*Tetrahedron*. Vol. 30, pp. 659 to 666. Pergamon Press 1974. Printed in Great Britain

# DEOXYGENATION OF QUINOXALINE N-OXIDES AND RELATED COMPOUNDS

M. J. HADDADIN,* G. E. ZAHR, T. N. RAWDAH, N. C. CHELHOT and C. H. ISSIDORIDES
Department of Chemistry, American University of Beirut, Beirut, Lebanon

(*Received in the UK 3 September* 1973; *Accepted for publication 16 October* 1973)

**Abstract**—The alkali induced deoxygenation of 3-(α-hydroxyalkyl)-quinoxaline-1-oxides is shown to be first order in substrate and in hydroxide ion. Examples are given to illustrate the synthetic utility of this reaction for the synthesis of quinoxaline and quinoline derivatives of type **4**, **5**, **8**, and **11**. The mechanism of the reaction is related to the mechanism of deoxygenation of heteroaromatic N-oxides by sodium dithionite.

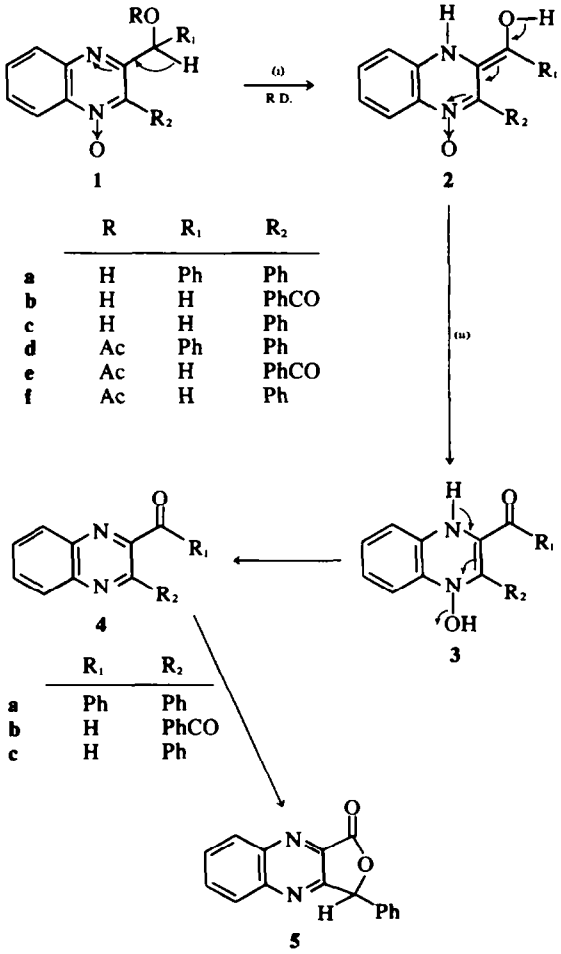
Heteroaromatic N-oxides can be deoxygenated by catalytic hydrogenation as well as by reducing agents such as complex hydrides, trivalent phosphorus compounds, dissolving metals, and sodium dithionite.[1] In certain cases deoxygenation is possible even in the absence of reducing agents, through a remarkable intramolecular oxidation-reduction first observed by Chilton and Butler in the base-catalyzed conversion of 2-hydroxymethylpyridine-1-oxide into pyridine-2-aldehyde.[2] Another example of this reaction under acid datalysis has been reported by Tennant[3] for 3-(α-hydroxybenzyl)-1,2,4-benzotriazine-1-oxide.

This paper describes results obtained in the quinoxaline and quinoline series. The first part deals with alkali-induced deoxygenations of certain substituted quinoxaline-1-oxides and related compounds; the second, with deoxygenations of quinoxaline-1-oxides and 1,4-dioxides by sodium dithionite.

A. *Alkali induced deoxygenations.* In a preliminary communication[4] we reported that hot methanolic potassium hydroxide readily converted **1a** into ketone **4a**, and **1b** into lactone **5**. The intermediacy of keto-aldehyde **4b** in the formation of **5** was substantiated by the finding that, under the same conditions, independently synthesized **4b** gave **5**.

We now present experimental details, kinetic evidence in support of our earlier mechanism,[4] and additional examples of the synthetic utility of this reaction (**1a**→**4a**; **1b**→**5**; **1c**→**4c**; **9a**→**11**).

The kinetics were studied with **1a** as the substrate. Although no information could be obtained in the UV region owing to the proximity of the UV maxima of substrate and product (244 nm for **1a** *vs* 250 nm for **4a**), the reaction was conveniently monitored in the IR by the CO absorption of the product at 1673 $cm^{-1}$. The data show that the reaction is first order in substrate and in hydroxide ion, as would be expected of the mechanism outlined in Scheme 1.




| | R | $R_1$ | $R_2$ |
|---|---|---|---|
| **a** | H | Ph | Ph |
| **b** | H | H | PhCO |
| **c** | H | H | Ph |
| **d** | Ac | Ph | Ph |
| **e** | Ac | H | PhCO |
| **f** | Ac | H | Ph |

| | $R_1$ | $R_2$ |
|---|---|---|
| **a** | Ph | Ph |
| **b** | H | PhCO |
| **c** | H | Ph |

SCHEME 1.

