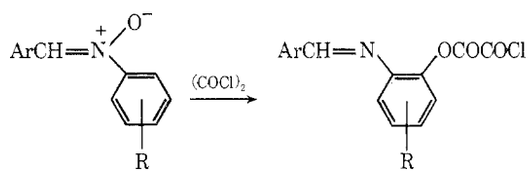
Communications

Reactions of *N*-Aryl Nitrogen Oxides. 2. The Reaction of *N*-Aryl Nitrones with Oxalyl Chloride

Summary: *N*-Aryl nitrones react rapidly with oxalyl chloride yielding imines in which the chloroglyoxalate group, -OCOCOCl, has been specifically introduced into the ortho position of the *N*-aryl ring.

Sir: Attention has been drawn to the need for the development of new ortho selective aromatic substitution reactions.[1] We have reported that phosgene or thionyl chloride react with *N*-aryl nitrones or amine oxides yielding the corresponding *o*-chloro imine hydrochlorides in high yield.[2,3]

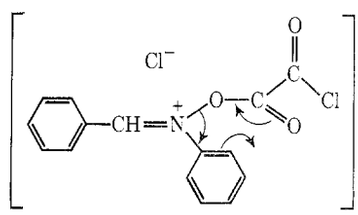
We now wish to report the positionally specific introduction of the chloroglyoxalate grouping into an aromatic ring, ortho to a nitrogen function, by the reaction of *N*-aryl nitrones with oxalyl chloride.



The reaction is performed by the addition of oxalyl chloride in 10% molar excess to a solution of the nitrone in dichloromethane or to a suspension of the nitrone in pentane, allowing the mixture to stand for 10 min. The latter method is particularly convenient since the product may be isolated simply by filtration. As the chloroglyoxalates are heat sensitive, purification is effected most efficiently by dissolving the product in a minimum amount of chloroform and reprecipitating it with pentane.

The chloroglyoxalates could be stored under nitrogen at the low temperature, but thermal decomposition and reactions with moisture and oxygen prevented adequate elemental analyses.[4] The products were characterized by spectra and by independent synthesis by the reaction of the appropriate *N*-(*o*-hydroxyphenyl) imine[5,6] with oxalyl chloride. Also, acid hydrolysis to the appropriately substituted 2-aminophenol and the appropriate aldehyde and quantitative ammonia hydrolysis to obtain the corresponding *N*-(*o*-hydroxyphenyl) imine. The mass spectra verified the proposed molecular weights and exhibited sequential fragmentation confirming the chloroglyoxalate linkage (Table I).

The mechanisms of the nitrone–oxalyl chloride reaction has not been established as yet, but, by analogy with other previously reported similar systems,[7] it most probably involves a cyclic six-centered transition state (intermediate I). Certainly the fact that only ortho ring substitution is observed would tend to indicate an intramolecular pathway.

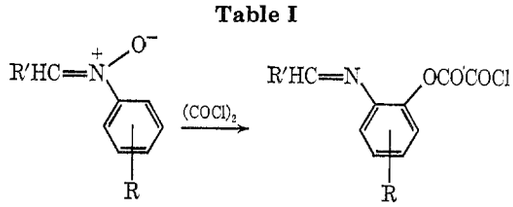


intermediate I

Since *N*-aryl nitrones are readily available starting materials,[8] the reaction with oxalyl chloride apparently affords an excellent route to ortho oxygenated products. To our knowledge, this is the only general method for oxygenating an aromatic ring ortho to a nitrogen function in a rapid, high yield, and positionally specific manner. The only other reported methods involve reactions of *N,N*-dialkylaniline *N*-oxides with acetic anhydride[9] or benzenesulfonyl chloride.[10] These suffer from the disadvantages of either low yields (~20%) or poor positional selectivity (ortho:para ratio of <3) which necessitates isomer separation, sometimes quite tedious.

Since we have now shown that nitrones are viable substances for introducing either a chlorine atom[2,3] or an oxygen function into the ortho position of the benzene ring, we are currently investigating the feasibility of specifically substituting other functionalities ortho to the nitrogen.

Table I



Reactants[a]			Products[b]			
Compd	R	R′	Compd	Mp, °C	Yield, %	Ir frequencies
1	H	C_6H_5	**2**	183–186	78	1780, 1710, 1600[c]
3	H	4-$NO_2C_6H_4$	**4**	100 dec	72	1770, 1695, 1598[d]
5	H	4-$MeOC_6H_4$	**6**	147–149	76	1785, 1710, 1610[c]
7	4-Me	4-$MeOC_6H_4$	**8**	264–266	73	1785, 1715, 1612[c]
9	H	C_6H_5CH=CH	**10**	157–161	80	1792, 1721, 1620, 1605[c]

