

tetrachloroethylene in the thermolysis of $\text{PhHgCCl}_2\text{Br}$ in the absence of a substrate capable of trapping CCl_2 occurs by such a route.¹

We report our results at the present time because the $(\text{Me}_3\text{SiCCl}_2)_2\text{Hg}$ reagent adds two new, potentially useful species to the arsenal of synthetic organosilicon chemistry: trimethylsilylchlorocarbene and the trimethylsilyldichloromethyl radical. Our recent report of Me_3SiCH transfer to olefins *via* CuCl -catalyzed reactions of trimethylsilyldiazomethane also should be noted in this connection.⁹ Our efforts in this area are continuing.

All new compounds reported in this communication had satisfactory analyses, and known compounds were identified by means of their infrared or nmr spectroscopic properties.

Acknowledgments. The authors are grateful to AFOSR(SRC)-OAR, U. S. Air Force (Grant No. AFOSR-68-1350), for generous support of this research. This investigation was supported in part by Public Health Service Fellowship 5-F1-GM-28,934 (to E. M. H.).

(9) D. Seyferth, A. W. Dow, H. Menzel, and T. C. Flood, *J. Am. Chem. Soc.*, **90**, 1080 (1968).

(10) National Institutes of Health Predoctoral Fellow, 1965–present.

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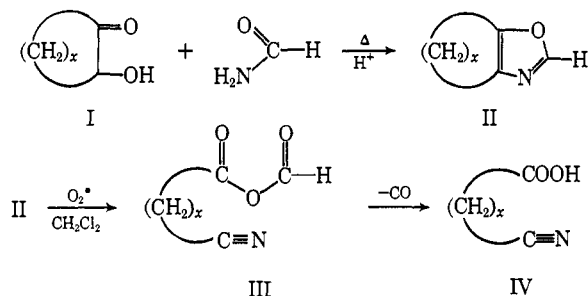
Received February 15, 1968

The Reaction of Oxazoles with Singlet Oxygen. II.¹ A Novel Method for the Preparation of ω -Cyano Acids

Sir:

We have previously described the conversion of oxazoles to triamides by dye-photosensitized autoxidation in methanol.¹ We now wish to report that, in inert solvents such as methylene chloride, the reaction of singlet oxygen with 4,5-condensed oxazoles of type II takes a different course, providing a useful method for the preparation of ω -cyano acids.

The fused-ring oxazoles were readily prepared from the acyloins (I) by condensation with formamide in acidic medium.² Systems studied included II, $x = 4, 5, 6$, and 10, based on their ready availability. In a typical oxidation, the oxazole II, $x = 4$ (4 g), was irradiated in CH_2Cl_2 (1000 ml) with a 275-W sunlamp³



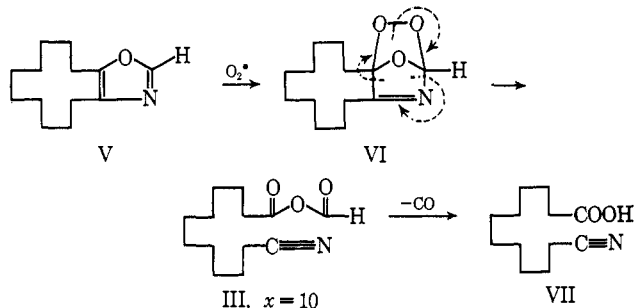
(1) For the first paper in this series see H. H. Wasserman and M. B. Floyd, *Tetrahedron Suppl.*, **7**, 551 (1966).

(2) H. Bredereck and R. Gompfer, *Chem. Ber.*, **87**, 726 (1954).

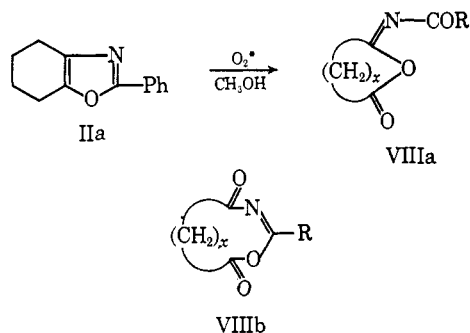
(3) The reaction also proceeds with a 150-W floodlamp, but at a much slower rate.

for 12–14 hr while dry oxygen was bubbled through the stirred solution. Methylene blue was used as a sensitizer. After evaporation of the solvent at room temperature a crude product was obtained showing sharp nitrile (2250 cm^{-1}) and anhydride absorption (1785 and 1765 cm^{-1}) in the ir. The nmr spectrum exhibits a characteristic sharp singlet at τ 0.9 (formyl hydrogen). The anhydride thus obtained readily liberated CO during work-up to yield the nitrile acid IV ($x = 4$).⁴ The structure of the product was shown by ir (broad OH absorption near 3100 cm^{-1} , $\text{C}\equiv\text{N}$ at 2250 cm^{-1} , and $\text{C}=\text{O}$ at 1705 cm^{-1}) and nmr spectra (singlet at $\tau -1.4$ (carboxylic proton) and two multiplets centered at τ 7.6 and 8.5). Hydrolysis of IV, $x = 4$, yielded adipic acid. The yields in the conversions II \rightarrow IV ($x = 4, 5, 6$, and 10) were 80–90%.

