The Preparation of 2*H*-1,4-benzoxazin-3-(4*H*)-ones *via* Palladium-Catalyzed Intramolecular C-O Bond Formation.

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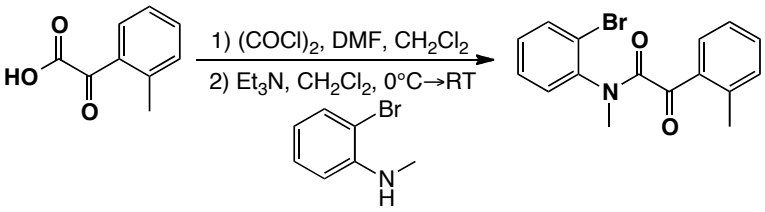
Supporting Information.

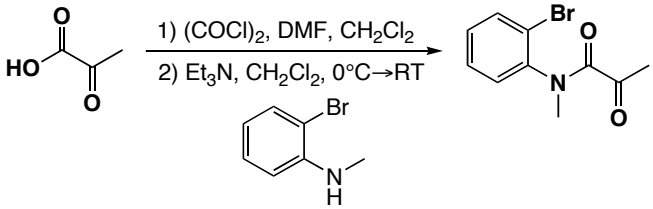
General experimental. All manipulations on air sensitive compounds were performed under nitrogen atmosphere using standard Schlenk techniques or in a drybox. All solvents were dried by passing them through activated Al_2O_3 (SolvtekH purification system). All other reagents were used without further purification. Flash column chromatography was performed with Silicycle silca gel (40 – 63 μm). IR spectra were recorded on a Perkin-Elmer Spectrum One spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on either a Bruker Avance300 (^{1}H, 300 MHz) or Bruker AMX-400 (^{1}H, 400 MHz; ^{13}C, 100 MHz) spectrometer. High-resolution mass spectra, performed by the Université de Genève Laboratoire de Science Mass Spectrometrie, were obtained on a quadrupoletime-of-flight Q STAR XL AppliedBiosystems/MDS Sciex mass spectrometer (electrospray ionization). Optical rotations were obtained on a Perkin-Elmer 241 polarimeter equipped with a quartz cell (l = 10 cm) and a Na high-pressure lamp (λ = 589 nm). HPLC was performed on an Agilent 1100 series chromatograph. ^{1}H NMR chemical shifts are reported relative to residual protiated solvent. ^{13}C NMR chemical shifts are reported relative to the deuterated solvent. Values of the coupling constants are obtained directly from the spectrum. Although generally measured to ±0.1 Hz, J values are self-consistent to only ±0.5 Hz. Data for the ^{1}H-^{1}H COSY is presented such that correlations are listed only once. Compounds prepared by published procedures: 2-bromo-*N*-methylaniline,[1] 3-bromo-*N*-methylpyridin-2-amine,[2] *N*-(2-bromophenyl)-*N*-methyl-2-oxo-2-phenylacetamide,[3] *N*-(2-bromophenyl)-2-(4-methoxyphenyl)-*N*-methyl-2-oxoacetamide,[3] *N*-(2-bromophenyl)-2-(4-trifluoromethylphenyl)-*N*-methyl-2-oxoacetamide,[3] *N*-(2-bromophenyl)-*N*-methyl-2-(naphthalene-1-yl)-2-oxoacetamide,[3] *N*-(2-bromophenyl)-2-(2-methoxyphenyl)-*N*-methyl-2-oxoacetamide,[3] [HP*t*Bu$_3$]BF$_4$,[4] and Pd(dba)$_2$.[5] Ketocarboxylic acids were prepared via addition of the appropriate Grignard reagent to diethyl oxalate,[6] followed by saponification.

[1] Würtz, S.; Lohre, C.; Fröhlich, R.; Bergander, K.; Glorius, F. *J. Am. Chem. Soc.* **2009**, *131*, 8344.
[2] Patriciu, O.-I.; Pillard, C.; Fînaru, A.-L.; Sandulescu, I.; Guillaumet, G. *Synthesis* **2007**, 3868.
[3] Jia, Y.-X.; Katayev, D.; Kündig, E. P. *Chem. Commun.* **2010**, *46*, 130.
[4] Netherton, M. R.; Fu, G. C. *Org. Lett.* **2001**, *3*, 4295.
[5] Rettig, M. F.; Maitlis, P. M. *Inorg. Synth.* **1990**, *28*, 110.
[6] Fizet, C. *Helv. Chim. Acta* **1982**, *65*, 2024.

Experimental Details.

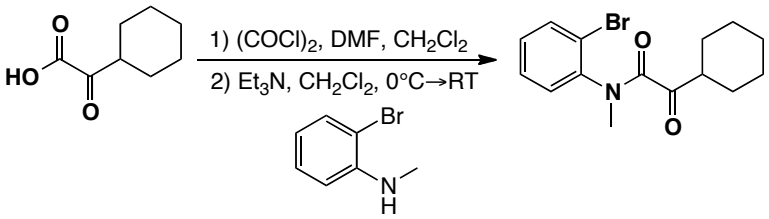


***N*-(2-bromophenyl)-*N*-methyl-2-oxo-(*o*-tolyl)acetamide.** In a Schlenk flask, carboxylic acid (0.54 g, 3.3 mmol) was dissolved in CH_2Cl_2 (5 mL) under a nitrogen atmosphere. To this, oxalyl chloride (0.28 mL, 3.3 mmol) was added, followed by one drop of dimethylformamide. The reaction was stirred until gas evolution ceased. The solution was cooled to 0 °C and 2-bromo-*N*-methylaniline (0.62 g, 3.31 mmol) was added, followed by triethylamine (1 mL, 6.62 mmol). The reaction was allowed to warm to room temperature overnight. The reaction was acidified with 1N HCl, diluted with diethyl ether, and the layers separated. The aqueous layer was extracted with diethyl ether, and the combined extracts were washed with water, then brine, and dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue purified by silica gel chromatography using 15% EtOAc/pentane to yield 0.86 g (79%) of product as a yellow oil. Spectroscopically, the product is a 5:1 mixture of rotamers. IR (neat, cm^{-1}): 2932 (w), 1735 (m), 1653 (s), 1600 (w), 1572 (w), 1477 (s), 1381 (s), 1289 (w), 1226 (s), 1119 (m), 1032 (s), 955 (m), 855 (w), 738 (s), 722 (s); ^1H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, J = 7.7 Hz, 0.2H), 7.95 (d, J = 7.7 Hz, 1H), 7.78 (d, J = 8.0 Hz, 0.2H), 7.56 (d, J = 7.9 Hz, 1H, overlaps 0.2H from other rotomer), 7.44 (t, J = 7.5 Hz, 1H, overlaps 0.6H from other rotomer), 7.34-7.25 (m, 3H, overlaps 0.4H from other rotomer), 7.21-7.17 (m, 2H), 3.44 (s, 3H), 3.33 (s, 0.6H), 2.79 (s, 0.6H), 2.26 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 192.9, 167.2, 140.6, 139.7, 133.9, 133.2, 132.7, 132.5, 132.0, 131.9, 131.4, 130.2, 128.4, 125.7, 123.4, 35.4, 21.1; Electrospray MS *m/z* calculated for $C_{16}H_{15}NO_2Br$ (M^+ + H): 332.0280; found: 332.0279.

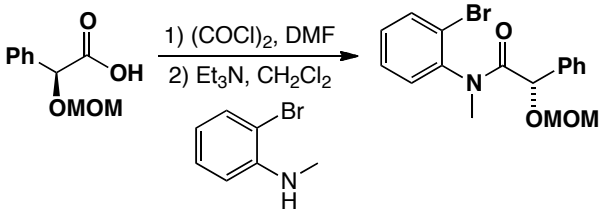


***N*-(2-bromophenyl)-*N*-methyl-2-oxopropanamide.** In a Schlenk flask, pyruvic acid (0.155 mL, 2.23 mmol) was dissolved in CH_2Cl_2 (5 mL) under a nitrogen atmosphere. To this, oxalyl chloride (0.190 mL, 2.23 mmol) was added, followed by one drop of dimethylformamide. The reaction was stirred until gas evolution ceased. The solution was cooled to 0 °C and 2-bromo-*N*-methylaniline (0.500 g, 2.68 mmol) was added, followed by triethylamine (1 mL, 7.22 mmol). The reaction was allowed to warm to room temperature overnight. The reaction was acidified with 1N HCl, diluted with diethyl ether, and the layers separated. The aqueous layer was extracted with diethyl ether, and the combined extracts were washed with water and brine. The solvent was removed *in vacuo* and the residue purified by silica gel chromatography using 15% EtOAc/pentane to yield 0.234 g (41%) of product as a yellow oil. IR (MeOH cast, cm^{-1}): 1720 (m), 1658 (s), 1584 (w), 1478 (m), 1435 (w), 1387 (w), 1351 (m), 1194 (m), 1116 (m), 1030 (m), 959 (w), 878 (w), 764 (m), 726

(w); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.43 (d, *J* = 7.9 Hz, 1H), 7.37 (td, *J* = 8.0, 1.3 Hz, 1H), 7.31 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.23 (td, *J* = 7.8, 1.7 Hz, 2H), 6.73 (br. d, *J* = 5.8 Hz, 1H), 6.63 (br. t, *J* = 7.6 Hz, 1H), 3.27 (s, 3H), 2.91 (s, 3H), 2.33 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 196.8, 165.9, 140.9, 133.6, 130.1, 130.0, 128.9, 122.5, 36.1, 26.9; Electrospray MS *m/z* calculated for $C_{10}H_{11}O_2NBr$ (M^+ + H): 255.9967; found: 255.9959.

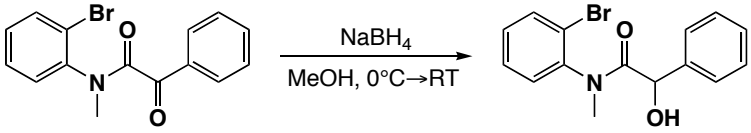


***N*-(2-bromophenyl)2-cyclohexyl-*N*-methyl-2-oxoacetamide.** In a Schlenk flask, carboxylic acid (0.76 g, 4.8 mmol) was dissolved in CH_2Cl_2 (5 mL) under a nitrogen atmosphere. To this, oxalyl chloride (0.50 mL, 4.8 mmol) was added, followed by one drop of dimethylformamide. The reaction was stirred until gas evolution ceased. All volatiles were removed *in vacuo* and the residue was redissolved in CH_2Cl_2 (5 mL). The solution was cooled to 0 °C and 2-bromo-*N*-methylaniline (0.90 g, 4.8 mmol) was added, followed by triethylamine (1.3 mL, 9.7 mmol). The reaction was allowed to warm to room temperature overnight. The reaction was acidified with 1N HCl, diluted with diethyl ether, and the layers separated. The aqueous layer was extracted with diethyl ether, and the combined extracts were washed with water, then brine, and dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue purified by silica gel chromatography using 15% EtOAc/pentane to yield 1.24 g (79%) of product as a yellow oil. Spectroscopically, the product is a 7:1 mixture of rotamers. IR (neat, cm^{-1}): 2929 (m), 2855 (m), 1709 (m), 1652 (s), 1583 (m), 1477 (s), 1447 (m), 1383 (m), 1363 (m), 1292 (w), 1237 (w), 1158 (w), 1134 (w), 1092 (m), 1030 (m), 976 (s), 893 (w), 763 (s), 722 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (dd, *J* = 8.0, 0.8 Hz, 0.13H), 7.51 (dd, *J* = 7.9, 0.9 Hz, 1H), 7.28 (td, *J* = 7.4, 1.0 Hz, 0.15H), 7.21 (app. qd, *J* = 5.2, 1.3 Hz, 1H), 7.15-7.08 (m, 2.3H), 3.15 (s, 3H), 3.13 (s, 0.4H), 2.95 (tt, *J* = 8.3, 3.4 Hz, 0.15H), 2.73 (tt, *J* = 8.0, 4.4 Hz, 1H), 2.00 (m, 0.30H), 1.80 (d, 12.6 Hz, 1H), 1.70 (m, 0.3H), 1.63-1.48 (m, 4.3H), 1.28-0.95 (m, 7H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 203.12, 202.07, 166.80, 166.10, 140.67, 140.53, 133.68, 133.64, 130.32, 130.08, 129.36, 128.54, 122.87, 121.88, 46.75, 37.73, 35.85, 28.40, 27.22, 25.66, 25.54, 25.19; Electrospray MS *m/z* calculated for $C_{15}H_{19}NO_2Br$ (M^+ + H): 324.0593; found: 324.0588.



(*S*)-*N*-(2-bromophenyl)-2-(methoxymethoxy)-*N*-methyl-2-phenylacetamide. In a Schlenk flask, carboxylic acid (200 mg, 1.01 mmol) was dissolved in CH_2Cl_2 (3 mL) under a nitrogen atmosphere. To this, oxalyl chloride (95 μL, 1.11 mmol) was added, followed by one drop of dimethylformamide. The reaction was stirred until gas evolution ceased. The volatiles were removed under vacuum and the residue dissolved in CH_2Cl_2 (3 mL) and cooled to 0 °C. To this solution, 2-Bromo-*N*-methylaniline (206 mg, 1.11 mmol) was added, followed by

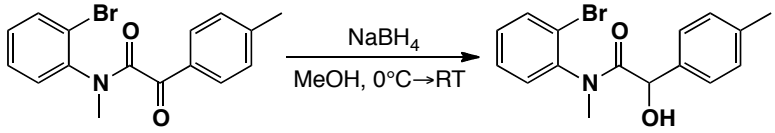
triethylamine (500 μL, 3.61 mmol). The reaction was allowed to warm to room temperature overnight. The reaction was acidified with 1N HCl, diluted with diethyl ether, and the layers separated. The aqueous layer was extracted with diethyl ether, and the combined extracts were washed with water, then brine, and dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue purified by silica gel chromatography using 20% EtOAc/pentane to yield 123 mg (46%) of product as a white solid in 70% *ee*. Spectroscopically, the product is a 2:1 mixture of rotamers. $[\alpha]_D^{20}$ = +41 (*c* = 0.655, $CHCl_3$); HPLC: Chiralcel OD-H, 1% *i*PrOH/hexane for 10 min then 1→20% *i*PrOH/hexane over 45 min, 1 mL/min, 240 nm; t_R = 24.54 min (major), t_R = 31.06 min (minor); IR ($CDCl_3$ cast, cm^{-1}): 2925 (w), 1674 (s), 1584 (w), 1476 (m), 1455 (m), 1287 (w), 1248 (w), 1213 (w), 1148 (m), 1103 (m), 1024 (s), 971 (m), 917 (m), 823 (w), 758 (s), 726 (m), 698 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (dd, *J* = 8.0, 1.3 Hz, 2H), 7.52 (dd, *J* = 8.8, 1.1 Hz, 1H), 7.44-7.39 (m, 2H), 7.27-7.18 (m, 12H), 7.09-7.00 (m, 8H), 6.48 (dd, *J* = 7.8, 1.6 Hz, 2H), 5.00 (s, 1H), 4.81 (s, 2H), 4.67 (d, *J* = 6.9 Hz, 2H), 4.62 (d, *J* = 6.9 Hz, 1H), 4.49 (d, *J* = 6.9 Hz, 3H), 3.27 (s, 3H), 3.26 (s, 6H), 3.18 (s, 3H), 3.16 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 169.64, 169.39, 141.28, 140.73, 135.77, 135.11, 133.89, 133.60, 131.26, 130.23, 129.95, 129.92, 128.62 (2 overlapping signals), 128.58, 128.49, 128.46, 128.32, 128.28, 128.16, 124.11, 123.32, 94.39, 93.91, 75.29, 74.70, 55.67, 55.55, 36.29, 36.21; Electrospray MS *m/z* calculated for $C_{17}H_{18}O_3NBrNa$ (M^+ + Na): 386.0362; found: 386.0351.



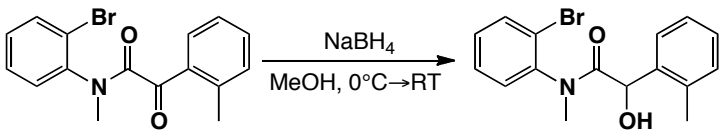
***N*-(2-bromophenyl)-2-hydroxy-*N*-methyl-2-phenylacetamide (3a).** Phenylketoamide (3.40 g, 11.1 mmol) was dissolved in MeOH (20 mL) under nitrogen and cooled to 0°C in an ice bath. To this, $NaBH_4$ (0.50 g, 13.3 mmol) was added and the reaction was allowed to warm slowly to room temperature overnight. The reaction was then diluted with Et_2O and acidified with 1N HCl to a pH of 6. The layers were separated and the aqueous layer extracted with Et_2O. The organic fractions were combined and washed with brine and dried over $MgSO_4$. The solvent was removed *in vacuo* and the product purified by silica gel chromatography with 20% EtOAc/pentane. The fractions were concentrated and residual solvent removed under vacuum to yield 3.14 g (92%) of the desired alcohol as a white solid. The enantioenriched product was obtained from deprotection of the MOM protected alcohol. The protected alcohol (123 mg, 0.34 mmol) was dissolved in MeOH (10 mL) and one drop of conc. HCl was added. The reaction was heated at reflux for 20 min, then quenched with sat. $NaHCO_3$ solution. The mixture was extracted with diethyl ether, and the aqueous phase was concentrated and extracted with the diethyl ether. The combined organics were washed with brine and dried over Na_2SO_4 to yield 72 mg (67%) of product as a white solid. The product spectra were similar, but not identical to those previously reported.[7] Spectroscopically, the product is a 2:1 mixture of amide rotamers favouring rotomer A. 70% *ee*; $[\alpha]_D^{20}$ = +14 (*c* = 0.910, $CHCl_3$); HPLC: Chiralpak AS-H, 1% *i*PrOH/hexane for 10 min then 1→20% *i*PrOH/hexane over 45 min, 1 mL/min, 240 nm; t_R = 32.19 min (major), t_R = 40.13 min (minor); IR ($CDCl_3$ cast, cm^{-1}): 3420 (br. w), 3030 (w), 1651 (s), 1584 (w), 1477 (m), 1437 (m), 1360 (m), 1300 (m), 1191 (w), 1136 (w), 1087 (m), 1047 (s), 1016 (m), 934 (w), 820 (w), 760 (s), 727 (m), 713 (m), 698 (s); ^{1}H NMR (400 MHz, $CDCl_3$, Rotomer A): δ 7.69 (dd, $J_{4\text{-}3}$ = 8.0 Hz, $J_{4\text{-}2}$ = 1.3 Hz, 1H, H_4), 7.26-7.10 (m, 4H, H_3, H_7, H_8, overlaps signals from

[7] Hillgren, J. M.; Marsden, S. P. *J. Org. Chem.* **2008**, *73*, 6459.

rotomer B), 6.98 (td, $J_{2\text{-}1} = J_{2\text{-}3} = 7.8$ Hz, $J_{2\text{-}4} = 1.3$ Hz, 1H, H_2), 6.81 (dd, $J_{6\text{-}7} = 7.0$ Hz, $J_{6\text{-}8} = 2.0$ Hz, 2H, H_6), 6.36 (dd, $J_{1\text{-}2} = 7.9$ Hz, $J_{1\text{-}3} = 1.5$ Hz, 1H, H_1), 4.73 (s, 1H, H_5), 4.49 (br. s, 1H, -OH), 3.24 (s, 3H, Me); ^{1}H-^{1}H COSY (400 MHz, $CDCl_3$, Rotomer A): δ 7.69 (H_4) ↔ δ 7.26-7.10 (H_3); δ 7.26-7.10 (H_3) ↔ δ 6.98 (H_2); δ 7.26-7.10 (H_7) ↔ δ 6.81 (H_6); δ 6.98 (H_2) ↔ δ 6.36 (H_1); ^{1}H NMR (400 MHz, $CDCl_3$, Rotomer B): δ 7.40 (td, $J_{2\text{-}1} = J_{2\text{-}3} = 9.0$ Hz, $J_{2\text{-}4} = 1.3$ Hz, 1H, H_2), 7.38 (td, $J_{3\text{-}2} = J_{3\text{-}4} = 9.0$ Hz, $J_{3\text{-}1} = 1.6$ Hz, 1H, H_3), 7.26-7.10 (m, 4H, H_1, H_7, H_8, overlaps signals from rotomer A), 6.69 (dd, $J_{6\text{-}7} = 8.4$ Hz, $J_{6\text{-}8} = 1.3$ Hz, 2H, H_6), 5.00 (s, 1H, H_5), 4.63 (br. s, 1H, -OH), 3.26 (s, 3H, Me); ^{1}H-^{1}H COSY (400 MHz, $CDCl_3$, Rotomer B): δ 7.40 (H_2) ↔ δ 7.38 (H_3), 7.26-7.10 (H_1); δ 7.26-7.10 (H_7) ↔ δ 6.69 (H_6); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, Rotamers A + B): δ 173.02, 172.60, 140.17, 140.10, 139.30, 137.71, 134.18, 133.56, 131.33, 130.31, 130.22, 130.17, 128.59, 128.54, 128.47, 128.40, 128.35, 128.31, 127.59, 127.48, 124.79, 123.38, 72.86, 71.85, 37.08, 36.97.

