Formation of Quinoxaline Monoxides from Reaction of Benzofurazan Oxide with Enones and ^{13}C NMR Correlations of Quinoxaline *N*-Oxides[1]

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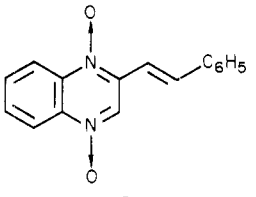
Benzofuran oxide (1) reacts with a variety of enones and amines to give quinoxaline monoxides. The nature of the amine determines the regiochemistry of the product: secondary amines give a type 4 product and primary amines give a type 5 product. Reaction of 1, cinnamaldehyde, and morpholine gave both **4a** and **8a**. The regiochemistry of these *N*-oxide products is discussed in terms of intermediate 11. Principal limitations of these reactions for synthesis are the low yields and the lack of universality for enones as substrates. ^{13}C NMR correlations for quinoxaline monoxides and dioxides are presented.

Benzofurazan oxide (1) reacts with enamines that are preformed or generated in situ, and also with enolates, to form quinoxaline di-*N*-oxides (Scheme I). This reaction, which has been referred to as the Beirut reaction, is an excellent method for preparing a variety of heterocyclic compounds that possess a range of antimicrobial activities.[2]

Our interest in preparing the styryl-substituted quinoxaline di-*N*-oxide **2** led to an investigation of the reaction



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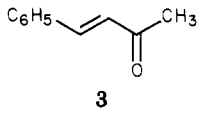

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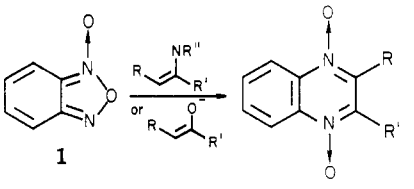
of benzalacetone (**3**) and 1 with an amine. We expected that **3** and an amine might react to form an enamine (or an enolate), which could then combine with 1 to form the desired **2**. When morpholine was used as the amine, none of the desired **2** was observed in the product mixture; however, the quinoxaline mono-*N*-oxide **4a** (R′ = C_6H_5) was obtained in 22% yield. Furthermore, a change of the amine reactant from morpholine to *n*-butylamine resulted in the formation of the acetylquinoxaline mono-*N*-oxide **5a** (R = CH_3, R′ = C_6H_5). By their unexpected nature, the products **4a** and **5a** presented a challenge for further work.

Results and Discussion

Benzofurazan oxide (1) reacts with a variety of enones and amines to give quinoxaline monoxides. The structure of the quinoxaline product is determined by the amine reactant: a primary amine gives a 3-acylquinoxaline 1-oxide (**5**) while a secondary amine gives a deacylated quinoxaline 1-oxide (**4**). Tertiary amines give no quinoxaline product derived from the enone **3**.[3] These reactions are summarized in Scheme II and Table I.[4]

Structure Proof and ^{13}C NMR Correlations. The assignment of gross structural features for each of the compounds in Table I was straightforward, and the structure assignment problem for each compound centered on which of the two ring nitrogens was the *N*-oxide. A recent report by Dirlam[5] on selective monodeoxygenation of quinoxaline 1,4-dioxides provided a route, in several cases, for preparing comparison samples. Structure **4b** was based on the facts that it differed from 2-methylquinoxaline 1-oxide,[5] and it was transformed to 2-methylquinoxaline 1,4-dioxide by oxidation with *m*-chloroperbenzoic acid (MCPBA). **5b** prepared by our route was identical with a sample prepared by the Dirlam route.[5]

Scheme I. The Beirut Reaction



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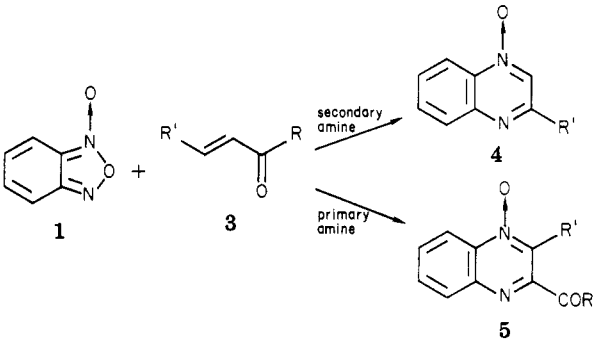
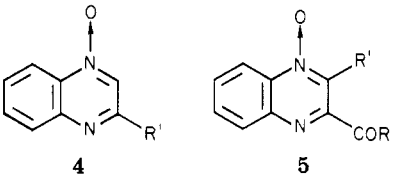
Scheme II



1 3 4 5

Table I. Quinoxaline Monoxides Prepared by Scheme II



4 5

enone	amine[a]	quinoxaline monoxide (% yield)
4-phenyl-3-buten-2-one	M	**4a**, R′ = C_6H_5 (22)
	P	**4a** (35)
	B	**5a**, R = CH_3; R′ = C_6H_5 (16)
	C	**5a** (27)
3-penten-2-one	M	**4b**, R′ = CH_3 (26)
	B	**5b**, R = R′ = CH_3 (24)
2-cyclohexen-1-one	M	**4c**, R′ = $(CH_2)_3CON$⟨O⟩

[a] M = morpholine, P = pyrrolidine, B = *n*-butylamine, C = cyclohexylamine.

