Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

Acetyl Nitrate Mediated Conversion of Methyl Ketones to Diverse Carboxylic Acid Derivatives

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GENERAL EXPERIMENTAL.

Unless otherwise noted, all reactions were performed in flame-dried glassware under an atmosphere of nitrogen or argon using dried reagents and solvents. All chemicals were purchased from commercial vendors and used without further purification. Anhydrous solvents were purchased from commercial vendors.

Flash chromatography was performed using standard grade silica gel 60 230-400 mesh from SORBENT Technologies or was performed using a Biotage Flash Purification system equipped with Biotage SNAP columns. Silica gel was loaded into glass columns as a slurry. All purifications were performed using gradients of mixtures of ethyl acetate and hexanes. Analytical thin-layer chromatography was carried out using Silica G TLC plates, 200 μm with UV_{254} fluorescent indicator (SORBENT Technologies), and visualization was performed by staining and/or by absorbance of UV light.

NMR spectra were recorded using a Varian Mercury Plus spectrometer (400 MHz for ^{1}H-NMR; 101 MHz for $^{13}C\{^{1}H\}$ NMR) or a Bruker Avance Neo spectrometer (400 MHz for ^{1}H-NMR; 101 MHz for $^{13}C\{^{1}H\}$ NMR). Chemical shifts are reported in parts per million (ppm) and were calibrated according to residual protonated solvent or TMS. Mass spectroscopy data was collected using an Agilent 1100-Series LC/MSD Trap LC-MS or a Micromass Quattromicro with a Waters 2795 Separations Module LC-MS with acetonitrile containing 0.1% formic acid as the mobile phase in positive ionization mode. Purity was determined on a Agilent 1100 series equipped with a Phenomenex Kinetex 2.6 μm C18-UPLC column using a gradient of water to acetonitrile with 0.1% TFA. IR spectra were recorded on a Perkin Elmer Spectrum 100 FT-IR spectrometer equipped with a Universal Diamond/ZnSe ATR. UV spectra were recorded on a Perkin Elmer Lambda XLS spectrometer.

All final compounds were evaluated to be of greater then 90% purity by analysis of ^{1}H-NMR, $^{13}C\{^{1}H\}$ NMR, and analytical HPLC.

EXPERIMENTAL PROCEDURES.

General Experimental Procedure:

A solution of methyl ketone (1.0 equiv.) in acetonitrile (0.5M) was cooled to 0 ºC (ice water bath) and was treated with acetic anhydride (3.0 equiv.) and nitric acid (6.0 equiv.; fuming, >90%) dropwise. This solution was allowed to react with stirring for 12h with warming to ambient temperature. The resulting mixture was cooled to 0 ºC (ice water bath) and was treated with N-ethyldiisopropylamine (12.0 equiv.) followed by the appropriate heteroatom nucleophile (0.5 equiv., unless otherwise stated). The resulting mixture was allowed to warm to ambient temperature and react overnight (12-18h.) with stirring and was quenched with HCl (1.0M). The reaction mixture was extracted with CH_2Cl_2 (3 x 20mL), combined organics were washed with sat. $NaHCO_3$ (*only for non-acidic products*), washed with brine, dried over Na_2SO_4 and concentrated *in vacuo*. The crude material was purified using Flash silica gel chromatography (hexane/EtOAc gradient) to provide the product.

1-(4-bromophenyl)-2,2-dinitroethen-1-ol, 2. A solution of 4-bromoacetophenone (122.2mg, 0.614mmol, 1.0 equiv.) in acetonitrile (1.2 mL, 0.5M) was cooled to 0 ºC (ice water bath) and was treated with acetic anhydride (0.171mL, 1.55mmol, 3.0 equiv.) and nitric acid (0.171mL, 6.0 equiv.). This solution was allowed to react with stirring for 12h with warming to ambient temperature. The reaction mixture was concentrated to dryness and was purified by flash column chromatography (silica gel, hexanes/EtOAc) to provide 1-(4-bromophenyl)-2,2-dinitroethen-1-ol, 2. The product was unstable to hydrolysis upon standing and could not be characterized by ESI-MS however was stable for immediate NMR, IR and UV characterization.
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, 2H), 7.72 (d, 2H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 181.8, 152.6, 133.5, 132.7, 131.8, 131.4. IR (neat) 3414, 2962, 2931, 2858, 1739, 1652, 1590, 1535, 1254, 1171, 1071, 1013, 923, 843, 774 cm^{-1}, UV λ_{max} (MeOH)/nm 307 (ε/dm^3 mol^{-1} cm^{-1} 11,500).

Methyl 4-bromobenzoate, 6. Product was produced following the General Procedure with 4'-bromoacetophenone as the methyl ketone and methanol as nucleophile providing Methyl 4-bromobenzoate, **6** (53.4 mg, 0.248 mmol, 81%). Characterization data matches previously reported data for this compound.[1]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, 2H), 7.58 (d, 2H), 3.91 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 166.6, 131.9, 131.3, 129.3, 128.3, 52.5.

Benzyl 4-bromobenzoate, 7. Product was produced following General Procedure with 4'-bromoacetophenone as the methyl ketone and benzyl alcohol as nucleophile providing Benzyl 4-bromobenzoate, **7** (49.8 mg, 0.171 mmol, 56%). Characterization data matches previously reported data for this compound.[2]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, 2H), 7.58 (d, 2H), 7.47 – 7.31 (m, 5H), 5.36 (s, 2H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 165.8, 135.9, 132.6, 131.9, 131.4, 129.2, 128.8, 128.5, 128.4, 67.1.

Phenyl 4-bromobenzoate, 8. Product was produced following the General Procedure with 4'-bromoacetophenone as the methyl ketone and phenol as nucleophile providing Phenyl 4-bromobenzoate, **8** (54.3 mg, 0.196 mmol, 64%). Characterization data matches previously reported data for this compound.[3]
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, 2H), 7.66 (d, 2H), 7.44 (t, 2H), 7.29 (t, 1H), 7.21 (dd, 2H).
$^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 164.7, 151.0, 132.2, 131.9, 129.8, 129.1, 128.7, 126.3, 121.8.

4-bromo-*N*-butylbenzamide, 9. Product was produced following the General Procedure with 4'-bromoacetophenone as the methyl ketone and 1-butyl amine as nucleophile providing 4-bromo-*N*-butylbenzamide, **9** (63.4 mg, 0.258 mmol, 81%). Characterization data matches previously reported data for this compound.[4]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, 2H), 7.55 (d, 2H), 6.15 (s, 1H), 3.44 (q, J = 7.2, 5.6 Hz, 2H), 1.66 – 1.52 (m, 2H), 1.47 – 1.33 (m, 2H), 0.95 (t, J = 7.3 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 166.7, 133.7, 131.9, 128.6, 126.1, 40.1, 31.8, 20.3, 13.9.

***N*-benzyl-4-bromobenzamide, 10.** Product was produced following the General Procedure with 4'-bromoacetophenone as the methyl ketone and benzyl amine as nucleophile providing *N*-benzyl-4-bromobenzamide, **10** (70.6 mg, 0.243 mmol, 80%). Characterization data matches previously reported data for this compound.[5]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, 2H), 7.55 (d, 2H), 7.39 – 7.27 (m, 5H), 6.49 (s, 1H), 4.61 (d, *J* = 5.6 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 166.5, 138.0, 133.3, 131.9, 129.0, 128.7, 128.1, 127.9, 126.4, 44.4.

(4-bromophenyl) (piperidin-1-yl) methanone, 11. Product was produced following the General Procedure with 4'-bromoacetophenone as the methyl ketone and piperidine as nucleophile providing (4-bromophenyl) (piperidin-1-yl) methanone, **11** (48.7 mg, 0.182 mmol, 59%). Characterization data matches previously reported data for this compound.[6]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, 2H), 7.26 (d, 2H), 3.68 (s, 2H), 3.32 (s, 2H), 1.80 – 1.40 (m, 6H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 169.4, 135.4, 131.8, 128.7, 123.8, 48.9, 43.4, 26.6, 25.8, 24.7.

4-bromo-*N*-methoxy-*N*-methylbenzamide, 12. Product was produced following the General Procedure with 4'-bromoacetophenone as the methyl ketone and N,O dimethyl hydroxylamine hydrochloride as nucleophile to provide 4-bromo-*N*-methoxy-*N*-methylbenzamide, **12** (58.1 mg, 0.238 mmol, 78%). Characterization data matches previously reported data for compound **12**.[7]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, 2H), 7.54 (d, 2H), 3.53 (s, 3H), 3.35 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 168.9, 132.9, 131.4, 130.2, 125.3, 61.3, 33.6.

3-(4-bromobenzoyl) oxazolidin-2-one, 13. Product was produced following the General Procedure with 4'-bromoacetophenone as the methyl ketone and oxazolidinone as nucleophile to provide 3-(4-bromobenzoyl) oxazolidin-2-one, **13** (9.2 mg, 0.034 mmol, 11%). Characterization data matches previously reported data for compound **15**.[8]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, 2H), 7.55 (d, 2H), 4.51 (t, 2H), 4.18 (t, 2H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 169.0, 153.3, 131.4, 131.4, 130.8, 127.6, 62.5, 43.8.

4-bromo-*N*-phenylbenzamide, 14. Product was produced following the General Procedure with 4'-bromoacetophenone as the methyl ketone and aniline as nucleophile to provide 4-bromo-*N*-phenylbenzamide, **14** (34.1 mg, 0.124 mmol, 40%) Characterization data matches previously reported data for compound **14**.[9]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.5 Hz, 3H), 7.62 (d, 4H), 7.38 (t, 2H), 7.17 (t, *J* = 7.5, 1.1 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 164.9, 137.7, 133.9, 132.2, 129.3, 128.8, 126.8, 125.0, 120.4.

2-bromobenzoic acid, *o*-15. Product was produced following the General Procedure with 2'-bromoacetophenone as the methyl ketone and 1M NaOH (12.0 equiv.) as nucleophile and base providing 2-bromobenzoic acid, ***o*-15** (47.8 mg, 0.237 mmol, 78%). Characterization data matches previously reported data for this compound.[10]
^{1}H NMR (400 MHz, DMSO-d_6) δ 13.43 (s, 1H), 7.72 (td, *J* = 7.6, 1.8 Hz, 2H), 7.45 (pd, *J* = 7.3, 1.6 Hz, 3H).. $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3OD) δ 167.4, 133.8, 132.6, 130.6, 127.8, 120.0, 39.5.

3-bromobenzoic acid, *m*-15. Product was produced following the General Procedure with 3'-bromoacetophenone as the methyl ketone and 1M NaOH (12.0 equiv.) as nucleophile and base providing 3-bromobenzoic acid, ***m*-15** (37.4 mg, 0.185 mmol, 61%). Characterization data matches previously reported data for this compound.[11]
^{1}H NMR (400 MHz, DMSO-d_6) δ 13.34 (s, 1H), 8.03 (s, 1H), 7.93 (d, J = 7.8 Hz, 1H), 7.82 (d, J = 8.9 Hz, 1H), 7.46 (t, J = 7.9 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, CD_3OD) δ 166.1, 135.7, 133.1, 131.8, 131.0, 128.3, 121.8, 39.5.

4-bromobenzoic acid, *p*-15. Product was produced following the General Procedure with 4'-bromoacetophenone as the methyl ketone and water (0.5 equiv.) as nucleophile providing 4-bromobenzoic acid, **15** (42.9 mg, 0.213 mmol, 70%). Characterization data matches previously reported data for this compound.[12]
^{1}H NMR (400 MHz, CD_3OD) δ 12.0(1H) 7.91 (d, 2H), 7.64 (d, 2H). ^{13}C{^{1}H} NMR (101 MHz, CD_3OD) δ 168.8, 132.8, 132.5, 131.1, 128.8.

4-fluorobenzoic acid, 16. Product was produced following the General Procedure with 4'-fluoroacetophenone as the methyl ketone and 1M NaOH (12.0 equiv.) as nucleophile and base providing 4-fluorobenzoic acid, **16** (70.5 mg, 0.503 mmol, 82%). Characterization data matches previously reported data for this compound.[13]
^{1}H NMR (400 MHz, DMSO-d6) δ 12.92 (br. s, 1H), 8.03−7.96 (m, 2H), 7.36−7.22 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d6) δ 166.4, 165.0 (d, J = 250.5 Hz), 132.1 (d, J = 9.5 Hz), 127.4 (d, J = 2.9 Hz), 115.6 (d, J = 22.0 Hz).

4-chlorobenzoic acid, 17. Product was produced following the General Procedure with 4'-chloroacetophenone as the methyl ketone and 1M NaOH (12.0 equiv.) as nucleophile and base providing 4-chlorobenzoic acid, **17** (68.3 mg, 0.436 mmol, 71%). Characterization data matches previously reported data for this compound.[14]
^{1}H NMR (400 MHz, DMSO-d6) δ 12.87 (br. s, 1H), 7.93 (d, J = 8.5 Hz, 2H), 7.52 (d, J = 8.4 Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d6) δ 166.5, 137.9, 131.2, 129.7, 128.7.

4-iodobenzoic acid, 18. Product was produced following the General Procedure with 4'-iodoacetophenone as the methyl ketone and 1M NaOH (12.0 equiv.) as nucleophile and base providing 4-iodobenzoic acid, **18** (120.3 mg, 0.485 mmol, 79%). Characterization data matches previously reported data for this compound.[15]
^{1}H NMR (400 MHz, DMSO-d6) δ 13.06 (br. s, 1H), 7.87 (d, J = 8.3 Hz, 2H), 7.69 (d, J = 8.3 Hz, 2H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d6) δ 166.9, 137.6, 131.1, 130.3, 101.2.

2-nitrobenzoic acid, *o*-19. Product was produced following the General Procedure with 2'-nitroacetophenone as the methyl ketone and 1M NaOH (12.0 equiv.) as nucleophile and base providing 2-nitrobenzoic acid, ***o*-19** (53.3 mg, 0.319 mmol, 52%). Characterization data matches previously reported data for this compound.[16]
^{1}H NMR (400 MHz, DMSO-d6) δ 8.01-7.96 (m, 1H), 7.88-7.83 (m, 1H), 7.82-7.74 (m, 2H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d6) δ 166.0, 148.4, 133.2, 132.5, 130.0, 127.3, 123.8, 39.5.

3-nitrobenzoic acid, *m*-19. Product was produced following the General Procedure with 3'-nitroacetophenone as the methyl ketone and 1M NaOH (12.0 equiv.) as nucleophile and base providing 3-nitrobenzoic acid, ***m*-19** (52.3 mg, 0.313 mmol, 51%). Characterization data matches previously reported data for this compound.[17]
^{1}H NMR (400 MHz, DMSO-d6) δ 13.66 (br. s, 1H), 8.61-8.56 (m, 1H), 8.43 (dd, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 1H), 8.32 (dd, J_1 = 7.6 Hz, J_2 = 0.8 Hz, 1H), 7.79 (t, J = 8.0 Hz, 1H). ^{13}C{^{1}H} NMR (101 MHz, DMSO-d6) δ 165.5, 147.9, 135.4, 132.5, 130.5, 127.3, 123.7.

4-nitrobenzoic acid, *p*-19. Product was produced following the General Procedure with 4'-nitroacetophenone as the methyl ketone and 1M NaOH (12.0 equiv.) as nucleophile and base providing 4-nitrobenzoic acid, ***p*-19** (82.1 mg, 0.490 mmol, 80%). Characterization data matches previously reported data for this compound.[18]
^{1}H NMR (400 MHz, DMSO-d6) δ 13.66 (s, 1H), 8.33 (d, J = 8.7 Hz, 2H), 8.17 (d, J = 8.7 Hz, 3H).
^{13}C{^{1}H} NMR (101 MHz, DMSO-d6) δ 166.3, 150.5, 137.0, 131.2, 124.2.

***N*-benzylpivalamide, 20.** Product was produced following the General Proceedure with 3,3-dimethyl-2-butanone as methyl ketone and benzylamine as nucleophile to provide *N*-benzylpivalamide, **20** (114.7 mg, 0.600 mmol, 58%). Characterization data matches previously reported data for this compound.[19]
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.20 (m, 5H), 6.14 (s, 1H), 4.39 (d, J = 5.7 Hz, 2H), 1.21 (s, 9H).
^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 178.4, 138.7, 128.7, 127.5, 127.3, 43.5, 38.7, 27.6.

