide. Purification by flash column chromatography (PE/EtOAc 8/2 v/v) gave **2j** as a white solid (38.5 mg, 57% yield, R_f = 0.26 PE/EtOAc 8/2 v/v), mp 91-93 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.04 (d, *J* = 7.2 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.07 (s, 2H), 7.04 (s, 1H), 4.59 (d, *J* = 17.1 Hz, 1H), 4.19 (d, *J* = 17.0 Hz, 1H), 3.84 (sept, *J* = 6.5 Hz, 1H), 3.39 (sept, *J* = 6.7 Hz, 1H), 2.32 (s, 3H), 1.51 (d, *J* = 6.5 Hz, 3H), 1.33 (d, *J* = 6.5 Hz, 3H), 1.11 (d, *J* = 6.4 Hz, 3H), 1.00 (d, *J* = 6.4 Hz, 3H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 197.9, 170.7, 138.4, 136.7, 135.9, 133.3, 132.1, 131.7, 128.8, 128.6, 127.6, 125.1, 51.1, 45.8, 42.5, 21.4, 21.0, 20.7, 20.6, 20.5. EI-MS *m/z* (%): 337 (M^+, 37), 336 (52), 237 (100),

236 (47), 209 (96), 194 (43), 133 (26), 105 (92), 86 (41), 77 (53). ESI-HRMS $[M+Na]^+$: *m/z* 360.1939, $C_{22}H_{27}NO_2Na^+$ requires 360.1934.

6-(Deuteriomethyl)-*N,N*-diisopropyl-2-methylbenzamide (*Bn-D*-1j): General procedure starting from **1j** and CD_3OD. Purification by flash column chromatography (9/1 PE/EtOAc v/v) gave *Bn-D*-**1j** (71% D incorporation) as white solid (37.6 mg, 80%, R*f* = 0.35 9/1 PE/EtOAc v/v). ^1H NMR (600 MHz, $CDCl_3$): δ 7.09 (t, *J* = 7.6 Hz, 1H), 6.99 (d, *J* = 7.6 Hz, 2H), 3.61 (sept, *J* = 6.7 Hz, 1H), 3.51 (sept, *J* = 6.8 Hz, 1H), 2.30-2.24 (m, 5H) 1.60 (d, *J* = 6.9 Hz, 6H), 1.11 (d, *J* = 6.9 Hz, 6H).$^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$): δ 170.3, 138.2, 133.4, 133.4, 127.6, 127.6, 50.9, 46.0, 21.2, 20.7, 18.85 (*t, J* = 19.1 Hz, 1C). ^2H NMR (92.07 MHz, CH_2Cl_2): 2.22 (t, *J* = 2.3 Hz). EI-MS *m/z* (%): 234 (M^+, 4), 218 (27), 191 (10), 134 (100), 133 (75). ESI-HRMS $[M+Na]^+$: *m/z* 257.1736, $C_{15}H_{22}DNONa^+$ requires 257.1735.

2-(2-Hydroxy-2-phenylethyl)-*N,N*-diisopropyl-6-methylbenzamide (2k): General procedure starting from **1j** and benzaldehyde. Purification by flash column chromatography (85/15 PE/EtOAc v/v) gave **2k** as colourless semi-solid (48 mg, 70%, R_f = 0.33 85/15 PE/EtOAc v/v). ^1H NMR (600 MHz, $CDCl_3$): δ 7.44 (d, *J* = 6.9 Hz, 2H), 7.35 (t, *J* = 7.6 Hz, 2H), 7.29-7.21 (m, 3H), 7.10 (d, *J* = 7.6 Hz, 1H), 4.76 (dd, *J* = 11.0, 3.4 Hz, 1H), 3.65-3.54 (m, 3H), 2.96 (dd, *J* = 13.8, 3.4 Hz, 1H), 2.72 (dd, *J* = 13.8, 10.5 Hz, 1H), 2.33 (s, 3H), 1.68 (d, *J* = 6.9 Hz, 3H), 1.62 (d, *J* = 6.9 Hz, 3H), 1.19 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 6.2 Hz, 3H).$^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$): δ 172.3, 146.4, 137.8, 135.3, 133.2, 128.9, 128.5, 128.5, 127.4, 127.1, 125.7, 76.1, 51.5, 46.6, 44.5, 21.5, 20.7, 20.5, 19.3. EI-MS *m/z* (%): 339 (M^+, 2), 233 (61), 218 (100), 190 (46), 133 (75). ESI-HRMS $[M+Na]^+$: *m/z* 362.2094, $C_{22}H_{29}NO_2Na^+$ requires 362.2091.

***N,N*-diisopropyl-2-methyl-6-(2-phenyl-2-(phenylamino)ethyl)benzamide (2l)**: General procedure starting from **1j** and *N*-benzylidene aniline. Purification by flash column chromatography (9/1 PE/EE v/v) gave **2l** as white semi-solid (55.5 mg, 67%, R_f = 0.25 9/1 PE/EE v/v). ^1H NMR (600 MHz, $CDCl_3$, 1:1 mixture of diastereoisomers): δ 7.49 (d, *J* = 7.2 Hz, 2H), 7.35 (t, *J* = 7.4 Hz, 2H), 7.30-7.16 (m, 8H), 7.06-7.00 (m, 4H), 6.97-6.93 (m, 3H), 6.57-6.45 (m, 6H), 6.31-6.30 (m, 1H), 4.75-4.73 (m, 1H), 4.40-4.38 (m, 1H), 3.61-3.49 (m, 4H), 3.19 (dd, *J* = 13.9, 3.5 Hz, 1H), 3.03-2.95 (m, 2H), 2.82-2.82 (m, 1H), 2.34 (s, 3H) superimposed to 2.44 (s, 3H), 1.68 (d, *J* = 6.9 Hz, 3H) superimposed to 1.67 (d, *J* = 6.8 Hz, 3H) superimposed to 1.64 (d, *J* = 6.8 Hz, 3H) superimposed to 1.63 (d, *J* = 6.8 Hz, 3H), 1.15 (d, *J* = 6.7 Hz, 3H) superimposed to 1.13 (d, *J* = 6.7 Hz, 3H) 1.08 (d, *J* = 6.5 Hz, 3H), 0.96 (d, J = 6.9 Hz, 3H). $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$): δ 171.4, 171.1, 148.4, 145.4, 138.5, 138.3, 134.8, 133.4, 133.3, 132.5, 128.9, 128.8, 128.7, 128.7, 128.5, 128.5, 128.4, 127.2, 127.0, 126.9, 126.3, 116.7, 115.8, 113.7, 113.0, 61.1, 58.6, 51.2, 51.1, 46.3, 46.3, 42.9, 41.4, 21.3, 21.2, 21.1, 21.0, 20.8, 20.6, 20.5, 19.3, 19.3. EI-MS *m/z* (%): 414 (M^+, 5), 298 (23), 233 (15), 190 (10), 182 (100). ESI-HRMS $[M+Na]^+$: *m/z* 437.2561, $C_{28}H_{34}N_2ONa^+$ requires 437.2563.

2-(Deuteriomethyl)-*N,N*-diisopropyl-4,6-dimethylbenzamide (*Bn-D*-1k): general procedure starting from **1k** and CD_3OD. Purification by flash column chromatography (PE/EtOAc 8/2 v/v) gave *Bn-D*-**1k** (60% D incorporation) as a white solid (36 mg, 73%, R_f = 0.38 PE/EtOAc 8/2 v/v), mp 115.3-116.5 °C. ^1H NMR (600

MHz, $CDCl_3$): δ 6.81 (s, 2H), 3.63 (sept, *J* = 6.6 Hz, 1H), 3.49 (sept, *J* = 6.8 Hz, 1H), 2.26 (s, 3H), 2.24 (s, 3H), 2.23-2.21 (m, 2H), 1.59 (d, *J* = 6.8 Hz, 6H), 1.10 (d, *J* = 6.6 Hz, 6H). $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$): δ 170.7, 137.2, 135.6, 133.3, 133.3, 128.3 (2C), 50.9, 45.9, 21.2, 21.2, 20.7, 19.0, 18.8 (t, *J* = 19.5 Hz). ^{2}H NMR (92.07 MHz, CH_2Cl_2): δ 2.20 (t, *J* = 2.3 Hz). EI-MS *m/z* (%): 248 (M^+, 3), 233 (23), 232 (27), 148 (100), 147 (49). ESI-HRMS $[M+Na]^+$: *m/z* 271.1893, $C_{16}H_{24}DNONa^+$ requires 271.1891.

2-(3-Hydroxybutyl)-*N*,*N*-diisopropyl-4,6-dimethylbenzamide (2m): general procedure starting from **1k** and propylene oxide. Purification by flash column chromatography (PE/EtOAc 7/3 v/v) gave **2m** as a colourless oil (33 mg, 54% yield, R_f = 0.36 PE/EtOAc 7/3 v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 6.86 (s, 1H), 6.84 (s, 1H), 3.60 (sept, *J* = 6.6 Hz,, 1H), 3.52 (sept, *J* = 6.8 Hz, 1H), 3.45-3.39 (m, 1H), 2.61 (dd, *J* = 8.0, 4.7 Hz, 2H), 2.29 (s, 3H), 2.23 (s, 3H), 1.74-1.65 (m, 2H), 1.61 (d, *J* = 6.8 Hz, 3H), 1.57 (d, *J* = 6.8 Hz, 3H), 1.13 (d, *J* = 6.7 Hz, 3H), 1.08 (d, *J* = 6.2 Hz, 3H), 1.06 (d, *J* = 6.7 Hz, 3H). $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$): δ 172.4, 137.8, 137.4, 135.4, 132.9, 128.7, 127.3, 63.5, 51.4, 46.4, 41.0, 28.4, 23.3, 21.4, 21.0, 21.0, 20.8, 20.4, 19.1. EI-MS *m/z* (%): 305 (M^+, 2), 290 (37), 288 (27), 272 (38), 232 (38), 205 (24), 187 (29), 186 (35), 163 (56), 161 (54), 159 (100), 145 (29), 119 (65), 84 (58), 43 (35). ESI-HRMS $[M+Na]^+$: *m/z* 328.2251, $C_{19}H_{31}NO_2Na^+$ requires 328.2247.

***N*,*N*-diisopropyl-2,4-dimethyl-6-(2-oxo-2-phenylethyl)benzamide (2n):** general procedure starting from **1k** and *N*-methoxy-*N*-methylbenzamide. Purification by flash column chromatography (PE/EtOAc 8/2 v/v) gave **2n** as a white solid (37 mg, 53%, R_f = 0.25 PE/EtOAc 8/2 v/v), mp 147.6-148.5 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.08-8.04 (m, 2H), 7.55-7.50 (m, 1H), 7.47-7.41 (m, 2H), 6.90 (s, 1H), 6.83 (s, 1H), 4.41 (d, *J* = 16.2 Hz, 1H), 4.03 (d, *J* = 16.2 Hz, 1H), 3.67 (sept, *J* = 6.7 Hz, 1H), 3.47 (sept, *J* = 6.9 Hz, 1H), 2.28 (s, 3H), 2.25 (s, 3H), 1.59 (d, *J* = 6.8 Hz, 3H), 1.52 (d, *J* = 6.8 Hz, 3H), 1.10 (d, *J* = 6.7 Hz, 3H). 0.98 (d, *J* = 6.7 Hz, 3H). $^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$): δ 197.9, 170.3, 137.6, 136.4, 135.4, 133.7, 133.3, 130.2, 129.8, 128.9, 128.8, 128.2, 51.0, 46.1, 42.7, 21.4, 21.3, 21.1, 20.8, 20.4, 19.3. EI-MS *m/z* (%): 351 (M^+, 3), 336 (100), 251 (58), 223 (45), 105 (63). ESI-HRMS $[M+Na]^+$: *m/z* 374.2078, $C_{23}H_{29}NO_2Na^+$ requires 374.2091.

2-(2-Ethylphenyl)-4,4-dimethyl-4,5-dihydrooxazole (2o): General procedure starting from **1d** and iodomethane. Purification by flash column chromatography (96/4 PE/EtOAc v/v) gave **2o** as colourless oil (32 mg, 78%, R_f = 0.33 96/4 PE/EtOAc v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.71 (d, *J* = 7.6 Hz, 1H), 7.35 (t, *J* = 7.2 Hz, 1H), 7.25 (d, *J* = 7.6 Hz, 1H), 7.21 (t, *J* = 7.4 Hz, 1H), 4.09 (s, 2H), 2.96 (q, *J* = 7.5 Hz, 2H), 1.40 (s, 6H), 1.21 (t, *J* = 7.4 Hz, 3H).$^{13}C\{1H\}$ NMR (150 MHz, $CDCl_3$): δ 163.2, 144.6, 130.8, 130.2, 129.6, 127.3, 125.7, 79.0, 67.8, 28.5, 27.4, 15.8. EI-MS *m/z* (%): 203 (M^+, 100), 188 (30), 160 (19), 148 (95), 132 (35), 117 (45), 104 (21).[13]

1-(2-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)phenyl)-2-phenylpropan-2-ol (2p): General procedure starting from **1d** and acetophenone. Purification by flash column chromatography (9/1 PE/EtOAc v/v) gave **2p** as colourless oil (37 mg, 60%, R_f = 0.30 9/1 PE/EtOAc v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.85 (brs, 1H), 7.77-7.73 (m, 1H), 7.56-7.52 (m, 2H), 7.35 (t, *J* = 7.7 Hz, 2H), 7.28-7.23 (m, 3H), 6.87-6.85 (m, 1H), 4.16 (d, *J* =

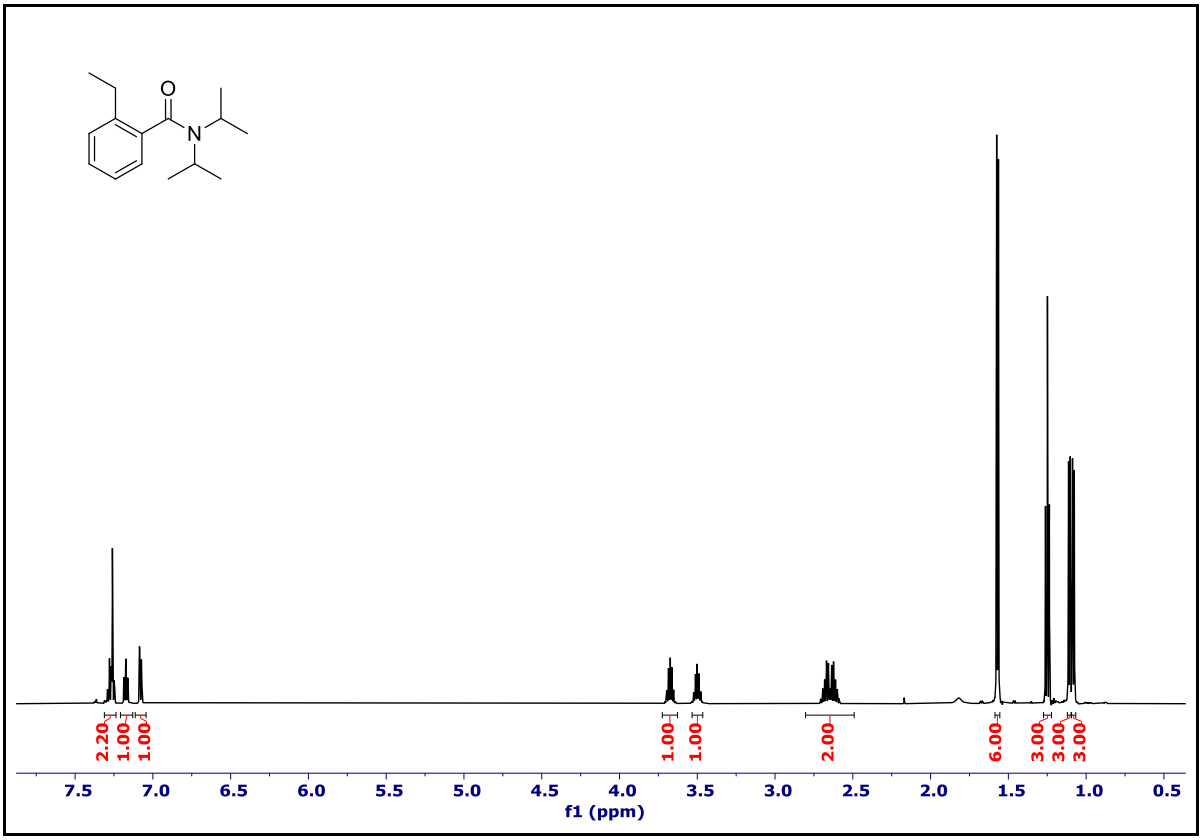
8.3 Hz, 1H), 4.13 (d, *J* = 8.3 Hz, 1H), 3.39 (d, *J* = 13.4 Hz, 1H), 3.33 (d, *J* = 13.4 Hz, 1H), 1.64 (s, 3H), 1.49 (s, 3H), 1.40 (s, 3H) .^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 163.5, 149.8, 138.8, 132.9, 130.3, 129.6, 127.9, 126.3, 126.2, 125.3, 79.3, 74.8, 68.1, 47.8, 29.9, 28.7, 28.7. EI-MS *m/z* (%): 309 (M^+, 1), 276 (5), 189 (100), 174 (41). ESI-HRMS $[M+H]^+$: *m/z* 310.1805, $C_{20}H_{24}NO_2^+$ requires 310.1802.

***N,N*-Diethyl-2-(3-hydroxybutyl)-4-methylbenzenesulfonamide (2q):** general procedure starting from **1f** and propylene oxide. Purification by flash column chromatography (PE/EtOAc 8/2 v/v) gave **2q** as a colourless semi-solid (39 mg, 65% yield, R_f = 0.10 PE/EtOAc 8/2 v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.2 Hz, 1H), 7.16 (s, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 3.83-3.77 (m, 1H), 3.30 (q, *J* = 7.2 Hz, 2H) superimposed to 3.29 (q, *J* = 7.1 Hz, 2H), 3.08-2.96 (m, 2H), 2.37 (s, 3H), 2.13 (br s, 1H), 1.88-1.75 (m, 2H), 1.21 (d, *J* = 6.2 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 6H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 143.3, 142.0, 135.6, 132.7, 129.7, 126.8, 67.1, 41.2, 41.1, 28.8, 23.6, 21.4, 13.9. EI-MS *m/z* (%): 299 (M^+, 8), 284 (15), 254 (27), 209 (22), 185 (25), 129 (27), 119 (30), 117 (33), 115 (26), 105 (31), 91 (36), 74 (47), 73 (37), 72 (60), 58 (100). ESI-HRMS $[M+Na]^+$: *m/z* 322.1451, $C_{15}H_{22}NO_3SNa^+$ requires 322.1447.

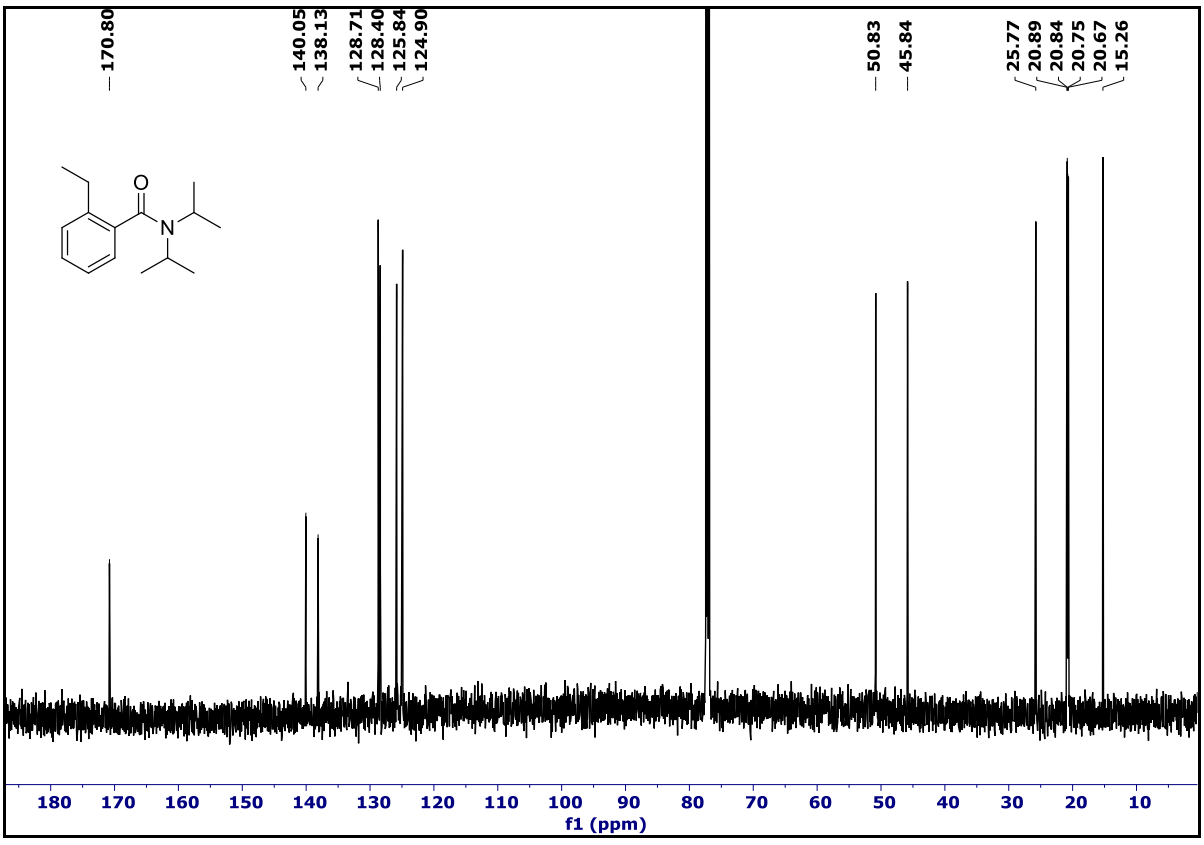
***N,N*-Diethyl-2-(2-hydroxy-2-phenylethyl)-4-methylbenzenesulfonamide (2r):** general procedure starting from **1f** and benzaldehyde. Purification by flash column chromatography (PE/EtOAc 9/1 v/v) gave **2r** as a colourless semi-solid (29 mg, 60% yield, R_f = 0.13 PE/EtOAc 9/1 v/v). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.75 (d, *J* = 7.8 Hz, 1H), 7.46 (d, *J* = 7.2 Hz, 2H), 7.37 (t, *J* = 7.6 Hz, 2H), 7.29 (t, *J* = 7.3 Hz, 1H), 7.16 (s, 2H), 7.14 (s, 1H), 5.01 (dd, *J* = 8.3, 5.1 Hz 1H), 3.35-3.27 (m, 6H), 2.37 (s, 3H), 1.13 (t, *J* = 7.1 Hz, 6H). ^{13}C{1H} NMR (150 MHz, $CDCl_3$): δ 145.0, 143.3, 138.0, 136.2, 134.0, 129.3, 128.5, 127.5, 127.5, 125.8, 75.1, 43.1, 41.4, 21.4, 13.9. ESI-HRMS $[M+Na]^+$: *m/z* 370.1453, $C_{19}H_{25}NO_3SNa^+$ requires 370.1447.

