SHORT PAPER

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Reaction between isocyanides and N,N′-dimethylbarbituric acid. Synthesis of push–pull olefinic systems†

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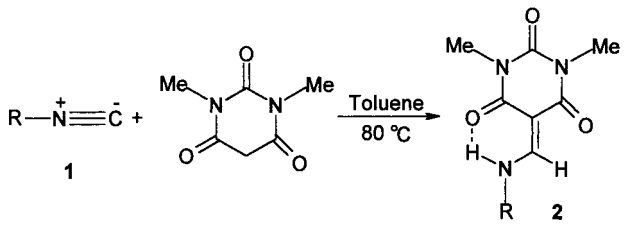
Polarised olefinic systems are synthesised from the reaction between alkyl or aryl isocyanides and N,N′-dimethylbarbituric acid in 62–74% yield.

Keywords: enaminones; isocyanides, pyrimidinones

The most usual reactivity observed in isocyanides is reaction of the functional group with acidic reactants.[1-4] A general feature of isocyanide reactions is the formation of α,α-addition reaction products: *i.e.* two new bonds are formed to the terminal isocyanide carbon atom. Typical examples are the reaction of isocyanides with protonic acids.[1,2] We report here that CH-acids such as *N,N′*-dimethylbarbituric acid react with alkyl or aryl isocyanides (**1**) producing 1:1 adducts. This two-component reaction produces the enaminones **2a–d**. These compounds may be formulated as having been derived from initial α,α-addition of CH-acids to the isocyanide and subsequent proton transfer reaction to produce the polarized olefinic systems **2a–d**. The reactions proceed in fairly high yields.

Previous reports of the preparation of enaminones analogous to those reported here have involved fusing the barbituric acid analogue with formanilide or its derivatives,[5,6] and the three-component condensation of dimethylbarbituric acid, trimethyl orthoformate, and aniline.[7]



1 **2**

1,2	R	%Yield of **2**
a	2,6-Dimethylphenyl	65
b	Benzyl	70
c	Cyclohexyl	74
d	*tert*-Bu	62

All the products (**2**) are stable crystalline solids whose structure is fully supported by elemental analyses and IR, ^{1}H NMR, ^{13}C NMR and mass spectral data. The mass spectra of these 1:1 adducts displayed molecular ion peaks at the appropriate *m/z* values.

The ^{1}H NMR spectrum of 5-(2,6-dimethylphenylaminomethylidene)-*N,N′*-dimethylbarbituric acid (**2a**) exhibited three sharp singlets, readily recognisable as arising from the *C*-methyl (δ 2.36) and *N*-methyl (δ 3.34 and 3.37) protons, along with a mutiplet (δ 7.19) for the aromatic protons. The HC-NH moiety showed an AX spin system (δ_{CH} 8.30, δ_{NH} 11.6, ^3J = 14 Hz). The ^{13}C NMR spectrum showed 12 distinct resonances consistent with the structure **2a**. Partial assignments of these resonances are given in the Experimental section. The ^{1}H NMR and ^{13}C NMR spectra of **2b–d** are similar to those of **2a** except for the isocyanide residues, which displayed characteristic resonances with appropiate chemical shifts.

The structural assignments of compounds **2a–d** made on the basis of their NMR specta are supported by their IR spectra. Of special interest are the strong carbonyl absorption bands at 1705–1662 cm^{-1} for all compounds and a fairly broad NH peak at about 3220 cm^{-1} for amino groups (see Experimental section).

We have not established the mechanism of the reaction between isocyanides and *N,N′*-dimethylbarbituric acid, however, a possible explanation is proposed in Scheme 1. On the basis of the well established chemistry of isocyanides,[1-4] it is reasonable to assume that compound **2** results from initial protonation of the isocyanide carbon atom by the CH-acid. The positively charged ion is then attacked by the enolate anion of the CH-acid to produce the α,α-addition product **3**. Such addition product tautomerises under reaction conditions to produce the enaminone **2** (see Scheme 1).

In summary, the reaction between alkyl or aryl isocyanides and *N,N′*-dimethylbarbituric acid provides a simple one-pot entry into the synthesis of polyfunctional pyrimidine derivatives of potential synthetic interest.

