

Mitchel M. Roland (1) and Richard C. Anderson

Department of Chemistry and Biochemistry, Utah State University, Logan, Utah 84322

Received February 14, 1977

The transient existence of thieno[3,4-*b*]quinoxaline (**2d**) as a product of dehydration of 1,3-dihydrothieno[3,4-*b*]quinoxaline 2-oxide (**5**) was demonstrated by trapping experiments with *N*-phenylmaleimide and dimethyl acetylenedicarboxylate. Attempts to isolate **2d** from reaction mixtures arising from dehydration of **5** and from dehydrogenation of 1,3-dihydrothieno[3,4-*b*]quinoxaline (**8**) were unsuccessful.

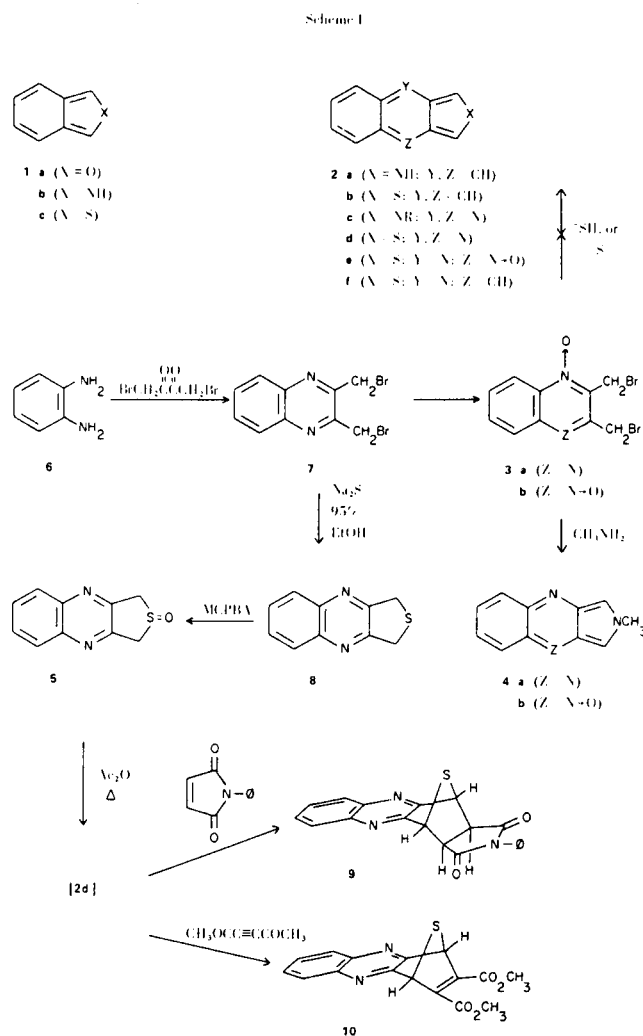
J. Heterocyclic Chem., 14, 541 (1977).

Isobenzofuran (**1a**), isoindole (**1b**), and isothianaphthene (**1c**) have all been isolated and characterized (2). Analogous systems having an additional six membered ring fused in a linear mode, (2), have proven elusive and appear to be less stable. Thus, benzo[*f*]isoindole (**2a**) and benzo[*f*]isothianaphthene (**2b**) have resisted isolation, but have been characterized *via* their adducts with *N*-phenylmaleimide (3). Pyrrolo[3,4-*b*]quinoxalines (**2c**) have been isolated and are relatively stable (4). We report here attempts to synthesize and characterize thieno[3,4-*b*]quinoxaline (**2d**). Key intermediates in this study were 2,3-bisbromomethylquinoxaline (**7**) and its mono- and di-*N*-oxides (**3a** and **3b**, respectively).

2-Methylpyrrolo[3,4-*b*]quinoxaline 4-oxide (**4b**) and 2-methylpyrrolo[3,4-*b*]quinoxaline (**4a**) are formed in good yield by reaction of methylamine with **3b** and **3a**, respectively (4). By analogy, it was reasoned that treatment **3a** or **3b** with sulfide or hydrosulfide salts might yield **2d** or **2e**. Actually, only dark intractable products were obtained, even though reaction conditions were varied over a wide range.

The synthesis of 1,3-dihydrothieno[3,4-*b*]quinoxaline 2-oxide (**5**) was accomplished as outlined in Scheme I. Reaction of *o*-phenylenediamine (**6**) with 1,4-dibromo-2,3-butanedione at 0° in ethanol gave 2,3-bisbromomethylquinoxaline (**7**) in 81% yield. Ring closure to 1,3-dihydrothieno[3,4-*b*]quinoxaline (**8**) was accomplished in 40% yield by reaction of **7** with sodium sulfide in ethanol at room temperature. Selective oxidation of **8** to **5** was carried out in 75% yield, using one equivalent of *m*-chloroperbenzoic acid in chloroform at -25°. Use of sodium metaperiodate as an oxidant gave unsatisfactory results.