***N,N*-Diisopropyl-2-ethylbenzamide (2a)**

^{1}H NMR (600 MHz, $CDCl_3$)

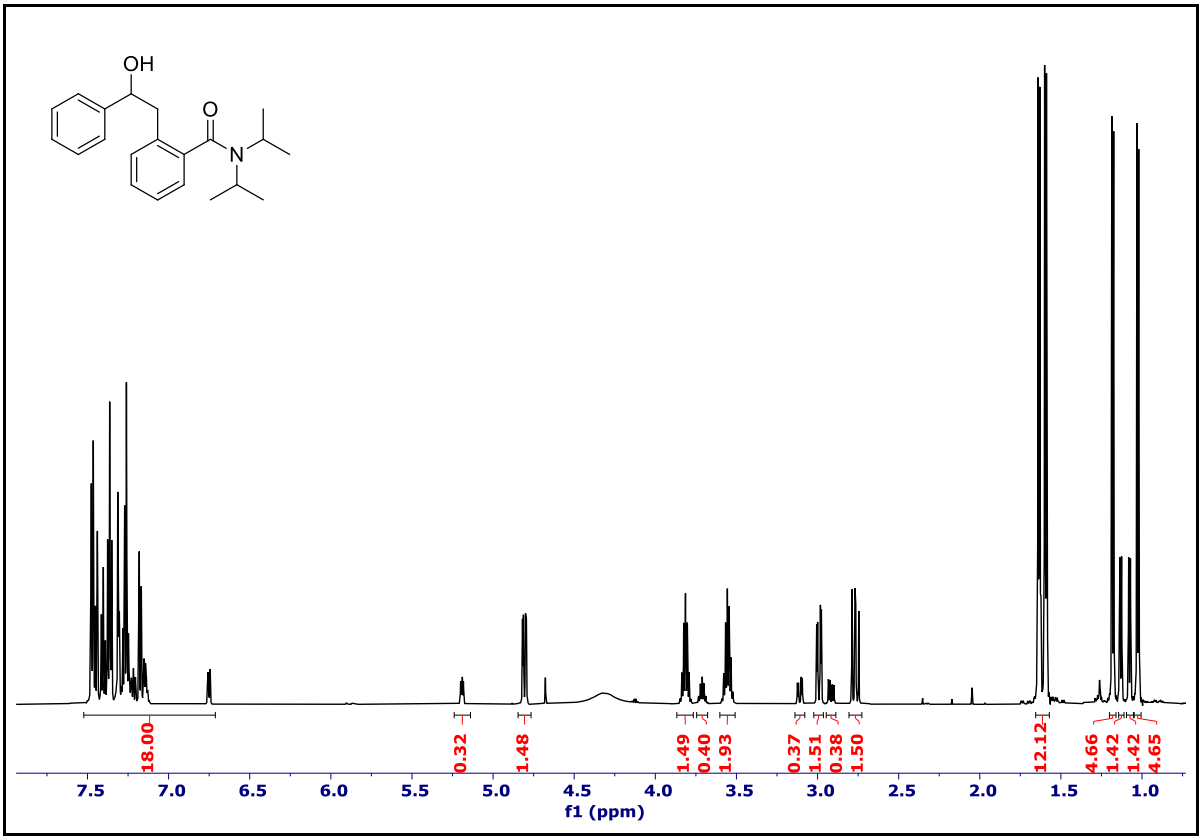


^{13}C NMR (150 MHz, $CDCl_3$)

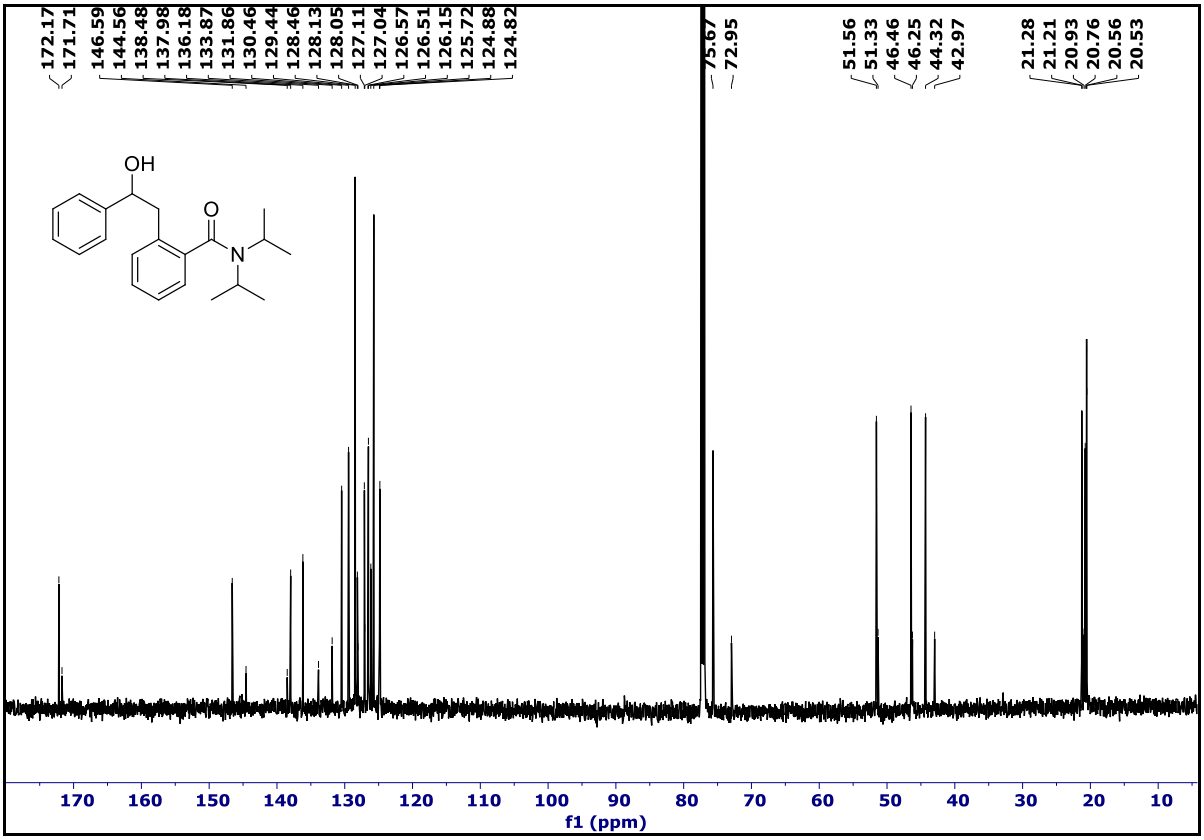


2-(2-Hydroxy-2-phenylethyl)-*N*,*N*-diisopropylbenzamide (2b)

^{1}H NMR (600 MHz, $CDCl_3$)

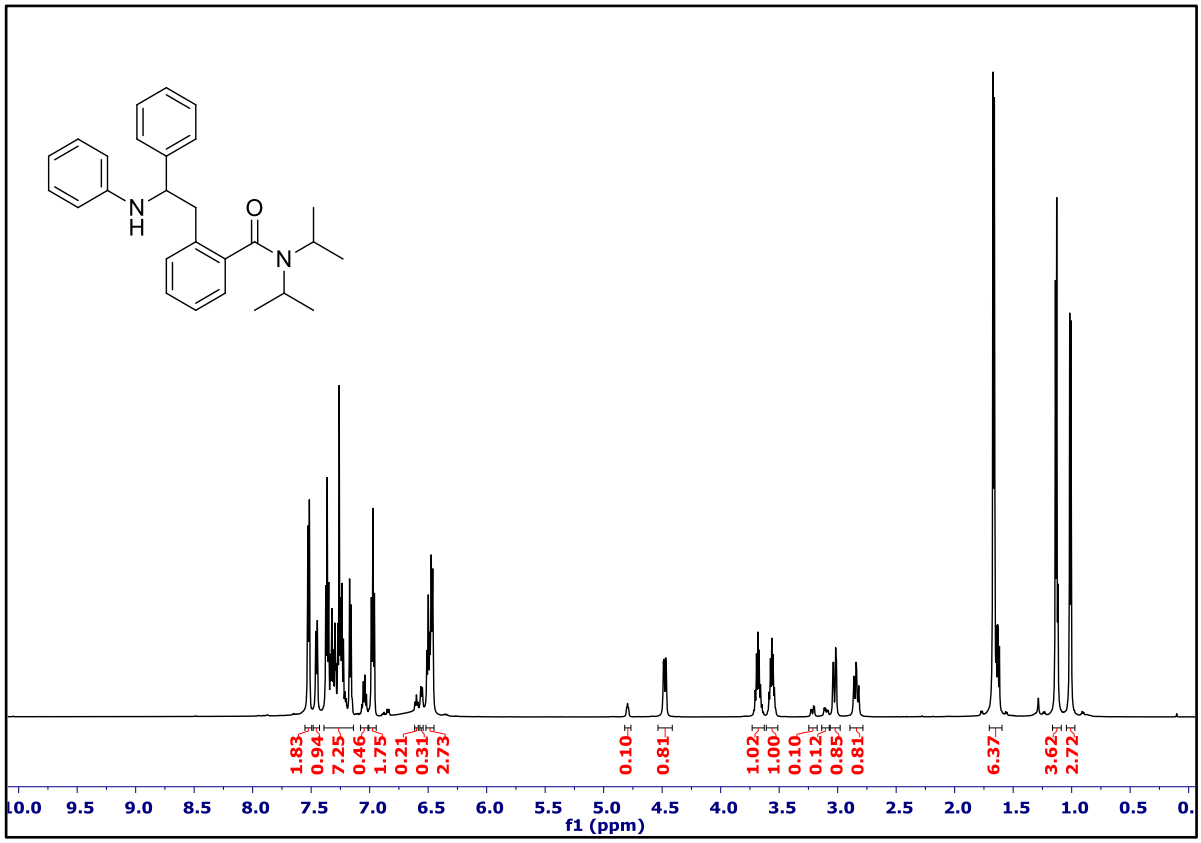


^{13}C NMR (150 MHz, $CDCl_3$)

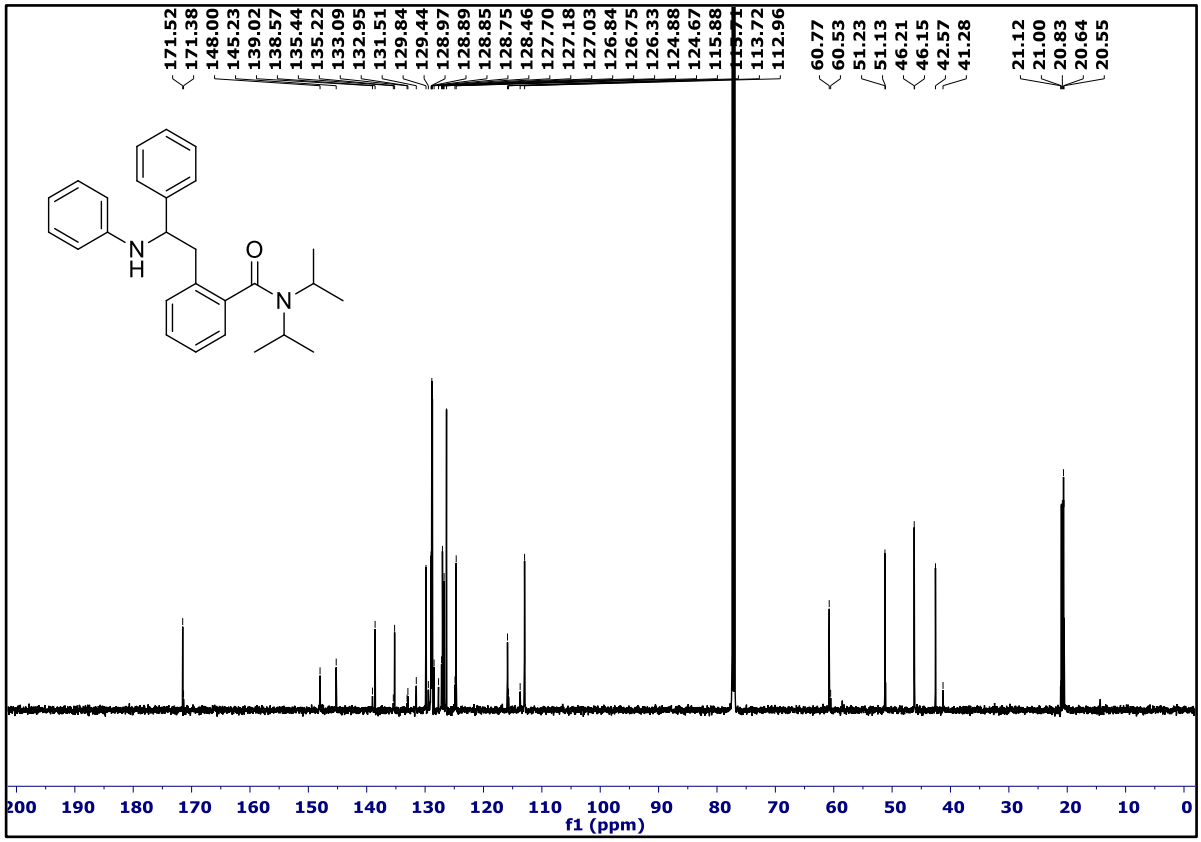


***N*,*N*-Diisopropyl-2-(2-phenyl-2-(phenylamino)ethyl)benzamide (2c)**

^{1}H NMR (600 MHz, $CDCl_3$)

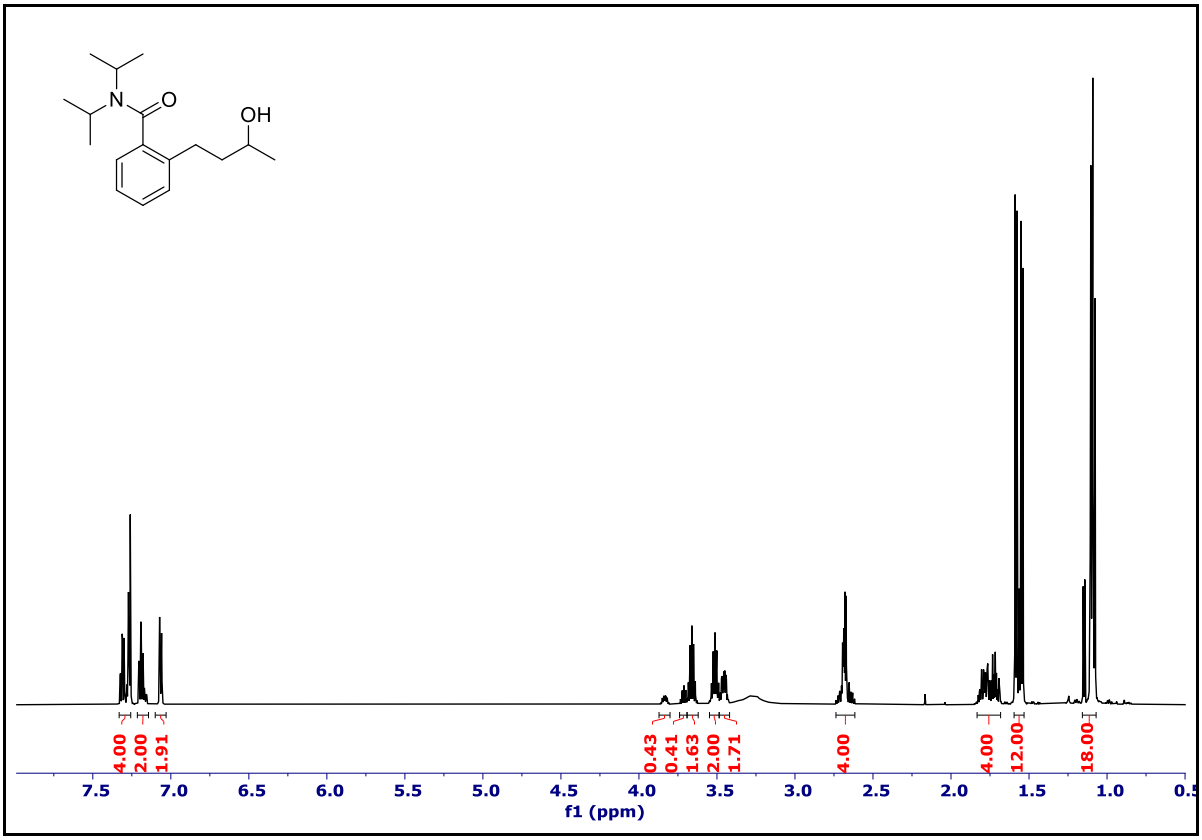


^{13}C NMR (150 MHz, $CDCl_3$)

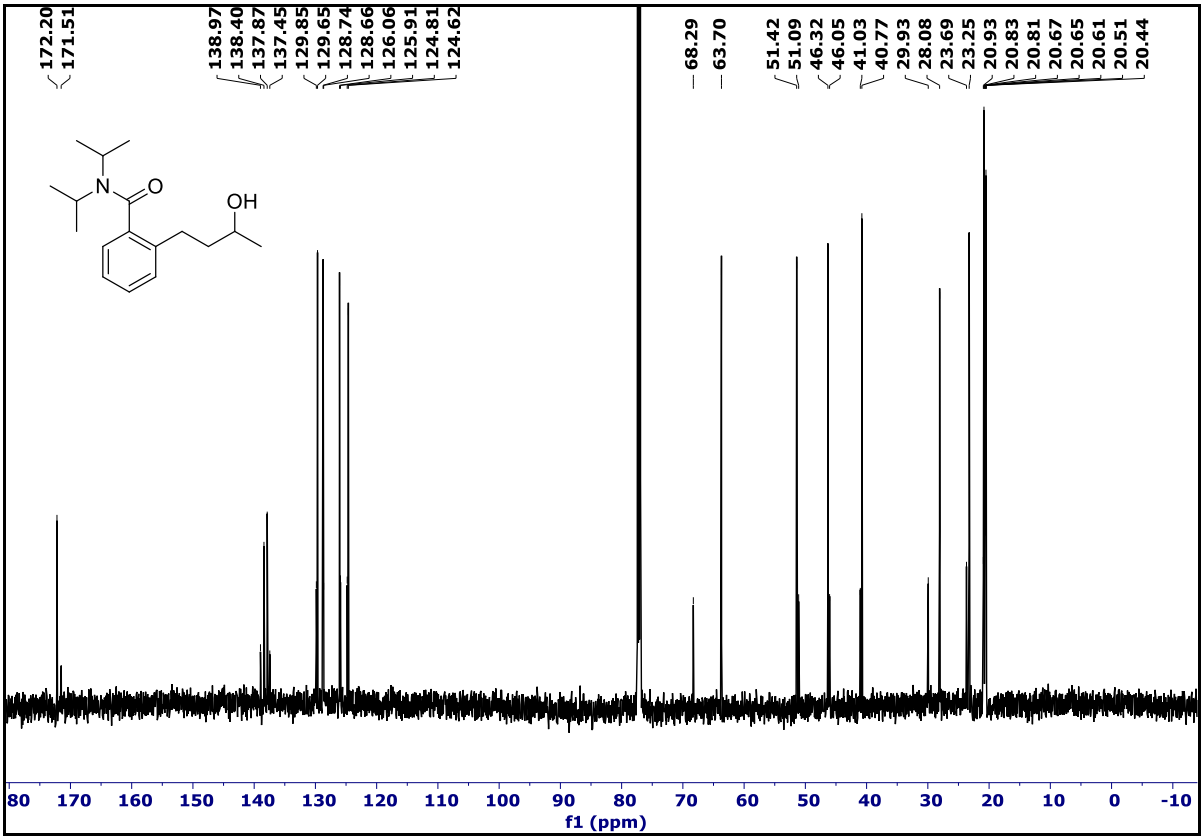


2-(3-Hydroxybutyl)-*N*,*N*-diisopropylbenzamide (2d)