[a] References for the syntheses of these known nitrones are as follows: O. H. Wheeler and P. H. Gore, *J. Amer. Chem. Soc.*, **78**, 3363 (1956); G. E. Utzinger and F. A. Regenass, *Helv. Chim. Acta*, **37**, 1892 (1954); T. Kubota, M. Yamakawa, and Y. Mori, *Bull. Chem. Soc. Jap.*, **36**, 1552 (1963); J. H. Bowie, R. G. Cooks, and G. E. Lewis, *Aust. J. Chem.*, **20**, 1601 (1967). [b] All products were examined by mass spectrometry. Peaks corresponding to M^+, $(M - 35)^+$, $(M - 63)^+$, $(M - 72)^+$, and $(M - 91)^+$ were observed, corresponding to the parent ion, loss of ^-Cl, ^-COCl, $^-C_2O_3$, and ^-COCOCl. [c] $CHCl_3$ solution. [d] Nujol mull.

References and Notes

(1) J. B. Hendrickson, *J. Amer. Chem. Soc.*, **93**, 6854 (1971).
(2) D. Liotta, A. D. Baker, F. Weinstein, D. Felsen, R. Engel, and N. L. Goldman, *J. Org. Chem.*, **38**, 3445 (1973).
(3) D. Liotta, A. D. Baker, S. Goldstein, N. L. Goldman, F. Weinstein-

Lanse, D. Felsen-Reingold, and R. Engel, manuscript submitted for publication in J. Org. Chem.
(4) The stability of alkyl chloroglyoxalates is discussed by S. J. Rhoads and R. E. Michel, J. Amer. Chem. Soc., 85, 585 (1963).
(5) The o-hydroxy imines were obtained by direct condensation of 2-aminophenol with the appropriate aromatic aldehyde in benzene solution via Dean–Stark apparatus. All products exhibited the expected -OH and C=N bands in their spectra.
(6) Authentication of N-(o-hydroxyphenyl) imines was by independent preparation as described in ref 5 above and (1) comparison with previous reports in the literature (listed below) and (2) complete spectrometric analyses (ir, nmr, mass spectra). The previous reports of interest are (a) F. G. Singleton and C. B. Pollard, J. Amer. Chem. Soc., 62, 2288 (1940); (b) F. R. Bean, U. S. Patent 2,338,482 (Jan 4, 1944), U. S. Patent 2,394,587 (Feb 12, 1946); (c) T. J. Lane and A. J. Kandathil, J. Amer. Chem. Soc., 83, 3782 (1961); (d) K. K. Chatterjee, N. Farrier, and B. E. Douglas, ibid., 85, 2919 (1963); (e) N. K. S. Rao, K. R. Chandran, and U. P. Basu, J. Indian Chem. Soc., 26, 133 (1949); (f) T. G. Levi, Gazz. Chim. Ital., 59, 544 (1929); (g) R. Shimizn, Am. Rept. Research Inst. Tuberc., Kanazawa Univ., 11 (2), 1 (1953).
(7) See ref 3 and reference therein.
(8) J. Harner and A. Macaluso, Chem. Rev., 64, 489 (1964).
(9) R. Huisgen, F. Bayerlein, and W. Heydkamp, Chem. Ber., 92, 3223 (1959).
(10) S. Oae, T. Maeda, S. Kozuka, and M. Nakai, Bull. Chem. Soc., Jap., 44, 2495 (1971).

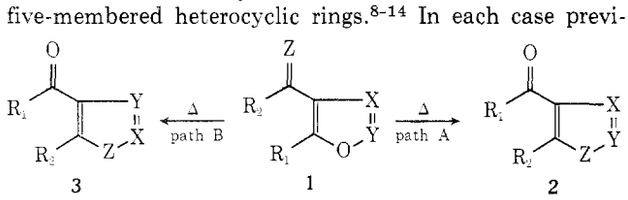
Department of Chemistry **Dennis Liotta**
Queens College of the **A. D. Baker**
City University of New York **Norman L. Goldman**
Flushing, New York 11367 **Robert Engel***

Received March 11, 1974

Thermal Valence Rearrangement of 4-Acylisoxazoles to 4-Acyloxazoles

Summary: A number of 3-phenyl-4-acyl-5-alkylisoxazoles have been found to undergo thermal rearrangement to 2-phenyl-4-acyl-5-alkyloxazoles; the formation of the rearranged oxazole requires bonding between the 3 carbon of the isoxazole ring with the oxygen atom of the acyl group; a mechanism involving the intermediacy of a 2*H*-azirine is suggested.