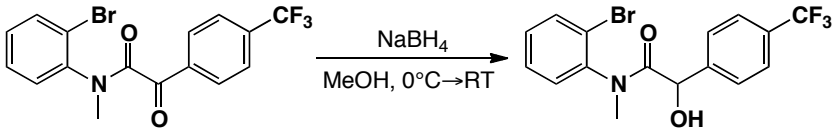


***N*-(2-bromophenyl)-2-hydroxy-*N*-methyl-2-(*p*-tolyl)acetamide (3b).** Ketoamide (0.40 g, 1.2 mmol) was dissolved in MeOH (5 mL) under nitrogen and cooled to 0 °C in an ice bath. To this, $NaBH_4$ (0.059 g, 1.6 mmol) was added and the reaction was allowed to warm slowly to room temperature overnight. The reaction was then diluted with Et_2O and acidified with 1N HCl to a pH of 6. The layers were separated and the aqueous layer extracted with Et_2O. The organic fractions were combined and washed with water, then brine, and dried over $MgSO_4$. The solvent was removed *in vacuo* and the product purified by silica gel chromatography with 20% EtOAc/pentane. The fractions were concentrated and residual solvent removed under vacuum to yield 0.342 g (86%) of the desired alcohol as a yellow oil. Spectroscopically, the product is a 2:1 mixture of rotamers. IR ($CDCl_3$ cast, cm^{-1}): 3428 (w), 2923 (w), 1652 (s), 1584 (w), 1512 (w), 1477 (m), 1437 (w), 1358 (m), 1299 (m), 1252 (w), 1192 (w), 1116 (w), 1081 (m), 1046 (m), 1015 (m), 910 (w), 833 (w), 803 (w), 765 (m), 724 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (dd, J = 8.1, 1.4 Hz, 1H), 7.45-7.33 (m, 2H), 7.22 (m, 1H), 7.17 (td, J = 7.9, 1.6 Hz, 1H), 7.00 (td, J = 7.7, 1.4 Hz, 1H), 6.95 (d, J = 7.8 Hz, 2H), 6.91 (d, J = 7.9 Hz, 1H), 6.70 (d, J = 8.0 Hz, 2H), 6.59 (d, J = 8.0 Hz, 1H), 6.40 (dd, J = 7.9, 1.6 Hz, 1H), 4.95 (s, 0.5H), 4.69 (s, 1H), 4.57 (br. s, 0.5H), 4.44 (br. s, 1H), 3.23 (s, 1.5H), 3.21 (s, 3H), 2.27 (s, 3H), 2.25 (s, 1.5H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 173.19, 172.80, 140.23, 140.12, 138.07, 137.77, 136.36, 134.81, 134.13, 133.52, 131.39, 130.27, 130.22, 130.19, 129.13, 129.01, 128.60, 128.55, 127.45, 127.37, 124.74, 123.34, 72.53, 71.55, 37.00, 36.89, 21.24; Electrospray MS *m/z* calculated for $C_{16}H_{17}NO_2Br$ (M^+ + H): 334.0437; found: 334.0441.

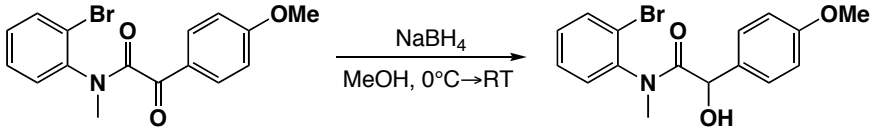


***N*-(2-bromophenyl)-2-hydroxy-*N*-methyl-2-(*o*-tolyl)acetamide (3c).** Ketoamide (0.40 g, 1.2 mmol) was dissolved in MeOH (5 mL) under nitrogen and cooled to 0 °C in an ice bath. To this, $NaBH_4$ (0.055 g, 1.4 mmol) was added and the reaction was allowed to warm slowly to room temperature overnight. The reaction was then diluted with Et_2O and acidified with 1N HCl to a pH of 6. The layers were separated and the aqueous layer extracted with Et_2O.

The organic fractions were combined and washed with water, then brine, and dried over $MgSO_4$. The solvent was removed *in vacuo* and the product purified by silica gel chromatography with 20% EtOAc/pentane. The fractions were concentrated and residual solvent removed under vacuum to yield 0.35 g (87%) of the desired alcohol as a white solid. Spectroscopically, the product is a 2.5:1 mixture of rotamers. IR ($CDCl_3$ cast, cm^{-1}): 3446 (w), 2933 (w), 1654 (s), 1584 (w), 1477 (m), 1435 (w), 1358 (m), 1298 (m), 1251 (w), 1178 (w), 1136 (w), 1080 (w), 1045 (m), 1014 (m), 908 (s), 828 (w), 760 (m), 724 (s); ^1H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, J = 8.0 Hz, 1H), 7.38-7.30 (m, 1.3H), 7.25 (m, 0.4H), 7.12-6.98 (m, 5.2H), 6.95-6.85 (m, 2.8H), 6.80 (d, J = 7.6 Hz, 0.4H), 6.19 (dd, J = 7.9, 0.8 Hz, 1H), 5.20 (d, J = 5.8 Hz, 0.4H), 4.94 (d, J = 5.9 Hz, 1H), 4.44 (d, J = 5.9 Hz, 0.4H), 4.33 (d, J = 5.9 Hz, 1H), 3.23 (s, 1.2H), 3.21 (s, 3H), 1.75 (s, 1.2H), 1.68 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 173.48, 173.16, 140.24, 139.90, 137.53, 136.86, 136.74, 135.49, 134.25, 133.45, 131.18, 130.71, 130.42, 130.13, 130.08, 128.78, 128.71, 128.56, 128.33, 128.17, 127.27, 126.42, 126.17, 124.29, 123.35, 69.69, 69.64, 37.01, 36.97, 18.37, 18.21; Electrospray MS *m/z* calculated for $C_{16}H_{17}NO_2Br$ (M^+ + H): 334.0437; found: 334.0441.

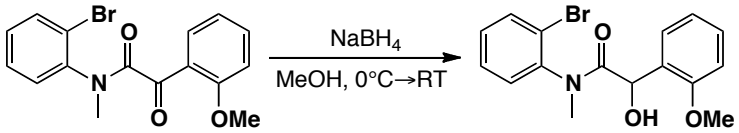


***N*-(2-bromophenyl)-2-hydroxy-*N*-methyl-2-(4-(trifluoromethyl)phenyl)acetamide (3d).** Ketoamide (0.43 g, 1.12 mmol) was dissolved in MeOH (5 mL) under nitrogen and cooled to 0 °C in an ice bath. To this, $NaBH_4$ (0.051 g, 1.33 mmol) was added and the reaction was allowed to warm slowly to room temperature overnight. The reaction was then diluted with Et_2O and acidified with 1N HCl to a pH of 6. The layers were separated and the aqueous layer extracted with Et_2O. The organic fractions were combined and washed with water, then brine, and dried over $MgSO_4$. The solvent was removed *in vacuo* and the product purified by silica gel chromatography with 20% EtOAc/pentane. The fractions were concentrated and residual solvent removed under vacuum to yield 0.36 g (82%) of the desired alcohol as a yellow oil. Spectroscopically, the product is a 1.2:1 mixture of rotamers. IR ($CDCl_3$ cast, cm^{-1}): 3422 (w), 2937 (w), 1744 (w), 1656 (s), 1598 (w), 1511 (w), 1478 (w), 1420 (w), 1362 (w), 1323 (s), 1164 (s), 1120 (s), 1085 (m), 1066 (s), 1048 (m), 1016 (s), 927 (w), 847 (w), 810 (w), 765 (w), 727 (s); ^1H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, J = 8.1 Hz, 1H), 7.60 (m, 0.8H), 7.43-7.37 (m, 7.2H), 7.28-7.18 (m, 3H), 7.01 (t, J = 7.6 Hz, 1H), 6.95 (d, J = 8.1 Hz, 2H), 6.83 (d, J = 8.1 Hz, 1.6H), 6.62 (d, J = 8.1 Hz, 0.8H), 6.56 (t, J = 7.8 Hz, 0.8H), 6.41 (d, J = 7.9 Hz, 1H), 5.07 (s, 0.8H), 4.83 (s, 1H), 3.26 (s, 2.4H), 3.24 (s, 3H), 2.87 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 172.27, 171.82, 145.95, 143.20, 141.69, 139.85, 134.29, 133.81, 132.25, 131.09, 130.49, 130.25, 128.83, 128.70, 128.59, 128.04, 127.87, 126.99, 125.37 (q, J = 3.8 Hz), 125.26 (q, J = 3.8 Hz), 125.57, 123.39, 122.62, 117.60, 110.79, 109.59, 72.26, 71.26, 37.21, 37.07, 30.58 (CF_3 signals not observed); Electrospray MS *m/z* calculated for $C_{16}H_{14}NO_2F_3$ (M^+ + H): 388.0154; found: 388.0153.



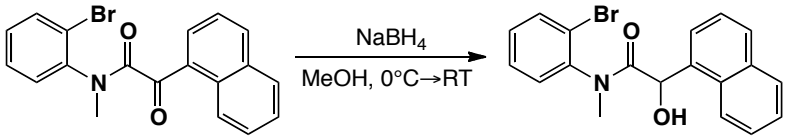
***N*-(2-bromophenyl)-2-hydroxy-2-(4-methoxyphenyl)-*N*-methylacetamide (3e).** Ketoamide (0.57 g, 1.6 mmol) was dissolved in MeOH (20 mL) under nitrogen and cooled to 0°C in an ice bath. To this, $NaBH_4$ (0.74 g, 2.0 mmol) was added and the reaction was

allowed to warm slowly to room temperature overnight. The reaction was then diluted with Et_2O and acidified with 1N HCl to a pH of 6. The layers were separated and the aqueous layer extracted with Et_2O. The organic fractions were combined and washed with brine and dried over $MgSO_4$. The solvent was removed *in vacuo* and the product purified by silica gel chromatography with 20% EtOAc/pentane. The fractions were concentrated and residual solvent removed under vacuum to yield 0.52 g (90%) of the desired alcohol as a yellow oil. IR ($CDCl_3$ cast, cm^{-1}): 3414 (br. w), 2928 (w), 1652 (s), 1611 (m), 1585 (m), 1511 (s), 1477 (m), 1439 (m), 1358 (m), 1302 (m), 1247 (s), 1175 (m), 1135 (w), 1113 (w), 1080 (m), 1046 (s), 1031 (s), 1017 (s), 939 (w), 839 (m), 809 (m), 766 (m), 727 (m); ^{1}H NMR (400 MHz, $CDCl_3$, Rotomer A): δ 7.68 (dd, $J_{1\text{-}2}$ = 8.1 Hz, $J_{1\text{-}3}$ = 1.3 Hz, 1H, H_1), 7.19 (td, $J_{2\text{-}1} = J_{2\text{-}3}$ = 8.0 Hz, $J_{2\text{-}4}$ = 1.1 Hz, 1H, H_2), 7.03 (td, $J_{3\text{-}2} = J_{3\text{-}4}$ = 7.8 Hz, $J_{3\text{-}1}$ = 1.4 Hz, 1H, H_3), 6.75 (d, $J_{6\text{-}7}$ = 8.8 Hz, 2H, H_6), 6.69 (d, $J_{7\text{-}6}$ = 8.8 Hz, 2H, H_7), 6.41 (dd, $J_{4\text{-}3}$ = 7.9 Hz, $J_{4\text{-}2}$ = 1.5 Hz, 1H, H_4), 4.68 (s, 1H, H_5), 3.77 (s, 3H, -OMe), 3.23 (s, 3H, -NMe), -OH proton not observed; ^{1}H-^{1}H COSY (400 MHz, $CDCl_3$, Rotomer A): δ 7.68 (H_1) ↔ δ 7.19 (H_2); δ 7.19 (H_2) ↔ δ 7.03 (H_3); δ 7.03 (H_3) ↔ δ 6.41 (H_4); δ 6.75 (H_6) ↔ δ 6.69 (H_7); ^{1}H NMR (400 MHz, $CDCl_3$, Rotomer B): δ 7.41 (app. q, $J_{2\text{-}1} = J_{2\text{-}3} = J_{3\text{-}2} = J_{3\text{-}4}$ = 7.8 Hz, 2H, H_2, H_3), 7.35 (dd, $J_{1\text{-}2}$ = 8.1 Hz, $J_{1\text{-}3}$ = 1.6 Hz, 1H, H_1), 7.22 (dd, $J_{4\text{-}3}$ = 7.6 Hz, $J_{4\text{-}3}$ = 1.6 Hz, 1H, H_4), 6.66 (d, $J_{6\text{-}7}$ = 9.3 Hz, 2H, H_6), 6.62 (d, $J_{7\text{-}6}$ = 9.0 Hz, 2H, H_7), 5.30 (s, 1H, H_5), 4.95 (s, 1H, -OH), 3.75 (s, 3H, -OMe), 3.26 (s, 3H, -NMe); ^{1}H-^{1}H COSY (400 MHz, $CDCl_3$, Rotomer B): δ 7.41 (H_2) ↔ δ 7.35 (H_1); δ 7.41 (H_3) ↔ δ 7.22(H_4); δ 6.66 (H_6) ↔ δ 6.62 (H_7); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, Rotamers A + B): δ 173.26, 172.85, 159.70, 159.60, 140.27, 140.20, 134.15, 133.55, 131.66, 131.35, 130.24, 130.19, 130.14, 130.10, 128.83, 128.73, 128.57, 128.50, 124.84, 123.36, 113.84, 72.23, 71.27, 55.36, 55.32, 37.00, 36.89; Electrospray MS *m/z* calculated for $C_{16}H_{17}O_3NBr$ (M^+ + H): 350.0386; found: 350.0382.

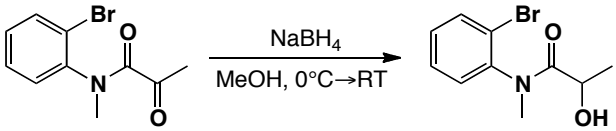


***N*-(2-bromophenyl)-2-hydroxy-2-(2-methoxyphenyl)-*N*-methylacetamide (3f).** Ketoamide (0.30 g, 0.86 mmol) was dissolved in MeOH (5 mL) under nitrogen and cooled to 0 °C in an ice bath. To this, $NaBH_4$ (0.039 g, 1.0 mmol) was added and the reaction was allowed to warm slowly to room temperature overnight. The reaction was then diluted with Et_2O and acidified with 1N HCl to a pH of 6. The layers were separated and the aqueous layer extracted with Et_2O. The organic fractions were combined and washed with water, then brine, and dried over $MgSO_4$. The solvent was removed *in vacuo* and the product purified by silica gel chromatography with 20% EtOAc/pentane. The fractions were concentrated and residual solvent removed under vacuum to yield 0.20 g (23%) of the desired alcohol as a yellow oil. Spectroscopically, the product is a 2:1 mixture of rotamers. IR ($CDCl_3$ cast, cm^{-1}): 3439 (w), 2924 (w), 1652 (s), 1600 (m), 1586 (m), 1492 (m), 1462 (m), 1437 (m), 1360 (s), 1297 (m), 1247 (s), 1187 (w), 1164 (w), 1108 (m), 1077 (m), 1045 (s), 1015 (s), 910 (w), 850 (w), 825 (w), 753 (s), 725 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (d, J = 8.0 Hz, 1H), 7.39-7.31 (m, 2H), 7.18-7.09 (m, 3.5H), 7.01 (d, J = 7.4 Hz, 1H), 6.90-6.85 (m, 1.5H), 6.80 (t, J = 7.4 Hz, 1H), 6.72 (t, J = 7.4 Hz, 0.5H), 6.61 (d, J = 8.4 Hz, 0.5H), 6.57 (d, J = 8.3 Hz, 1H), 6.29 (d, J = 7.8 Hz, 1H), 5.43 (d, J = 5.4 Hz, 0.5H), 5.22 (d, J = 5.1 Hz, 1H), 4.45 (d, J = 6.1 Hz, 0.5H), 4.36 (d, J = 5.7 Hz, 1H), 3.43 (s, 1.5H), 3.40 (s, 3H), 3.24 (s, 1.5H), 3.22 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 173.62, 173.17, 156.78, 140.34, 140.07, 133.73, 133.27, 130.96, 130.31, 129.69, 129.61, 129.53, 129.24, 128.48, 128.31, 128.11, 123.61,

120.68, 120.65, 110.24, 110.20, 66.47, 54.97, 54.91, 36.98, 36.93; Electrospray MS *m/z* calculated for $C_{16}H_{16}NO_2Br$ (M^+ + H): 372.0205; found: 372.0203.

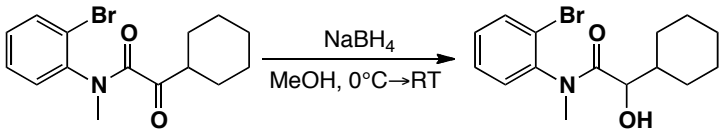


***N*-(2-bromophenyl)-2-hydroxy-*N*-methyl-2-(naphthalen-1-yl)acetamide (3g).** Ketoamide (0.519 g, 1.41 mmol) was dissolved in MeOH (5 mL) under nitrogen and cooled to 0 °C in an ice bath. To this, $NaBH_4$ (0.063 g, 1.69 mmol) was added and the reaction was allowed to warm slowly to room temperature overnight. The reaction was then diluted with Et_2O and acidified with 1N HCl to a pH of 6. The layers were separated and the aqueous layer extracted with Et_2O. The organic fractions were combined and washed with water, then brine, and dried over $MgSO_4$. The solvent was removed *in vacuo* and the product purified by silica gel chromatography with 20% EtOAc/pentane. The fractions were concentrated and residual solvent removed under vacuum to yield 0.429 g (82%) of the desired alcohol as a yellow oil. Spectroscopically, the product is a 2.5:1 mixture of rotamers. IR ($CDCl_3$ cast, cm^{-1}): 3412 (w), 3061 (w), 1651 (s), 1583 (w), 1511 (w), 1477 (m), 1438 (w), 1351 (m), 1297 (m), 1250 (w), 1165 (w), 1138 (w), 1091 (m), 1046 (m), 907 (s), 862 (w), 799 (w), 777 (m), 724 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82-7.73 (m, 4H), 7.62 (dd, *J* = 8.0, 1.0 Hz, 1H), 7.47-7.31 (m, 4H), 7.24 (t, *J* = 7.3 Hz, 1H), 7.18 (t, *J* = 7.9 Hz, 0.4H), 7.08-7.02 (m, 1.8H), 6.94 (td, *J* = 7.9, 1.4 Hz, 1H), 6.84 (d, *J* = 7.0 Hz, 0.4H), 6.52 (td, *J* = 7.8, 1.2 Hz, 1H), 5.92 (dd, *J* = 7.9, 1.3 Hz, 1H), 5.70 (d, *J* = 4.8 Hz, 0.4H), 5.49 (d, *J* = 4.7 Hz, 1H), 4.77 (d, *J* = 5.0 Hz, 0.4H), 4.68 (d, *J* = 4.8 Hz, 1H), 3.31 (s, 1.2H), 3.30 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 173.57, 173.39, 140.30, 139.94, 135.06, 134.08, 134.05, 133.76, 133.38, 131.52, 131.06, 130.73, 129.99, 129.84, 129.65, 129.05, 128.96, 128.64, 128.59, 128.51, 128.22, 127.53, 126.63, 126.50, 126.19, 125.67, 125.41, 125.18, 125.08, 124.01, 123.33, 123.02, 122.71, 71.21, 70.90, 37.30, 37.20; Electrospray MS *m/z* calculated for $C_{19}H_{17}NO_2Br$ (M^+ + H): 370.0437; found: 370.0436.

