Strained Heterocyclic Systems. VI. Basicities of Some Quinoxalines[1]

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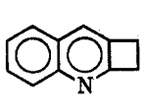
The basicities of a series of 2,3-disubstituted quinoxalines were determined by potentiometric titration in acetic anhydride. A decrease in basicity was observed for those compounds containing a fused, strained ring adjacent to the heteroatoms. Such an effect was consistent with previous interpretations based on orbital rehybridization. In conjunction with the present study, J (^{13}C–H) values were determined for the benzylic protons of acenaphthene and pyracene.

It has recently been established that a fused strained ring adjacent to the nitrogen atom in a quinoline ring causes a marked decrease in the basicity of such heterocyclic compounds.[2-4] These observations are in accord with the concept of orbital rehybridization developed by Streitwieser and coworkers to account for the changes in kinetic acidity and reactivity toward electrophilic substitution observed with strained carbocyclic systems.[5] This interpretation has gained support from a variety of studies: J (^{13}C–H) nmr data,[6,7] esr data,[8,9] rates of protodesilylation,[10] polarographic reduction potentials,[11] and molecular orbital calculations.[12]

In our earlier studies of 1,2-dihydrocyclobuta[*b*]quinoline (**1**) and acenaphtho[1,2-*b*]quinoline (**2**) de-



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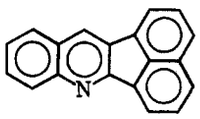

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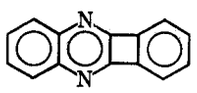
creases in basicity of ten- and fivefold, respectively, were observed relative to model compounds. Since there is greater strain in biphenylene than in benzocyclobutene,[13] it was anticipated that pK_a data for an azabiphenylene would exhibit a further substantial decrease in basicity. Although no monoazabiphenylenes have been reported in the literature, the diazabiphenylene, benzo[3,4]cyclobuta[1,2-*b*]quinoxaline (**3**), has been known for some time.[14] This report, therefore, presents the synthesis and basicity measurements of a series of strained quinoxaline derivatives.



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Results and Discussion

The compounds selected for this study are listed in Table I. Basicities were determined as half-neutralization potentials (HNP) at 25° in acetic anhydride by titration with perchloric acid in acetic acid. The apparent acid dissociation constants (pK_a) were calculated from the known values of selected quinoxalines and the assumption that HNP (Ac_2O) and pK_a (H_2O) are linearly related.[15] Structures **4**, **5**, and **7** of known aqueous acidities[16] were used to calibrate the above extrapolation. Compounds **8** and **10** were model compounds of previously unknown basicity. Compounds **3**, **6**, and **9** were the desired quinoxalines containing strained fused rings adjacent to the heteroatoms. Those compounds, not commercially available, were prepared by condensation of *o*-phenylenediamine with the appropriate α diketone.

TABLE I

BASICITIES OF 2,3-DISUBSTITUTED QUINOXALINES

Compound	HNP,[a] mV	pK_a
2,3-Dimethylquinoxaline (**4**)	468	2.08[c]
Phenazine (**5**)	536	1.23[d]
1,2-Dihydrocyclopent[5,6]acenaphtho-[1,2-*b*]quinoxaline (**6**)	536[b]	1.23
Quinoxaline (**7**)	548	1.03[d]
2,3-Diphenylquinoxaline (**8**)	564	0.85
Acenaphtho[1,2-*b*]quinoxaline (**9**)	573	0.72
Benzo[3,4]cyclobuta[1,2-*b*]quinoxaline (**3**)	581[b]	0.62
Dibenzo[*a*,*c*]phenazine (**10**)	607	0.30

[a] Duplicate runs, ±2 mV, at 25° unless otherwise stated. [b] At 30°. [c] Reference 16a. [d] Reference 16b.

The basicity data are presented in Table I. The sequence of relative base strengths (**7** > **8** > **9** > **3**) was in accord with prediction. The diphenyl (**8**) and acenaphtho (**9**) derivatives exhibited the same relative effects in the quinoline series.[3] The fact that **3** was the least basic in the above series confirmed our expectations, although the decrease in basicity relative to **8** (*ca.* twofold) was less than that anticipated. This discrepancy may be attributed to the effect of the second nitrogen atom, which is the dominant influence. The difference between the basicities of

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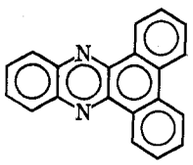
quinoline (pK_a 4.94) and quinoxaline (pK_a 1.03) is quite striking.[16b] Compared to the heteroatom effect, the influence of a strained ring is clearly secondary.

