Supporting Information for:

Enantioselective Desymmetrization via Carbonyl-Directed Catalytic Asymmetric Hydroboration and Suzuki-Miyaura Cross-Coupling

Gia L. Hoang,[‡] Zhao-Di Yang,[†‡] Sean M. Smith,[‡] Rhitankar Pal,[§] Judy L. Miska,[‡] Damaris E. Pérez,[‡] Libbie S. W. Pelter,[f] Xiao Cheng Zeng,[‡] and James M. Takacs*[‡]

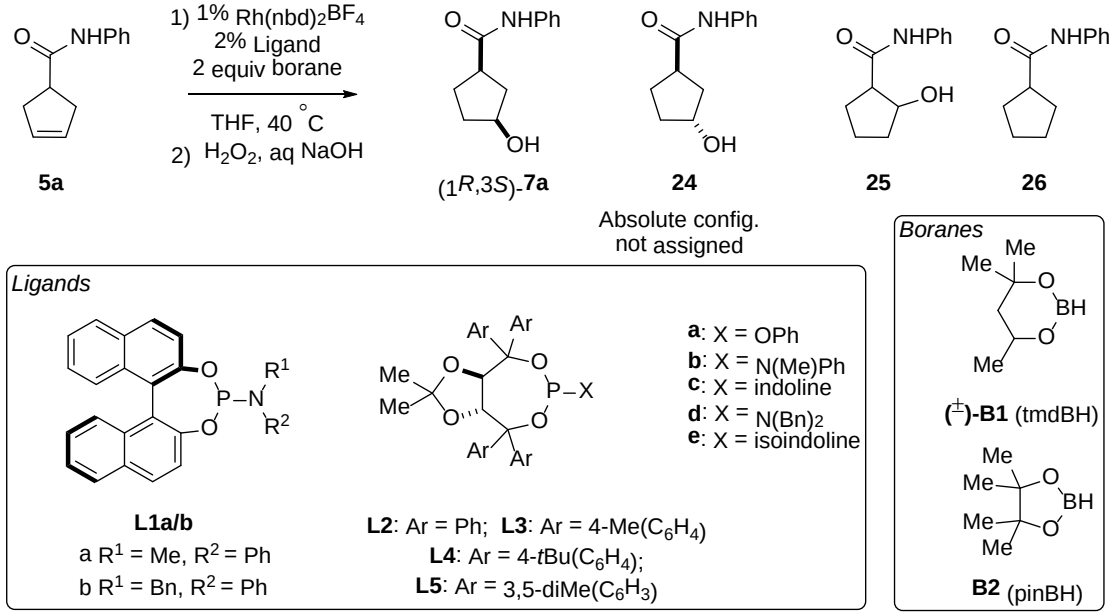
[‡] Department of Chemistry, University of Nebraska-Lincoln, Lincoln, NE 68588, USA
[†] Key Laboratory of Green Chemical Engineering and Technology, College of Heilongjiang Province, College of Chemical and Environmental Engineering, Harbin University of Science and Technology, Harbin 150040, P. R. China
[§] Department of Chemistry, Yale University, New Haven, CT 06518, United States
[f] Department of Chemistry and Physics, Purdue University Calumet, Department of Chemistry and Physics, Hammond, IN, 46323-2094, United States

jtakacs1@unl.edu

Table of Contents

General procedures. Reactions were carried out in a dry nitrogen atmosphere. Dichloromethane (DCM) and tetrahydrofuran (THF) were freshly distilled under the following conditions: THF from sodium metal and benzophenone, and DCM from calcium hydride. HPLC solvents were filtered through Millipore filter paper. When indicated in the following procedures, solvents were degassed by freezing under reduced pressure followed by a dry nitrogen atmosphere thaw (3–4 times). 4,4,6-Trimethyl-1,3,2-dioxaborinane (**B1,** tmdBH) was distilled immediately before use. All synthesized compounds were purified with flash chromatography using EMD Silica Gel 60 Geduran®, distilled via short path distillation, or triturated. Thin Layer Chromatography analyses were performed on Analtech Silica Gel HLF (0.25 mm) precoated analytical plates and visualized with use of handheld short wavelength UV light, Iodine stain (I_2 and EMD Silica Gel 60 Geduran®) and Vanillin stain (Ethanol, H_2SO_4, and vanillin). HPLC analyses were performed with use of an ISCO model 2360 HPLC and Chiral Technologies, Inc. chiral HPLC columns (Chiralcel OD; column: 250 x 4.6 mm, Chiralpak-AD; column: 250 x 4.6 mm, Chiralpak-IC; column: 4.6 x 250 mm). Data were recorded and analyzed with ChromPerfect chromatography software (version 5.1.0). NMR spectra were recorded on 700, 400, and 300 MHz Bruker Advance NMR spectrometers using residue $CHCl_3$ (δ 7.27 ppm) or $CDCl_3$ (δ 77.0 ppm) for reference unless otherwise specified. Peaks are expressed as m (unresolved multiplet), q (quartet), t (triplet), d (doublet) or s (singlet). IR spectra were recorded using an Avatar 360 FT-IR. Optical rotations were measured as solutions, 1.0 g/100 mL in chloroform or methanol unless indicated otherwise, and recorded using an Autopol III automatic polarimeter. HRMS analyses were performed by the Nebraska Center for Mass Spectrometry.

Table S1. Enantioselective desymmetrization via CAHB of **5a** with **B1** (tmdBH).



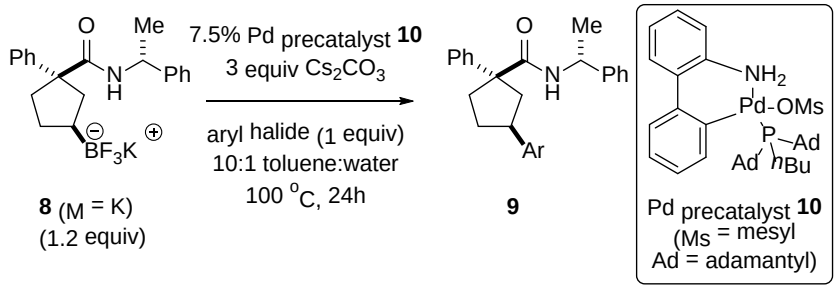
Ligand	Abs. Config. (**7a**)	% ee (**7a**)	% Yield (**7a**)	% Yield (**24**)	**%** Yield (**25**)	**%** Yield (**26**)
L1a	(1*R*,3*S*)	94	80	1	2	14
L1b	(1*R*,3*S*)	94	80	1	1	12
L2a	(1*R*,3*S*)	88	60	2	4	27
L3a	(1*R*,3*S*)	87	59	2	4	32
L4a	(1*R*,3*S*)	92	65	1	3	25
L5a	(1*R*,3*S*)	83	70	1	3	25
L2b	(1*R*,3*S*)	35	47	3	5	41
L3b	(1*R*,3*S*)	23	45	2	5	45
L4b	(1*R*,3*S*)	30	37	3	4	52
L5b	(1*R*,3*S*)	26	35	2	4	55
L2c	(1*R*,3*S*)	10	29	1	5	60
L3c	(1*S*,3*R*)	40	22	1	4	68
L4c	(1*R*,3*S*)	49	30	2	6	60
L5c	(1*R*,3*S*)	11	9	3	5	81

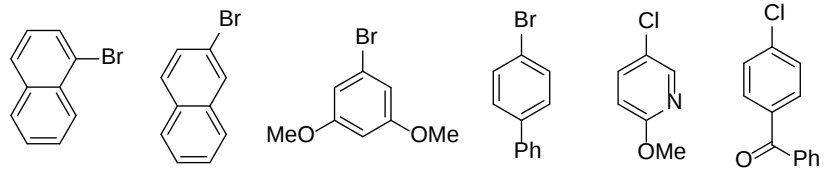
L2d	(1*R*,3*S*)	1	2	2	16	71
L3d	(1*R*,3*S*)	2	5	3	17	69
L4d	(1*R*,3*S*)	11	9	3	19	65
L5d	(1*R*,3*S*)	20	2	2	4	81
L3e	(1*S*,3*R*)	45	8	2	7	74
L4e	(1*R*,3*S*)	50	9	3	7	70
L5e	(1*R*,3*S*)	11	5	2	4	71

Table S2. Enantioselective desymmetrization via CAHB of **5a** with **B2** (pinBH).

Ligand	Abs. Config. (**7a**)	% ee (**7a**)	% Yield (**7a**)	% Yield (**24**)	**%** Yield (**25**)	**%** Yield (**26**)
L1a	(1*R*,3*S*)	80	45	3	7	25
L1b	(1*R*,3*S*)	81	52	3	8	28
L2a	(1*R*,3*S*)	60	66	8	7	16
L3a	(1*R*,3*S*)	55	60	10	7	20
L4a	(1*R*,3*S*)	68	62	9	8	18
L5a	(1*R*,3*S*)	70	59	8	13	17
L2b	(1*S*,3*R*)	75	64	6	11	16
L3b	(1*S*,3*R*)	65	66	5	12	14
L4b	(1*S*,3*R*)	60	62	4	15	16
L5b	(1*S*,3*R*)	60	62	4	14	17
L2c	(1*S*,3*R*)	60	75	5	8	15
L3c	(1*S*,3*R*)	78	77	7	6	14
L4c	(1*R*,3*S*)	15	63	4	15	16
L5c	(1*S*,3*R*)	6	25	4	22	47
L2d	(1*S*,3*R*)	13	48	8	18	20
L3d	(1*S*,3*R*)	50	46	5	25	20
L4d	(1*S*,3*R*)	10	23	34	8	22
L5d	(1*S*,3*R*)	10	11	19	10	51
L3e	(1*S*,3*R*)	70	55	8	12	19
L4e	(1*R*,3*S*)	2	40	17	15	25
L5e	(1*R*,3*S*)	5	27	5	22	31

Figure S1. Palladium-catalyzed cross-coupling of potassium trifluoroborate salt **8.**[a]

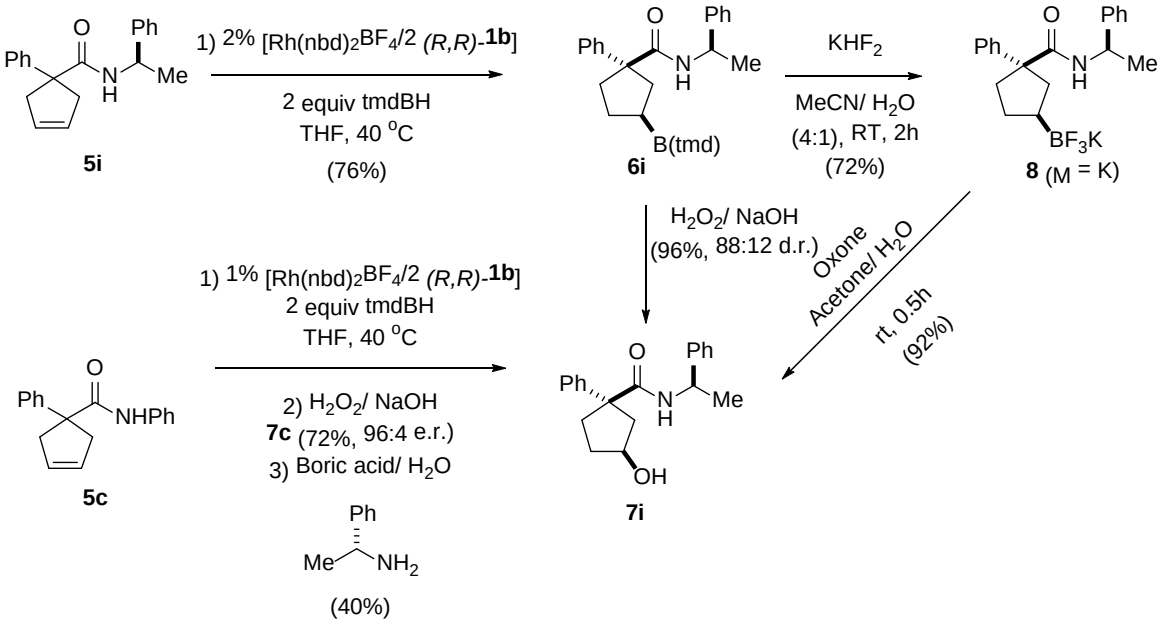




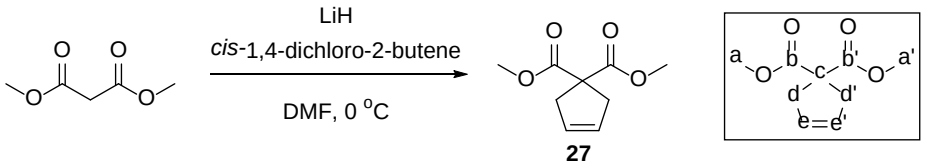
aryl halides	11	12	13	14	15	16
% Yield of 9	**9c** (92%)	**9d** (68%)	**9e** (73%)	**9f** (73%)	**9g** (66%)	**9h** (68%)

[a] Isolated yields based on limiting aryl halide, an average (±2%) of two runs

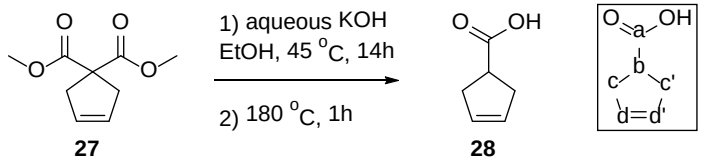
Figure S2. Confirmation of CAHB absolute configuration



Preparation sequence of 3-cyclopentenecarboxylic acid.[1]



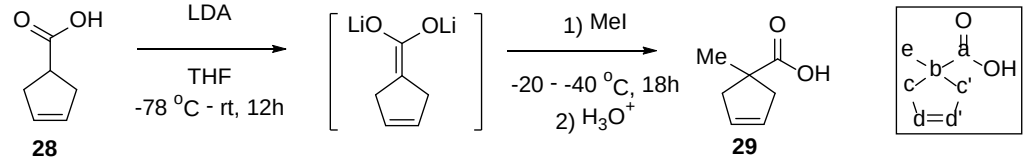
Preparation of 3-cyclopentene-1,1-dicarboxylic acid dimethyl ester (27).[1] To a cooled (0 °C) solution of dimethylmalonate (6.6 g, 50.0 mmol) in dry *N*,*N*-dimethylformamide (DMF, 75 mL) was added LiH (1.0 g, 126 mmol) under nitrogen atmosphere. The reaction was stirred at this temperature for 2 h, then *cis*-1,4-dichloro-2-butene (6.94 g, 55.5 mmol) was added dropwise, and the resultant mixture was slowly warm to room temperature. After 72 h, the mixture was diluted with 20% diethyl ether in hexanes (100 mL) and poured into cold water (100 mL). The organic layer was washed with brine (3 x 50 mL). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to afford the title compound (8.06 g, 87%) as a white solid: mp 169.5–171.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.59 (2H, s, e,e'), 3.72 (6H, s, a,a'), 3.01 (4H, s, d,d'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.60 (b,b'), 127.76 (e,e'), 58.74 (c), 52.77 (a,a'), 40.90 (d,d'); IR (neat) 2983, 2897, 1720 (C=O stretch), 1430, 1258 (C-O-C antisymmetrical stretch), 752, 694 (O-C-O bend) cm^{-1}.



Preparation of 3-cyclopentenecarboxylic acid (28).[1] To the stirring solution of 3-cyclopentene-1,1-dicarboxylic acid dimethyl ester (5.01g, 27.2 mmol) in 4:1 ethanol:water (55 mL) was added KOH (5.02g, 89.1 mmol). The reaction was stirred at 45 °C for 14h. The reaction mixture was then concentrated under reduced pressure and poured into a solution of 1:4 ether:hexanes (20 mL) and water (30 mL). The mixture was acidified with concentrated sulfuric acid (ca. 4.5 mL) until pH = 1 and then extracted with ethyl acetate (3 x 30 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure to afford a crude white solid. The

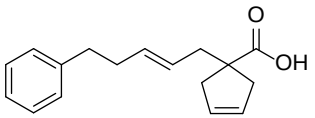
solid was heated at 180 °C for 1 h and then cooled to room temperature. Flash chromatography on silica gel (90:10 hexanes:ethyl acetate) affords the title compound (2.21 g, 73%, 2 steps) as a yellow oil: TLC analysis R_f 0.35 (70:30 hexanes:ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 10.99 (1H, br s, OH), 5.68 (2H, s, d,d'), 3.25–31.0 (1H, m, b), 2.75–2.65 (4H, m, c,c'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.88 (a), 128.91 (d,d'), 41.40 (b), 36.20 (c,c'); IR (neat) 3265 (O-H stretch), 3064, 2929, 1695 (C=O stretch), 1614 (C=C stretch), 1422, 931, 678 cm^{-1}. HRMS (FAB) calcd. for $C_6H_9O_2$ (M+H): 113.0603, found 113.1603 *m/z*.

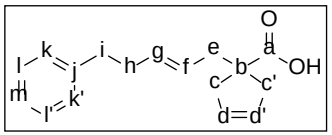
General procedure for α-alkylation of carboxylic acid via dianion intermediate.



28 **29**

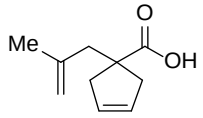
Preparation of 1-methyl-3-cyclopentenecarboxylic acid (29). To a cooled (–78 °C) solution of diisopropylamine (8.15 mL, 58.0 mmol) in THF (200 mL) was slowly added *n*-butyllithium (20.5 mL, 2.5 M solution in hexanes, 51.3 mmol). The resultant mixture was stirred at that temperature for 1 h followed by a 1 h-stir at room temperature. The reaction mixture was then cooled to –20 °C – – 40°C and a solution of 3-cyclopentenecarboxylic acid **28** (2.54 g, 22.6 mmol) in THF (15 mL) was slowly added over 1 h. The resultant mixture was slowly rised to room temperature and stir for the total of 12 h. After that, the mixture was cooled to –20 °C – – 40°C and methyl iodide (2.15 mL, 34.3 mmol) was added dropwise. The resultant mixture was slowly rised to room temperature and stir for the total of 18 h. The mixture was quenched with dilute HCl (3M) and extracted with ethyl acetate (3 x 25 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. Flash chromatography on silica gel (80:20 hexanes:ethyl acetate) affords the title compound (2.45 g, 87%) as a dark oil: TLC analysis R_f 0.40 (70:30 hexanes:ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.06 (1H, br s, OH), 5.63 (2H, s, d,d'), 2.97 (2H, d, J = 14.4 Hz, c,c'), 2.27 (2H, d, J = 14.7 Hz, c,c'), 1.35 (3H, s, e); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.41 (a), 128.22 (d,d'), 47.71 (b), 44.53 (c,c'), 25.71 (e); IR (neat) 3195 (O-H stretch), 3064, 2970, 2917, 1695 (C=O stretch), 1467, 1405, 1287, 944, 670 cm^{-1}. HRMS (EI) calcd. for $C_7H_{10}O_2$: 126.0681, found 126.0676 *m/z*.

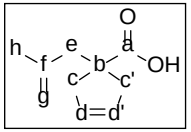




30

***(E)*-1-(5-phenylpent-2-en-1-yl)cyclopent-3-ene-1-carboxylic acid (30).** Using the general procedure with diisopropylamine (4.5 mL, 32.0 mmol in 100 mL THF), *n*-butyllithium (11.3 mL, 2.5 M solution in hexanes, 28.3 mmol), 3-cyclopentenecarboxylic acid **28** (1.4 g, 12.5 mmol in 10 mL THF), and allylic bromide **34** affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (2.95 g, 92 %) as a yellow oil: TLC analysis R_f 0.50 (70:30 hexanes:ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 12.05 (1H, br s, OH), 7.40–7.20 (5H, j, k,k',l,l',m), 5.63 (2H, s, d,d'), 5.60–5.40 (2H, m, f,g), 2.92 (2H, d, *J* = 14.7 Hz, c,c'), 2.75–2.65 (2H, m, c,c'), 2.50–2.30 (6H, m, e,h,i); ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.34 (a), 141.92 (j), 133.56 (d,d'), 128.49 (g), 128.35 (l,l'), 128.31 (k,k'), 126.02 (m), 125.80 (f), 51.99 (b), 41.93 (e), 41.84 (c,c'), 36.00 (i), 34.41 (h); IR (neat) 2918 (O-H stretch), 1694 (C=O stretch), 1277, 1226 (C-O stretch), 967, 951 (O-H bend), 697, 670 cm^{-1}. HRMS (ESI) calcd. for $C_{17}H_{19}Na_2O_2$ (M-H+2Na): 301.1180, found 301.1190 *m/z*.



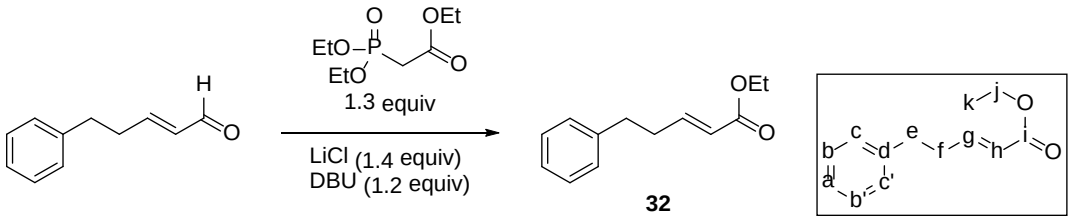


31

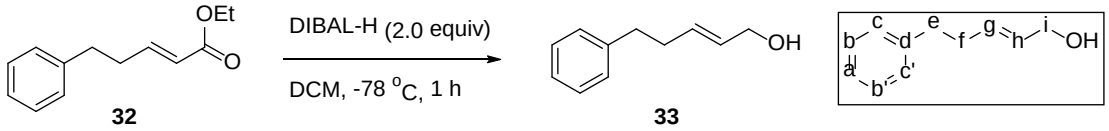
1-(2-methylallyl)cyclopent-3-ene-1-carboxylic acid (31). Using the general procedure with diisopropylamine (4.5 mL, 32.0 mmol) in 100 mL THF, *n*-butyllithium (11.3 mL, 2.5 M solution in hexanes, 28.3 mmol), 3-cyclopentenecarboxylic acid **28** (1.4 g, 12.5 mmol in 10 mL THF), and 3-bromo-2-methylpropene (1.9 mL, 18.8 mmol) affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (1.85 g, 89 %) as a yellow oil: TLC analysis R_f 0.55 (70:30 hexanes:ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.02 (1H, br s, OH), 5.63 (2H, s, d,d'), 4.84 (1H, s, g), 4.70 (1H, s, g), 2.96 (2H, d, *J* = 14.4 Hz, c,c'), 2.52 (2H, s, e), 2.44 (2H, d, *J* = 14.8 Hz, c,c'), 1.73 (3H, s, h); ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.59 (a), 142.39 (f), 128.36 (d,d'), 113.60 (g),

51.66 (a), 46.57 (e), 42.49 (c,c'), 23.21 (h); IR (neat) 2911 (O-H stretch), 1694 (C=O stretch), 1229 (C-O stretch), 951 (O-H bend), 893, 693, 663 cm^{-1}. HRMS (ESI) calcd. for $C_{10}H_{13}Na_2O_2$ (M-H+2Na): 211.0711, found 211.0719 *m/z*.

Preparation sequence of (*E*)-(5-bromopent-3-en-1-yl)benzene (34).

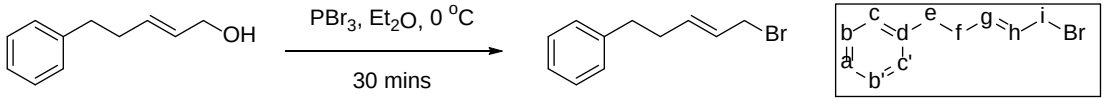


Preparation of ethyl (*E*)-5-phenylpent-2-enoate (32).[2] To a suspension of LiCl (2.21 g, 1.4 equiv, 52.0 mmol) in MeCN (50 mL) were added DBU (6.7 mL, 1.2 equiv, 45.0 mmol) and triethyl phosphonoacetate (9.7 mL, 1.3 equiv, 48.5 mmol). The resulting mixture was stirred at rt for 15 mins. After cooling to 0 ^oC, 3-phenylpropionaldehyde (4.9 mL, 37.2 mmol) was added slowly in 5 mins. The resultant mixture was slowly warmed to rt for the total of 1 h and quenched by saturated ammonium chloride. The resultant mixture was extract with ethyl acetate (3 x 50 mL). The combined organic extracts were dried (anhyd. Na_2SO_4) and concentrated under reduced pressure. Flash chromatography on silica gel (95:5 hexanes:ethyl acetate) affords the title compound (6.9 g, 91%) as a colorless liquid: TLC analysis R_f 0.50 (90:10 hexanes:ethyl acetate); ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.30 (2H, m, b,b'), 7.30–7.15 (3H, m, a,c,c'), 7.05 (1H, dt, *J* = 15.7 and 6.8 Hz, g), 5.89 (1H, dt, *J* = 15.7 and 1.5 Hz, h), 4.22 (2H, q, *J* = 15.7 Hz, j), 2.81 (2H, t, *J* = 7.3 Hz, e), 2.60–2.50 (2H, m, f) 1.32 (3H, t, *J* = 7.1 Hz, k); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.56 (i), 148.04 (g), 140.83 (d), 128.51 (b,b'), 128.35 (c,c'), 126.19 (a), 121.90 (h), 60.20 (j), 34.38 (e), 33.91 (f), 14.30 (k).



Preparation of (*E*)-5-phenylpent-2-en-1-ol (33).[3] To a solution of ester **32** (6.8 g, 33.3 mmol) in dichloromethane was added DIBAL-H (67 mL, 2.0 equiv, 67 mmol, 1M in hexane) slowly at -78 ^oC. The resultant mixture was stirred at -78 ^oC and carefully

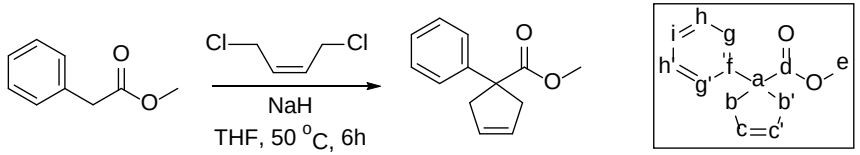
quenched with saturated aq. potassium sodium tartrate. The layers were separated and the aqueous layer was washed with dichloromethane (2 x75 mL). The combined organic extracts were dried (anhyd. Na_2SO_4) and concentrated under reduced pressure to afford the title compound (5.0 g, 93%) as a colorless liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.30 (2H, m, b,b'), 7.30–7.20 (3H, m, a,c,c'), 5.90–5.60 (2H, m, g,h), 4.11 (2H, d, *J* = 4.9 Hz, i), 2.78 (2H, t, *J* = 7.3 Hz, e), 2.50–2.40 (2H, m, f), 2.40–2.25 (1H, br s, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.79 (d), 132.04 (h), 129.71 (g), 128.49 (b,b'), 128.40 (c,c'), 125.94 (a), 63.49 (i), 35.61 (e), 34.04 (f).



33 **34**

Preparation of (*E*)-(5-bromopent-3-en-1-yl)benzene (34).[3] To a cooled (0 °C) solution of allylic alcohol **33** (5.0 g, 30.8 mmol) in Et_2O (50 mL) was added phosphorous tribromide (1.45 mL, 0.5 equiv, 15.4 mmol). The resultant mixture was stirred at 0 °C for 30 mins and quenched by saturated brine solution. The layers were separated and the aqueous layer was washed with Et_2O (2 x 30 mL). The combined organic extracts were dried (anhyd. Na_2SO_4) and concentrated under reduced pressure. The residue was passed through a short pad of silica and concentrated under reduced pressure to afford the title compound (6.6 g, 95%) as yellow liquid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.30 (2H, m, b,b'), 7.30–7.20 (3H, m, a,c,c'), 5.90–5.70 (2H, m, g,h), 3.98 (2H, d, *J* = 6.8 Hz, i), 2.75 (2H, t, *J* = 7.3 Hz, e), 2.50–2.40 (2H, m, f); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.36 (d), 135.49 (h), 128.45 (b,b'), 128.41 (c,c'), 127.01 (g'), 126.01 (a), 35.24 (i), 33.82 (e), 33.34 (f).

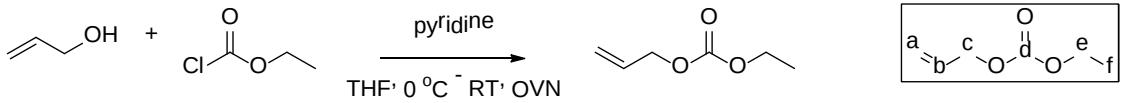
Preparation of methyl 1-phenyl-3-cyclopentenecarboxylate (35).[4]



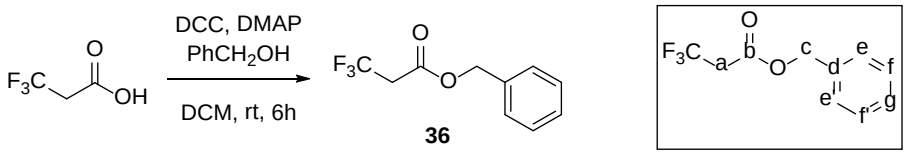
35

To a cooled (0 ^{o}C) solution of methyl phenylacetate (6.0 g, 39.6 mmol) in THF (80 mL) and *N,N'*-dimethylpropyleneurea (20 mL) was carefully added NaH (1.9 g, 79.7 mmol) and the mixture was stirred at 50 ^{o}C. After 2 h, the resultant mixture was allowed to cool to room temperature, and *cis*-1,4-dichloro-2-butene (5.2 mL, 47.3 mmol) was added dropwise. The resultant mixture was then stirred at 50 ^{o}C for 3 h. After cooling to room temperature, the mixture was quenched with saturated ammonium chloride and extracted with ethyl acetate (2 x 25 mL). The combined organic layers were dried (Na_2SO_4) and concentrated under reduced pressure. Flash chromatography on silica gel (97:3 hexanes:ethyl acetate) affords the title compound (3.51 g, 44%) as a yellow oil: TLC analysis R_f 0.80 (70:30 hexanes:ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45–7.20 (5H, m, g,g',h,h',i), 5.82 (2H, s, c,c'), 3.68 (3H, s, e), 3.48 (2H, d, *J* = 14.6, b,b'), 2.82 (2H, d, *J* = 14.8, b,b'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.58 (d), 143.78 (f), 129.18 (g,g'), 128.44 (c,c'), 126.79 (h,h'), 126.58 (i), 58.42 (e), 52.49 (a), 42.88 (b,b').

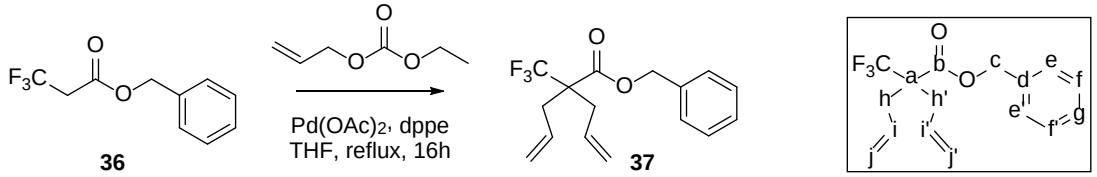
Preparation sequence of benzyl 1-(trifluoromethyl)cyclopent-3-enecarboxylate (38).[5]



Preparation of allyl ethyl carbonate. To a cooled (0 ^{o}C) solution of allylic alcohol (13.6 mL, 0.2 mol) and DMAP (0.6 g, 5 mmol) in dichloromethane (300 mL) was slowly added pyridine (32 mL, 2 equiv, 0.4 mol). Ethyl chloroformate (19.1 mL, 1 equiv, 0.2 mol) was added dropwise to the above mixture. The resultant mixture was slowly warmed to room temperature and stirred overnight. The reaction mixture was washed with water (3 x 100 mL). The organic extracts were dried (anhyd. Na_2SO_4) and concentrated under reduced pressure. Flash chromatography on silica gel (95:5 hexanes:ethyl acetate) affords the title (24.3 g, 93%) as a colorless liquid; TLC analysis R_f 0.55 (90:10 hexanes:ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.05–5.80 (1H, m, b), 5.29 (1H, dd, *J* = 31.5 Hz, 17.1 Hz, a), 4.61 (2H, d, *J* = 5.7 Hz, c), 4.19 (2H, q, *J* = 7.1 Hz, e), 1.30 (3H, t, *J* = 7.1 Hz, f); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.94 (d), 131.67 (b), 118.65 (a), 68.19 (c), 63.96 (e), 14.20 (f).

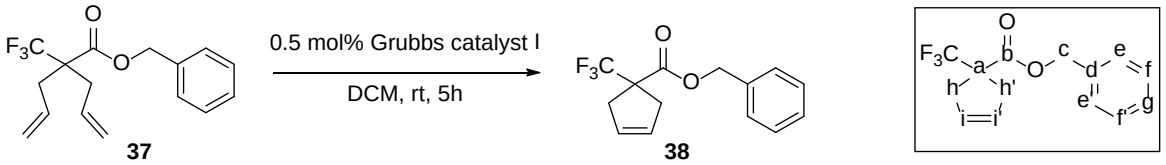


Preparation of benzyl 3,3,3-trifluoropropanoate (36).[5] Using the general procedure of DCC-mediated condensation with 3,3,3-trifluoropropanoic acid (3.0 g, 23.4 mmol), DMAP (72.0 mg, 0.025 equiv, 0.59 mmol), DCC (4.8 g, 1 equiv, 23.4 mmol), and benzyl alcohol (4.85 mL, 2 equiv, 46.8 mmol) affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (4.9 g, 96%) as a colorless liquid: TLC analysis R_f 0.55 (80:20 hexanes:ethyl acetate); ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.43 (t, J = 9.6 Hz, CF_3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.35 (5H, m, e,e',f,f',g), 5.26 (2H, s, c), 3.26 (2H, q, J = 14.6, a); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.00 (q, J = 4.1 Hz, b), 134.91 (d), 128.71 (f), 128.66 (e), 128.37 (g), 123.43 (q, J = 274.4 Hz, CF_3), 67.50 (c), 39.59 (q, J = 30.9 Hz, a).



Preparation of benzyl 2-allyl-2-(trifluoromethyl)pent-4-enoate (37).[5] To a refluxed solution of $Pd(OAc)_2$ (203 mg, 0.04 equiv, 0.87 mmol) and 1,2-bis(diphenylphosphanyl)ethane (dppe; 1.07 g, 0.12 equiv, 2.6 mmol) in THF (50 mL) was added a solution of benzyl 3,3,3-trifluoropropanoate **36** (4.85 g, 22.2 mmol) and allyl ethyl carbonate (8.9 mL, 66.7 mmol, 3.0 equiv) in THF (250 mL) via cannula. After 16 h of reflux, the resultant mixture was cooled to rt and concentrated under reduced pressure. Flash chromatography on silica gel (95:5 hexanes:ethyl acetate) affords the title compound (6.1 g, 92%) as a colorless oil: TLC analysis R_f 0.85 (70:30 hexanes:ethyl acetate); ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.05 (s, CF_3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.35 (5H, m, e,e',f,f',g), 5.85–5.70 (2H, m, i,i'), 5.24 (2H, s, c), 5.20–5.10 (4H, m, j,j'), 2.70–2.60 (4H, m, h,h'); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.40 (b),

135.11 (d), 131.50 (i,i'), 128.61 (f,f'), 128.46 (g), 128.23 (e,e'), 125.91 (q, J = 283.24 Hz, CF_3), 119.69 (j,j'), 67.49 (c), 55.94 (q, J = 23.14 Hz, a), 36.19 (h,h').

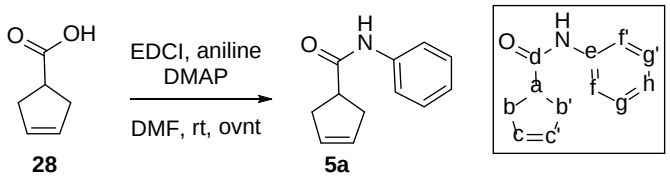


Preparation of benzyl 1-(trifluoromethyl)cyclopent-3-enecarboxylate (38).[5] A solution of diallyl benzyl ester **37** (599 mg, 2.0 mmol) and Grubbs' I catalyst (8.3 mg, 0.01 mmol, 0.005 equiv) in dichloromethane (20 mL) was stirred at rt for 5 h. The resultant mixture was then concentrated under reduced pressure. Flash chromatography on silica gel (90:10 hexanes:ethyl acetate) affords the title compound (535 mg, 99%) as a colorless oil: TLC analysis R_f 0.75 (80:20 hexanes:ethyl acetate); ^{19}F NMR (376 MHz, $CDCl_3$) δ -72.73 (s, CF_3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.35 (5H, m, e,e',f,f',g), 5.67 (2H, s, i,i'), 5.27 (2H, s, c), 3.11 (2H, d, J = 15.2, h,h'), 2.92 (2H, d, J = 15.8, h,h'); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.12 (b), 135.29 (d), 128.63 (i,i'), 128.40 (f,f'), 127.89 (g), 127.67 (e,e'), 126.67 (q, J = 279.0 Hz, CF_3), 67.66 (c), 57.14 (q, J = 25.7 Hz, a), 38.87 (h,h').

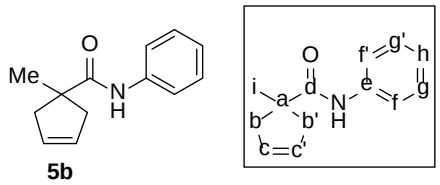
General procedure for the preparation of *γ,δ*-unsaturated carboxylic acids via hydrolysis of esters.

To a carboxylate ester was added a solution of KOH 1 M in ethanol (5 equiv), and the reaction was heated at reflux for 2 h. The reaction mixture was cooled to rt and partially concentrated under reduced pressure. The residue was added water and extracted twice with dichloromethane. The aqueous layer was acidified until pH = 1 with HCl (3M) and extracted twice with dichloromethane. The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to afford a corresponding carboxylic acid which was used in the next step without further purification.

General procedure for the preparation of *γ,δ*-unsaturated phenyl amides via EDCI-mediated condensation.



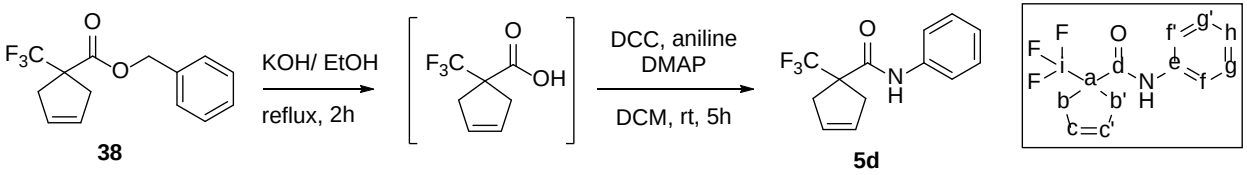
Preparation of 3-cyclopentenecarboxylic acid phenyl amide (5a). To a cooled (0 °C) degassed solution of 3-cyclopentenecarboxylic acid **28** (562 mg, 5.0 mmol) in *N*,*N*-dimethylformamide (DMF, 40 mL) was slowly added aniline (0.46 mL, 5.0 mmol). The resulting solution was stirred (0.5 h, 0 °C) and then *N*-(3-dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride (EDCI, 1.06 g, 5.5 mmol) and 4-(dimethylamino)pyridine (DMAP, 612 mg, 5.0 mmol) were added. The resulting mixture was allowed to slowly warm to room temperature and stirred overnight. The reaction mixture was quenched by the addition of satd. aq. sodium bicarbonate (50 mL) and extracted with ethyl acetate (2 x 50 mL). The combined organic extracts were washed with HCl (3M, 2 x 30 mL) and dried (anhyd. Na_2SO_4) and concentrated under reduced pressure. Flash chromatography on silica gel (85:15 hexanes:ethyl acetate) affords the title (815 mg, 87%) as a white solid: mp 83.0–84.5 °C; TLC analysis R_f 0.5 (75:25 hexanes:ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (1H, br s, NH), 7.56 (2H, d, *J* = 7.8 Hz, f,f'), 7.30 (2H, t, *J* = 7.6 Hz, g,g'), 7.10 (1H, t, *J* = 7.4 Hz, h), 5.71 (2H, s, c,c'), 3.25–3.05 (1H, m, a), 2.85–2.55 (4H, m, b,b'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.80 (d), 138.23 (e), 129.19 (c,c'), 128.90 (g,g'), 124.13 (h), 120.10 (f,f'), 44.28 (a), 37.15 (b,b'); IR (neat) 3288 (N-H stretch), 3253, 3142, 1655 (C=O stretch), 1544 (N-H bend), 1439, 1310, 750 cm^{-1}. HRMS (FAB) calcd. for $C_{12}H_{14}NO$ (M+H): 188.0997, found 188.1081 *m/z*.



1-methyl-3-cyclopentenecarboxylic acid phenyl amide (5b). Following the general procedure, 3-cyclopentene-1-methylcarboxylic acid **29** (632 mg, 5.0 mmol) affords, after flash chromatography on silica gel (85:15 hexanes:ethyl acetate), the title compound (854 mg, 85%) as a white solid: mp 91.0–93.5 °C; TLC analysis R_f 0.5 (75:25 hexanes:ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52

(2H, d, *J* = 8.0 Hz, f,f'), 7.48 (1H, br s, NH), 7.30 (2H, t, *J* = 7.7 Hz, g,g'), 7.09 (1H, t, *J* = 7.4 Hz, h), 5.73 (2H, s, c,c'), 2.97 (2H, d, *J* = 14.5 Hz, b,b'), 2.36 (2H, d, *J* = 14.5 Hz, b,b'), 1.42 (3H, s, i); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.73 (d), 138.21 (e), 129.13 (c,c'), 128.92 (g,g'), 124.13 (h), 120.09 (f,f'), 48.96 (a), 45.10 (b,b'), 26.14 (i); IR (neat) 3657 (N-H stretch), 2974, 2897, 1679 (C=O stretch), 1593 (C=C stretch), 1520 (N-H bend), 1438, 1303, 727 cm^{-1}. HRMS (FAB) calcd. for $C_{13}H_{16}NO$ (M+H): 202.1232, found 202.1228 *m/z*.

General procedure for the preparation of *γ,δ*-unsaturated phenyl amides via DCC-mediated condensation.

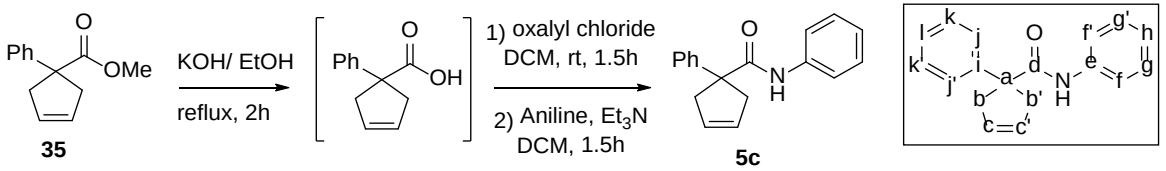


Preparation of 1-(trifluoromethyl)-3-cyclopentenecarboxylic acid phenyl amide (5d). Using the general procedure for the preparation of *γ,δ*-unsaturated carboxylic acids via hydrolysis of esters with benzyl ester **38** (501 mg, 1.85 mmol) affords the crude carboxylic acid (327 mg) as yellow oil used in the next step without further purification.

To a solution of the crude *γ,δ*-unsaturated carboxylic acid (327 mg, 1.82 mmol) in dichloromethane (6 mL) was added DMAP (5.6 mg, 0.025 equiv, 0.046 mmol) and aniline (0.33 mL, 2 equiv, 3.64 mmol). The resultant mixture was stirred at 0 ^{o}C for 15 mins and DCC (374 mg, 1 equiv, 1.82 mmol) was added. The reaction mixture was slowly warm to rt and stir for 5 h. After filtration, the filtrate was washed twice with HCl (3M) and once with satd. $NaHCO_3$. The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Flash chromatography on silica gel (90:10 hexanes:ethyl acetate) affords, the title compound (321 mg, 68%, 2 steps) as a white solid: mp 69.5–72.5 ºC; TLC analysis R_f 0.60 (70:30 hexanes:ethyl acetate); ^{19}F NMR (376 MHz, $CDCl_3$) δ -71.86 (s, CF_3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (2H, d, *J* = 7.7 Hz, f,f'), 7.60–7.45 (1H, m, NH), 7.36 (2H, t, *J* = 7.6 Hz, g,g'), 7.17 (1H, t, *J* = 7.4 Hz, h), 5.74 (2H, s, c,c'), 3.21 (2H, d, *J* = 15.5 Hz, b,b'), 2.97 (2H, d, *J* = 15.3 Hz, b,b'); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.06 (d), 137.32 (e), 129.07 (c,c'), 128.05 (g,g'), 127.24 (q, *J* = 278.7 Hz, i), 124.98 (h), 120.43 (f,f'), 58.11 (q, *J* = 24.7, a), 38.89 (q, *J* =

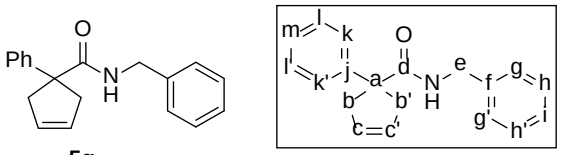
2.0 Hz, b,b'); IR (neat) 3309 (N-H stretch), 2924, 2867, 1667 (C=O stretch), 1599 (C=C stretch), 1535 (N-H bend), 1476, 1301, 1263, 1148, 753, 739, 662 (C-F stretch) cm^{-1}. HRMS (ESI) calcd. for $C_{13}H_{12}F_3NaNO$ (M+Na): 278.0769, found 278.0766 *m/z*.

General procedure for the preparation of *γ,δ*-unsaturated amides via acid chloride intermediates.



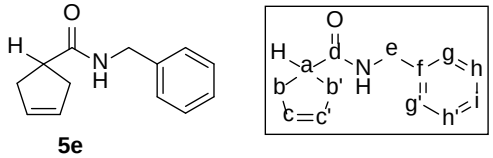
Preparation of 1-phenyl-3-cyclopentenecarboxylic acid phenyl amide (5c). Using the general procedure for the preparation of *γ,δ*-unsaturated carboxylic acids via hydrolysis of esters with methyl ester **35** (1.66 g, 8.2 mmol) affords the crude carboxylic acid (1.47 g) as yellow solid used in the next step without further purification.

To a cooled solution (0 ^oC) of the crude *γ,δ*-unsaturated carboxylic acid (1.47 g, 7.8 mmol) in dichloromethane (50 mL) was added dropwise oxalyl chloride (2.68 mL, 4.0 equiv, 31.2 mmol) followed by 3 drops of DMF. The resultant mixture was slowly warm to rt and stir for the total of 1.5 h. The reaction mixture was then concentrated. The resulting acid chloride was redissolved in dichloromethane (50 mL) and cooled to 0 ^oC. The resultant mixture was then added dropwise aniline (1.1 mL, 1.5 equiv, 11.7 mmol) followed by dropwise addition of triethylamine (2.18 mL, 2.0 equiv, 15.6 mmol). The reaction mixture was slowly warm to rt and stir for the total of 1.5 h. Whereupon it was diluted, it was washed twice with HCl (3M), once with satd. $NaHCO_3$ solution, and once with brine. The organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure. Flash chromatography on silica gel (90:10 hexanes:ethyl acetate) affords, the title compound (1.55 g, 72%, 3 steps) as a white solid: mp 90.5–92.5 ºC; TLC analysis R_f 0.6 (70:30 hexanes:ethyl acetate); ^1H NMR (300 MHz, $CDCl_3$) δ 7.50–7.20 (9H, m, f,f',g,g',h,j,j'k,k'), 7.08 (1H, t, *J* = 7.4 Hz, l), 5.81 (2H, s, c,c'), 3.43 (2H, d, *J* = 14.6, b,b'), 2.92 (2H, d, *J* = 14.6, b,b'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.49 (d), 144.53 (e), 138.12 (i), 129.03 (j,j'), 128.90 (c,c'), 128.73 (k,k'), 127.28 (g,g'), 126.75 (h), 124.12 (l), 119.62 (f,f'), 59.24 (a), 43.89 (b,b'); IR (neat) 3286 (N-H stretch), 3056, 2846, 2917, 1648 (C=O stretch), 1595 (C=C stretch), 1518 (N-H bend), 1497, 1436, 1312, 1239, 753, 742, 732, 688, 655 cm^{-1}. HRMS (ESI) calcd. for $C_{18}H_{17}NaNO$ (M+Na): 286.1208, found 286.1197 *m/z*.



5g

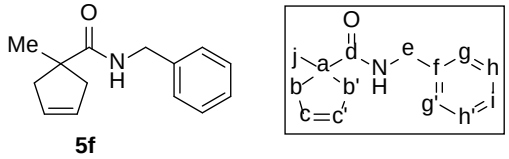
1-phenyl-3-cyclopentenecarboxylic acid benzyl amide (5g). Using the general procedure with benzylamine (1.28 mL, 1.5 equiv, 11.7 mmol) affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (1.48 g, 65%, 3 steps) as a white solid: mp 68.0–70.5 ºC; TLC analysis R_f 0.50 (70:30 hexanes:ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.30 (4H, m, g,g',k,k'), 7.35–7.25 (4H, m, i,l,l',m), 7.13 (2H, d, J = 6.4 Hz, h,h'), 5.79 (2H, s c,c'), 5.69 (1H, br s, NH), 4.41 (2H, d, J = 5.8 Hz, e), 3.37 (2H, dd, J = 14.3 Hz, b,b'), 2.85 (2H, d, J = 14.4 Hz, b,b'); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.35 (d), 144.97 (f), 138.57 (j), 128.81 (c,c'), 128.75 (k,k'), 128.59 (l,l'), 127.37 (h,h'), 127.28 (m), 126.95 (g,g'), 126.74 (i), 58.44 (a), 43.83 (e), 43.80 (b,b'); IR (neat) 3393, 3351 (N-H stretch), 3057, 3029, 1637 (C=O stretch), 1518 (N-H bend), 1497, 1446, 1027, 1005, 718 cm^{-1}. HRMS (ESI) calcd. for $C_{19}H_{19}NaNO$ (M+Na): 300.1364, found 300.1364 *m/z*.



5e

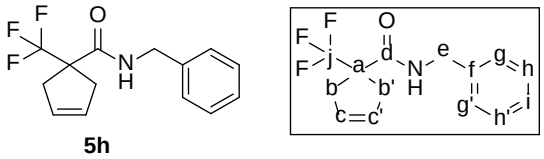
3-cyclopentenecarboxylic acid benzyl amide (5e). Using the general procedure with carboxylic acid **28** (562 mg, 5.0 mmol), oxalyl chloride (1.72 mL, 4.0 equiv, 20 mmol), triethyl amine (1.4 mL, 2.0 equiv, 10.0 mmol), and benzylamine (0.82 mL, 1.5 equiv, 7.5 mmol) affords, after flash chromatography on silica gel (85–70:15–30 hexanes:ethyl acetate), the title compound (684 mg, 68%, 2 steps) as a white solid: mp 103.5–105.5 ºC; TLC analysis R_f 0.35 (70:30 hexanes:ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.30 (2H, m, h,h'), 7.35–7.25 (2H, m, g,g',i), 5.94 (1H, br s, NH), 5.70 (2H, s, c,c'), 4.46 (2H, d, J = 5.7 Hz, e), 3.05–2.95 (1H, m, a), 2.75–2.60 (4H, m, b,b'); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.82 (d), 138.55 (f), 129.26 (c,c'), 128.71 (h,h'), 127.75 (g,g'), 127.46 (i),

43.62 (e), 43.51 (a), 37.02 (b,b'); IR (neat) 3271 (N-H stretch), 3054, 2898, 2837, 1635 (C=O stretch), 1551 (C=C stretch), 1497 (N-H bend), 1454, 1449, 1389, 1033, 746, 693 cm^{-1}. HRMS (ESI) calcd. for $C_{13}H_{15}NaNO$ (M+Na): 224.1051, found 224.1059 *m/z*.



5f

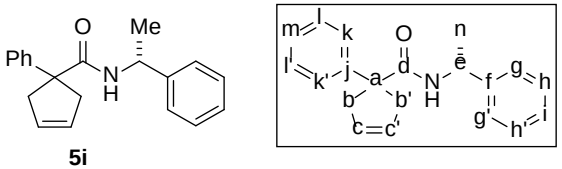
1-methyl-3-cyclopentenecarboxylic acid benzyl amide (5f). Using the general procedure with carboxylic acid **29** (632 mg, 5.0 mmol), oxalyl chloride (1.72 mL, 4.0 equiv, 20 mmol), triethyl amine (1.4 mL, 2.0 equiv, 10.0 mmol), and benzylamine (0.82 mL, 1.5 equiv, 7.5 mmol) affords, after flash chromatography on silica gel (85–70:15–30 hexanes:ethyl acetate), the title compound (667 mg, 62%, 2 steps) as a white solid: mp 72.5–74.5 ºC; TLC analysis R_f 0.40 (70:30 hexanes:ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40–7.30 (2H, m, h,h'), 7.35–7.25 (2H, m, g,g',i), 5.91 (1H, br s, NH), 5.68 (2H, s, c,c'), 4.48 (2H, d, *J* = 5.7 Hz, e), 2.89 (2H, d, *J* = 14.4 Hz, b,b'), 2.29 (2H, d, *J* = 14.7 Hz, b,b'), 1.35 (3H, s, j); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.27 (d), 138.70 (f), 128.89 (c,c'), 128.72 (h,h'), 127.64 (g,g'), 127.43 (i), 48.17 (a), 45.12 (b,b'), 43.69 (e), 26.33 (j); IR (neat) 3369 (N-H stretch), 3305, 2916, 1637 (C=O stretch), 1528 (N-H bend), 1414, 1289, 1235, 948, 714 cm^{-1}. HRMS (ESI) calcd. for $C_{14}H_{17}NaNO$ (M+Na): 238.1208, found 238.1218 *m/z*.



5h

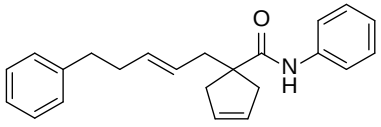
1-(trifluoromethyl)-3-cyclopentenecarboxylic acid benzyl amide (5h). Using the general procedure with carboxylic ester **38** (1.36 g, 5.0 mmol), oxalyl chloride (1.72 mL, 4.0 equiv, 20 mmol), triethyl amine (1.4 mL, 2.0 equiv, 10.0 mmol), and benzylamine (0.82 mL, 1.5 equiv, 7.5 mmol) affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (702 mg,

52%, 3 steps) as a white solid: mp 77.5–78.5 ºC; TLC analysis R_f 0.5 (70:30 hexanes:ethyl acetate); ^{19}F NMR (282 MHz, $CDCl_3$) δ -72.11 (s, CF_3); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45–7.20 (5H, m, g,g',h,h',i), 6.21 (1H, br s, NH), 5.68 (2H, s, c,c'), 4.51 (2H, d, *J* = 5.6 Hz, e), 3.12 (2H, d, *J* = 15.6 Hz, b,b'), 2.88 (2H, d, *J* = 15.4 Hz, b,b'); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.04 (d), 137.72 (f), 128.82 (c,c'), 127.90 (h,h'), 127.67 (i), 127.53 (g,g'), 127.33 (q, *J* = 278.7, j), 57.28 (q, J = 24.6, a), 44.20 (e), 38.91 (b,b'); IR (neat) 3338 (N-H stretch), 3030, 2922, 1660 (C=O stretch), 1533 (C=C stretch), 1496 (N-H bend), 1419, 1302, 1127 (C-N stretch), 954, 712, 697, 655 cm^{-1}. HRMS (ESI) calcd. for $C_{14}H_{14}F_3NaNO$ (M+Na): 292.0925, found 292.0923 *m/z*.

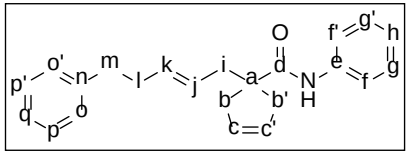


5i

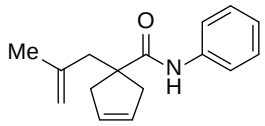
***(R)*-1-phenyl-*N*-(1-phenylethyl)cyclopent-3-ene-1-carboxamide (5i).** Using the general procedure with *(R)*-(+)-α-methylbenzylamine (1.5 mL, 1.5 equiv, 11.7 mmol) affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (1.67 g, 70%, 3 steps) as a white solid: mp 73.5–75.5 ºC; TLC analysis R_f 0.6 (70:30 hexanes:ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45–7.20 (8H, m, h,h',i,k,k',l,l',m), 7.14 (2H, t, *J* = 6.7 Hz, g,g'), 5.76 (2H, s c,c'), 5.44 (1H, br s, NH), 5.20–5.05 (1H, m, e), 3.32 (2H, dd, *J* = 16.6 and 10.5 Hz, b,b'), 2.81 (2H, dd, *J* = 15.9 and 14.8 Hz, b,b'), 1.38 (3H, d, *J* = 6.9 Hz, n); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.46 (d), 145.11 (j), 143.35 (f), 128.76 and 128.66 (c,c'), 128.69 (k,k'), 128.52 (l,l'), 127.12 (h,h'), 126.89 (m), 126.64 (i), 125.90 (g,g'), 58.25 (a), 48.93 (e), 43.87 and 43.79 (b,b'), 21.60 (n); IR (neat) 3290 (N-H stretch), 3053, 1644 (C=O stretch), 1623 (C=C stretch), 1526 (N-H bend), 1493, 1444, 741, 695, 662 cm^{-1}. HRMS (ESI) calcd. for $C_{20}H_{21}NaNO$ (M+Na): 314.1521, found 314.1510 *m/z*.



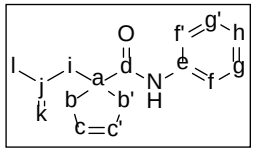
5k



(*E*)-1-(5-phenyl-2-pentenyl)-3-cyclopentenecarboxylic acid phenyl amide (5k). Using the general procedure with carboxylic acid **30** (1.40 g, 5.46 mmol), oxalyl chloride (1.88 mL, 4.0 equiv, 21.8 mmol), triethyl amine (1.53 mL, 2.0 equiv, 10.9 mmol), and aniline (0.77 mL, 1.5 equiv, 8.2 mmol) affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (1.36 g, 75%, 2 steps) as a light yellow solid: mp 82.5–83.0 ºC; TLC analysis R_f 0.7 (70:30 hexanes:ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (2H, dd, *J* = 8.7 and 1.2 Hz, f,f'), 7.40–7.25 (4H, m, g,g',p,p'), 7.27 (1H, br s, NH), 7.25–7.15 (3H, m, o,o',q), 7.14 (1H, t, *J* = 7.4 Hz, h), 5.73 (2H, s, c,c'), 5.65–5.45 (2H, m, j,k), 2.85 (2H, d, *J* = 14.4 Hz, b,b'), 2.70 (2H, t, *J* = 7.3 Hz, m), 2.50–2.40 (4H, m, b,b',i), 2.40–2.35 (2H, m, l); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.54 (d), 141.85 (n), 138.15 (e), 133.74 (k), 129.13 (c,c'), 128.97 (g,g'), 128.51 (p,p'), 128.31 (o,o'), 126.44 (j), 125.82 (q), 124.15 (h), 120.03 (f), 53.00 (a), 42.38 (i), 42.16 (b,b'), 35.87 (m), 34.40 (l); IR (neat) 3329 (N-H stretch), 3060, 2916, 2844, 1659 (C=O stretch), 1598 (C=C stretch), 1529 (N-H bend), 1497, 1436, 1309, 1233, 976, 951, 755, 692, 677 cm^{-1}. HRMS (ESI) calcd. for $C_{23}H_{25}NaNO$ (M+Na): 354.1834, found 354.1833 *m/z*.



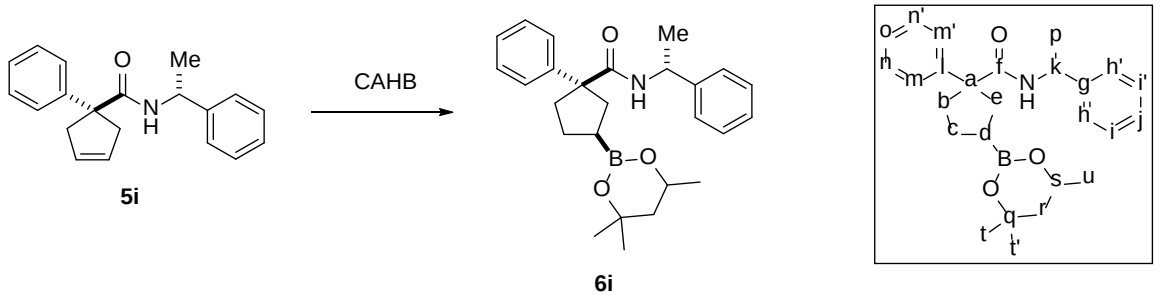
5l



1-(2-methylallyl)-3-cyclopentenecarboxylic acid phenyl amide (5l). Using the general procedure with carboxylic acid **31** (454 mg, 2.73 mmol), oxalyl chloride (0.94 mL, 4.0 equiv, 10.9 mmol), triethyl amine (0.77 mL, 2.0 equiv, 5.45 mmol), and aniline (0.39 mL, 1.5 equiv, 4.1 mmol) affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (468 mg, 71%, 2 steps) as an off-white solid: mp 109.0–110.0 ºC; TLC analysis R_f 0.7 (70:30 hexanes:ethyl acetate); ^{1}H NMR (400 MHz,

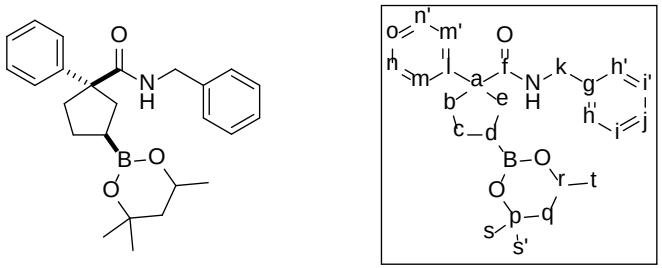
$CDCl_3$) δ 7.51 (2H, d, *J* = 7.6 Hz, f,f'), 7.40–7.30 (3H, m, g,g',NH), 7.12 (1H, t, *J* = 7.4 Hz, h), 5.74 (2H, s, c,c'), 4.92 (1H, s, k), 4.75 (1H, s, k), 2.95 (2H, d, *J* = 14.5 Hz, b,b'), 2.60–2.50 (4H, m, b,b',i), 1.76 (3H, s, l); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.37 (d), 142.51 (j), 138.12 (e), 129.01 (c,c'), 128.97 (g,g'), 124.17 (h), 120.01 (f,f'), 114.21 (k), 52.90 (a), 46.78 (i), 42.99 (b,b'), 23.84 (l); IR (neat) 3240 (N-H stretch), 3066, 2925, 1646 (C=O stretch), 1597 (C=C stretch), 1531 (N-H bend), 1485, 1438, 951, 749, 729, 690, 661 cm^{-1}. HRMS (ESI) calcd. for $C_{16}H_{19}NaNO$ (M+Na): 264.1364, found 264.1357 *m/z*.

General procedure for CAHB of *γ,δ*-unsaturated amides without subsequent oxidation.



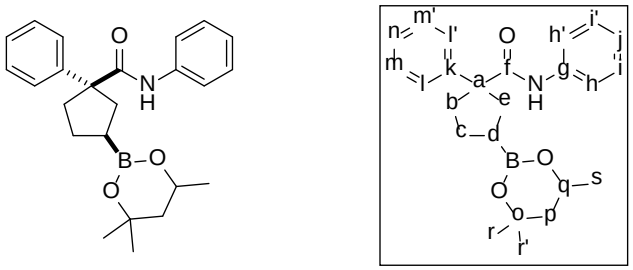
Preparation of (1*R*,3*S*)-1-phenyl-*N*-((*R*)-1-phenylethyl)-3-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)cyclopentane-1-carboxamide (6i). To a yellow solution of $Rh(nbd)_2BF_4$ (3.9 mg, 0.011 mmol) and (*R*,*R*)-(BINOL)PN(Bn)Ph **L1b** (10.5 mg, 0.021 mmol) in THF (2.0 mL) was added *γ,δ*-unsaturated amide **5i** (154 mg, 0.528 mmol) as a solution in THF (2.0 mL). To the resulting solution was slowly added (i.e., dropwise over the course of 0.5 h) a solution of 4,4,6-trimethyl-1,3,2-dioxaborinane (tmdBH, **B1**, 134 mg, 1.10 mmol) in THF (1.0 mL). The mixture was then stirred at 40 ^{o}C for 20 h. Afterwards, the reaction was concentrated under reduced pressure and purified via flash chromatography on silica gel (90:10 hexanes:ethyl acetate) to afford the title compound (173.1 mg, 78%) as a yellow oil: TLC analysis R_f 0.7 (70:30 hexanes:ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.20 (8H, m, f,g,h,h',i,i',j,m,m',n,n'), 7.15–7.05 (2H, m, j,o), 5.47 (1H, dd, *J* = 11.2 and 1.9 Hz, NH), 5.15–5.00 (1H, m, k), 4.20–4.00 (1H, m, s), 2.50–2.30 (2H, m, b,e), 2.30–2.05 (2H, m, b,e), 1.85–1.70 (3H, m, c,r), 1.50–1.40 (1H, m, r), 1.34 (3H, dd, *J* = 6.8 and 4.0 Hz, p), 1.25 (6H, s, t,t'), 1.23 (3H, d, *J* = 6.2 Hz, u), 1.30–1.20 (1H, m, d); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.96 and 175.89 (f), 144.22 and 144.05

(l), 143.58 and 143.57 (g), 128.51 and 128.48 (i,i'), 128.42 (n,n'), 127.04 and 127.02 (h,h'), 126.95 (m,m'), 126.68 and 126.64 (j), 125.90 and 125.86 (o), 70.40 (q), 64.58 and 64.54 (s), 60.10 and 60.06 (a), 48.55 (k), 45.92 and 45.88 (r), 39.33 and 39.04 (b), 37.60 and 37.49 (e), 31.26 and 31.23 (t,t'), 28.07 and 28.03 (d), 26.55 (c), 23.23 and 23.19 (u), 21.75 and 21.69 (p); IR (neat) 3345 (N-H stretch), 2970, 2932, 1649 (C=O stretch), 1600 (N-H bend), 1493 (C=C stretch, aromatic), 1446, 1300 (C-O stretch), 1207, 765, 697 cm^{-1}.



6g

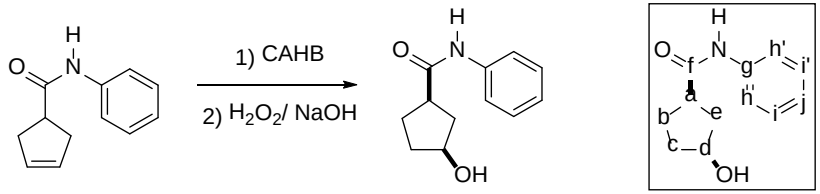
(1*R*,3*S*)-1-phenyl-3-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)-1-cyclopentanecarboxylic acid benzyl amide (6g). Using the general procedure for CAHB of *γ,δ*-unsaturated amides without subsequent oxidation [$Rh(nbd)_2BF_4$ (2.0 mg, 0.0053 mmol) and (*R*,*R*)-(BINOL)PN(Bn)Ph **L1b** (5.3 mg, 0.011 mmol)], CAHB of *γ,δ*-unsaturated amide **5g** (146.5 mg, 0.528 mmol) affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (154.2 mg, 72%) as a yellow oil: TLC analysis R_f 0.6 (70:30 hexanes:ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.35 (2H, m, m,m'), 7.35–7.30 (2H, m, i,i'), 7.30–7.20 (2H, m, j,n,n',o), 7.15–7.05 (2H, m, h,h'), 5.70 (1H, d, *J* = 31.3 Hz, NH), 4.50–4.30 (2H, m, k), 4.20–3.95 (1H, m, r), 2.55–2.40 (2H, m, b,e), 2.30–2.10 (2H, m, b,e), 1.85–1.70 (3H, m, c,q), 1.44 (1H, dd, *J* = 13.8 and 11.7 Hz, q), 1.26 (6H, s, s,s'), 1.23 (3H, dd, *J* = 6.2 and 6.2 Hz, t), 1.35–1.15 (1H, m, d); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.77 and 176.71 (f), 144.13 and 144.04 (l), 138.83 and 138.82 (g), 128.54 (i,i'), 128.51 (n,n'), 127.31 and 127.25 (h,h'), 127.13 and 127.12 (m,m'), 127.07 and 127.06 (j), 126.70 and 126.68 (o), 70.50 and 70.47 (p), 64.64 and 64.59 (r), 60.18 and 60.15 (a), 45.92 and 45.87 (q), 43.57 and 43.52 (k), 39.17 and 39.03 (b), 37.65 and 37.61 (e), 31.26 and 31.24 (s,s'), 28.09 and 28.05 (d), 26.54 and 26.52 (c), 23.21 and 23.20 (t); IR (neat) 3339 (N-H stretch), 2970, 1645 (C=O stretch), 1600 (N-H bend), 1512 (C=C stretch, aromatic), 1300 (C-O stretch), 1207, 724, 696 cm^{-1}.



6c

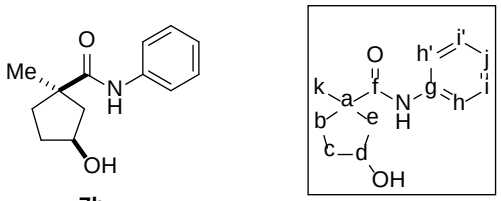
(1*R*,3*S*)-1-phenyl-3-(4,4,6-trimethyl-1,3,2-dioxaborinan-2-yl)-1-cyclopentanecarboxylic acid phenyl amide (6c). Using the general procedure for CAHB of *γ,δ*-unsaturated amides without subsequent oxidation [$Rh(nbd)_2BF_4$ (2.0 mg, 0.0053 mmol) and (*R*,*R*)-(BINOL)PN(Bn)Ph **L1b** (5.3 mg, 0.011 mmol)], CAHB of *γ,δ*-unsaturated amide **5c (**139.2 mg, 0.528 mmol) affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (151 mg, 73%) as a light yellow solid: mp 112.5–114.0 ºC; TLC analysis R_f 0.75 (70:30 hexanes:ethyl acetate); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (1H, d, *J* = 7.4 Hz, l,l'), 7.45–7.35 (4H, m, h,h',m,m'), 7.35–7.20 (2H, m, i,i',j), 7.05 (1H, t, *J* = 7.4 Hz, n), 6.92 (1H, d, *J* = 18.6 Hz, NH), 4.25–4.10 (2H, m, q), 2.60–2.45 (2H, m, b,e), 2.40–2.25 (2H, m, b), 2.20–2.10 (2H, m, e), 1.95–1.80 (3H, m, c), 1.76 (1H, dd, *J* = 13.9 and 3.0 Hz, p), 1.46 (1H, dd, *J* = 12.5 and 12.5 Hz, p), 1.40–1.30 (1H, m, d), 1.27 (6H, d, *J* = 3.9 Hz, r,r'), 1.24 (3H, dd, *J* = 6.2 and 4.1 Hz, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.95 and 174.91 (f), 143.63 and 143.57 (k), 138.33 and 138.30 (g), 128.84 (i,i'), 128.79 (m,m'), 127.04 (j), 127.03 (l,l'), 123.87 and 123.85 (n), 119.60 and 119.55 (h,h'), 70.52 and 70.50 (o), 64.69 and 64.62 (q), 61.03 and 61.02 (a), 45.93 and 45.89 (p), 39.40 and 39.31 (b), 37.67 (e), 31.27 and 31.24 (r,r'), 28.10 and 28.07 (d), 26.60 and 26.53 (c), 23.20 and 23.18 (s); IR (neat) 3408 (N-H stretch), 2971, 1677 (C=O stretch), 1596 (N-H bend), 1519, 1493, 1436, 1303 (C-O stretch), 1208 (C-N stretch), 1163, 700, 690 cm^{-1}.

General procedure for CAHB-oxidation sequence with H_2O_2.



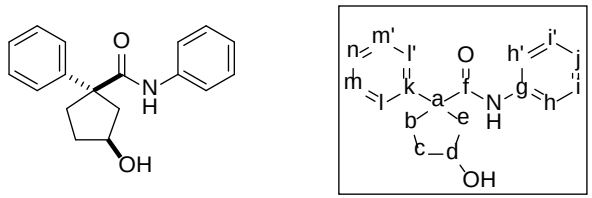
5a **7a**

Preparation of (1*R*,3*S*)-3-hydroxycyclopentanecarboxylic acid phenyl amide (7a). After the CAHB [using general CAHB procedure of *γ,δ*-unsaturated amides without subsequent oxidation with $Rh(nbd)_2BF_4$ (2.0 mg, 0.0053 mmol) and (*R*,*R*)-(BINOL)PN(Bn)Ph **L1b** (5.3 mg, 0.011 mmol)] of **5a** (99.1 mg, 0.528 mmol), the resultant mixture was diluted with THF (10 mL) followed by addition of methanol (8 mL), sodium hydroxide (6 mL of a 3.0 M soln.), and the slow addition of H_2O_2 (1.0 mL of a 30% solution). The resulting mixture stirred (2 h) and then extracted with dichloromethane (3 x 15 mL). The combined organic extracts were dried (anhyd. Na_2SO_4) and concentrated under reduced pressure. Flash chromatography on silica gel (80–40:20–60 hexanes:ethyl acetate) affords the title compound (86.7 mg, 80%) as a white solid: mp 100.5–102.5 ºC; TLC analysis R_f 0.4 (50:50 hexanes:ethyl acetate); $[\alpha]_D^{20}$ = -14º (*c* 1.0, $CHCl_3$); Chiral HPLC analysis (Chiralpak-IC, 80:20 hexanes:isopropanol, flow rate = 1.0 mL/min) showed peaks at 56 minutes (3.0% (1*S*,3*R*)) and 64 minutes (97.0% (1*R*,3*S*); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (1H, br s, NH), 7.54 (2H, d, *J* = 7.9 Hz, h,h'), 7.31 (2H, t, *J* = 7.8 Hz, i,i'), 7.11 (1H, t, *J* = 7.3 Hz, j), 4.56 (1H, d, *J* = 6.6 Hz, d), 4.40 (1H, br s, OH), 3.05–2.90 (1H, m, a), 2.20–1.90 (5H, m, b,c,e), 1.80–1.65 (1H, m, c); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.41 (f), 138.18 (a), 128.93 (i,i'), 124.32 (j), 120.11 (h,h'), 73.89 (d), 45.28 (a), 38.94 (e), 36.50 (b), 29.20 (c); IR (neat) 3677 (N-H stretch, O-H stretch), 2907, 2803, 1728 (C=O stretch), 1663, 1597 (N-H bend), 1565, 1389 (C-N stretch), 1238 (C-OH bend), 1050 (C-OH stretch) cm^{-1}; HRMS (ESI) calcd. for $C_{12}H_{15}NNaO_2$ (M+Na): 228.1000, found 228.1002 *m/z*.



7b

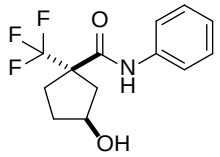
(*1R*, 3*S*)-3-hydroxy-1-methylcyclopentanecarboxylic acid phenyl amide (7b). Using the general procedure for CAHB-oxidation sequence with H_2O_2, CAHB of *γ,δ*-unsaturated amide **5b** (106.4 mg, 0.528 mmol) affords, after flash chromatography on silica gel (85:15 dichloromethane:ethyl acetate), the title compound (76.2 mg, 65 %) as a white solid: mp 91.0–93.5 ºC; TLC analysis R_f 0.5 (80:20 dichloromethane:ethyl acetate); $[\alpha]_D^{20}$ = -13º (*c* 0.7, $CHCl_3$); Chiral HPLC analysis (Chiralcel-OD, 90:10 hexanes:isopropanol, flow rate = 1.3 mL/min) showed peaks at 87 minutes (96.0% (1*R*,3*S*)) and 105 minutes (4.0% (1*S*,3*R*)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (1H, br s, NH), 7.54 (2H, d, *J* = 7.6 Hz, h,h'), 7.31 (2H, t, *J* = 7.5 Hz, i,i'), 7.08 (1H, t, *J* = 7.4 Hz, j), 4.55 (1H, s, d), 3.44 (1H, br s, OH), 2.40 (1H, ddd, *J* = 18.8 Hz, 10.9 Hz, 7.9 Hz, b), 2.31 (1H, dd, *J* = 14.9 Hz, 1.6 Hz, e), 2.00–1.85 (2H, m, c), 1.80–1.70 (2H, m, b,e), 1.37 (3H, s, k); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.32 (f), 138.78 (g), 128.88 (i,i'), 123.78 (j), 119.64 (h,h'), 75.18 (d), 48.98 (a), 47.64 (e), 38.52 (b), 36.03 (c), 25.91 (k); IR (neat) 3318 (O-H stretch, N-H stretch), 2962, 2901, 1663 (C=O stretch), 1536 (C-OH bend), 1495, 1434, 1311 (C-N stretch), 657 cm^{-1}; HRMS (CI) calcd. for $C_{13}H_{18}NO_2$ (M+H): 220.1338, found 220.1346 *m/z*.



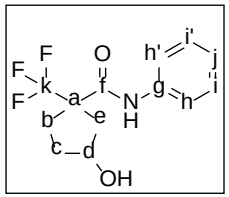
7c

(*1R*, 3*S*)-3-hydroxy-1-phenylcyclopentanecarboxylic acid phenyl amide (7c). Using the general procedure for CAHB-oxidation sequence with H_2O_2, CAHB of *γ,δ*-unsaturated amide **5c** (139.2 mg, 0.528 mmol) affords, after flash chromatography on silica gel (85:15 dichloromethane:ethyl acetate), the title compound (106.7 mg, 72 %) as a white solid: mp 113.5–114.5 ºC; TLC analysis R_f 0.5

(80:20 dichloromethane:ethyl acetate); $[\alpha]_D^{20}$ = -43° (*c* 0.8, $CHCl_3$); Chiral HPLC analysis (Chiralcel-OD, 60:40 hexanes:isopropanol, flowrate = 1.4 mL/min) showed peaks at 14 minutes (96.0% (1*R*,3*S*)) and 22 minutes (4.0% (1*S*,3*R*)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50–7.40 (4H, m, h,h',i,i'), 7.40–7.35 (1H, m, j), 7.40–7.35 (4H, m, l,l',m,m'), 7.15–7.05 (2H, m, n,NH), 4.47 (2H, br s, d,OH), 2.80 (1H, d, *J* = 14.2 Hz, e), 2.75–2.60 (1H, m, b), 2.40–2.30 (1H, m, b), 2.30–2.20 (2H, m, c,e), 2.00–1.90 (1H, m, c); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.02 (f), 143.60 (k), 137.42 (g), 129.34 (i,i'), 128.96 (m,m'), 127.81 (j), 127.19 (l,l'), 124.74 (n), 120.15 (h,h'), 73.01 (d), 59.39 (a), 47.12 (e), 36.33 (b), 36.01 (c); IR (neat) 3492 (O-H stretch), 3400 (N-H stretch), 2896, 1668 (C=O stretch), 1596 (C-=C stretch), 1522 (C-OH bend), 1492, 1437, 1311 (C-N stretch), 1033, 751, 733, 691 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{19}NNaO_2$ (M+Na): 304.1313, found 304.1299 *m/z*.

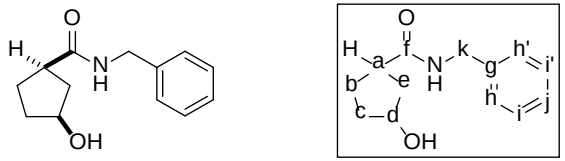


7d



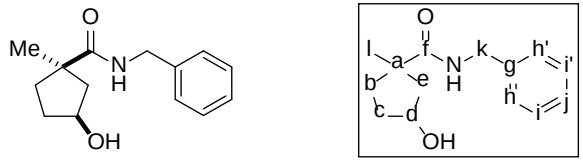
***(1S,* 3*S*)-3-hydroxy-1-(trifluoromethyl)cyclopentanecarboxylic acid phenyl amide (7d).** Using the general procedure for CAHB-oxidation sequence with H_2O_2, CAHB of *γ,δ*-unsaturated amide **5d** (135.2 mg, 0.528 mmol) affords, after flash chromatography on silica gel (90:10 dichloromethane:ethyl acetate), the title compound (111.9 mg, 78 %) as a white solid: mp 129.0–130.5 ºC; TLC analysis R_f 0.75 (80:20 dichloromethane:ethyl acetate); $[\alpha]_D^{20}$ = -22° (*c* 1.3, $CHCl_3$); Chiral HPLC analysis (Chiralpak-IC with OD guard column, 80:20 hexanes:isopropanol, flowrate = 1.0 mL/min) showed peaks at 14 minutes (97.0% (1*S*,3*S*)) and 21 minutes (3.0% (1*R*,3*R*)); ^{19}F NMR (282 MHz, $CDCl_3$) δ -71.94; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.53 (1H, br s, NH), 7.49 (2H, d, *J* = 7.6 Hz, h,h'), 7.30 (2H, t, *J* = 7.5 Hz, i,i'), 7.11 (1H, t, *J* = 7.4 Hz, j), 4.65 (1H, s, d), 3.88 (1H, br s, OH), 2.55–2.25 (4H, m, b,e), 2.10–1.95 (1H, m, c), 1.95–1.80 (1H, m, c); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.51 (f), 137.92 (g), 128.95 (i,i'), 127.3 (q, *J* = 279 Hz, k), 124.52 (j), 120.00 (h,h'), 74.16 (d), 58.58 (q, *J* = 24 Hz, a), 40.88 (e), 36.20 (c), 32.21 (b); IR (neat) 3416 (O-H stretch), 3263 (N-H stretch),

3089, 2376, 1669 (C=O stretch), 1624, 1599 (C-=C stretch), 1567 (C-OH bend), 1450, 1157, 1131, 752, 692, 653 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{14}F_3NNaO_2$ (M+Na): 296.0874, found 296.0870 *m/z*.



7e

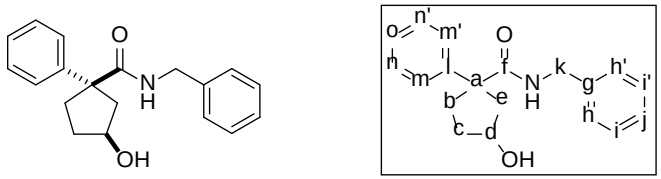
(1*R*,3*S*)-3-hydroxycyclopentanecarboxylic acid benzyl amide (7e). Using the general procedure for CAHB-oxidation sequence with H_2O_2, CAHB of *γ,δ*-unsaturated amide **5e** (106.3 mg, 0.528 mmol) affords, after flash chromatography on silica gel (80–30:20–70 hexanes:ethyl acetate), the title compound (80.0 mg, 69 %) as a white solid: mp 115.5–116.0 ºC; TLC analysis R_f 0.3 (20:80 hexanes:ethyl acetate); $[\alpha]_D^{20}$ = -12º (*c* 1.4, $CHCl_3$); chiral HPLC analysis determined by converting to the corresponding phenyl amide **7a** using boric acid-catalyzed transamidation;[6] Chiralpak-IC, 80:20 hexanes:isopropanol, flow rate = 1.4 mL/min, showed peaks at 40 minutes (6.0% (1*S*,3*R*)) and 45 minutes (94.0% (1*R*,3*S*)). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.20 (5H, m, h,h',i,i',j), 6.27 (1H, br s, NH), 4.45 (2H, d, *J* = 5.7 Hz, k), 4.40–4.25 (2H, m, d,OH), 2.85–2.70 (1H, m, a), 2.20–1.80 (5H, m, b,c,e), 1.80–1.60 (1H, m, c); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.42 (f), 138.02 (g), 128.78 (i,i'), 127.74 (h,h'), 127.61 (j), 73.65 (d), 44.09 (a), 43.87 (k), 38.99 (e), 36.56 (c), 28.93 (b); IR (neat) 3259 (O-H stretch), 3085 (N-H stretch), 2937, 1634 (C=O stretch), 1573, 1551 (C=C stretch), 1233, 1001, 752, 727, 700 cm^{-1}; HRMS (ESI) calcd. for $C_{13}H_{17}NaNO_2$ (M+Na): 242.1157, found 242.1153 *m/z*.



7f

(*1R,* 3*S*)-3-hydroxy-1-methylcyclopentanecarboxylic acid benzyl amide (7f). Using the general procedure for CAHB-oxidation sequence with H_2O_2, CAHB of *γ,δ*-unsaturated amide **5f** (114.0 mg, 0.528 mmol) affords, after flash chromatography on silica gel (85:15 dichloromethane:ethyl acetate), the title compound (76.4 mg, 62 %) as a colorless oil: TLC analysis R_f 0.4 (80:20

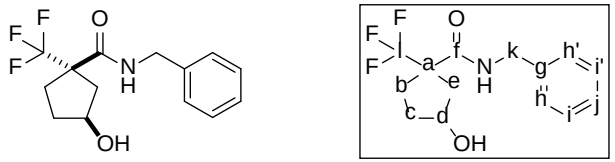
dichloromethane:ethyl acetate); $[\alpha]_D^{20}$ = -12° (*c* 1.6, $CHCl_3$); chiral HPLC analysis determined by converting to the corresponding phenyl amide **7b** using boric acid-catalyzed transamidation;[6] Chiral HPLC analysis (Chiralcel-OD, 90:10 hexanes:isopropanol, flow rate = 1.3 mL/min) showed peaks at 87 minutes (92.0% (1*R*,3*S*)) and 105 minutes (8.0% (1*S*,3*R*)); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40–7.20 (5H, m, h,h',i,i',j), 6.60 (1H, br s, NH), 4.47 (2H, d, *J* = 5.6 Hz, k), 4.45–4.35 (1H, m, d), 4.00 (1H, d, *J* = 7.2 Hz, OH), 2.40–2.15 (2H, m, b,e), 1.95–1.80 (2H, m, c), 1.75–1.60 (2H, m, b,e), 1.32 (3H, s, l); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.08 (f), 138.35 (g), 128.74 (i,i'), 127.61 (j), 127.47 (h,h'), 74.59 (d), 48.18 (e), 47.81 (a), 43.89 (k), 38.29 (b), 36.21 (c), 25.66 (l); IR (neat) 3299 (O-H stretch, N-H stretch), 2958, 1636 (C=O stretch), 1535 (C-=C stretch), 1453 (C-OH bend), 1227, 1190, 961, 721, 696 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{19}NaNO_2$ (M+Na): 256.1313, found 256.1325 *m/z*.



7g

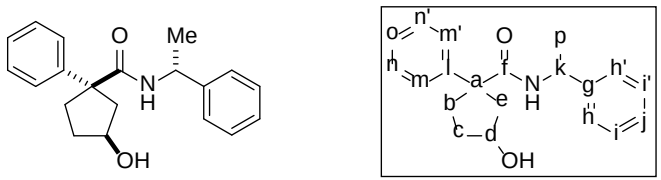
(*1R*, 3*S*)-3-hydroxy-1-phenylcyclopentanecarboxylic acid benzyl amide (7g). Using the general procedure for CAHB-oxidation sequence with H_2O_2, CAHB of *γ,δ*-unsaturated amide **5g** (146.5 mg, 0.528 mmol) affords, after flash chromatography on silica gel (85:15 dichloromethane:ethyl acetate), the title compound (109.3 mg, 70 %) as a white solid: mp 91.0–93.5 ºC; TLC analysis R_f 0.4 (80:20 dichloromethane:ethyl acetate); $[\alpha]_D^{20}$ = -45° (*c* 1.3, $CHCl_3$); Chiral HPLC analysis (Chiralpak-AD, 70:30 hexanes:isopropanol, flowrate = 1.0 mL/min) showed peaks at 15 minutes (93.0% (1*R*,3*S*)) and 20 minutes (7.0% (1*S*,3*R*)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.30 (4H, m, i,i',n,n'), 7.35–7.25 (4H, m, h,h',j,o), 7.08 (2H, d, *J* = 6.5 Hz, m,m'), 5.61 (2H, br s, NH), 4.70 (1H, d, *J* = 10.1 Hz, OH), 4.45–4.35 (2H, m, d,k), 4.33 (1H, dd, *J* = 15.2 and 5.8 Hz, k), 2.75 (1H, dd, *J* = 14.1 and 1.3 Hz, e), 2.65–2.55 (1H, m, b), 2.35–2.25 (1H, m, b), 2.25–2.10 (1H, m, c,e), 2.00–1.90 (1H, m, c); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.88 (f), 143.95 (l), 137.96 (g), 129.11 (i,i'), 128.67 (n,n'), 127.52 (h,h'), 127.41 (j), 127.17 (o), 127.01 (m,m'), 73.02 (d), 58.46 (a), 47.14 (e), 43.81 (k), 36.35 (b),

36.11 (c); IR (neat) 3316 (O-H stretch, N-H stretch), 1638 (C=O stretch), 1532 (C-OH bend), 1494, 1450, 1282, 1062, 1027, 992, 743, 719, 697, 662 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{21}NaNO_2$ (M+Na): 318.1470, found 318.1456 *m/z*.



7h

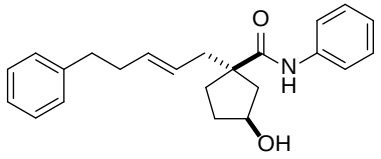
(*1S*, 3*S*)-3-hydroxy-1-(trifluoromethyl)cyclopentanecarboxylic acid benzyl amide (7h). Using the general procedure for CAHB-oxidation sequence with H_2O_2, CAHB of *γ,δ*-unsaturated amide **5h** (142.2 mg, 0.528 mmol) affords, after flash chromatography on silica gel (85:15 dichloromethane:ethyl acetate), the title compound (107.8 mg, 71 %) as a white solid: mp 100.5–102.0 ºC; TLC analysis R_f 0.5 (80:20 dichloromethane:ethyl acetate); $[\alpha]_D^{20}$ = -16º (*c* 1.3, $CHCl_3$); Chiral HPLC analysis (Chiralcel-OD, 70:30 hexanes:isopropanol, flowrate = 1.0 mL/min) showed peaks at 12 minutes (3.5% (1*R*,3*R*)) and 18 minutes (96.5% (1*S*,3*S*)); ^{19}F NMR (282 MHz, $CDCl_3$) δ -71.04 (s, CF_3); ^1H NMR (300 MHz, $CDCl_3$) δ 7.45–7.20 (5H, m, h,h',i,i',j), 7.09 (1H, br s, NH), 4.60–4.40 (3H, m, d,k), 3.71 (1H, br s, OH), 2.50–2.15 (4H, m, b,e), 2.20–1.80 (2H, m, c); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.70 (f), 137.58 (g), 129.29 (l), 128.80 (i,i'), 127.62 (j), 127.44 (h,h'), 73.57 (d), 57.96 (q, *J* = 24.5 Hz, a), 44.04 (k), 40.74 (e), 36.18 (c), 31.70 (b); IR (neat) 3421 (O-H stretch), 3311 (N-H stretch), 3269, 3084, 2944, 2360, 1657 (C=O stretch), 1526 (C-OH bend), 1455, 1362, 1301 (C-N stretch), 1169, 1123, 746, 696, 648 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{16}F_3NaNO_2$ (M+Na): 310.1031, found 310.1026 *m/z*.



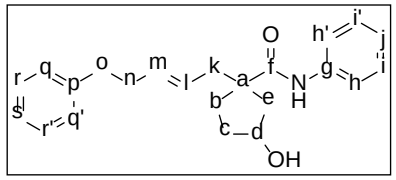
7i

(1*R*,3*S*)-3-hydroxy-1-phenyl-*N*-((R)-1-phenylethyl)cyclopentane-1-carboxamide (7i).[a] Using the general procedure for CAHB-

oxidation sequence with H_2O_2 with $Rh(nbd)_2BF_4$ (3.9 mg, 0.011 mmol) and (*R*,*R*)-(BINOL)PN(Bn)Ph **L1b** (10.5 mg, 0.021 mmol), CAHB of *γ,δ*-unsaturated amide **5i** (154.2 mg, 0.528 mmol) affords, after flash chromatography on silica gel (85:15 dichloromethane:ethyl acetate), the title compound (124.3 mg, 76 %) as a white solid: mp 98.5–99.5 ºC; TLC analysis R_f 0.5 (80:20 dichloromethane:ethyl acetate); $[\alpha]_D^{20}$ = -80º (*c* 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.35 (2H, m, i,i'), 7.35–7.30 (3H, m, j,n,n'), 7.30–7.20 (3H, m, h,h',o), 6.99 (2H, d, *J* = 7.3 Hz, m,m'), 5.47 (1H, d, *J* = 6.9 Hz, NH), 5.05–4.95 (1H, m, k), 4.62 (1H, d, *J* = 10.0 Hz, OH), 4.45–4.35 (1H, m, d), 2.67 (1H, d, *J* = 14.2 Hz, e), 2.60–2.50 (1H, m, b), 2.35–2.25 (1H, m, b), 2.25–2.15 (1H, m, c), 2.10 (1H, d, *J* = 14.1 Hz and 6.8 Hz, e), 2.20–1.85 (1H, m, c), 1.34 (2.63H, d, *J* = 6.9 Hz, p major), 1.28 (0.33H, d, *J* = 6.7 Hz, p minor) [the peaks at 1.34 and 1.28 ppm are used to determined the diastereoselectivity (88:12 major:minor]; ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.84 (f), 143.99 (l), 143.00 (g), 129.04 (i,i'), 128.56 (n,n'), 127.46 (h,h'), 127.17 (j), 127.06 (o), 125.53 (m,m'), 72.84 (d), 58.43 (a), 49.16 (k), 46.86 (e), 36.12 (b), 35.99 (c), 22.00 (p, major), 21.69 (p, minor); IR (neat) 3368 (O-H stretch, N-H stretch), 1633 (C=O stretch), 1540 (C-=C stretch), 1493, 1445, 1096, 760, 736, 695 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{23}NaNO_2$ (M+Na): 332.1626, found 332.1619 *m/z*.



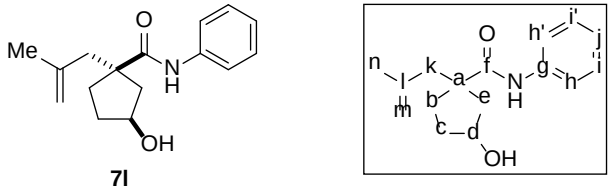
7k



(1*S*,3*S*)-3-hydroxy-1-((*E*)-5-phenylpent-2-en-1-yl)cyclopentanecarboxylic acid phenyl amide (7k). Using the general procedure for CAHB-oxidation sequence with H_2O_2 with $Rh(nbd)_2BF_4$ (3.9 mg, 0.011 mmol) and (*R*,*R*)-(BINOL)PN(Bn)Ph **L1b** (10.5 mg, 0.021 mmol), CAHB of *γ,δ*-unsaturated amide **5k** (175.0 mg, 0.528 mmol) affords, after flash chromatography on silica gel (90:10 dichloromethane:ethyl acetate), the title compound (147.9 mg, 80%) as a light yellow oil: TLC analysis R_f 0.75 (80:20

[a] The disastereoselectivity obtained using chiral ligand (*R*)-**L1b** affords an 88:12 dr; using (±)-**L1b** affords a 61:39 mixture with the same major diastereomer

dichloromethane:ethyl acetate); $[\alpha]_D^{20}$ = +17° (*c* 1.8, $CHCl_3$); Chiral HPLC analysis (Chiralpak-ASH with OD guard column, 70:30 hexanes:isopropanol, flowrate = 1.0 mL/min) showed peaks at 15 minutes (99.0% (1*S*,3*S*)) and 20 minutes (1.0% (1*R*,3*R*)); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.07 (1H, br s, NH), 7.54 (2H, d, *J* = 7.6 Hz, h,h'), 7.35–7.25 (4H, m, i,i',r,r'), 7.25–7.15 (3H, m, j,q,q'), 7.10 (1H, t, *J* = 7.4 Hz, s), 5.65–5.50 (2H, m, l,m), 4.55–4.45 (1H, m, d), 3.51 (1H, br s, OH), 2.71 (2H, t, *J* = 7.3 Hz, o), 2.61 (1H, dd, *J* = 13.9 Hz and 6.1 Hz, k), 2.45–2.35 (2H, m, b), 2.35–2.20 (2H, m, k,n), 2.12 (1H, d, *J* = 15.0 Hz, e), 1.90–1.70 (4H, m, c,e,n) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.56 (f), 141.81 (p), 138.82 (g), 133.54 (m), 128.90 (i,i'), 128.49 (r,r'), 128.31 (j), 127.18 (l), 125.81 (q,q'), 123.81(s), 119.72 (h,h'), 74.81 (d), 52.75 (a), 44.15 (e), 41.86 (k), 36.56 (n), 36.06 (c), 35.86 (o), 34.36 (b); IR (neat) 3296 (O-H stretch), 2935 (N-H stretch), 1660 (C=O stretch), 1597 (C-=C stretch), 1555 (C-OH bend), 1497, 1442, 1333, 1308 (C-N stretch), 1254, 960, 907, 752, 692 cm^{-1}; HRMS (ESI) calcd. for $C_{23}H_{27}NaNO_2$ (M+Na): 372.1939, found 372.1939 *m/z*.