^{1}H NMR (600 MHz, $CDCl_3$)

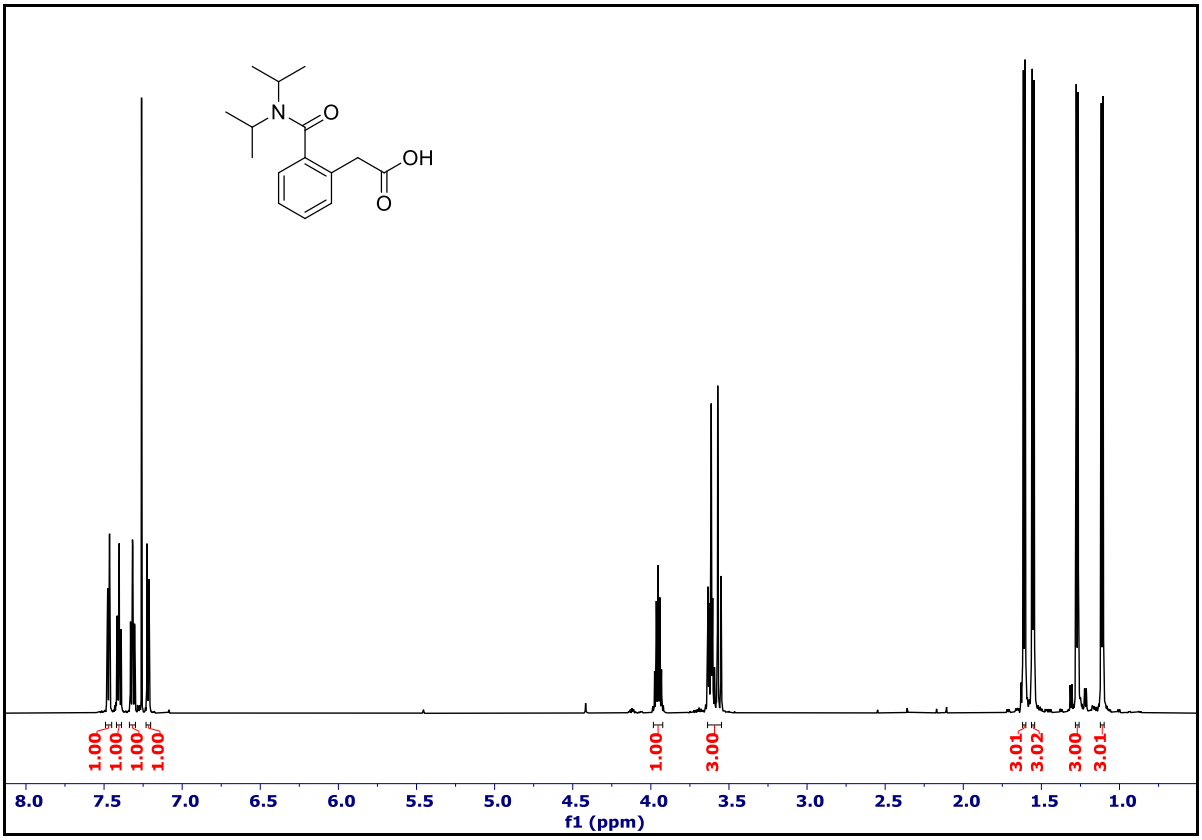


^{13}C NMR (150 MHz, $CDCl_3$)

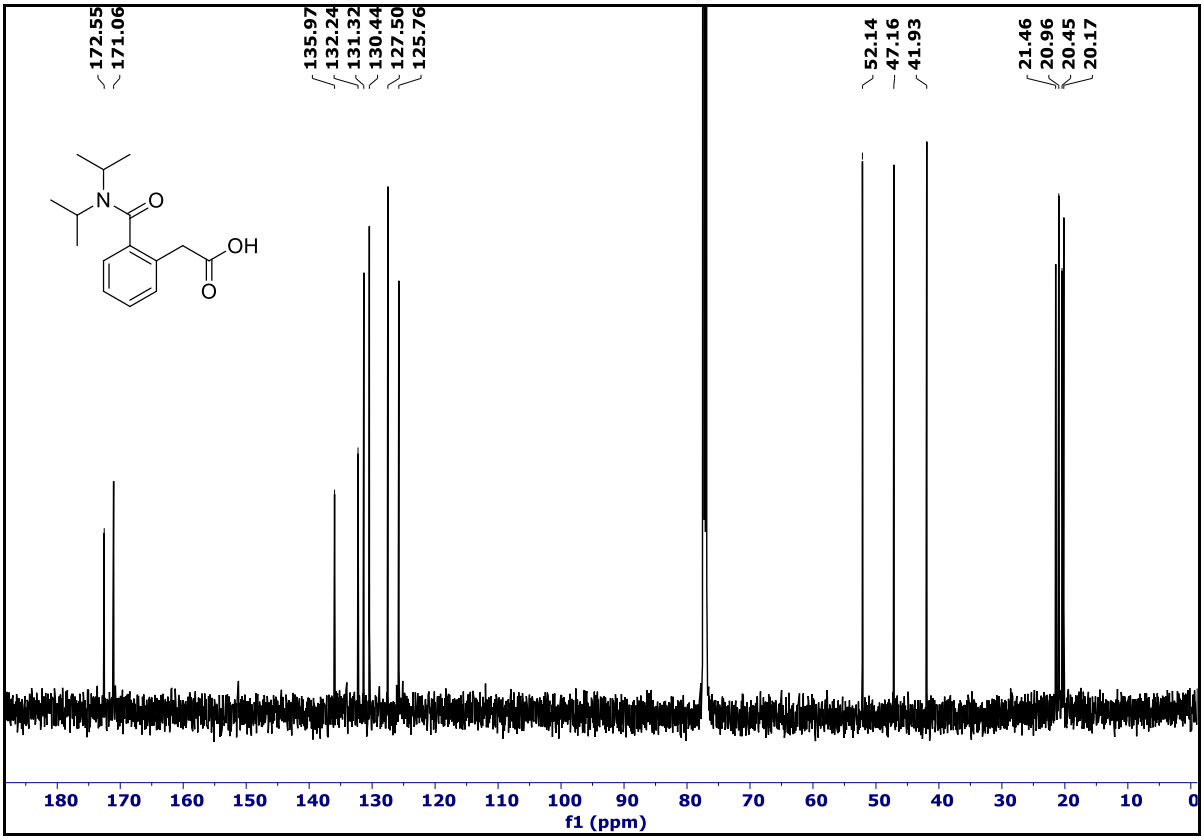


2-(2-(Diisopropylcarbamoyl)phenyl)acetic acid (2e)

^{1}H NMR (600 MHz, $CDCl_3$)

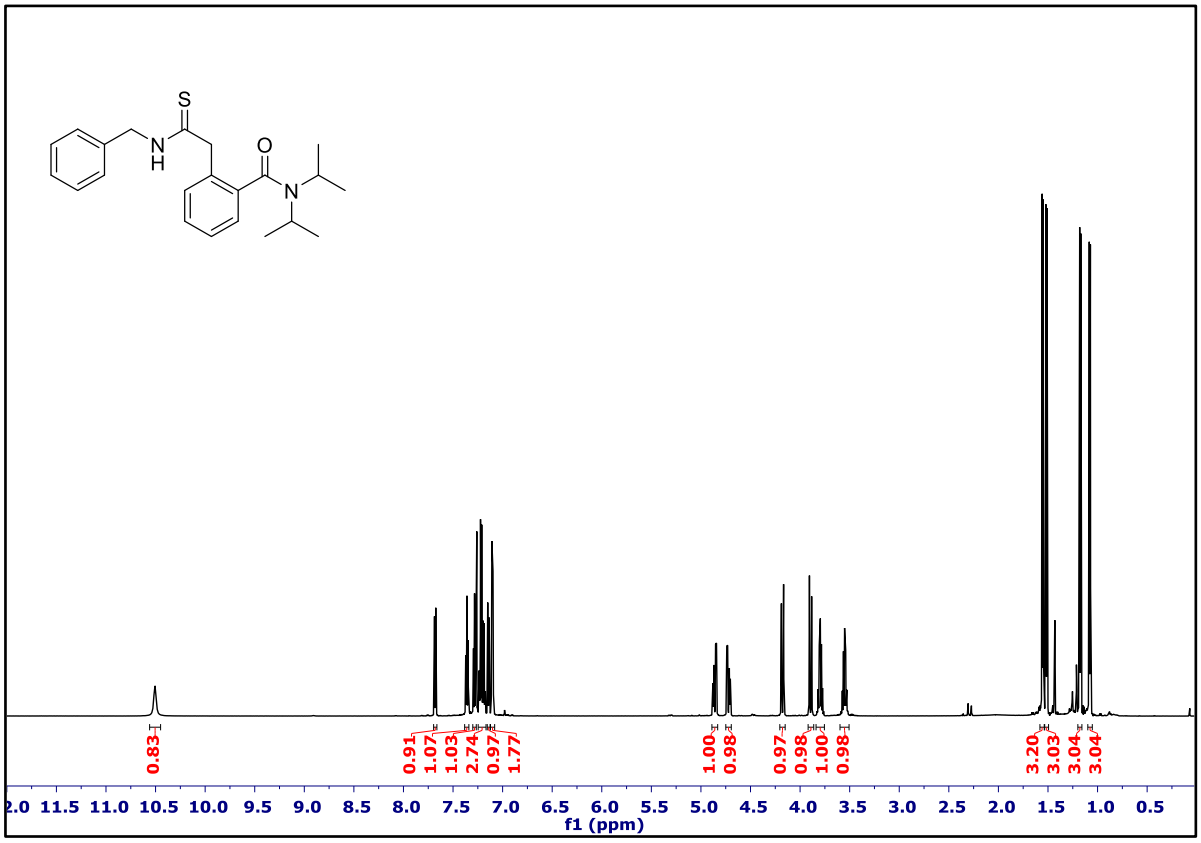


^{13}C NMR (150 MHz, $CDCl_3$)

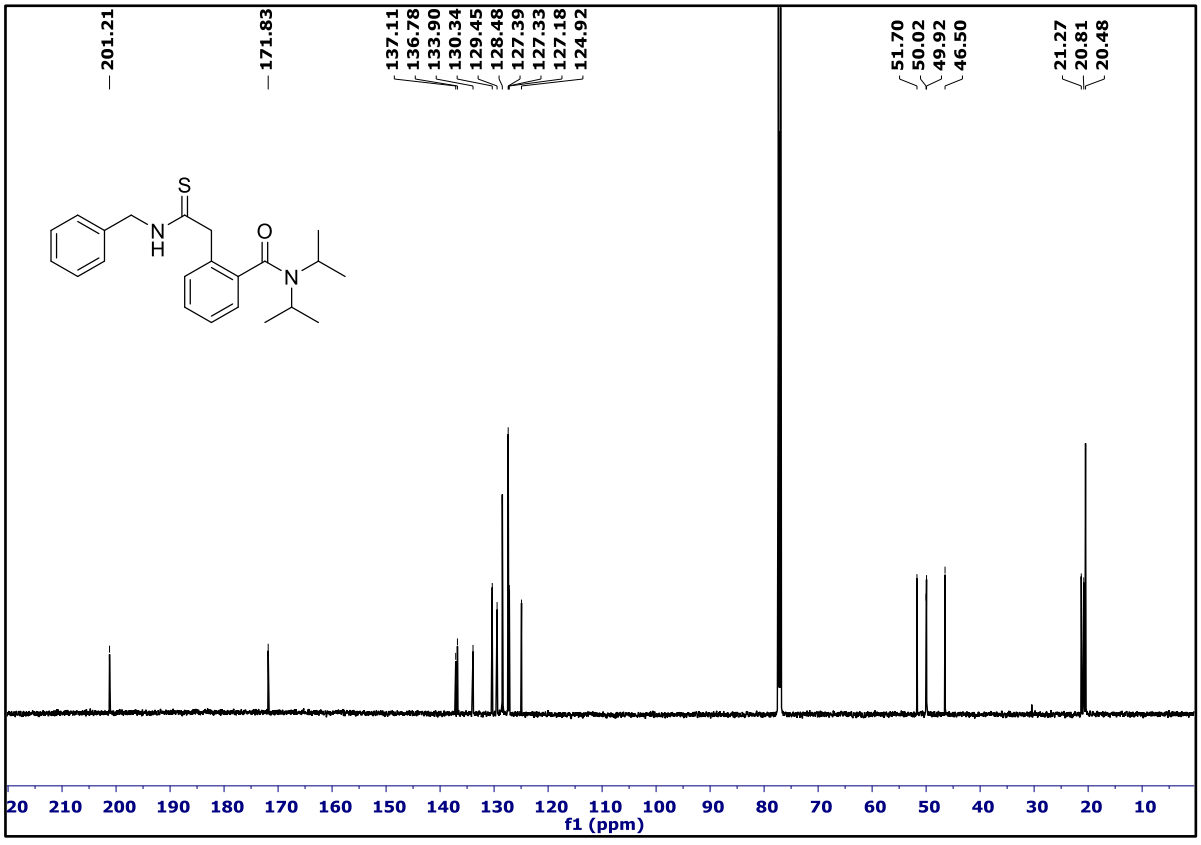


2-(2-Hydroxy-2-phenylethyl)-*N*,*N*-diisopropyl-6-methylbenzamide (2f)

^{1}H NMR (600 MHz, $CDCl_3$)

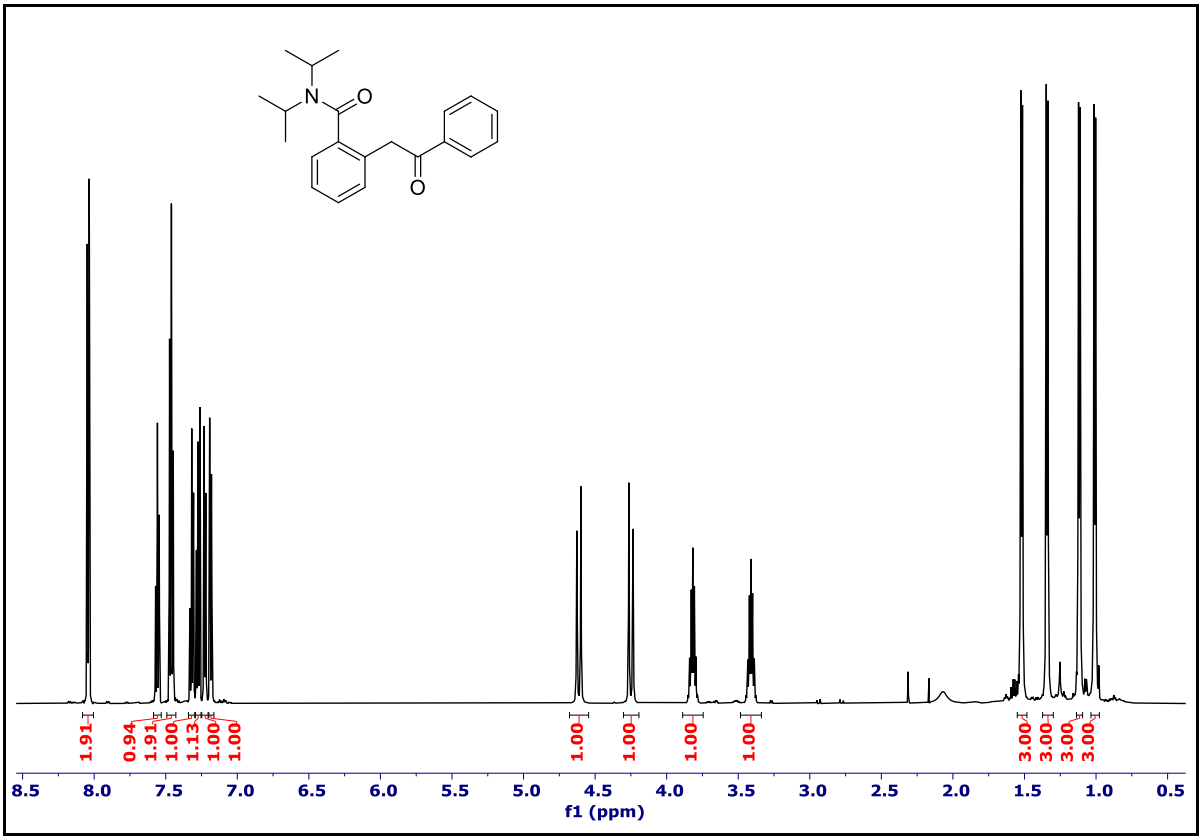


^{13}C NMR (150 MHz, $CDCl_3$)

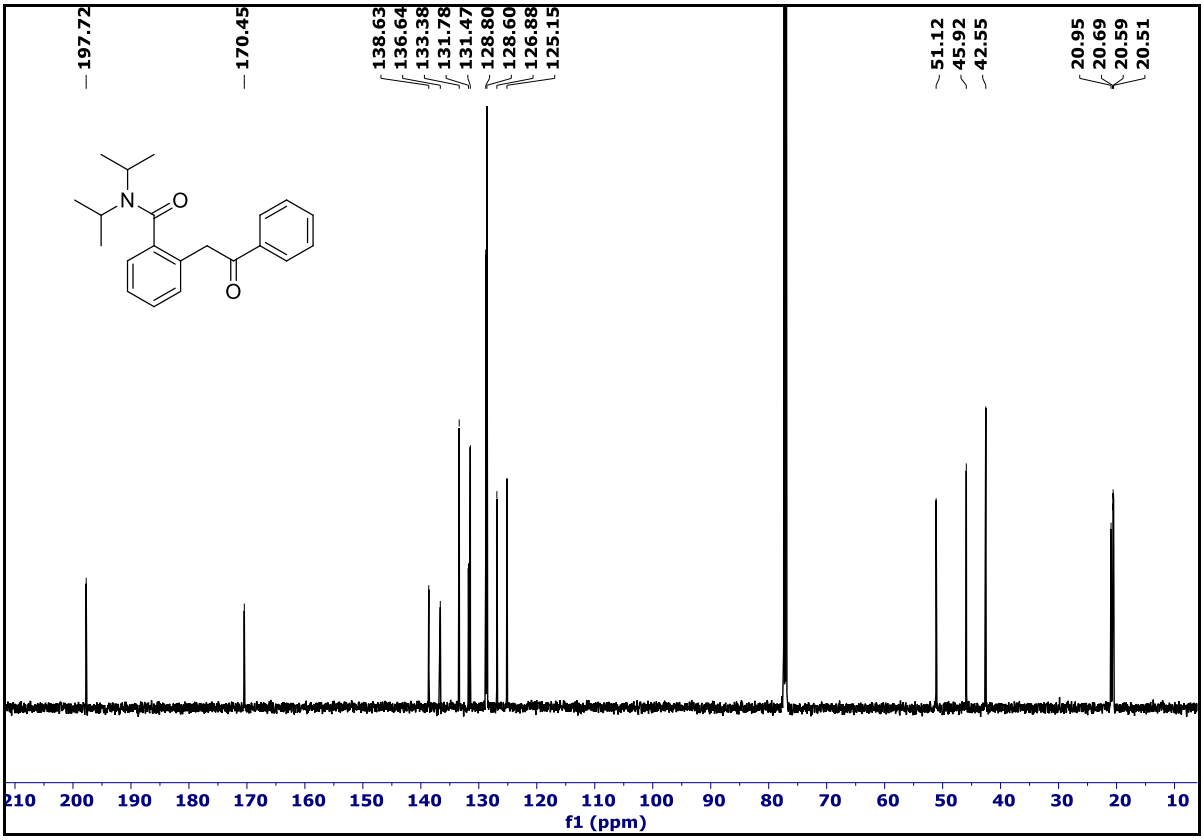


***N*,*N*-Diisopropyl-2-(2-oxo-2-phenylethyl)benzamide (2g)**

^{1}H NMR (600 MHz, $CDCl_3$)