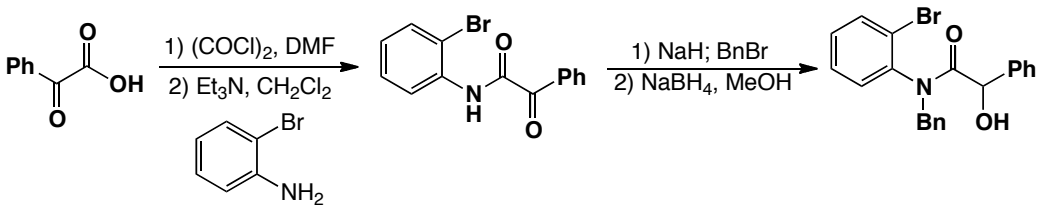


***N*-(2-bromophenyl)-2-hydroxy-*N*-methylpropanamide (3h).** Ketoamide (0.70 g, 2.9 mmol) was dissolved in MeOH (10 mL) under nitrogen and cooled to 0 °C in an ice bath. To this, $NaBH_4$ (0.13 g, 3.4 mmol) was added and the reaction was allowed to warm slowly to room temperature overnight. The reaction was then diluted with Et_2O and acidified with 1N HCl to a pH of 6. The layers were separated and the aqueous layer extracted with Et_2O. The organic fractions were combined and washed with water, then brine, and dried over $MgSO_4$. The solvent was removed *in vacuo* and the product purified by silica gel chromatography with 20% EtOAc/pentane. The fractions were concentrated and residual solvent removed under vacuum to yield 0.48 g (68%) of the desired alcohol as a white solid. Spectroscopically, the product is a 1:1 mixture of rotamers. IR ($CDCl_3$ cast, cm^{-1}): 3436 (br), 2980 (w), 1652 (s), 1584 (w), 1476 (m), 1356 (m), 1294 (m), 1117 (s), 1051 (m), 1029 (s), 878 (w), 767 (m), 729 (m); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.0 Hz, 2H), 7.41 (m, 2H), 7.32 (m, 4H), 4.16 (quint, *J* = 6.6 Hz, 1H), 3.93 (quint, *J* = 6.8 Hz, 1H), 3.43 (app. t, *J* = 8.3 Hz, 2H), 3.27 (s, 3H), 3.25 (s, 3H), 1.12 (app. t, *J* = 6.7 Hz, 6H); ^{13}C{^{1}H} NMR (100

MHz, $CDCl_3$): δ 175.94, 175.49, 141.99, 134.37, 134.14, 130.34, 130.32, 130.28, 130.18, 129.10, 129.08, 123.71, 123.02, 65.56, 64.86, 36.77, 36.65, 21.59, 20.67; Electrospray MS *m/z* calculated for $C_{10}H_{13}NO_2Br$ (M^+ + H): 258.0124; found: 258.0125.

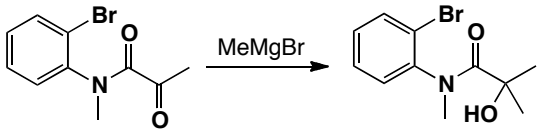


***N*-(2-bromophenyl)-2-cyclohexyl-2-hydroxy-*N*-methylacetamide (3i).** Ketoamide (0.28 g, 0.86 mmol) was dissolved in MeOH (5 mL) under nitrogen and cooled to 0 °C in an ice bath. To this, $NaBH_4$ (0.039 g, 1.0 mmol) was added and the reaction was allowed to warm slowly to room temperature overnight. The reaction was then diluted with Et_2O and acidified with 1N HCl to a pH of 6. The layers were separated and the aqueous layer extracted with Et_2O. The organic fractions were combined and washed with water, then brine, and dried over $MgSO_4$. The solvent was removed *in vacuo* and the product purified by silica gel chromatography with 20% EtOAc/pentane. The fractions were concentrated and residual solvent removed under vacuum to yield 0.16 g (59%) of the desired alcohol as a yellow oil. Spectroscopically, the product is a 1:1 mixture of rotamers. IR ($CDCl_3$ cast, cm^{-1}): 3445 (w), 2925 (s), 2952 (m), 1650 (s), 1584 (w), 1477 (m), 1447 (m), 1355 (m), 1299 (m), 1108 (m), 1051 (m), 1030 (m), 995 (w), 909 (m), 809 (w), 764 (m), 726 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.69 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.44 (td, *J* = 7.7, 1.2 Hz, 1H), 7.39 (td, *J* = 8.2, 1.2 Hz, 1H), 7.34 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.31-7.26 (m, 3H), 3.93 (d, *J* = 5.5 Hz, 1H), 3.63 (dd, *J* = 7.0, 3.1 Hz, 1H), 3.37 (d, *J* = 7.3 Hz, 1H), 3.22 (s, 3H), 3.20 (s, 3H), 3.16 (d, *J* = 8.0 Hz, 1H), 1.80-1.37 (m, 8H), 1.31-0.98 (m, 14H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 174.60, 174.27, 141.14, 141.11, 134.24, 133.99, 130.47, 130.19, 130.11, 130.05, 128.91, 128.85, 123.65, 123.08, 73.47, 72.83, 41.69, 39.70, 36.82, 36.79, 29.74, 29.71, 26.42, 26.37, 26.03, 25.97, 25.93, 25.80, 25.71, 25.28; Electrospray MS *m/z* calculated for $C_{15}H_{21}NO_2Br$ (M^+ + H): 326.0750; found: 326.0752.



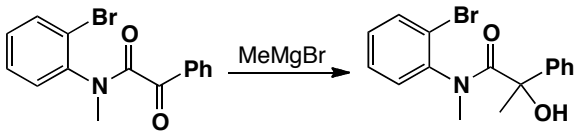
***N*-benzyl-*N*-(2-bromophenyl)-2-hydroxy-2-phenylacetamide (3j).** In a Schlenk flask, carboxylic acid (1.04 g, 6.93 mmol) was dissolved in CH_2Cl_2 (10 mL) under a nitrogen atmosphere. To this, oxalyl chloride (712 μL, 8.32 mmol) was added, followed by one drop of dimethylformamide. The reaction was stirred until gas evolution ceased. The volatiles were removed under vacuum and the residue dissolved in CH_2Cl_2 (20 mL) and cooled to 0 °C. To this solution, 2-bromoaniline (784 μL, 6.93 mmol) was added, followed by triethylamine (2 mL, 27 mmol). The reaction was allowed to warm to room temperature overnight. The reaction was acidified with 1N HCl, diluted with diethyl ether, and the layers separated. The aqueous layer was extracted with diethyl ether, and the combined extracts were washed with water, then brine, and dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue purified by silica gel chromatography using 10% EtOAc/pentane to yield 1.68 g (80%) of product as a yellow. IR (CH_2Cl_2 cast, cm^{-1}): 3340 (w), 3070 (w), 1698 (s), 1672 (s), 1592 (m), 1520 (s), 1437 (m), 1273 (m), 1165 (m), 1047 (w), 1026 (w), 989

(w), 940 (w), 880 (w), 823 (w), 801 (w), 742 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.59 (br. s, 1H), 8.50 (dd, *J* = 8.2, 1.3 Hz, 1H), 8.43 (d, *J* = 7.3 Hz, 2H), 7.66 (t, *J* = 7.4 Hz, 1H), 7.60 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.52 (t, *J* = 7.9 Hz, 2H), 7.38 (td, *J* = 8.3, 1.0 Hz, 1H), 7.06 (td, *J* = 7.9, 1.4 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 186.6, 158.7, 134.7, 134.6, 132.9, 132.6, 131.4, 128.5, 128.4, 126.1, 121.3, 114.2. Electrospray MS *m/z* calculated for $C_{14}H_{10}NO_2Br$ (M^+): 302.9895; found: 302.9893. The solid amide (1.68 g, 5.52 mmol) was dissolved in THF (10 mL) and cooled to 0 °C. To this, NaH (442 mg, 11 mmol, 60% suspension) was added and stirred for one hour at 0 °C, then one hour at room temperature. The solution was cooled to 0 °C, and benzylbromide (1.32 mL, 11 mmol) was added slowly. The reaction was allowed to warm to room temperature overnight, then was quenched with sat. NH_4Cl solution. The mixture was diluted with diethyl ether and the aqueous phase was extracted. The combined organics were washed with brine and dried over Na_2SO_4. The product was purified by silica gel chromatography using 10% EtOAc/pentane to yield 770 mg (1.95 mmol, 35%) of product as a white solid. This material was dissolved in MeOH (10 mL) and cooled to 0 °C. $NaBH_4$ (90 mg, 2.38 mmol) was added and allowed to stir overnight. The reaction was quenched with 1M HCl and diluted with ether. The layers were separated and the aqueous phase extracted with ether. The combined organics were washed with brine and dried over Na_2SO_4. The product was purified by column using 10% EtOAc/pentane to yield 445 mg (58%) of product as a white solid. Spectroscopically, the product is a 1.7:1 mix of rotamers. IR ($CDCl_3$ cast, cm^{-1}): 3449 (br, w), 3065 (w), 3030 (w), 2925 (w), 1652 (s), 1584 (w), 1520 (w), 1494 (w), 1475 (m), 1454 (w), 1436 (w), 1375 (m), 1284 (m), 1253 (w), 1188 (m), 1060 (m), 990 (w), 909 (m), 848 (w), 816 (w), 761 (w), 725 (s), 696 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.37 (dd, *J* = 7.3, 1.8 Hz, 0.6H), 7.23-7.06 (m, 16H), 6.81 (dd, *J* = 7.2, 1.6 Hz, 2.6H), 6.75-6.70 (m, 2H), 5.83 (dd, *J* = 7.9, 1.5 Hz, 1H), 5.74 (d, *J* = 14.0 Hz, 0.6H), 5.54 (d, *J* = 14.3 Hz, 1H), 4.92 (d, *J* = 6.5 Hz, 0.6H), 4.74 (d, *J* = 6.5 Hz, 1H), 4.70 (d, *J* = 6.6 Hz, 0.6H), 4.56 (d, *J* = 6.5 Hz, 1H), 4.10 (d, *J* = 14.3 Hz, 1H), 3.99 (d, *J* = 14.3 Hz, 0.6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 173.11, 172.49, 139.25, 138.23, 137.84, 137.74, 136.08, 134.10, 133.51, 132.54, 132.24, 130.36, 130.24, 129.42, 129.25, 129.13, 128.57, 128.54, 128.52, 128.50, 128.43, 128.39, 128.06, 127.94, 127.86, 127.85, 127.72, 127.54, 125.11, 123.91, 73.05, 72.02, 53.03, 52.26; Electrospray MS *m/z* calculated for $C_{21}H_{18}O_2NBrNa$ (M^+ + Na): 418.0413; found: 418.0398.

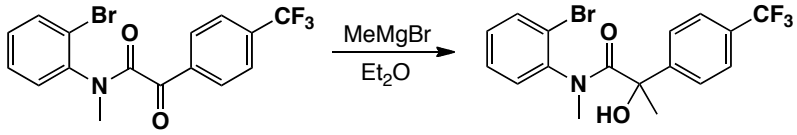


***N*-(2-bromophenyl)-2-hydroxy-*N*,2-dimethylpropanamide (3k).** In a Schlenk flask, ketoamide (571 mg, 2.23 mmol) was dissolved in THF (10 mL) under a nitrogen atmosphere and cooled to 0 °C. To this, MeMgBr (0.96 mL, 2.9 mmol, 3M in diethyl ether) was added and allowed to warm to room temperature overnight. The reaction was quenched with saturated NH_4Cl solution and the layers separated. The aqueous layer was extracted with diethyl ether, and the combined organic fractions were washed with brine and dried over Na_2SO_4. The solvent was removed and the residue purified by silica gel chromatography using 20% EtOAc/pentane to yield 454 mg (75%) of product as a cloudy oil. IR ($CDCl_3$ cast, cm^{-1}): 3423 (br., w), 2928 (w), 1628 (s), 1582 (w), 1475 (m), 1437 (w), 1381 (m), 1346 (s), 1288 (m), 1251 (w), 1182 (m), 1119 (m), 1091 (w), 1054 (w), 1028 (w), 967 (w), 880 (w), 765 (s), 730 (s); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.67 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.42-7.32 (m, 2H), 7.25 (m, 1H), 4.07 (s, 1H), 3.27 (s, 3H), 1.32 (s, 3H), 1.11 (s, 3H); ^{13}C{^{1}H} NMR (100

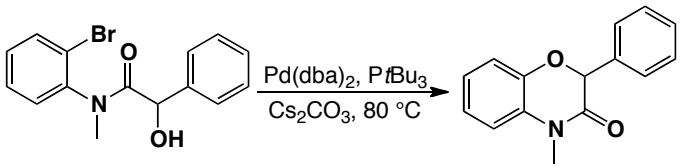
MHz, $CDCl_3$): δ 176.9, 142.9, 134.0, 130.6, 130.2, 128.6, 124.2, 73.2, 31.0, 29.9, 26.5; Electrospray MS *m/z* calculated for $C_{11}H_{15}O_2NBr$ (M^+ + H): 270.1124; found: 270.1117.



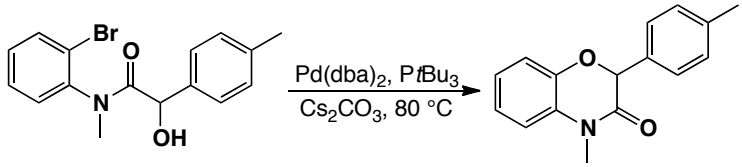
***N*-(2-bromophenyl)-2hydroxyl-*N*-methyl-2-phenylpropanamide (3l).** In a Schlenk flask, ketoamide (580 mg, 1.82 mmol) was dissolved in THF (10 mL) under a nitrogen atmosphere and cooled to –78 °C. To this, MeMgBr (1.2 mL, 3.6 mmol, 3M in diethyl ether) was added and allowed to warm to room temperature overnight. The reaction was quenched with saturated NH_4Cl solution and the layers separated. The aqueous layer was extracted with diethyl ether, and the combined organic fractions were washed with brine and dried over Na_2SO_4. The solvent was removed and the residue purified by silica gel chromatography using 20% EtOAc/pentane to yield 256 mg (42%) of product as a white solid. The NMR spectra are extremely complicated. We therefore carried the product forward with further characterization. IR ($CDCl_3$ cast, cm^{-1}): 3363 (br, m), 3967 (w), 2980 (w), 2931 (w), 1630 (s), 1580 (m), 1475 (m), 1444 (m), 1370 (m), 1289 (w), 1202 (w), 1116 (w), 1071 (m), 1028 (m), 939 (w), 912 (w), 760 (m), 726 (s), 702 (s); Electrospray MS *m/z* calculated for $C_{16}H_{17}NO_2Br$ (M^+ + H): 334.0437; found: 334.0454.



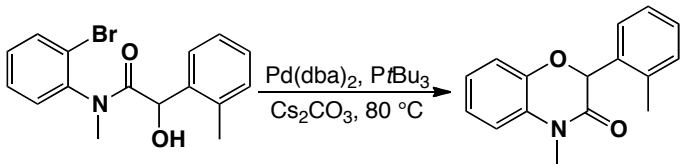
***N*-(2-bromophenyl)-2-hydroxy-*N*-methyl-2-(4-(trifluoromethyl)phenyl)propanamide (3m).** In a Schlenk flask, amidoketone (100 mg, 0.26 mmol) was dissolved in diethyl ether (3 mL) under a nitrogen atmosphere. Methyl magnesium bromide (0.087 mL, 0.26 mmol, 3.0 M) was added and the reaction stirred for three hours. Saturated ammonium chloride solution was added, the layers separated, and the aqueous layer extracted with diethyl ether. The combined extracts were washed were brine and dried over Na_2SO_4. The solvent was removed and the residue purified by silica gel chromatography (neutralized with 1 mL of Et_3N) with 30% Et_2O/pentane to yield 73 mg (70%) of product as a white powder. The ^1H NMR spectrum is very complicated, suggesting a mixture of several rotamers. IR ($CDCl_3$ cast, cm^{-1}): 3395 (br., w), 2928 (w), 1637 (s), 1583 (w), 1478 (w), 1442 (w), 1413 (w), 1354 (w), 1325 (s), 1251 (w), 1163 (s), 1121 (s), 1074 (s), 1029 (w), 1017 (w), 936 (w), 897 (w), 846 (w), 764 (w); ^1H NMR (300 MHz, $CDCl_3$): δ 7.72 (br. s, 1H), 7.60-7.36 (m, 3.13H), 7.21-7.11 (m, 3.37H), 6.88-6.75 (m, 0.86H), 6.08 (m, 0.49H), 5.40 (s, 0.51H), 4.93-4.78 (m, 0.25H), 4.24 (s, 0.36H), 3.25 (s, 1.54H), 3.22 (s, 0.96H), 2.93 (br. s, 0.76H), 1.99 (br. s, 0.71H), 1.81 (br. s, 1.22H), 1.64 and 1.62 (both s, 2.37H), 1.30 (s, 1.39H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 174.6, 147.4, 140.8, 133.6, 131.4, 129.9, 129.7, 127.8, 126.6, 126.3, 125.2, 124.7, 123.6, 29.7, 23.9.