1-Adamantanecarboxylic acid, 21. Product was produced following the General Procedure with 1-Adamantane methyl ketone as the methyl ketone and 1M NaOH (12.0 equiv.) as nucleophile and base providing 1-Adamantanecarboxylic acid, **21 (**93.0 mg, 0.516 mmol, 84%). Characterization data matches previously reported data for this compound.[20]
^{1}H NMR (400 MHz, $CDCl_3$) δ 11.85 (br. s, 1H), 2.06-1.99 (m, 3H), 1.94-1.87 (m, 6H), 1.77 –1.66 (m, 6H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 184.5, 40.5, 38.5, 36.4, 27.8.

***N*-butyl-3-(4-nitrophenyl) propenamide, 22.** Product was produced following the General Procedure with 4-(4-aminophenyl)butan-2-one as the methyl ketone and butylamine as nucleophile to provide *N*-butyl-3-(4-nitrophenyl) propenamide, **22 (**44.0mg, 0.176 mmol, 25%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, 2H), 7.36 (d, 2H), 5.44 (s, 1H), 3.20 (q, 2H), 3.07 (t, J = 7.5 Hz, 2H), 2.48 (t, J = 7.7, 1.0 Hz, 2H), 1.46 – 1.34 (m, 2H), 1.31 – 1.20 (m, 2H), 0.88 (t, J = 7.2, 0.9 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 171.0, 149.0, 146.7, 129.4, 123.8, 39.5, 37.7, 31.7, 31.4, 20.1, 13.8. ESI-MS calculated from $C_{13}H_{19}N_2O_3^+$, 251.1396 $[M+H]^+$, observed, 251.1399; HPLC purity=91.3%.

Cyclohexanecarboxylic acid, 23. Product was produced following the General Procedure with Cyclohexyl methyl ketone as the methyl ketone and 1M NaOH (12.0 equiv.) as nucleophile and base providing cyclohexanecarboxylic acid, **23 (**68.5 mg, 0.534 mmol, 87%). Characterization data matches previously reported data for this compound.[21]
^{1}H NMR (400 MHz, $CDCl_3$) δ 12.1 (br. s, 1H), 2.37-2.26 (m, 1H), 1.98-1.87 (m, 2H), 1.80-1.69 (m, 2H), 1.67-1.58 (m, 1H), 1.51-1.38 (m, 2H), 1.34-1.18 (m, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 183.0, 42.9, 28.7, 25.6, 25.3.

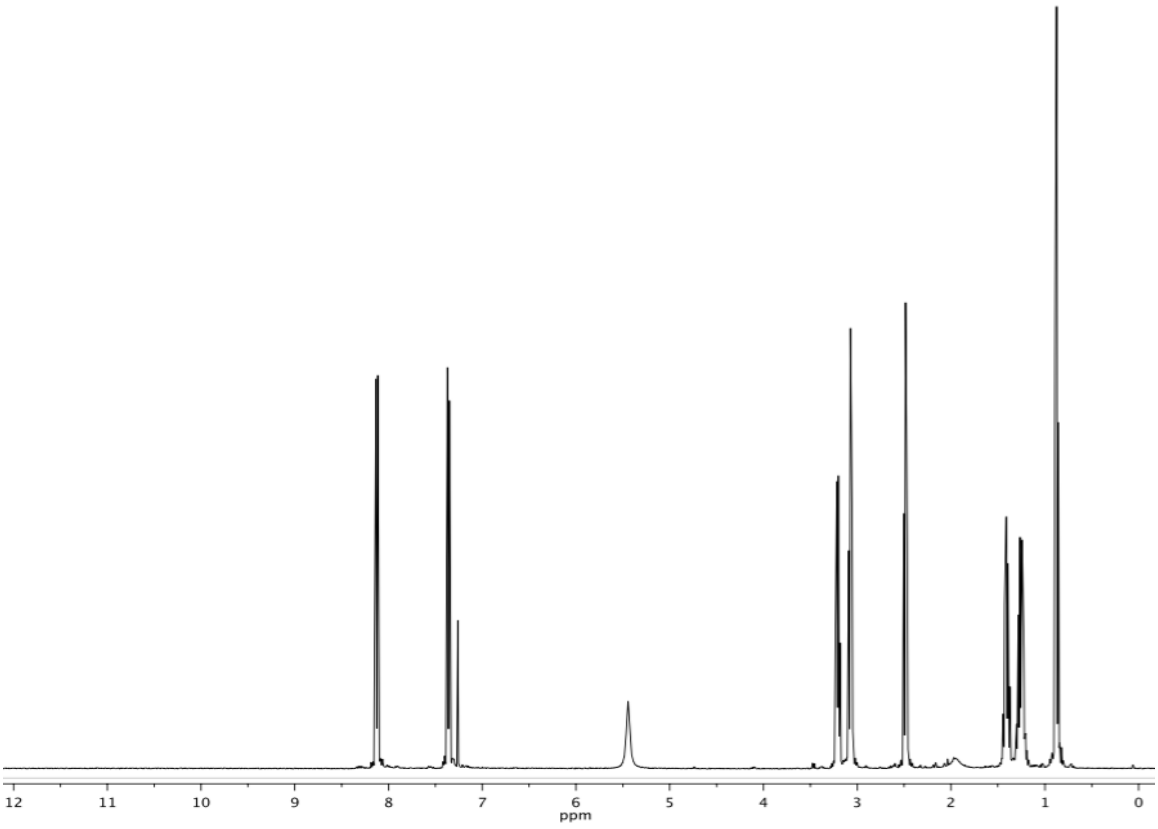
2-(4-bromophenyl)-1*H*-benzo[*d*]imidazole, 26. Product was produced following the General Procedure with 4'-bromoacetophenone as the methyl ketone and ortho-phenyllene diamine as heteroatom nucleophile with the following modifications. In leiu of the reaction quench described in the general procedure, the mixture was concentrated *in vacuo* and was suspended in AcOH (0.5M). The resulting solution was heated to 60ºC for 12h. and was concentrated to dryness to provide a crude product. This crude product was directly purified by column chromatography to yield 2-(4-bromophenyl)-1*H*-benzo[*d*]imidazole, **26** (42.0 mg, 0.154 mmol, 86%.) Characterization data matches previously reported data for compound **20**.[22]
^{1}H NMR (400 MHz, CD_3OD) δ 8.00 (d, 2H), 7.72 (d, 2H), 7.65 – 7.58 (m, 2H), 7.31 – 7.25 (m, 2H). $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3OD) δ 152.2, 133.4, 130.1, 129.5, 125.5, 124.2.

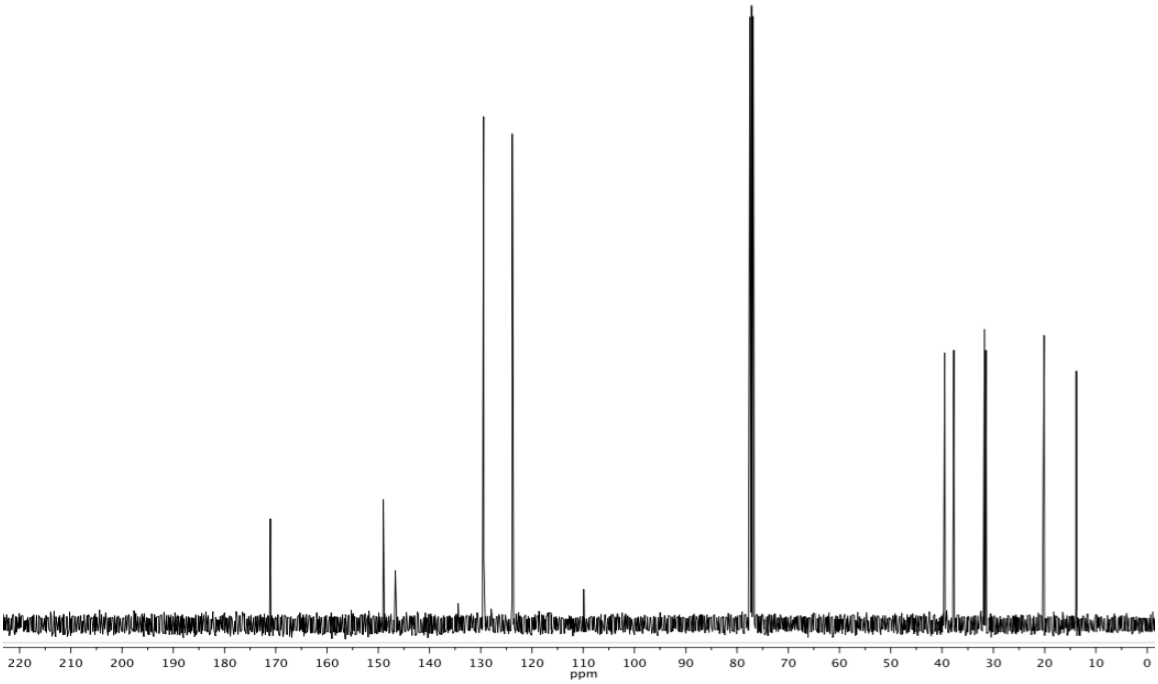
2-(4-bromophenyl)-6-methylbenzo[d]oxazole, 27. Product was produced following the General Procedure with 4'-bromoacetophenone as the methyl ketone and 2-amino-5-methylphenol as heteroatom nucleophile with the following modifications. In leiu of the reaction quench described in the general procedure, the mixture was concentrated *in vacuo* and was suspended in AcOH (0.5M). The resulting solution was heated to 60ºC for 12h. and was concentrated to dryness to provide a crude product. This crude product was directly purified by column chromatography to yield 2-(4-bromophenyl)-6-methylbenzo[d]oxazole, **27 (**36.3 mg, 0.126 mmol, 41%). Characterization data matches previously reported data for this compound.[23]
^{1}H NMR (400 MHz, DMSO-d_6) δ 7.77 (d, J = 8.3 Hz, 2H), 7.60 (d, J = 8.3 Hz, 2H), 7.31 (d, J = 8.0 Hz, 1H), 6.61 (s, 1H), 6.52 (d, J = 8.4 Hz, 1H), 2.10 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, DMSO-d_6) δ 164.9, 150.2, 136.0, 134.1, 132.0, 130.2, 125.8, 125.2, 123.4, 120.2, 117.1, 21.3.

2-(4-bromophenyl) benzo[*d*]oxazole, 28. Product was produced following the General Procedure with 4'-bromoacetophenone as the methyl ketone and 2-amino phenol as heteroatom nucleophile with the following modifications. In leiu of the reaction quench described in the general procedure, the mixture was concentrated *in vacuo* and was suspended in AcOH. The resulting solution was heated to 60ºC for 12h. and was concentrated to dryness to provide a crude product. This crude product was directly purified by column chromatography to yield 2-(4-bromophenyl) benzo[*d*]oxazole, **28** (80.6 mg, 0.294 mmol, 91%). Characterization data matches previously reported data for this compound.[24]
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.78 (d, J = 8.6 Hz, 2H), 7.66 (d, J = 8.5 Hz, 2H), 7.25 (d, J = 8.9 Hz, 3H), 7.20 – 7.15 (m, 1H), 7.07 (dd, J = 8.1, 1.4 Hz, 1H), 6.94 (td, J = 7.9, 1.4 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $cdcl_3$) δ 166.0, 148.6, 132.2, 132.1, 132.1, 132.0, 128.9, 127.4, 127.4, 125.4, 122.3, 120.8, 119.7.

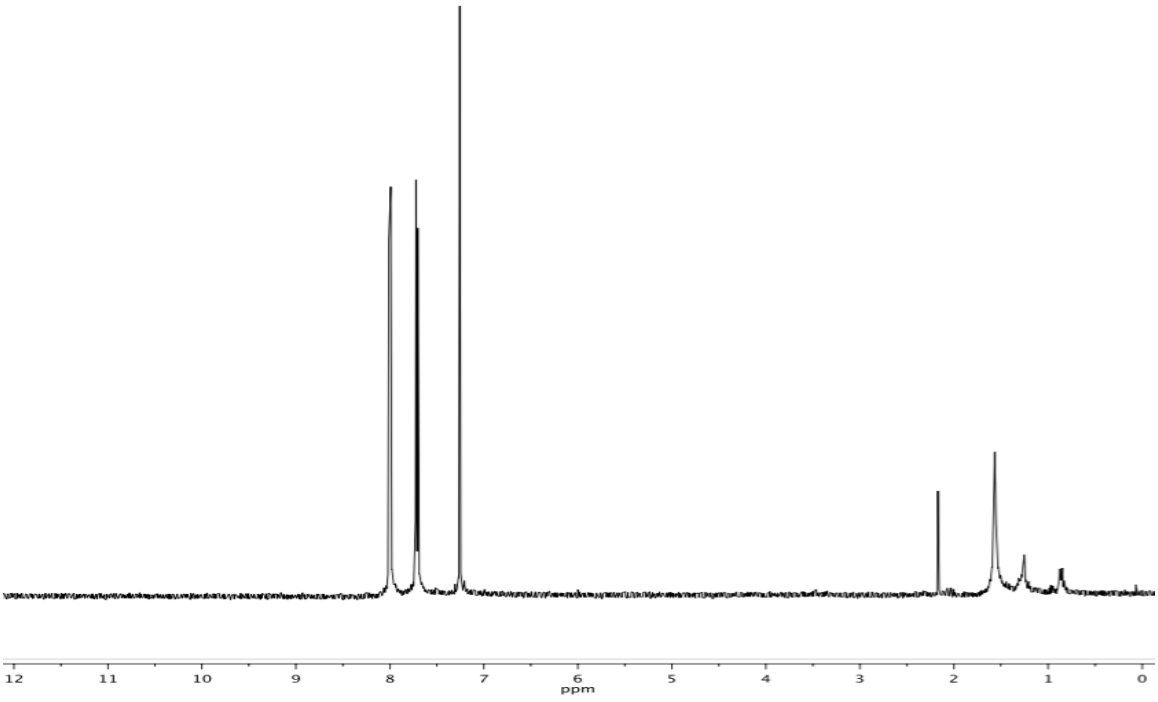
^{1}H-NMR and ^{13}C{^{1}H} NMR Spectra for New Compounds.