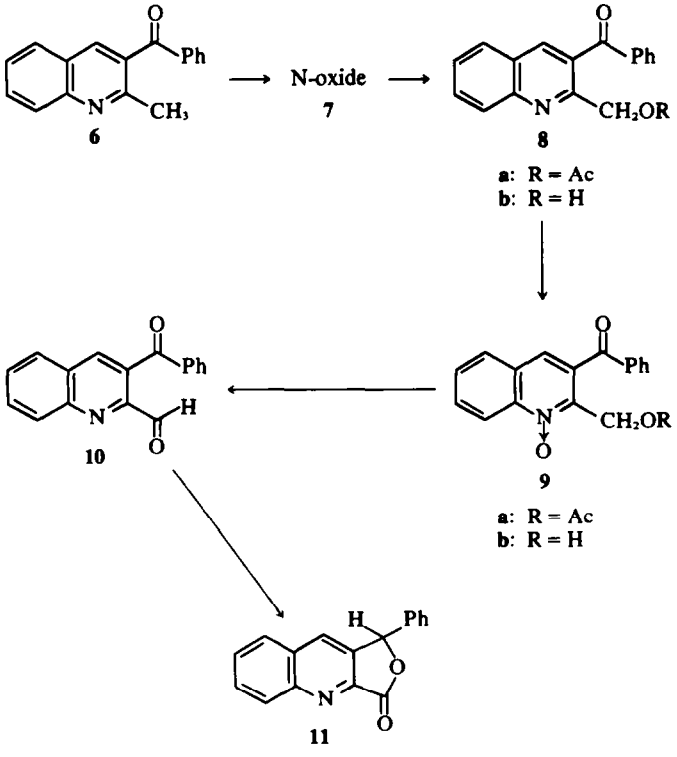
Further support for this mechanism is the finding that no deuterium is incorporated in starting material (**1a**) that has been recovered from partial reac-

tion in $CD_3OD$-$CD_3ONa$. Although the benzylic protons of 2-benzylpyridine-1-oxide and 4-benzylpyridine-1-oxide are exchanged with deuterium under conditions comparable to those of the present study,[5] the mechanism outlined in Scheme 1 is consistent with the non-occurrence of deuterium exchange, provided that intermediate **2** goes to product fast enough to make step (i) irreversible. Whether the tautomerization **1**→**2** is a two-stage reaction involving an azaallylic carbanion,[6] or whether it is concerted, cannot be established from our data.

The transformations described here set the stage for a general synthesis of lactones such as **11**, which are potential precursors of quinolino [2,3:c]furans. Treatment of **6** with *m*-chloroperbenzoic acid gave the 1-oxide **7** (strong N→O absorption at 1350 $cm^{-1}$; downfield shift of $C_8$ proton as compared with that of **6**). Acetic acid–acetic anhydride at reflux[7] converted **7** into the acetate **8a** (CO bands at 1730 and 1650 $cm^{-1}$; two methylene protons at 4·58τ and three Me protons at 8·20τ). This acetate was oxidized to the N-oxide **9a** which was converted into lactone **11** (5% methanolic potassium hydroxide at reflux, followed by acidification). The lactone showed only one CO absorption band (1770 $cm^{-1}$), and had a singlet for one aliphatic proton at 3·42τ. By analogy to the formation of **5** from **4b**, **11** most likely arises from the intermediate keto-aldehyde **10** by an intramolecular Cannizzaro reaction (Scheme 2). This assumption is corroborated by the finding that, under the conditions of the reaction (**9a**→**11**), independently synthesized **10** (prepared by manganese dioxide oxidation of keto-alcohol **8b**) produces **11**.

The deoxygenations described here are internal oxidation-reductions and can occur only if the side chain containing the function to be oxidized is properly located with respect to the N-oxide function. For example, whereas 2- and 4-hydroxymethylpyridine-1-oxide undergo deoxygenation fairly easily (one prototropic shift followed by dehydration), 3-hydroxymethylpyridine-1-oxide fails to react.[2] Although compounds **1a**, **1b**, and **1c** are partially related to 3-hydroxymethylpyridine-1-oxide, they can accomodate the required two prototropic shifts (Scheme 1, (i) and (ii)) via the N atom at position 4.

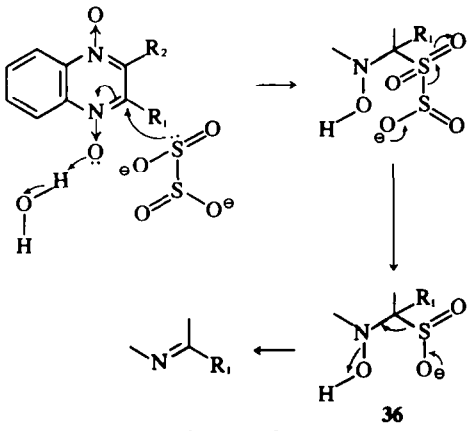
B. *Deoxygenations with sodium dithionite.* Reductions with sodium dithionite were carried out in aqueous ethanol (60%)[8] for 3–4 hr at reflux. In the case of di-N-oxides, shorter reflux periods often gave products contaminated with mono-N-oxides. The choice of an initially neutral medium was dictated by the desire to preserve base-labile functions such as carboalkoxyl, acyl, aroyl, and alkyl groups at positions 2 and 3.[9] Optimum yields were obtained with 4:1 molar ratio of reductant:di-N-oxide. The




SCHEME 2.

results are summarized in Tables 1 and 2. Many of the deoxygenations reported here (N-oxide to parent heterocyclic base) can be effected also with phosphorus trichloride in refluxing chloroform solution. In general, we found reactions with phosphorus trichloride to be somewhat faster, but yields with sodium dithionite to be considerably higher.

Although sodium dithionite has been used in several instances for the deoxygenation of heterocyclic N-oxides, its applications in the quinoxaline-di-N-oxide series[1] are few, and its mode of action is not well established. A plausible mechanism is suggested in Scheme 3 (partial structures shown for first-stage deoxygenation to the mono-oxide). The first step entails nucleophilic attack by dithionite at position 2 (or 3) of the 1,4-dioxide. The electrophilicity of these positions in quinoxalines and their oxides is well documented[1,10] and, in this case, enhanced by hydrogen bonding between the oxide and the solvent. The resulting intermediate is postulated to lose $SO_2$ to give the sulfinate anion **36** which decomposes to product in a manner analogous to the decarboxylation of β-hydroxy- and β-bromocarboxylic acid salts.[11]

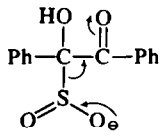


**36**

SCHEME 3.