Experimental

Melting points were measured on an Electrothermal 9100 apparatus. Elemental analyses for C, H, and N were performed using a Heraeus CHN-O-Rapid analyzer. IR spectra were measured on a Shimadzu IR 460 spectrometer. ^{1}H and ^{13}C NMR spectra were measured with BRUKER DRX-500 AVANCE instrument with $CDCl_3$ as solvent at 500 and 125.7 MHz, respectively. Mass spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionisation potential of 70 eV. Isocyanides **1a–d** and *N,N′*-dimethylbarbituric acid were obtained from Fluka (Buchs, Switzerland) and were used without further purification.

Preparation of 5-(2,6-dimethylphenylaminomethylene)-N,N′-*dimethyl barbituric acid* (**2a**): *General procedure*: To a magnetically stirred solution of *N,N′*-dimethylbarbituric acid (0.312 g, 2 mmol) in toluene (10 ml) was added, dropwise, a mixture of 2,6-dimethylphenyl isocyanide (0.262 g, 2 mmol) in toluene (3 ml) at –5 °C over 10 min. The reaction mixture then kept for 48 h at 80 °C. The solvent was removed under reduced pressure and the solid residue was washed with cold diethyl ether (2×5 ml) and the product

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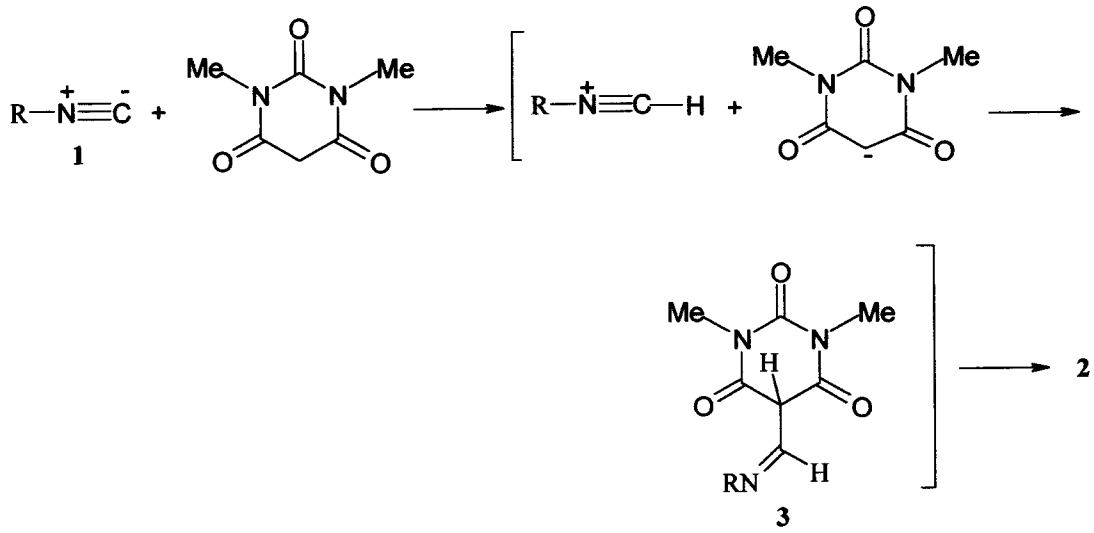

Scheme 1

2a was recrystallised from ethanol. Colourless crystals, m.p. 201–204 °C, yield 0.37 g (65%). IR (KBr) (ν_{max}, cm^{-1}): 3218 (N-H), 1705 and 1664 (C=O), 1632 (C=C). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 2.36 (6 H, s, 2 Ar-CH_3), 3.34 and 3.37 (6 H, 2 s, 2 NCH_3), 7.19 (3 H, m, arom.), 8.30 (1 H, d, ^3J = 14 Hz, CH), 11.60 (1 H, br d, ^3J = 14 Hz, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C 18.79 (Ar-CH_3), 27.55 and 28.26 (2 NCH_3), 92.43 (*C*=CHN), 128.33 (C_{para}), 129.49 (C_{meta}), 133.00 (N-CH), 137.26 (*C*-CH_3), 152.40 (N-C-N), 159.56 (N-CH), 163.18 and 165.58 (2 C=O). MS (*m/z*, %): 287 (M^+, 45); 286 (10); 144 (16); 132 (35); 131 (100); 77 (18). (Found: C, 62.8; H, 5.9; N, 14.5%. $C_{15}H_{17}N_3O_3$ requires C, 62.70; H, 5.96; N, 14.62 %).