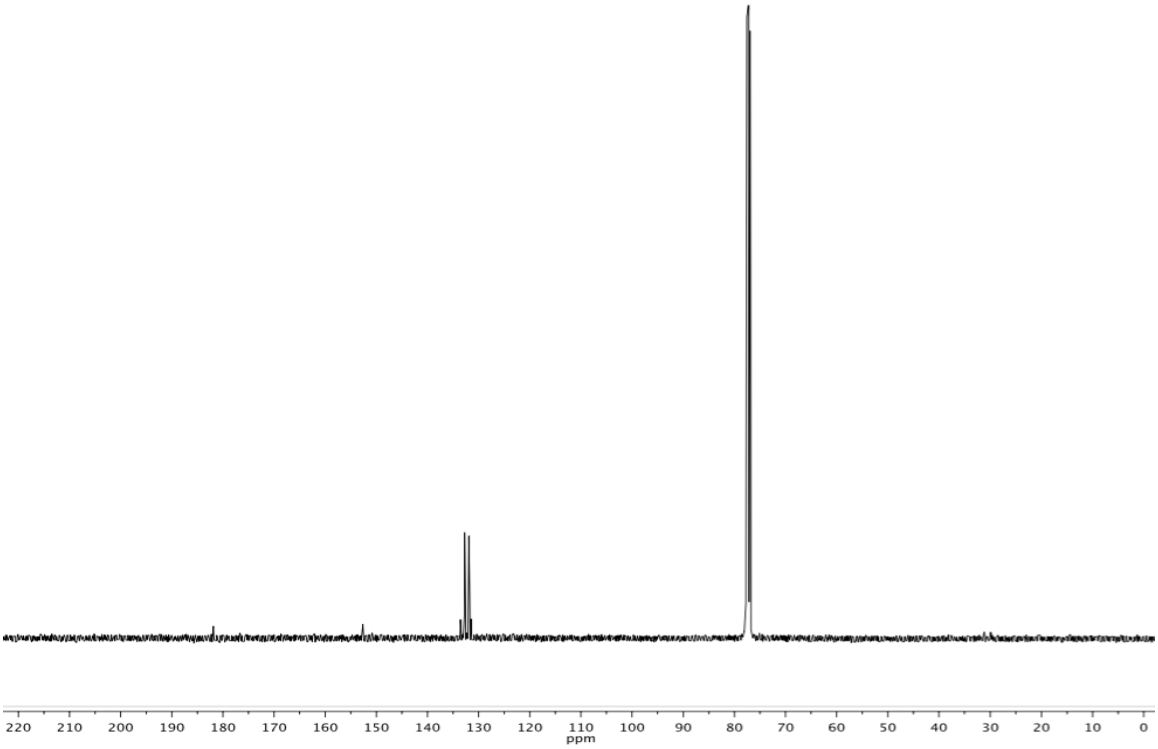
***N*-butyl-3-(4-nitrophenyl) propenamide, 22.**





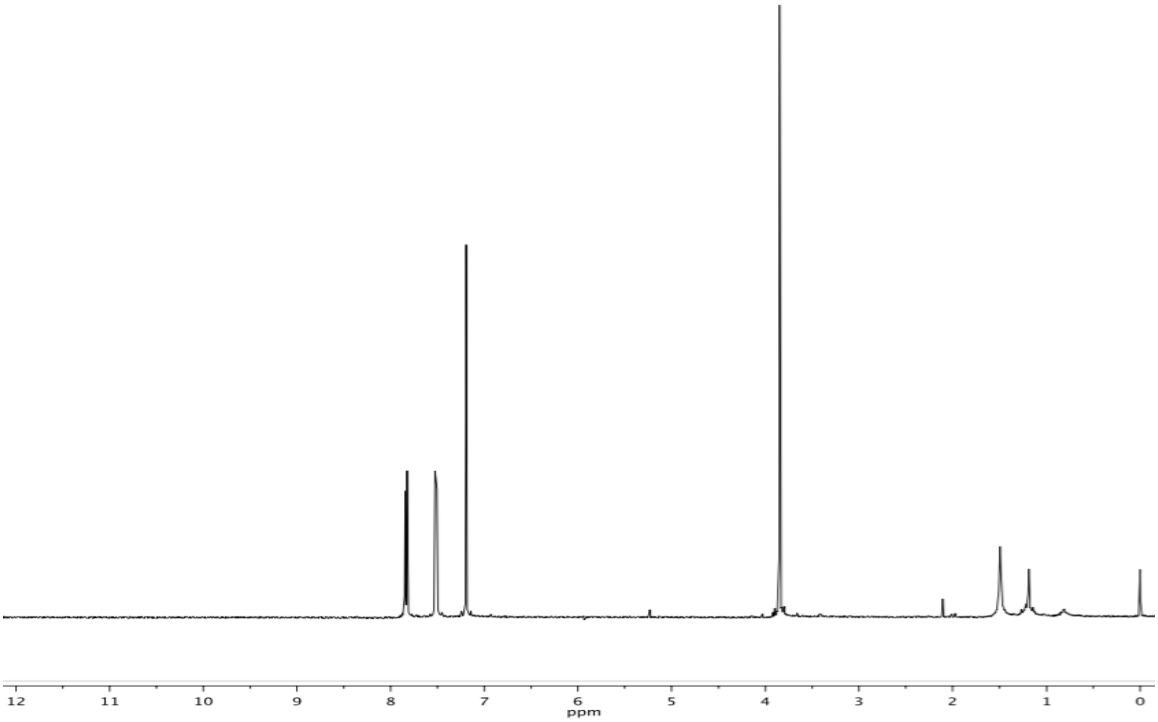
1-(4-bromophenyl)-2,2-dinitroethen-1-ol, 2 (*isolated reaction intermediate*)**.**



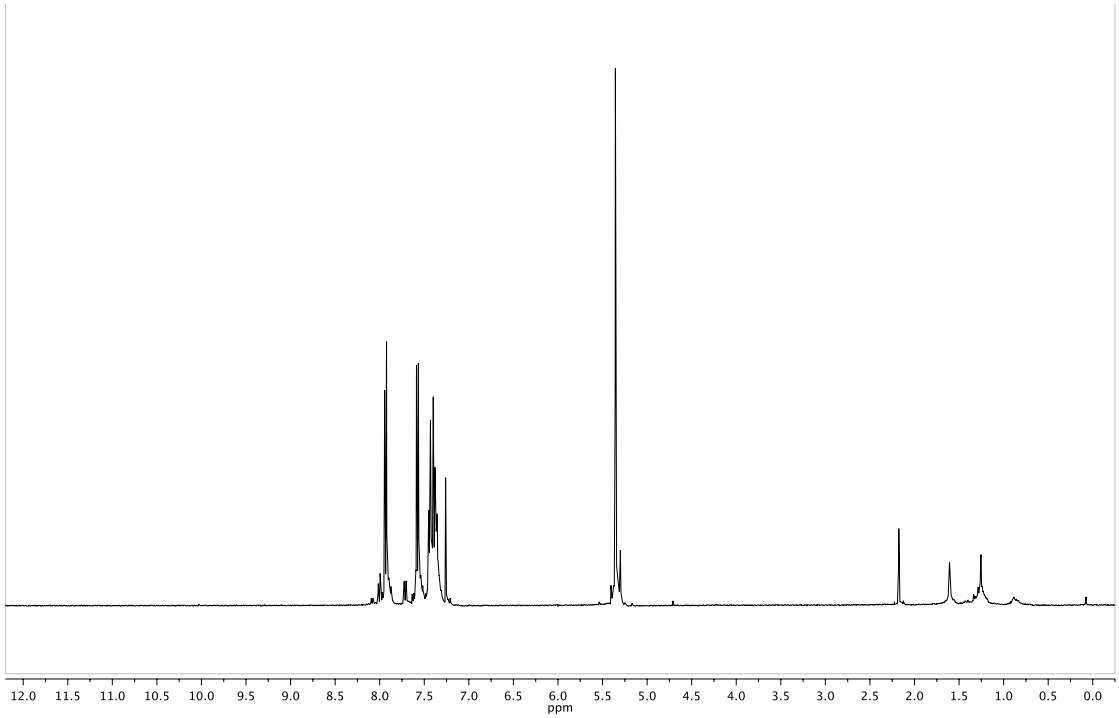


^{1}H-NMR for Previously Isolated Compounds.

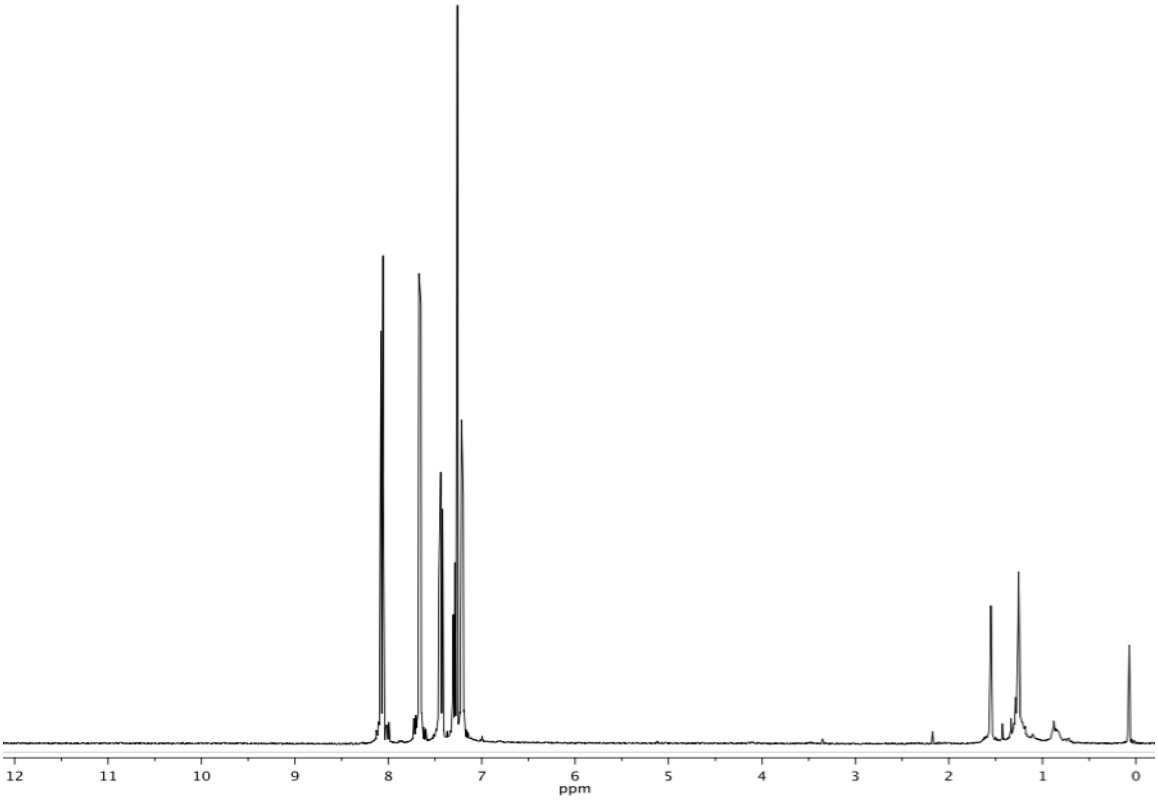
Methyl 4-bromobenzoate, 6.



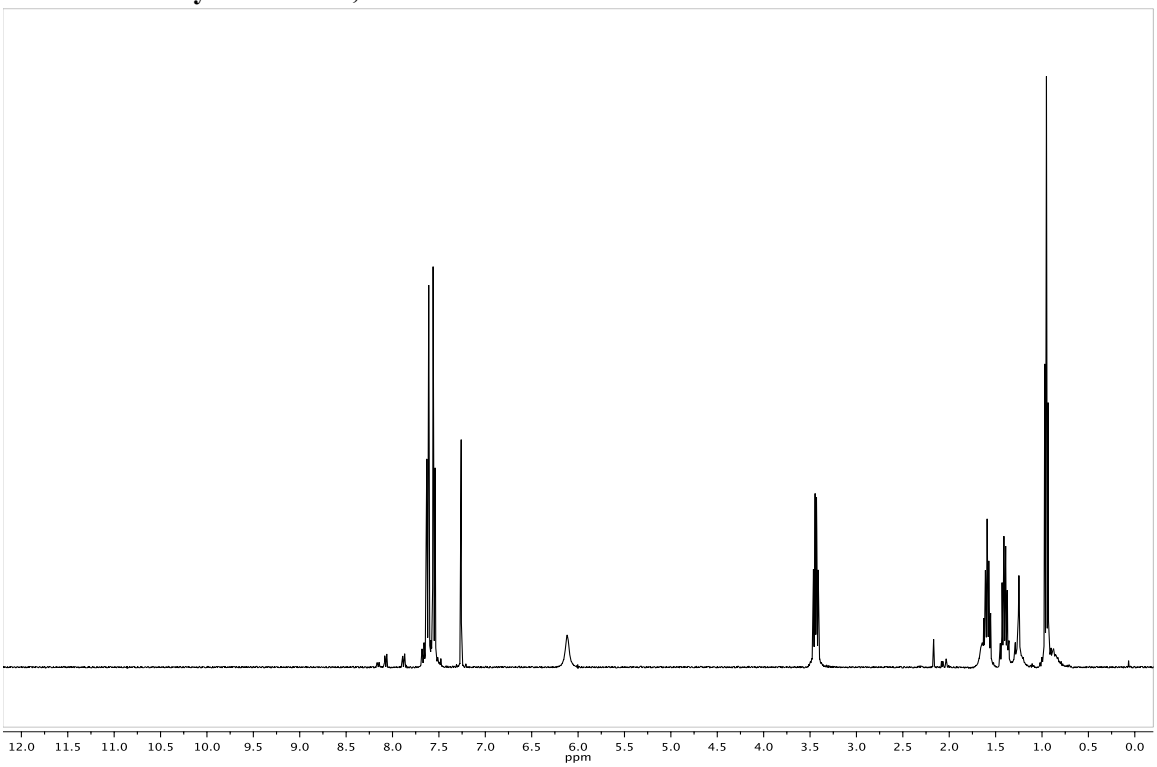
Benzyl 4-bromobenzoate, 7.



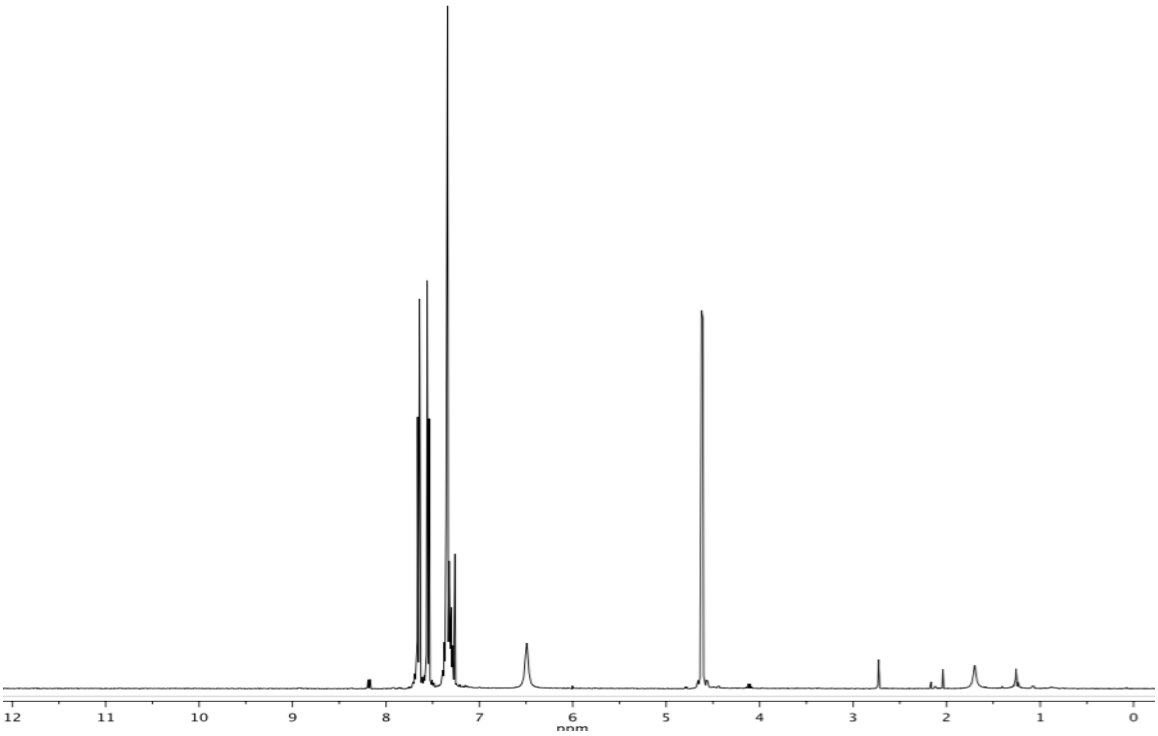
Phenyl 4-bromobenzoate, 8.



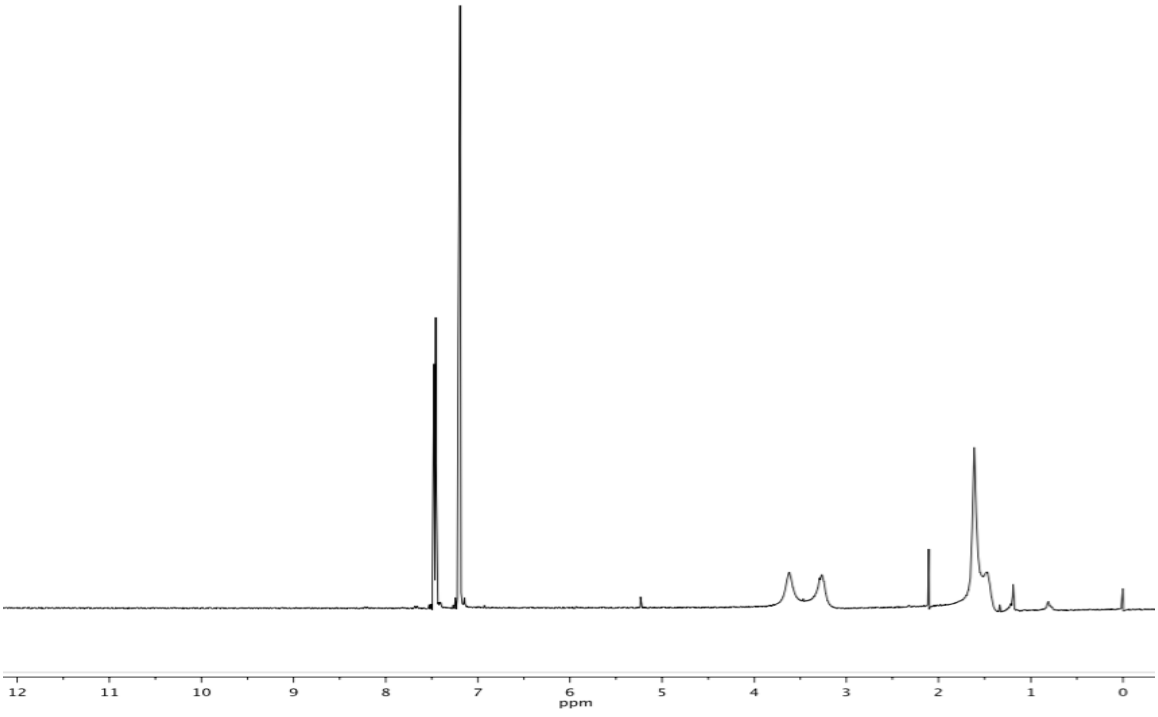
4-bromo-*N*-butylbenzamide, 9.