The following evidence is in support of the proposed mechanism:

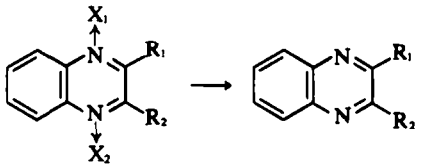
(i) The affinity of dithionite for certain electrophilic centers is demonstrated by the ease with which it reduces benzil to benzoin (93% yield) under the conditions used for deoxygenation of N-oxides:



The reduction of quinones to hydroquinones by dithionite[12] is a closely related reaction.

(ii) Intermediates **37** and **38**, analogous to **36**, have been isolated recently during reductions of pyridinium compounds with dithionite.[13,14] In the present case, elimination to the fully aromatic pro-

Table 1.



| Reactants | | | | | Products | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| No. | $R_1$ | $R_2$ | $X_1$ | $X_2$ | No. | $R_1$ | $R_2$ | Yield | m.p. | Ref |
| 12 | $CH_3$ | Ph | 0 | 0 | 13[a] | $CH_3$ | Ph | 73 | 53–54 | m.p. 57–58[b] |
| 14[c] | $CH_3$ | $COCH_3$ | 0 | 0 | 15[d] | $CH_3$ | $COCH_3$ | 78 | 85–86 | m.p. 87–88[b] |
| 16[c] | $CH_3$ | $CO_2Et$ | 0 | 0 | 17[e] | $CH_3$ | $CO_2Et$ | 69 | 72–73 | *f* |
| 18 | $CH_2Ph$ | Ph | 0 | 0 | 19[g] | $CH_2Ph$ | Ph | 95 | 96–97 | m.p. 97[b] |
| 20[c] | Ph | COPh | 0 | 0 | 21 | Ph | COPh | 93 | 150–151 | m.p. 150[h] |
| 1d | CH(OAc)Ph | Ph | — | 0 | 19 | $CH_2Ph$ | Ph | 50 | 96–97 | m.p. 97[b] |
| 1a | CH(OH)Ph | Ph | — | 0 | 19 | $CH_2Ph$ | Ph | 55 | 96–97 | m.p. 97[b] |

[a] NMR: m 1·95 (2H), m 2·40 (7H), s 7·29 (3H).

[b] J. C. E. Simpson, *The Chemistry of Heterocyclic Compounds: Condensed Pyridazine and Pyrazine Rings*, Interscience, New York (1953).

[c] C. H. Issidorides and M. J. Haddadin, *J. Org. Chem.* **31**, 4067 (1966).

[d] NMR: m 2·17 (4H), s 7·08 (3H), s 7·21 (3H).

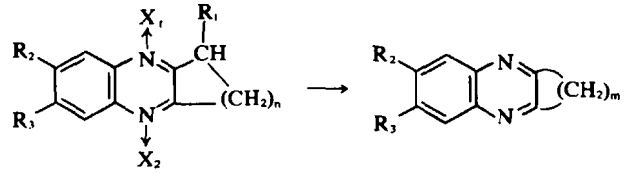
[e] NMR: m 2·15 (4H), q 5·52 (2H), s 7·14 (3H), t 8·58 (3H).

[f] Calcd: C, 66·65; H, 5·59; N, 12·96. Found: C, 66·79; H, 5·63; N, 12·93.

[g] NMR: m 1·98 (2H), m 2·70 (12H), s 5·68 (2H).

[h] C. Brandt, G. V. Foerster, F. Krohnke, *Liebig. Ann.* **688**, 189 (1965).

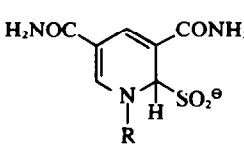
Table 2.



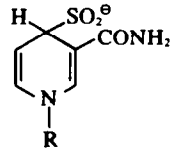
Reactants | Products

| No. | $R_1$ | $R_2$ | $R_3$ | $X_1$ | $X_2$ | n | No. | $R_2$ | $R_3$ | m | Yield | m.p. | Ref |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 22[a] | H | H | H | 0 | 0 | 2 | 23 | H | H | 3 | 80 | 98–99 | m.p. 99–100[b,c] |
| 24[a] | H | H | H | 0 | 0 | 3 | 25 | H | H | 4 | 91 | 92–93 | *d* |
| 26[a] | H | Cl | Cl | 0 | 0 | 3 | 27[e] | Cl | Cl | 4 | 86 | 185–186 | m.p. 183·5[f] |
| 28[a] | H | $CH_3$ | $CH_3$ | 0 | 0 | 3 | 29 | $CH_3$ | $CH_3$ | 4 | 94 | 145–146 | *g* |
| 30[h] | OAc | H | H | — | 0 | 3 | 25 | H | H | 4 | 42 | 92–93 | *d* |
| 31 | OAc | H | H | — | — | 3 | 25 | H | H | 4 | 50 | 90–91 | *d* |
| 32[a] | H | H | H | 0 | 0 | 4 | 33 | H | H | 5 | 89 | 84–85 | m.p. 83–85[c,i] |
| 34[a] | H | H | H | 0 | 0 | 5 | 35 | H | H | 6 | 90 | 120–121 | m.p. 120·2–120·7[c,i] |

