

# Reissert Compound Studies. XLIII. The Pyrido[2,3-*b*]pyrazine Reissert Compound

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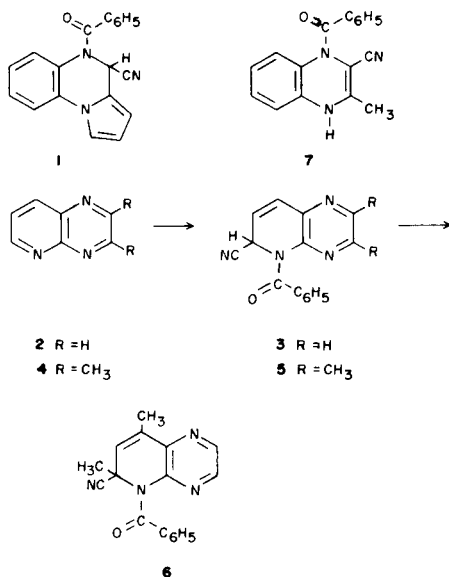
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Both pyrido[2,3-*b*]pyrazine (5-azaquinoxaline) and 2,3-dimethyl-5-azaquinoxaline undergo Reissert compound formation across the 5,6-position.

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Recently we reported (1) that, although quinoxaline does not give rise to a Reissert compound, the quinoxaline derivative, pyrrolo[1,2-*a*]quinoxaline gives the Reissert compound **1**. Continuing this study of compounds related to quinoxaline we now report on the behavior of pyrido[2,3-*b*]pyrazine (5-azaquinoxaline) (**2**) towards Reissert compound formation.



Treatment of 5-azaquinoxaline (**2**) with trimethylsilyl cyanide (2), benzoyl chloride, and a catalytic amount of aluminum chloride afforded a mono-Reissert compound in

49% yield. This is the first example of a Reissert compound formed from a triaza system. Theoretically, six structural possibilities exist for this compound (three 1,4-dihydro structures and three 1,2-dihydro structures). The infrared spectrum did not show NH stretching which excluded the possibility of the 1,4-dihydro-structures. The pmr spectrum of the compound revealed two sets of nuclei, an ABX pattern (A at  $\delta$  6.98, B at  $\delta$  6.39, and X at  $\delta$  5.98;  $J_{AB} = 9$  Hz,  $J_{BX} = 6$  Hz, and  $J_{AX} = 0$ ) and an AB pattern (A at  $\delta$  8.18 and B at  $\delta$  7.76,  $J_{AB} = 3$  Hz). The ABX pattern, which compared well with that for 1,2-dicyano-1,2-dihydroquinoline (**3**), strongly favored structure **3** for the Reissert compound.

Additional evidence in support of structure **3** for the Reissert compound was obtained by the synthesis of a Reissert compound from 2,3-dimethyl-5-azaquinoxaline (**4**) (**4**). This compound (**5**) showed an ABX system in its pmr spectrum that had a striking similarity to the ABX region of the pmr spectrum of **3**.

Reaction of the Reissert compound **3** with methyl iodide and sodium hydride in dimethylformamide gave the dimethyl derivative **6**.

In view of the success in obtaining Reissert compounds from **2** and **4**, and particularly as a result of the synthesis of **1** (1), the reaction of 2-methylquinoxaline was reinvestigated. Treatment of freshly distilled 2-methylquinoxaline with trimethylsilyl cyanide (2) and benzoyl chloride in the presence of a catalytic amount of anhydrous aluminum chloride gave a compound identified as **7** in only 6% yield. The structure **7** is proposed on the basis of its in-

