

An Octahydropyrido[3,4-g]isoquinoline, A New Ring System

Thomas J. Schwan and Guy S. Lougheed

Research and Development Department, Norwich Pharmacal Company,
Division of Morton-Norwich Products, Inc., Norwich, New York 13815

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In connection with our previous reports on the synthesis of 4-phenyl-1,2,3,4-tetrahydroisoquinolines (1,2), we have investigated the ring closure of *N,N'*-bis(1-hydroxy-1-phenyl-2-propyl)-*p*-xylene- α,α' -diamine dihydrochloride (**1**) with polyphosphoric acid (PPA).

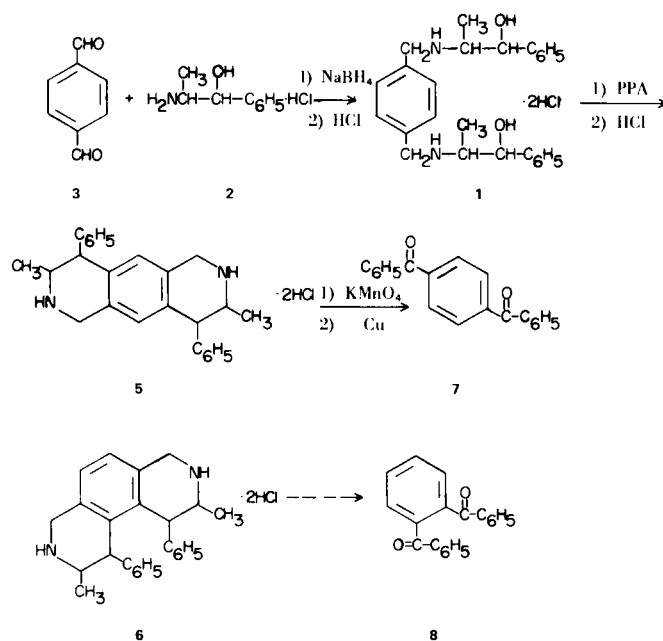
Compound **1** was prepared by reductive condensation of 2-amino-1-phenyl-1-propanol hydrochloride (**2**) and terephthalic dicarboxaldehyde (**3**) using sodium borohydride (**4**). Cyclization of **1** in PPA and treatment of the resultant product with hydrogen chloride gave a product, the infrared spectrum and elemental analysis of which were consistent with a tricyclic material of molecular formula $C_{26}H_{28}N_2 \cdot 2HCl$. Although the insolubility of this compound precluded nuclear magnetic resonance spectral determination, the spectrum of the corresponding free base was also consistent with that of a tricyclic compound. The nmr spectrum of the crude free base indicated that only one product was formed in the cyclization.

None of these properties permitted a distinction between the linear pyrido[3,4-g]isoquinoline (**5**) and the angular 3,8-phenanthroline (**6**) as the product of cyclization. The nmr spectrum of the material exhibited an aromatic singlet significantly upfield from the unsubstituted phenyl protons in a relative ratio of 2:10 and this singlet is attributed to the protons of the tetrasubstituted phenyl. Although this singlet would normally suggest that the linear product **5** was formed, the two aromatic protons in the symmetrical angular product **6** occupy the same environment and would similarly be expected to appear as a singlet.

To permit a selection between **5** and **6** as a cyclization product of **1**, an oxidation-decarboxylation degradation sequence was utilized. Potassium permanganate oxidation of this product followed by copper powder-catalyzed decarboxylation afforded the known *p*-dibenzoylbenzene (**7**), thereby indicating the material in question to be the linear compound **5**. The angular substance **6** would be expected to yield *o*-dibenzoylbenzene **8** by this degradative scheme.

The aliphatic C-H signals in the nuclear magnetic resonance spectrum of the product was not sufficiently resolved to permit a decision regarding the stereochemistry of **5**.

This apparently is the first reported example of the pyrido[3,4-g]isoquinoline ring system.



EXPERIMENTAL

Melting points were taken in a Mel-Temp apparatus in open capillary tubes and are uncorrected. The nuclear magnetic resonance spectrum was taken on a Varian A-60A instrument and was compared with TMS as an internal standard. Infrared spectra were determined on a Perkin-Elmer 137B spectrophotometer.