[a] N. A. Mufarrij, M. J. Haddadin, C. H. Issidorides, J. W. McFarland and J. D. Johnston, *J. Chem. Soc.* (Perkin I) 965 (1972).
[b] J. R. Landquist and J. A. Silu, *J. Am. Chem. Soc.* **78**, 2052 (1956).
[c] M. J. Haddadin, H. N. Alkaysi and S. E. Saheb, *Tetrahedron* **26**, 1115 (1970).
[d] M. J. Haddadin and C. H. Issidorides, *Tetrahedron Letters* 3253 (1965).
[e] Calcd: C, 56·95; H, 3·96; N, 11·07, Cl, 28·02. Found: C, 56·91; H, 4·18; N, 11·04; Cl, 27·83.
[f] R. Scott and M. Tomlinson, *J. Chem. Soc.* 417 (1959).
[g] Calcd: C, 79·21; H, 7·60; N, 13·20. Found: C, 79·13; H, 7·61; N, 13·36. NMR: s 2·40 (2H), m 6·92 (4H), s 7·60 (6H), m 8·00 (4H).
[h] M. J. Haddadin and A. S. Salameh, *J. Org. Chem.* **33**, 2127 (1968).
[i] A. T. Blomquist and L. Haung Lin, *J. Am. Chem. Soc.* **75**, 2153 (1953).



37



38

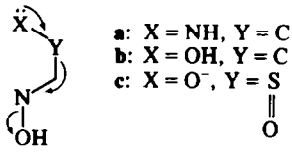
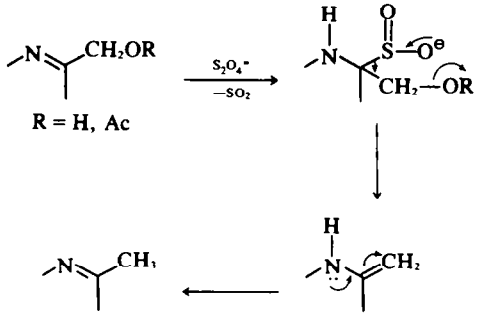


Fig 1.

duct occurs much too readily to permit isolation of the intermediate.

(iii) Of the two positions (2 and 3) available for attack in quinoxaline-di-N-oxides, dithionite is expected to initially attack the more electrophilic center. For example, controlled reduction of 2 - methyl - 3 - trifluoromethylquinoxaline - di - N - oxide has been reported[15] to give 2-methyl-3-trifluoromethylquinoxaline-1-oxide, just as would be expected of initial attack at position 3.

(iv) In certain cases, reductive elimination of hydroxy or acetoxy groups occurs, provided these are located alpha to a position vulnerable to attack by dithionite. This side reaction (**1d→19**, **1a→19**, **30→25**, **31→25**) is consistent with the postulated mechanism, and can be rationalized as outlined below (partial structures).



The NMR spectra of **12**, **14**, and **16** showed sharp signals for the methyl protons at position 2. Deoxygenation to the corresponding quinoxaline was attended in every case by readily detectable downfield shifts for the Me signals (**12→13**, 7·55 to 7·29; **14→15**, 7·51 to 7·08; **16→17**, 7·45 to 7·14). A similar trend has been reported recently for 2-methyl-3-trifluoromethylquinoxaline-di-N-oxide.[15] Interestingly, only a small downfield shift was observed for the methylene protons signal upon reduction of **18** to **19** (5·78 to 5·68).

In conclusion, we draw attention to the common salient feature of the deoxygenations described here, whether induced by dithionite or by internal oxidation-reduction (Fig 1—partial structures, with double bonds omitted).

Fig 1 depicts the conversion of **3** into **4** (Fig 1a), the deoxygenation of **9b** (after one prototropic prototropic shift) to **10** (Fig 1b), and the terminal step in dithionite reductions (Fig 1c).

## EXPERIMENTAL

M.ps were determined on a Fisher–Johns apparatus, and are uncorrected. IR spectra were recorded on a Perkin–Elmer model 257 spectrophotometer. Unless specified otherwise, NMR spectra are reported in tau values and were taken on a Varian A60-D spectrometer in $CDCl_3$ with TMS as internal reference. Elemental analyses were performed by F. Pascher, Bonn, Germany.

*2-Phenyl-3-benzylquinoxaline-1,4-dioxide* (**18**). Dibenzyl ketone (52·5 g) was dissolved in dry ether (200 ml). Granular sodamide (10 g) was added to the ether soln and the mixture was stirred for 10 min. An ether soln of benzofurazan oxide (34 g) was added gradually with stirring. The dark red mixture was stirred for an additional 10 min and water was added slowly to destroy the unreacted sodamide. Evaporation of the ether yielded a yellow solid which upon recrystallization from EtOH gave the yellow title compound in 55% yield, m.p. 191°, IR: 1600, 1345, 1310, 1275, 1090, 985, 770, 715, 675, and 640 $cm^{-1}$, NMR: S 5·78 (2H), m 2·75 (10H), m 2·25 (2H), m 1·45 (2H). (Found: C, 76·71; H, 4·91; N, 8·48. $C_{21}H_{16}N_2O_2$ requires: C, 76·81, H 4·91; N, 8·53%).

*2-Phenyl-3-(α-acetoxybenzyl)quinoxaline-1-oxide* (**1d**). 2-Phenyl-3-benzylquinoxaline-1,4-dioxide (15 g) was dissolved in glacial AcOH (40 ml) and $Ac_2O$ (80 ml). The soln was refluxed for 30 min and then concentrated to about 100 ml by distillation of the solvent at reduced pressure. Addition of water to the soln gave a gummy product which, upon scratching, yielded 2-phenyl-3-(α-acetoxybenzyl)quinoxaline-1-oxide in 77% yield. The product was recrystallized from MeOH, m.p. 143–144°, IR: 1730, 1575, 1350, 1330, 1245, 1175, 1040, 1020, 985, 935, 905, 775, 740, and 700 $cm^{-1}$; NMR: S 7·85 (3H), S 3·48 (1H), m 2·9, 2·6 (12H), m 1·9 (1H), m 1·6 (1H). (Found: C, 74·19; H, 4·89; N, 7·52. $C_{23}H_{18}N_2O_3$ requires: C, 74·58; H, 4·90; N, 7·56%).