(1) Contribution no. 536 from the Institute of Organic Chemistry and Contribution no. 3 from Analytic Research.

(2) See: Haddadin, M. J.; Issidorides, C. H. *Heterocycles* **1976**, *4*, 767.

(3) A reviewer has pointed out that heating benzofurazan oxide with triethylamine gives quinoxaline 1,4-dioxide in 5–8% yield.

(4) For a preliminary account of this work see: Lewis, G. S.; Kluge, A. F. *Tetrahedron Lett.* **1977**, 2491.

(5) Dirlam, J. P.; McFarland, J. W. *J. Org. Chem.* **1977**, *42*, 1360.

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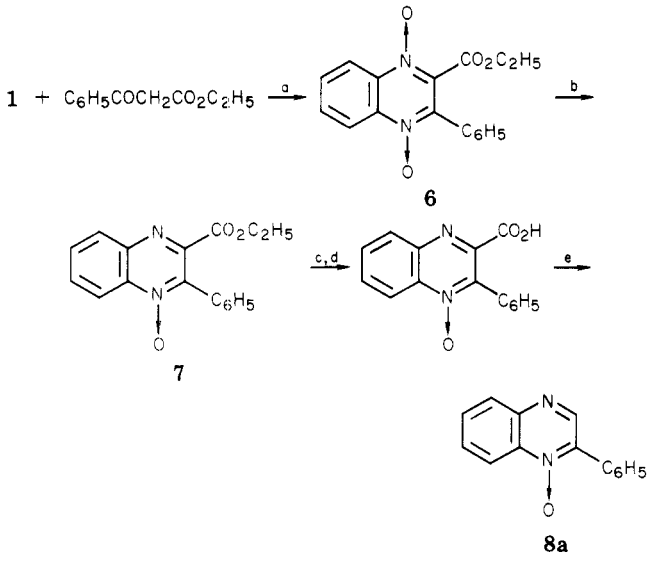
Scheme III[a]

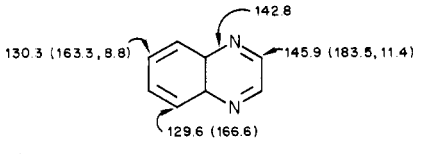


[a] (a) $Ca(OH)_2$, 2-PrOH; (b) $P(OCH_3)_3$, PrOH; (c) NaOH; (d) HCl; (e) toluene, reflux.

The assignment given to **4a** was based on the following arguments: (1) its identity with an independently prepared sample,[6] (2) its difference from 2-phenylquinoxaline 1-oxide (**8a**) (Scheme III),[7,8] and (3) its transformation with MCPBA to the known 2-phenylquinoxaline 1,4-dioxide.

We were unable to make structural assignments for **4c** and **5a** by using the chemical transformations of a quinoxaline 1-oxide into a 2-chloroquinoxaline with phosphorus oxychloride. **5a** could not undergo chlorine substitution without undergoing radical fragmentation, and **4c** produced an intractable tar.[4] Both the lack of suitable reference compounds and the lack of universality in degradation procedures made it highly desirable to develop spectral correlations which could be used for assigning structures in quinoxaline monoxides.

By compiling ^{13}C NMR spectra for our products, the monoxides described by Dirlam,[5] and various quinoxaline dioxides prepared by the Beirut reaction, we were able to assign the key carbon absorptions (Table II). The assignments in Table II are based on off-resonance decoupling (OFDR), selective decoupling (SFDR), examination of coupled spectra, and analogy with other aromatic systems. Data for quinoxaline have been reported;[9] however,



for a more direct comparison with the *N*-oxides, chemical shifts and coupling constants (in parentheses) measured in Me_2SO-d_6 are shown here. In the spectrum of quinoxaline 1-oxide (**9**), C-8 was identified by SFDR and by analogy with the well-known shifts caused by peri substituents in naphthalenes.[10] Peaks assignable to C-2 and C-3 were identified by SFDR and from the coupled spectrum. Peaks assignable to C-9 and C-10 were obvious in the OFDR spectrum. The assignments of C-2 and C-9 were given to the higher-field resonance of the pairs C-2/C-3 and C-9/C-10 by analogy with the relative proton and carbon chemical shifts of the double bond in an enone system. The assignments of C-2 and C-3 were confirmed by examination of the spectra of **4b** and **8b**, compounds whose structure had been established by chemical means. In addition, the relative chemical shifts of the methyl carbons of **4b** and **8b** provided confirmation of the structural assignments since the methyl carbon of **8b** was 7.3 ppm upfield from that of **4b** by virtue of the shielding effect of the ortho oxygen.[11] In the spectrum of **4b**, the methyl substituent caused a 9.1-ppm downfield shift of C-3 relative to the position of C-3 in **9**. The magnitude of this shift was quite close to that of the substituent effect of a methyl group in benzene[12] or naphthalene.[10] Also, in comparison to **9**, it was seen that C-2 in **8b** was shifted 10 ppm downfield while C-3 was shifted only 0.8 ppm.