As illustrated in the case of oxazole V, formed from cyclododecanone, the reaction appears to proceed through the intermediate transannular peroxide, VI, which then undergoes rearrangement⁵ to form the cyano anhydride III, $x = 10$. Loss of CO from this mixed anhydride of formic acid⁶ leads to VII, the observed product. Further evidence for the participation of singlet oxygen in this reaction was provided by the thermal reaction of V with 9,10-diphenylanthracene peroxide⁷ (19 hr in boiling toluene) which yielded the nitrile acid VII (75%).⁸



Oxazoles of type II substituted in the 2 position (CH_3 , C_6H_5) also undergo the same rearrangement, yielding cyano anhydrides which may react further by hydrolysis or alcoholysis to form the corresponding ω -cyano acids or esters. By-products in these reactions are N-acylimino anhydrides VIIIa or VIIIb. The



(4) Satisfactory C, H, and N analyses were obtained for all new compounds.

(5) D. W. Kurtz and H. Shechter (*Chem. Commun.*, 689 (1966)) have observed that benzonitrile and benzoic anhydride are among the products formed in the photolysis of 2,4,5-triphenyloxazole in oxygen. An analogous mechanism has been suggested by these authors to explain their results.

(6) G. F. Fanta, *J. Org. Chem.*, **29**, 981 (1964).

(7) H. H. Wasserman and J. R. Scheffer, *J. Am. Chem. Soc.*, **89**, 3073 (1967).

(8) H. H. Wasserman and J. Cooper, to be published.

latter are isolated as the principal products if the photosensitized autoxidation is carried out in methanol. Thus, the photosensitized autoxidation of the phenyl-substituted oxazole IIa in methanol yields VIII, a or b, $x = 4$, $R = C_6H_5$, mp 125–126° (65%),⁹ ir, 1745, 1695, and 1655 cm^{-1} ; nmr, peaks at τ 2.12 (multiplet, 2 H) and 2.46 (multiplet, 3 H), and an A_2B_2 pattern of peaks (8 H) centered at τ 7.58. In addition to the molecular ion peak at m/e 231 in the mass spectrum, there is a base peak at m/e 105 corresponding to the loss of COC_6H_5 .

Acknowledgments. We wish to acknowledge support of this work by Grant GM 13854 from the National Institutes of Health. We also wish to thank Drs. S. Lipsky and W. McMurray for assistance in obtaining the mass spectrometric analyses.

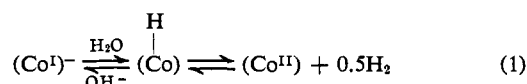
(9) The reaction mixture also contains a small amount of nitrile.

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Received January 31, 1968

The Nucleophilicity of Vitamin B_{12s}

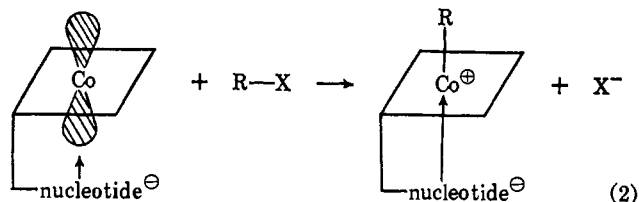
Sir:

One of the most unusual features of vitamin B₁₂ is its reducibility to vitamin B_{12s}, the highly reactive species which is now well recognized to be a Co(I) complex.^{1–4} Vitamin B_{12s} is at equilibrium with vitamin B_{12r} and molecular hydrogen, as represented by



In alkaline solutions the predominant form of vitamin B_{12s} is the spin-paired species “(Co^I)[−]” in which the cobalt atom has the properties of a strong nucleophile. This is because its highest occupied orbital is the probably weakly antibonding d_{z^2} orbital, which forms a center of high polarizability and charge density on the cobalt atom.³ The concentration of the unstable acid “(H–Co)” is very small both in alkaline or acidic solutions.^{3,4}

Many conventional alkylating agents react with vitamin B_{12s} to produce organocobalt derivatives. These reactions can be formulated as nucleophilic displacement processes,³ although their SN2 character has not yet been rigorously established (eq 2). A mechanistic



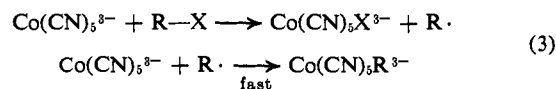
(1) (a) G. H. Beaven and E. A. Johnson, *Nature*, **176**, 1264 (1955); (b) O. Müller and G. Müller, *Biochem. Z.*, **336**, 299 (1962); (c) E. L. Smith and L. Mervyn, *Biochem. J.*, **86**, 2P (1963).