*2 - Phenyl - 3 - (α - hydroxybenzyl)quinoxaline - 1 - oxide* (**1a**). 2-Phenyl-3-(α-acetoxybenzyl)quinoxaline-1-oxide (15 g) was dissolved in 5% methanolic KOH (80 ml). The soln was heated for 2 min on the steam bath, and immediately cooled in an ice bath. The title compound precipitated out as a white solid (86%) which was recrystallized from EtOH, m.p. 188–189°, IR: 3410, 1595, 1390, 1350, 1210, 1075, 1010, 930, 780, 750, 710, 670, and 640 $cm^{-1}$; NMR: S 4·36 (1H), m 2·7 (13H), m 1·8 (1H), m 1·35 (1H). (Found: C, 76·68; H, 5·01; N, 8·42. $C_{21}H_{16}N_2O_2$ requires: C, 76·81; H, 4·91; N, 8·53%).

*2-Phenyl-3-benzoylquinoxaline* (**4a**). 2-Phenyl-3-(α-hydroxybenzyl)quinoxaline-1-oxide (5 g) was refluxed in 10% methanolic KOH (80 ml) for 1 hr. The soln was concentrated to about 40 ml and allowed to cool to room temp. Immersion of the reaction flask in an ice bath resulted in the precipitation of 2-phenyl-3-benzoylquinoxaline in 85% yield, m.p. 159–160° (lit.[16] 150). The product was identical with an authentic sample of **4a**.

*2-Benzoyl-3-acetoxymethylquinoxaline-1-oxide* (**1e**). 2-Benzoyl-3-methylquinoxaline-1,4-dioxide[16] (8 g) was dis-

solved in a mixture of $Ac_2O$ (20 ml) and glacial AcOH (10 ml). The soln was refluxed for 0·5 hr. The deep brown soln was cooled and the precipitated brownish solid was filtered, washed with AcOH and MeOH. Recrystallization from benzene gave yellowish prisms of 2-benzoyl-3-acetoxymethylquinoxaline-1-oxide in 50% yield, m.p. 177–178°; IR: 1745, 1670, 1355, 1225, 1100, 960, 780, 740, 690, and 660 $cm^{-1}$; NMR: S 8·45 (3H), S 4·8 (2H), m 2·4 (8H), m 1·7 (1H). (Found: C, 66·77; H, 4·41; N, 8·65. $C_{18}H_{14}N_2O_4$ requires: C, 67·07; H, 4·38; N, 8·69%).

*2-Benzoyl-3-hydroxymethylquinoxaline-1-oxide* (**1b**). 2-Benzoyl-3-acetoxymethylquinoxaline-1-oxide (6 g) was dissolved, with stirring at room temp, in 10% methanolic KOH (30 ml). The solid dissolved in 10 min and the soln developed a red color. Dilution with ice-water followed by acidification with conc HCl gave a pale pink solid which, upon recrystallization from MeOH, afforded fluffy needles in 77% yield, m.p. 164–165°; IR: 3230, 1670, 1350, 1230, 1045, 950, 765, and 690 $cm^{-1}$; NMR: broad s 5·3 (3H), m 2·5 (8H), m 1·65 (1H). (Found: C, 68·40; H, 4·41; N, 9·83. $C_{16}H_{12}N_2O_3$ requires: C, 68·56; H, 4·32; N, 10·00%).

*1,3-Dihydro-3-phenylfuro[3,4-b]quinoxaline-1-one* (**5**). The title compound was prepared by the following methods: (a) 2-benzoyl-3-acetoxymethylquinoxaline-1-oxide (2 g) was refluxed for 5 min in 10% methanolic KOH (15 ml). The colored soln was treated with charcoal and filtered. Dilution with water (150 ml) and acidification with conc HCl (3–4 ml) gave lactone **5** in 43% yield, (b) **1b** (0·3 g) and **4b** (0·3 g) were converted, by procedure (a) into lactone **5** in 74% and 67% yield respectively. The product was recrystallized from MeOH, m.p. 183–185°; IR: 1770, 1500, 1360, 1275, 1260, 1170, 1120, 975, 790–780 and 710–700 $cm^{-1}$; NMR: s 3·4 (1H), m 2·3 (9H). (Found: C, 73·05; H, 3·80; N, 10·70. $C_{16}H_{10}N_2O_2$ requires: C, 73·27; H, 3·84; N, 10·68%).

*2-Benzoyl-3-hydroxymethylquinoxaline.* In a 200 ml 3-necked round bottom flask equipped with a mechanical stirrer, a reflux condenser, and a dropping funnel, 2-benzoyl-3-hydroxymethylquinoxaline-1-oxide (3·8 g) was dissolved in refluxing 60% EtOH (60 ml). A 0·02M sodium dithionite soln was added dropwise, with stirring, until the developed red color remained unchanged for 15 min. The hot soln was transferred into an Erlenmeyer flask, diluted with water, and allowed to cool. The 2-benzoyl-3-hydroxymethylquinoxaline crystallized in fine needles (75% yield). The analytical sample was recrystallized from EtOH, m.p. 134–135°. IR: 3420, 1660, 1450, 1340, 1055, 970, 770, 690 and 650–641 $cm^{-1}$, NMR: s 5·8 (1H), s 5 (2H), m 2·35 (9H). (Found: C, 72·55; H, 4·57; N, 10·6. $C_{16}H_{12}N_2O_2$ requires: C, 72·71; H, 4·58; N, 10·6%).