Features common to the spectra of **4b**, **8b**, and **9** provide the basis for establishing the location of a substituent in a monosubstituted structure such as **4** and **8**. Since the signals due to C-2 and C-3 in **9** are separated by 17.5 ppm, a determination of the chemical shift of the unsubstituted carbon immediately establishes the point of attachment of the substituent in a monosubstituted structure each as **4** or **8**. In this same context if the proton-bearing carbon has a chemical shift greater than 145 ppm, then the substituent must be at C-2, and if the proton-bearing carbon has a shift less than 130 ppm, then the substituent is attached to C-3. Moreover, if one of the substituents is methyl, then the chemical shift of the methyl carbon can be used to establish the point of attachment: methyl groups attached to C-2 have chemical shifts less than 15 ppm, while those attached to C-3 have shifts greater than 20 ppm.

The trends seen in the chemical shifts in the quinoxaline dioxides in Table II are those expected for the shielding effects resulting from transforming N-4 to an *N*-oxide. Comparison of comparably substituted monoxide and dioxide pairs shows that both C-3 and C-5 have experienced upfield shifts in the dioxide.

Mechanism. The initial stage of the reaction between **1** and an enone requires the generation of a nucleophilic species. Typically **1** behaves as an electrophile.[2] A role for the amine reactant in the generation of the required nucleophile is implied from the observation that no reaction occurs between **1** and an enone in the absence of a primary or secondary amine.

A mechanism for the combination of **1**, an enone, and an amine to form a quinoxaline monoxide is shown in Scheme IV. The reaction is initiated by a nucleophile generated through Michael addition of morpholine to *trans*-3-penten-2-one. **10**[5] was not detected in the course of the reaction, hence, there must necessarily be a re-

(6) Landquist, J. K.; Stacy, G. J. *J. Chem. Soc.* **1953**, 2822. The crude product from this procedure contains ca. 20% 2-phenylquinoxaline 1,4-dioxide as an impurity. This impurity persisted through repeated recrystallizations, so a pure sample of **4a** could be obtained only by chromatography. **8a** was not detected in the crude product mixture.

(7) The synthesis of **8a** is directly analogous to that described in ref 5.

(8) **8a** has been prepared by selective monodeoxygenation of 2-phenylquinoxaline 1,4-dioxide by sulfurous acid in methanol: Hayashi, E.; Iijima, C. *Yakugaku Zasshi* **1962**, *82*, 1093; *Chem. Abstr* **1963**, *58*, 4551.

(9) (a) Pugmire, R. J.; Grant, D. M.; Robins, M. J.; Robins, R. K. *J. Am. Chem. Soc.* **1969**, *91*, 6381. (b) Tori, K.; Nakagawa, *J. Phys. Chem.* **1964**, *68*, 3163. (c) Johannesen, R. B. *J. Chem. Phys.* **1967**, *47*, 3088.

(10) (a) Ernst, L. *Chem. Ber.* **1975**, *108*, 2030. (b) Seita, J.; Sandstrom, J.; Drakenberg, T. *Org. Magn. Reson.* **1978**, *11*, 239. (c) Kitching, W.; Bullpitt, M.; Garshore, D.; Adcock, W.; Khor, T. C.; Doddrell, D.; Rae, I. D. *J. Org. Chem.* **1977**, *42*, 2411. (d) Wilson, N. K.; Stothers, J. B. *J. Magn. Reson.* **1974**, *15*, 31.

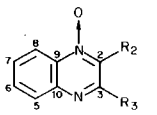
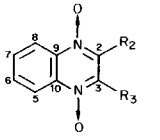
(11) Woolfenden, W. R.; Grant, D. M. *J. Am. Chem. Soc.* **1966**, *88*, 1496.

(12) Levy, G. C.; Nelson, G. L. "Carbon-13 Nuclear Magnetic Resonance for Organic Chemists"; Wiley-Interscience: New York, 1972; p 81.

(13) (a) Latham, D. W. S.; Meth-Cohn, O.; Suschitzky, H. *Tetrahedron Lett.* **1972**, 5365. (b) *J. Chem. Soc., Perkin Trans. 1* **1976**, 2216.

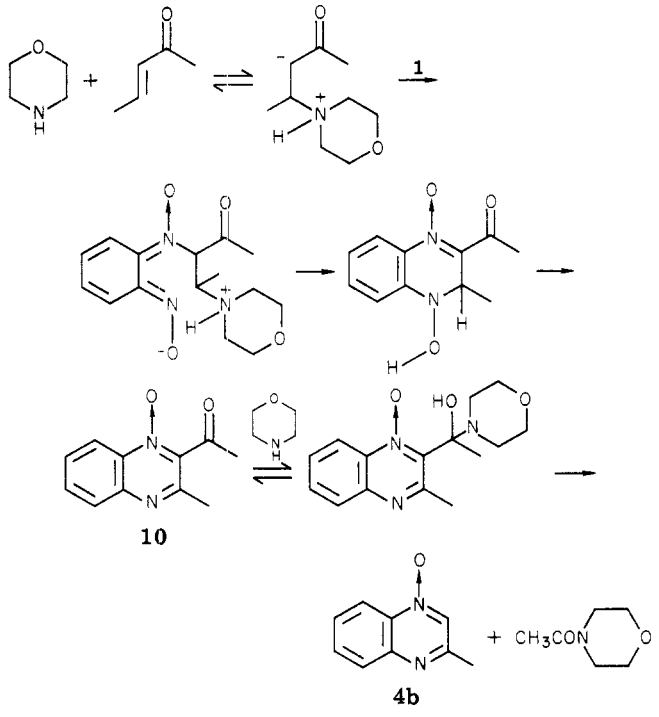
(14) We mistakenly reported in ref 4 that this reaction gave only **4a**.

