

Organic Letters

Supporting Information

Efficient Addition Reaction of Bromonitromethane to Aldehydes Catalyzed by NaI:

A New Route to 1-Bromo-1-nitroalkan-2-ols Under Very Mild Conditions

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GENERAL

Reactions requiring an inert atmosphere were conducted under dry nitrogen, and the glassware was oven dried (120 °C). THF was distilled from sodium/benzophenone ketyl immediately prior to use. All reagents were purchased in the higher quality available and were used without further purification. Flash column chromatography was carried out on silica gel 230-400 mesh. Compounds were visualized on analytical thin layer chromatograms (TLC) by UV light (254 nm). ¹H NMR spectra were recorded at 200, 300 or 400 MHz. ¹³C NMR spectra and DEPT experiments were determined at 50 or 75 MHz. Chemical shifts are given in ppm relative to tetramethylsilane (TMS), which is used as an internal standard, and coupling constants (*J*) are reported in Hz. The diastereomeric excesses were obtained using ¹H NMR analysis and GC-MS of crude products. GC-MS and HRMS were measured at 70 eV or using FAB conditions. When HRMS could not be measured on molecular ion the HRMS of a significant fragment is given. Only the most important IR absorptions (cm⁻¹) and the molecular ions and/or base peaks in MS are given.

General Procedure. NaI (0.12 mmol, 0.15 equiv.) was added to a stirred solution of bromonitromethane **1** (0.8 mmol, 1 equiv.) and the corresponding aldehyde **3** or **8** (0.8 mmol, 1 equiv.) in THF (10 ml). After stirring the reaction at room temperature for two hours it was quenched with aqueous HCl (10 mL, 0.1 M) before the organic material was extracted with diethyl ether. The combined extracts were washed with an aqueous saturated solution of Na₂S₂O₃ and then dried over Na₂SO₄ and the solvent was removed under reduced pressure affording products **5** or **9** which were purified by column chromatography when necessary.

Spectral and analytical data for products 5 and 9

Products **5** were obtained as a diastereoisomeric mixture.

1-Bromo-1-nitrononan-2-ol (5a): ^1H NMR (300 MHz, CDCl_3): 5.87 (d, $J = 3.4$ Hz, 1 H), 5.62 (d, $J = 7.90$ Hz, 1 H), 4.13-4.05 (m, 2 H), 1.50-1.04 (m, 24 H), 0.75 (t, $J = 6.7$ Hz, 6 H); ^{13}C NMR (75 MHz, CDCl_3): δ 86.2 (CH), 81.5 (CH), 73.2 (CH), 72.5 (CH), 33.6 (CH_2), 31.9 (CH_2), 31.6 (CH_2), 29.0 (CH_2), 28.9 (CH_2), 25.1 (CH_2), 24.7 (CH_2), 22.5 (CH_2), 13.9 (CH_2); IR (neat): 3410, 2928, 1712, 1569, 1465, 1356 cm^{-1} ; $R_f = 0.6, 0.7$ (hexane/EtOAc 3:1); Anal. Calcd for $\text{C}_9\text{H}_{18}\text{BrNO}_3$: C, 40.31; H, 6.77; N, 5.22. Found: C, 40.40; H, 6.82; N, 5.27.

2-Bromo-1-cyclohexyl-2-nitroethanol (5b): ^1H NMR (300 MHz, CDCl_3): 6.01 (d, $J = 2.8$ Hz, 1 H), 5.72 (d, $J = 9.0$ Hz, 1 H), 3.90 (dd, $J = 3.4, 9.0$ Hz, 1 H), 3.78 (dd, $J = 2.8, 7.9$ Hz, 1 H), 3.39 (br s, 2 H), 1.84-0.93 (m, 22H); ^{13}C NMR (75 MHz, CDCl_3): δ 86.2 (CH), 79.6 (CH), 76.6 (CH), 76.4 (CH), 41.2 (CH), 38.2 (CH), 29.5 (CH_2), 28.2 (CH_2), 28.1 (CH_2), 25.8 (CH_2), 25.7 (CH_2), 25.6 (CH_2), 25.4 (CH_2), 25.3 (CH_2), 25.2 (CH_2), 24.4 (CH_2); HRMS (70 eV) calc. for $[\text{C}_8\text{H}_{14}\text{BrNO}_3\text{-OH}]$ 234.0208, found 234.0210; IR (neat): 3428, 2926, 1705, 1564, 1450, 1357 cm^{-1} ; $R_f = 0.5, 0.6$ (hexane/EtOAc 3:1); Anal. Calcd for $\text{C}_8\text{H}_{14}\text{BrNO}_3$: C, 38.11; H, 5.60; N, 5.56. Found: C, 38.04; H, 5.66; N, 5.48.