The sulfoxide (**5**) was mixed with alumina and heated to 150° at 0.5 mm in a sublimation apparatus. It was anticipated that pyrolytic dehydration of **5** to form **2d** would occur and that **2d** might sublime from the alumina quickly enough to avoid decomposition (5). Only a small amount of **5** was obtained as a sublimate and extraction of the residual alumina with chloroform yielded an amorphous, intractable residue. Neither catalytic dehydrogenation of **8** using palladium on carbon, nor oxidation of **8** using chloranil or DDQ yielded **2d** as a reaction product.



Dehydration of **5** in refluxing acetic anhydride and with trifluoroacetic anhydride in anhydrous ether gave extensive decomposition. When the reaction in hot acetic anhydride was carried out in the presence of *N*-phenylmaleimide, a crystalline product (**9**) was obtained which was characterized as the exo Diels-Alder adduct of **2d**. Similarly, a crystalline adduct **10** of **2d** was obtained when dimethyl acetylenedicarboxylate was employed as a trapping agent.

The structures of **9** and **10** were assigned on the basis of their elemental analyses and spectroscopic properties. The nmr spectrum of **9** (DMSO- d_6) has two singlets of equal intensity at 3.58 (2H) and 4.45 (2H) corresponding to the hydrogens α to the imido carbonyls and the bridge-head hydrogens, respectively, as well as broad multiplets from 7.65-8.20 (9H) for aromatic hydrogens. These data are in very close agreement with those reported by MacDowell (3c) and Cava (3b) for the *exo*-*N*-phenylmaleimide adducts of **2b** and **2f**, and differ substantially from the spectra reported for the *endo* stereoisomers. The mass spectrum of **9** has a weak peak at *m/e* 359 which corresponds to the molecular ion, and the base peak is at *m/e* 186 which corresponds to loss of *N*-phenylmaleimide to give a cation corresponding to the molecular ion of **2d**.

The nmr spectrum of **10** (DMSO- d_6) exhibited singlets at 3.33 (3H) and 4.90 (1H) and a broad multiplet in the range 7.65-8.25 (2H). The molecular ion in the mass spectrum of **10** was observed at *m/e* 328 and the base peak was *m/e* 186.

It appears certain, therefore, that **2d** is formed by dehydration of **5** in refluxing acetic anhydride, but that **2d** is not sufficiently stable to survive the conditions of the reaction and/or work-up and permit isolation. Thus, if the presence of two nitrogen atoms in **2d** as compared to **2b** does have a stabilizing effect as proposed by MacDowell (3c), the effect is not great enough to permit isolation of **2d**.

EXPERIMENTAL (6)

2,3-Bisbromomethylquinoxaline (**3a**).

1,4-Dibromo-2,3-butanedione (45 g., 0.18 mole) and *o*-phenylenediamine (**6**) (19.9 g., 0.18 mole) were dissolved in ethanol in separate flasks. The solutions were cooled to 0° and poured together. After a few seconds, the solution became tea-colored, and a precipitate formed. After thirty minutes, the precipitate was collected and purified by recrystallization from aqueous to yield 47 g. (81%) of **3a**, m.p. 151-152° [lit. (7) m.p. 150-151°]; ir: 3000, 2950, 1480, 1420, 1358, 1200, 760, and 685 cm^{-1} ; nmr: δ 4.91 (s, 1H), and 7.65-8.20 (m, 1H).

1,3-Dihydrothieno[3,4-*b*]quinoxaline (**8**).

2,3-Bisbromomethylquinoxaline (**3a**) (21.0 g., 0.067 mole) was added in one portion to a stirred solution of sodium sulfide nonahydrate (36.0 g., 0.15 mole) in 300 ml. of 95% ethanol. The reaction mixture became yellow immediately, then orange, then red over a ten minute period. The mixture was stirred at room temperature for a total of 40 minutes and filtered using suction. The filtrate was diluted with 100 ml. of water and extracted overnight in a liquid-liquid extractor with petroleum ether (30-60°). The ether extract was dried with anhydrous sodium sulfate and evaporated to give 5.5 g. of crude **8** as a yellow colored solid which was sublimed at 90° and 0.1 mm to give pure **8** (5.0 g., 40%) as white crystals having m.p. 111-112° (lit. (2b) m.p. 112-113°); ir (potassium bromide): 2940, 2910, 1485, 1330, 1355, 1115 and 740 cm^{-1} ; nmr (deuteriochloroform): δ 4.35 (s, 1H) and 7.58-8.12 (m, 1H).

1,3-Dihydrothieno[3,4-*b*]quinoxaline 2-Oxide (**5**).

1,3-Dihydrothieno[3,4-*b*]quinoxaline (**8**) (3.0 g., 0.016 mole) was dissolved in chloroform (150 ml.) and cooled at -20° in a dry ice-acetone bath. *m*-Chloroperbenzoic acid (3.0 g., 0.17 mole) was dissolved in chloroform (100 ml.) and cooled to -20° and was then added in ten portions to the stirred, cooled, original solution. The addition was complete in five minutes. The stirred reaction mixture was allowed to warm to room temperature and was washed three times with 25 ml. portions of saturated sodium carbonate solution and then dried over anhydrous sodium sulfate. Evaporation of the reaction mixture gave the sulfoxide, (**5**), as a white solid. Recrystallization from benzene yielded 2.6 g. (78.5%) of **5** as white plates, having m.p. 157-158° dec.; ir: 3050, 2980, 2900, 1490, 1380, 1320, 1200, 1100, 1035, and 775 cm^{-1} ; nmr: δ 4.45 (s, 1H) and 7.65-8.20 (m, 1H).