(2) S. L. Tackett, J. W. Collatt, and J. C. Abbott, *Biochemistry*, **2**, 919 (1963).

(3) G. N. Schrauzer, R. J. Windgassen, and J. Kohnle, *Chem. Ber.*, **98**, 3324 (1965).

(4) P. K. Das, H. A. O. Hill, J. M. Pratt, and R. J. P. Williams, *Biochim. Biophys. Acta*, **141**, 644 (1967).

alternative would be an electron-transfer process similar to that postulated for the reactions of $Co(CN)_5^{3-}$ with alkylating agents⁵



Such a mechanism is difficult to distinguish from simple nucleophilic displacement. However, we feel that it does not apply for vitamin B_{12s} reactions on the basis of the following evidence. (1) The relative rates of the reaction of vitamin B_{12s} with methyl, ethyl, *n*-propyl, and *n*-butyl chlorides (180:1.7:1.3:1.0 in methanol at 25°) are very similar to the relative rates of reaction of iodide ion with the same alkyl chlorides (200:2.5:1.1:1.0 in acetone at 50°).⁶ (2) Vitamin B_{12s} reacts much faster with primary halides than with secondary halides; Halpern and Maher observed the opposite effect in the pentacyanocobaltate(II) reactions.⁵ (3) The solvent dependence of the vitamin B_{12s} reactions, which is still under study, seems to be typical for nucleophilic displacement reactions.

Since vitamin B_{12s} has been proposed to be an intermediate in certain B₁₂-dependent enzymatic reactions, it is of interest to determine its position on a relative nucleophilic reactivity scale similar to that proposed by Swain and Scott.⁷ Following Pearson, *et al.*,⁸ we define the nucleophilic reactivity constant, n_{CH_3I} , as

$$n_{CH_3I} = \log(k_Y/k_{CH_3OH})$$

where k_Y and k_{CH_3OH} are respectively the second-order specific rate constants for attack by a nucleophile Y and methanol on the substrate CH_3I , at 25° in methanol as the solvent. Using the rate constants from Table I

Table I. Rate Constants in Methanol at 25°

Halide	$k_2, M^{-1} sec^{-1}$	
	Vitamin B _{12s} ^a	Tributylphosphine-cobaloxime ₈ ^a
CH ₃ I ^b	$3.4 \pm 0.2 \times 10^4$	$2.5 \pm 0.2 \times 10^3$
CH ₃ Br ^b	$1.57 \pm 0.07 \times 10^8$	$2.2 \pm 0.1 \times 10^2$
CH ₃ Cl ^c	5.0 ± 0.5	0.85 ± 0.03

^a Reduced cobalt species prepared by NaBH₄ reduction in 0.1 *F* NaOH. Rates are not dependent on concentration of NaBH₄ or concentration of base. ^b Determined by stopped-flow technique. ^c Determined by conventional spectrophotometric technique.

and a value of $1.3 \times 10^{-10} M^{-1} sec^{-1}$ for k_{CH_3OH} ,⁸ n_{CH_3I} for vitamin B_{12s} is calculated to be 14.4. Values of n_{CH_3I} of some other nucleophiles are listed in Table II (a more complete list is given in Pearson, *et al.*⁸).

Vitamin B_{12s} is obviously the most powerful nucleophile known to date. Its reactivity is matched only by vitamin B₁₂ model compounds such as cobaloxime₈.

Vitamin B_{12s} has not yet been directly observed in any of the biochemical systems where it has been suggested as a reaction intermediate.⁹ Equilibrium amounts of it are probably present in nonenzymatic systems containing vitamin B₁₂ and a mercaptan at pH 7, since the

(5) J. Halpern and J. P. Maher, *J. Am. Chem. Soc.*, **87**, 5361 (1965).

(6) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., New York, N. Y., 1962, p 176.

(7) C. G. Swain and C. B. Scott, *J. Am. Chem. Soc.*, **75**, 141 (1953).

(8) R. G. Pearson, H. Sobel, and J. Songstad, *ibid.*, **90**, 319 (1968).

(9) See H. A. Barker, *Biochem. J.*, **105**, 1 (1967), for detailed discussion and references.