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DNA: a novel catalyst for nitro-Aldol or Henry reaction

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General Remarks: ^1H NMR and ^{13}C NMR were recorded on a Bruker AC-300 FT (^1H : 300 MHz, ^{13}C : 75 MHz) using TMS as internal reference. The chemical shifts (δ) and coupling constants (J) were expressed in ppm and Hz respectively. Infrared samples were recorded on a Perkin-Elmer 2000 FTIR spectrometer. Herring sperm DNA was purchased from BIO BASIC INC, Salmon testes DNA, MOPS and MES were purchased from Sigma. The synthetic 16-mer d(TCAG)₂(CTGA)₂ was obtained from Shanghai Sangon Biological Engineering Technology & Services Co., Ltd. All substrates were purchased from Aldrich and used as supplied. The pH value of DNA solution (in super-pure water) was recorded on a pH-3C precision acidity meter. Other reagents and solvents were used as supplied.

Dissolution of synthetic oligonucleotide.

The synthetic 16-mer d(TCAG)₂(CTGA)₂ was obtained from Shanghai Sangon Biological Engineering Technology & Services Co., Ltd. The lyophilized powder was dissolved in buffer (20 mM Mops, 150 mM NaCl, 50 mM MgCl₂, pH 6.5), heated to 94 °C and slowly cooled to room temperature. After centrifugation the supernatant, containing the dissolved oligonucleotide, was decanted. Concentration was determined by UV/Vis, using $\epsilon_{260} = 31.2 \text{ OD}/\mu\text{g}$.

Control and additional experiments (Table 1)

Table S1 Control and additional experiments^a

Catalysts and Modification	Yield(%) ^b
DNA source = Herring sperm	90
DNA(3.3 mg mL ⁻¹)	92
DNA(2.0 mg mL ⁻¹)	70
DNA(1.0 mg mL ⁻¹)	45
DNA(0.5 mg mL ⁻¹)	28
Without DNA	0
NaCl(3.3 mg mL ⁻¹)	0
MgCl ₂ (3.3 mg mL ⁻¹)	0
FeCl ₃ (3.3 mg mL ⁻¹)	0
CaCl ₂ (3.3 mg mL ⁻¹)	0
H ₃ PO ₄ (3.3 mg mL ⁻¹)	0
Synthetic DNA ^c	87
Synthetic DNA ^d	63
MOPS, pH = 6.5, without DNA	Trace
Substrate = acetone	Trace
Substrate =acetophenone	0

^a Except as noted otherwise, all experiments were carried out between 0.5 mmol *p*-nitrobenzaldehyde and 0.5 mL of nitromethane in 3 mL of super-pure water with salmon testes DNA (3.3 mg mL⁻¹) at 12 °C for 8h. ^b Isolated yields were the average values of duplicate experiments (standard deviation: ±4%). ^c Synthetic DNA = synthetic duplex d(TCAG)₂(CTGA)₂ (2.8 mM), *p*-nitrobenzaldehyde (46.4 mM), nitromethane (186.0 mM). Buffer: 20 mM MOPS, pH = 6.5, 150 mM NaCl, 50 mM MgCl₂. ^d Synthetic DNA = synthetic duplex d(TCAG)₂(CTGA)₂ (0.28 mM), *p*-nitrobenzaldehyde (46.4 mM), nitromethane (186.0 mM). Buffer: 20 mM MOPS, pH = 6.5, 150 mM NaCl, 50 mM MgCl₂.

UV/Vis spectra of the synthetic DNA (Figure 1)

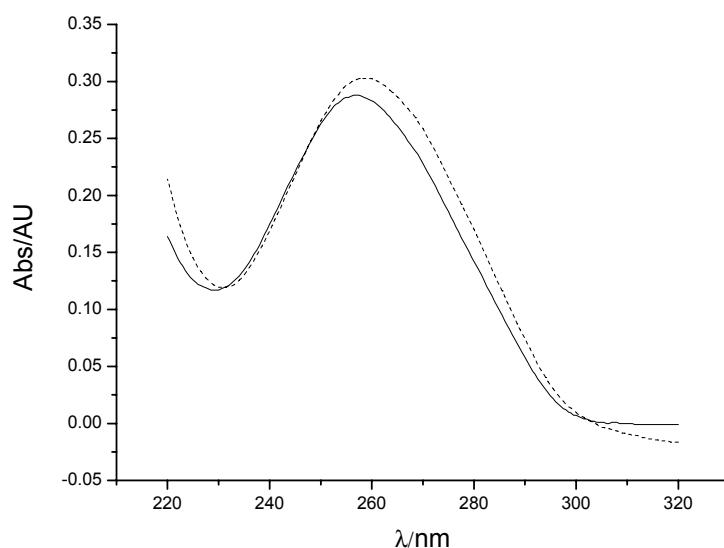


Figure S1. UV/Vis spectra. The synthetic duplex d(TCAG)₂(CTGA)₂ before reaction (Solid line) and the recovered aqueous (hashed line). The solution was buffered (20 mM MOPS, pH = 6.5, 150 mM NaCl, 50 mM MgCl₂).

Determination of the pH value of DNA aqueous solution. (Table 2)

The pH value of salmon testes DNA solution was recorded on a pHS-3C precision acidity meter calibrated by NaH₂PO₄/Na₂HPO₄ standard buffer solution (pH = 6.86, 25 °C) and Na₂B₄O₇·10H₂O (pH = 9.18, 25 °C) standard buffer solution.

Table S2 Determination of the PH value of DNA aqueous solution

Catalyst system			pH ^a		
Catalyst	Reactiom medium	No substrate	Substrate added		
			0h	2h	8h
DNA	3 mLsuper-pure water	6.82	6.73	6.72	6.79
DNA	30mM MES,pH=5.5	5.63	5.63	5.62	5.69
Synthetic duplex d(TCAG) ₂ (CTGA) ₂ ^b		6.42	6.28	6.26	6.21

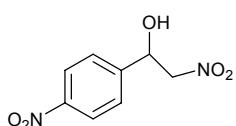
^a All experiments were carried out between 0.5 mmol *p*-nitrobenzaldehyde and 0.5 mL nitromethane in 3 mL of reaction medium with salmon testes DNA (3.3 mg mL⁻¹) at 25 °C, pH values were the average values of duplicate experiments (standard deviation: ±2%). ^b Reaction medium: 20 mM MOPS, pH = 6.5, 150 mM NaCl, 50 mM MgCl₂.

Procedure of catalyst recycles.

To an aqueous MES buffer solution (20 mM, pH = 5.5) was added DNA (Herring sperm DNA, purchased from BIO BASIC INC, DNA content >90% or Salmon testes DNA 10 mg, purchased from Sigma, 17.5 A₂₆₀ units/mg). After 10 minutes, 0.5 mmol of *p*-nitrobenzaldehyde in 0.5 ml of CH₃NO₂ was added. After the mixture was heated at 37 °C for 12 h, the mixture was extracted three times with ethyl acetate. The combined organic extracts were dried using anhydrous Na₂SO₄ and evaporated under reduced pressure; the residue was then purified by column chromatography over silica gel to afford the corresponding Henry product with high purity (run 1).

The corresponding recovered aqueous solution was used as the reaction medium for the next run. To this recovered aqueous solution, 0.5 mmol of *p*-nitrobenzaldehyde in 0.5 ml of CH₃NO₂ was added. After the mixture was heated at 37 °C for 12 h, the mixture was extracted three times with ethyl acetate. Repeating the procedure described above, the corresponding products were obtained.

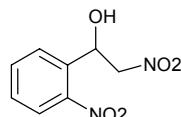
Characterization data for the products.



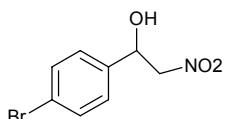
2-nitro-1-(4-nitrophenyl)ethanol (Table 2; Entry 1)
 ^1H NMR (CDCl_3 , 300 MHz, ppm): $\delta = 8.25$ (d, $J = 8.4$ Hz, 2 H), 7.61 (d, $J = 8.4$ Hz, 2 H), 5.62-5.57 (m, 1 H), 4.59-4.53 (m, 2 H), 3.18 (br, 1 H). ^{13}C NMR(CDCl_3 , 75 MHz, ppm): $\delta = 70.1, 80.7, 124.3, 127.1, 145.1, 148.3$.

IR (KBr film, cm^{-1}): $\nu = 3401, 2919, 1555, 1416, 1382, 1349, 1086, 856, 754, 727, 697$.

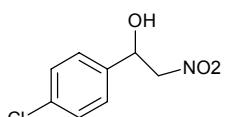
HRMS: calcd for $\text{C}_8\text{H}_8\text{N}_2\text{O}_5$: 212.0433, found: 212.0443.



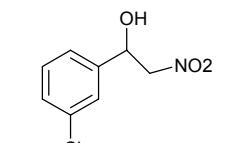
2-nitro-1-(2-nitrophenyl)ethanol (Table 2; Entry 2)
 ^1H NMR (CDCl_3 , 300 MHz, ppm): $\delta = 8.07$ (d, $J = 8.1$ Hz, 1 H), 7.95 (d, $J = 7.8$ Hz, 1 H), 7.77-7.65 (m, 1 H), 7.58-7.53 (m, 1 H), 6.06-6.03 (m, 1 H), 4.87 (dd, $J = 13.8, 2.1$ Hz, 1 H), 4.56 (dd, $J = 13.8, 7.8$ Hz, 1 H), 3.70 (br, 1 H). ^{13}C NMR(CDCl_3 , 75 MHz, ppm): $\delta = 66.8, 80.1, 124.9, 128.7, 129.7, 134.3, 134.5, 147.0$. IR (KBr film, cm^{-1}): $\nu = 3537, 1587, 1533, 1422, 1380, 1365, 1091, 1071, 866$. HRMS: calcd for $\text{C}_8\text{H}_8\text{N}_2\text{O}_5$: 212.0433, found: 212.0452.



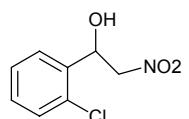
1-(4-bromophenyl)-2-nitroethanol (Table 2; Entry 3)
 ^1H NMR (CDCl_3 , 300 MHz, ppm): $\delta = 7.54$ (d, $J = 8.1$ Hz, 2 H), 7.29 (d, $J = 8.1$ Hz, 2 H), 5.45-5.42 (m, 1 H), 4.61-4.46(m, 2 H), 2.87 (br, 1 H). ^{13}C NMR(CDCl_3 , 75 MHz, ppm): $\delta = 70.4, 81.0, 123.0, 127.7, 132.2, 137.2$. IR (KBr film, cm^{-1}): $\nu = 3540, 2922, 1592, 1554, 1489, 1412, 1344, 1292, 1212, 1075, 1011, 907, 825, 733, 646$. HRMS: calcd for $\text{C}_8\text{H}_8\text{BrNO}_3$: 244.9688, found: 244.9676.



