Synthesis of a Pyrano[2,3-*b*]pyridine with Vinylogous Hydroxamic Acid Structures

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A new, two step synthesis of a pyrano[2,3-*b*]pyridine derivative **5** is described. Dehydroacetic acid and *N,N*-dimethylformamide dimethylacetal was condensed to form **2**. Compound **2** was converted into **5** by reaction with hydroxylamine which opens the lactone ring.

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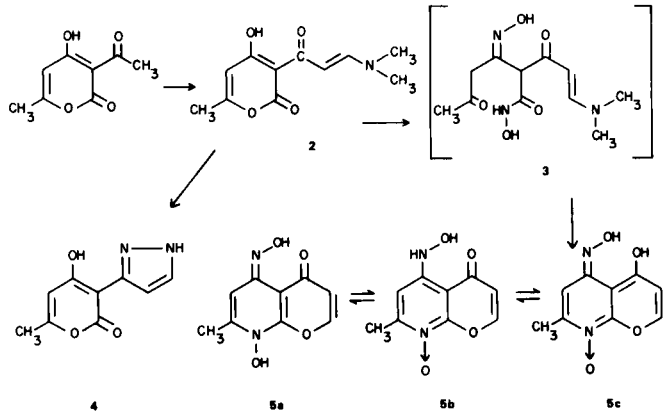
In the course of studies on the condensation reaction between the dehydroacetic acid **1** and *N,N*-dimethylformamide dimethylacetal, a new, high-yield synthesis of the pyrano[2,3-*b*]pyridine derivative **5** with vinylogous hydroxamic acid structures was discovered. Dimethylformamide dimethylacetal (1) and **1** react smoothly in either toluene or xylene to give the crystalline 4-hydroxy-2*H*-pyran-2-one (**2**). Treatment of **2** with an excess of aqueous hydroxylamine hydrochloride leads to the formation of the poorly soluble compound **5**.



The conversion of **2** → **3** is similar to the formation of 1-hydroxy-2-pyridone from 2-pyrone (2,3) in that nucleophilic attack by hydroxylamine at the C-2 position takes place. The open ring configuration reacts with a second molecule of hydroxylamine to give **3**. Acidification causes pyridone ring formation with accompanying loss of dimethylamine and closure of the 4-pyrone ring.

Compared with 4-hydroxylaminopyridine 1-oxide (4) or 4-hydroxylaminoquinoline 1-oxide (5), the number of tautomeric forms in which **5** can exist through pyrone ring annelation is increased by one. Compound **5** is a high melting point substance that is poorly soluble in the solvents used. A red colour with alcoholic iron(III) chloride solution and reduction with ammoniacal silver nitrate suggests a vinylogous hydroxamic acid. The infrared absorption at 1630 cm^{-1} indicates a pyrone-carbonyl group and therefore the existence of **5c** in the solid form is improbable. The N-O absorption at 1220 cm^{-1} is unfortunately produced by *N*-oxides and oximes and makes a distinction between **5a** and **5b** impossible. The elimination of oxygen on fragmentation of the molecular ion suggests at first **5b**, but the possibility of tautomerisation during ionization in the mass spectrometer cannot be excluded and is perhaps, a better explanation for the elimination of oxygen and subsequent M-16 ion. The AB spectrum (2-H, 3-H) measured in [D_6]DMSO is typical in position and distribution for a 4-pyrone ring. These results indicate that the existence of forms **5a-c** should first be studied in solution and from the ratios of **5** formed in the reaction. Studies in this direction are in progress.

The reaction of **2** with hydrazine dihydrate in sodium hydroxide produces **4**, a quite different result. Compared to the more nucleophilic hydroxylamine, here no lactone ring opening can be observed under basic conditions. The formation of **4** can best be explained by conversion of the enamine **2** into a vinylogous hydrazide followed by pyrazole ring closure on acidification.

EXPERIMENTAL

Melting points are uncorrected. The nmr spectra were recorded with a Varian A-60 spectrometer at 60 MHz. Chemical shifts are given in ppm (δ) relative to internal TMS. Ir spectra were recorded with a Perkin-Elmer spectrophotometer 237 (potassium bromide, cm^{-1}). Mass spectra were measured with Varian-MAT CH 7.

4-Hydroxy-6-methyl-3-[3-dimethylaminoacryloyl]-2*H*-pyran-2-one (**2**).

Dehydroacetic acid (6) (**1**) (5.0 g., 0.03 mole) and 3.9 g. (0.033 mole) of *N,N*-dimethylformamide dimethylacetal were heated under reflux in 180 ml. of anhydrous xylene. The crude product that precipitated on cooling was recrystallized from ethanol as yellow crystals (6.0 g., 90%) m.p. 169°; ir: 1710, 1620; mass spectrum: M^+ 223; nmr ([D_6]DMSO): δ = 2.15 (s, 3H, CH_3), 3.0 (s, 3H) and 3.3 (s, 3H, $N(CH_3)_2$), 5.85 (s, 1H, 5-H), 6.5 (d, 1H, J = 13 Hz) and 8.15 ppm (d, 1H, J = 13 Hz, CH=CH).

Anal. Calcd. for $C_{11}H_{13}NO_4$ (223.2): C, 59.19; H, 5.87; N, 6.27. Found: C, 59.02; H, 5.68; N, 6.20.

8-Hydroxy-5-oximino-7-methyl-5,8-dihydro-4*H*-pyrano[2,3-*b*]pyridin-4-one

or

4-Oxo-5-hydroxylamino-7-methyl-4*H*-pyrano[2,3-*b*]pyridine 8-Oxide (**5**).

Compound **2** (2.23 g., 0.01 mole) and 2.5 g. of hydroxyl-

amine hydrochloride were dissolved in 80 ml. of 2*N* sodium hydroxide and stirred at room temperature for 12 hours. After acidification with concentrated hydrochloric acid, **5** precipitated and was recrystallized from DMFA/water. The beige coloured crystals obtained (1.8 g., 87%) had m.p. 274° dec.; ir: 1630, 1220; mass spectrum: M^+ 208; nmr ([D_6]DMSO): δ = 2.3 (s, 3H, CH_3), 6.2 (d, 1H, J = 8 Hz) and 7.8 (d, 1H, J = 8 Hz, CH=CH), 6.76 ppm (s, 1H, 6-H).

Anal. Calcd. for $C_9H_8N_2O_4$ (208.2): C, 59.28; H, 3.87; N, 13.46. Found: C, 59.03; H, 3.95; N, 13.46.

3-[4-Hydroxy-2-oxo-6-methyl-2*H*-pyran-3-yl] pyrazole (**4**).

From compound **2** (2.23 g., 0.01 mole) above and 2.5 g. of hydrazine dihydrate in 80 ml. of 2*N* sodium hydroxide, after acidification with concentrated hydrochloric acid, there was obtained a crude product which was recrystallized from DMFA/water as yellow crystals (1.5 g., 78%) m.p. 287°; ir: 3180, 1700; mass spectrum: M^+ 192; nmr ([D_7]DMFA): δ = 2.3 (d, 3H, J = 1 Hz, CH_3), 6.2 (d, 1H, J = 1 Hz, 5-H), 7.05 (d, 1H, J = 2 Hz) and 7.9 ppm (d, 1H, J = 2 Hz, CH=CH).

Anal. Calcd. for $C_9H_8N_2O_3$ (192.2): C, 56.52; H, 4.20; N, 14.58. Found: C, 56.15; H, 4.26; N, 14.55.

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