1-Bromo-4-methyl-1-nitropentan-2-ol (5c): ^1H NMR (300 MHz, CDCl_3): δ 5.86 (d, $J = 3.3$ Hz, 1 H), 5.60 (d, $J = 6.6$ Hz, 1 H), 4.30-4.08 (m, 2 H), 3.49 (br s, 2 H), 1.71 (m, 2 H), 1.51-1.36 (m, 4H), 0.81 (t, $J = 7.0$ Hz, 12 H); ^{13}C NMR (50 MHz, CDCl_3): δ 86.6 (CH), 82.1 (CH), 71.7 (CH), 70.9 (CH), 42.2 (CH_2), 40.61 (CH_2); 24.5 (2 x CH), 23.3 (CH_3), 22.8 (CH_3), 21.5 (CH_3), 20.9 (CH_3); HRMS (70 eV) calc. for $\text{C}_6\text{H}_{12}\text{BrNO}_3$ 225.0001, found 224.9972, IR (neat): 3414, 2960, 1568, 1469, 1355 cm^{-1} ; $R_f = 0.5, 0.6$ (hexane/EtOAc 3:1); Anal. Calcd for $\text{C}_6\text{H}_{12}\text{BrNO}_3$: C, 31.88; H, 5.35; N, 6.20. Found: C, 31.92; H, 5.41; N, 6.29.

1-Bromo-3-methyl-1-nitropentan-2-ol (5d): ^1H NMR (300 MHz, CDCl_3): δ 6.05 (d, $J = 2.8$ Hz, 1 H), 5.98 (d, $J = 4.5$ Hz, 1 H), 5.78 (d, $J = 8.4$ Hz, 1 H), 5.65 (d, $J = 9.6$ Hz, 1 H), 4.14 (dd, $J = 2.3, 9.0$ Hz, 1 H), 3.97 (dd, $J = 3.9, 8.5$ Hz, 1 H), 3.88 (dd, $J = 4.5, 6.2$ Hz, 1 H), 3.81 (dd, $J = 2.3, 8.5$ Hz, 1 H), 2.65 (br s, 4 H), 1.82-1.11 (m, 12 H), 0.93-0.73 (m, 24 H); ^{13}C NMR (75 MHz, CDCl_3): $\delta = 86.6$ (CH), 85.3 (CH), 80.0 (CH), 79.9 (CH), 77.1 (CH), 76.2 (CH), 75.7 (CH), 74.7 (CH), 38.4 (CH), 37.5 (CH), 35.5 (CH), 34.9 (CH), 26.4 (CH_2), 25.3 (CH_2), 24.1 (CH_2), 21.7 (CH_2), 15.8 (CH_3), 14.3 (CH_3), 13.2 (CH_3), 11.4 (2 x CH_3), 11.3 (CH_3), 10.6 (CH_3), 10.4 (CH_3); HRMS (70 eV) calc. for $\text{C}_6\text{H}_{12}\text{BrNO}_3$ 225.0001, found

225.0025, IR (neat): 3437, 2968, 1568, 1463, 1352 cm^{-1} ; $R_f = 0.5, 0.6$ (hexane/EtOAc 3:1); Anal. Calcd for $\text{C}_6\text{H}_{12}\text{BrNO}_3$: C, 31.88; H, 5.35; N, 6.20. Found: C, 31.90; H, 5.38; N, 6.26.

