Strained Heterocyclic Systems. III. Cyclobuta[*b*]quinoxaline Derivatives (1)

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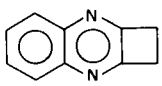
As an extension of our work on the influence of fused, strained rings on adjacent hetero atoms (1,3), we now report studies directed toward the synthesis of 1,2-dihydrocyclobuta[*b*]quinoxaline (**1**), an analog of 1,2-dihydrocyclobuta[*b*]quinoline (**2**) (3,4). Compound **1** has



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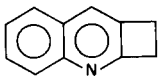

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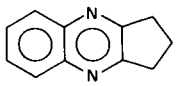
proved to be elusive and remains unknown. Starting with 2,3-bis(bromomethyl)quinoxaline and a variety of derivatives, Moriconi and Fritsch were unable to effect the desired intramolecular cyclizations (5). Mindful of these difficulties, we directed our attention to condensations of cyclobutanone derivatives.

Initially, two known pathways to **3** were considered appropriate models (6). Landquist obtained **3** from the acid-catalyzed condensation of cyclopentanone with *o*-phenylazoaniline (9). More recently, Haddadin and Issidorides prepared the 4,9-dioxide derivative (**4**) by the novel reaction of benzofurazan oxide with an enamine of



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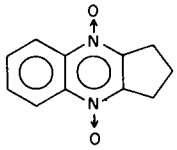

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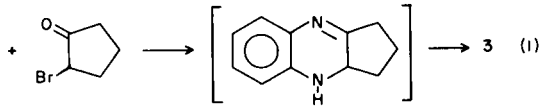
cyclopentanone (10). The latter authors, in the analogous case of 1,2,3,4-tetrahydrophenazine 5,10-dioxide, smoothly effected bis-deoxygenation with sodium dithionite. In the present study **3** was prepared by both routes in low overall yield. These two schemes failed, however, when applied to cyclobutanone. The recent report of the abnormal behavior of cyclobutanone enamines (11) undoubtedly accounts for the difficulties in the latter case.

A condensation previously reported with acyclic ketones proved more interesting. Based on the preparation of 2-benzoyl-3-phenylquinoxaline from *o*-phenylenediamine (**5**) and dibenzoylbromomethane (12,13), treatment of **5** with 2-bromocyclopentanone gave **3** in satisfactory yield. Compared to the routes outlined above, this reaction (Eq. 1) is the method of choice for **3**. Similarly from 2-bromocyclobutanone, 1,2,2a,3-tetrahydrocyclobuta[*b*]-quinoxaline (6) was obtained.



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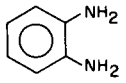

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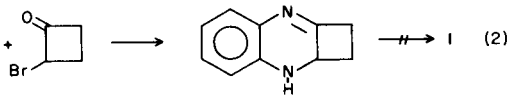

(2)

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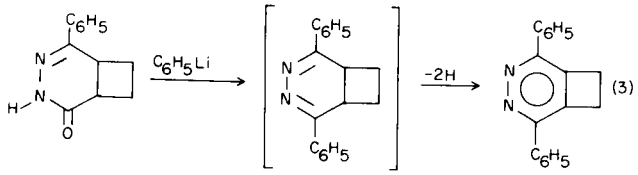
The structural assignment was based on mass spectral and proton magnetic resonance data. The mass spectrum contained only two major peaks: the molecular ion at *m/e* 158 and the base peak at *m/e* 157. The absence of peaks higher than M^+ established the intramolecular nature of the condensation. The predominance of the M-1 peak is consistent with loss of a hydrogen from C-2a with concomitant aromatization (14). The nmr spectrum was consistent with only one tautomer. The absence of vinyl protons and the presence of one methine and one N-H proton require the postulated structure.

Compound **6** represents the nearest approach yet reported to the desired system. The final conversion of **6** to **1**, however, could not be effected. Attempted dehydrogenations with chloranil, lead tetraacetate, or 30% palladium on charcoal led to recovery of starting material. Such inability to achieve aromatization is in marked contrast to the spontaneous loss of hydrogen observed in closely related systems: the present route to **3** (Eq. 1) and the recently reported preparation of **7**, 2,5-diphenyl-3,4-diazabicyclo[4.2.0]octa-1,3,5-triene, (Eq. 3) (15). The influence of a fused, four-membered ring on the chemical reactivity in a related system has been noted previously (3).



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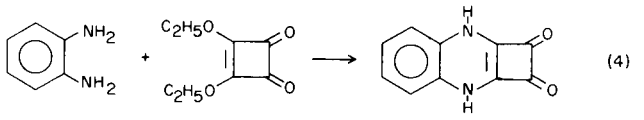
As an adjunct to the present studies, the reaction of *o*-phenylenediamine with 1,2-diethoxycyclobutenedione (diethyl squarate) was investigated (Eq. 4). The product, 1,2,3,8-tetrahydro-1,2-dioxocyclobuta[*b*]quinoxaline (**8**), was identical with that reported by Skujins and Webb (16), who described the first preparation of **8** by an alternate route.



8

EXPERIMENTAL (17)

2,3-Dihydro-1*H*-cyclopenta[*b*]quinoxaline (**3**).