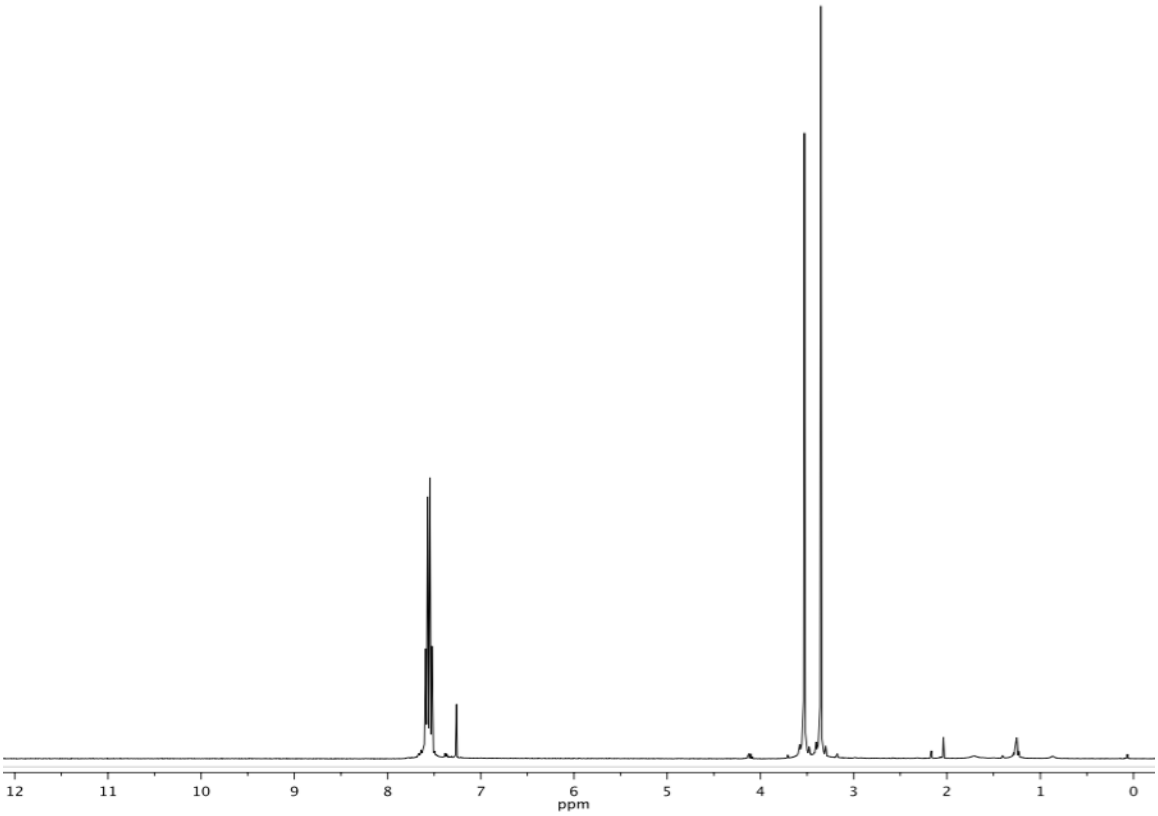
***N*-benzyl-4-bromobenzamide, 10.**



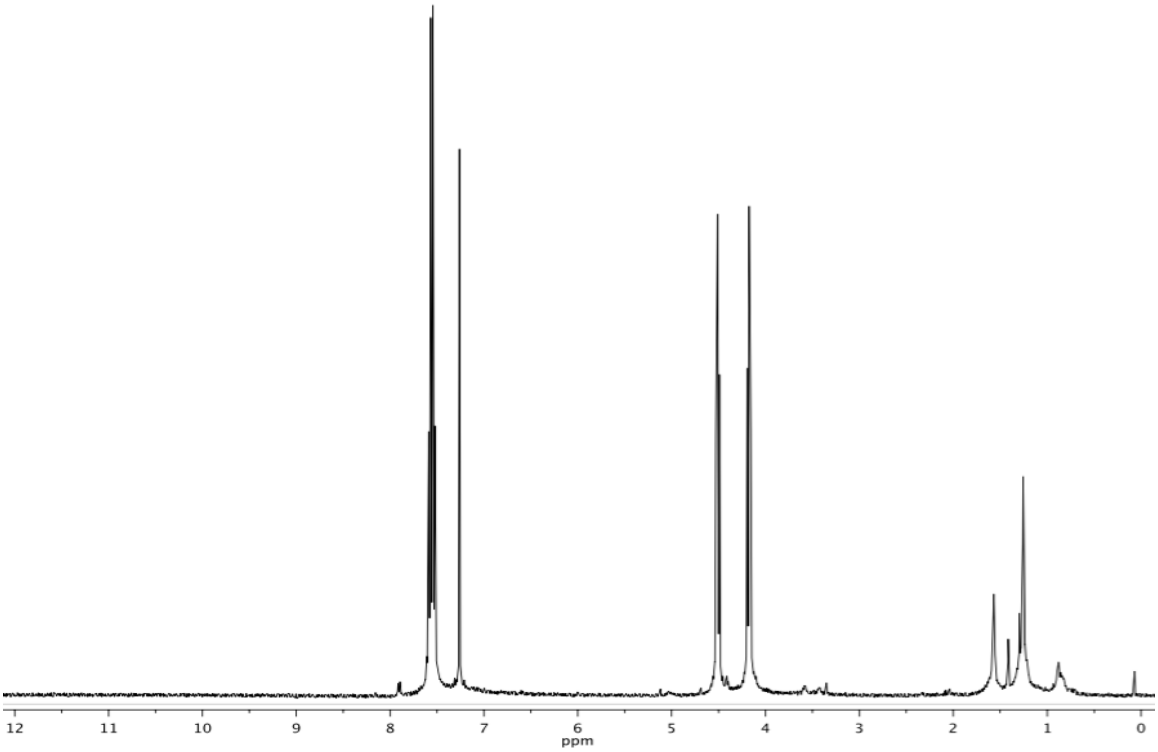
(4-bromophenyl) (piperidin-1-yl) methanone, 11.



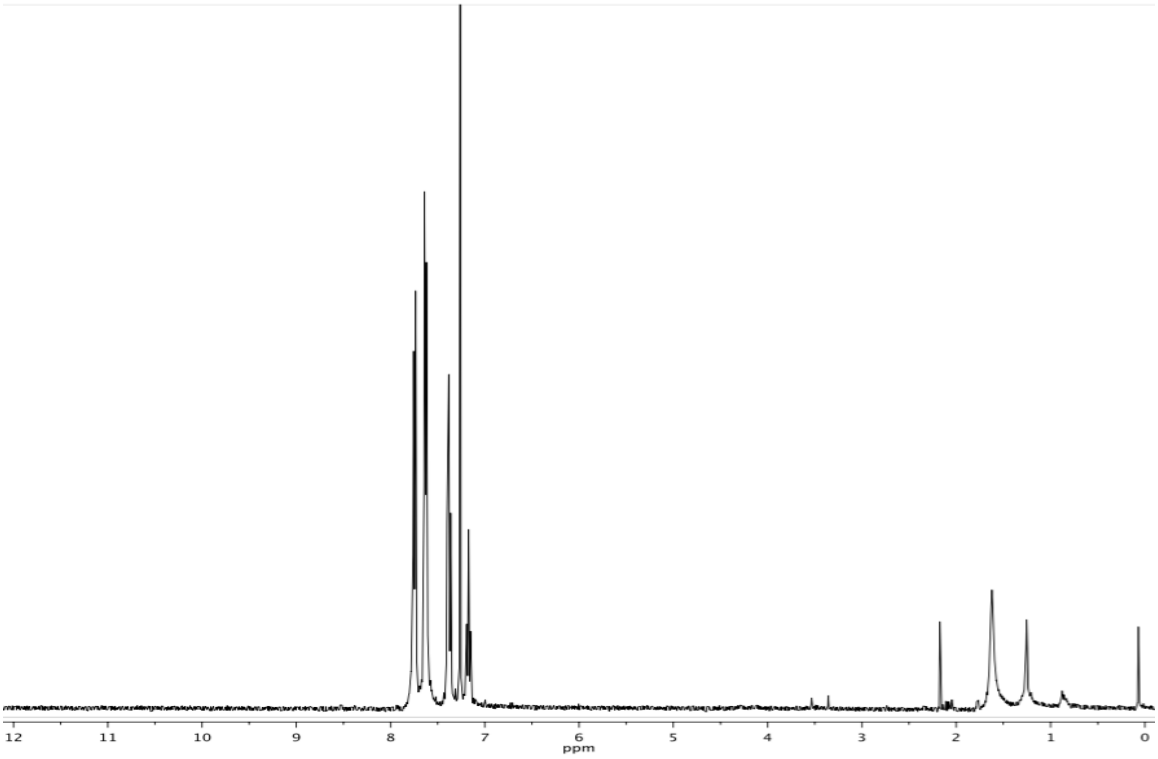
4-bromo-*N*-methoxy-*N*-methylbenzamide, 12.



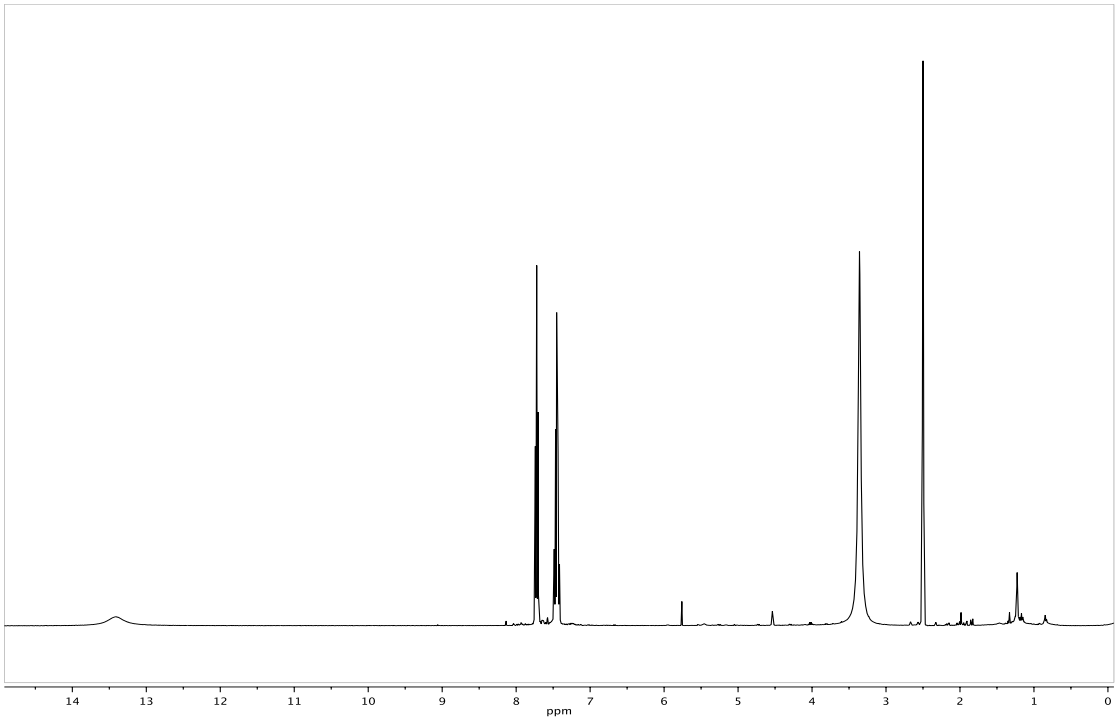
3-(4-bromobenzoyl) oxazolidin-2-one, 13.



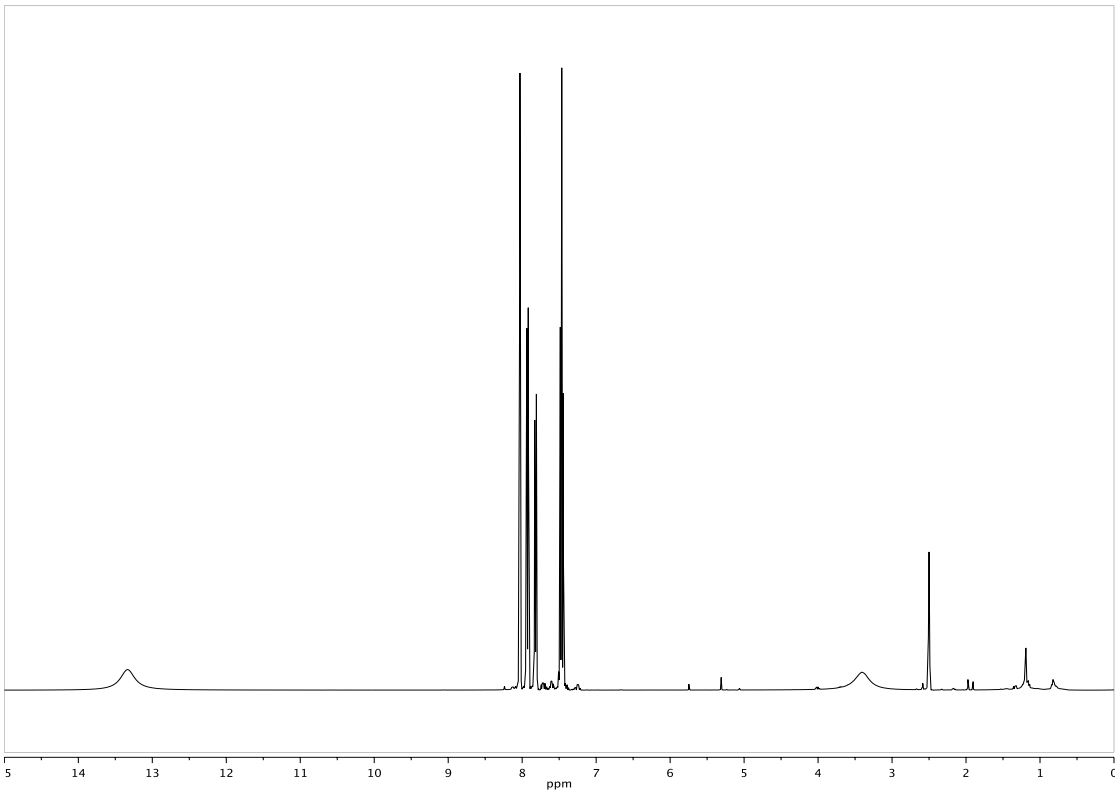
4-bromo-*N*-phenylbenzamide, 14.