1-Bromo-4,8-dimethyl-1-nitronon-7-en-2-ol (5e): ^1H NMR (300 MHz, CDCl_3): δ 5.86-5.83 (m, 2 H), 5.59-5.56 (m, 2 H), 4.92-4.74 (m, 4 H), 4.35-4.20 (m, 4 H), 2.03-1.81 (m, 8 H), 1.74-1.30 (m, 20 H), 1.64 (s, 12 H), 1.56 (s, 12 H), 0.81-0.78 (m, 12 H); ^{13}C NMR (75 MHz, CDCl_3): δ 131.4 (2 x C), 131.3 (2 x C), 124.2 (CH), 124.1 (CH), 124.0 (2 x CH), 86.7 (2 x CH), 82.1 (CH), 82.0 (CH), 71.6 (CH), 71.3 (CH), 70.8 (CH), 70.6 (CH), 40.6 (CH_2), 40.3 (CH_2), 39.0 (CH_2), 38.8 (CH_2), 37.5 (CH_2), 37.1 (CH_2), 36.0 (CH_2), 35.2 (CH_2), 28.8 (2 x CH), 28.3 (2 x CH), 25.4 (2 x CH_3), 25.2 (CH_2), 25.1 (CH_2), 24.9 (CH_2), 24.8 (CH_2), 20.1 (2 x CH_3), 19.7 (2 x CH_3), 18.7 (2 x CH_3), 18.3 (2 x CH_3), 17.4 (2 x CH_3); HRMS (70 eV) calc. for $[\text{C}_{11}\text{H}_{20}\text{BrNO}_3\text{-Br}]$ 214.1444, found 214.1490; IR (neat): 3389, 2925, 1700, 1568, 1456, 1355 cm^{-1} ; $R_f = 0.5, 0.6$ (hexane/EtOAc 3:1); Anal. Calcd for $\text{C}_{11}\text{H}_{20}\text{BrNO}_3$: C, 44.91; H, 6.85; N, 4.76. Found: C, 44.88; H, 6.79; N, 4.71.