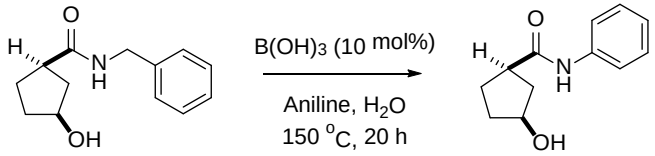


7l

(1*S*,3*S*)-3-hydroxy-1-(2-methylallyl)cyclopentanecarboxylic acid phenyl amide (7l). Using the general procedure for CAHB-oxidation sequence with H_2O_2 with $Rh(nbd)_2BF_4$ (3.9 mg, 0.011 mmol) and (*R*,*R*)-(BINOL)PN(Bn)Ph **L1b** (10.5 mg, 0.021 mmol), CAHB of *γ,δ*-unsaturated amide **5l** (127.5 mg, 0.528 mmol) affords, after flash chromatography on silica gel (90:10 dichloromethane:ethyl acetate), the title compound (102.5 mg, 75%) as a white solid: mp 76.5–78.5 ºC; TLC analysis R_f 0.6 (80:20 dichloromethane:ethyl acetate); $[\alpha]_D^{20}$ = +10° (*c* 1.7, $CHCl_3$); Chiral HPLC analysis (Chiralpak-AD, 80:20 hexanes:isopropanol, flowrate = 1.0 mL/min) showed peaks at 16 minutes (97.0% (1*S*,3*S*)) and 21 minutes (3.0% (1*R*,3*R*)); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.75 (1H, br s, NH), 7.52 (2H, d, *J* = 7.6 Hz, h,h'), 7.31 (2H, t, *J* = 7.6 Hz, i,i'), 7.10 (1H, t, *J* = 7.4 Hz, j), 4.89 (1H, s, m), 4.72 (1H, s, m), 4.55–4.45 (1H, m, d), 3.46 (1H, br s, OH), 2.93 (1H, d, *J* = 15.4 Hz, k), 2.40–2.30 (2H, m, b,e), 2.16 (1H, d, *J* = 15.4 Hz, k), 2.20–1.80 (4H, m, b,c,e), 1.76 (3H, s, n); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.01 (f), 143.01 (l), 138.57 (g), 128.90 (i,i'), 124.01 (j), 119.98

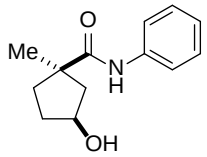
(h,h'), 113.76 (m), 74.29 (d), 52.79 (a), 47.14 (k), 44.38 (e), 38.60 (b), 35.45 (c), 23.86 (n); IR (neat) 3348 (O-H stretch), 3081 (N-H stretch), 2954, 2916, 1653 (C=O stretch), 1621, 1597 (C-=C stretch), 1556 (C-OH bend), 1499, 1442, 1352 1307 (C-N stretch), 1259, 1072, 1027, 970, 959, 891, 750, 688 cm^{-1}; HRMS (ESI) calcd. for $C_{16}H_{21}NaNO_2$ (M+Na): 282.1470, found 282.1459 *m/z*.

General procedure for boric acid-catalyzed transamidation for chiral HPLC analysis.[6]



7e **7a**

(1*R*,3*S*)-3-hydroxycyclopentanecarboxylic acid phenyl amide (7a). A mixture of benzyl amide **7e** (47.6 mg, 0.217 mmol 1.0 equiv), aniline (0.02 mL, 0.217 mmol, 1.0 equiv), water (7.9 mg, 0.434 mmol, 2.0 equiv), and boric acid (1.4 mg, 0.022 mmol, 0.1 equiv) was stirred at 150 °C for 20 h. After being cooled to room temp, the crude mixture was purified by flash chromatography on silica gel (80–40:20–60 hexanes:ethyl acetate) to afford the title compound (23.3 mg, 52%) as a white solid: TLC analysis R_f 0.4 (50:50 hexanes:ethyl acetate); Chiral HPLC analysis (Chiralpak-IC, 80:20 hexanes:isopropanol, flow rate = 1.4 mL/min) showed peaks at 40 minutes (6.0% (1*S*,3*R*)) and 45 minutes (94.0% (1*R*,3*S*)).

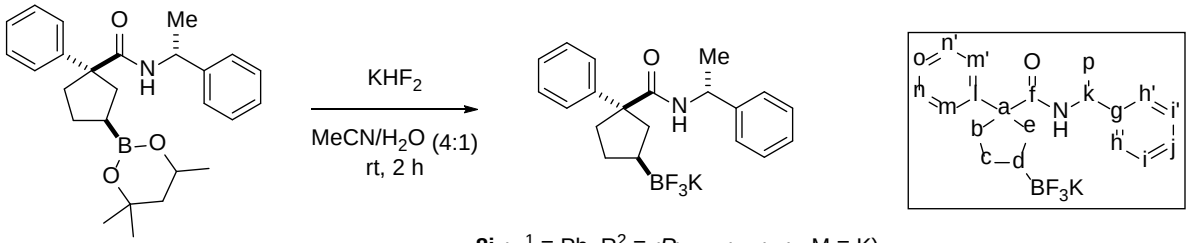


7b

(*1R*, 3*S*)-3-hydroxy-1-methylcyclopentanecarboxylic acid phenyl amide (7b). Using the general procedure for boric acid-catalyzed transamidation with benzyl amide **7f** (50.5 mg, 0.217 mmol, 1.0 equiv) affords, after flash chromatography on silica gel (85:15 dichloromethane:ethyl acetate), the title compound (22.9 mg, 48 %) as a white solid: TLC analysis R_f 0.5 (80:20

dichloromethane:ethyl acetate); Chiral HPLC analysis (Chiralcel-OD, 90:10 hexanes:isopropanol, flow rate = 1.3 mL/min) showed peaks at 87 minutes (92.0% (1*R*,3*S*)) and 105 minutes (8.0% (1*S*,3*R*)).

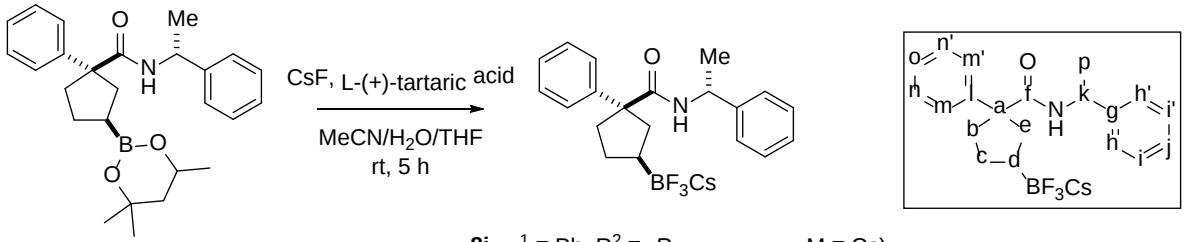
General procedure for the preparation of potassium trifluoroborate salts.[7]



6i **8i** (R^1 = Ph, R^2 = (*R*)-CH(Me)Ph, M = K)

Preparation of (1*R*,3*S*)-1-phenyl-*N*-((*R*)-1-phenylethyl)-3-(trifluoroborato)cyclopentane-1-carboxamide, potassium salt [8i (R^1 = Ph, R^2 = (*R*)-CH(Me)Ph, M = K)]**.** To a solution of *γ*-dioxaborato amide **6i** (839 mg, 2.0 mmol, 1.0 equiv) in acetonitrile (MeCN, 4.0 mL) was slowly added a solution of KHF_2 (467 mg, 6.0 mmol, 3.0 equiv) in H_2O (1.2 mL). After a 2 h stir, the reaction mixture was concentrated under reduced pressure and allowed to dry under vacuum. The resultant crude solid was extracted with acetone (2 x 5 mL) and the combined organic extracts were concentrated under reduced pressure. Diethyl ether (10.0 mL) was added to precipitate the product. Filtration affords the title compound (575 mg, 72%) as a white solid: mp 214.0–216.0 ºC; $[\alpha]_D^{20}$ = +17º (*c* 1.0, MeOH); ^{19}F NMR (282 MHz, MeOD) δ -147.27 (s, BF_3K); ^{1}H NMR (300 MHz, MeOD) δ 7.40 (2H, d, *J* = 7.5 Hz, h,h'), 7.35–7.10 (8H, m, i,i',j,m,m',n,n',o), 5.00–4.90 (1H, m, k), 2.30–2.10 (2H, m, b,e), 1.65–1.55 (2H, m, c), 1.36 (3H, d, *J* = 7.0 Hz, p), 1.05–0.85 (1H, m, d); ^{13}C NMR (75 MHz, MeOD) δ 178.16 (f), 145.39 (l), 144.11 (g), 127.86 (i,i'), 127.68 (n,n'), 126.58 (h,h'), 126.29 (m,m'), 125.69 (j), 125.61 (o), 60.20 (a), 48.86 (k), 38.82 (b), 37.25 (e), 26.24 (c), 20.78 (p); IR (neat) 3438 (N-H stretch), 2941, 2867, 1662 (C=O stretch), 1500 (N-H bend), 1461, 1446, 1320 (C-N stretch), 1172, 997, 958, 890, 696 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{22}BF_3NO$ (M-K): 360.1747, found 360.1761 *m/z*. The salt was recrystallized (3:1 Et_2O/ MeOH) to give off-white single crystals, and an X-ray crystal structure was obtained.

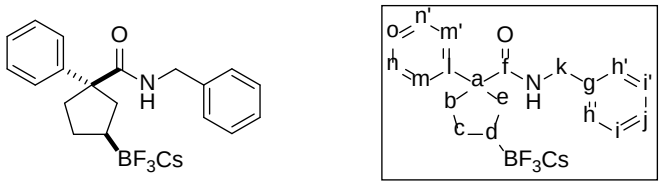
General procedure for the preparation of cesium trifluoroborate salts.[8]



6i

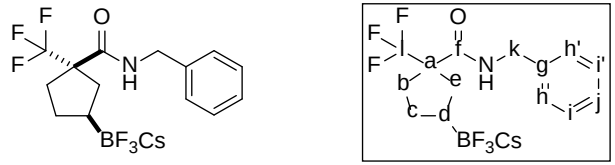
8i (R^1 = Ph, R^2 = (*R*)-CH(Me)Ph, M = Cs)

Preparation of (1*R*,3*S*)-1-phenyl-*N*-((*R*)-1-phenylethyl)-3-(trifluoroborato)cyclopentane-1-carboxamide, cesium salt [8i (R^1 = Ph, R^2 = (*R*)-CH(Me)Ph, M = Cs)]**.** To a solution of *γ*-dioxaborato amide **6i** (839 mg, 2.0 mmol, 1.0 equiv) in acetonitrile (MeCN, 8.0 mL) was added a solution of CsF (1.21 g, 8.0 mmol, 4.0 equiv) in H_2O (0.8 mL). The resultant mixture was stirred at room temp for 2 mins, and a solution of L-(+)-tartaric acid (614 mg, 4.1 mmol, 2.05 equiv) in THF (3.0 mL) was added dropwise. After a 5 h stir, the mixture was filtered, washed through with more MeCN, and the filtrate was concentrated under reduced pressure to afford the crude mixture of trifluorborate salt. Afterward, diethyl ether was added to the crude mixture to dissolve undesired products. Following a decantation to remove the solvent and undesired products, the precipitate was further dried under vacuum to afford the title compound (947 mg, 96%) as an off-white solid: mp 246.0–247.5 ºC; $[\alpha]_D^{20}$ = +16º (*c* 1.0, MeOH); ^{19}F NMR (376 MHz, MeOD) δ -145.41 (s, BF_3Cs); ^{1}H NMR (400 MHz, MeOD) δ 7.40 (2H, d, *J* = 7.3 Hz, h,h'), 7.35–7.15 (8H, m, i,i',j,m,m',n,n',o), 5.00–4.90 (1H, m, k), 2.35–2.20 (2H, m, b,e), 2.20–2.00 (2H, m, b,e), 1.70–1.55 (2H, m, c), 1.37 (3H, d, *J* = 7.0 Hz, p), 1.05–0.80 (1H, m, d); ^{13}C NMR (100 MHz, MeOD) δ 178.21 (f), 145.43 (l), 144.20 (g), 127.90 (i,i'), 127.69 (n,n'), 126.60 (h,h'), 126.32 (m,m'), 125.71 (j), 125.64 (o), 60.21 (a), 48.93 (k), 38.86 (b), 37.30 (e), 26.28 (c), 20.81 (p); IR (neat) 3441 (N-H stretch), 2941, 2851, 2830, 1659 (C=O stretch), 1497 (N-H bend), 1297 (C-N stretch), 929, 895, 696 cm^{-1}; HRMS (ESI) calcd. for $C_{20}H_{22}BF_3NO$ (M-Cs): 360.1747, found 360.1736 *m/z*.



8g (R^1 = Ph, R^2 = CH_2Ph, M = Cs)

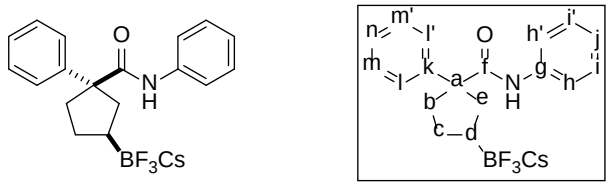
(1*R*,3*S*)-1-phenyl-3-(trifluoroborato)1-1-cyclopentanecarboxylic acid benzyl amide, cesium salt [8g (R^1 = Ph, R^2 = CH_2Ph, M = Cs)]**.** Following the general procedure for the preparation of cesium trifluoroborate salts with *γ*-dioxaborato amide **6g** (203 mg, 0.50 mmol, 1.0 equiv) affords the title compound (196 mg, 82 %) as the white solid: mp 167.5–169.0 ºC; $[\alpha]_D^{20}$ = +3.2º (*c* 1.0, MeOH); ^{19}F NMR (376 MHz, MeOD) δ -144.61 (s, BF_3Cs); ^{1}H NMR (400 MHz, MeOD) δ 7.44 (2H, d, *J* = 7.2 Hz, h,h'), 7.30 (2H, t, *J* = 7.4 Hz, n,n'), 7.25–7.15 (4H, m, i,i',j,o), 7.12 (2H, d, *J* = 6.8 Hz, m,m'), 4.40–4.25 (2H, m, k), 2.35–2.25 (2H, m, b,e), 2.20–2.05 (2H, m, b,e), 1.65–1.55 (2H, m, c), 1.05–0.85 (1H, m, d); ^{13}C NMR (100 MHz, MeOD) δ 179.07 (f), 145.12 (l), 139.22 (g), 127.91 (i,i'), 127.79 (n,n'), 126.67 (h,h'), 126.59 (m,m'), 126.40 (j), 125.81 (o), 60.24 (a), 42.66 (k), 38.79 (b), 37.22 (e), 26.17 (c); IR (neat) 3354 (N-H stretch), 2936, 2872, 1656 (C=O stretch), 1628 (C=C stretch), 1514 (N-H bend), 1443, 1287 (C-N stretch), 1091, 948, 919, 897, 728, 696 cm^{-1}; HRMS (ESI) calcd. for $C_{19}H_{20}BF_3NO$ (M-Cs): 346.1590, found 346.1573 *m/z*.



8h (R^1 = CF_3, R^2 = CH_2Ph, M = Cs)

(1*R*,3*S*)-1-trifluoromethyl-3-(trifluoroborato)-1-cyclopentanecarboxylic acid benzyl amide, cesium salt [8h (R^1 = CF_3, R^2 = CH_2Ph, M = Cs)]**.** Using the general procedure for CAHB of *γ,δ*-unsaturated amides without subsequent oxidation [$Rh(nbd)_2BF_4$ (2.0 mg, 0.0053 mmol) and (*R,R*)-(BINOL)PN(Bn)Ph **L1b** (5.3 mg, 0.011 mmol)], CAHB of *γ,δ*-unsaturated amide **5h** (142.5 mg, 0.528 mmol) affords, after passing through a short pad of silica gel and concentrating under reduced pressure, the crude *γ*-dioxaborato amide **6h** as the dark oil used in the next step without further purification.

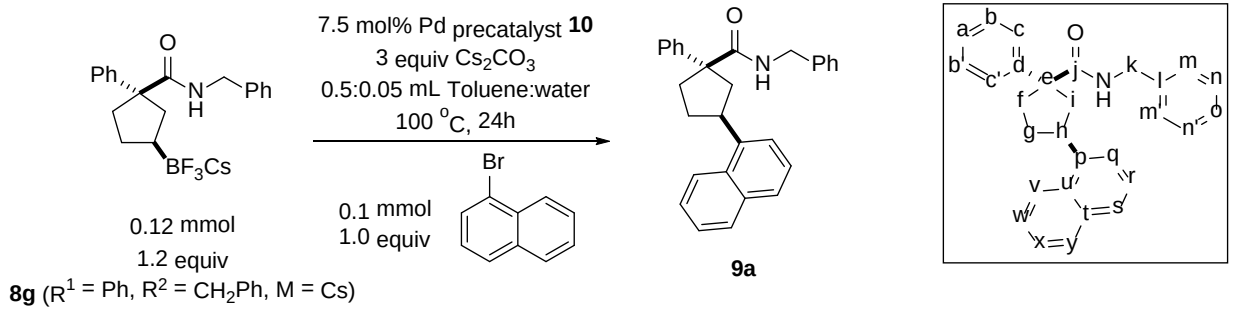
Following the general procedure for the preparation of cesium trifluoroborate salts with crude *γ*-dioxaborato amide **6h** (200 mg, 0.50 mmol, 1.0 equiv) affords the title compound (147 mg, 59%, 2 steps) as a white foamy solid: mp 73.0–75.5 ºC; $[\alpha]_D^{20}$ = -26º (*c* 2.0, $CHCl_3$); ^{19}F NMR (376 MHz, $CDCl_3$) δ -69.90 (s, CF_3), -133.70 (s, BF_3Cs); ^1H NMR (400 MHz, $CDCl_3$) δ 7.30–7.25 (2H, m, i,i'), 7.21 (1H, d, *J* = 7.1 Hz, j), 7.17 (1H, d, *J* = 7.0 Hz, h,h'), 6.51 (1H, br s, NH), 4.35 (2H, d, *J* = 5.2 Hz, k), 2.20–2.05 (2H, m, b,e), 2.05–1.95 (2H, m, e), 1.90–1.85 (1H, m, b), 1.75–1.60 (1H, m, c), 1.45–1.30 (1H, m, c), 1.05–0.85 (1H, m, d); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.29 (f), 138.16 (g), 128.76 (i,i'), 127.46 (j), 127.11 (h,h'), 59.85 (q, *J* = 93.3 Hz, a), 43.95 (k), 34.84 (b), 33.71 (e), 29.37 (c); IR (neat) 3373 (N-H stretch), 2956, 2870, 1657 (C=O stretch), 1523 (N-H bend), 1497, 1454, 1293 (C-N stretch), 1273, 1146, 1090, 1001, 926, 895, 729, 697 cm^{-1}; HRMS (ESI) calcd. for $C_{14}H_{15}BF_6NO$ (M-Cs): 338.1151, found 338.1179 *m/z*.



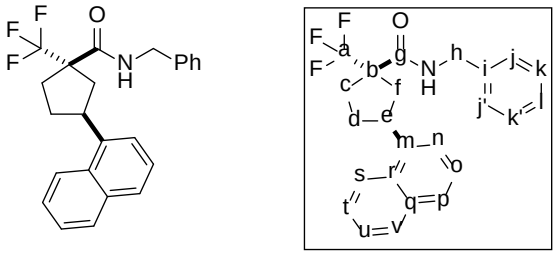
22

(1*R*,3*S*)-1-phenyl-3-(trifluoroborato)-1-cyclopentanecarboxylic acid phenyl amide, cesium salt (22). Following the general procedure for the preparation of cesium trifluoroborate salts with *γ*-dioxaborato amide **6c** (196 mg, 0.50 mmol, 1.0 equiv) affords the title compound (186 mg, 80 %) as the white solid: mp 173.5–177.0 ºC; $[\alpha]_D^{20}$ = +11º (*c* 1.0, MeOH); ^{19}F NMR (376 MHz, MeOD) δ -144.25 (s, BF_3Cs); ^1H NMR (400 MHz, MeOD) δ 7.50–7.40 (4H, m, h,h',l,l'), 7.33 (2H, t, *J* = 7.4 Hz, m,m'), 7.26 (2H, t, *J* = 7.5 Hz, i,i'), 7.21 (1H, t, *J* = 7.3 Hz, j), 7.06 (1H, t, *J* = 7.4 Hz, n), 2.50–2.30 (2H, m, b,e), 2.30–2.10 (2H, m, b,e), 1.75–1.60 (2H, m, c), 1.10–0.95 (1H, m, d); ^{13}C NMR (100 MHz, MeOD) δ 177.61 (f), 145.34 (k), 138.55 (g), 128.18 (i,i'), 127.89 (m,m'), 126.51 (l,l'), 125.89 (j), 123.79 (n), 120.85 (h,h'), 61.13 (a), 38.97 (b), 37.77 (e), 26.60 (c); IR (neat) 3402 (N-H stretch), 2947, 2842, 1663 (C=O stretch), 1596 (C=C stretch), 1516 (N-H bend), 1493, 1436, 1311 (C-N stretch), 1241, 1080, 994, 901, 897, 745, 696 cm^{-1}; HRMS (ESI) calcd. for $C_{18}H_{18}BF_3NO$ (M-Cs): 332.1434, found 332.1426 *m/z*.

General procedure for Suzuki-Miyaura cross-coupling reactions.

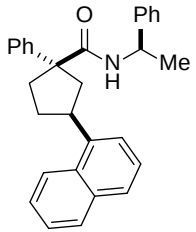


(1*R*,3*S*)-3-(naphthalen-1-yl)-1-phenylcyclopentanecarboxylic acid benzyl amide (9a). An 8-mL vial was charged with Pd precatalyst **10** (5.5 mg, 0.0075 mmol, 0.075 equiv), Cs_2CO_3 (98 mg, 0.3 mmol, 3.0 equiv), γ-trifluoroborato amide **8g** (R^1 = CF_3, R^2 = CH_2Ph, M = Cs) (57.5 mg, 0.12 mmol, 1.2 equiv), 1-bromonaphthalene **11** (20.7 mg, 0.1 mmol, 1.0 equiv), toluene (0.5 mL), and water (0.05 mL). The resultant mixture was stirred at 100 °C for 24 h. After cooling to room temperature, the organic layer was separated, and water (1.0 mL) was added to the aqueous layer following by extraction with ethyl acetate (2 x 2 mL). The combined organic extracts were dried (anhyd. Na_2SO_4) and concentrated under reduced pressure. Flash chromatography on silica gel (90:10–85:15 hexanes:ethyl acetate) affords the tile compound (28.1 mg, 69%) as a yellow oil; TLC analysis R_f = 0.55 (70:30 hexanes:ethyl acetate); $[\alpha]_D^{20}$ = -3.2° (*c* 1.3, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10–8.00 (1H, m, v), 7.95–7.85 (1H, m, y), 7.76 (1H, d, *J* = 8.2 Hz, s), 7.69 (1H, d, *J* = 7.1 Hz, q), 7.60–7.45 (6H, m, a,n,n',o,w,x), 7.40–7.35 (1H, m, r), 7.35–7.25 (4H, m, b,b',m,m'), 7.09 (2H, d, *J* = 6.4 Hz, c,c'), 5.49 (1H, br s, NH), 4.45–4.35 (2H, m, k), 4.00–3.90 (1H, m, h), 2.95–2.80 (3H, m, f,i), 2.50–2.40 (1H, m, f), 2.40–2.30 (1H, m, g), 2.20–2.10 (1H, m, g); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.52 (j), 143.90 (d), 140.67 (p), 138.47 (l), 133.90 (t), 132.12 (u), 129.12 (n,n'), 128.88 (y), 128.60 (b,b'), 127.30 (r), 127.27 (m,m'), 127.19 (c,c'), 126.97 (o,o'), 126.65 (s), 125.83 (w), 125.70 (a), 125.33 (x), 123.53 (v), 122.65 (q), 58.98 (e), 43.75 (k), 43.69 (i), 39.41 (h), 37.04 (f), 32.59 (g); IR (neat) 3325 (N-H stretch), 1646 (C=O stretch), 1598 (C=C stretch), 1533 (N-H bend), 1449, 1418, 1285, 795, 775, 718, 695 cm^{-1}; HRMS (ESI) calcd. for $C_{29}H_{27}NaNO$ (M+Na): 428.1990, found 428.1992 *m/z*.

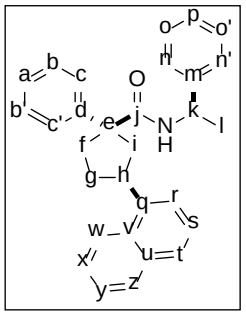


9b

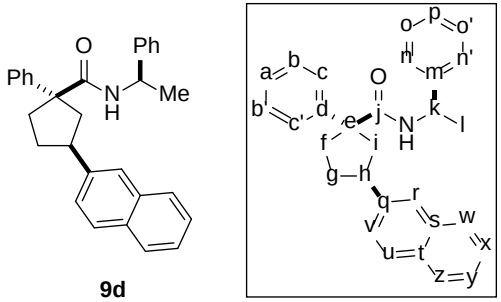
(1*S*,3*S*)-3-(naphthalen-1-yl)-1-(trifluoromethyl)cyclopentanecarboxylic acid benzyl amide (9b). Using the general procedure with 1-bromonaphthalene **11** (20.7 mg, 0.1 mmol, 1.0 equiv), cross-coupling of γ-trifluoroborato amide **8h** (R^1 = CF_3, R^2 = CH_2Ph, M = Cs) (56.5 mg, 0.12 mmol, 1.2 equiv) affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (25.0 mg, 63%) as a yellow oil; TLC analysis R_f = 0.75 (70:30 hexanes:ethyl acetate); $[\alpha]_D^{20}$ = -16° (*c* 0.5, $CHCl_3$); ^{19}F NMR (376 MHz, $CDCl_3$) δ -70.47; ^1H NMR (400 MHz, $CDCl_3$) δ 8.11 (1H, d, *J* = 8.4 Hz, v), 7.90 (1H, dd, *J* = 7.6 Hz, s), 7.77 (1H, dd, *J* = 7.9 Hz, n), 7.60–7.40 (4H, m, l,p,t,u), 7.40–7.20 (5H, m, j,j',k,k',o), 6.12 (1H, br s, NH), 4.60–4.45 (2H, m, h), 4.10–3.95 (1H, m, e), 2.80–2.65 (2H, m, c,f), 2.60–2.55 (1H, m, f), 2.40–2.20 (2H, m, c,d), 2.20–2.10 (1H, m, d); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.18 (g), 138.32 (m), 137.61 (i), 133.89 (q), 131.97 (r), 128.96 (v), 128.85 (k,k'), 127.70 (j,j'), 127.53 (o), 127.17 (l), 126.08 (p), 125.66 (t), 125.55 (u), 123.16 (s), 122.40 (n), 58.45 (d, *J* = 24 Hz, b), 44.41 (h), 41.13 (e), 39.01 (f), 32.70 (d), 31.73 (c); IR (neat) 3341 (N-H stretch), 3052, 2957, 1657 (C=O stretch), 1598 (C=C stretch), 1522 (N-H bend), 1496, 1453, 1287,1147, 1111, 777, 726, 695 cm^{-1}; HRMS (ESI) calcd. for $C_{24}H_{22}F_3NaNO$ (M+Na): 420.1551, found 420.1534 *m/z*.



9c

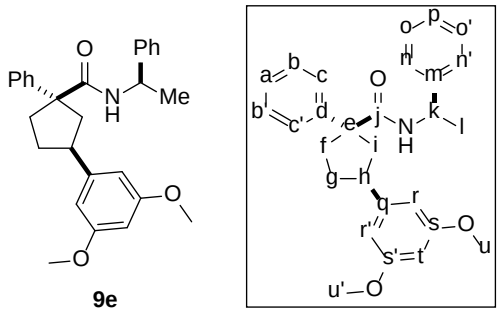


Preparation of (1*R*,3*S*)-3-(naphthalen-1-yl)-1-phenyl-N-((*R*)-1-phenylethyl)cyclopentane-1-carboxamide (9c). Using the general procedure with 1-bromonaphthalene **11** (20.7 mg, 0.1 mmol, 1.0 equiv), cross-coupling of γ-trifluoroborato amide **8i** (R^1 = Ph, R^2 = (*R*)-CH(Me)Ph, M = Cs) (59.2 mg, 0.12 mmol, 1.2 equiv) affords, after flash chromatography on silica gel (90:10–85:15 hexanes:ethyl acetate), the title compound (36.0 mg, 86%) as a yellow oil; TLC analysis R_f = 0.6 (70:30 hexanes:ethyl acetate); $[\alpha]_D^{20}$ = -20° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05–8.00 (1H, m, w), 7.90–7.85 (1H, m, z), 7.80–7.70 (1H, m, t), 7.70–7.60 (1H, m, y), 7.55–7.45 (7H, m, a,c,c',n,p,o,o'), 7.40–7.35 (1H, m, s), 7.30–7.20 (3H, m, n',r,x), 7.07 (2H, d, *J* = 6.9 Hz, b.b'), 5.34 (1H, br s, NH), 5.20–5.00 (1H, m, k), 4.00–3.85 (1H, m, h), 2.90–2.70 (3H, m, f,i), 2.50–2.40 (1H, m, f), 2.40–2.30 (1H, m, g), 2.20–2.10 (1H, m, g), 1.35 (3H, d, *J* = 6.9 Hz, l); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.63 (j), 144.10 (d), 143.33 (q), 140.65 (m), 133.87 (u), 132.10 (v), 129.07 (o,o'), 128.86 (z), 128.53 (b,b'), 127.25 (s), 127.08 (n,n'), 126.91 (c,c'), 126.60 (t), 125.83 (p), 125.72 (x), 125.67 (a), 125.29 (r), 123.50 (w), 122.69 (y), 58.94 (e), 48.88 (k), 43.57 (i), 37.47 (h), 37.01 (f), 32.71 (g), 21.82 (l); IR (neat) 3337 (N-H stretch), 3053, 2923, 1644 (C=O stretch), 1597 (C=C stretch), 1493 (N-H bend), 1445, 796, 777, 732, 696 cm^{-1}; HRMS (ESI) calcd. for $C_{30}H_{29}NaNO$ (M+Na): 442.2147, found 442.2151 *m/z*.



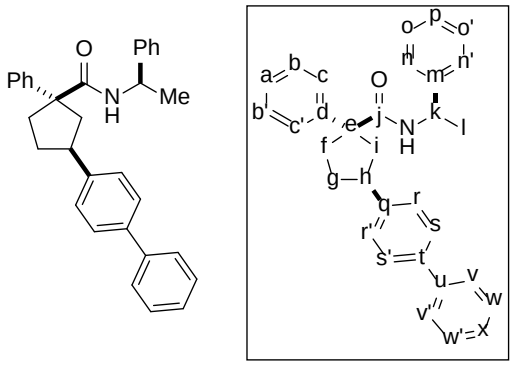
9d

(1*R*,3*S*)-3-(naphthalen-2-yl)-1-phenyl-N-((*R*)-1-phenylethyl)cyclopentane-1-carboxamide (9d). Using the general procedure with 2-bromonaphthalene **12** (20.7 mg, 0.1 mmol, 1.0 equiv), cross-coupling of γ-trifluoroborato amide **8i** (R^1 = Ph, R^2 = (*R*)-CH(Me)Ph, M = Cs) (59.2 mg, 0.12 mmol, 1.2 equiv) affords, after flash chromatography on silica gel (90:10–85:15 hexanes:ethyl acetate), the title compound (28.0 mg, 66%) as a yellow oil; TLC analysis R_f = 0.6 (70:30 hexanes:ethyl acetate); $[\alpha]_D^{20}$ = +48° (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90–7.75 (3H, m, w,z,u), 7.75–7.70 (1H, m, r), 7.55–7.50 (1H, m, x), 7.50–7.40 (5H, m, c,c',o,o',y), 7.40–7.30 (2H, m, n,n'), 7.30–7.20 (3H, m, a,p,v), 7.09 (2H, d, *J* = 6.8 Hz, b.b'), 5.35 (1H, br s, NH), 5.15–5.05 (1H, m, k), 3.40–3.20 (1H, m, h), 2.90–2.75 (2H, m, f,i), 2.75–2.65 (1H, m, i), 2.45–2.35 (1H, m, f), 2.35–2.20 (1H, m, g), 2.15–2.05 (1H, m, g), 1.37 (3H, d, *J* = 6.9 Hz, l); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.70 (j), 144.04 (d), 143.36 (q), 142.59 (m), 133.53 (s), 132.24 (t), 129.00 (o,o'), 128.71 (b,b'), 128.53 (z), 128.08 (w), 127.58 (u), 127.21 (n,n'), 127.09 (c,c'), 126.94 (p), 126.12 (x), 125.90 (a), 125.72 (v), 125.32 (y), 125.22 (r), 59.24 (e), 48.89 (k), 44.77 (i), 44.64 (h), 37.30 (f), 33.72 (g), 21.87 (l); IR (neat) 3325 (N-H stretch), 2920, 1708 (C=O stretch), 1644 (C=C stretch), 1598 (N-H bend), 1493, 1446, 888, 857, 817, 745, 696 cm^{-1}; HRMS (ESI) calcd. for $C_{30}H_{29}NaNO$ (M+Na): 442.2147, found 442.2151 *m/z*.



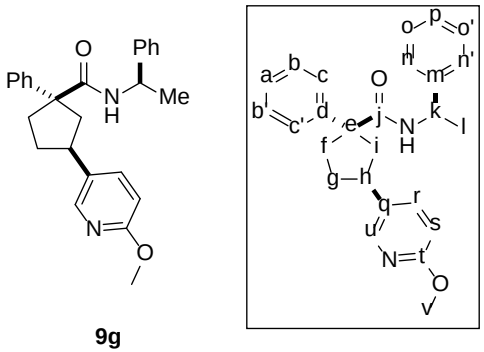
9e

(1*R*,3*S*)-3-(3,5-dimethoxyphenyl)-1-phenyl-*N*-((*R*)-1-phenylethyl)cyclopentane-1-carboxamide (9e). Using the general procedure with 1-bromo-3,5-dimethoxybenzene **13** (21.7 mg, 0.1 mmol, 1.0 equiv), cross-coupling of γ-trifluoroborato amide **8i** (R^1 = Ph, R^2 = (*R*)-CH(Me)Ph, M = Cs) (59.2 mg, 0.12 mmol, 1.2 equiv) affords, after flash chromatography on silica gel (90:10–85:15 hexanes:ethyl acetate), the title compound (28.5 mg, 66%) as a yellow oil; TLC analysis R_f = 0.5 (70:30 hexanes:ethyl acetate); $[\alpha]_D^{20}$ = +15° (*c* 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45–7.40 (4H, m, o,o',c,c'), 7.35–7.30 (1H, m, p), 7.30–7.20 (3H, m, a,n,n'), 7.07 (2H, d, *J* = 6.8 Hz, b,b'), 6.49 (2H, d, *J* = 2.1 Hz, r,r'), 6.33 (1H, t, *J* = 2.2 Hz, t), 5.30 (1H, d, *J* = 7.5 Hz, NH), 5.20–5.00 (1H, m, k), 3.80 (6H, s, u,u'), 3.15–3.00 (1H, m, h), 2.80–2.70 (1H, m, f), 2.70–2.55 (2H, m, i), 2.40–2.25 (1H, m, f), 2.25–2.10 (1H, m, g), 2.05–1.90 (1H, m, g), 1.34 (3H, d, *J* = 6.9 Hz, l); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.55 (j), 160.79 (s,s'), 147.65 (q), 143.94 (d), 143.33 (m), 128.95 (o,o'), 128.51 (n,n'), 127.16 (p), 127.07 (a), 126.85 (c,c'), 125.71 (b,b'), 105.25 (r,r'), 98.22 (t), 59.06 (e), 55.31 (u,u'), 48.83 (k), 44.70 (h), 44.54 (i), 36.98 (f), 33.41 (g), 21.81 (l); IR (neat) 3348 (N-H stretch), 2930, 1654 (C=O stretch), 1593 (C=C stretch), 1493 (N-H bend), 1451, 1427, 1203, 1149, 1059, 924. 831, 733, 697 cm^{-1}; HRMS (ESI) calcd. for $C_{28}H_{31}NaNO_3$ (M+Na): 452.2202, found 452.2195 *m/z*.



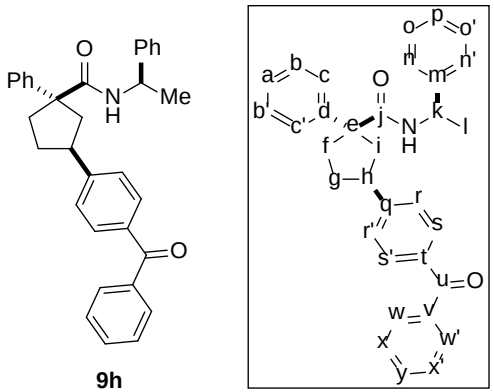
9f

(1*R*,3*S*)-3-([1,1'-biphenyl]-4-yl)-1-phenyl-*N*-((*R*)-1-phenylethyl)cyclopentane-1-carboxamide (9f). Using the general procedure with 4-bromo-1,1'-biphenyl **14** (23.3 mg, 0.1 mmol, 1.0 equiv), cross-coupling of γ-trifluoroborato amide **8i** (R^1 = Ph, R^2 = (*R*)-CH(Me)Ph, M = Cs) (59.2 mg, 0.12 mmol, 1.2 equiv) affords, after flash chromatography on silica gel (90:10–85:15 hexanes:ethyl acetate), the title compound (31.8 mg, 71%) as a yellow oil; TLC analysis R_f = 0.6 (70:30 hexanes:ethyl acetate); $[\alpha]_D^{20}$ = +49° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (2H, d, *J* = 8.1 Hz, v,v'), 7.56 (2H, d, *J* = 8.2 Hz, s,s'), 7.50–7.40 (8H, m, b,b'c,c',r,r',w,w'), 7.40–7.30 (2H, m, n,n'), 7.30–7.20 (3H, m, o,o',x), 7.10–7.00 (2H, m, a,p), 5.34 (3H, d, *J* = 7.3 Hz, NH), 5.15–5.05 (1H, m, k), 3.25–3.10 (1H, m, h), 2.80–2.70 (2H, m, f,i), 2.70–2.60 (1H, m, i), 2.40–2.30 (1H, m, f), 2.30–2.15 (1H, m, g), 2.10–2.00 (1H, m, g), 1.36 (3H, d, *J* = 6.9 Hz, l); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.68 (j), 144.38 (q), 144.12 (d), 143.36 (u), 141.12 (t), 139.08 (m), 128.98 (w,w'), 128.72 (r,r'), 128.53 (b,b'), 127.76 (v,v'), 127.19 (x), 127.15 (s,s'), 127.09 (n,n'), 127.04 (c,c'), 126.90 (p), 125.72 (p,a), 59.19 (e), 48.87 (k), 44.86 (i), 44.25 (h), 37.35 (f), 33.92 (g), 21.86 (l); IR (neat) 3334 (N-H stretch), 3026, 1651 (C=O stretch), 1598 (C=C stretch), 1486 (N-H bend), 1446, 1234, 1073, 837, 761, 732, 695 cm^{-1}; HRMS (ESI) calcd. for $C_{32}H_{31}NaNO$ (M+Na): 468.2303, found 468.2293 *m/z*.



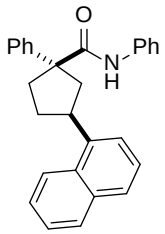
9g

(1*R*,3*S*)-3-(6-methoxypyridin-3-yl)-1-phenyl-*N*-((*R*)-1-phenylethyl)cyclopentane-1-carboxamide (9g). Using the general procedure with 5-chloro-2-methoxypyridine **15** (71.8 mg, 0.5 mmol, 1.0 equiv), cross-coupling of γ-trifluoroborato amide **8i** (R^1 = Ph, R^2 = (*R*)-CH(Me)Ph, M = Cs) (298 mg, 0.6 mmol, 1.2 equiv) affords, after flash chromatography on silica gel (85:15 hexanes:ethyl acetate), the title compound (150.2 mg, 75%) as a yellow oil; TLC analysis R_f = 0.25 (80:20 hexanes:ethyl acetate); $[\alpha]_D^{20}$ = +8.2° (*c* 0.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (1H, d, *J* = 2.4 Hz, u), 7.68 (1H, dd, *J* = 8.6 Hz and 2.4 Hz, r), 7.45–7.40 (4H, m, c,c',o,o'), 7.40–7.30 (2H, m, n,n'), 7.30–7.20 (2H, m, b,b'), 7.10–7.00 (2H, m, a,p), 6.72 (1H, d, *J* = 8.6 Hz, s), 5.33 (1H, d, *J* = 7.8 Hz, NH), 5.15–5.00 (1H, m, k), 3.93 (3H, s, v), 3.15–3.05 (1H, m, h), 2.75–2.65 (2H, m, f,i), 2.60–2.50 (1H, m, i), 2.40–2.30 (1H, m, f), 2.20–2.10 (1H, m, g), 2.00–1.85 (1H, m, g), 1.34 (3H, d, *J* = 6.9 Hz, l); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.61 (j), 162.91 (t), 145.24 (u), 143.95 (d), 143.30 (m), 137.65 (r), 133.13 (q), 129.00 (o,o'), 128.51 (b,b'), 127.25 (n,n'), 127.09 (c,c'), 126.86 (p), 125.64 (a), 110.82 (s), 59.10 (e), 53.32 (v), 48.89 (k), 44.59 (i), 41.03 (h), 37.29 (f), 33.88 (g), 21.89 (l); IR (neat) 3323 (N-H stretch), 2942, 1645 (C=O stretch), 1604 (C=C stretch), 1491 (N-H bend), 1446, 1282, 1252, 1128, 1026, 829, 760, 697 cm^{-1}; HRMS (ESI) calcd. for $C_{26}H_{28}NaN_2O_2$ (M+Na): 423.2048, found 423.2033 *m/z*.

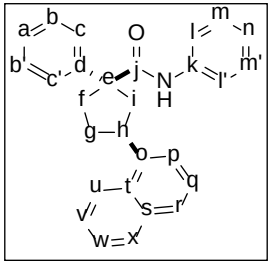


9h

(1*R*,3*S*)-3-(4-benzoylphenyl)-1-phenyl-*N*-((*R*)-1-phenylethyl)cyclopentane-1-carboxamide (9h). Using the general procedure with 4-chlorobenzophenone **16** (21.7 mg, 0.1 mmol, 1.0 equiv), cross-coupling of γ-trifluoroborato amide **8i** (R^1 = Ph, R^2 = (*R*)-CH(Me)Ph, M = Cs) (59.2 mg, 0.12 mmol, 1.2 equiv) affords, after flash chromatography on silica gel (90:10–85:15 hexanes:ethyl acetate), the title compound (33.1 mg, 70%) as a yellow oil; TLC analysis R_f = 0.5 (70:30 hexanes:ethyl acetate); $[\alpha]_D^{20}$ = +63° (*c* 1.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85–7.80 (2H, m, s,s'), 7.76 (2H, d, *J* = 8.2 Hz, w,w'), 7.60 (1H, t, *J* = 7.4 Hz, y), 7.50 (2H, t, *J* = 7.7 Hz, b,b'), 7.45–7.40 (5H, m, c,c',o,o',p), 7.40–7.30 (2H, m, n,n'), 7.30–7.15 (4H, m, r,r',x,x'), 7.05 (1H, d, *J* = 6.8 Hz, a), 5.36 (1H, br s, NH), 5.15–5.05 (1H, m, k), 3.30–3.15 (1H, m, h), 2.85–2.70 (2H, m, f,i), 2.65–2.55 (1H, m, i), 2.45–2.30 (1H, m, f), 2.30–2.20 (1H, m, g), 2.10–2.00 (1H, m, g), 1.35 (3H, d, *J* = 6.9 Hz, l); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.47 (u), 175.53 (j), 150.51 (q), 143.83 (d), 143.30 (v), 137.93 (t), 135.48 (m), 132.21 (y), 130.45 (w,w'), 130.00 (s,s'), 129.04 (o,o'), 128.53 (x,x'), 128.23 (b,b'), 127.30 (n,n'), 127.11 (c,c'), 126.88 (p), 125.68 (a), 59.22 (e), 48.94 (k), 44.62 (i), 44.52 (h), 37.28 (f), 33.75 (g), 21.90 (l); IR (neat) 3346 (N-H stretch), 3054, 1651 (C=O stretch), 1598 (C=C stretch), 1493 (N-H bend), 1445, 1315, 1277, 923. 742, 696 cm^{-1}; HRMS (ESI) calcd. for $C_{33}H_{31}NaNO_2$ (M+Na): 496.2252, found 496.2245 *m/z*.

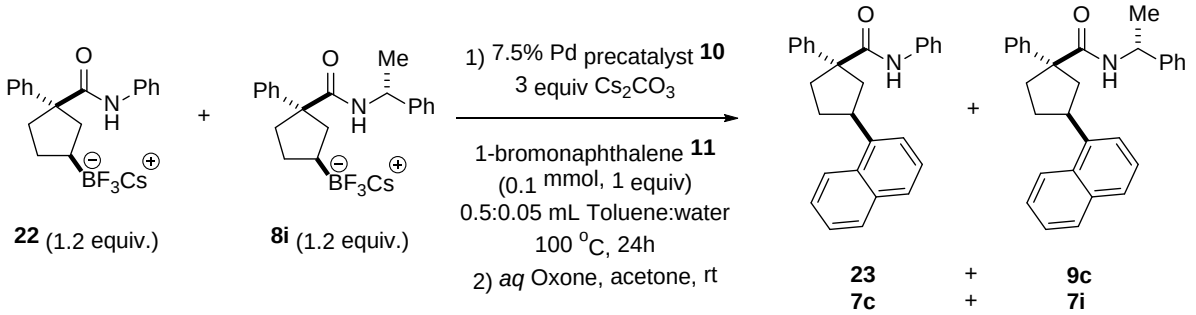


23



(1*R*,3*S*)-3-(naphthalen-1-yl)-1-phenylcyclopentanecarboxylic acid phenyl amide (23). Using the general procedure with 1-bromonaphthalene **11** (20.7 mg, 0.1 mmol, 1.0 equiv), cross-coupling of γ-trifluoroborato amide **22** (55.8 mg, 0.12 mmol, 1.2 equiv) affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (7.9 mg, 20%) as a yellow oil; TLC analysis R_f = 0.70 (70:30 hexanes:ethyl acetate); $[\alpha]_D^{20}$ = -23° (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10–8.00 (1H, m, u), 7.95–7.85 (1H, m, x), 7.76 (1H, d, *J* = 8.2 Hz, r), 7.70 (1H, d, *J* = 7.1 Hz, w), 7.65–7.55 (2H, m, b,b'), 7.55–7.25 (10H, m, a,c,c',l,l',m,m',n,q,v), 7.09 (1H, tt, *J* = 7.3 and 1.2 Hz, p), 6.83 (1H, br s, NH), 4.05–3.90 (1H, m, h), 3.00–2.80 (3H, m, i,f), 2.55–2.45 (1H, m, f), 2.45–2.35 (1H, m, g), 2.25–2.15 (1H, m, g); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.70 (j), 143.52 (d), 140.42 (o), 137.98 (k), 133.91 (s), 132.09 (t), 129.40 (m,m'), 128.91 (x), 127.63 (n), 127.00 (b,b'), 126.72 (q), 125.83 (c,c'), 125.74 (r), 125.35 (a), 124.22 (v), 123.47 (w), 122.63 (u), 119.70 (p), 110.61 (l,l'), 59.84 (e), 43.70 (i), 39.59 (h), 37.16 (f), 32.70 (g); IR (neat) 3332 (N-H stretch), 3055, 2948, 1661 (C=O stretch), 1596 (C=C stretch), 1515 (N-H bend), 1498, 1435, 1308, 1240, 905, 777, 751, 691 cm^{-1}; HRMS (ESI) calcd. for $C_{28}H_{25}NaNO$ (M+Na): 414.1834, found 414.1846 *m/z*.

Direct competition experiment of Suzuki-Miyaura cross-coupling.

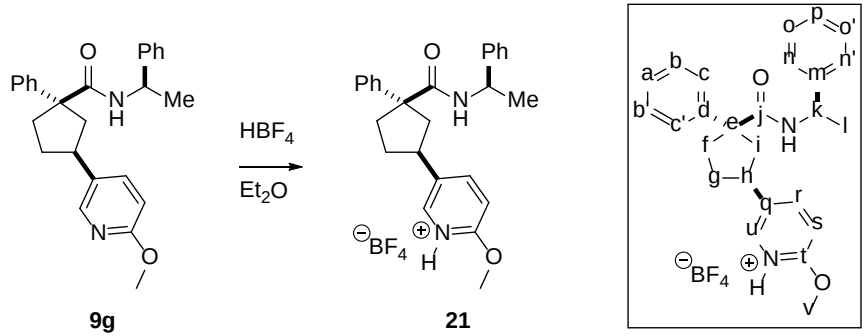


An 8-mL vial was charged with Pd precatalyst **10** (5.5 mg, 0.0075 mmol, 0.075 equiv), Cs_2CO_3 (98 mg, 0.3 mmol, 3.0 equiv), γ-trifluoroborato amide **8i** (R^1 = Ph, R^2 = (*R*)-CH(Me)Ph, M = Cs) (59.2 mg, 0.12 mmol, 1.2 equiv), γ-trifluoroborato amide **22** (55.8 mg, 0.12 mmol, 1.2 equiv), 1-bromonaphthalene **11** (20.7 mg, 0.1 mmol, 1.0 equiv), toluene (0.5 mL), and water (0.05 mL). The resultant mixture was stirred at 100 ^oC for 24 h. After cooling to room temperature, the organic layer was separated, and water (1.0 mL) was added to the aqueous layer following by extraction with ethyl acetate (2 x 2 mL). The combined organic extracts were dried (anhyd. Na_2SO_4) and concentrated under reduced pressure. The resulting mixture was diluted with 1.2 mL acetone and Oxone (0.6 mL of a 0.2 M solution in H_2O, 1.2 mmol, 1.2 equiv) was added in one portion. After a 0.5 h-stir, to the crude mixture was added water (1 mL) and HCl (1 mL of the 1M solution). The resultant mixture was extracted with DCM (3 x 2 mL). The combined organic extracts were dried (Na_2SO_4), and concentrated under reduced pressure. Flash chromatography on silica gel (90:10 hexanes:ethyl acetate) affords **23** (18.8 mg, 48%, TLC analysis R_f = 0.70 (70:30 hexanes:ethyl acetate) as a yellow oil and **9c** (17.6 mg, 42%, TLC analysis R_f = 0.60 (70:30 hexanes:ethyl acetate) as a yellow oil. The eluent was then switched to 85:15 DCM:EtOAc to afford a mixture of alcohols **7c** (61%) and **7i** (60%) (mass was calculated using ^1H NMR ratio (1:0.98 **7c:7i**); total mass of **7c** and **7i** was 43.1 mg).

Using the same procedures of the direct competition experiment described above with only 10% of γ-trifluoroborato amide **8i** (R^1 = Ph, R^2 = (*R*)-CH(Me)Ph, M = Cs) (5.0 mg, 0.01 mmol, 0.1 equiv) affords, after flash chromatography on silica gel (90:10

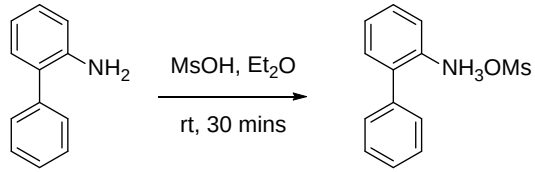
hexanes:ethyl acetate then 85:15 DCM:EtOAc), **23** (20.3 mg, 52%) and **7c** (20.0 mg, 59%); only trace amount of **9c** and **7i** were obtained.

Preparation of tetrafluoroborate salt 21 for x-ray crystallography

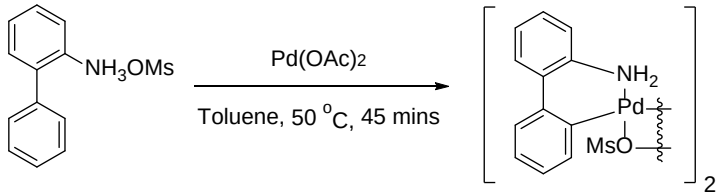


2-methoxy-5-((1*S*,3*R*)-3-phenyl-3-(((*R*)-1-phenylethyl)carbamoyl)cyclopentyl)pyridin-1-ium tetrafluoroborate (21). A solution of (1*R*,3*S*)-pyridinyl amide **9g** (64.9 mg, 0.162 mmol) in Et_2O (4.0 mL) was treated with HBF_4 (54% in Et_2O, 15 μL, 1.2 equiv), which immediately produced a light yellow precipitate. The liquid was pipetted out and washed with Et_2O (2 x 2 mL) and then dried under vacuum to give a white solid (69.6 mg, 88%). The salt was recrystallized (5:1 TBME/ MeOH) to give off-white single crystals (59.2 mg, 85%), and an X-ray crystal structure was obtained; $[\alpha]_D^{20}$ = +25 (*c* 1.2, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (1H, dd, *J* = 9.1 and 2.4 Hz, r), 8.24 (1H, d, *J* = 2.1 Hz, u), 7.48 (1H, d, *J* = 9.2 Hz, s), 7.45–7.35 (4H, m, b,b',o,o'), 7.30 (1H, tt, *J* = 7.0 and 1.4 Hz, p), 7.20–7.10 (3H, m, a,b,b'), 7.01 (2H, dd, *J* = 7.8 and 2.1 Hz, n,n'), 5.05–4.95 (1H, m, k), 4.21 (3H, s, v), 3.40–3.30 (1H, m, h), 2.80–2.65 (2H, m, f,i), 2.60–2.40 (2H, m, f,i), 2.40–2.25 (1H, m, g), 1.85–1.75 (1H, m, g), 1.37 (3H, d, *J* = 7.0 Hz, l); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.96 (j), 159.80 (t), 147.81 (r), 143.77 (d), 143.42 (m), 136.91 (u), 136.89 (q), 128.35 (o,o'), 127.89 (b,b'), 126.70 (p), 126.41 (a), 126.29 (c,c'), 125.44 (n,n'), 110.24 (s), 59.40 (e), 57.26 (v), 49.07 (k), 43.40 (i), 39.73 (h), 35.70 (f), 32.89 (g), 20.64 (l); IR (neat) 3378 (N-H stretch), 1646 (C=O stretch), 1597 (C=C stretch), 1555, 1529 (N-H bend), 1495, 1444, 1330, 1303, 1060, 1014, 836, 766, 703, 643 cm^{-1}; HRMS (ESI) calcd. for $C_{26}H_{28}NaN_2O_2$ (M-HBF_4+Na): 423.2048, found 423.2044 *m/z*.

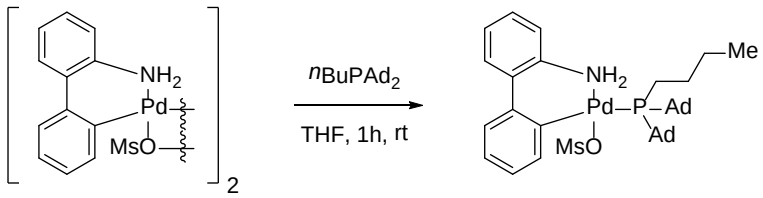
Preparation sequence of Palladium-precatalyst 10.[9]



2-Ammoniumbiphenyl mesylate.[9] To a solution of 2-aminobiphenyl (2.54 g, 15.0 mmol, 1.0 equiv) in diethyl ether (50 mL) was added a solution of methanesulfonic acid (0.97 mL, 15.0 mmol, 1.0 equiv) in diethyl ether (8 mL). After 30 min of stir, the resultant mixture was filtered and washed with diethyl ether (2 x 10 mL). The precipitate was dried under vacuum to provide the title compound (3.97 g, 99%) as a white solid: mp 152.5–153.0 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.17 (3H, br s, NH_3), 7.50 (1H, dd, *J* = 7.9 and 0.8 Hz), 7.45–7.35 (6H, m), 7.35–7.25 (2H, m), 2.38 (3H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.76, 136.18, 131.16, 129.42, 128.97, 128.65, 128.24, 128.19, 124.42, 38.85.



***μ*-OMs dimer.[9]** The solution of 2-ammoniumbiphenyl mesylate (789 mg, 3.0 mmol, 1.0 equiv) and $Pd(OAc)_2$ (672 mg, 3.0 mmol, 1.0 equiv) in 12 mL anhydrous toluene was stirred at 50 °C for 1 h. After cooling to room temp, the suspension was filtered, washed with toluene (5 mL) and diethyl ether (3 x 5 mL) and dried under vacuum for 24 h to afford the title compound (1.01 g, 91%) as an off-white solid: mp 200.5–202.0 ºC; ^{1}H NMR (400 MHz, CD_3CN) δ 7.65–7.55 (1H, m), 7.48 (1H, dd, *J* = 7.5 and 1.2 Hz), 7.45–7.35 (1H, m), 7.35–7.25 (2H, m), 7.22 (1H, d, *J* = 7.6 Hz), 7.18 (1H, t, *J* = 7.4 Hz), 7.08 (1H, td, *J* = 7.6 and 1.4 Hz), 6.38 (2H, br s), 2.58 (3H, s); ^{13}C NMR (100 MHz, CD_3CN) δ 139.19, 138.83, 136.81, 136.39, 135.55, 127.89, 127.86, 127.18, 126.28, 126.14, 125.22, 120.49, 39.10.

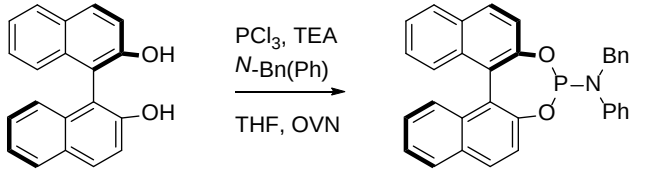


Pd-precatalyst **10**

Preparation of Pd-precatalyst (10). The solution of μ-OMs dimer (370 mg, 0.5 mmol, 0.5 equiv) and *n*BuPAd_2 (359 mg, 1.0 mmol, 1.0 equiv) in anhydrous THF (5 mL) was stirred at room temp for 1 h. The solvent was then concentrated under reduced pressure at room temp until ~ 0.5 mL remained. The residue was then added pentane (5 mL) to crystalize out the product. The solvent was removed by pipet and the solid was dried under vacuum to afford the title compound (671 mg, 92%) as an off-white solid: mp 219.0–220.5 ºC; ^{31}P NMR (283 MHz, $CDCl_3$) δ 47.97; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.45–7.35 (3H, m), 7.30–7.20 (3H, m), 7.16 (1H, t, *J* = 7.4 Hz), 7.08 (1H, t, *J* = 7.2 Hz), 7.01 (1H, t, *J* = 7.3 Hz), 4.18 (1H, br s), 2.83 (3H, s), 2.30–2.15 (6H, m), 2.10–2.00 (9H, m), 2.85–2.75 (9H, m), 1.65–1.55 (7H, m), 1.45–1.35 (1H, m), 1.10–1.00 (1H, m), 0.95–0.90 (1H, m), 0.60 (3H, t, *J* = 7.2 Hz), 0.60–0.50 (1H, m), 0.40–0.20 (1H, m); ^{13}C NMR (176 MHz, $CDCl_3$) δ 140.16, 137.58 and 137.55, 136.63 and 136.61, 128.12, 127.63, 126.91, 125.33, 125.26, 124.65, 119.83, 41.34 and 41.26, 40.55 and 40.45, 40.08, 39.87, 36.65 and 36.46, 28.84 and 28.79, 28.65 and 28.61, 27.73, 25.41 and 25.34, 17.63 and 17.51, 13.80 (observed complexity due to P-C splitting). IR (neat) 2898, 2841, 1611, 1492, 1419, 1341, 1300, 1249, 1239, 1166, 1141, 1034, 1021, 771, 754, 735, 709 cm^{-1}; HRMS (ESI) calcd. for $C_{36}H_{49}NPPd$ (M-OMs): 632.2637, found 632.2637 *m/z*.

General procedure for the preparation of ligands (*R*,*R*)-L1-5 and dioxaborinane tmdBH (B1).

Ligands (*R*,*R*)-**L1a** and (*R*,*R*)-**L2-5** and dioxaborinane tmdBH (**B1**) were prepared as previously described.[10,11] The preparation of the new ligand **L1b** was obtained by You's protocol[12] with some modifications.

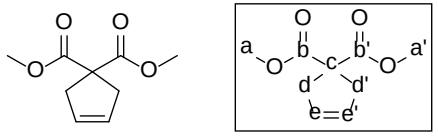


(*R*,*R*)-BINOL (*R*,*R*)-(BINOL)PN(Bn)Ph (**L1b**)

Preparation of (BINOL)PN(Bn)Ph (L1b). To a cooled (0 ^{o}C) of *N*-benzylaniline (1.41 g, 1.1 equiv, 7.7 mmol) and TEA (1.8 mL, 1.84 equiv, 12.9 mmol) in THF (50 mL) was added PCl_3 (0.67 mL, 1.1 equiv, 7.7 mmol) dropwise. The resultant mixture was refluxed for 6 h and slowly cooled to -78 ^{o}C. A solution of (*R*,*R*)-BINOL (2.0 g, 7.0 mmol) and TEA (3.5 mL, 3.6 equiv, 25.2 mmol) in THF (35 mL) was then added slowly to the above mixture at -78 ^{o}C. The resulting mixture was stirred at rt overnight, then filtered through a pad of celite, and washed with THF. The organic phase was concentrated under reduced pressure. Flash chromatography on silica gel (80:20–70:30 hexanes:DCM) affords the tile compound (3.01 g, 86%) as a white foamy solid: mp 99.5–100.0 ^{o}C; TLC analysis R_f = 0.6 (50:50 hexanes:DCM); $[\alpha]_D^{20}$ = -165^{o} (*c* 1.0, $CHCl_3$); ^{31}P NMR (121 MHz, $CDCl_3$) δ 140.95; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (1H, d, *J* = 8.8 Hz), 8.00–7.90 (3H, m), 7.67 (1H, dd *J* = 8.8 and 0.5 Hz), 7.50–7.40 (5H, m), 7.35–7.25 (6H, m), 7.25–7.05 (6H, m), 4.56 (1H, dd, *J* = 15.7 and 2.1 Hz), 4.06 (1H, dd, *J* = 15.7 and 1.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 149.56 (J_{CP} = 4.9 Hz), 149.15, 143.78, 143.47, 138.45, 132.87, 132.64, 131.58, 130.89, 130.48, 130.27, 129.09, 128.41, 128.34, 128.10, 127.84, 127.08, 126.99, 126.73, 126.24, 125.02, 124.82, 124.71, 124.55, 124.32, 124.18, 124.11, 122.69, 122.08, 121.71, 50.37; IR (neat) 3052, 1618, 1589, 1489, 1462, 1359, 1324, 1223, 1096, 1063, 947, 819, 747, 692 cm^{-1}; HRMS (EI) calcd. for $C_{33}H_{24}NO_2P$ (M): 497.1545, found 497.1545 *m/z*.

References

1. Depres, J. P.; Greene, A. E. *J. Org. Chem.* **1984**, *49*, 928-31.
2. Kiyotsuka, Y.; Acharya, H. P.; Katayama, Y.; Hyodo, T.; Kobayashi, Y. *Org. Lett.* **2008**, *10*, 1719-1722.
3. Race, N. J.; Bower, J. F. *Org. Lett.* **2013**, *15*, 4616-4619.
4. DeMartino, J.; Akiyama, T.; Struthers, M.; Yang, L.; Berger, J. P.; Morriello, G.; Pastemak, A.; Zhou, C.; Mills, S. G.; Butora, G.; Kothandaraman, S.; Guiadeen, D.; Tang, C.; Jiao, R.; Goble, S. D.; Moyes, C. US20060030582A1, 2006.
5. Grellepois, F.; Kikelj, V.; Coia, N.; Portella, C. *Eur. J. Org. Chem.* **2012**, *2012*, 509-517,
6. Nguyen, T. B.; Sorres, J.; Tran, M. Q.; Ermolenko, L.; Al-Mourabit, A. *Org. Lett.* **2012**, *14*, 3202-3205.
7. Molander, G. A.; Shin, I.; Jean-Gerard, L. *Org. Lett.* **2010**, *12*, 4384-4387.
8. Lennox, A. J. J.; Lloyd-Jones, G. *Angew. Chem. , Int. Ed.* **2012**, *51*, 9385-9388.
9. Bruno, N. C.; Tudge, M. T.; Buchwald, S. L. *Chem. Sci.* **2013**, *4*, 916-920.
10. Smith, S. M.; Takacs, J. M. *Org. Lett.* **2010**, *12*, 4612-4615.
11. Smith, S. M.; Thacker, N. C.; Takacs, J. M. *J. Am. Chem. Soc.* **2008**, *130*, 3734-3735.
12. Liu, W.; Zheng, C.; Zhuo, C.; Dai, L.; You, S. *J. Am. Chem. Soc.* **2012**, *134*, 4812-4821.

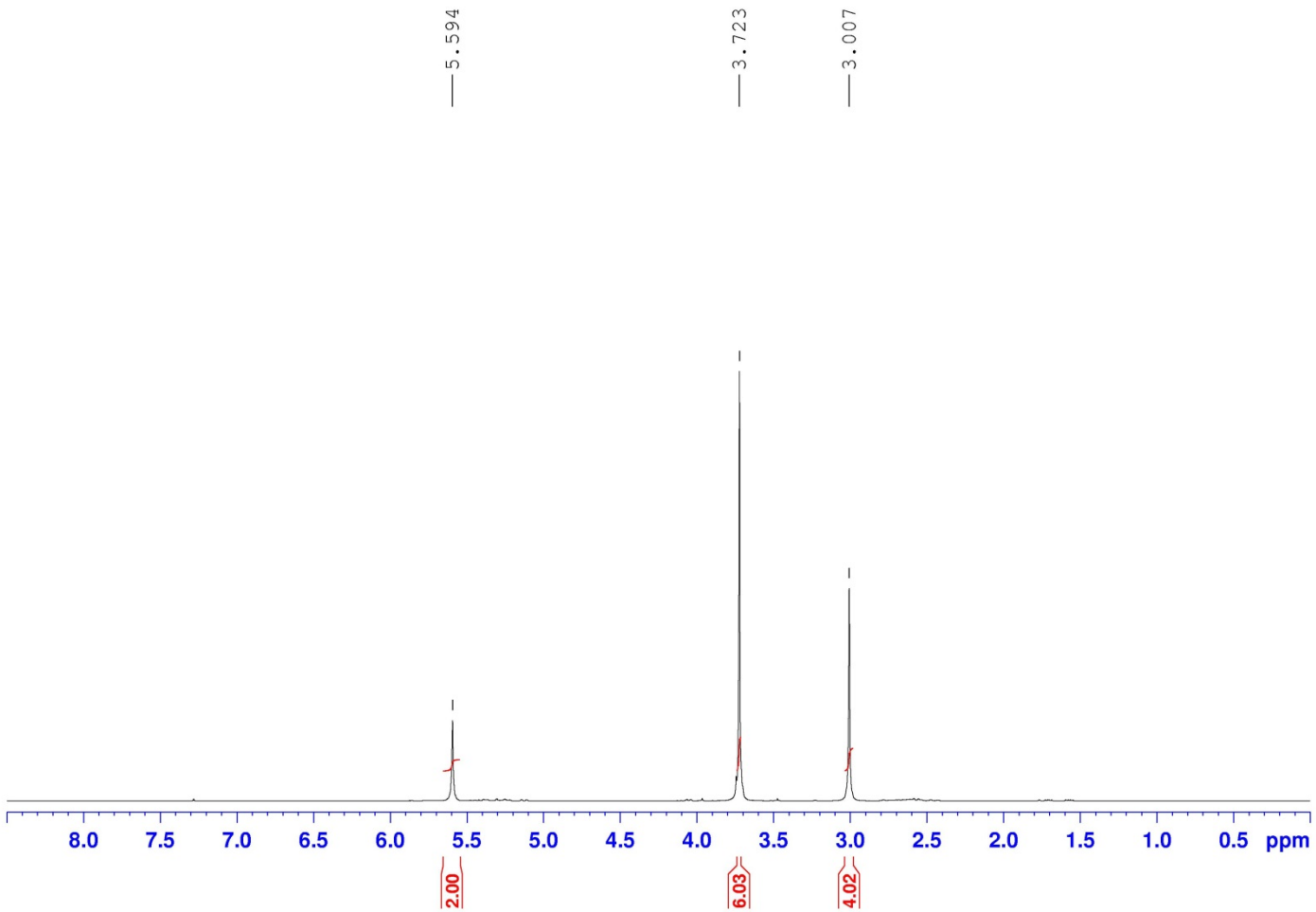


27

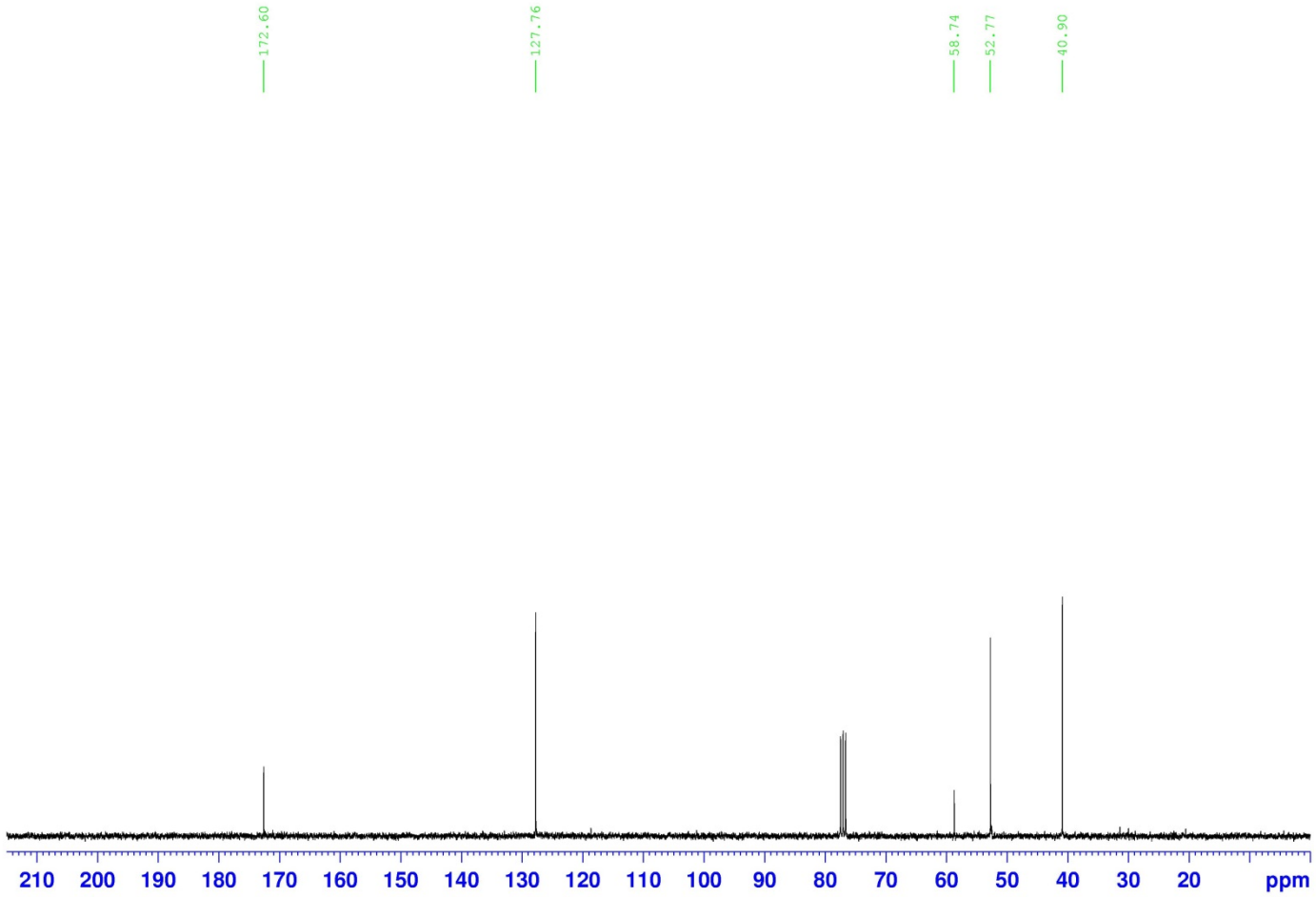
Following the procedure of preparing 3-cyclopentene-1,1-dicarboxylic acid dimethyl ester affords the title compound (87%) as a white solid.

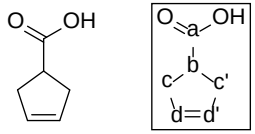
m.p.	169.5–171.0 ^{o}C.
^{1}H NMR (300 MHz, $CDCl_3$)	δ 5.59 (2H, s, e,e'), 3.72 (6H, s, a,a'), 3.01 (4H, s, d,d').
^{13}C NMR (75 MHz, $CDCl_3$)	δ 172.60 (b,b'), 127.76 (e,e'), 58.74 (c), 52.77 (a,a'), 40.90 (d,d').
IR (neat)	2983, 2897, 1720 (C=O stretch), 1430, 1258 (C-O-C antisymmetrical stretch), 752, 694 (O-C-O bend) cm^{-1}.

^{1}H NMR of 27


5.594
3.723
3.007
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.00
6.03
4.02

^{13}C NMR of 27


172.60
127.76
58.74
52.77
40.90
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

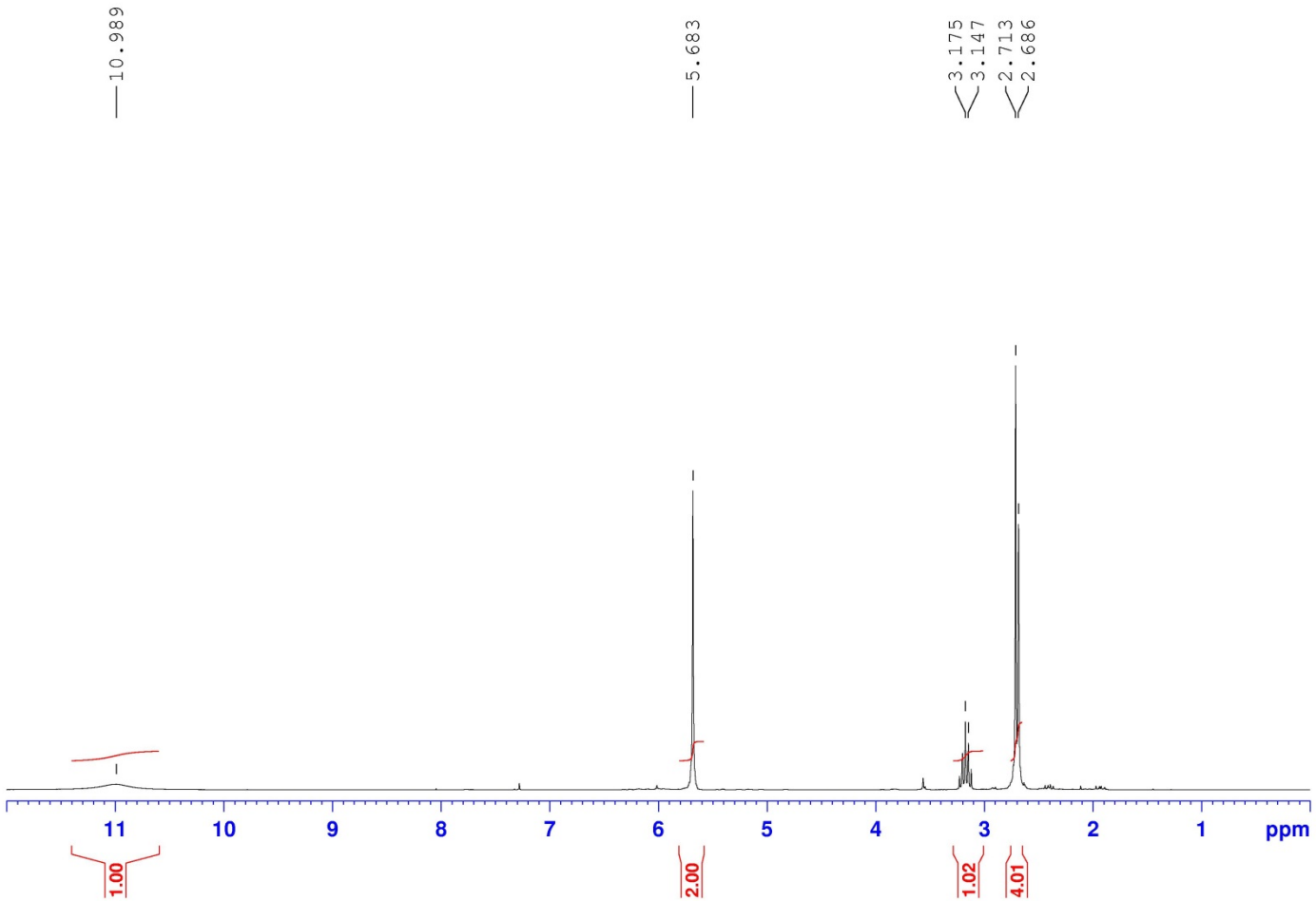


28

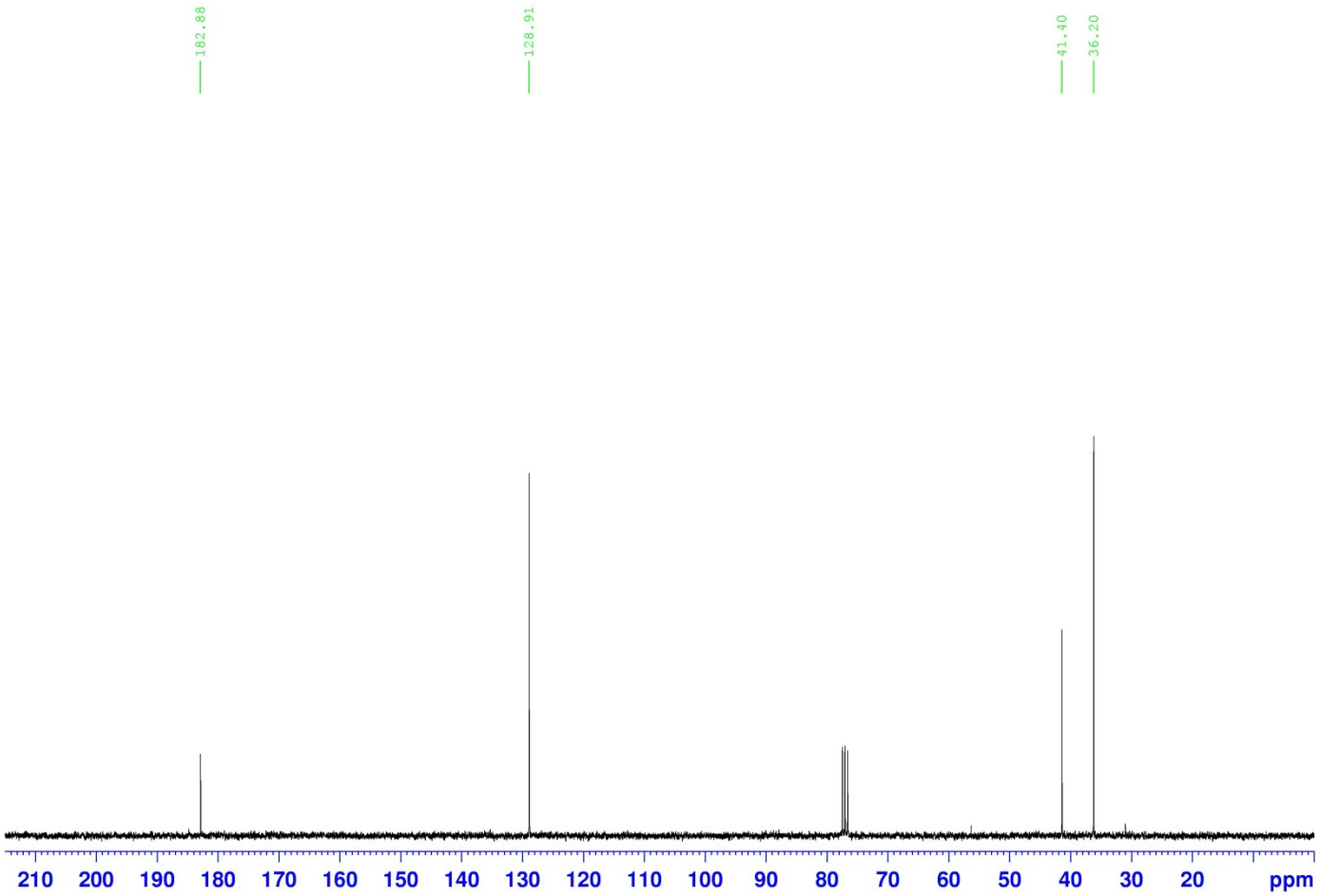
Following the procedure of preparing 3-cyclopentenecarboxylic acid affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (73%, 2 steps) as a yellow oil.

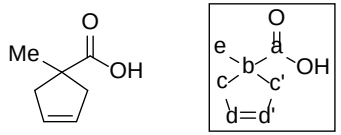
TLC analysis	R_f 0.35 (70:30 hexanes:ethyl acetate)
^{1}H NMR (300 MHz, $CDCl_3$)	δ 10.99 (1H, br s, OH), 5.68 (2H, s, d,d'), 3.25–31.0 (1H, m, b), 2.75–2.65 (4H, m, c,c').
^{13}C NMR (75 MHz, $CDCl_3$)	δ 182.88 (a), 128.91 (d,d'), 41.40 (b), 36.20 (c,c').
IR (neat)	3265 (O-H stretch), 3064, 2929, 1695 (C=O stretch), 1614 (C=C stretch), 1422, 931, 678 cm^{-1}.

^{1}H NMR of 28


10.989
5.683
3.175
3.147
2.713
2.686
11
10
9
8
7
6
5
4
3
2
1
ppm
1.00
2.00
1.02
4.01

^{13}C NMR of 28


182.88
128.91
41.40
36.20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

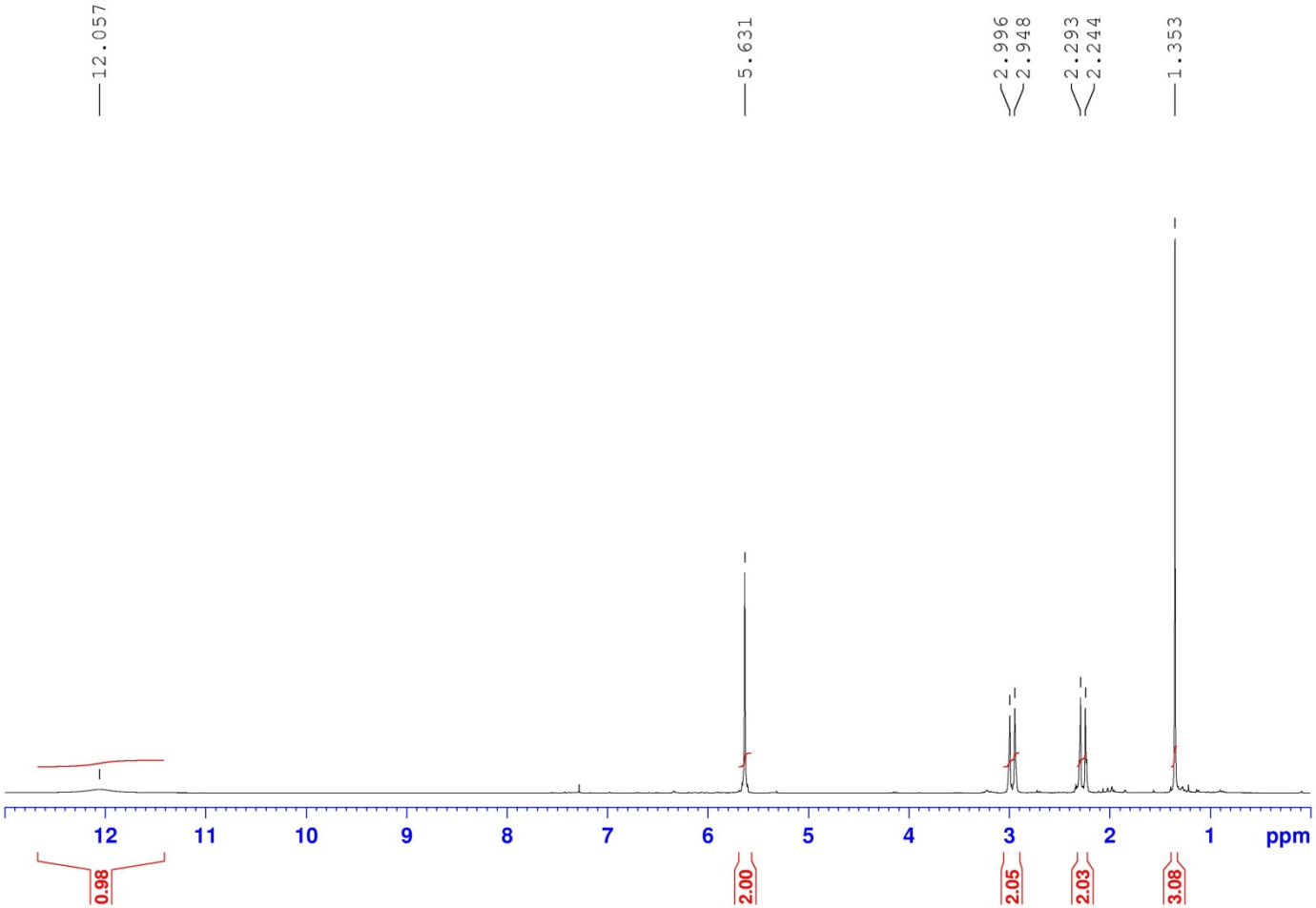


29

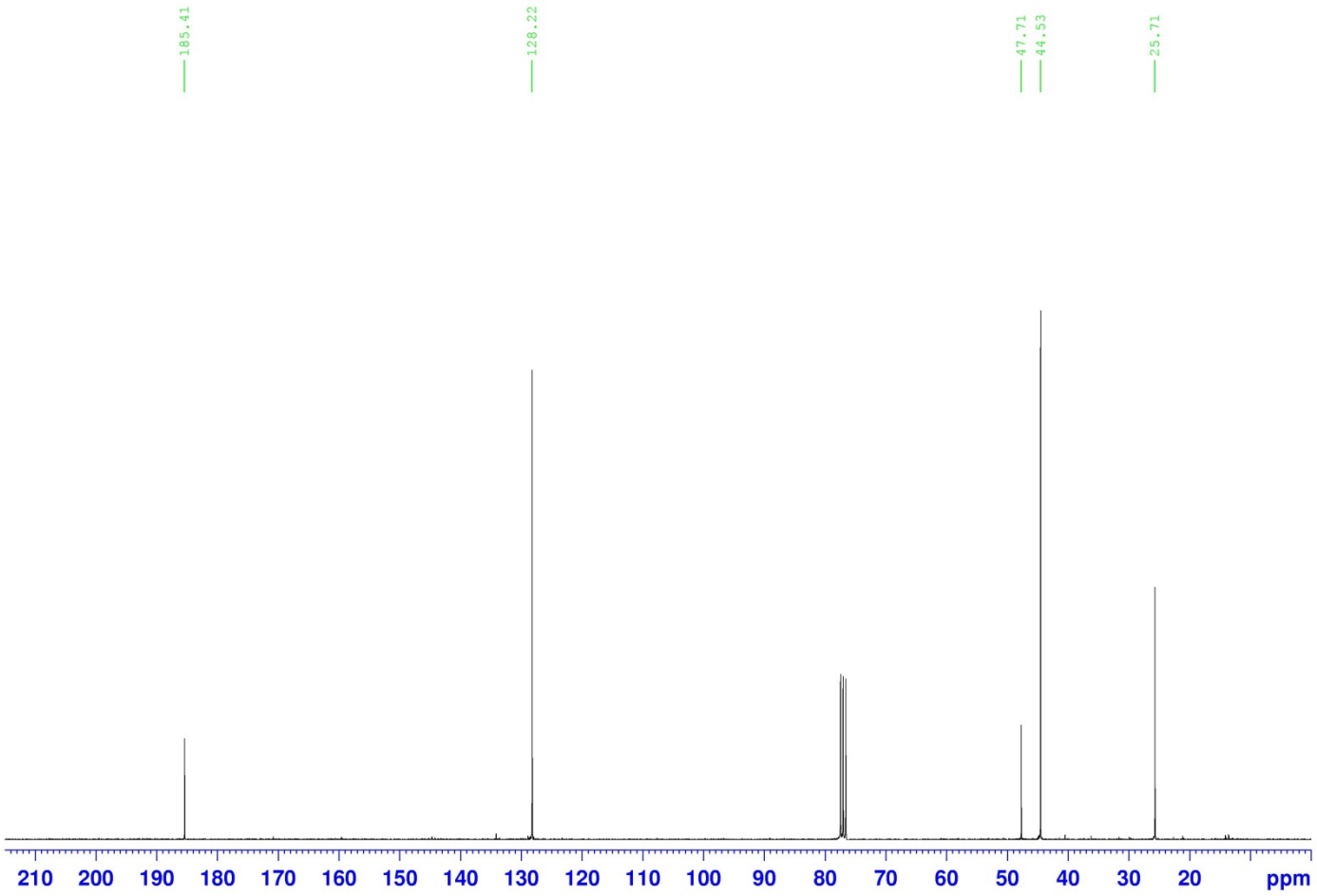
Following general procedure for α-alkylation of carboxylic acid via dianion intermediate, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (87%) as a dark oil.

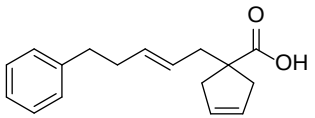
TLC analysis	R_f 0.40 (70:30 hexanes:ethyl acetate)
^{1}H NMR (300 MHz, $CDCl_3$)	δ 12.06 (1H, br s, OH), 5.63 (2H, s, d,d'), 2.97 (2H, d, *J* = 14.4, c,c'), 2.27 (2H, d, *J* = 14.7, c,c'), 1.35 (3H, s, e).
^{13}C NMR (75 MHz, $CDCl_3$)	δ 185.41 (a), 128.22 (d,d'), 47.71 (b), 44.53 (c,c'), 25.71 (e).
IR (neat)	3195 (O-H stretch), 3064, 2970, 2917, 1695 (C=O stretch), 1467, 1405, 1287, 944, 670 cm^{-1}.
HMRS (EI)	Calcd. for $C_7H_{10}O_2$: 126.0681, found 126.0676 *m/z*.

^{1}H NMR of 29

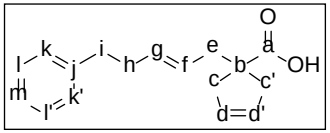

12.057
5.631
2.996
2.948
2.293
2.244
1.353
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.98
2.00
2.05
2.03
3.08

^{13}C NMR of 29


185.41
128.22
47.71
44.53
25.71
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm



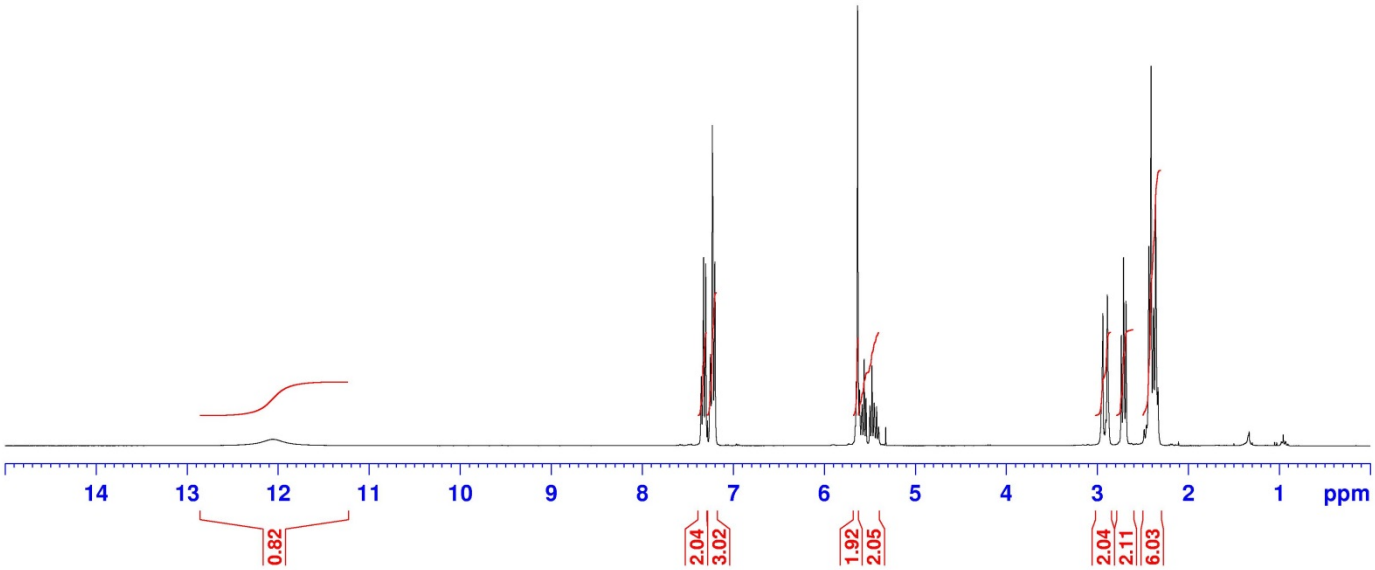
30



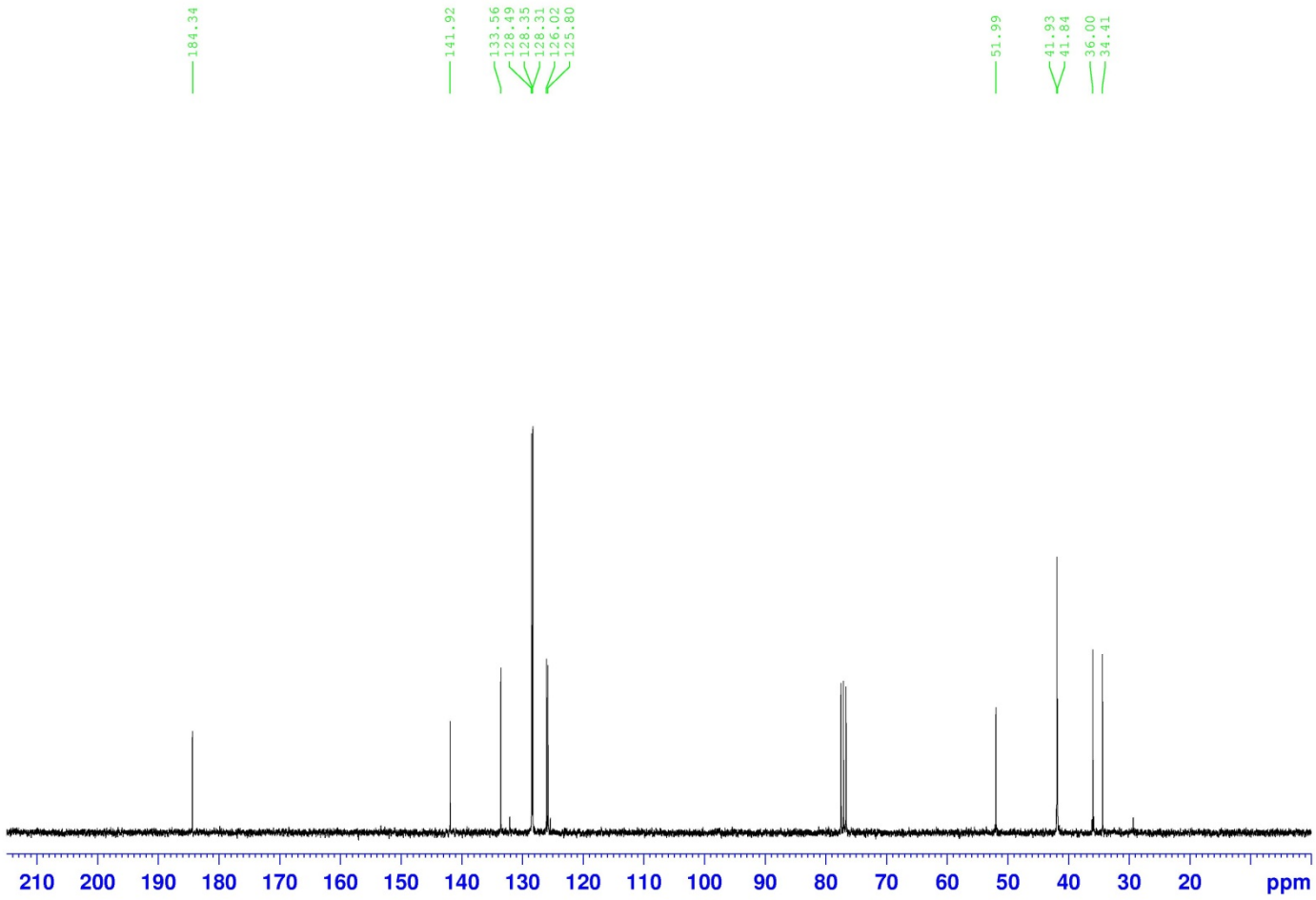
Following general procedure for α-alkylation of carboxylic acid via dianion intermediate, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (92%) as a yellow oil.