Table II. ^{13}C NMR Chemical Shifts (ppm)

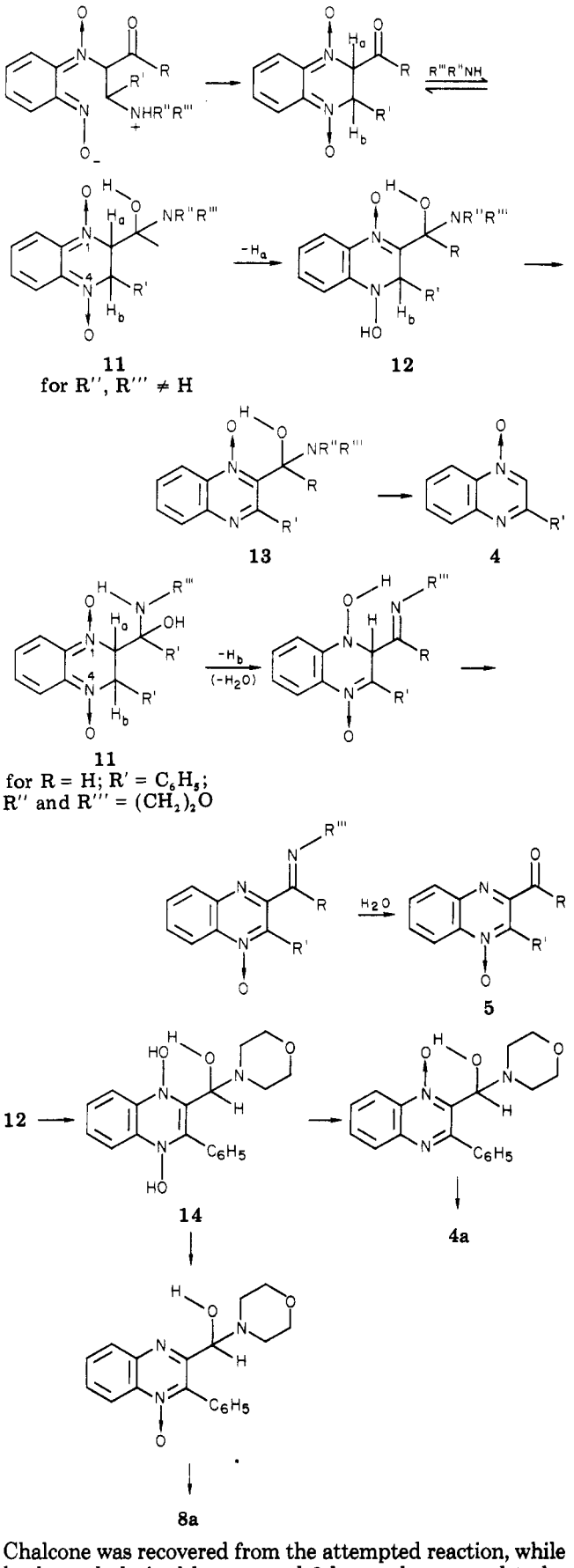
	C-2	C-3	C-5	C-6	C-7	C-8	C-9	C-10	other
 quinoxaline monoxides									
9, $R_2 = R_3 = H$[a]	129.7	147.2	129.9	132.0	130.4	118.4	136.8	145.4	
4b, $R_2 = H$; $R_3 = CH_3$[b]	129.1	156.3	129.2	131.8	129.5	118.2	135.0	144.6	22.2 (CH_3)
8b, $R_2 = CH_3$; $R_3 = H$[c]	139.7	148.0	129.8	130.7	130.1	118.2	136.3	144.0	14.9 (CH_3)
4a, $R_2 = H$; $R_3 = C_6H_5$[d]	127.5	153.7	129.0	132.3	130.9	118.3	135.4	144.6	129.0 (C-4′), 129.9 (C-3′), 135.1 (C-1′), 127.3 (C-2′)
8a, $R_2 = C_6H_5$; $R_3 = H$[e]	138.6	148.0	130.0	131.5	130.6	118.8	136.7	144.0	136.7 (C-1′), 128.4 (C-2′), 129.6 (C-3′), 129.8 (C-4′)
4c, $R_3 = CH_2CH_2CH_2CON$ (morpholino)	129.4	159.5	129.3	131.9	129.4	118.3	135.1	144.6	170.7 (CO), 66.1 (OCH_2), 45.4 (NCH_2), 41.4 (NCH_2), 34.9 ($COCH_2$), 31.3 ($ArCH_2$), 23.5 (CH_2)
10, $R_2 = COCH_3$; $R_3 = CH_3$[c]	137.5	152.2	129.1	132.5	130.0	118.0	134.5	143.7	197.7 (CO), 29.5 (CH_3CO), 21.8 (CH_3)
5b, $R_2 = CH_3$; $R_3 = COCH_3$	139.5	150.6	130.3	132.0	131.4	118.3	136.3	141.2	200.0 (CO), 27.8 (CH_3CO), 13.4 (CH_3)
15, $R_2 = CO_2CH_3$; $R_3 = CH_3$[c]	134.4	152.0	129.2	132.8	130.3	118.2	133.0	143.8	162.2 (CO_2), 53.7 (OCH_3), 21.6 (CH_3)
16, $R_2 = CH_3$; $R_3 = CO_2CH_3$[c]	139.7	146.7	130.2	131.9	131.5	118.2	136.5	141.8	164.9 (CO_2), 53.2 (OCH_3), 13.8 (CH_3)
7, $R_2 = C_6H_5$; $R_3 = CO_2CH_2CH_3$	138.6	148.7	130.2	132.4	131.9	118.8	137.2	143.0	164.3 (CO_2), 62.0 (OCH_2), 13.4 (CH_3), 129.9 (C-3′), 129.6 (C-4′), 129.6 (C-1′), 128.4 (C-2′)
5a, $R_2 = C_6H_5$; $R_3 = COCH_3$	137.1	152.8	130.2	132.3	132.0	118.9	138.4	142.5	199.1 (CO), 130.0 (C-1′), 130.0 (C-3′), 129.3 (C-4′), 128.2 (C-2′), 28.3 (CH_3)
19, $R_2 = R_3 = H$[c]	131.2	131.2	120.0	132.0	132.0	120.0	138.2	138.2	
20, $R_2 = H$; $R_3 = CH_3$[d]	131.7	141.4	119.5	131.9	130.9	119.8	136.9	137.6	15.0 (CH_3)
21, $R_2 = H$; $R_3 = C_6H_5$[e]	131.6	140.5	120.2	132.2	131.6	119.8	137.0	138.3	130.4 (C-4′), 129.8 (C-3′), 128.2 (C-2′), 129.1 (C-1′)
22, $R_2 = COCH_3$; $R_3 = CH_3$[b]	138.4	139.5	119.5	132.5	131.5	119.4	136.2	137.5	195.6 (CO), 29.6 (CH_3CO), 13.5 (CH_3)
23, $R_2 = CO_2CH_3$; $R_3 = CH_3$[b]	134.8	138.5	119.7	132.8	131.7	119.7	136.3	137.6	160.3 (CO_2), 53.9 (OCH_3), 14.1 (CH_3)
 quinoxaline dioxides									
17, $R_2 = R_3 = H$[c]	131.2	131.2	120.0	132.0	132.0	120.0	138.2	138.2	
18, $R_2 = H$; $R_3 = CH_3$[d]	131.7	141.4	119.5	131.9	130.9	119.8	136.9	137.6	15.0 (CH_3)
19, $R_2 = H$; $R_3 = C_6H_5$[e]	131.6	140.5	120.2	132.2	131.6	119.8	137.0	138.3	130.4 (C-4′), 129.8 (C-3′), 128.2 (C-2′), 129.1 (C-1′)
20, $R_2 = COCH_3$; $R_3 = CH_3$[b]	138.4	139.5	119.5	132.5	131.5	119.4	136.2	137.5	195.6 (CO), 29.6 (CH_3CO), 13.5 (CH_3)
21, $R_2 = CO_2CH_3$; $R_3 = CH_3$[b]	134.8	138.5	119.7	132.8	131.7	119.7	136.3	137.6	160.3 (CO_2), 53.9 (OCH_3), 14.1 (CH_3)
6, $R_2 = CO_2CH_2CH_3$; $R_3 = C_6H_5$	135.5	139.1	120.3	132.9	132.4	119.8	136.9	138.2	130.5 (C-4′), 130.0 (C-3′), 129.4 (C-1′), 128.5 (C-2′), 165.0 (CO_2), 62.3 (OCH_2), 13.9 (CH_3)
22, $R_3 = CH_2CH_2CH_2CON$ (morpholino)	131.4	144.1	119.7	132.0	131.0	119.7	137.0	137.8	170.4 (CO), 66.2 (OCH_2), 45.4 and 41.4 (NCH_2), 31.5 (CH_2CO), 27.8 ($ArCH_2$), 20.7 (CH_2)

