Microwave Enhanced Reaction of Thio Acids with Azides In Aqueous Media

Pallavi Sharma, Adam D. Moorhouse, and John E. Moses*

School of Chemistry, University of Nottingham, UK, NG2 7RD
Fax: ++ 44 (0)115 951 3564; E-mail: john.moses@nottingham.ac.uk

General

$^1$H and $^{13}$C-NMR spectra were recorded on a Bruker AV (III) 400, Bruker AV 400, Bruker DPX 400 (400 MHz ($^1$H NMR), and 100 MHz ($^{13}$C NMR)) spectrometers. Chemical shifts are expressed in parts per million (ppm) and the spectra calibrated to residual solvent signals of CDCl$_3$ (7.26 ppm ($^1$H) and 77.0 ppm ($^{13}$C)), MeOD-$d_4$ (3.31 ppm ($^1$H) and 49.0 ppm ($^{13}$C), DMSO-$d_6$ 2.50 ppm ($^1$H) and 39.4 ppm ($^{13}$C). Coupling constants are given in hertz (Hz) and the following notations indicate the multiplicity of the signals: s (singlet), brs (broad singlet), brd (broad doublet) t (triplet), apt t (apparent triplet) and m (multiplet).

High Resolution Mass Spectra were recorded on a VG micron Autospec or Bruker microTOF. Fourier Transform Infrared Spectroscopy (FT-IR) spectra were obtained using a Perkin Elmer 1600 series or Bruker Tensor 27 spectrometer.

Melting points were recorded using a STUART SMP3 apparatus and are uncorrected. Thin layer chromatography were carried out on Merck pre-coated silica gel plates (60F-254) and visualised using ultra violet light, KMnO$_4$ solution or p-anisaldehyde solution.
General Procedure: To a stirred solution of aniline (0.840 mmol) in MeCN (1 mL) was added t-BuONO (0.840 mmol) at 0 °C in a 2-5 mL microwave reaction vial. To this solution was added TMSN₃ (0.840 mmol) dropwise at 0 °C. The solution was stirred for required amount of time, before completion of transformation to azide (monitored by TLC). At this point, the reaction was diluted with H₂O (1 mL) and 2,6-lutidine (1.09 mmol), thio acid (1.09 mmol) was added to the reaction mixture. The vial was capped then placed in a microwave and heated to 80 °C for required amount of time. After cooling, the solvent was evaporated under reduced pressure and product purified by column chromatography.

\[
\text{N-(4-Nitrophenyl)benzamide (7):} \quad \text{The product was purified by re-suspending the solid residue, obtained after removal of solvents, in water, filtration and washing with diethyl ether. White powder, Yield: >99%, mp: 199-201 °C (lit² 197-198 °C), } \\
\nu_{\text{max}}/\text{cm}^{-1}(\text{solid}): 1657, 1504; \quad ^1\text{H NMR (DMSO-d₆, 400 MHz): } \delta 10.81 (s, 1H), 8.27 (d, J = 9.3 Hz, 2H), 8.07 (d, J = 9.3 Hz, 2H), 7.98 (d, J = 7.4 Hz, 2H), 7.64 (apt t, J = 7.4 Hz, 1H), 7.57 (apt t, J = 7.4 Hz, 2H); \quad ^{13}\text{C NMR (DMSO-d₆, 100 MHz): } \delta 166.7, 145.9, 142.9, 134.6, 132.6, 128.9, 128.3, 124.7, 119.7; \quad \text{HRMS: calculated for } C_{13}H_{11}N_{2}O_{3} [M+H]^+ 243.0770 obtained 243.0761.
\]

\[
\text{N-(4-Nitrophenyl)acetamide (10):} \quad \text{The product was purified by re-suspending the solid residue, obtained after removal of solvents, in water, filtration and washing with }
\]
diethyl ether. White powder, **Yield**: 99%, **mp** 212-214 °C (lit\(^2\) 208-209 °C), \(v_{\text{max/cm}^{-1}}\) (solid): 1680, 1503; \(^1\)H NMR (DMSO-\(d_6\), 400 MHz): \(\delta\) 10.55 (s, 1H), 8.20 (d, \(J = 9.3\) Hz, 2H), 7.81 (d, \(J = 9.3\) Hz, 2H), 2.12 (s, 3H); \(^{13}\)C NMR (DMSO-\(d_6\), 100 MHz): \(\delta\) 169.2, 145.3, 141.9, 124.9, 118.4, 24.1; **HRMS**: calculated for C\(_8\)H\(_8\)N\(_2\)O\(_3\) \([M+H]^+\) 181.0613 obtained 181.0608.

![Structure of N-(4-Cyanophenyl)benzamide (11)](image)

**N-(4-Cyanophenyl)benzamide (11):**\(^3\) Yellow powder, **Yield**: 77%, **mp**: 165-167 °C (lit\(^3\) 167 °C), \(v_{\text{max/cm}^{-1}}\) (solid): 2227, 1660; \(^1\)H NMR (Acetone-\(d_6\), 400 MHz): \(\delta\) 9.88 (s, 1H), 8.07 (d, \(J = 8.8\) Hz, 2H), 8.00 (d, \(J = 7.4\) Hz, 2H), 7.76 (d, \(J = 8.8\) Hz, 2H), 7.61 (t, \(J = 7.4\) Hz, 1H), 7.53 (t, \(J = 7.4\) Hz, 2H); \(^{13}\)C NMR (DMSO-\(d_6\), 100 MHz): \(\delta\) 167.8, 145.4, 136.6, 134.8, 133.8, 130.4, 129.5, 121.9, 120.5, 108.3; **HRMS**: calculated for C\(_{14}\)H\(_9\)N\(_2\)O \([M-H]^−\) 221.0715 obtained 221.0714.