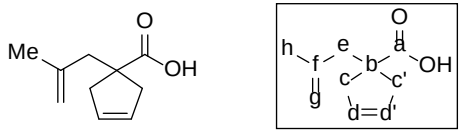
TLC analysis	R_f 0.50 (70:30 hexanes:ethyl acetate)
^{1}H NMR (300 MHz, $CDCl_3$)	δ 12.05 (1H, br s, OH), 7.40–7.20 (5H, j, k,k',l,l',m), 5.63 (2H, s, d,d'), 5.60–5.40 (2H, m, f,g), 2.92 (2H, d, *J* = 14.7, c,c'), 2.75–2.65 (2H, m, c,c'), 2.50–2.30 (6H, m, e,h,i).
^{13}C NMR (75 MHz, $CDCl_3$)	δ 184.34 (a), 141.92 (j), 133.56 (d,d'), 128.49 (g), 128.35 (l,l'), 128.31 (k,k'), 126.02 (m), 125.80 (f), 51.99 (b), 41.93 (e), 41.84 (c,c'), 36.00 (i), 34.41 (h).
IR (neat)	2918 (O-H stretch), 1694 (C=O stretch), 1277, 1226 (C-O stretch), 967, 951 (O-H bend), 697, 670 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{17}H_{19}Na_2O_2$ (M-H+2Na): 301.1180, found 301.1190 *m/z.*

^{1}H NMR of 30



^{13}C NMR of 30


184.34
141.92
133.56
128.49
128.35
128.31
126.02
125.80
51.99
41.93
41.84
36.00
34.41
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

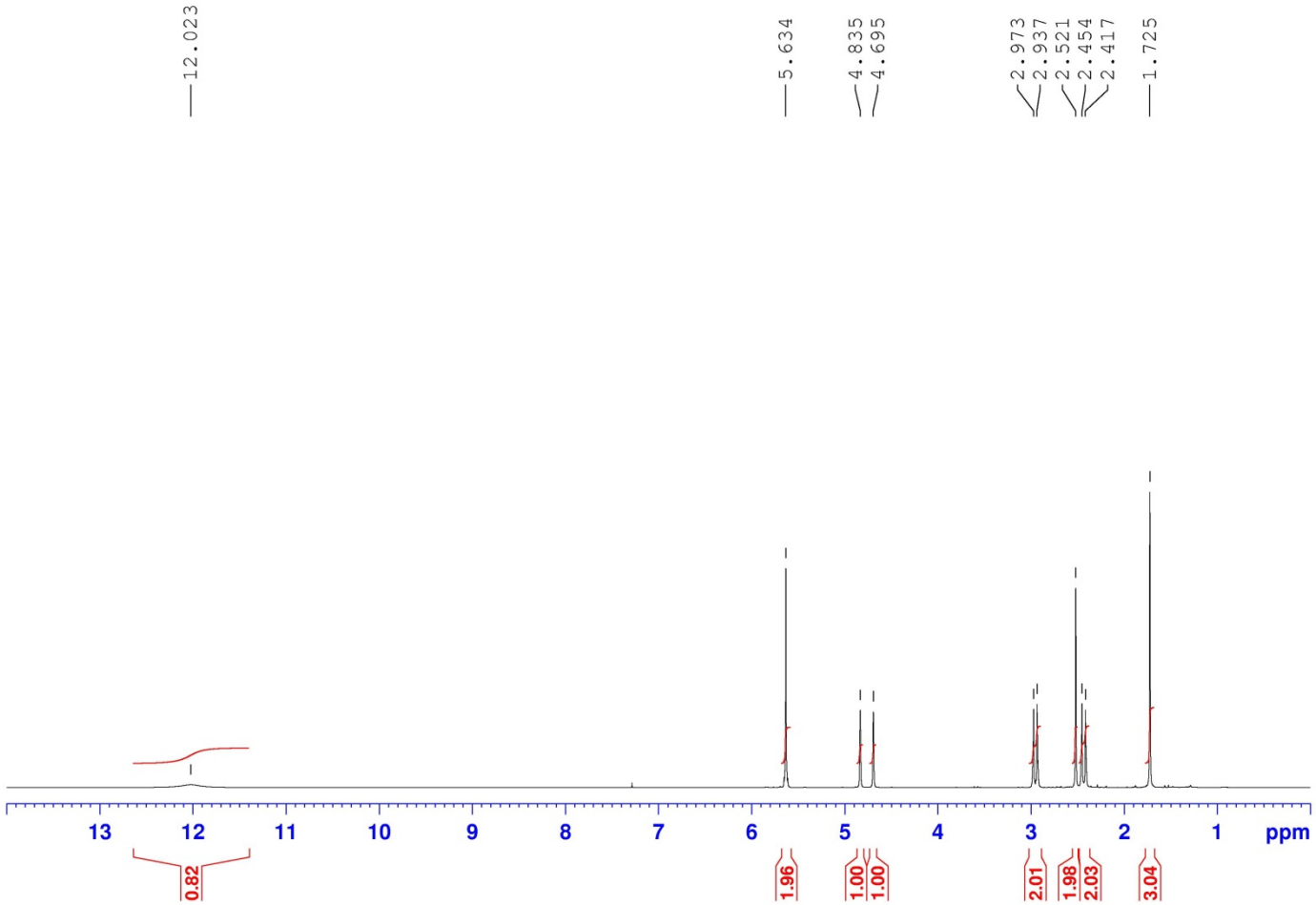


31

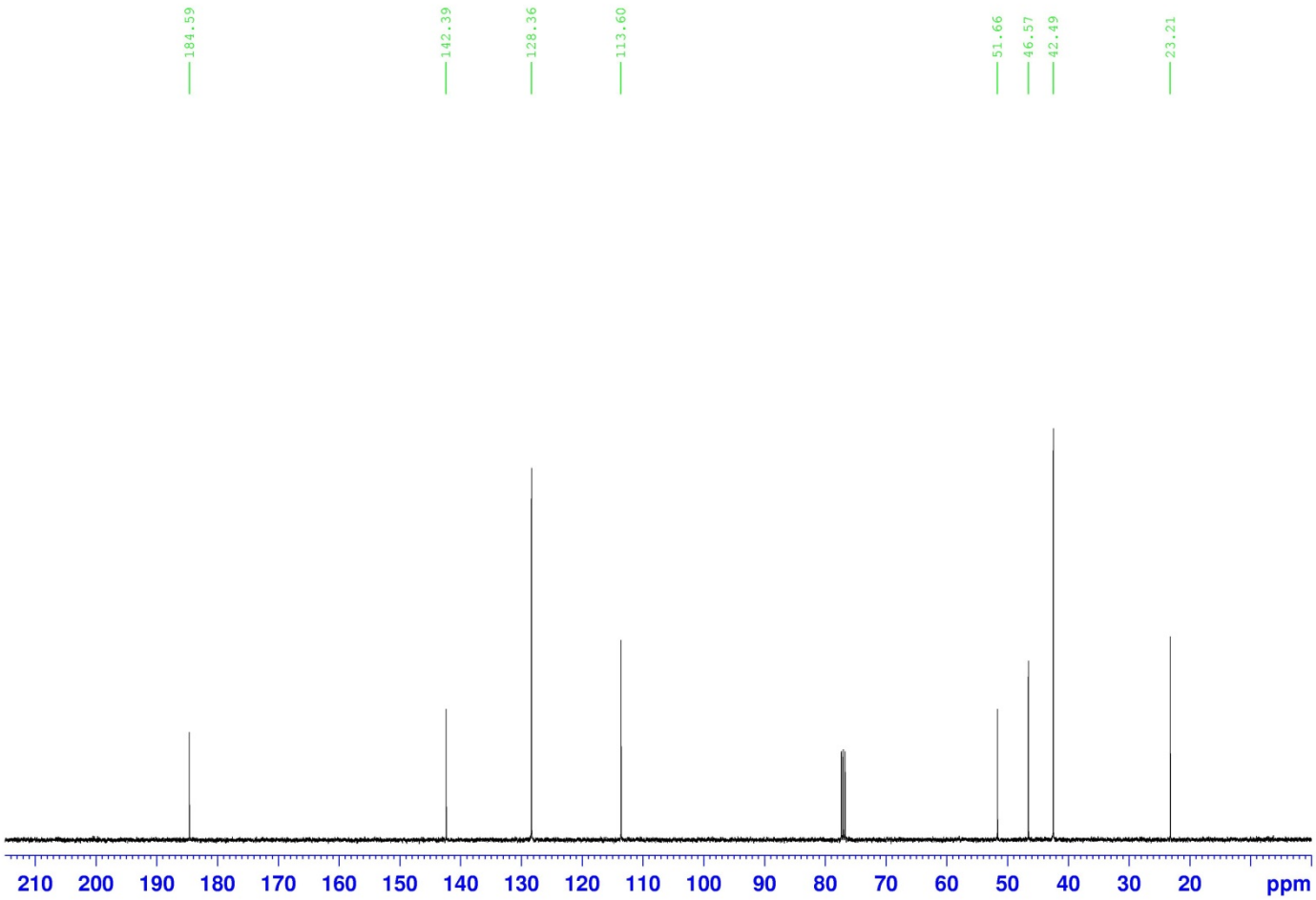
Following general procedure for α-alkylation of carboxylic acid via dianion intermediate, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (89%) as a yellow oil.

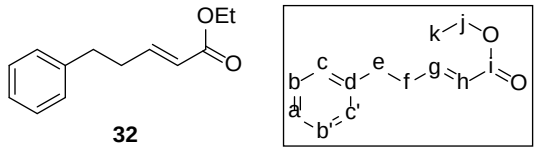
TLC analysis	R_f 0.55 (70:30 hexanes:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 12.02 (1H, br s, OH), 5.63 (2H, s, d,d'), 4.84 (1H, s, g), 4.70 (1H, s, g), 2.96 (2H, d, *J* = 14.4, c,c'), 2.52 (2H, s, e), 2.44 (2H, d, *J* = 14.8, c,c'), 1.73 (3H, s, h).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 184.59 (a), 142.39 (f), 128.36 (d,d'), 113.60 (g), 51.66 (a), 46.57 (e), 42.49 (c,c'), 23.21 (h).
IR (neat)	2911 (O-H stretch), 1694 (C=O stretch), 1229 (C-O stretch), 951 (O-H bend), 893, 693, 663 cm^{-1}.
HRMS	Calcd. for $C_{10}H_{13}Na_2O_2$ (M-H+2Na): 211.0711, found 211.0719 *m/z.*

^{1}H NMR of 31


12.023
5.634
4.835
4.695
2.973
2.937
2.521
2.454
2.417
1.725
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
0.82
1.96
1.00
1.00
2.01
1.98
2.03
3.04

^{13}C NMR of 31


184.59
142.39
128.36
113.60
51.66
46.57
42.49
23.21
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

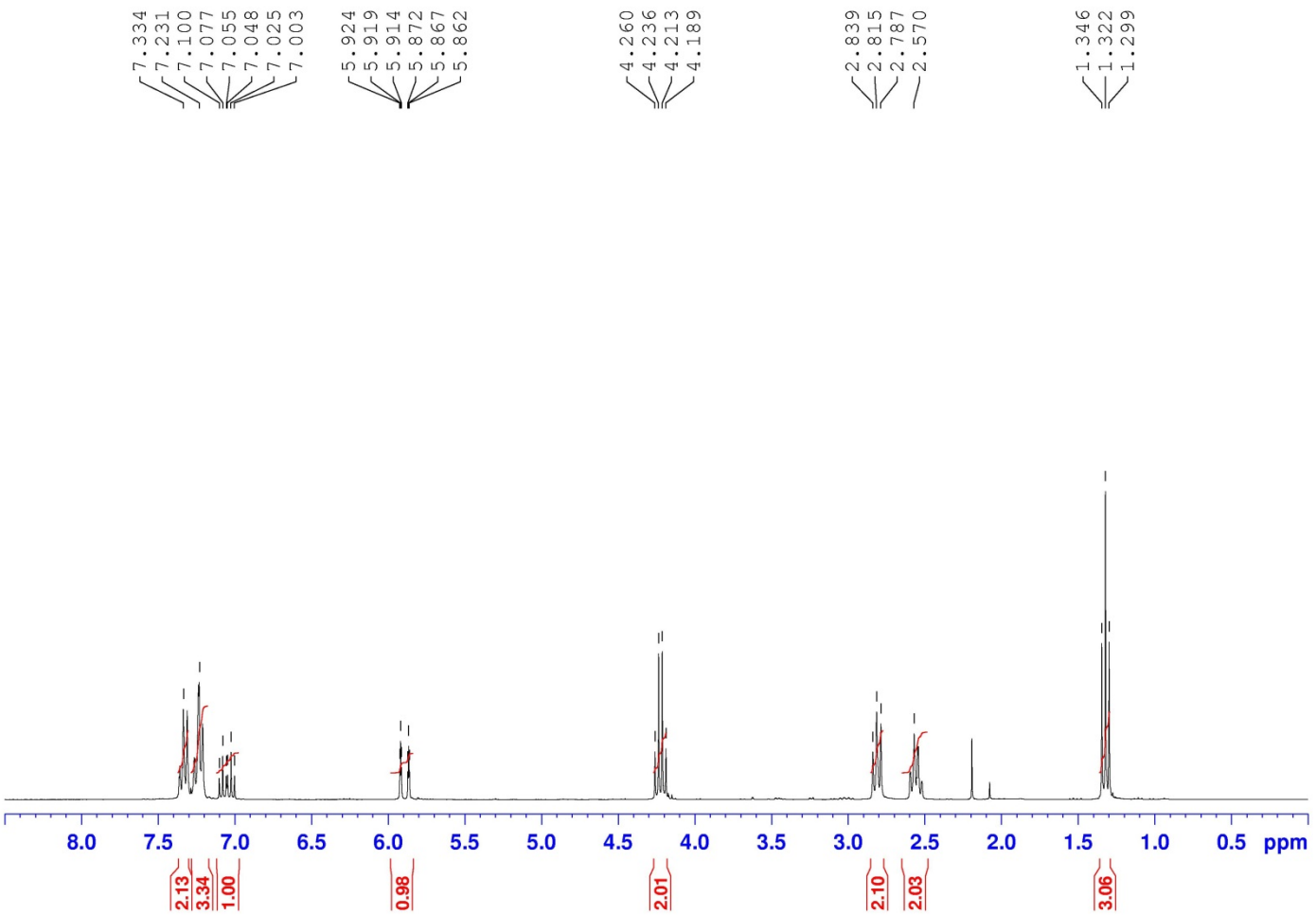


32

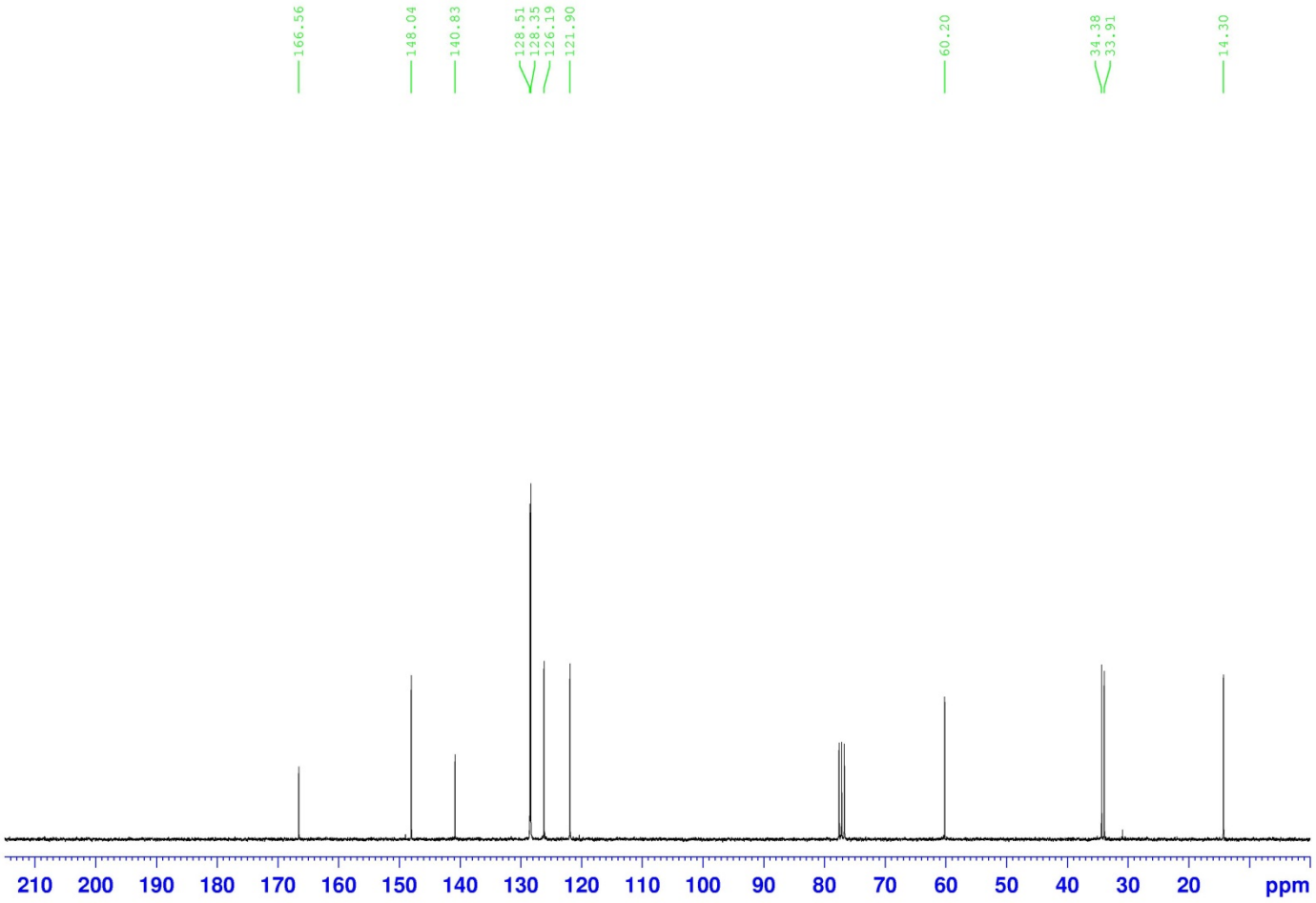
Following the procedure of preparing ethyl (*E*)-5-phenylpent-2-enoate, after flash chromatography on silica gel (95:5 hexanes:ethyl acetate), the title compound (91%) as a colorless liquid.

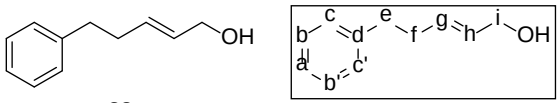
TLC analysis	R_f 0.50 (90:10 hexanes:ethyl acetate)
^{1}H NMR (300 MHz, $CDCl_3$)	δ 7.35–7.30 (2H, m, b,b'), 7.30–7.15 (3H, m, a,c,c'), 7.05 (1H, dt, *J* = 15.7 and 6.8 Hz, g), 5.89 (1H, dt, *J* = 15.7 and 1.5 Hz, h), 4.22 (2H, q, *J* = 15.7 Hz, j), 2.81 (2H, t, *J* = 7.3 Hz, e), 2.60–2.50 (2H, m, f) 1.32 (3H, t, *J* = 7.1 Hz, k).
^{13}C NMR (75 MHz, $CDCl_3$)	δ 166.56 (i), 148.04 (g), 140.83 (d), 128.51 (b,b'), 128.35 (c,c'), 126.19 (a), 121.90 (h), 60.20 (j), 34.38 (e), 33.91 (f), 14.30 (k).

^{1}H NMR of 32


7.334
7.231
7.100
7.077
7.055
7.048
7.025
7.003
5.924
5.919
5.914
5.872
5.867
5.862
4.260
4.236
4.213
4.189
2.839
2.815
2.787
2.570
1.346
1.322
1.299
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.13
3.34
1.00
0.98
2.01
2.10
2.03
3.06

^{13}C NMR of 32


166.56
148.04
140.83
128.51
128.35
126.19
121.90
60.20
34.38
33.91
14.30
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

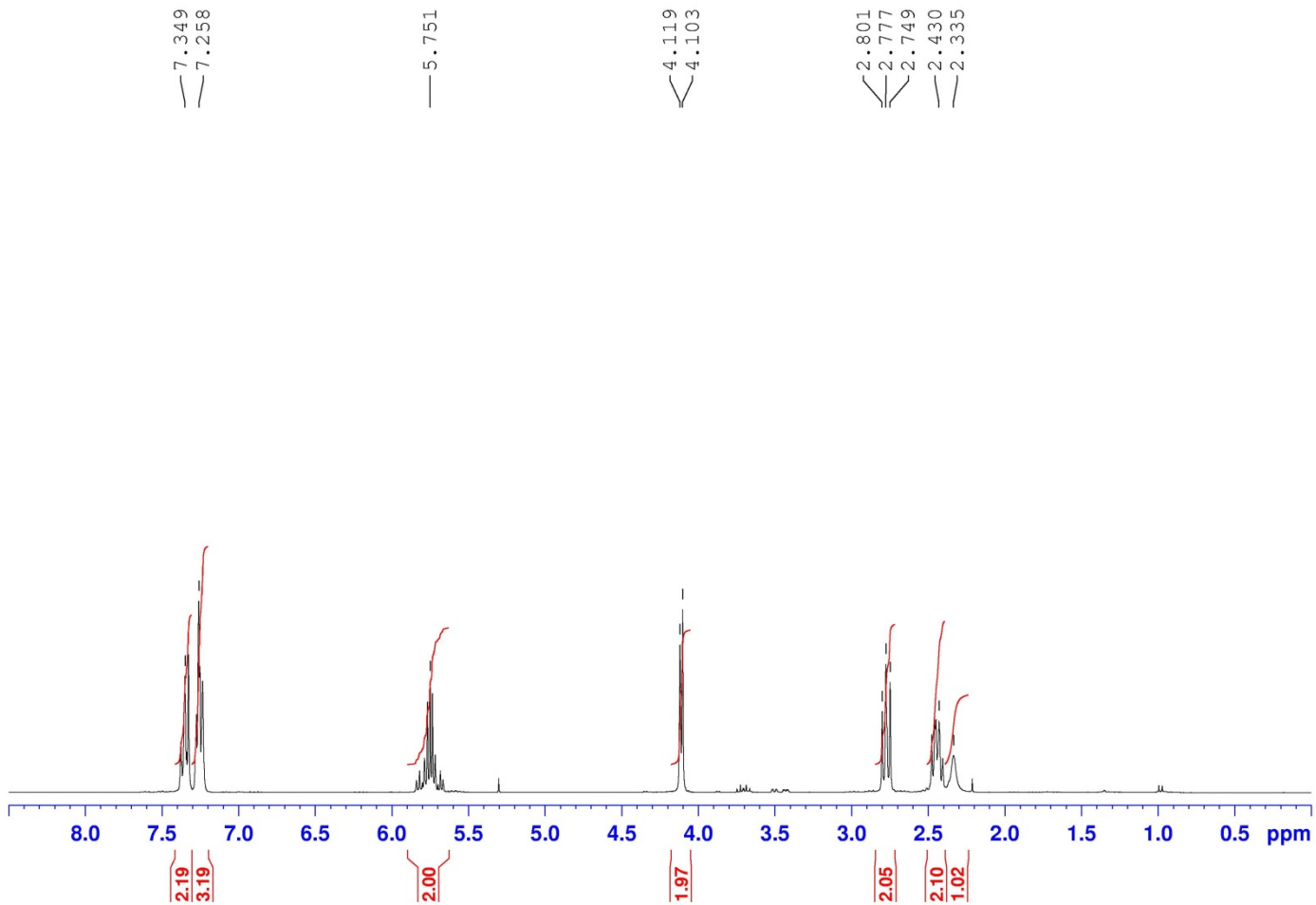


33

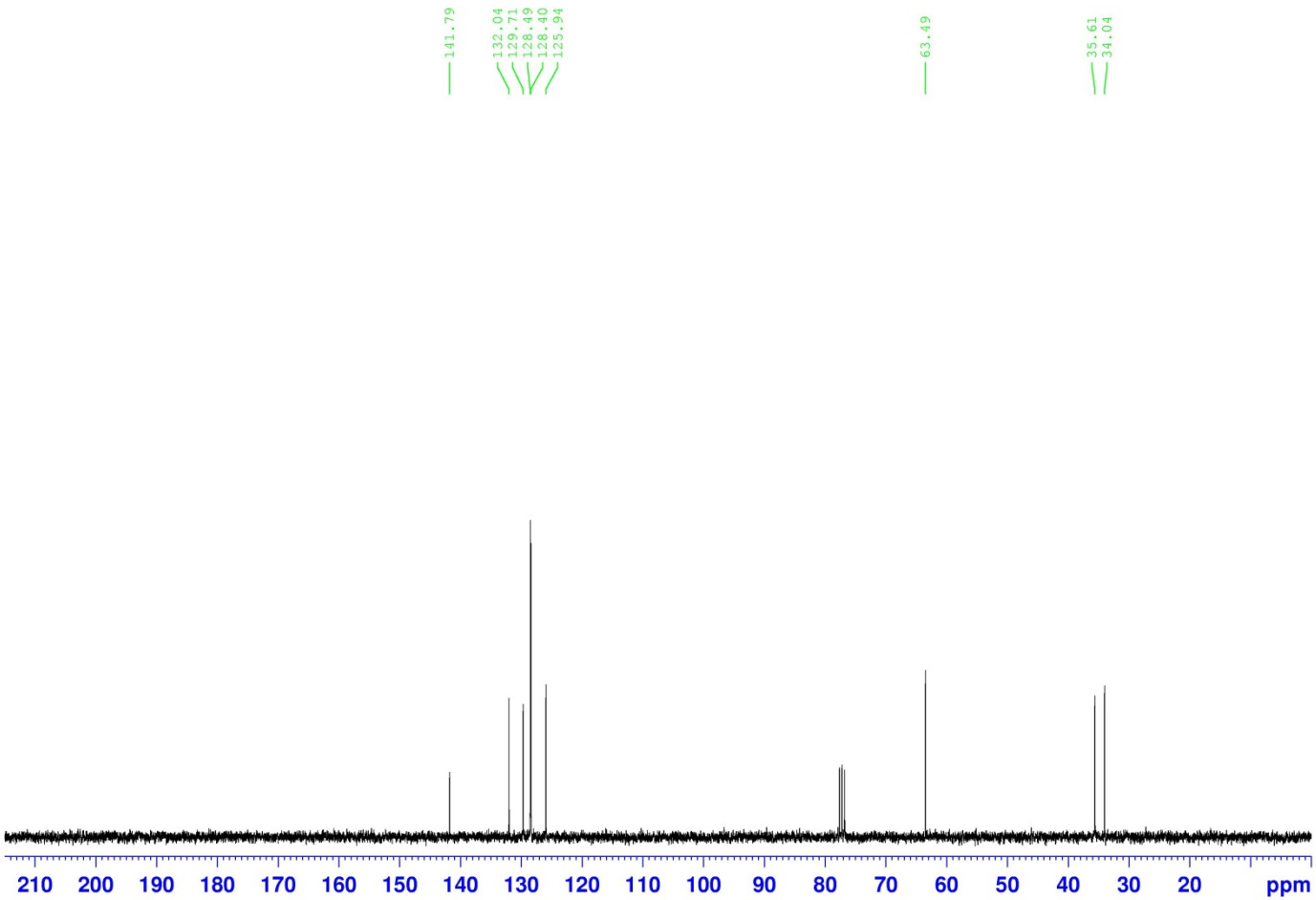
Following the procedure of preparing (*E*)-5-phenylpent-2-en-1-ol affords the title compound (93%) as a colorless liquid.

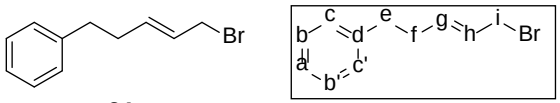
^{1}H NMR (300 MHz, $CDCl_3$)	δ 7.40–7.30 (2H, m, b,b'), 7.30–7.20 (3H, m, a,c,c'), 5.90–5.60 (2H, m, g,h), 4.11 (2H, d, *J* = 4.9 Hz, i), 2.78 (2H, t, *J* = 7.3 Hz, e), 2.50–2.40 (2H, m, f), 2.40–2.25 (1H, br s, OH).
^{13}C NMR (75 MHz, $CDCl_3$)	δ 141.79 (d), 132.04 (h), 129.71 (g), 128.49 (b,b'), 128.40 (c,c'), 125.94 (a), 63.49 (i), 35.61 (e), 34.04 (f).

^{1}H NMR of 33


7.349
7.258
5.751
4.119
4.103
2.801
2.777
2.749
2.430
2.335
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.19
3.19
2.00
1.97
2.05
2.10
1.02

^{13}C NMR of 33


141.79
132.04
129.71
128.49
128.40
125.94
63.49
35.61
34.04
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

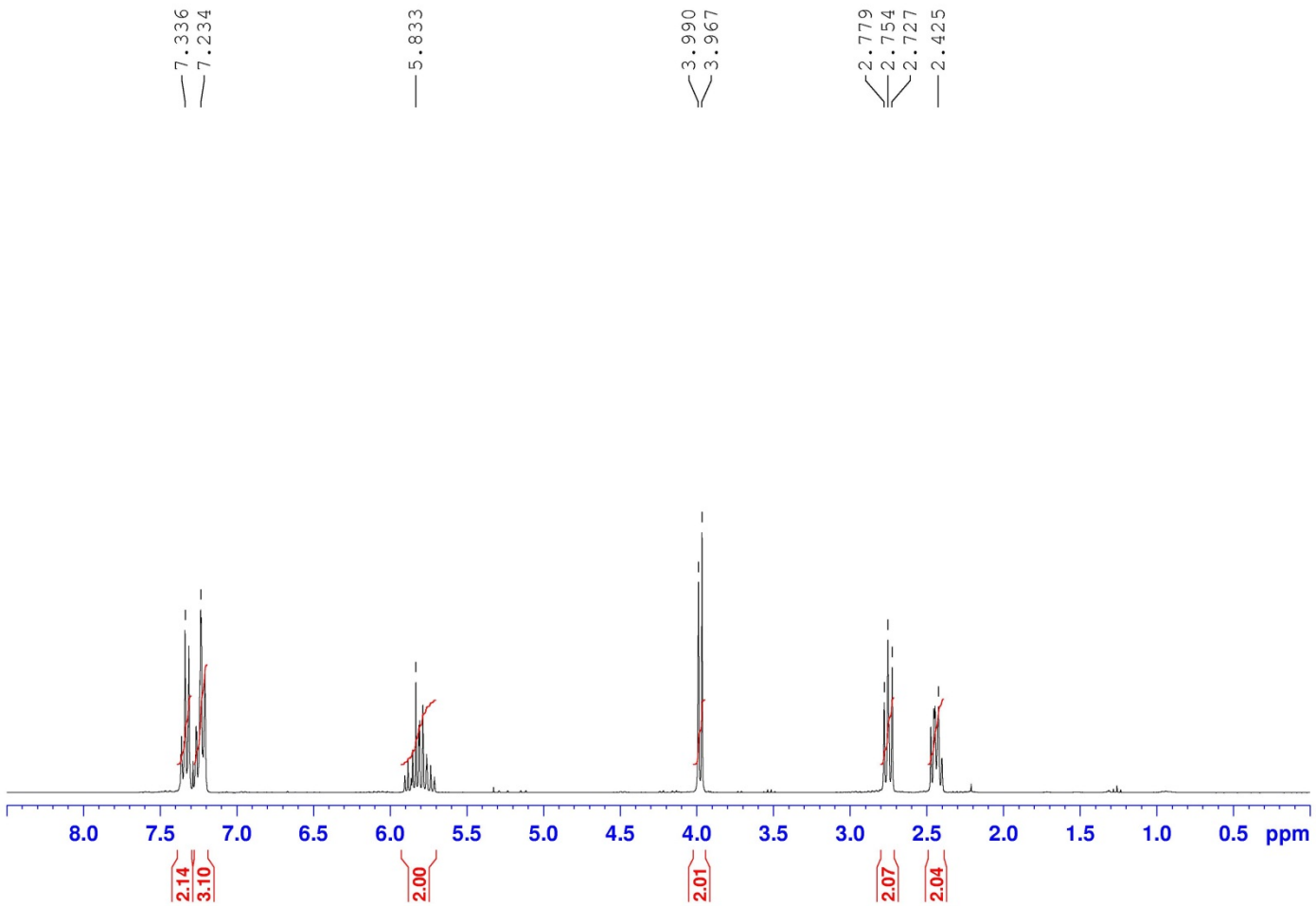


34

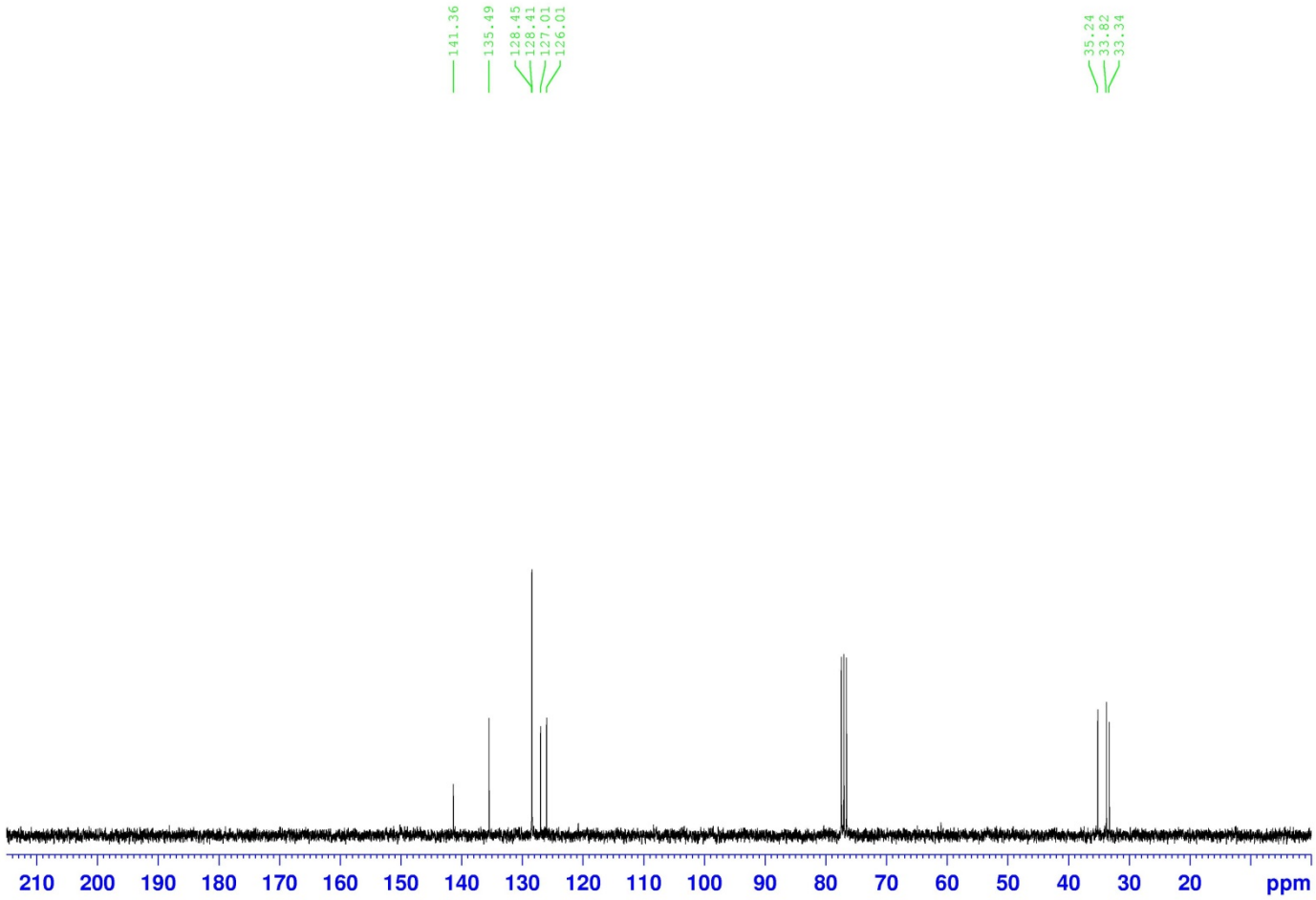
Following the procedure of preparing (*E*)-(5-bromopent-3-en-1-yl)benzene affords the title compound (95%) as a colorless liquid.

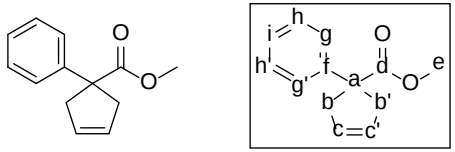
^{1}H NMR (300 MHz, $CDCl_3$)	δ 7.40–7.30 (2H, m, b,b'), 7.30–7.20 (3H, m, a,c,c'), 5.90–5.70 (2H, m, g,h), 3.98 (2H, d, *J* = 6.8 Hz, i), 2.75 (2H, t, *J* = 7.3 Hz, e), 2.50–2.40 (2H, m, f).
^{13}C NMR (75 MHz, $CDCl_3$)	δ 141.36 (d), 135.49 (h), 128.45 (b,b'), 128.41 (c,c'), 127.01 (g'), 126.01 (a), 35.24 (i), 33.82 (e), 33.34 (f).

^{1}H NMR of 34


7.336
7.234
5.833
3.990
3.967
2.779
2.754
2.727
2.425
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.14
3.10
2.00
2.01
2.07
2.04

^{13}C NMR of 34


141.36
135.49
128.45
128.41
127.01
126.01
35.24
33.82
33.34
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

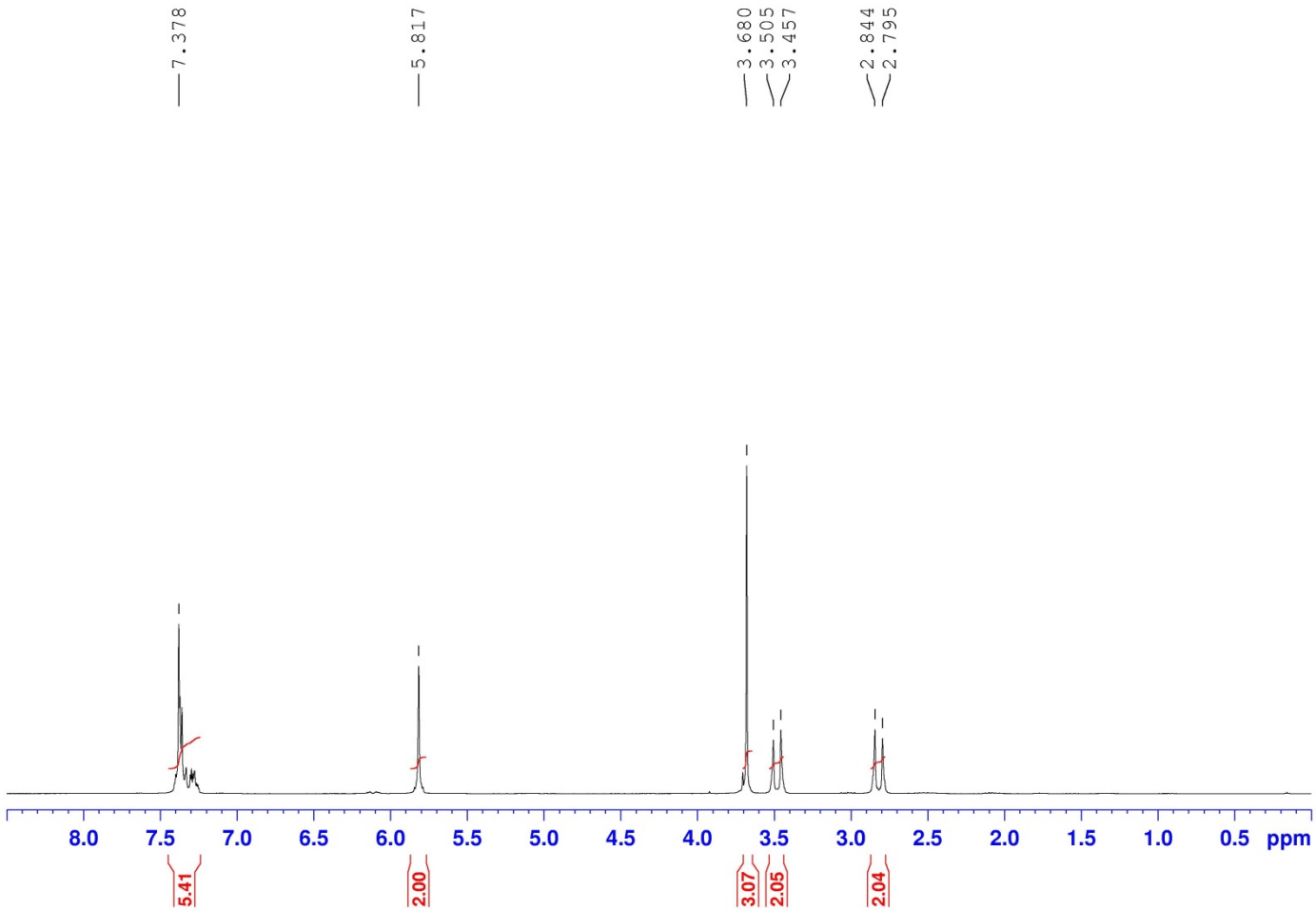


35

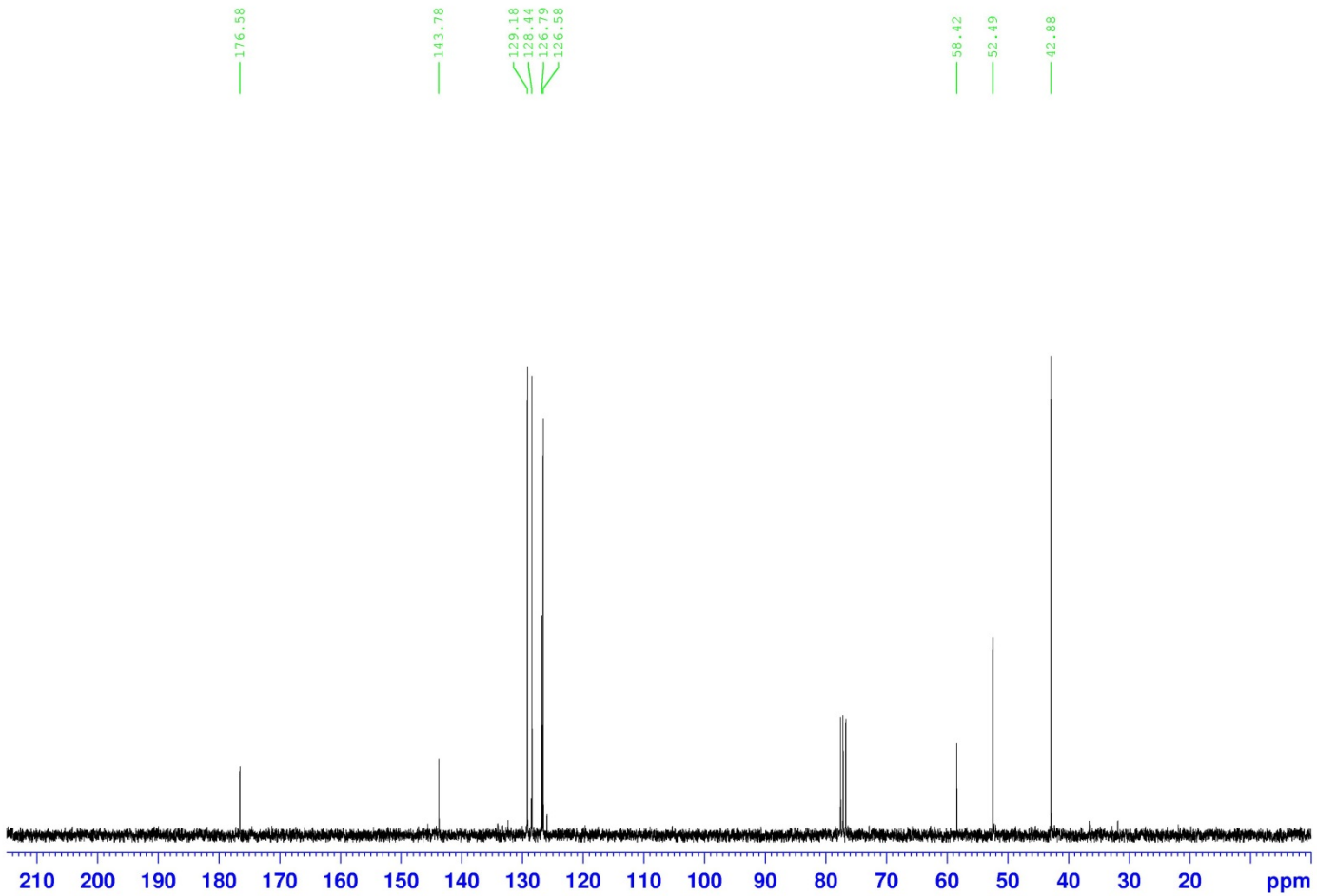
Following the procedure of preparing methyl 1-phenyl-3-cyclopentenecarboxylate affords, after flash chromatography on silica gel (97:3 hexanes:ethyl acetate), the title compound (44%) as a yellow oil.

TLC analysis	R_f 0.80 (70:30 hexanes:ethyl acetate)
^{1}H NMR (300 MHz, $CDCl_3$)	δ 7.45–7.20 (5H, m, g,g',h,h',i), 5.82 (2H, s, c,c'), 3.68 (3H, s, e), 3.48 (2H, d, J = 14.6, b,b'), 2.82 (2H, d, J = 14.8, b,b').
^{13}C NMR (75 MHz, $CDCl_3$)	δ 176.58 (d), 143.78 (f), 129.18 (g,g'), 128.44 (c,c'), 126.79 (h,h'), 126.58 (i), 58.42 (e), 52.49 (a), 42.88 (b,b').

^{1}H NMR of 35


7.378
5.817
3.680
3.505
3.457
2.844
2.795
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
5.41
2.00
3.07
2.05
2.04

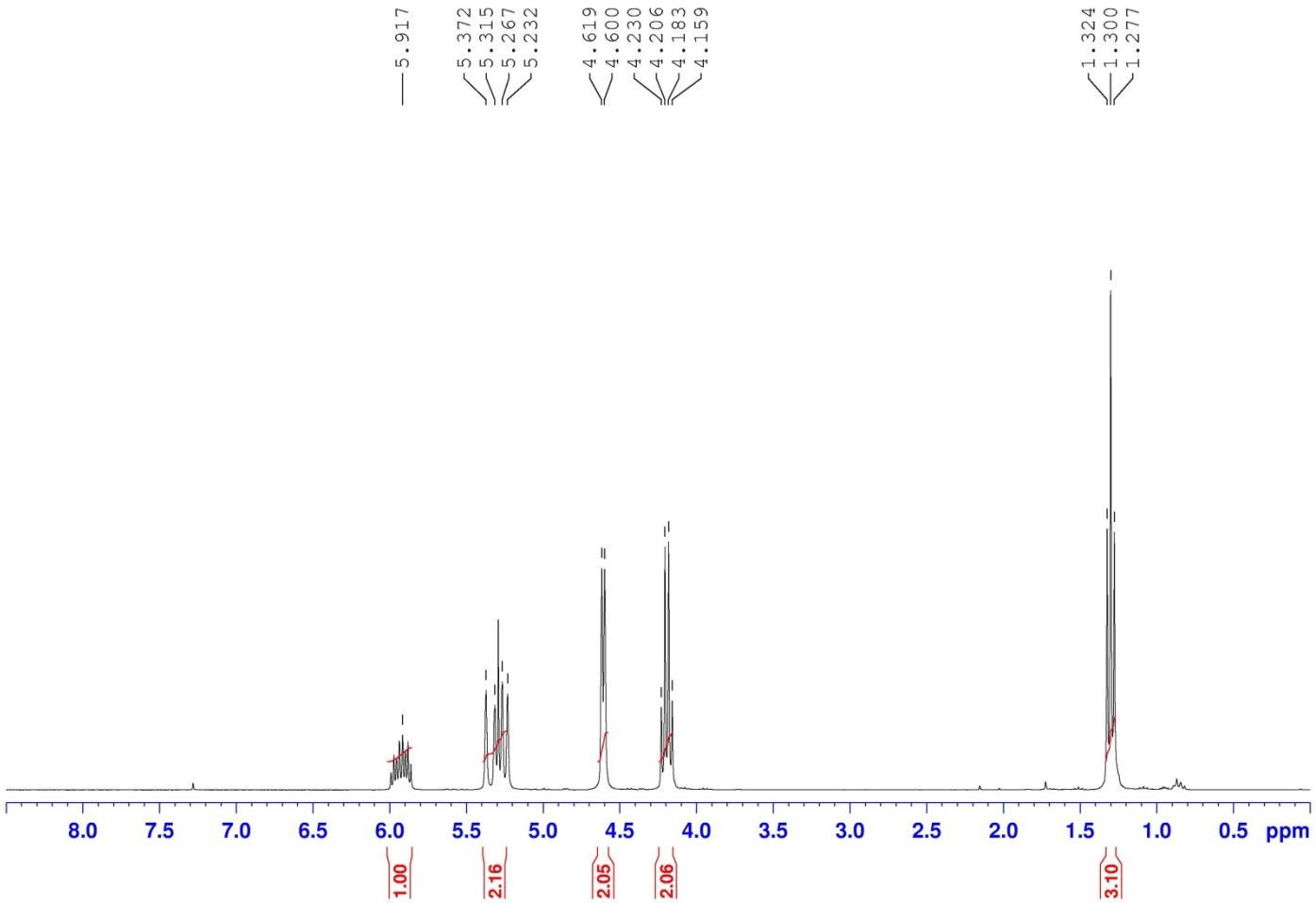
^{13}C NMR of 35


176.58
143.78
129.18
128.44
126.79
126.58
58.42
52.49
42.88
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

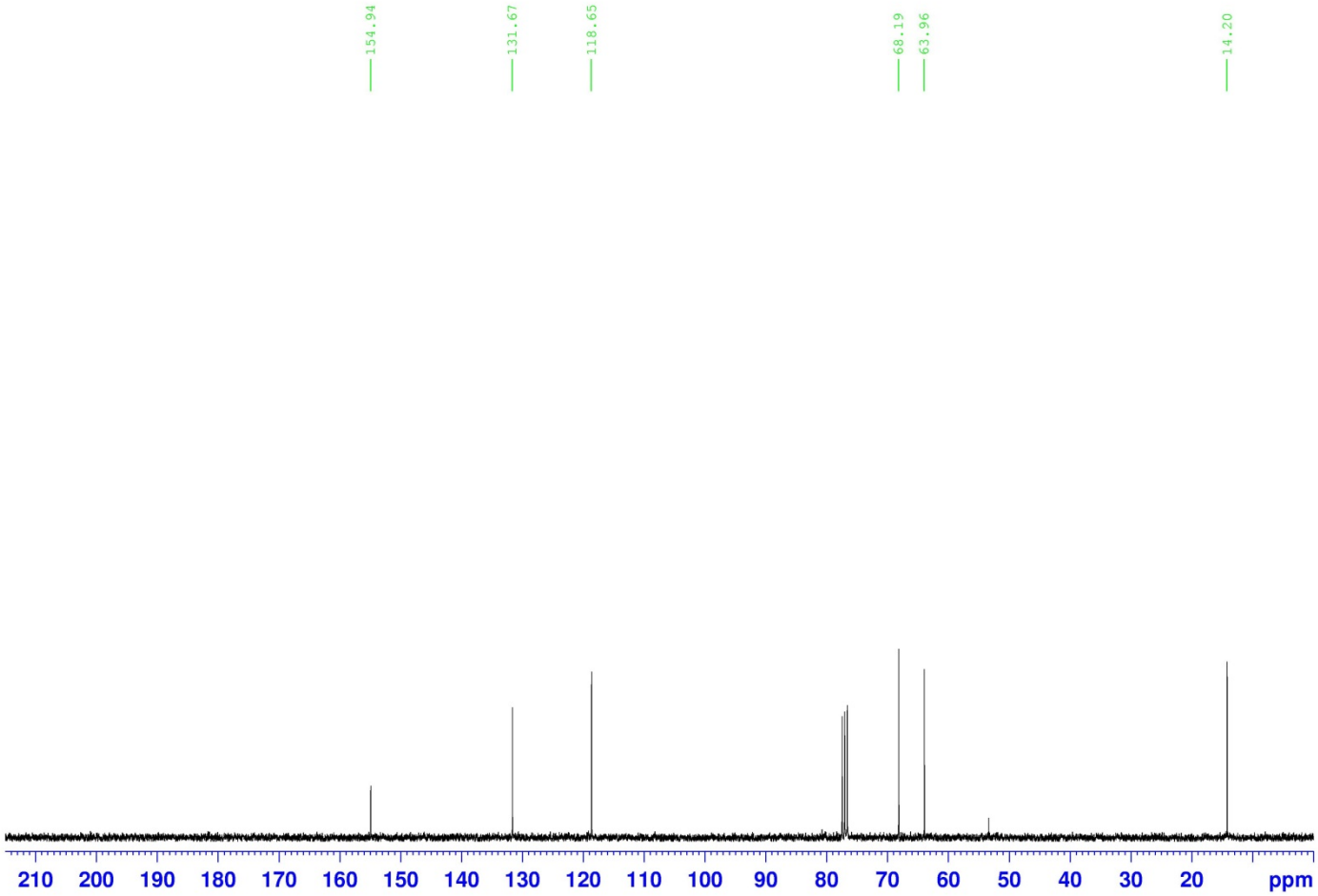
Following the procedure of preparing allyl ethyl carbonate affords, after flash chromatography on silica gel (95:5 hexanes:ethyl acetate), the title compound (93%) as a colorless oil.

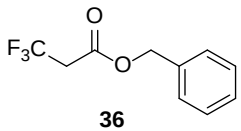
TLC analysis	R_f 0.55 (90:10 hexanes:ethyl acetate);
^{1}H NMR (300 MHz, $CDCl_3$)	δ 6.05–5.80 (1H, m, b), 5.29 (1H, dd, *J* = 31.5 Hz, 17.1 Hz, a), 4.61 (2H, d, *J* = 5.7 Hz, c), 4.19 (2H, q, *J* = 7.1 Hz, e), 1.30 (3H, t, *J* = 7.1 Hz, f).
^{13}C NMR (75 MHz, $CDCl_3$)	δ 154.94 (d), 131.67 (b), 118.65 (a), 68.19 (c), 63.96 (e), 14.20 (f).

^{1}H NMR of allyl ethyl carbonate

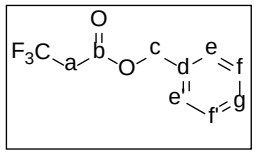


^{13}C NMR of allyl ethyl carbonate





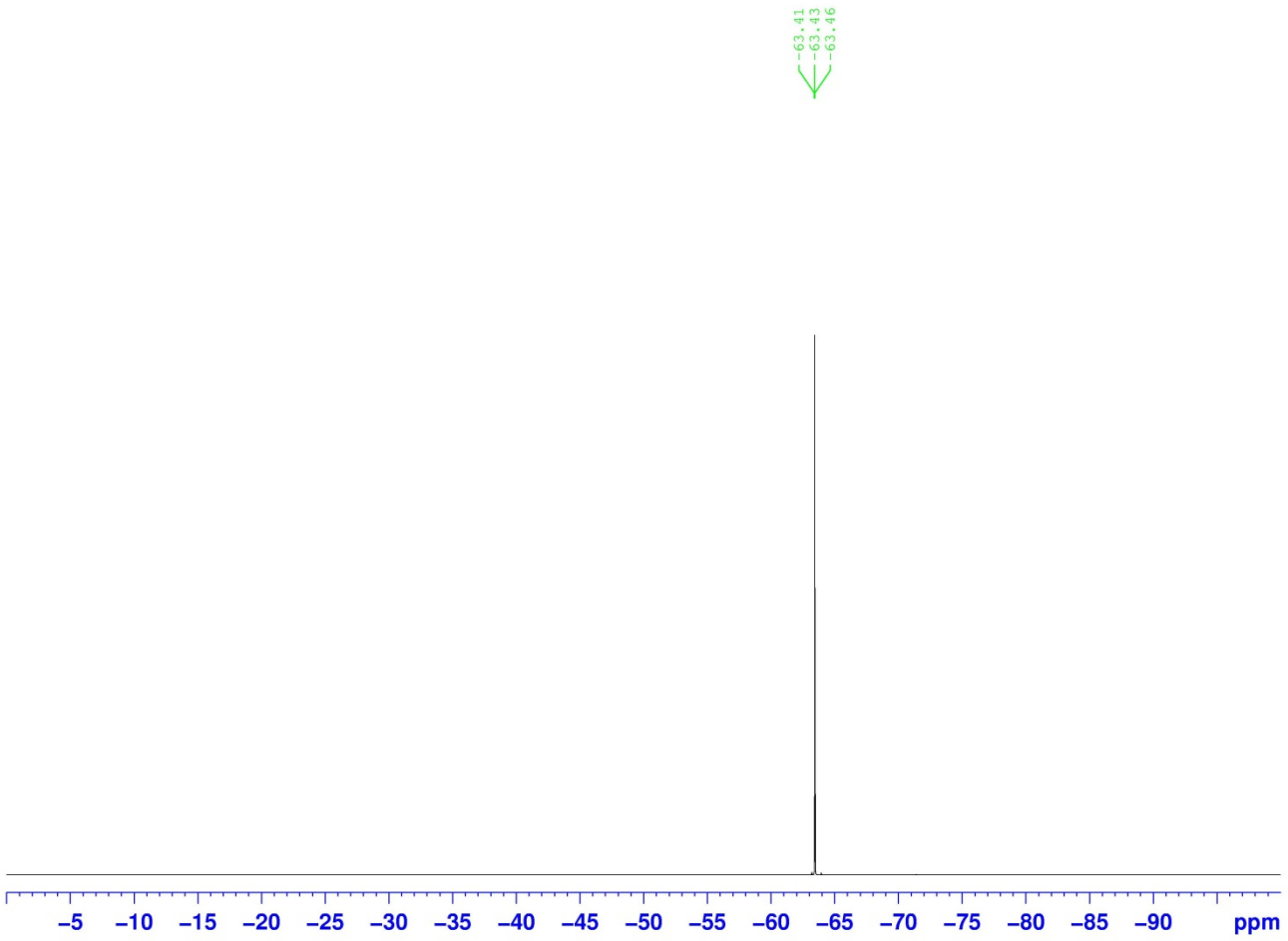
36



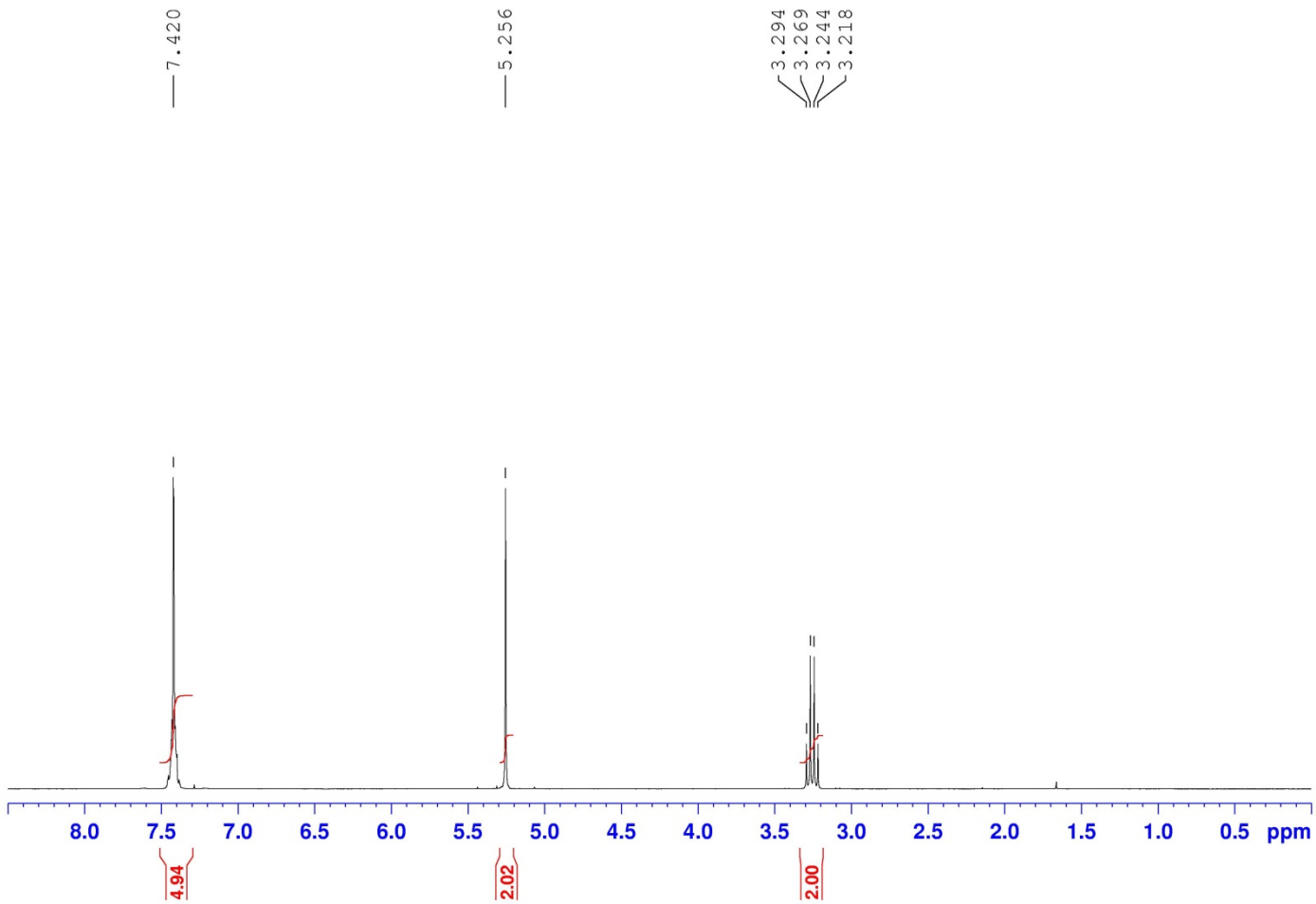
Following the general procedure of DCC-mediated condensation affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (96%) as a colorless oil.

TLC analysis	R_f 0.55 (80:20 hexanes:ethyl acetate).
^{19}F NMR (376 MHz, $CDCl_3$)	δ -63.43 (t, *J* = 9.6 Hz, CF_3).
^{1}H NMR (400 MHz, $CDCl_3$)	δ 7.50–7.35 (5H, m, e,e',f,f',g), 5.26 (2H, s, c), 3.26 (2H, q, *J* = 14.6, a).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 163.00 (q, *J* = 4.1 Hz, b), 134.91 (d), 128.71 (f), 128.66 (e), 128.37 (g), 123.43 (q, *J* = 274.4 Hz, CF_3), 67.50 (c), 39.59 (q, *J* = 30.9 Hz, a).

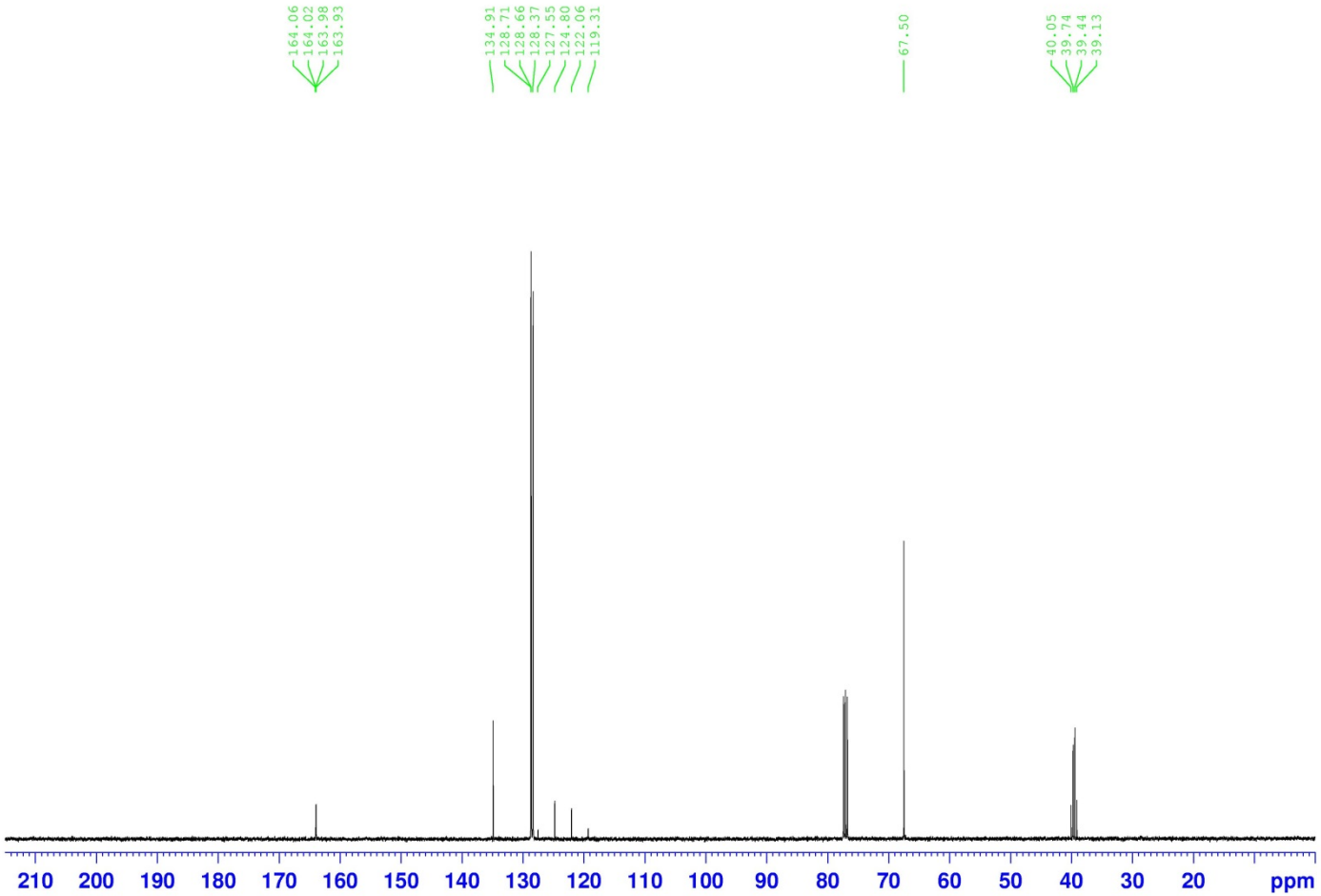
^{19}F NMR of 36

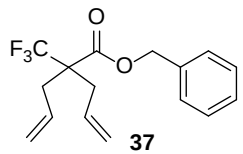

-63.41
-63.43
-63.46
-5
-10
-15
-20
-25
-30
-35
-40
-45
-50
-55
-60
-65
-70
-75
-80
-85
-90
ppm

^{1}H NMR of 36

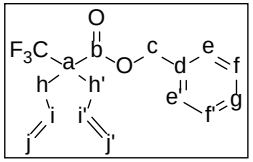

7.420
5.256
3.294
3.269
3.244
3.218
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.94
2.02
2.00

^{13}C NMR of 36


164.06
164.02
163.98
163.93
134.91
128.71
128.66
128.37
127.55
124.80
122.06
119.31
67.50
40.05
39.74
39.44
39.13
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm



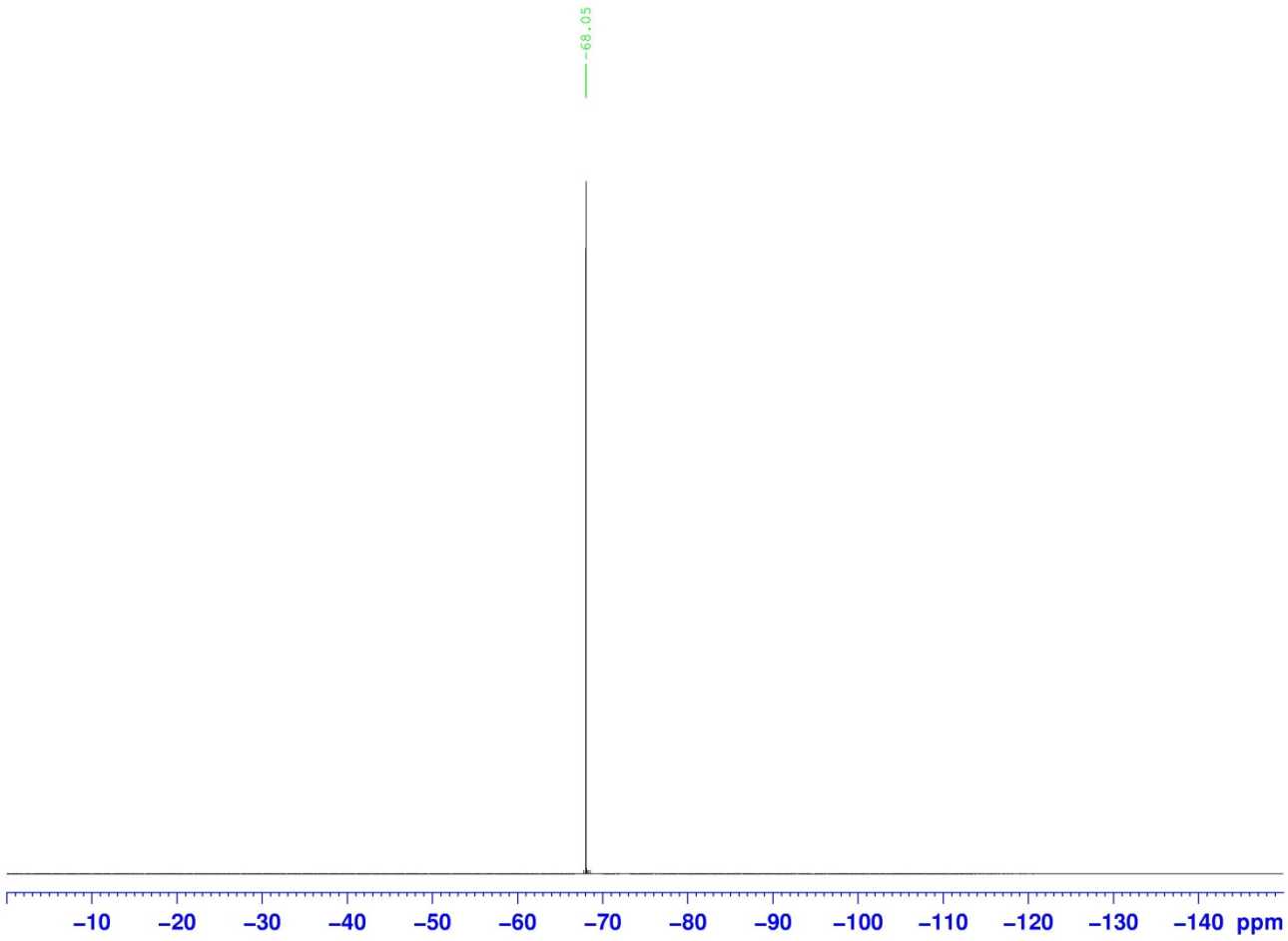
37



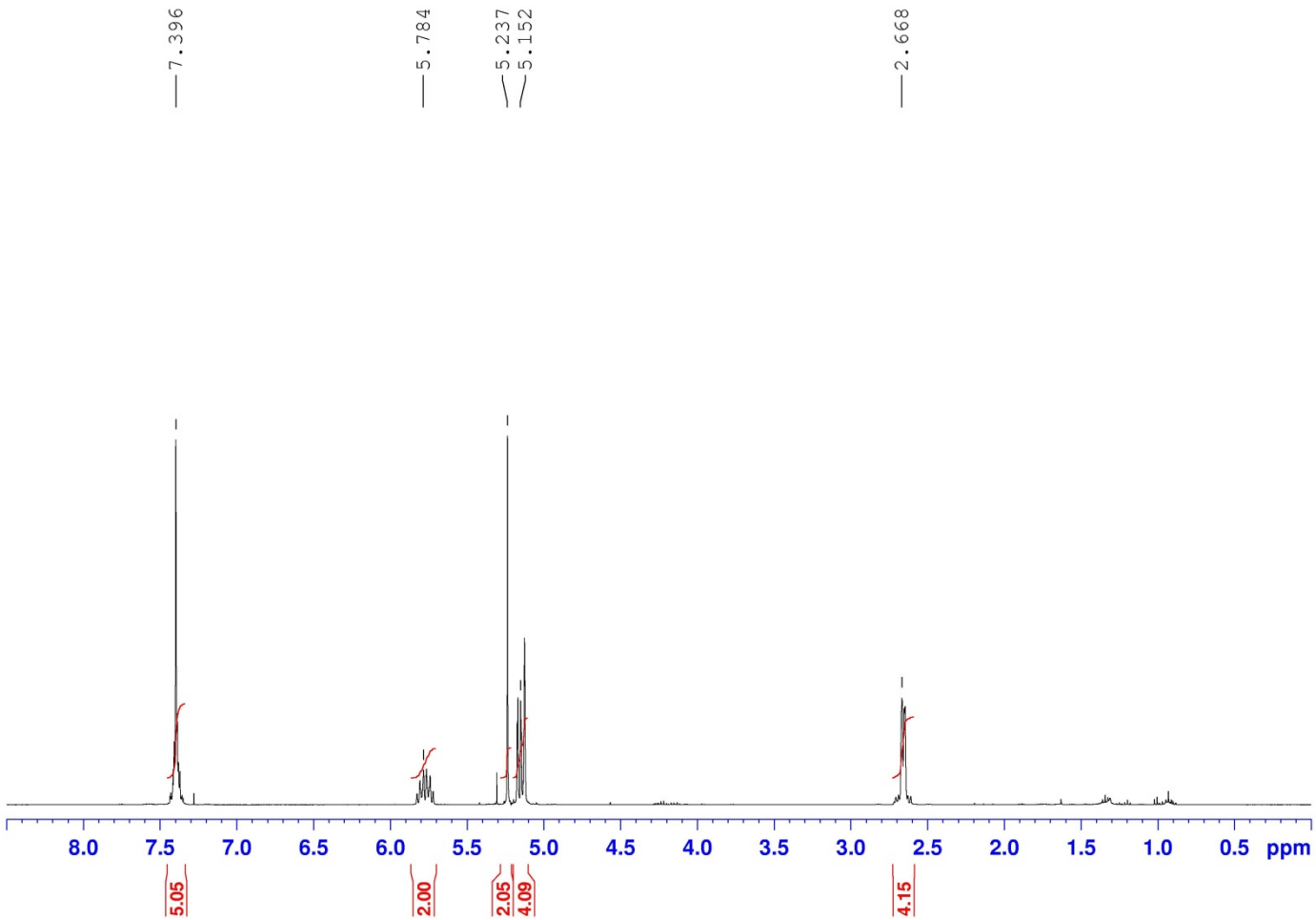
Following the procedure of preparing benzyl 2-allyl-2-(trifluoromethyl)pent-4-enoate affords, after flash chromatography on silica gel (95:5 hexanes:ethyl acetate), the title compound (92%) as a colorless oil.

TLC analysis	R_f 0.85 (70:30 hexanes:ethyl acetate)
^{19}F NMR (376 MHz, $CDCl_3$)	δ -68.05 (s, CF_3).
^{1}H NMR (400 MHz, $CDCl_3$)	δ 7.45–7.35 (5H, m, e,e',f,f',g), 5.85–5.70 (2H, m, i,i'), 5.24 (2H, s, c), 5.20–5.10 (4H, m, j,j'), 2.70–2.60 (4H, m, h,h').
^{13}C NMR (100 MHz, $CDCl_3$)	δ 168.40 (b), 135.11 (d), 131.50 (i,i'), 128.61 (f,f'), 128.46 (g), 128.23 (e,e'), 125.91 (q, J = 283.24 Hz, CF_3), 119.69 (j,j'), 67.49 (c), 55.94 (q, J = 23.14 Hz, a), 36.19 (h,h').

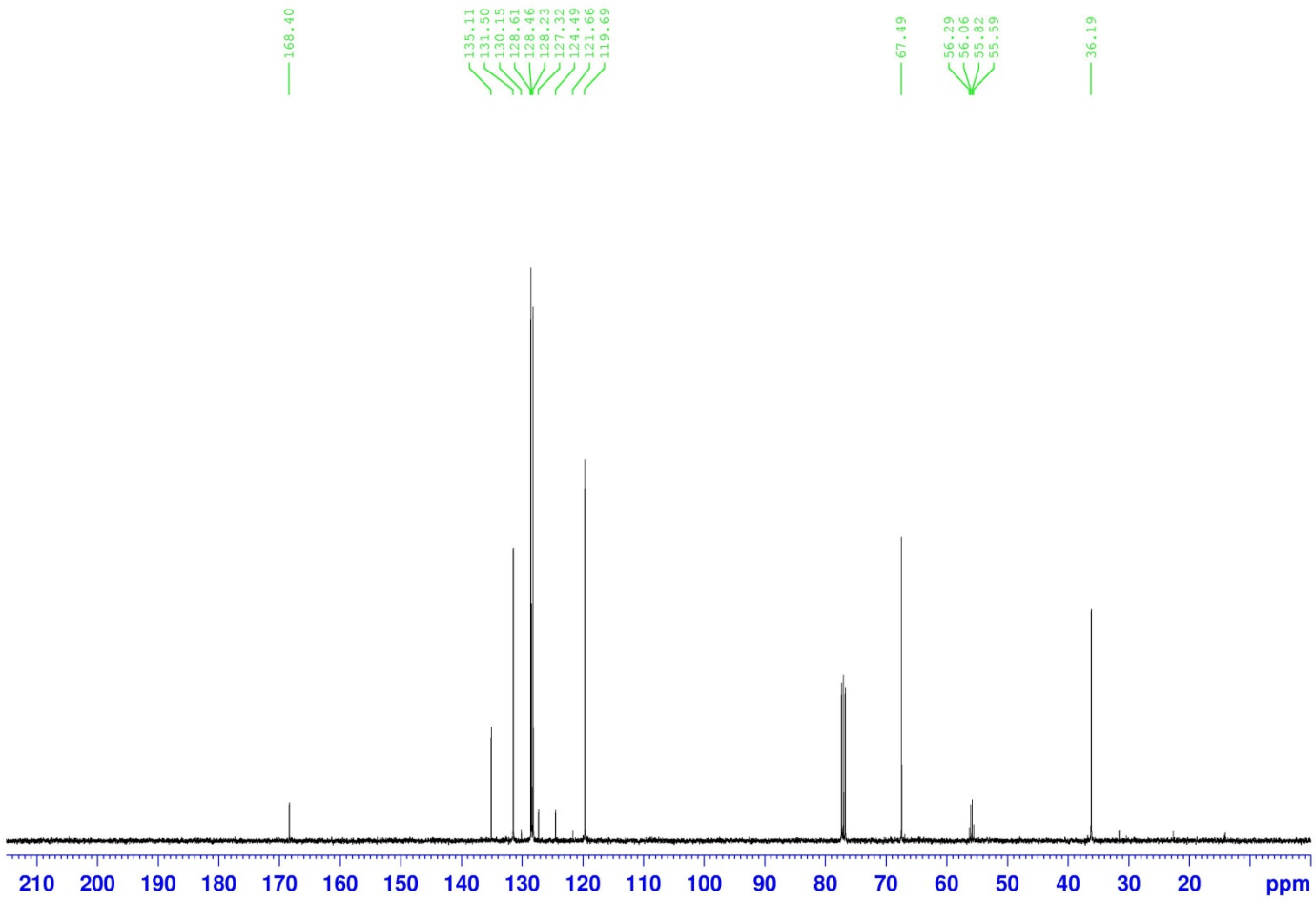
^{19}F NMR of 37

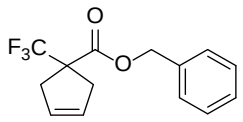


^{1}H NMR of 37

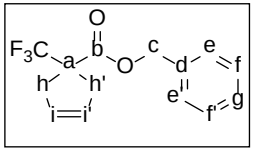

7.396
5.784
5.237
5.152
2.668
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
5.05
2.00
2.05
4.09
4.15

^{13}C NMR of 37


168.40
135.11
131.50
130.15
128.61
128.46
128.23
127.32
124.49
121.66
119.69
67.49
56.29
56.06
55.82
55.59
36.19
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm



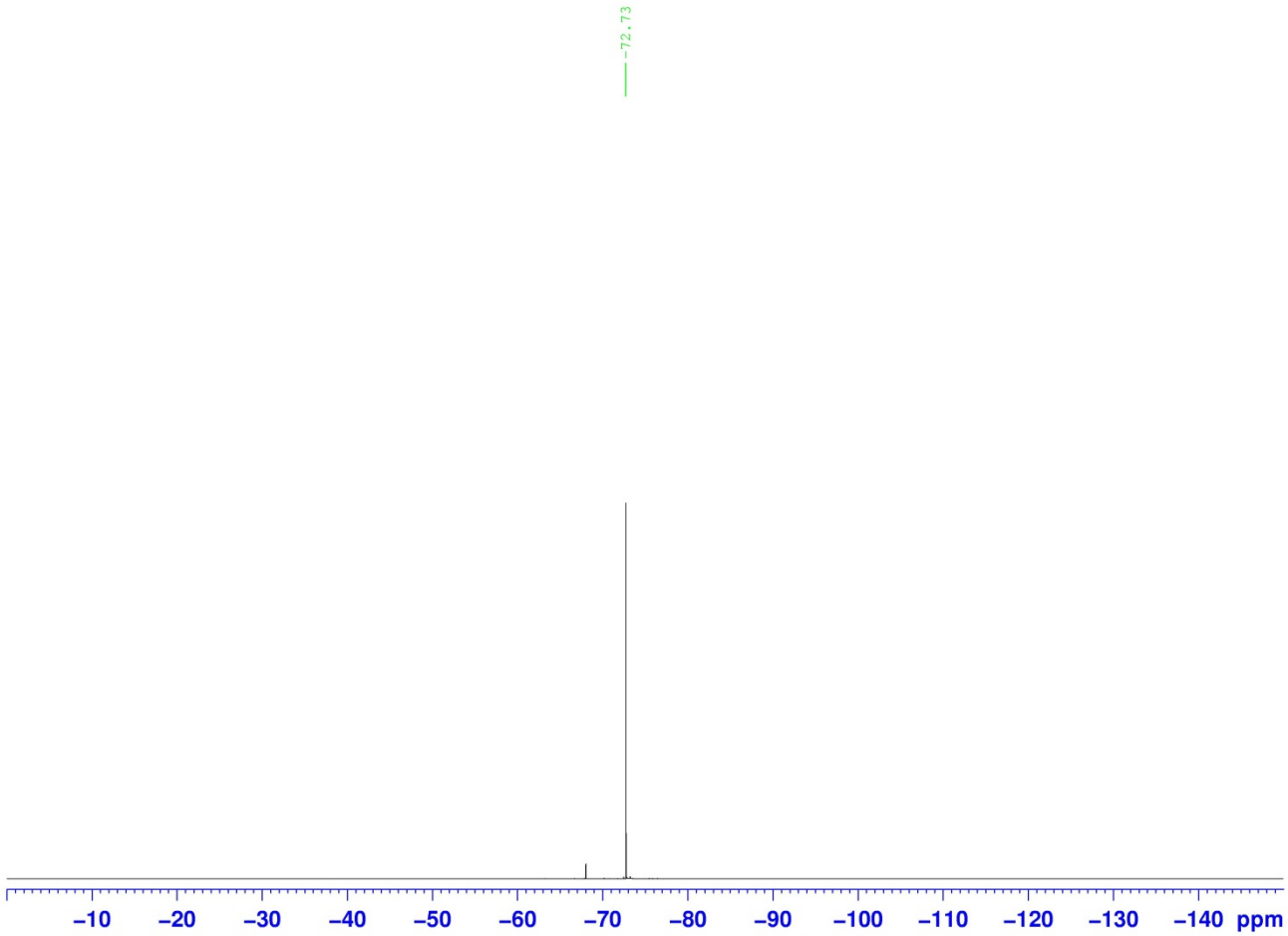
38



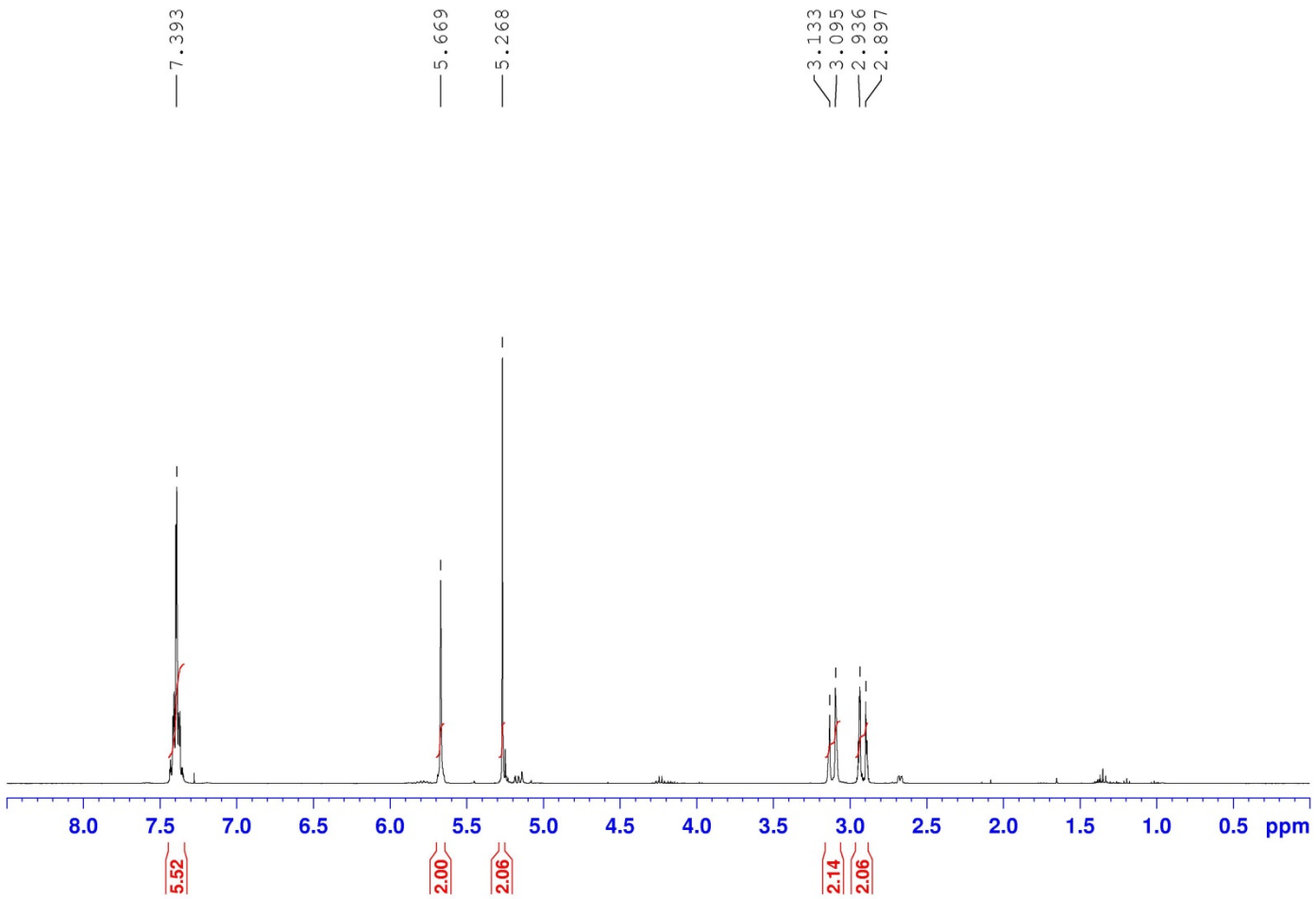
Following the procedure of preparing benzyl 1-(trifluoromethyl)cyclopent-3-enecarboxylate affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (99%) as a colorless oil.

TLC analysis	R_f 0.75 (80:20 hexanes:ethyl acetate)
^{19}F NMR (376 MHz, $CDCl_3$)	δ -72.73 (s, CF_3).
^{1}H NMR (400 MHz, $CDCl_3$)	δ 7.45–7.35 (5H, m, e,e',f,f',g), 5.67 (2H, s, i,i'), 5.27 (2H, s, c), 3.11 (2H, d, *J* = 15.2, h,h'), 2.92 (2H, d, *J* = 15.8, h,h').
^{13}C NMR (100 MHz, $CDCl_3$)	δ 170.12 (b), 135.29 (d), 128.63 (i,i'), 128.40 (f,f'), 127.89 (g), 127.67 (e,e'), 126.67 (q, *J* = 279.0 Hz, CF_3), 67.66 (c), 57.14 (q, *J* = 25.7 Hz, a), 38.87 (h,h').

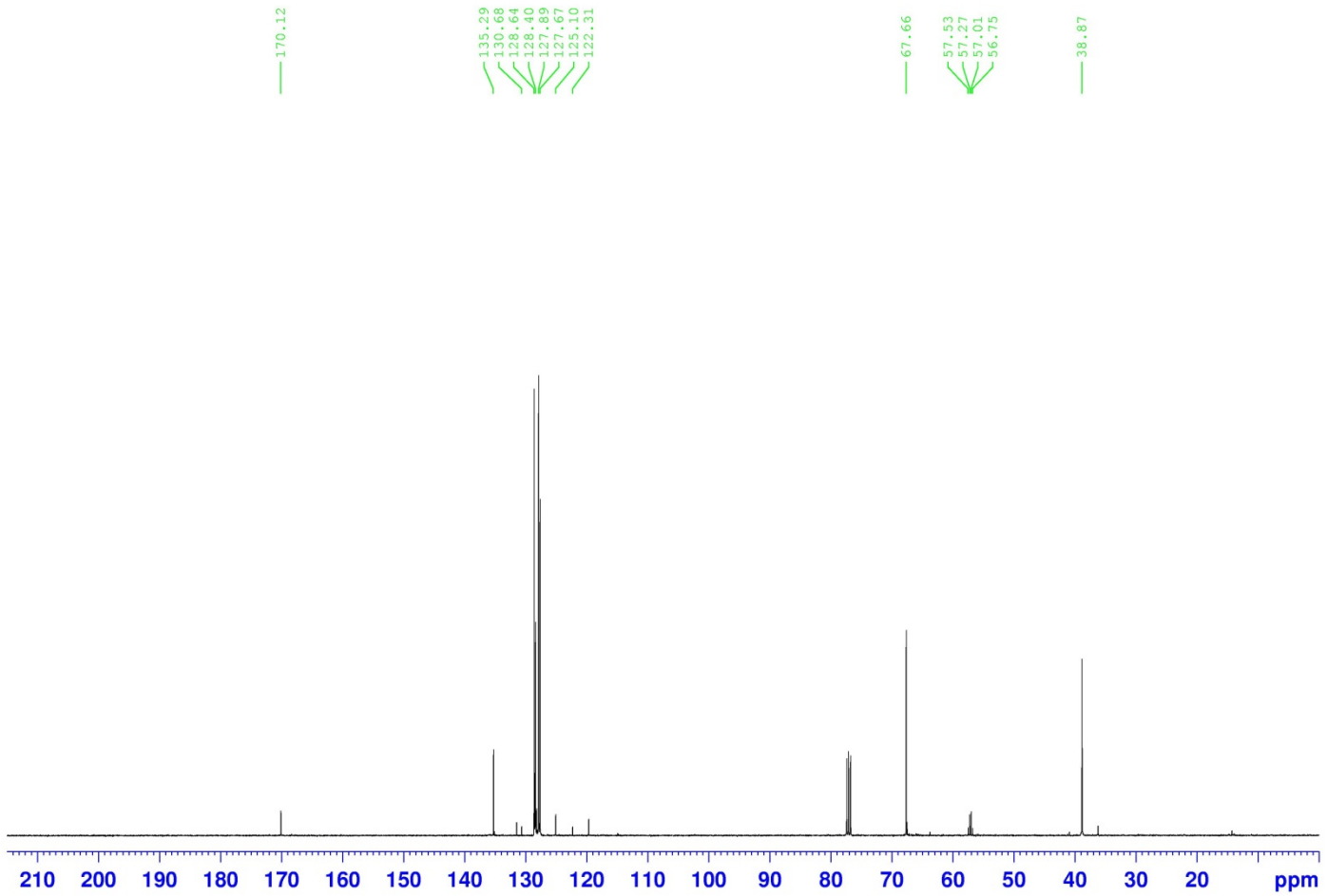
^{19}F NMR of 38

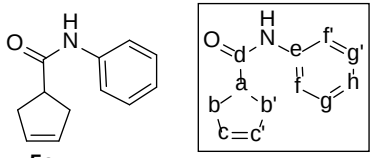


^{1}H NMR of 38


7.393
5.669
5.268
3.133
3.095
2.936
2.897
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
5.52
2.00
2.06
2.14
2.06

^{13}C NMR of 38


170.12
135.29
130.68
128.64
128.40
127.89
127.67
125.10
122.31
67.66
57.53
57.27
57.01
56.75
38.87
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

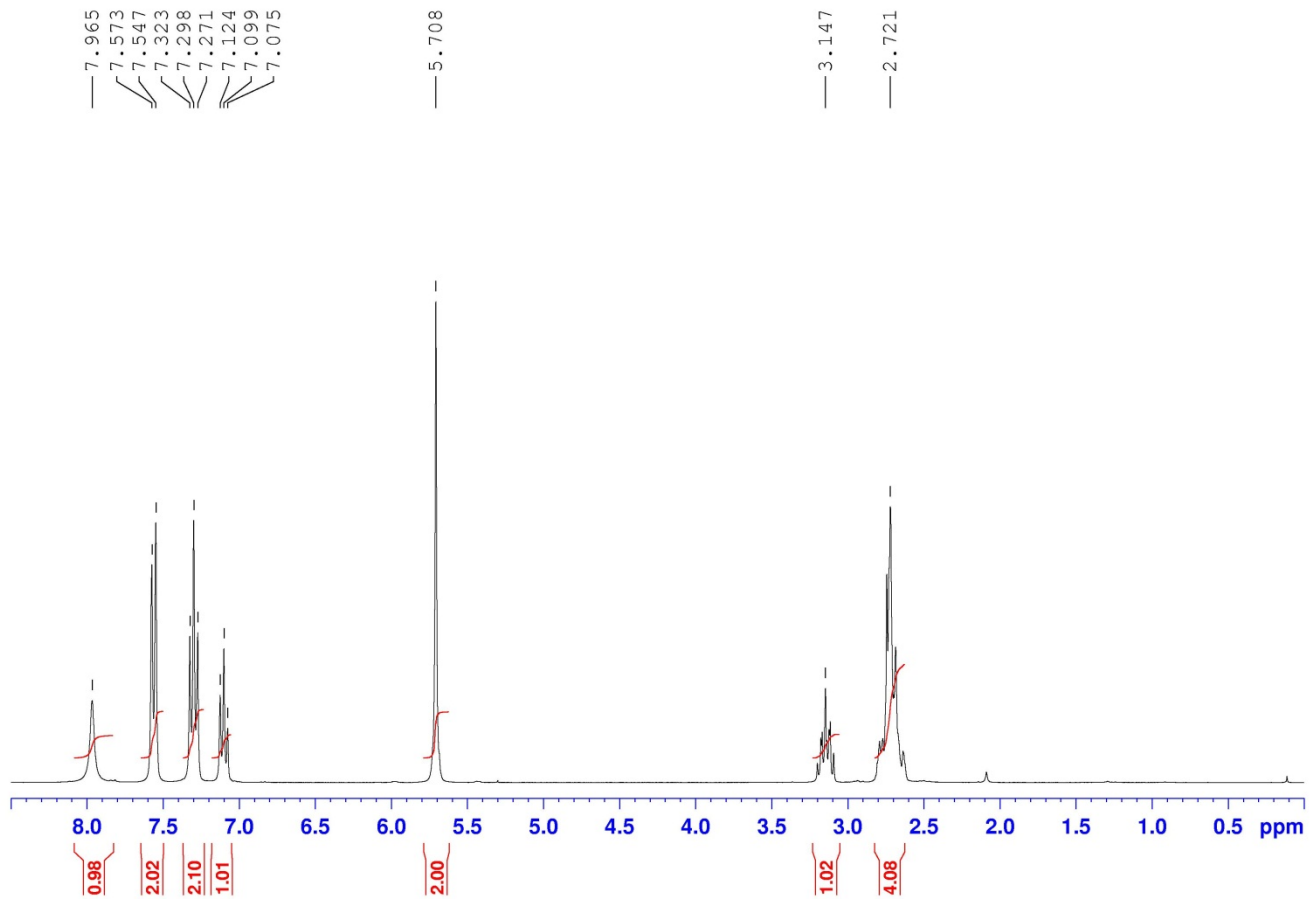


5a

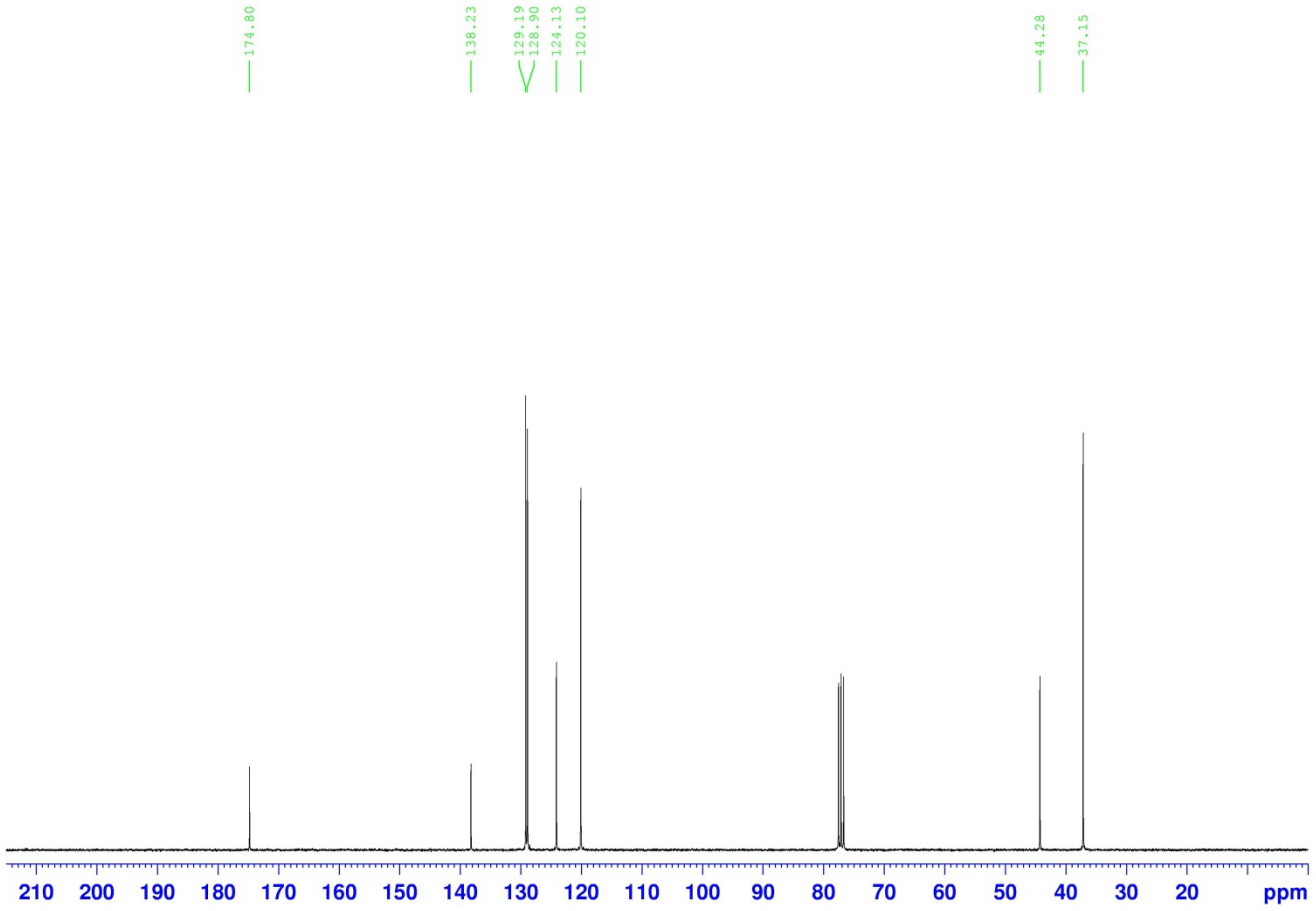
Following the general amidation procedure with EDCI affords, after flash chromatography on silica gel (85:15 hexanes:ethyl acetate), the title compound (87%) as a white solid.