1-(4-chlorophenyl)-2-nitroethanol (Table 2; Entry 4)
 ^1H NMR (CDCl_3 , 300 MHz, ppm): $\delta = 7.39-7.32$ (m, 4 H), 5.45-5.42 (m, 1 H), 4.56-4.49 (m, 2 H), 3.03 (br, 1 H). ^{13}C NMR(CDCl_3 , 75 MHz, ppm): $\delta = 70.4, 81.1, 127.4, 129.3, 134.9, 136.7$. IR (KBr film, cm^{-1}): $\nu = 3446, 2924, 2255, 1557, 1493, 1379, 1090, 1015, 909, 829, 735, 651, 530$. HRMS: calcd for $\text{C}_8\text{H}_8\text{ClNO}_3$: 201.0193, found: 201.0194

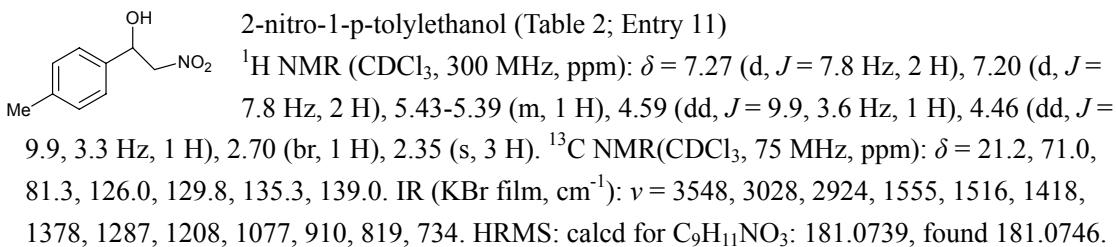
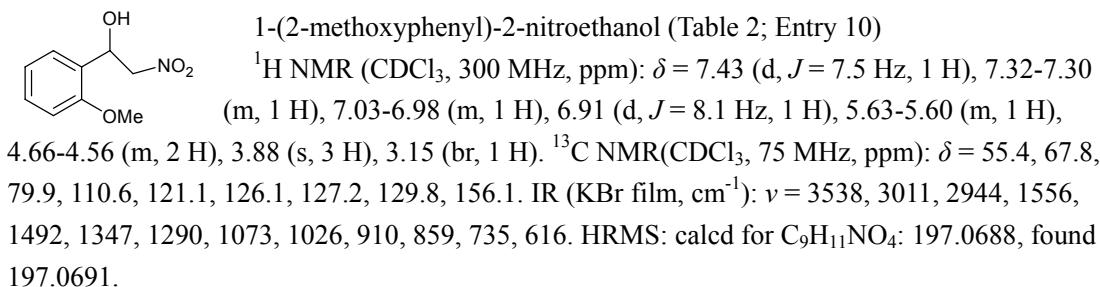
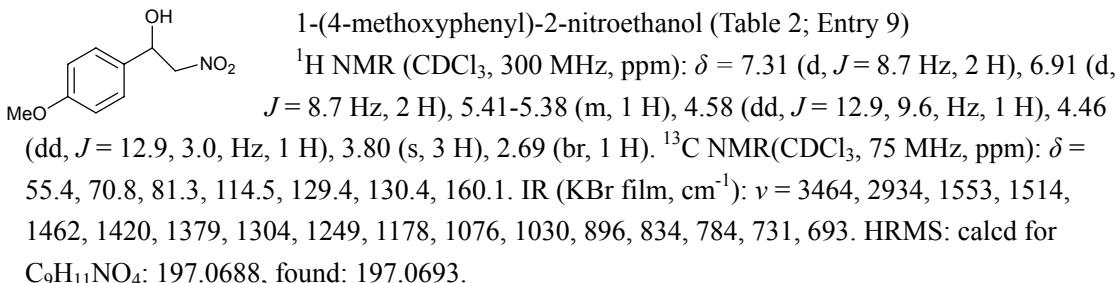
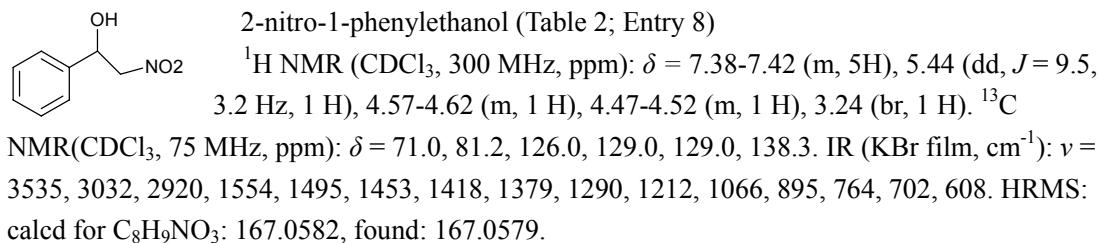
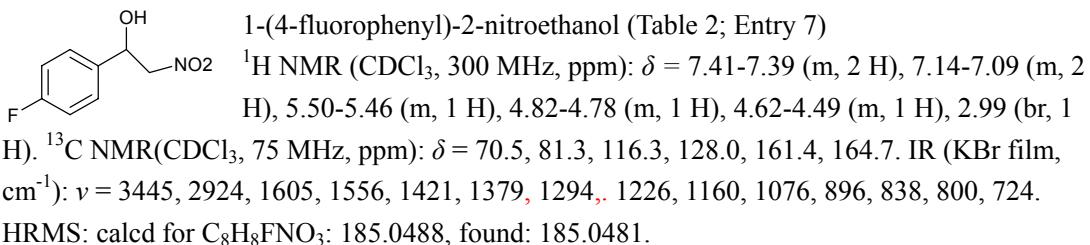


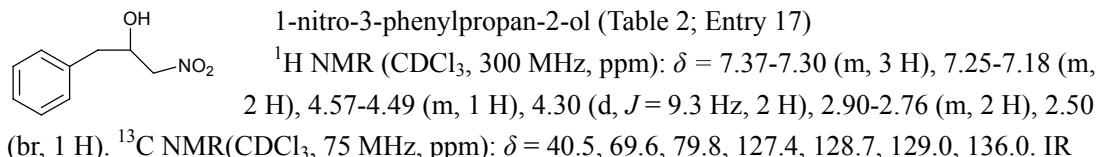
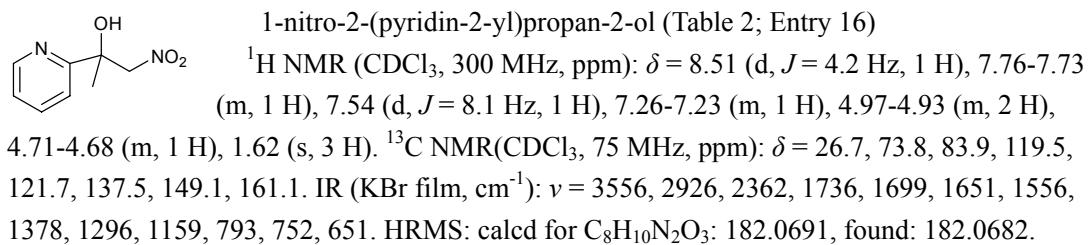
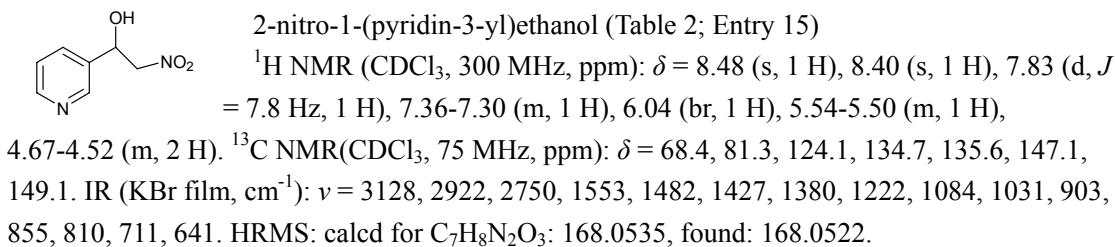
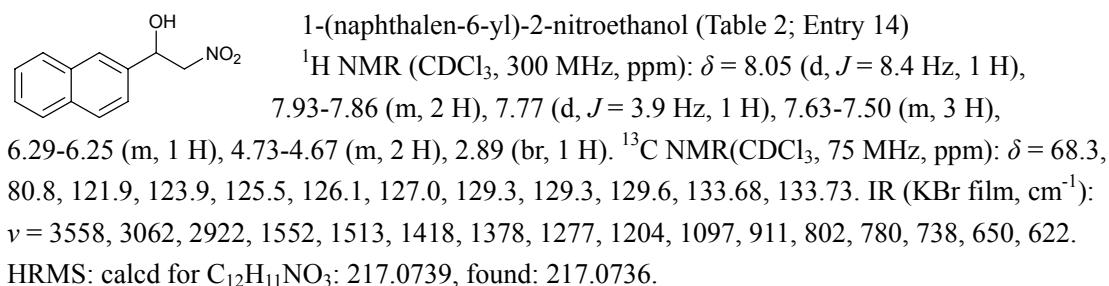
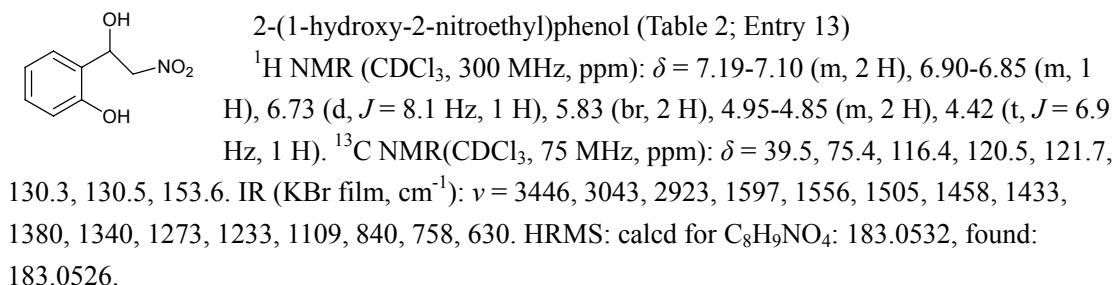
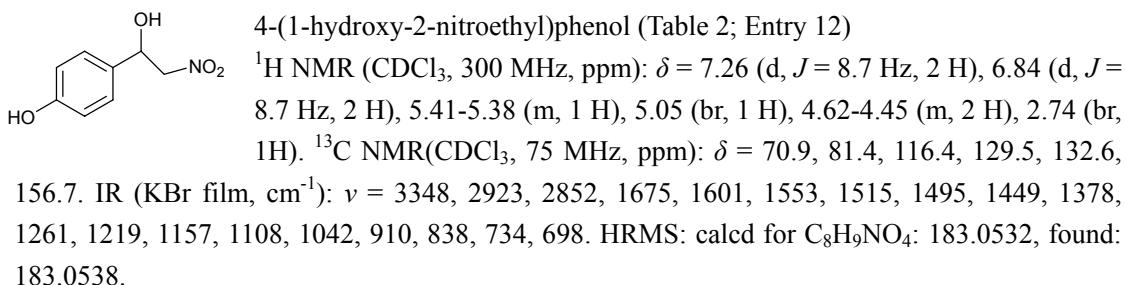
1-(3-chlorophenyl)-2-nitroethanol (Table 2; Entry 5)
 ^1H NMR (CDCl_3 , 300 MHz, ppm): $\delta = 7.42$ (s, 1 H), 7.34-7.33 (m, 2 H), 7.29-7.25 (m, 1 H), 5.46-5.43 (m, 1 H), 4.57-4.52 (m, 2 H), 2.30 (s, 1 H). ^{13}C NMR(CDCl_3 , 75 MHz, ppm): $\delta = 70.4, 81.1, 124.2, 126.3, 129.2, 130.4, 135.1, 140.2$. IR (KBr film, cm^{-1}): $\nu = 3563, 1597, 1557, 1477, 1422, 1378, 910, 739$. HRMS: calcd for $\text{C}_8\text{H}_8\text{ClNO}_3$: 201.0193, found: 201.0195.



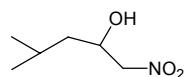
1-(2-chlorophenyl)-2-nitroethanol (Table 2; Entry 6)
 ^1H NMR (CDCl_3 , 300 MHz, ppm): $\delta = 7.67-7.64$ (m, 1 H), 7.39-7.29 (m, 3 H)

H), 5.85-5.82 (m, 1 H), 4.67 (dd, $J = 13.5, 2.1$, Hz, 1 H), 4.46 (d, $J = 13.5, 9.6$, Hz, 1 H), 3.08 (br, 1 H). ^{13}C NMR(CDCl_3 , 75 MHz, ppm): $\delta = 68.0, 79.4, 127.6, 127.7, 129.8, 130.0, 131.6, 135.7$. IR (KBr film, cm^{-1}): $\nu = 3589, 2924, 2256, 1557, 1473, 1442, 1416, 1379, 1344, 1285, 1211, 1131, 1086, 1037, 905, 734, 650, 610$. HRMS: calcd for $\text{C}_8\text{H}_8\text{ClNO}_3$: 201.0193, found: 201.0188.