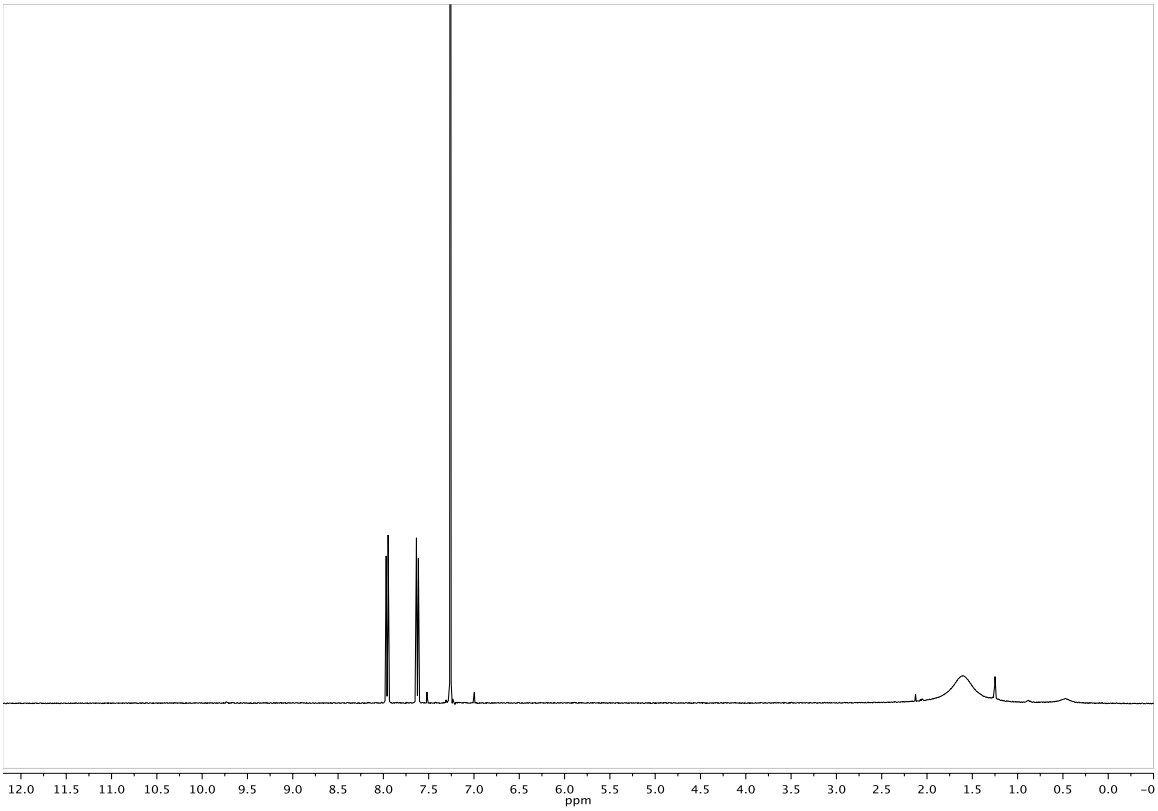
2-bromobenzoic acid, *o*-15.



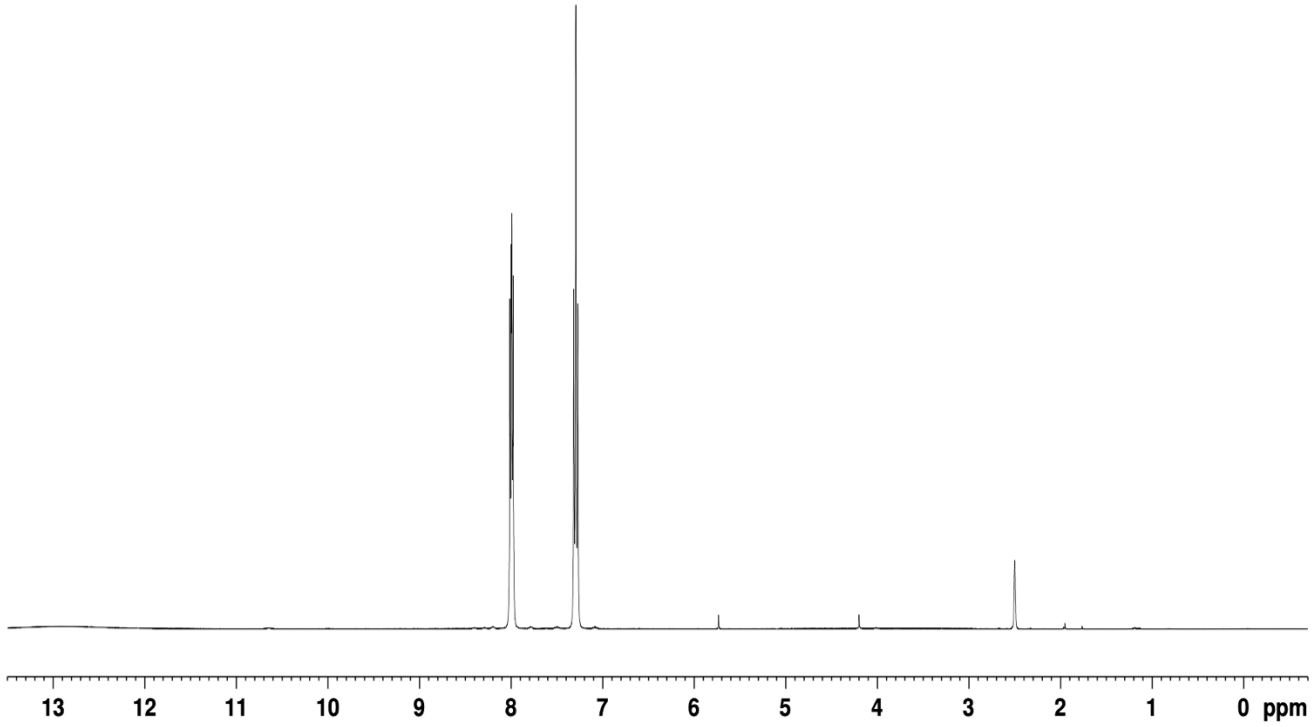
3-bromobenzoic acid, *m*-15.



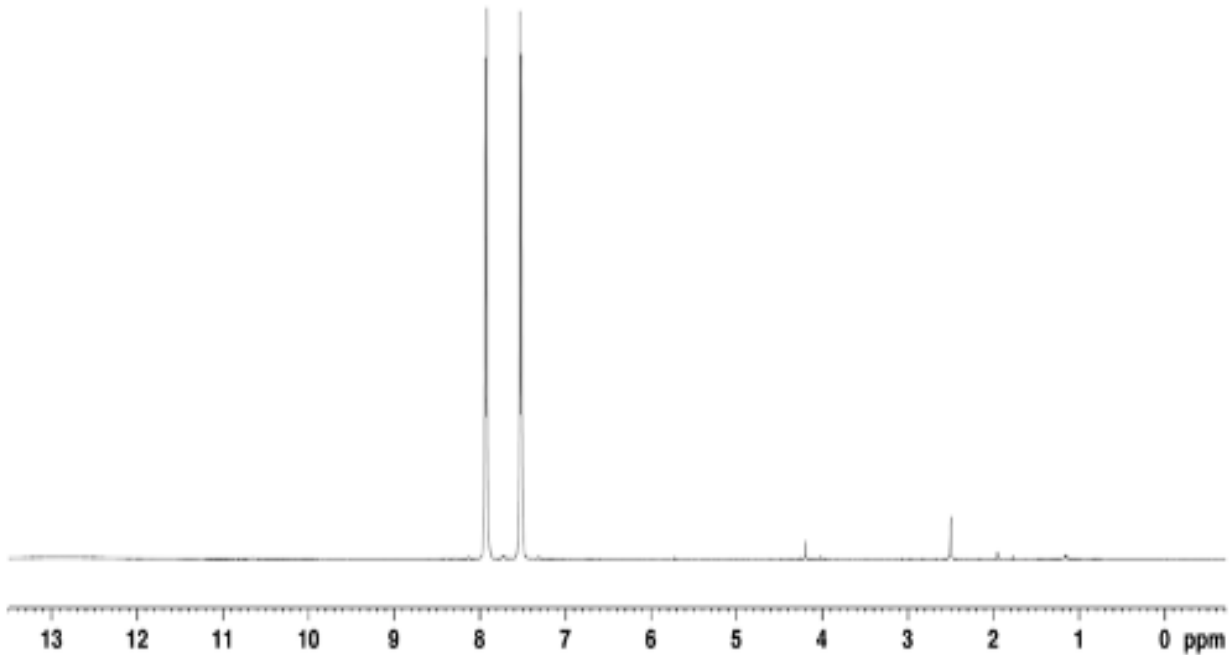
4-bromobenzoic acid, *p*-15.



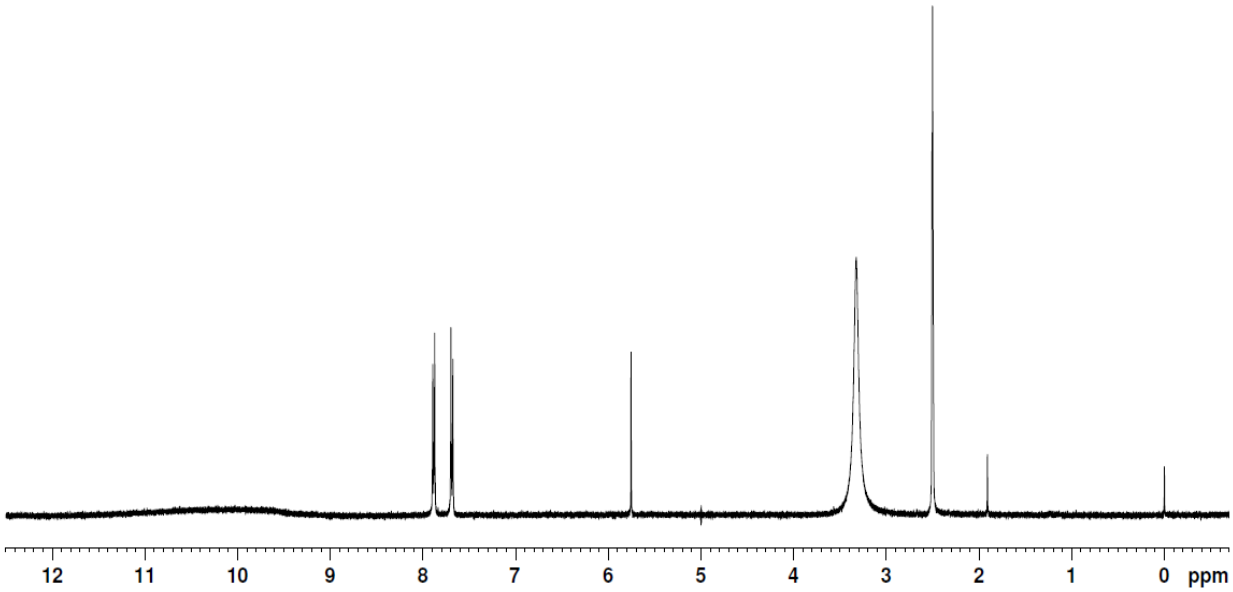
4-fluorobenzoic acid, 16.



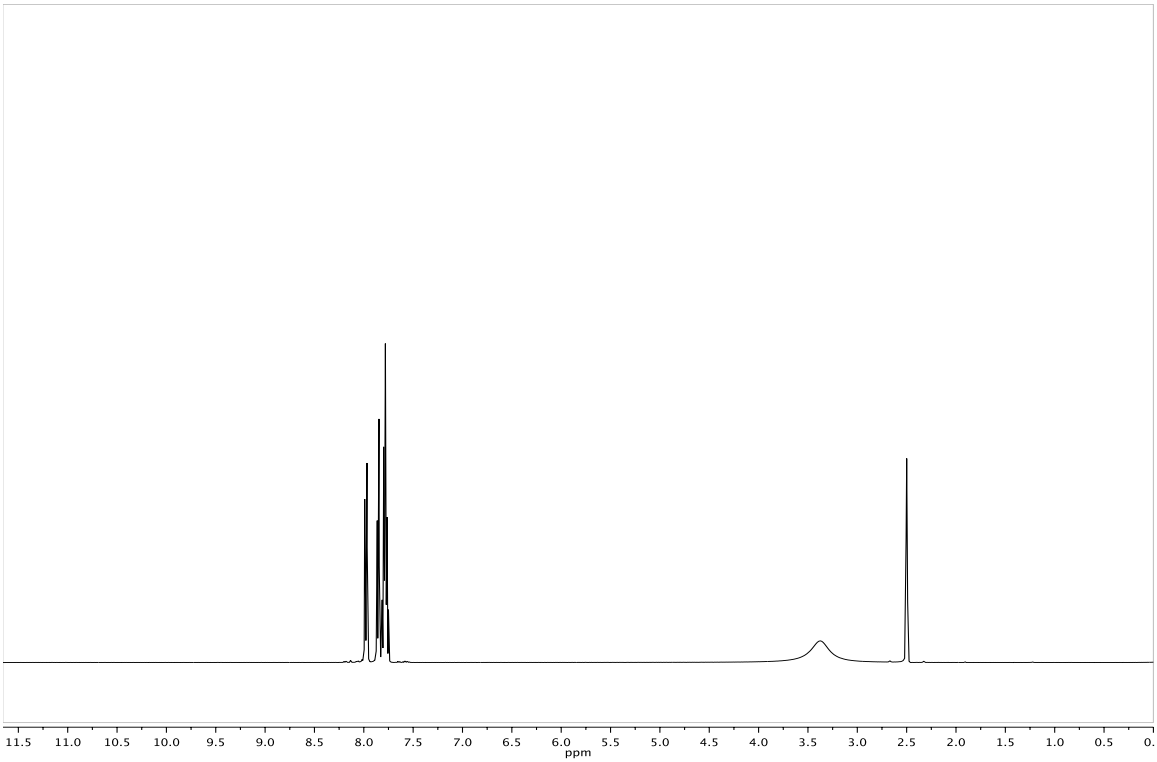
4-chlorobenzoic acid, 17.



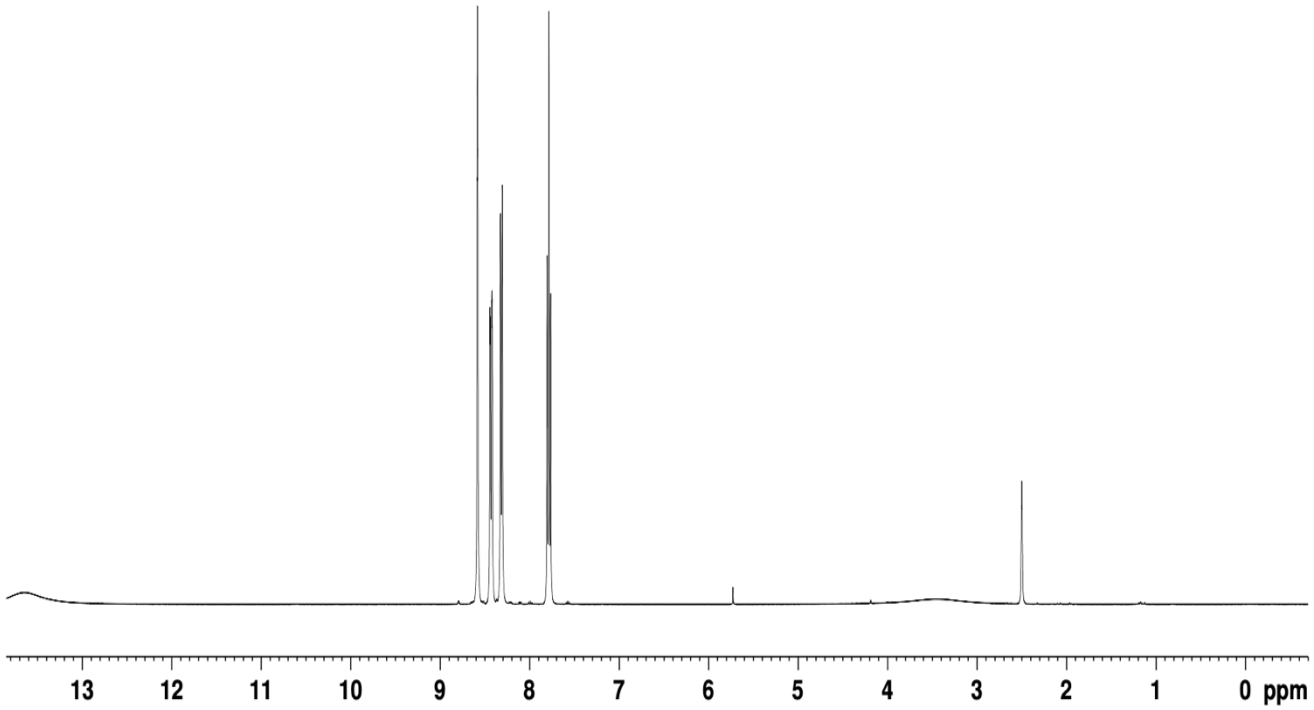
4-iodobenzoic acid, 18.