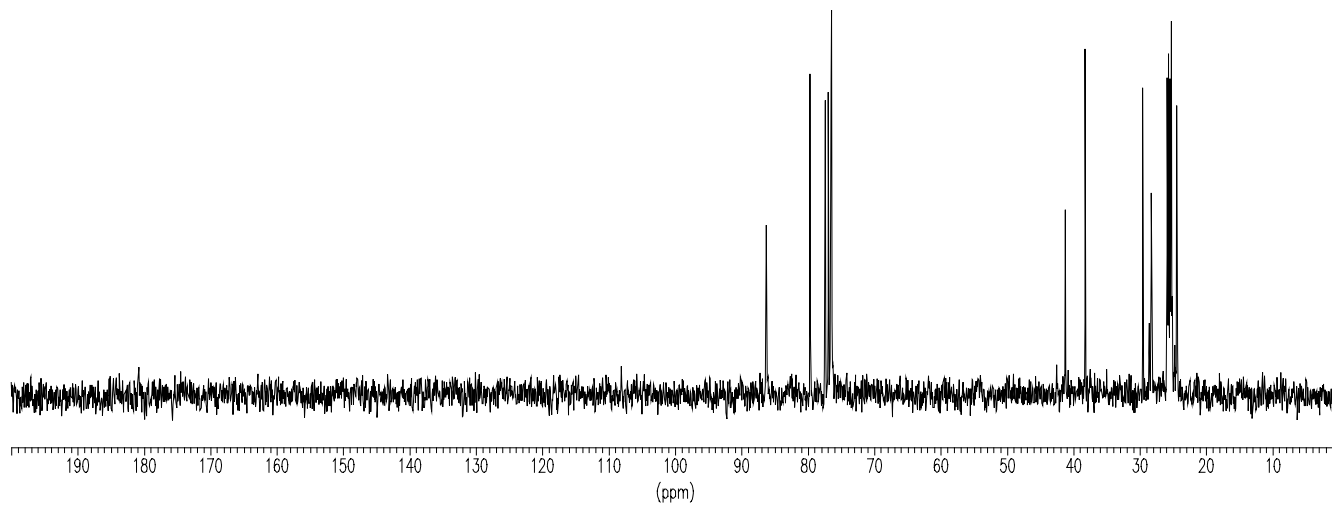
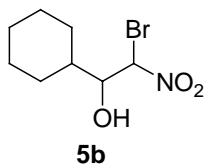
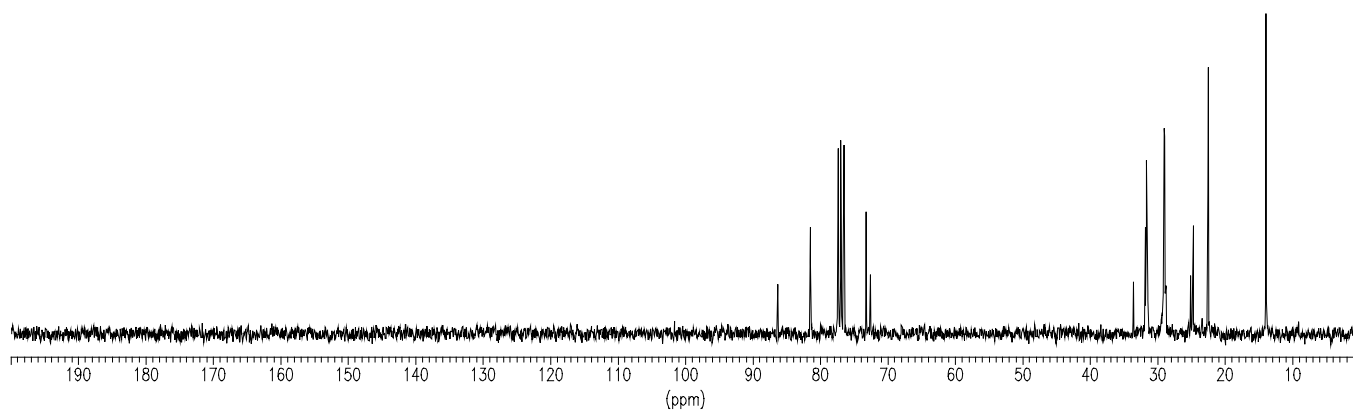
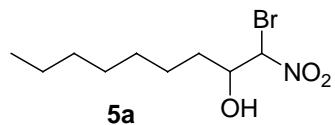
1-Bromo-1-nitro-3-phenylpropan-2-ol (5f): ^1H NMR (300 MHz, CDCl_3): δ 7.29-7.13 (m, 10 H), 5.77 (d, $J = 2.3$ Hz, 1 H), 5.61 (d, $J = 7.5$ Hz, 1 H), 4.37 (dd, $J = 2.8, 7.3$ Hz, 1 H), 4.32 (dd, $J = 3.4, 7.9$ Hz, 1H), 3.31 (dd, $J = 3.4, 14.1$ Hz, 1H), 2.94 (br s, 2 H), 2.87 (dd, $J = 7.3, 13.6$ Hz, 1H), 2.76 (dd, $J = 1.7, 6.8$ Hz, 1H), 2.71 (dd, $J = 2.3, 6.8$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3): δ 135.2 (C), 134.9 (C), 129.4 (2 x CH), 129.0 (2 x CH), 128.7 (2 x CH), 128.5 (2 x CH), 127.2 (CH), 127.1 (CH), 85.8 (CH), 80.5 (CH), 73.7 (CH), 73.2 (CH), 39.9 (CH_2), 37.9 (CH_2); HRMS (70 eV) calc. for $\text{C}_9\text{H}_{10}\text{BrNO}_3$ 258.9844, found 258.9857; IR (neat): 3536, 3029, 2924, 1560, 1496, 1455, 1351 cm^{-1} ; $R_f = 0.4, 0.5$ (hexane/EtOAc 3:1); Anal. Calcd for $\text{C}_9\text{H}_{10}\text{BrNO}_3$: C, 41.56; H, 3.88; N, 5.39. Found: C, 41.60; H, 3.93; N, 5.34.