*3-Benzoylquinoxaline-2-carboxaldehyde* (**4b**).* 2-Benzoyl-3-hydroxymethylquinoxaline (2 g) and freshly prepared $MnO_2$ (6 g) were heated in refluxing $CHCl_3$ (30 ml) for 20 hr. The mixture was filtered through a charcoal pad, and the $MnO_2$ was washed thoroughly with $CHCl_3$. Evaporation of the solvent gave the title compound, which was recrystallized from $CCl_4$, yield 50%, m.p. 187–190°; IR: 1700, 1670, 1450, 1340, 1155, 980, 940, 930, 890, 830, 770, and 760 $cm^{-1}$; NMR: m 2·2 (9H), s −0·1 (1H). (Found: C, 72·13; H, 3·82; N, 10·66. $C_{16}H_{10}N_2O_2$ requires: C, 73·27; Y 3·84; N, 10·68%).

*Aldehydes **4b** and **4c** are very reactive and could not be obtained sufficiently pure due to lack of a suitable crystallizing solvent.

*2-Phenyl-3-methylquinoxaline-1,4-dioxide* (**12**). The procedure used in the preparation of 2-phenyl-3-benzylquinoxaline-1,4-dioxide was employed. The title compound was obtained in 77% yield from benzyl methyl ketone (13·4 g), benzofurazan oxide (13·6 g), and sodamide (5 g) in ether. The yellow product was recrystallized from MeOH and melted at 192°; IR: 3040, 1500, 1485, 1333, 1320, 1287, 1095, 830, 760, 700, 648, and 636 $cm^{-1}$; NMR: s 7·5 (3H); m 2·7 (7H), m 1·3 (2H). (Found: C, 71·58; H, 4·83; N, 11·27. $C_{15}H_{12}N_2O_2$ requires: C, 71·41; H, 4·80; N, 11·11%).

*2-Phenyl-3-acetoxymethylquinoxaline-1-oxide* (**1f**) *and 2-phenyl-3-hydroxymethylquinoxaline-1-oxide* (**1c**). Treatment of 2-phenyl-3-methylquinoxaline-1,4-dioxide (5 g) with $Ac_2O$–AcO–AcOH (80:40 ml) for 24 hr at room temp, followed by evaporation of the solvent at reduced pressure gave a gummy residue which, upon recrystallization from MeOH, afforded **1f** in 82% yield, m.p. 118°, IR: 3030, 1732, 1580, 1480, 1445, 1350, 1300, 1230, 1060, 860, 840, 780, 760, 705, and 660 $cm^{-1}$; NMR: s 7·5 (3H), 4·8 (2H), m 2·7 (7H), m 1·8 (1H), m 1·3 (1H). (Found: C, 69·64; H, 4·89; N, 9·35. $C_{17}H_{14}N_2O_3$ requires: C, 69·37; H, 4·80; N, 9·52%).

Acetate **1f** (4 g) was dissolved in MeOH (10 ml), treated with 5% methanolic KOH (3 ml), and immediately placed in an ice bath. The product (**1c**) precipitated out and was recrystallized from MeOH, yield 87%, m.p. 153°; IR: 3470, 1575, 1485, 1360, 1075, 995, 770, 720, 705, and 640 $cm^{-1}$; NMR: s 5·6 (1H), s 5·4 (2H), m 2·85 (7H), m 1·8 (1H), m 1·35 (1H). (Found: C, 71·54; H, 4·91; N, 11·27. $C_{15}H_{12}N_2O_2$ requires: C, 71·41; H, 4·80; N, 11·11%).

*2-Formyl-3-phenylquinoxaline* (**4c**).* 2-Phenyl-3-hydroxymethylquinoxaline-1-oxide (1 g) was heated in 5% methanolic KOH at reflux temp for 10 min. Dilution with water and recrystallization of the resulting solid from MeOH gave presumably the hemi-acetal of the title compound, yield 66%, m.p. 134°; IR: 3430, 3040, 2850, 1710, 1530, 1480, 1350, 1195, 1078, 1010, 810, 765, 700, and 690 $cm^{-1}$; NMR: (before crystallization from MeOH) m 2·7 (9H), s −0·42 (1H). (Found: C, 72·92; H, 5·20; N, 10·37. $C_{15}H_{10}N_2O.CH_3OH$ requires: C, 72·16; H, 5·30; N, 10·52%).

*2-Methyl-3-benzoylquinoline-1-oxide* (**7**). Compound **6** (5 g) was dissolved in benzene (25 ml). A soln of *m*-chloroperbenzoic acid (4·1 g) in benzene (25 ml) was added and the soln was allowed to stand at room temp for 18 hr. Excess peracid was destroyed by treatment with $Na_2S_2O_3$ aq, followed by extraction with NaOH. The benzene layer was washed with water, dried, and evaporated to yield a yellowish solid which was recrystallized from acetone, yield 80%, m.p. 158–159°, IR: 1665, 1325, 1290, 1250, 910, 880, 800, 790, 775, 760–750, 730, and 710 $cm^{-1}$; NMR: s 7·3 (3H), m 2·4 (10H). (Found: C, 77·89; H, 5·06; N, 5·48. $C_{17}H_{13}NO_2$ requires: C, 77·55; H, 4·98; N, 5·32%).