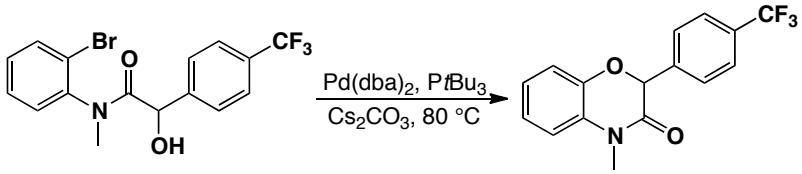
4-Methyl-2-phenyl-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4a). In a Schlenk flask, $Pd(dba)_2$ (4.0 mg, 7.0 μmol), $[HPtBu_3]BF_4$ (4.1 mg, 14.0 μmol), and Cs_2CO_3 (300 mg, 0.92 mmol) were dissolved in toluene (5 mL) and heated at 80 °C for 30 min. To this, amidoalcohol (216 mg, 0.77 mmol) was added and stirred for 16 hours. The solvent was removed *in vacuo* and the residue filtered through Celite with diethyl ether. The solvent was removed and the residue purified by silica gel chromatography with 5% EtOAc/pentane to yield 141 mg (84%) of product as a pale yellow solid. The enantioenriched product was prepared in an analogous fashion from the enantioenriched alcohol. 70% *ee*; $[\alpha]_D^{20} = -22$ (c = 0.187, $CHCl_3$); HPLC: Chiralpak AS-H, 1% *i*PrOH/hexane for 10 min then 1→10% *i*PrOH/hexane over 45 min, 1.0 mL/min, 254 nm, t_R = 23.70 min (minor), t_R = 33.15 min (major); IR ($CDCl_3$ cast, cm^{-1}): 2922 (w), 1676 (s), 1608 (w), 1501 (m), 1476 (m), 1450 (m), 1419 (w), 1382 (s), 1323 (w), 1301 (w), 1276 (m), 1221 (m), 1184 (w), 1123 (m), 1042 (m), 924 (m), 872 (w), 825 (w), 746 (s), 694 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.41 (dd, $J_{ortho\text{-}meta}$ = 7.1 Hz, $J_{ortho\text{-}para}$ = 2.0 Hz, 2H, H_{ortho}), 7.35-7.30 (m, 3H, H_{ortho}, H_{para}), 7.08-6.94 (m, 4H), 5.74 (s, 1H, -OCHPh), 3.42 (s, 3H, Me); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 164.7, 144.0, 135.4, 129.3, 128.7, 128.6, 126.9, 124.1, 122.8, 117.5, 114.8, 78.6, 28.6; Electrospray MS *m/z* calculated for $C_{15}H_{14}NO_2$ (M^+ + H): 240.1019; found: 240.1022 (100%).



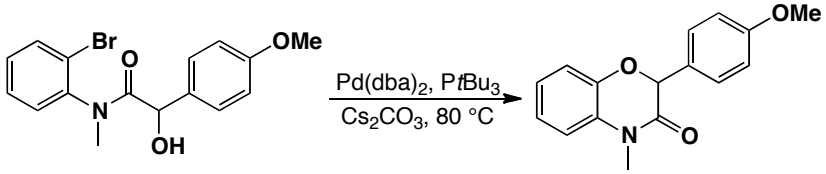
4-methyl-2-(*p*-tolyl)-2*H*-benzo[*b*][1,4]oxazin-3-(4*H*)-one (4b). In a Schlenk flask, $Pd(dba)_2$ (2.9 mg, 5.1 μmol), $[HPtBu_3]BF_4$ (2.9 mg, 10.2 μmol), Cs_2CO_3 (198 mg, 0.61 mmol), and amidoalcohol (170 mg, 0.51 mmol) were dissolved in toluene (5 mL) and heated at 80 °C for 16 hours. The solvent was removed *in vacuo* and the residue filtered through Celite with diethyl ether. The solvent was removed and the residue purified by silica gel chromatography with 5% EtOAc/pentane to yield 103 mg (80%) of product as a yellow oil. IR ($CDCl_3$ cast, cm^{-1}): 2921 (w), 1677 (s), 1609 (w), 1502 (s), 1476 (m), 1419 (w), 1381 (s), 1322 (w), 1301 (w), 1275 (m), 1221 (m), 1182 (w), 1122 (m), 1040 (m), 1019 (w), 923 (m), 877 (w), 810 (m), 786 (w), 744 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.1 Hz, 2H), 7.07-7.00 (m, 3H), 6.96-6.94 (m, 2H), 5.71 (s, 1H), 3.42 (s, 3H), 2.32 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 164.91, 144.09, 138.61, 132.45, 129.38, 129.36, 126.91, 124.04, 122.70, 117.50, 114.76, 78.53, 28.54, 21.23; Electrospray MS *m/z* calculated for $C_{16}H_{16}NO_2$ (M^+ + H): 254.1175; found: 254.1181.



4-methyl-2-(*o*-tolyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4c). In a Schlenk flask, $Pd(dba)_2$ (1.7 mg, 3.1 μmol), $[HPtBu_3]BF_4$ (1.7 mg, 6.2 μmol), and Cs_2CO_3 (120 mg, 0.37 mmol) were dissolved in toluene (5 mL) and heated a 80 °C for 30 min. To this, amidoalcohol (100 mg, 0.31 mmol) was added and stirred for 16 hours. The solvent was removed *in vacuo* and the residue filtered through Celite with diethyl ether. The solvent was removed and the residue purified by silica gel chromatography with 10% EtOAc/pentane to yield 66 mg (87%) of product as a pale yellow solid. IR ($CDCl_3$ cast, cm^{-1}): 2929 (w), 1677 (s), 1607 (w), 1501 (s), 1476 (m), 1419 (w), 1381 (s), 1323 (w), 1300 (w), 1265 (m), 1218 (m), 1125 (w), 1039 (m), 1016 (w), 926 (w), 872 (w), 831 (w), 805 (w), 744 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (m, 2H), 7.15 (m, 2H), 7.04 (m, 2H), 6.97 (m, 2H), 5.80 (s, 1H), 3.48 (s, 3H), 2.49 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.3, 144.3, 137.6, 133.5, 130.9, 129.7, 129.0, 127.3, 125.9, 123.9, 122.7, 117.2, 114.6, 77.0, 28.5, 19.5; Electrospray MS *m/z* calculated for $C_{16}H_{16}NO_2$ (M^+ + H): 254.1175; found: 254.1181.

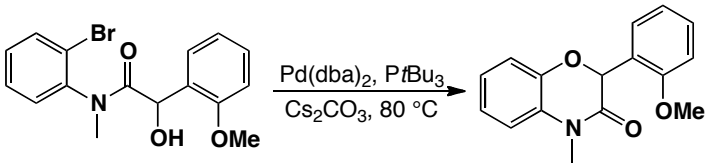


4-methyl-2-(4-(trifluoromethyl)phenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4d). In a Schlenk flask, $Pd(dba)_2$ (2.2 mg, 3.8 μmol), $[HPtBu_3]BF_4$ (2.2 mg, 7.6 μmol), and Cs_2CO_3 (150 mg, 0.46 mmol) were dissolved in toluene (5 mL) and heated at 80 °C for 30 min. To this, amidoalcohol (150 mg, 0.38 mmol) was added as a solution in toluene (1 mL) and stirred for 16 hours. The solvent was removed *in vacuo* and the residue filtered through Celite with diethyl ether. The solvent was removed and the residue purified by silica gel chromatography with 5% EtOAc/pentane to yield 97 mg (87%) of product as a yellow solid. IR ($CDCl_3$ cast, cm^{-1}): 2924 (w), 1684 (s), 1611 (w), 1503 (m), 1478 (w), 1415 (w), 1387 (m), 1325 (s), 1276 (w), 1228 (w), 1167 (m), 1124 (s), 1068 (m), 1018 (w), 825 (w), 749 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, J = 8.8 Hz, 2H), 7.57 (d, J = 8.5 Hz, 2H), 7.11-7.09 (m, 1H), 7.06-7.04 (m, 2H), 6.98-6.96 (m, 1H), 5.77 (s, 1H), 3.42 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 164.0, 143.8, 139.3, 131.0, 129.0, 127.2, 125.5 (q, J = 3.8 Hz), 124.3, 123.1, 117.4, 115.0, 77.9, 28.7 (CF_3 signal not observed); Electrospray MS *m/z* calculated for $C_{16}H_{16}NO_2$ (M^+ + H): 308.0887; found: 308.0892.

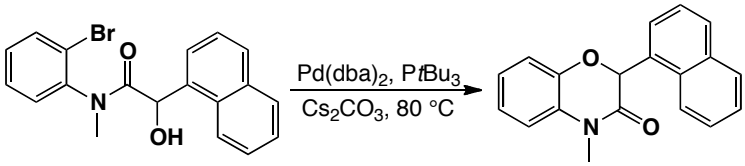


2-(4-methoxyphenyl)-4-methyl-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4e). In a Schlenk flask, $Pd(dba)_2$ (3.7 mg, 6.3 μmol), $[HPtBu_3]BF_4$ (3.7 mg, 13 μmol), Cs_2CO_3 (248 mg, 0.76 mmol), and amidoalcohol (223 mg, 0.63 mmol) were dissolved in toluene (5 mL) and heated at 80 °C for 16 hours. The solvent was removed *in vacuo* and the residue filtered through

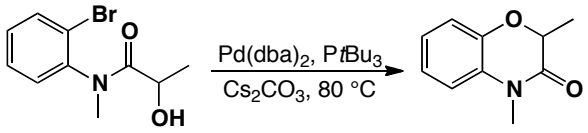
Celite with diethyl ether. The solvent was removed and the residue purified by silica gel chromatography with 5% EtOAc/pentane to yield 154 mg (90%) of product as a pale yellow solid. IR ($CDCl_3$ cast, cm^{-1}): 2927 (w), 1680 (s), 1610 (m), 1504 (s), 1477 (m), 1419 (w), 1384 (s), 1304 (w), 1248 (s), 1177 (s), 1122 (w), 1031 (m), 925 (w), 823 (m), 749 (s); ^1H NMR (400 MHz, $CDCl_3$): δ 7.30 (d, J = 8.8 Hz, 2H), 7.02 (m, 3H), 6.96 (m, 1H), 6.84 (d, J = 8.8 Hz, 2H), 5.66 (s, 1H), 3.76 (s, 3H), 3.43 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.0, 159.9, 144.1, 129.4, 128.4, 127.5, 124.0, 122.7, 117.5, 114.7, 114.1, 78.4, 55.3, 28.6; Electrospray MS *m/z* calculated for $C_{16}H_{16}O_3N$ (M^+ + H): 272.0280; found: 272.0277.



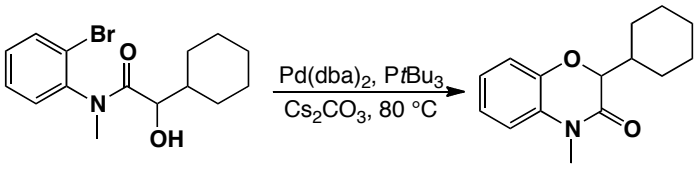
2-(2-methoxyphenyl)-4-methyl-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4f). In a Schlenk flask, $Pd(dba)_2$ (1 mg, 1.7 μmol), P*t*Bu_3 (1 mg, 3.4 μmol), and Cs_2CO_3 (51 mg, 0.15 mmol) were dissolved in toluene (5 mL) and heated at 80 °C for 30 min. To this, amidoalcohol (55 mg, 0.15 mmol) was added and stirred for 16 hours. The solvent was removed *in vacuo* and the residue filtered through Celite with diethyl ether. The solvent was removed and the residue purified by silica gel chromatography with 10% EtOAc/pentane to yield 40 mg (95%) of product as a yellow oil. IR ($CDCl_3$ cast, cm^{-1}): 2927 (w), 1676 (s), 1604 (m), 1500 (s), 1463 (m), 1419 (w), 1382 (s), 1344 (w), 1325 (w), 1300 (m), 1248 (s), 1224 (m), 1191 (w), 1163 (w), 1124 (w), 1025 (m), 926 (w), 878 (w), 830 (w), 801 (w), 747 (s); ^1H NMR (300 MHz, $CDCl_3$): δ 7.36 (td, J = 6.8, 1.6 Hz, 1H), 7.26 (dd, J = 7.1, 1.3 Hz, 1H), 7.08-6.92 (m, 6H), 6.00 (s, 1H), 3.85 (s, 3H), 3.47 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.6, 157.8, 144.8, 130.6, 129.9, 128.8, 124.2, 123.8, 122.6, 120.7, 117.2, 114.5, 111.3, 74.4, 55.9, 28.6; Electrospray MS *m/z* calculated for $C_{16}H_{16}NO_3$ (M^+ + H): 270.1124; found: 270.1114.



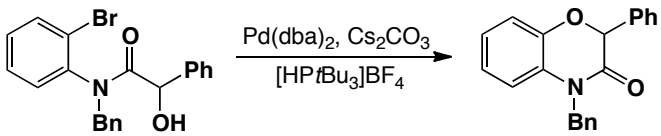
4-methyl-2-(naphthalen-1-yl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4g). In a Schlenk flask, $Pd(dba)_2$ (3.2 mg, 5.6 μmol), [HP*t*Bu_3]BF_4 (3.2 mg, 11 μmol), and Cs_2CO_3 (196 mg, 0.97 mmol) were dissolved in toluene (5 mL) and heated at 80 °C for 30 min. To this, amidoalcohol (203 mg, 0.55 mmol) was added and stirred for 16 hours. The solvent was removed *in vacuo* and the residue filtered through Celite with diethyl ether. The solvent was removed and the residue purified by silica gel chromatography with 5% EtOAc/pentane to yield 132 mg (84%) of product as a yellow oil. IR ($CDCl_3$ cast, cm^{-1}): 2925 (w), 1681 (s), 1608 (w), 1502 (s), 1477 (m), 1419 (w), 1385 (s), 1302 (w), 1274 (m), 1219 (w), 1124 (w), 1043 (w), 1017 (w), 925 (w), 791 (m), 774 (m), 749 (s); ^1H NMR (300 MHz, $CDCl_3$): δ 8.30 (d, J = 8.2 Hz, 1H), 7.87 (t, J = 9.0 Hz, 2H), 7.61 (t, J = 6.8 Hz, 1H), 7.55 (t, J = 6.9 Hz, 1H), 7.37-7.34 (m, 2H), 7.08-7.06 (m, 2H), 6.98-6.88 (m, 2H), 6.35 (s, 1H), 3.56 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.36, 144.12, 134.12, 131.62, 130.68, 130.18, 129.84, 128.85, 126.74, 126.03, 126.01, 124.87, 124.26, 124.05, 122.89, 117.54, 114.70, 77.36, 28.72; Electrospray MS *m/z* calculated for $C_{19}H_{16}NO_2$ (M^+ + H): 290.1175; found: 290.1171.



2,4-dimethyl-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4h). In a Schlenk flask, $Pd(dba)_2$ (4.7 mg, 2.1 μmol), $[HPtBu_3]BF_4$ (4.7 mg, 16 μmol), and Cs_2CO_3 (291 mg, 1.44 mmol) were dissolved in toluene (5 mL) and heated a 80 °C for 30 min. To this, amidoalcohol (200 mg, 0.81 mmol) was added and stirred for 16 hours. The solvent was removed *in vacuo* and the residue filtered through Celite with diethyl ether. The solvent was removed and the residue purified by silica gel chromatography with 5% EtOAc/pentane to yield 90 mg (62%) of product as a yellow oil. IR ($CDCl_3$ cast, cm^{-1}): 2932 (w), 1682 (s), 1609 (w), 1503 (m), 1478 (w), 1419 (w), 1386 (m), 1311 (w), 1274 (m), 1235 (w), 1129 (w), 1109 (w), 1070 (w), 1039 (w), 750 (m); ^1H NMR (400 MHz, $CDCl_3$): δ 7.05-6.95 (m, 4H), 4.63 (q, J = 6.8 Hz, 1H), 3.36 (s, 3H), 1.56 (d, J = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 167.0, 144.4, 129.9, 123.8, 122.6, 117.1, 114.6, 73.6, 28.5, 16.5; Electrospray MS *m/z* calculated for $C_{10}H_{12}NO_2$ (M^+ + H): 178.0862; found: 178.0863.

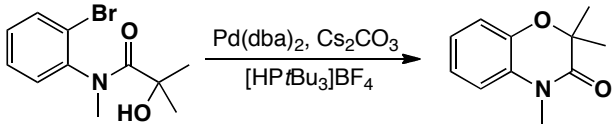


2-cyclohexyl-4-methyl-4*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4i). In a Schlenk flask, $Pd(dba)_2$ (2.5 mg, 4.3 μmol), $[HPtBu_3]BF_4$ (2.5 mg, 8.6 μmol), and Cs_2CO_3 (168 mg, 0.50 mmol) were dissolved in toluene (5 mL) and heated a 80 °C for 30 min. To this, amidoalcohol (140 mg, 0.43 mmol) was added as a solution in toluene (1 mL) and stirred for 16 hours. The solvent was removed *in vacuo* and the residue filtered through Celite with diethyl ether. The solvent was removed and the residue purified by silica gel chromatography with 5% EtOAc/pentane to yield 63 mg (60%) of product as a yellow oil. IR ($CDCl_3$ cast, cm^{-1}): 2926 (m), 2853 (m), 1677 (s), 1608 (w), 1502 (s), 1477 (m), 1450 (w), 1419 (w), 1381 (s), 1320 (w), 1275 (m), 1230 (m), 1186 (w), 1129 (w), 1040 (w), 993 (w), 923 (w), 894 (w), 826 (w), 745 (s); ^1H NMR (400 MHz, $CDCl_3$): δ 7.03-6.91 (m, 4H), 4.36 (d, J = 6.4 Hz, 1H), 3.35 (s, 3H), 1.88-1.64 (m, 5H), 1.36-1.15 (m, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.5, 144.4, 129.5, 123.8, 122.2, 116.9, 114.5, 81.4, 38.9, 29.0, 28.2, 27.8; Electrospray MS *m/z* calculated for $C_{15}H_{20}NO_2$ (M^+ + H): 246.1488; found: 246.1491.

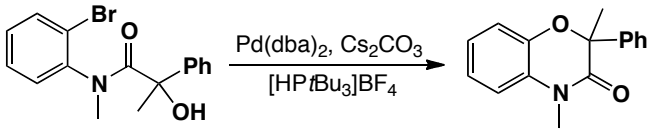


4-benzyl-2-phenyl-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4j). In a Schlenk flask, $Pd(dba)_2$ (71 mg, 0.12 mmol), $[HPtBu_3]BF_4$ (72 mg, 0.24 mmol), and Cs_2CO_3 (404 mg, 1.24 mmol) were dissolved in toluene (20 mL) and heated a 80 °C for 30 min. To this, amidoalcohol (246 mg, 0.62 mmol) was added and stirred for 16 hours. The solvent was removed *in vacuo* and the residue filtered through Celite with diethyl ether. The crude product was dissolved in MeOH (10 mL) and cooled to 0 °C. $NaBH_4$ (40 mg) was added and stirred for two hours. The reaction was quenche with 1M HCl, and extracted with diethyl ether. The combined organics were washed with brine and dried over $MgSO_4$. The solvent was removed and the

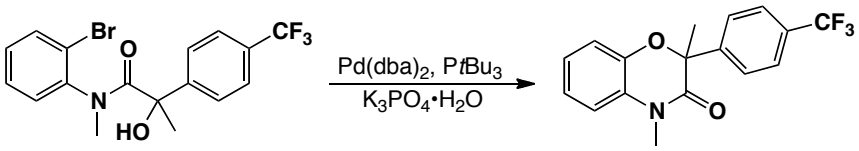
residue purified by silica gel chromatography with 5% EtOAc/pentane to yield 74 mg (38%) of product as a pale yellow solid. IR ($CDCl_3$ cast, cm^{-1}): 3032 (w), 2926 (w), 2855 (w), 1680 (s), 1606 (w), 1499 (s), 1466 (w), 1453 (w), 1396 (s), 1326 (m), 1301 (w), 1277 (m), 1245 (m), 1205 (w), 1184 (w), 1159 (w), 125 (w), 1084 (w), 1049 (m), 1030 (w), 923 (w), 885 (w), 834 (w), 749 (s), 696 (s); ^1H NMR (400 MHz, $CDCl_3$): δ 7.44 (m, 2H), 7.34-7.18 (m, 8H), 7.05 (dd, J = 7.5, 0.9 Hz, 1H), 6.93 (ddd, J = 8.9, 6.0, 3.0 Hz, 1H), 6.83 (m, 2H), 5.82 (s, 1H), 5.30 (d, J = 16.1 Hz, 1H), 5.04 (d, J = 16.1 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 164.8, 144.0, 136.0, 135.1, 128.8, 128.7, 128.6, 128.4, 127.4, 126.7, 126.5, 124.1, 122.6, 117.6, 115.5, 78.5, 45.2; Electrospray MS *m/z* calculated for $C_{21}H_{18}NO_2$ (M^+ + H): 316.1332; found: 316.1333.