(KBr film, cm^{-1}): $\nu = 3431, 2924, 1554, 1453, 1422, 1383, 1089, 756, 702$. HRMS: calcd for $\text{C}_9\text{H}_{11}\text{NO}_3$: 181.0739, found: 181.0741.

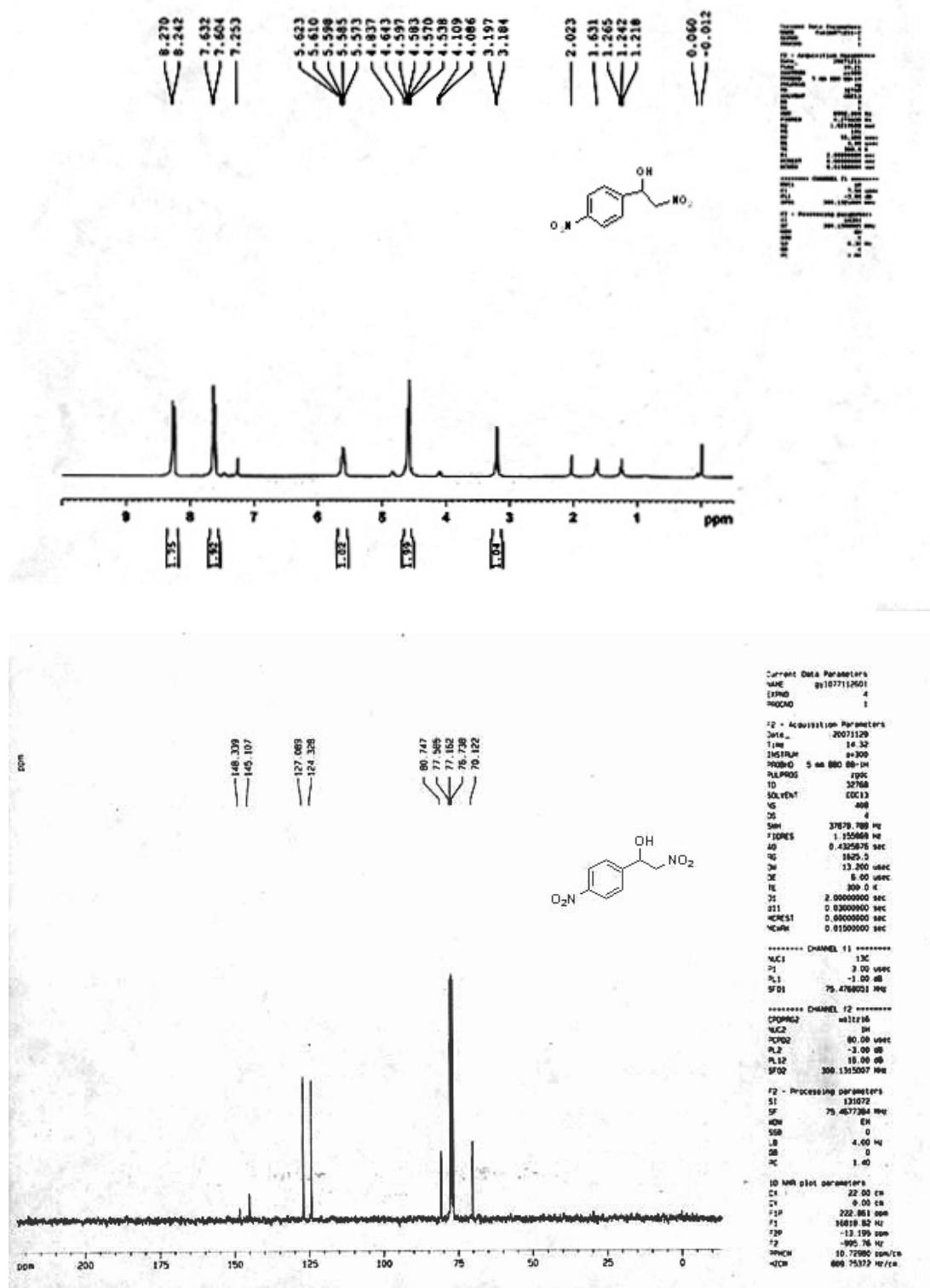


4-methyl-1-nitropentan-2-ol (Table 2; Entry 18)

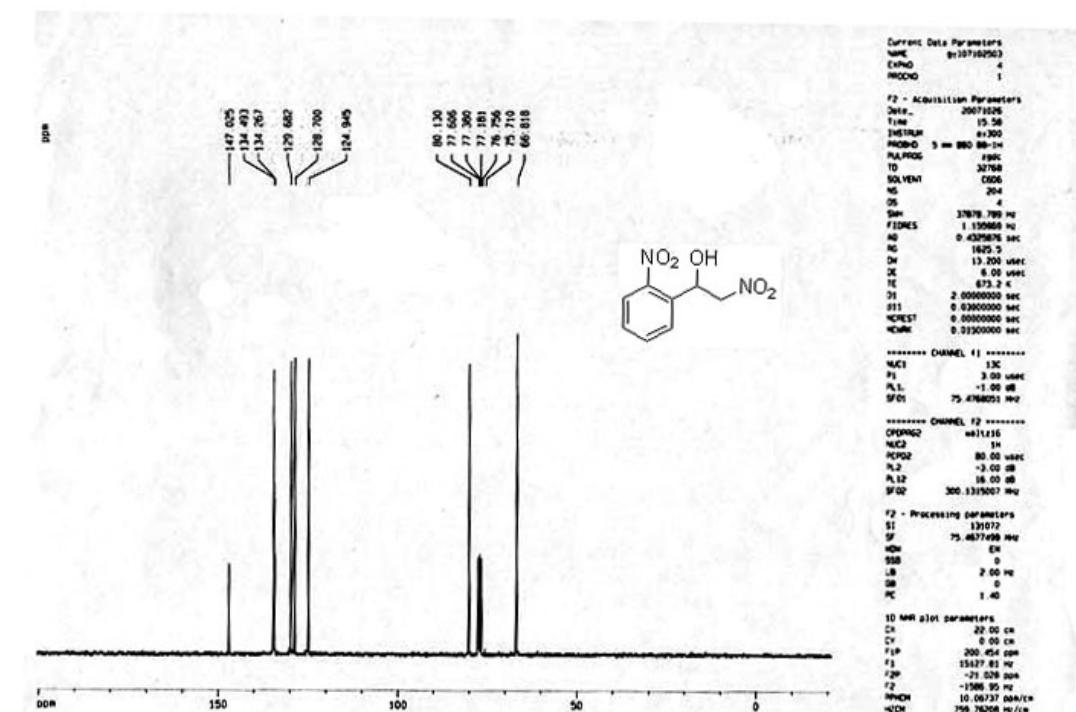
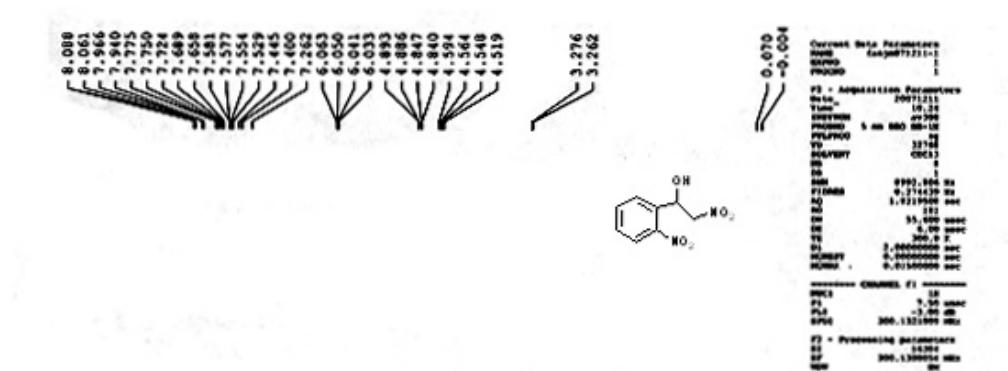
^1H NMR (CDCl_3 , 300 MHz, ppm): $\delta = 4.42\text{-}4.33$ (m, 2 H), 2.46 (br, 1 H), 1.87-1.78 (m, 1 H), 1.54-1.45 (m, 2 H), 1.26-1.18 (m, 1 H), 0.96 (d, $J = 4.5$ Hz, 3 H), 0.94 (d, $J = 4.5$ Hz, 3 H). ^{13}C NMR (CDCl_3 , 75 MHz, ppm): $\delta = 21.8, 23.1, 24.3, 42.5, 67.1, 81.1$. IR (KBr film, cm^{-1}): $\nu = 3416, 2960, 1557, 1467, 1384, 1296, 1206, 1144, 1089, 1045, 891, 848, 735, 646$. HRMS: calcd for $\text{C}_6\text{H}_{13}\text{NO}_3$: 147.0895, found: 147.0889.

¹H NMR and ¹³C NMR Spectrum of the products.

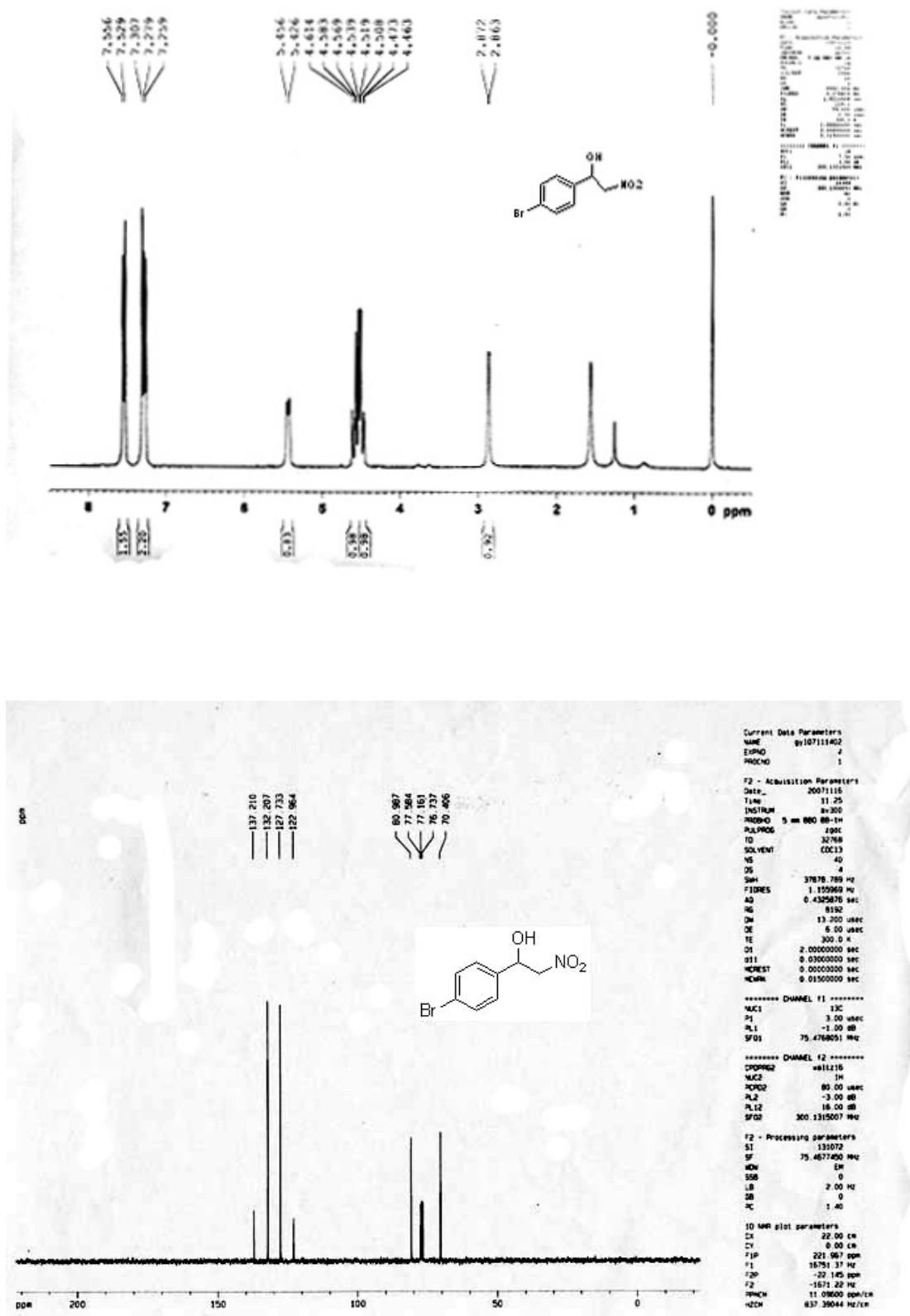
2-nitro-1-(4-nitrophenyl)ethanol (Table 2; Entry 1)



