TABLE I

Compd no.	R_1	R_2	X	Mp, °C	% yield	Ref
3	CH_3	CH_3	O	181–183	16	a
4	CH_2CH_2-	CH_2CH_2	O	170–172	7	b
5	CH_3	H	H, OH	178–179	14	b
6	H	H	H, OH	227–229	5	b
7	CH_2OH	H	H, OH	198–199	16	b

a British Patent 668,412 (1958). *b* H. McIlwain, *J. Chem. Soc.*, 322 (1943).

SCHEME III

SCHEME IV

8a, R = H
b, R = CH₃
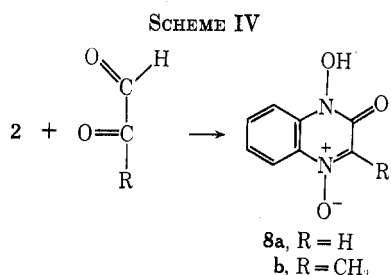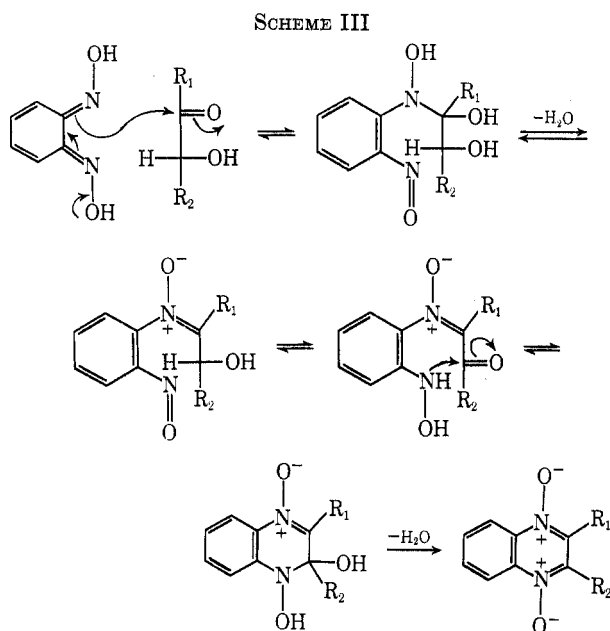
lier routes for the synthesis of 1-hydroxyquinoxalin-2-one 4-oxides.[7]

Experimental Section

General Procedure for Quinoxaline 1,4-Dioxides (3–7).—A mixture of equimolar quantities of *o*-quinone dioxime and the carbonyl compound was dissolved in tetrahydrofuran (0.01 mol/ 30 ml) and refluxed for few hours. The solvent was then evaporated and the residue chromatographed on acid-washed Florisil, eluting first with benzene and then with chloroform. The CHCl₃ eluates were crystallized from methanol or a mixture of methanol–chloroform. The compounds isolated had identical physical data to authentic samples.

1-Hydroxyquinoxalin-2-one 4-Oxide (8a).—*o*-Quinone dioxime (6.9 g, 0.05 mol) was suspended in water (50 ml) and glyoxal (20 ml of 30% aqueous solution) was added. The suspension was heated on the steam bath for 5 min and a precipitate formed

(6.0 g) (65%). This crystallized from methanol had mp 255–257°. The nmr spectrum had the following chemical shifts: δ 7.3–7.9 (3 H, m); 8.1 (1 H, s); 8.26 (1 H, q, $J_{5,6}$ = 8 Hz, $J_{5,7}$ = 2 Hz); 11.6 (1 H, broad multiplet, exchanges with D₂O). Ir (KBr) showed absorptions at 2.8, 6.2, and 7.5 μ; uv λ_{max}^{MeOH} 420 mμ (ε 470), 327 (470), 257 (2800), and 230 (1870).

Anal. Calcd for $C_8H_6O_3N_2$: C, 53.93; H, 3.37; N, 15.17. Found: C, 53.83; H, 3.37; N, 15.37.

3-Methyl-1-hydroxyquinoxalin-2-one 4-Oxide (8b).—Following the procedure for 8a using methyl glyoxal, the product was formed in 50% yield, mp 231–232° (lit.[7] 216–217°). The physical data were similar to those of 8a.

Anal. Calcd for $C_9H_8O_3N_2$: C, 56.25; H, 4.20; N, 14.58. Found: C, 56.77; H, 4.44; N, 14.44.

Substituent Effects on Hydrogen Bonding of Monosubstituted Phenols to Chloride Ion

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Recent publications[1,2] dealing with hydrogen bonding of chloride ion in nonpolar media prompted us to report some of our data on the interaction of monosubstituted phenols with chloride ion in methylene chloride.