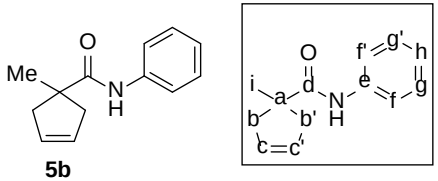
m.p.	83.0–84.5 °C
TLC analysis	R_f 0.5 (75:25 hexanes:ethyl acetate)
^{1}H NMR (300 MHz, $CDCl_3$)	δ 7.97 (1H, br s, NH), 7.56 (2H, t, *J* = 7.8 Hz, f,f'), 7.30 (2H, t, *J* = 7.6 Hz, g,g'), 7.10 (1H, t, *J* = 7.4 Hz, h), 5.71 (2H, s, c,c'), 3.25–3.05 (1H, m, a), 2.85–2.55 (4H, m, b,b').
^{13}C NMR (75 MHz, $CDCl_3$)	δ 174.80 (d), 138.23 (e), 129.19 (c,c'), 128.90 (g,g'), 124.13 (h), 120.10 (f,f'), 44.28 (a), 37.15 (b,b').
IR (neat)	3288 (N-H stretch), 3253, 3142, 1655 (C=O stretch), 1544 (N-H bend), 1439, 1310, 750 cm^{-1}.
HRMS (FAB)	Calcd. for $C_{12}H_{14}NO$ (M+H): 188.0997, found 188.1081 *m/z*.

^{1}H NMR of 5a


7.965
7.573
7.547
7.323
7.298
7.271
7.124
7.099
7.075
5.708
3.147
2.721
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.98
2.02
2.10
1.01
2.00
1.02
4.08

^{13}C NMR of 5a


174.80
138.23
129.19
128.90
124.13
120.10
44.28
37.15
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

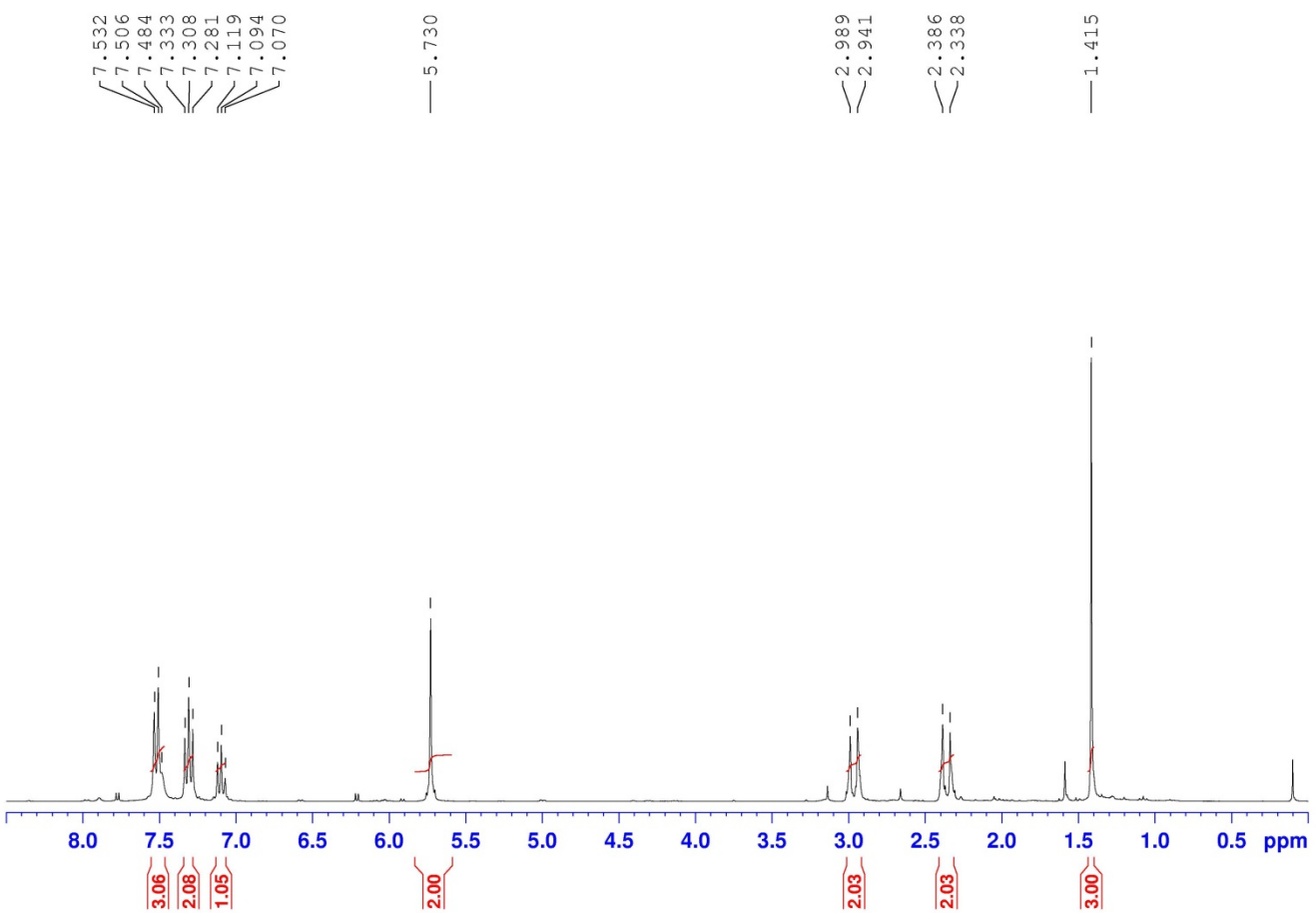


5b

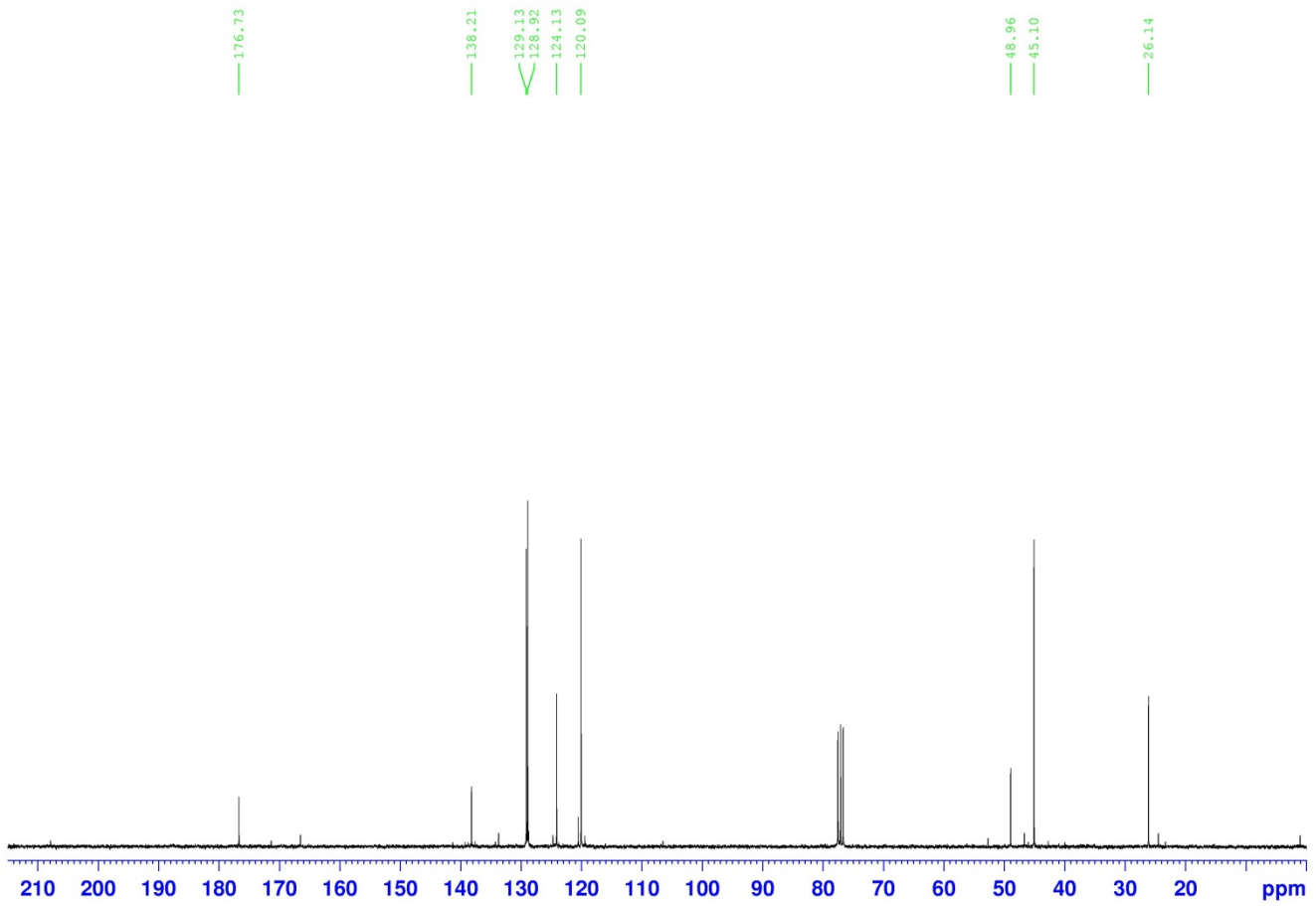
Following the general amidation procedure with EDCI affords, after flash chromatography on silica gel (85:15 hexanes:ethyl acetate), the title compound (85%) as a white solid.

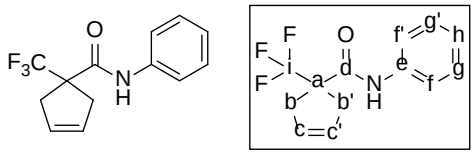
m.p.	91.0–93.5 ºC
TLC analysis	R_f 0.5 (75:25 hexanes:ethyl acetate)
^{1}H NMR (300 MHz, $CDCl_3$)	δ 7.52 (2H, t, *J* = 8.0 Hz, f,f'), 7.48 (1H, br s, NH), 7.30 (2H, t, *J* = 7.7 Hz, g,g'), 7.09 (1H, t, *J* = 7.4 Hz, h), 5.73 (2H, s, c,c'), 2.97 (2H, t, *J* = 14.5 Hz, b,b'), 2.36 (2H, t, *J* = 14.5 Hz, b,b'), 1.42 (3H, s, i).
^{13}C NMR (75 MHz, $CDCl_3$)	δ 176.73 (d), 138.21 (e), 129.13 (c,c'), 128.92 (g,g'), 124.13 (h), 120.09 (f,f'), 48.96 (a), 45.10 (b,b'), 26.14 (i).
IR (neat)	IR (neat) 3657 (N-H stretch), 2974, 2897, 1679 (C=O stretch), 1593 (C=C stretch), 1520 (N-H bend), 1438, 1303, 727 cm^{-1}.
HRMS (FAB)	Calcd. for $C_{13}H_{16}NO$ (M+H): 202.1232, found 202.1228 *m/z*.

^{1}H NMR of 5b


7.532
7.506
7.484
7.333
7.308
7.281
7.119
7.094
7.070
5.730
2.989
2.941
2.386
2.338
1.415
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
3.06
2.08
1.05
2.00
2.03
2.03
3.00

^{13}C NMR of 5b


176.73
138.21
129.13
128.92
124.13
120.09
48.96
45.10
26.14
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

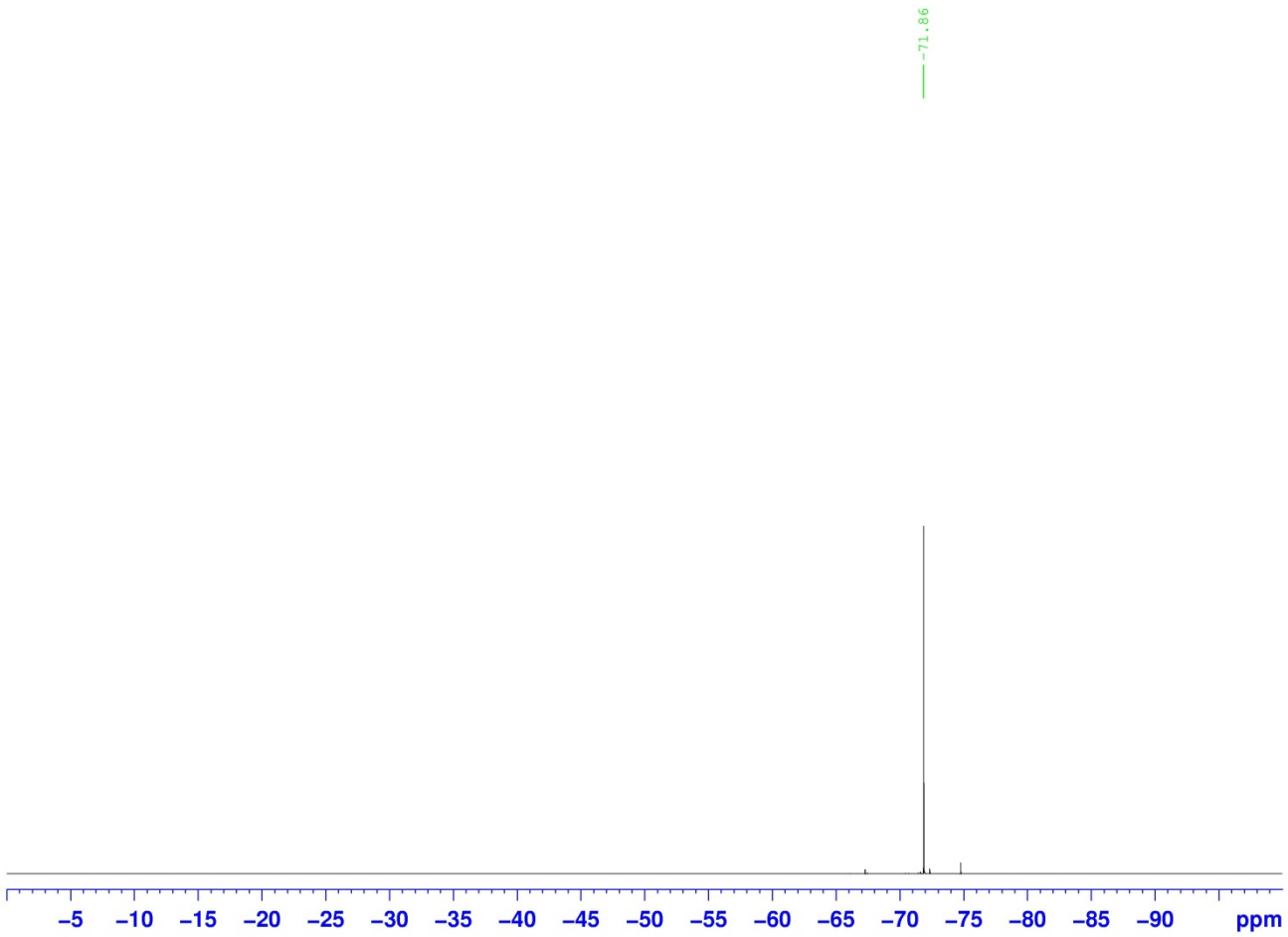


5d

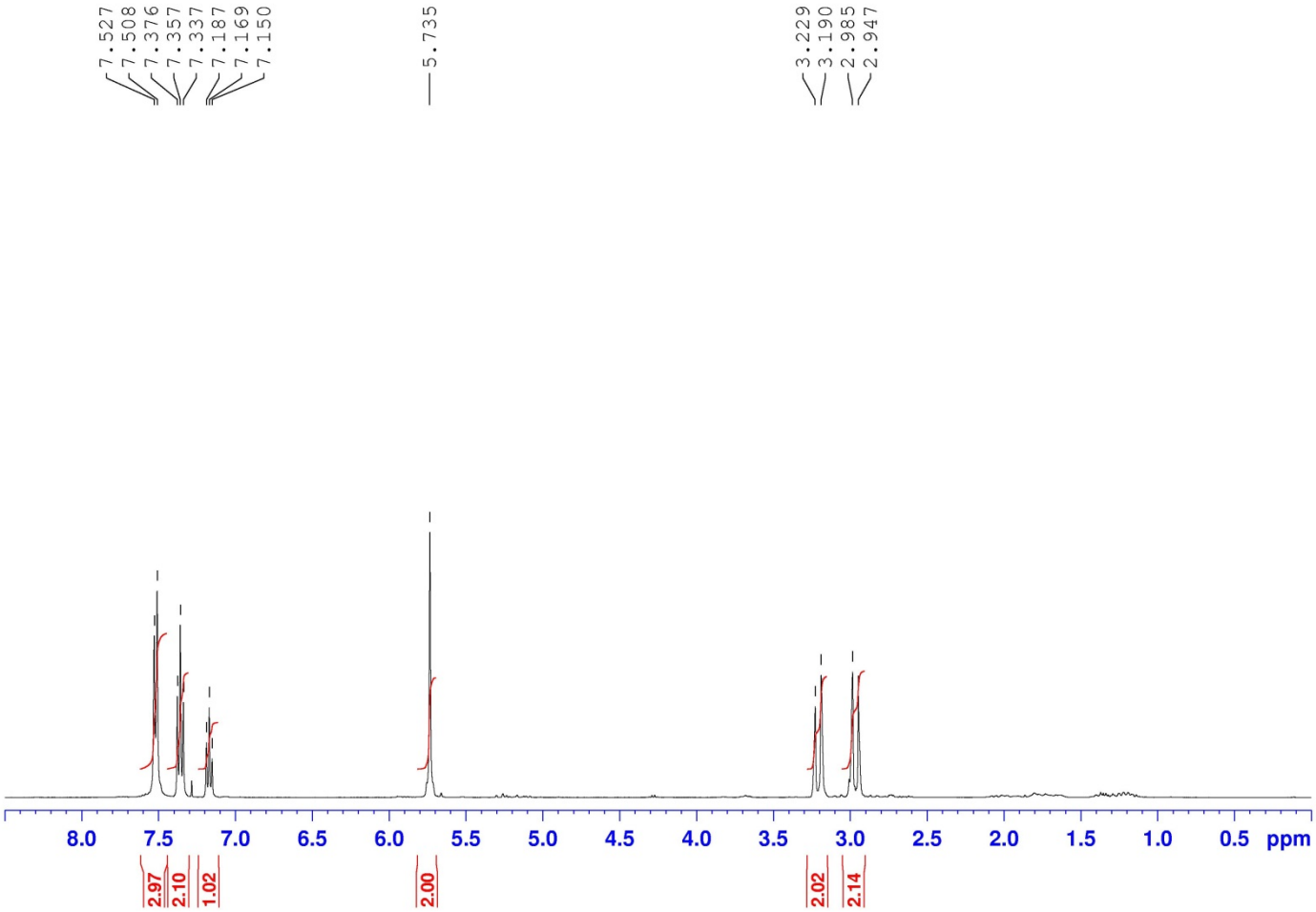
Following the general procedure of hydrolysis of esters followed by amidation via DCC condensation affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (68%, 2 steps) as a white solid.

m.p.	69.5–72.5 ºC
TLC analysis	R_f 0.60 (70:30 hexanes:ethyl acetate)
^{19}F NMR (376 MHz, $CDCl_3$)	δ -71.86 (s, CF_3).
^{1}H NMR (400 MHz, $CDCl_3$)	δ 7.52 (2H, d, *J* = 7.7 Hz, f,f'), 7.60–7.45 (1H, m, NH), 7.36 (2H, t, *J* = 7.6 Hz, g,g'), 7.17 (1H, t, *J* = 7.4 Hz, h), 5.74 (2H, s, c,c'), 3.21 (2H, d, *J* = 15.5 Hz, b,b'), 2.97 (2H, d, *J* = 15.3 Hz, b,b').
^{13}C NMR (100 MHz, $CDCl_3$)	δ 167.06 (d), 137.32 (e), 129.07 (c,c'), 128.05 (g,g'), 127.24 (q, *J* = 278.7 Hz, i), 124.98 (h), 120.43 (f,f'), 58.11 (q, *J* = 24.7, a), 38.89 (q, *J* = 2.0 Hz, b,b').
IR (neat)	3309 (N-H stretch), 2924, 2867, 1667 (C=O stretch), 1599 (C=C stretch), 1535 (N-H bend), 1476, 1301, 1263, 1148, 753, 739, 662 (C-F stretch) cm^{-1}.
HRMS (ESI)	Calcd. for $C_{13}H_{12}F_3NaNO$ (M+Na): 278.0769, found 278.0766 *m/z*.

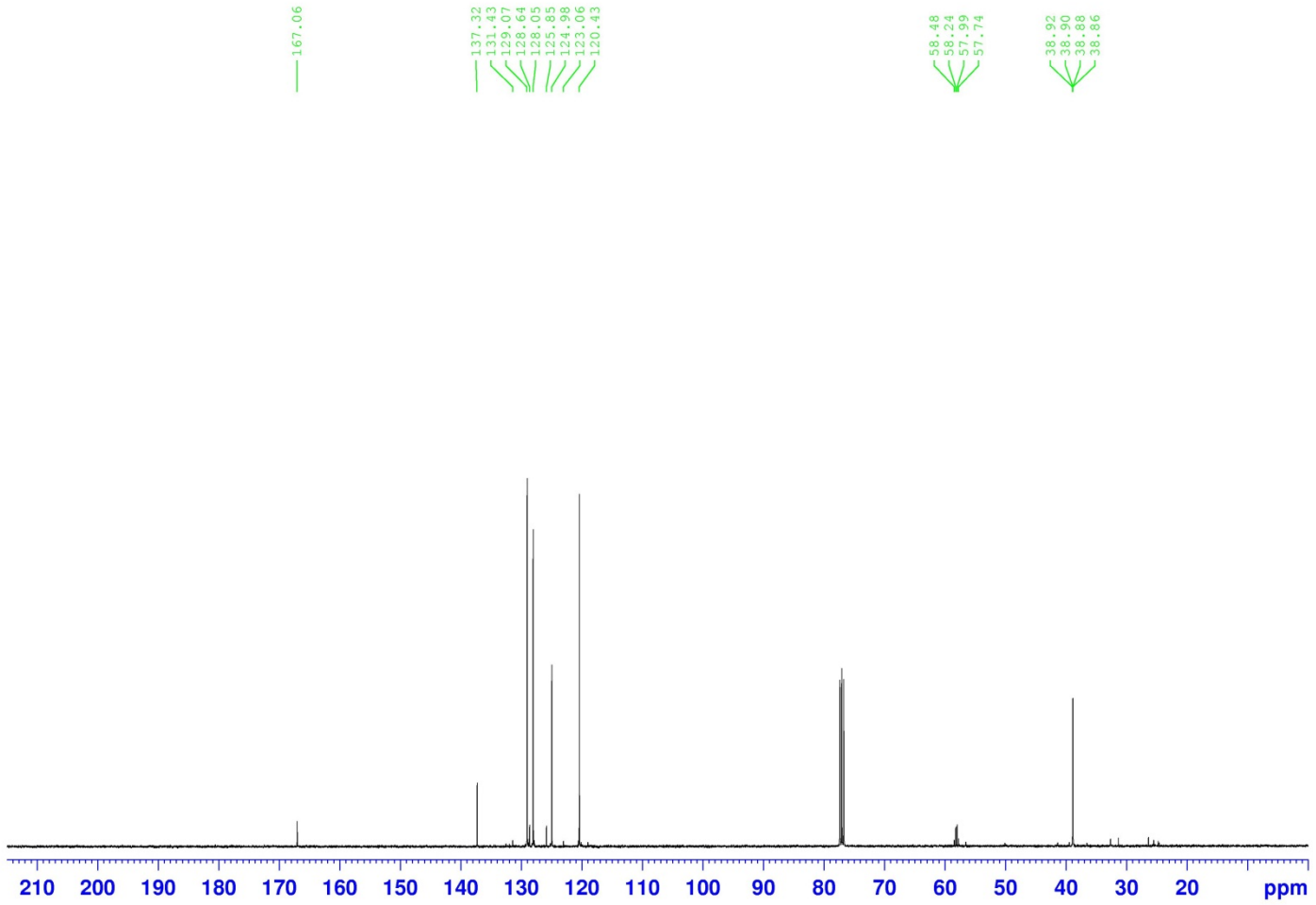
^{19}F NMR of 5d

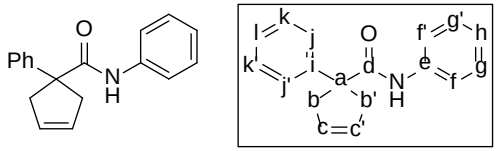


^{1}H NMR of 5d


7.527
7.508
7.376
7.357
7.337
7.187
7.169
7.150
5.735
3.229
3.190
2.985
2.947
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.97
2.10
1.02
2.00
2.02
2.14

^{13}C NMR of 5d


167.06
137.32
131.43
129.07
128.64
128.05
125.85
124.98
123.06
120.43
58.48
58.24
57.99
57.74
38.92
38.90
38.88
38.86
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

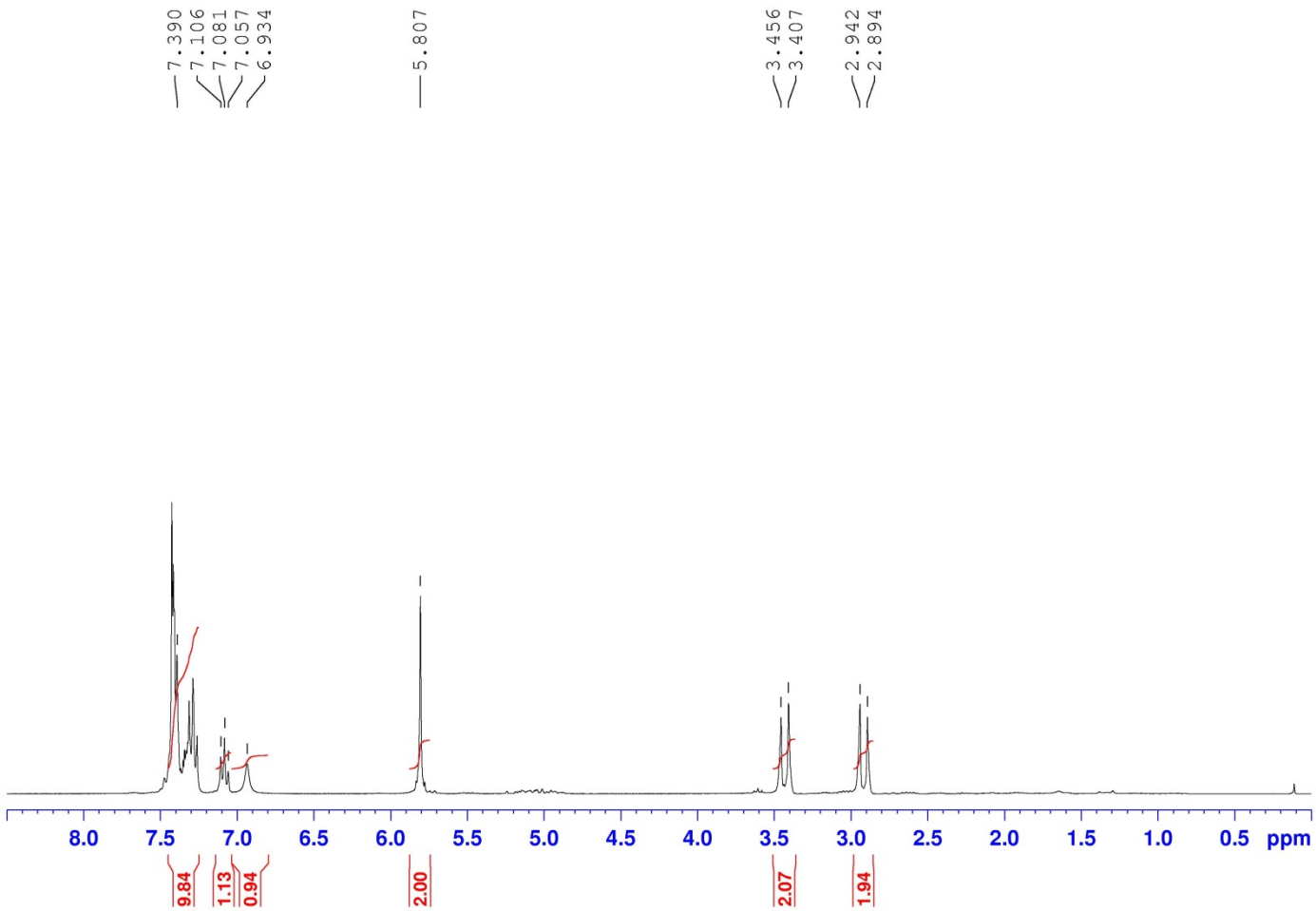


5c

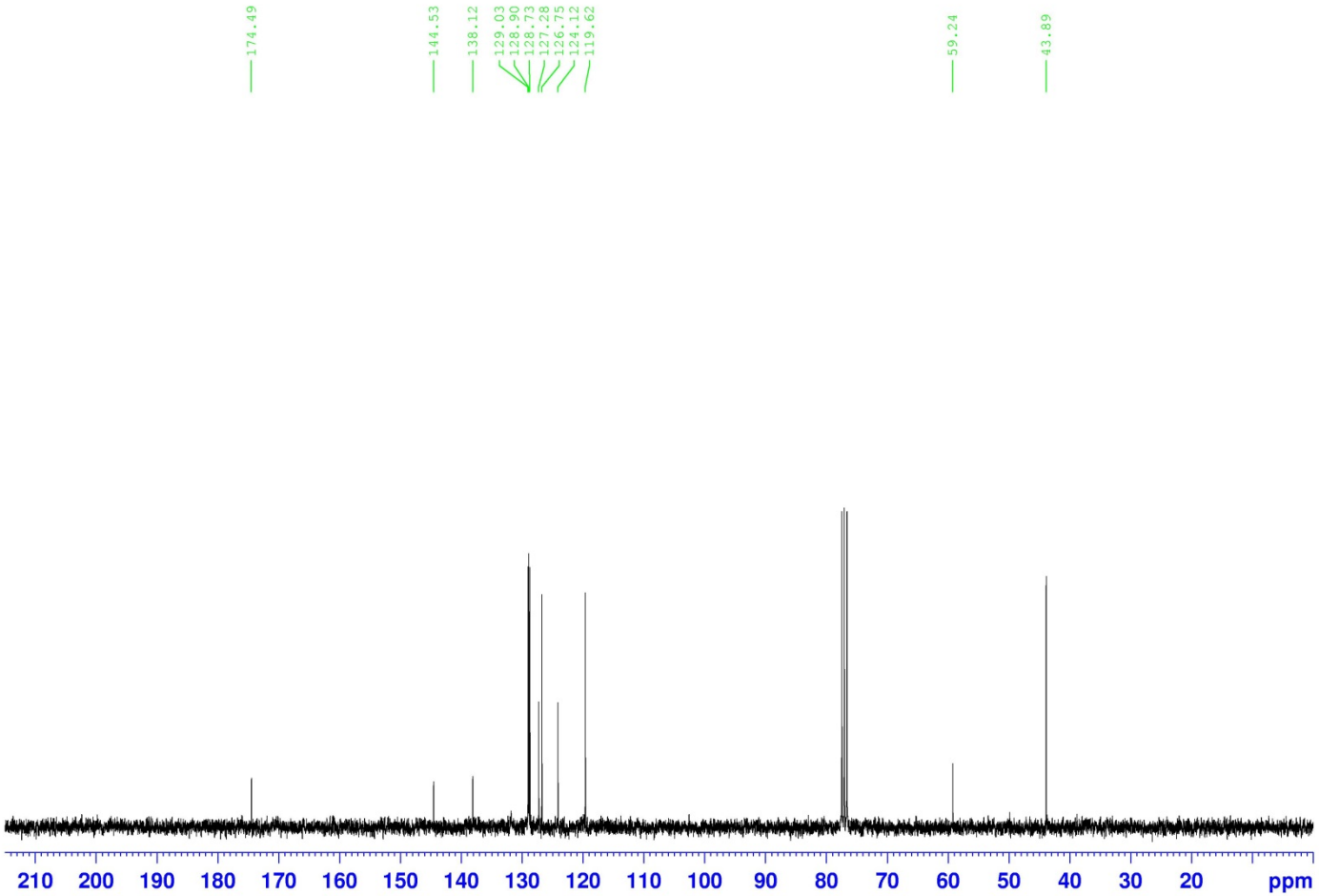
Following the general procedure of hydrolysis of esters followed by amidation via acid chloride intermediates affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (72%, 3 steps) as a white solid.

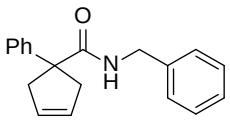
m.p.	90.5–92.5 ºC
TLC analysis	R_f 0.6 (70:30 hexanes:ethyl acetate)
^{1}H NMR (300 MHz, $CDCl_3$)	δ 7.50–7.20 (9H, m, f,f',g,g',h,j,j'k,k'), 7.08 (1H, t, *J* = 7.4 Hz, l), 5.81 (2H, s, c,c'), 3.43 (2H, d, *J* = 14.6, b,b'), 2.92 (2H, d, *J* = 14.6, b,b').
^{13}C NMR (75 MHz, $CDCl_3$)	δ 174.49 (d), 144.53 (e), 138.12 (i), 129.03 (j,j'), 128.90 (c,c'), 128.73 (k,k'), 127.28 (g,g'), 126.75 (h), 124.12 (l), 119.62 (f,f'), 59.24 (a), 43.89 (b,b').
IR (neat)	3286 (N-H stretch), 3056, 2846, 2917, 1648 (C=O stretch), 1595 (C=C stretch), 1518 (N-H bend), 1497, 1436, 1312, 1239, 753, 742, 732, 688, 655 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{18}H_{17}NaNO$ (M+Na): 286.1208, found 286.1197 *m/z*.

^{1}H NMR of 5c

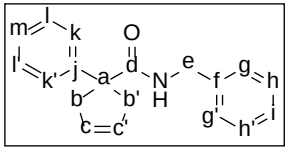

7.390
7.106
7.081
7.057
6.934
5.807
3.456
3.407
2.942
2.894
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
9.84
1.13
0.94
2.00
2.07
1.94

^{13}C NMR of 5c


174.49
144.53
138.12
129.03
128.90
128.73
127.28
126.75
124.12
119.62
59.24
43.89
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm



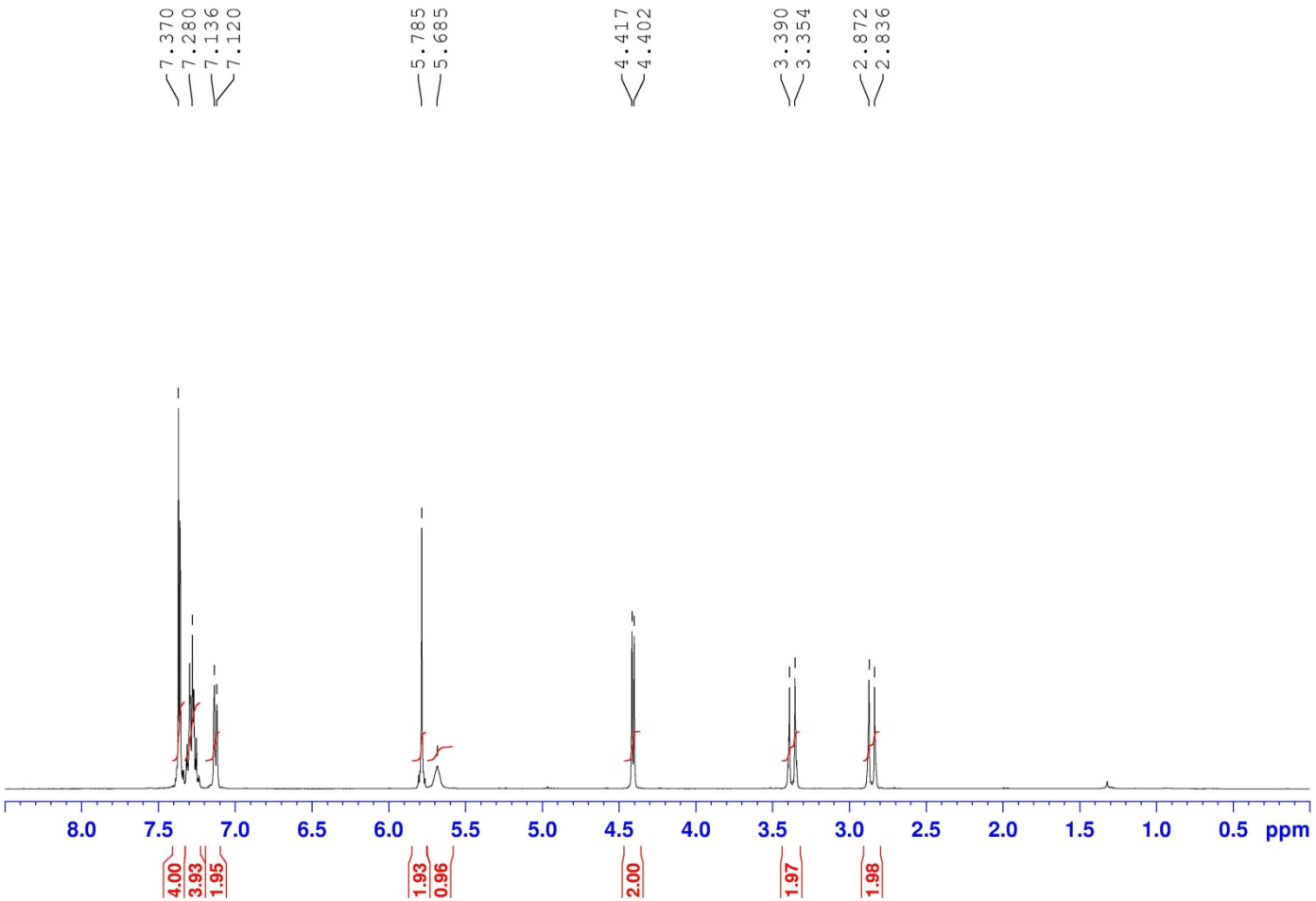
5g



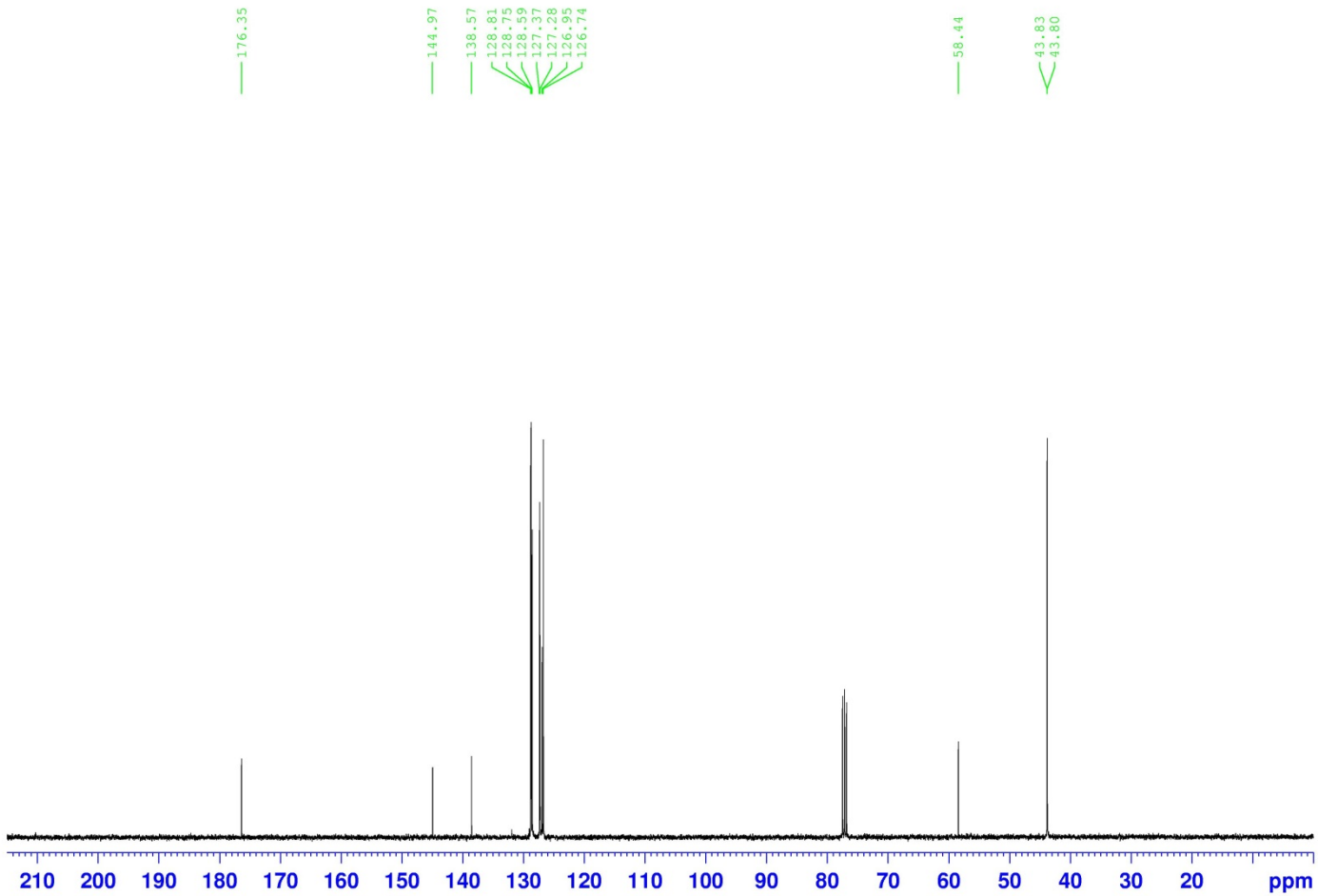
Following the general procedure of hydrolysis of esters followed by amidation via acid chloride intermediates affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (65%, 3 steps) as a white solid.

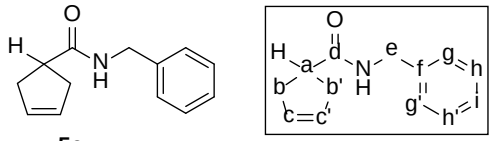
m.p.	68.0–70.5 ºC
TLC analysis	R_f 0.50 (70:30 hexanes:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 7.40–7.30 (4H, m, g,g',k,k'), 7.35–7.25 (4H, m, i,l,l',m), 7.13 (2H, d, *J* = 6.4 Hz, h,h'), 5.79 (2H, s c,c'), 5.69 (1H, br s, NH), 4.41 (2H, d, *J* = 5.8 Hz, e), 3.37 (2H, dd, *J* = 14.3 Hz, b,b'), 2.85 (2H, d, *J* = 14.4 Hz, b,b').
^{13}C NMR (100 MHz, $CDCl_3$)	δ 176.35 (d), 144.97 (f), 138.57 (j), 128.81 (c,c'), 128.75 (k,k'), 128.59 (l,l'), 127.37 (h,h'), 127.28 (m), 126.95 (g,g'), 126.74 (i), 58.44 (a), 43.83 (e), 43.80 (b,b').
IR (neat)	3393, 3351 (N-H stretch), 3057, 3029, 1637 (C=O stretch), 1518 (N-H bend), 1497, 1446, 1027, 1005, 718 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{19}H_{19}NaNO$ (M+Na): 300.1364, found 300.1364 *m/z*.

^{1}H NMR of 5g


7.370
7.280
7.136
7.120
5.785
5.685
4.417
4.402
3.390
3.354
2.872
2.836
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.00
3.93
1.95
1.93
0.96
2.00
1.97
1.98

^{13}C NMR of 5g


176.35
144.97
138.57
128.81
128.75
128.59
127.37
127.28
126.95
126.74
58.44
43.83
43.80
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

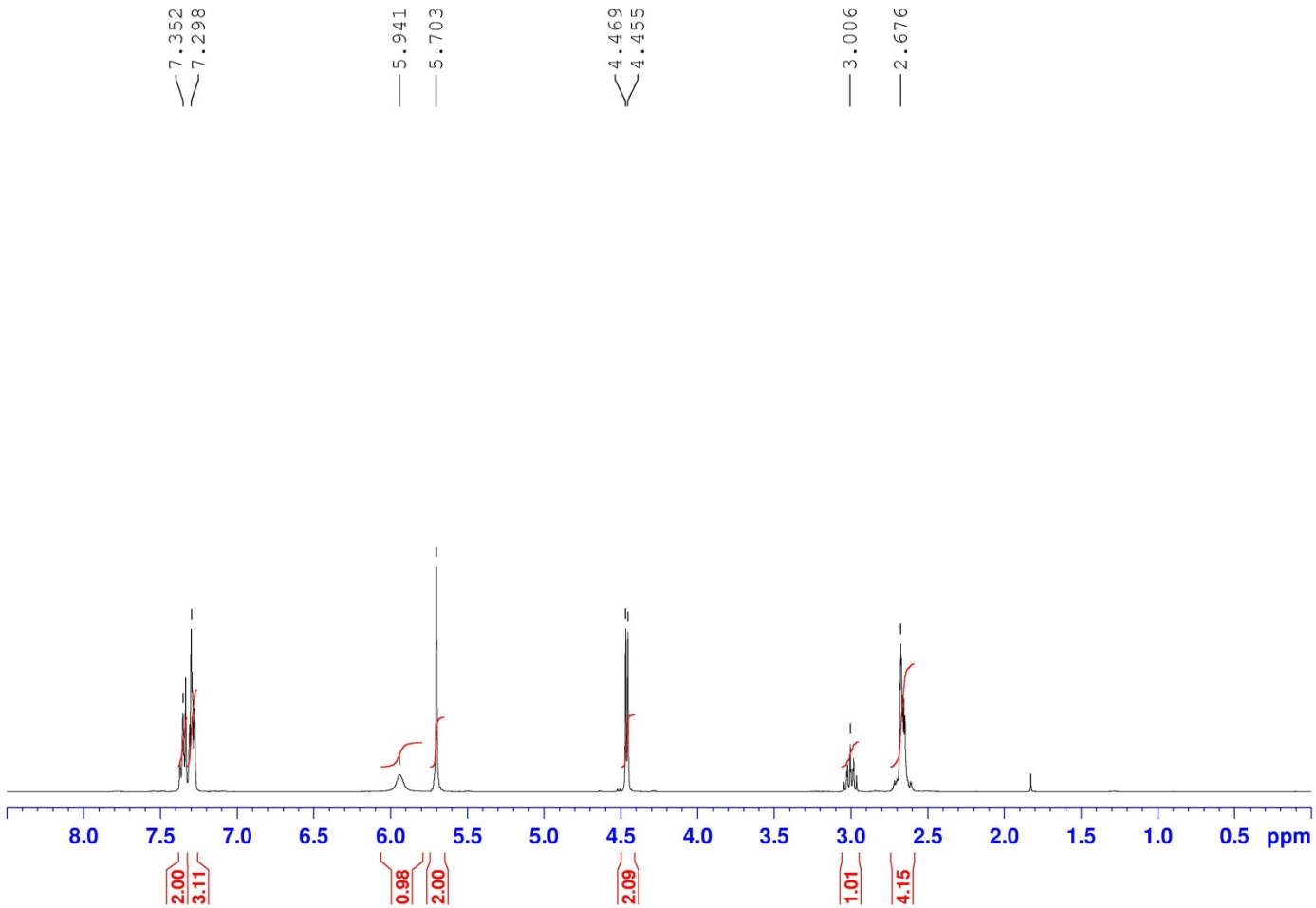


5e

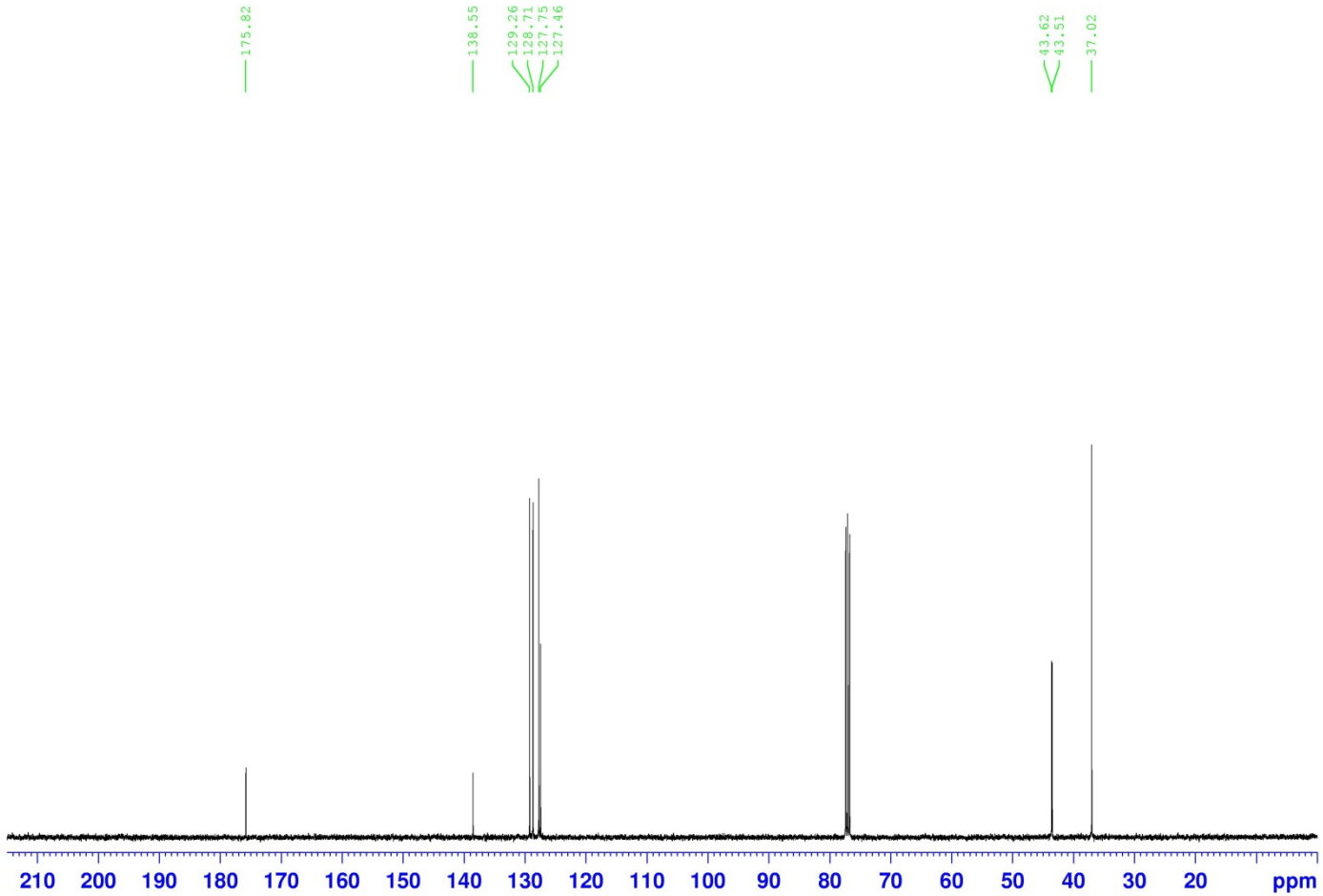
Following the general amidation procedure via acid chloride intermediates affords, after flash chromatography on silica gel (85–70:15–30 hexanes:ethyl acetate), the title compound (68%, 2 steps) as a white solid.

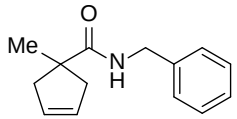
m.p.	103.5–105.5 ºC
TLC analysis	R_f 0.35 (70:30 hexanes:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 7.40–7.30 (2H, m, h,h'), 7.35–7.25 (2H, m, g,g',i), 5.94 (1H, br s, NH), 5.70 (2H, s, c,c'), 4.46 (2H, d, *J* = 5.7 Hz, e), 3.05–2.95 (1H, m, a), 2.75–2.60 (4H, m, b,b').
^{13}C NMR (100 MHz, $CDCl_3$)	δ 175.82 (d), 138.55 (f), 129.26 (c,c'), 128.71 (h,h'), 127.75 (g,g'), 127.46 (i), 43.62 (e), 43.51 (a), 37.02 (b,b').
IR (neat)	3271 (N-H stretch), 3054, 2898, 2837, 1635 (C=O stretch), 1551 (C=C stretch), 1497 (N-H bend), 1454, 1449, 1389, 1033, 746, 693 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{13}H_{15}NaNO$ (M+Na): 224.1051, found 224.1059 *m/z*.

^{1}H NMR of 5e

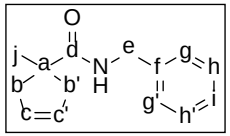

7.352
7.298
5.941
5.703
4.469
4.455
3.006
2.676
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.00
3.11
0.98
2.00
2.09
1.01
4.15

^{13}C NMR of 5e


175.82
138.55
129.26
128.71
127.75
127.46
43.62
43.51
37.02
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm



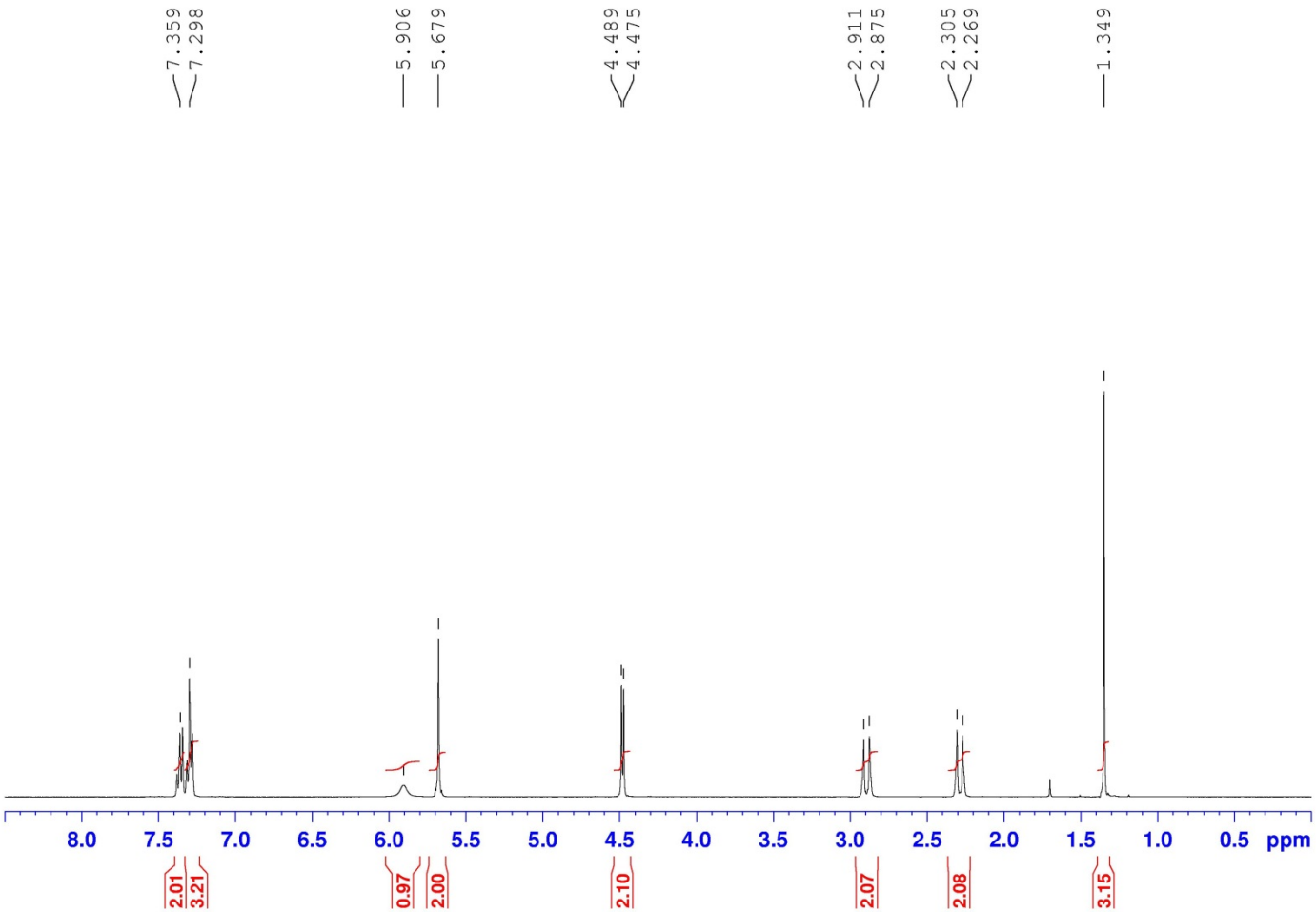
5f



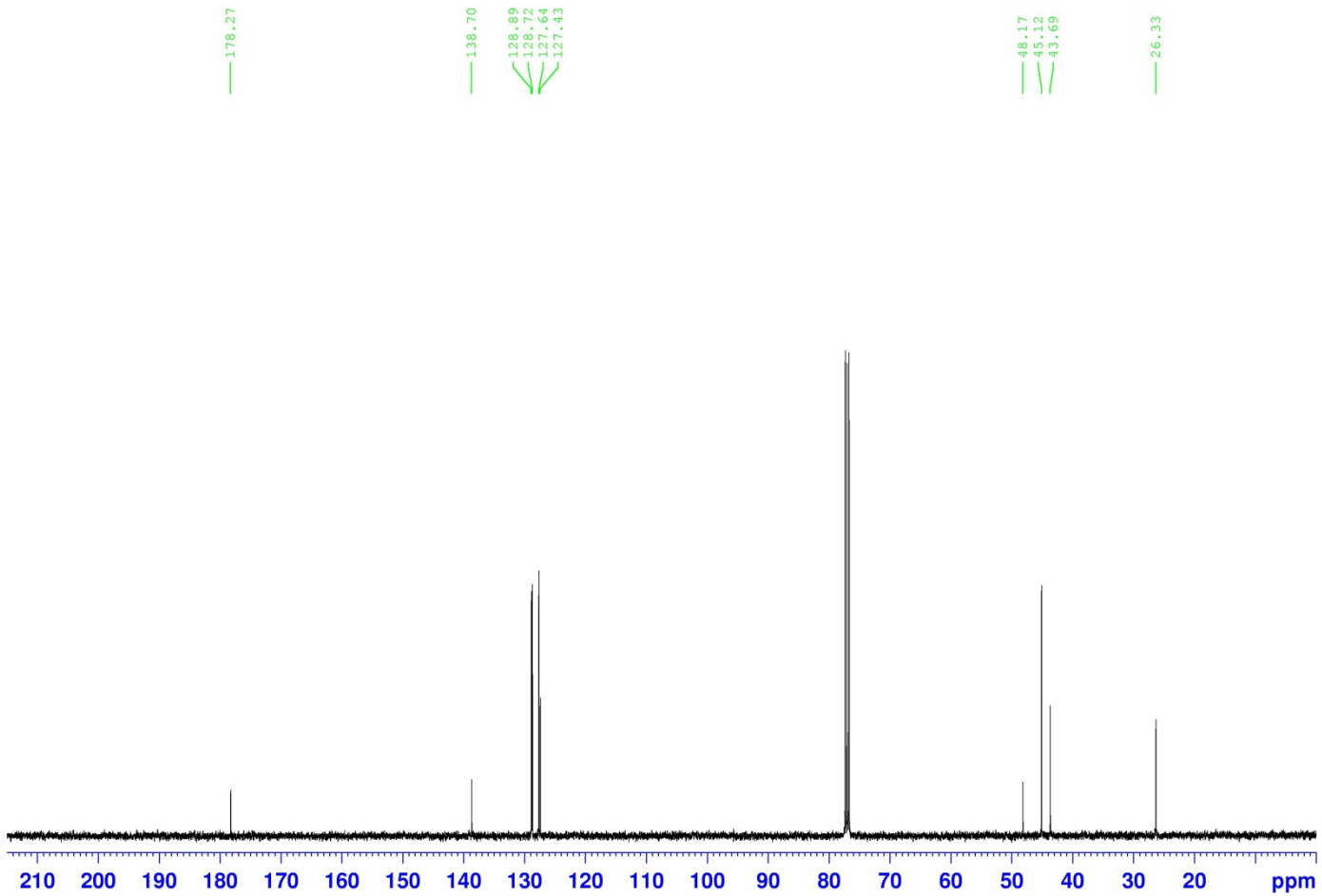
Following the general amidation procedure via acid chloride intermediates affords, after flash chromatography on silica gel (85–70:15–30 hexanes:ethyl acetate), the title compound (62%, 2 steps) as a white solid.

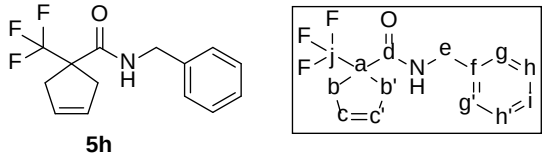
m.p.	72.5–74.5 ºC
TLC analysis	R_f 0.40 (70:30 hexanes:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 7.40–7.30 (2H, m, h,h'), 7.35–7.25 (2H, m, g,g',i), 5.91 (1H, br s, NH), 5.68 (2H, s, c,c'), 4.48 (2H, d, *J* = 5.7 Hz, e), 2.89 (2H, d, *J* = 14.4 Hz, b,b'), 2.29 (2H, d, *J* = 14.7 Hz, b,b'), 1.35 (3H, s, j).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 178.27 (d), 138.70 (f), 128.89 (c,c'), 128.72 (h,h'), 127.64 (g,g'), 127.43 (i), 48.17 (a), 45.12 (b,b'), 43.69 (e), 26.33 (j).
IR (neat)	3369 (N-H stretch), 3305, 2916, 1637 (C=O stretch), 1528 (N-H bend), 1414, 1289, 1235, 948, 714 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{14}H_{17}NaNO$ (M+Na): 238.1208, found 238.1218 *m/z*.

^{1}H NMR of 5f


7.359
7.298
5.906
5.679
4.489
4.475
2.911
2.875
2.305
2.269
1.349
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.01
3.21
0.97
2.00
2.10
2.07
2.08
3.15

^{13}C NMR of 5f


178.27
138.70
128.89
128.72
127.64
127.43
48.17
45.12
43.69
26.33
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

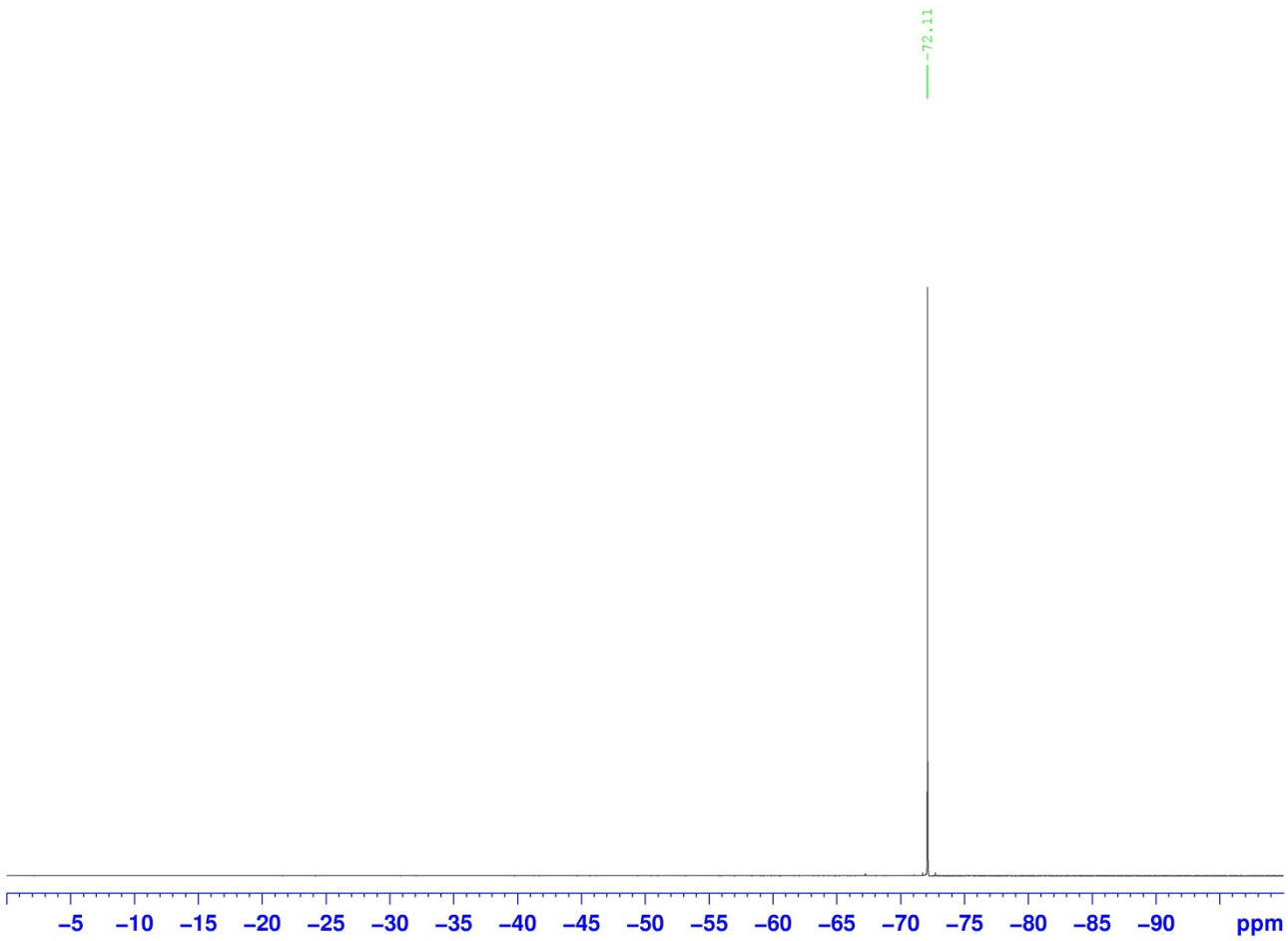


5h

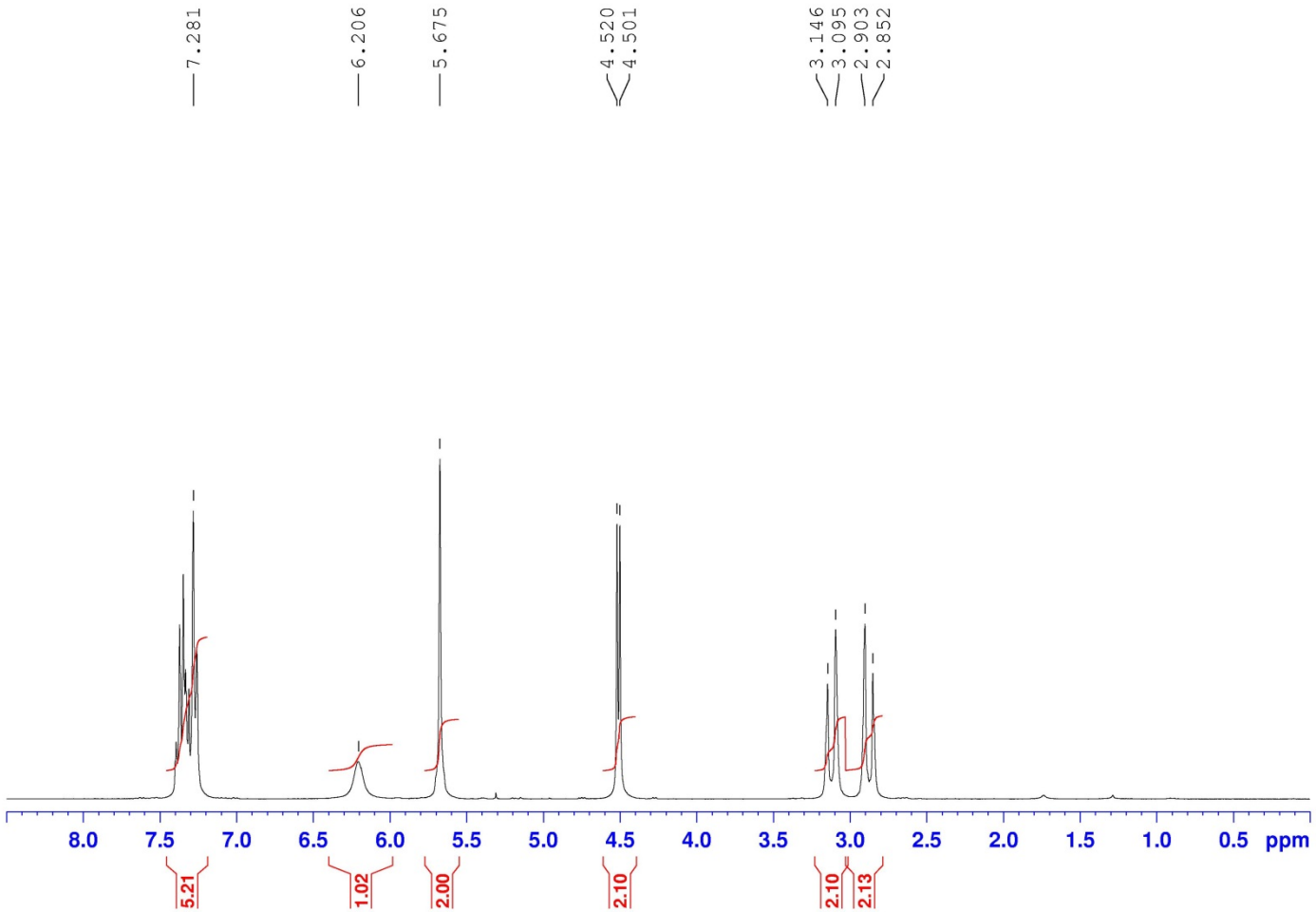
Following the general procedure of hydrolysis of esters followed by amidation via acid chloride intermediates affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (52%, 3 steps) as a white solid.

m.p.	77.5–78.5 ºC
TLC analysis	R_f 0.5 (70:30 hexanes:ethyl acetate)
^{19}F NMR (282 MHz, $CDCl_3$)	δ -72.11 (s, CF_3).
^{1}H NMR (300 MHz, $CDCl_3$)	δ 7.45–7.20 (5H, m, g,g',h,h',i), 6.21 (1H, br s, NH), 5.68 (2H, s, c,c'), 4.51 (2H, d, *J* = 5.6 Hz, e), 3.12 (2H, d, *J* = 15.6 Hz, b,b'), 2.88 (2H, d, *J* = 15.4 Hz, b,b').
^{13}C NMR (75 MHz, $CDCl_3$)	δ 169.04 (d), 137.72 (f), 128.82 (c,c'), 127.90 (h,h'), 127.67 (i), 127.53 (g,g'), 127.33 (q, *J* = 278.7, j), 57.28 (q, J = 24.6, a), 44.20 (e), 38.91 (b,b').
IR (neat)	3338 (N-H stretch), 3030, 2922, 1660 (C=O stretch), 1533 (C=C stretch), 1496 (N-H bend), 1419, 1302, 1127 (C-N stretch), 954, 712, 697, 655 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{14}H_{14}F_3NaNO$ (M+Na): 292.0925, found 292.0923 *m/z*.

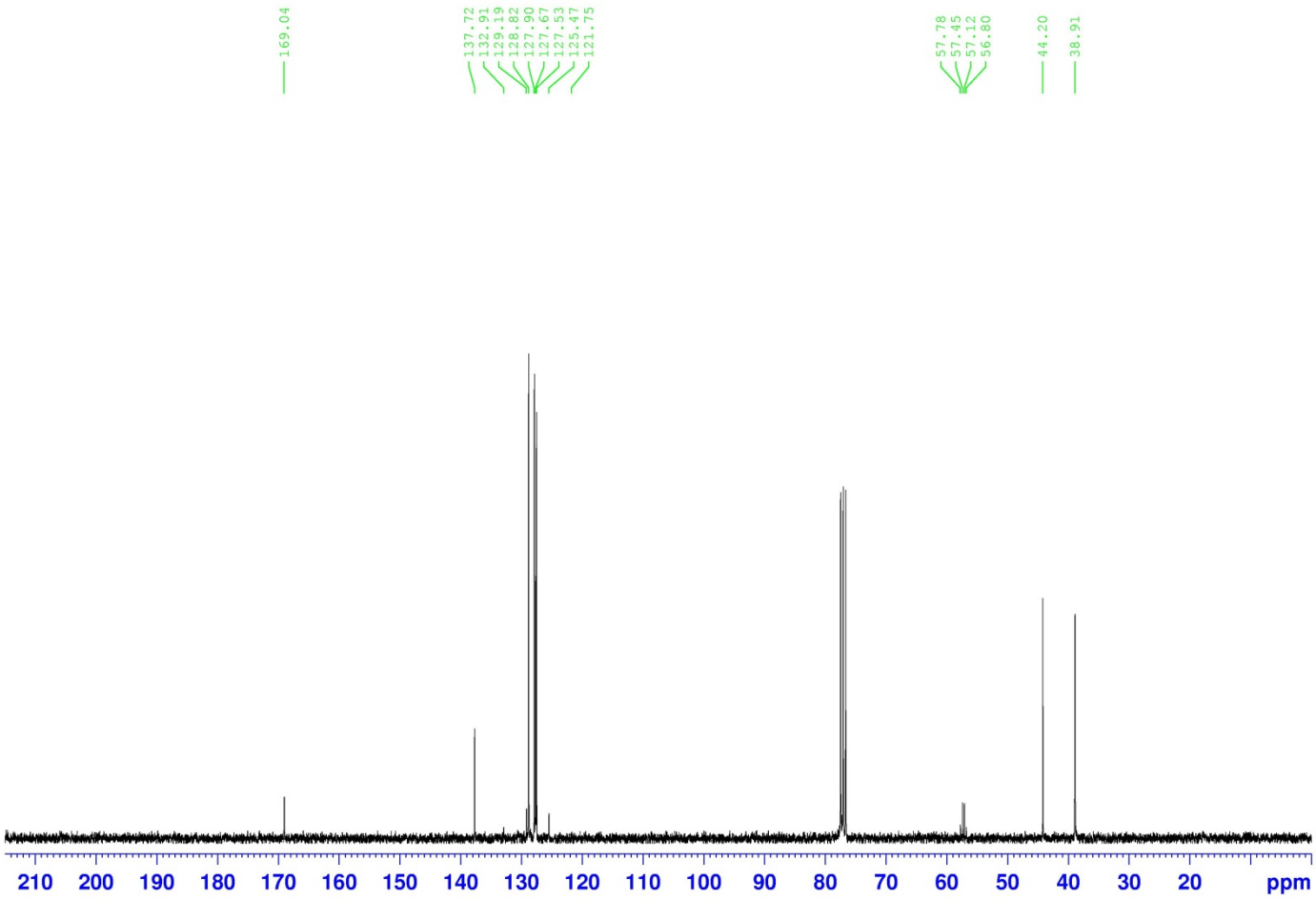
^{19}F NMR of 5h

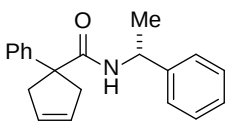


^{1}H NMR of 5h

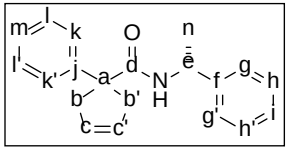

7.281
6.206
5.675
4.520
4.501
3.146
3.095
2.903
2.852
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
5.21
1.02
2.00
2.10
2.10
2.13

^{13}C NMR of 5h


169.04
137.72
132.91
129.19
128.82
127.90
127.67
127.53
125.47
121.75
57.78
57.45
57.12
56.80
44.20
38.91
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm



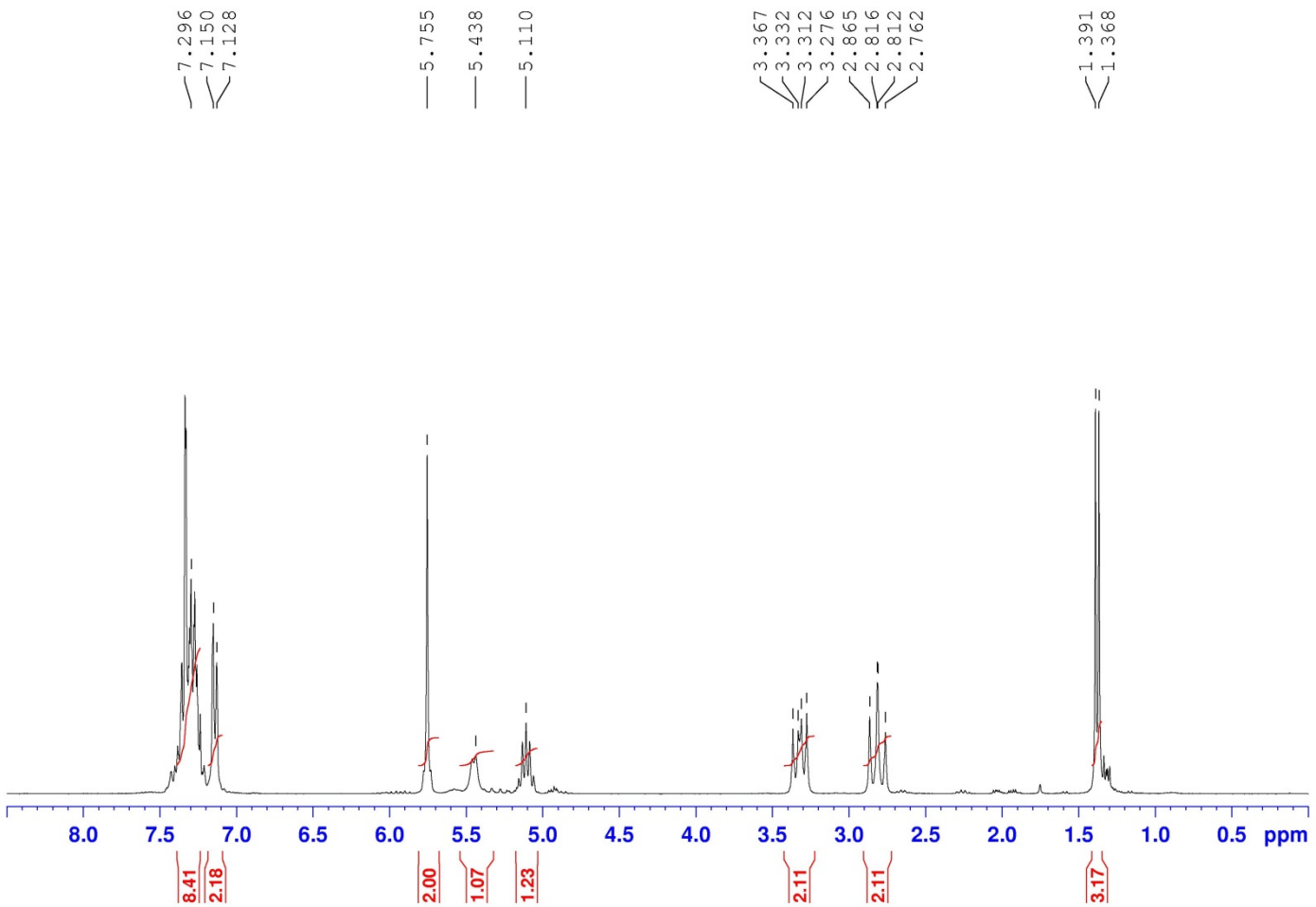
5i



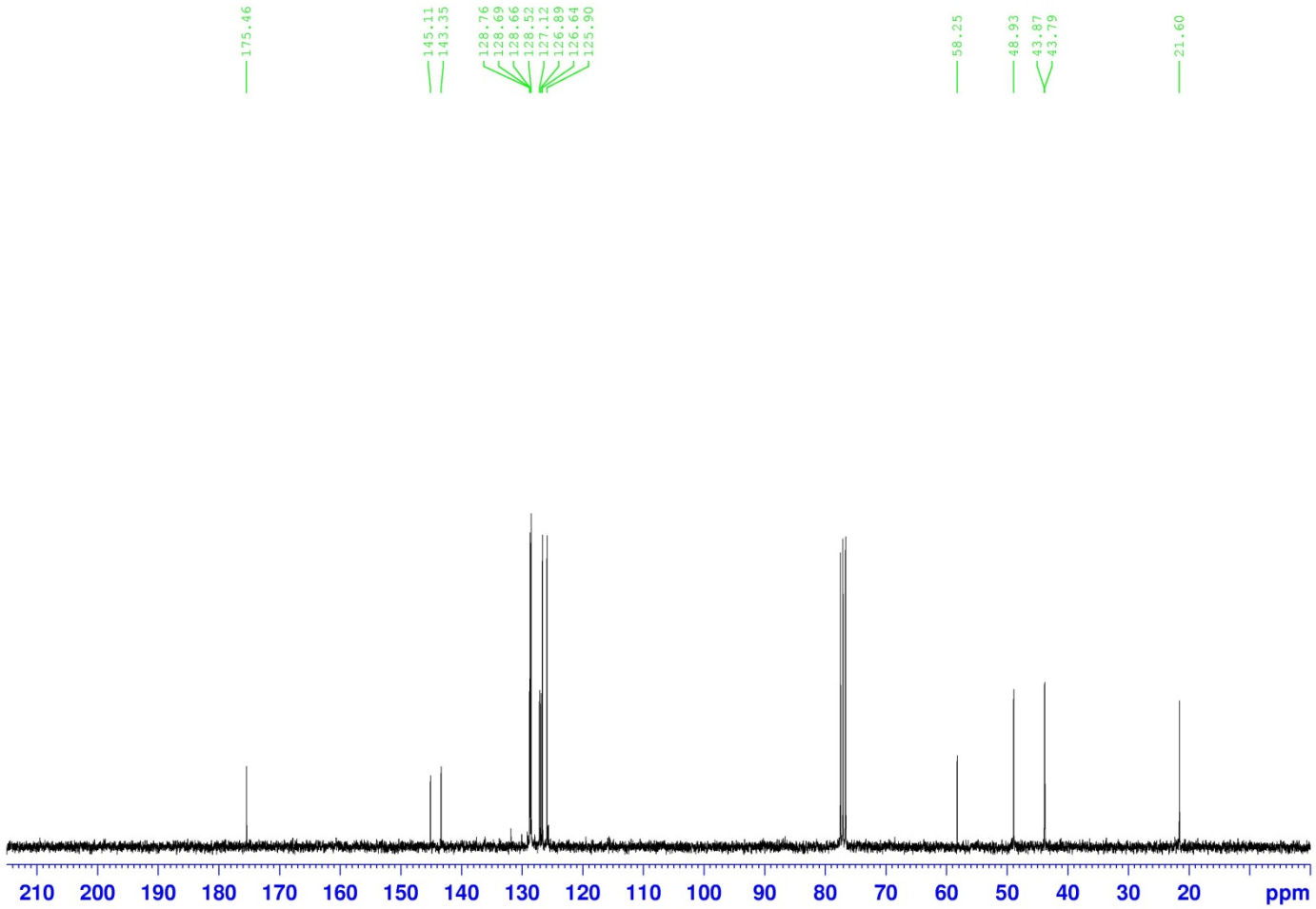
Following the general procedure of hydrolysis of esters followed by amidation via acid chloride intermediates affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (70%, 3 steps) as a white solid.

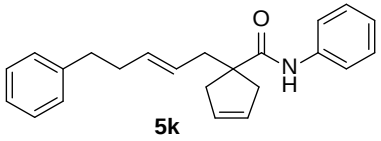
m.p.	73.5–75.5 ºC
TLC analysis	R_f 0.6 (70:30 hexanes:ethyl acetate)
^{1}H NMR (300 MHz, $CDCl_3$)	δ 7.45–7.20 (8H, m, h,h',i,k,k',l,l',m), 7.14 (2H, t, *J* = 6.7 Hz, g,g'), 5.76 (2H, s c,c'), 5.44 (1H, br s, NH), 5.20–5.05 (1H, m, e), 3.32 (2H, dd, *J* = 16.6 and 10.5 Hz, b,b'), 2.81 (2H, dd, *J* = 15.9 and 14.8 Hz, b,b'), 1.38 (3H, d, *J* = 6.9 Hz, n).
^{13}C NMR (75 MHz, $CDCl_3$)	δ 175.46 (d), 145.11 (j), 143.35 (f), 128.76 and 128.66 (c,c'), 128.69 (k,k'), 128.52 (l,l'), 127.12 (h,h'), 126.89 (m), 126.64 (i), 125.90 (g,g'), 58.25 (a), 48.93 (e), 43.87 and 43.79 (b,b'), 21.60 (n).
IR (neat)	3290 (N-H stretch), 3053, 1644 (C=O stretch), 1623 (C=C stretch), 1526 (N-H bend), 1493, 1444, 741, 695, 662 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{20}H_{21}NaNO$ (M+Na): 314.1521, found 314.1510 *m/z*.

^{1}H NMR of 5i

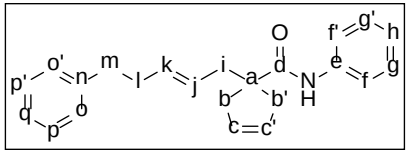

7.296
7.150
7.128
5.755
5.438
5.110
3.367
3.332
3.312
3.276
2.865
2.816
2.812
2.762
1.391
1.368
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
8.41
2.18
2.00
1.07
1.23
2.11
2.11
3.17

^{13}C NMR of 5i


175.46
145.11
143.35
128.76
128.69
128.66
128.52
127.12
126.89
126.64
125.90
58.25
48.93
43.87
43.79
21.60
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm



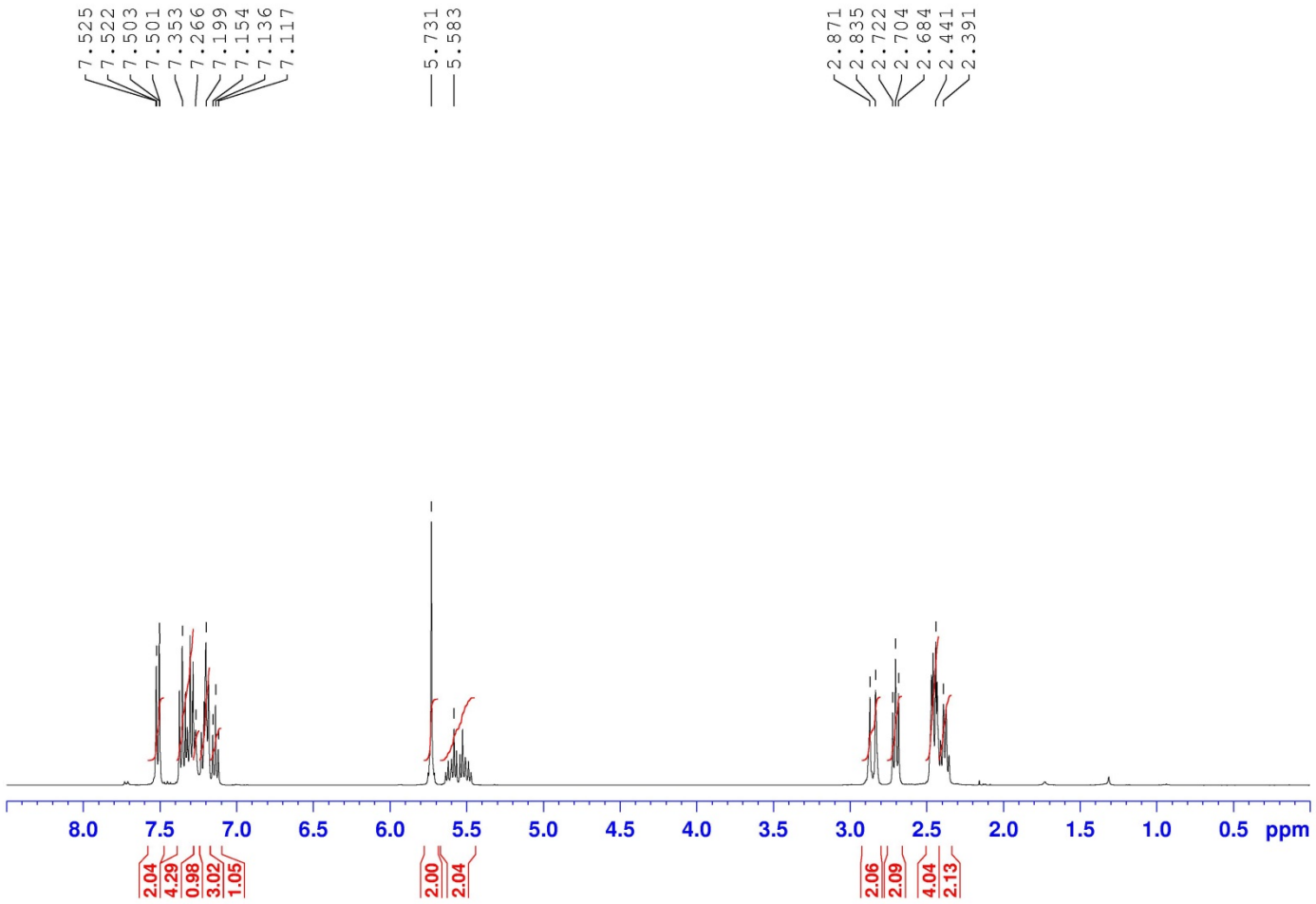
5k



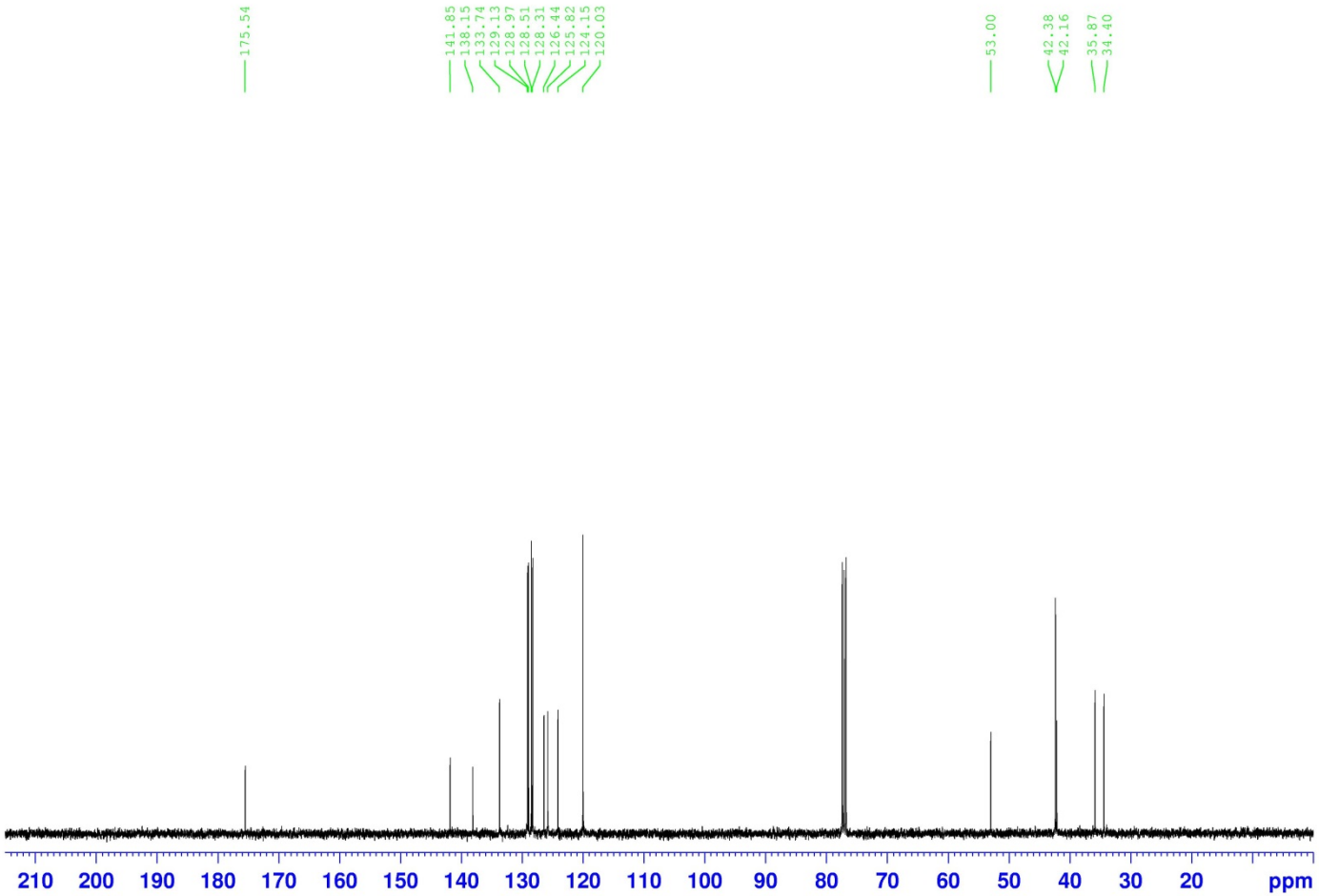
Following the general amidation procedure via acid chloride intermediates affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (75%, 2 steps) as a light yellow solid.

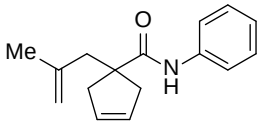
m.p.	82.5–83.0 ºC
TLC analysis	R_f 0.7 (70:30 hexanes:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 7.51 (2H, dd, *J* = 8.7 and 1.2 Hz, f,f'), 7.40–7.25 (4H, m, g,g',p,p'), 7.27 (1H, br s, NH), 7.25–7.15 (3H, m, o,o',q), 7.14 (1H, t, *J* = 7.4 Hz, h), 5.73 (2H, s, c,c'), 5.65–5.45 (2H, m, j,k), 2.85 (2H, d, *J* = 14.4 Hz, b,b'), 2.70 (2H, t, *J* = 7.3 Hz, m), 2.50–2.40 (4H, m, b,b',i), 2.40–2.35 (2H, m, l).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 175.54 (d), 141.85 (n), 138.15 (e), 133.74 (k), 129.13 (c,c'), 128.97 (g,g'), 128.51 (p,p'), 128.31 (o,o'), 126.44 (j), 125.82 (q), 124.15 (h), 120.03 (f), 53.00 (a), 42.38 (i), 42.16 (b,b'), 35.87 (m), 34.40 (l).
IR (neat)	3329 (N-H stretch), 3060, 2916, 2844, 1659 (C=O stretch), 1598 (C=C stretch), 1529 (N-H bend), 1497, 1436, 1309, 1233, 976, 951, 755, 692, 677 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{23}H_{25}NaNO$ (M+Na): 354.1834, found 354.1833 *m/z*.