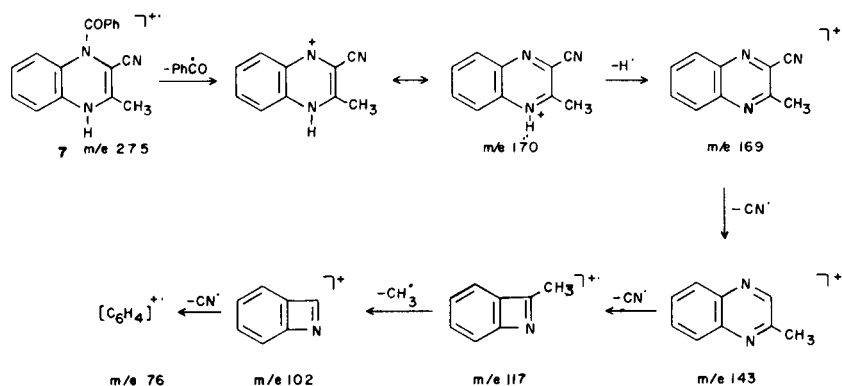


Figure 1

frared and mass spectral data. The infrared spectrum showed a broad absorption in the region 3250-3000  $\text{cm}^{-1}$ , an intense peak at 2230  $\text{cm}^{-1}$  and a shoulder at 1640  $\text{cm}^{-1}$  attributable to the N-H,  $\text{C}\equiv\text{N}$  and  $\text{C}=\text{O}$  stretching vibrations, respectively. The mass spectrum, in addition to the benzoylium ion ( $m/e$  105, 100%), had peaks at  $m/e$  275, 170, 169, 143, 117, 102, and 76 assignable to the ions shown in Figure 1. Undoubtedly, compound **7** arises from an isomerization of the initially formed Reissert compound. 1,2-Dicyano-1,2-dihydroquinoline has been reported to readily undergo a similar rearrangement to 1,2-dicyano-1,4-dihydroquinoline (**3**).

## EXPERIMENTAL

### General.

All melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 710B spectrometer as potassium bromide pellets. Proton magnetic resonance spectra were determined with a Hitachi Perkin-Elmer Model R-24B instrument using tetramethylsilane as an internal standard. Chemical shifts are expressed in parts per million ( $\delta$ ) downfield from tetramethylsilane. Mass spectra were obtained at the Midwest Center for Mass Spectrometry at the University of Nebraska (Supported under the N. S. F. Regional Instrumentation Facilities Program). Microanalyses were performed by Spang Microanalytical Laboratories, Eagle Harbor, Michigan.

### Pyrido[2,3-*b*]pyrazine(5-Azaquinoxaline) (**2**).

This compound was obtained from Aldrich Chemical Company and recrystallized from *n*-heptane before use.

### 2,3-Dimethylpyrido[2,3-*b*]pyrazin (2,3-Dimethyl-5-azaquinoxaline) (**4**).

2,3-Dimethylpyrido[2,3-*b*]pyrazine was synthesized by a slight modification of a literature procedure (4). Freshly crystallized 2,3-diaminopyridine (3.45 g, 31.6 mmoles) was added to 2.85 g (33.1 mmoles) of freshly distilled diacetyl. An exothermic reaction took place immediately. The contents were diluted with 30 ml of anhydrous benzene and refluxed gently for 1 hour. The solution was cooled and the water formed was removed. Evaporation of the benzene yielded the crude pyridopyrazine which was purified by vacuum sublimation at 70°, to give 84% of **4** mp 143-144°, reported (4) mp 148-149°; ir 3000, 1595, 1560, 1460, 1400, 1240, 1200, 1000, 810  $\text{cm}^{-1}$ ; pmr (deuteriochloroform):  $\delta$  8.92 (q, 1H, 6-H), 8.22 (q, 1H, 8-H), 7.51 (q, 1H, 7-H), 2.78 (s, 3H), 2.72 (s, 3H),  $J_{67} = 4$  Hz,  $J_{68} = 2$  Hz and  $J_{78} = 8$  Hz.

### 5-Benzoyl-6-cyano-5,6-dihydropyrido[2,3-*b*]pyrazine (**3**).

A mixture of 1.5 g (11.44 mmoles) of **2**, 3.92 g (39.51 mmoles) of trimethylsilyl cyanide, 0.05 g of anhydrous aluminum chloride and 5.6 g (39.72 mmoles) of benzoyl chloride was stirred for 48 hours in 40 ml of anhydrous dichloromethane. The dichloromethane was then washed successively with water (2  $\times$  20 ml), 10% aqueous sodium hydroxide (2  $\times$

25 ml) and water (2  $\times$  20 ml). Removal of the solvent from the dried (magnesium sulfate) organic extract followed by trituration with ethanol afforded 1.47 g (49%) of the title compound, mp 170-173° (from *n*-heptane-dichloromethane); ir: 3070, 2950, 1670, 1600, 1560, 1430, 1330, 1200, 1170, 1060, 960, 905, 850, 740  $\text{cm}^{-1}$ ; pmr (deuteriochloroform):  $\delta$  8.18 (d, 1H,  $J = 3$  Hz), 7.76 (d, 1H,  $J = 3$  Hz), 7.28 (m, 5H), 6.98 (q, 1H, 8-H), 6.39 (q, 1H, 7-H), 5.98 (q, 1H, 6-H),  $J_{67} = 6$  Hz;  $J_{68} \cong 0$  Hz;  $J_{78} = 9$  Hz).