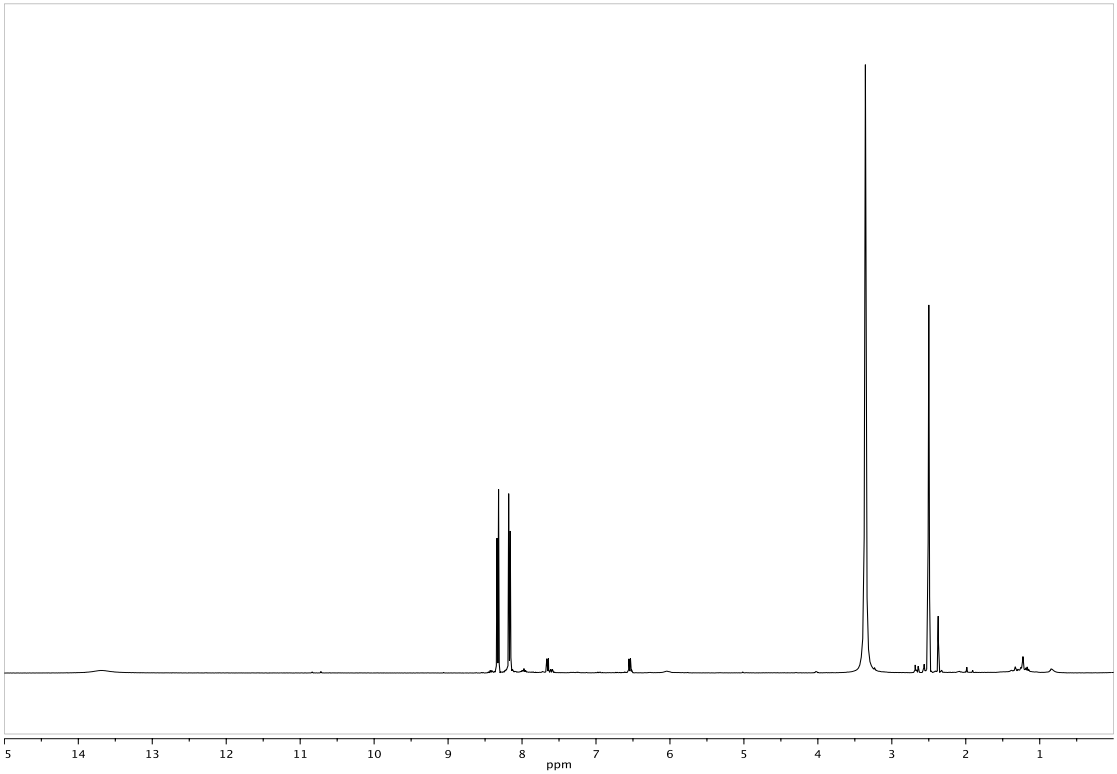
2-nitrobenzoic acid, *o*-19.



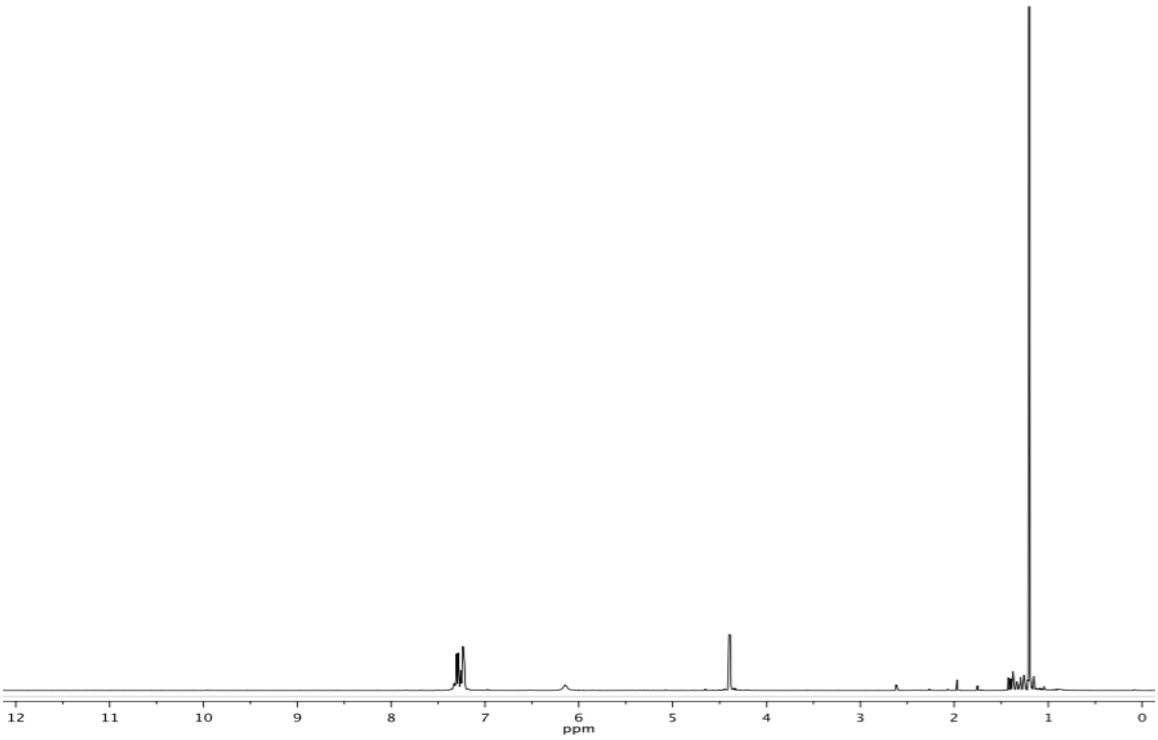
3-nitrobenzoic acid, *m*-19.



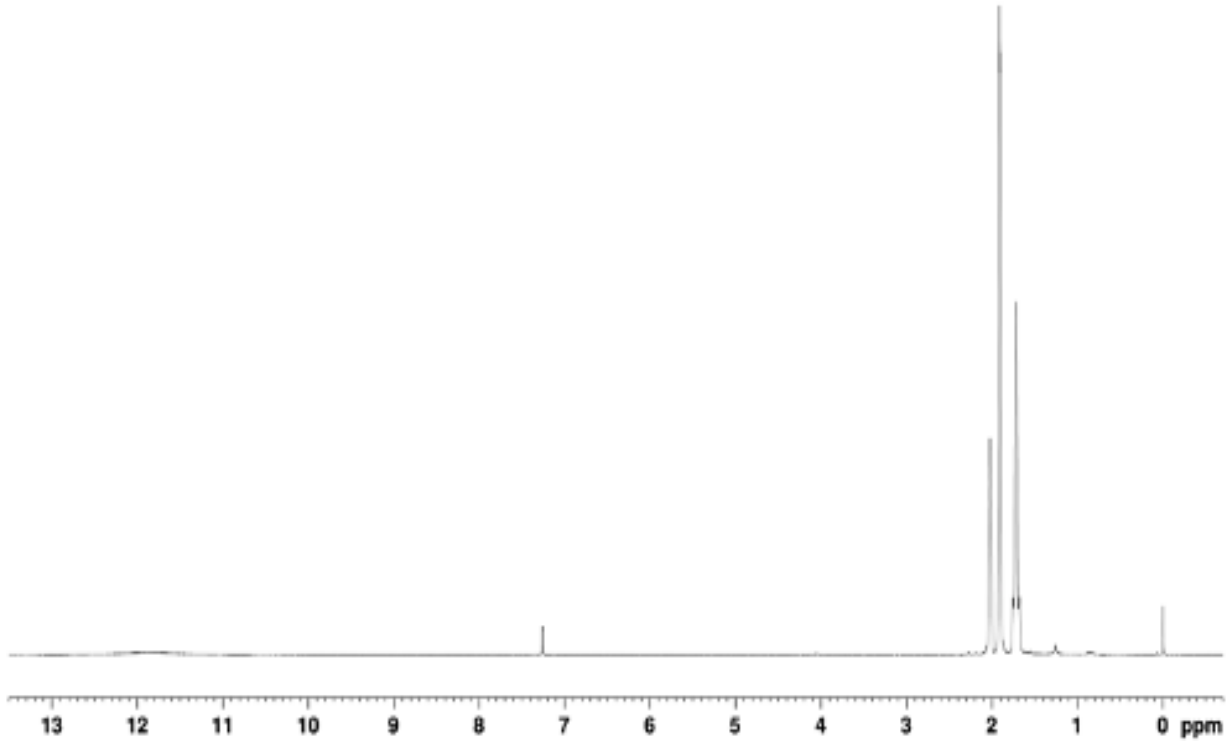
4-nitrobenzoic acid, *p*-19.



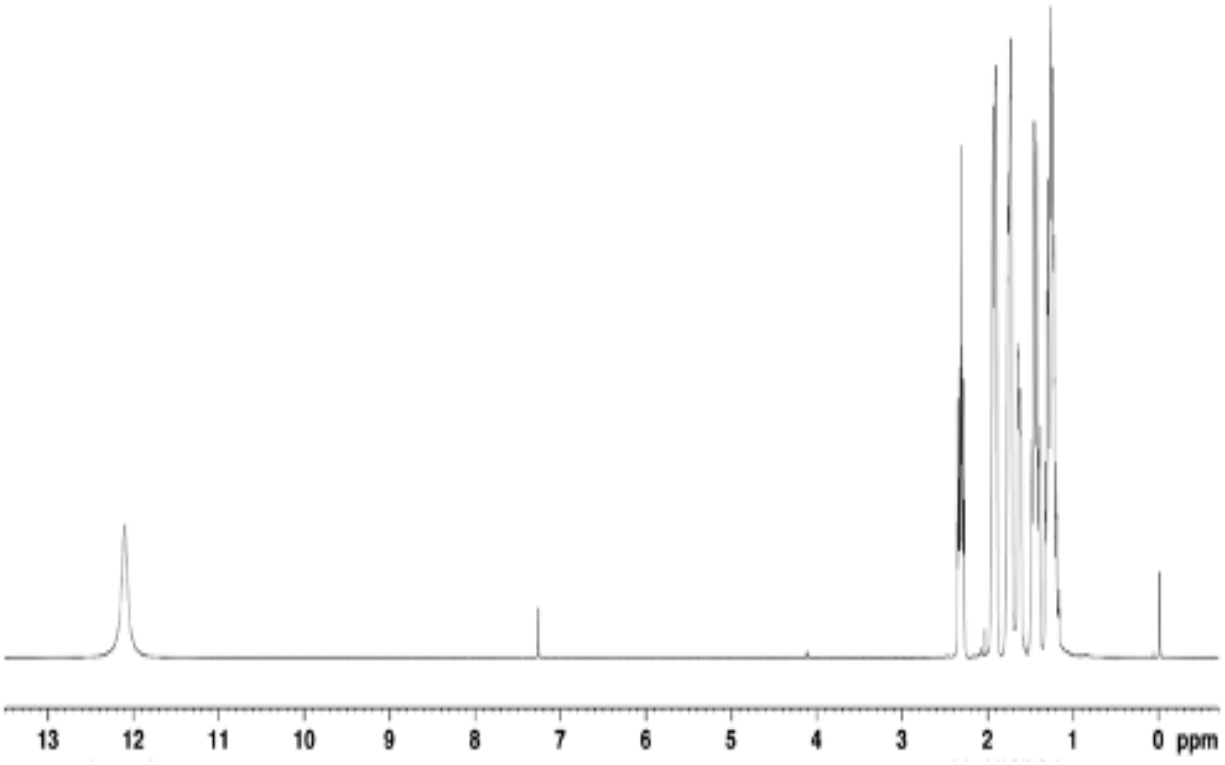
***N*-benzylpivalamide, 20.**



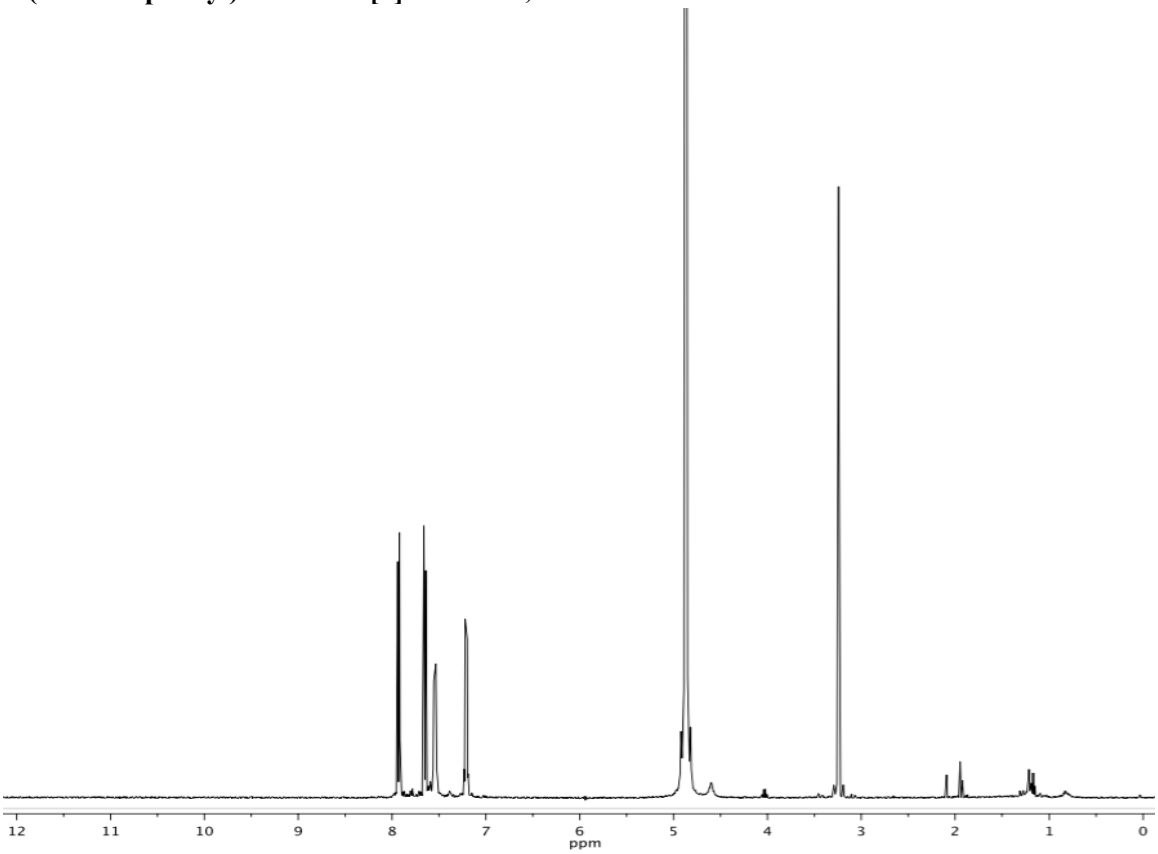
1-Adamantanecarboxylic acid, 21.