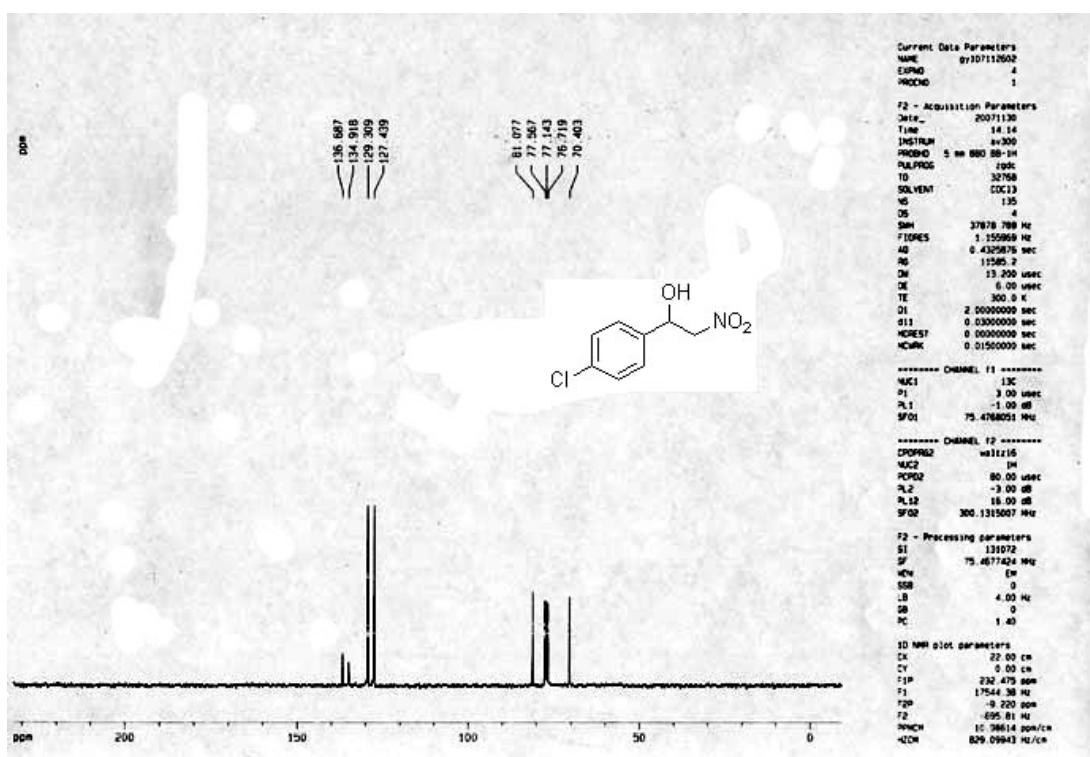
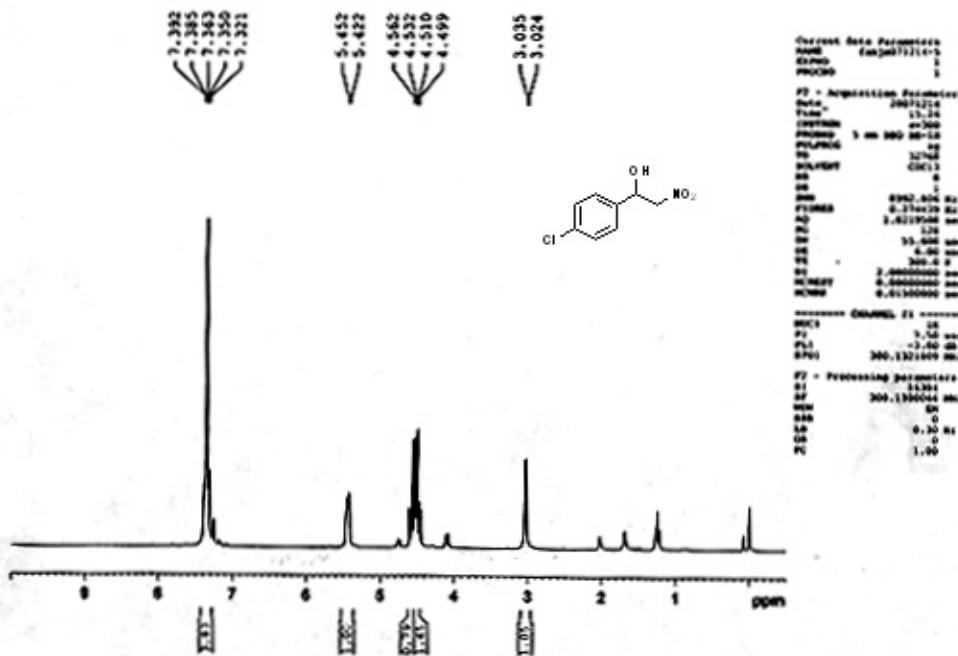
2-nitro-1-(2-nitrophenyl)ethanol (Table 2; Entry 2).



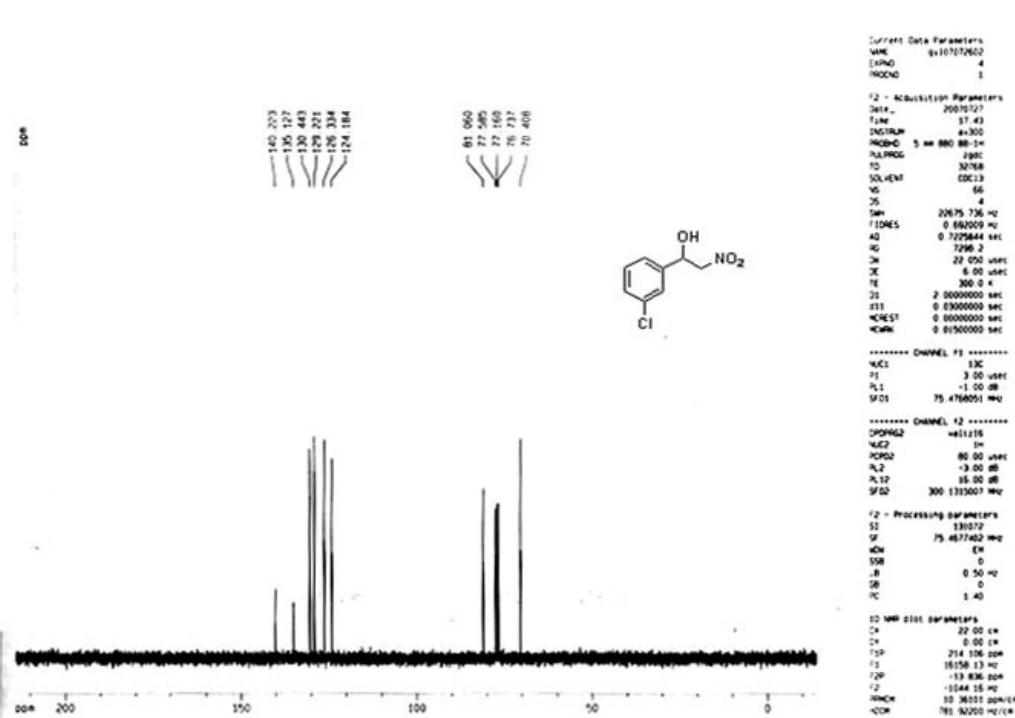
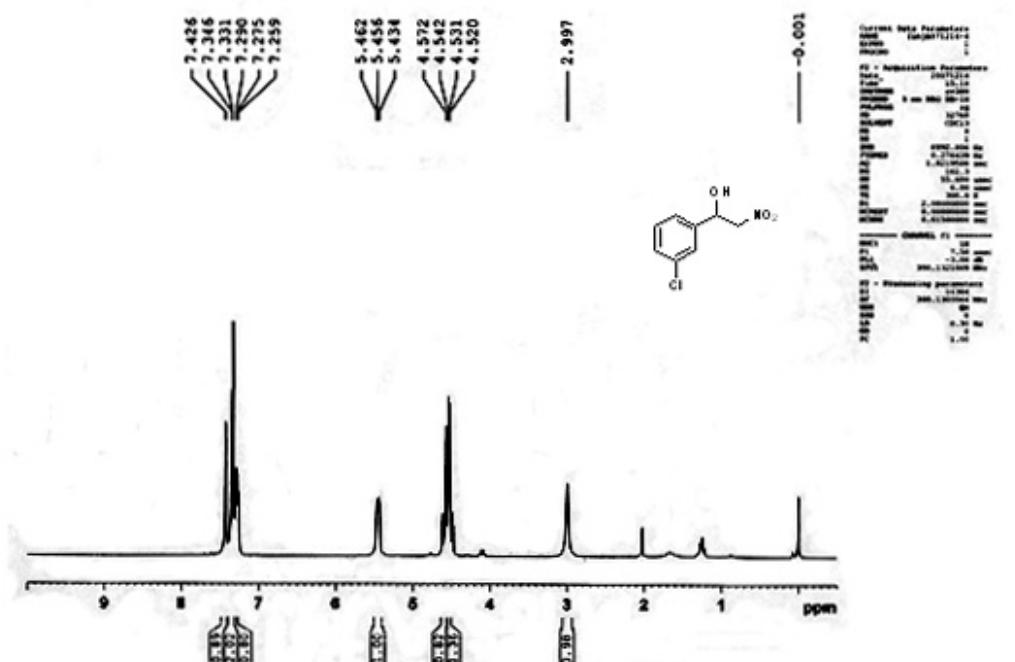
1-(4-bromophenyl)-2-nitroethanol (Table 2; Entry 3).