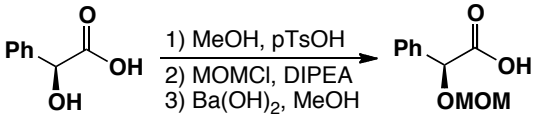
2,2,4-trimethyl-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4k). In a Schlenk flask, $Pd(dba)_2$ (9.6 mg, 17 μmol), $[HPtBu_3]BF_4$ (10 mg, 34 μmol), Cs_2CO_3 (652 mg, 2.00 mmol) were combined and heated at 80 °C under a nitrogen atmosphere for 30 min. To this, tertiary alcohol (454 mg, 1.67 mmol) was added and stirred for 16 hours. The solvent was removed *in vacuo* and the residue filtered through Celite with diethyl ether. The product was purified by silica gel chromatography using 5% EtOAc/pentane to yield 216 mg (68%) of product as an oil. IR ($CDCl_3$ cast, cm^{-1}): 2925 (m), 2855 (w), 1681 (s), 1609 (w), 1503 (m), 1477 (w), 1418 (w), 1384 (m), 1307 (w), 1284 (w), 1260 (m), 1198 (w), 1165 (m), 1125 (w), 1044 (w), 955 (w), 748 (m); ^1H NMR (400 MHz, $CDCl_3$): δ 7.03-6.92 (m, 4H), 3.36 (s, 3H), 1.50 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 169.0, 143.4, 129.9, 123.8, 122.3, 117.5, 114.3, 77.9, 28.7, 23.9. Electrospray MS *m/z* calculated for $C_{11}H_{14}NO_2$ (M^+ + H): 192.1019; found: 192.1011.



2,4-dimethyl-2-phenyl-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4l). In a Schlenk flask, $Pd(dba)_2$ (4.4 mg, 7.7 μmol), $[HPtBu_3]BF_4$ (4.4 mg, 15 μmol), Cs_2CO_3 (301 mg, 0.92 mmol) were combined and heated at 80 °C under a nitrogen atmosphere for 30 min. To this, tertiary alcohol (256 mg, 0.77 mmol) was added and stirred for 16 hours. The solvent was removed *in vacuo* and the residue filtered through Celite with diethyl ether. The product was purified by silica gel chromatography using 5% EtOAc/pentane to yield 136 mg (70%) of product a pale yellow solid. IR ($CDCl_3$ cast, cm^{-1}): 2934 (w), 1679 (s), 1610 (w), 1503 (m), 1477 (w), 1448 (w), 1418 (w), 1379 (s), 1306 (w), 1281 (w), 1247 (w), 1220 (w), 1135 (w), 1040 (w), 750 (w), 700 (w); ^1H NMR (400 MHz, $CDCl_3$): δ 7.43 (m, 2H), 7.25 (m, 2H), 7.18 (tt, J = 7.2, 1.3 Hz, 1H), 7.09 (dd, J = 7.8, 1.6 Hz, 1H), 6.97 (td, J = 7.5, 1.6 Hz, 1H), 6.92 (td, J = 7.5, 1.6 Hz, 1H), 6.80 (dd, J = 7.8, 1.6 Hz, 1H), 3.38 (s, 3H), 1.92 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 166.7, 144.0, 140.15, 129.7, 128.3, 127.8, 125.1, 123.6, 122.4, 117.5, 114.5, 81.9, 28.8, 27.5; Electrospray MS *m/z* calculated for $C_{16}H_{16}O_2N$ (M^+ + H): 254.1175; found: 254.1167.



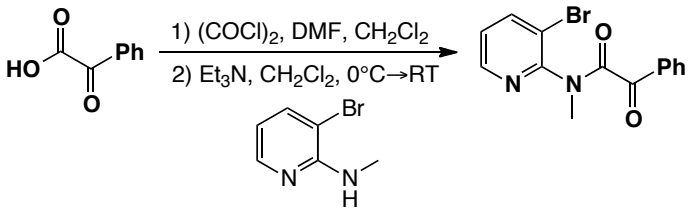
2,4-dimethyl-2-(4-(trifluoromethyl)phenyl)-2*H*-benzo[*b*][1,4]oxazin-3(4*H*)-one (4m). In a Schlenk flask, $Pd(dba)_2$ (31 mg, 0.054 mmol), P*t*Bu_3 (22 mg, 0.11 mmol), and K_3PO_4•H_2O (84 mg, 0.36 mmol) were dissolved in toluene (5 mL) and heated at 80 °C for one hour under a nitrogen atmosphere. To this, amidoalcohol (73 mg, 0.18 mmol) was added and the reaction was allowed to proceed for 16 hours. The solvent was removed *in vacuo* and the residue filtered through Celite with diethyl ether. The solvent was removed and the product residue purified by silica gel chromatography with 5% EtOAc/pentane to yield approximately 58 mg (77%). Some phosphine oxide by product contaminates the final product. IR ($CDCl_3$ cast, cm^{-1}): 2922 (w), 1677 (s), 1613 (w), 1593 (w), 1503 (s), 1477 (w), 1410 (w), 1379 (s), 1323 (s), 1280 (m), 1246 (w), 1166 (m), 1123 (s), 1107 (s), 1081 (s), 1065 (m), 1040 (w), 1017 (m), 951 (w), 906 (w), 843 (m), 748 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 (d, J = 8.5 Hz, 2H), 7.51 (d, J = 8.5 Hz, 2H), 7.11 (dd, J = 7.8, 1.9 Hz, 1H), 6.99 (app. quintd, 7.4, 1.7 Hz, 2H), 6.85 (dd, J = 7.5, 1.9 Hz, 1H), 3.41 (s, 3H), 1.91 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 166.2, 144.4, 143.7, 130.4, 130.0, 129.5, 125.7, 125.5 (q, J = 3.7 Hz), 124.0, 122.9, 117.6, 114.8, 81.7, 29.1, 27.5 (CF_3 signal not observed); Electrospray MS *m/z* calculated for $C_{17}H_{15}O_2NF_3$ (M^+ + H): 322.1049; found: 322.1052.



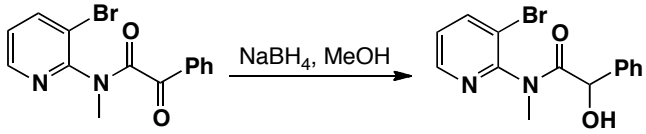
(S)-2-(methoxymethoxy)2-phenylacetic acid (5). (S)-Mandelic acid (2.00 g, 13.2 mmol) was dissolved in MeOH (25 mL) and *p*TsOH (65 mg) was added. The solution was heated at reflux for 16 hours, then the solvent was removed and the residue dissolved in diethyl ether. The solution was washed with $NaHCO_3$ solution, extracted with diethyl ether, washed with brine, and dried over Na_2SO_4 to provide 1.64 g (75%) of the crude ester.[8] The crude product (1.64 g, 9.87 mmol) was dissolved in CH_2Cl_2 (25 mL) and cooled to 0 °C in an ice bath. MOMCl (18.0 mL, 37.8 mmol, 2.1 M sol. in toluene) was added, followed by slow addition of diisopropylethylamine (3.5 mL, 20.0 mmol). The reaction was allowed to warm to room temperature overnight. Water was added and the product extracted with CH_2Cl_2. The combined organics were washed with brine and dried over Na_2SO_4 to provide 2.33 g of crude protected alcohol.[8] The material (2.33 g) was dissolved in MeOH (50 mL) and $Ba(OH)_2$•$8H_2O$ was added. The reaction was stirred for 20 min then cooled to 0 °C in an ice bath, followed by addition of 22.2 mL of 1M HCl to bring the pH to 6. The solution was diluted with water and extracted with CH_2Cl_2. The combined extracts were washed with brine and dried over Na_2SO_4 to proved 588 mg (23% overall) of product as a white solid with 90% *ee*; $[\alpha]_D^{20}$ = +144 (c = 2.94, $CHCl_3$); HPLC: Chiralpak AD-H, 1% *i*PrOH/hexane for 10 min then 1→20% *i*PrOH/hexane over 45 min, 1 mL/min, 240 nm; t_R = 26.55 min (minor), t_R = 28.34 min (major); IR ($CDCl_3$ cast, cm^{-1}): 3690-2300 (br, m), 1725 (s), 1495 (w), 1455 (w), 1402 (w), 1212 (m), 1149 (s), 1108 (s), 1040 (s), 989 (m), 919 (m), 765 (w), 722 (m), 698 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.16 (br. s, 1H), 7.47 (m, 2H), 7.37 (m, 3H), 5.19 (s, 1H), 4.74 (d, J = 6.9 Hz, 1H), 4.69 (d, J = 6.9 Hz, 1H), 3.39 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$):

[8] Barret, A. G. M.; Rys, D. J. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1009.

δ 176.0, 135.4, 129.1, 128.8, 127.5, 94.9, 76.3, 56.1; Electrospray MS *m/z* calculated for $C_{10}H_{12}O_4Na$ (M^+ + Na): 219.0627; found: 219.0620.

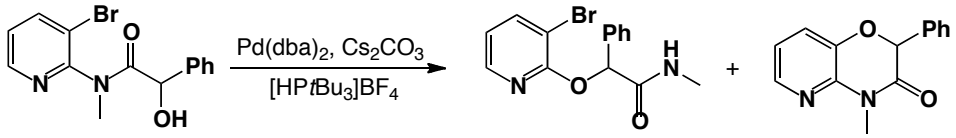


***N*-(3-bromopyridin-2-yl)-*N*-methyl-2-oxo-2-phenylacetamide.** In a Schlenk flask, benzoylformic acid (255 mg, 1.70 mmol) was dissolved in CH_2Cl_2 (5 mL) under a nitrogen atmosphere. To this, oxalyl chloride (0.175 mL, 2.04 mmol) was added, followed by one drop of dimethylformamide. The reaction was stirred until gas evolution ceased, then all volatiles were removed under vacuum. The residue was redissolved in CH_2Cl_2 (5 mL) and was cooled to 0 °C. 3-bromo-*N*-methylpyridin-2-amine (332 mg, 1.80 mmol) was added, followed by triethylamine (0.700 mL, 5.05 mmol). The reaction was allowed to warm to room temperature overnight. Volatiles were removed under vacuum and the residue taken up in CH_2Cl_2 and washed with water. The aqueous layer was extracted with CH_2Cl_2 and the combined extracts were washed with brine and dried over $MgSO_4$. The solvent was removed *in vacuo* and the residue purified by silica gel chromatography using 15% EtOAc/pentane to yield 235 mg (41%) of product as a white solid. IR ($CDCl_3$ cast, cm^{-1}): 1662 (s), 1596 (w), 1570 (m), 1432 (m), 1375 (w), 1316 (w), 1233 (m), 1146 (m), 1052 (w), 1024 (w), 964 (w), 854 (w), 803 (w), 735 (m); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.17 (dd, $J_{1\text{-}2}$ = 4.7 Hz, $J_{1\text{-}3}$ = 1.6 Hz, 1H, H_1), 8.02 (app. d, $J_{4\text{-}5}$ = 5.1 Hz, 2H, H_4), 7.98 (dd, $J_{3\text{-}2}$ = 8.0 Hz, $J_{3\text{-}4}$ = 1.6 Hz, 1H, H_3), 7.61 (tt, $J_{6\text{-}5}$ = 7.4 Hz, $J_{6\text{-}4}$ = 1.3 Hz, 1H, H_6), 7.48 (t, $J_{5\text{-}4}$ = $J_{5\text{-}6}$ = 7.8 Hz, 2H, H_5), 7.10 (dd, $J_{2\text{-}3}$ = 8.0 Hz, $J_{2\text{-}1}$ = 4.7 Hz, 1H, H_2), 3.51 (s, 3H, Me); ^{1}H-^{1}H COSY (300 MHz, $CDCl_3$): δ 8.17 (H_1) ↔ δ 7.10 (H_2); δ 8.02 (H_4) ↔ δ 7.48 (H_5); δ 7.98 (H_3) ↔ δ 7.10 (H_2); δ 7.61 (H_6) ↔ δ 7.48 (H_5); ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ 189.2, 166.9, 153.0, 147.4, 143.0, 134.0, 133.6, 130.2, 128.4, 124.5, 117.4, 34.4; Electrospray MS *m/z* calculated for $C_{14}H_{12}N_2O_2Br$ (M^+ + H): 319.0076; found: 319.0076.



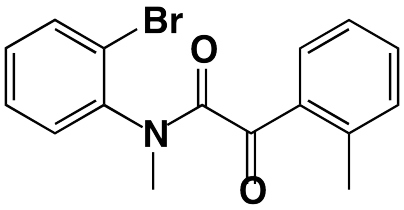
***N*-(3-bromopyridin-2-yl)-2-hydroxy-*N*-methyl-2-phenylacetamide (6).** Ketoamide (235 mg, 0.74 mmol) was dissolved in MeOH (5 mL) under nitrogen and cooled to 0 °C in an ice bath. To this, $NaBH_4$ (33 mg, 0.87 mmol) was added and the reaction was allowed to warm slowly to room temperature overnight. The reaction was then diluted with Et_2O and acidified with 1N HCl to a pH of 6. The layers were separated and the aqueous layer extracted with Et_2O. The organic fractions were combined and washed with water, then brine, and dried over $MgSO_4$. The solvent was removed *in vacuo* and the product purified by silica gel chromatography with 70% EtOAc/pentane to provide 108 mg (46%) the desired alcohol as a white solid. Spectroscopically, the product is mainly one rotomer with ≈15% of a second compound. IR ($CDCl_3$ cast, cm^{-1}): 3413 (br, w), 3064 (w), 2932 (w), 1655 (s), 1566 (m), 1429 (s), 1353 (s), 1305 (m), 1231 (w), 1191 (w), 1145 (m), 1092 (m), 1062 (s), 1021 (s), 937 (w), 911 (m), 849 (w), 800 (m), 762 (m), 727 (s), 698 (s); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (br. s, 1H), 7.70 (br. s, 1H), 7.15-7.08 (m, 4H), 6.72 (d, J = 7.1 Hz, 2H), 5.14 (br. s, 1H),

4.60 (br. s, 1H), 3.27 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 173.1 (br), 152.2, 147.7 (br), 142.6, 137.8 (br), 128.3, 128.2, 127.1, 124.9, 119.9, 72.4 (br), 35.5; Electrospray MS *m/z* calculated for $C_{14}H_{14}O_2N_2Br$ (M^+ + H): 321.0233; found: 321.0231.

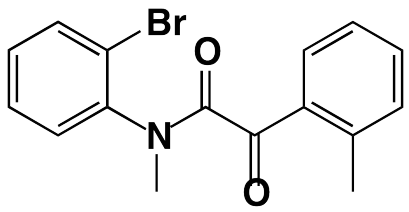


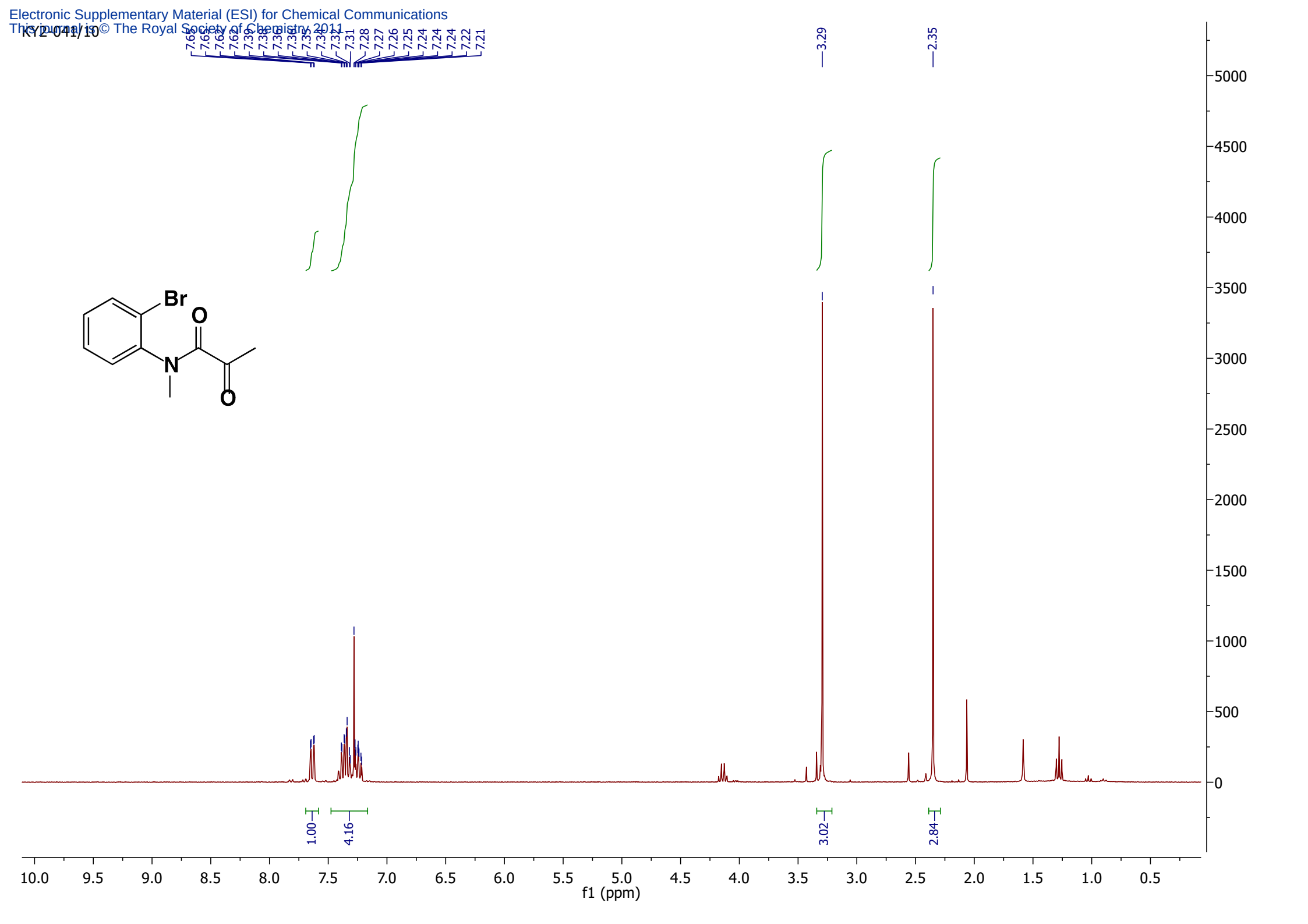
2-((2-bromopyridin-2-yl)oxy)-*N*-methyl-2-phenylacetamide (8) and 4-methyl-2-phenyl-2*H*-pyrido[3,2-*b*][1,4]oxazin-3(4*H*)-one (7). Amide (23 mg, 0.072 mmol), $Pd(dba)_2$ (1 mg, 1.7 μmol), $[HPtBu_3]BF_4$ (1 mg, 3.4 μmol), and Cs_2CO_3 (28 mg, 0.086 mmol) were combined in toluene (5 mL) and heated at 80 °C for 16 hours. The solvent was removed and the residue filtered through Celite. The product was purified by silica gel chromatography using 10% EtOAc/pentane to provide 13 mg (56%) of **8** as an oil. The crude mixture was a 1:2 mixture of **7**:**8**. After purification, only **8** was fully characterized. IR ($CDCl_3$ cast, cm^{-1}): 3298 (w), 3063 (w), 2929 (w), 1665 (s), 1582 (m), 1533 (m), 1496 (w), 1427 (s), 1366 (w), 1307 (m), 1243 (m), 1189 (w), 1159 (w), 1127 (w), 1071 (m), 1031 (m), 893 (w), 788 (m), 748 (m), 732 (m), 697 (m); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (dd, J = 4.8, 1.6 Hz, 1H), 7.85 (dd, J = 7.6, 1.6 Hz, 1H), 7.60 (d, J = 7.0 Hz, 2H), 7.38-7.28 (m, 3H), 6.83 (dd, J = 7.6, 4.8 Hz, 1H), 6.71 (br. s, 1H), 6.51 (s, 1H), 2.88 (d, J = 4.9 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 169.93, 157.52, 145.75, 141.98, 136.35, 128.45, 128.39, 126.80, 119.13, 107.09, 77.36, 26.14; Electrospray MS *m/z* calculated for $C_{14}H_{13}O_2N_2BrNa$ (M^+ + Na): 343.0052; found: 343.0063. Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (dd, J = 4.8, 1.6 Hz, 1H), 7.64 (m, 1H, overlaps), 6.96 (dd, J = 7.9, 4.9 Hz, 1H), 5.79 (s, 1H), 3.57 (s, 3H), remaining signals are buried under other isomer peaks).