Solutions of various phenols and benzyltriphenylphosphonium chloride (1:1 mol ratio) were prepared in anhydrous methylene chloride and the nmr chemical shifts of the hydroxyl protons were determined at 35°. The results are listed in Table I. A good linear correlation (see Figure 1) was obtained by plotting the chemical shift for the meta- and para-substituted phenols against σ values[3,4] (or σ⁻ values[3] in the special cases of

(1) G. G. Arzoumanidis, *Chem. Commun.*, 217 (1969).
(2) D. B. Denney, D. Z. Denney, and B. C. Chang, *J. Amer. Chem. Soc.*, **90**, 6332 (1968).
(3) H. H. Jaffé, *Chem. Rev.*, **53**, 191 (1953).
(4) M. T. Tribble and J. G. Traynham, *J. Amer. Chem. Soc.*, **91**, 379 (1969).

(7) A. S. Elina and L. G. Tsirul'nikova, *Zh. Obshch. Khim.*, **33**, 1544 (1963).

TABLE I

HYDROXYL-PROTON CHEMICAL SHIFTS $(\delta)^a$ FOR MONOSUBSTITUTED PHENOLS IN METHYLENE CHLORIDE IN THE PRESENCE OF 1 EQUIV[b] OF CHLORIDE ION[c]

No.	Substituent	Para isomer	Meta isomer	Ortho isomer
1	–OCH$_3$	9.32	9.78	7.76
2	–t-C$_4$H$_9$	9.41	9.50	9.49
3	–CH$_3$	9.40	9.57	9.48
4	–CH$_2$C$_6$H$_5$	9.57		9.70
5	–SCH$_3$	9.90		
6	–OC$_6$H$_5$	9.76	10.04	9.36
7	–H	9.69	(9.69)	(9.69)
8	–F	9.74	10.22	9.98
9	–Cl	10.04	10.22	10.22
10	–Br	10.09	10.25	10.34
11	–I	10.12	10.18	10.60
12	–CO$_2$CH$_3$	10.67		10.62
13	–COCH$_3$	10.75	10.23	12.11
14	–CN	10.98	10.60	10.12
15	–CHO	11.01	10.39	11.00
16	–NO$_2$	11.41	10.81	10.91
17	–C$_6$H$_5$	9.96	9.97	9.69
18	–COC$_6$H$_5$	10.83		11.76
19	–CH=CHC$_6$H$_5$ (trans)	10.07		
20	–C(CH$_3$)$_2$C$_6$H$_5$	9.53		
21	–N=NC$_6$H$_5$	10.69		
22	–N(CH$_3$)$_2$			9.38

^{a} Parts per million downfield from tetramethylsilane; measured by determining the chemical shift from CH$_2$Cl$_2$ and adding 5.23 ppm (the chemical shift of CH$_2$Cl$_2$). ^{b} Molality of the phenol and the chloride ion were each 0.25. ^{c} As benzyltriphenylphosphonium chloride.

Figure 1.—Plot of hydroxyl-proton chemical shift *vs. σ*. Numbers refer to those in Table I.

–R para substituents[5]). The least-squares equation for this data, omitting p-20, as no σ value has previously been reported, and p-17–19 and p-21, as σ^- values, appropriate in these cases, have not previously been reported, is $\sigma = 0.741\ \delta_{\text{OH}} - 7.196$ where $r = 0.970$, $s = 0.070$, and $n = 30$. Using this equation, new substituent constants were calculated for p-17–21 and these are listed in Table II.

TABLE II

CALCULATED SUBSTITUTED CONSTANTS

Substituent	σ	σ^-
p-C(CH$_3$)$_2$C$_6$H$_5$	−0.134	
p-C$_6$H$_5$	(0.009)^a	0.184^b
p-CH=CHC$_6$H$_5$ (trans)	(.....)^c	0.266
p-N=NC$_6$H$_5$	(0.640)^a	0.725
p-COC$_6$H$_5$	(0.459)^a	0.829

^{a} Data from ref 3. ^{b} Value of 0.195 can be calculated from data in DMSO.[4] ^{c} Value given in ref 3 was incorrectly cited from the original reference.^{d} ^{d} L. P. Hammett "Physical-Organic Chemistry," McGraw-Hill, New York, N. Y., 1940, p 188.