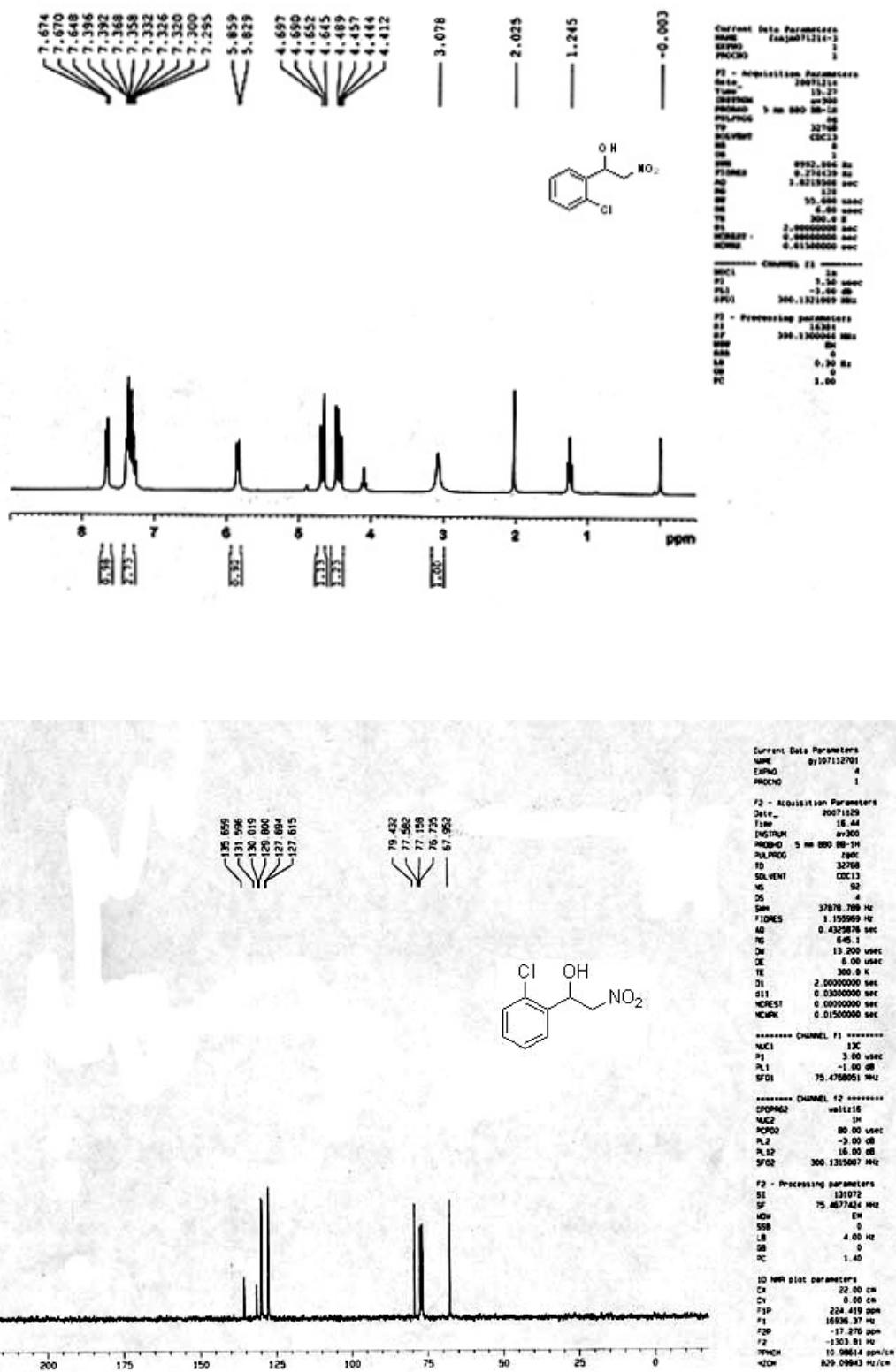
1-(4-chlorophenyl)-2-nitroethanol (Table 2; Entry 4).



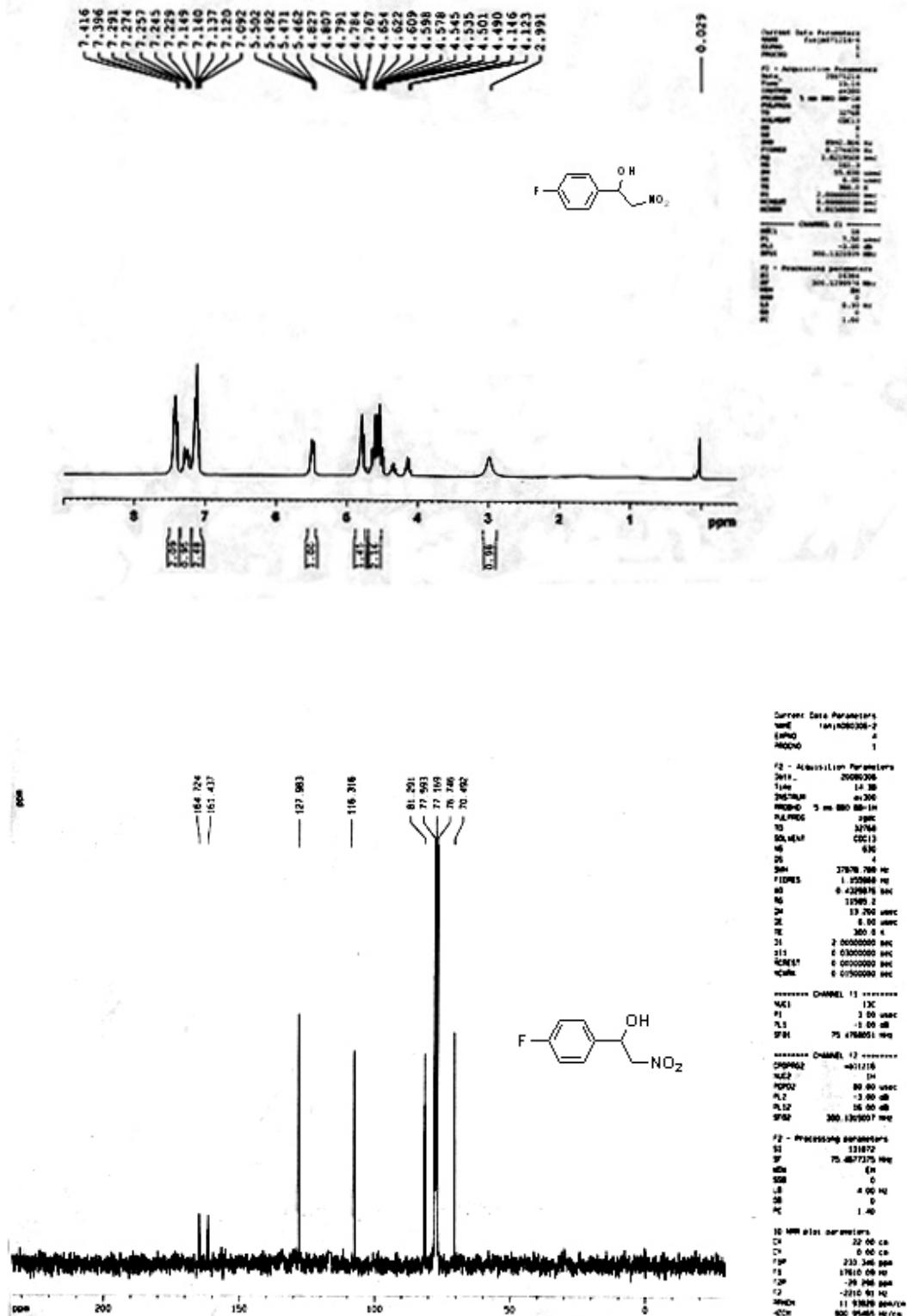
1-(3-chlorophenyl)-2-nitroethanol (Table 2; Entry 5).



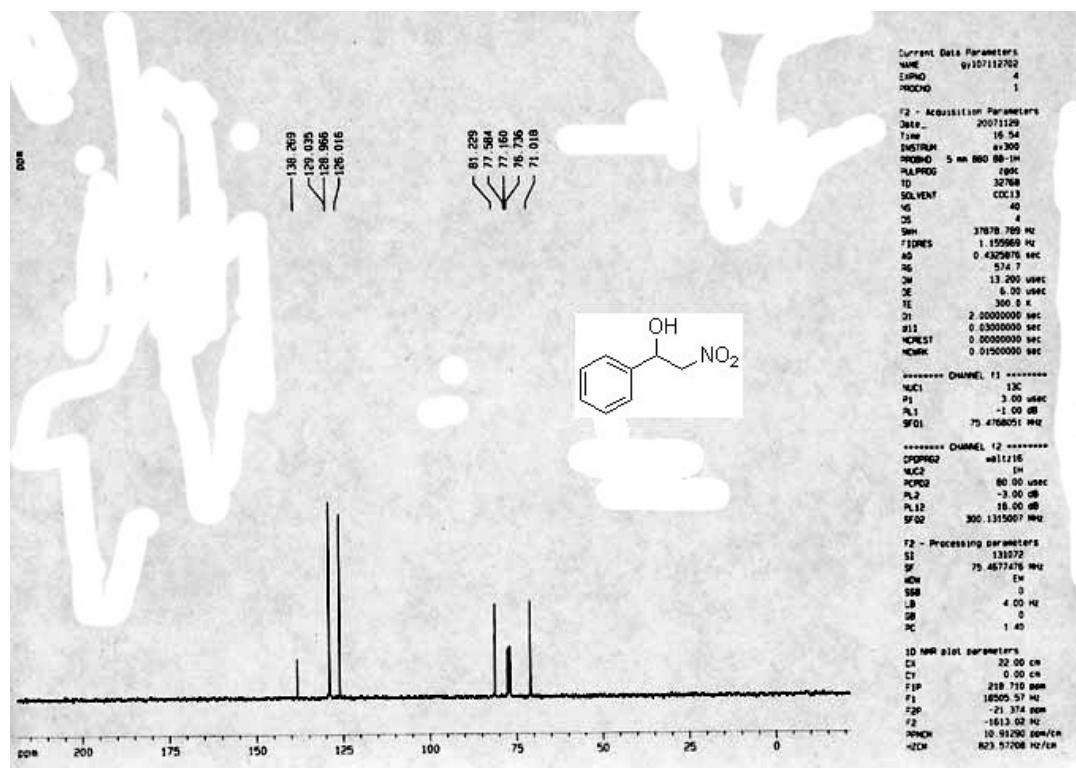
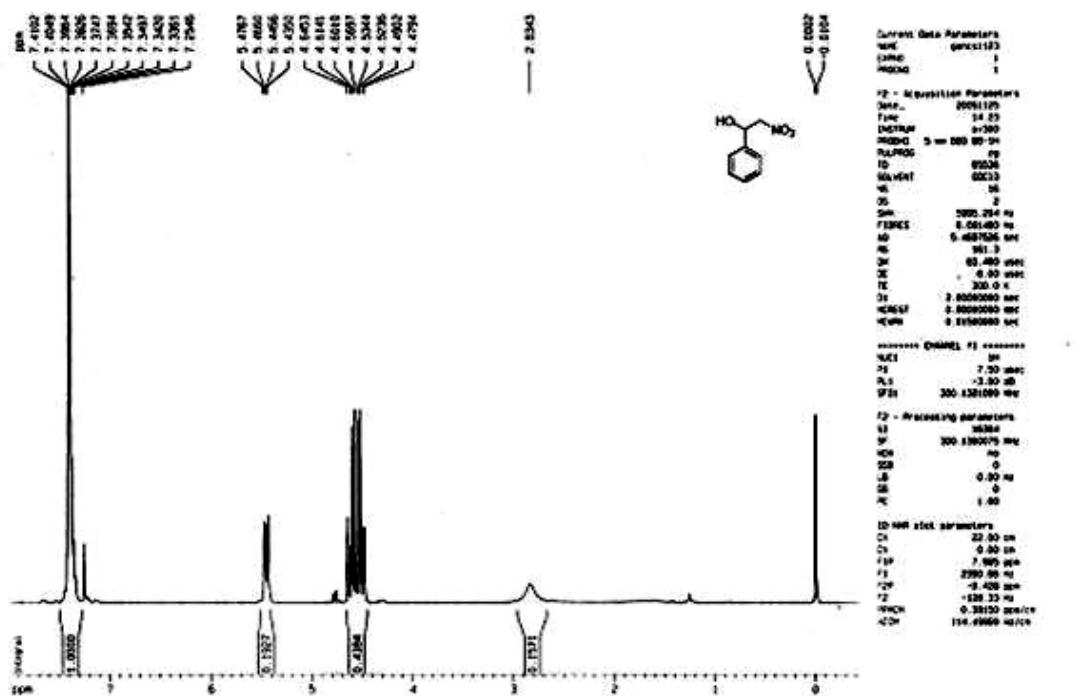
1-(2-chlorophenyl)-2-nitroethanol (Table 2; Entry 6).