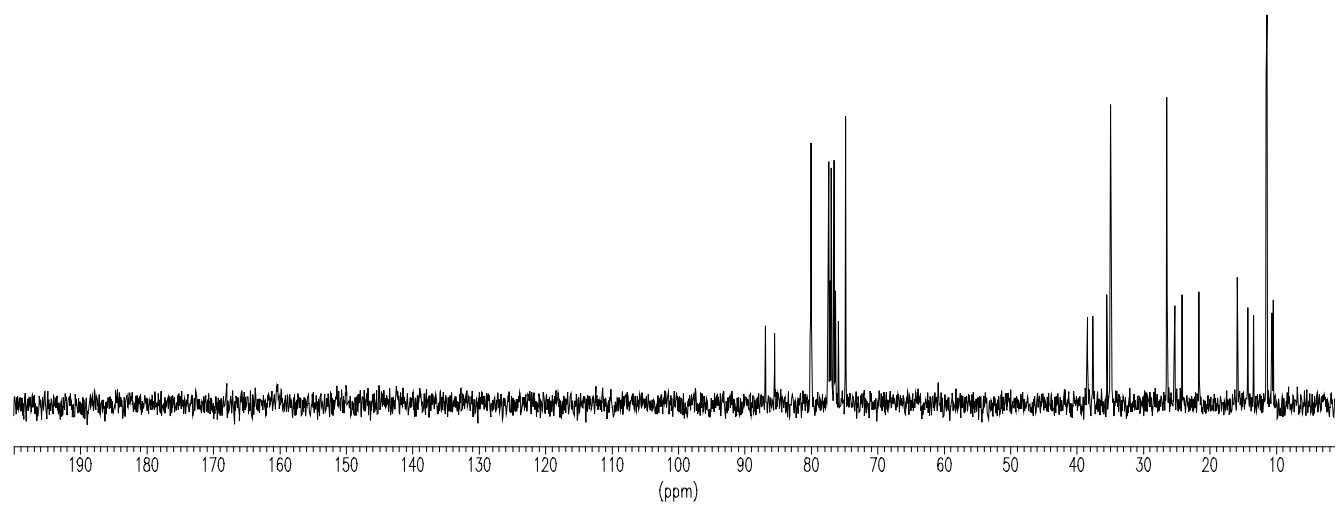
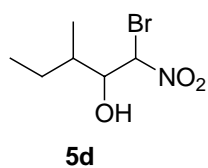
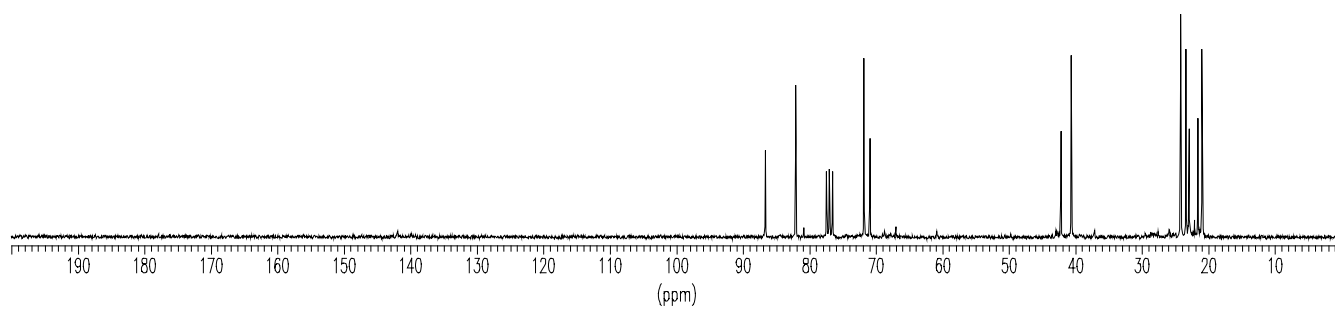
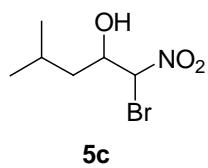
1-Bromo-2-hydroxy-2-phenyl-1-nitroethane (5g): ^1H NMR (300 MHz, CDCl_3): δ 7.39-7.25 (m, 10 H), 5.97 (d, $J = 5.1$ Hz, 1 H), 5.85 (d, $J = 9.0$ Hz, 1 H), 5.25 (d, $J = 5.1$ Hz, 1 H), 5.18 (d, $J = 9.0$ Hz, 1 H), 3.10 (br s, 2 H); ^{13}C NMR (75 MHz, CDCl_3): δ 236.0 (C), 135.9 (C), 129.7 (3 x CH); 129.4 (2 x CH), 127.3 (3 x CH), 126.4 (2 x CH), 85.5 (CH), 81.0 (CH), 76.2 (CH), 74.6 (CH); IR (neat): 3537, 3031, 1565, 1451, 1360 cm^{-1} ; $R_f = 0.3, 0.4$ (hexane/EtOAc 3:1); Anal. Calcd for $\text{C}_8\text{H}_8\text{BrNO}_3$: C, 39.05; H, 3.28; N, 5.69. Found: C, 39.10; H, 3.22; N, 5.71.

