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Intramolecular Nitrile Imide Cycloadditions onto the Furan Ring: Synthesis of the New 3a,4-Dihydro-6*H*-difuro[3,2-*c*;3,4-*d*]pyrazole Skeleton†

Gianluigi Broggini, Giorgio Molteni* and Gaetano Zecchi

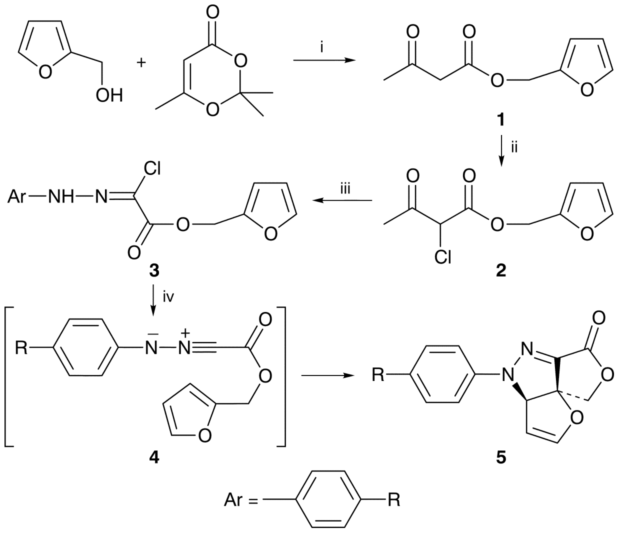
Dipartimento di Chimica Organica e Industriale dell'Università and Centro CNR, Via Golgi 19, 20133, Milano, Italy

Intramolecular nitrile imide cycloadditions onto the furan ring have been exploited in the construction of the hitherto unknown 3a,4-dihydro-6*H*-difuro[3,2-*c*;3,4-*d*]pyrazole skeleton.

The behaviour of the furan ring as dipolarophile in both inter- and intra-molecular 1,3-dipolar cycloadditions is a documented matter.[1–3] However, few reports are concerned with cycloadditions between nitrile imides and furan derivatives.[4–6] In pursuing our interest in the synthesis of new heterocyclic systems, we have undertaken a study on the intramolecular reactivity of a series of nitrile imides **4** containing the furan moiety as a potential dipolarophile.

The hydrazonoyl chlorides **3**, which we devised as suitable precursors of the nitrile imide intermediates **4**, were synthesised as depicted in Scheme 1.‡

The *in situ* generation of **4** was usually accomplished by treating **3** under a nitrogen stream with a twofold molar excess of silver carbonate in dry dioxane at room temperature. In the case of **3c** a better result was obtained by using silver acetate. However, since extensive formation of dark-coloured decomposition materials was observed, the reactions were stopped before the conversion of **3** was complete; so that some amount of the starting hydrazonoyl chloride was always recovered. The difuropyrazolines **5** were isolated in an analytically pure state with yields ranging from 11–37%. Their chromatographic treatment required eluents added with a small amount of triethylamine in order to prevent acid-catalysed decomposition of the products. The assigned structures were supported by ^{1}H NMR and IR spectroscopy as well as FAB–MS spectrometry. In conclusion, intramolecular nitrile imide cycloadditions to the furan ring were proven to be an effective route to the new 3a,4-dihydro-6*H*-difuro[3,2-*c*;3,4-*d*]pyrazole skeleton. The lability of the latter spiro-tricyclic system must be underlined and can plausibly be ascribed to the strain of the dihydrofuran ring.



a, R = H; **b**, R = Cl; **c**, R = F; **d**, R = NO_2

Scheme 1 *Reagents and conditions*: i, xylene, heat; ii, SO_2Cl_2 0 °C; iii, $ArN_2{}^+Cl^-$ 0 °C iv, Ag_2CO_3 (entries **a**, **b**, **d**) or AcOAg (entry **c**), dioxane, room temp.

Experimental

Analytical and spectroscopic instruments were as described in a previous paper.[7]

Preparation of Acetoacetate **1**.—A solution of 2-hydroxymethylfuran (9.9 g, 0.1 mol) in xylene (20 ml) was treated with 2,2,6-trimethyl-4*H*-1,3-dioxin-4-one (14.2 g, 0.1 mol). The mixture was refluxed for 1.5 h. Evaporation of the solvent under reduced pressure gave crude **1** as an 'undistillable' oil (17.6 g, 97%); ν_{max}/cm^{-1} (neat) 1745, 1720; δ_H 2.25 (3 H, s), 3.44 (2 H, s), 5.12 (2 H, s), 6.30–6.45 (2 H, m), 7.40–7.50 (1 H, m); *m*/*z* 182 (M^+).