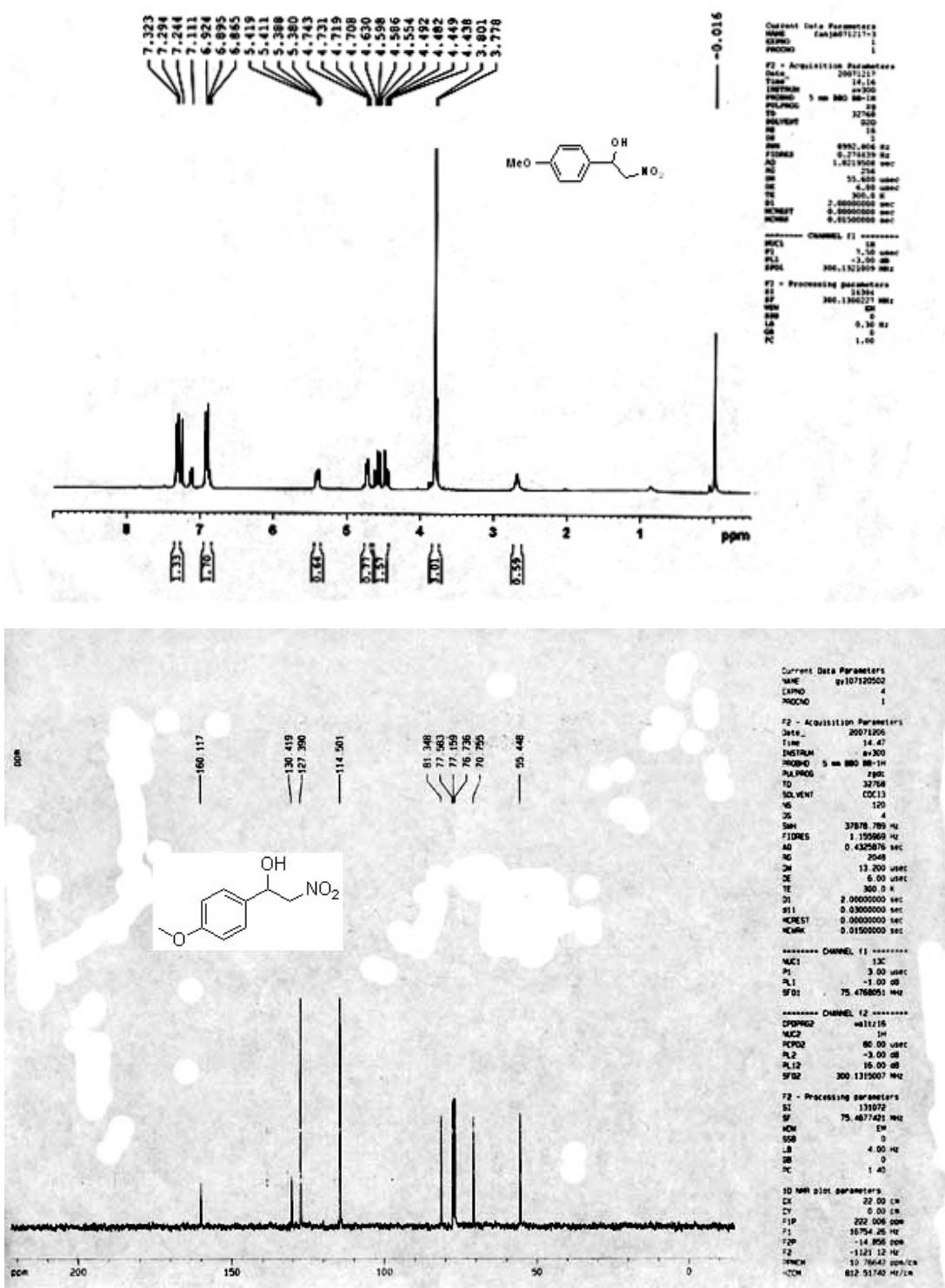
1-(4-fluorophenyl)-2-nitroethanol (Table 2; Entry 7).



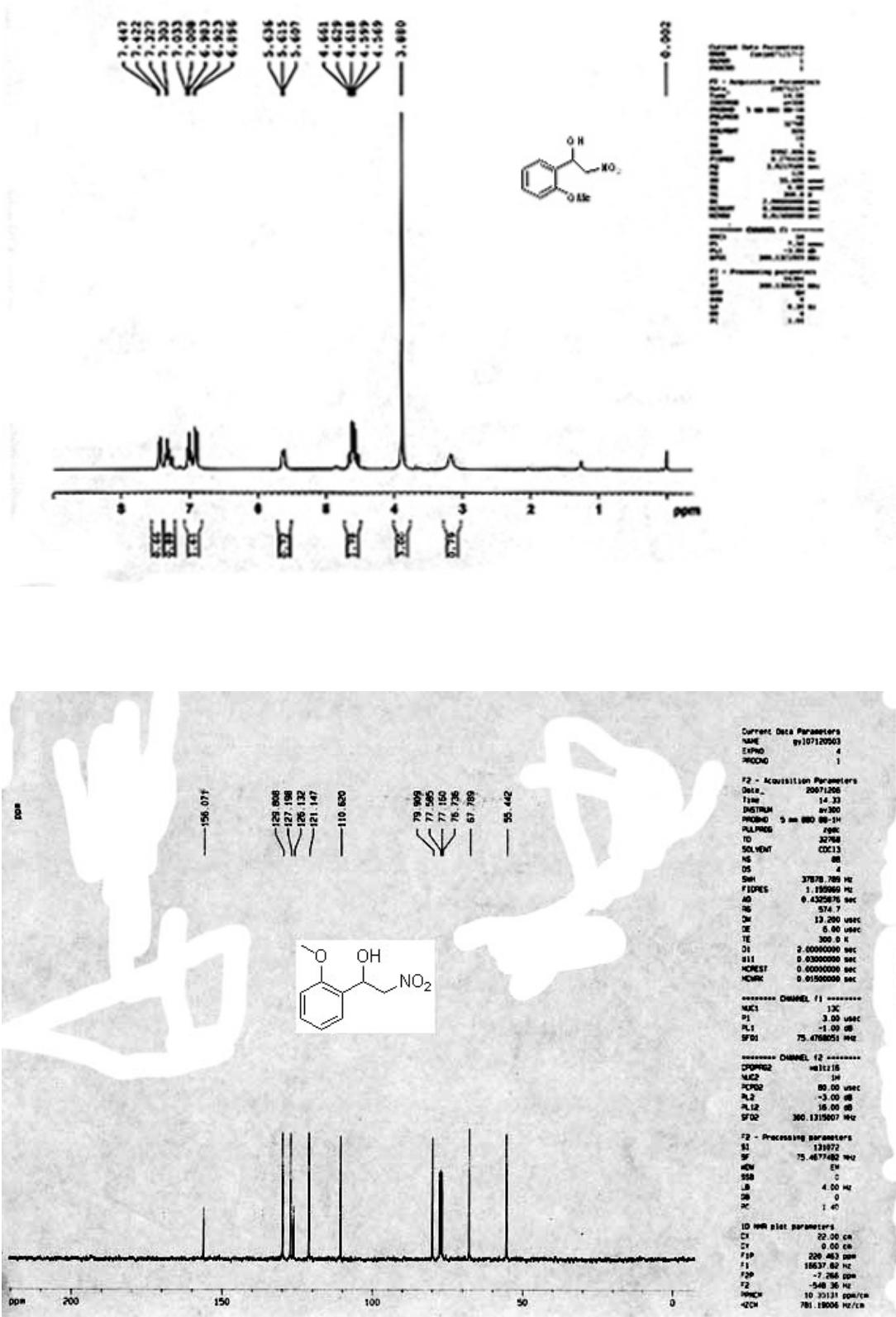
2-nitro-1-phenylethanol (Table 2; Entry 8).



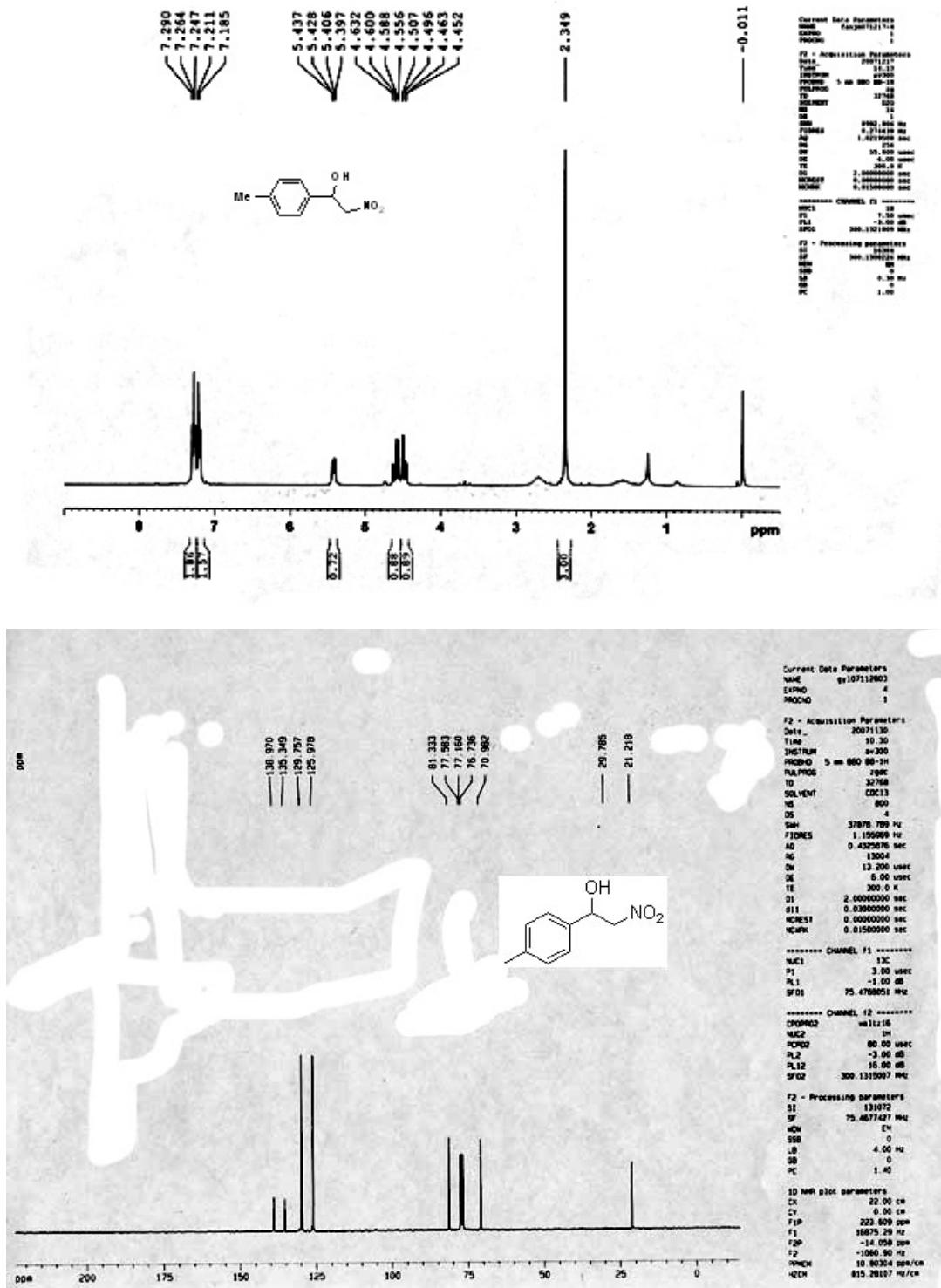
1-(4-methoxyphenyl)-2-nitroethanol (Table 2; Entry 9).