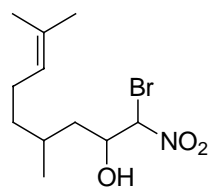
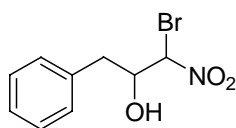
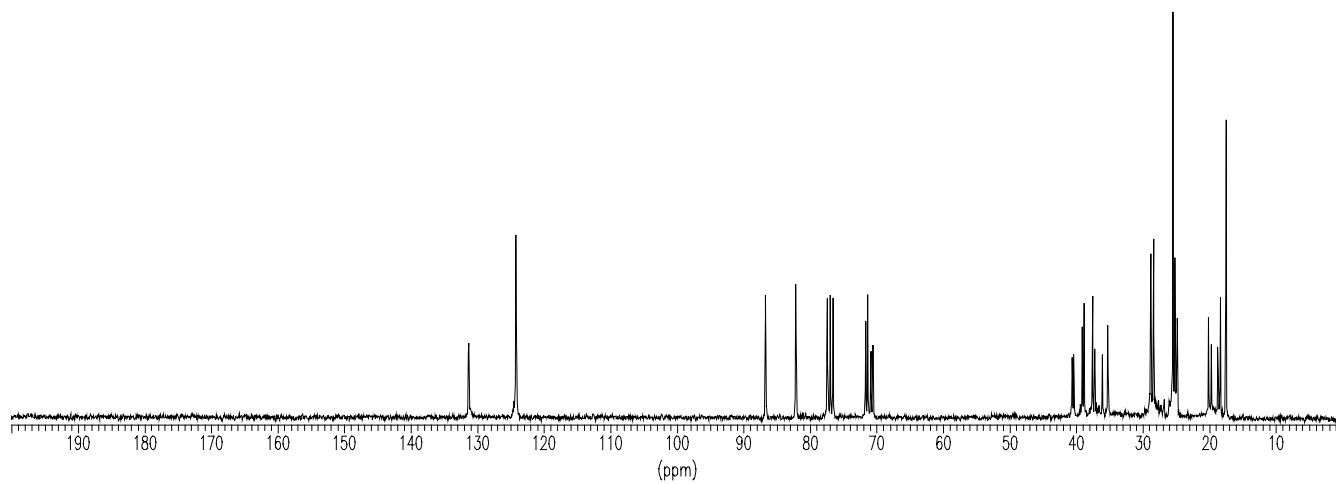
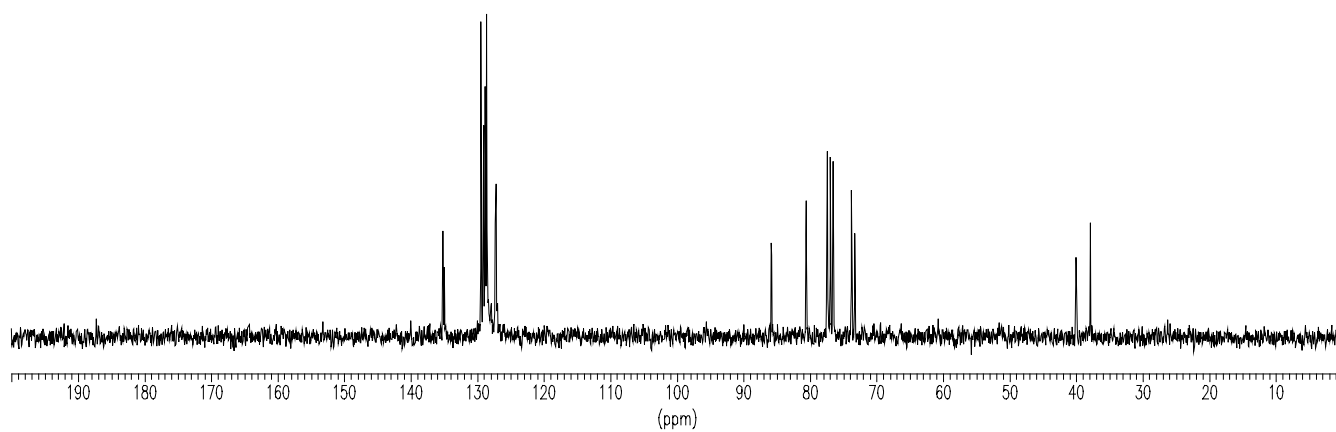
(E)-1-Bromo-1-nitropent-3-en-2-ol (5h): ^1H NMR (300 MHz, CDCl_3): δ 5.87-5.63 (m, 4 H), 5.37-5.30 (m, 2 H), 4.57-4.46 (m, 2 H), 1.63-1.59 (m, 6 H); ^{13}C NMR (75 MHz, CDCl_3): δ 133.8 (CH), 133.3 (CH), 125.5 (CH), 125.1 (CH), 84.7 (CH), 81.1 (CH), 74.3 (CH), 73.8 (CH), 17.6 (2 x CH_3); HRMS (70