*2-Acetoxymethyl-3-benzoylquinoline* (**8a**) *and 2-hydroxymethyl-3-benzoylquinoline* (**8b**). 2-Methyl-3-benzoylquinoline-1-oxide (8 g) was dissolved in a mixture of $Ac_2O$–AcOH (15:5 ml). The soln was allowed to stand at room temp for 40 hr, diluted with ice-water, and stirred until the gummy substance solidified. The crude product was chromatographed on neutral alumina and eluted with benzene. The product (**8a**) was recrystallized from MeOH, 45% yield, m.p. 97–98°; IR: 1730, 1650, 1270, 1255, 1230, 1200, 1090, 910, 780, 760, 735, 705, and 680 $cm^{-1}$; NMR: s 8·2 (3H), s 4·6 (2H), m 2·4 (10H). (Found: C, 74·79; H, 5·17; N, 4·75. $C_{19}H_{15}NO_3$ requires: C, 74·74; H, 4·95; N, 4·59%).

Quinolinoacetate **8a** (3·5 g) was dissolved in hot MeOH (20 ml) and 10% methanolic KOH soln (5 ml) was added dropwise to the refluxing soln. After 10 min the soln was cooled, diluted with water, and placed in the cold for 12 hr. The product was recrystallized from EtOH-water to give **8b** in 80% yield, m.p. 75°; IR: 3330, 1650, 1590, 1450, 1380, 1280, 1030, 910, 880, 790, 770, 760, 745, 700, and 680 $cm^{-1}$; NMR: broad s 5·18 (3H), m 2·5 (10H). (Found: C, 77·73; H, 4·94; N, 5·20. $C_{17}H_{13}NO_2$ requires: C, 77·55; H, 4·98; N, 5·32%).

*3-Benzoylquinoline-2-carboxaldehyde* (**10**). The title compound was prepared from **8b** by the same procedure used for the preparation of 3-benzoylquinoxaline-2-carboxaldehyde, yield 50%, m.p. 132–133°; IR: 1700, 1670, 1450, 1320, 1260, 945, 890, 825, and 770–760 $cm^{-1}$; NMR: m 2·5 (8H), m 1·9 (2H), s 0·0 (1H). (Found: C, 77·96; H, 4·23; N, 5·35. $C_{17}H_{11}NO_2$ requires: C, 78·15; H, 4·24; N, 5·36%).

*2-Acetoxymethyl-3-benzoylquinoline-1-oxide* (**9a**). 2-Acetoxymethyl-3-benzoylquinoline (8 g) was converted into **9a** by the procedure used for the oxidation of 2-methyl-3-benzoylquinoline methyl-3-benzoylquinoline into **7**. The product **9a** was recrystallized from acetone, 60% yield, m.p. 174–176°; IR; 1745, 1665, 1590, 1450, 1330, 1210, 1050, 970, 945, 910, 895, 800, 780, 750, 705, and 670 $cm^{-1}$; NMR: s 8·3 (3H), s 4·57 (2H), m 2·5 (10H). (Found: C, 71·03; H, 4·71; N, 4·54. $C_{19}H_{15}NO_4$ requires: C, 71·02; H, 4·71; N, 4·36%).

*1,3-Dihydro-1-phenylfuro[3,4-b]quinoline-3-one* (**11**). The title lactone was prepared by the following two methods: (a) 2-acetoxymethyl-3-benzoylquinoline-1-oxide (2 g) was heated in refluxing 10% methanolic KOH (20 ml) for 1 min. The brown soln was diluted with hot water (150 ml), treated with charcoal and filtered. The hot orange-red soln was acidified with conc HCl (5 ml). The cold soln yielded fluffy needles of **11** in 35% yield. Recrystallization from EtOH gave white needles, m.p. 203°. (b) Procedure (a) was applied to 3-benzoylquinoline-2-carboxaldehyde (0·1 g). Lactone **11** was obtained in 70% yield, m.p. 203°; IR: 1770, 1300, 1160, 1125, 1070, 960, 785–775, and 700 $cm^{-1}$; NMR: s 3·4 (1H), m 1·8, 2·7 (10H). (Found: C, 78·45; H, 4·37; N, 5·37. $C_{17}H_{11}NO_2$ requires: C, 78·15; H, 4·24; N, 5·36%).

*Kinetic measurements.* A Perkin–Elmer model 621 IR Spectrophotometer was used. The soln cells were NaCl, 0·5 mm thickness. A plot of concentration *vs* absorbance of pure 2-phenyl-3-benzoylquinoxaline, at 1673 $cm^{-1}$, was used as a standard. The presence of starting material (**1a**), was found not to affect the determination of the product (**4a**).

The kinetic measurements were performed by mixing a thermostated (50°) 1:1 dioxane-MeOH soln of **1a**, and a thermostated (50°) methanolic KOH soln. The reaction was allowed to proceed at 50° for 90 min, afterwhich it was quenched with water and extracted with $CCl_4$ (3 times). The extract was made to volume, and the IR absorbance was measured at 1673 $cm^{-1}$ and related to the standard curve. Table 3 summarizes the results, which fit a reaction first order in **1a** and in KOH.

*Incomplete reaction in tetradeuterated methanol.* Compound **1a** (0·75 g) was dissolved in MeOD (10 ml) in which NaO metal (2 g) was dissolved. The soln was refluxed for 15 min and, on cooling, white crystals of unreacted **1a** and product **4a** precipitated. The NMR spectrum of this mixture showed a multiplet centered at 1·35 (proton at $C_8$) the integration of which was equal to that of the singlet at 4·36 (benzylic proton). The IR spectrum of the dried mixture showed absorptions at 3400, 1673, and 1350 $cm^{-1}$.

*Reduction of quinoxaline-N-oxides with sodium dithionite.* The general procedure was as follows: To a stirred, refluxing soln of the quinoxaline-N-oxide (0·005 moles) in 60% EtOH was added dropwise aqueous sodium dithionite (0·02 moles) over a period of 20 min. The mixture was refluxed for 3 to 4 hr, diluted with cold water, and extracted with ether. The ether extract was dried, filtered, and evaporated to dryness. The product was recrystallized from MeOH or MeOH-$H_2O$ (charcoal). The results are summarized in Tables 1 and 2.