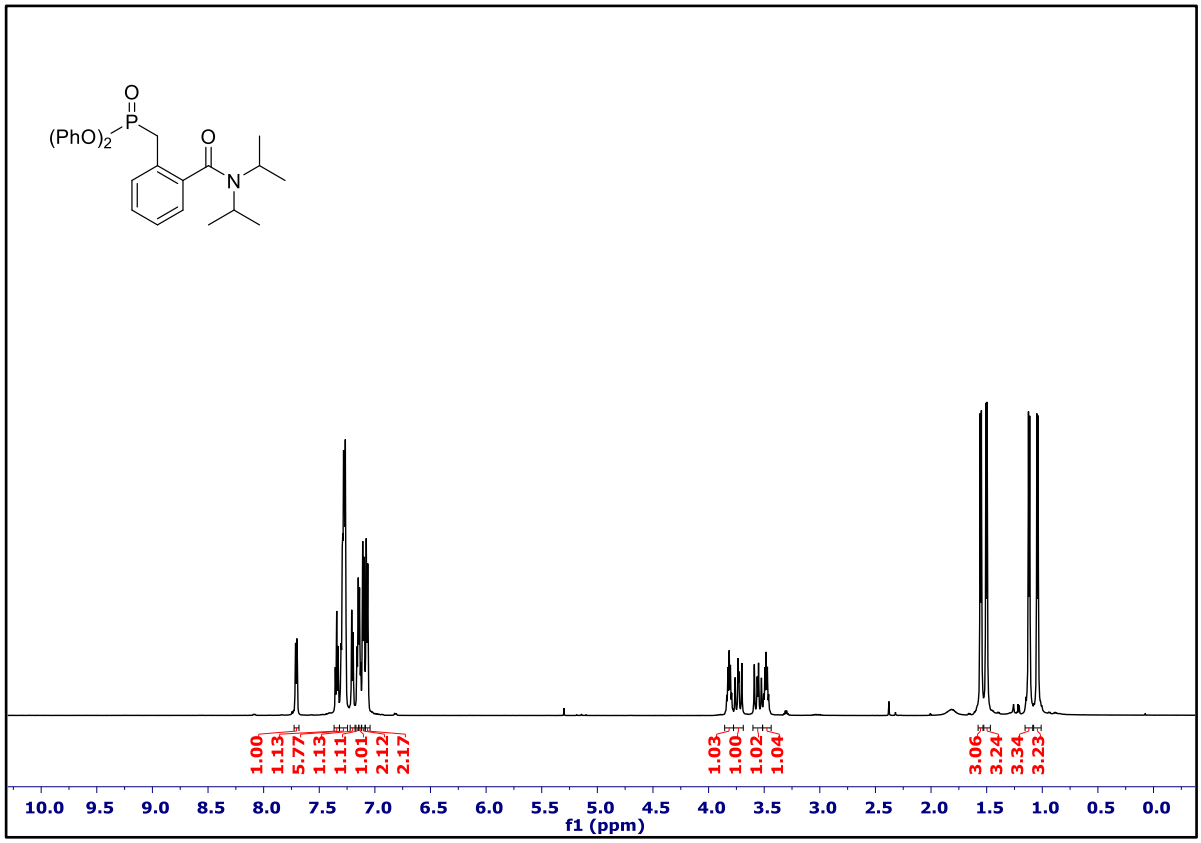


^{13}C NMR (150 MHz, $CDCl_3$)

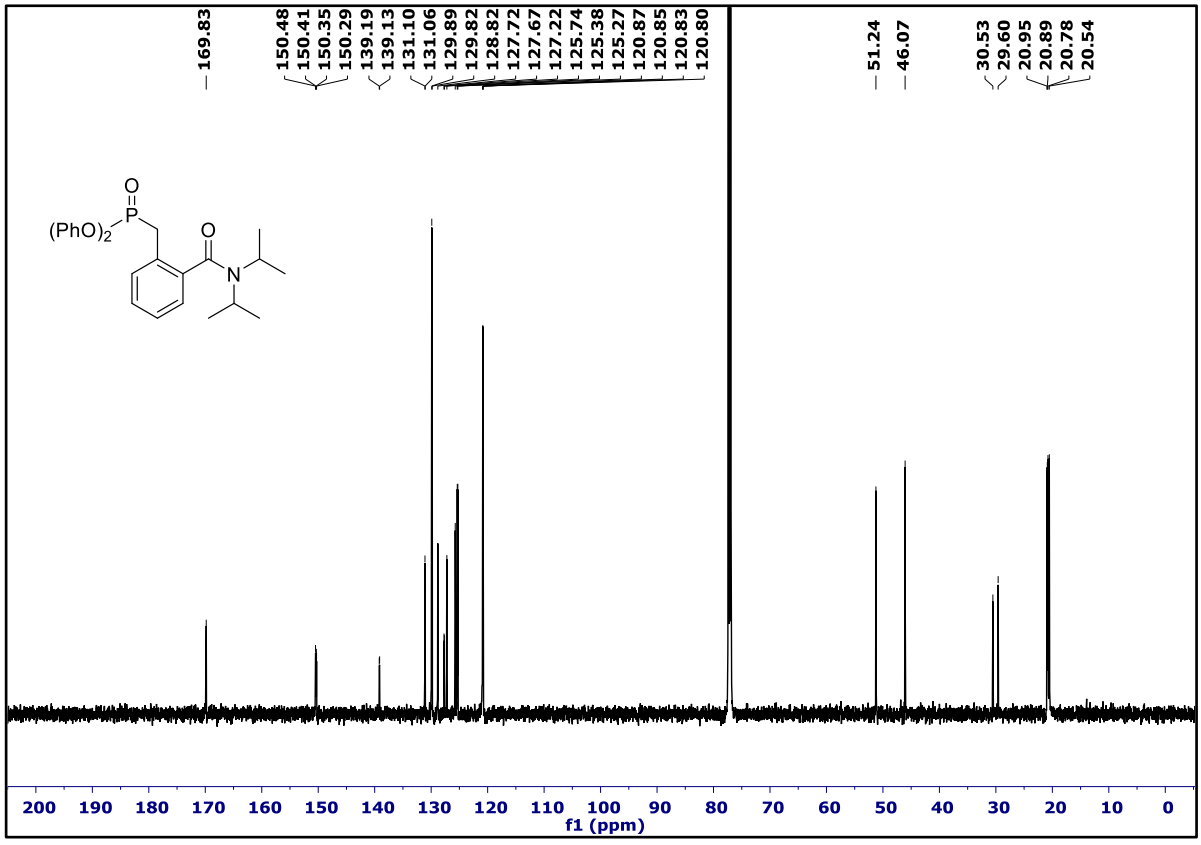


Diphenyl (2-(diisopropylcarbamoyl)benzyl)phosphonate (2h)

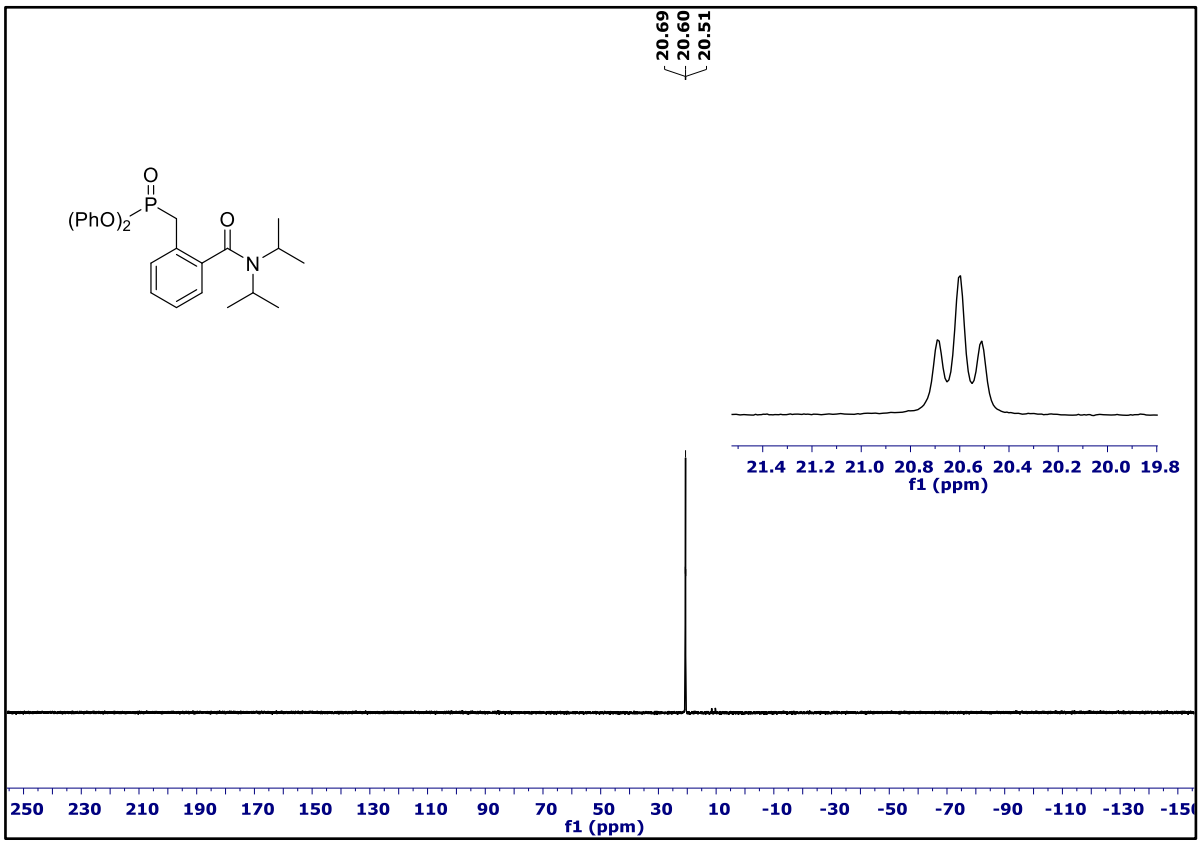
^{1}H NMR (600 MHz, $CDCl_3$)



^{13}C NMR (150 MHz, $CDCl_3$)

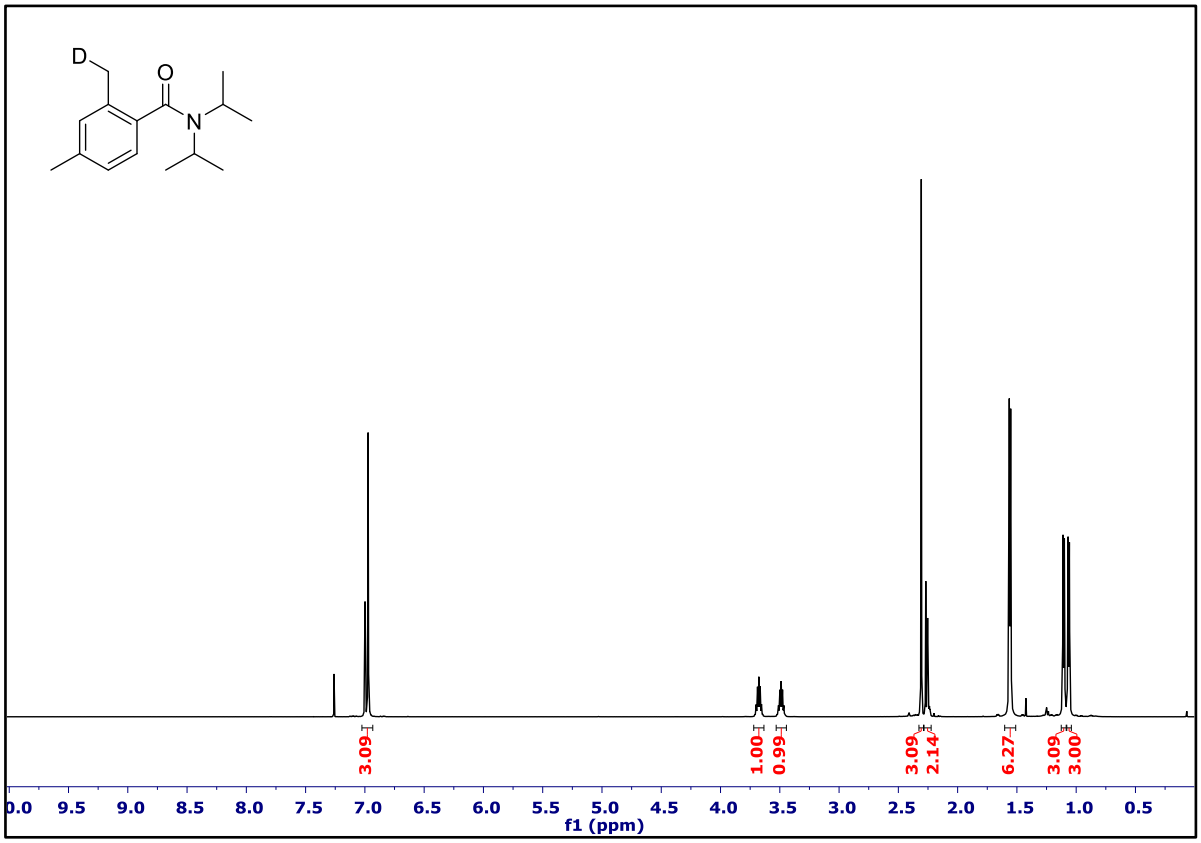


^{31}P NMR (242 MHz, $CDCl_3$)

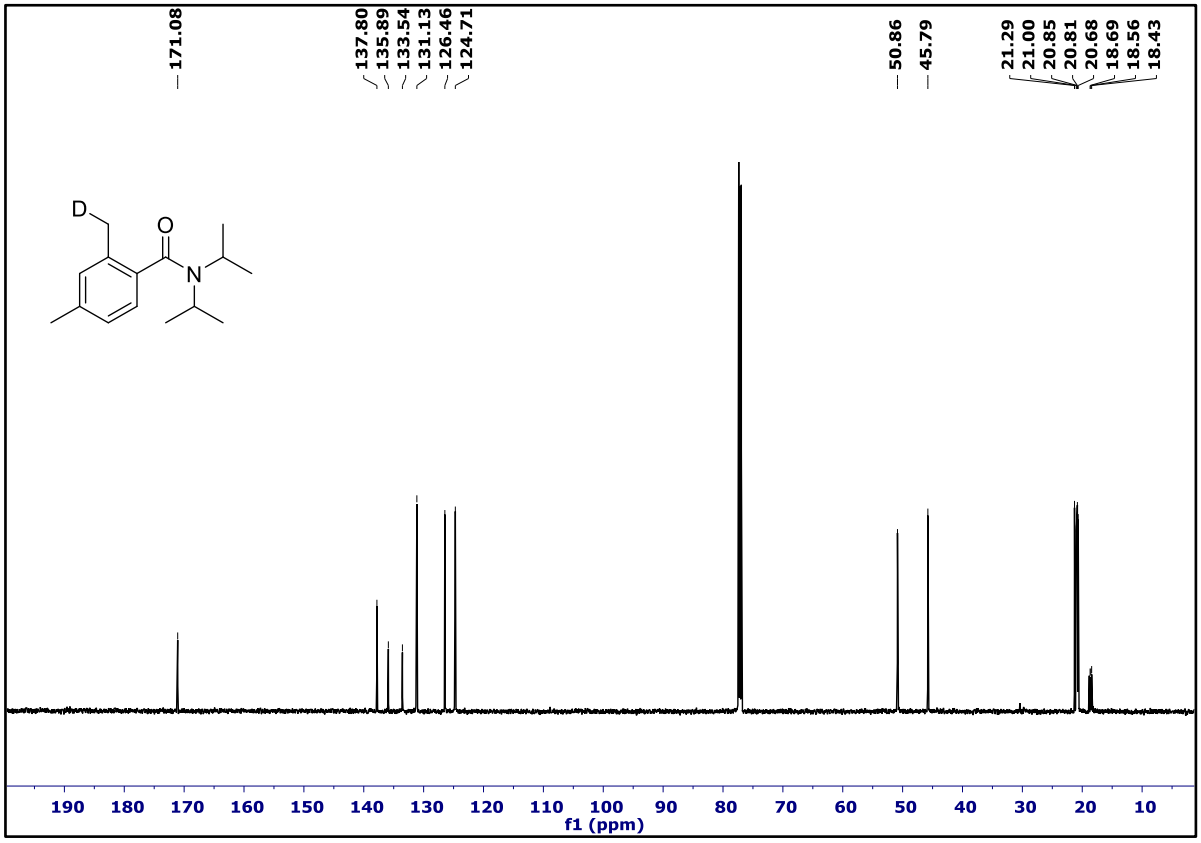


2-(Deuteriomethyl)-*N*,*N*-diisopropyl-4-methylbenzamide (*Bn*-*D*-1i)

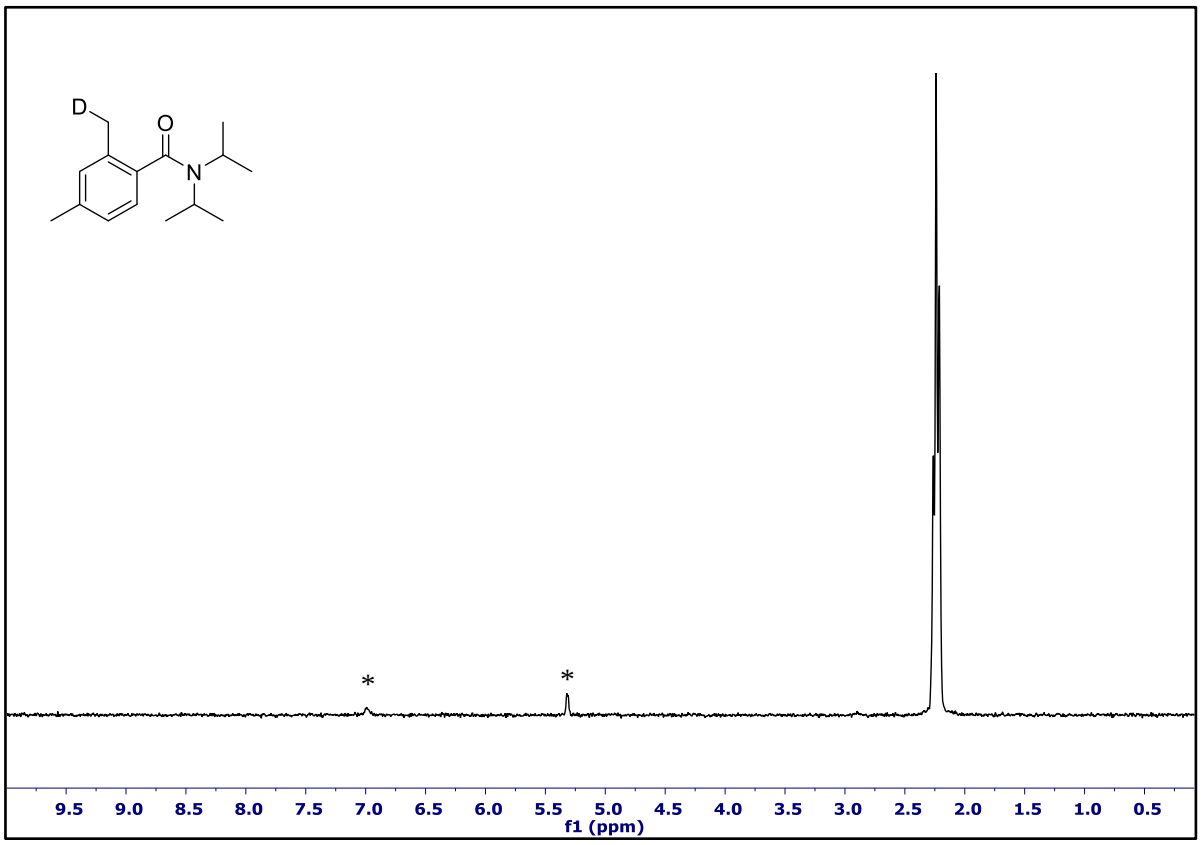
^{1}H NMR (600 MHz, $CDCl_3$)



^{13}C NMR (150 MHz, $CDCl_3$)



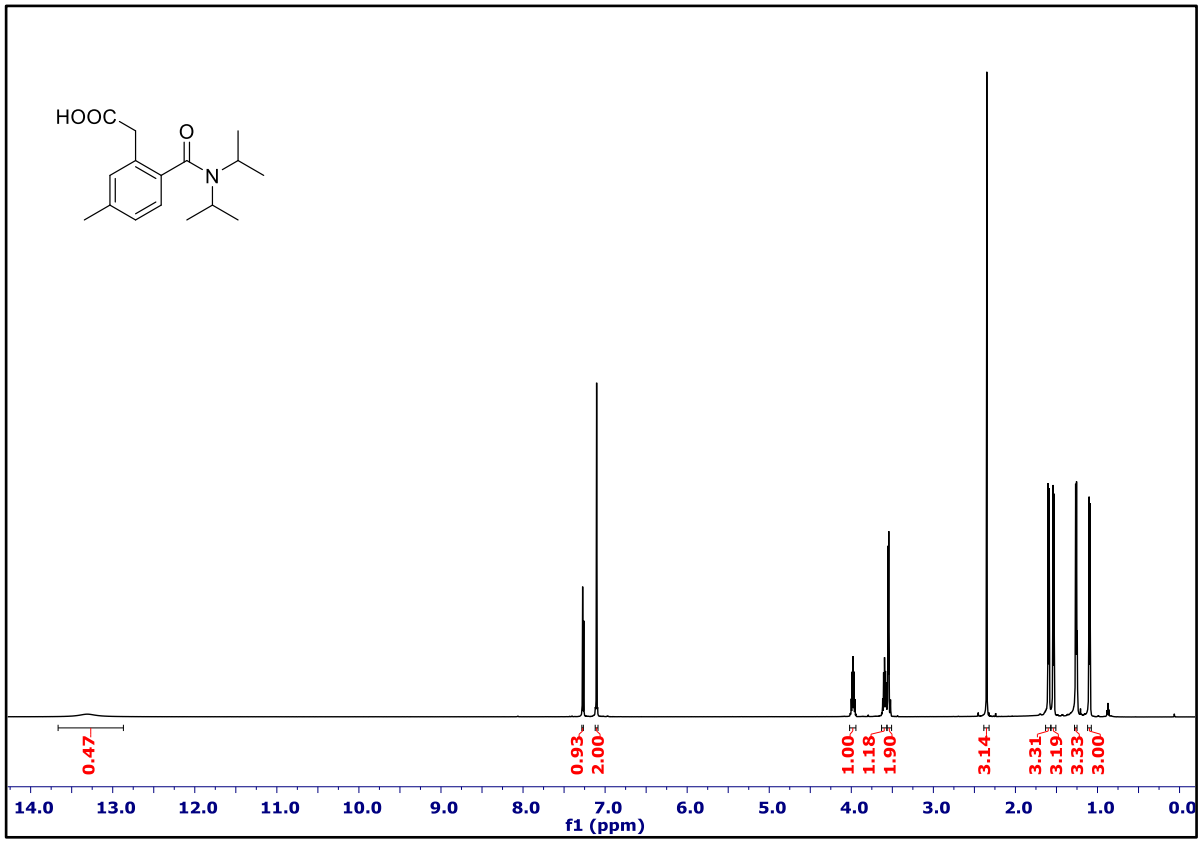
^{2}H NMR (92.07 MHz, CH_2Cl_2)