Preparation of Hydrazonoyl Chlorides **3**. *General Procedure*.—A solution of sulfuryl chloride (3.35 g, 25 mmol) in dry chloroform (5 ml) was slowly added (2 h) to a mixture of **1** (4.55 g, 25 mmol) and sodium hydrogencarbonate (2.10 g, 25 mmol) in dry chloroform (40 ml), keeping the temperature in the range 0–5 °C. After 1.5 h at room temperature, chloroform (80 ml) was added, and the mixture was washed with water (25 ml). The organic layer was dried over sodium sulfate and the solvent was removed under reduced pressure to afford **2** in the crude state (3.51 g, 65%); ν_{max}/cm^{-1} (neat) 1760, 1730; δ_H 2.30 (3 H, s), 4.75 (1 H, s), 5.48 (2 H, s), 6.50–6.80 (2 H, m), 7.40–7.50 (1 H, m). Crude **2** was dissolved in cold methanol (45 ml), and sodium acetate (2.72 g, 20 mmol) was added. A cold aqueous solution of the appropriate arenediazonium chloride (17 mmol) was added dropwise under vigorous stirring and ice-cooling. The mixture was allowed to stand overnight with stirring at room temperature. The solvent was partly removed under reduced pressure and the resulting mixture was extracted with diethyl ether (150 ml). The organic layer was washed firstly with 5% aqueous sodium hydrogencarbonate (50 ml), then with water (100 ml), and dried over sodium sulfate. Evaporation of the solvent and subsequent crystallisation of the residue from diisopropyl ether gave the hydrazonoyl chlorides **3** in the pure state.

3a (3.48 g, 50%) had mp 118 °C; ν_{max}/cm^{-1} (Nujol) 3270, 1700; δ_H ($CDCl_3$) 5.31 (2 H, s), 6.40 (1 H, dd, *J* 3.3, 1.6), 6.52 (1 H, d, *J* 3.3), 7.00–7.40 (5 H, m), 7.46 (1 H, d, *J* 1.6), 8.35 (1 H, br s) (*J* values in Hz throughout); *m*/*z* 278 (M^+) (Found: C, 56.06; H, 4.03; Cl, 12.49; N, 10.13. $C_{13}H_{11}ClN_2O_3$ requires C, 56.11; H, 3.99; Cl, 12.58; N, 10.07%).

3b (4.68 g, 60%) had mp 111 °C; ν_{max}/cm^{-1} (Nujol) 3270, 1700; δ_H ($CDCl_3$) 5.30 (2 H, s), 6.35 (1 H, dd, *J* 3.2, 1.8), 6.50 (1 H, d, *J* 3.2), 7.00–7.35 (4 H, m), 7.45 (1 H, d, *J* 1.8), 8.30 (1 H, br s); *m*/*z* 312 (M^+) (Found: C, 49.94; H, 3.26; Cl, 22.49; N, 9.06. $C_{13}H_{10}Cl_2N_2O_3$ requires C, 50.00; H, 3.23; Cl, 22.42; N, 8.98%).

3c (3.33 g, 45%) had mp 112 °C; ν_{max}/cm^{-1} (Nujol) 3270, 1715; δ_H ($CDCl_3$) 5.29 (2 H, s), 6.37 (1 H, dd, *J* 3.2, 1.8), 6.50 (1 H, d, *J* 3.2), 6.90–7.30 (4 H, m), 7.48 (1 H, d, *J* 1.8), 8.30 (1 H, br s); *m*/*z* 296 (M^+) (Found: C, 52.77; H, 3.34; N, 9.46. $C_{13}H_{10}ClFN_2O_3$ requires C, 52.70; H, 3.40; N, 9.46%).

3d (3.63 g, 45%) had mp 152 °C; ν_{max}/cm^{-1} (Nujol) 3280, 1710; δ_H ($CDCl_3$) 5.33 (2 H, s), 6.40 (1 H, dd, *J* 3.3, 1.7), 6.52 (1 H, d, *J* 3.3), 7.30–7.40 (2 H, m), 7.47 (1 H, d, *J* 1.7), 8.20–8.30 (2 H, m),

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*To receive any correspondence.

†This is a **Short Paper** as defined in the Instructions for Authors, Section 5.0 [see *J. Chem. Research (S)*, 1998, Issue 1]; there is therefore no corresponding material in *J. Chem. Research (M)*.