In the case of 22 of the meta- and para-substituted phenols, direct comparisons could be made with the hydroxyl chemical shifts in dimethyl sulfoxide (DMSO) solution recently reported by Tribble and Traynham.[4] A plot of the two sets of data gave a straight line ($r =$

$$\delta_{\text{OH-DMSO}} = 0.991\ \delta_{\text{OH-Cl}} - 0.358 \qquad (1)$$

0.994) which is defined by eq 1. Since hydrogen bonding of phenols in DMSO appears to be well established,[4]

(5) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York, N. Y., 1959, p 217.
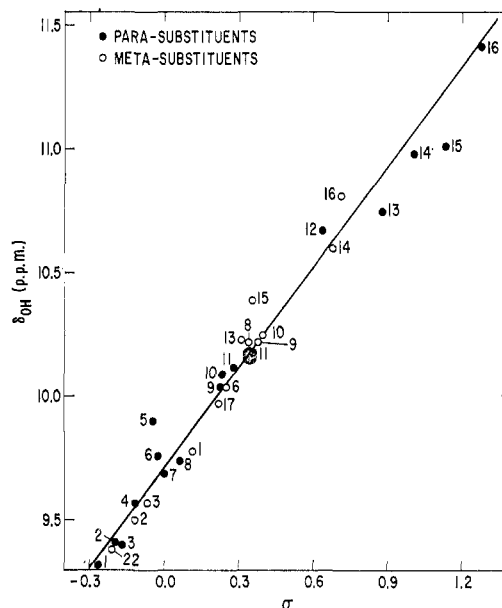
this correlation (as well as our correlation of δ_{OH} with σ) strongly suggests that phenol hydrogen bonding is also occurring in the present system. (In methylene chloride, in the absence of the phosphonium chloride, the δ_{OH} values for all of the meta- and para-substituted phenols occurred in the 4–6-ppm range.)

Comparison of our δ_{OH} values with those of Tribble and Traynham[4] for 13 ortho-substituted phenols (omitting data for o-1, o-14, and o-18) also gave a good correlation ($r = 0.987$). Since steric effects appear to be of little importance in DMSO hydrogen bonding,[4] this correlation suggests the same to be true for chloride ion–hydrogen bonding.

Further support for hydrogen bonding in our systems is evident from a complimentary infrared study. In the absence of the phosphonium chloride, the phenols (0.25 m in methylene chloride), except those having o-carbonyl substituents or an o-nitro substituent, showed –OH stretching vibrations in the 3500–3600-cm^{-1} region. In the presence of 1 equiv of the phosphonium chloride, these bands were either very weak or completely absent and new, very broad bands in the 3000–3100-cm^{-1} region were present. Phenols such as o-13, o-15, and o-18 showed very broad bands in the latter region even without added phosphonium chloride because of intramolecular hydrogen bonding. Thus, no conclusions can be drawn from the infrared spectra concerning interaction of chloride ion with these phenols.

In the absence of added chloride ion, the δ_{OH} in CH$_2$Cl$_2$ for o-12, o-13, o-15, o-16, and o-18 are 10.63, 12.14, 10.91, 10.44, and 11.90, respectively, indicating strong intramolecular hydrogen bonding in each. Since these values are altered very little by the addition of chloride ion, any conclusions regarding the interaction of chloride ion with these phenols would be conjectural at best, at this time. In this regard, σ_{ortho}^- values given by Tribble and Traynham[4] for o-carbonyl substituents must be used with caution since they were determined under conditions where DMSO may or may not have been involved in strong hydrogen bonding with the corresponding phenols.

Proton exchange processes, which also occur in our systems, will be the subject of future publications. We are also involved in experiments to determine the effect of other phosphonium halides as well as ammonium halides on hydrogen bonding in nonpolar media. Acids, other than phenols, are also being investigated.

Nitrones. IV.[1a] A Facile Cope-Type Reaction

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Hess & Clark, Division of Richardson-Merrell, Inc., Ashland, Ohio 44805

As part of a study of nitrofurylnitrones,[1a] we wanted a compound containing a nitro group in the *N*-alkyl portion of α-(5-nitro-2-furyl)-*N*-alkylnitrone. Attempts to synthesize α-(5-nitro-2-furyl)-*N*-(1-furyl-2-nitroethyl)nitrone (**3a**) by the reaction of 5-nitro-furfural (**1a**) and *N*-(1-furyl-2-nitroethyl)hydroxylamine (**2a**)[2] at room temperature gave unexpected results. Thin layer chromatography (tlc) of the reaction mixture revealed two components which were readily separated by column chromatography to give 2-(2-nitrovinyl)furan (**5a**)[3] and 5-nitro-2-furaldehyde *anti*-oxime (**4a**).[4] Their identity was proven by comparison with authentic samples (Scheme I).

While we were unable to isolate any reaction intermediates, we believe nitrone **3a** is formed as an intermediate and rearranges spontaneously to the observed products. This reaction is analogous to the pyrolysis of tertiary amine oxides[5] (the Cope reaction), of aldazine

(1) (a) For paper III, see H. K. Kim, R. E. Bambury, and H. K. Yaktin, *J. Med. Chem.*, submitted for publication. (b) Research Division, Bristol Laboratories, Division of Bristol-Meyers Company, Syracuse, N. Y. 13201. (c) Wm. S. Merrell, Division of Richardson-Merrell, Inc., Cincinnati, Ohio 45215.