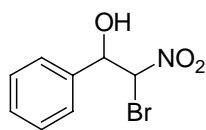
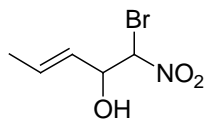
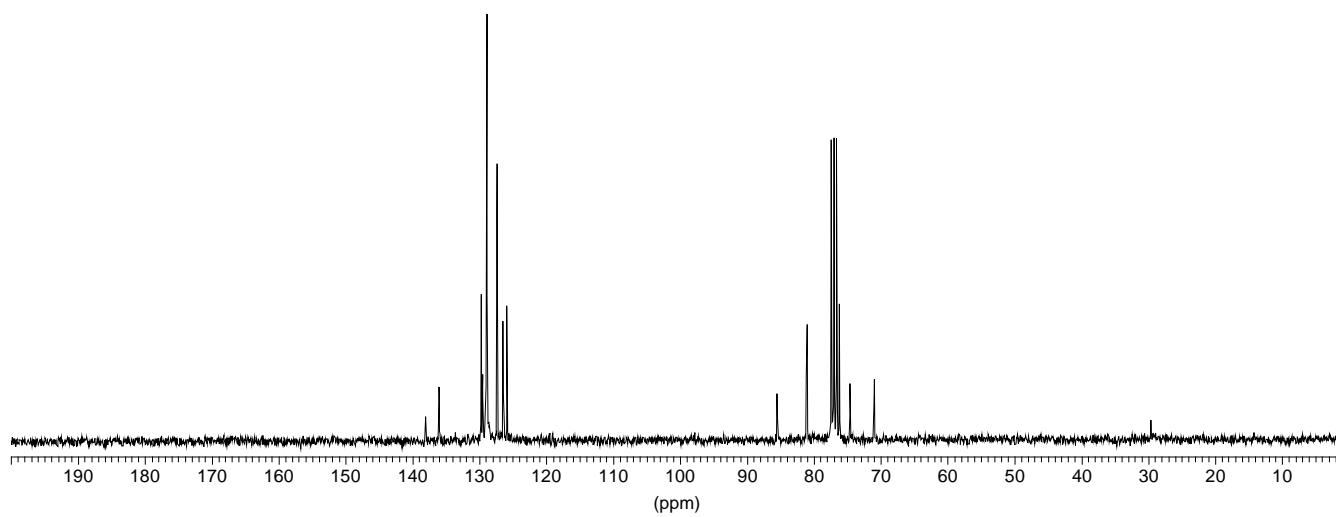
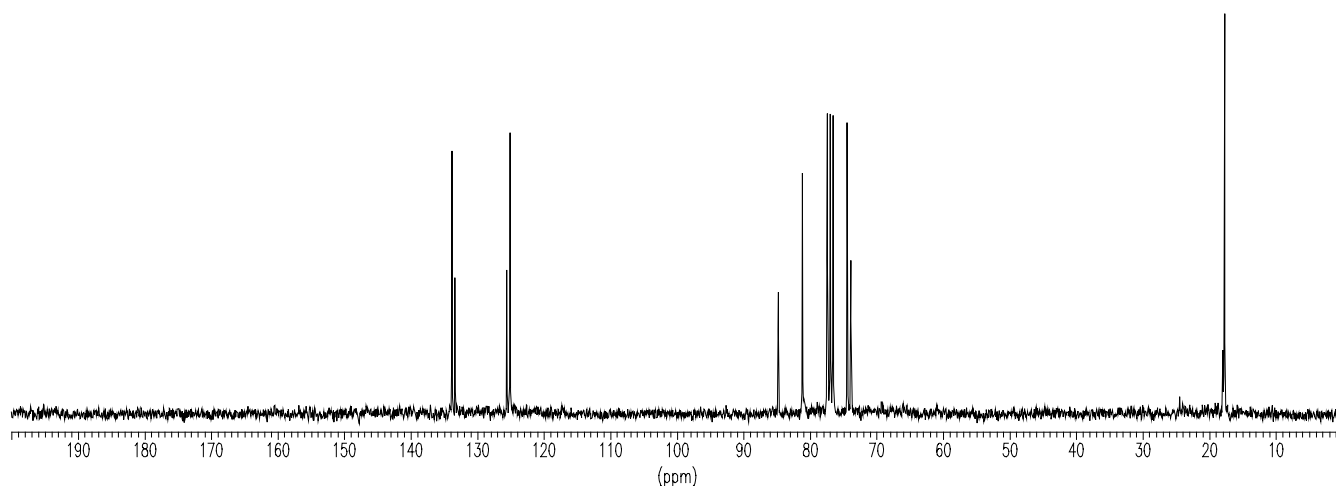
eV) calc. for $C_5H_8BrNO_3$ 208.9688, found 208.9693; IR (neat): 3410, 2919, 1692, 1674, 1568, 1448, 1359 cm^{-1} ; $R_f = 0.3, 0.4$ (hexane/EtOAc 3:1); Anal. Calcd for $C_5H_8BrNO_3$: C, 28.59; H, 3.84; N, 6.67. Found: C, 28.64; H, 3.88; N, 6.70.