‡Owing to its instability, the α-chloroacetoacetate **2** was used as a crude material without full characterisation.

8.78 (1 H, br s); *m*/*z* (M^+) (Found: C, 48.35; H, 3.08; Cl, 10.90; N, 12.96. $C_{13}H_{10}ClN_3O_5$ requires C, 48.29; H, 3.12; Cl, 10.83; N, 13.00%).

Treatment of Hydrazonoyl Chlorides **3a**,**b**,**d** *with Silver Carbonate. General Procedure*.—A solution of **3a**, **3b** or **3d** (5.0 mmol) in dry dioxane (250 ml) was treated with silver carbonate (2.76 g, 10.0 mmol) under a nitrogen stream, and the mixture was stirred in the dark at room temperature for 100 h. The undissolved material was filtered off, the solvent was evaporated and then the residue was chromatographed on a silica gel column with diethyl ether–ethyl acetate–triethylamine (89:10:1). Unchanged **3** was eluted first (**a**, 25%; **b**, 20%, **d** 44%), followed by crude cycloadduct **5**. Recrystallisation from diisopropyl ether gave analytically pure **5**.

5a (0.36 g, 34%) had mp 120 °C (decomp.); ν_{max}/cm^{-1} (Nujol) 1745; δ_H ($CDCl_3$) 4.45 and 4.81 (2 H, AB type, *J* 10.5), 5.49 (1 H, dd, *J* 3.0, 2.8), 5.70 (1 H, d, *J* 3.0) 6.68 (1 H, d, *J* 2.8), 7.00–7.40 (5 H, m); *m*/*z* 242 (M^+) (Found: C, 64.40; H, 4.11; N, 11.49. $C_{13}H_{10}N_2O_3$ requires C, 64.44; H, 4.16; N, 11.57%).

5b (0.28 g, 23%) had mp 117 °C (decomp.); ν_{max}/cm^{-1} (Nujol) 1750; δ_H ($CDCl_3$) 4.48 and 4.81 (2 H, AB type, *J* 10.5), 5.48 (1 H, dd, *J* 3.0, 2.9), 5.70 (1 H, d, *J* 3.0), 6.70 (1 H, d, *J* 2.9), 7.15–7.35 (4 H, m); *m*/*z* 276 (M^+) (Found: C, 56.57; H, 3.33; Cl, 12.76; N, 10.21. $C_{13}H_9ClN_2O_3$ requires C, 56.52; H, 3.29; Cl, 12.67; N, 10.15%).

5d (0.14 g, 11%) had mp 142 °C (decomp.); ν_{max}/cm^{-1} (Nujol) 1750; δ_H ($CDCl_3$) 4.45 and 4.81 (2 H, AB type, *J* 10.5), 5.49 (1 H, dd, *J* 3.0, 2.8), 5.70 (1 H, d, *J* 3.0), 6.68 (1 H, d, *J* 2.8), 7.00–7.40 (4 H, m); *m*/*z* 287 (M^+) (Found: C, 54.30; H, 3.11; N, 14.70. $C_{13}H_9N_3O_5$ requires C, 54.35; H, 3.16; N, 14.63%).

Treatment of Hydrazonoyl Chloride **3c** *with Silver Acetate*.—A solution of **3c** (1.39 g, 5.0 mmol) in dry dioxane (250 ml) was treated with silver acetate (1.68 g, 10.0 mmol) under a nitrogen stream, and the mixture was stirred in the dark at room temperature for 3 h. The undissolved material was filtered off, the solvent was evaporated and then the residue was taken up with diethyl ether (100 ml). The organic solution was washed with 2.5% aqueous sodium hydrogencarbonate (20 ml) and then with water (20 ml), dried over sodium sulfate and evaporated. The residue was chromatographed on a silica gel column with diethyl ether–triethylamine (99:1). Unchanged **3c** was eluted first (33%), followed by crude cycloadduct **5c**. Recrystallisation from diisopropyl ether gave analytically pure **5c** (0.48 g, 37%), mp 115 °C; ν_{max}/cm^{-1} (Nujol) 1745; δ_H ($CDCl_3$) 4.47 and 4.80 (2 H, AB type, *J* 10.5), 5.46 (1 H, dd, *J* 3.1, 2.8), 5.70 (1 H, d, *J* 3.1), 6.68 (1 H, d, *J* 2.8), 6.90–7.40 (4 H, m); *m*/*z* 242 (M^+) (Found: C, 60.06; H, 3.52; N, 10.81. $C_{13}H_9FN_2O_3$ requires C, 59.99; H, 3.49; N, 10.77%).

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