(2) C. D. Hurd and J. Patterson, *J. Amer. Chem. Soc.*, **75**, 285 (1953). All the *N*-(1-aryl-2-nitroethyl)hydroxylamines showed a single spot on tlc in 2-propanol and also gave a positive Tollens test.

(3) J. Thiele and H. Landers, *Justus Liebigs Ann. Chem.*, **369**, 303 (1909).

(4) (a) H. Gilman and G. F Wright, *J. Amer. Chem. Soc.*, **52**, 2550 (1930); (b) R. F. Raffauf, *ibid.*, **68**, 1765 (1946).

(5) A. C. Cope, T. T. Foster, and P. H. Towle, *ibid.*, **71**, 3929 (1949).

Scheme I

Scheme I
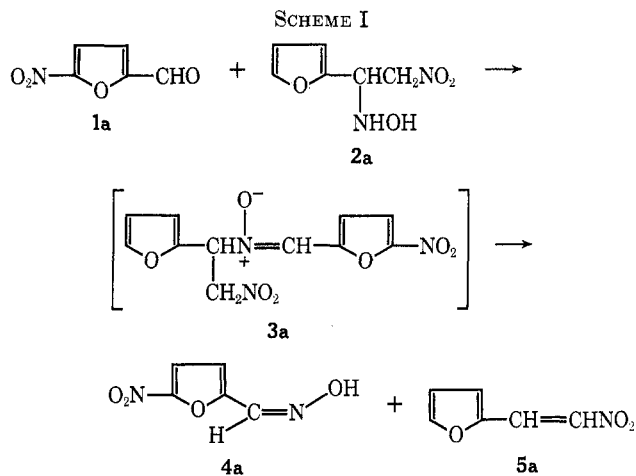
monoxides,[6] and of the methoxazonyl group.[7] The presence of a strong electron-withdrawing group on the α carbon of the nitrone must be essential for spontaneous rearrangement since Hurd and Patterson[2] were able to isolate α-phenyl-*N*-(1-phenyl-2-nitroethyl)nitrone. We propose a mechanism involving a five-membered transition state[8,9] as shown below.
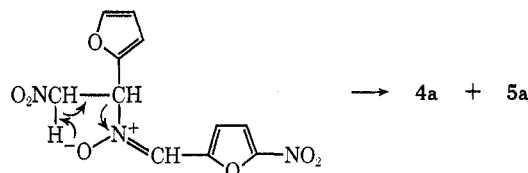
To study the scope of this rearrangement, we successfully extended the reaction to other aromatic carboxaldehydes: 5-nitro-2-thiophenecarboxaldehyde (**1e**), 5-nitro-2-pyrrolecarboxaldehyde (**1f**), *p*-nitrobenzaldehyde (**1g**), 5-nitro-2-furanacrolein (**1h**), and *o*-nitrocinnamaldehyde (**1i**), and to other *N*-(1-aryl-2-nitroethyl)hydroxylamines, **2b**, **2c**, and **2d**.

Yields of aldoximes and nitro olefins isolated by silica gel column chromatography were 46–83 and 35–97%, respectively (see Table I). Assignments to *anti*-aldoximes were based on comparisons of nmr spectra[10] (DMSO-*d₆*) and melting points with authentic samples.

Although authentic samples of anti and syn isomers of **4e** are not reported, the assignment was made on the basis that rearrangement would produce an anti isomer. The nmr spectrum of **4f** showed the presence of two nitrone methine protons at 8.21 (syn) and 7.65 (anti) in a 1:1 ratio. Nmr analysis could not be applied to the vinyl oximes **4h** and **4i**. The spectra of the anti isomers **4h** and **4i** were different from those of the syn isomers; however, signals due to the nitrone methine proton were

(6) W. M. Williams and W. R. Dolbier, Jr., *J. Org. Chem.*, **34**, 155 (1969).

(7) R. B. Woodward and C. Winter, *Tetrahedron Lett.*, 2689 (1969).

(8) A. C. Cope and A. C. Haven [*J. Amer. Chem. Soc.*, **72**, 4896 (1950)], proposed this mechanism to explain an in-acid rearrangement. We do not believe the mechanism is operative in that example.

(9) One of the referees suggested that the initial intermediate i of **1a** and **2a** might collapse directly to products without nitrone formation.
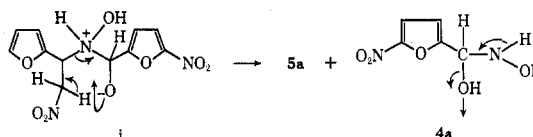
(10) I. Pejkovic-Tadic, M. Hranisvljevic-Jakovljevic, S. Nesic, C. Pascual, and W. Simon, *Helv. Chim. Acta*, **48**, 1157 (1965).