Anal. Calcd. for  $\text{C}_{15}\text{H}_{10}\text{N}_4\text{O}$ : C, 68.69; H, 3.84; N, 21.36. Found: C, 68.74; H, 3.84; N, 21.41.

### 5-Benzoyl-6-cyano-2,3-dimethyl-5,6-dihydropyrido[2,3-*b*]pyrazine (**5**).

Following the procedure described for the preparation of **3**, 1.14 g (7.16 mmoles) of **4**, 1.63 g (16.4 mmoles) of trimethylsilyl cyanide and 2.1 g (14.9 mmoles) of benzoyl chloride in the presence of a catalytic amount of anhydrous aluminum chloride afforded 1.64 g (79%) of **5**, mp 157-159° (from *n*-heptane-dichloromethane); ir: 3060, 2950, 1660, 1600, 1560, 1450, 1410, 1360, 1210, 1050, 985, 940, 890, 860, 800  $\text{cm}^{-1}$ ; pmr (deuteriochloroform):  $\delta$  7.30 (m, 5H), 6.96 (q, 1H, 8-H), 6.32 (q, 1H, 7-H), 6.05 (q, 1H, 6-H), 2.44 (s, 3H), 2.02 (s, 3H),  $J_{67} = 6$  Hz;  $J_{68} = 0$  Hz;  $J_{78} = 9$  Hz.

Anal. Calcd. for  $\text{C}_{17}\text{H}_{14}\text{N}_4\text{O}$ : C, 70.33; H, 4.86; N, 19.30. Found: C, 70.35; H, 4.88; N, 19.41.

### 5-Benzoyl-6-cyano-6,8-dimethyl-5,6-dihydropyrido[2,3-*b*]pyrazine (**6**).

The title compound was prepared in 22% yield from **3** by reaction with methyl iodide and sodium hydride in dimethylformamide using the general procedure for alkylation of Reissert compounds, mp 143-145° (from *n*-heptane); ir: 3075, 2940, 1690, 1600, 1560, 1450, 1420, 1385, 1280, 1185, 1150, 1110, 1020, 880, 860, 730  $\text{cm}^{-1}$ .

Anal. Calcd. for  $\text{C}_{17}\text{H}_{14}\text{N}_4\text{O}$ : C, 70.33; H, 4.86; N, 19.30. Found: C, 70.41; H, 4.78; N, 19.48.

### 1-Benzoyl-2-cyano-3-methyl-1,4-dihydroquinoxaline (**7**).

Benzoyl chloride (2.45 g, 17.38 mmoles) was added to a well-stirred mixture of 1.0 g (6.94 mmoles) of freshly distilled 2-methylquinoxaline, 1.72 g (17.34 mmoles) of trimethylsilyl cyanide and 0.05 g of anhydrous aluminum chloride (catalyst) in 30 ml of anhydrous dichloromethane. The solution, after stirring for 48 hours, was allowed to stand for 15 days and then worked-up as described for the preparation of **3** to obtain 0.12 g (6%) of **7** mp 211-213° (from ethanol); ir: 3250-3000 (b), 2230, 1640 (sh), 1620, 1485, 1280, 1080, 1040, 960, 760  $\text{cm}^{-1}$ ; ms:  $m/e$  (%) 275.1052 (6.72,  $\text{C}_{17}\text{H}_{13}\text{N}_3\text{O}$ ,  $\text{M}^+$ ), 170.0714 (67.26,  $\text{C}_{10}\text{H}_8\text{N}_3$ ,  $[\text{M-PhCO}]^+$ ), 169.0640 (8.64,  $\text{C}_{10}\text{H}_7\text{N}_3$ ,  $[\text{M-PhCO-H}]^+$ ), 143.0607 (2.48,  $\text{C}_8\text{H}_7\text{N}_2$ ,  $[\text{M-PhCO-H-CN}]^+$ ), 117.0581 (8.76,  $\text{C}_8\text{H}_7\text{N}$ ,  $[\text{M-PhCO-H-2CN}]^+$ ), 105.0343 (100,  $\text{C}_7\text{H}_5\text{O}$ ), 102.0346 (5.32,  $\text{C}_7\text{H}_4\text{N}$ ,  $[\text{M-PhCO-H-2CN-Me}]^+$ ), 77.0395 (34.11,  $\text{C}_6\text{H}_5$ ), 76.0318 (5.31,  $\text{C}_6\text{H}_4$ ).

Anal. Calcd. for  $\text{C}_{17}\text{H}_{13}\text{N}_3\text{O}$ : C, 74.16; H, 4.76; N, 15.26. Found: C, 74.06; H, 4.73; N, 15.24.

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