Sir: The photoisomerization of many different five-membered heterocyclic ring compounds has been shown to proceed by a path in which two of the ring atoms interchange their position under the influence of uv light.[1] The demonstration of a ring-contraction–ring-expansion process in these reactions was first documented by Ullman and Singh for the photorearrangement of 3,5-diarylisoxazoles to 2,5-diaryloxazoles.[2] An analogous pathway nicely rationalizes the major products produced in the photoisomerization of other five-membered heterocyclic rings.[3-7] There are also a number of reports in the literature which describe the thermally induced valence isomerizations of five-membered heterocyclic rings.[8-14] In each case previ-

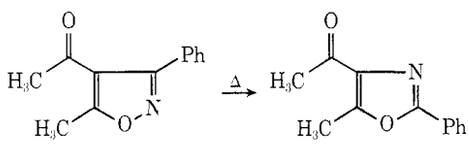


3 1 2

X = N, C; Z = N, O; Y = N, C

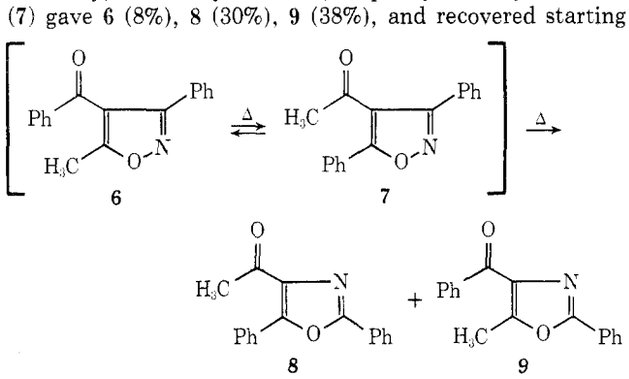
ously studied, the product obtained can only be rationalized by a sequence involving homolytic cleavage of the O–Y bond to produce a reactive acyclic intermediate which subsequently recloses to produce the rearranged heteroaromatic compound (*i.e.*, **1** → **2** *via* path A). In this communication we wish to describe the thermally induced rearrangement of several 4-acylisoxazoles which follow a ring-contraction–ring-expansion sequence (path B).

It is well known that, when two heteroatoms of higher electronegativity than carbon (*e.g.*, nitrogen, oxygen) are linked together through a single bond, the bond dissociation energy of such a linkage is considerably lower than that of a C–C single bond.[15,16] Taking this into consideration, we decided to examine the thermal behavior of 3-phenyl-4-acetyl-5-methylisoxazole (**4**).[17] Thermolysis of isoxazole **4** at 230° under a nitrogen atmosphere for 2 hr afforded 2-phenyl-4-acetyl-5-methyloxazole (**5**), mp 78–79°, in quantitative yield [nmr ($CDCl_3$) τ 7.50 (s, 3 H), 7.42 (s, 3 H)]. The structure of the rearranged product was unambiguously established by an independent synthesis.[18]



4 5

When 3-phenyl-4-benzoyl-5-methylisoxazole[17] (**6**) was subjected to similar thermolysis conditions, a mixture of three new compounds was produced. Analysis of the crude reaction mixture by nmr showed that it contained 3,5-diphenyl-4-acetylisoxazole (**7**, 8%), 2,5-diphenyl-4-acetyloxazole (**8**, 29%), and 2-phenyl-4-benzoyl-5-methyloxazole (**9**, 39%), as well as unreacted starting material (24%). Similarly, thermolysis of 3,5-diphenyl-4-acetylisoxazole (**7**) gave **6** (8%), **8** (30%), **9** (38%), and recovered starting



6 7 8 9

material (24%). Confirmation of the structure of isoxazole **7**, mp 93–94°, nmr ($CDCl_3$) τ 7.8 (s, 3 H), was obtained by comparison with an authentic sample prepared by treating 4-phenyl-3-butyn-2-one with benzonitrile oxide.[19] Structure **8** was established by comparison with an authentic sample.[18] Oxazole **9**,[19] mp 61–62°, nmr ($CDCl_3$) τ 7.32 (s, 3 H), was also independently synthesized by treating 5-methyl-2-phenyloxazole-4-carboxylic acid[18] with thionyl chloride in dimethylformamide to give the corresponding acid chloride, mp 131–133°, which in turn was treated with diphenylcadmium in benzene.

The thermal rearrangement of 4-carbonyl substituted oxazoles is a general reaction[8-12] which was first observed by Cornforth.[8] Consequently, it was of interest to determine whether oxazoles **8** and **9** were interconverted during the thermolysis conditions. Oxazole **8**, when subjected to thermolysis at 230° for 5 hr gave only a 5% yield of **9**. Similarly, **9** produced an insignificant (~4%) amount of **8** under identical reaction conditions. The lack of significant thermal interconversion of oxazoles **8** and **9** under the reaction conditions used rules out any regiospecific mechanism for the thermal rearrangement of **6** and/or **7**.

The formation of oxazole **8** from isoxazole **6** (or **9** from **7**) requires bonding, at some point in the reaction, between C-3 of the isoxazole ring and the oxygen of the benzoyl group. We believe that the experiments reported here require the intermediacy of a 2*H*-azirine (*i.e.*, **10**) to rationalize the transposition of the two ring atoms. The most reasonable pathway for the formation of **10** involves homo-