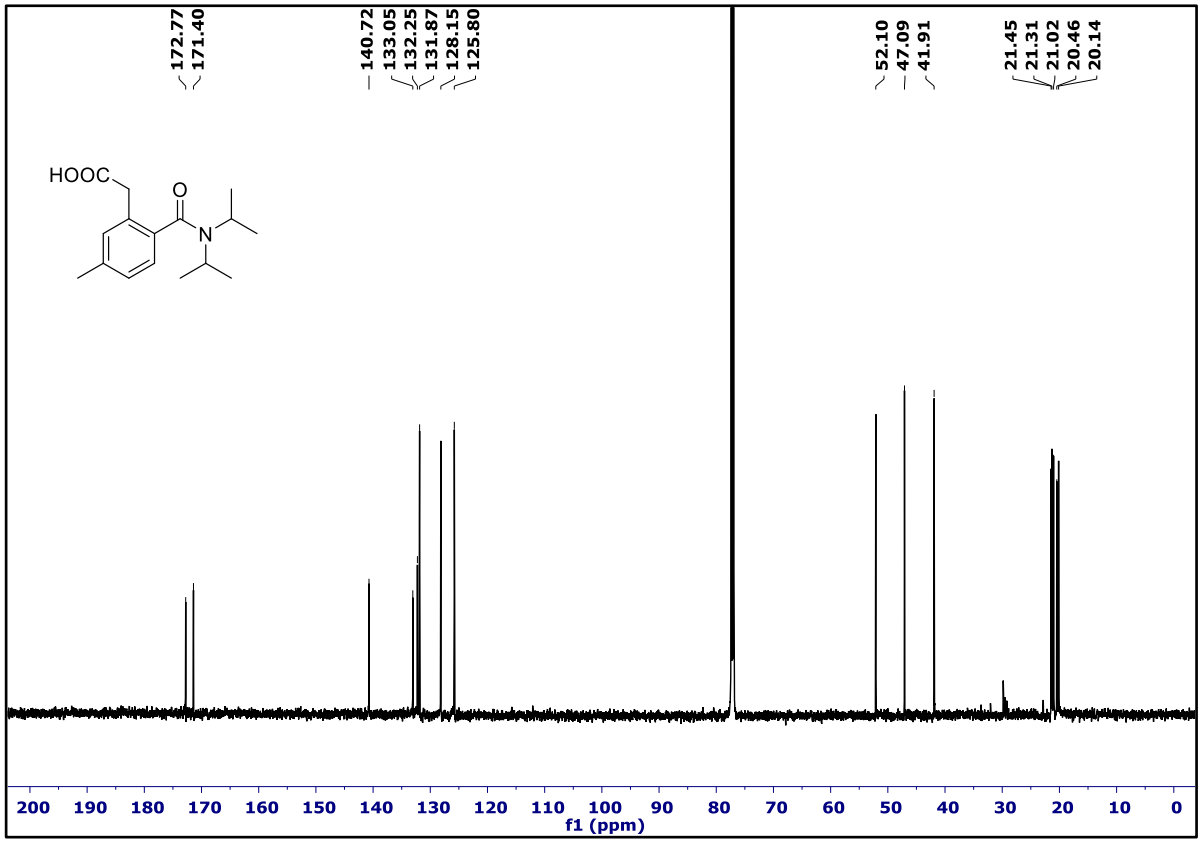
* residual CD_2Cl_2 and $CDCl_3$ solvent peaks

2-(2-(Diisopropylcarbamoyl)-5-methylphenyl)acetic acid (2i)

^{1}H NMR (600 MHz, $CDCl_3$)

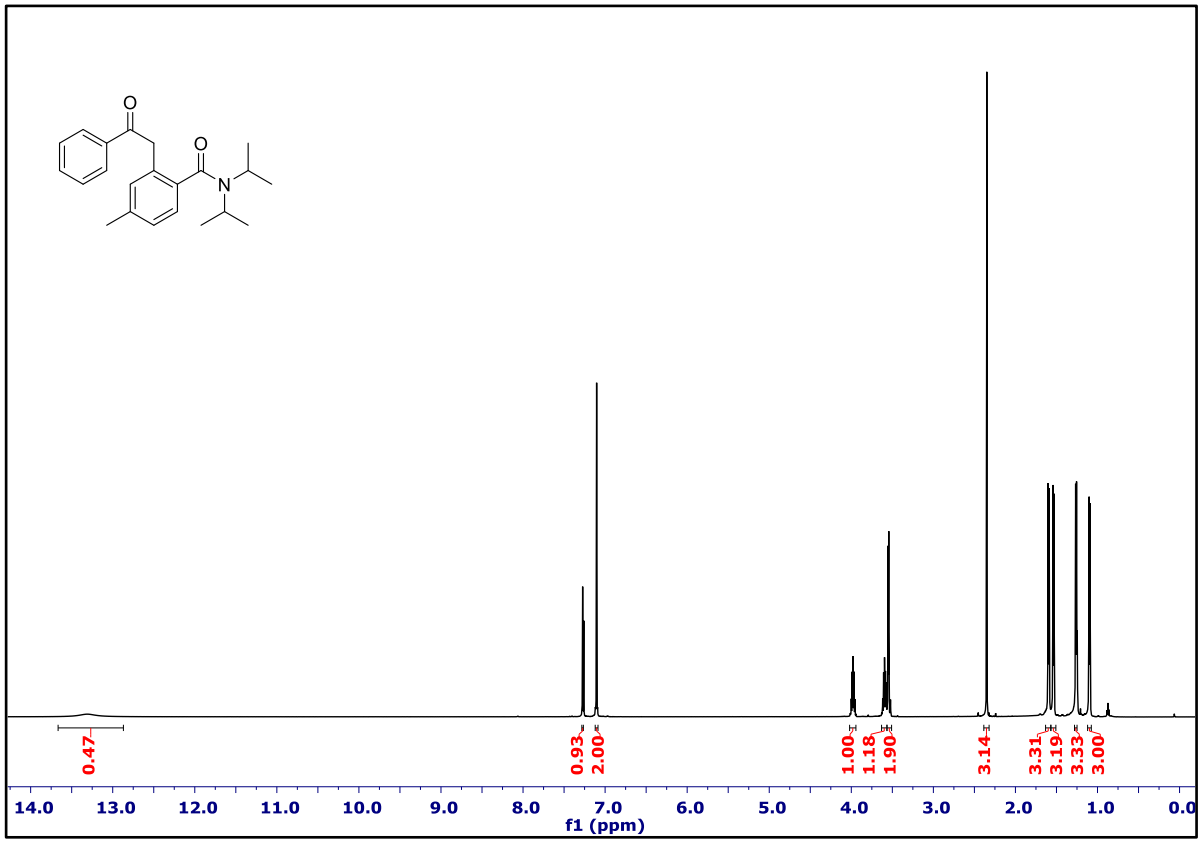


^{13}C NMR (150 MHz, $CDCl_3$)

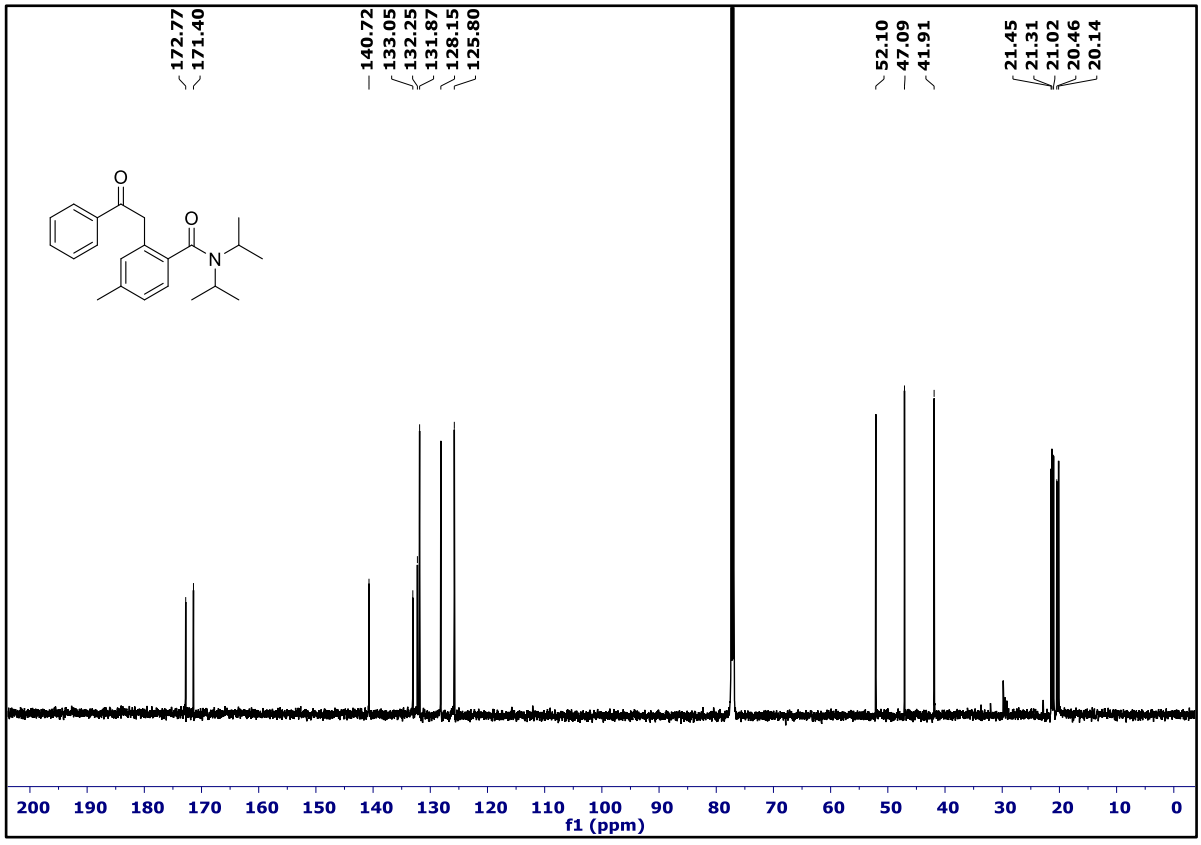


***N*,*N*-Diisopropyl-4-methyl-2-(2-oxo-2-phenylethyl)benzamide (2j)**

^{1}H NMR (600 MHz, $CDCl_3$)

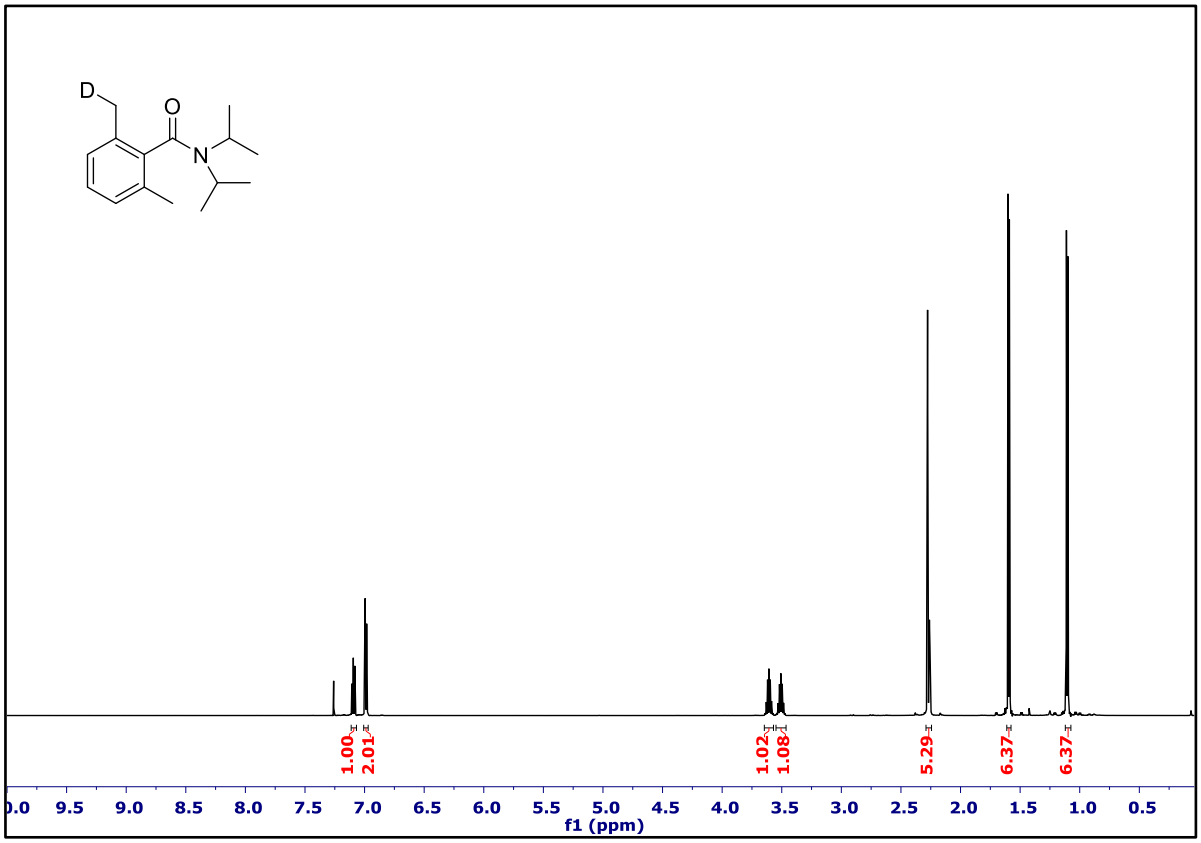


^{13}C NMR (150 MHz, $CDCl_3$)

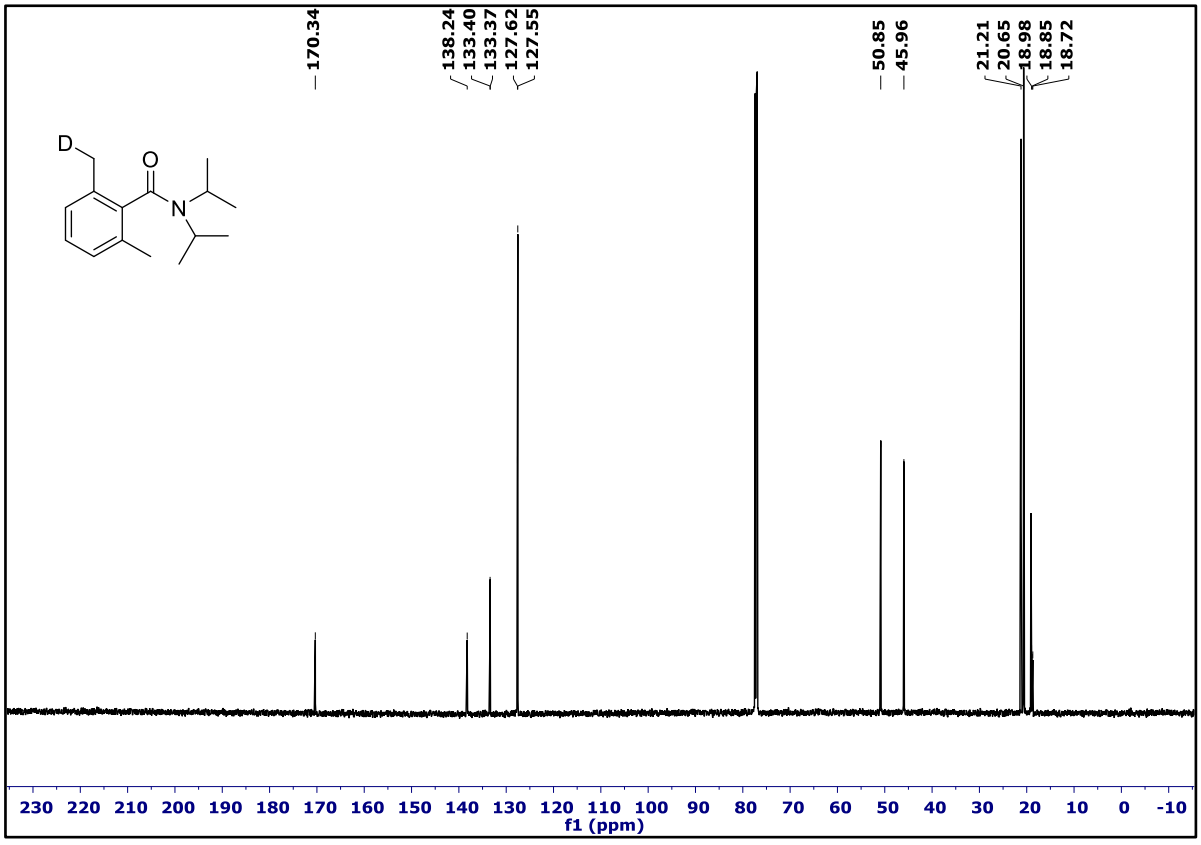


6-(Deuteriomethyl)-*N*,*N*-diisopropyl-2-methylbenzamide (*Bn*-*D*-1j)

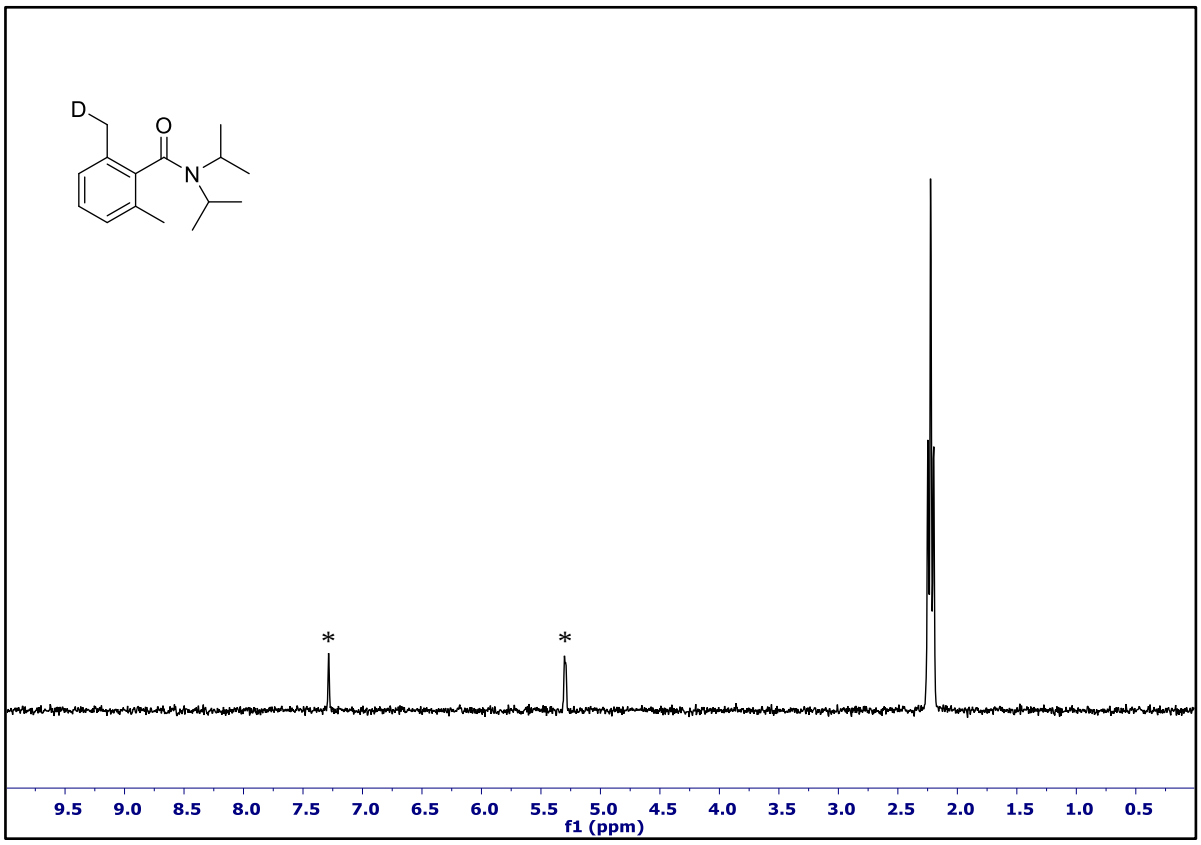
^{1}H NMR (600 MHz, $CDCl_3$)