5-(Benzylaminomethylene)-N,N′-*dimethylbarbituric acid* (**2b**): Colourless crystals, m.p. 130–132 °C, yield 0.38 g (70%). IR (KBr) (ν_{max}, cm^{-1}): 3220 (N-H), 1705 (C=O) and 1647 (C=C). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 3.28 and 3.31 (6 H, 2 s, 2 N-CH_3); 4.64 (2 H, d, ^3J = 6 Hz,CH_2); 7.2 (5 H, m, C_6H_5), 8.30 (1 H, d, ^3J = 14 Hz, CH), 10.60 (1 H, br m, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C 26.87 and 27.57 (2 NCH_3); 53.79 (CH_2); 90.89 (N-CH=*C*); 127.25 (2 CH); 128.35 (CH); 128.92 (2 CH); 135.15 (C_{ipso}); 151.85 (N-C-N); 159.26 (N-CH); 162.68 and 164.71 (2 C=O). MS (*m/z*, %): 273 (M^+, 40), 256 (20), 199 (18), 182 (32), 169 (33), 91 (100), 65 (55), 58 (35). (Found: C, 61.4; H, 5.6; N,15.5. $C_{14}H_{15}N_3O_3$ requires C,61.53; H, 5.53; N, 15.38%).

5-(Cyclohexylaminomethylene)-N,N′-*dimethylbarbituric acid* (**2c**): Colourless crystals, m.p. 208–211 °C yield 0.39g (74%). IR (KBr) (ν_{max}, cm^{-1}): 3220 (N-H), 1702 and 1662 (C=O), 1637 (C=C). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.2-2.2 (10 H, m, 5 CH_2); 3.25 (1 H, m, CHN); 3.30 and 3.32 (6 H, 2 s, 2 NCH_3); 8.25 (1 H, d, ^3J= 14 Hz, CH); 10.4 (1H, br d, ^3J= 14 Hz, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C 24.06, 24.72 (CH_2); 26.83 and 27.57 (2 NCH_3); 33.27 (2 CH_2); 58.59 (CHN); 90.23 (N-CH-*C*); 151.97 (N-C-N); 157.22 (CH-N); 162.80 and 164.83 (2 C=O). MS (*m/z*, %): 265 (M^+, 65), 222 (100), 169 (22), 48 (50), 97 (90), 69 (45), 55 (80). (Found: C, 58.3; H, 7.0; N, 16.1. $C_{13}H_{19}N_3O_3$ requires C,58.85; H, 7.22; N, 15.84%).

5-(t-Butylaminomethylene)-N,N′-*dimethylbarbituric acid* (**2d**): colourless crystals, m.p. 96–97 °C yield 0.30 g (62%). IR (KBr) (ν_{max}, cm^{-1}): 3222 (N-H), 1700 and 1668 (C=O), 1639 (C=C). ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.42 (9 H, s, CMe_3); 3.29 and 3.32 (6 H, 2 s, 2 NCH_3); 8.27 (1 H, d, ^3J= 15 Hz, CH); 10.65 (1 H, br d, ^3J= 15 Hz, NH···O=C). ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C 27.34 and 28.10 (2 NCH_3); 29.98 (C-Me_3); 55.17 (*C*Me_3); 90.57 (*C*=C-N); 152.48 (N-C-N); 155.64 (N-*C*=C); 163.39 and 165.39 (2 N-C=O). MS (*m/z*, %): 239 (M^+, 100), 207 (44), 182 (68), 155 (92), 125 (41), 97 (45), 57 (47). (Found: C, 55.1; H, 7.3; N, 17.6. $C_{11}H_{17}N_3O_3$ requires C, 55.41; H, 7.22; N, 17.49%).

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M)*.