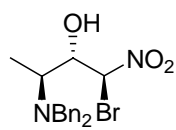
(1*S*,2*S*,3*S*)-1-Bromo-3-(dibenzylamino)-1-nitrobutan-2-ol (9): $[\alpha]_D^{25} = +98.1$ (*c* 1.3, $CHCl_3$); 1H NMR (300 MHz, $CDCl_3$): δ 7.25-7.14 (m, 10 H), 6.57 (d, $J = 1.0$ Hz, 1 H), 3.94-3.89 (m, 1 H), 3.64 (d, $J = 13.1$ Hz, 2 H), 3.27 (d, $J = 13.1$ Hz, 2H), 2.77-2.67 (m, 1H), 2.25 (br s, 1 H), 1.15 (d, $J = 6.64$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.6 (2 x C), 129.2 (4 x CH), 128.6 (4 x CH), 127.4 (2 x CH), 86.1 (CH), 73.8 (CH), 55.7 (CH), 54.5 (2 x CH_2), 8.2 (CH_3); HRMS (70 eV) calc. for $[C_{18}H_{21}BrN_2O_3-NO_2]$ 346.0807, found 346.0809; IR (neat): 3553, 3490, 3095, 2923, 1555, 1488, 1376 cm^{-1} ; $R_f = 0.5$ (hexane/EtOAc 3:1); Anal. Calcd for $C_{18}H_{21}BrN_2O_3$: C, 54.97; H, 5.38; N, 7.12. Found: C, 54.90; H, 5.42; N, 7.17.

^{13}C NMR of products 5 and 9:



**5e****5f**

**5g****5h**

**9**