![Structure of N-(4-Cyanophenyl)acetamide (12)](image)

**N-(4-Cyanophenyl)acetamide (12):**\(^4\) White powder, **Yield**: 77%, **mp**: 204-206 °C (lit\(^4\) 206-208 °C), \(v_{\text{max/cm}^{-1}}\) (solid): 2221, 1667; \(^1\)H NMR (DMSO-\(d_6\), 400 MHz): \(\delta\) 10.39 (s, 1H), 7.75 (s, 4H), 2.09 (s, 3H); \(^{13}\)C NMR (DMSO-\(d_6\), 100 MHz): \(\delta\) 169.1, 143.4, 133.1, 118.9, 118.8, 104.6, 24.1; **HRMS**: calculated for C\(_9\)H\(_9\)N\(_2\)O \([M+H]^+\) 161.0715 obtained 161.0710.
N-(4-Fluorophenyl)benzamide (14): Yellow powder, **Yield**: 70%, **mp**: 179-181 °C (lit 184-185 °C), ν max/cm⁻¹(solid): 2985, 2904, 1652, 1519, 1385; ¹H NMR (MeOH-d₄, 400 MHz): δ 7.92 (brd, J = 7.1 Hz, 2H), 7.70-7.67 (m, 2H), 7.58-7.56 (m, 1H), 7.52-7.49 (m, 2H0, 7.09 (apt t, J = 8.8 Hz, 2H) ¹³C NMR (MeOH-d₄, 100 MHz): δ 168.9, 161.0 (d, J = 242 Hz), 136.1, 136.0 (d, J = 3.0 Hz), 135.8, 132.9 129.6, 124.2 (d, J = 7.9 Hz), 116.2 (d, J = 22.6 Hz); HRMS: calculated for C₁₃H₁₁FNO [M+H]+ 216.0819 obtained 216.0822.

N-(4-Flurophenyl)acetamide (13): Yellow powder, **Yield**: 70%; **mp**: 152-153 °C (lit 156-157 °C); ν max/cm⁻¹(solid): 3301, 1664, 1559, 1504, 1208; ¹H NMR (MeOH-d₄, 400 MHz): δ 7.52-7.49 (m, 2H), 7.03-6.99 (m, 2H), 2.10 (s, 3H); ¹³C NMR (MeOH-d₄, 100 MHz): δ 171.8, 160.6 (d, J = 241 Hz), 135.9 (d, J = 2.8 Hz), 123.2 (d, J = 7.8 Hz), 116.2 (d, J = 22.6 Hz), 23.7; HRMS: calculated for C₈H₉FNO (M+H⁺) 154.0663 obtained 154.0664.

N-(p-Tolyl)benzamide (15): Off white powder, **Yield**: 60%; **mp**: 152-154 °C (lit 157-158 °C); ν max/cm⁻¹(solid): 3338, 1650, 1521, 1319; ¹H NMR (MeOH-d₄, 400 MHz): δ 7.90 (d, J = 7.2 Hz, 2H), 7.58-7.48 (m, 5H), 7.17 (d, J = 8.2 Hz, 2H), 2.31
N-(p-Tolyl)acetamide (16): Off white powder, Yield: 72%; mp: 144-148 °C (Lit. 149-150 °C), ν_max/cm⁻¹(solid): 3288, 1656, 1604, 1513, 1320; ¹H NMR (CDCl₃, 400 MHz): δ 7.55 (brs, 1H), 7.36 (d, J = 8.3 Hz, 2H), 7.09 (d, J = 8.1 Hz, 2H), 2.29 (s, 3H), 2.13 (s, 3H); ¹³C NMR (CDCl₃, 100 MHz): δ 168.4, 135.3, 133.8, 129.3, 12.0, 24.3, 20.7; HRMS: calculated for C₉H₁₂NO [M+H]+ 150.0913 obtained 150.0928.
$^1$H NMR: $N$-(4-Nitrophenyl)benzamide (7)
$^{13}$C NMR: $N$-(4-Nitrophenyl)benzamide (7)
$^1$H NMR: $N$-(4-Nitrophenyl)acetamide (10)
$^{13}$C NMR: \textit{N-(4-Nitrophenyl)acetamide (10)}
$^1$H NMR: N-(4-Cyanophenyl)benzamide (11)
$^{13}$C NMR: $N$-(4-Cyanophenyl)benzamide (11)
$^1$H NMR: N-(4-Cyanophenyl)acetamide (12)
$^{13}$C NMR: $N$-(4-Cyanophenyl)acetamide (12)
$^1$H NMR: N-(4-Flurophenyl)acetamide (13)
$^{13}$C NMR: $N$-(4-Flurophenyl)acetamide (13)
$^1$H NMR: $N$-(4-Fluorophenyl)benzamide (14)
$^{13}$C NMR: $N$-(4-Fluorophenyl)benzamide (14)
$^1$H NMR: $N$-(p-Tolyl)benzamide (15)
$^{13}$C NMR: $N$-($\rho$-Tolyl)benzamide (15)
$^1$H NMR: N-(p-Tolyl)acetamide (16)
$^{13}$C NMR: $N$-(p-Tolyl)acetamide (16)