Anal. Calcd. for $\text{C}_{10}\text{H}_8\text{N}_2\text{OS}$: C, 58.80; H, 3.95; N, 13.72; S, 15.70. Found: C, 58.78; H, 4.03; N, 13.58; S, 15.82.

exo-*N*-Phenylmaleimide Adduct (**9**) of Thieno[3,4-*b*]quinoxaline (**2d**).

1,3-Dihydrothieno[3,4-*b*]quinoxaline 2-oxide (**5**) (0.1 g., 0.0049 mole) was dissolved in 35 ml. of freshly distilled acetic anhydride and the system was purged with dry nitrogen. *N*-Phenylmaleimide (0.85 g., 0.0048 mole) was added, and the mixture was refluxed for 20 minutes during which time it became quite dark, and it was then poured into a slurry 300 ml. of water and cracked ice. The mixture was stirred and then extracted with two 50 ml. portions of chloroform. The chloroform extract was washed three times with water and then dried over anhydrous sodium sulfate. After filtration, the orange-yellow solution was evaporated to small volume. A grey-white precipitate formed which was collected by filtration and recrystallized from benzene/hexane to yield 0.86 g. (47%) of **9** having m.p. 310° dec.; ir: 1775, 1700, 1385, 1185, 750, and 685 cm^{-1} ; nmr: δ 4.98 (s, 2H), 3.58 (s, 2H), and 6.60-7.80 (m, 9); mass spectrum: (70 eV) *m/e* 359 (M^+), 186 (base peak).

Anal. Calcd. for $\text{C}_{20}\text{H}_{13}\text{N}_3\text{O}_2\text{S}$: C, 66.80; H, 3.66; N, 11.70. Found: C, 66.80; H, 3.39; N, 11.79.

Dimethyl Acetylenedicarboxylate Adduct (**10**) of Thieno[3,4-*b*]quinoxaline (**2d**).

The reaction was carried out as described above for the *N*-phenylmaleimide adduct. Evaporation of the reaction mixture gave a dark viscous residue, which was treated with 25 ml. of an ice-water slurry, then extracted with three 10 ml. portions of chloroform. Evaporation of the dried (magnesium sulfate) chloroform extract, followed by recrystallization of the residue from acetonitrile gave 0.62 g. of **10** having m.p. 87-90°; ir: 1740, 1310, 1220, 770, and 760 cm^{-1} ; nmr: δ 3.33 (s, 3H), 4.90 (s, 1H), 7.65-8.25 (m, 2H); mass spectrum: (70 eV) *m/e* 328 (M^+), 186 (base peak).

Anal. Calcd. for $\text{C}_{16}\text{H}_{12}\text{N}_2\text{O}_4\text{S}$: C, 58.52; H, 3.69; N, 8.53. Found: C, 58.28; H, 3.79; N, 8.41.

REFERENCES AND NOTES

- (1a) This investigation was partially supported by an NSF Traineeship (NSF-GZ977, 1339, and 1743) to M.M.R. (b) Present address: Thiokol Chemical Corporation, Promontory, Utah.
- (2a) R. Mayer, H. Kleinert, S. Richter, and K. Gewalt, *Angew. Chem., Int. Ed. Engl.*, **1**, 115 (1962); (b) M. P. Cava and N. M. Pollack, *J. Am. Chem. Soc.*, **88**, 4112 (1966); (c) D. Wege, *Tetrahedron Letters*, 2337 (1971); (d) R. N. Warrener, *J. Am. Chem. Soc.*, **93**, 2346 (1971); (e) R. Bonnett and R. F. C. Brown,

J. Chem. Soc., Chem. Commun., 393 (1972); G. M. Priestley and R. N. Warrener, *Tetrahedron Letters*, 4295 (1972).

(3a) J. E. Shields and J. Bornstein, *Chem. Ind. (London)*, 1404 (1967); (b) M. P. Cava, N. M. Pollack, O. A. Manner, and J. M. Mitchell, *J. Org. Chem.*, **36**, 3932 (1971); (c) D. W. H. MacDowell, A. J. Jeffries, and M. B. Meyers, *ibid.*, **36**, 1416 (1971).

(4) R. C. Anderson and R. H. Fleming, *Tetrahedron Letters*,

(5) By analogy with a procedure for preparation of isothianaphthene described in (2b).

(6) Melting points were determined by the capillary method and are uncorrected. Mass spectra were taken using Perkin-Elmer RMU-6E mass spectrometer. Elemental analyses were performed by M-H-W Laboratories, Garden City, Michigan.

(7) J. Wegmann and H. Dahn, *Helv. Chem. Acta*, **29**, 95 (1946).