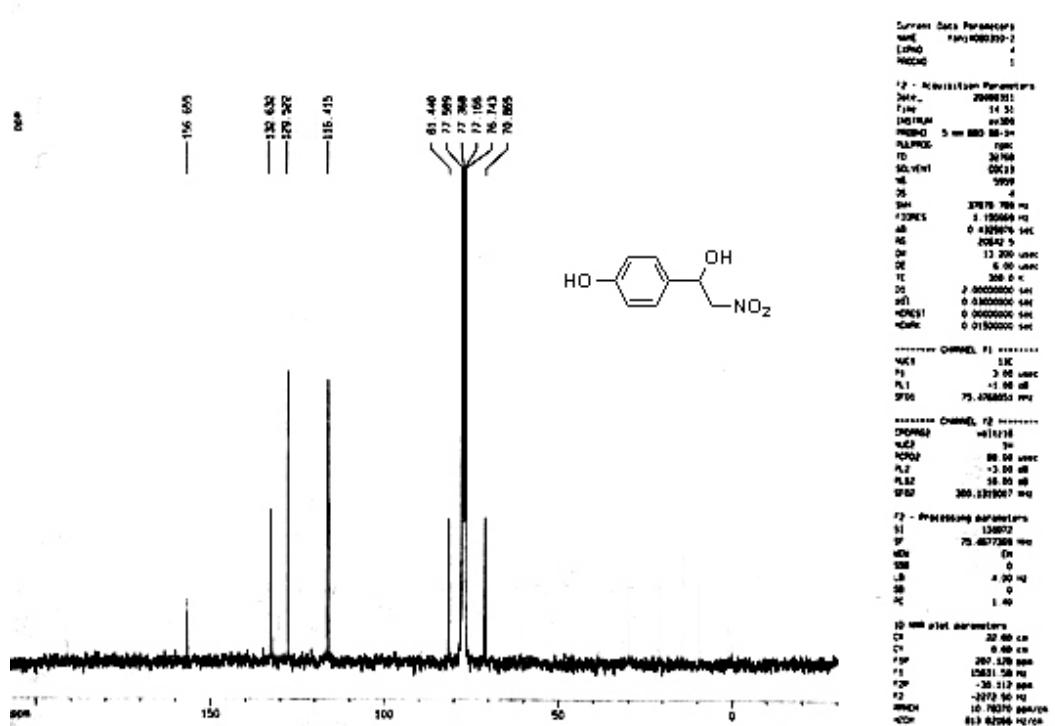
1-(2-methoxyphenyl)-2-nitroethanol (Table 2; Entry 10).



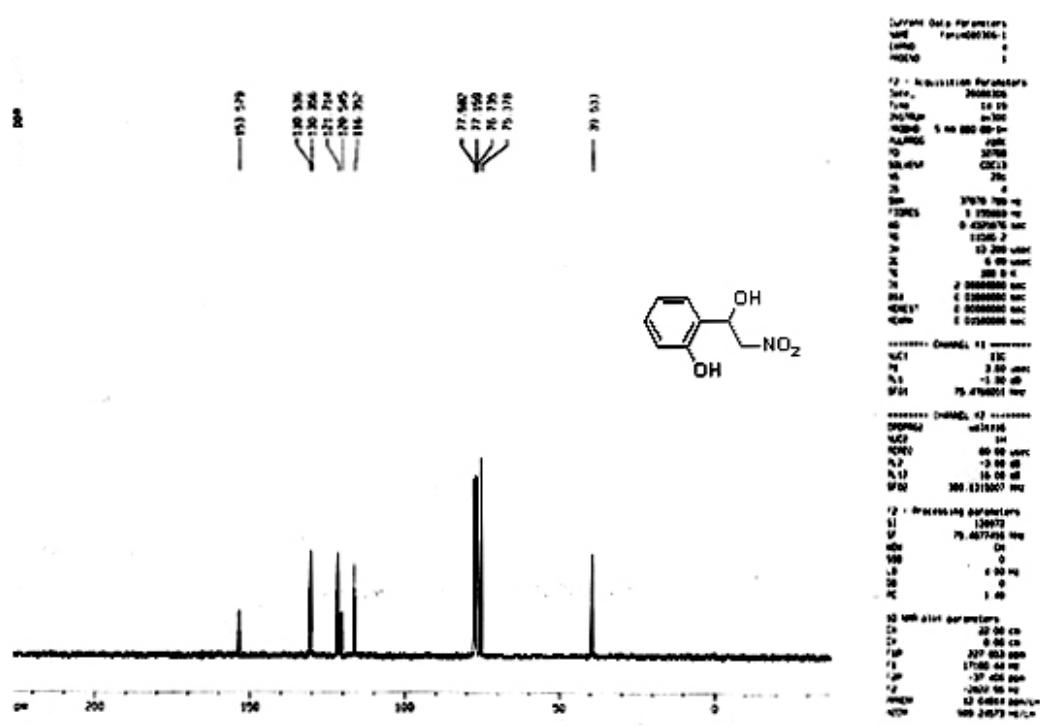
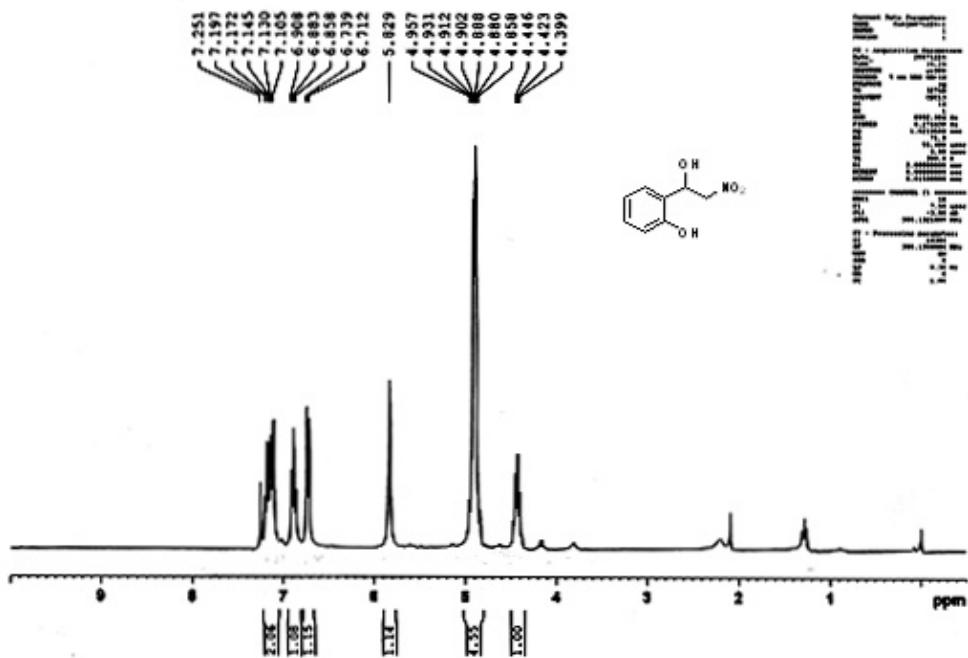
2-nitro-1-p-tolylethanol (Table 2; Entry 11).



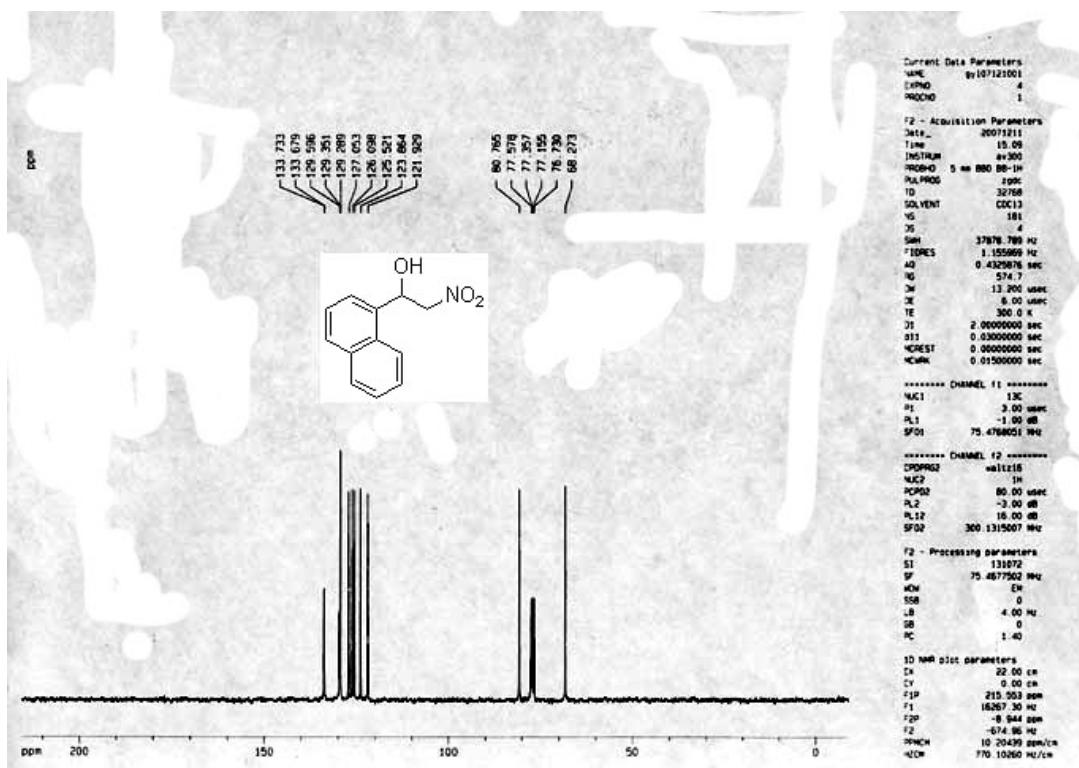
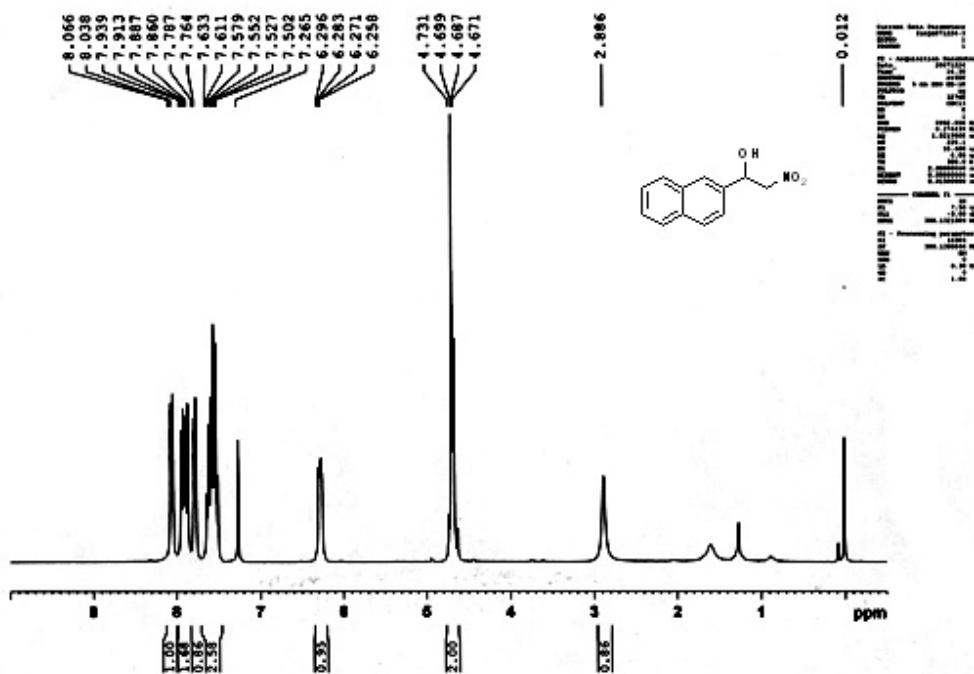
4-(1-hydroxy-2-nitroethyl) phenol (Table 2; Entry 12).



