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[1+4] Cycloaddition of Isocyanides with 3-(1-Hydroxyethylidene)pentane-2,4-dione. A Convenient Synthesis of Iminolactones†

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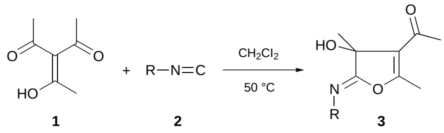
Isocyanides undergo formal [1 + 4] cycloaddition with 3-(1-hydroxyethylidene)pentane-2,4-dione to afford five-membered iminolactone derivatives in high yields.

Formal [1 + 4] cycloaddition reactions that incorporate an isocyanide carbon atom are an elegant approach to a range of cyclic systems which are often inaccessible by other methods.[1–3] This is specially true of five-membered ring systems.[4–9] Electron-deficient α,β-unsaturated carbonyl compounds which are capable of assuming a *cisoid* configuration in general lead to five-membered 1:1 adducts. 3-(1-Hydroxyethylidene)pentane-2,4-dione (**1**) has been shown to be almost completely enolic both in organic solvents (CCl_4) and in the solid,[10] thus providing an electron-deficient hetero-1,3-diene. The work reported here was undertaken in order to study the possibility of trapping this heterodiene by a formal [1 + 4] cycloaddition reaction using isocyanides such as *tert*-butyl isocyanide, cyclohexyl isocyanide and benzyl isocyanide.

The [1 + 4] cycloaddition of isocyanides **2** with the heterodiene **1** afforded the iminolactone derivatives (**3**) in high yields. The structures of compounds **3a**, **3b** and **3c** were deduced from elemental analysis and ^{1}H and ^{13}C NMR and IR spectra. The nature of these compounds as 1 : 1 adducts was also apparent from the elemental analyses as well as from the mass spectra, which for **3a** and **3b** displayed M + 1 peaks instead of molecular ion peaks at *m/z* 226 and 252 respectively. For **3c** a molecular ion peak was seen at *m/z* 259.



2a, 3a R = Bu^t
2b, 3b R = cyclohexyl
2c, 3c R = benzyl

The ^{1}H NMR spectra of **3a** exhibited five single lines, readily recognizable as arising from a *tert*-butyl group (δ 1.62), three methyl groups (δ 1.80, 2.20 and 2.50) and a hydroxy (δ 3.85) group. The proton-decoupled ^{13}C NMR spectrum of **3a** displayed 10 single lines. The ^{1}H and ^{13}C NMR spectra of **3b** and **3c** are similar to that of **3a**, except for the methylene group of **3c**. The methylene group in **3c** is attached to a ring system bearing an asymmetric carbon atom, and appears as an AB quartet (δ 4.50, J_{AB} 16.50 Hz).

The structural assignments made on the basis of the NMR spectra of compounds **3a**, **3b** and **3c** were supported by their IR spectra. Of special interest are the hydroxy absorptions at 3280, 3290 and 3325 cm^{-1} of **3a**, **3b** and **3c**, respectively.

In summary, the major synthetic advantages of this reaction are the mild reaction conditions, the excellent yields and the experimental simplicity.

Experimental

All melting points are uncorrected. Elemental analyses were performed using a Heraeus CHN-O rapid analyser. Mass spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 70 eV. IR spectra were measured on a Shimadzu IR-470 spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Jeol EX-90A spectrometer at 90 and 22.6 MHz, respectively.