^{1}H NMR of 5k

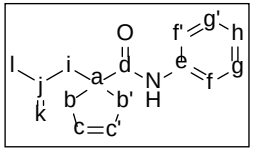

7.525
7.522
7.503
7.501
7.353
7.266
7.199
7.154
7.136
7.117
5.731
5.583
2.871
2.835
2.722
2.704
2.684
2.441
2.391
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.04
4.29
0.98
3.02
1.05
2.00
2.04
2.06
2.09
4.04
2.13

^{13}C NMR of 5k


175.54
141.85
138.15
133.74
129.13
128.97
128.51
128.31
126.44
125.82
124.15
120.03
53.00
42.38
42.16
35.87
34.40
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm



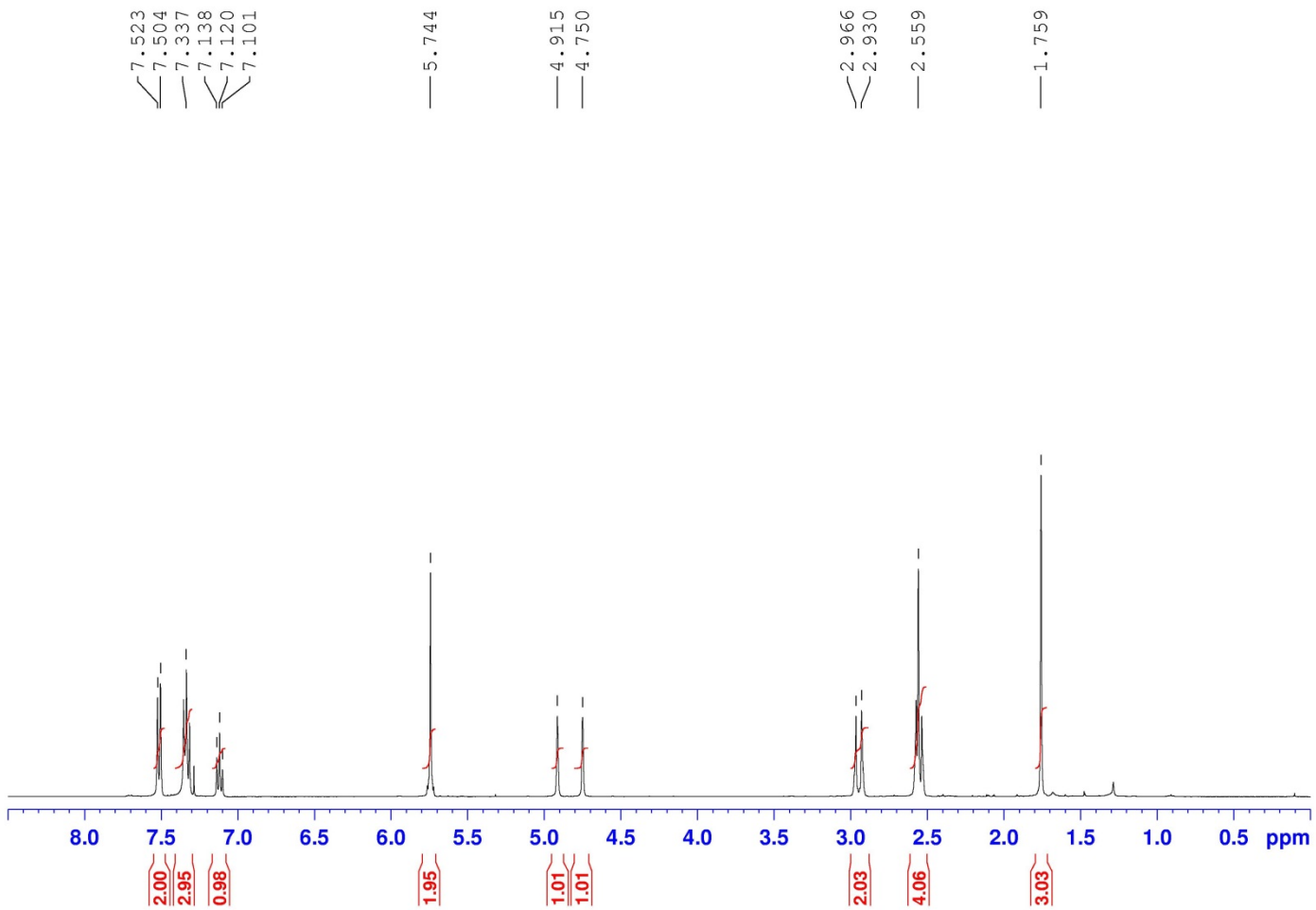
5l



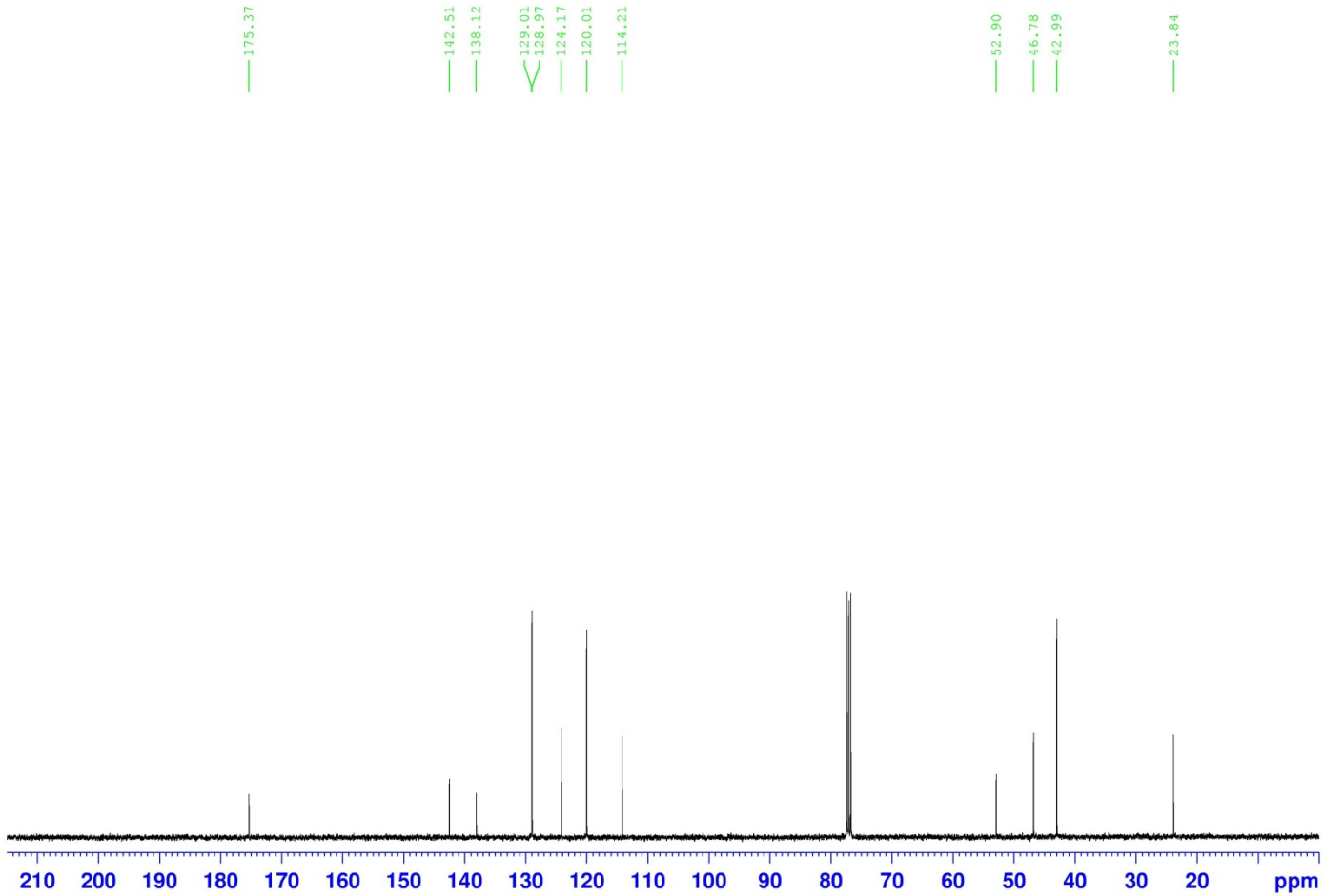
Following the general amidation procedure via acid chloride intermediates affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (71%, 2 steps) as an off-white solid.

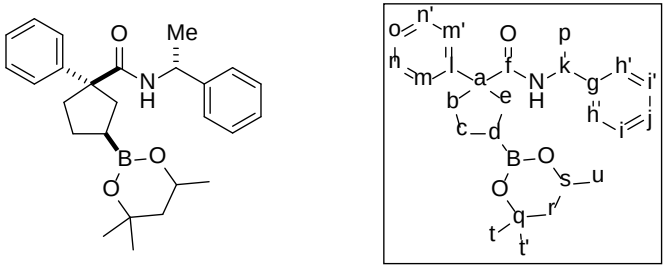
m.p.	109.0–110.0 ºC
TLC analysis	R_f 0.7 (70:30 hexanes:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 7.51 (2H, d, *J* = 7.6 Hz, f,f'), 7.40–7.30 (3H, m, g,g',NH), 7.12 (1H, t, *J* = 7.4 Hz, h), 5.74 (2H, s, c,c'), 4.92 (1H, s, k), 4.75 (1H, s, k), 2.95 (2H, d, *J* = 14.5 Hz, b,b'), 2.60–2.50 (4H, m, b,b',i), 1.76 (3H, s, l).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 175.37 (d), 142.51 (j), 138.12 (e), 129.01 (c,c'), 128.97 (g,g'), 124.17 (h), 120.01 (f,f'), 114.21 (k), 52.90 (a), 46.78 (i), 42.99 (b,b'), 23.84 (l).
IR (neat)	3240 (N-H stretch), 3066, 2925, 1646 (C=O stretch), 1597 (C=C stretch), 1531 (N-H bend), 1485, 1438, 951, 749, 729, 690, 661 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{16}H_{19}NaNO$ (M+Na): 264.1364, found 264.1357 *m/z*.

^{1}H NMR of 5l


7.523
7.504
7.337
7.138
7.120
7.101
5.744
4.915
4.750
2.966
2.930
2.559
1.759
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.00
2.95
0.98
1.95
1.01
1.01
2.03
4.06
3.03

^{13}C NMR of 5l


175.37
142.51
138.12
129.01
128.97
124.17
120.01
114.21
52.90
46.78
42.99
23.84
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

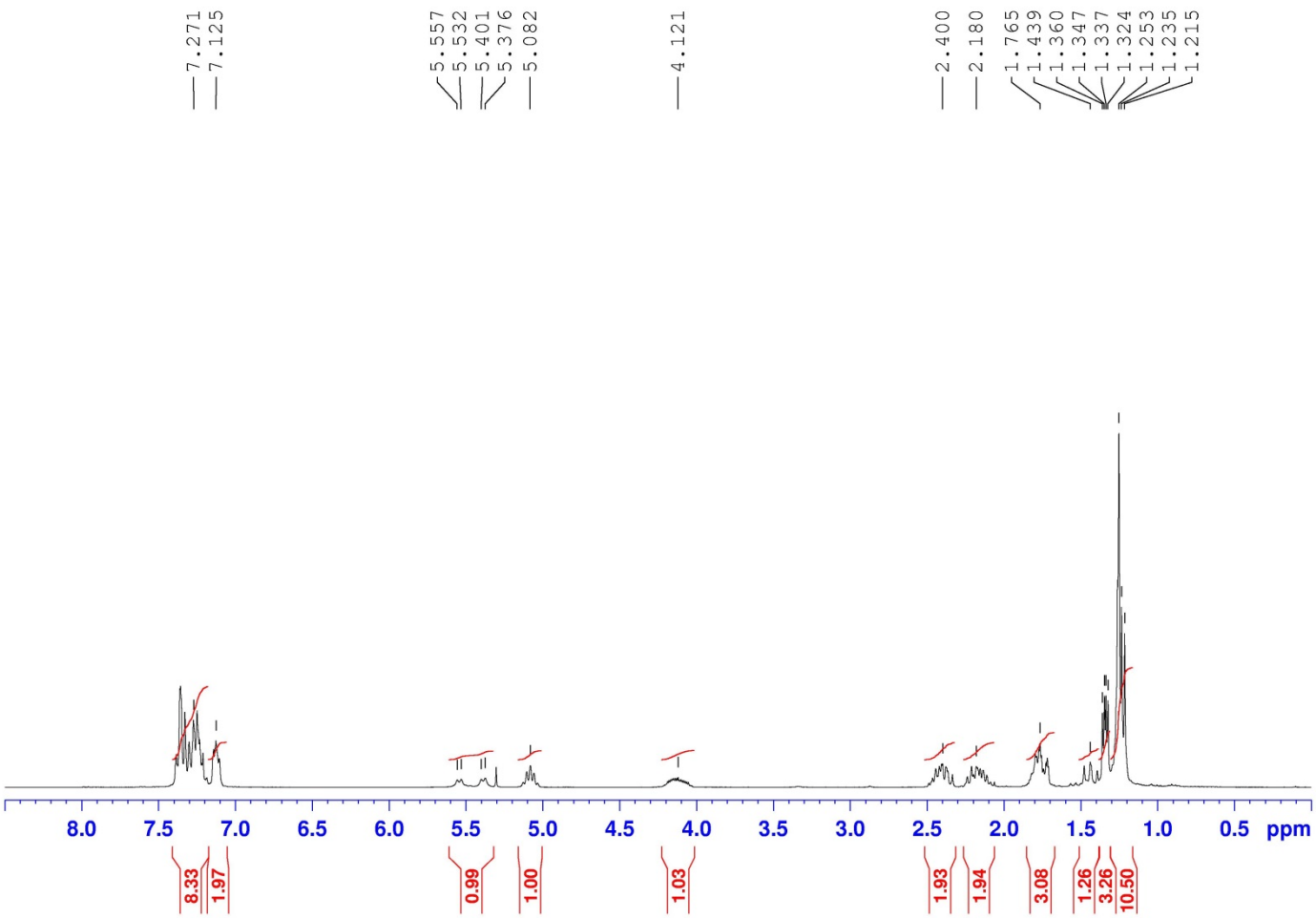


6i

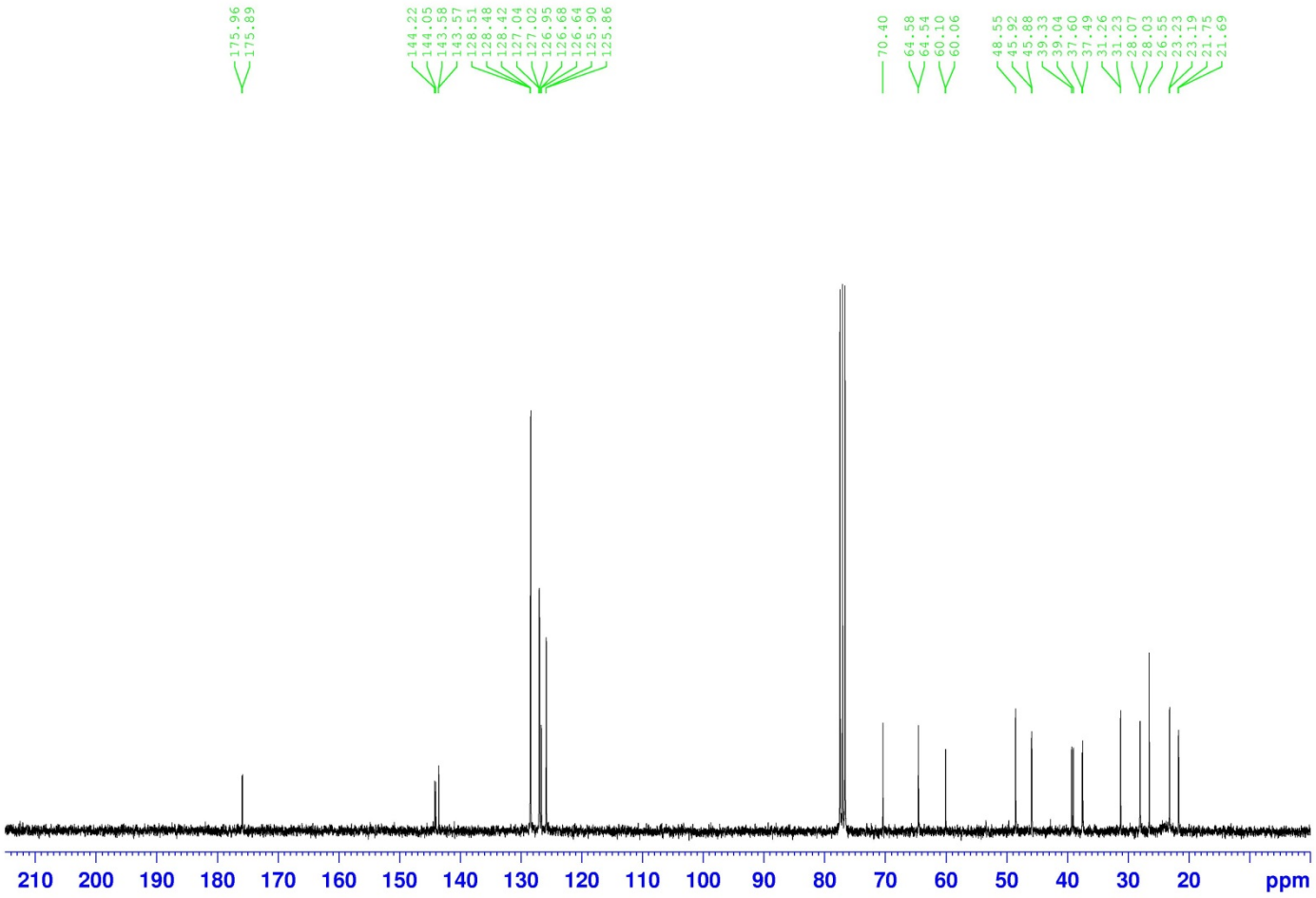
Following the general procedure for CAHB of *γ,δ*-unsaturated amides without subsequent oxidation affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (78%) as a yellow oil.

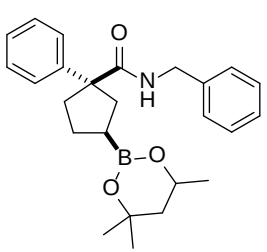
TLC analysis	R_f 0.7 (70:30 hexanes:ethyl acetate)
^{1}H NMR (300 MHz, $CDCl_3$)	δ 7.40–7.20 (8H, m, f,g,h,h',i,i',j,m,m',n,n'), 7.15–7.05 (2H, m, j,o), 5.47 (1H, dd, *J* = 11.2 and 1.9 Hz, NH), 5.15–5.00 (1H, m, k), 4.20–4.00 (1H, m, s), 2.50–2.30 (2H, m, b,e), 2.30–2.05 (2H, m, b,e), 1.85–1.70 (3H, m, c,r), 1.50–1.40 (1H, m, r), 1.34 (3H, dd, *J* = 6.8 and 4.0 Hz, p), 1.25 (6H, s, t,t'), 1.23 (3H, d, *J* = 6.2 Hz, u), 1.30–1.20 (1H, m, d).
^{13}C NMR (75 MHz, $CDCl_3$)	δ 175.96 and 175.89 (f), 144.22 and 144.05 (l), 143.58 and 143.57 (g), 128.51 and 128.48 (i,i'), 128.42 (n,n'), 127.04 and 127.02 (h,h'), 126.95 (m,m'), 126.68 and 126.64 (j), 125.90 and 125.86 (o), 70.40 (q), 64.58 and 64.54 (s), 60.10 and 60.06 (a), 48.55 (k), 45.92 and 45.88 (r), 39.33 and 39.04 (b), 37.60 and 37.49 (e), 31.26 and 31.23 (t,t'), 28.07 and 28.03 (d), 26.55 (c), 23.23 and 23.19 (u), 21.75 and 21.69 (p).
IR (neat)	3345 (N-H stretch), 2970, 2932, 1649 (C=O stretch), 1600 (N-H bend), 1493 (C=C stretch, aromatic), 1446, 1300 (C-O stretch), 1207, 765, 697 cm^{-1}.

^{1}H NMR of 6i

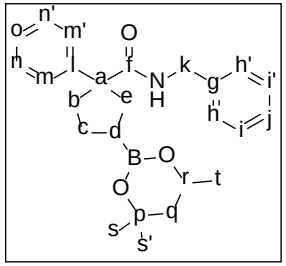

7.271
7.125
5.557
5.532
5.401
5.376
5.082
4.121
2.400
2.180
1.765
1.439
1.360
1.347
1.337
1.324
1.253
1.235
1.215
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
8.33
1.97
0.99
1.00
1.03
1.93
1.94
3.08
1.26
3.26
10.50

^{13}C NMR of 6i


175.96
175.89
144.22
144.05
143.58
143.57
128.51
128.48
128.42
127.04
127.02
126.95
126.68
126.64
125.90
125.86
70.40
64.58
64.54
60.10
60.06
48.55
45.92
45.88
39.33
39.04
37.60
37.49
31.26
31.23
28.07
28.03
26.55
23.23
23.19
21.75
21.69
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm



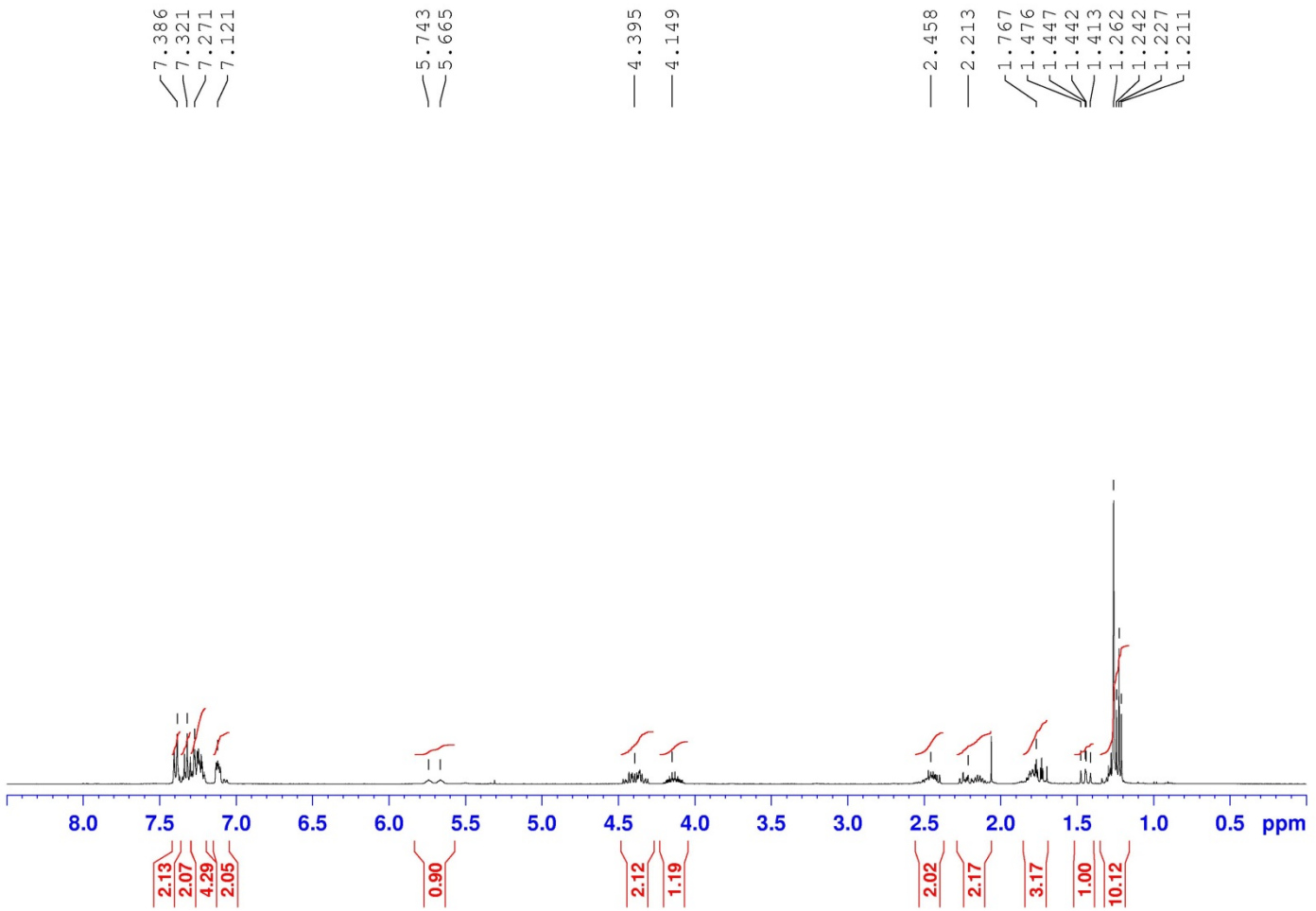
6g



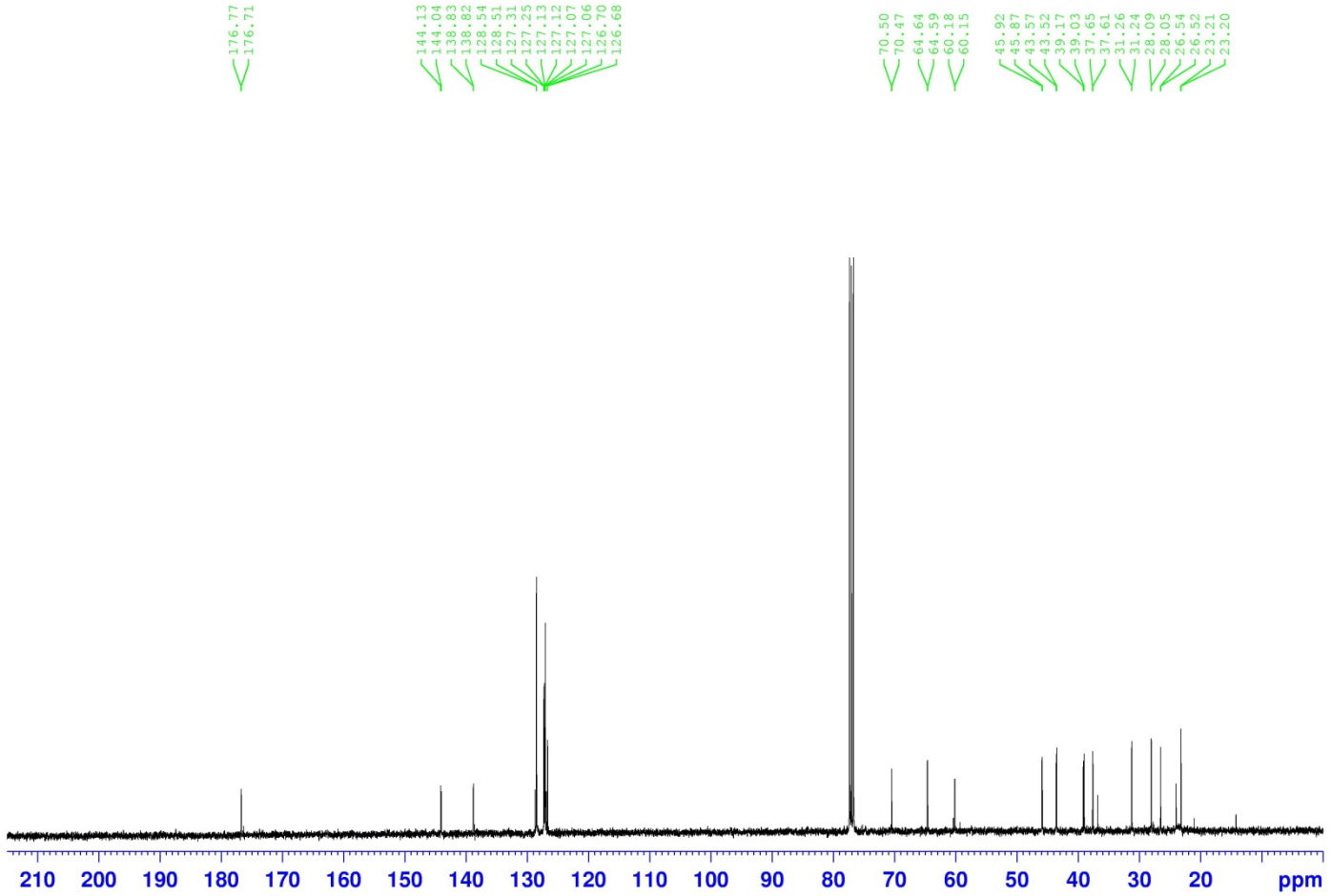
Following the general procedure for CAHB of *γ,δ*-unsaturated amides without subsequent oxidation affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (72%) as a yellow oil.

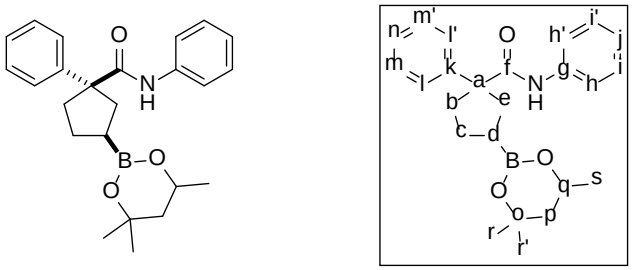
TLC analysis	R_f 0.6 (70:30 hexanes:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 7.45–7.35 (2H, m, m,m'), 7.35–7.30 (2H, m, i,i'), 7.30–7.20 (2H, m, j,n,n',o), 7.15–7.05 (2H, m, h,h'), 5.70 (1H, d, *J* = 31.3 Hz, NH), 4.50–4.30 (2H, m, k), 4.20–3.95 (1H, m, r), 2.55–2.40 (2H, m, b,e), 2.30–2.10 (2H, m, b,e), 1.85–1.70 (3H, m, c,q), 1.44 (1H, dd, *J* = 13.8 and 11.7 Hz, q), 1.26 (6H, s, s,s'), 1.23 (3H, dd, *J* = 6.2 and 0.0 Hz, t), 1.35–1.15 (1H, m, d).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 176.77 and 176.71 (f), 144.13 and 144.04 (l), 138.83 and 138.82 (g), 128.54 (i,i'), 128.51 (n,n'), 127.31 and 127.25 (h,h'), 127.13 and 127.12 (m,m'), 127.07 and 127.06 (j), 126.70 and 126.68 (o), 70.50 and 70.47 (p), 64.64 and 64.59 (r), 60.18 and 60.15 (a), 45.92 and 45.87 (q), 43.57 and 43.52 (k), 39.17 and 39.03 (b), 37.65 and 37.61 (e), 31.26 and 31.24 (s,s'), 28.09 and 28.05 (d), 26.54 and 26.52 (c), 23.21 and 23.20 (t).
IR (neat)	3339 (N-H stretch), 2970, 1645 (C=O stretch), 1600 (N-H bend), 1512 (C=C stretch, aromatic), 1300 (C-O stretch), 1207, 724, 696 cm^{-1}.

^{1}H NMR of 6g


7.386
7.321
7.271
7.121
5.743
5.665
4.395
4.149
2.458
2.213
1.767
1.476
1.447
1.442
1.413
1.262
1.242
1.227
1.211
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.13
2.07
4.29
2.05
0.90
2.12
1.19
2.02
2.17
3.17
1.00
10.12

^{13}C NMR of 6g


176.77
176.71
144.13
144.04
138.83
138.82
128.54
128.51
127.31
127.25
127.13
127.12
127.07
127.06
126.70
126.68
70.50
70.47
64.64
64.59
60.18
60.15
45.92
45.87
43.57
43.52
39.17
39.03
37.65
37.61
31.26
31.24
28.09
28.05
26.54
26.52
23.21
23.20
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

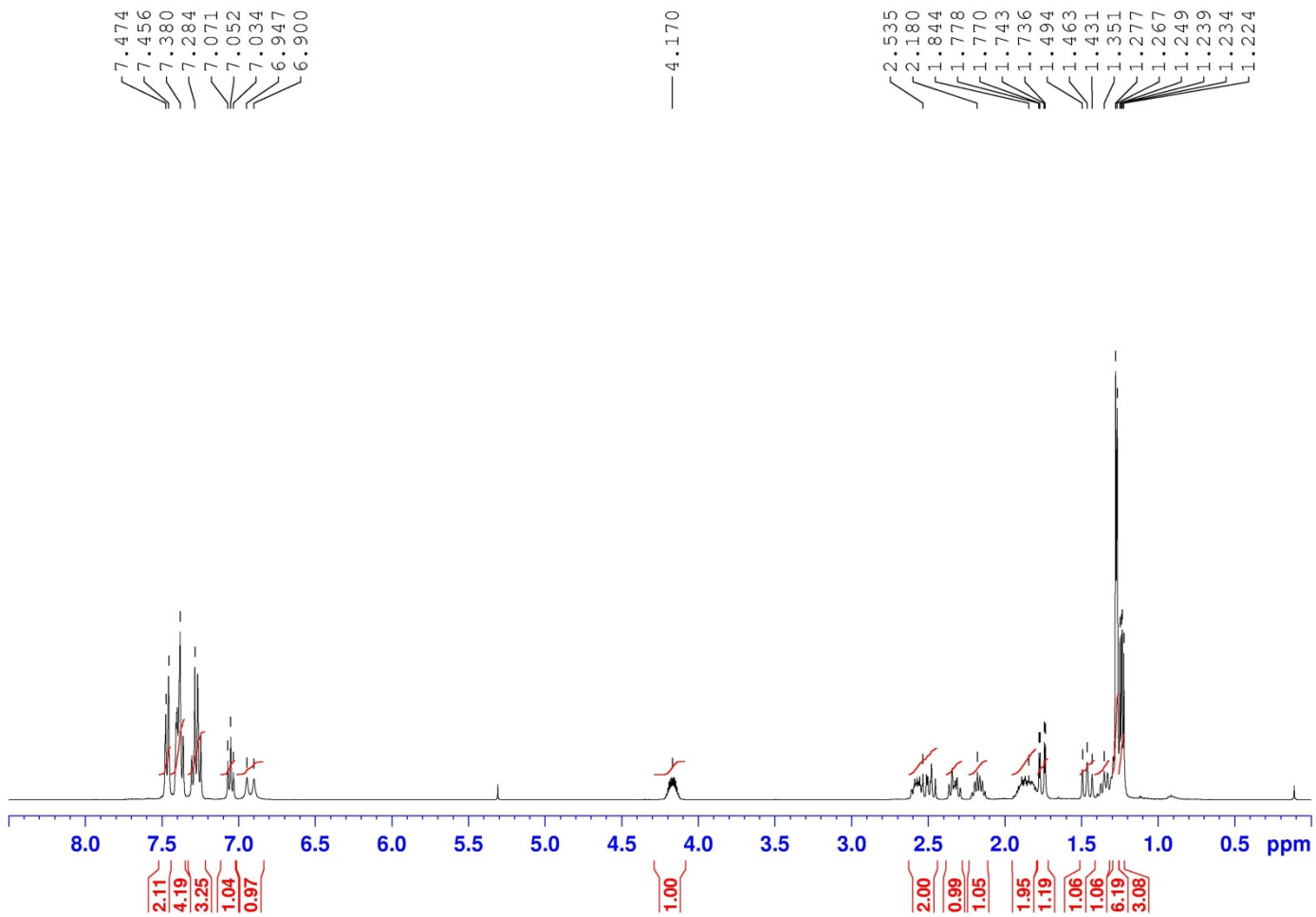


6c

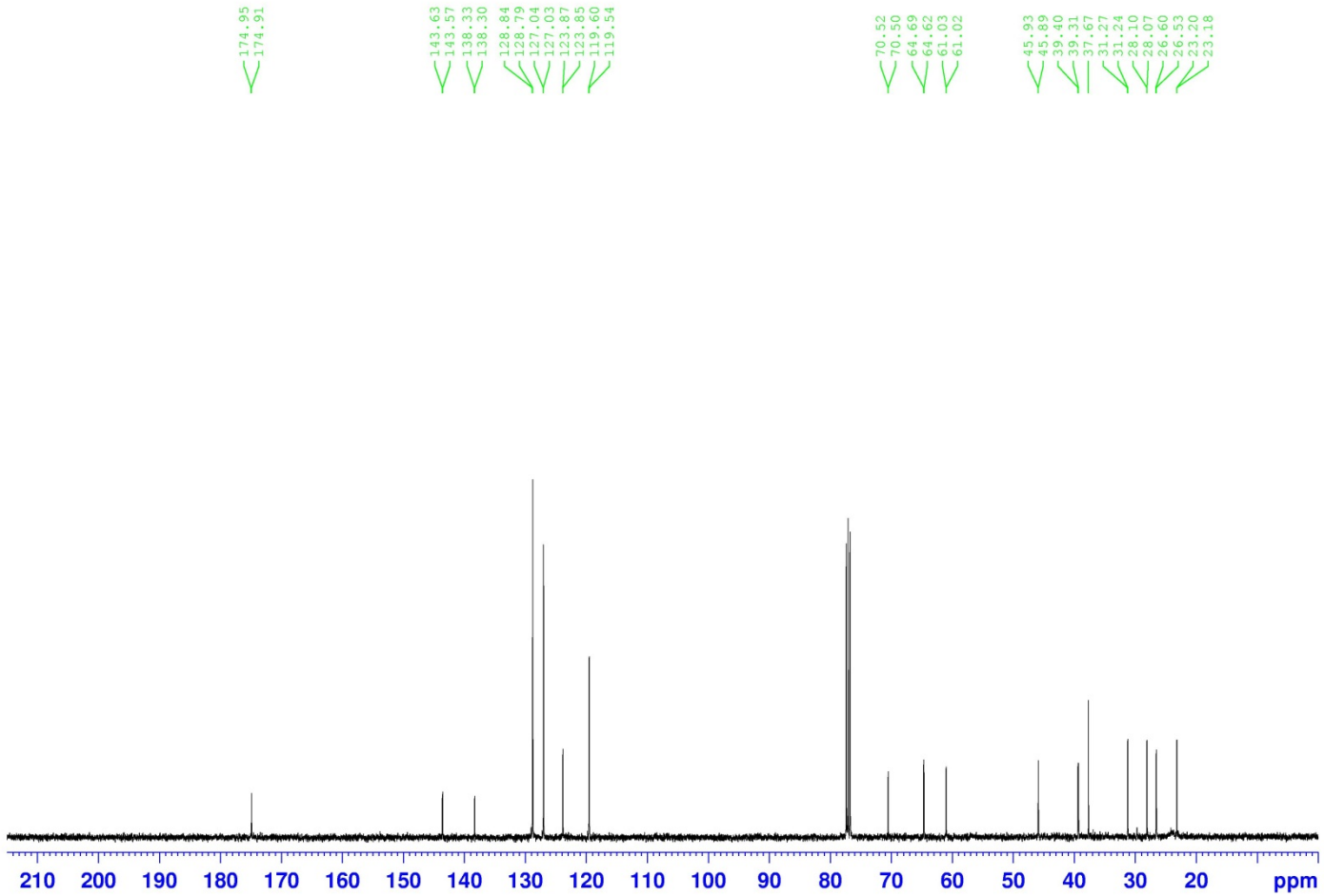
Following the general procedure for CAHB of *γ,δ*-unsaturated amides without subsequent oxidation affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (73%) as a light yellow solid.

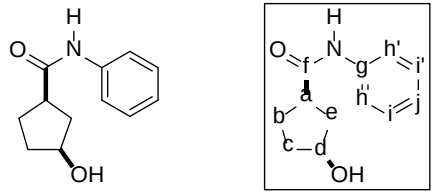
m.p.	112.5–114.0 ºC
TLC analysis	R_f 0.75 (70:30 hexanes:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 7.46 (1H, d, *J* = 7.4 Hz, l,l'), 7.45–7.35 (4H, m, h,h',m,m'), 7.35–7.20 (2H, m, i,i',j), 7.05 (1H, t, *J* = 7.4 Hz, n), 6.92 (1H, d, *J* = 18.6 Hz, NH), 4.25–4.10 (2H, m, q), 2.60–2.45 (2H, m, b,e), 2.40–2.25 (2H, m, b), 2.20–2.10 (2H, m, e), 1.95–1.80 (3H, m, c), 1.76 (1H, dd, *J* = 13.9 and 3.0 Hz, p), 1.46 (1H, dd, *J* = 12.5 and 12.5 Hz, p), 1.40–1.30 (1H, m, d), 1.27 (6H, d, *J* = 3.9 Hz, r,r'), 1.24 (3H, dd, *J* = 6.2 and 4.1 Hz, s).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 174.95 and 174.91 (f), 143.63 and 143.57 (k), 138.33 and 138.30 (g), 128.84 (i,i'), 128.79 (m,m'), 127.04 (j), 127.03 (l,l'), 123.87 and 123.85 (n), 119.60 and 119.55 (h,h'), 70.52 and 70.50 (o), 64.69 and 64.62 (q), 61.03 and 61.02 (a), 45.93 and 45.89 (p), 39.40 and 39.31 (b), 37.67 (e), 31.27 and 31.24 (r,r'), 28.10 and 28.07 (d), 26.60 and 26.53 (c), 23.20 and 23.18 (s).
IR (neat)	3408 (N-H stretch), 2971, 1677 (C=O stretch), 1596 (N-H bend), 1519, 1493, 1436, 1303 (C-O stretch), 1208 (C-N stretch), 1163, 700, 690 cm^{-1}.

^{1}H NMR of 6c


7.474
7.456
7.380
7.284
7.071
7.052
7.034
6.947
6.900
4.170
2.535
2.180
1.844
1.778
1.770
1.743
1.736
1.494
1.463
1.431
1.351
1.277
1.267
1.249
1.239
1.234
1.224
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.11
4.19
3.25
1.04
0.97
1.00
2.00
0.99
1.05
1.95
1.19
1.06
1.06
6.19
3.08

^{13}C NMR of 6c


174.95
174.91
143.63
143.57
138.33
138.30
128.84
128.79
127.04
127.03
123.87
123.85
119.60
119.54
70.52
70.50
64.69
64.62
61.03
61.02
45.93
45.89
39.40
39.31
37.67
31.27
31.24
28.10
28.07
26.60
26.53
23.20
23.18
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

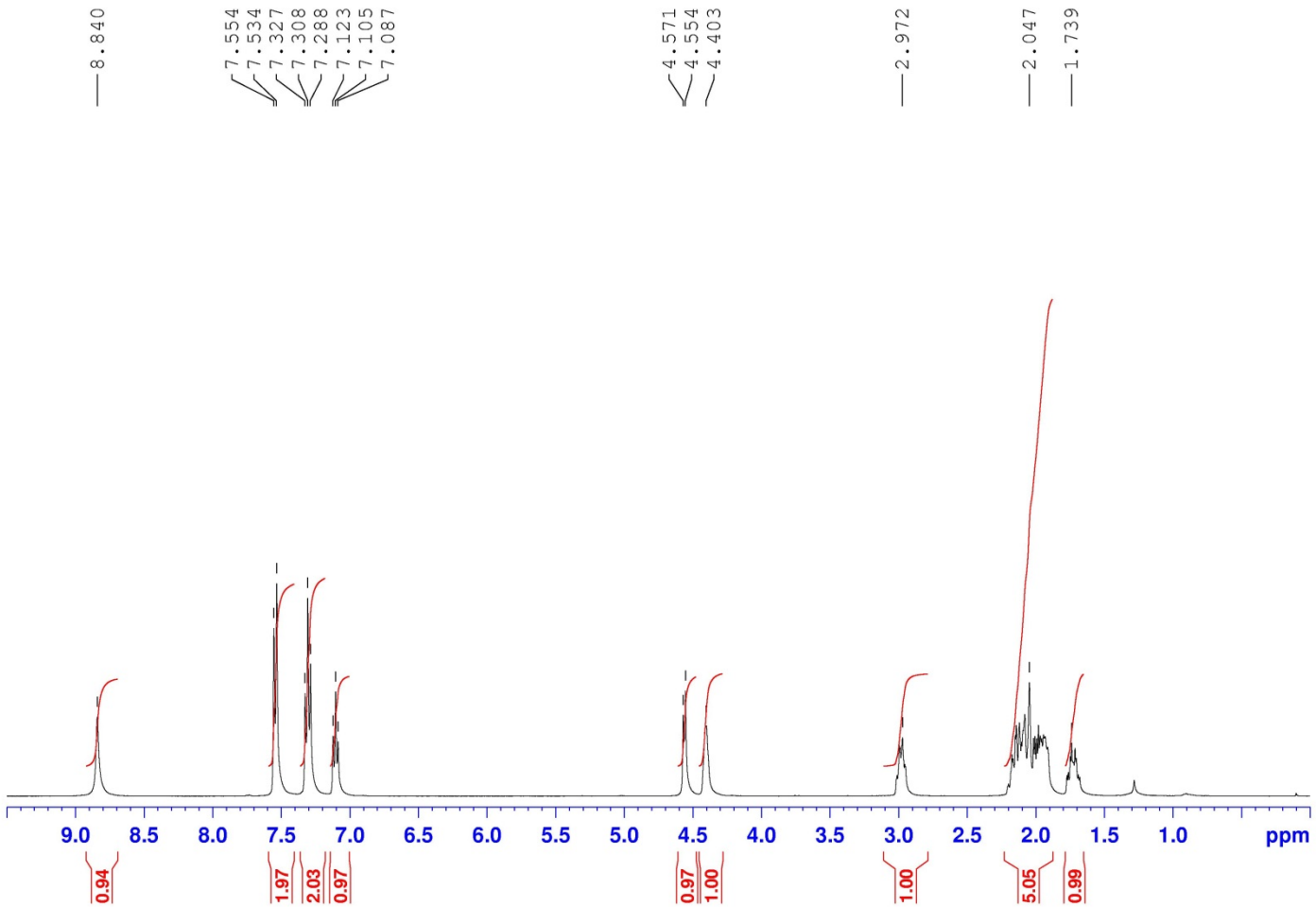


7a

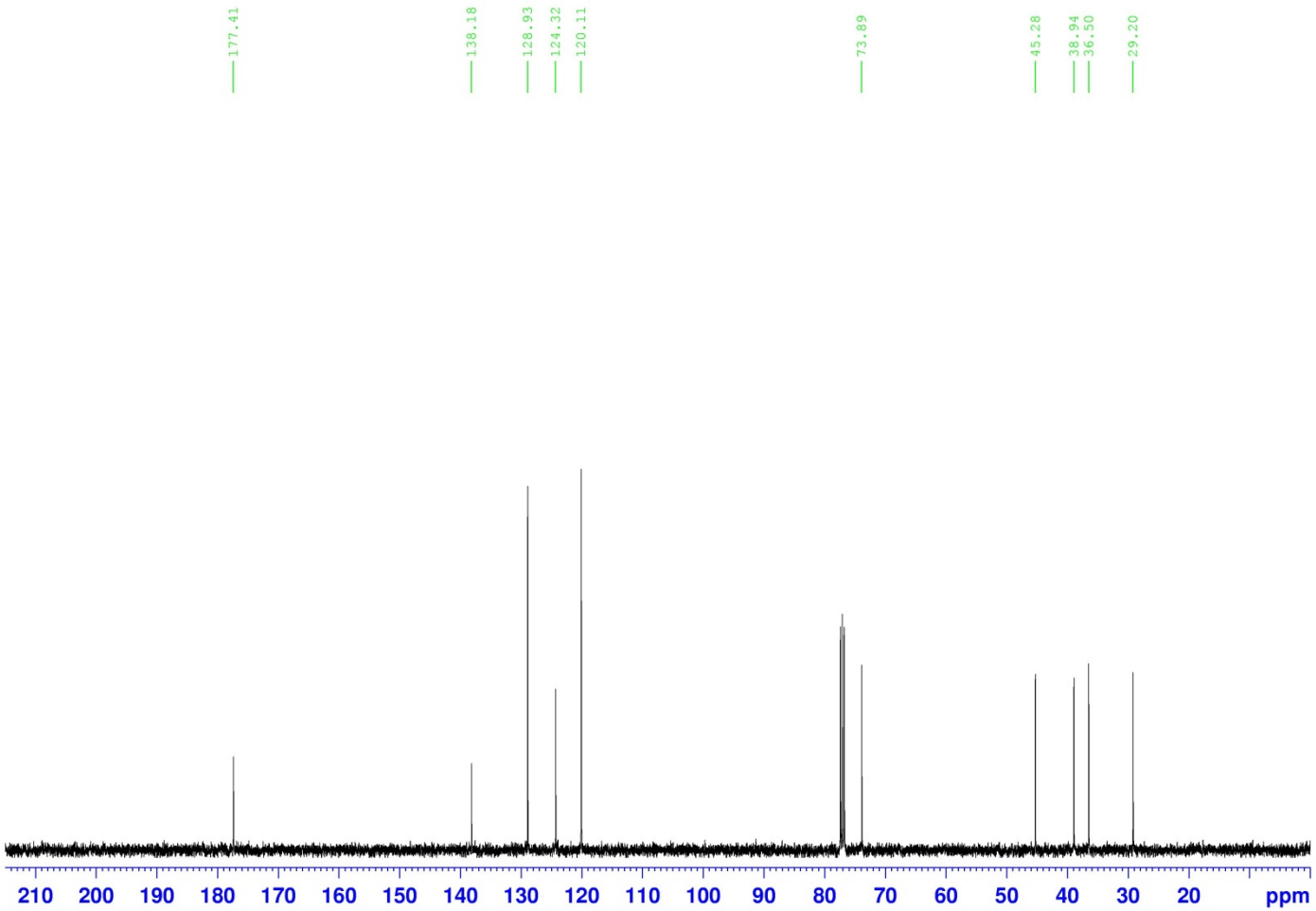
Following the general procedure for CAHB-oxidation sequence with H_2O_2 affords, after flash chromatography on silica gel (80–40:20–60 hexanes:ethyl acetate), the title compound (80%) as a white solid.

m.p.	100.5–102.5 ºC
Optical rotation	$[\alpha]_D^{20} = -14^o$ (*c* 1.0, $CHCl_3$).
HPLC analysis	Chiralpak-IC, 80:20 hexanes:isopropanol, flow rate = 1.0 mL/min, showed peaks at 56 minutes (3.0% (1*S*,3*R*)) and 64 minutes (97.0% (1*R*,3*S*)).
TLC analysis	R_f 0.4 (50:50 hexanes:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 8.84 (1H, br s, NH), 7.54 (2H, d, *J* = 7.9 Hz, h,h'), 7.31 (2H, t, *J* = 7.8 Hz, i,i'), 7.11 (1H, t, *J* = 7.3 Hz, j), 4.56 (1H, d, *J* = 6.6 Hz, d), 4.40 (1H, br s, OH), 3.05–2.90 (1H, m, a), 2.20–1.90 (5H, m, b,c,e), 1.80–1.65 (1H, m, c).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 177.41 (f), 138.18 (g), 128.93 (i,i'), 124.32 (j), 120.11 (h,h'), 73.89 (d), 45.28 (a), 38.94 (e), 36.50 (b), 29.20 (c).
IR (neat)	3677 (N-H stretch, O-H stretch), 2907, 2803, 1728 (C=O stretch), 1663, 1597 (N-H bend), 1565, 1389 (C-N stretch), 1238 (C-OH bend), 1050 (C-OH stretch) cm^{-1}.
HRMS (ESI)	Calcd. for $C_{12}H_{15}NNaO_2$ (M+Na): 228.1000, found 228.1002 *m/z*.

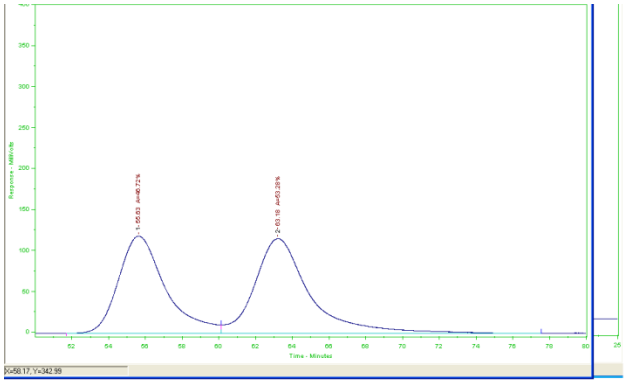
^{1}H NMR of 7a


8.840
7.554
7.534
7.327
7.308
7.288
7.123
7.105
7.087
4.571
4.554
4.403
2.972
2.047
1.739
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.94
1.97
2.03
0.97
0.97
1.00
1.00
5.05
0.99

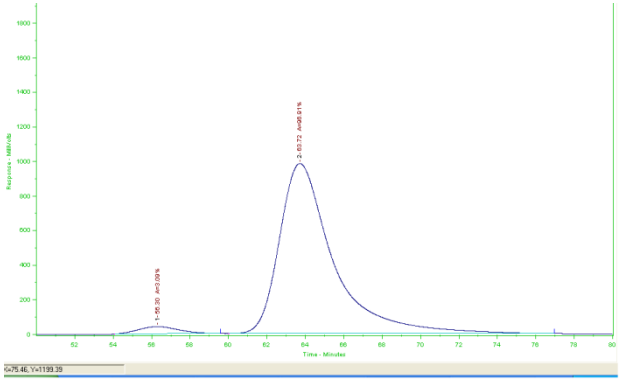
^{13}C NMR of 7a


177.41
138.18
128.93
124.32
120.11
73.89
45.28
38.94
36.50
29.20
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

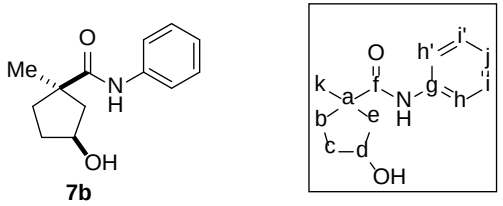
HPLC analysis of **7a**



Racemic



CAHB product

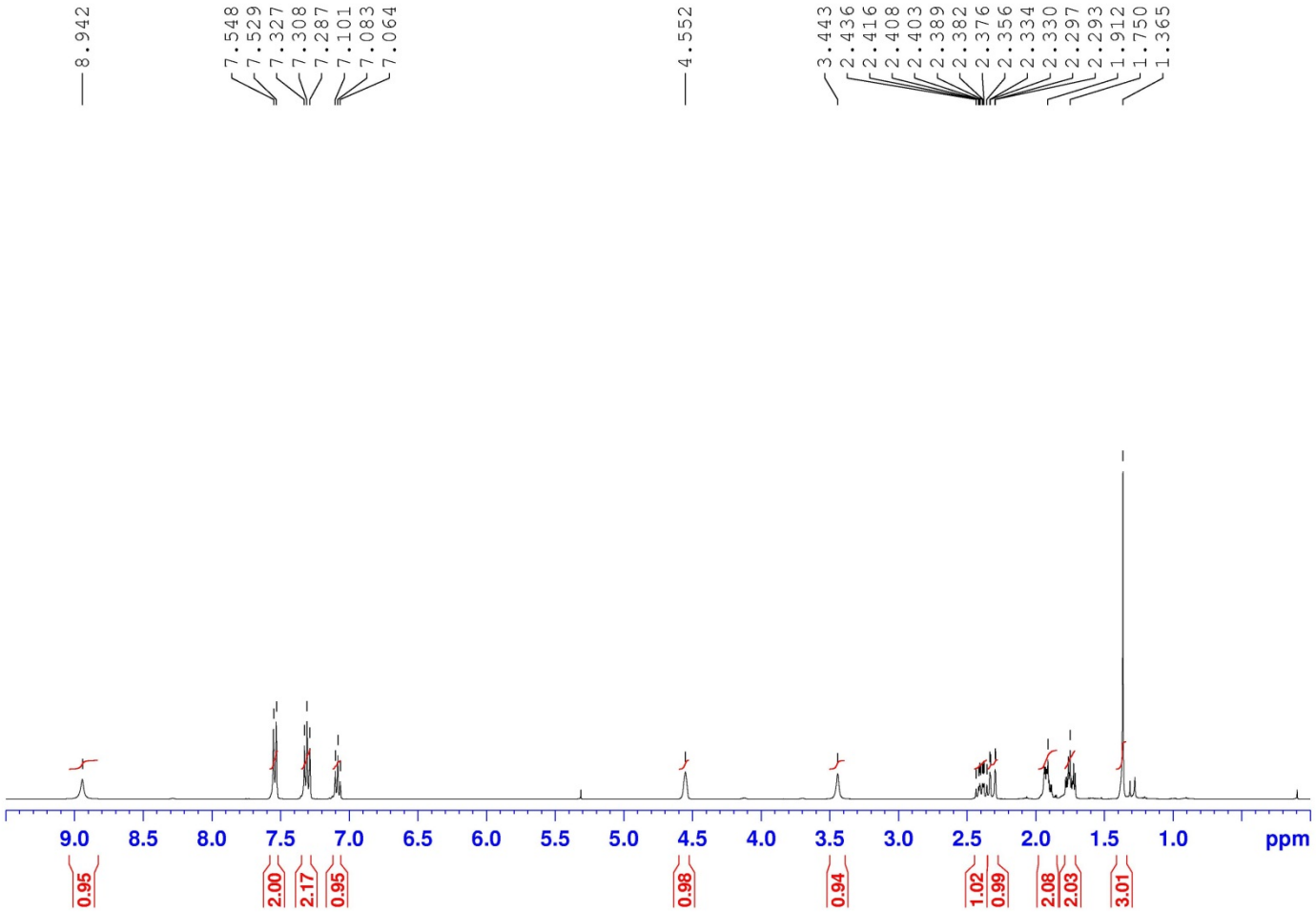


7b

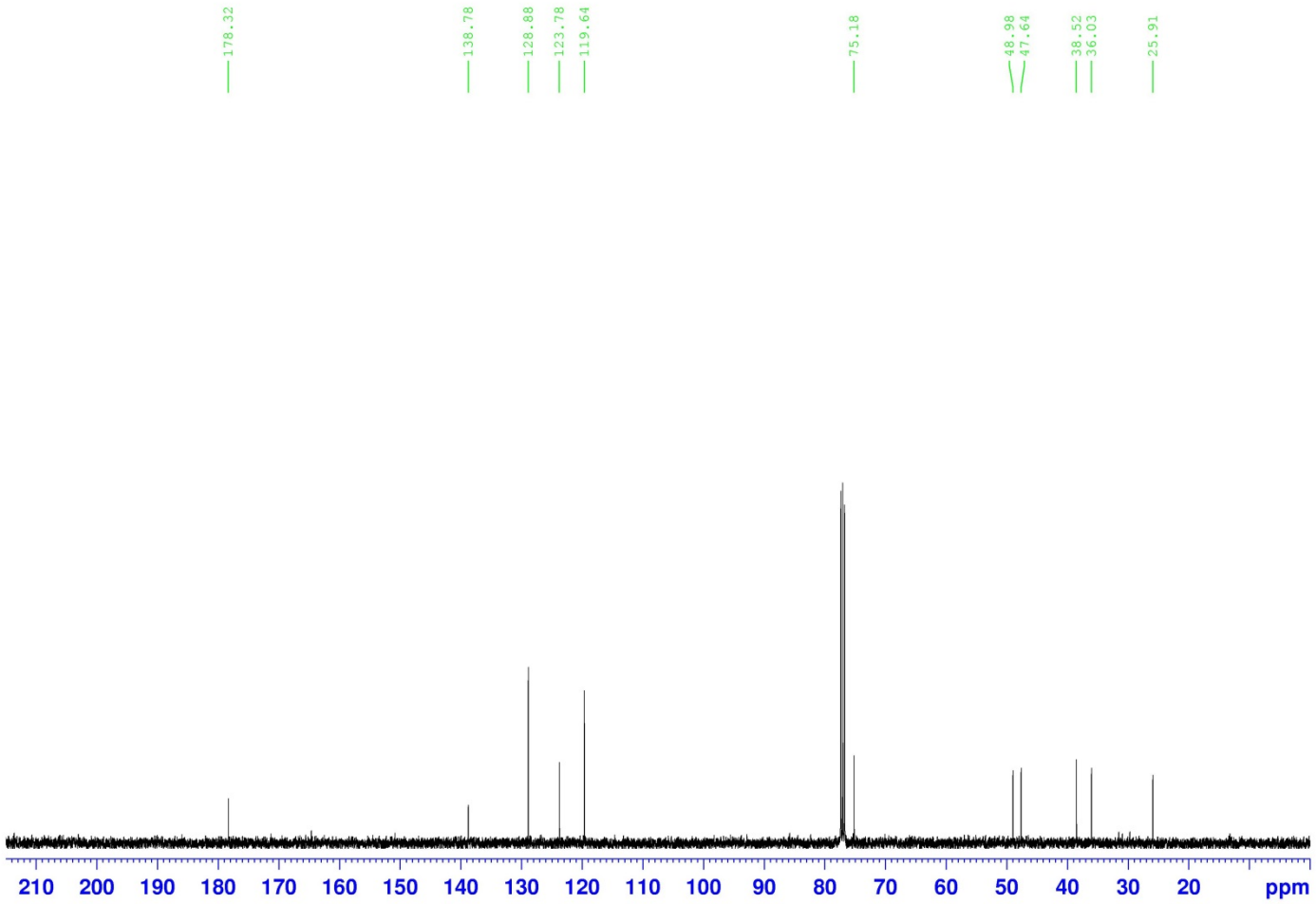
Following the general procedure for CAHB-oxidation sequence with H_2O_2 affords, after flash chromatography on silica gel (85:15 dichloromethane:ethyl acetate), the title compound (65%) as a white solid.

m.p.	91.0–93.5 °C
Optical rotation	$[\alpha]_D^{20} = -13^o$ (*c* 0.7, $CHCl_3$).
HPLC analysis	Chiralcel-OD, 90:10 hexanes:isopropanol, flow rate = 1.3 mL/min, showed peaks at 87 minutes (96.0% (1*R*,3*S*)) and 105 minutes (4.0% (1*S*,3*R*))
TLC analysis	R_f 0.5 (80:20 dichloromethane:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 8.94 (1H, br s, NH), 7.54 (2H, d, *J* = 7.6 Hz, h,h'), 7.31 (2H, t, *J* = 7.5 Hz, i,i'), 7.08 (1H, t, *J* = 7.4 Hz, j), 4.55 (1H, s, d), 3.44 (1H, br s, OH), 2.40 (1H, ddd, *J* = 18.8 Hz, 10.9 Hz, 7.9 Hz, b), 2.31 (1H, dd, *J* = 14.9 Hz, 1.6 Hz, e), 2.00–1.85 (2H, m, c), 1.80–1.70 (2H, m, b,e), 1.37 (3H, s, k).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 178.32 (f), 138.78 (g), 128.88 (i,i'), 123.78 (j), 119.64 (h,h'), 75.18 (d), 48.98 (a), 47.64 (e), 38.52 (b), 36.03 (c), 25.91 (k).
IR (neat)	3318 (O-H stretch, N-H stretch), 2962, 2901, 1663 (C=O stretch), 1536 (C-OH bend), 1495, 1434, 1311 (C-N stretch), 657 cm^{-1}.
HRMS (CI)	Calcd. for $C_{13}H_{18}NO_2$ (M+H): 220.1338, found 220.1346 *m/z*.

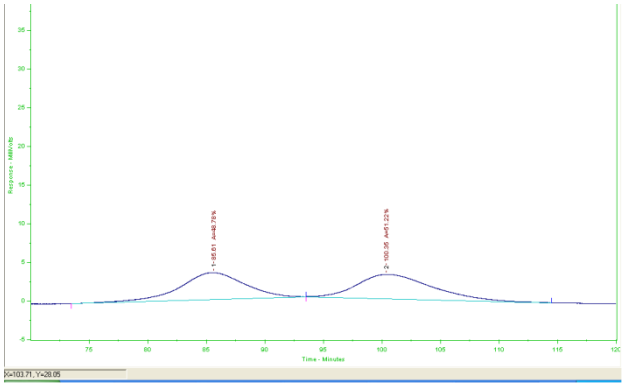
^{1}H NMR of 7b


8.942
7.548
7.529
7.327
7.308
7.287
7.101
7.083
7.064
4.552
3.443
2.436
2.416
2.408
2.403
2.389
2.382
2.376
2.356
2.334
2.330
2.297
2.293
1.912
1.750
1.365
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.95
2.00
2.17
0.95
0.98
0.94
1.02
0.99
2.08
2.03
3.01

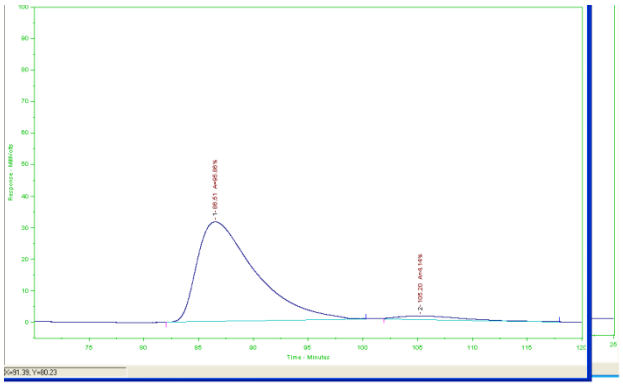
^{13}C NMR of 7b


178.32
138.78
128.88
123.78
119.64
75.18
48.98
47.64
38.52
36.03
25.91
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

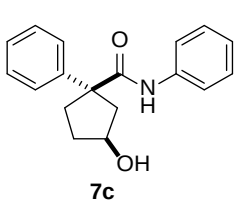
HPLC analysis of 7b



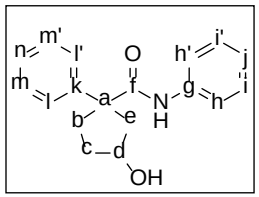
Racemic



CAHB product



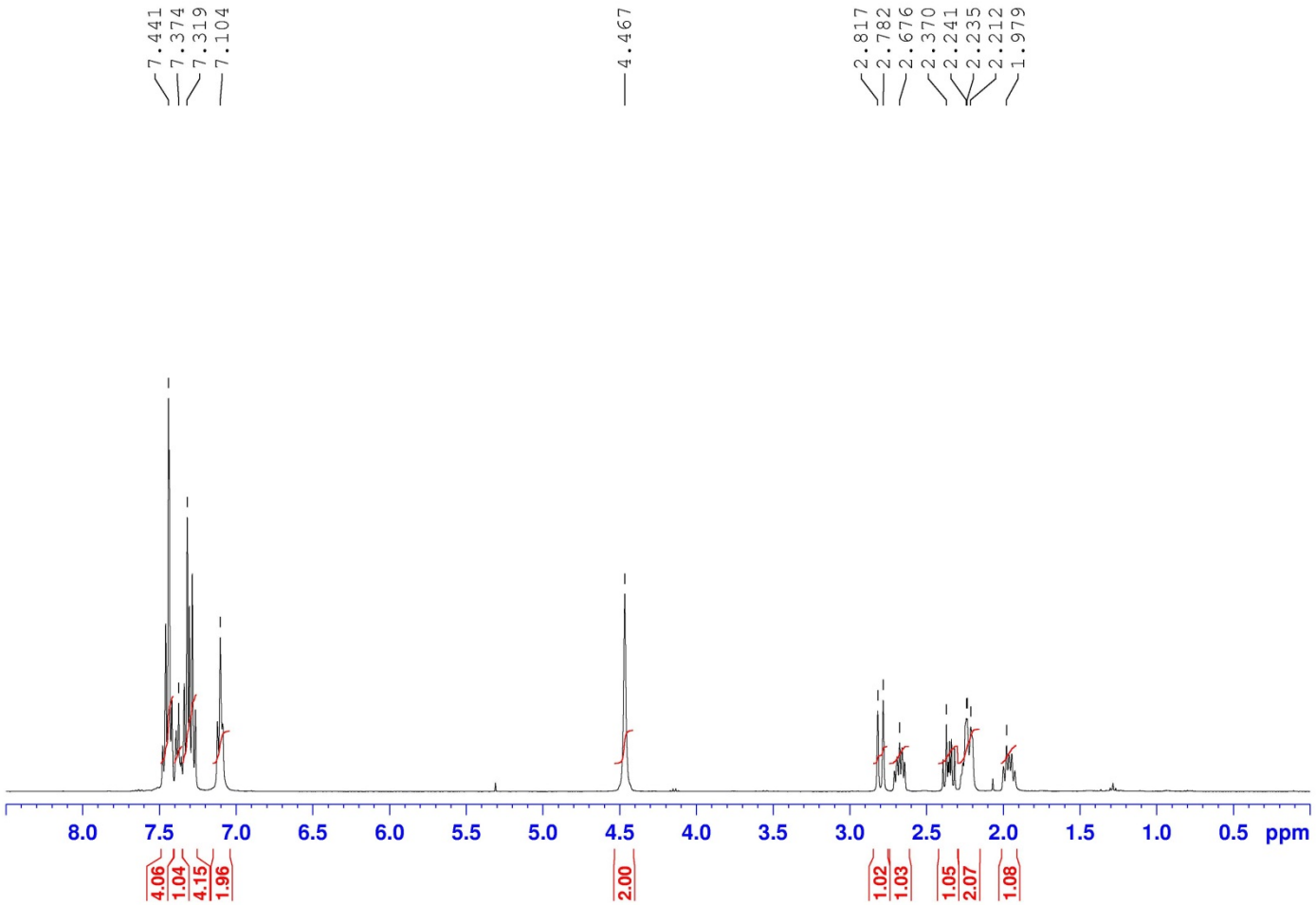
7c



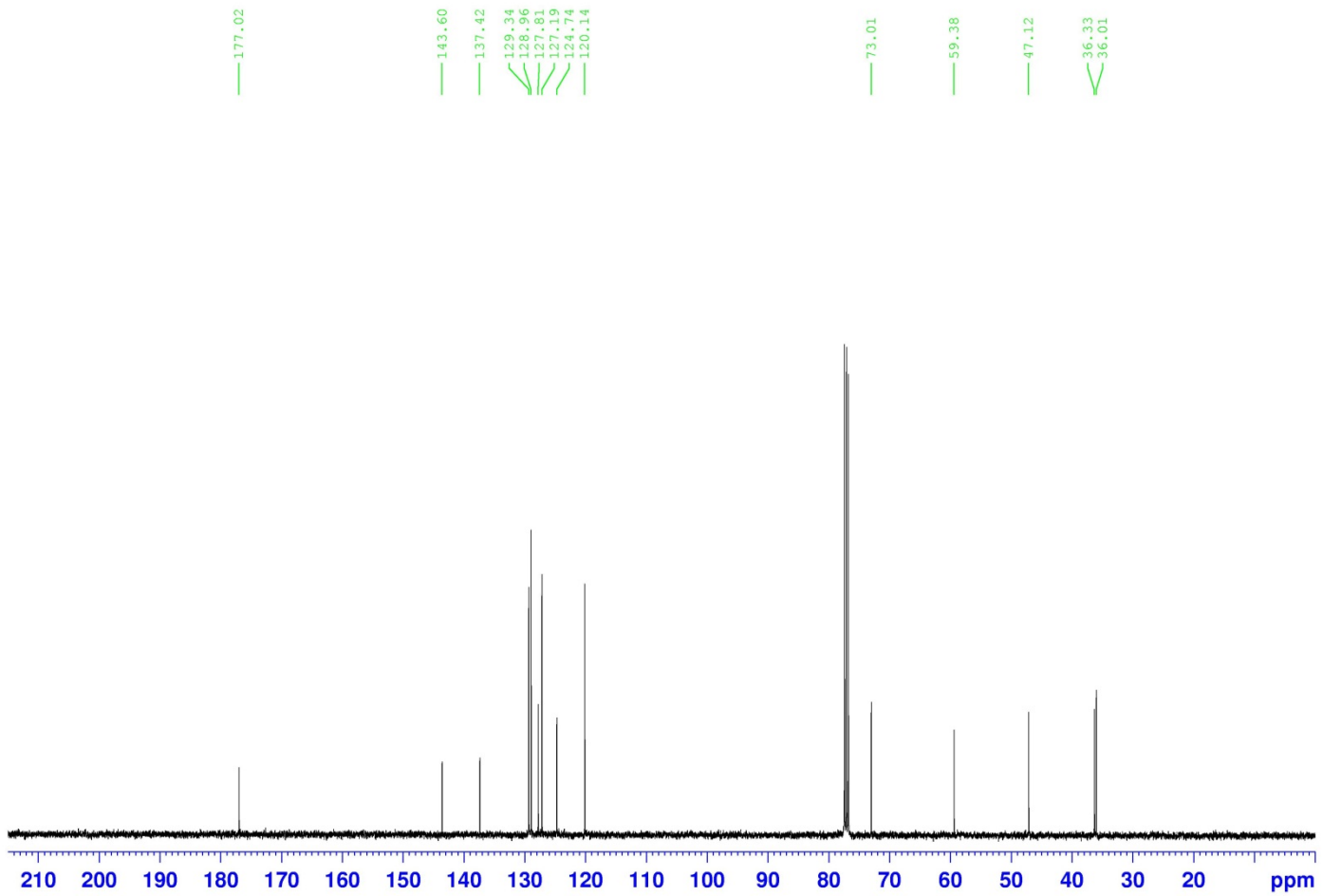
Following the general procedure for CAHB-oxidation sequence with H_2O_2 affords, after flash chromatography on silica gel (85:15 dichloromethane:ethyl acetate), the title compound (72%) as a white solid.

m.p.	113.5–114.5 ºC
Optical rotation	$[\alpha]_D^{20} = -43^o$ (*c* 0.8, $CHCl_3$)
HPLC analysis	Chiralcel-OD, 60:40 hexanes:isopropanol, flowrate = 1.4 mL/min, showed peaks at 14 minutes (96.0% (1*R*,3*S*)) and 22 minutes (4.0% (1*S*,3*R*)).
TLC analysis	R_f 0.5 (80:20 dichloromethane:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 7.50–7.40 (4H, m, h,h',i,i'), 7.40–7.35 (1H, m, j), 7.40–7.35 (4H, m, l,l',m,m'), 7.15–7.05 (2H, m, n,NH), 4.47 (2H, br s, d,OH), 2.80 (1H, d, *J* = 14.2 Hz, e), 2.75–2.60 (1H, m, b), 2.40–2.30 (1H, m, b), 2.30–2.20 (2H, m, c,e), 2.00–1.90 (1H, m, c).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 177.02 (f), 143.60 (k), 137.42 (g), 129.34 (i,i'), 128.96 (m,m'), 127.81 (j), 127.19 (l,l'), 124.74 (n), 120.15 (h,h'), 73.01 (d), 59.39 (a), 47.12 (e), 36.33 (b), 36.01 (c).
IR (neat)	3492 (O-H stretch), 3400 (N-H stretch), 2896, 1668 (C=O stretch), 1596 (C-=C stretch), 1522 (C-OH bend), 1492, 1437, 1311 (C-N stretch), 1033, 751, 733, 691 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{18}H_{19}NNaO_2$ (M+Na): 304.1313, found 304.1299 *m/z*.

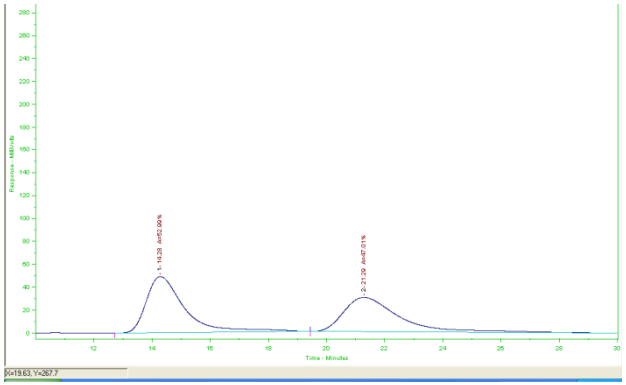
^{1}H NMR of 7c


7.441
7.374
7.319
7.104
4.467
2.817
2.782
2.676
2.370
2.241
2.235
2.212
1.979
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.06
1.04
4.15
1.96
2.00
1.02
1.03
1.05
2.07
1.08

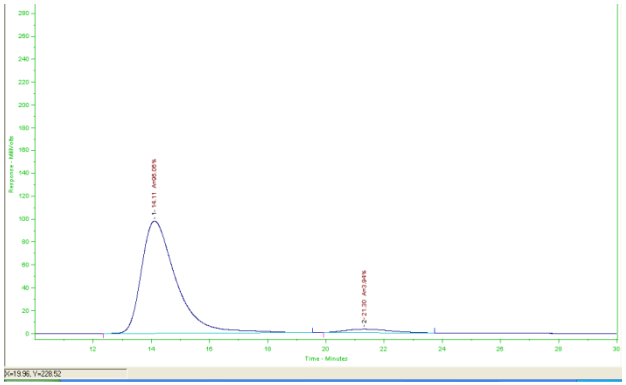
^{13}C NMR of 7c


177.02
143.60
137.42
129.34
128.96
127.81
127.19
124.74
120.14
73.01
59.38
47.12
36.33
36.01
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

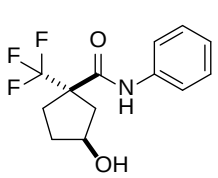
HPLC analysis of 7c



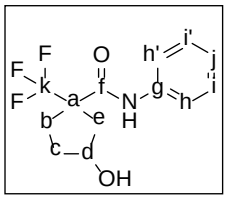
Racemic



CAHB product



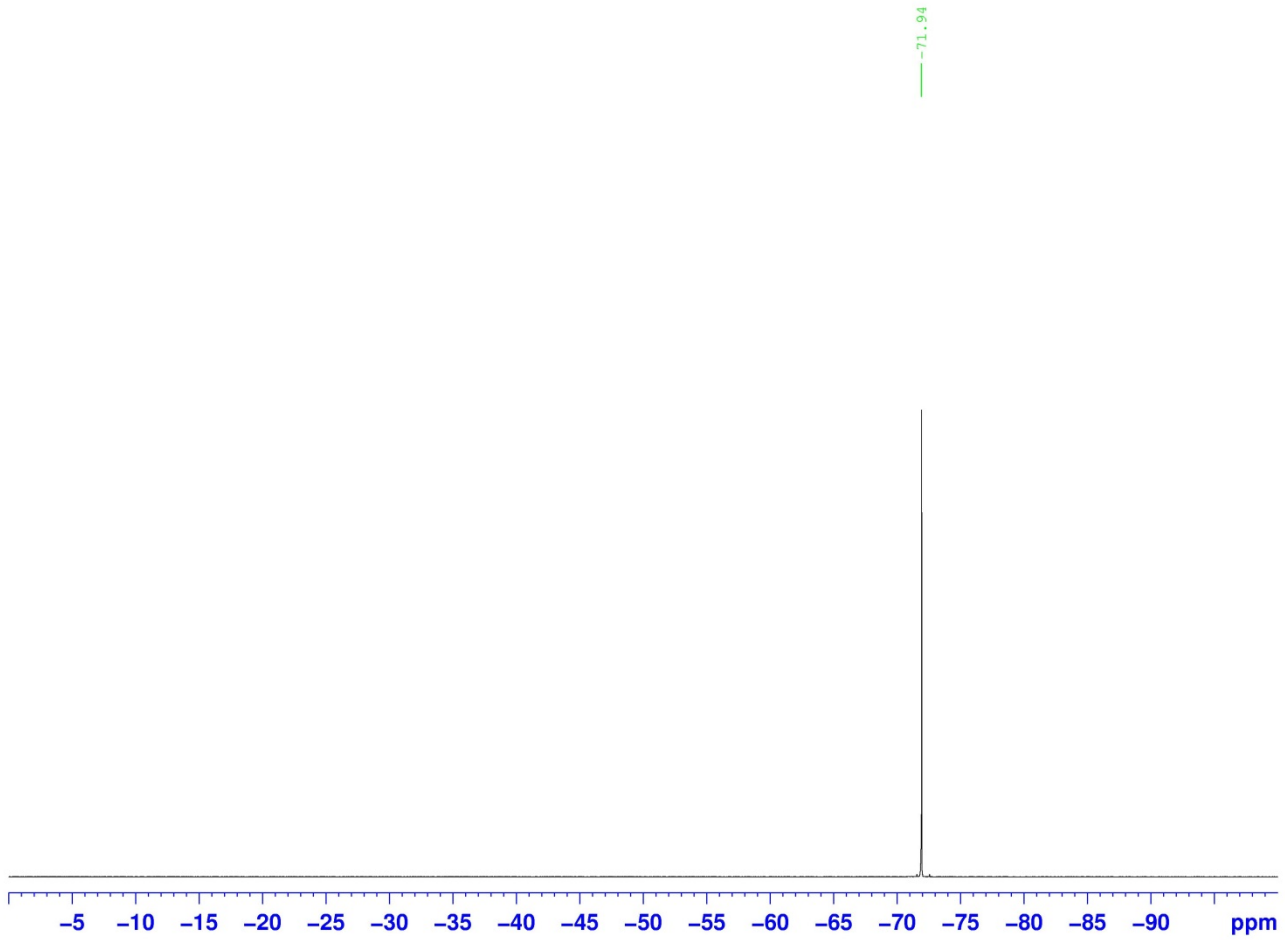
7d



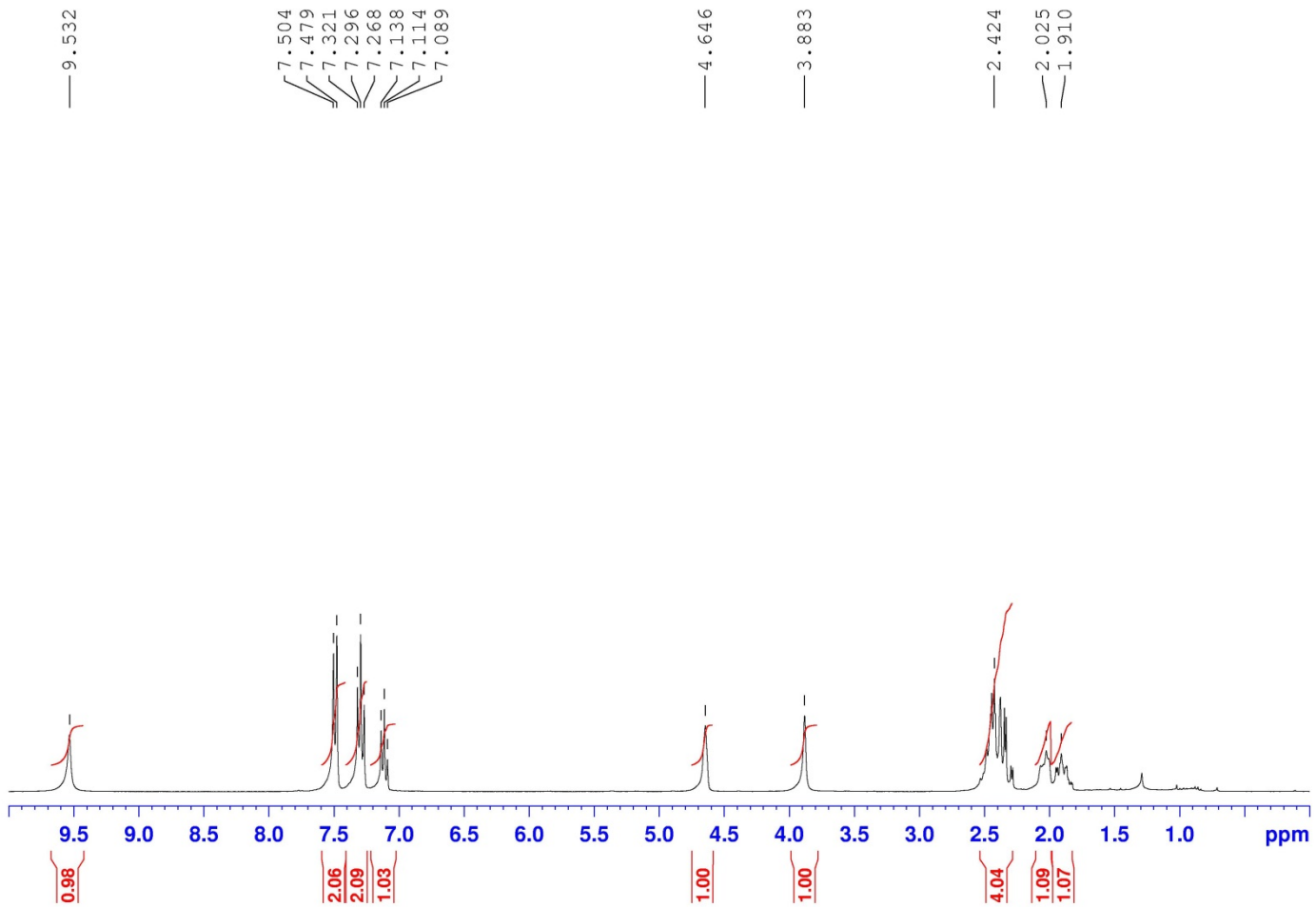
Following the general procedure for CAHB-oxidation sequence with H_2O_2 affords, after flash chromatography on silica gel (90:10 dichloromethane:ethyl acetate), the title compound (78%) as a white solid.

m.p.	129.0–130.5 ºC
Optical rotation	$[\alpha]_D^{20} = -22^o$ (*c* 1.3, $CHCl_3$).
HPLC analysis	Chiralpak-IC with OD guard column, 80:20 hexanes:isopropanol, flowrate = 1.0 mL/min, showed peaks at 14 minutes (97.0% (1*S*,3*S*)) and 21 minutes (3.0% (1*R*,3*R*)).
TLC analysis	R_f 0.75 (80:20 dichloromethane:ethyl acetate)
^{19}F NMR (282 MHz, $CDCl_3$)	δ -71.94.
^{1}H NMR (300 MHz, $CDCl_3$)	δ 9.53 (1H, br s, NH), 7.49 (2H, d, *J* = 7.6 Hz, h,h'), 7.30 (2H, t, *J* = 7.5 Hz, i,i'), 7.11 (1H, t, *J* = 7.4 Hz, j), 4.65 (1H, s, d), 3.88 (1H, br s, OH), 2.55–2.25 (4H, m, b,e), 2.10–1.95 (1H, m, c), 1.95–1.80 (1H, m, c).
^{13}C NMR (75 MHz, $CDCl_3$)	δ 170.51 (f), 137.92 (g), 128.95 (i,i'), 127.3 (q, *J* = 279 Hz, k), 124.52 (j), 120.00 (h,h'), 74.16 (d), 58.58 (q, *J* = 24 Hz, a), 40.88 (e), 36.20 (c), 32.21 (b).
IR (neat)	3416 (O-H stretch), 3263 (N-H stretch), 3089, 2376, 1669 (C=O stretch), 1624, 1599 (C-=C stretch), 1567 (C-OH bend), 1450, 1157, 1131, 752, 692, 653 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{13}H_{14}F_3NNaO_2$ (M+Na): 296.0874, found 296.0870 *m/z*.

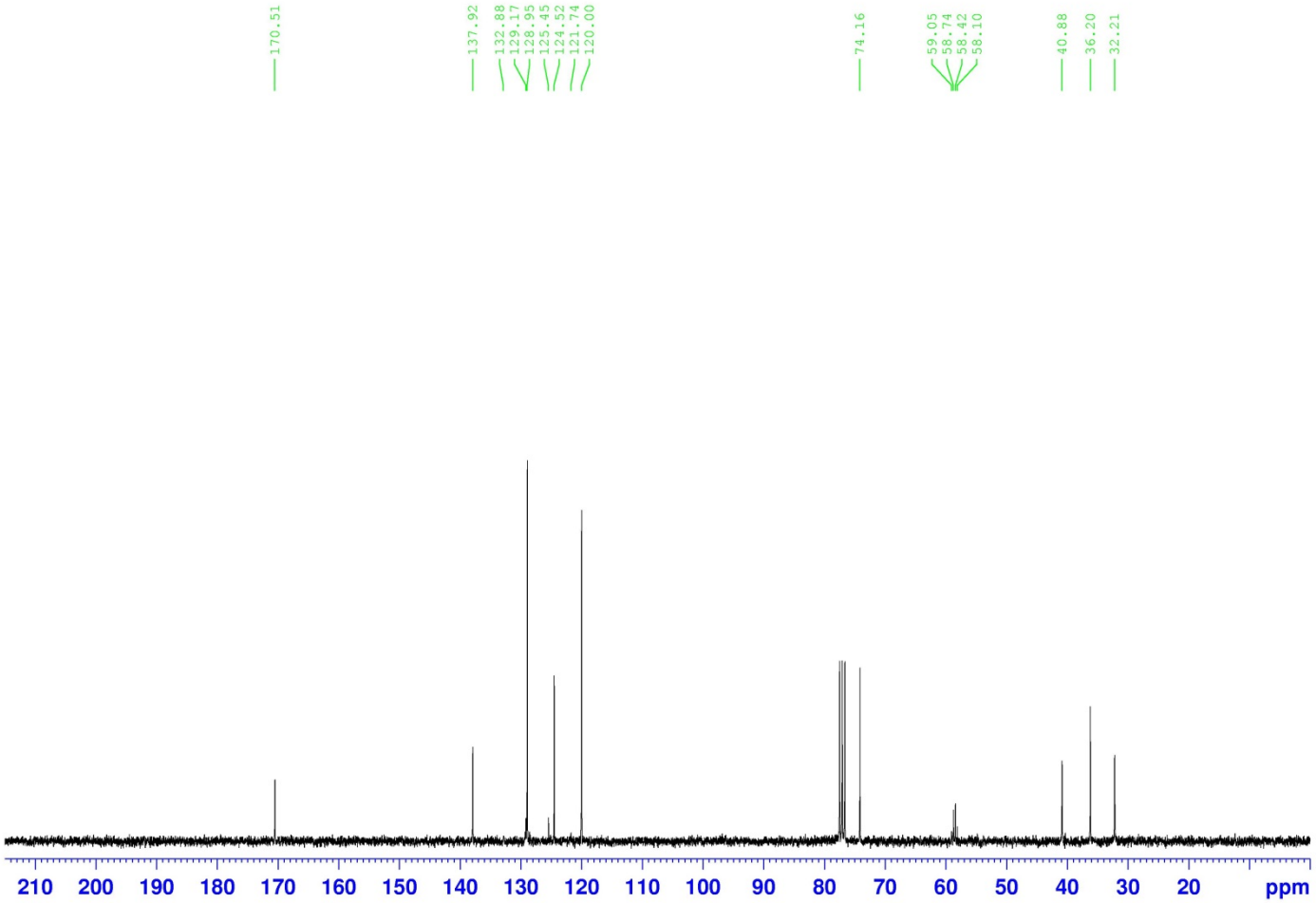
^{19}F NMR of 7d



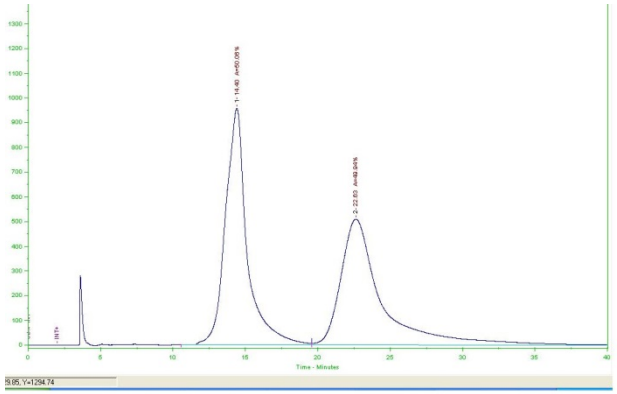
^{1}H NMR of 7d


9.532
7.504
7.479
7.321
7.296
7.268
7.138
7.114
7.089
4.646
3.883
2.424
2.025
1.910
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.98
2.06
2.09
1.03
1.00
1.00
4.04
1.09
1.07

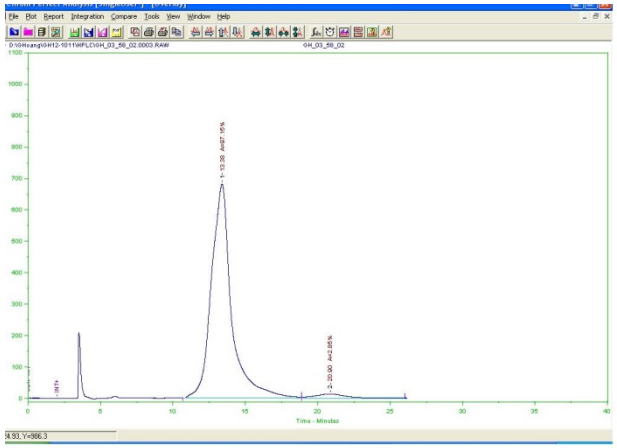
^{13}C NMR of 7d


170.51
137.92
132.88
129.17
128.95
125.45
124.52
121.74
120.00
74.16
59.05
58.74
58.42
58.10
40.88
36.20
32.21
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

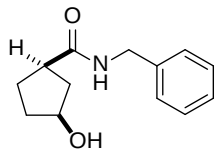
HPLC analysis of 7d



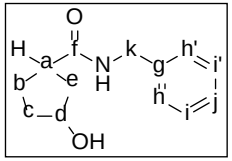
Racemic



CAHB product



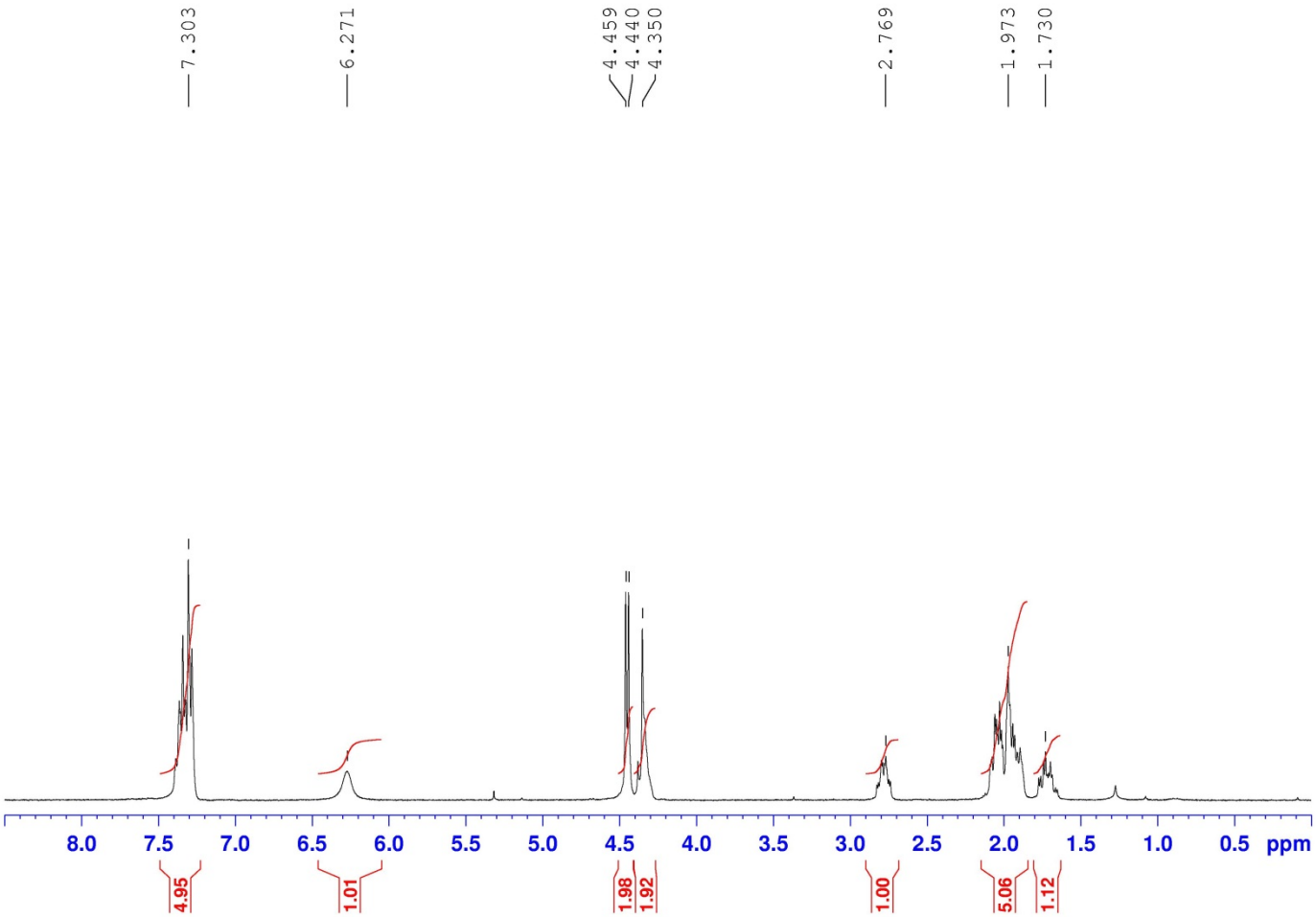
7e



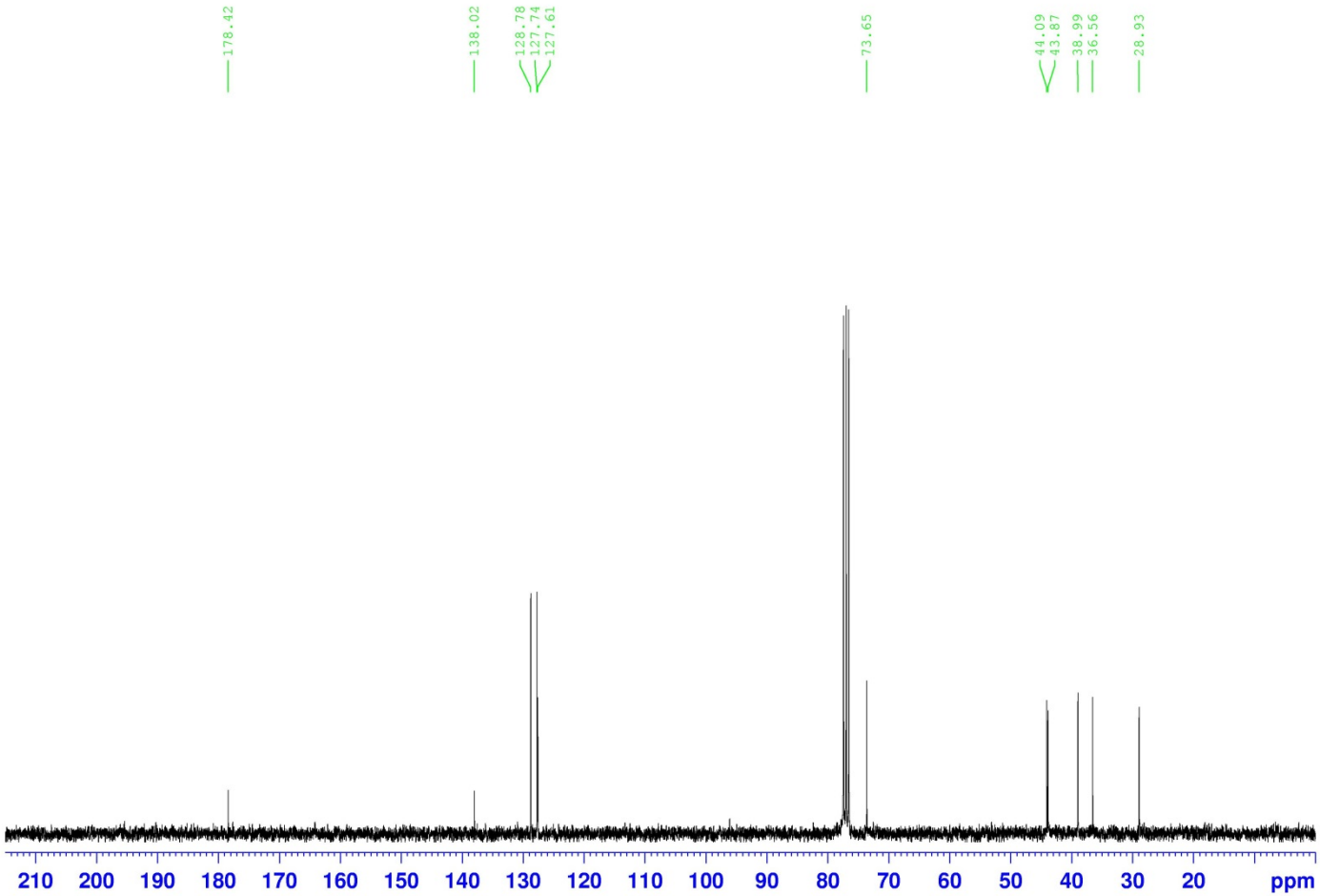
Following the general procedure for CAHB-oxidation sequence with H_2O_2 affords, after flash chromatography on silica gel (80–30:20–70 hexanes:ethyl acetate), the title compound (69%) as a white solid.

m.p.	115.5–116.0 ºC
Optical rotation	$[\alpha]_D^{20} = -12^o$ (*c* 1.4, $CHCl_3$)
HPLC analysis	Chiral HPLC analysis determined by converting to the corresponding phenyl amide **7a** using boronic acid-catalyzed transamidation.[6] Chiralpak-IC, 80:20 hexanes:isopropanol, flow rate = 1.4 mL/min, showed peaks at 40 minutes (6.0% (1*S*,3*R*)) and 45 minutes (94.0% (1*R*,3*S*)).
TLC analysis	R_f 0.3 (20:80 hexanes:ethyl acetate)
^{1}H NMR (300 MHz, $CDCl_3$)	δ 7.40–7.20 (5H, m, h,h',i,i',j), 6.27 (1H, br s, NH), 4.45 (2H, d, *J* = 5.7 Hz, k), 4.40–4.25 (2H, m, d,OH), 2.85–2.70 (1H, m, a), 2.20–1.80 (5H, m, b,c,e), 1.80–1.60 (1H, m, c).
^{13}C NMR (75 MHz, $CDCl_3$)	δ 178.42 (f), 138.02 (g), 128.78 (i,i'), 127.74 (h,h'), 127.61 (j), 73.65 (d), 44.09 (a), 43.87 (k), 38.99 (e), 36.56 (c), 28.93 (b).
IR (neat)	3259 (O-H stretch), 3085 (N-H stretch), 2937, 1634 (C=O stretch), 1573, 1551 (C=C stretch), 1233, 1001, 752, 727, 700 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{13}H_{17}NaNO_2$ (M+Na): 242.1157, found 242.1153 *m/z*.