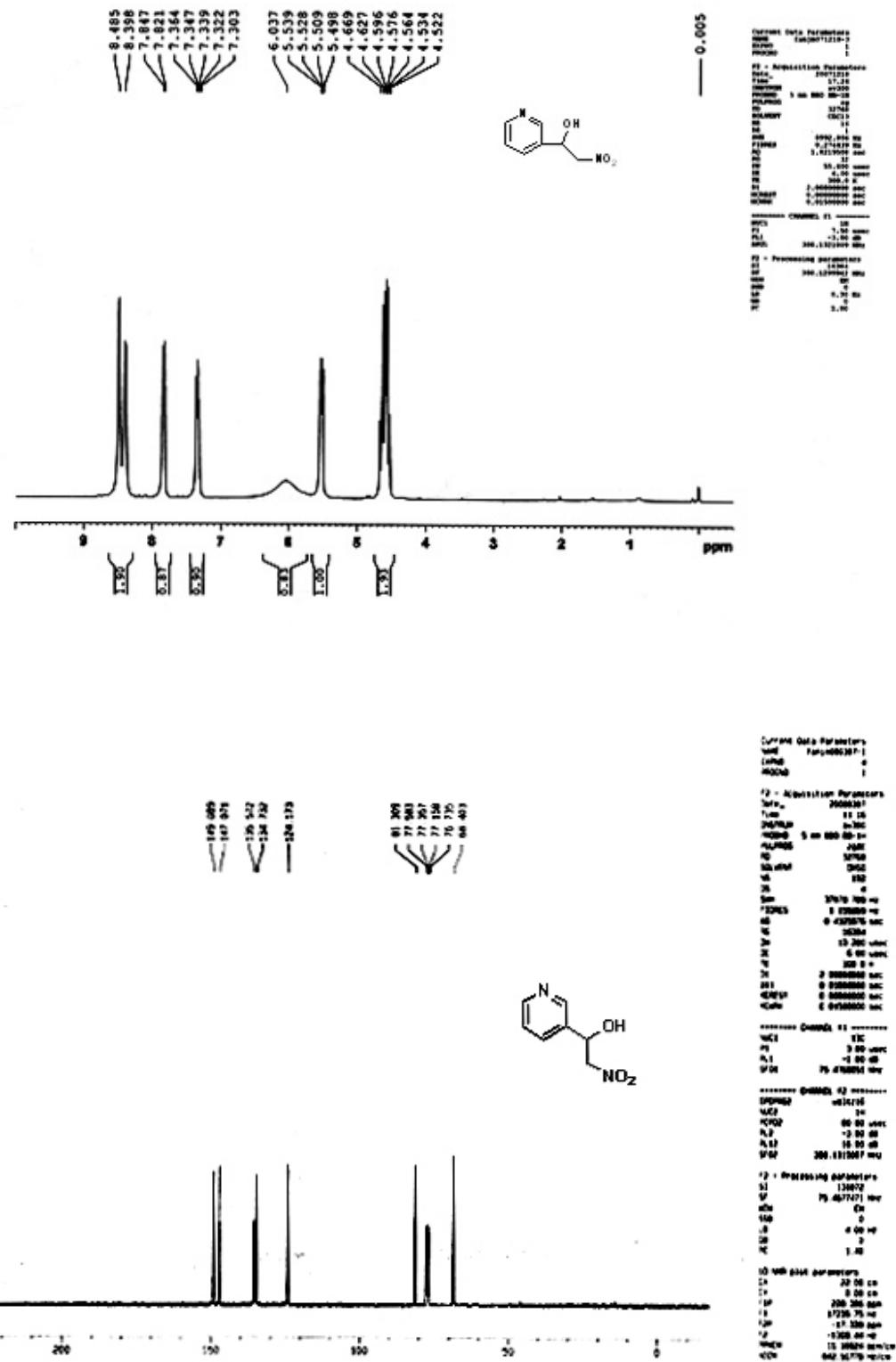
2-(1-hydroxy-2-nitroethyl)phenol (Table 2; Entry 13).



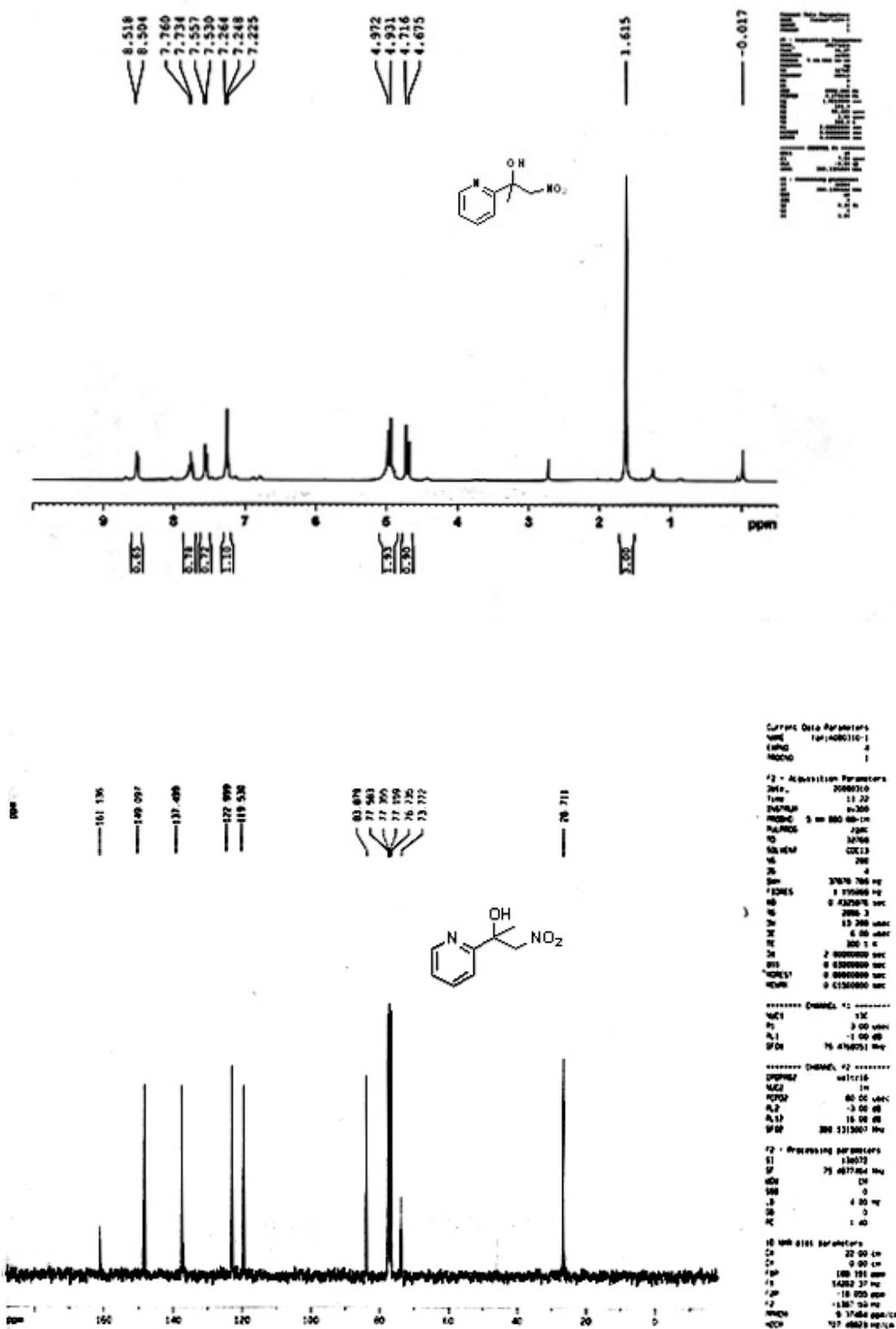
1-(naphthalen-6-yl)-2-nitroethanol (Table 2; Entry 14).



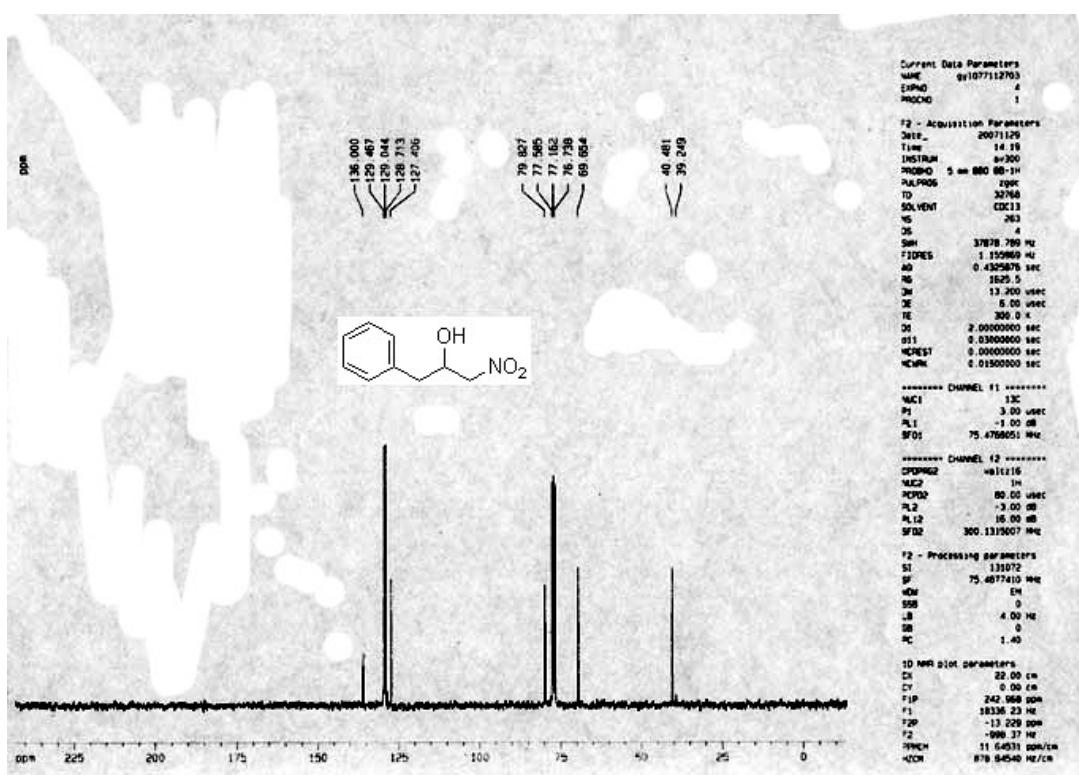
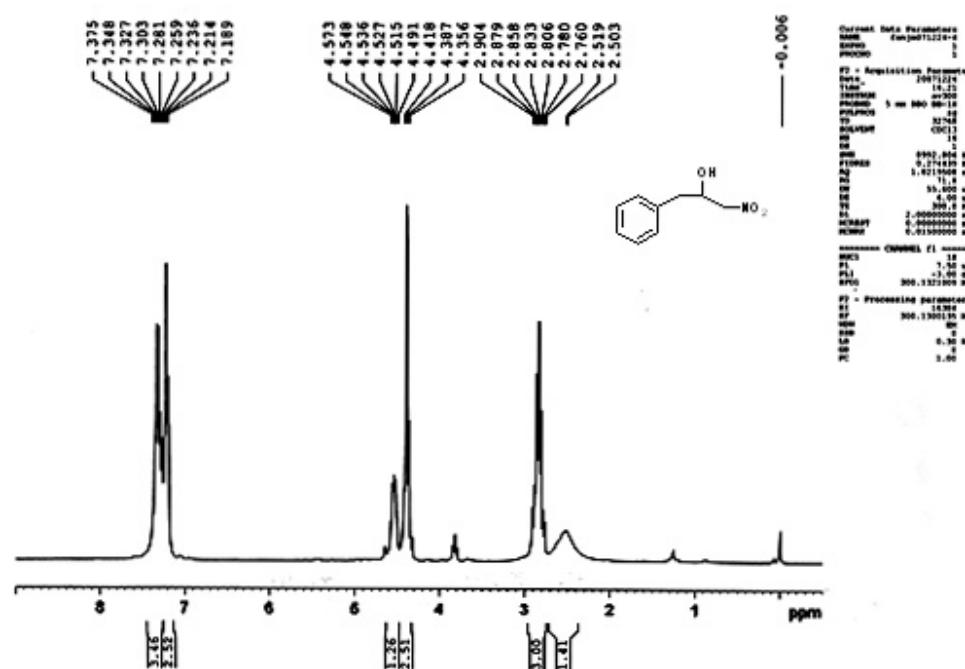
2-nitro-1-(pyridin-3-yl)ethanol (Table 2; Entry 15).



1-nitro-2-(pyridin-2-yl)propan-2-ol (Table 2; Entry 16).



1-nitro-3-phenylpropan-2-ol (Table 2; Entry 17).



4-methyl-1-nitropentan-2-ol (Table 2; Entry 18).

