The Preparation of the Benzo[4,5]cyclohepta[1,2-*b*]pyrazine and Benzo[4,5]cyclohepta[1,2-*b*]quinoxaline Systems

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Benzo[4,5]cyclohepta[1,2-*b*]quinoxaline **2**, benzo[4,5]cyclohepta[1,2-*b*]pyrazine **3a** and benzo[4,5]cyclohepta[1,2-*b*]quinoxaline **4** were prepared from 4,5-benzotropolone and 1,2-phenylenediamine, ethylenediamine and 1,2-diaminocyclohexane, respectively. Compound **3a** was methylated to **3b**.

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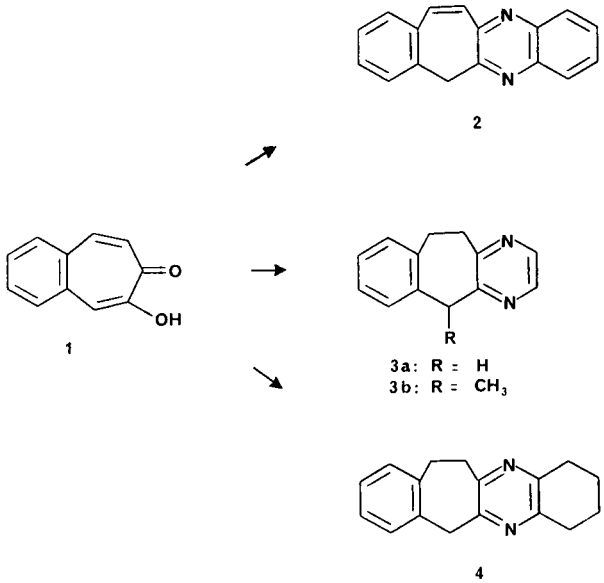
The 4,5-benzotropolone system (1) is known to undergo reactions with amines to give 6-amino-7*H*-benzocyclohepten-2-one (2). Since these intermolecular reactions allow the introduction of only one amino group into the benzotropolone, we have investigated (3) the feasibility of introducing a second amino group *via* an intramolecular condensation, since such reactions would give access to hitherto unknown heterocyclic systems. This is in analogy to the condensation between tropolone methyl ether and 1,2-phenylenediamine which gave 5*H*-cyclohepta[*b*]quinoxaline (4).

An analogous compound was obtained when we heated 4,5-benzotropolone (**1**) with 1,2-phenylenediamine in the presence of hydrochloric acid. The structure of the product **2** was assigned based on nmr and ir spectral data.

Scheme 1



When 4,5-benzotropolone (**1**) was treated with ethylenediamine in the presence of a catalytic amount of hydrochloric acid a condensation between the two components took place as expected. In this case however the double bonds migrated into the heterocyclic ring to form the pyrazine **3a** in 85% yield. This assignment was based on the nmr spectrum of **3a**. The quartet at δ 8.16 ppm (J = 3 Hz) was found to collapse to a singlet when the spectrum of **3a** was recorded in the presence of trifluoroacetic acid and shifted to lower field (8.9 ppm). The chemical shift observed below δ 8 ppm therefore seemed to exclude the presence of the 2,3-dihydro isomer in favor of the 10,11-dihydro isomer **3a**.

Proof for the position of the double bond in question was available from the nmr spectrum of compound **4**. This was prepared from 4,5-benzotropolone and 1,2-diaminocyclohexane, albeit in low yield. If the isolated material were the 1,2,3,4,4a,13a-hexahydro-6*H*-isomer, the ratio of low field to high field protons would be 6:12 while in fact the nmr spectrum of **4** clearly showed a ratio of 4:14 (see experimental section). Direct comparison of the spectra for **3** and **4** further supported these assignments.

The methylene bridges between the aromatic rings of compounds described above should be acidic enough to permit the abstraction of a proton. This was demonstrated with compound **3a** in the presence of sodium hydride in dimethyl formamide followed by the treatment with methyl iodide to give compound **3b**. However an alkylation of **3b** under similar conditions was not successful.

EXPERIMENTAL

Melting points were determined on a Thomas Hoover capillary melting point apparatus and were not corrected. Nmr spectra were measured on either a Varian A-60 and/or T-60 spectrometer and were recorded in δ ppm values from TMS as internal standard. Ir spectra were taken on a Perkin-Elmer Model 257 or 457. Gas-liquid chromatography was carried out on a Hewlett-Packard 5750 Chromatograph. Mass spectra were taken on a LKB 9000 Mass spectrometer.

6*H*-Benzo[4,5]cyclohepta[1,2-*b*]quinoxaline (**2**).