*1-Acetoxy-1,2,3,4-tetrahydrophenazine* (**31**). Metachlorperbenzoic acid (10 g), suspended in benzene (50 ml), was gradually added to a soln of 1,2,3,4-tetrahydrophenazine[19] (10 g) in warm benzene (50 ml). An exothermic reaction ensued, and the mixture was allowed to stand at room temp for 12 hr. The mixture was extracted once with $Na_2S_2O_3$ aq and several times with 10% KOHaq. Evaporation of the benzene layer to dryness gave a solid which, upon recrystallization from MeOH, gave cream-colored crystals of the hygroscopic 1,2,3,4-tetrahydrophenazine-5-oxide (7 g), melting over a wide range (87–96°). A soln of this product (5 g) in glacial HOAc (10 ml) and $Ac_2O$ (20 ml) was refluxed for 1 hr, cooled, poured onto crushed ice, and treated to saturation with KOAc. The ppt was collected by filtration and recrystallized from MeOH to give **31** (3 g) m.p. 119–120°; IR: 2940, 1730, 1580, 1480, 1420, 1370, 1350, 1300, 1240, 1050, 980, 910, 850, 760 $cm^{-1}$; NMR: m 1·7–2·5 (4H), m 3·7–4 (1H), m 6·7–7 (2H), m 7·7–8·2 (7H). (Found: C, 69·30; H, 5·75; N, 11·48. $C_{14}H_{14}N_2O_2$ requires: C, 69·40; H, 5·83; N, 11·56%).

*1,2,3,4-Tetrahydrophenazine* (**25**) *from 1-acetoxy-1,2,3,4-tetrahydrophenazine* (**31**). Treatment of **31** (0·25 g)

Table 3.

| Run No. | Initial conc of **1a** in m/lit. (a) $a \times 10^2$ | Conc of **4a** at end of Rx. in m/lit. (c) $c \times 10^2$ | Conc of KOH in m/lit. (b) | $\log \frac{a}{a-c}$ |
|---|---|---|---|---|
| 1 | 1·528 | 0·588 | 1·80 | 0·2115 |
| 2 | 2·286 | 0·887 | 1·80 | 0·2135 |
| 3 | 3·048 | 1·258 | 1·80 | 0·2033 |
| 4 | 3·810 | 1·500 | 1·80 | 0·2174 |
| 5 | 3·810 | 1·000 | 1·07 | 0·1323 |
| 6 | 3·810 | 1·242 | 1·43 | 0·1714 |

with sodium dithionite, according to the general procedure for dithionite reductions, gave **25** (m.p. 90–91°, 50% yield), identical with an authentic sample.[19]

*Reduction of benzil by sodium dithionite.* Benzil (2·1 g) gave benzoin (1·95 g, 93% yield) upon treatment with sodium dithionite according to the general procedure for dithionite reductions. The product was identical with an authentic sample (mixture m.p., IR).

*Acknowledgement*—We are grateful to Chas. Pfizer Co. for a generous grant in support of this work.

## REFERENCES

[1a] A. R. Katritzky and J. M. Lagowski, *Chemistry of the Heterocyclic N-Oxides* pp. 166–231. Academic Press, New York (1971); [b] E. Ochiai, *Aromatic Amine Oxides* pp. 184–206. Elsevier, Amsterdam (1967)
[2] W. S. Chilton and A. K. Butler, *J. Org. Chem.* **32**, 1270 (1967)
[3] G. Tennant, *J. Chem. Soc.* C, 2658 (1967)
[4] M. J. Haddadin and C. H. Issidorides, *Tetrahedron Letters* 4609 (1968)
[5] SR A. I. Gallagher, I.H.M., B. A. Lalinsky and C. M. Cuper, *J. Org. Chem.* **35**, 1175 (1970) and refs cited
[6a] D. J. Cram and R. D. Guthrie, *J. Am. Chem. Soc.* **88**, 5760 (1966); [b] F. D. Bordwell, *Acc. Chem. Research* **3**, 281 (1970)
[7] M. J. Haddadin and A. S. Salameh, *J. Org. Chem.* **33**, 2127 (1968)
[8] M. J. Haddadin, H. N. Alkaysi and S. E. Saheb, *Tetrahedron* **26**, 1115 (1970)
[9] Table 1, Ref *c*
[10] Table 1, Ref *b*
[11] J. March, *Advanced Organic Chemistry* p. 699. McGraw-Hill, New York (1968)
[12] L. F. Fieser and M. Fieser, *Reagents for Organic Synthesis* p. 1081. Wiley, New York (1967)
[13a] K. Wallenfels and H. Schuly, *Liebigs Ann.* **621**, 178 (1959); [b] *Chem. Ber.* **91**, 487 (1958)
[14a] J. F. Biellman and H. Callot, *Tetrahedron Letters* 3991 (1966); [b] J. F. Biellman and J. Henry, *Bull. Soc. Chim. Fr.* 1154 (1968); *Chem. Abstr.* **69**, 59060 (1968)
[15] E. Abushanab, *J. Am. Chem. Soc.* **93**, 6532 (1971)
[16] C. H. Issidorides and M. J. Haddadin, *J. Org. Chem.* **31**, 4067 (1966)
[17] O. Stark and F. Hoffman, *Chem. Ber.* **42**, 716 (1909)
[18] H. N. Al-Kaysi, M.S. Thesis, American University of Beirut, Beirut, Lebanon (1968)
[19] Table 2, Ref *d*