A. From *o*-Phenylazoaniline (9).

A solution of *o*-phenylazoaniline (99 mg., 0.50 mmole) (18) and cyclopentanone (42 mg., 0.50 mmole) in 15 ml. of toluene containing 2 mg. of *p*-toluenesulfonic acid was refluxed for 4 hours in an apparatus fitted with a Dean-Stark trap and then concentrated at reduced pressure to give a viscous residual oil, which slowly crystallized at room temperature. The solid was chromatographed in carbon tetrachloride on 10 g. of alumina to give 33 mg. (39%) of **3**, m.p. 97-98.6°; recrystallization from water gave m.p. 99.2-99.7° (lit. (9) m.p. 99-100°). When the same condensation was tried with cyclobutanone, column chromatography of the residue gave no isolable products.

B. From Benzofurazan Oxide.

The method of Haddadin and Issidorides (10) afforded **4** (47% after recrystallization from methanol), m.p. 181° dec. (lit. (10) m.p. 182° dec.). It was discovered that the preparation of the enamine could be omitted. Thus, a solution of benzofurazan oxide (19) (0.53 g., 0.0039 mole) and cyclopentanone (0.33 g., 0.0039 mole) in 10 ml. of morpholine was left at room temperature for 16 hours and then chilled to give 0.64 g. (81%) of **4**. When the simplified procedure was attempted with cyclobutanone, only recovered benzofurazan oxide was obtained.

Several reagents were employed for the conversion of **4** to **3**. The use of sulfur dioxide (20) gave 1.5% of **3**. Phosphorus trichloride (21) or triethyl phosphite (22) gave a residual solid which was chromatographed as above to give **3** in yields of 4% and 6%, respectively. The use of sodium dithionite (13) gave intractable solids from which no material with m.p. $<300°$ could be isolated.

C. From *o*-Phenylenediamine (12).

A solution of 2-bromocyclopentanone (23) (0.49 g., 0.0030 mole) and **5** (0.32 g., 0.0030 mole) in 90 ml. of diethyl ether was stirred for 1.5 hours at room temperature while dry air was bubbled into the mixture, then diluted with an equal volume of water, basified, washed twice with aqueous alkaline portions, and dried. Removal of the solvent yielded 0.39 g. (77%) of crude product which was chromatographed as above to give **3**.

1,2,2a,3-Tetrahydrocyclobuta[*b*]quinoxaline (**6**).

To a solution of 2-bromocyclobutanone (23) (0.50 g., 0.0034 mole) and **5** (0.72 g., 0.0067 mole) in 13 ml. of methanol-water (10:3, v/v) was added 1 ml. of concentrated sulfuric acid. The mixture was refluxed for 1 hour, concentrated at reduced pressure, diluted with 10 ml. of water, neutralized with 10% sodium bicarbonate solution, and extracted with chloroform. The combined extract was washed, dried and evaporated to give 0.41 g. of residual solid which, when chromatographed in chloroform on an alumina column, afforded 0.13 g. (25%) of **6** m.p. 224-226°. The crude product was dissolved in sulfuric acid and precipitated with base to give **6**, m.p. 227-228.2°: infrared (potassium bromide) cm^{-1}, 3125-2950, 1548, 1455, 1420, 1246, and 752; nmr (DMSO-d_6) δ 7.5-7.0 (m, 4), *ca.* 3.3 (1, N-H), 2.05 (m,1,H-2a), 1.08 (d,2,H-2), and 0.98 (s,2,H-1); mass spectrum (70 eV) ***m/e*** (relative intensity) 158 (86), 157 (100), 156 (15), 132 (22), and 66 (8).

Anal. Calcd. for $C_{10}H_{10}N_2$: C, 75.92; H, 6.37; N, 17.71. Found: C, 75.83; H, 6.25; N, 18.00.

Attempted Dehydrogenation of **6**.

Recovered starting material was the only substance obtained from the following treatments of **6**: 30% palladium on charcoal in refluxing *p*-cymene for 2.5 hours (24); chloranil in refluxing xylene for 5 hours (25); chloranil in refluxing *t*-butyl alcohol for 4 hours (26); and lead tetraacetate in pyridine (27).

1,2,3,8-Tetrahydro-1,2-dioxocyclobuta[*b*]quinoxaline (**8**).

A mixture of **5** (1.08 g., 0.010 mole) and 1,2-diethoxycyclobutenedione (1.70 g., 0.010 mole) in 25 ml. of benzene was refluxed for 2 hours in an apparatus fitted with a Dean-Stark trap and then evaporated to dryness at reduced pressure. The quantitative yield of crude product, m.p. 315-320° dec., was recrystallized from dimethylformamide-water (charcoal) to give 0.88 g. (47%) of **8**, m.p. 325° dec. (lit. (16) m.p. 330° dec.). The infrared and nmr spectra were identical to those of an authentic sample (m.p. 327° dec.).

Anal. Calcd. for $C_{10}H_6N_2O_2$: C, 64.52; H, 3.25; H, 15.05. Found: C, 64.21; H, 3.32; N, 15.24.

Acknowledgments.

We are indebted to Mr. W. C. Jankowski (Varian) for the nmr spectra and to Miss Sherri Firth (University of California, Berkeley) for the mass spectra. Professor G. A. Webb (University of Surry) kindly provided a sample of **8**. We thank Dr. K. L. Loening (Chemical Abstracts Service) for consultation on Nomenclature. Acknowledgment if made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this work.

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(17) Melting points and boiling points are uncorrected. Infrared spectra were obtained in potassium bromide with a Perkin-Elmer Model 237B spectrophotometer. Nmr spectra were determined in dimethylsulfoxide-d_6 on a Varian A-60D spectrometer; the data are reported in ppm downfield from tetramethylsilane as internal standard. Mass spectra were measured on a CEC 21-103C instrument. Analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

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Received October 16, 1968 Williamstown, Mass. 01267