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PYRRO[3,4-b]QUINOXALINES. STABLE ANALOGS OF BENZO[f]ISOINDOLE

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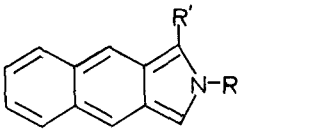
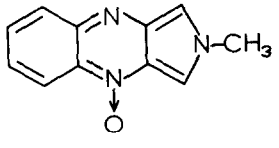
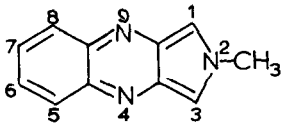
A recent communication by Shields and Bornstein (1) reported the synthesis of benzo[f]isoindole (Ia) and its 1-phenyl derivative (Ib). These compounds were found to be unstable under the conditions used in attempts to effect their isolation from solution, and were characterized *via* their stable N-phenylmaleimide adducts. Wittig (2) has reported an unsuccessful attempt to prepare 2-methylbenzo[f]isoindole (Ic), but it is not clear whether this failure indicates instability of Ic relative to the stable 2-substituted isoindole system, or simply an enhanced reactivity of an intermediate species in a competing side-reaction. In this paper we report the preparation of stable diaza-analogs of Ic, *vis.*, 2-methylpyrro[3,4-b]quinoxalines (II, III).



I a. R = R' = H
b. R = H, R' = Ph
c. R = Me, R' = H



II



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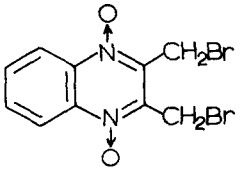
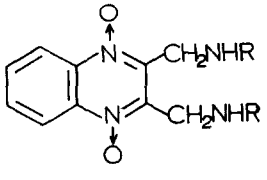


IV



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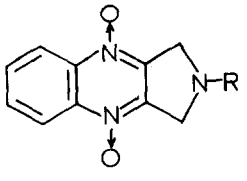
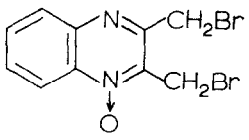


VI

Landquist and Silk (3) reported that 2,3-bisbromomethylquinoxaline 1,4-dioxide (IV) gave "red mixtures which did not yield the desired derivatives" rather than simple displacement products (V) or cyclic tertiary amines (VI) upon treatment with aliphatic primary amines, but gave the expected tertiary amine products upon reaction with secondary amines. On the basis of mechanistic considerations, it appeared likely to us that IV should be converted to II by reaction with methylamine under appropriate conditions. This expectation was realized when IV was added to liquid methylamine at -80° and the mixture was stirred and allowed to warm to room temperature. Compound II was obtained in 85% yield. Purification by repeated recrystallization from benzene gave lustrous red needles having mp 174°d which were stable to storage at room temperature in air.

Compound II was converted to the desoxy derivative (III) by treatment with phosphorus trichloride in chloroform (4) and also by treatment with Raney nickel in methanol (5). Compound III was also prepared conveniently in 80% yield by reaction of 2,3-bisbromomethylquinoxaline 1-oxide (VII) (3) with liquid methylamine. Repeated



VII

recrystallization from benzene gave dark red prisms which decomposed above 170°, but which were stable to storage in air at room temperature.

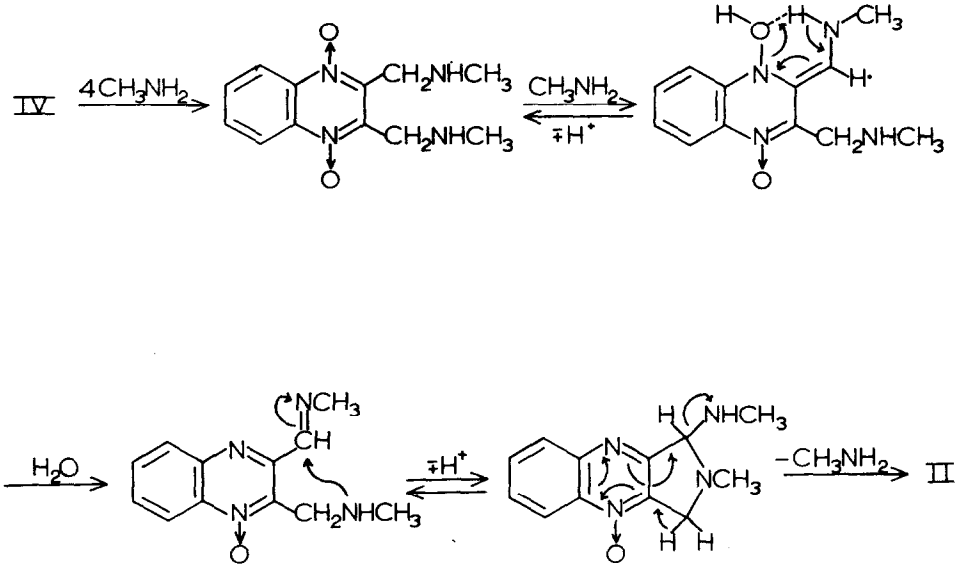
The mass spectra of II and III indicate divergent fragmentation behavior, but both exhibit intense peaks corresponding to the molecular ions (M^+) at m/e 199 and 183, respectively. Peaks corresponding to loss of an oxygen atom from II (183) and M^+-1 (182) and M^{++} (91.5) for III were also relatively intense. The N-methyl pmr absorptions occur as sharp singlets at δ4.17 in II and 4.26 in III, which is well downfield of the usual N-methyl region and indicated that N-2 serves as an efficient π-electron donor in the ground states of pyrro[3,4-b]quinoxalines. The signals due to protons at positions 1 and 3 are not resolved at 60 MHz, and appear as a singlet at δ7.55 in II and 7.56 in III. The protons at positions 5,6,7, and 8 give rise to a complex multiplet ranging

from δ7.40 - 8.50 in II, and a well-defined ABB'A' multiplet centered about δ7.80 in III. The ir spectrum of II exhibits a very strong band at 7.55μ (1320 cm^{-1}) which is attributed to N-O stretching. No comparable band is present in the ir spectrum of III. Compounds II and III both give intense red solutions in protonic solvents. Addition of HCl causes a large bathochromic shift and the solutions become blue in color. The uv-vis spectral characteristics of II and III are given in Table I.

Table I

		methanol	Methanol-HCl
II	λ_{max} (Log ε)	261 (4.78), 348 (3.97), 506 (3.63)	263 (4.54), 362 (4.08), 584 (3.38)
III		258 (4.53), 344 (3.88), 352 (3.96), 356 (3.90), 504 (3.24)	250 (4.26), 265 (4.36), 362 (4.05), 372 (4.03), 578 (3.18)

A variety of plausible mechanistic schemes can be written for the conversion of IV to II. One such scheme is shown below.



Extensions and adaptations of this method of synthesis of pyrro[3,4-b]-quinoxalines appear to offer access to a wide variety of aza-isoindoles and their oxygen, sulfur, and

selenium analogs, which are ring systems that have not been reported at the present time. Further work to establish the scope and utility of this method is being carried out in our laboratories. Acknowledgments. Mass spectra were obtained using an instrument purchased through an N.S.F. Scientific Equipment Grant (GP 5503).

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