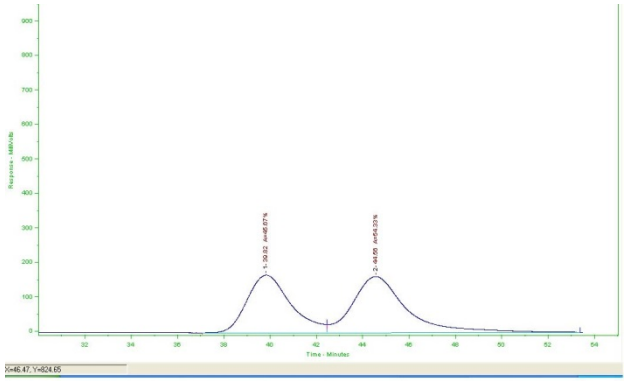
^{1}H NMR of 7e


7.303
6.271
4.459
4.440
4.350
2.769
1.973
1.730
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.95
1.01
1.98
1.92
1.00
5.06
1.12

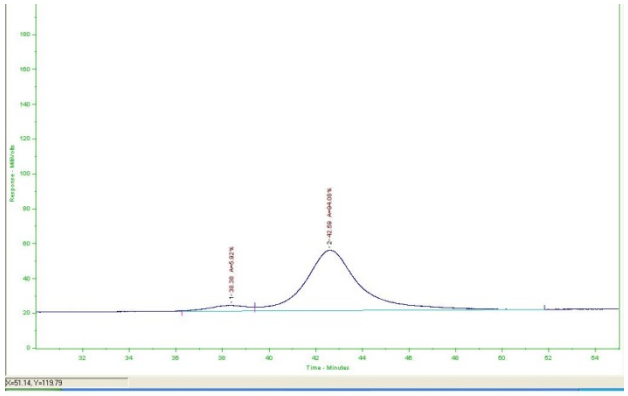
^{13}C NMR of 7e


178.42
138.02
128.78
127.74
127.61
73.65
44.09
43.87
38.99
36.56
28.93
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

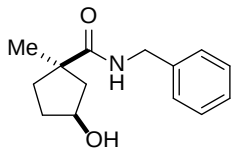
HPLC analysis of 7a (from transamidation of 7e)



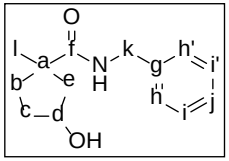
Racemic



CAHB product



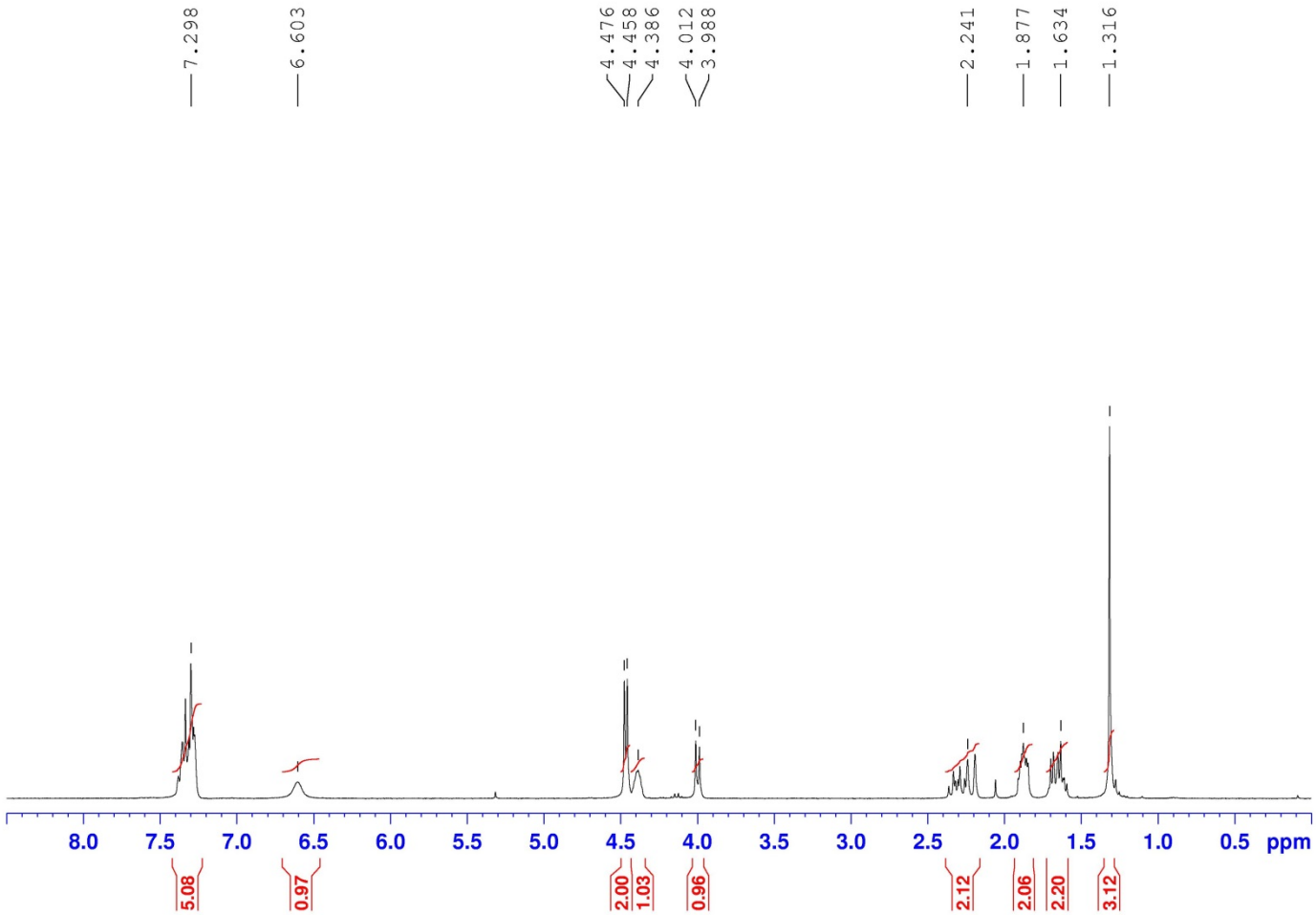
7f



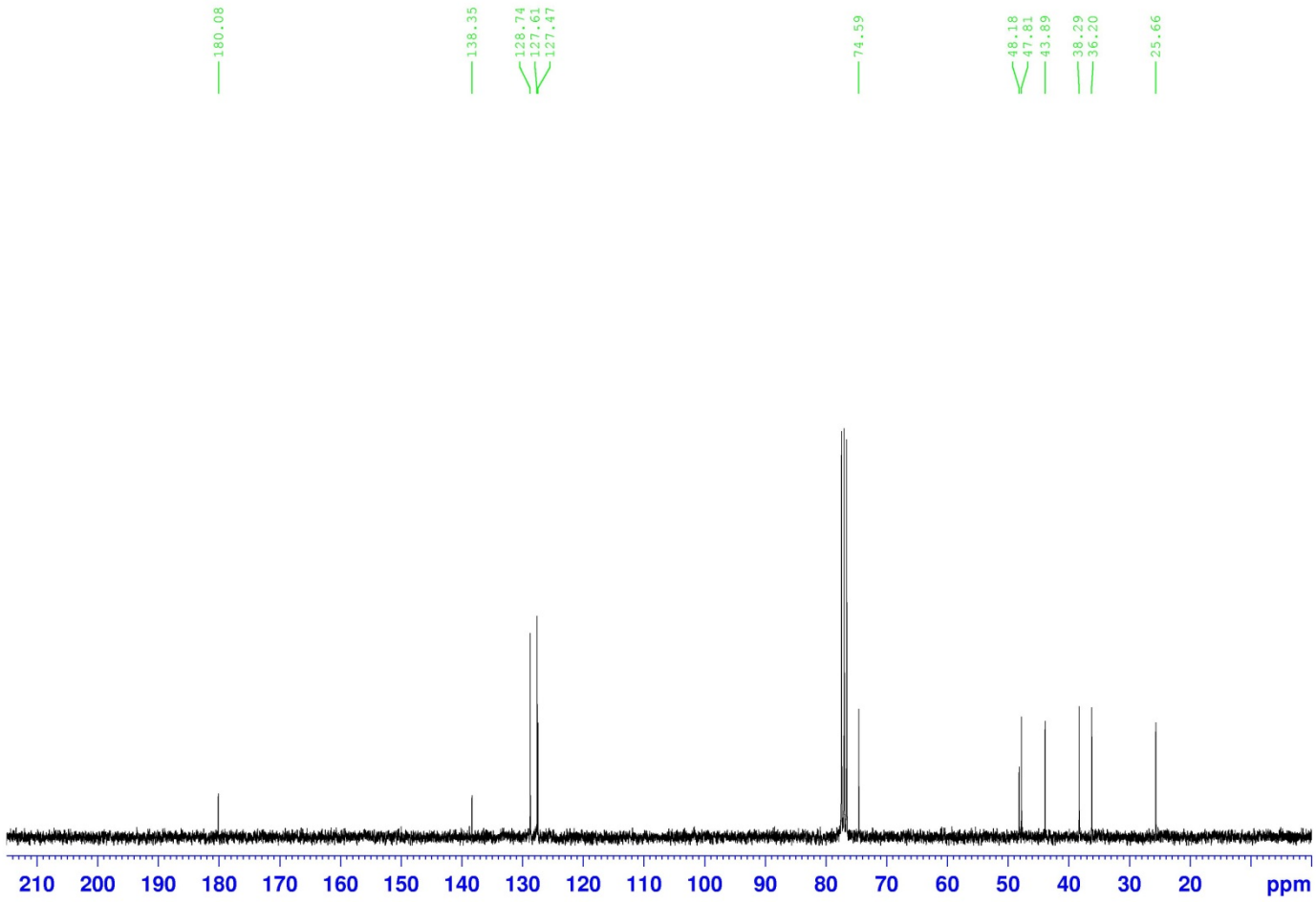
Following the general procedure for CAHB-oxidation sequence with H_2O_2 affords, after flash chromatography on silica gel (85:15 dichloromethane:ethyl acetate), the title compound (62%) as a colorless oil.

Optical rotation	$[\alpha]_D^{20} = -12^o$ (*c* 1.6, $CHCl_3$)
HPLC analysis	Chiral HPLC analysis determined by converting to the corresponding phenyl amide **7b** using boronic acid-catalyzed transamidation.[6] Chiral HPLC analysis (Chiralcel-OD, 90:10 hexanes:isopropanol, flow rate = 1.3 mL/min) showed peaks at 87 minutes (92.0% (1*R*,3*S*)) and 105 minutes (8.0% (1*S*,3*R*)).
TLC analysis	R_f 0.4 (80:20 dichloromethane:ethyl acetate)
^{1}H NMR (300 MHz, $CDCl_3$)	δ 7.40–7.20 (5H, m, h,h',i,i',j), 6.60 (1H, br s, NH), 4.47 (2H, d, *J* = 5.6 Hz, k), 4.45–4.35 (1H, m, d), 4.00 (1H, d, *J* = 7.2 Hz, OH), 2.40–2.15 (2H, m, b,e), 1.95–1.80 (2H, m, c), 1.75–1.60 (2H, m, b,e), 1.32 (3H, s, l).
^{13}C NMR (75 MHz, $CDCl_3$)	δ 180.08 (f), 138.35 (g), 128.74 (i,i'), 127.61 (j), 127.47 (h,h'), 74.59 (d), 48.18 (e), 47.81 (a), 43.89 (k), 38.29 (b), 36.21 (c), 25.66 (l).
IR (neat)	3299 (O-H stretch, N-H stretch), 2958, 1636 (C=O stretch), 1535 (C-=C stretch), 1453 (C-OH bend), 1227, 1190, 961, 721, 696 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{14}H_{19}NaNO_2$ (M+Na): 256.1313, found 256.1325 *m/z*.

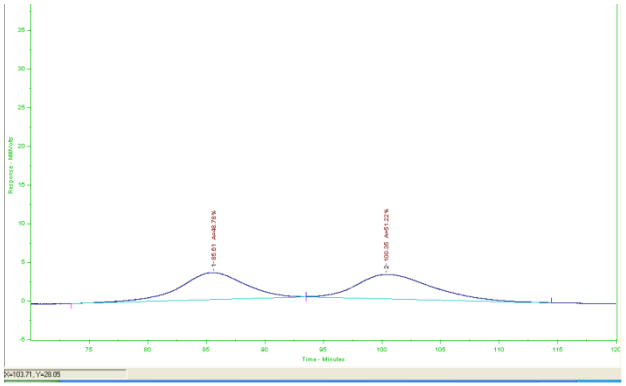
^{1}H NMR of 7f


7.298
6.603
4.476
4.458
4.386
4.012
3.988
2.241
1.877
1.634
1.316
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
5.08
0.97
2.00
1.03
0.96
2.12
2.06
2.20
3.12

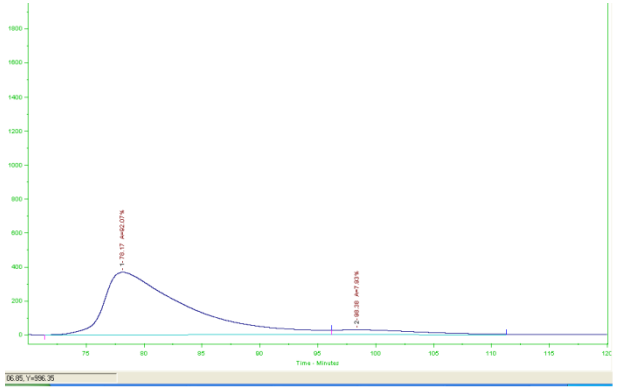
^{13}C NMR of 7f


180.08
138.35
128.74
127.61
127.47
74.59
48.18
47.81
43.89
38.29
36.20
25.66
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

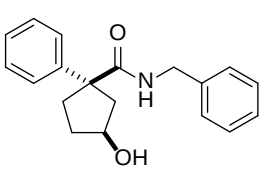
HPLC analysis of 7b (from transamidation of 7f)



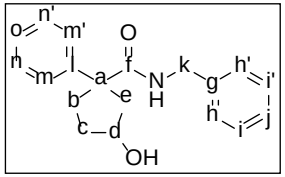
Racemic



CAHB product



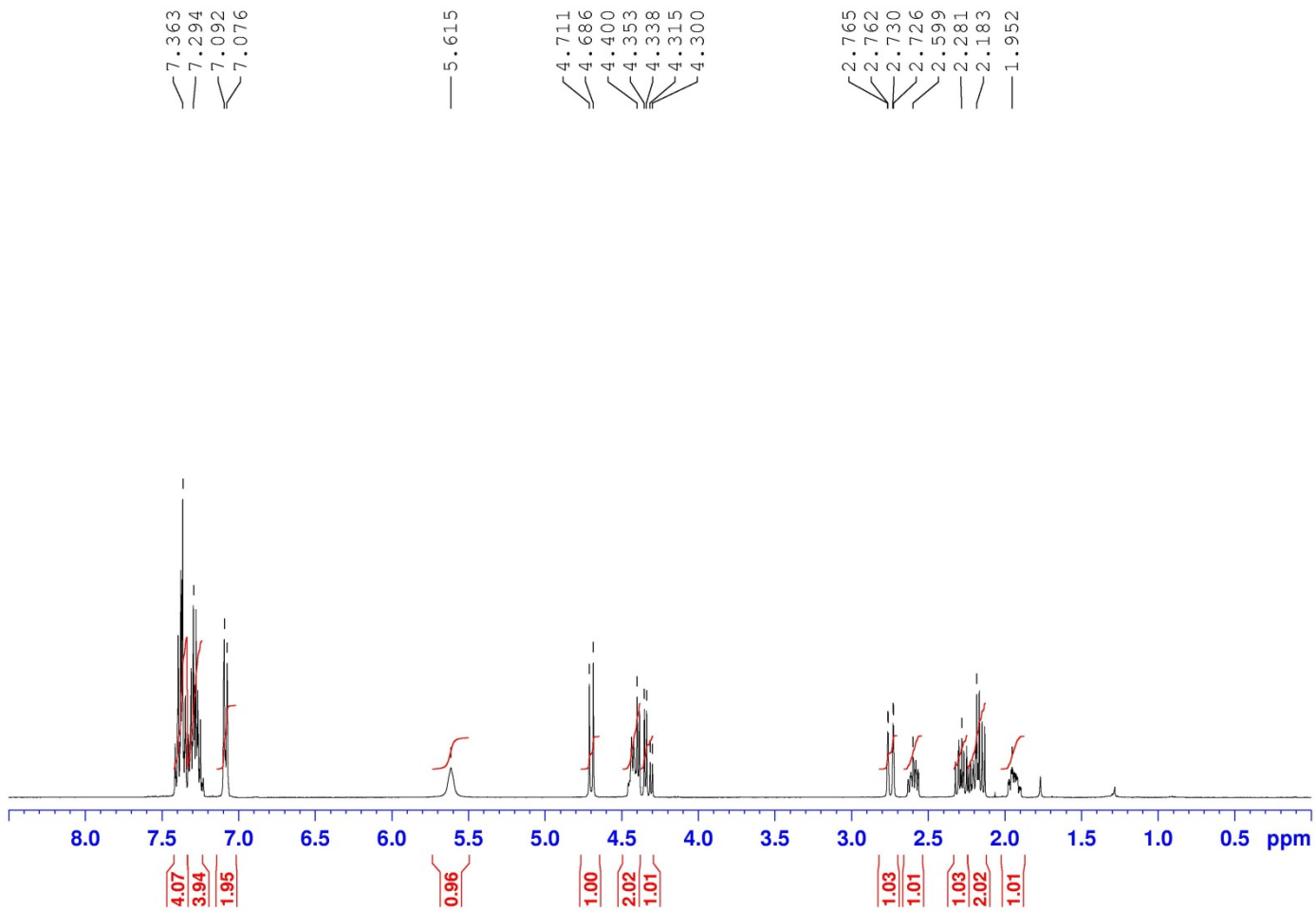
7g



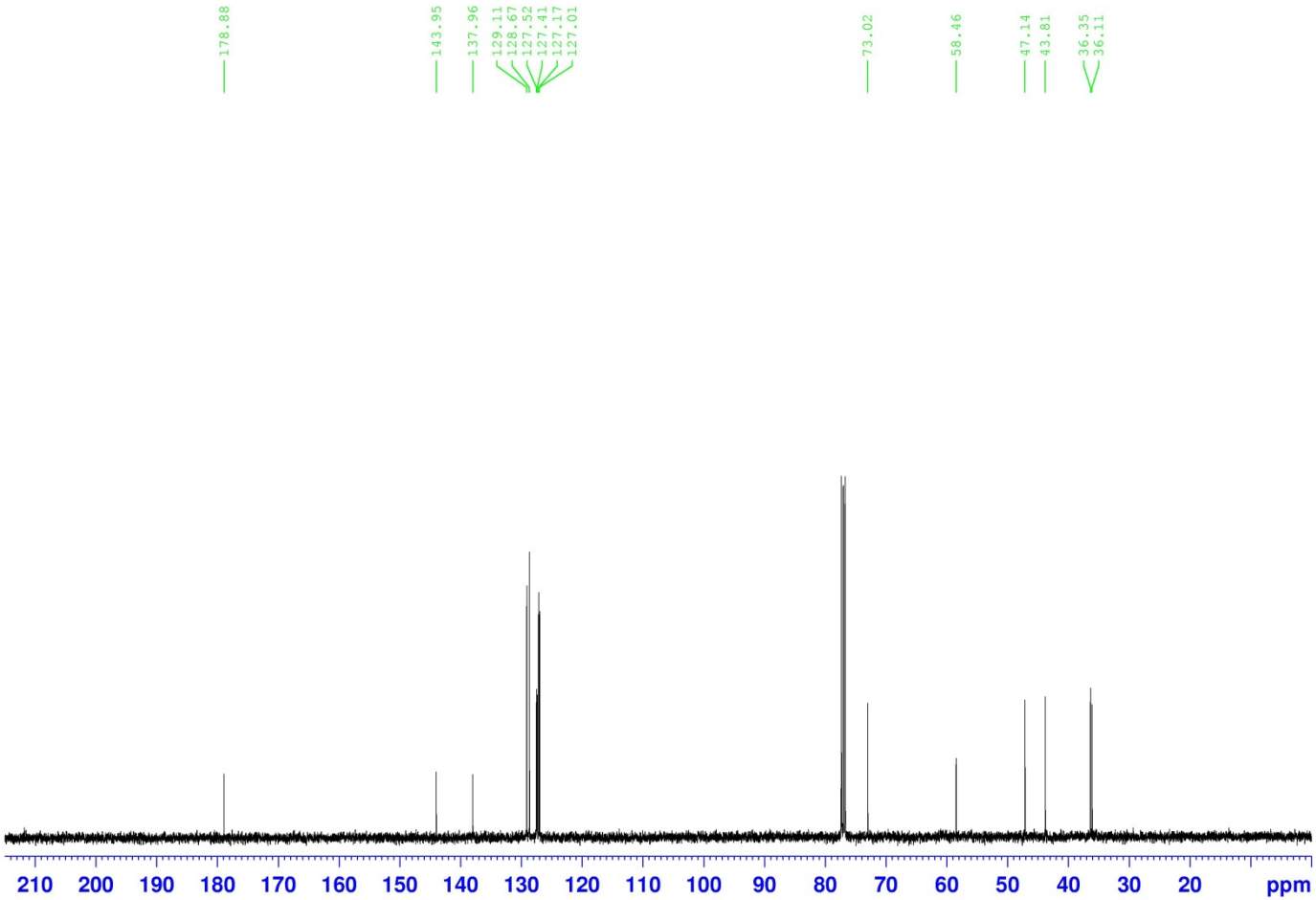
Following the general procedure for CAHB-oxidation sequence with H_2O_2 affords, after flash chromatography on silica gel (85:15 dichloromethane:ethyl acetate), the title compound (70%) as a white solid.

m.p.	91.0–93.5 °C
Optical rotation	$[\alpha]_D^{20} = -45^o$ (*c* 1.3, $CHCl_3$).
HPLC analysis	Chiralpak-AD, 70:30 hexanes:isopropanol, flowrate = 1.0 mL/min, showed peaks at 15 minutes (93.0% (1*R*,3*S*)) and 20 minutes (7.0% (1*S*,3*R*)).
TLC analysis	R_f 0.4 (80:20 dichloromethane:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 7.45–7.30 (4H, m, i,i',n,n'), 7.35–7.25 (4H, m, h,h',j,o), 7.08 (2H, d, *J* = 6.5 Hz, m,m'), 5.61 (2H, br s, NH), 4.70 (1H, d, *J* = 10.1 Hz, OH), 4.45–4.35 (2H, m, d,k), 4.33 (1H, dd, *J* = 15.2 and 5.8 Hz, k), 2.75 (1H, dd, *J* = 14.1 and 1.3 Hz, e), 2.65–2.55 (1H, m, b), 2.35–2.25 (1H, m, b), 2.25–2.10 (1H, m, c,e), 2.00–1.90 (1H, m, c).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 178.88 (f), 143.95 (l), 137.96 (g), 129.11 (i,i'), 128.67 (n,n'), 127.52 (h,h'), 127.41 (j), 127.17 (o), 127.01 (m,m'), 73.02 (d), 58.46 (a), 47.14 (e), 43.81 (k), 36.35 (b), 36.11 (c).
IR (neat)	3316 (O-H stretch, N-H stretch), 1638 (C=O stretch), 1532 (C-OH bend), 1494, 1450, 1282, 1062, 1027, 992, 743, 719, 697, 662 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{19}H_{21}NaNO_2$ (M+Na): 318.1470, found 318.1456 *m/z*.

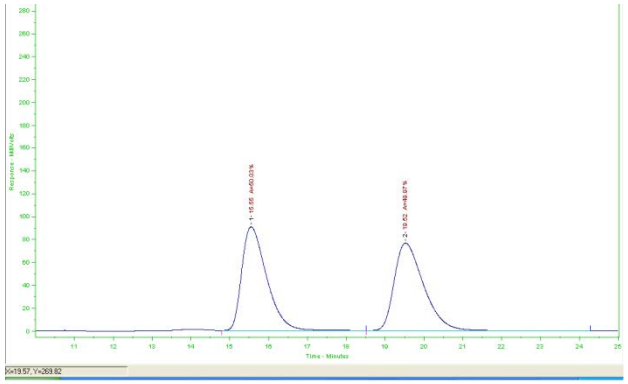
^{1}H NMR of 7g


7.363
7.294
7.092
7.076
5.615
4.711
4.686
4.400
4.353
4.338
4.315
4.300
2.765
2.762
2.730
2.726
2.599
2.281
2.183
1.952
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.07
3.94
1.95
0.96
1.00
2.02
1.01
1.03
1.01
1.03
2.02
1.01

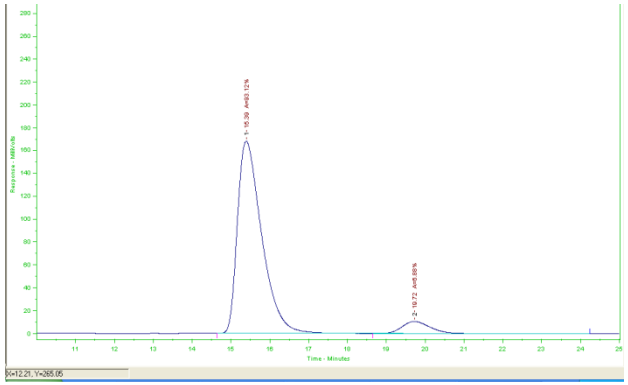
^{13}C NMR of 7g


178.88
143.95
137.96
129.11
128.67
127.52
127.41
127.17
127.01
73.02
58.46
47.14
43.81
36.35
36.11
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

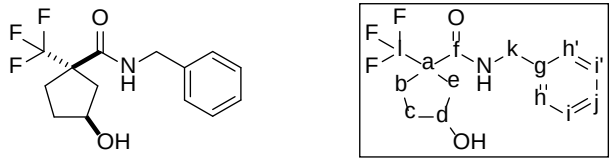
HPLC analysis of 7g



Racemic



CAHB product

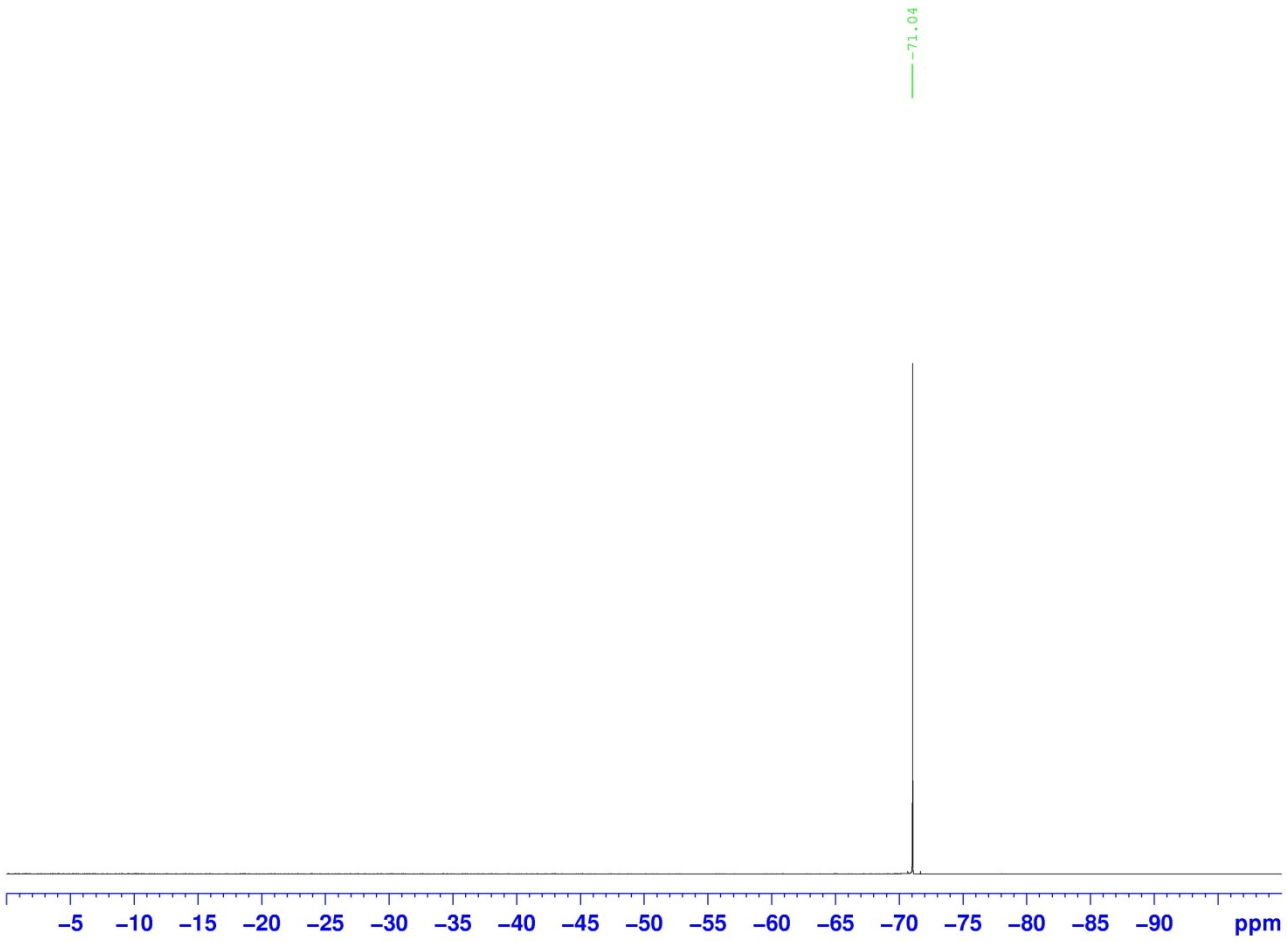


7h

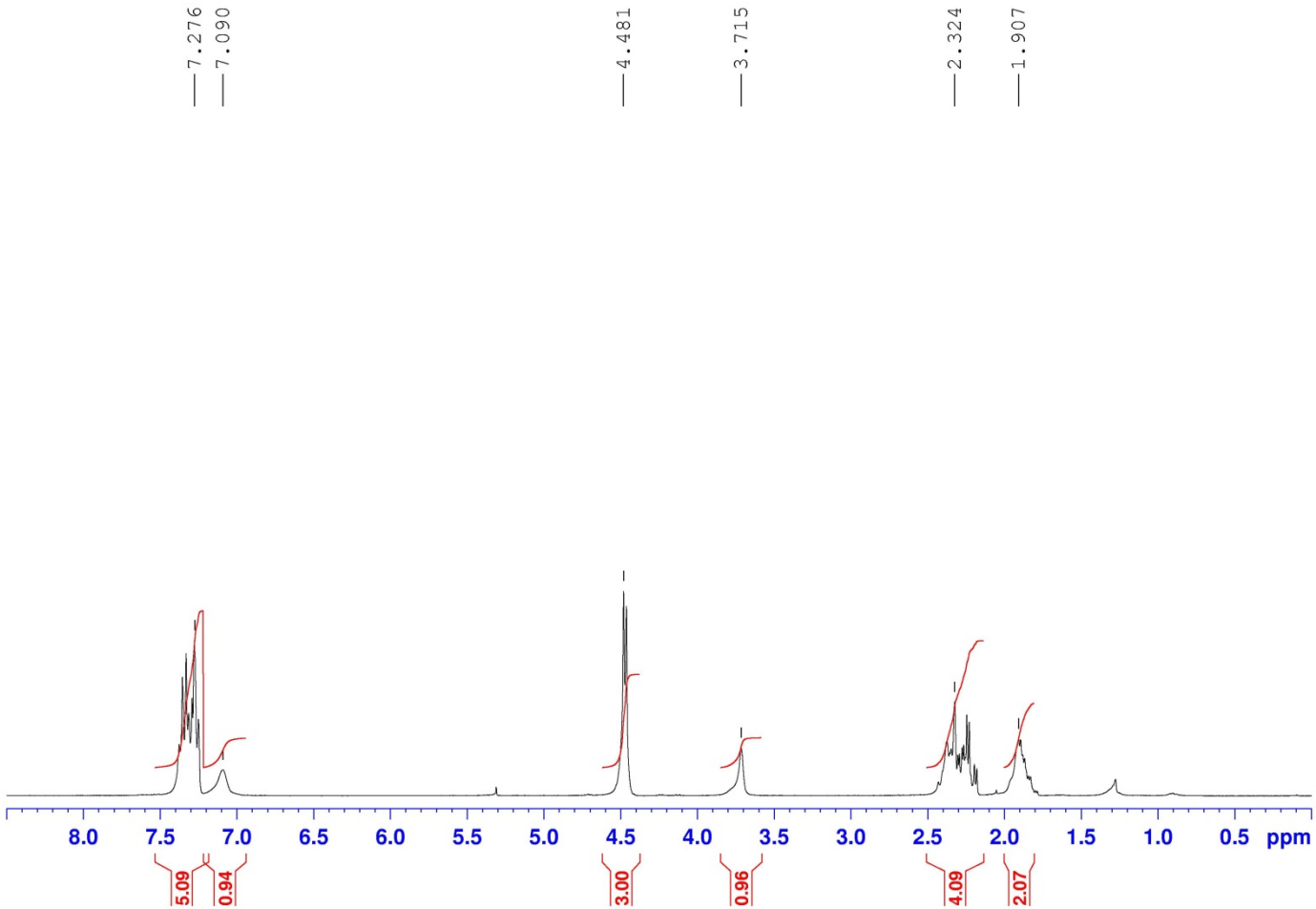
Following the general procedure for CAHB-oxidation sequence with H_2O_2 affords, after flash chromatography on silica gel (85:15 dichloromethane:ethyl acetate), the title compound (71%) as a white solid.

m.p.	100.5–102.0 ºC
Optical rotation	$[\alpha]_D^{20} = -16^o$ (*c* 1.3, $CHCl_3$)
HPLC analysis	Chiralcel-OD, 70:30 hexanes:isopropanol, flowrate = 1.0 mL/min, showed peaks at 12 minutes (3.5% (1*R*,3*R*)) and 18 minutes (96.5% (1*S*,3*S*)).
TLC analysis	R_f 0.5 (80:20 dichloromethane:ethyl acetate)
^{19}F NMR (282 MHz, $CDCl_3$)	δ -71.04 (s, CF_3).
^{1}H NMR (300 MHz, $CDCl_3$)	δ 7.45–7.20 (5H, m, h,h',i,i',j), 7.09 (1H, br s, NH), 4.60–4.40 (3H, m, d,k), 3.71 (1H, br s, OH), 2.50–2.15 (4H, m, b,e), 2.20–1.80 (2H, m, c).
^{13}C NMR (75 MHz, $CDCl_3$)	δ 171.70 (f), 137.58 (g), 129.29 (l), 128.80 (i,i'), 127.62 (j), 127.44 (h,h'), 73.57 (d), 57.96 (q, *J* = 24.5 Hz, a), 44.04 (k), 40.74 (e), 36.18 (c), 31.70 (b).
IR (neat)	3421 (O-H stretch), 3311 (N-H stretch), 3269, 3084, 2944, 2360, 1657 (C=O stretch), 1526 (C-OH bend), 1455, 1362, 1301 (C-N stretch), 1169, 1123, 746, 696, 648 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{14}H_{16}F_3NaNO_2$ (M+Na): 310.1031, found 310.1026 *m/z*.

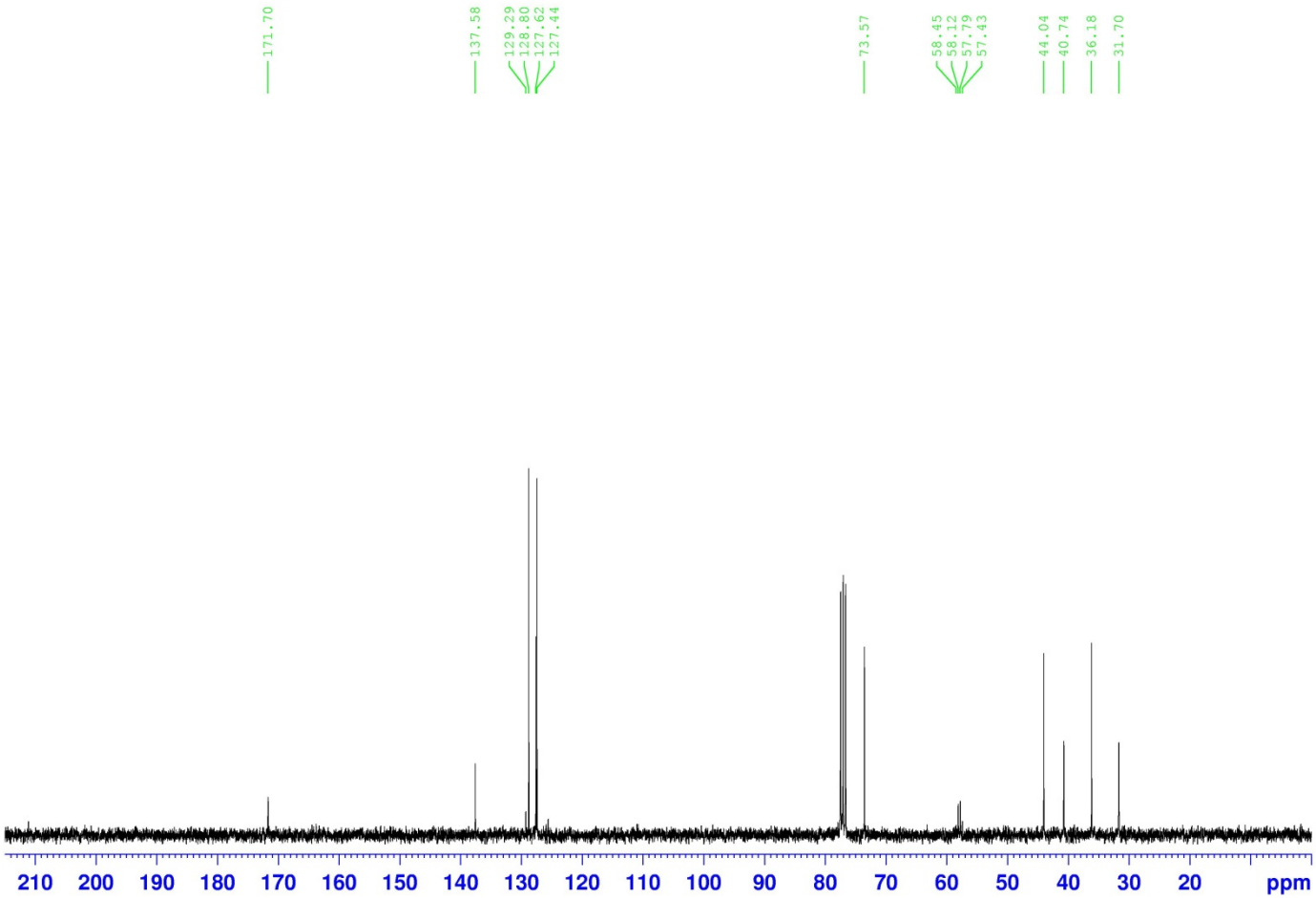
^{19}F NMR of 7h



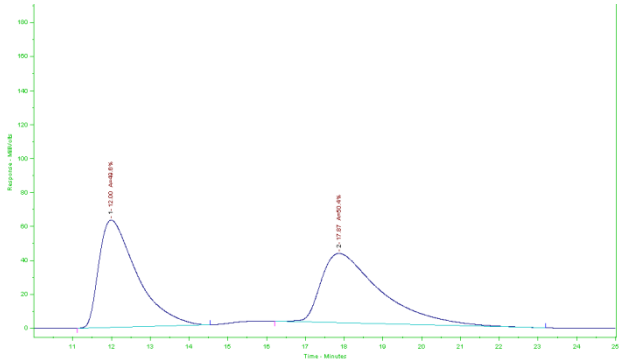
^{1}H NMR of 7h


7.276
7.090
4.481
3.715
2.324
1.907
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
5.09
0.94
3.00
0.96
4.09
2.07

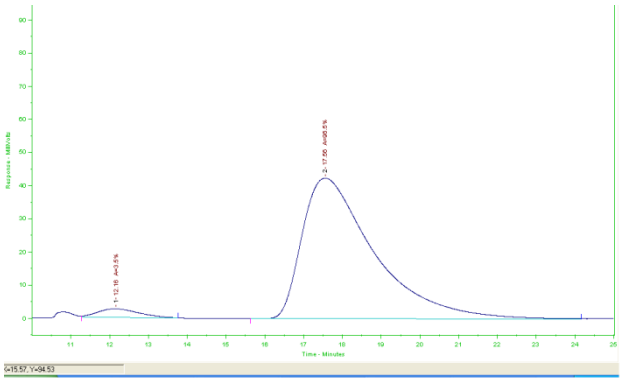
^{13}C NMR of 7h


171.70
137.58
129.29
128.80
127.62
127.44
73.57
58.45
58.12
57.79
57.43
44.04
40.74
36.18
31.70
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
ppm

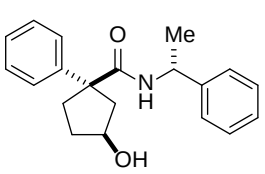
HPLC analysis of 7h



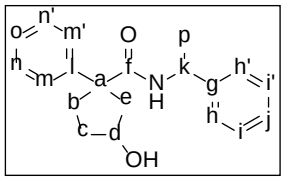
Racemic



CAHB product



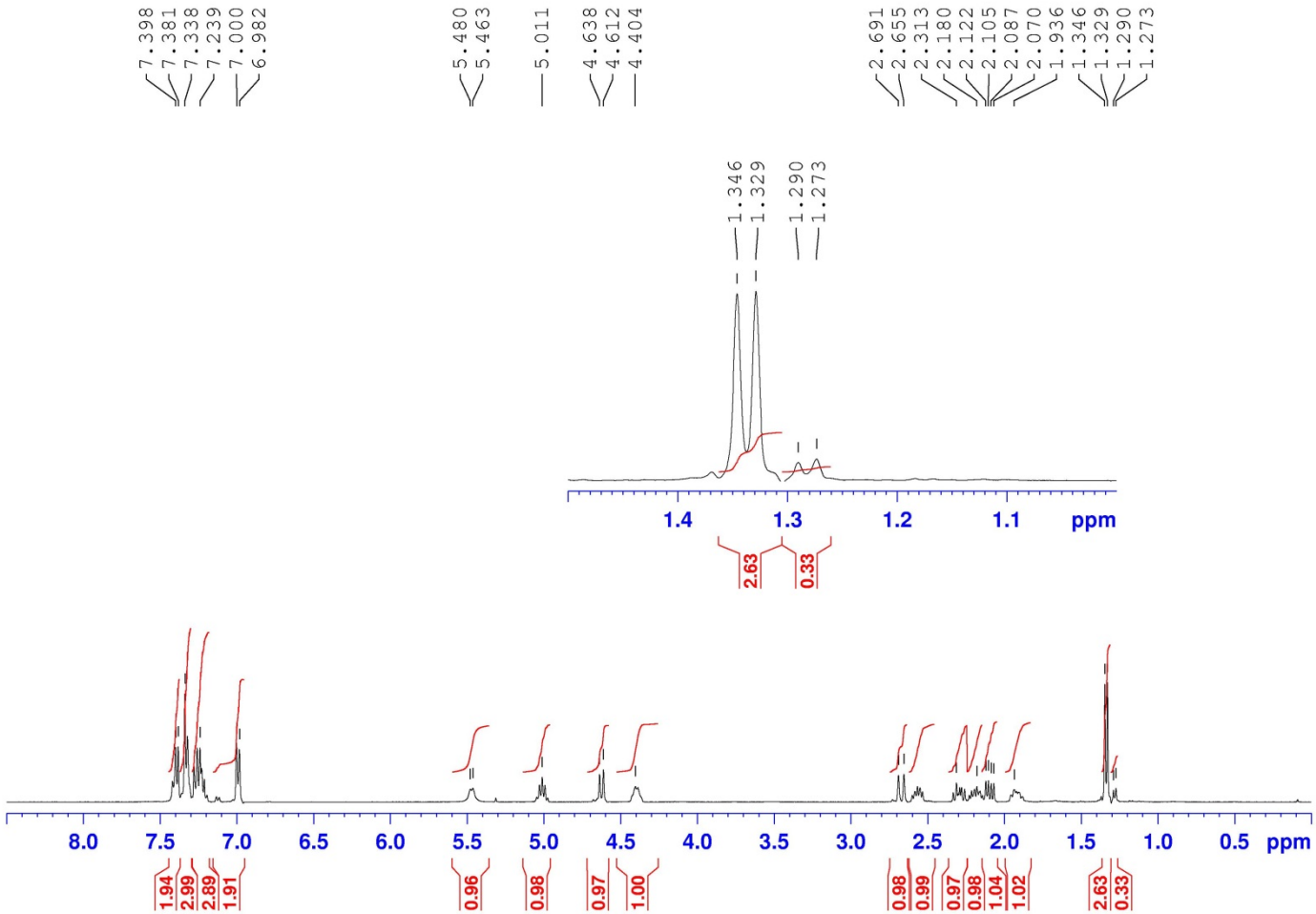
7i



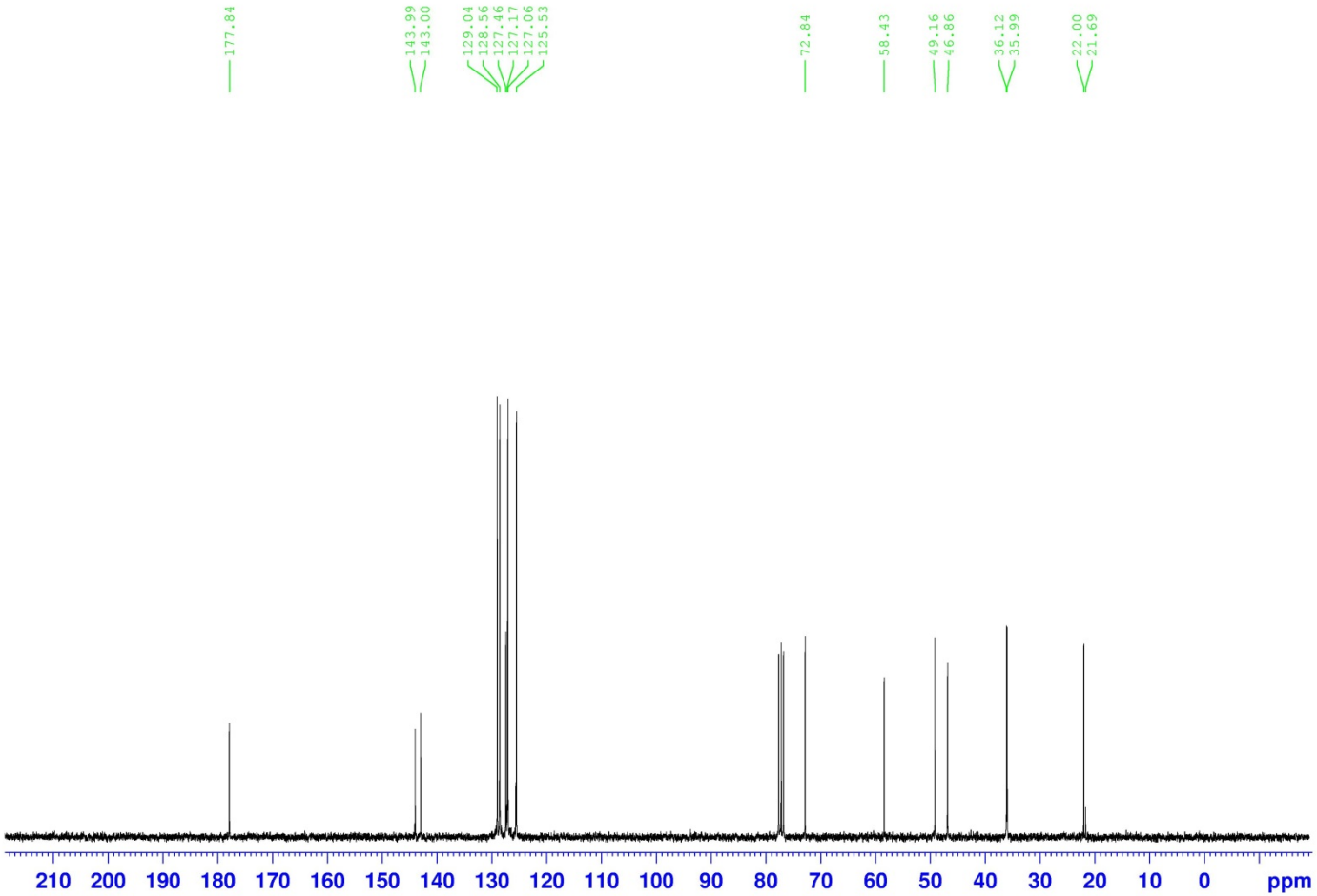
Following the general procedure for CAHB-oxidation sequence with H_2O_2 affords, after flash chromatography on silica gel (85:15 dichloromethane:ethyl acetate), the title compound (76%) as a white solid.

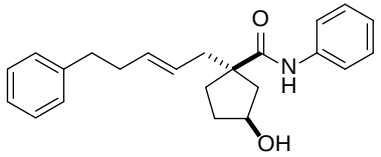
m.p.	98.5–99.5 °C
Optical rotation	$[\alpha]_D^{20} = -80^o$ (*c* 1.3, $CHCl_3$).
TLC analysis	R_f 0.5 (80:20 dichloromethane:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 7.45–7.35 (2H, m, i,i'), 7.35–7.30 (3H, m, j,n,n'), 7.30–7.20 (3H, m, h,h',o), 6.99 (2H, d, *J* = 7.3 Hz, m,m'), 5.47 (1H, d, *J* = 6.9 Hz, NH), 5.05–4.95 (1H, m, k), 4.62 (1H, d, *J* = 10.0 Hz, OH), 4.45–4.35 (1H, m, d), 2.67 (1H, d, *J* = 14.2 Hz, e), 2.60–2.50 (1H, m, b), 2.35–2.25 (1H, m, b), 2.25–2.15 (1H, m, c), 2.10 (1H, d, *J* = 14.1 Hz and 6.8 Hz, e), 2.20–1.85 (1H, m, c), 1.34 (2.63H, d, *J* = 6.9 Hz, p major), 1.28 (0.33H, d, *J* = 6.7 Hz, p minor); the peaks at 1.34 and 1.28 ppm are used to determined the diastereoselectivity (88:12 major:minor).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 177.84 (f), 143.99 (l), 143.00 (g), 129.04 (i,i'), 128.56 (n,n'), 127.46 (h,h'), 127.17 (j), 127.06 (o), 125.53 (m,m'), 72.84 (d), 58.43 (a), 49.16 (k), 46.86 (e), 36.12 (b), 35.99 (c), 22.00 (p, major), 21.69 (p, minor).
IR (neat)	3368 (O-H stretch, N-H stretch), 1633 (C=O stretch), 1540 (C-=C stretch), 1493, 1445, 1096, 760, 736, 695 cm^{-1}.
HRMS (ESI)	$C_{20}H_{23}NaNO_2$ (M+Na): 332.1626, found 332.1619 *m/z*.

^{1}H NMR of 7i

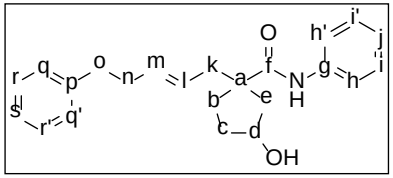

7.398
7.381
7.338
7.239
7.000
6.982
5.480
5.463
5.011
4.638
4.612
4.404
2.691
2.655
2.313
2.180
2.122
2.105
2.087
2.070
1.936
1.346
1.329
1.290
1.273
1.346
1.329
1.290
1.273
1.4
1.3
1.2
1.1
ppm
2.63
0.33
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.94
2.99
2.89
1.91
0.96
0.98
0.97
1.00
0.98
0.99
0.97
0.98
1.04
1.02
2.63
0.33

^{13}C NMR of 7i


177.84
143.99
143.00
129.04
128.56
127.46
127.17
127.06
125.53
72.84
58.43
49.16
46.86
36.12
35.99
22.00
21.69
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm



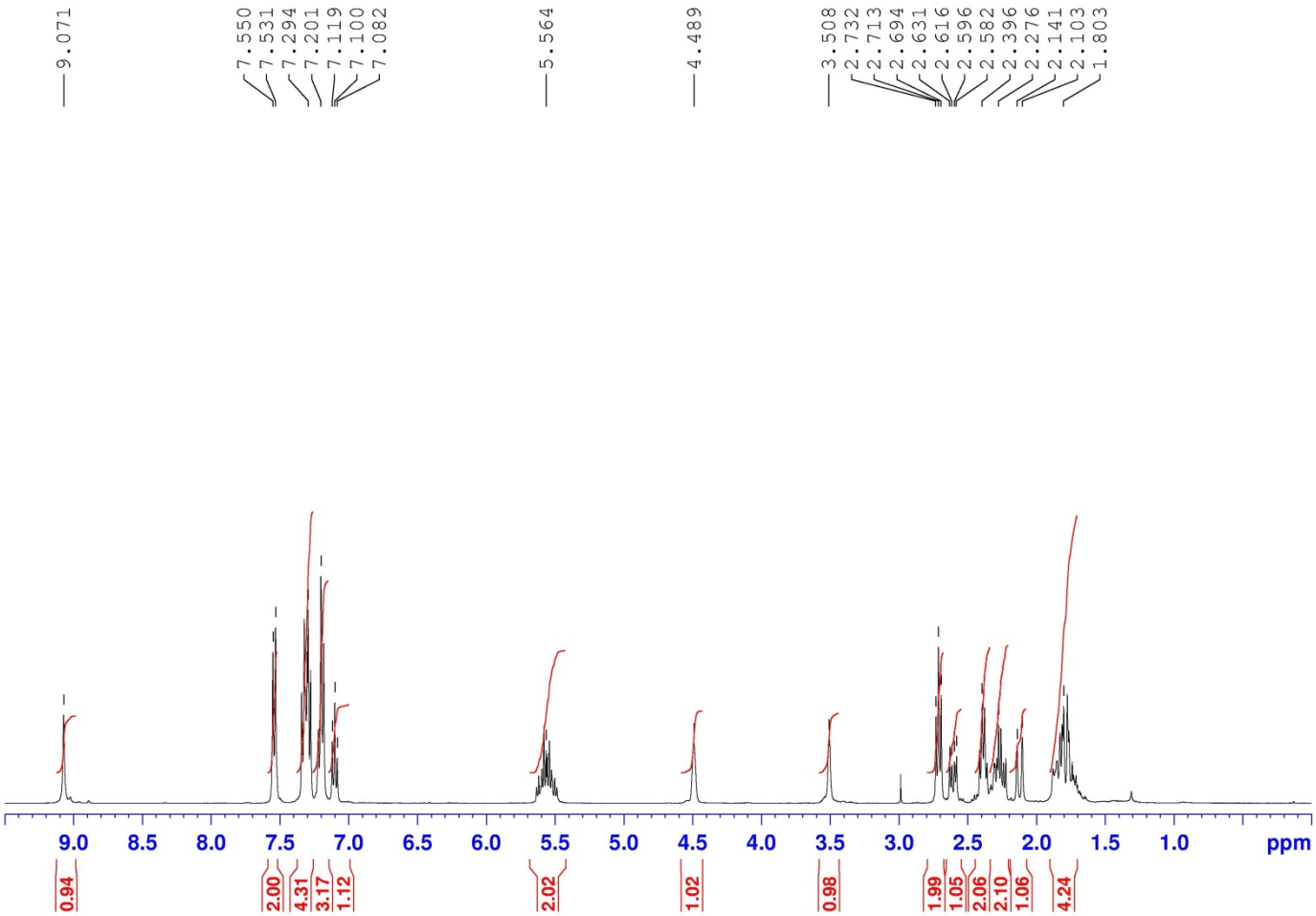
7k



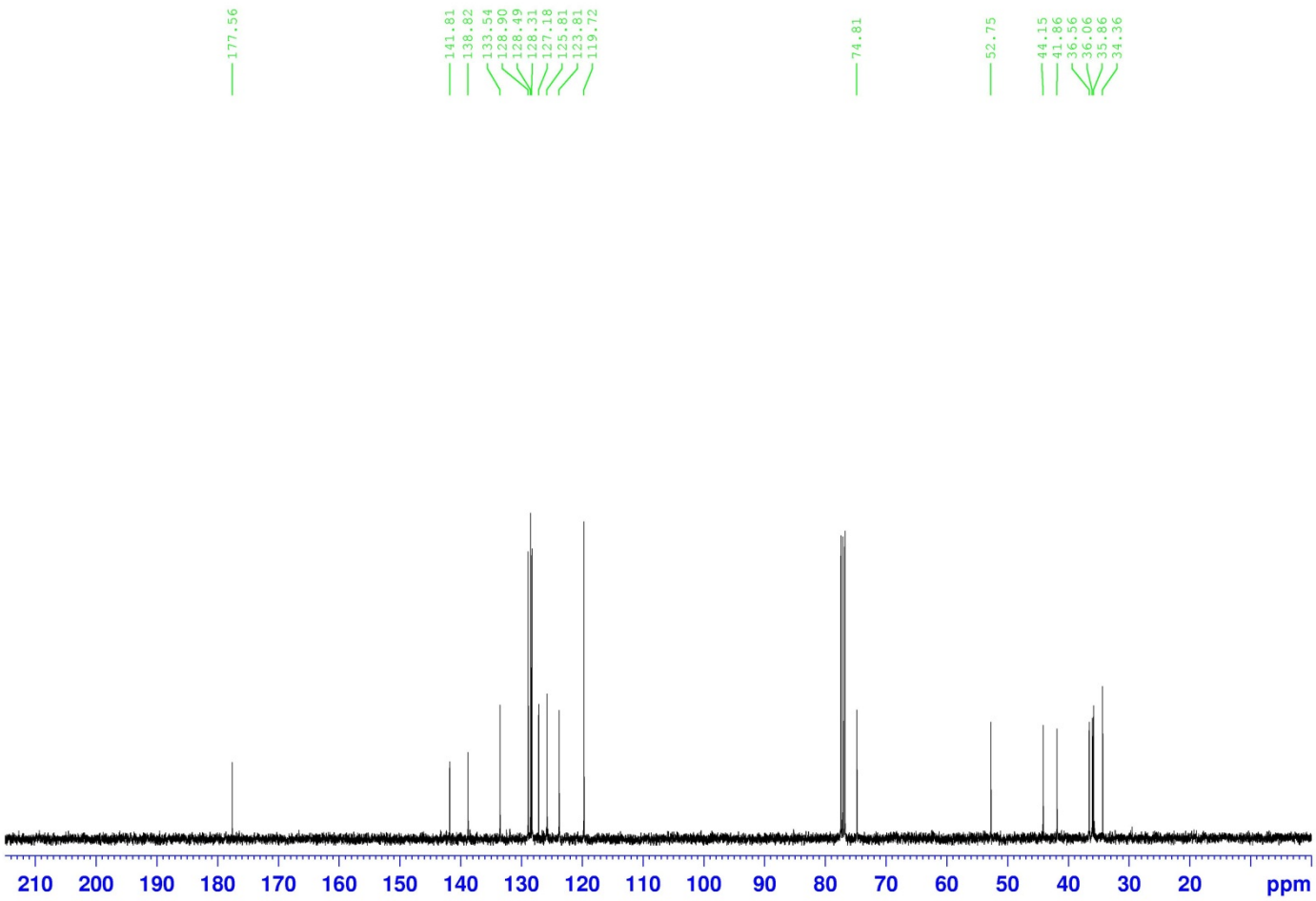
Following the general procedure for CAHB-oxidation sequence with H_2O_2 affords, after flash chromatography on silica gel (90:10 dichloromethane:ethyl acetate), the title compound (80%) as a light yellow oil.

Optical rotation	$[\alpha]_D^{20} = +17^o$ (*c* 1.8, $CHCl_3$)
HPLC analysis	Chiralpak-ASH with OD guard column, 70:30 hexanes:isopropanol, flowrate = 1.0 mL/min, showed peaks at 15 minutes (99.0% (1*S*,3*S*)) and 20 minutes (1.0% (1*R*,3*R*)).
TLC analysis	R_f 0.75 (80:20 dichloromethane:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 9.07 (1H, br s, NH), 7.54 (2H, d, *J* = 7.6 Hz, h,h'), 7.35–7.25 (4H, m, i,i',r,r'), 7.25–7.15 (3H, m, j,q,q'), 7.10 (1H, t, *J* = 7.4 Hz, s), 5.65–5.50 (2H, m, l,m), 4.55–4.45 (1H, m, d), 3.51 (1H, br s, OH), 2.71 (2H, t, *J* = 7.3 Hz, o), 2.61 (1H, dd, *J* = 13.9 Hz and 6.1 Hz, k), 2.45–2.35 (2H, m, b), 2.35–2.20 (2H, m, k,n), 2.12 (1H, d, *J* = 15.0 Hz, e), 1.90–1.70 (4H, m, c,e,n).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 177.56 (f), 141.81 (p), 138.82 (g), 133.54 (m), 128.90 (i,i'), 128.49 (r,r'), 128.31 (j), 127.18 (l), 125.81 (q,q'), 123.81(s), 119.72 (h,h'), 74.81 (d), 52.75 (a), 44.15 (e), 41.86 (k), 36.56 (n), 36.06 (c), 35.86 (o), 34.36 (b).
IR (neat)	3296 (O-H stretch), 2935 (N-H stretch), 1660 (C=O stretch), 1597 (C-=C stretch), 1555 (C-OH bend), 1497, 1442, 1333, 1308 (C-N stretch), 1254, 960, 907, 752, 692 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{23}H_{27}NaNO_2$ (M+Na): 372.1939, found 372.1939 *m/z*.

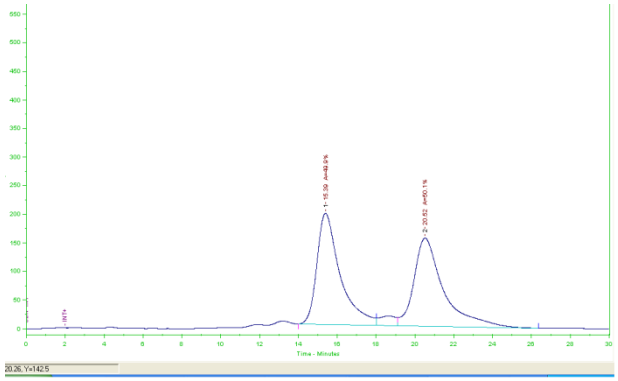
^{1}H NMR of 7k


9.071
7.550
7.531
7.294
7.201
7.119
7.100
7.082
5.564
4.489
3.508
2.732
2.713
2.694
2.631
2.616
2.596
2.582
2.396
2.276
2.141
2.103
1.803
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.94
2.00
4.31
3.17
1.12
2.02
1.02
0.98
1.99
1.05
2.06
2.10
1.06
4.24

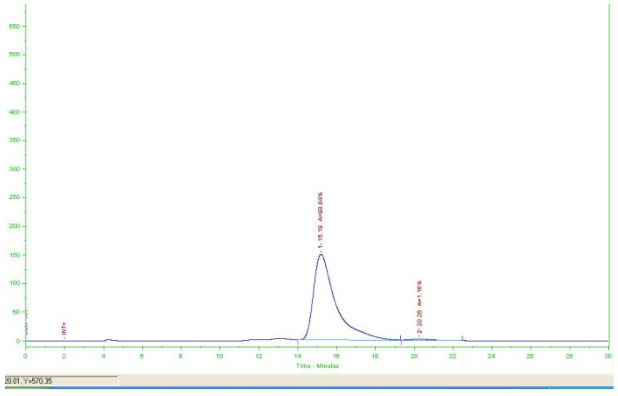
^{13}C NMR of 7k


177.56
141.81
138.82
133.54
128.90
128.49
128.31
127.18
125.81
123.81
119.72
74.81
52.75
44.15
41.86
36.56
36.06
35.86
34.36
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

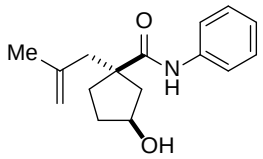
HPLC analysis of 7k



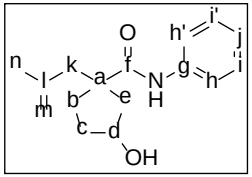
Racemic



CAHB product



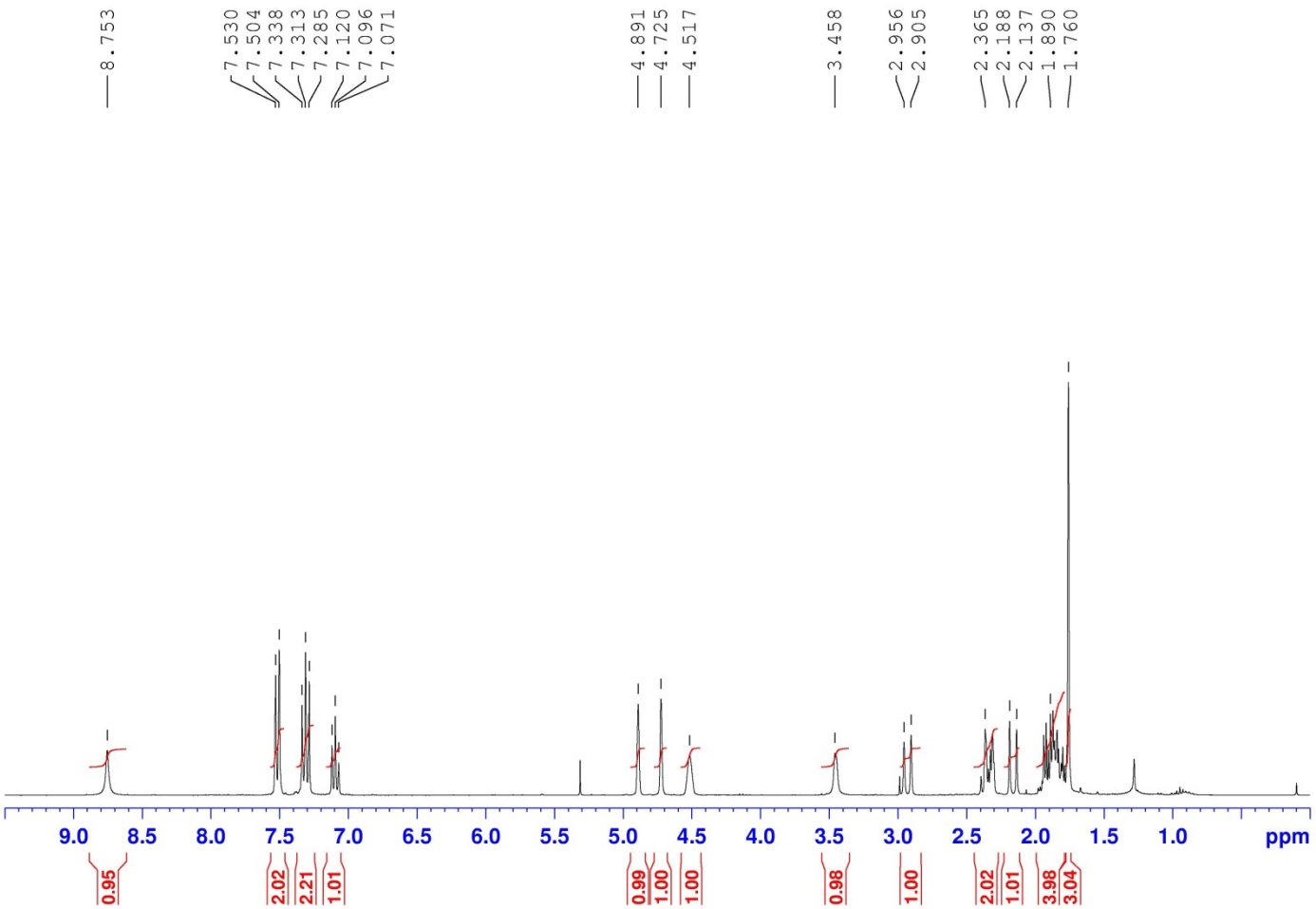
7l



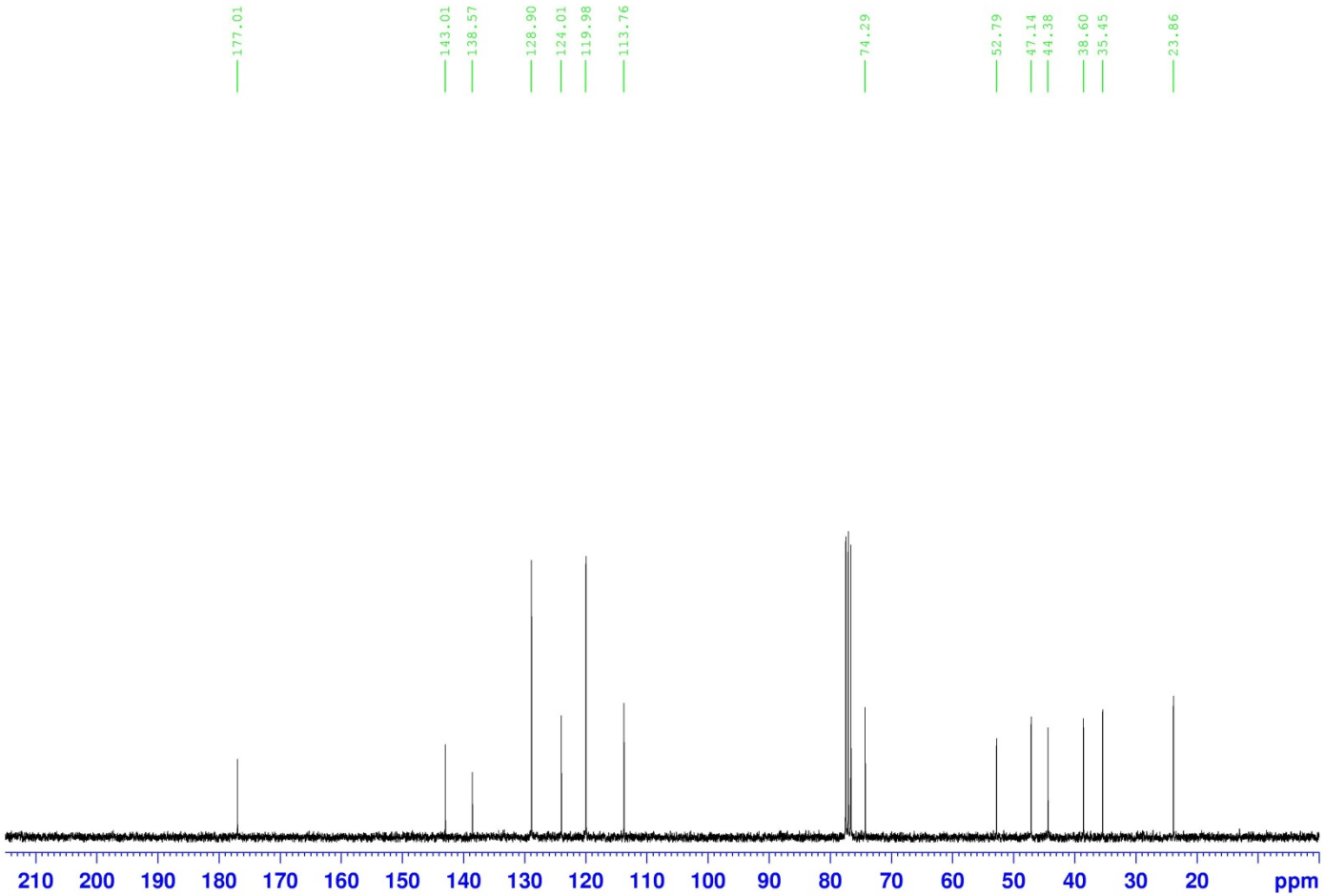
Following the general procedure for CAHB-oxidation sequence with H_2O_2 affords, after flash chromatography on silica gel (90:10 dichloromethane:ethyl acetate), the title compound (75%) as a white solid.

m.p.	76.5–78.5 ºC
Optical rotation	$[\alpha]_D^{20} = +10^o$ (*c* 1.7, $CHCl_3$)
HPLC analysis	Chiralpak-AD, 80:20 hexanes:isopropanol, flowrate = 1.0 mL/min, showed peaks at 16 minutes (97.0% (1*S*,3*S*)) and 21 minutes (3.0% (1*R*,3*R*)).
TLC analysis	R_f 0.6 (80:20 dichloromethane:ethyl acetate)
^{1}H NMR (300 MHz, $CDCl_3$)	δ 8.75 (1H, br s, NH), 7.52 (2H, d, *J* = 7.6 Hz, h,h'), 7.31 (2H, t, *J* = 7.6 Hz, i,i'), 7.10 (1H, t, *J* = 7.4 Hz, j), 4.89 (1H, s, m), 4.72 (1H, s, m), 4.55–4.45 (1H, m, d), 3.46 (1H, br s, OH), 2.93 (1H, d, *J* = 15.4 Hz, k), 2.40–2.30 (2H, m, b,e), 2.16 (1H, d, *J* = 15.4 Hz, k), 2.20–1.80 (4H, m, b,c,e), 1.76 (3H, s, n).
^{13}C NMR (75 MHz, $CDCl_3$)	δ 177.01 (f), 143.01 (l), 138.57 (g), 128.90 (i,i'), 124.01 (j), 119.98 (h,h'), 113.76 (m), 74.29 (d), 52.79 (a), 47.14 (k), 44.38 (e), 38.60 (b), 35.45 (c), 23.86 (n).
IR (neat)	3348 (O-H stretch), 3081 (N-H stretch), 2954, 2916, 1653 (C=O stretch), 1621, 1597 (C-=C stretch), 1556 (C-OH bend), 1499, 1442, 1352 1307 (C-N stretch), 1259, 1072, 1027, 970, 959, 891, 750, 688 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{16}H_{21}NaNO_2$ (M+Na): 282.1470, found 282.1459 *m/z*.

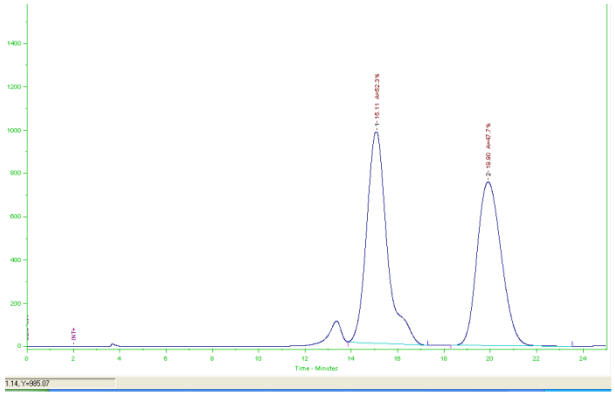
^{1}H NMR of 7l


8.753
7.530
7.504
7.338
7.313
7.285
7.120
7.096
7.071
4.891
4.725
4.517
3.458
2.956
2.905
2.365
2.188
2.137
1.890
1.760
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.95
2.02
2.21
1.01
0.99
1.00
1.00
0.98
1.00
2.02
1.01
3.98
3.04

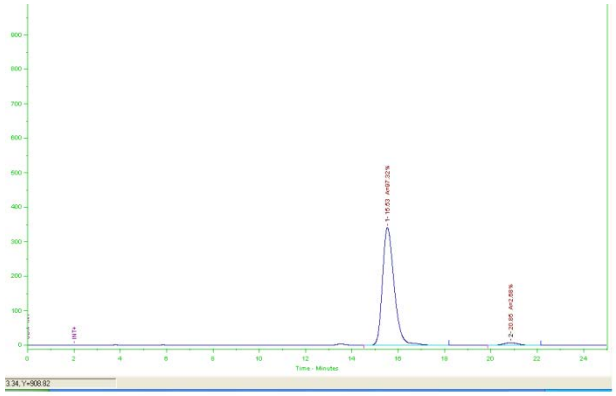
^{13}C NMR of 7l


177.01
143.01
138.57
128.90
124.01
119.98
113.76
74.29
52.79
47.14
44.38
38.60
35.45
23.86
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

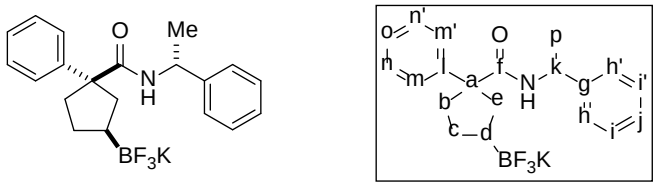
HPLC analysis of 7l



Racemic



CAHB product

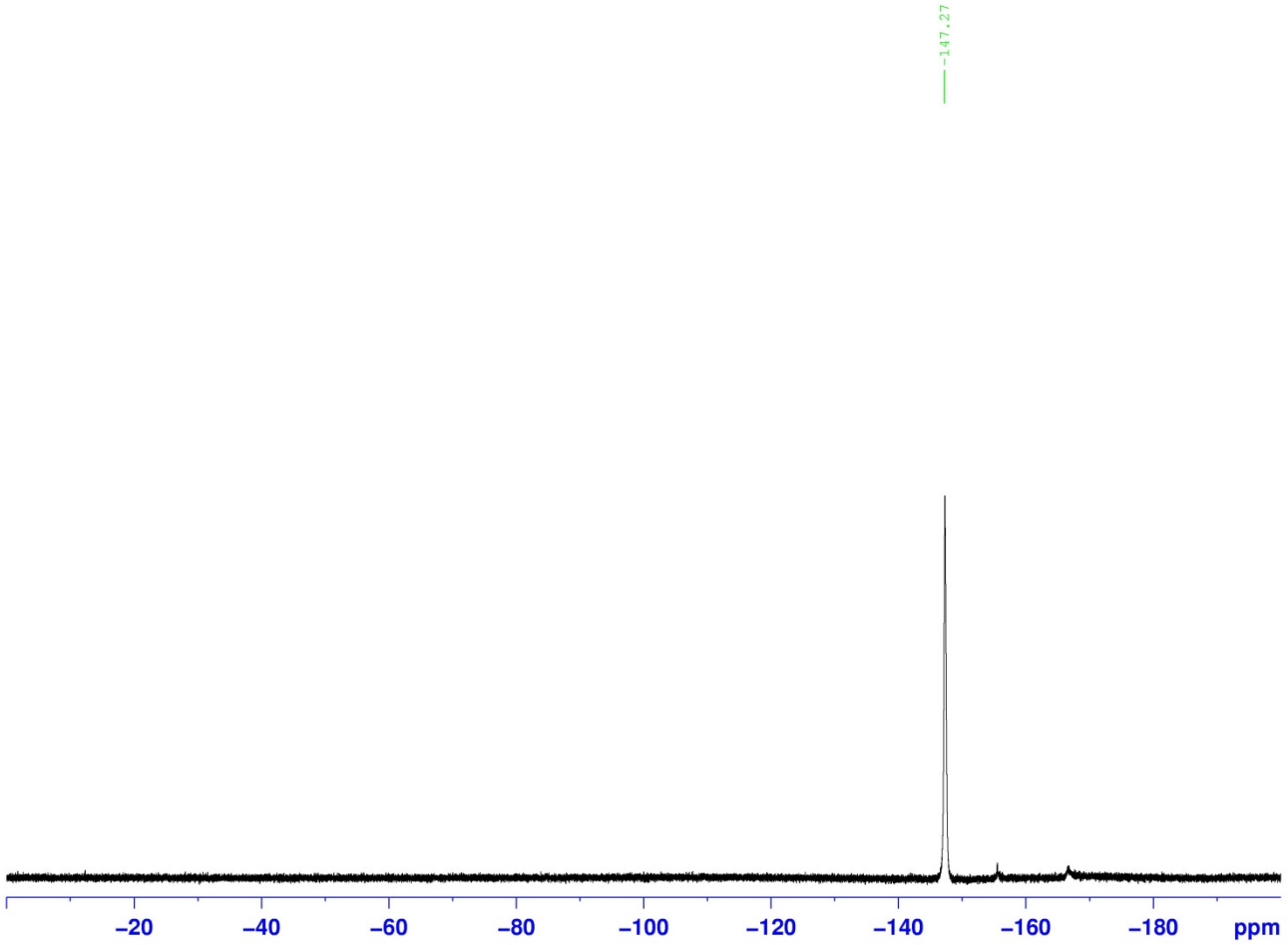


8i (R^1 = Ph, R^2 = (*R*)-CH(Me)Ph, M = K)

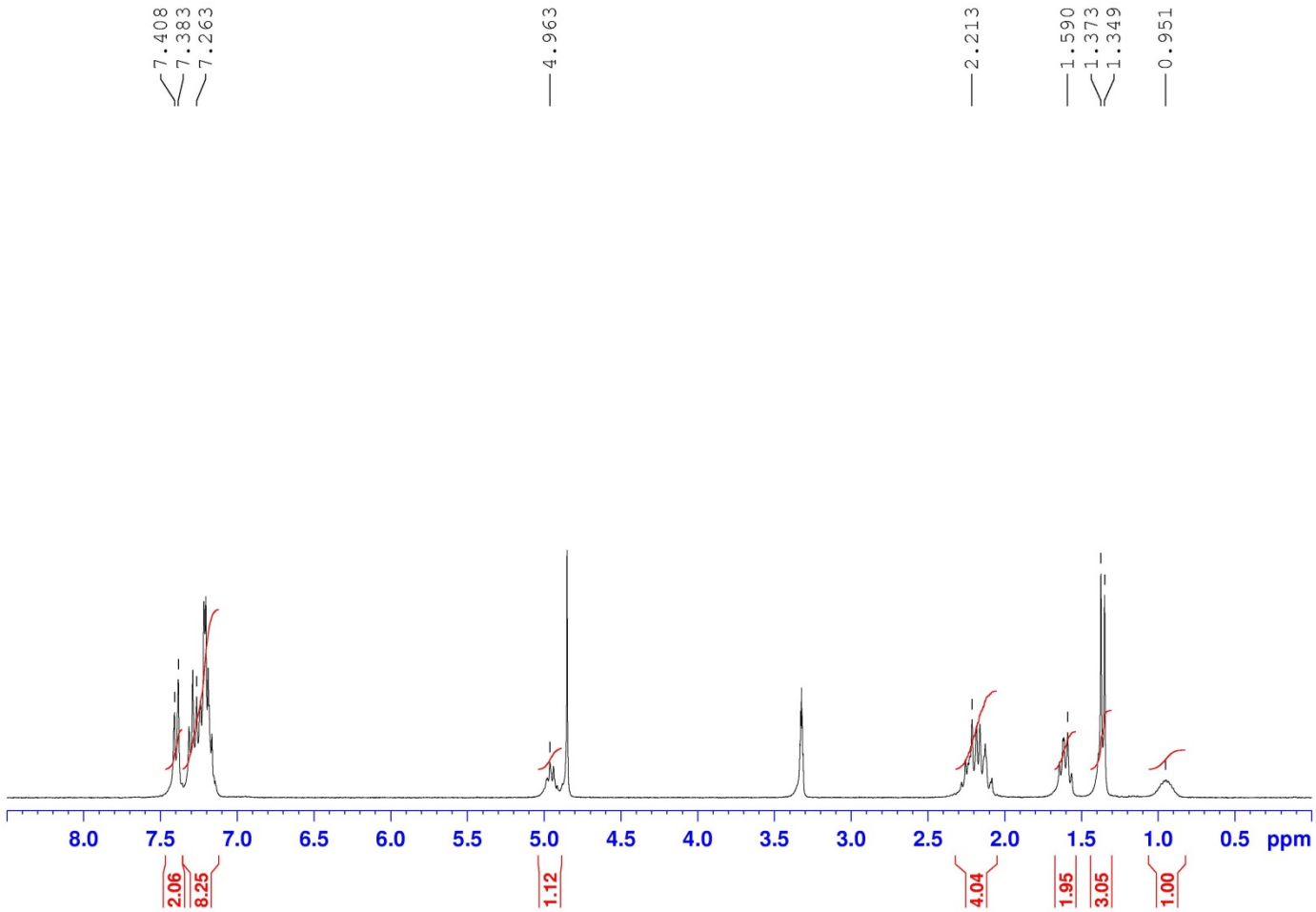
Following the general procedure for the preparation of potassium trifluoroborate salts affords the title compound (72%) as a white solid.

m.p.	214.0–216.0 ºC
Optical rotation	$[\alpha]_D^{20}$ = +17º (*c* 1.0, MeOH)
^{19}F NMR (282 MHz, MeOD)	δ -147.27 (s, BF_3K)
^{1}H NMR (300 MHz, MeOD)	δ 7.40 (2H, d, *J* = 7.5 Hz, h,h'), 7.35–7.10 (8H, m, i,i',j,m,m',n,n',o), 5.00–4.90 (1H, m, k), 2.30–2.10 (2H, m, b,e), 1.65–1.55 (2H, m, c), 1.36 (3H, d, *J* = 7.0 Hz, p), 1.05–0.85 (1H, m, d).
^{13}C NMR (75 MHz, MeOD)	δ 178.16 (f), 145.39 (l), 144.11 (g), 127.86 (i,i'), 127.68 (n,n'), 126.58 (h,h'), 126.29 (m,m'), 125.69 (j), 125.61 (o), 60.20 (a), 48.86 (k), 38.82 (b), 37.25 (e), 26.24 (c), 20.78 (p).
IR (neat)	3438 (N-H stretch), 2941, 2867, 1662 (C=O stretch), 1500 (N-H bend), 1461, 1446, 1320 (C-N stretch), 1172, 997, 958, 890, 696 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{20}H_{22}BF_3NO$ (M-K): 360.1747, found 360.1761 *m/z*.

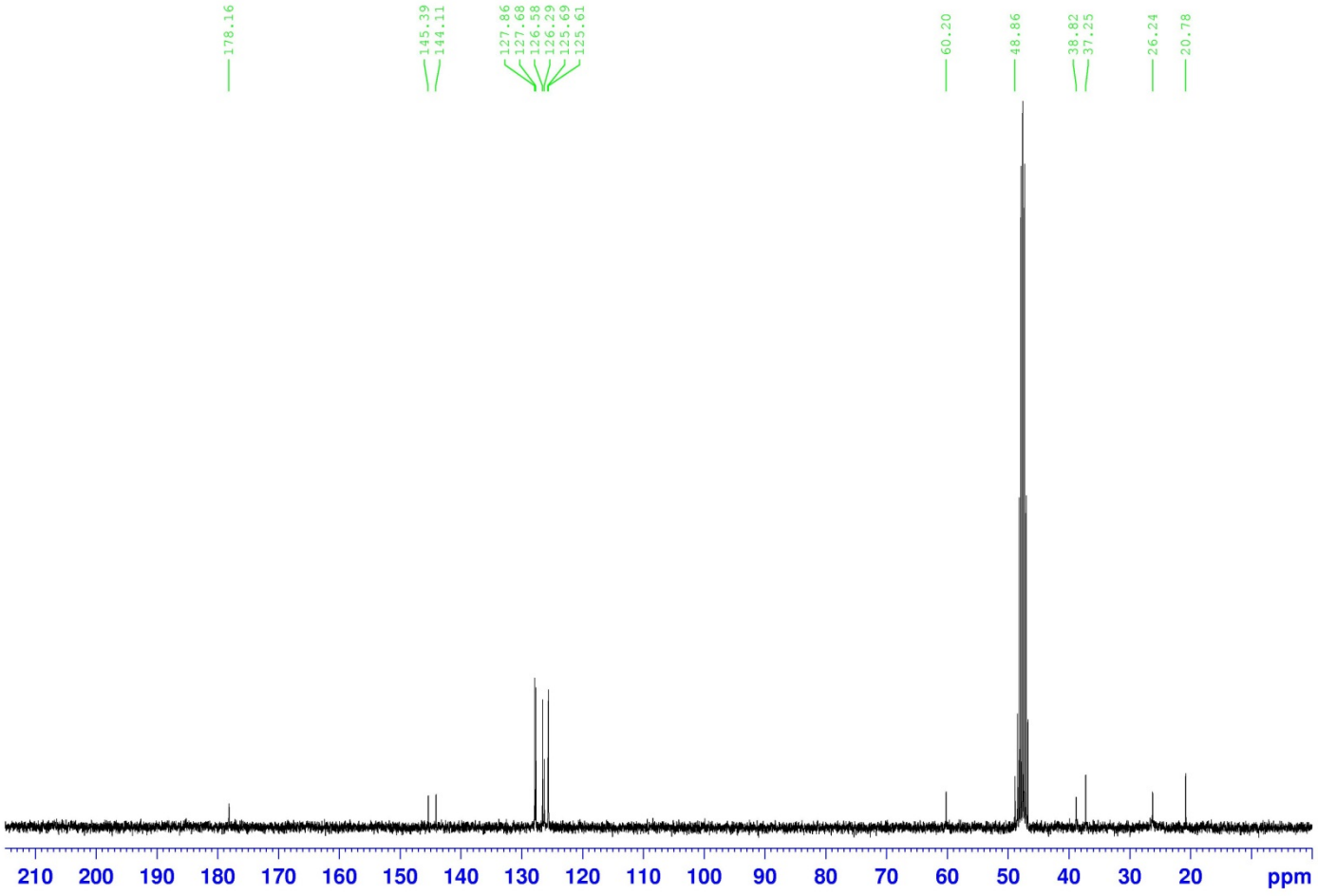
^{19}F NMR of 8i (R^1 = Ph, R^2 = (*R*)-CH(Me)Ph, M = K)

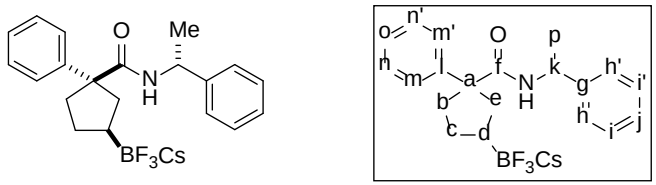


^{1}H NMR of 8i (R^1 = Ph, R^2 = (*R*)-CH(Me)Ph, M = K)



^{13}C NMR of 8i (R^1 = Ph, R^2 = (*R*)-CH(Me)Ph, M = K)



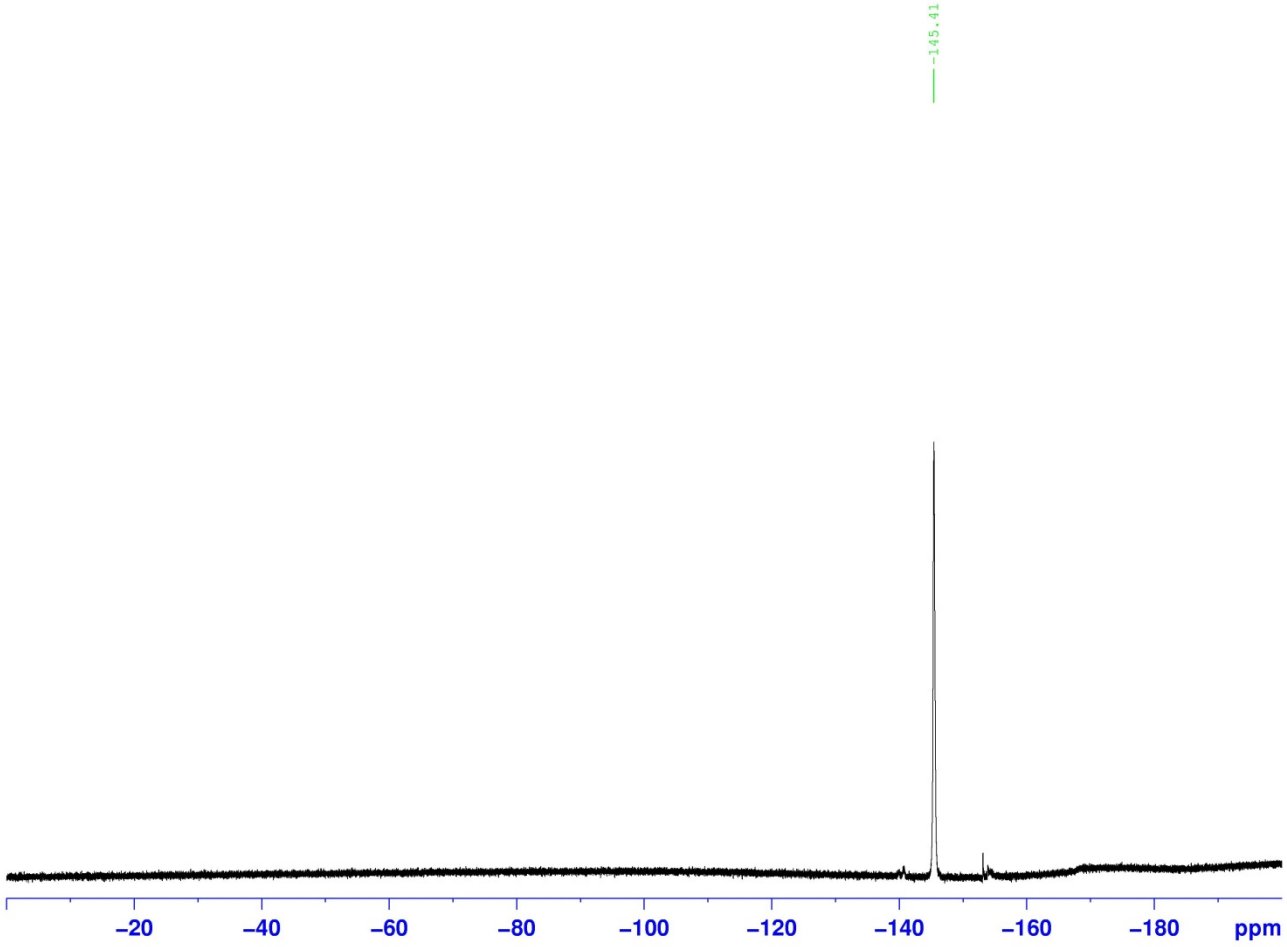


8i (R^1 = Ph, R^2 = *(R)*-CH(Me)Ph, M = Cs)

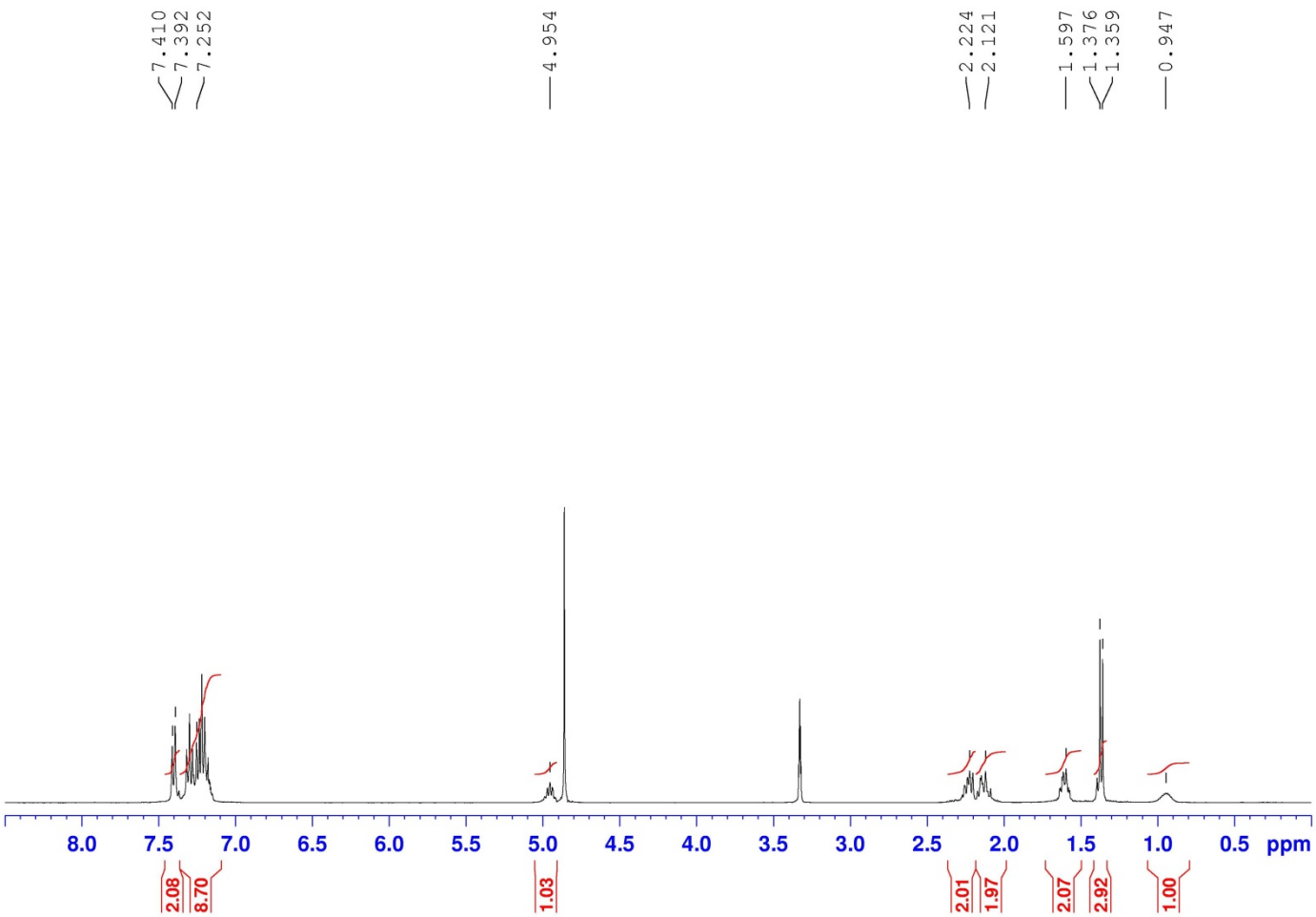
Following the general procedure for the preparation of cesium trifluoroborate salts affords the title compound (96%) as an off-white solid.

m.p.	246.0–247.5 ºC
Optical rotation	$[\alpha]_D^{20} = +16^o$ (*c* 1.0, MeOH)
^{19}F NMR (376 MHz, MeOD)	δ -145.41 (s, BF_3Cs)
^{1}H NMR (400 MHz, MeOD)	δ 7.40 (2H, d, *J* = 7.3 Hz, h,h'), 7.35–7.15 (8H, m, i,i',j,m,m',n,n',o), 5.00–4.90 (1H, m, k), 2.35–2.20 (2H, m, b,e), 2.20–2.00 (2H, m, b,e), 1.70–1.55 (2H, m, c), 1.37 (3H, d, *J* = 7.0 Hz, p), 1.05–0.80 (1H, m, d).
^{13}C NMR (100 MHz, MeOD)	δ 178.21 (f), 145.43 (l), 144.20 (g), 127.90 (i,i'), 127.69 (n,n'), 126.60 (h,h'), 126.32 (m,m'), 125.71 (j), 125.64 (o), 60.21 (a), 48.93 (k), 38.86 (b), 37.30 (e), 26.28 (c), 20.81 (p).
IR (neat)	3441 (N-H stretch), 2941, 2851, 2830, 1659 (C=O stretch), 1497 (N-H bend), 1297 (C-N stretch), 929, 895, 696 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{20}H_{22}BF_3NO$ (M-Cs): 360.1747, found 360.1736 *m/z*.