KTZ-050
1H Spectrum

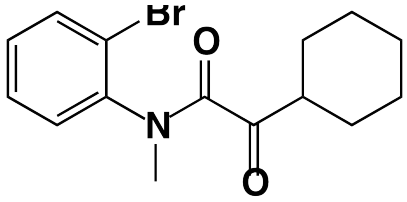


KYZ-050
13C CPD-Spectrum



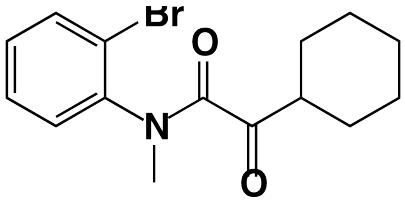


KTZ-039/2
1H Spectrum

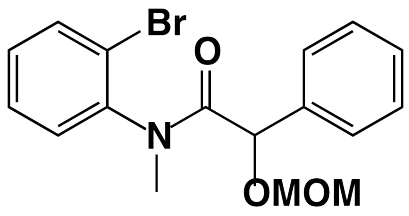


KYZ-039_c13/2

13C CPD-Spectrum



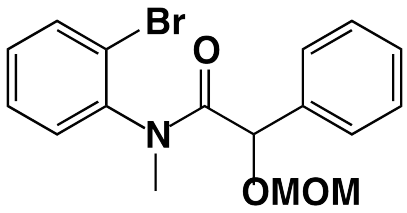
KYP-04-13
1H Spectrum



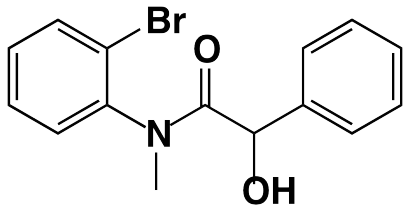
f1 (ppm)