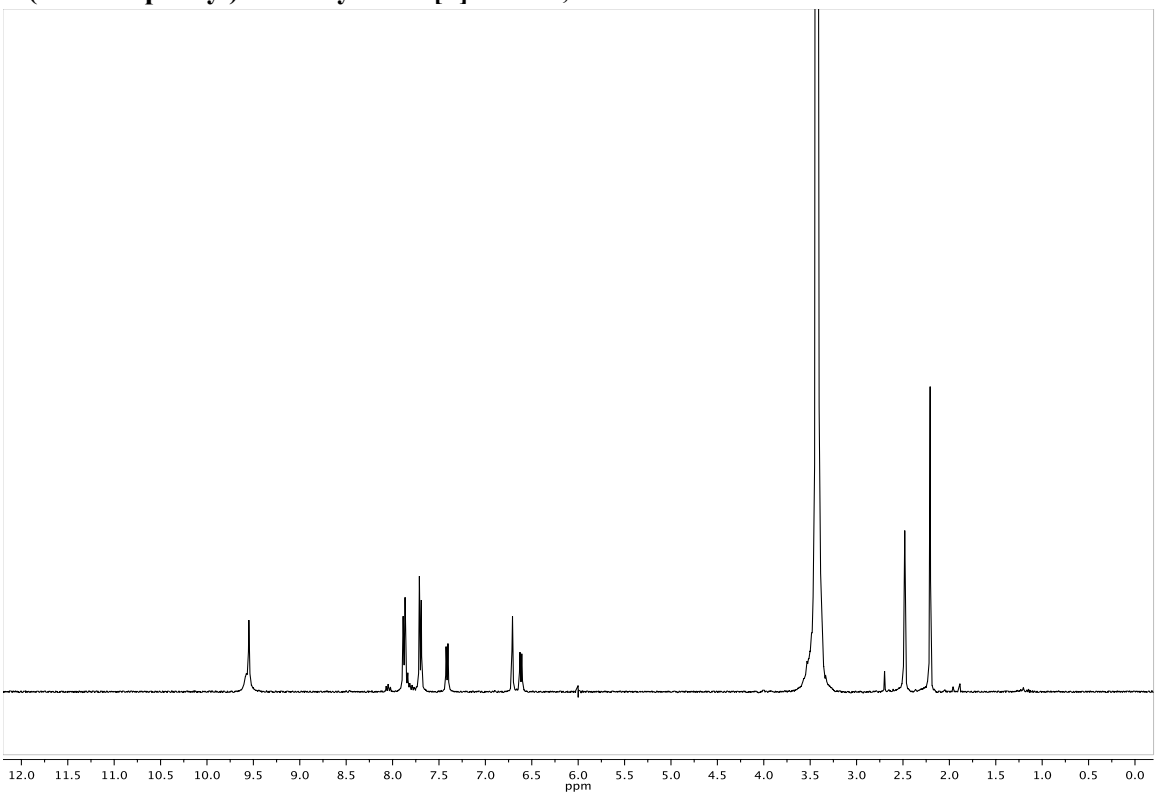
Cyclohexanecarboxylic acid, 23.



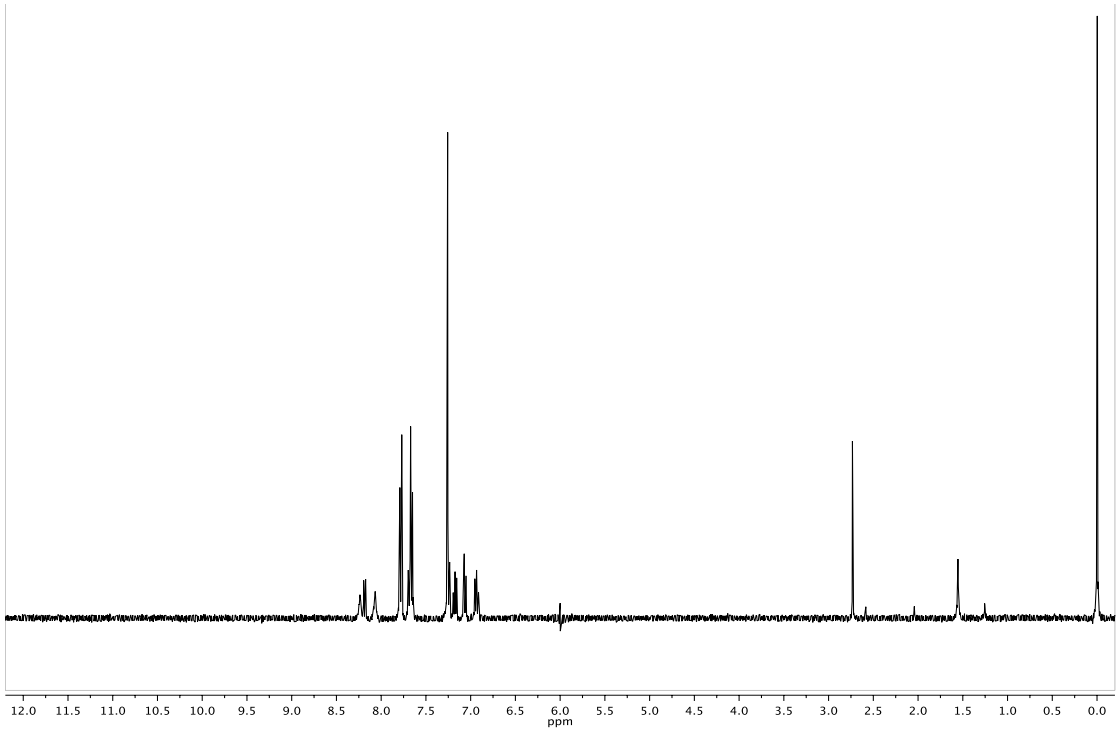
2-(4-bromophenyl)-1*H*-benzo[*d*]imidazole, 26.



2-(4-bromophenyl)-6-methylbenzo[d]oxazole, 27.



2-(4-bromophenyl) benzo[*d*]oxazole, 28.



Computational Methods

All calculations were obtained using the Schrodinger 2020 software package.[25,26] The ground state and transition state structures from Figure 5 were optimized using the wB97x-D functional and the 6-31G**++ basis set. The SCF calculations were converged to an energy tolerance of 0.5E-08 Hartrees. All transition state and minima geometries were verified using frequency calculations with all transition states having only 1 imaginary frequency and all minima having zero imaginary frequencies. The frequency calculations were performed using the same functional and basis set as the electronic structure calculations. The geometry was first optimized in the gas phase. Using the gas phase geometries as a starting point, the final optimized solution-phase geometries were obtained in an implicit acetonitrile solvent. This solvent was included in all calculations using the Poisson Boltzmann Finite element method which determines the solvent interactions using a numerical solution to the Poisson-Boltzmann equations. For the acetonitrile implicit solution, a dielectric constant of 37.5 and a probe radius of 2.19 Angstroms was used. The final reported Gibb's free energies included thermal corrections calculated at 298.15 K calculated using the same functional and basis set as the electronic structure calculations. The additional calculations in the supporting information were carried out using the same settings as described previously but with either a different basis set (cc-pVDZ++), a different functional (B3PW91-D3, B3LYP-D3, M06-2X-D3), or implicit PBF solvent (chloroform).

Summary of Electronic Structure Calculations.

#	QM Basis	QM Method	Solvation Energy (kcal/mol)	Imaginary Freq.	Total Energy (au)	Zero Point Energy (kcal/mol)	Total Free Energy (au) 298.15K 1.00atm
Hydroxide	6-31g++**	ωB97X-D	-99.86	0	-75.933062	5.488	-75.940572
33	6-31g++**	ωB97X-D	-13.26	0	-793.660871	92.292	-793.55207
33-TS	6-31g++**	ωB97X-D	-58.46	1	-869.563091	98.338	-869.444138
34	6-31g++**	ωB97X-D	-17.82	0	-793.649678	92.81	-793.539524
34-TS	6-31g++**	ωB97X-D	-58.26	1	-869.573096	100.987	-869.451273
35	6-31g++**	ωB97X-D	*-14.4*	0	-869.643525	102.969	-869.517766
5	6-31g++**	ωB97X-D	-10.629	0	-420.727004	74.629	-420.639169
$CH(NO2)_2^-$	6-31g++**	ωB97X-D	-61.25	0	-448.942616	26.113	-448.931071
Products	6-31g++**	ωB97X-D	-71.879	0	-869.669620	100.742	-869.57024
Hydroxide	6-31g++**	B3PW91-D3	-99.86	0	-75.933062	5.488	-75.935273
33	6-31g++**	B3PW91-D3	-12.91	0	-793.66057	92.378	-793.533649
34	6-31g++**	B3PW91-D3	-17.73	0	-793.64968	92.81	-793.532963
35	6-31g++**	B3PW91-D3	-13.93	0	-869.63129	102.884	-869.497056
33	6-31g++**	B3LYP-D3	-13.06	0	-793.94497	96.98	-793.829239
34	6-31g++**	B3LYP-D3	-17.64	0	-793.93408	98.04	-793.815766
33	6-31g++**	M06-2X-D3	-13.33	0	-793.59881	97.256	-793.482595
34	6-31g++**	M06-2X-D3	-18.07	0	-793.58909	99.365	-793.468639
33	cc-pvdz++	B3LYP-D3	-12.25	0	-794.0174	96.593	-793.902362
34	cc-pvdz++	B3LYP-D3	-16.66	0	-794.00765	98.089	-793.889558
33	cc-pvdz++	B3PW91-D3	-12.09	0	-793.71653	97.241	-793.600309
34	cc-pvdz++	B3PW91-D3	-16.59	0	-793.70755	99.373	-793.587322
33	cc-pvdz++	M06-2X-D3	-12.53	0	-793.71184	96.823	-793.596299
34	cc-pvdz++	M06-2X-D3	-16.51	0	-793.7024	99.275	-793.582042
33	cc-pvdz++	ωB97X-D	-12.46	0	-793.73628	97.051	-793.620521
34	cc-pvdz++	ωB97X-D	-16.7	0	-793.72551	98.35	-793.607068

Energetic Difference Results.

#	QM Basis	QM Method	Free Energy Difference from 33(+OH^-)* (kcal/mol)	Total Energy+ZPE Difference from 33(+OH^-)* (kcal/mol)
Hydroxide	6-31g++**	ωB97X-D		
33	6-31g++**	ωB97X-D	0.00	0.00
33-TS	6-31g++**	ωB97X-D	30.44	2.92
34	6-31g++**	ωB97X-D	7.87	7.02
34-TS	6-31g++**	ωB97X-D	25.96	13.08
35	6-31g++**	ωB97X-D	-8.19	-18.33
5	6-31g++**	ωB97X-D		
$CH(NO2)_2^-$	6-31g++**	ωB97X-D		
Products	6-31g++**	ωB97X-D	-48.69	-44.53
Hydroxide	6-31g++**	B3PW91-D3		
33	6-31g++**	B3PW91-D3		
34	6-31g++**	B3PW91-D3	0.43	7.27
35	6-31g++**	B3PW91-D3	-17.65	-18.61
33	6-31g++**	B3LYP-D3		
34	6-31g++**	B3LYP-D3	8.45	7.90
33	6-31g++**	M06-2X-D3		
34	6-31g++**	M06-2X-D3	8.76	8.21
33	cc-pvdz++	B3LYP-D3		
34	cc-pvdz++	B3LYP-D3	8.03	7.61
33	cc-pvdz++	B3PW91-D3		
34	cc-pvdz++	B3PW91-D3	8.15	7.77
33	cc-pvdz++	M06-2X-D3		
34	cc-pvdz++	M06-2X-D3	8.95	8.37
33	cc-pvdz++	ωB97X-D		
34	cc-pvdz++	ωB97X-D	8.44	8.06

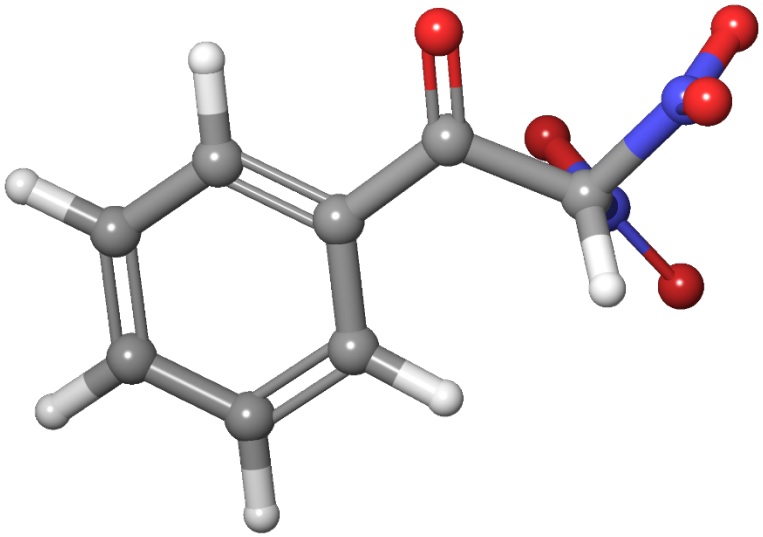
**For the energy differences between the transition states/ 33 and 34, the hydroxide ion energies are included with 33.*

Keto-Enol Results (Acetonitrile vs Chloroform)

#	QM Basis	QM Method	Implicit Solvent	Solvation Energy (kcal/mol)	Imaginary Freq.	Total Energy (au)	Zero Point Energy (kcal/mol)	Total Free Energy (au) 298.15K 1.00atm
33	6-31g++**	ωB97X-D	Acetonitrile	-13.26	0	-793.660871	92.292	-793.55207
34	6-31g++**	ωB97X-D	Acetonitrile	-17.82	0	-793.649678	92.81	-793.539524
33	6-31g++**	ωB97X-D	Chloroform	-9.19	0	-793.654428	92.399	-793.545489
34	6-31g++**	ωB97X-D	Chloroform	-12.76	0	-793.641637	93.012	-793.531481

#	QM Basis	QM Method	Implicit Solvent	Free Energy Difference from 33(+OH^-)* (kcal/mol)	Total Energy+ZPE Difference from 33(+OH^-)* (kcal/mol)
33	6-31g++**	ωB97X-D	Acetonitrile	0.00	0.00
34	6-31g++**	ωB97X-D	Acetonitrile	7.87	7.02
33	6-31g++**	ωB97X-D	Chloroform	0.00	0.00
34	6-31g++**	ωB97X-D	Chloroform	8.79	8.64

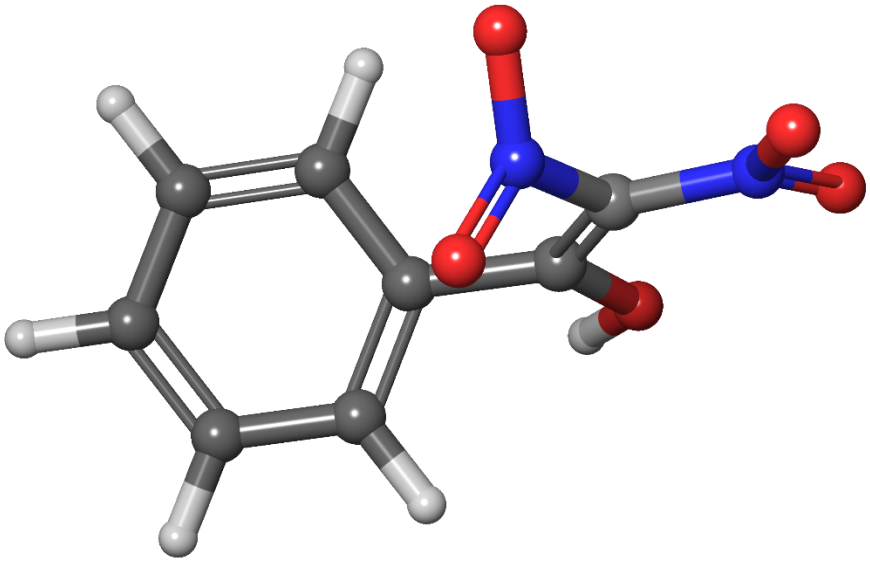
Pictures and Cartesian Coordinates for Reported Structures.