Prepared from 1.7 g. (0.01 mole) of 4,5-benzotropolone and 0.5 g. (0.005 mole) of 1,2-phenylenediamine hydrochloride in 1.5 g. of 1,2-phenylenediamine at 125°. The product was treated with 2*N* sodium hydroxide solution in the presence of ether and dried over sodium sulfate. The crude product was recrystallized from ethanol, yield 0.7 g. (29%); m.p. 144-146°; m/e 244 [M$^+$]; nmr (deuteriochloroform): δ 4.19 (s, 2, CH_2) 7.1-8.1 (m, 10, 2 C_6H_4 + CH=CH); ir (dichloromethane): 1625 cm^{-1}.

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Anal. Calcd. for $C_{17}H_{12}N_2$ (244.3): C, 83.6; H, 5.0; N, 11.5. Found: C, 83.2; H, 4.9; N, 11.1.

10,11-Dihydro-5*H*-benzo[4,5]cyclohepta[1,2-*b*]pyrazine (**3a**).

A mixture of 15.0 g. (0.087 mole) of 4,5-benzotropolone, 5.7 g. (0.043 mole) of ethylenediamine hydrochloride in 100 ml. of ethylenediamine was heated to reflux for 2.5 hours under an atmosphere of nitrogen. The solvent was evaporated under reduced pressure, the residue dissolved in chloroform, washed with 2*N* sodium hydroxide and dried over sodium sulfate. The crude product was distilled twice in a Kugelrohr (b.p. 125-150°/0.05 mm) to give 14.5 g. (85%) of the product; m.p. 35-36°; m/e 196 [M⁺]; nmr (deuteriochloroform): δ 3.1-3.3 (m, 4, CH_2CH_2) 4.34 (s, 2, CH_2) 7.1-7.4 (m, 4, C_6H_4) 8.1-8.3 (m, 2, $C_4H_2N_2$); ir (film): 1560, 1480 cm^{-1}.

Anal. Calcd. for $C_{13}H_{12}N_2$ (196.2): C, 79.6; H, 6.2; N, 14.3. Found: C, 79.3; H, 6.4; N, 14.3.

10,11-Dihydro-5-methylbenzo[4,5]cyclohepta[1,2-*b*]pyrazine (**3b**).

To a suspension of 0.1 g. (0.005 mole) of sodium hydride in 10 ml. of absolute DMF a solution of 0.5 g. (0.0025 mole) of **2a** in 10 ml. of DMF was added under an atmosphere of nitrogen. After 1 hour at RT, 0.4 g. (0.028 mole) of methyl iodide was added. After 2 hours at RT the solvent was evaporated under reduced pressure and the residue worked up as usual in chloroform. The crude material was chromatographed on silica gel to give 0.5 g. (56%) of product, m.p. 75-76° (ethanol/water); m/e 210 [M⁺]; nmr (deuteriochloroform): δ 1.75 (d, 3, J = 7 Hz, CH_3) 3.1-3.5 (m, 4, CH_2CH_2) 4.64 (q, 1, J = 7 Hz, CH), 7.0-7.4 (m, 4, C_6H_4) 8.27 (s, 2, $C_4H_2N_2$).

Anal. Calcd. for $C_{14}H_{14}N_2$ (210.3): C, 80.0; H, 6.7; N, 13.3. Found: C, 80.3; H, 6.3; N, 13.6.

1,2,3,4,11,12-Hexahydro-6*H*-benzo[4,5]cyclohepta[1,2-*b*]quinoxaline (**4**).

A mixture of 8.3 g. (0.048 mole) of 4,5-benzotropolone and 9.5 g. (0.05 mole) of 1,2-diaminocyclohexane hydrochloride in 30.0 g. of 1,2-diaminocyclohexane was heated to 125° under nitrogen for 2.5 hours. The crude material was worked up in chloroform as described above. Column chromatography (silica gel) gave 1.2 g. of material from which the crystalline product was obtained; yield 0.520 g. (4%), m.p. 76-77°; m/e 250 [M⁺]; nmr (deuteriochloroform): δ 1.4-2.1 (m, 4, $2CH_2$) 2.5-3.0 (m, 4, $2CH_2$) 3.20 (s, 4, $C_6H_4CH_2CH_2$) 4.28 (s, 2, $C_6H_4CH_2C_4N_2$) 7.1-7.4 (m, 4, C_6H_4).

Anal. Calcd. for $C_{17}H_{18}N_2$ (250.4): C, 81.6; H, 7.2; N, 10.9. Found: C, 81.3; H, 7.2; N, 10.9.

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