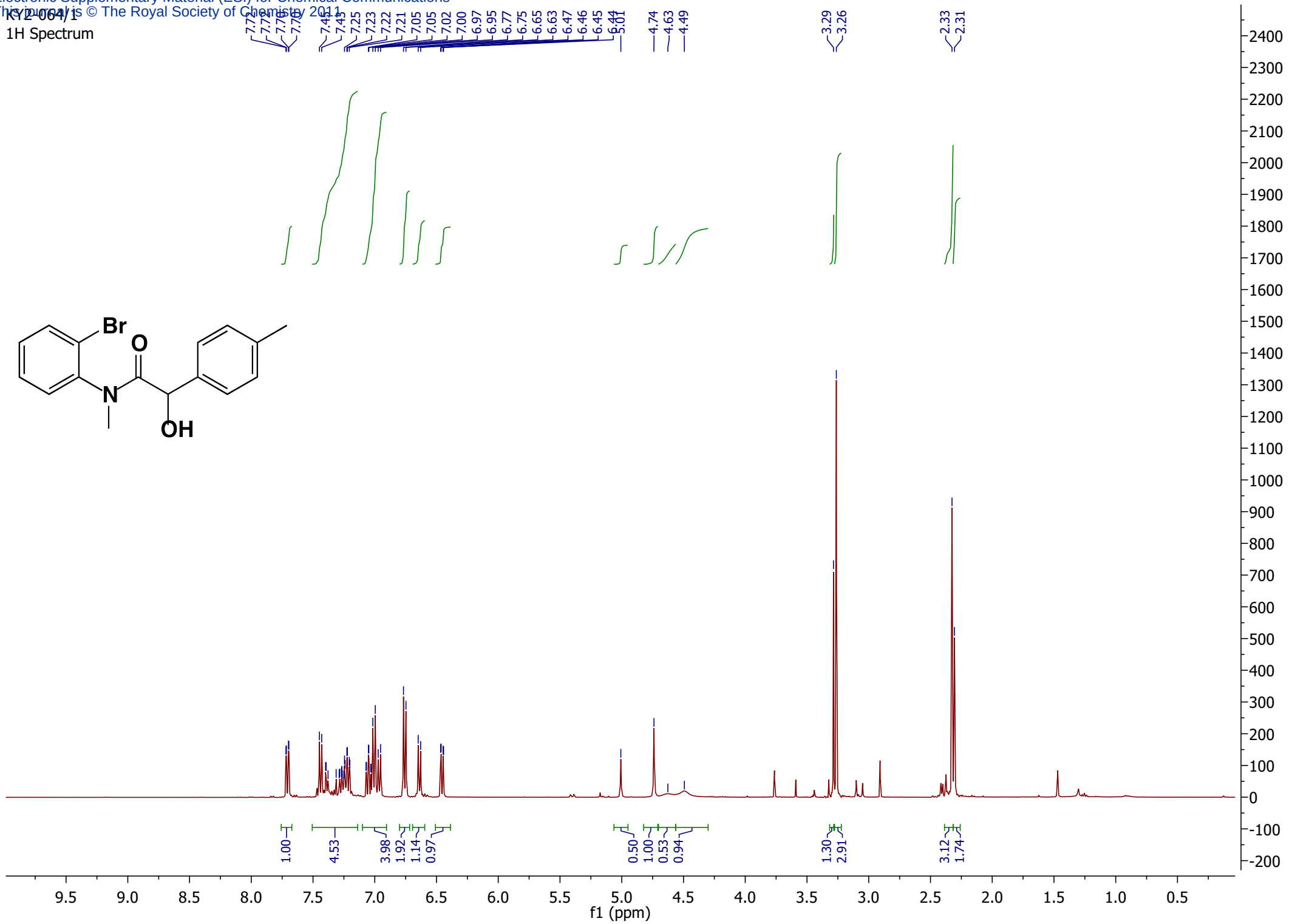
KYB-049_c13/1

13C CPD-Spectrum

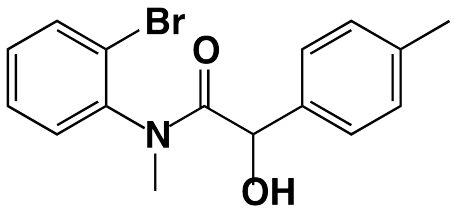


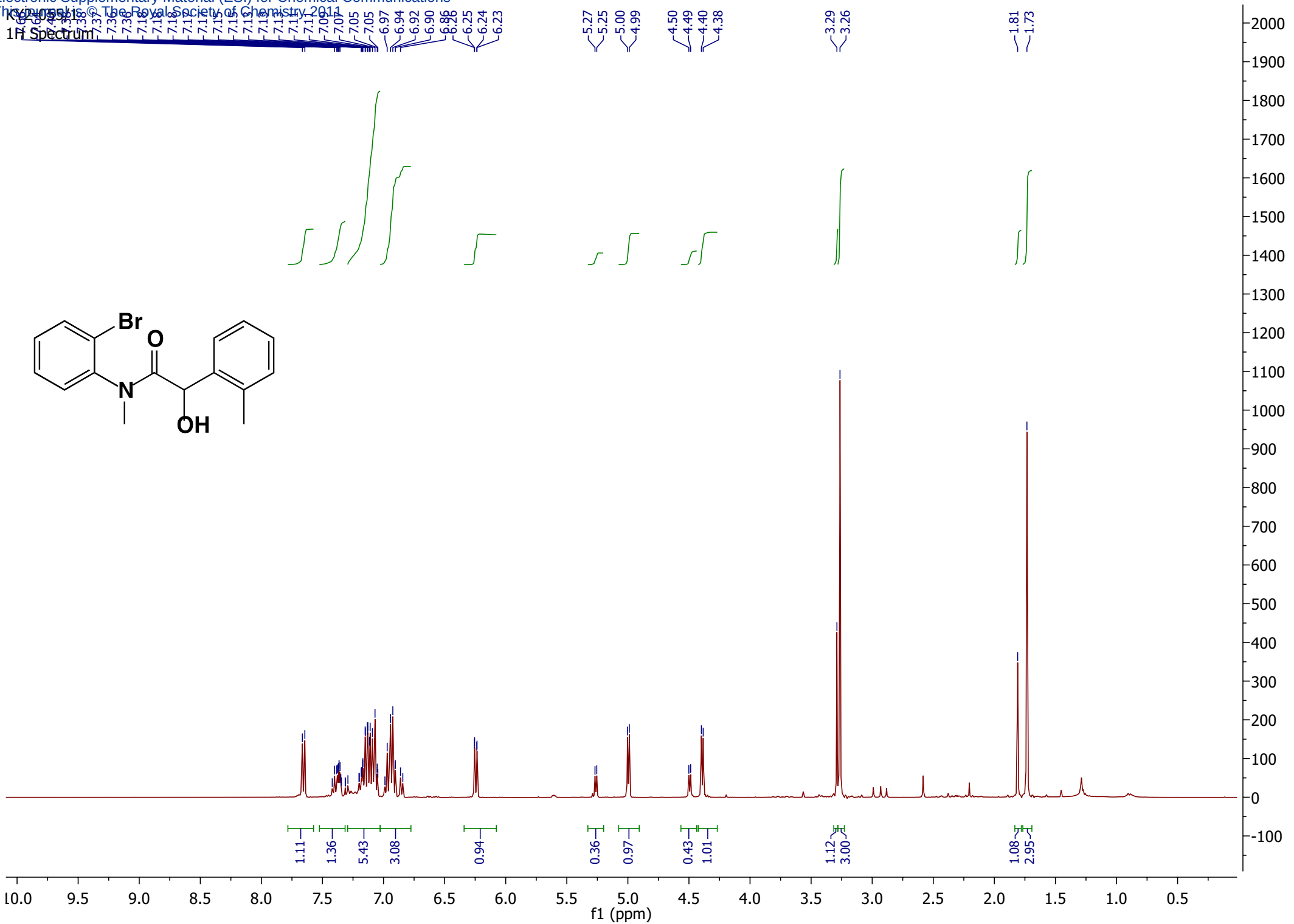
KR3-046-2
1H Spectrum



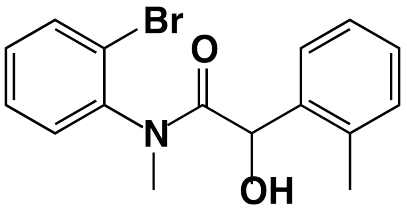


KYZ-064_C13
13C CPD-Spectrum

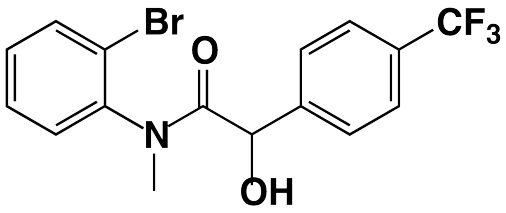




KYZ-059_c13/1
13C CPD-Spectrum

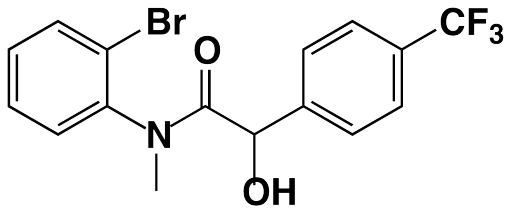


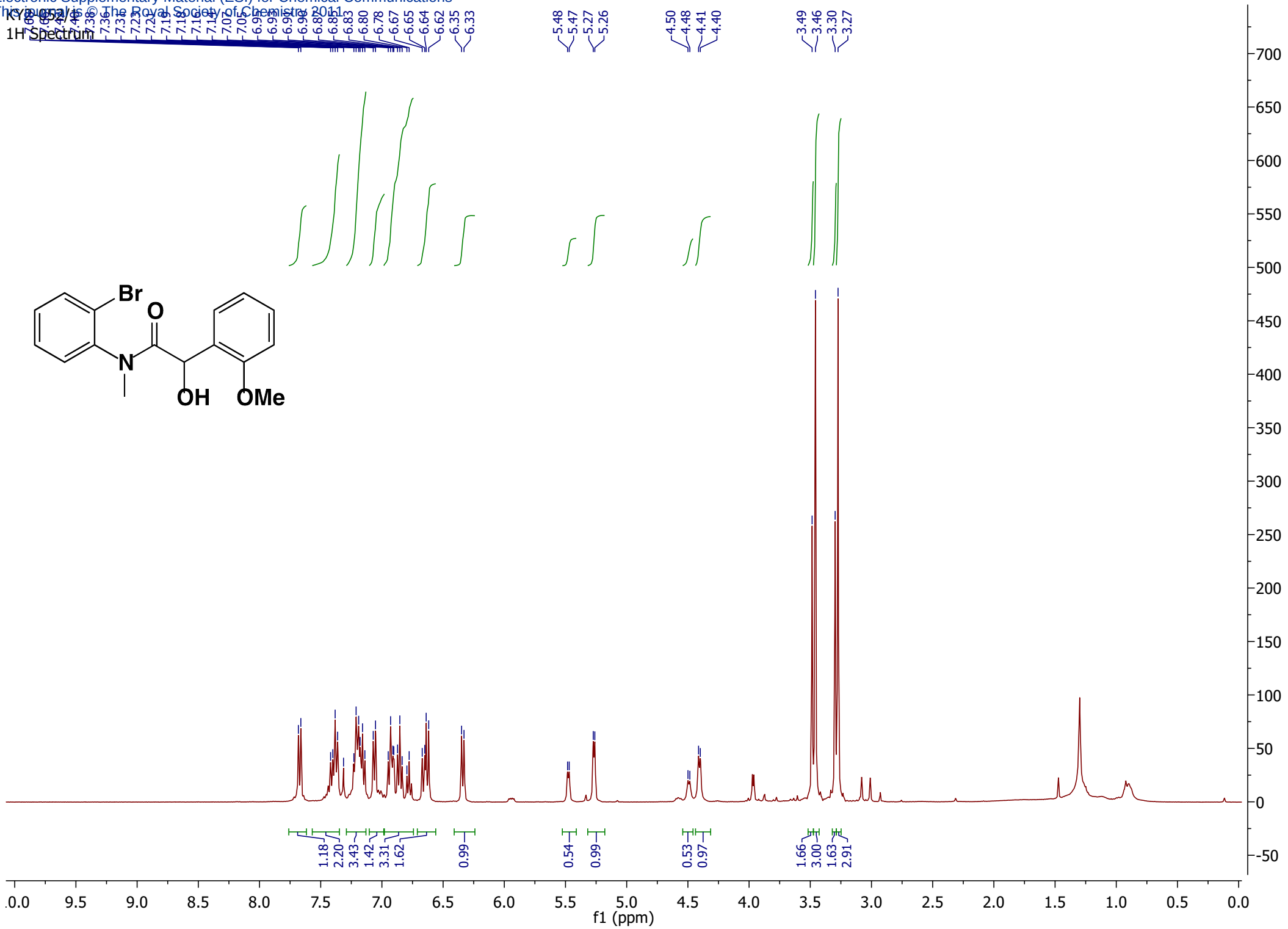
KYZ-05-11
1H Spectrum



KYZ-054_C13/1

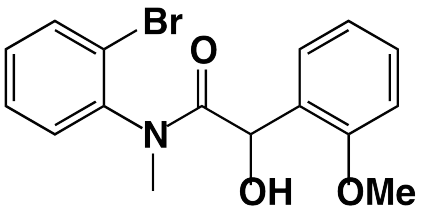
13C CPD-Spectrum

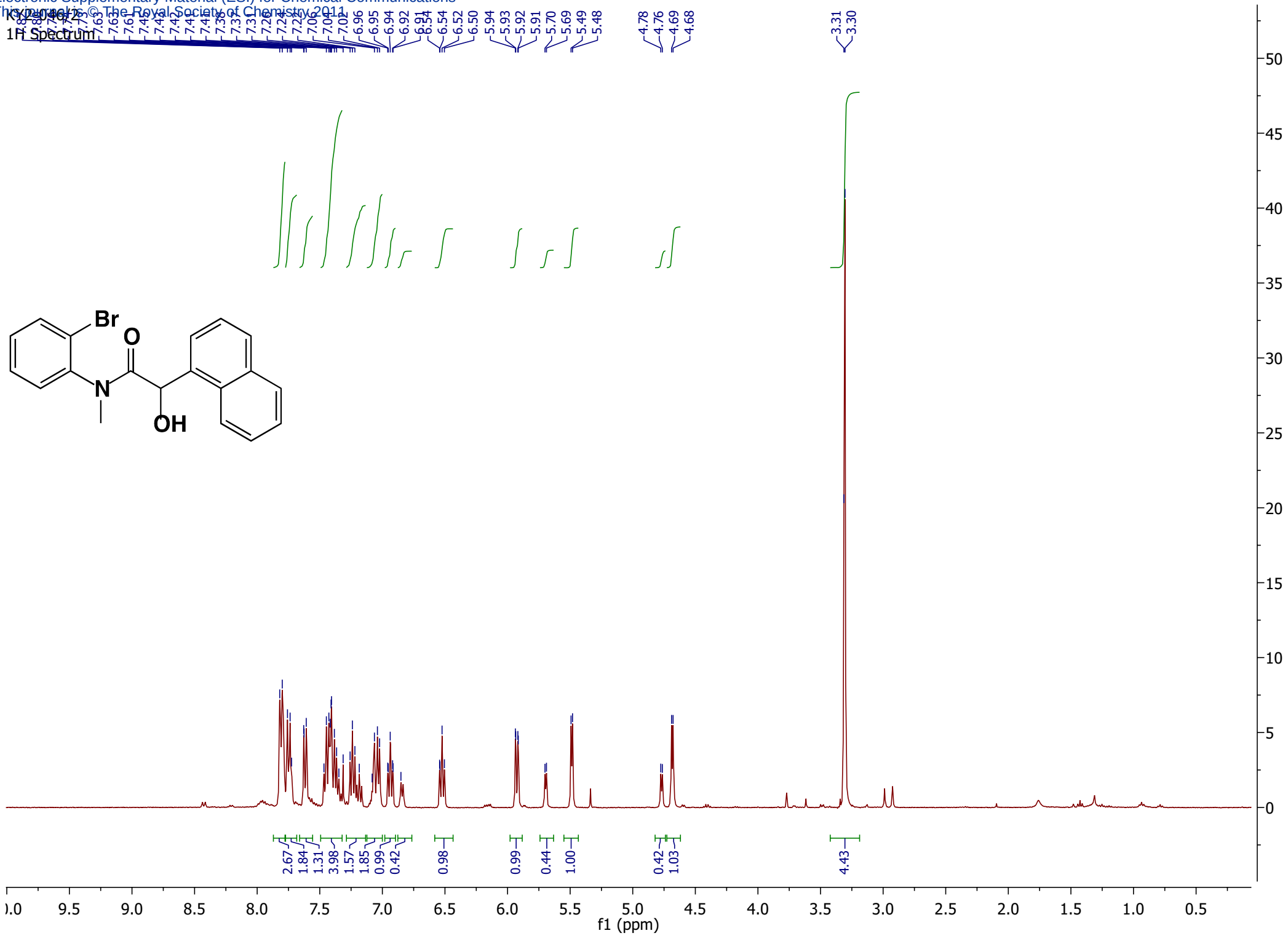




KYZ-052_C13/1

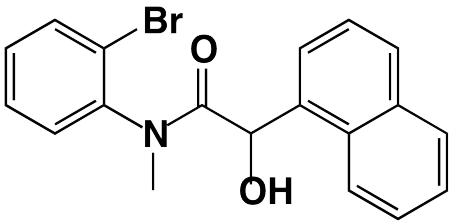
13C CPD-Spectrum





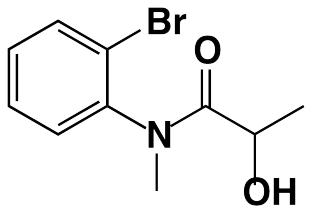
KYZ-046_c13/2

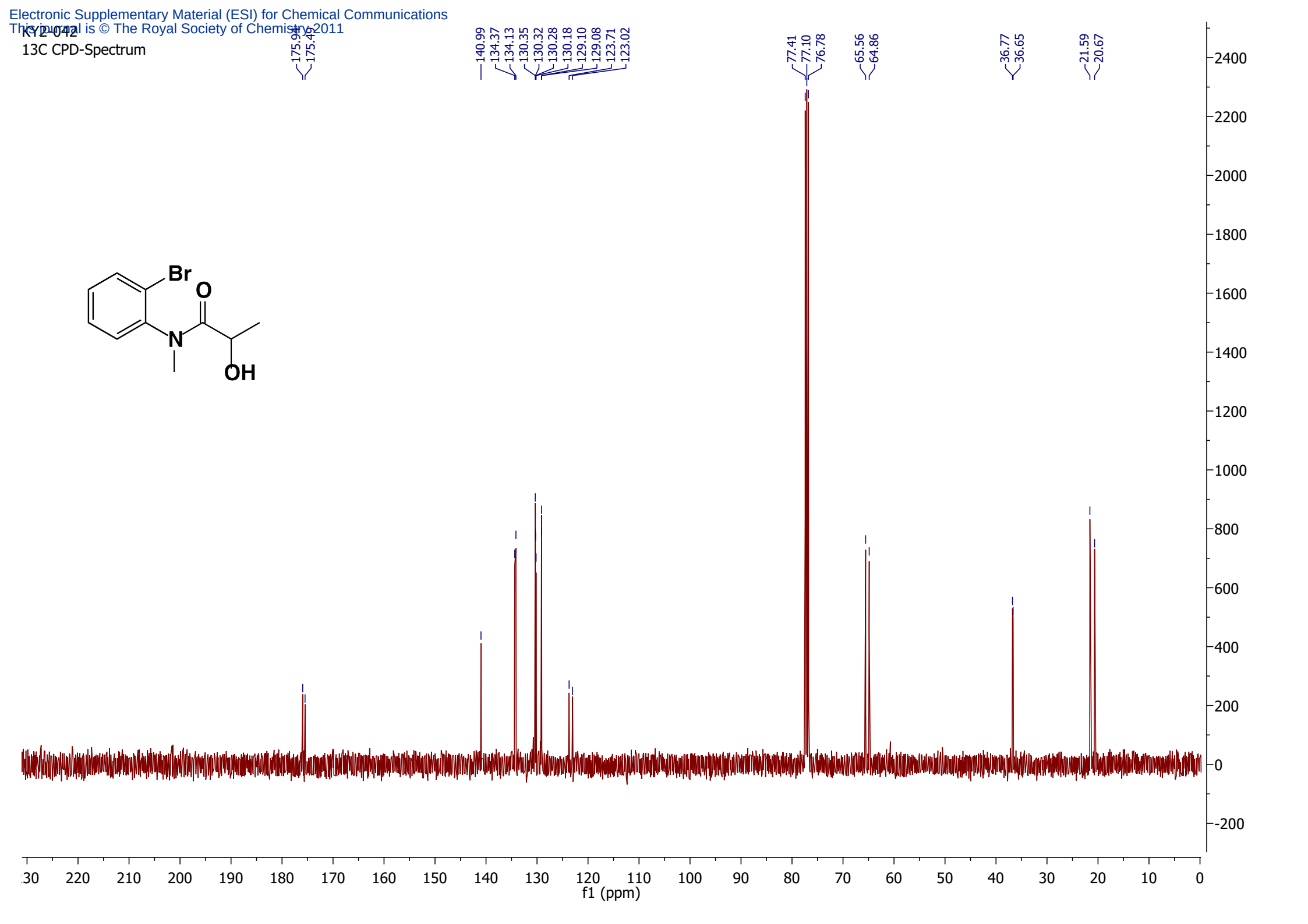
13C CPD-Spectrum



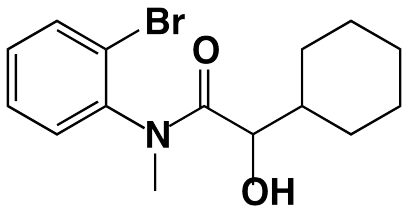
KYZ-042

13C CPD-Spectrum



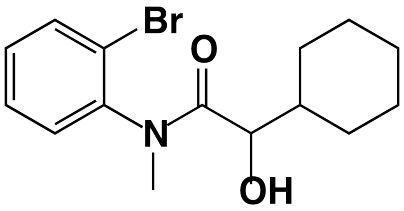


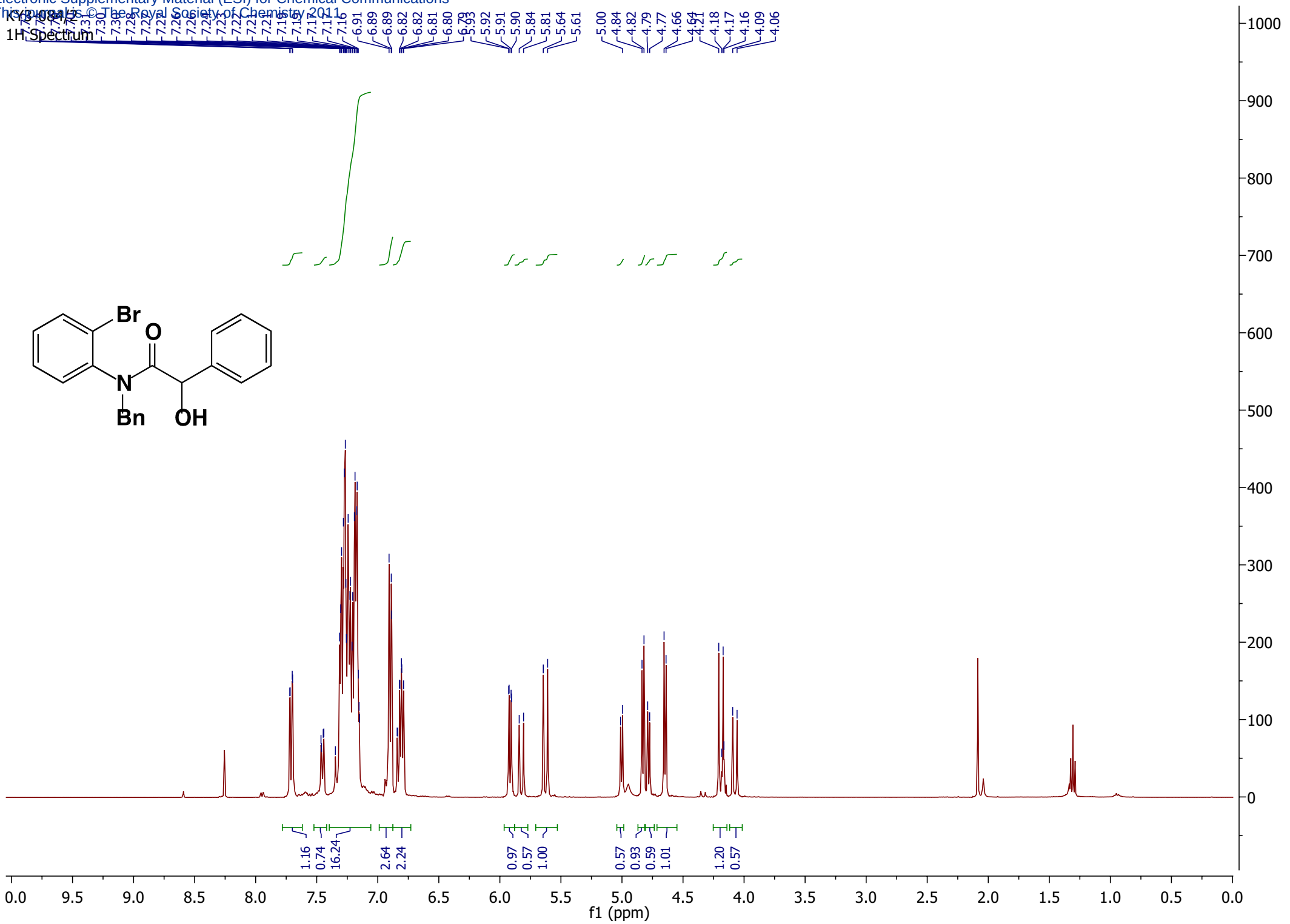
KTZ-047/2
1H Spectrum



KTZ-047_C13/2

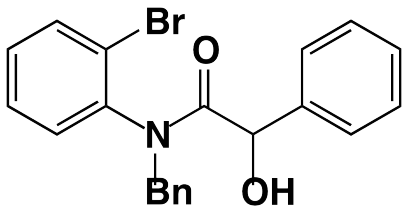
13C CPD-Spectrum



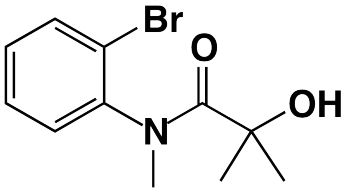


KYB-084_c13/2

13C CPD-Spectrum

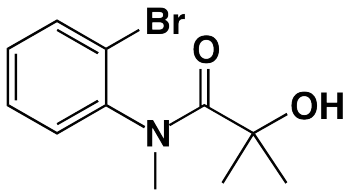


KTB-091/1
1H Spectrum

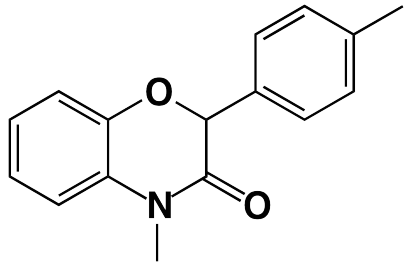


KTB-091_c13/1

13C CPD-Spectrum

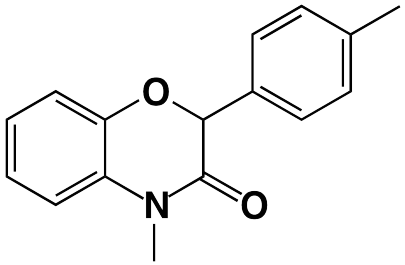


KTZ-066
1H Spectrum

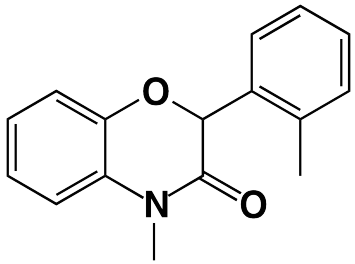


KYZ-066_C13

13C CPD-Spectrum

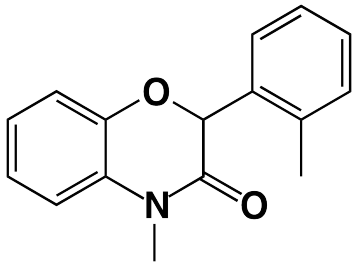


KYZ-062/1
1H Spectrum

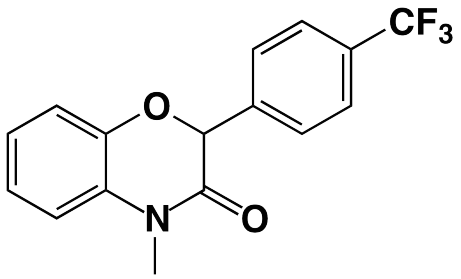


KYZ-062_c13/1

13C CPD-Spectrum

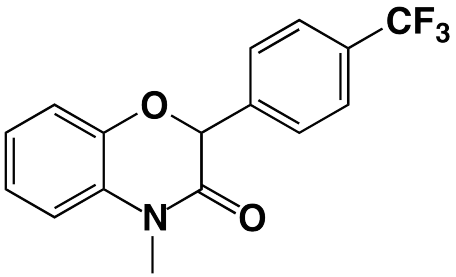