21
XYZ Coordinates for #33

C	-1.16640	-4.68800	-0.04290
C	-0.39930	-3.78850	-0.77120
C	-0.31770	-2.44480	-0.36150
C	-1.01730	-2.01560	0.77820
C	-1.78930	-2.92180	1.49840

C	-1.86150	-4.25550	1.09170
C	0.52930	-1.53400	-1.14540
C	0.95970	-0.20480	-0.43690
N	1.79500	0.62080	-1.39260
N	1.83790	-0.53320	0.76320
O	1.15830	1.20550	-2.24490
O	3.00390	0.61210	-1.26890
O	1.80230	0.24380	1.69840
O	2.51410	-1.54280	0.69000
O	0.95060	-1.75590	-2.25850
H	-1.22200	-5.72650	-0.35180
H	0.15270	-4.11590	-1.64480
H	-0.99490	-0.98060	1.10230
H	-2.33450	-2.58640	2.37340
H	-2.46020	-4.96020	1.65950
H	0.14110	0.43470	-0.10780

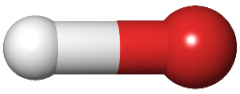


21

XYZ Coordinates for #34

C	-2.04810	-0.68700	0.95970
C	-0.65920	-0.65070	1.03670
C	0.06470	0.01320	0.03700
C	-0.59220	0.64990	-1.02310
C	-1.98310	0.62430	-1.07810
C	-2.70860	-0.04890	-0.09320
C	1.53920	0.02320	0.11170
C	2.27620	-0.56040	-0.88420
N	3.69240	-0.63790	-0.99220
N	1.58610	-1.28100	-1.97780
O	4.15960	-1.38260	-1.85930

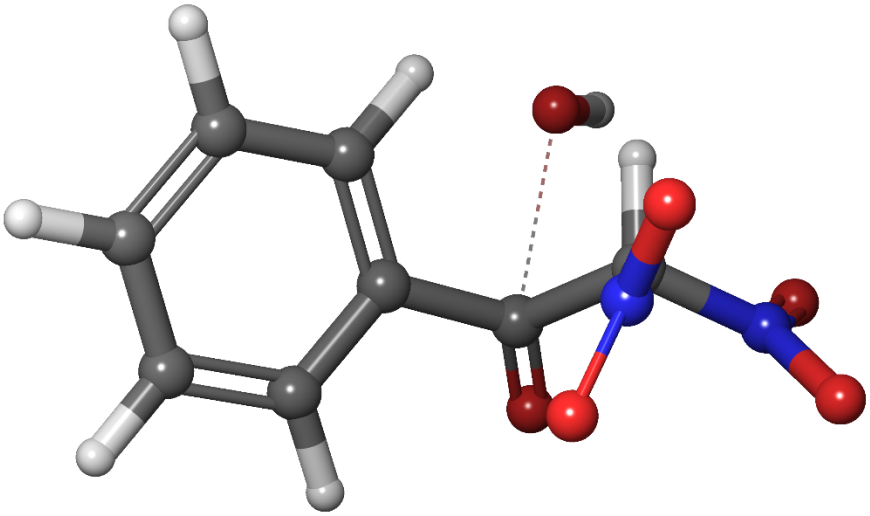
O	4.37540	0.01650	-0.20870
O	0.99150	-2.31040	-1.69540
O	1.66200	-0.79980	-3.09740
O	2.12140	0.57460	1.16130
H	-2.61360	-1.21970	1.71650
H	-0.13900	-1.16500	1.83870
H	-0.02210	1.17580	-1.78130
H	-2.49810	1.12900	-1.88850
H	-3.79180	-0.07630	-0.14570
H	1.47430	1.03960	1.72740



2

XYZ Coordinates for OH-

O	0.00000	0.00000	-0.05730
H	0.00000	0.00000	0.9094

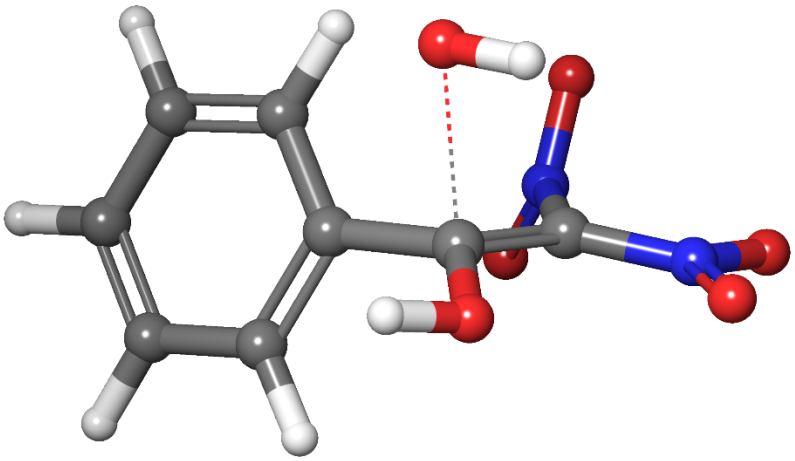


23

XYZ Coordinates for #33TS

C	-0.85350	-3.79060	-1.36100
C	-0.49720	-2.45740	-1.54710
C	-0.61960	-1.54040	-0.49820
C	-1.12540	-1.95540	0.73410
C	-1.48050	-3.29200	0.91660
C	-1.33720	-4.21350	-0.12210

C	-0.11150	-0.15760	-0.75810
C	0.91760	0.34020	0.28680
N	1.60440	1.58090	-0.13440
N	1.97440	-0.68740	0.54370
O	0.87970	2.60620	-0.29370
O	2.87290	1.57050	-0.29320
O	2.38590	-1.39040	-0.42920
O	2.37040	-0.82250	1.74470
H	-0.74270	-4.49920	-2.17570
H	-0.10220	-2.11680	-2.49780
H	-1.29900	-1.20100	1.49470
H	-1.88140	-3.61250	1.87280
H	-1.60670	-5.25430	0.03020
H	0.23000	0.58920	1.16020
O	-1.37220	0.79200	0.96830
O	-0.21360	0.38950	-1.86700
H	-1.75780	1.67120	0.74960

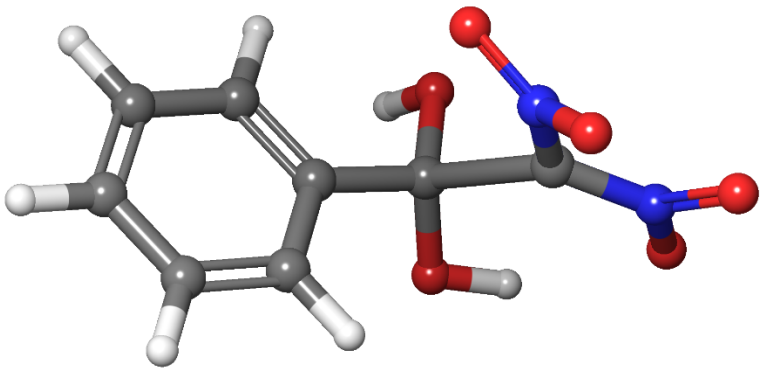


23

XYZ Coordinates for #34TS

C	-2.45860	-2.15410	0.28820
C	-1.46590	-1.19620	0.47300
C	-0.13080	-1.53590	0.25110
C	0.21210	-2.82820	-0.16630
C	-0.78710	-3.78180	-0.34800
C	-2.12230	-3.44590	-0.12070
C	0.97300	-0.53680	0.32180
C	1.06260	0.39350	-0.71530
N	2.09010	1.26610	-1.00910
N	-0.04970	0.51070	-1.67070
O	2.00210	1.93710	-2.05640

O	3.06750	1.34280	-0.25380
O	-0.82910	1.43910	-1.52770
O	-0.13330	-0.32260	-2.56000
O	2.07200	-0.85140	0.98330
O	0.04580	0.61310	2.12920
H	-1.70180	-0.19280	0.80800
H	1.24900	-3.07910	-0.37780
H	-0.52340	-4.78300	-0.67720
H	-2.90010	-4.19170	-0.26220
H	1.87260	-1.45990	1.71710
H	-3.49640	-1.88890	0.47020
H	0.83220	1.16720	2.21630

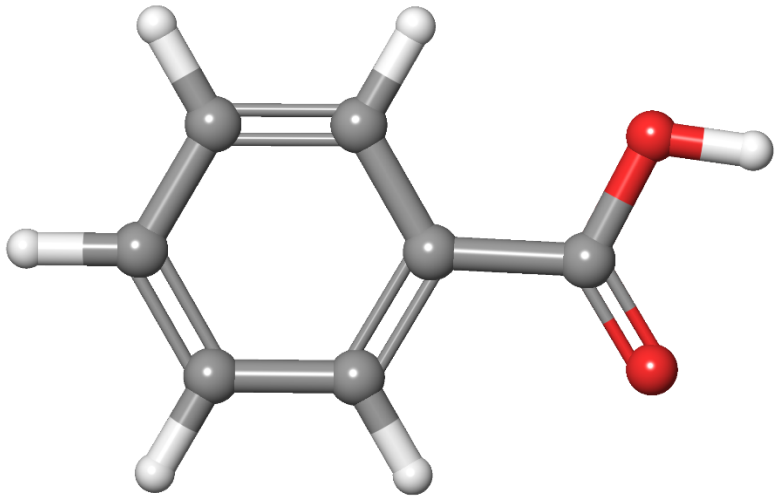


23

XYZ Coordinates for #35

C	-0.76580	-3.47610	-1.14770
C	-0.31050	-2.16310	-1.24360
C	-0.64060	-1.22480	-0.26260
C	-1.42870	-1.61430	0.81630
C	-1.89190	-2.92670	0.91100
C	-1.56270	-3.86120	-0.06910
C	-0.14510	0.21900	-0.42510
C	1.90980	0.32080	-0.35570
N	2.61200	1.31570	-0.97790
N	2.62480	-0.59350	0.44480
O	1.94930	2.18590	-1.63170
O	3.84650	1.43090	-0.89350
O	3.75510	-0.97540	0.12730
O	2.05050	-1.01580	1.46120
H	-0.50210	-4.19700	-1.91670
H	0.30880	-1.86600	-2.08550
H	-1.66350	-0.90030	1.59830
H	-2.50560	-3.22000	1.75820
H	-1.92270	-4.88360	0.00710

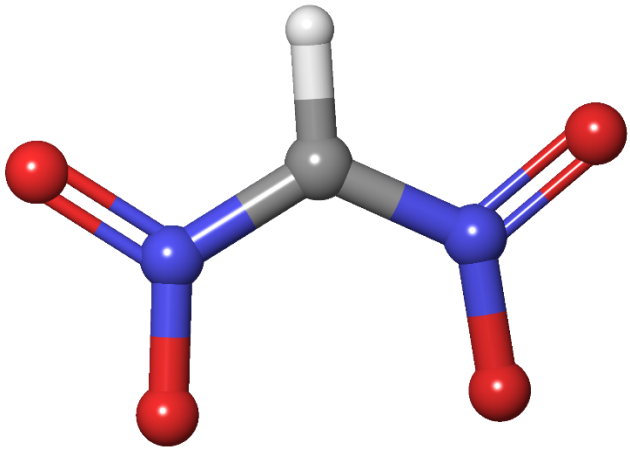
O	-0.66350	1.08920	0.56800
O	-0.62390	0.62550	-1.68740
H	-1.61530	1.20240	0.40750
H	-0.10080	1.42290	-1.92440



15

XYZ Coordinates for #5

C	-2.06120	-1.19750	0.14140
C	-2.78990	-0.00640	0.12860
C	-2.12320	1.22010	0.15240
C	-0.72940	1.26180	0.18870
C	0.00490	0.06770	0.20110
C	-0.66970	-1.16100	0.17750
C	1.49810	0.04400	0.23910
O	2.07440	1.25040	0.26160
O	2.15760	-0.98450	0.24940
H	-2.57760	-2.15350	0.12350
H	-3.87670	-0.03490	0.10040
H	-2.69210	2.14600	0.14290
H	-0.22080	2.22070	0.20730
H	-0.09940	-2.08490	0.18750
H	3.04520	1.14810	0.28630

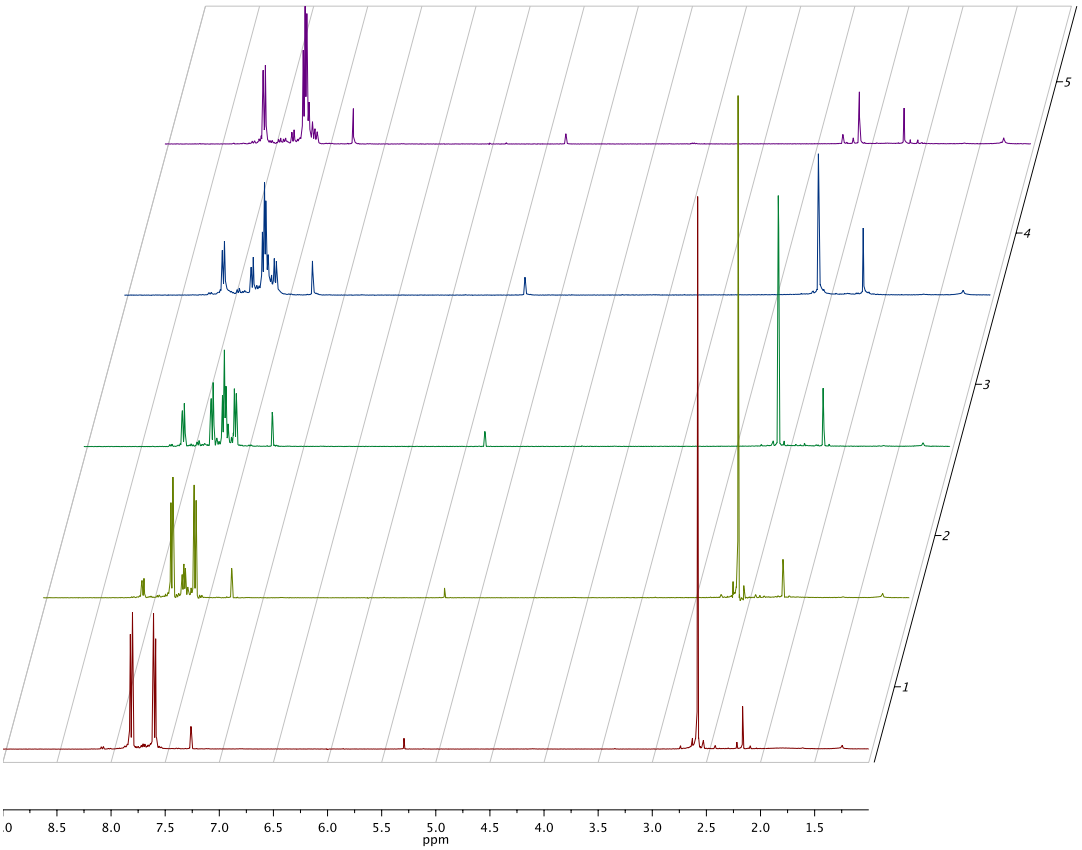


8

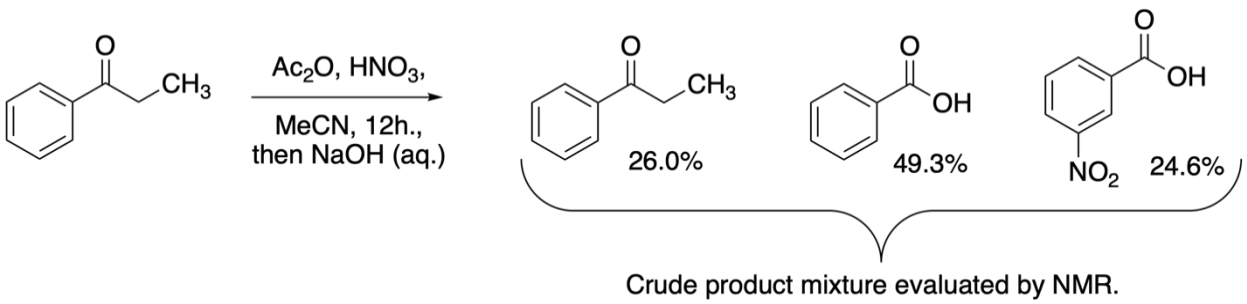
$CH(NO_2)_2^-$

C	0.06830	0.11310	-0.01290
N	1.42580	0.02020	0.10050
N	-0.63290	1.27870	0.12140
O	1.91080	-1.13230	-0.04690
O	2.16260	0.99240	0.33370
O	-0.10060	2.37540	0.35980
O	-1.88040	1.18510	-0.01170
H	-0.48400	-0.78650	-0.21970

Additional Studies Evaluating Reaction Mechanism.



Time course ^{1}HNMR for conversion of 4-bromoacetophenone to intermediate 2. The conversion of **1** to **2** as described in Table 1 was monitored by ^{1}H-NMR spectroscopy. Aliquots of the reaction were removed at the indicated time intervals, concentrated *in vacuo* and the residue was directly resuspended in $CDCl_3$ for ^{1}H-NMR analysis. Spectra are: 1-starting material; 2-reaction after 2h..; 3-reaction after 6h..; 4-reaction after 9h.; 5-reaction after 12h.



Trinitration is not required for oxidative C-C bond cleavage. Consistent with our mechanistic hypothesis for the formation of a dinitroalkyl ketone intermediate we confirmed that trinitration (which is possible with a methyl ketone, but not possible with propiophenone) is not required for conversion to the carboxylic acid. In the reaction with propiophenone, aromatic nitration is additionally observed as a competing reaction pathway. No efforts were made to further optimize this reaction.

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