^{13}C NMR (150 MHz, $CDCl_3$)



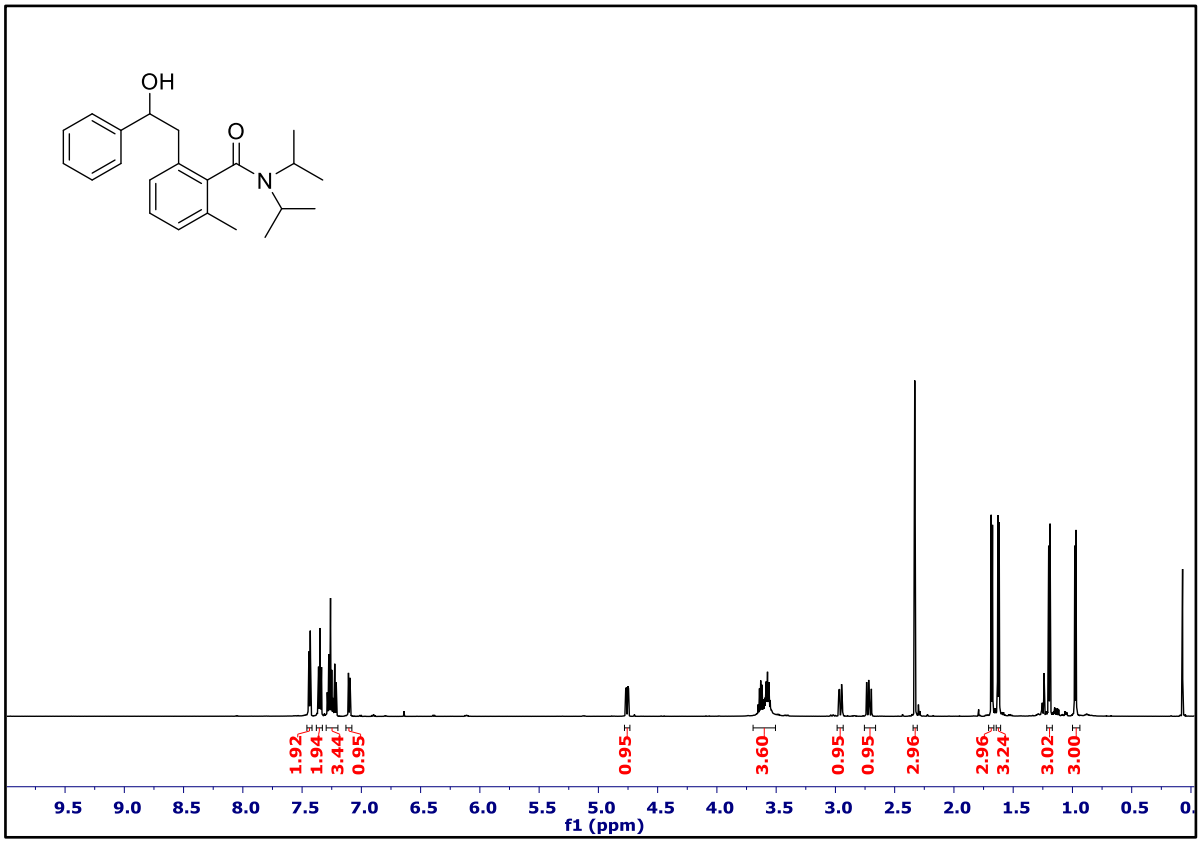
^{2}H NMR (92.07 MHz, CH_2Cl_2)



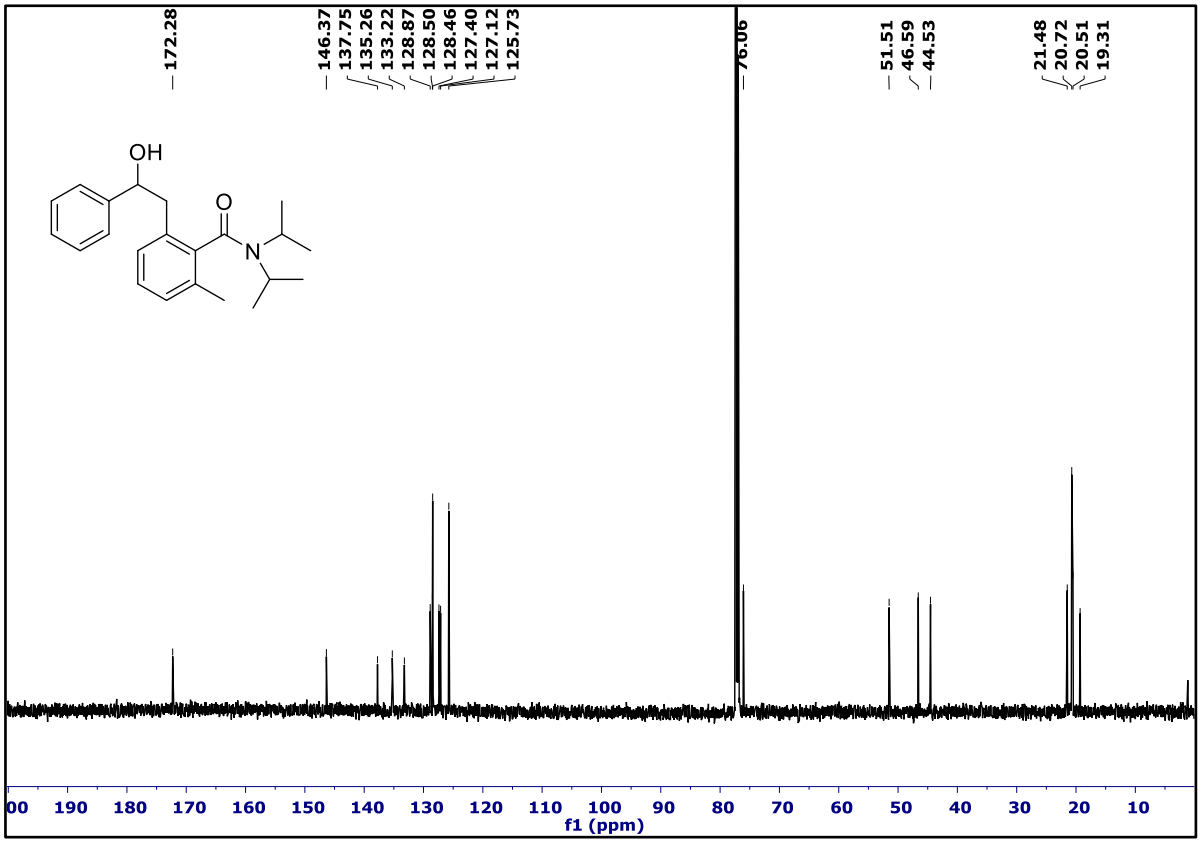
* residual CD_2Cl_2 and $CDCl_3$ solvent peaks

2-(2-Hydroxy-2-phenylethyl)-*N*,*N*-diisopropyl-6-methylbenzamide (2k)

^{1}H NMR (600 MHz, $CDCl_3$)

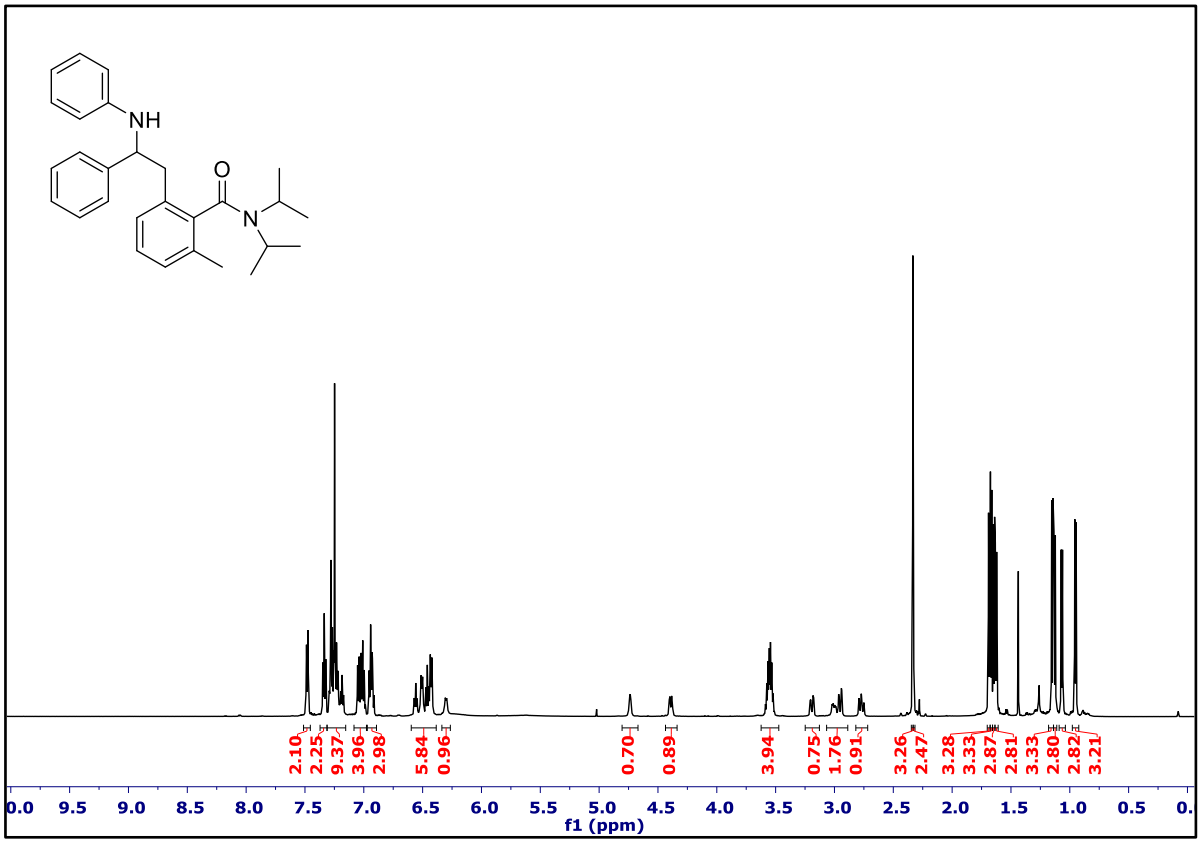


^{13}C NMR (150 MHz, $CDCl_3$)

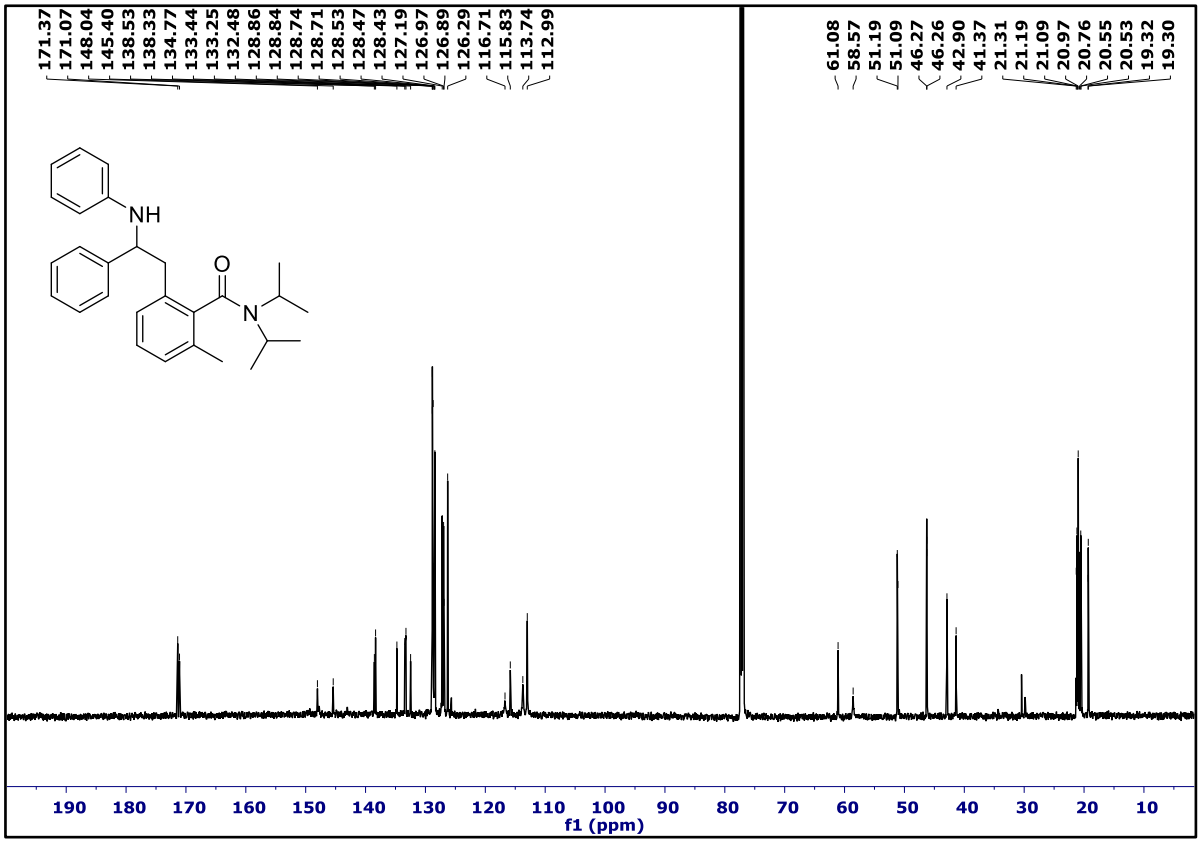


***N*,*N*-diisopropyl-2-methyl-6-(2-phenyl-2-(phenylamino)ethyl)benzamide (2l)**

^{1}H NMR (600 MHz, $CDCl_3$)

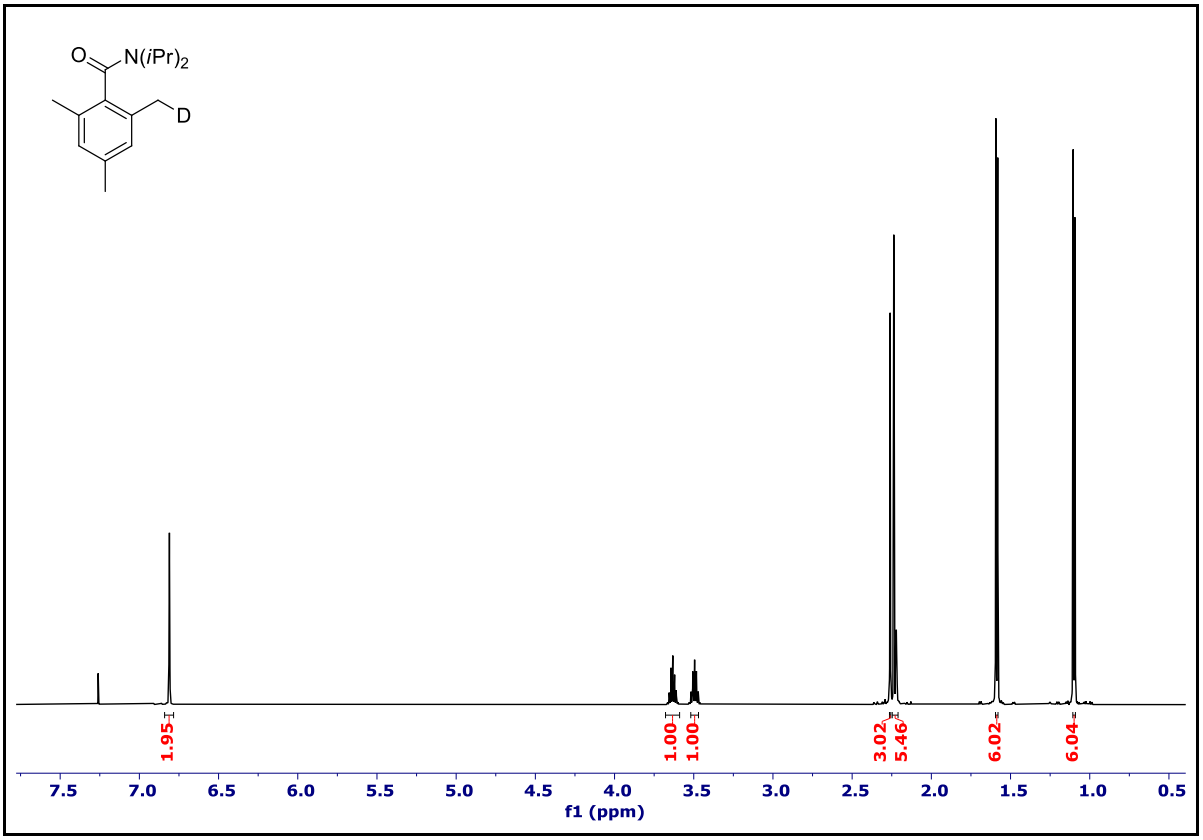


^{13}C NMR (150 MHz, $CDCl_3$)

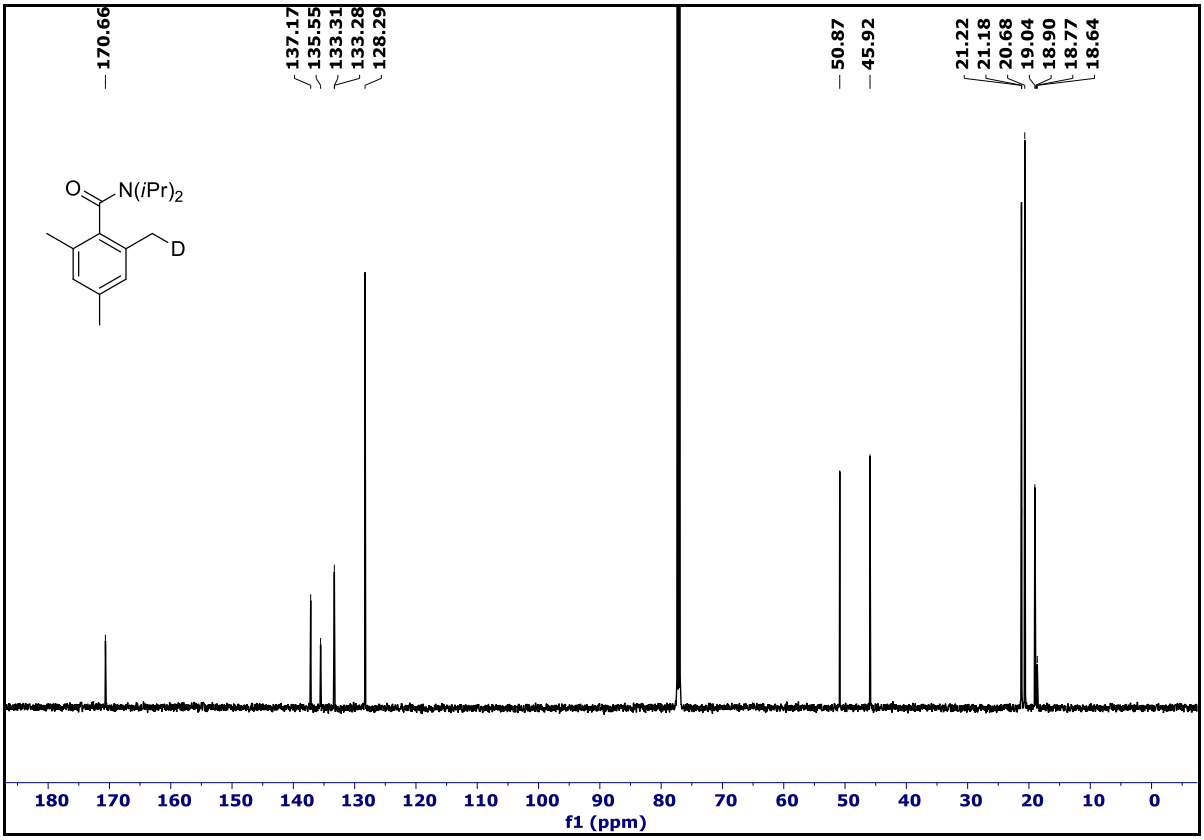


2-(Deuteriomethyl)-*N*,*N*-diisopropyl-4,6-dimethylbenzamide (*Bn-D*-1k)