[a] Landquist, J. K. *J. Chem. Soc.* **1953**, 2816. [b] Reference 16. [c] Reference 5. [d] Reference 6. [e] Reference 8.

Scheme IV



Scheme V



quirement for rapid deacylation[4,15] of **10** by morpholine as the reaction progresses. When **10** was combined with morpholine under standard reaction conditions, only 30% of **10** was deacylated to give **4b**.

Modification of Scheme IV provides a way of rationalizing both the above result with **10** and also the fact that a primary amine leads to a different product type than that which was obtained with a secondary amine (Scheme V). From intermediate **11** it can be seen in the secondary amine case (R″, R‴ ≠ H) that the loss of H_a and protonation of the oxygen on N-4 (**12**) lead through **13** to the formation of the type **4** product. In the primary amine case (R″ = H), the propinquity of the proton on the amine nitrogen to the oxygen on N-1 allows for the facile loss of H_b followed by the formation of the fully aromatic system and the hydrolysis of the imine to give the observed product **5**.

In the case of the reaction of **1**, cinnamaldehyde, and morpholine, we obtained both **4a** and **8a**. The appearance of these two products may be explained in terms of a lessened steric interaction between R (H) and R′ (C_6H_5) in **12**, enabling the transfer of H_b to the oxygen on N-1 to give **14**. Intermediate **14** may lose the elements of water followed by the fragmentation of morpholine formamide to give either **4a** or **8a**.