N,N'-bis(1-Hydroxy-1-phenyl-2-propyl)-*p*-xylene- α,α' -diamine Dihydrochloride (**1**).

A solution containing 149.6 g. (0.80 mole) of 2-amino-1-phenyl-1-propanol hydrochloride (**2**), 53.6 g. (0.40 mole) of terephthalic dicarboxaldehyde (**3**), 80.8 g. (0.80 mole) triethylamine, and 700 ml. of methanol was stirred at ambient temperature for 20 minutes. The solution was stirred at 20-30° while sodium borohydride (30 g., 0.80 mole) was added over 1 hour. The mixture was stirred for 2 hours, concentrated to dryness *in vacuo*, and the residue was partitioned between 1500 ml. of water and 500 ml. of chloroform. The aqueous layer was extracted with 2 x 500 ml. of chloroform and the combined extracts were dried (magnesium sulfate) and concentrated to dryness to give 160 g. (99%) of the product.

Treatment of the oil with methanolic hydrogen chloride gave **1** (95 g., 50%), m.p. > 320° after one recrystallization from methanol; ir (Nujol) μ : 3.00 (O-H); 9.25 (C-OH).

Anal. Calcd. for $C_{26}H_{32}N_2O_2 \cdot 2HCl$: C, 65.40; H, 7.18; N, 5.87. Found: C, 65.43; H, 7.18; N, 5.77.

1,2,3,4,6,7,8,9-Octahydro-3,8-dimethyl-4,9-diphenylpyrido[3,4-g]-isoquinoline Dihydrochloride (**5**).

To 960 g. of polyphosphoric acid was added 160 g. (0.395 mole) of **1**. The mixture was stirred and heated to 80° until the reaction became exothermic and the temperature rose to 130°. The mixture was stirred at ambient temperature for 18 hours and poured into 6 l. of cold tap water. The solution was stirred and made alkaline with 1 l. of 50% potassium hydroxide. The product was filtered to give 156 g. of a white solid; nmr (DMSO-d₆): δ 0.95 (d, 6, J = 6 Hz, CH₃); 3.50-4.10 (broad m, exchangeable, 2, N-H); 3.95 (m, 8, CH₂, CH); 6.33 (s, 2, aromatic C-H); 7.20-7.30 (m, 10, aromatic C-H).

The product was suspended in 2 l. of methanol. Methanolic hydrogen chloride was added to give in three crops 58 g. (33%) of the product. The analytical sample, m.p. 344° dec., was obtained by boiling the product with methanol and subsequent drying; infrared (Nujol) μ: 6.20, 6.30 (C=C); no O-H absorption at 3.00-3.10.

Anal. Calcd. for C₂₆H₂₈N₂·2HCl: C, 70.74; H, 6.85; N, 6.35. Found: C, 71.04; H, 6.99; N, 6.17.

Degradation of **5** to *p*-Dibenzoylbenzene (**7**).

A 5.10 g. (0.0117 mole) portion of **5** and 10 g. of potassium hydroxide in 500 ml. of water was heated to boiling. Potassium permanganate (12.0 g., 0.076 mole) was added and the solution was refluxed for 5.5 hours. Excess permanganate was destroyed with ethanol and the mixture was filtered and washed with chloro-

form. Acidification with hydrochloric acid gave 1.75 g. (40%) of a white solid which was mixed with 0.60 g. of copper metal (electrolytic dust, purified) and heated at 260-280° for 15 minutes. The cooled mixture was extracted with 4 x 20 ml. of boiling chloroform and the combined extracts were concentrated to dryness *in vacuo* to give 0.60 g. of product (18% overall from **5**). The infrared spectrum was identical with that of an authentic sample of **7**. Recrystallization and subsequent vacuum sublimation at 180-200° (0.1 mm) gave *p*-dibenzoylbenzene, observed m.p. 163-165°; m.p. of a commercially available sample of *p*-dibenzoylbenzene: 164-167°; literature m.p. 161° (3). A 50-50 mixture of the two substances melted at 164-166°. The nmr spectra of the two materials were identical.

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