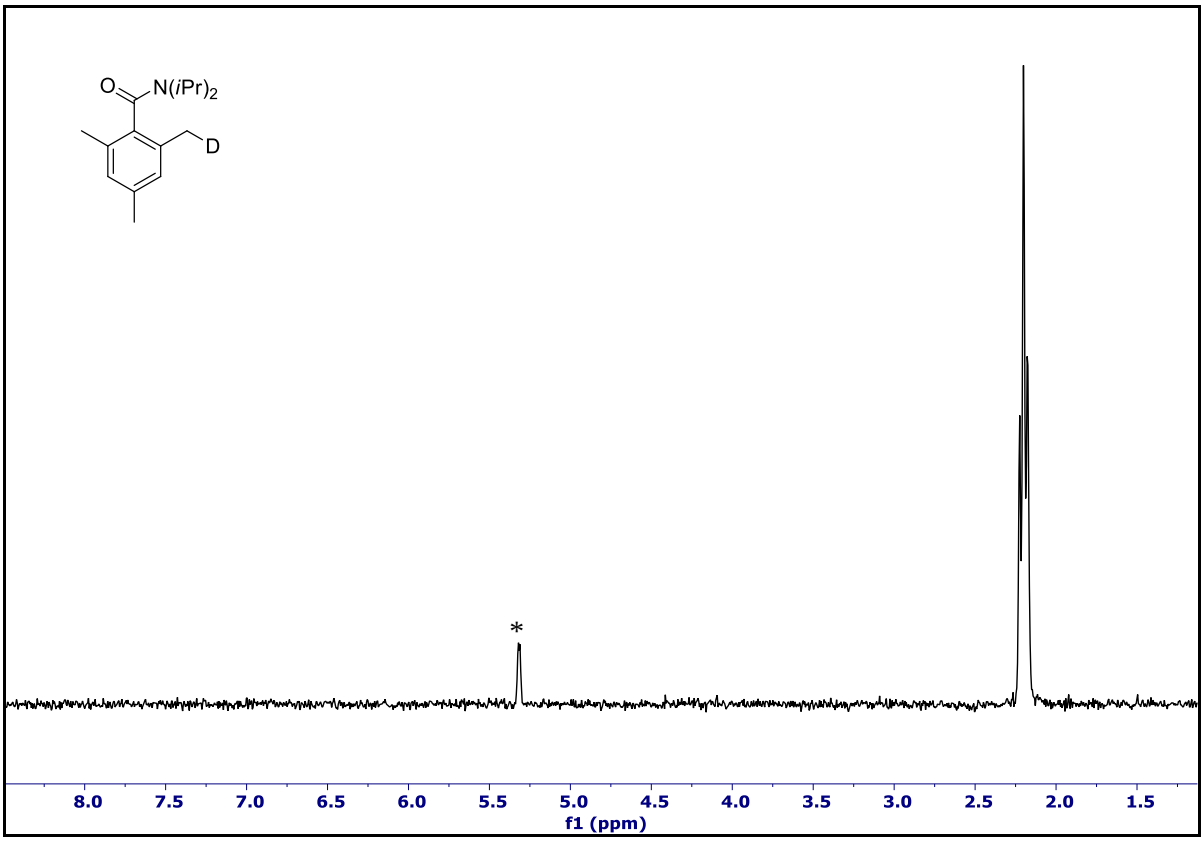
^{1}H NMR (600 MHz, $CDCl_3$)



^{13}C NMR (150 MHz, $CDCl_3$)



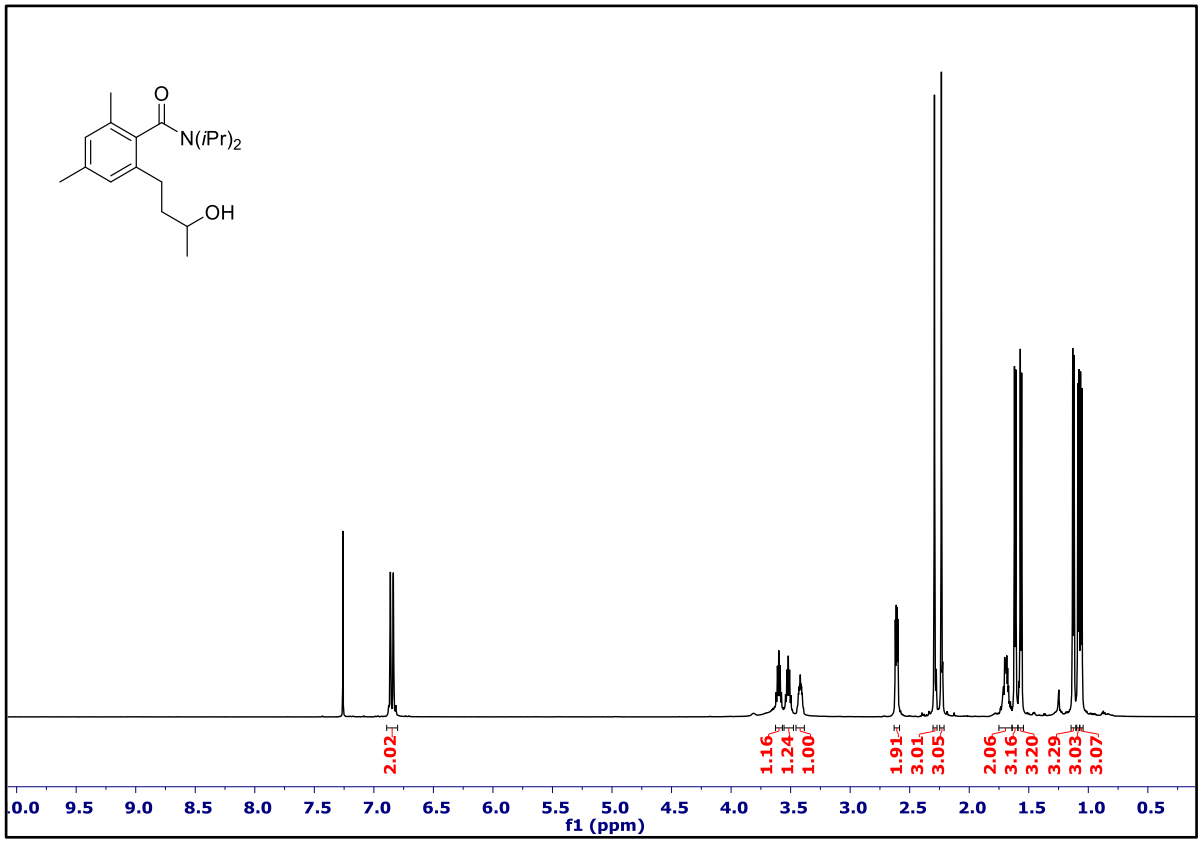
^{2}H NMR (92.07 MHz, CH_2Cl_2)



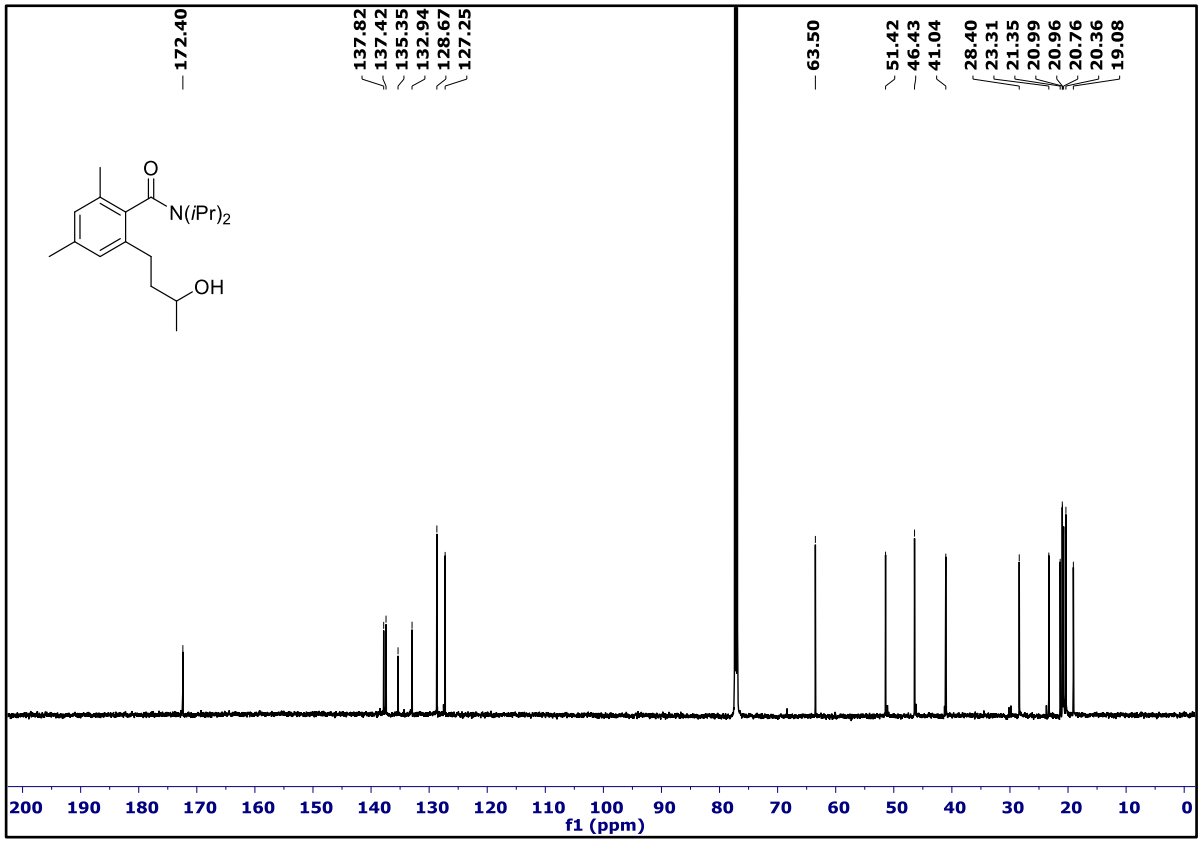
* residual CD_2Cl_2 solvent peak

2-(3-Hydroxybutyl)-*N*,*N*-diisopropyl-4,6-dimethylbenzamide (2m)

^{1}H NMR (600 MHz, $CDCl_3$)

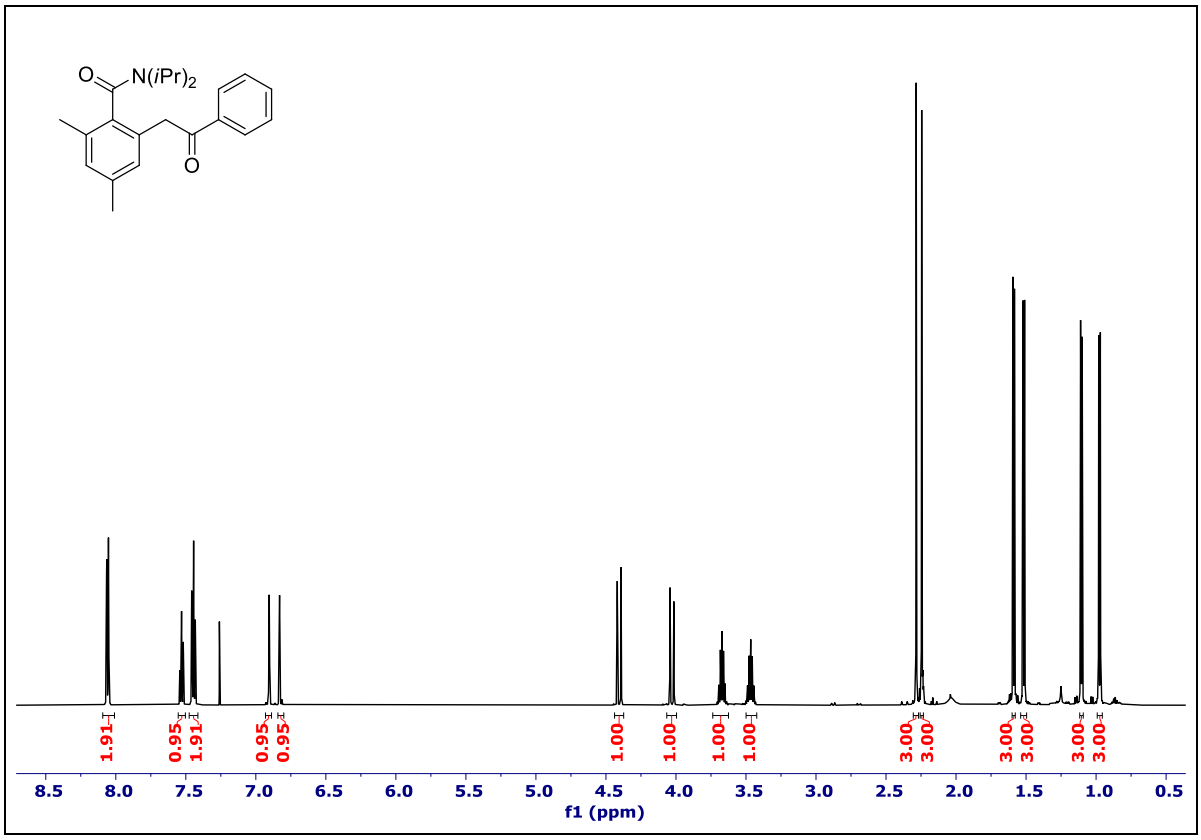


^{13}C NMR (150 MHz, $CDCl_3$)

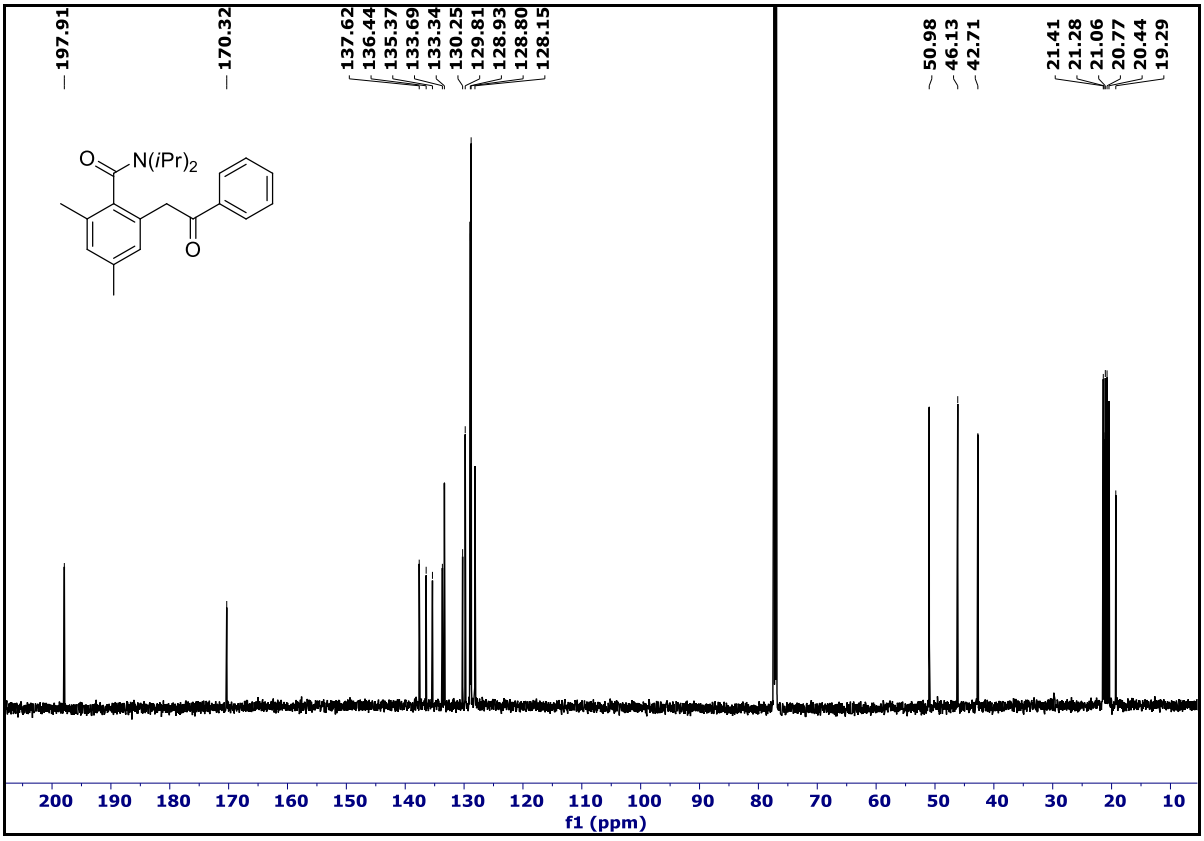


***N*,*N*-Diisopropyl-2,4-dimethyl-6-(2-oxo-2-phenylethyl)benzamide (2n)**

^{1}H NMR (600 MHz, $CDCl_3$)

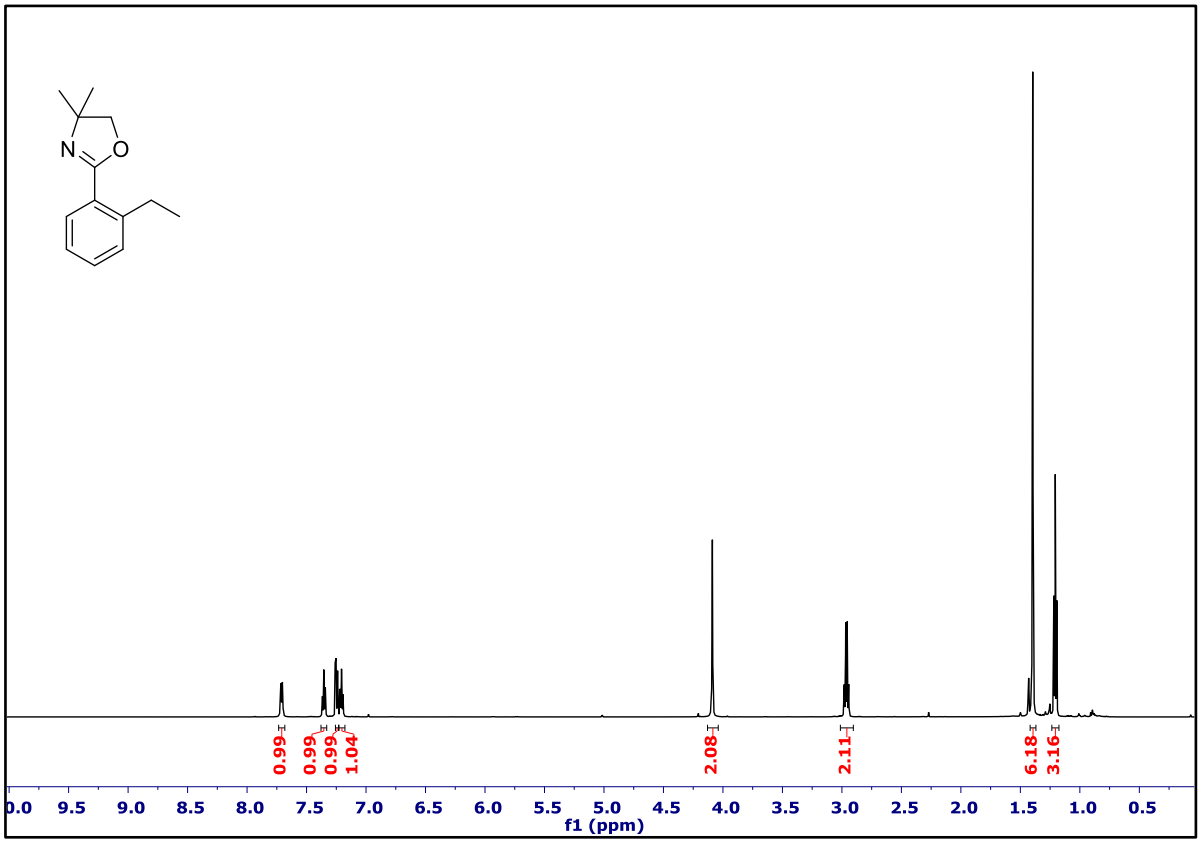


^{13}C NMR (150 MHz, $CDCl_3$)

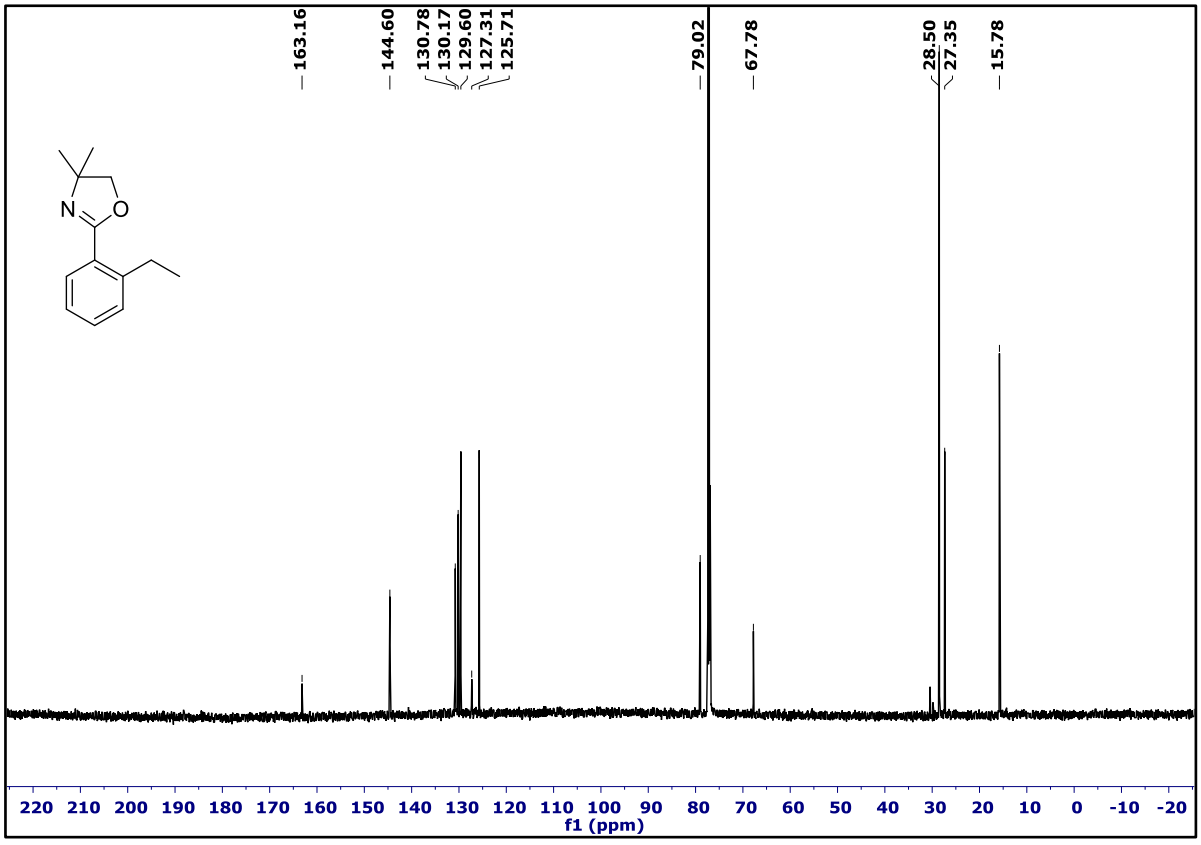


2-(2-ethylphenyl)-4,4-dimethyl-4,5-dihydrooxazole (2o)