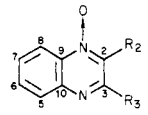
Limitations on Synthetic Utility. While the reaction of **1** with enones has the advantage of giving specific quinoxaline monoxides, the reaction suffers from the disadvantages that the yields are uniformly low and that several enones have failed to give quinoxaline products. Moreover, we have uncovered one case in which there was no specificity in the formation of the quinoxaline *N*-oxides.

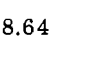
Several α,β-unsaturated carbonyl compounds were found to be unproductive substrates. No quinoxaline monoxide product was detected in each case from the reaction of **1** with 1,3-diphenyl-2-propenone (chalcone), methyl vinyl ketone or 2-butenal in the presence of morpholine. Chalcone was recovered from the attempted reaction, while both methyl vinyl ketone and 2-butenal appeared to be consumed in the reaction.

The low yields (13–35%) associated with the products in Table I can be explained in terms of competing side

(15) In addition to examples of this type of deacylation cited in ref 4, there is a general patent claim for deacylation of quinoxaline-2-carboxaldehyde 1,4-dioxide by secondary amines with $pK_a > 8$ to give high yields of quinoxaline 1,4-dioxides: Myers, R. F. U.S. Patent 3 947 438 (1976).

Table III. ^{1}H NMR Chemical Shifts (ppm)



	H-2	H-3	other
9, $R_2 = R_3 = H$	8.66 (d, J = 3.5 Hz)	8.81 (d, J = 3.5 Hz)	
4b, $R_2 = H$; $R_3 = CH_3$	8.61 (s)		2.62 (s, 3, CH_3)
8b, $R_2 = CH_3$; $R_3 = H$[c]		8.88 (s)	2.54 (s, 3, CH_3)
4a, $R_2 = H$; $R_3 = C_6H_5$	8.82		
8a, $R_2 = C_6H_5$; $R_3 = H$		9.07	
4c, $R_3 = CH_2CH_2CH_2CON$ 	8.64		

[a] Solvent Me_2SO-d_6. [b] McIlwain, H. *J. Chem. Soc.* **1943**, 322. [c] Reference 5.

reactions of the amine with **1**.[13] TLC analysis of a reaction mixture from **1** and morpholine showed two major components and ca. five minor ones. When this control TLC plate was compared with one from a reaction of an enone with **1** and morpholine, it was possible to detect the quinoxaline monoxide product by its superimposition on the control background. However, while the analytical problem of product detection was solved, the presence of numerous byproducts in the reaction mixture necessitated careful chromatography for product isolation. This requirement and the low yields detract from the advantage of regiospecificity.

Experimental Section

Melting points were determined on a Fisher-Johns apparatus. Proton NMR spectra were determined on a Varian HA-100 spectrometer and are reported in Table III. Chemical shifts (δ) refer to parts per million downfield from internal tetramethylsilane. Infrared spectra were obtained on a Perkin-Elmer 237 grating spectrophotometer. Mass spectra were obtained on an Atlaswerke CH-4 instrument. ^{13}C NMR spectra were measured at 22.62 MHz in rotating 10-mm tubes on a Bruker WH-90 operating in the pulse Fourier transform mode. The pulse width was 5 μs (15 μs = 90°). Dimethyl-d_6 sulfoxide was the solvent (100–300 mg of compound in 2 mL) with tetramethylsilane (1%) as an internal standard. The sample temperature was maintained at 305 K. The repetition rate for noise-decoupled spectra was 0.7 s and the free induction decays (6000–90000 accumulations) were stored in 8192 points. An 0.8-Hz line-broadening function was applied before zero filling to 16 384 points and Fourier transformation, yielding a digital resolution of 0.783 Hz.

General Procedure. A stirred mixture of 20 mmol of enone, 22 mmol of benzofurazan oxide (**1**), and 22 mmol of an amine in 50 mL of acetonitrile (or benzene) was heated at reflux for 24 h.

The solvent was removed by rotary evaporation and the residue was chromatographed on ca. 60 times its weight of Merck silica gel 60 (70–230 mesh) with one of the designated elution systems: (A) 2% methanol–dichloromethane, (B) 20% ethyl acetate–toluene, (C) 2% methanol–ethyl acetate, and (D) 25% ethyl acetate–hexane.

3-Phenylquinoxaline 1-Oxide (4a). Reaction of benzalacetone, **1**, and pyrrolidine followed by chromatography with system B afforded **4a** in 35% yield after recrystallization from acetone–hexane: mp 137–138 °C (lit.[6] mp 137–138 °C), mmp 137–138 °C. Use of morpholine in the reaction afforded **4a** in 22% yield. All of **1** was consumed in this reaction and the unreacted benzalacetone recovered by chromatography. It was determined that 89% of the consumed benzalacetone was accounted for in the isolated **4a**.

3-Methylquinoxaline 1-Oxide (4b). Reaction of *trans*-3-penten-2-one, morpholine, and **1** followed by chromatography with system B afforded **4b** in 26% yield after crystallization from diethyl ether–hexane: mp 107–108 °C (lit.[16] mp 118 °C). Anal. Calcd for $C_9H_8N_2O$: C, 67.48; H, 5.03; N, 17.49. Found: C, 67.20; H, 5.12; N, 17.62.

Oxidation of **4b** with *m*-chloroperbenzoic acid in dichloromethane at room temperature for 16 h gave 2-methylquinoxaline 1,4-dioxide in 90% yield: mp 185–185 °C (lit.[17] mp 180–181 °C), mmp 185–186 °C.