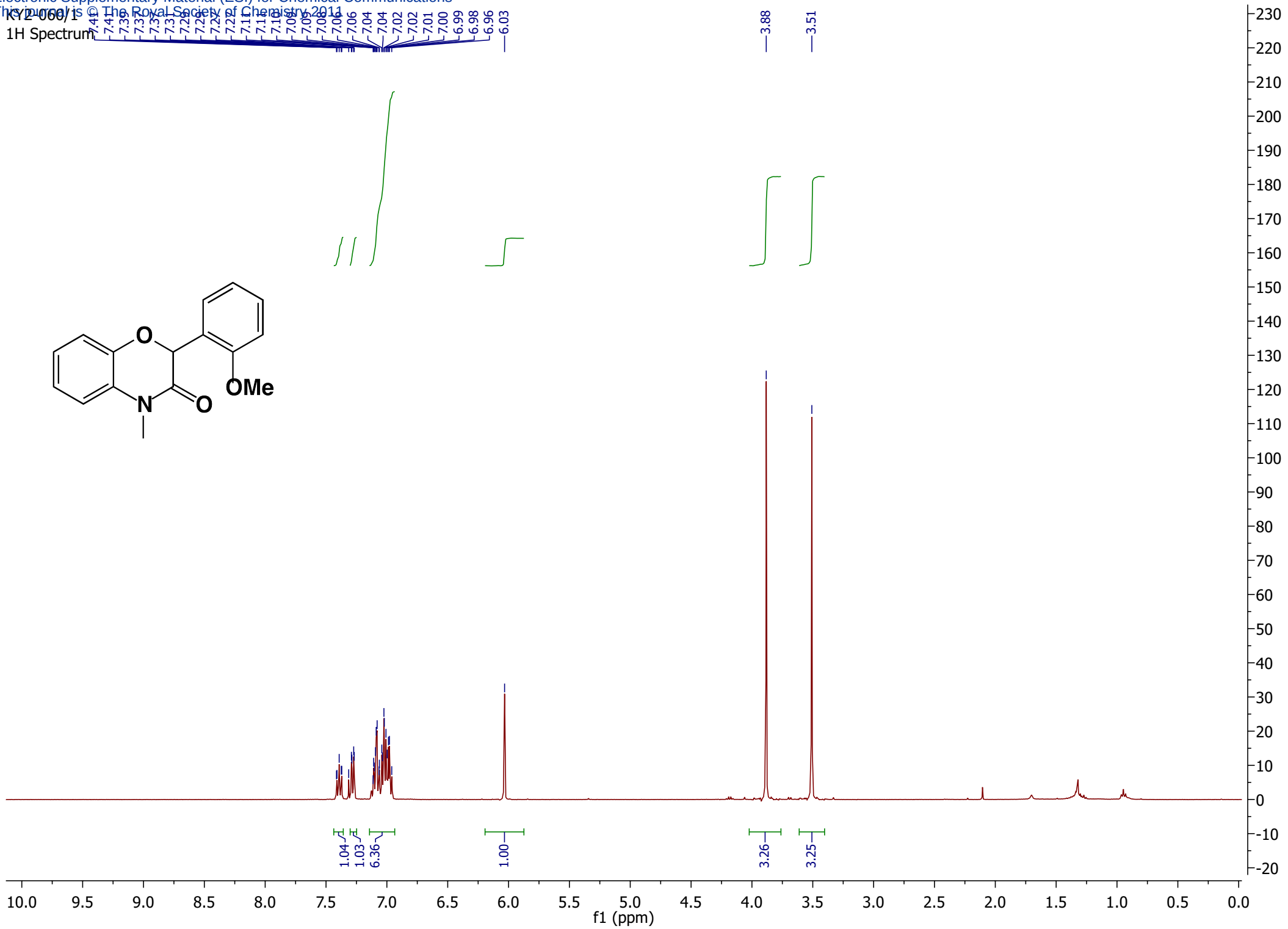
KTZ-069/1
1H Spectrum

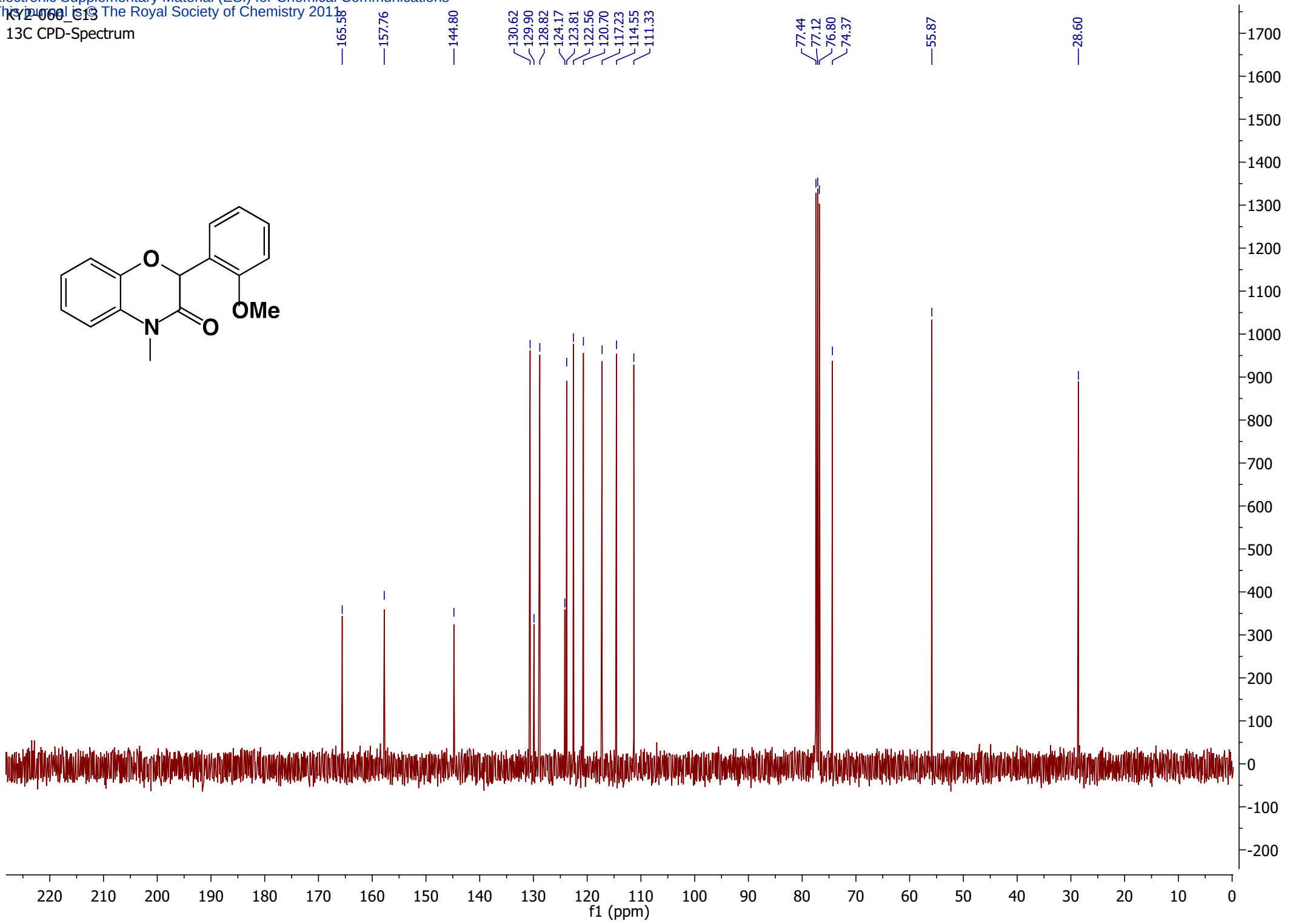


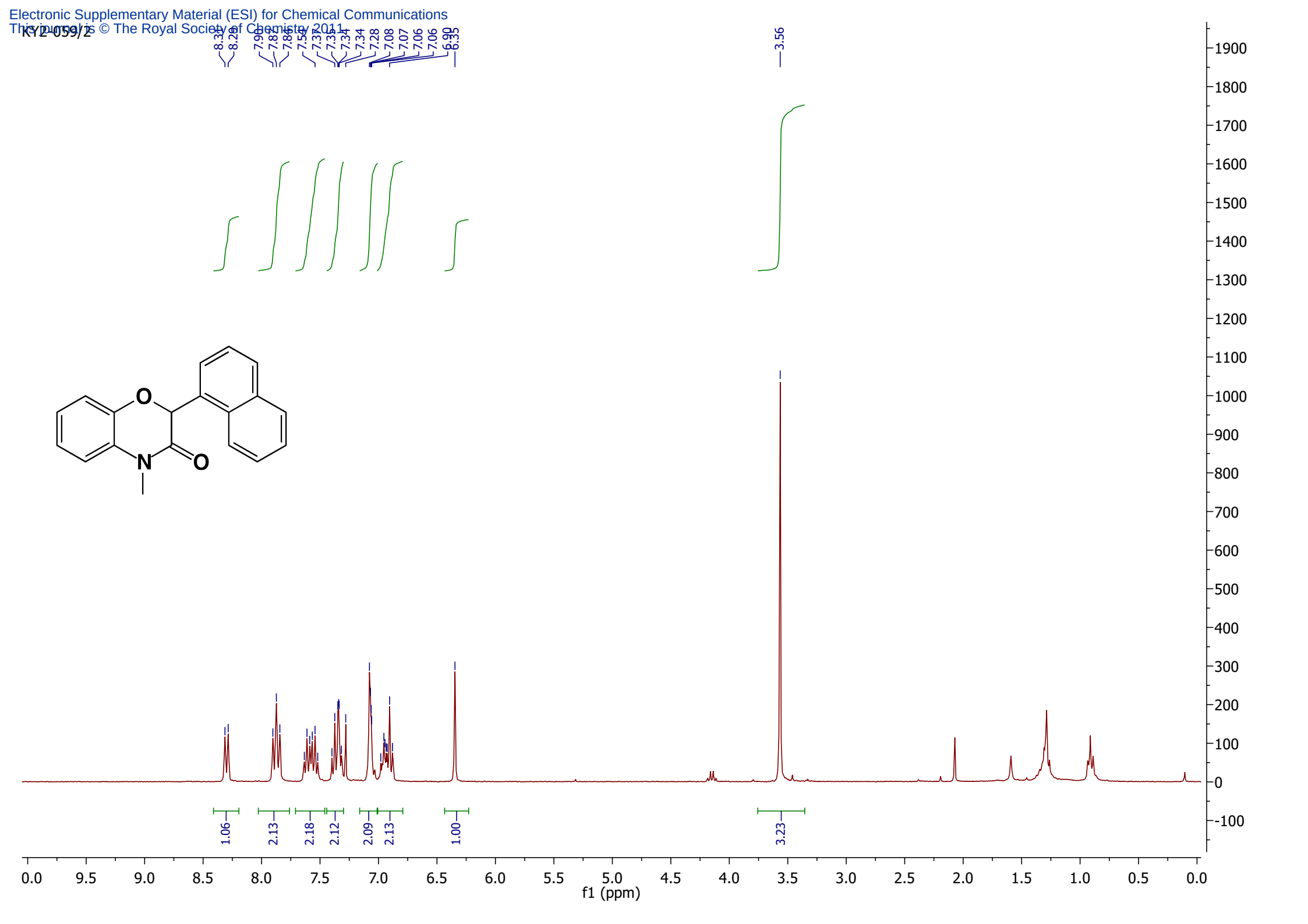
KYZ-069_C13/2

13C CPD-Spectrum



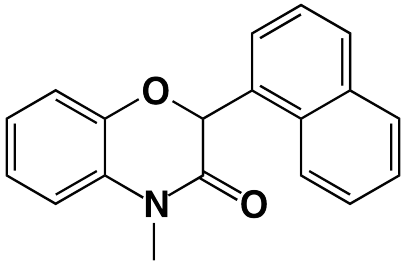


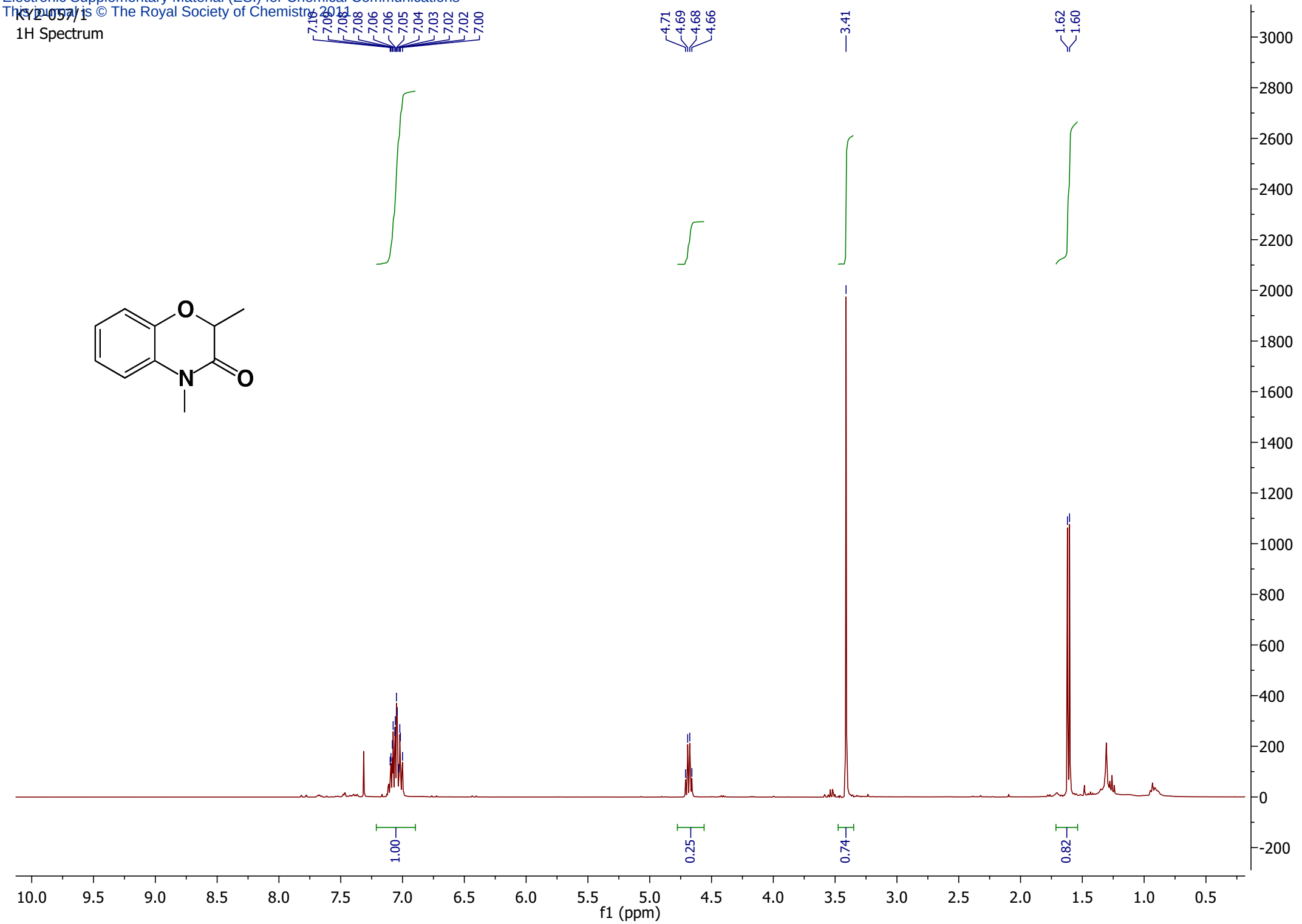




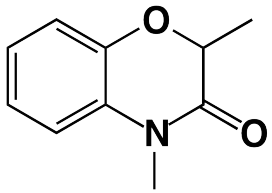
KYZ-059_C13

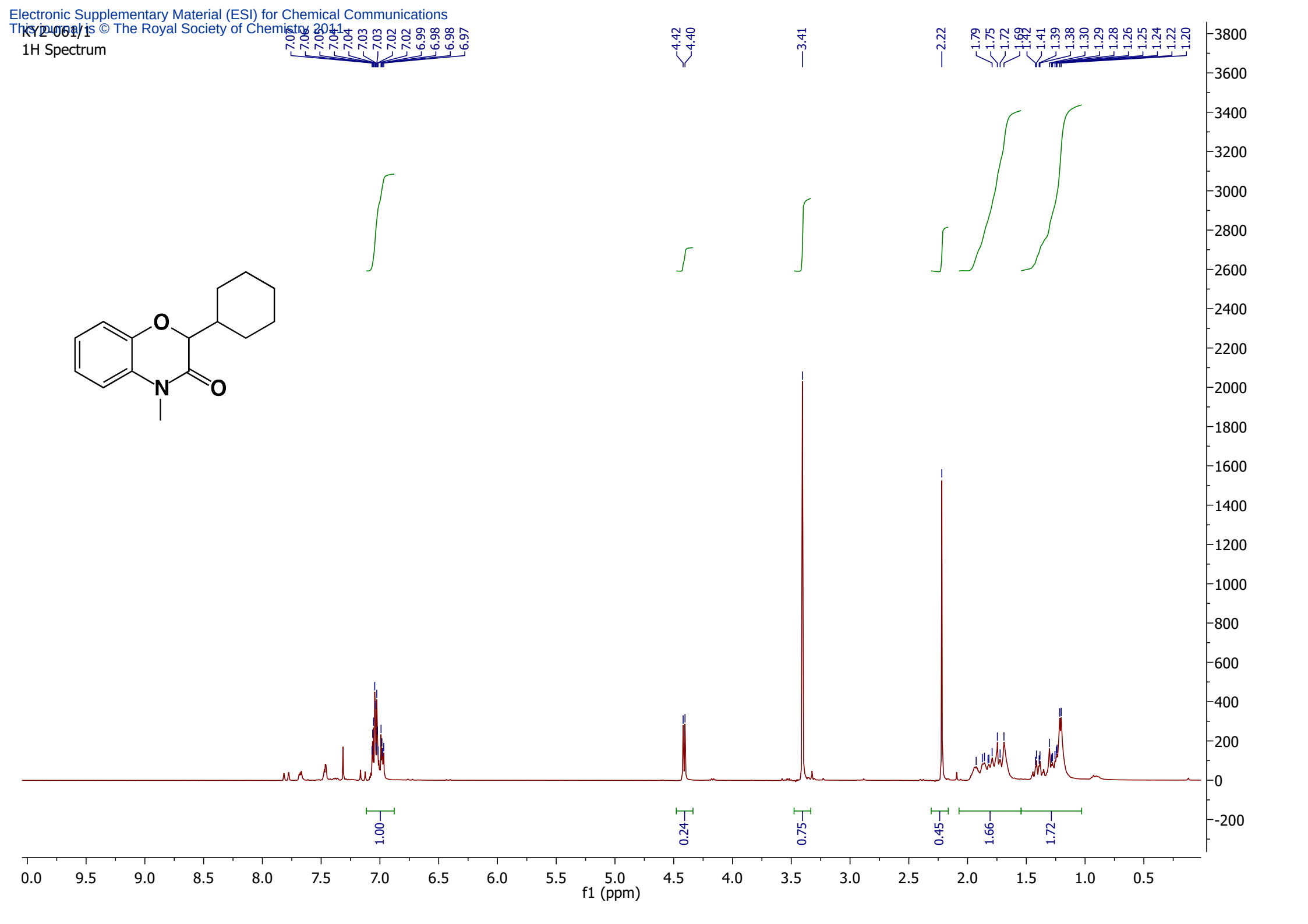
13C CPD-Spectrum



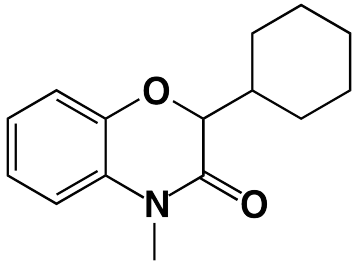


KYZ-057_C13/1
13C CPD-Spectrum

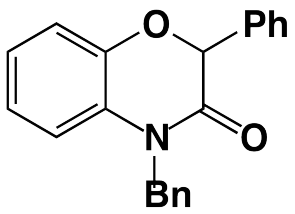




K12-061_c13/1
13C CPD-Spectrum

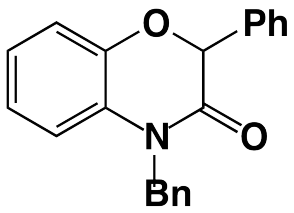


KYB-09-24
1H Spectrum

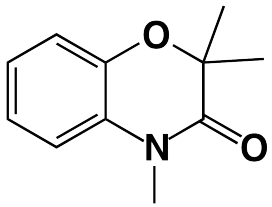


KYB-090_c13/2

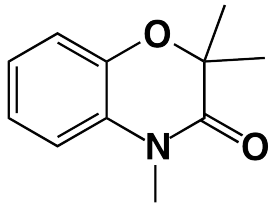
13C CPD-Spectrum



KYB-dime/1
1H Spectrum



KYB-dime_C13/1
13C CPD-Spectrum

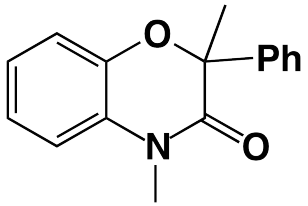


169.01
143.40
129.93
123.82
122.33
117.53
114.27
77.94
77.40
77.08
76.76
28.69
23.92

f1 (ppm)

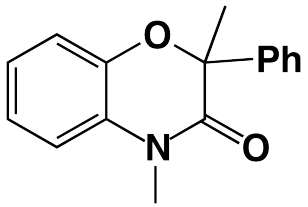
Electronic Supplementary Material (ESI) for Chemical Communications

KYB-076/1
1H Spectrum



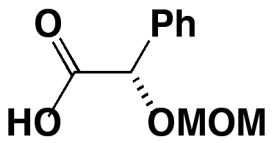
KYB-076_C13/1

13C CPD-Spectrum



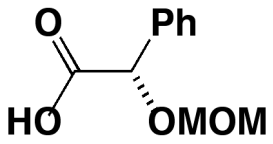
KTB-034/1

1H Spectrum

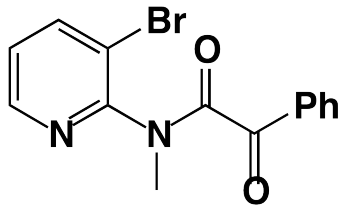


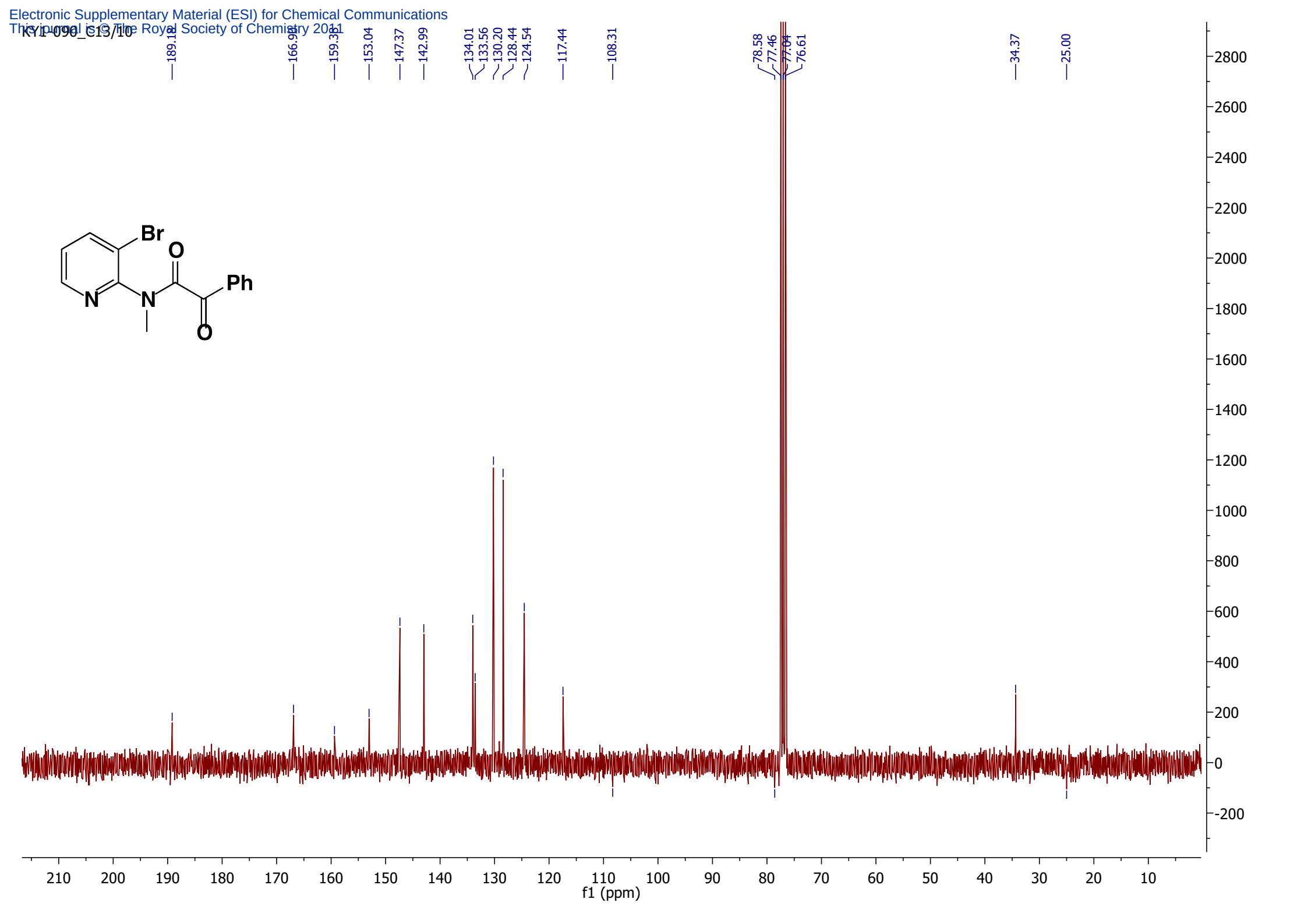
KYB-034_c13/2

13C CPD-Spectrum

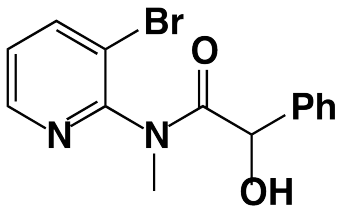


KYL-090
1H Spectrum



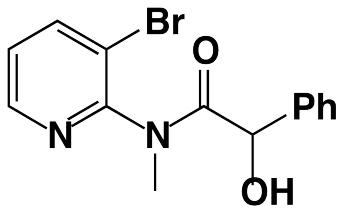


KTZ-043/1
1H Spectrum

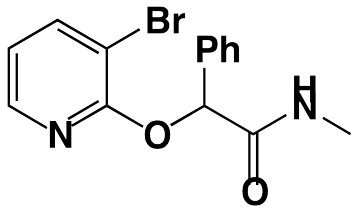


KYZ-043_C13/1

13C CPD-Spectrum



KYB-061/1
1H Spectrum



f1 (ppm)

KYB-061_c13/1
13C CPD-Spectrum