Preparation of 4-*Acetyl*-2-tert-*butylimino*-3-*hydroxy*-3,5-*dimethyl*-2,3-*dihydrofuran* (**3a**).—To a magnetically stirred solution of **1** (1.42 g, 10 mmol) in dichloromethane (10 ml) was added dropwise a mixture of *tert*-butyl isocyanide (0.83 g, 10 mmol) in dichloromethane (10 ml) at −5 °C over 10 min. The reaction mixture was allowed to warm up to room temperature and then stirred for 24 h at 50 °C. After 12 h in a refrigerator at 5 °C white crystals (2.0 g, 90%) were collected by filtration. Mp 80 °C. ν_{max} (KBr)/cm^{-1} 3280 (OH), 1690 (C=N), 1657 (C=O), 1634 (C=C). δ_H ($CDCl_3$, Me_4Si) 1.62 (9 H, s, Bu^t), 1.8 (3 H, s, Me), 2.2 (3 H, s, Me), 2.5 (3 H, s, Me), 3.85 (1 H, s, OH, exchange with D_2O). δ_C ($CDCl_3$, Me_4Si) 11.20 (CH_3), 26.31 (CH_3), 28.79 (CH_3), 31.56 (CH_3), 56.60 (*C*Me_3), 91.70 (C-OH), 140.40 (*C*=C-O), 147.94 (C=*C*-O), 169.03 (C=N), 197.37 (C=O). *m/z* 226 (MH^+, 12%), 210 (M-CH_3, 23), 152 (19), 83 (5), 58 (100). (Found: C, 63.9; H, 8.6; N, 6.1. $C_{12}H_{19}NO_3$ requires C, 64; H, 8.4; N, 6.1%).

Preparation of 4-*Acetyl*-2-*cyclohexylimino*-3-*hydroxy*-3,5-*dimethyl*-2,3-*dihydrofuran* (**3b**).—Similar reaction conditions as above but using cyclohexyl isocyanide instead of *tert*-butyl isocyanides yielded a white powder (2.0 g, 82%). Mp 110 °C. ν_{max} (KBr)/cm^{-1} 3290 (OH), 1690 (C=N), 1661 (C=O), 1620 (C=C). δ_H ($CDCl_3$, Me_4Si) 1–2.30 (11 H, m, C_6H_{11}), 1.65 (3 H, s, CH_3), 2.30 (3 H, s, CH_3), 2.52 (3 H, s, CH_3), 3.4 (1 H, s, OH). δ_C ($CDCl_3$, Me_4Si) 11.08 (CH_3), 23.86, 25.21 and 31.23 (3CH_2), 26.26 (CH_3), 29.93 (CH_3), 52.08 (CH), 89.63 (C-OH), 141.71 (*C*=C-O), 147.37 (C=*C*-O), 167.65 (C=N), 196.64 (C=O). *m/z* 252 (MH^+), 236, 170, 153, 125, 98, 83, 56. (Found: C, 67.0; H, 8.7; N, 5.5. $C_{14}H_{21}NO_3$ requires C, 67.0; H, 8.4; N, 5.6%).

Preparation of 4-*Acetyl*-2-*benzylimino*-3-*hydroxy*-3,5-*dimethyl*-2,3-*dihydrofuran* (**3c**).—Similar reaction conditions as **3a** but using benzyl isocyanide yielded a colourless powder (2.20 g, 85%). Mp 73 °C. ν_{max} (KBr)/cm^{-1} 3325 (OH), 1699 (C=N), 1680 (C=O), 1638 (C=C). δ_H ($CDCl_3$, Me_4Si) 1.50 (3 H, s, CH_3), 2.20 (3 H, s, CH_3), 2.44 (3 H, s, CH_3), 4.60 (AB-q, 2 H, $\Delta\nu$ 24.0 Hz, *J* 16.5 Hz, Ph-CH_2), 7.3 (5 H, m, C_6H_5). δ_C ($CDCl_3$, Me_4Si) 11.63 (CH_3), 24.67 (CH_3), 31.63 (CH_3), 42.53 (CH_2), 89.68 (C-OH), 127.59, 128.22, 128.79 and 138.32 (C_6H_5), 140.45 (*C*=C-O), 149.02 (C=*C*-O), 169.24 (C=N), 197.08 (C=O). *m/z* 259 (M^+), 241, 137, 106, 91, 65. (Found: C, 69.5; H, 6.5; N, 5.5. $C_{15}H_{17}NO_3$ requires C, 69.4; H, 6.5; N, 5.5%).

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