3-[3-(Morpholinecarboxamido)propyl]quinoxaline 1-Oxide (4c). Reaction of 2-cyclohexenone, morpholine, and **1** followed by chromatography with system C afforded **4c** as tan crystals in 13% yield after recrystallization from diisopropyl ether: mp 118–119 °C; mass spectrum, m/e 301 (M^+).

Anal. Calcd for $C_{16}H_{19}N_3O_3$: C, 63.77; H, 6.36; N, 13.95. Found: C, 64.16; H, 6.39; N, 13.94.

3-[3-(Morpholinecarboxamido)propyl]quinoxaline 1,4-Dioxide (22). A mixture of 0.45 g of **4c** (1.5 mmol), 0.37 g of 85% *m*-chloroperbenozic acid (1.8 mmol), and 5 mL of dichloromethane was left at room temperature for 16 h. The mixture was diluted with 50 mL of dichloromethane and was washed with two 20-mL portions of 2% sodium hydroxide solution. The extract was dried (Na_2SO_4) and the solvent was removed by evaporation to give a residue. Trituration of this residue with diethyl ether afforded 0.41 g (86%) of **24** as orange-yellow crystals: mp 155–157 °C; mass spectrum, m/e 301 ($M^+ - OH$).

Anal. Calcd for $C_{16}H_{19}N_3O_4$: C, 60.55; H, 6.04; N, 13.24. Found: C, 60.55; H, 6.03; N, 13.24.

3-Acetyl-2-phenylquinoxaline 1-Oxide (5a). Reaction of **3**, *n*-butylamine, and **1** followed by chromatography using system A afforded **5a** in 16% yield as off-white crystals after recrystallization from heptane: mp 126–127 °C; IR (KBr) 1705 cm^{-1}; mass spectrum, m/e 264 (M^+).

Anal. Calcd for $C_{16}H_{12}N_2O_2$: C, 72.71; H, 4.58; N, 10.60. Found: C, 72.54; H, 4.61; N, 10.53.

3-Acetyl-2-methylquinoxaline 1-Oxide (5b). Reaction of *trans*-3-penten-2-one, *n*-butylamine, and **1** followed by chromatography using system D afforded a 24% yield of **5b**: mp 94–95 °C (lit.[5] mp 93–94 °C), mmp 94–95 °C.

Deacylation of 2-Acetyl-3-methylquinoxaline 1-Oxide (10). A mixture of 0.38 g of **10** (1.88 mmol), 0.18 g of morpholine (2 mmol), and 5 mL of acetonitrile was heated at reflux for 24 h. Evaporation of the solvent gave a residue that was chromatographed with system A to give 90 mg of **4b** (30%) and 235 mg of **10** (62%). In a similar experiment using 10 equiv of morpholine, there was essentially the same conversion of **10** to **4b**.

2-(Carboethoxy)-3-phenylquinoxaline 1,4-Dioxide (6). A mixture of 13.6 g of **1** (0.1 mol), 21.5 g of ethyl benzoylacetate (0.112 mol), 0.2 g of calcium hydroxide, and 150 mL of 2-propanol was heated at reflux for 18 h. The hot mixture was filtered and 17.7 g of golden crystals deposited on cooling. Recrystallization from ethanol afforded 14.8 g (47%) of **6**: mp 123–125 °C; ^{1}H NMR (Me_2SO-d_6) δ 0.98 (t, 3 H, CH_3, J = 7 Hz), 4.17 (q, 2 H, CH_2, J = 7 Hz), 7.58 (s, 5 H, C_6H_5), 7.9–8.12 (m, 2 H), 8.4–8.65 (m, 2 H).

Anal. Calcd for $C_{17}H_{14}N_2O_4$: C, 65.8; H, 4.55; N, 9.03. Found: C, 65.56; H, 4.5; N, 9.1.

3-(Carboethoxy)-2-phenylquinoxaline 1-Oxide (7). A mixture of 14.6 g of **6** (47 mmol), 6.42 g of trimethylphosphite

(16) Hayashi, E.; Iijima, C. *Yakugaku Zasshi* **1964**, *84*, 163.

(17) McIlwain, H. *J. Chem. Soc.* **1943**, 322.

(51.8 mmol), and 100 mL of 1-propanol was heated at reflux for 1 h. The mixture was cooled in an ice bath and the precipitate was collected by filtration. After recrystallization from ethanol, there was obtained 8.76 g (63%) of **7** as yellow crystals: mp 115–116 °C; IR (KBr) 1740 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 0.96 (t, 3 H, CH_3, J = 7 Hz), 4.1 (q, 2 H, CH_2, J = 7 Hz), 7.54 (s, 5 H, C_6H_5), 7.8–8.6 (m, 4 H).

Anal. Calcd for $C_{17}H_{14}N_2O_3$: C, 69.37; H, 4.80; N, 9.52. Found: C, 69.03; H, 4.76; N, 9.73.