The basicities of two other compounds require comment. It was not anticipated that dibenzo[*a*,*c*]phenazine (**10**) would be the least basic of the present



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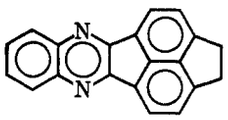
series. The difficulty in protonating **10**, however, can be ascribed to steric inhibition of solvation of the conjugate acid. Comparable effects have been observed with benzo[*a*]phenazine, in which the reactivity of N-12 is rendered much less than that of N-7,[17] and with benzo[*f*]- and benzo[*h*]quinoline, in which the latter is unreactive toward methyl iodide.[18] The enhanced basicity of **6** relative to **9** also was not expected. In



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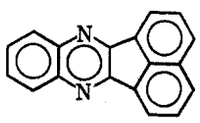

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fact, it was assumed initially that **6** would be less basic than **9**. The molecular geometry of acenaphthene is known,[19] and the strain is accommodated mainly by changes in bond angles. These adjustments result in a C_5–C_{5a}–C_6 bond angle of 128°. Although the geometry of pyracene has not been determined, it seemed reasonable that whatever strain is present in acenaphthene would be increased by the incorporation of an ethylene bridge across C_5–C_6. This was confirmed by nmr measurements on the ^{13}C–H coupling constants for the benzylic protons of acenaphthene (129 Hz) and pyracene (132.5 Hz). A threefold enhancement in the basicity of **6** compared to **9** was, therefore, quite remarkable. This change undoubtedly reflects the electron-releasing character of the ethylene bridge in **6**. A similar effect has been observed for product distribution and partial rate factors in the nitration of acenaphthene.[20]

Experimental Section[21]

Materials.—The following compounds were obtained from Aldrich Chemical Co.: phenazine (**5**), recrystallized from acetic acid, mp 175.3–175.9° (lit.[22] mp 174.9–175.6°); quinoxaline (**7**); 2,3-diphenylquinoxaline (**8**), recrystallized from 95% ethanol, mp 125.8–126.7° (lit.[23] mp 124.0–124.5°); and dibenzo[*a*,*c*]-phenazine (**10**), recrystallized from benzene, mp 224.8–225.7° (lit.[24] mp 220–222°). Benzo[3,4]cyclobuta[1,2-*b*]quinoxaline (**3**) was prepared from benzocyclobutenedione[25] by the method of Cava,[28] mp 229.3–229.9. (lit.[28] mp 238–239°). 2,3-Dimethylquinoxaline (**4**) was prepared from biacetyl and recrystallized from water, mp 105.9–106.3° (lit.[29] mp 106°). 1,2-Dihydrocyclopent[5,6]acenaphtho[1,2-*b*]quinoxaline (**6**) was prepared from 5,6-dihydrocyclopenta[*f*,*g*]acenaphthylene-1,2-dione (diketopyracene)[30] by the method Richter and Stocker[31] and recrystallized from benzene–ligroin, mp 275.5–276.5° (lit.[31] mp 275–276°). Acenaphtho[1,2-*b*]quinoxaline (**9**) was prepared from acenaphthenequinone and recrystallized from benzene, mp 239.5–240.3° (lit.[32] mp 241°). Acetic anhydride (J. T. Baker, assay 99.2%) and 0.10 *N* perchloric acid in acetic acid (Fisher Certified Reagent) were used without further purification.

Basicity Determinations.—Basicities were determined by potentiometric titration with a Beckman Model 76 expanded scale pH meter fitted with a glass indicator electrode and a saturated calomel reference electrode, previously equilibrated with acetic anhydride for 48 hr. Titrations were carried out at 25.00 ± 0.02° under a nitrogen atmosphere in a water-jacketed cell connected to a constant temperature bath and fitted with a Teflon cover drilled to accommodate two electrodes, buret, thermometer (certified by the Natioanl Bureau of Standards), and nitrogen inlet tube. In a typical run an accurately weighed amount of the compound (*ca.* 10^{-3} mol) was dissolved in acetic anhydride in a nitrogen-swept 50-ml volumetric flask; a 20-ml aliquot was transferred under nitrogen to the titration cell, diluted with 80 ml of acetic anhydride, and with magnetic stirring titrated with 0.10 *N* $HClO_4$ in acetic acid (*ca.* 7 ml). The end point and half-neutralization potential were determined graphically; all runs were carried out in duplicate, with a precision of ±2 mV. Compounds **3** and **6** were not completely soluble at 25°; these measurements were conducted at 30.00 ± 0.05°, along with redeterminations of **5**, **7**, and **10** for calibration purposes.

Nmr Data.—The ^{13}C–H coupling constants for the benzylic protons of acenaphthene and 1,2,5,6-tetrahydrocyclopent[*f*,*g*]-acenaphthylene (pyracene) were determined as saturated solutions in CCl_4 and $DCCl_3$, respectively, with tetramethylsilane as an internal standard. The acenaphthene spectrum was obtained with the aid of a Varian time-averaging computer attached to a Varian HA-100 instrument; 100 scans were required to delineate the sidebands. The low solubility of pyracene precluded the above procedures. Its spectrum was obtained by the Fourier transform pulse mode and required 13,500 scans. The J (^{13}C–H) values thus obtained for acenaphthene and pyracene were 129 ± 1 Hz and 132.5 ± 1 Hz, respectively, which correspond to 25.8 and 26.5% *s* character for the benzylic C–H bonds.

Registry No.—**3**, 259-57-4; **4**, 2379-55-7; **5**, 92-82-0; **6**, 33068-15-4; **7**, 91-19-0; **8**, 1684-14-6; **9**, 207-11-4; **10**, 215-64-5.

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