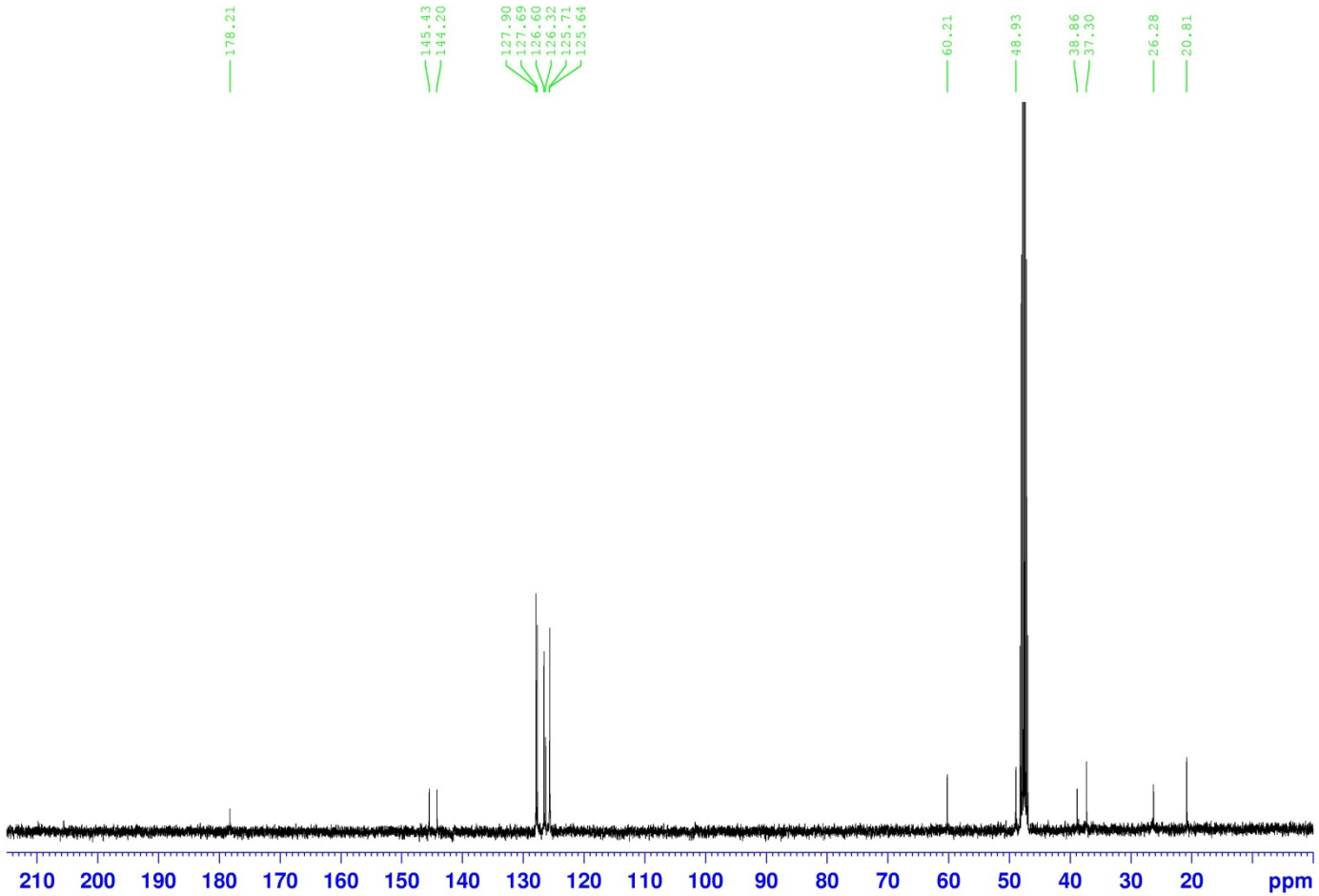
^{19}F NMR of 8i (R^1 = Ph, R^2 = (*R*)-CH(Me)Ph, M = Cs)

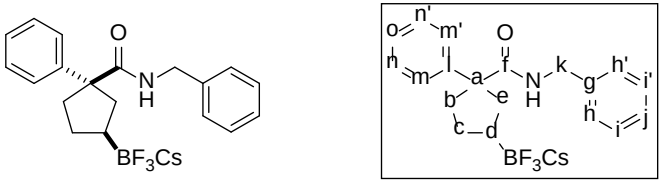


^{1}H NMR of 8i (R^1 = Ph, R^2 = (*R*)-CH(Me)Ph, M = Cs)



^{13}C NMR of 8i (R^1 = Ph, R^2 = (*R*)-CH(Me)Ph, M = Cs)



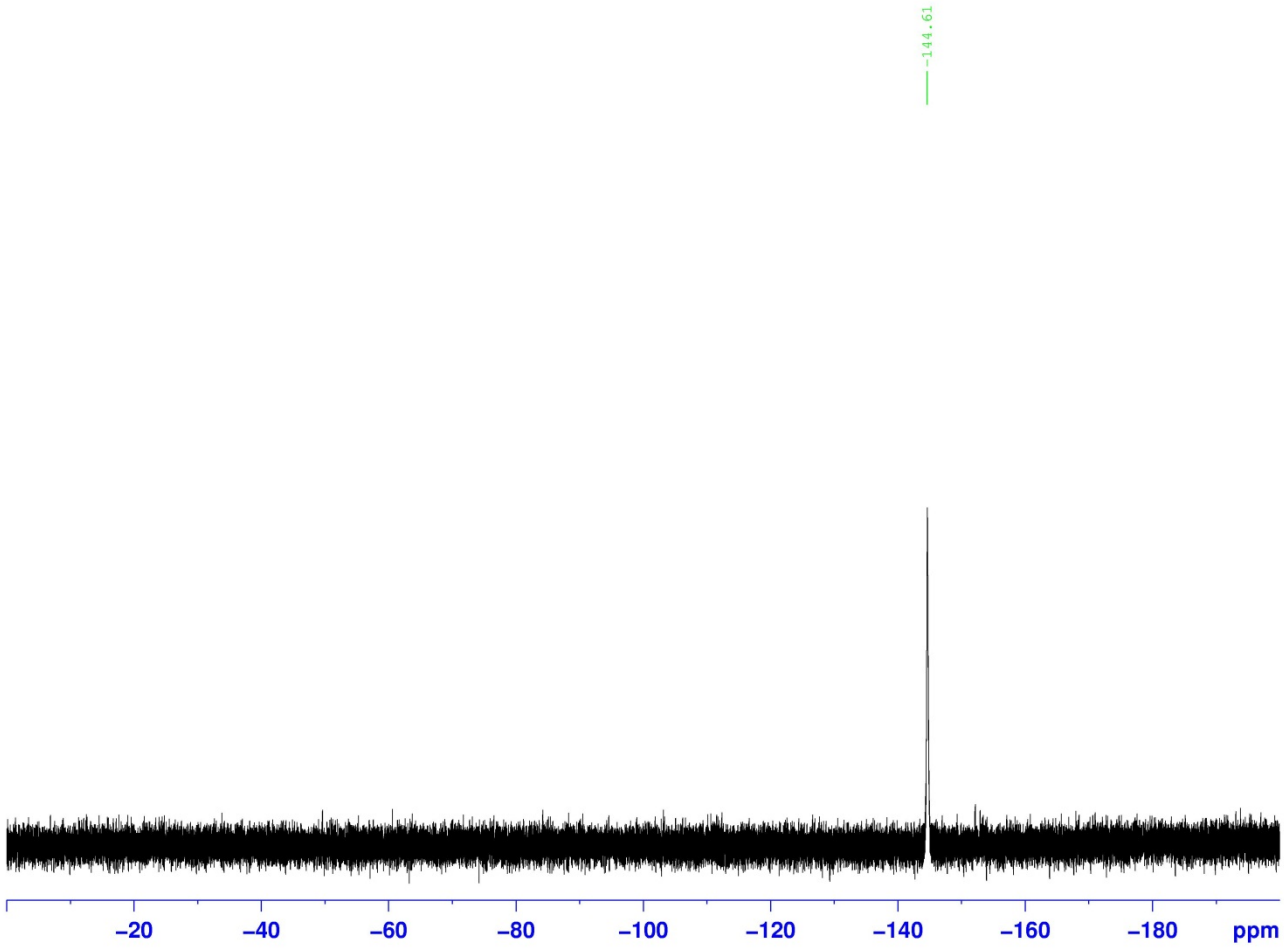


8g (R^1 = Ph, R^2 = CH_2Ph, M = Cs)

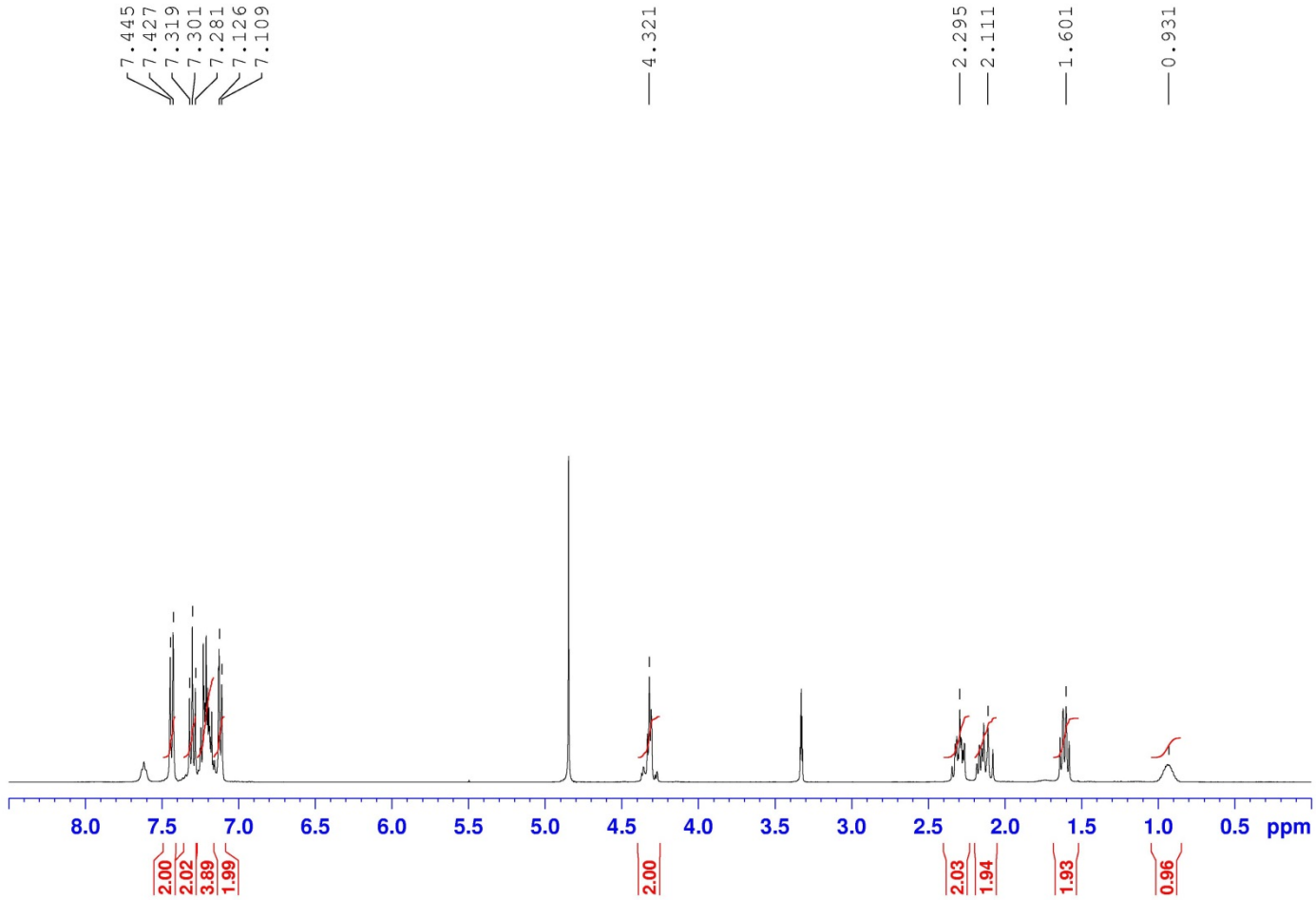
Following the general procedure for the preparation of cesium trifluoroborate salts affords the title compound (82%) as a white solid.

m.p.	167.5–169.0 ºC
Optical rotation	$[\alpha]_D^{20}$ = +3.2º (*c* 1.0, MeOH)
^{19}F NMR (376 MHz, MeOD)	δ -144.61 (s, BF_3Cs)
^{1}H NMR (400 MHz, MeOD)	δ 7.44 (2H, d, *J* = 7.2 Hz, h,h'), 7.30 (2H, t, *J* = 7.4 Hz, n,n'), 7.25–7.15 (4H, m, i,i',j,o), 7.12 (2H, d, *J* = 6.8 Hz, m,m'), 4.40–4.25 (2H, m, k), 2.35–2.25 (2H, m, b,e), 2.20–2.05 (2H, m, b,e), 1.65–1.55 (2H, m, c), 1.05–0.85 (1H, m, d).
^{13}C NMR (100 MHz, MeOD)	δ 179.07 (f), 145.12 (l), 139.22 (g), 127.91 (i,i'), 127.79 (n,n'), 126.67 (h,h'), 126.59 (m,m'), 126.40 (j), 125.81 (o), 60.24 (a), 42.66 (k), 38.79 (b), 37.22 (e), 26.17 (c).
IR (neat)	3354 (N-H stretch), 2936, 2872, 1656 (C=O stretch), 1628 (C=C stretch), 1514 (N-H bend), 1443, 1287 (C-N stretch), 1091, 948, 919, 897, 728, 696 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{19}H_{20}BF_3NO$ (M-Cs): 346.1590, found 346.1573 *m/z*.

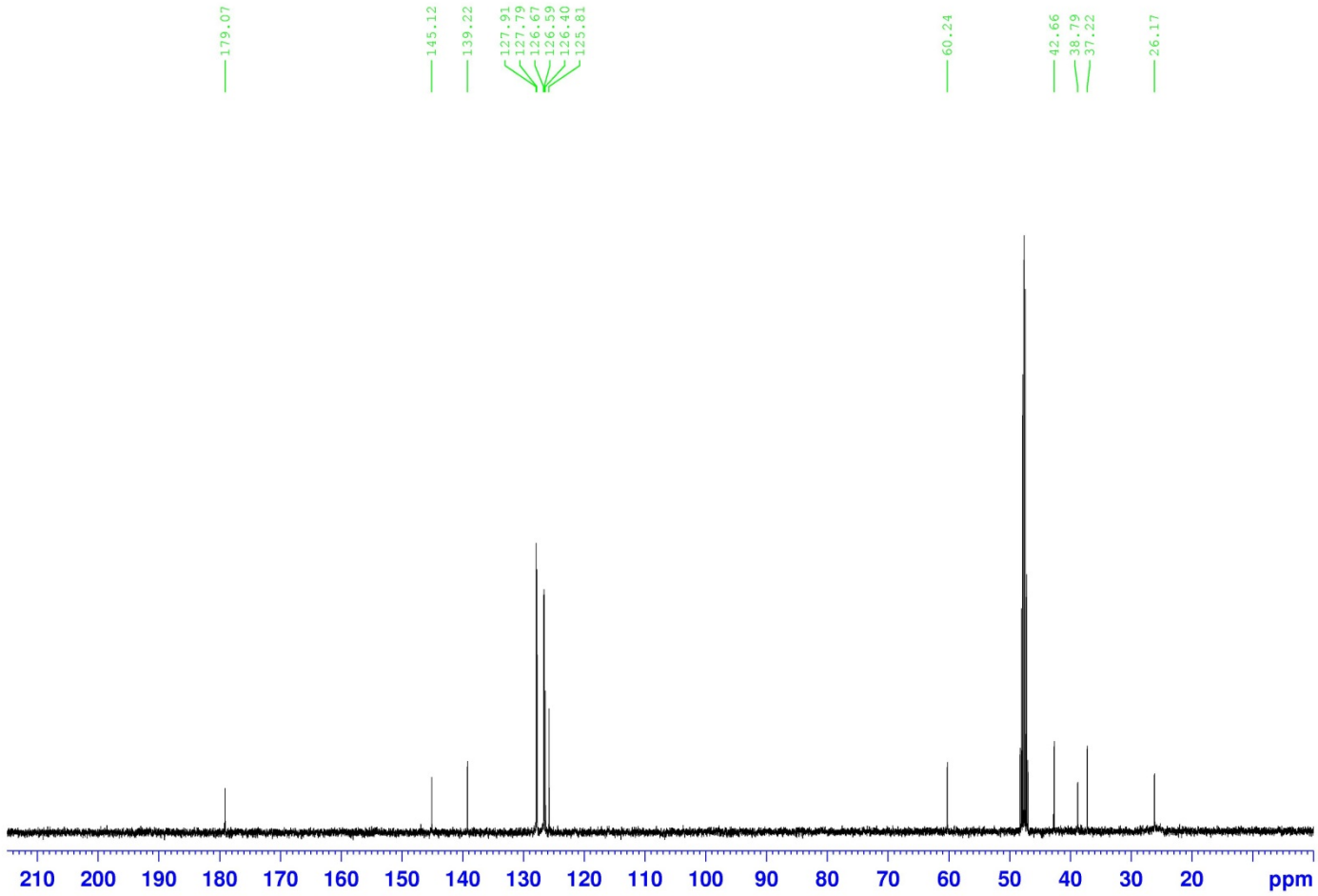
^{19}F NMR of 8g (R^1 = Ph, R^2 = CH_2Ph, M = Cs)

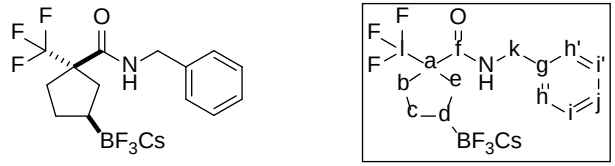


^{1}H NMR of 8g (R^1 = Ph, R^2 = CH_2Ph, M = Cs)



^{13}C NMR of 8g (R^1 = Ph, R^2 = CH_2Ph, M = Cs)



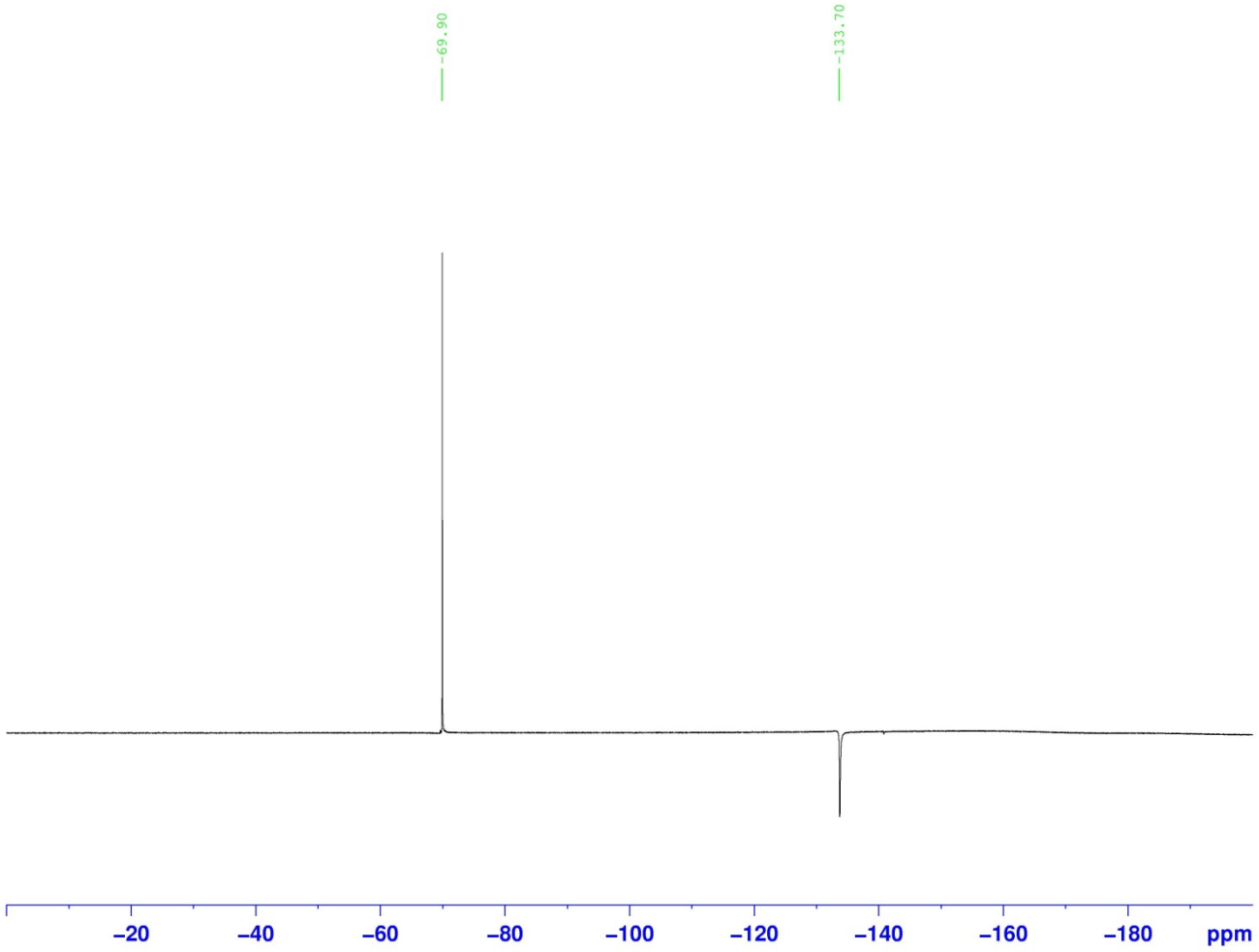


8h (R^1 = CF_3, R^2 = CH_2Ph, M = Cs)

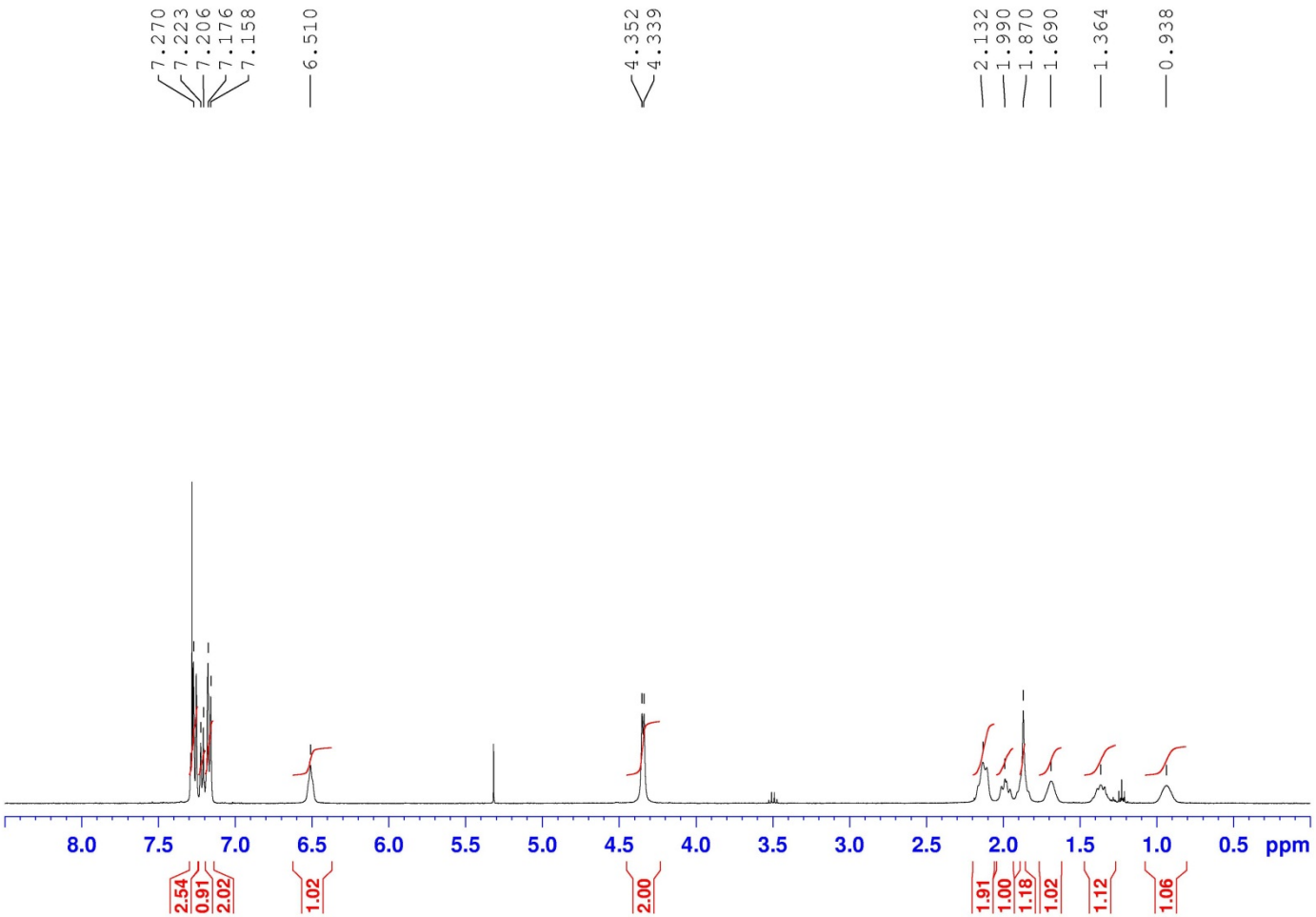
Following the general procedure for CAHB without oxidation following by the preparation of cesium trifluoroborate salts affords the title compound (59%, 2 steps) as a white foamy solid.

m.p.	73.0–75.5 ºC
Optical rotation	$[\alpha]_D^{20}$ = -26^o (*c* 2.0, $CHCl_3$)
^{19}F NMR (376 MHz, $CDCl_3$)	δ -69.90 (s, CF_3), -133.70 (s, BF_3Cs)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 7.30–7.25 (2H, m, i,i'), 7.21 (1H, d, *J* = 7.1 Hz, j), 7.17 (1H, d, *J* = 7.0 Hz, h,h'), 6.51 (1H, br s, NH), 4.35 (2H, d, *J* = 5.2 Hz, k), 2.20–2.05 (2H, m, b,e), 2.05–1.95 (2H, m, e), 1.90–1.85 (1H, m, b), 1.75–1.60 (1H, m, c), 1.45–1.30 (1H, m, c), 1.05–0.85 (1H, m, d).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 171.29 (f), 138.16 (g), 128.76 (i,i'), 127.46 (j), 127.11 (h,h'), 59.85 (q, *J* = 93.3 Hz, a), 43.95 (k), 34.84 (b), 33.71 (e), 29.37 (c).
IR (neat)	3373 (N-H stretch), 2956, 2870, 1657 (C=O stretch), 1523 (N-H bend), 1497, 1454, 1293 (C-N stretch), 1273, 1146, 1090, 1001, 926, 895, 729, 697 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{14}H_{15}BF_6NO$ (M-Cs): 338.1151, found 338.1179 *m/z*.

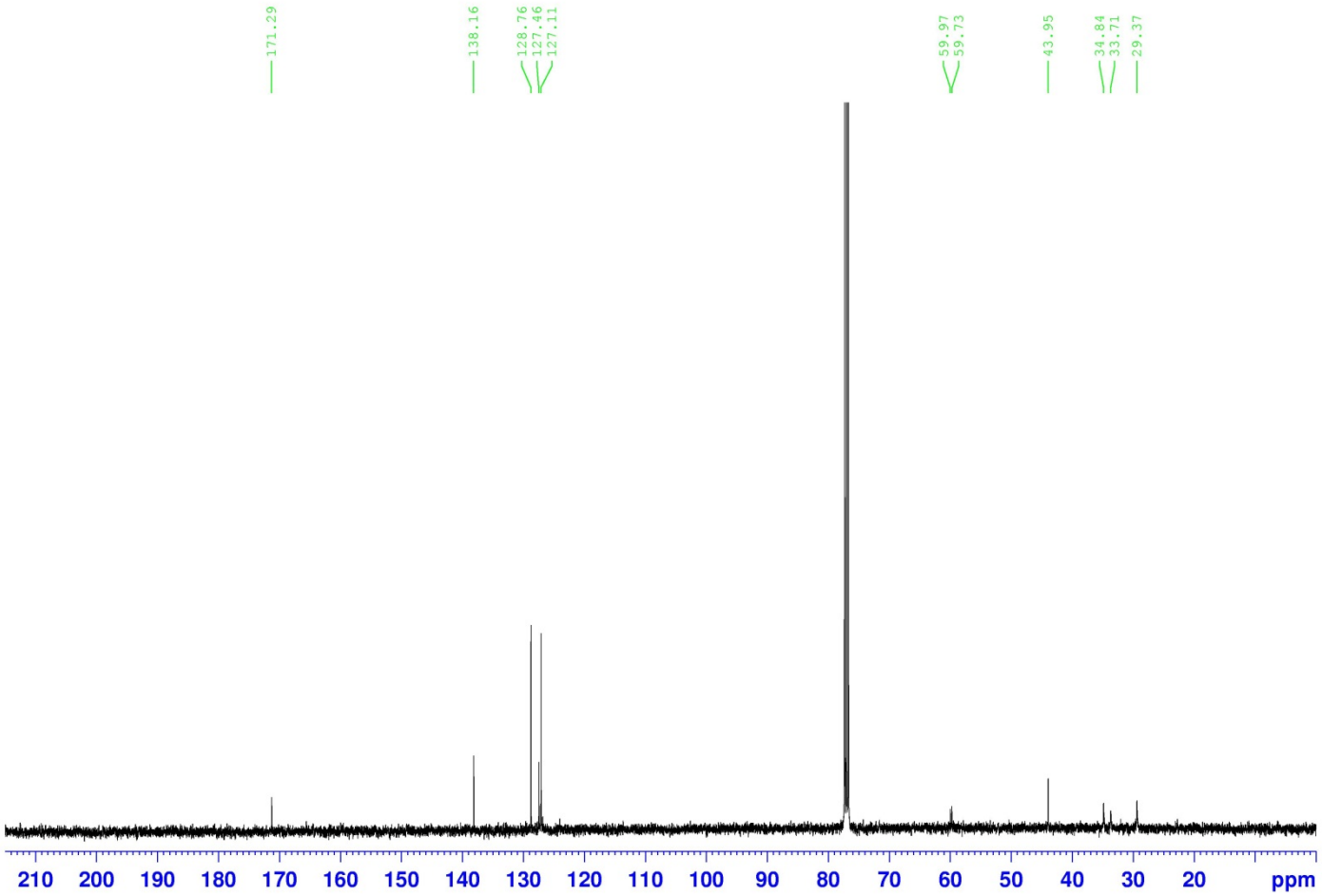
^{19}F NMR of 8h ($R^1 = CF_3$, $R^2 = CH_2Ph$, M = Cs)

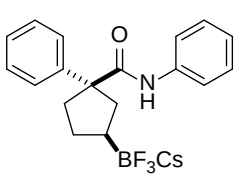


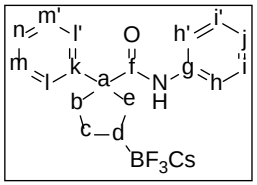
^{1}H NMR of 8h ($R^1 = CF_3$, $R^2 = CH_2Ph$, M = Cs)



^{13}C NMR of 8h ($R^1 = CF_3$, $R^2 = CH_2Ph$, M = Cs)





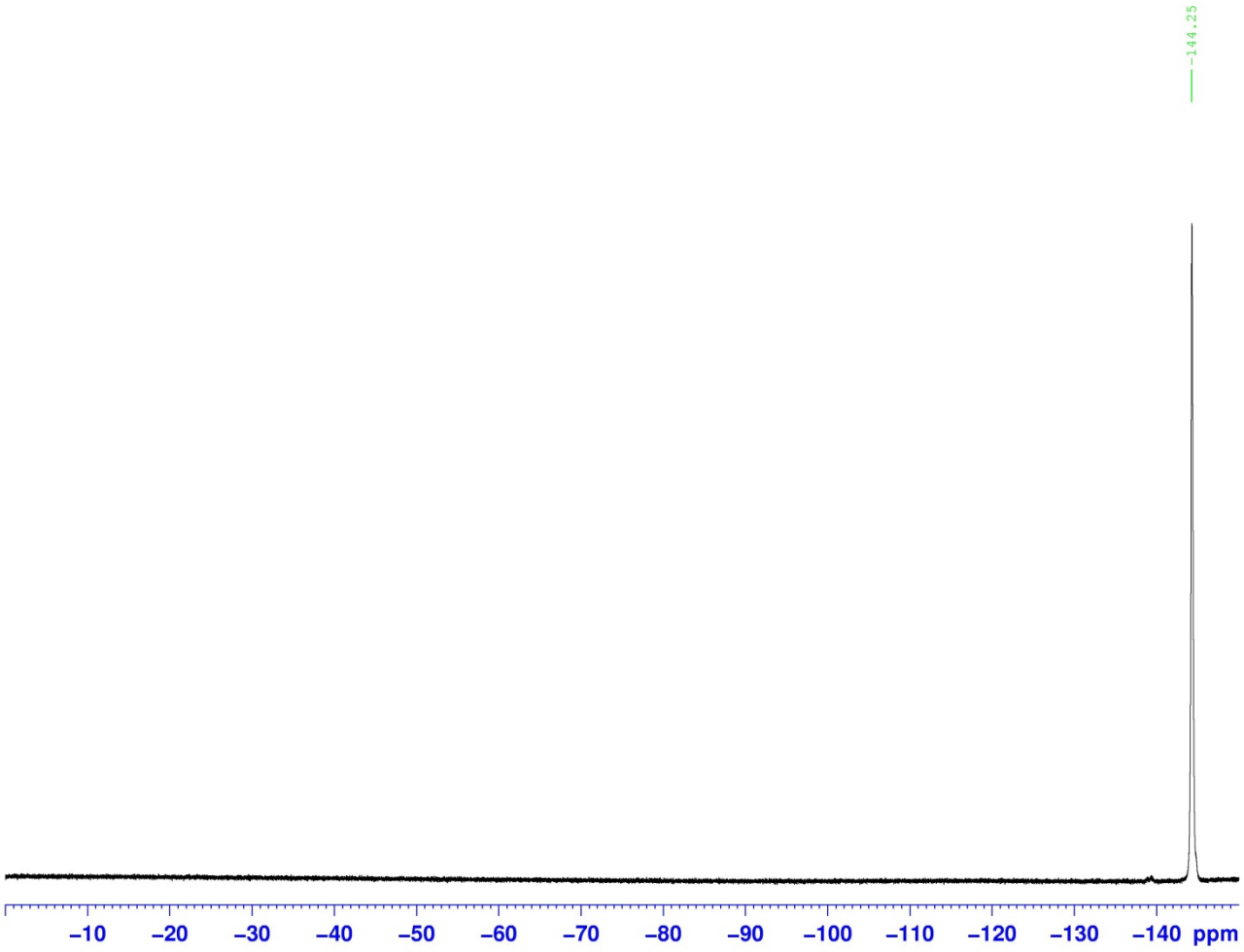


22

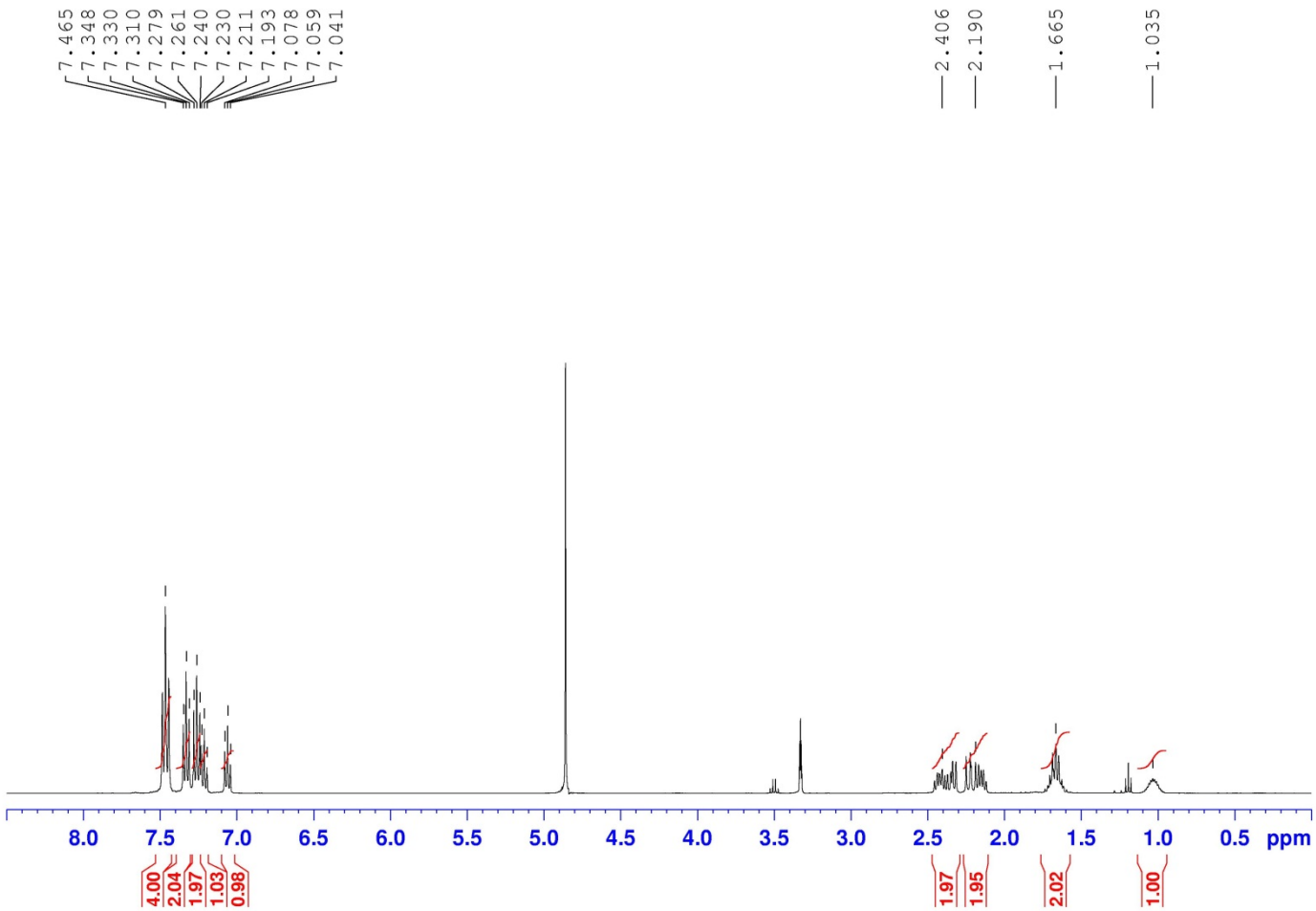
Following the general procedure for the preparation of cesium trifluoroborate salts affords the title compound (80%) as a white solid.

m.p.	173.5–177.0 ºC
Optical rotation	$[\alpha]_D^{20} = +11^o$ (*c* 1.0, MeOH)
^{19}F NMR (376 MHz, MeOD)	δ -144.25 (s, BF_3Cs)
^{1}H NMR (400 MHz, MeOD)	δ 7.50–7.40 (4H, m, h,h',l,l'), 7.33 (2H, t, *J* = 7.4 Hz, m,m'), 7.26 (2H, t, *J* = 7.5 Hz, i,i'), 7.21 (1H, t, *J* = 7.3 Hz, j), 7.06 (1H, t, *J* = 7.4 Hz, n), 2.50–2.30 (2H, m, b,e), 2.30–2.10 (2H, m, b,e), 1.75–1.60 (2H, m, c), 1.10–0.95 (1H, m, d).
^{13}C NMR (100 MHz, MeOD)	δ 177.61 (f), 145.34 (k), 138.55 (g), 128.18 (i,i'), 127.89 (m,m'), 126.51 (l,l'), 125.89 (j), 123.79 (n), 120.85 (h,h'), 61.13 (a), 38.97 (b), 37.77 (e), 26.60 (c).
IR (neat)	3402 (N-H stretch), 2947, 2842, 1663 (C=O stretch), 1596 (C=C stretch), 1516 (N-H bend), 1493, 1436, 1311 (C-N stretch), 1241, 1080, 994, 901, 897, 745, 696 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{18}H_{18}BF_3NO$ (M-Cs): 332.1434, found 332.1426 *m/z*.

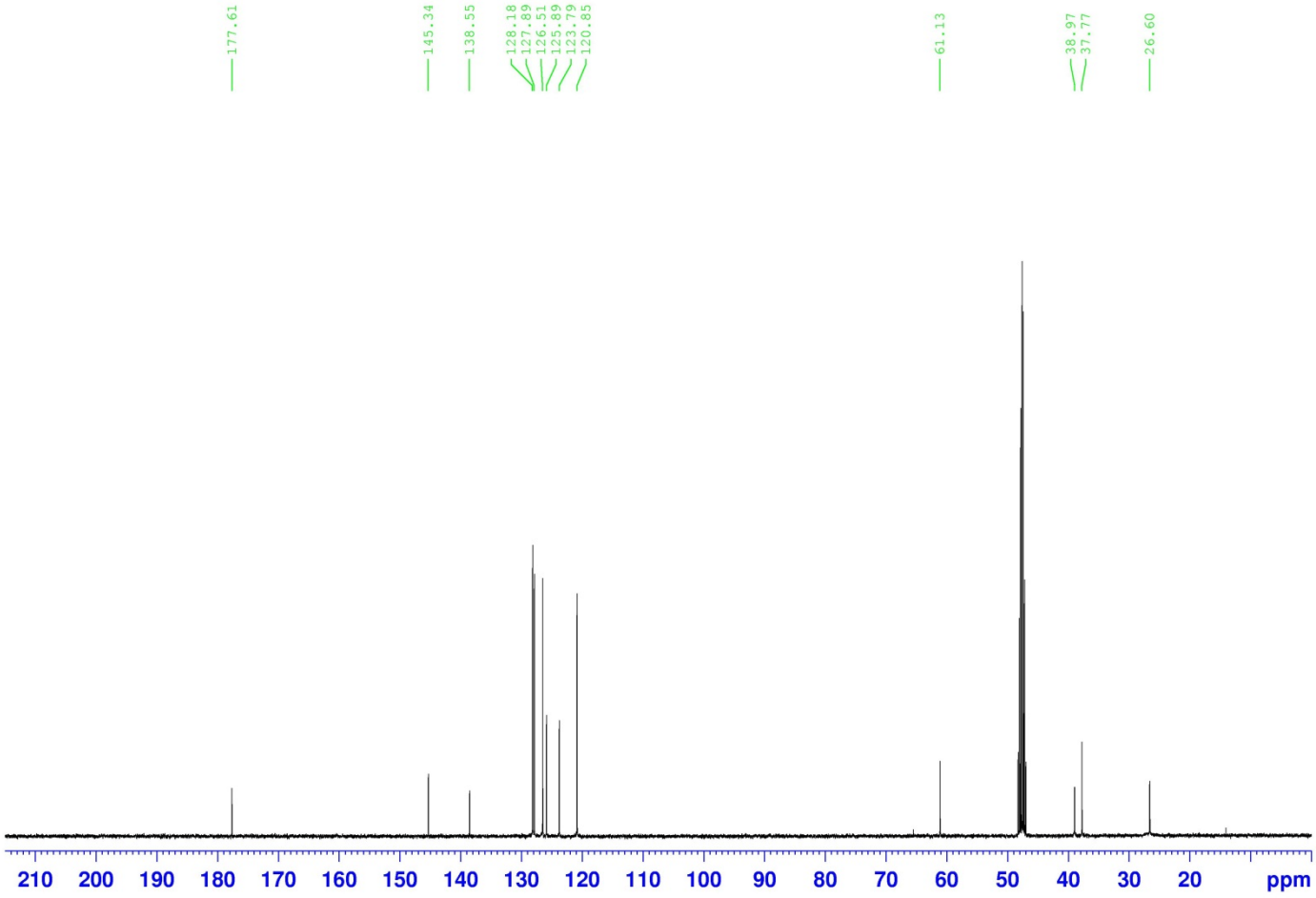
^{19}F NMR of 22

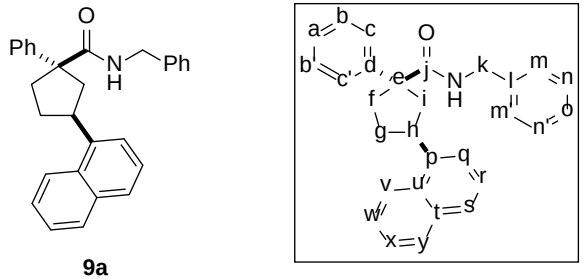


^{1}H NMR of 22


7.465
7.348
7.330
7.310
7.279
7.261
7.240
7.230
7.211
7.193
7.078
7.059
7.041
2.406
2.190
1.665
1.035
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.00
2.04
1.97
1.03
0.98
1.97
1.95
2.02
1.00

^{13}C NMR of 22


177.61
145.34
138.55
128.18
127.89
126.51
125.89
123.79
120.85
61.13
38.97
37.77
26.60
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

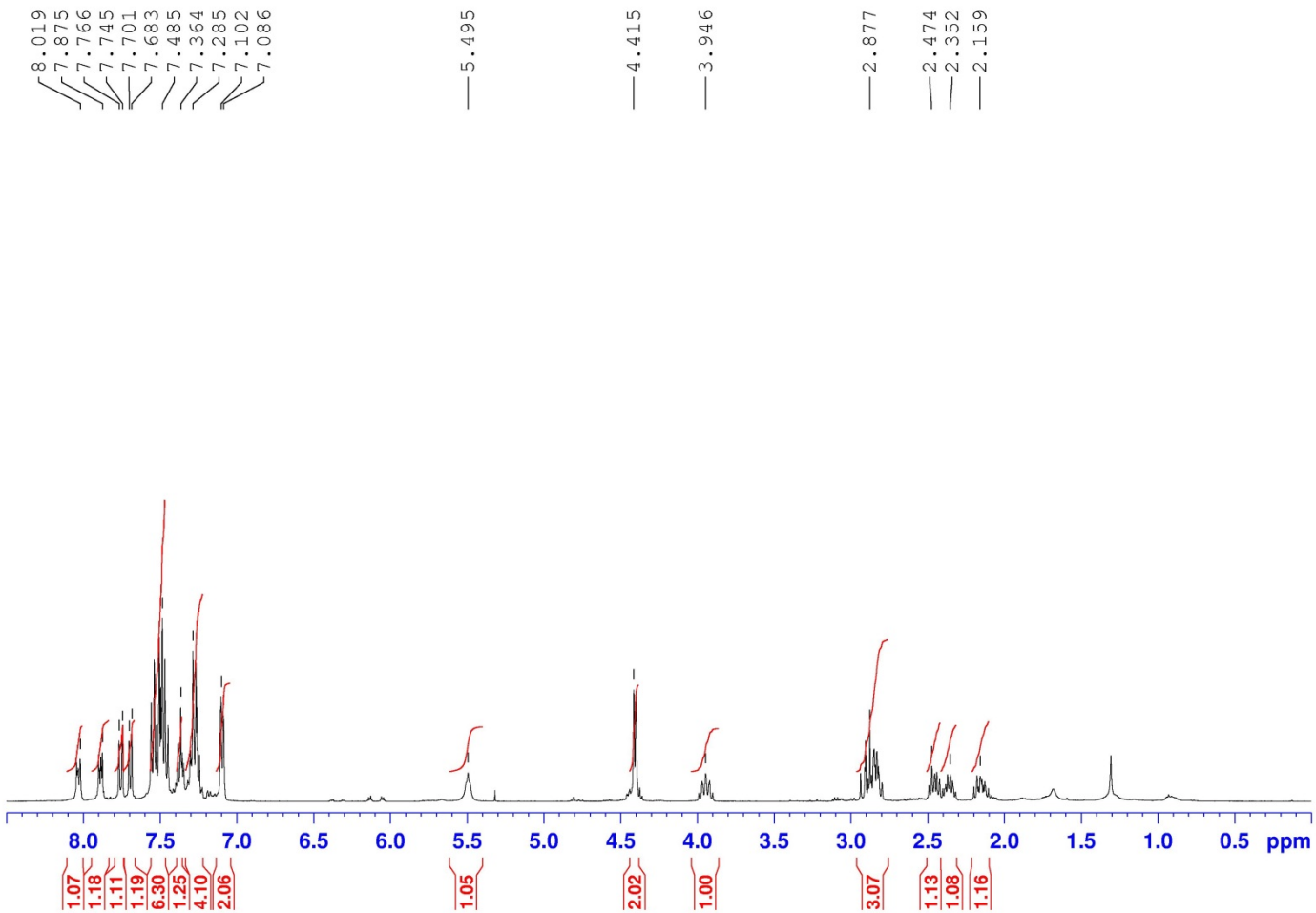


9a

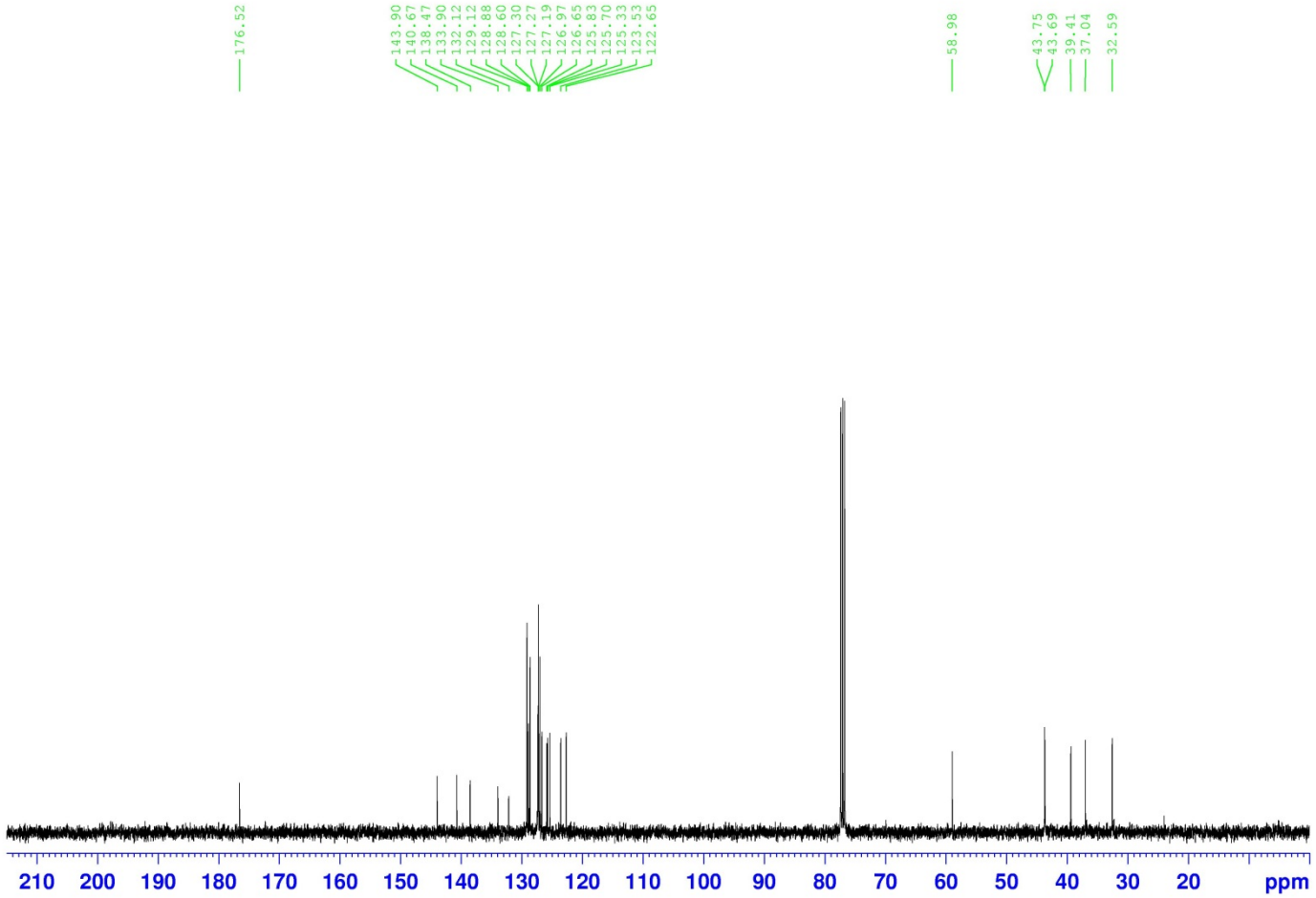
Following the general procedure for Suzuki-Miyaura cross-coupling reaction affords, after flash chromatography on silica gel (90:10–85:15 hexanes:ethyl acetate), the title compound (69%) as a yellow oil.

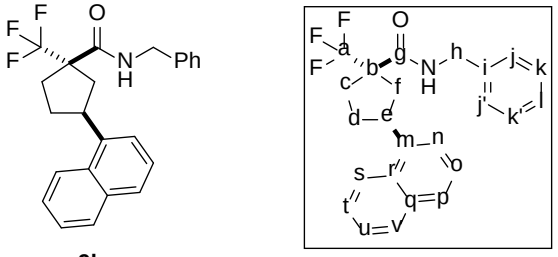
Optical rotation	$[\alpha]_D^{20}$ = -3.2° (*c* 1.3, $CHCl_3$)
TLC analysis	R_f = 0.55 (70:30 hexanes:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 8.10–8.00 (1H, m, v), 7.95–7.85 (1H, m, y), 7.76 (1H, d, *J* = 8.2 Hz, s), 7.69 (1H, d, *J* = 7.1 Hz, q), 7.60–7.45 (6H, m, a,n,n',o,w,x), 7.40–7.35 (1H, m, r), 7.35–7.25 (4H, m, b,b',m,m'), 7.09 (2H, d, *J* = 6.4 Hz, c,c'), 5.49 (1H, br s, NH), 4.45–4.35 (2H, m, k), 4.00–3.90 (1H, m, h), 2.95–2.80 (3H, m, f,i), 2.50–2.40 (1H, m, f), 2.40–2.30 (1H, m, g), 2.20–2.10 (1H, m, g).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 176.52 (j), 143.90 (d), 140.67 (p), 138.47 (l), 133.90 (t), 132.12 (u), 129.12 (n,n'), 128.88 (y), 128.60 (b,b'), 127.30 (r), 127.27 (m,m'), 127.19 (c,c'), 126.97 (o,o'), 126.65 (s), 125.83 (w), 125.70 (a), 125.33 (x), 123.53 (v), 122.65 (q), 58.98 (e), 43.75 (k), 43.69 (i), 39.41 (h), 37.04 (f), 32.59 (g).
IR (neat)	3325 (N-H stretch), 1646 (C=O stretch), 1598 (C=C stretch), 1533 (N-H bend), 1449, 1418, 1285, 795, 775, 718, 695 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{29}H_{27}NaNO$ (M+Na): 428.1990, found 428.1992 *m/z*.

^{1}H NMR of 9a


8.019
7.875
7.766
7.745
7.701
7.683
7.485
7.364
7.285
7.102
7.086
5.495
4.415
3.946
2.877
2.474
2.352
2.159
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.07
1.18
1.11
1.19
6.30
1.25
4.10
2.06
1.05
2.02
1.00
3.07
1.13
1.08
1.16

^{13}C NMR of 9a


176.52
143.90
140.67
138.47
133.90
132.12
129.12
128.88
128.60
127.30
127.27
127.19
126.97
126.65
125.83
125.70
125.33
123.53
122.65
58.98
43.75
43.69
39.41
37.04
32.59
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

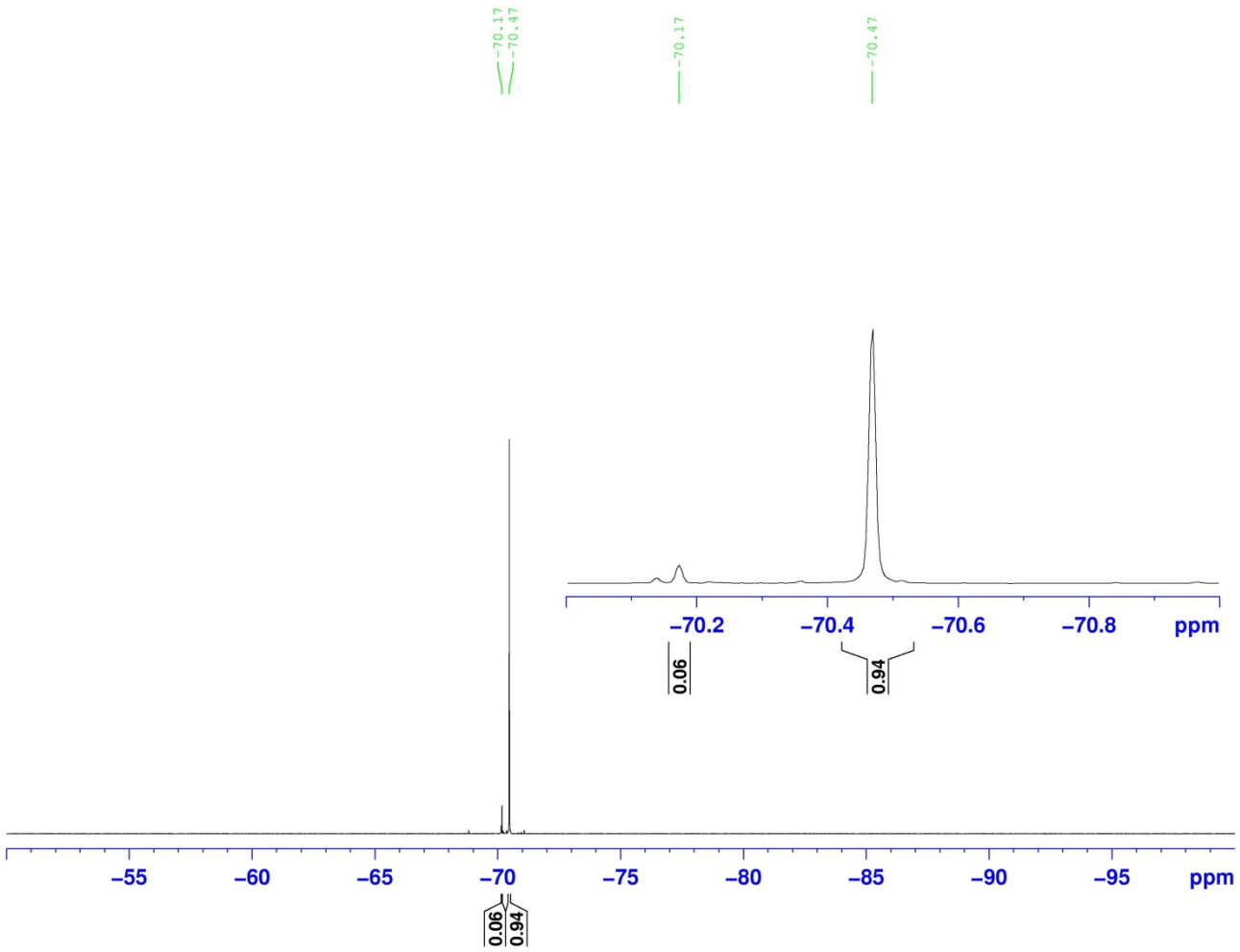


9b

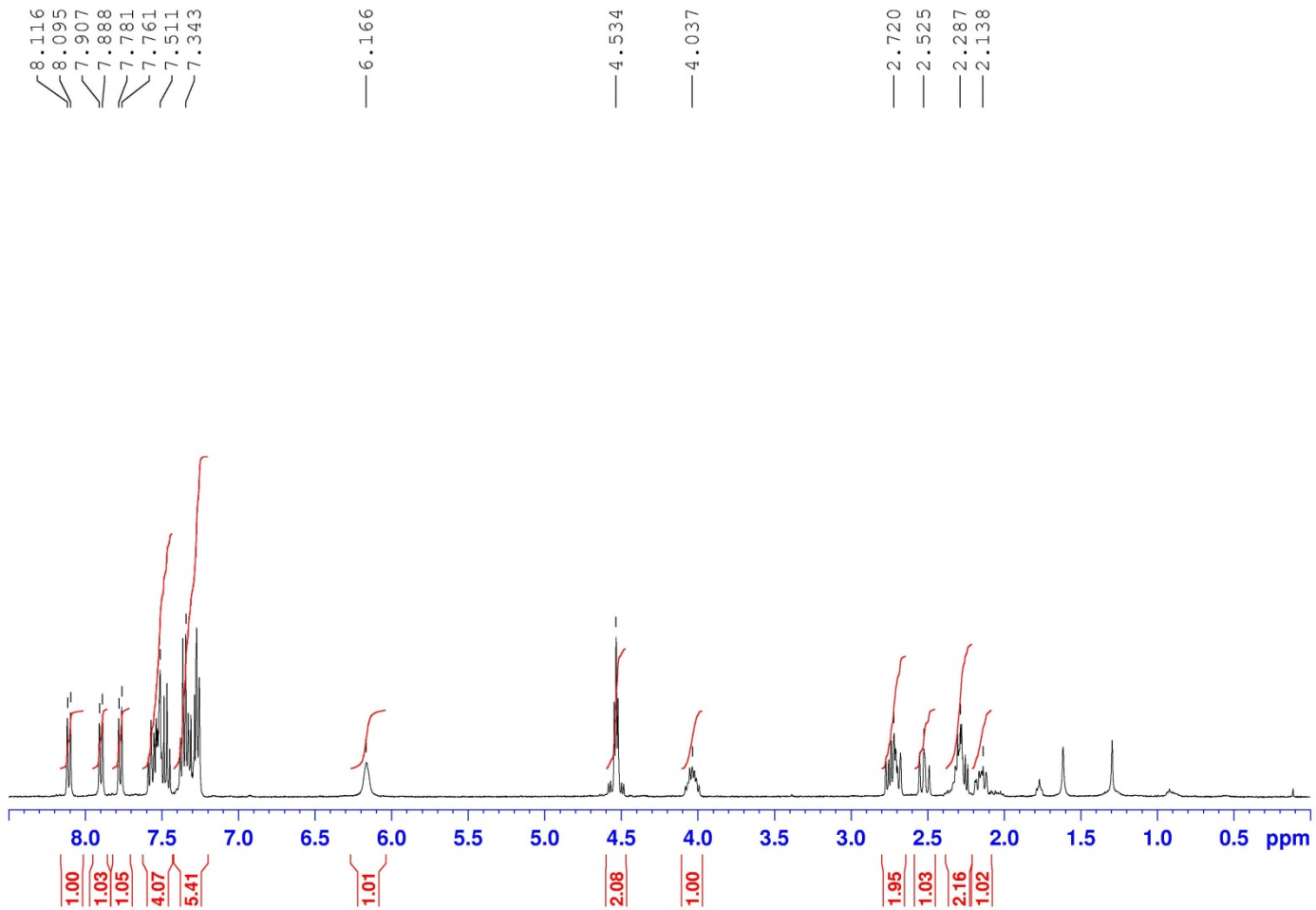
Following the general procedure for Suzuki-Miyaura cross-coupling reaction affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (63%) as a yellow oil.

Optical rotation	$[\alpha]_D^{20}$ = -16° (*c* 0.5, $CHCl_3$)
TLC analysis	R_f = 0.75 (70:30 hexanes:ethyl acetate)
^{19}F NMR (376 MHz, $CDCl_3$)	δ -70.47.
^{1}H NMR (400 MHz, $CDCl_3$)	δ 8.11 (1H, d, *J* = 8.4 Hz, v), 7.90 (1H, dd, *J* = 7.6 Hz, s), 7.77 (1H, dd, *J* = 7.9 Hz, n), 7.60–7.40 (4H, m, l,p,t,u), 7.40–7.20 (5H, m, j,j',k,k',o), 6.12 (1H, br s, NH), 4.60–4.45 (2H, m, h), 4.10–3.95 (1H, m, e), 2.80–2.65 (2H, m, c,f), 2.60–2.55 (1H, m, f), 2.40–2.20 (2H, m, c,d), 2.20–2.10 (1H, m, d).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 169.18 (g), 138.32 (m), 137.61 (i), 133.89 (q), 131.97 (r), 128.96 (v), 128.85 (k,k'), 127.70 (j,j'), 127.53 (o), 127.17 (l), 126.08 (p), 125.66 (t), 125.55 (u), 123.16 (s), 122.40 (n), 58.45 (d, *J* = 24 Hz, b), 44.41 (h), 41.13 (e), 39.01 (f), 32.70 (d), 31.73 (c).
IR (neat)	3341 (N-H stretch), 3052, 2957, 1657 (C=O stretch), 1598 (C=C stretch), 1522 (N-H bend), 1496, 1453, 1287,1147, 1111, 777, 726, 695 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{24}H_{22}F_3NaNO$ (M+Na): 420.1551, found 420.1534 *m/z*.

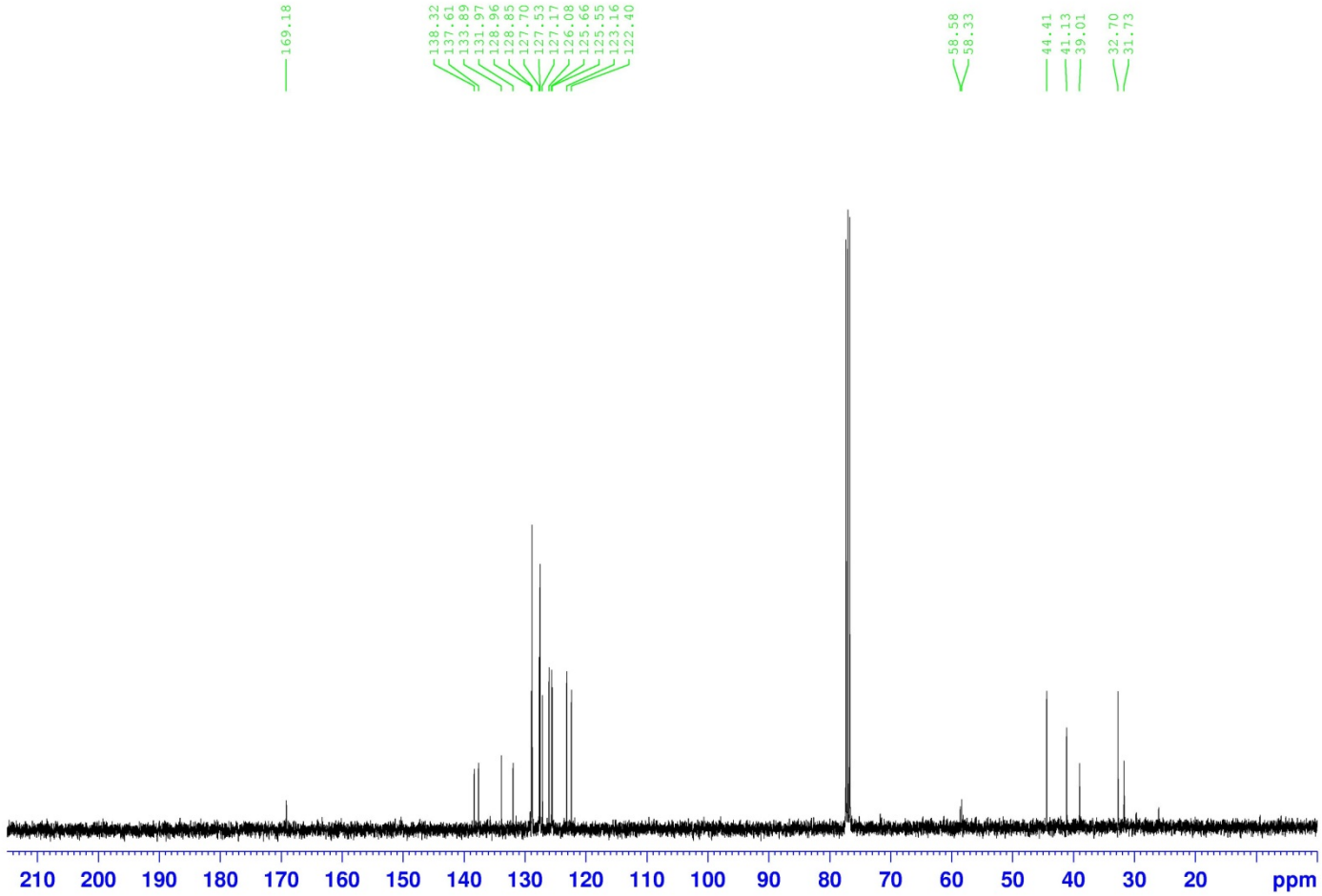
^{19}F NMR of 9b

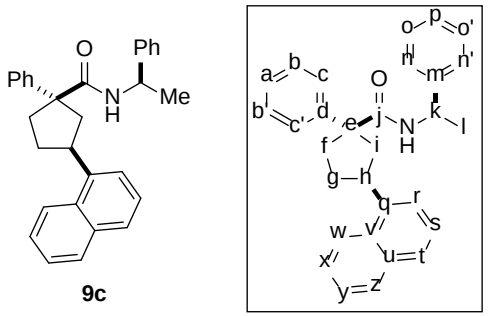

-70.17
-70.47
-70.17
-70.47
-70.2
-70.4
-70.6
-70.8
ppm
0.06
0.94
-55
-60
-65
-70
-75
-80
-85
-90
-95
ppm
0.06
0.94

^{1}H NMR of 9b


8.116
8.095
7.907
7.888
7.781
7.761
7.511
7.343
6.166
4.534
4.037
2.720
2.525
2.287
2.138
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.00
1.03
1.05
4.07
5.41
1.01
2.08
1.00
1.95
1.03
2.16
1.02

^{13}C NMR of 9b


169.18
138.32
137.61
133.89
131.97
128.96
128.85
127.70
127.53
127.17
126.08
125.66
125.55
123.16
122.40
58.58
58.33
44.41
41.13
39.01
32.70
31.73
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

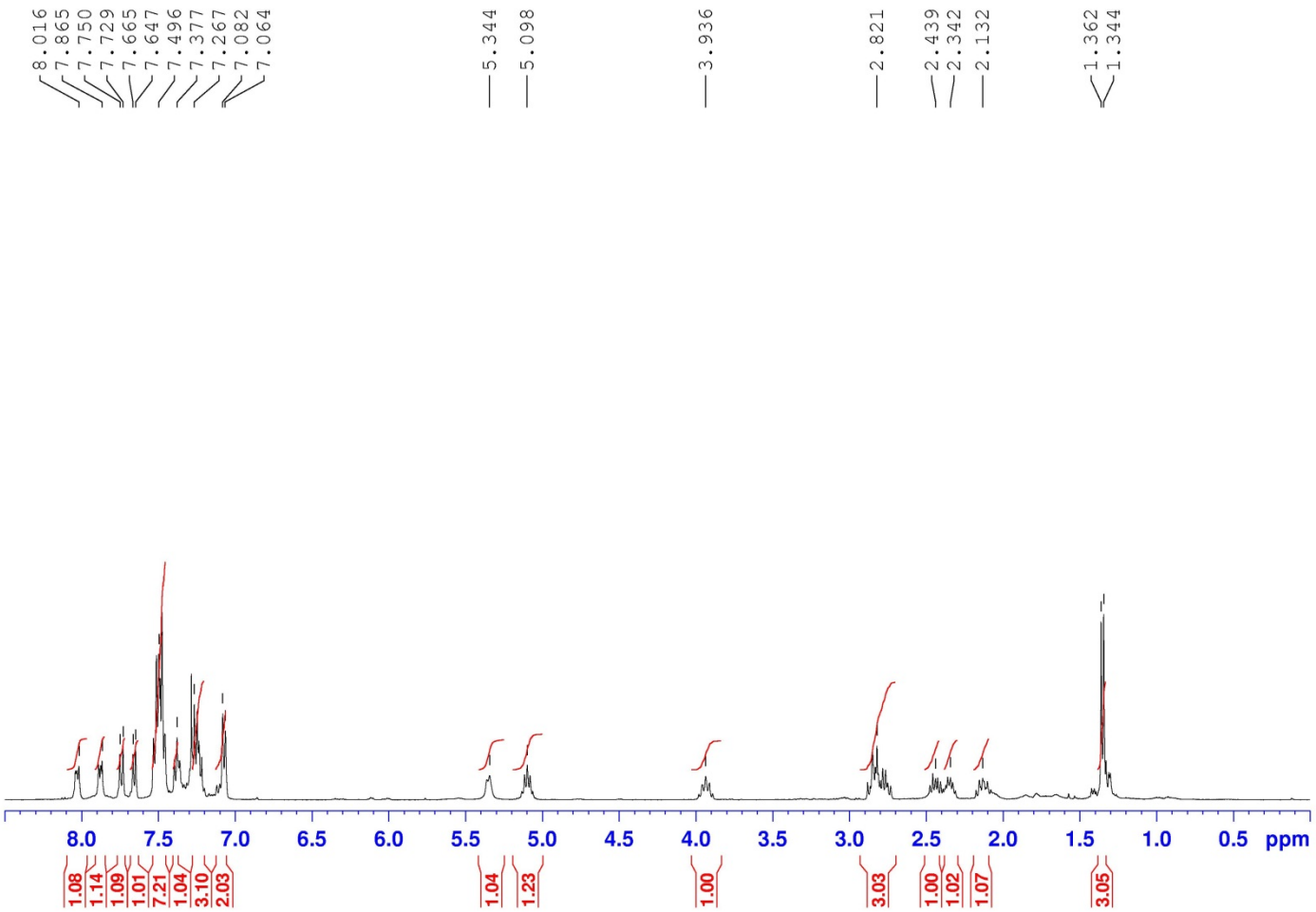


9c

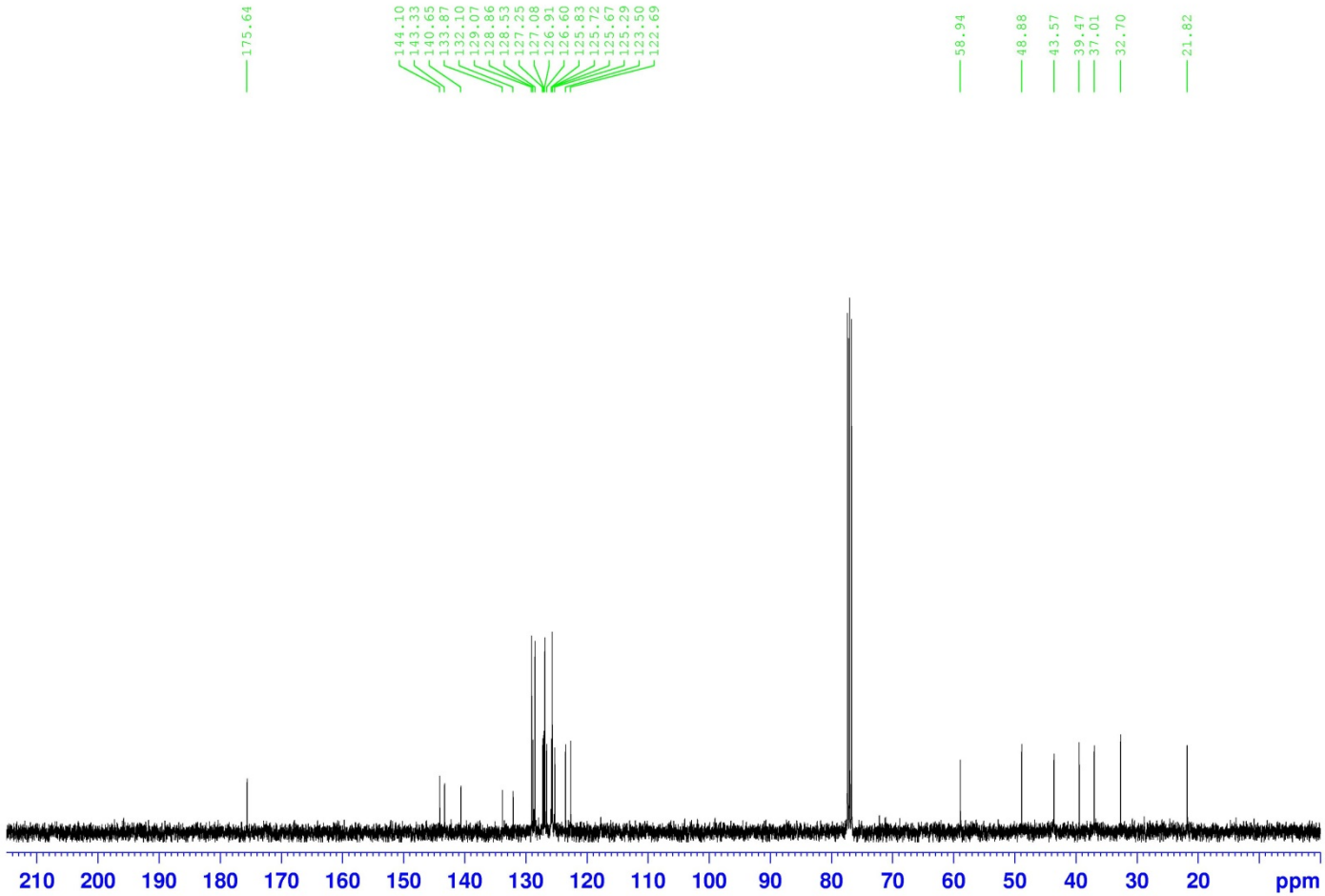
Following the general procedure for Suzuki-Miyaura cross-coupling reaction affords, after flash chromatography on silica gel (90:10–85:15 hexanes:ethyl acetate), the title compound (86%) as a yellow oil.

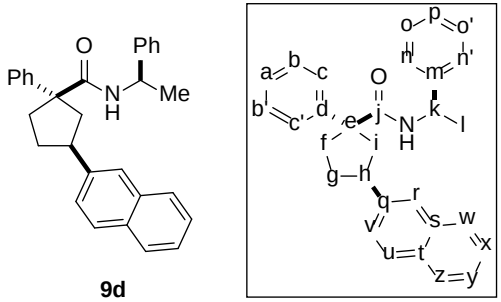
Optical rotation	$[\alpha]_D^{20} = -20^o$ (*c* 1.0, $CHCl_3$)
TLC analysis	R_f 0.6 (70:30 hexanes:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 8.05–8.00 (1H, m, w), 7.90–7.85 (1H, m, z), 7.80–7.70 (1H, m, t), 7.70–7.60 (1H, m, y), 7.55–7.45 (7H, m, a,c,c',n,p,o,o'), 7.40–7.35 (1H, m, s), 7.30–7.20 (3H, m, n',r,x), 7.07 (2H, d, *J* = 6.9 Hz, b.b'), 5.34 (1H, br s, NH), 5.20–5.00 (1H, m, k), 4.00–3.85 (1H, m, h), 2.90–2.70 (3H, m, f,i), 2.50–2.40 (1H, m, f), 2.40–2.30 (1H, m, g), 2.20–2.10 (1H, m, g), 1.35 (3H, d, *J* = 6.9 Hz, l).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 175.63 (j), 144.10 (d), 143.33 (q), 140.65 (m), 133.87 (u), 132.10 (v), 129.07 (o,o'), 128.86 (z), 128.53 (b,b'), 127.25 (s), 127.08 (n,n'), 126.91 (c,c'), 126.60 (t), 125.83 (p), 125.72 (x), 125.67 (a), 125.29 (r), 123.50 (w), 122.69 (y), 58.94 (e), 48.88 (k), 43.57 (i), 37.47 (h), 37.01 (f), 32.71 (g), 21.82 (l).
IR (neat)	3337 (N-H stretch), 3053, 2923, 1644 (C=O stretch), 1597 (C=C stretch), 1493 (N-H bend), 1445, 796, 777, 732, 696 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{30}H_{29}NaNO$ (M+Na): 442.2147, found 442.2151 *m/z*.

^{1}H NMR of 9c


8.016
7.865
7.750
7.729
7.665
7.647
7.496
7.377
7.267
7.082
7.064
5.344
5.098
3.936
2.821
2.439
2.342
2.132
1.362
1.344
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.08
1.14
1.09
1.01
7.21
1.04
3.10
2.03
1.04
1.23
1.00
3.03
1.00
1.02
1.07
3.05

^{13}C NMR of 9c


175.64
144.10
143.33
140.65
133.87
132.10
129.07
128.86
128.53
127.25
127.08
126.91
126.60
125.83
125.72
125.67
125.29
123.50
122.69
58.94
48.88
43.57
39.47
37.01
32.70
21.82
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

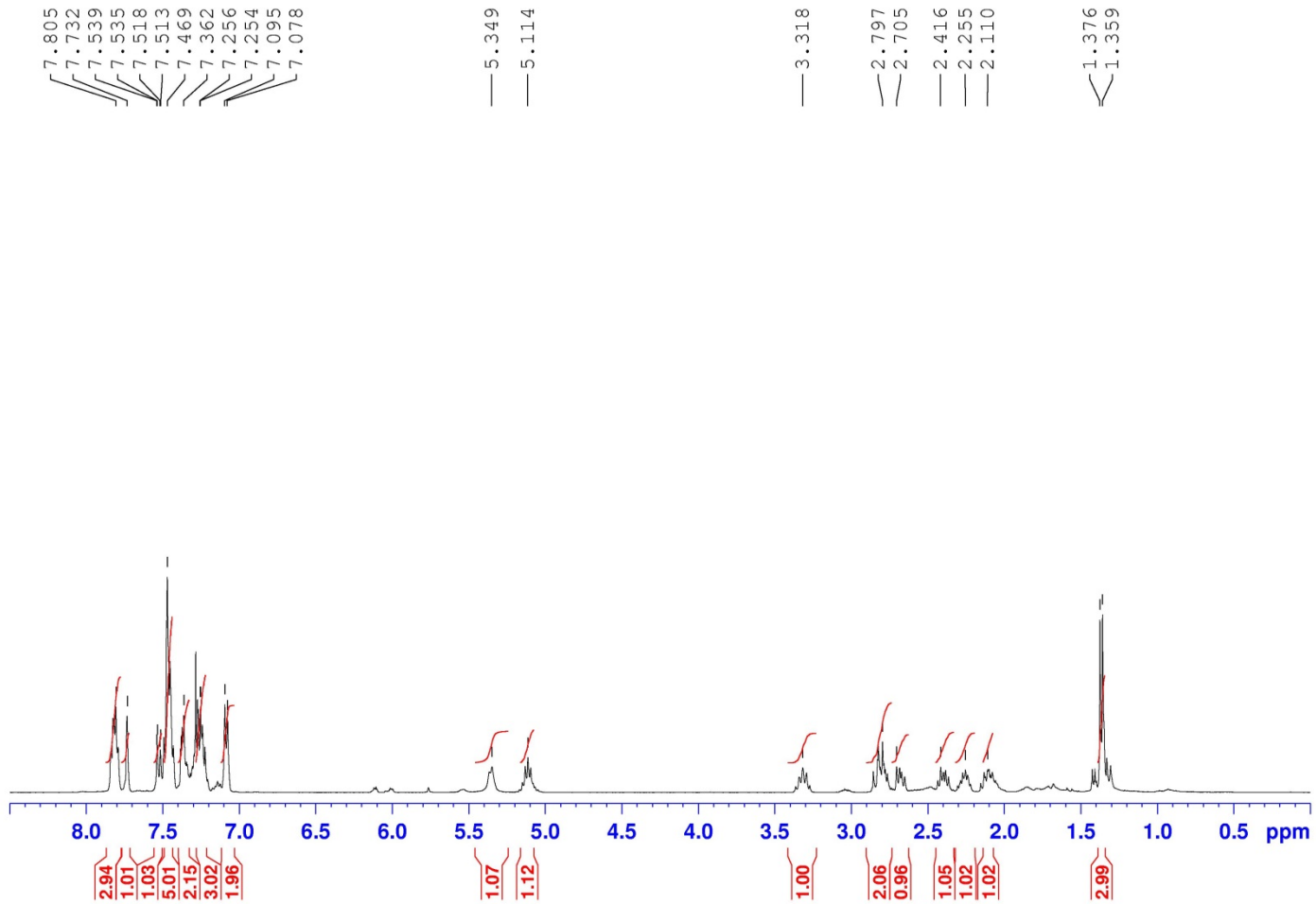


9d

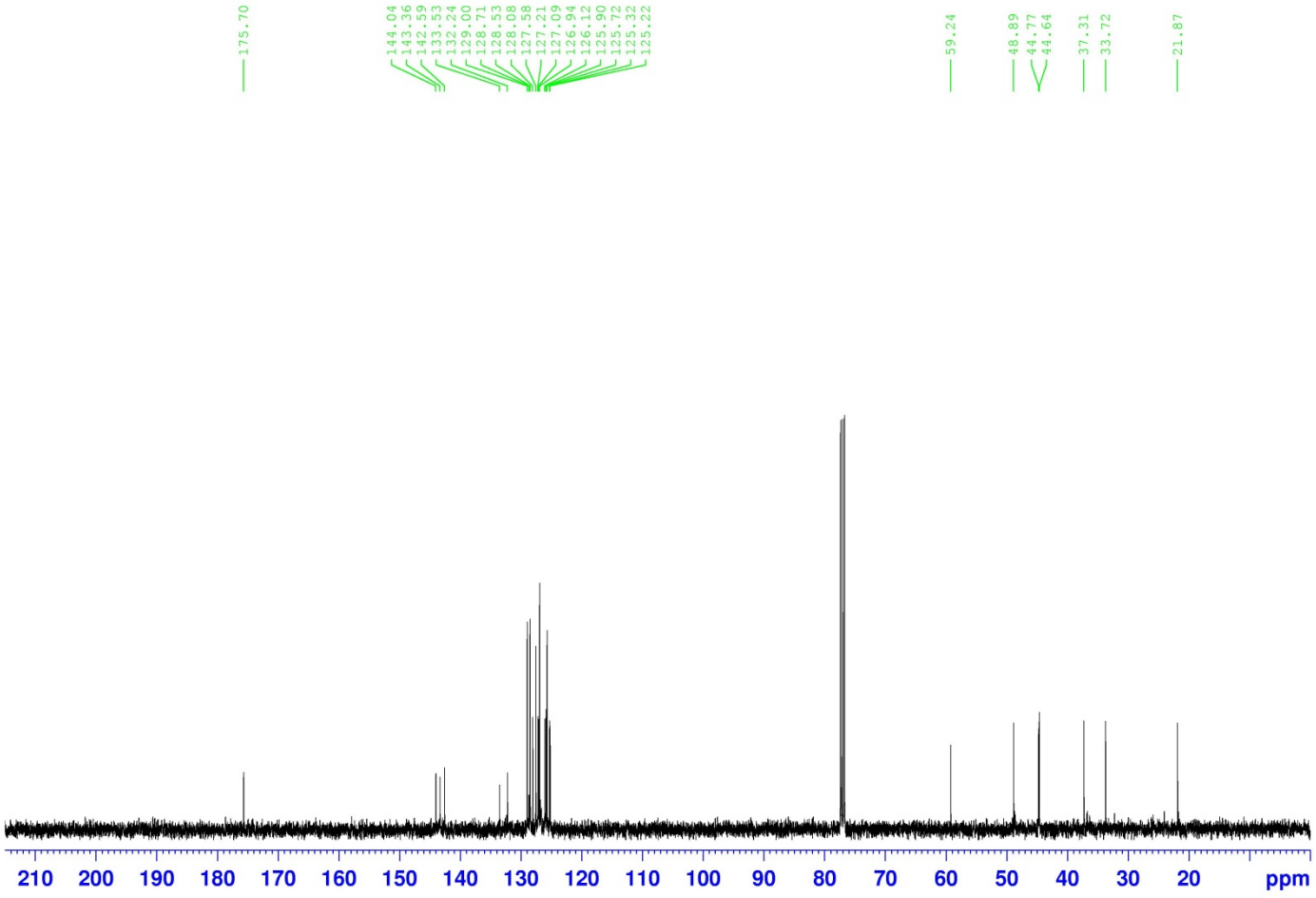
Following the general procedure for Suzuki-Miyaura cross-coupling reaction affords, after flash chromatography on silica gel (90:10–85:15 hexanes:ethyl acetate), the title compound (66%) as a yellow oil.

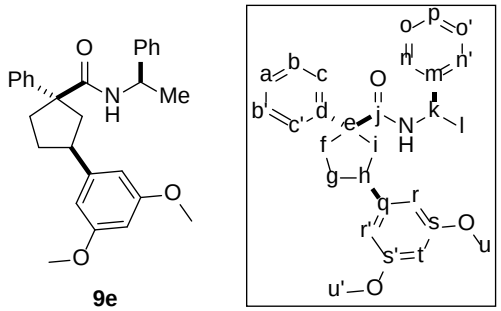
Optical rotation	$[\alpha]_D^{20} = +48^o$ (*c* 1.1, $CHCl_3$)
TLC analysis	R_f 0.6 (70:30 hexanes:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 7.90–7.75 (3H, m, w,z,u), 7.75–7.70 (1H, m, r), 7.55–7.50 (1H, m, x), 7.50–7.40 (5H, m, c,c',o,o',y), 7.40–7.30 (2H, m, n,n'), 7.30–7.20 (3H, m, a,p,v), 7.09 (2H, d, *J* = 6.8 Hz, b.b'), 5.35 (1H, br s, NH), 5.15–5.05 (1H, m, k), 3.40–3.20 (1H, m, h), 2.90–2.75 (2H, m, f,i), 2.75–2.65 (1H, m, i), 2.45–2.35 (1H, m, f), 2.35–2.20 (1H, m, g), 2.15–2.05 (1H, m, g), 1.37 (3H, d, *J* = 6.9 Hz, l).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 175.70 (j), 144.04 (d), 143.36 (q), 142.59 (m), 133.53 (s), 132.24 (t), 129.00 (o,o'), 128.71 (b,b'), 128.53 (z), 128.08 (w), 127.58 (u), 127.21 (n,n'), 127.09 (c,c'), 126.94 (p), 126.12 (x), 125.90 (a), 125.72 (v), 125.32 (y), 125.22 (r), 59.24 (e), 48.89 (k), 44.77 (i), 44.64 (h), 37.30 (f), 33.72 (g), 21.87 (l).
IR (neat)	3325 (N-H stretch), 2920, 1708 (C=O stretch), 1644 (C=C stretch), 1598 (N-H bend), 1493, 1446, 888, 857, 817, 745, 696 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{30}H_{29}NaNO$ (M+Na): 442.2147, found 442.2151 *m/z*.

^{1}H NMR of 9d


7.805
7.732
7.539
7.535
7.518
7.513
7.469
7.362
7.256
7.254
7.095
7.078
5.349
5.114
3.318
2.797
2.705
2.416
2.255
2.110
1.376
1.359
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.94
1.01
1.03
5.01
2.15
3.02
1.96
1.07
1.12
1.00
2.06
0.96
1.05
1.02
1.02
2.99

^{13}C NMR of 9d


175.70
144.04
143.36
142.59
133.53
132.24
129.00
128.71
128.53
128.08
127.58
127.21
127.09
126.94
126.12
125.90
125.72
125.32
125.22
59.24
48.89
44.77
44.64
37.31
33.72
21.87
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

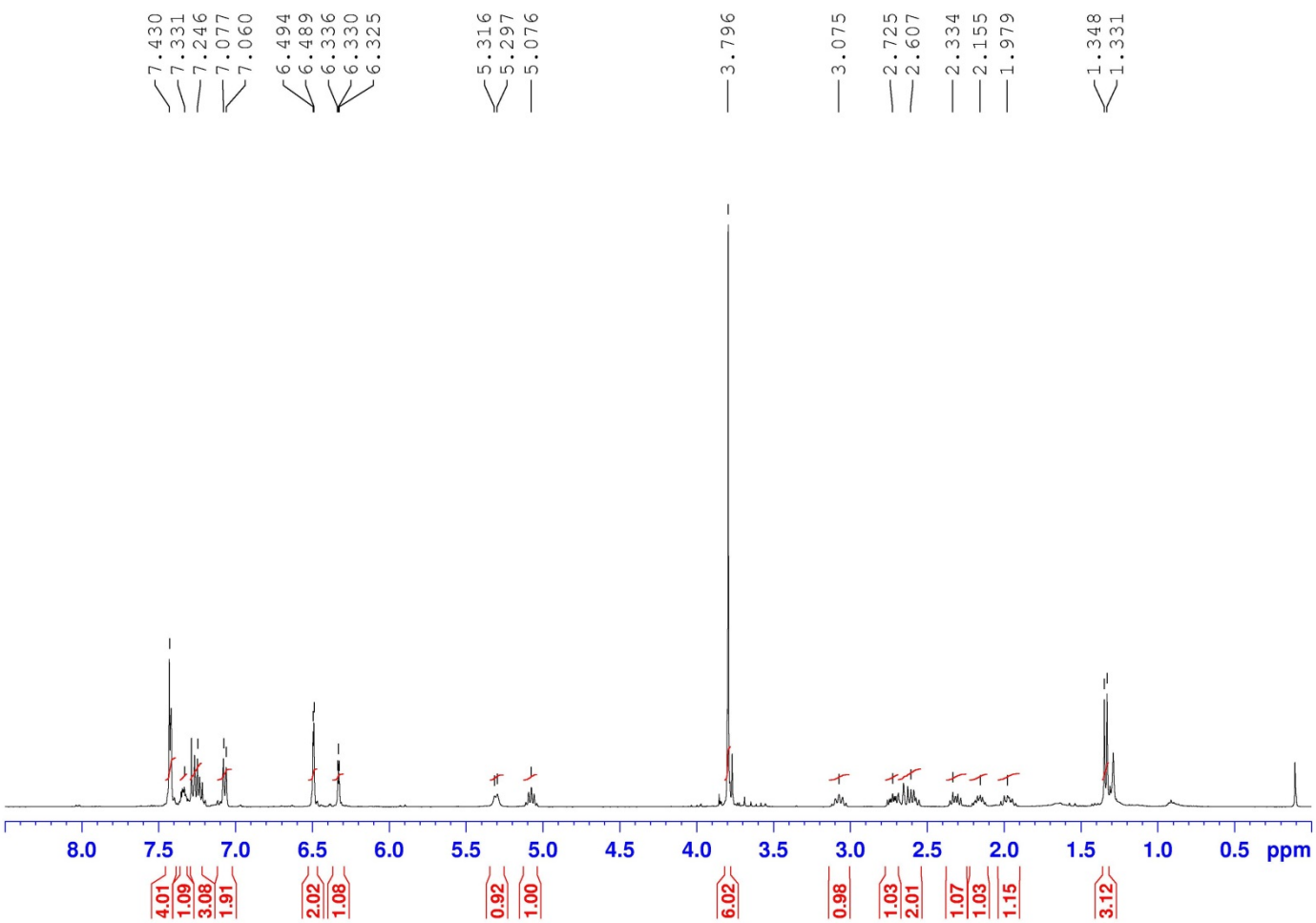


9e

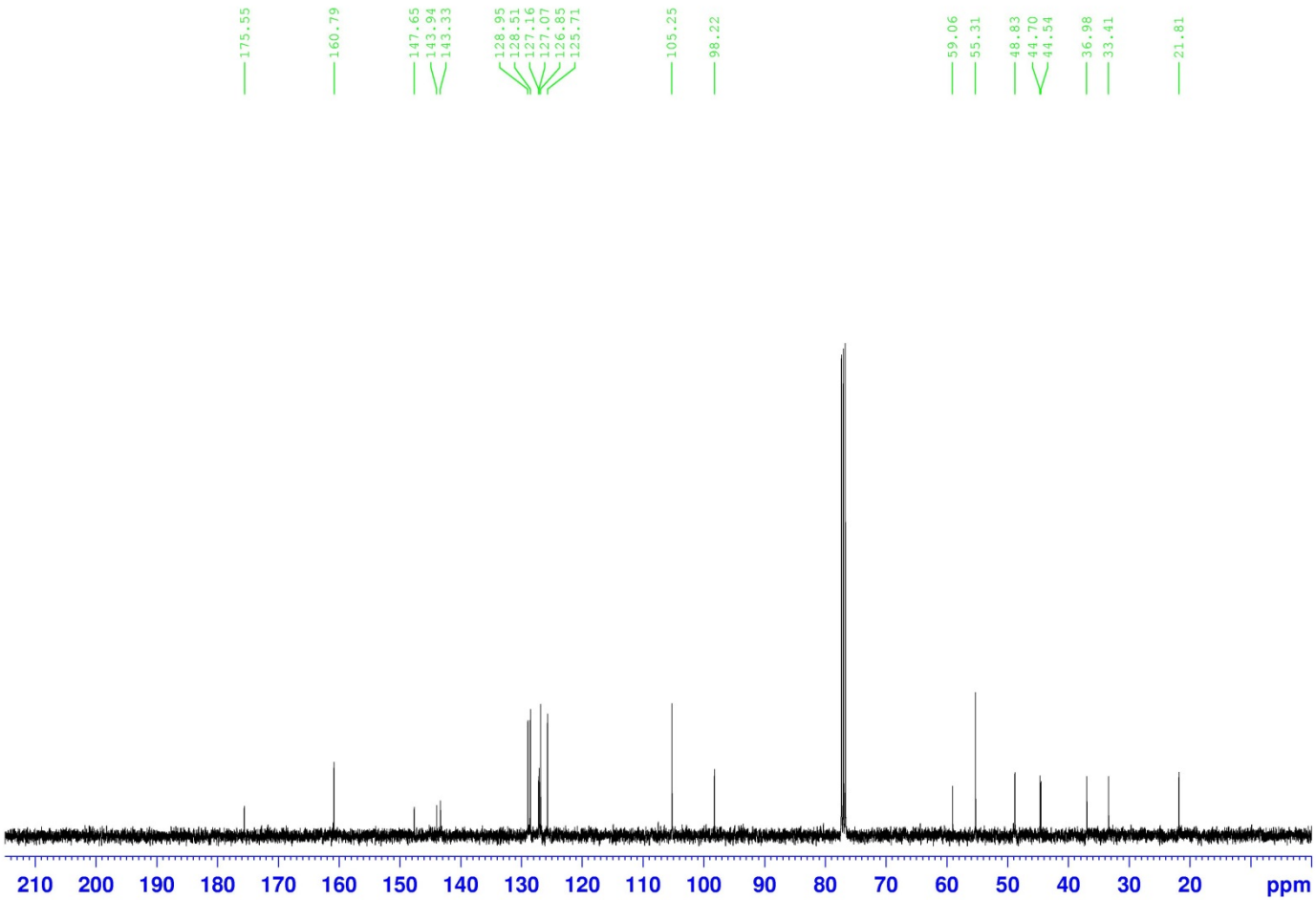
Following the general procedure for Suzuki-Miyaura cross-coupling reaction affords, after flash chromatography on silica gel (90:10–85:15 hexanes:ethyl acetate), the title compound (66%) as a yellow oil.