2-Phenylquinoxaline 1-Oxide (8a). A mixture of 8 g of **7** (27.2 mmol) and 60 mL of 0.5 N NaOH was stirred at room temperature for 1 h. The mixture was filtered from a small amount of suspended solid and the filtrate was neutralized with 65 mL of 0.5 N HCl. The precipitated solid was collected by filtration to give 4.5 g of crude 2-phenylquinoxaline-3-carboxylic acid 1-oxide, mp 142–144 °C dec. The crude acid was suspended in 60 mL of toluene and the mixture was heated at reflux for 2 h. The hot mixture was filtered and the filtrate was evaporated to give a residue. Trituration of this residue with diethyl ether gave 3.1 g of **8a** (51% from **7**) as light yellow crystals: mp 155–156.5 °C (lit.[8] mp 154 °C); ^1H NMR (Me_2SO-d_6) δ 7.5–7.66 (m, 3 H), 7.83–8.2 (m, 5 H), 8.5–8.62 (m, 1 H), 9.07 (s, 1 H).

Anal. Calcd for $C_{14}H_{10}N_2O$: C, 75.65; H, 4.45; N, 12.61. Found: C, 75.70; H, 4.52; N, 12.65.

Syntheses of 1,3-Bis(1′-alkylpyridinium)cyclopentadienides and the X-ray Crystal Structures of 1,3-Bis(1′-methyl-2′-pyridinium)indenide Bromide and 1-(1′-Methyl-2′-pyridinium)-3-(1″-methyl-4″-pyridinium)cyclopentadienide Bromide

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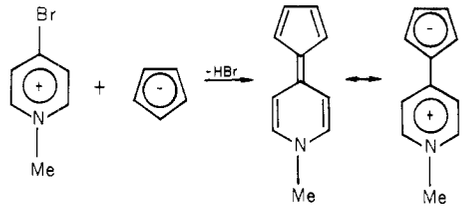
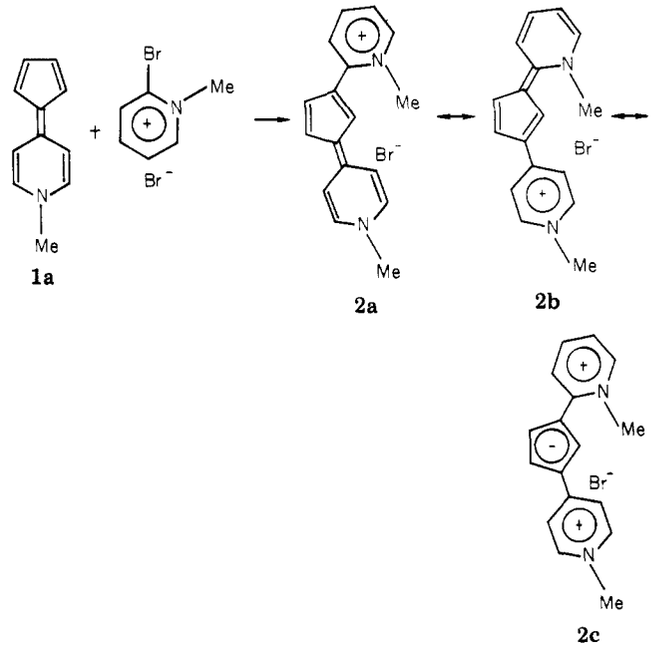
The reaction of cyclopentadienide with excess 2- or 4-bromo-1-alkypyridinium salts is described. The products may be thought of as alkylpyridinium-substituted fulvalenes or as 1,3-bis(alkylpyridinium)cyclopentadienides. The reaction probably proceeds via a fulvalene intermediate since the product can be obtained by starting with the appropriate fulvalene and 2- or 4-bromo-1-alkylpyridinium salt. Unsymmetrical products can be prepared from the fulvalene–pyridinium salt reaction. A similar kind of reaction occurs with indenides and their fulvalene analogues. X-ray crystallographic studies of a symmetrically substituted "indenide" and unsymmetrically substituted "cyclopentadienide" have been carried out. Bond lengths in the central five-membered ring suggest that the products are resonance hybirds of the two possible pyridinium–fulvalene structures that can be written for each compound. There is no evidence to support a tripolar structure, i.e., that of a bis(pyridinium)cyclopentadienide or indenide.

Cyclopentadienide reacts with 2- or 4-halo-1-alkylpyridinium salts to yield cyclopentadienylidene-1,2- or -1,4-dihydropyridines,[2] exemplied by the formation of 1-methyl-4-cyclopentadienylidene-1,4-dihydropyridine (**1**).



1a **1b**

Canonical structures **1a** and **1b** presumably are the major contributors to the resonance hybrid. We reported[3] previously that these cyclopentadienylidenedihydropyridines and their indenylidene analogues can react with 2- or 4-halo-1-alkylpyridinium salts to form cationic products, which can be envisaged as either 1-alkylpyridinium-substituted fulvalenes (e.g., **2a** and **2b**) or 1,3-bis(alkylpyridinium)cyclopentadienides (e.g., **2c**). By analogy to the structures of compounds similar to **2** but with pyridinium replaced by cyclopropenium, reported by Yoshida and co-workers,[4] structure **2c** can be termed a "tripolar mesomeric form". In this paper, we report the syntheses of **3a–g** and the results of X-ray crystallographic investigations of **3b** and **3e**.



1a **2a** **2b** **2c**

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(2) J. A. Berson, E. M. Evleth, and Z. Hamlet, *J. Am. Chem. Soc.*, 87, 2887 (1965).

(3) W. D. Erhardt and H. L. Ammon, *Tetrahedron Lett.*, 3997 (1975).

(4) Z. Yoshida, S. Araki, and H. Ogoshi, *Tetrahedron Lett.*, 19 (1975).

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