^{1}H NMR (600 MHz, $CDCl_3$)

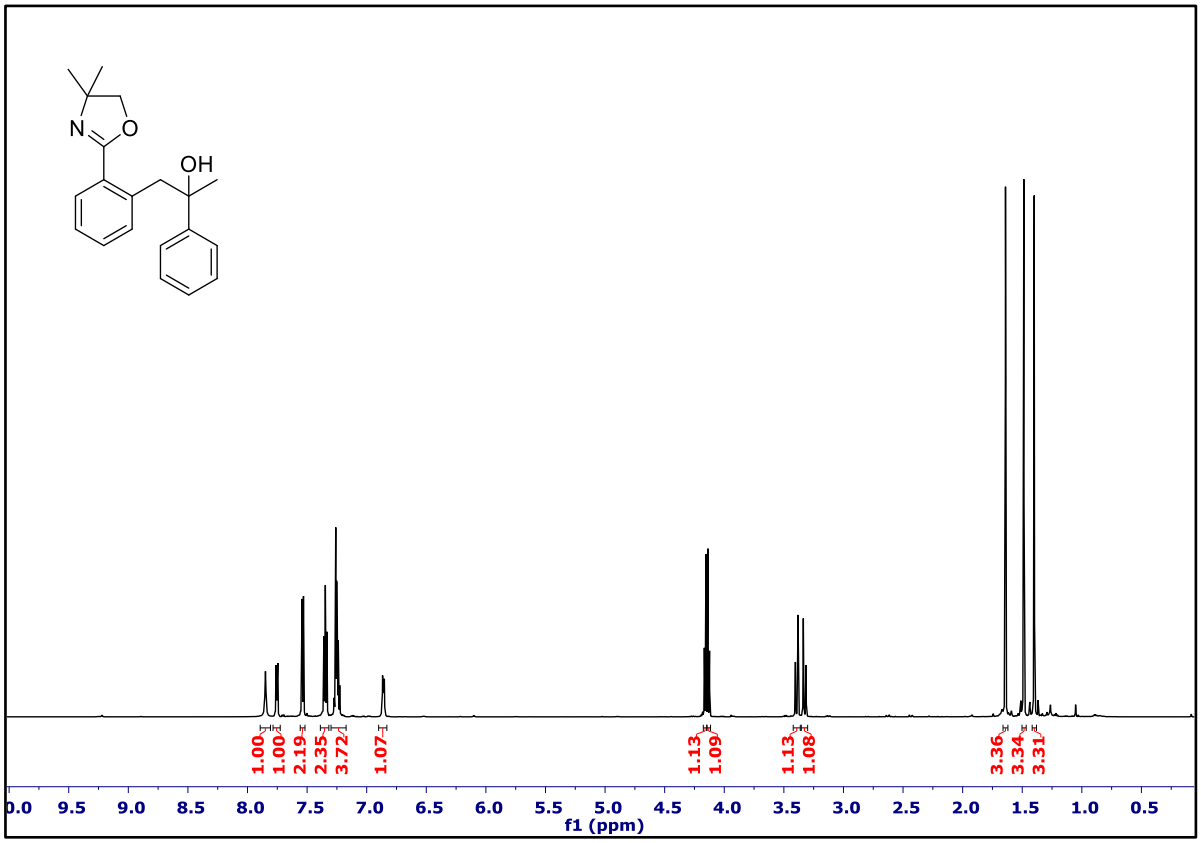


^{13}C NMR (150 MHz, $CDCl_3$)

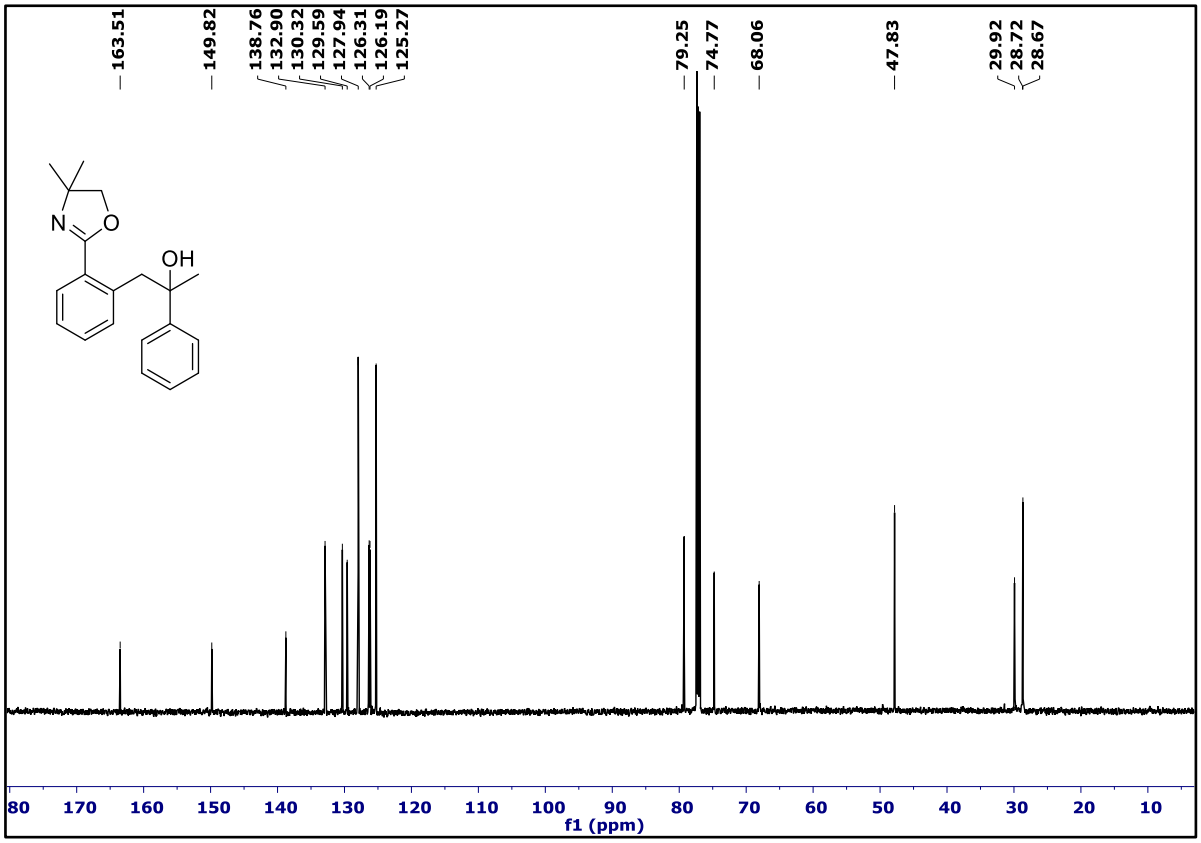


1-(2-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)phenyl)-2-phenylpropan-2-ol (2p)

^{1}H NMR (600 MHz, $CDCl_3$)

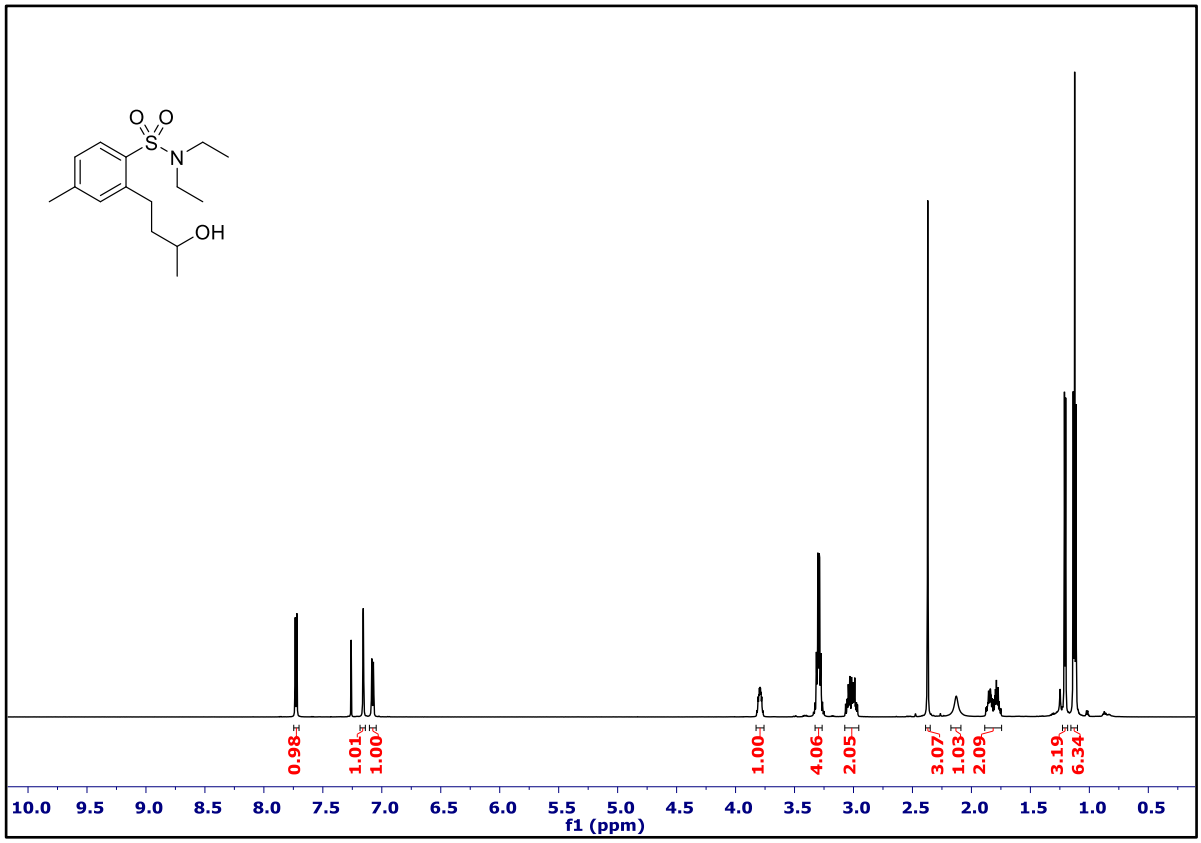


^{13}C NMR (150 MHz, $CDCl_3$)

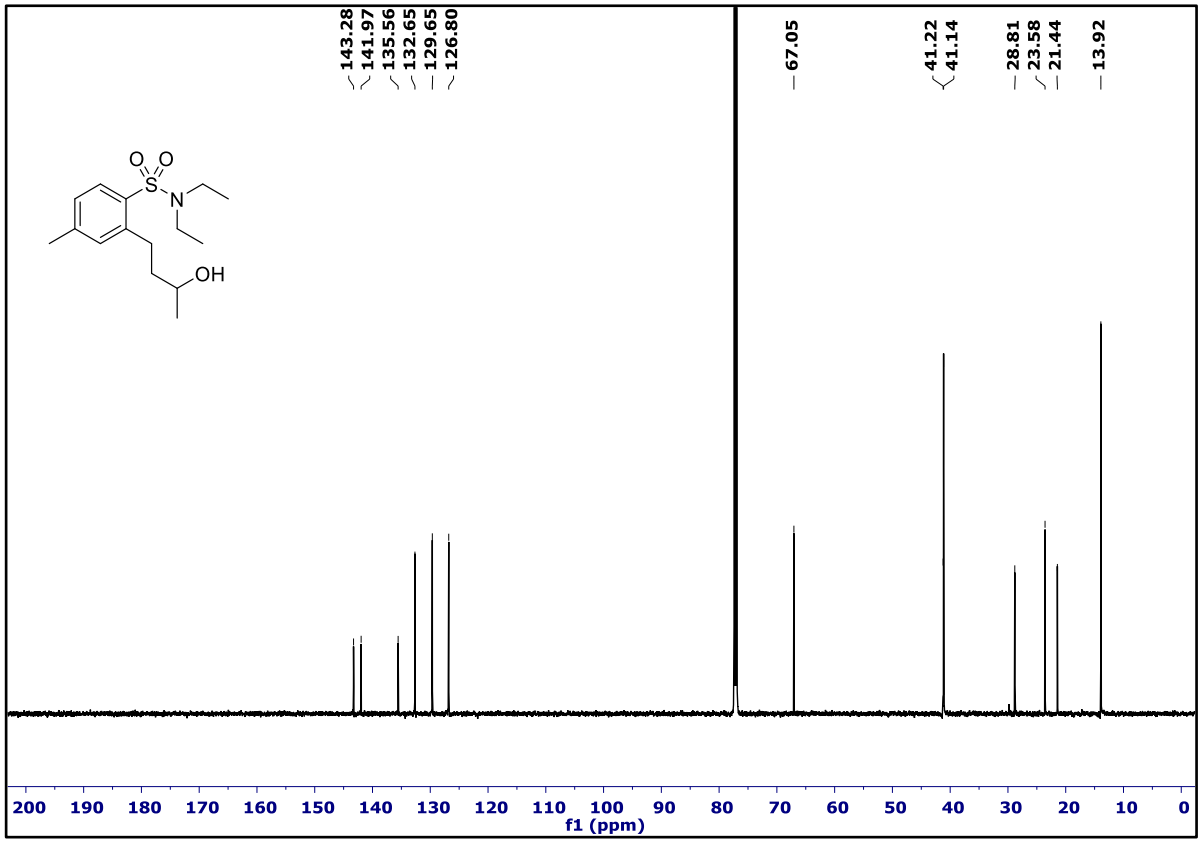


***N*,*N*-Diethyl-2-(3-hydroxybutyl)-4-methylbenzenesulfonamide (2q)**

^{1}H NMR (600 MHz, $CDCl_3$)

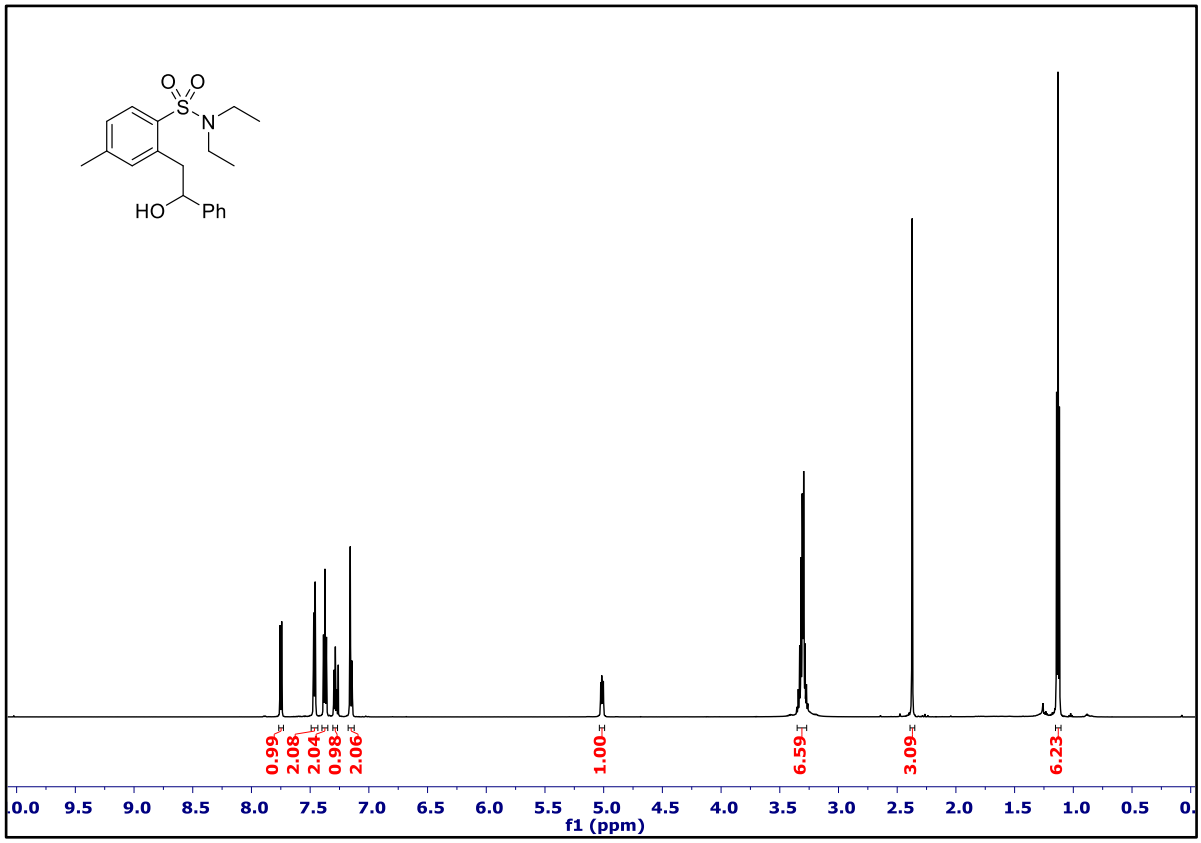


^{13}C NMR (150 MHz, $CDCl_3$)

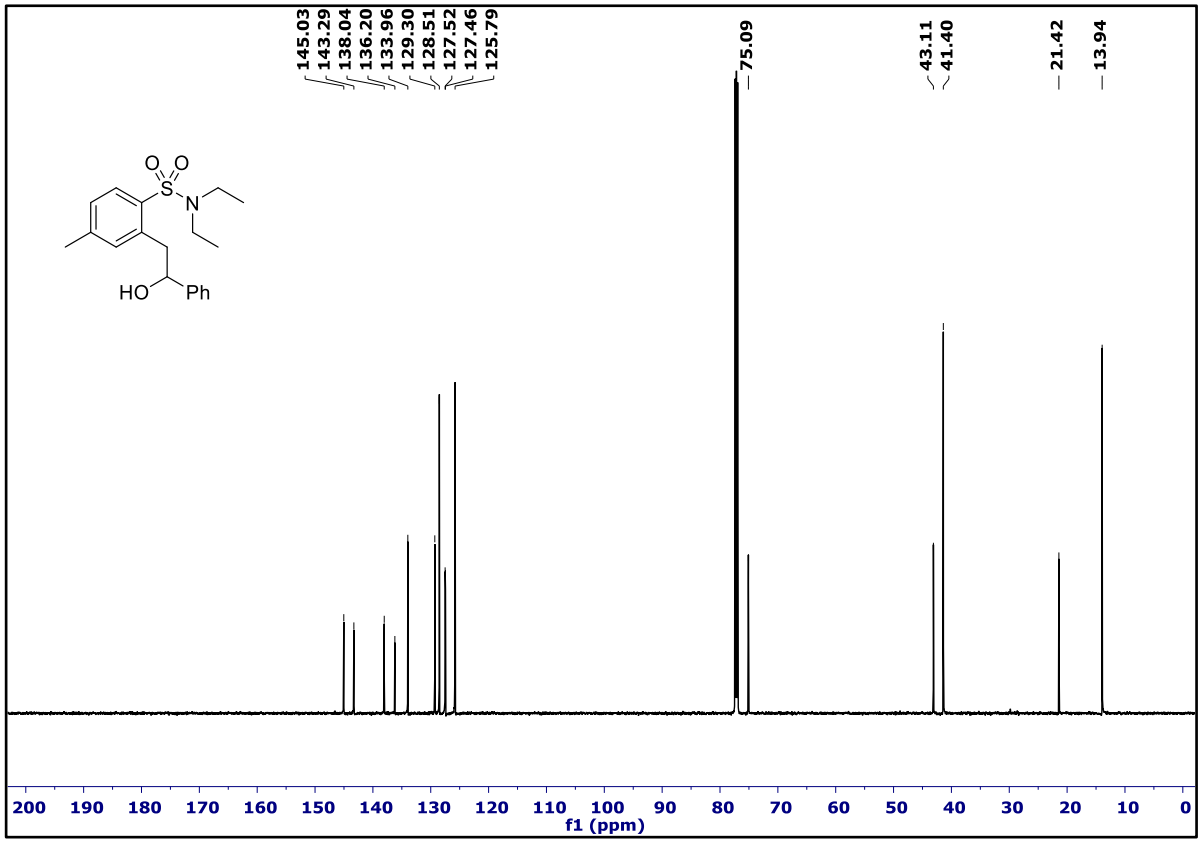


***N*,*N*-Diethyl-2-(2-hydroxy-2-phenylethyl)-4-methylbenzenesulfonamide (2r)**

^{1}H NMR (600 MHz, $CDCl_3$)



^{13}C NMR (150 MHz, $CDCl_3$)



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