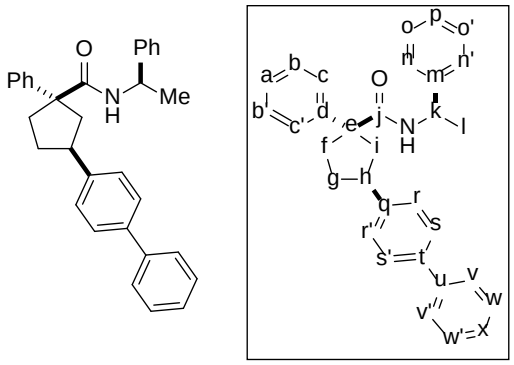
Optical rotation	$[\alpha]_D^{20} = +15^o$ (*c* 0.8, $CHCl_3$)
TLC analysis	R_f 0.5 (70:30 hexanes:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 7.45–7.40 (4H, m, o,o',c,c'), 7.35–7.30 (1H, m, p), 7.30–7.20 (3H, m, a,n,n'), 7.07 (2H, d, *J* = 6.8 Hz, b,b'), 6.49 (2H, d, *J* = 2.1 Hz, r,r'), 6.33 (1H, t, *J* = 2.2 Hz, t), 5.30 (1H, d, *J* = 7.5 Hz, NH), 5.20–5.00 (1H, m, k), 3.80 (6H, s, u,u'), 3.15–3.00 (1H, m, h), 2.80–2.70 (1H, m, f), 2.70–2.55 (2H, m, i), 2.40–2.25 (1H, m, f), 2.25–2.10 (1H, m, g), 2.05–1.90 (1H, m, g), 1.34 (3H, d, *J* = 6.9 Hz, l).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 175.55 (j), 160.79 (s,s'), 147.65 (q), 143.94 (d), 143.33 (m), 128.95 (o,o'), 128.51 (n,n'), 127.16 (p), 127.07 (a), 126.85 (c,c'), 125.71 (b,b'), 105.25 (r,r'), 98.22 (t), 59.06 (e), 55.31 (u,u'), 48.83 (k), 44.70 (h), 44.54 (i), 36.98 (f), 33.41 (g), 21.81 (l).
IR (neat)	3348 (N-H stretch), 2930, 1654 (C=O stretch), 1593 (C=C stretch), 1493 (N-H bend), 1451, 1427, 1203, 1149, 1059, 924. 831, 733, 697 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{28}H_{31}NaNO_3$ (M+Na): 452.2202, found 452.2195 *m/z*.

^{1}H NMR of 9e


7.430
7.331
7.246
7.077
7.060
6.494
6.489
6.336
6.330
6.325
5.316
5.297
5.076
3.796
3.075
2.725
2.607
2.334
2.155
1.979
1.348
1.331
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
4.01
1.09
3.08
1.91
2.02
1.08
0.92
1.00
6.02
0.98
1.03
2.01
1.07
1.03
1.15
3.12

^{13}C NMR of 9e


175.55
160.79
147.65
143.94
143.33
128.95
128.51
127.16
127.07
126.85
125.71
105.25
98.22
59.06
55.31
48.83
44.70
44.54
36.98
33.41
21.81
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

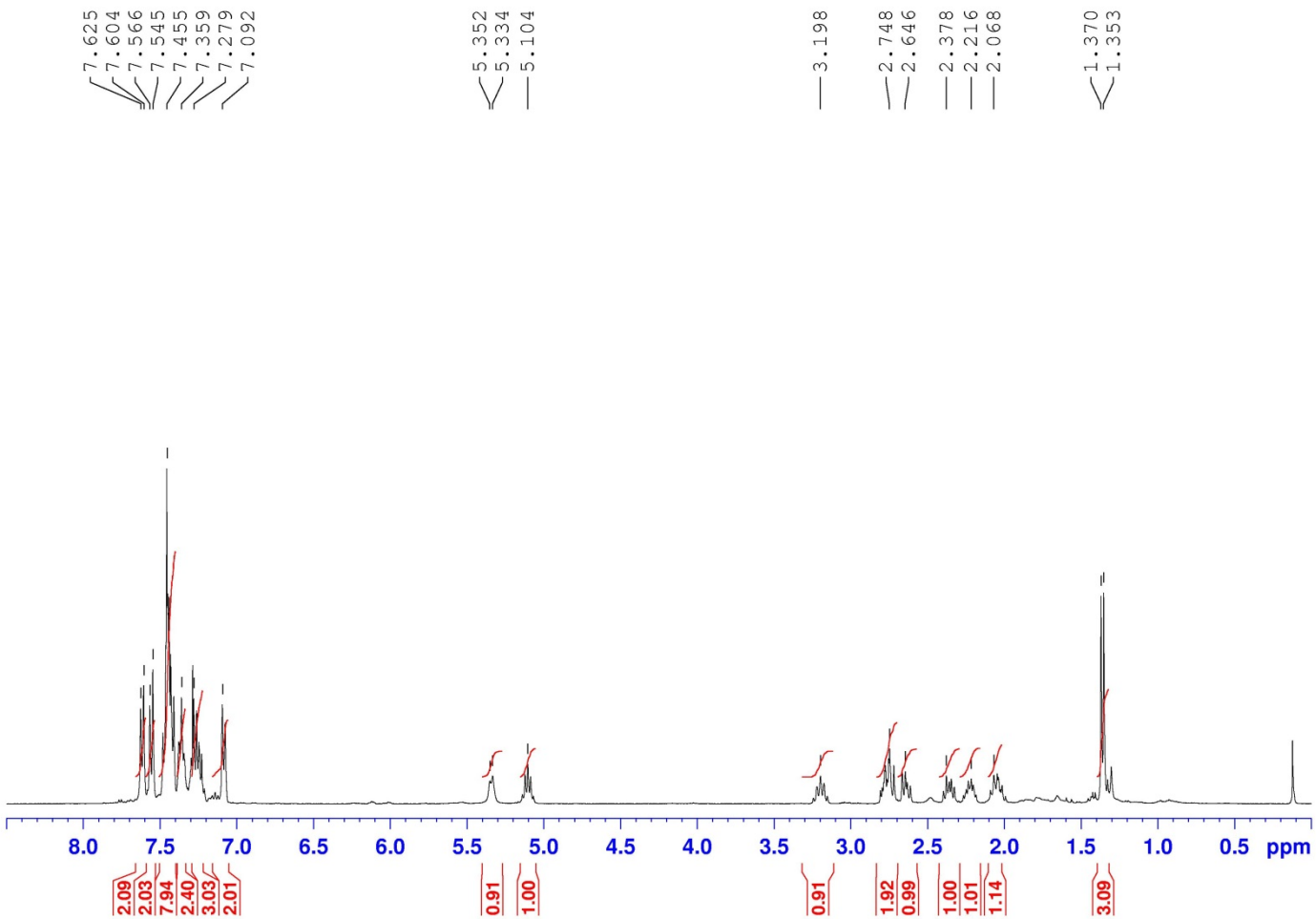


9f

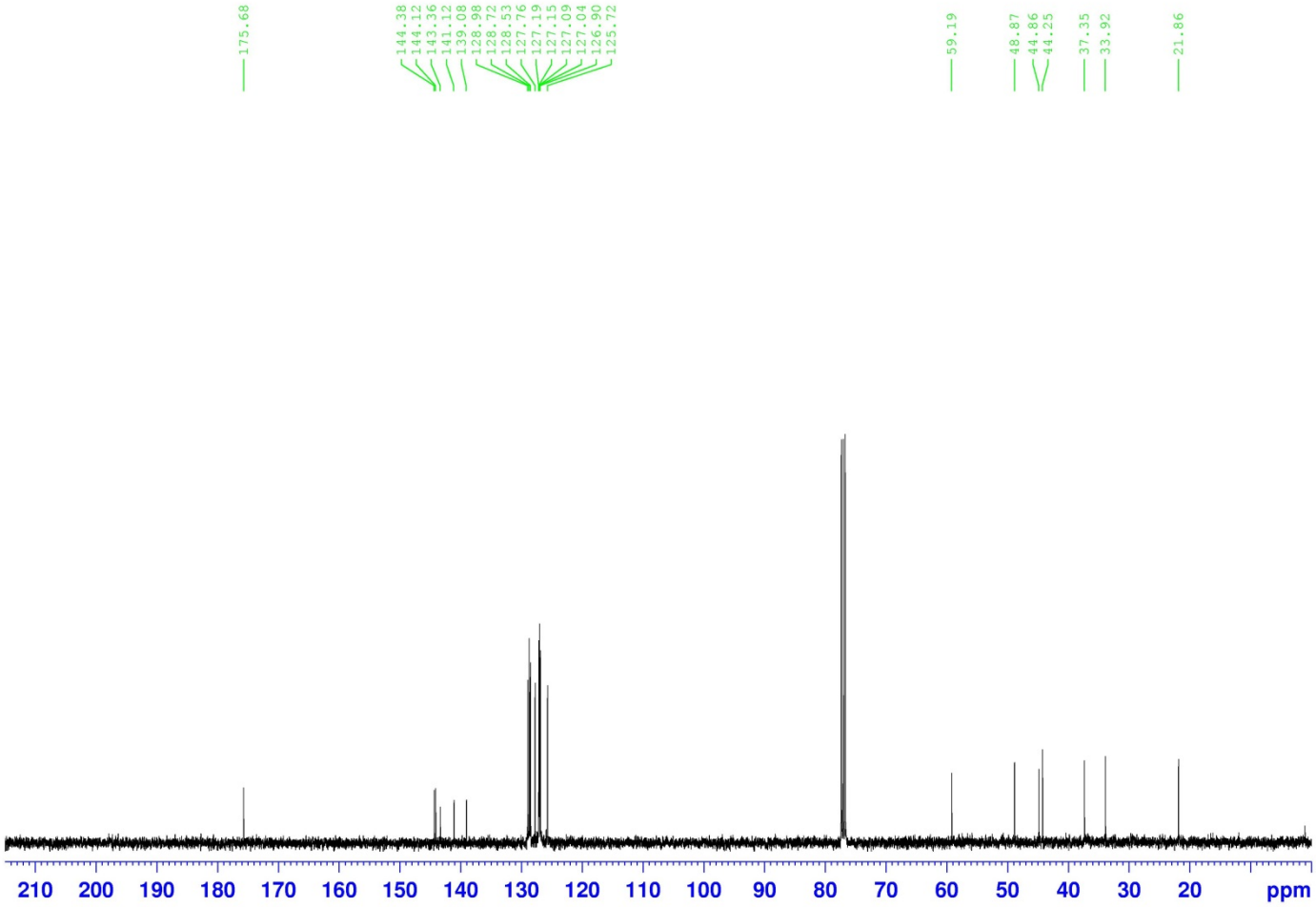
Following the general procedure for Suzuki-Miyaura cross-coupling reaction affords, after flash chromatography on silica gel (90:10–85:15 hexanes:ethyl acetate), the title compound (71%) as a yellow oil.

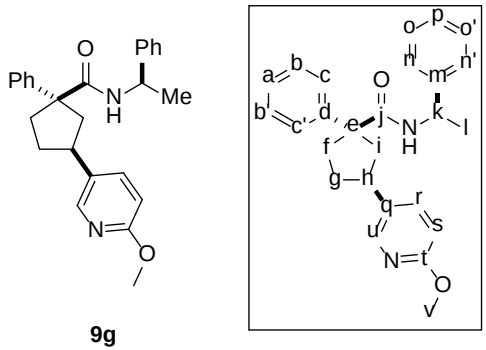
Optical rotation	$[\alpha]_D^{20} = +49^o$ (*c* 1.0, $CHCl_3$)
TLC analysis	R_f 0.6 (70:30 hexanes:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 7.61 (2H, d, *J* = 8.1 Hz, v,v'), 7.56 (2H, d, *J* = 8.2 Hz, s,s'), 7.50–7.40 (8H, m, b,b'c,c',r,r',w,w'), 7.40–7.30 (2H, m, n,n'), 7.30–7.20 (3H, m, o,o',x), 7.10–7.00 (2H, m, a,p), 5.34 (3H, d, *J* = 7.3 Hz, NH), 5.15–5.05 (1H, m, k), 3.25–3.10 (1H, m, h), 2.80–2.70 (2H, m, f,i), 2.70–2.60 (1H, m, i), 2.40–2.30 (1H, m, f), 2.30–2.15 (1H, m, g), 2.10–2.00 (1H, m, g), 1.36 (3H, d, *J* = 6.9 Hz, l).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 175.68 (j), 144.38 (q), 144.12 (d), 143.36 (u), 141.12 (t), 139.08 (m), 128.98 (w,w'), 128.72 (r,r'), 128.53 (b,b'), 127.76 (v,v'), 127.19 (x), 127.15 (s,s'), 127.09 (n,n'), 127.04 (c,c'), 126.90 (p), 125.72 (p,a), 59.19 (e), 48.87 (k), 44.86 (i), 44.25 (h), 37.35 (f), 33.92 (g), 21.86 (l).
IR (neat)	3334 (N-H stretch), 3026, 1651 (C=O stretch), 1598 (C=C stretch), 1486 (N-H bend), 1446, 1234, 1073, 837, 761, 732, 695 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{32}H_{31}NaNO$ (M+Na): 468.2303, found 468.2293 *m/z*.

^{1}H NMR of 9f


7.625
7.604
7.566
7.545
7.455
7.359
7.279
7.092
5.352
5.334
5.104
3.198
2.748
2.646
2.378
2.216
2.068
1.370
1.353
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.09
2.03
7.94
2.40
3.03
2.01
0.91
1.00
0.91
1.92
0.99
1.00
1.01
1.14
3.09

^{13}C NMR of 9f


175.68
144.38
144.12
143.36
141.12
139.08
128.98
128.72
128.53
127.76
127.19
127.15
127.09
127.04
126.90
125.72
59.19
48.87
44.86
44.25
37.35
33.92
21.86
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

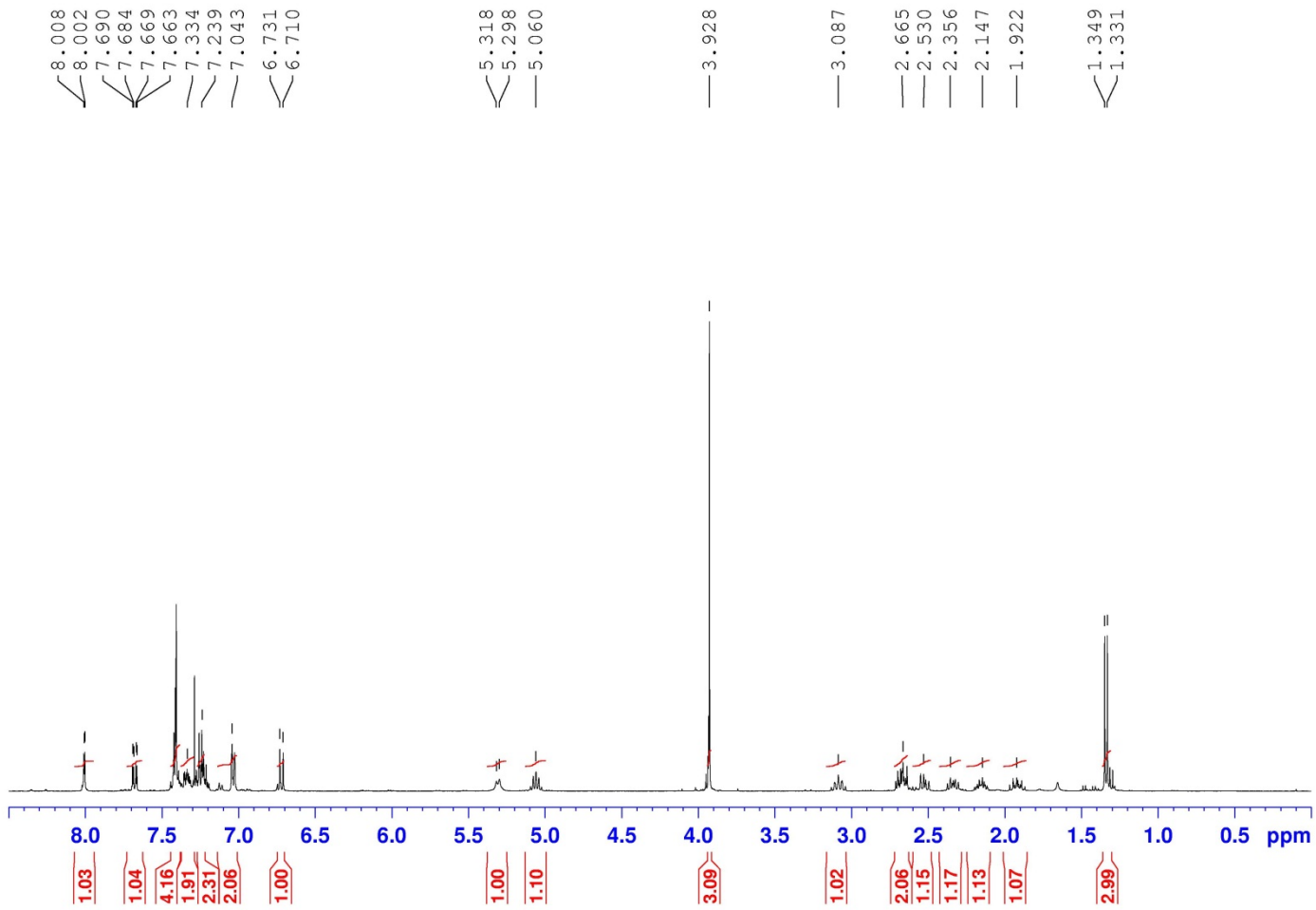


9g

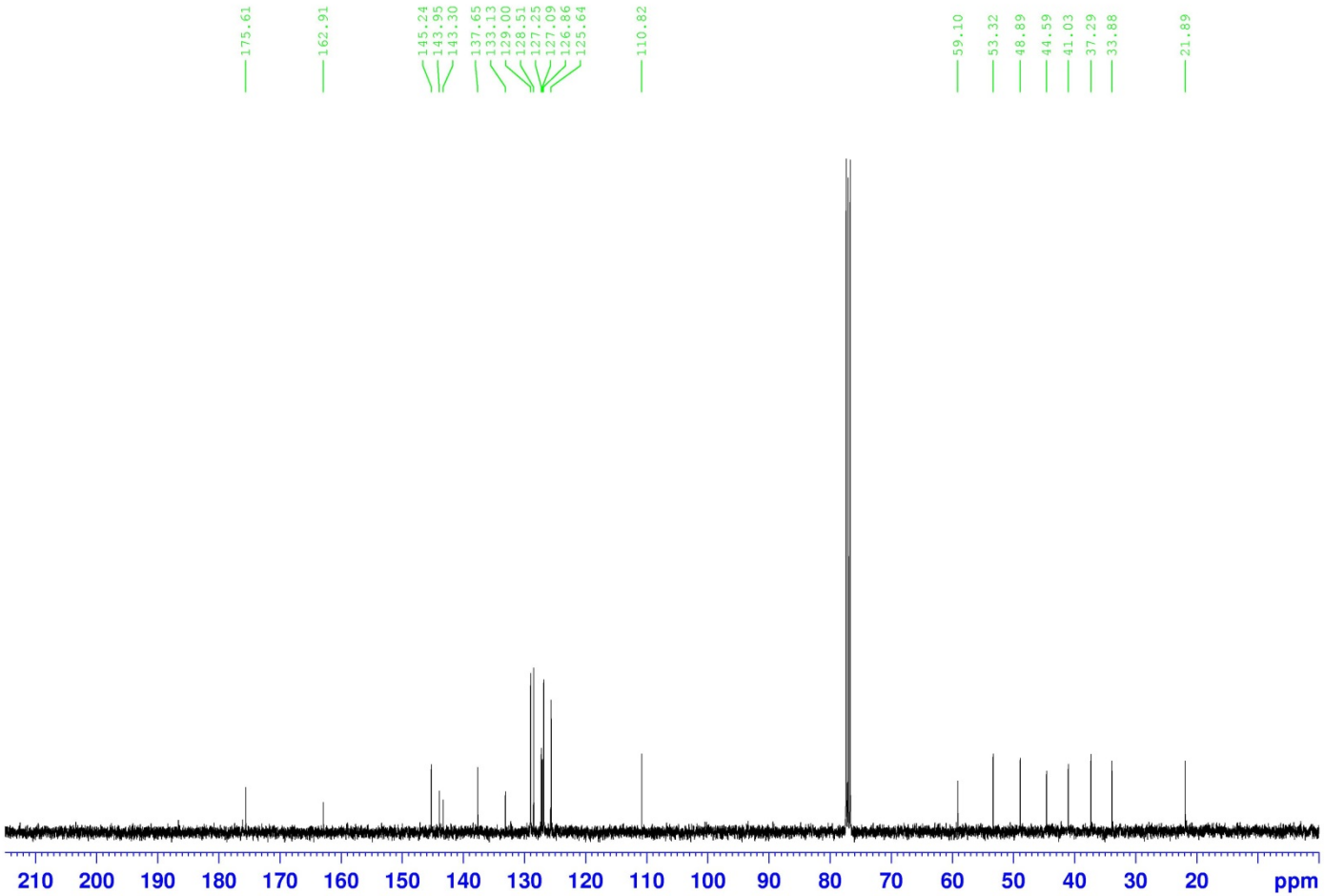
Following the general procedure for Suzuki-Miyaura cross-coupling reaction affords, after flash chromatography on silica gel (85:15 hexanes:ethyl acetate), the title compound (75%) as a yellow oil.

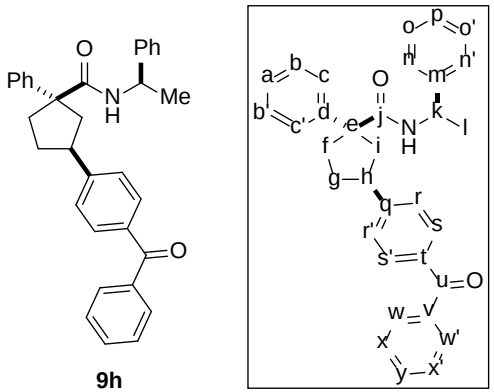
Optical rotation	$[\alpha]_D^{20} = +8.2^o$ (*c* 0.8, $CHCl_3$)
TLC analysis	R_f 0.25 (80:20 hexanes:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 8.00 (1H, d, *J* = 2.4 Hz, u), 7.68 (1H, dd, *J* = 8.6 Hz and 2.4 Hz, r), 7.45–7.40 (4H, m, c,c',o,o'), 7.40–7.30 (2H, m, n,n'), 7.30–7.20 (2H, m, b,b'), 7.10–7.00 (2H, m, a,p), 6.72 (1H, d, *J* = 8.6 Hz, s), 5.33 (1H, d, *J* = 7.8 Hz, NH), 5.15–5.00 (1H, m, k), 3.93 (3H, s, v), 3.15–3.05 (1H, m, h), 2.75–2.65 (2H, m, f,i), 2.60–2.50 (1H, m, i), 2.40–2.30 (1H, m, f), 2.20–2.10 (1H, m, g), 2.00–1.85 (1H, m, g), 1.34 (3H, d, *J* = 6.9 Hz, l).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 175.61 (j), 162.91 (t), 145.24 (u), 143.95 (d), 143.30 (m), 137.65 (r), 133.13 (q), 129.00 (o,o'), 128.51 (b,b'), 127.25 (n,n'), 127.09 (c,c'), 126.86 (p), 125.64 (a), 110.82 (s), 59.10 (e), 53.32 (v), 48.89 (k), 44.59 (i), 41.03 (h), 37.29 (f), 33.88 (g), 21.89 (l).
IR (neat)	3323 (N-H stretch), 2942, 1645 (C=O stretch), 1604 (C=C stretch), 1491 (N-H bend), 1446, 1282, 1252, 1128, 1026, 829, 760, 697 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{26}H_{28}NaN_2O_2$ (M+Na): 423.2048, found 423.2033 *m/z*.

^{1}H NMR of 9g


8.008
8.002
7.690
7.684
7.669
7.663
7.334
7.239
7.043
6.731
6.710
5.318
5.298
5.060
3.928
3.087
2.665
2.530
2.356
2.147
1.922
1.349
1.331
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.03
1.04
4.16
1.91
2.31
2.06
1.00
1.00
1.10
3.09
1.02
2.06
1.15
1.17
1.13
1.07
2.99

^{13}C NMR of 9g


175.61
162.91
145.24
143.95
143.30
137.65
133.13
129.00
128.51
127.25
127.09
126.86
125.64
110.82
59.10
53.32
48.89
44.59
41.03
37.29
33.88
21.89
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

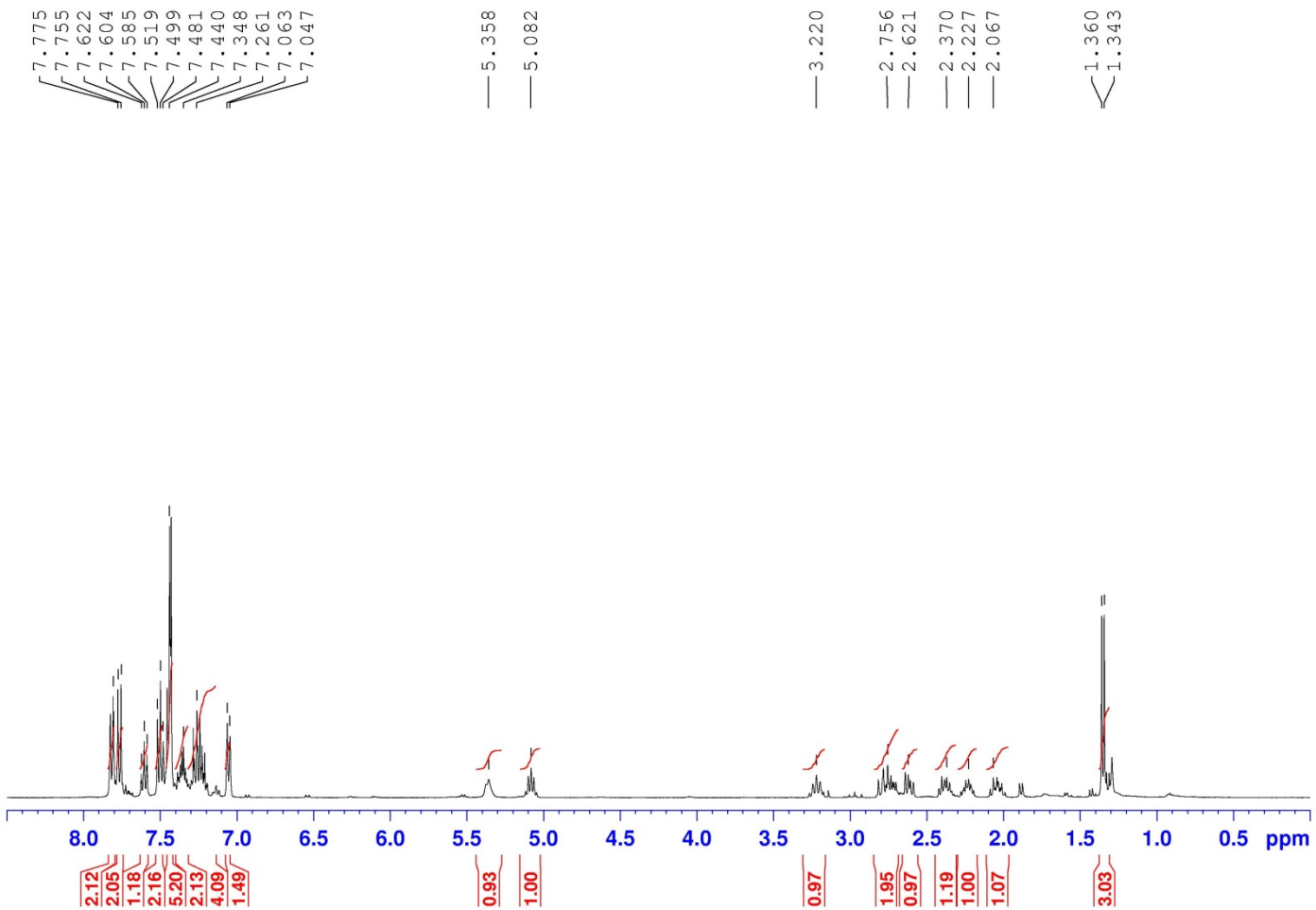


9h

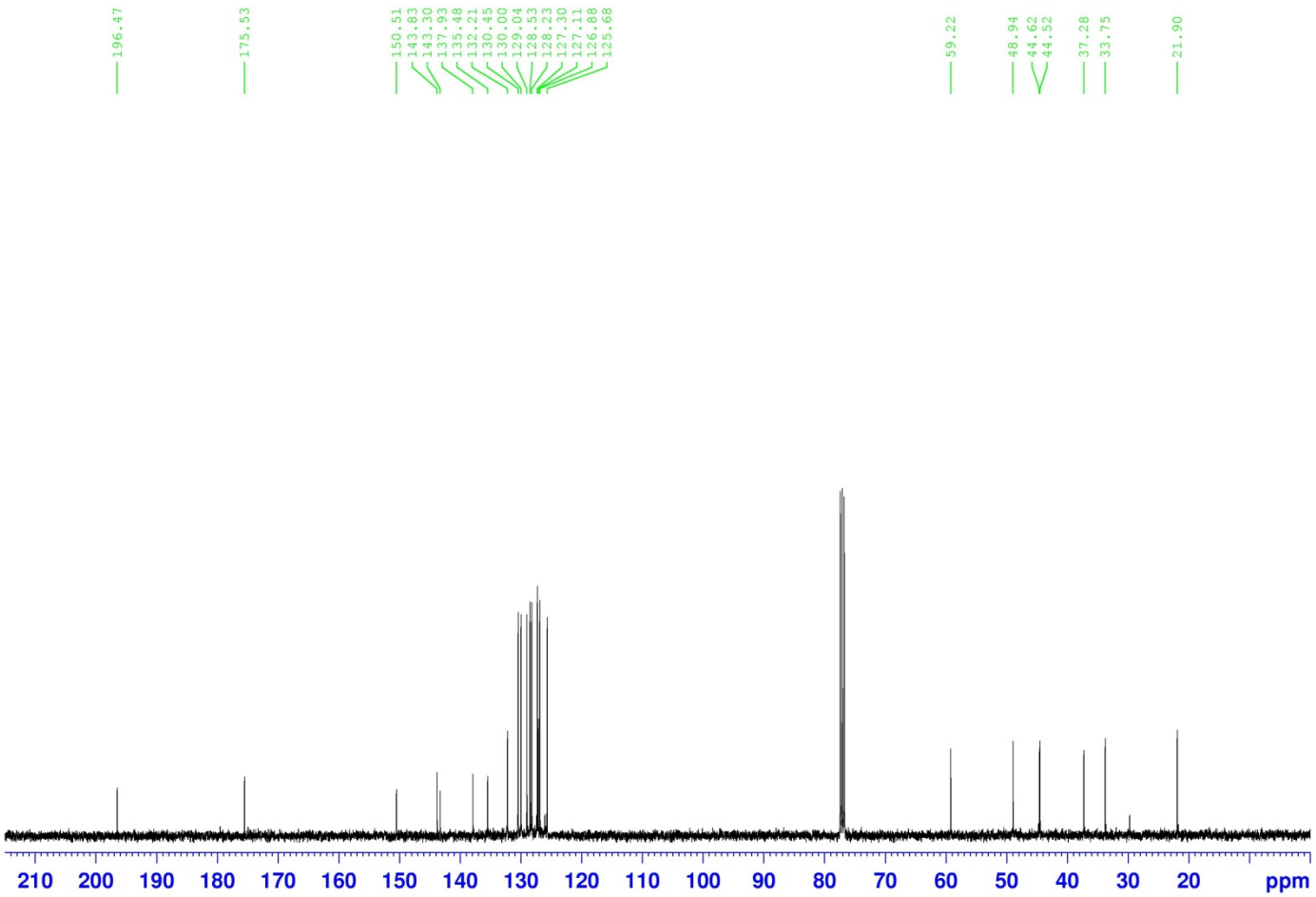
Following the general procedure for Suzuki-Miyaura cross-coupling reaction affords, after flash chromatography on silica gel (90:10–85:15 hexanes:ethyl acetate), the title compound (70%) as a yellow oil.

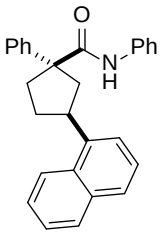
Optical rotation	$[\alpha]_D^{20} = +63^o$ (*c* 1.5, $CHCl_3$)
TLC analysis	R_f 0.5 (70:30 hexanes:ethyl acetate)
^{1}H NMR (400 MHz, $CDCl_3$)	δ 7.85–7.80 (2H, m, s,s'), 7.76 (2H, d, *J* = 8.2 Hz, w,w'), 7.60 (1H, t, *J* = 7.4 Hz, y), 7.50 (2H, t, *J* = 7.7 Hz, b,b'), 7.45–7.40 (5H, m, c,c',o,o',p), 7.40–7.30 (2H, m, n,n'), 7.30–7.15 (4H, m, r,r',x,x'), 7.05 (1H, d, *J* = 6.8 Hz, a), 5.36 (1H, br s, NH), 5.15–5.05 (1H, m, k), 3.30–3.15 (1H, m, h), 2.85–2.70 (2H, m, f,i), 2.65–2.55 (1H, m, i), 2.45–2.30 (1H, m, f), 2.30–2.20 (1H, m, g), 2.10–2.00 (1H, m, g), 1.35 (3H, d, *J* = 6.9 Hz, l).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 196.47 (u), 175.53 (j), 150.51 (q), 143.83 (d), 143.30 (v), 137.93 (t), 135.48 (m), 132.21 (y), 130.45 (w,w'), 130.00 (s,s'), 129.04 (o,o'), 128.53 (x,x'), 128.23 (b,b'), 127.30 (n,n'), 127.11 (c,c'), 126.88 (p), 125.68 (a), 59.22 (e), 48.94 (k), 44.62 (i), 44.52 (h), 37.28 (f), 33.75 (g), 21.90 (l).
IR (neat)	3346 (N-H stretch), 3054, 1651 (C=O stretch), 1598 (C=C stretch), 1493 (N-H bend), 1445, 1315, 1277, 923. 742, 696 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{33}H_{31}NaNO_2$ (M+Na): 496.2252, found 496.2245 *m/z*.

^{1}H NMR of 9h

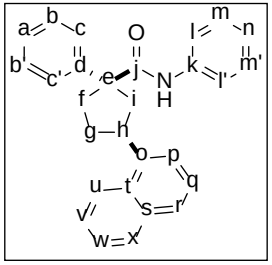

7.775
7.755
7.622
7.604
7.585
7.519
7.499
7.481
7.440
7.348
7.261
7.063
7.047
5.358
5.082
3.220
2.756
2.621
2.370
2.227
2.067
1.360
1.343
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.12
2.05
1.18
2.16
5.20
2.13
4.09
1.49
0.93
1.00
0.97
1.95
0.97
1.19
1.00
1.07
3.03

^{13}C NMR of 9h


196.47
175.53
150.51
143.83
143.30
137.93
135.48
132.21
130.45
130.00
129.04
128.53
128.23
127.30
127.11
126.88
125.68
59.22
48.94
44.62
44.52
37.28
33.75
21.90
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm



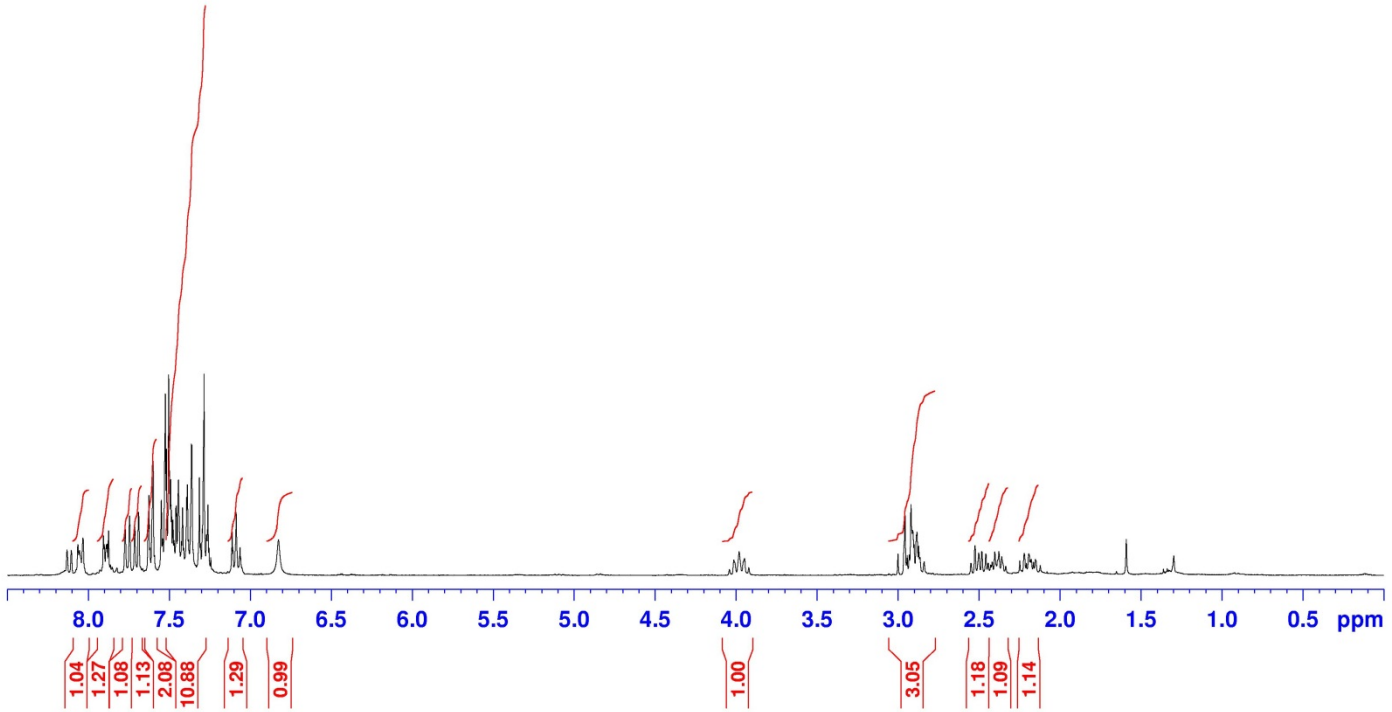
23



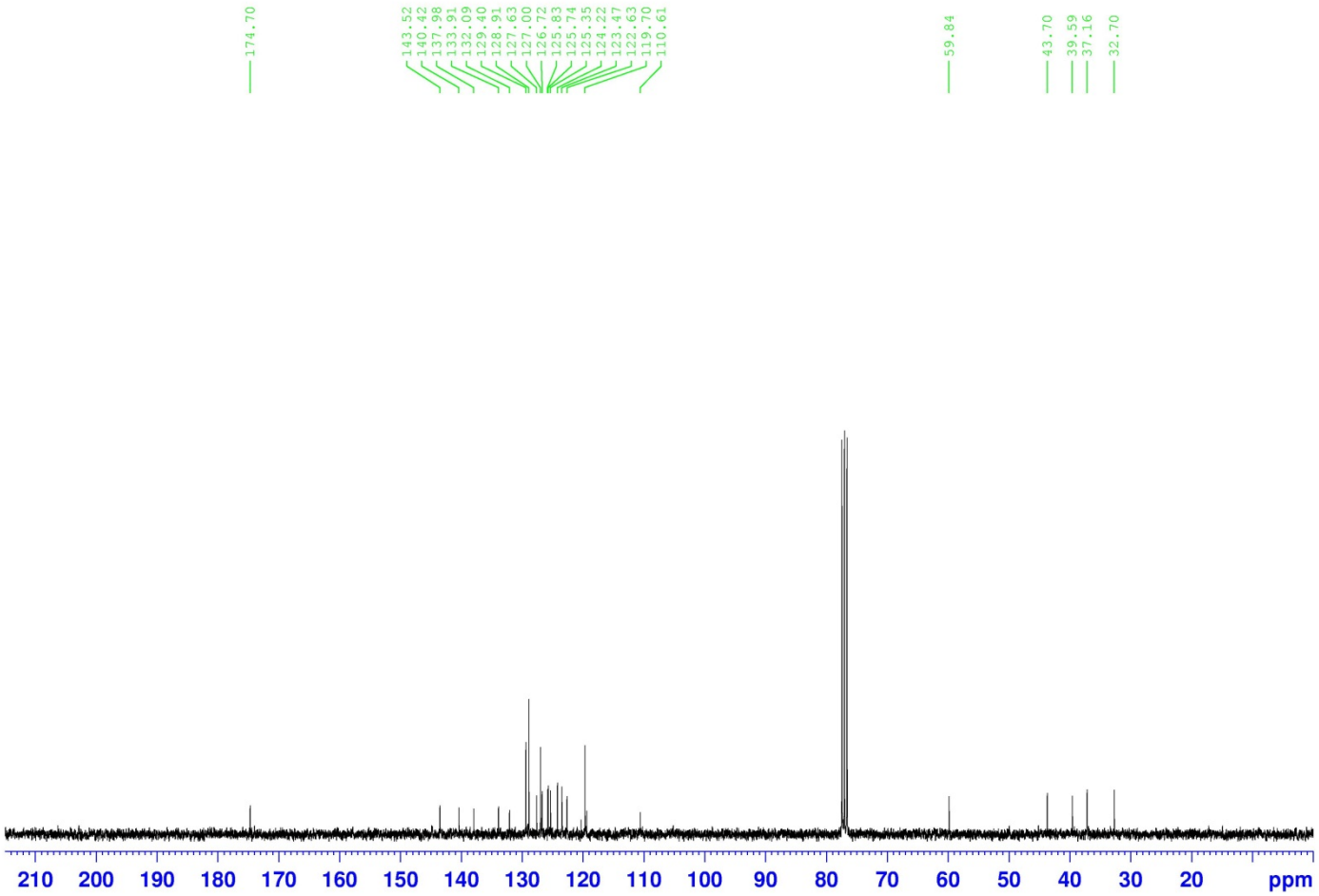
Following the general procedure for Suzuki-Miyaura cross-coupling reaction affords, after flash chromatography on silica gel (90:10 hexanes:ethyl acetate), the title compound (20%) as a yellow oil.

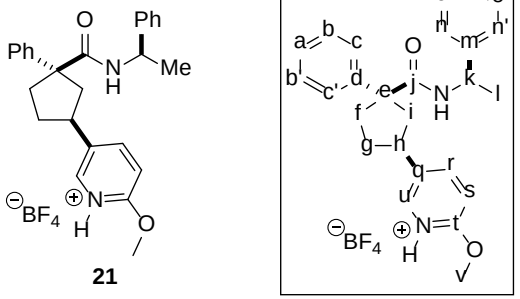
Optical rotation	$[\alpha]_D^{20} = -23^o$ (*c* 1.0, $CHCl_3$)
TLC analysis	R_f = 0.70 (70:30 hexanes:ethyl acetate)
^{1}H NMR (300 MHz, $CDCl_3$)	δ 8.10–8.00 (1H, m, u), 7.95–7.85 (1H, m, x), 7.76 (1H, d, *J* = 8.2 Hz, r), 7.70 (1H, d, *J* = 7.1 Hz, w), 7.65–7.55 (2H, m, b,b'), 7.55–7.25 (10H, m, a,c,c',l,l',m,m',n,q,v), 7.09 (1H, tt, *J* = 7.3 and 1.2 Hz, p), 6.83 (1H, br s, NH), 4.05–3.90 (1H, m, h), 3.00–2.80 (3H, m, i,f), 2.55–2.45 (1H, m, f), 2.45–2.35 (1H, m, g), 2.25–2.15 (1H, m, g).
^{13}C NMR (75 MHz, $CDCl_3$)	δ 174.70 (j), 143.52 (d), 140.42 (o), 137.98 (k), 133.91 (s), 132.09 (t), 129.40 (m,m'), 128.91 (x), 127.63 (n), 127.00 (b,b'), 126.72 (q), 125.83 (c,c'), 125.74 (r), 125.35 (a), 124.22 (v), 123.47 (w), 122.63 (u), 119.70 (p), 110.61 (l,l'), 59.84 (e), 43.70 (i), 39.59 (h), 37.16 (f), 32.70 (g).
IR (neat)	3332 (N-H stretch), 3055, 2948, 1661 (C=O stretch), 1596 (C=C stretch), 1515 (N-H bend), 1498, 1435, 1308, 1240, 905, 777, 751, 691 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{28}H_{25}NaNO$ (M+Na): 414.1834, found 414.1846 *m/z*.

^{1}H NMR of 23


8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
1.04
1.27
1.08
1.13
2.08
10.88
1.29
0.99
1.00
3.05
1.18
1.09
1.14

^{13}C NMR of 23


174.70
143.52
140.42
137.98
133.91
132.09
129.40
128.91
127.63
127.00
126.72
125.83
125.74
125.35
124.22
123.47
122.63
119.70
110.61
59.84
43.70
39.59
37.16
32.70
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

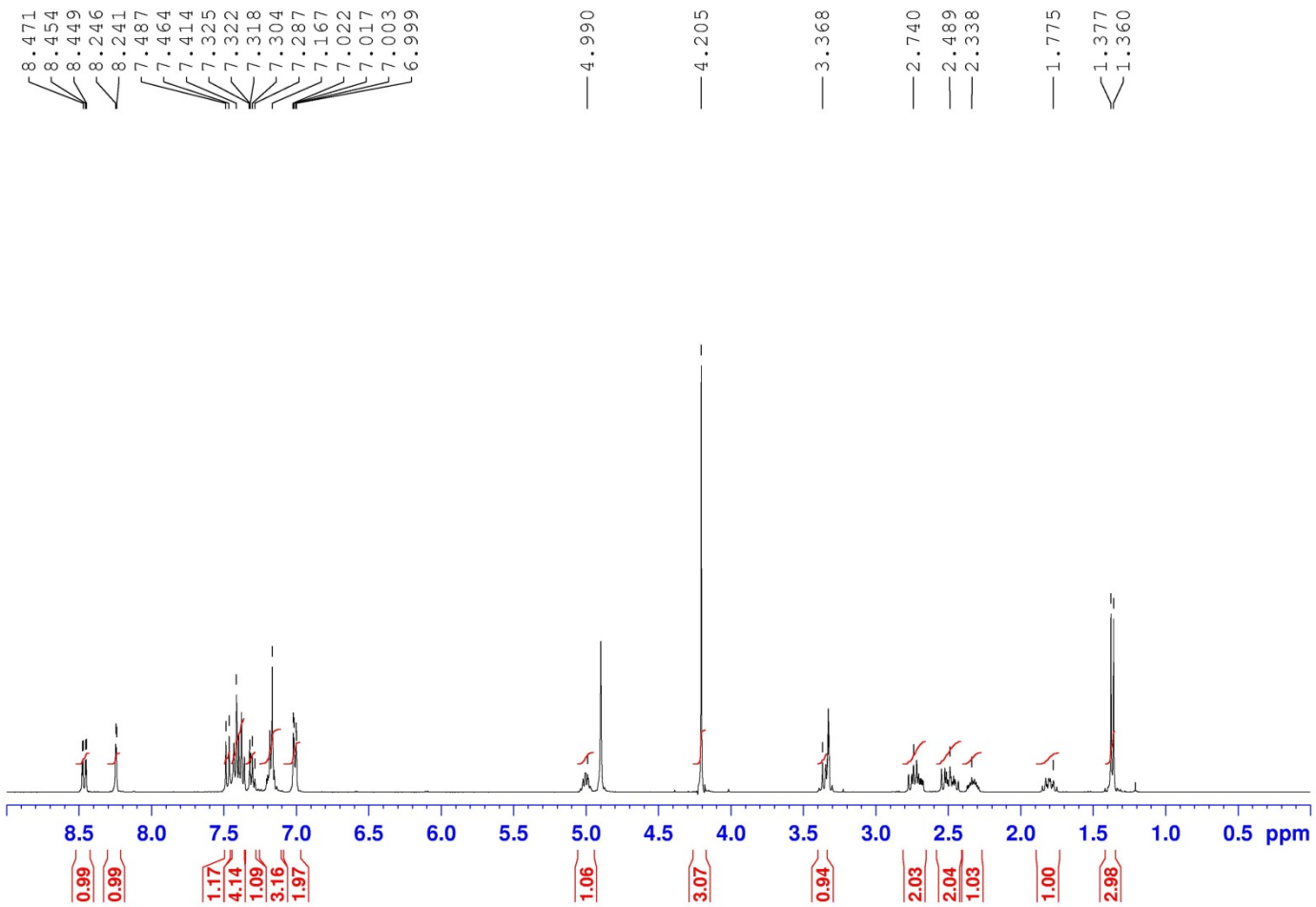


21

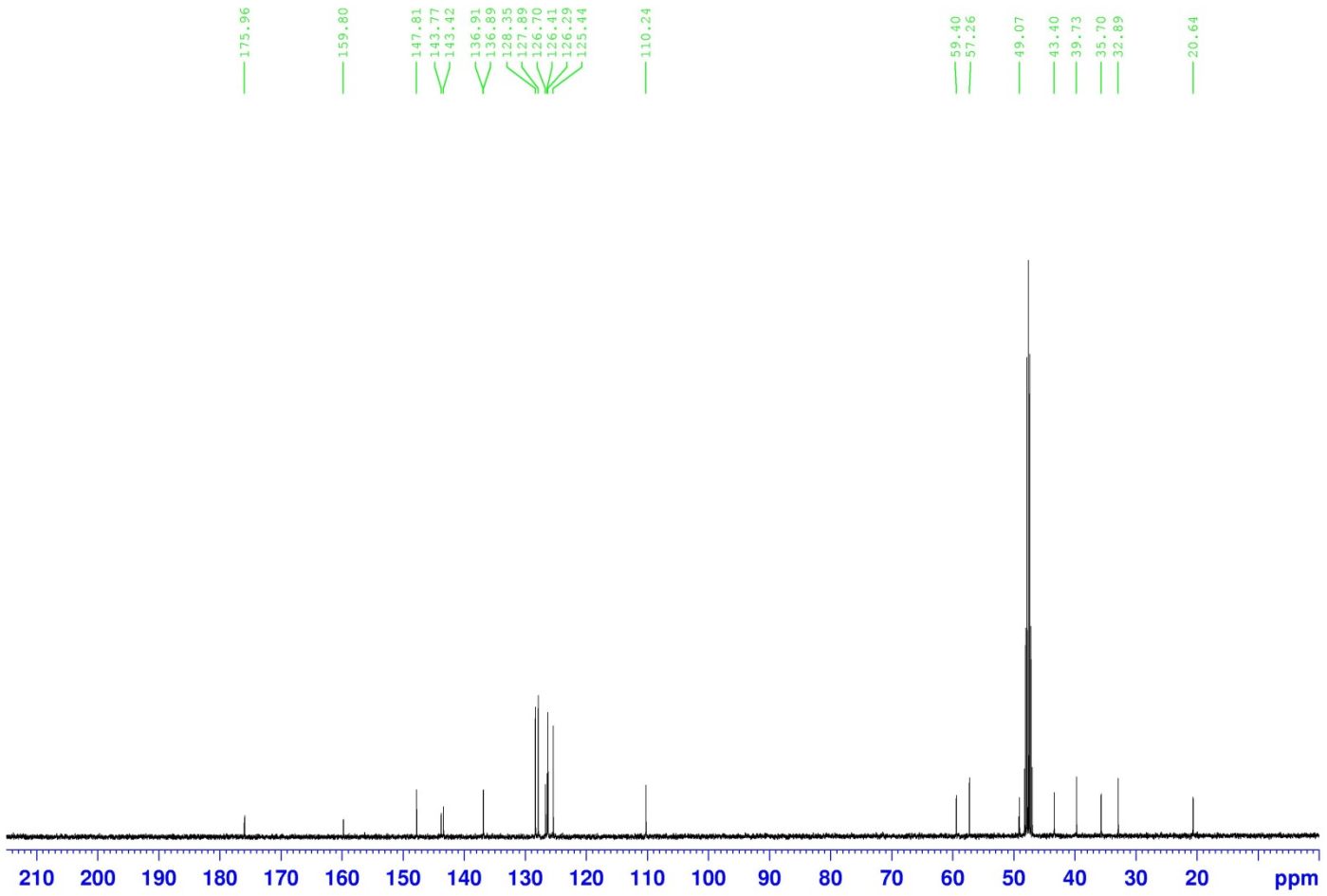
Following the procedure for the preparation of tetrafluoroborate salt of pyridinyl amide **9g** affords a light yellow precipitate (88%) and off-white single crystals (85%) after recrystallization with 5:1 TBME/ MeOH.

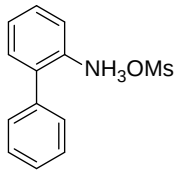
Optical rotation	$[\alpha]_D^{20} = +25^o$ (*c* 1.2, MeOH)
^{1}H NMR (400 MHz, MeOD)	δ 8.46 (1H, dd, *J* = 9.1 and 2.4 Hz, r), 8.24 (1H, d, *J* = 2.1 Hz, u), 7.48 (1H, d, *J* = 9.2 Hz, s), 7.45–7.35 (4H, m, b,b',o,o'), 7.30 (1H, tt, *J* = 7.0 and 1.4 Hz, p), 7.20–7.10 (3H, m, a,b,b'), 7.01 (2H, dd, *J* = 7.8 and 2.1 Hz, n,n'), 5.05–4.95 (1H, m, k), 4.21 (3H, s, v), 3.40–3.30 (1H, m, h), 2.80–2.65 (2H, m, f,i), 2.60–2.40 (2H, m, f,i), 2.40–2.25 (1H, m, g), 1.85–1.75 (1H, m, g), 1.37 (3H, d, *J* = 7.0 Hz, l).
^{13}C NMR (100 MHz, MeOD)	δ 175.96 (j), 159.80 (t), 147.81 (r), 143.77 (d), 143.42 (m), 136.91 (u), 136.89 (q), 128.35 (o,o'), 127.89 (b,b'), 126.70 (p), 126.41 (a), 126.29 (c,c'), 125.44 (n,n'), 110.24 (s), 59.40 (e), 57.26 (v), 49.07 (k), 43.40 (i), 39.73 (h), 35.70 (f), 32.89 (g), 20.64 (l).
IR (neat)	3378 (N-H stretch), 1646 (C=O stretch), 1597 (C=C stretch), 1555, 1529 (N-H bend), 1495, 1444, 1330, 1303, 1060, 1014, 836, 766, 703, 643 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{26}H_{28}NaN_2O_2$ (M-HBF_4+Na): 423.2048, found 423.2044 *m/z*.

^{1}H NMR of 21


8.471
8.454
8.449
8.246
8.241
7.487
7.464
7.414
7.325
7.322
7.318
7.304
7.287
7.167
7.022
7.017
7.003
6.999
4.990
4.205
3.368
2.740
2.489
2.338
1.775
1.377
1.360
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.99
0.99
1.17
4.14
1.09
3.16
1.97
1.06
3.07
0.94
2.03
2.04
1.03
1.00
2.98

^{13}C NMR of 21

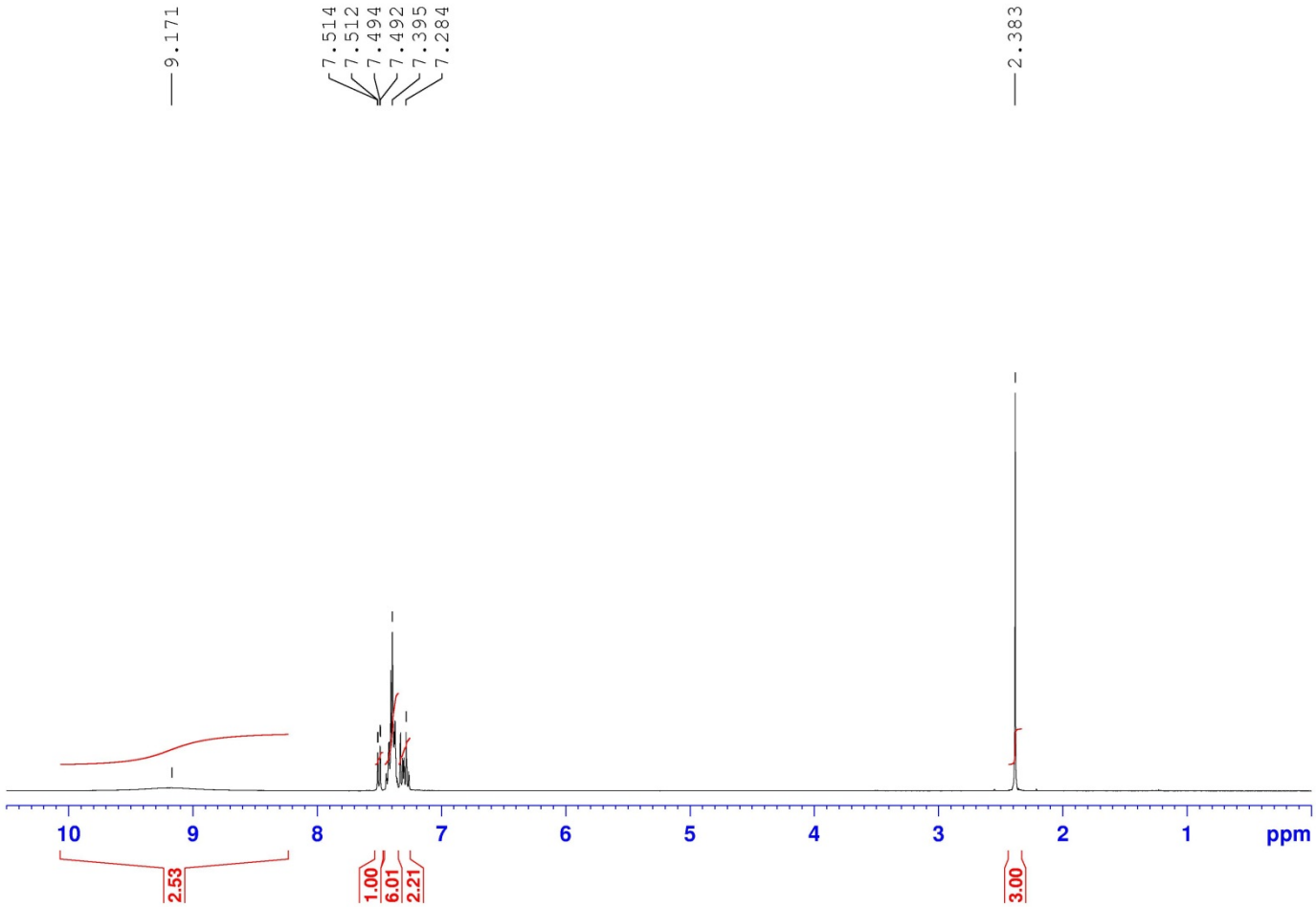

175.96
159.80
147.81
143.77
143.42
136.91
136.89
128.35
127.89
126.70
126.41
126.29
125.44
110.24
59.40
57.26
49.07
43.40
39.73
35.70
32.89
20.64
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm



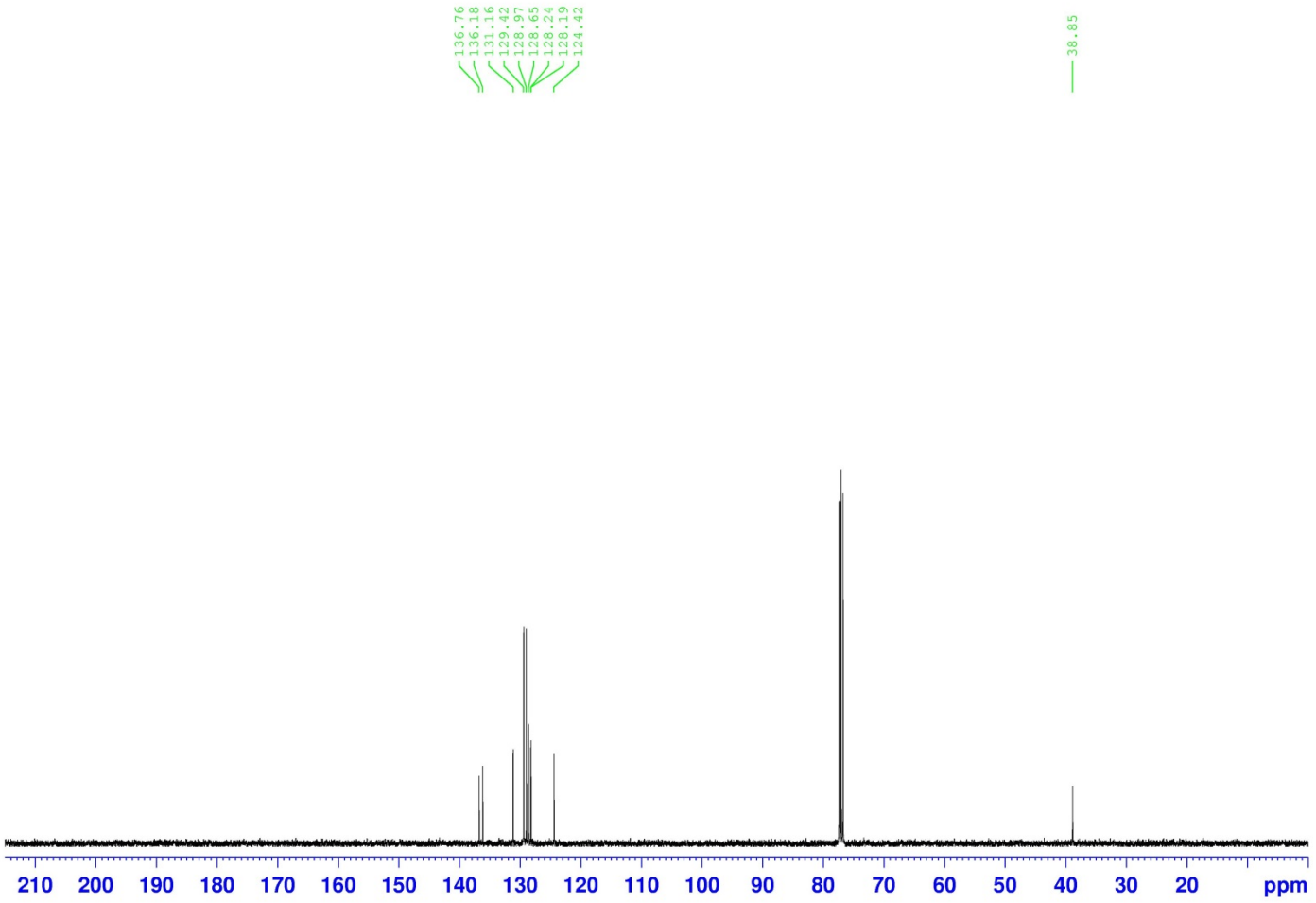
Following the procedure for the preparation of 2-ammoniumbiphenyl mesylate affords the title compound (99%) as a white solid.

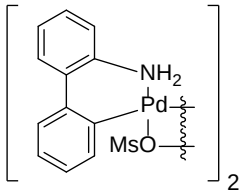
m.p.	152.5–153.0 ºC
^{1}H NMR (400 MHz, $CDCl_3$)	δ 9.17 (3H, br s, NH_3), 7.50 (1H, dd, *J* = 7.9 and 0.8 Hz), 7.45–7.35 (6H, m), 7.35–7.25 (2H, m), 2.38 (3H, s).
^{13}C NMR (100 MHz, $CDCl_3$)	δ 136.76, 136.18, 131.16, 129.42, 128.97, 128.65, 128.24, 128.19, 124.42, 38.85.

^{1}H NMR of 2-ammoniumbiphenyl mesylate



^{13}C NMR of 2-ammoniumbiphenyl mesylate

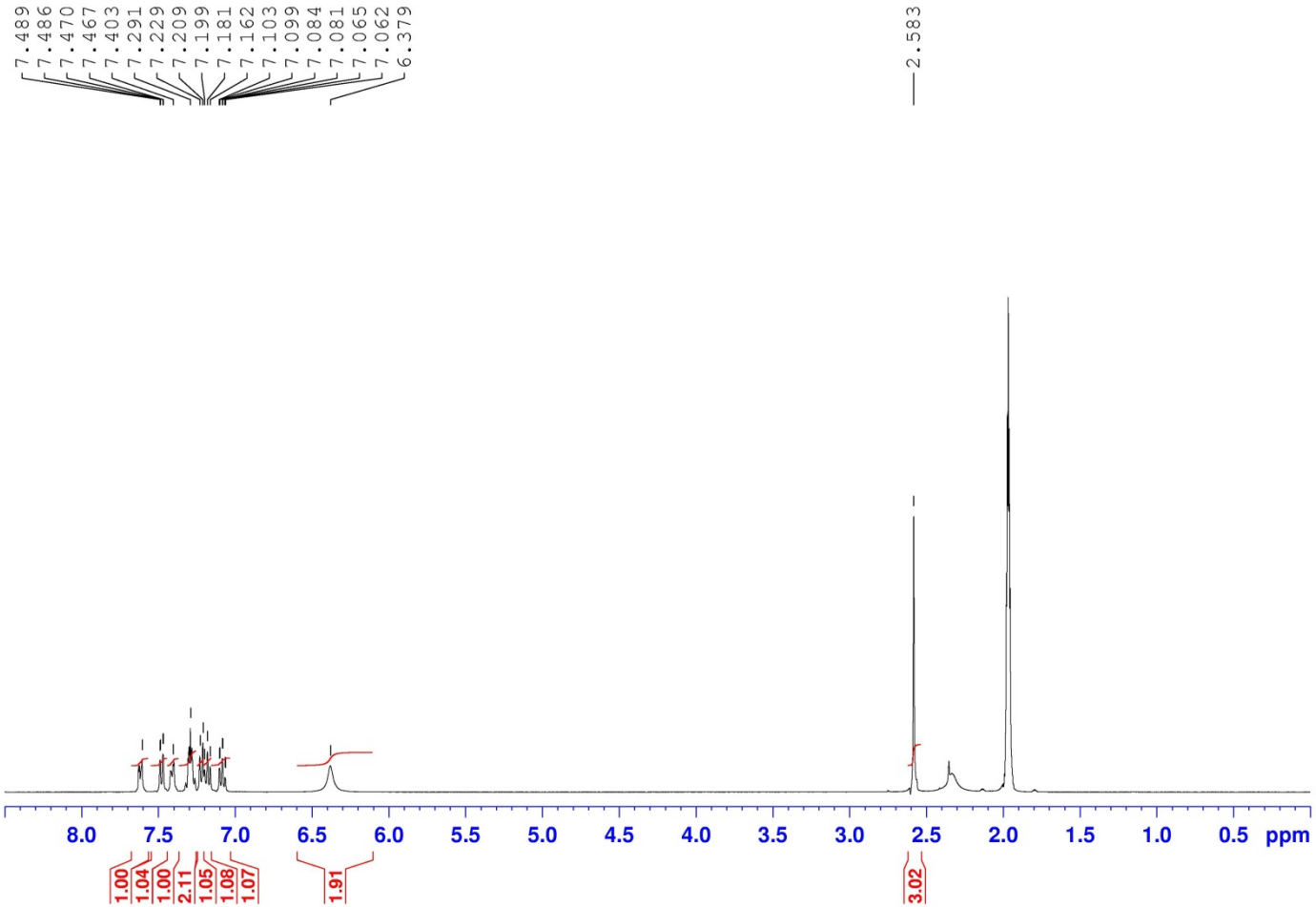




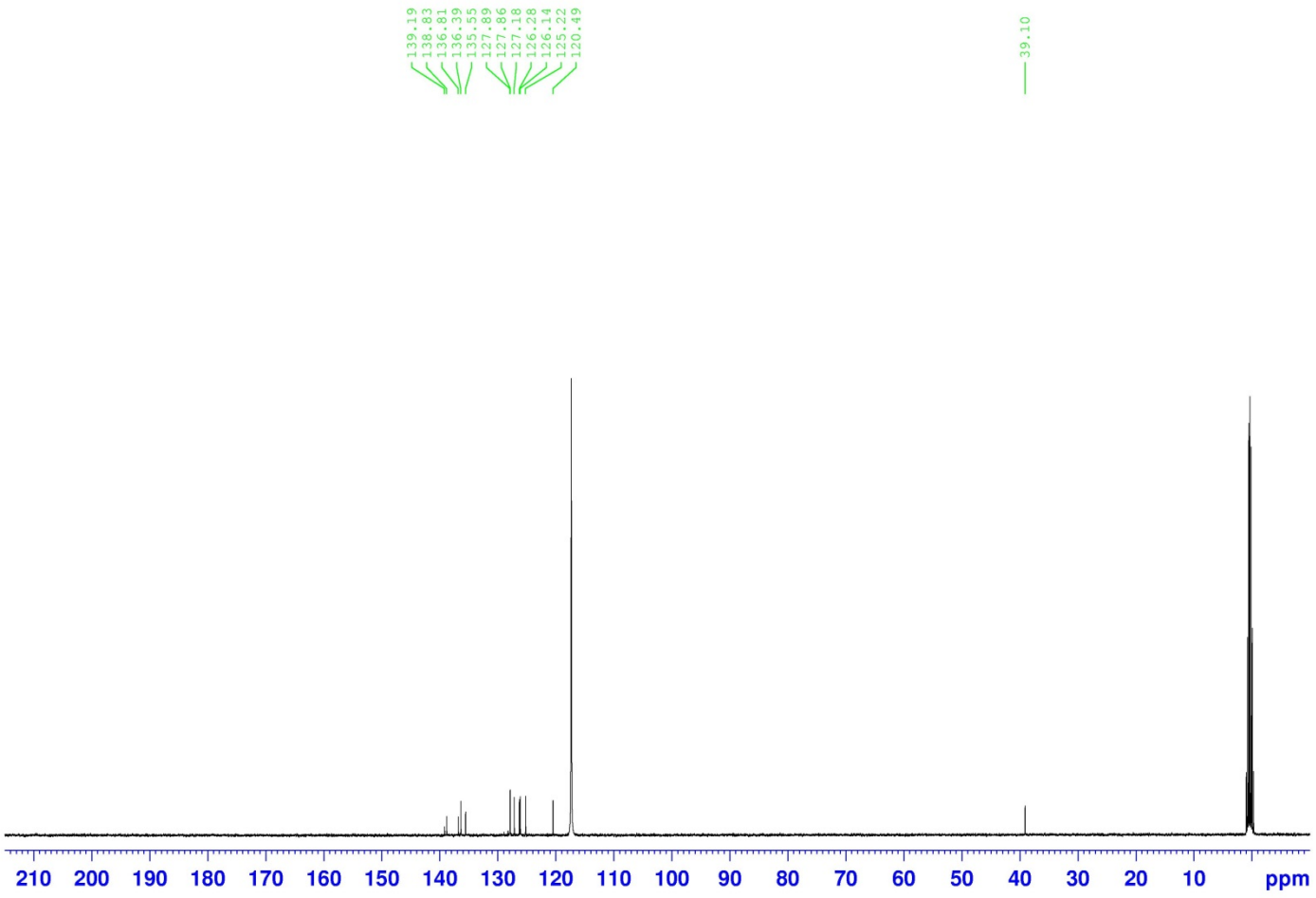
Following the procedure for the preparation of ***μ*-OMs dimer** affords the title compound (91%) as an off-white solid.

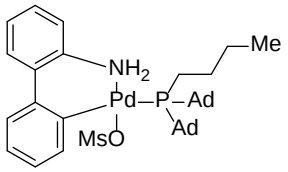
m.p.	200.5–202.0 ºC
^{1}H NMR (400 MHz, CD_3CN)	δ 7.65–7.55 (1H, m), 7.48 (1H, dd, *J* = 7.5 and 1.2 Hz), 7.45–7.35 (1H, m), 7.35–7.25 (2H, m), 7.22 (1H, d, *J* = 7.6 Hz), 7.18 (1H, t, *J* = 7.4 Hz), 7.08 (1H, td, *J* = 7.6 and 1.4 Hz), 6.38 (2H, br s), 2.58 (3H, s).
^{13}C NMR (100 MHz, CD_3CN)	δ 139.19, 138.83, 136.81, 136.39, 135.55, 127.89, 127.86, 127.18, 126.28, 126.14, 125.22, 120.49, 39.10.

^{1}H NMR of μ-OMs dimer



^{13}C NMR of μ-OMs dimer



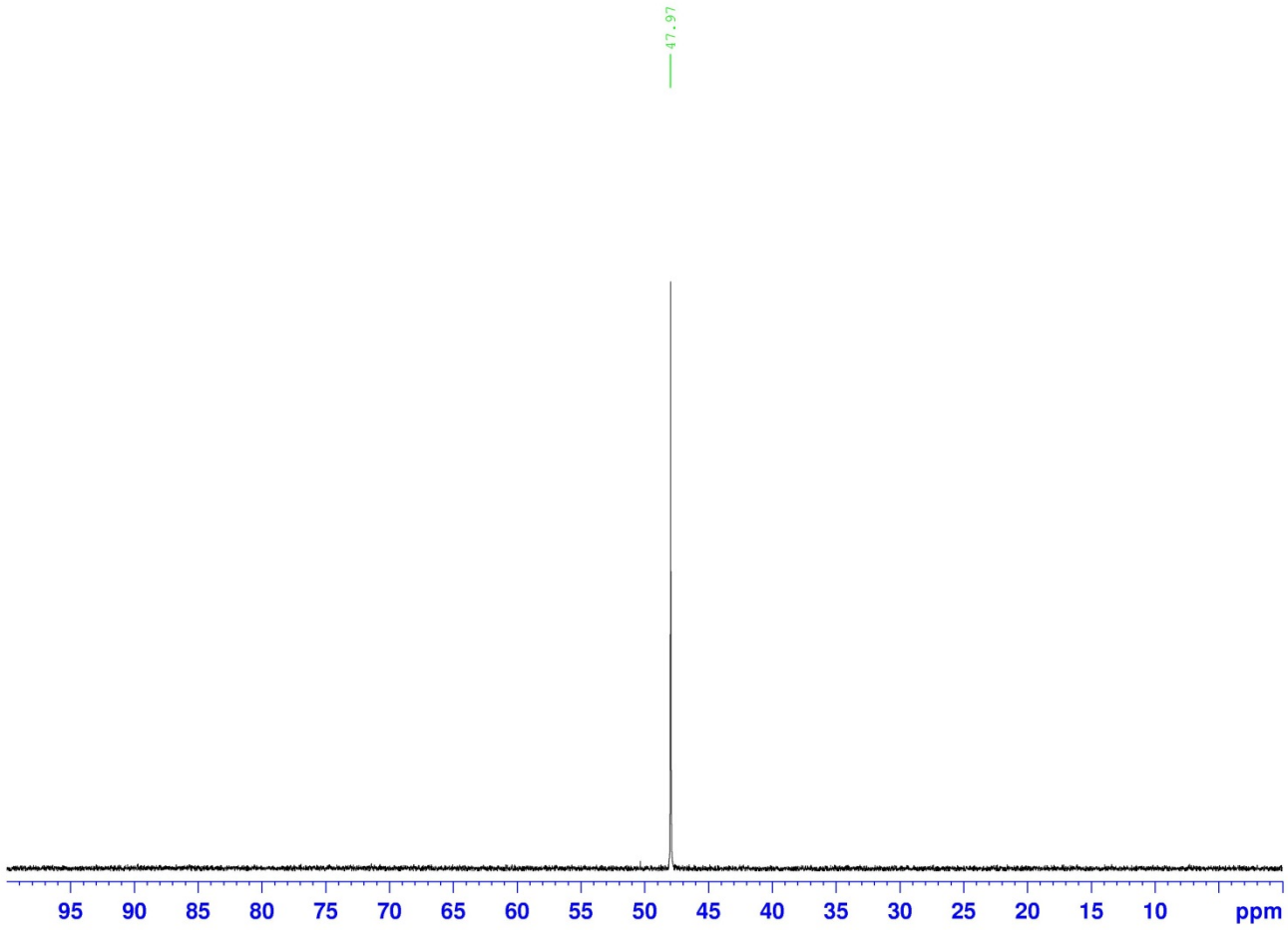


Pd-precatalyst **10**

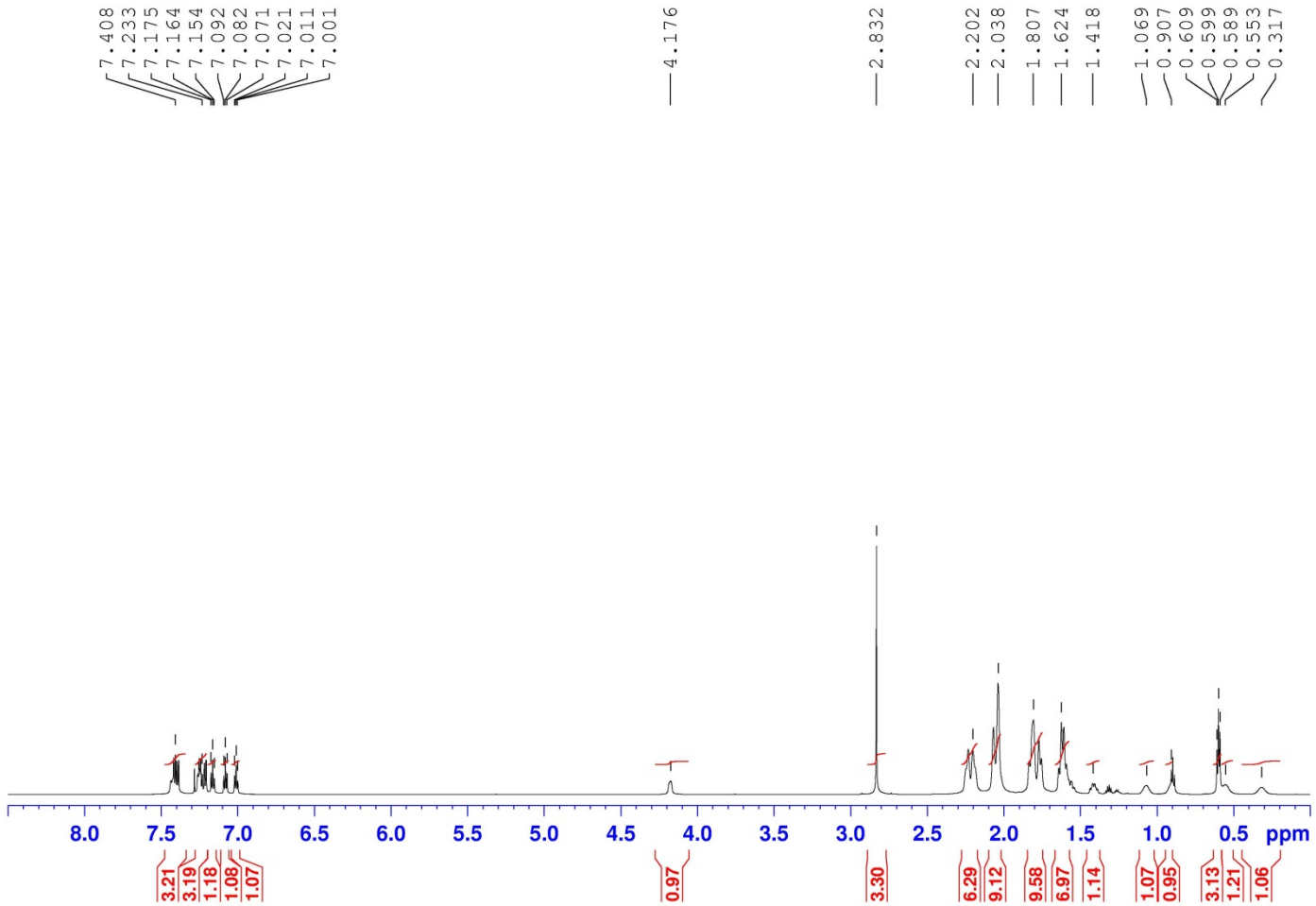
Following the procedure for the preparation of Pd-precatalyst **10** affords the title compound (92%) as an off-white solid.

m.p.	219.0–220.5 ºC
^{31}P NMR (283 MHz, $CDCl_3$)	δ 47.97
^{1}H NMR (700 MHz, $CDCl_3$)	δ 7.45–7.35 (3H, m), 7.30–7.20 (3H, m), 7.16 (1H, t, *J* = 7.4 Hz), 7.08 (1H, t, *J* = 7.2 Hz), 7.01 (1H, t, *J* = 7.3 Hz), 4.18 (1H, br s), 2.83 (3H, s), 2.30–2.15 (6H, m), 2.10–2.00 (9H, m), 2.85–2.75 (9H, m), 1.65–1.55 (7H, m), 1.45–1.35 (1H, m), 1.10–1.00 (1H, m), 0.95–0.90 (1H, m), 0.60 (3H, t, *J* = 7.2 Hz), 0.60–0.50 (1H, m), 0.40–0.20 (1H, m).
^{13}C NMR (176 MHz, $CDCl_3$)	δ 140.16, 137.58 and 137.55, 136.63 and 136.61, 128.12, 127.63, 126.91, 125.33, 125.26, 124.65, 119.83, 41.34 and 41.26, 40.55 and 40.45, 40.08, 39.87, 36.65 and 36.46, 28.84 and 28.79, 28.65 and 28.61, 27.73, 25.41 and 25.34, 17.63 and 17.51, 13.80 (observed complexity due to P-C splitting).
IR (neat)	2898, 2841, 1611, 1492, 1419, 1341, 1300, 1249, 1239, 1166, 1141, 1034, 1021, 771, 754, 735, 709 cm^{-1}.
HRMS (ESI)	Calcd. for $C_{36}H_{49}NPPd$ (M-OMs): 632.2637, found 632.2637 *m/z*.

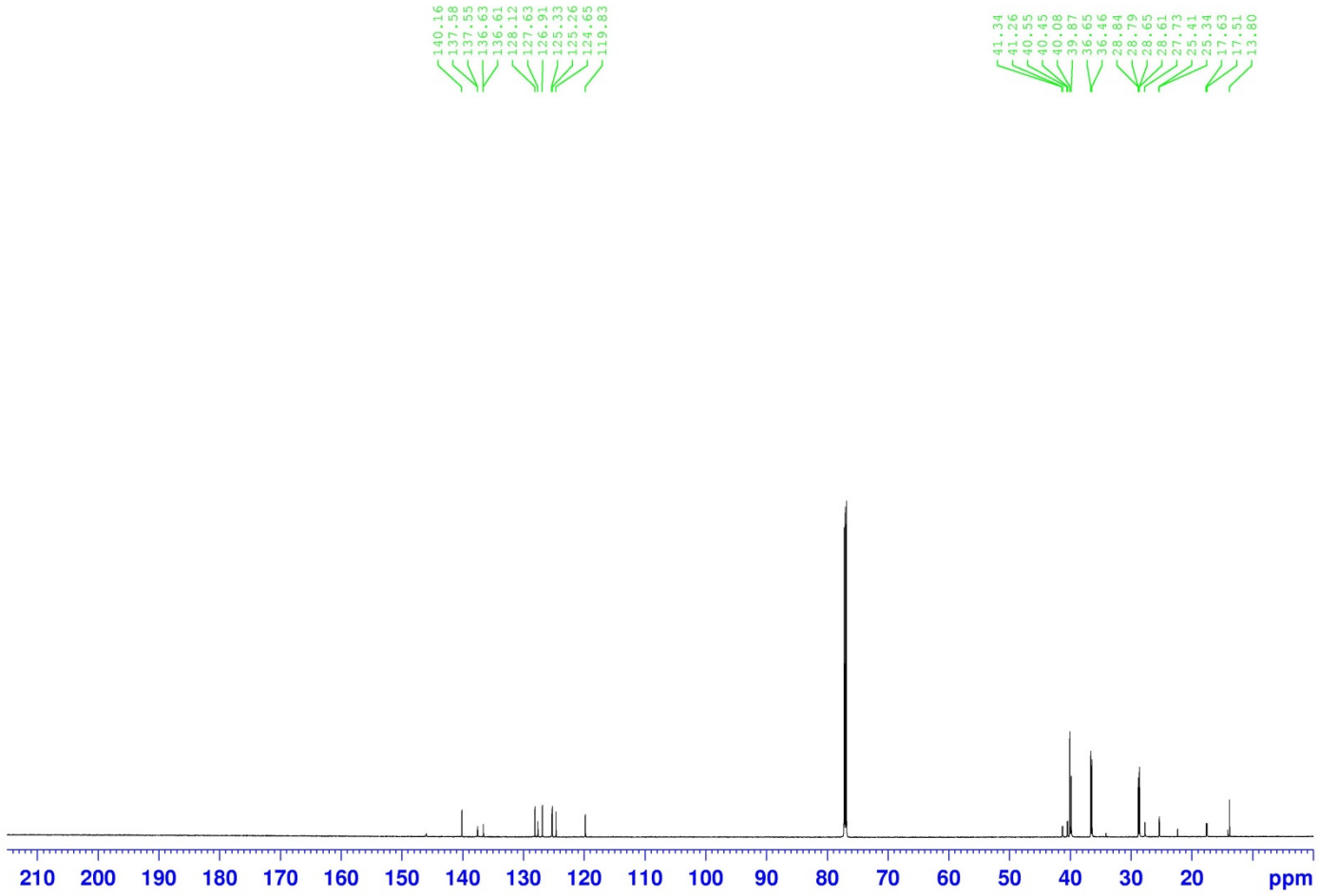
^{31}P NMR of Pd-precatalyst **10**

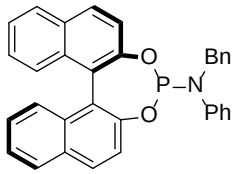


^{1}H NMR of Pd-precatalyst **10**



^{13}C NMR of Pd-precatalyst **10**



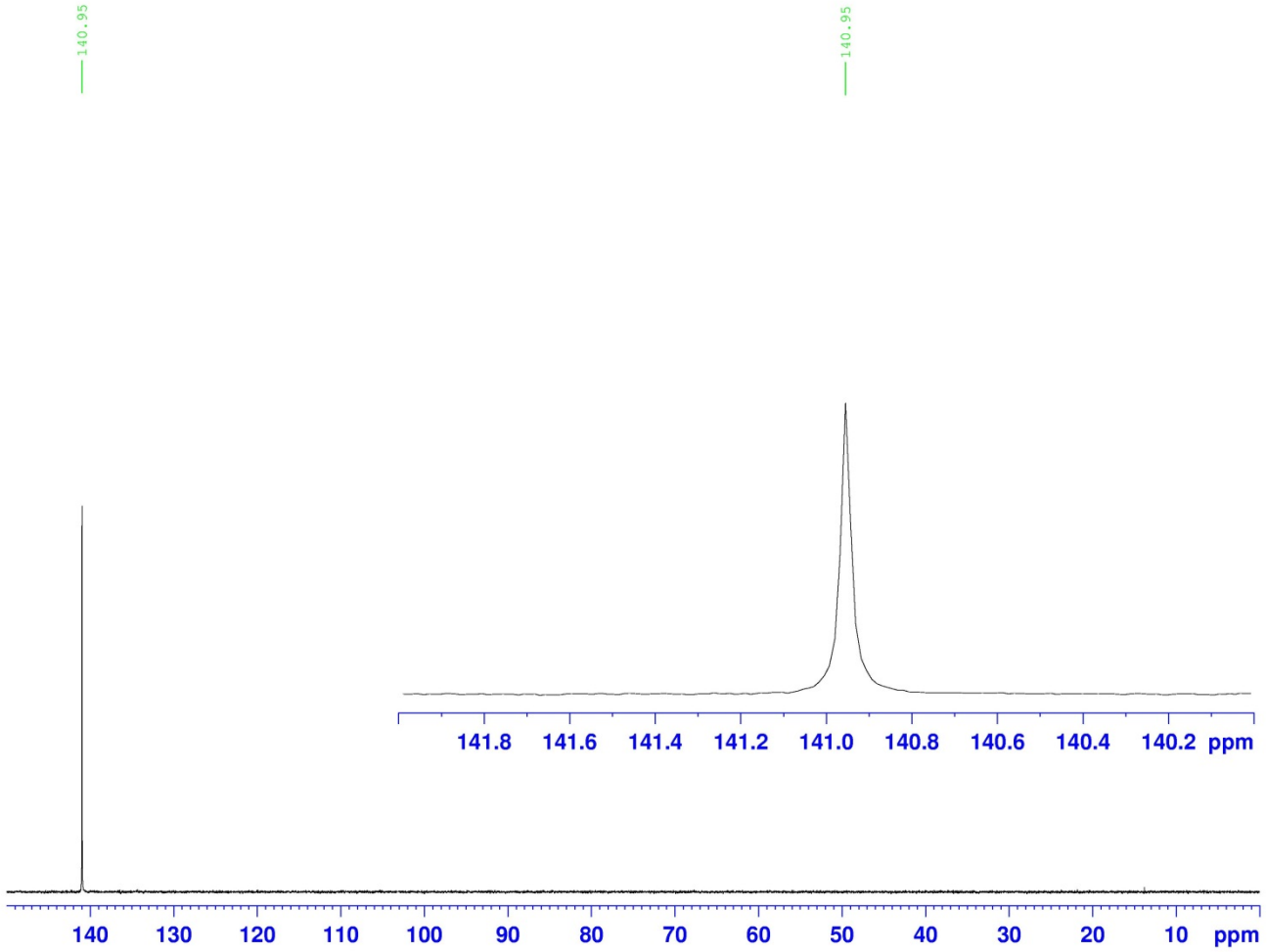


(*R*,*R*)-(BINOL)PN(Bn)Ph (**L1b**)

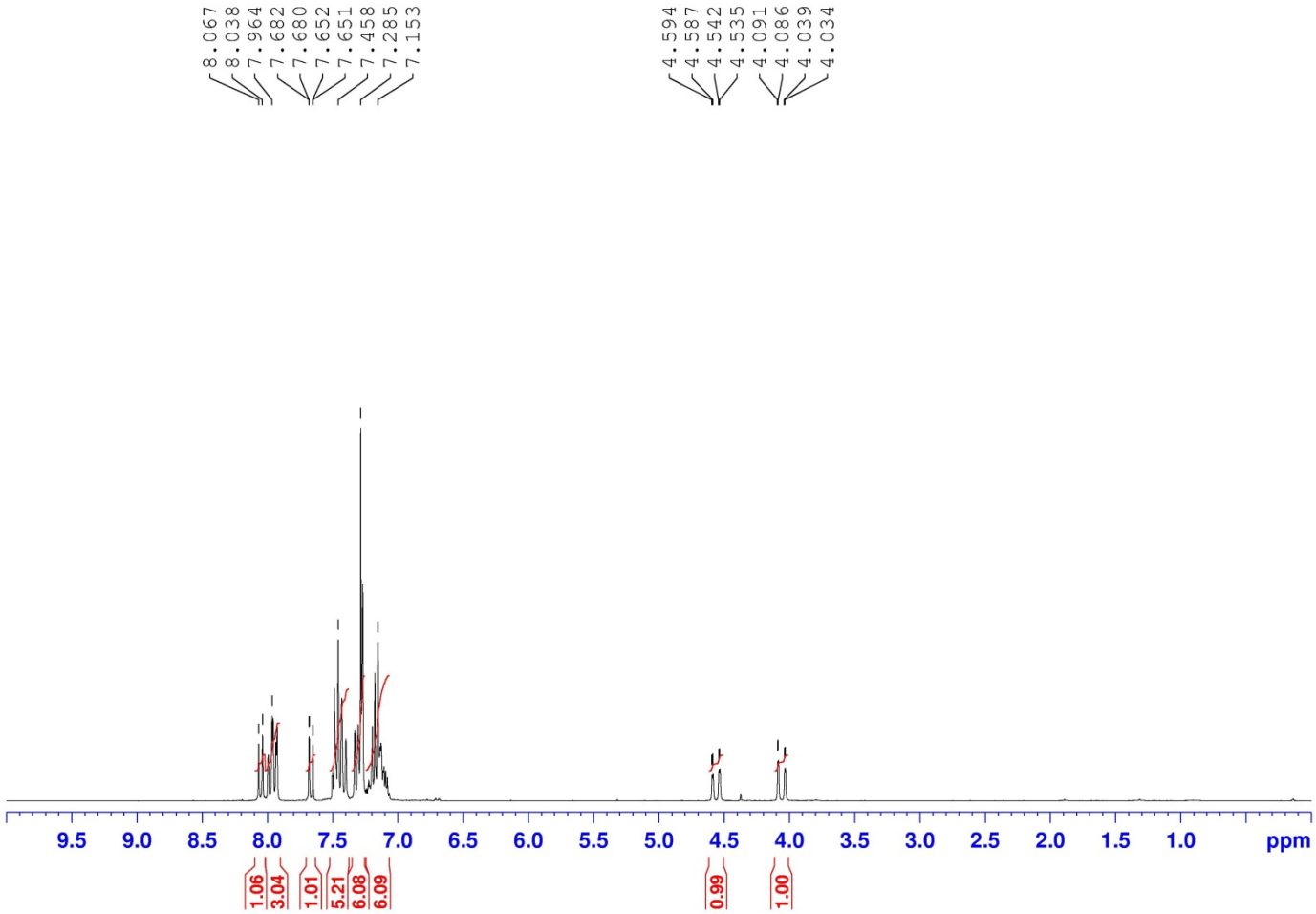
Following the procedure for the preparation of (BINOL)PN(Bn)Ph **(L1b)** affords, after flash chromatography in silica gel (80:20–70:30 hexanes:DCM) the title compound (86%) as a white foamy solid.

m.p.	99.5–100.0 ^{o}C
Optical rotation	$[\alpha]_D^{20}$ = -165^{o} (*c* 1.0, $CHCl_3$)
TLC analysis	R_f = 0.6 (50:50 hexanes:DCM)
^{31}P NMR (121 MHz, $CDCl_3$)	δ 140.95
^{1}H NMR (300 MHz, $CDCl_3$)	δ 8.05 (1H, d, *J* = 8.8 Hz), 8.00–7.90 (3H, m), 7.67 (1H, dd *J* = 8.8 and 0.5 Hz), 7.50–7.40 (5H, m), 7.35–7.25 (6H, m), 7.25–7.05 (6H, m), 4.56 (1H, dd, *J* = 15.7 and 2.1 Hz), 4.06 (1H, dd, *J* = 15.7 and 1.6 Hz).
^{13}C NMR (75 MHz, $CDCl_3$)	δ 149.56 (J_{CP} = 4.9 Hz), 149.15, 143.78, 143.47, 138.45, 132.87, 132.64, 131.58, 130.89, 130.48, 130.27, 129.09, 128.41, 128.34, 128.10, 127.84, 127.08, 126.99, 126.73, 126.24, 125.02, 124.82, 124.71, 124.55, 124.32, 124.18, 124.11, 122.69, 122.08, 121.71, 50.37.
IR (neat)	3052, 1618, 1589, 1489, 1462, 1359, 1324, 1223, 1096, 1063, 947, 819, 747, 692 cm^{-1}.
HRMS (EI)	Calcd. for $C_{33}H_{24}NO_2P$ (M): 497.1545, found 497.1545 *m/z*.

^{31}P NMR of (BINOL)PN(Bn)Ph **(L1b)**



^{1}H NMR of (BINOL)PN(Bn)Ph **(L1b)**



^{13}C NMR of (BINOL)PN(Bn)Ph **(L1b)**