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.

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

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The Nucleophilicity of Vitamin B_{12s}

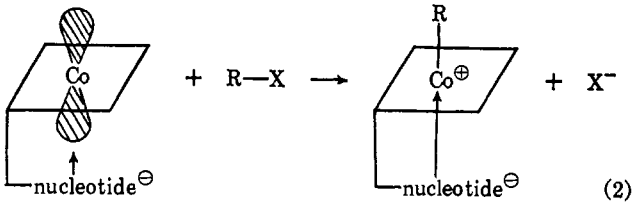
Sir:

One of the most unusual features of vitamin B_{12} 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

$$(Co^{I})^{-} \underset{OH^-}{\overset{H_2O}{\rightleftharpoons}} \overset{H}{\underset{|}{(Co)}} \rightleftharpoons (Co^{II}) + 0.5H_2 \qquad (1)$$

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



(2)

alternative would be an electron-transfer process similar to that postulated for the reactions of $Co(CN)_5^{3-}$ with alkylating agents[5]

$$Co(CN)_5^{3-} + R{-}X \longrightarrow Co(CN)_5X^{3-} + R\cdot$$
$$Co(CN)_5^{3-} + R\cdot \xrightarrow[fast]{} Co(CN)_5R^{3-} \qquad (3)$$

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 B_{12}-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]	k_2, M^{-1} sec^{-1}: Tributylphosphine-cobaloxime$_s$[a]
CH_3I[b]	$3.4 \pm 0.2 \times 10^4$	$2.5 \pm 0.2 \times 10^3$
CH_3Br[b]	$1.57 \pm 0.07 \times 10^3$	$2.2 \pm 0.1 \times 10^2$
CH_3Cl[c]	5.0 ± 0.5	0.85 ± 0.03

[a] Reduced cobalt species prepared by $NaBH_4$ reduction in 0.1 *F* NaOH. Rates are not dependent on concentration of $NaBH_4$ or concentration of base. [b] Determined by stopped-flow technique. [c] Determined by conventional spectrophotometric technique.

and a value of 1.3×10^{-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 B_{12} model compounds such as cobaloxime$_s$.

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 B_{12} and a mercaptan at pH 7, since the

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(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).
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(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.

Table II. Nucleophilic Reactivity Constants toward Methyl Iodide

Nucleophile	n_{CH_3I}[a]
CH_3OH	0.00
Cl^-	4.37
NH_3	5.50
Br^-	5.79
I^-	7.42
$(n\text{-}C_4H_9)_3P$	8.69
$S_2O_3^{2-}$	8.95
$(C_6H_5)_3Sn^-$	~11.5
$(C_6H_5)_3Ge^-$	~12
$Cobaloxime_s \cdot P(n\text{-}C_4H_9)_3$	13.3
$Cobaloxime_s \cdot pyridine$	13.8[b]
$Cobaloxime_s$ (aqua)	14.3[b]
Vitamin B_{12s}	14.4

[a] Except for the last four entries, data taken from ref 8. [b] Calculated from relative rates of reaction with *n*-propyl chloride.

addition of methyl iodide to such a mixture produces methylcobalamin.[10] To obtain further information on the position of the equilibria in eq 1, the stability of vitamin B_{12s} was determined as a function of pH. In the presence of 1 atm of hydrogen gas and a platinum catalyst, vitamin B_{12s} is stable *only above pH ~9.9*. At lower pH values, decomposition into vitamin B_{12r} and hydrogen takes place.[11] Vitamin B_{12r} and hydrogen (1 atm) in the presence of a platinum catalyst similarly proved unstable above pH 9.9, readily forming vitamin B_{12s}. In the absence of a catalyst the equilibrium between vitamin B_{12s} and vitamin $B_{12r} + H_2$ is achieved only slowly. For this reason it is possible to generate vitamin B_{12s} below pH 9.9 at higher than equilibrium concentrations. With metallic zinc or chromous ion as the reducing agents, the reduction is even possible in mildly acidic medium (*e.g.*, acetate buffer). The resulting solutions of vitamin B_{12s} are metastable under these conditions, however, and decompose into hydrogen and vitamin B_{12r}; we have observed that the decomposition proceeds much more rapidly upon the addition of a platinum catalyst.

Assuming that $[Co^I] \approx [Co^{II}]$ at the observed equivalence point (pH 9.9, at 1 atm of H_2), the standard reduction potential of the B_{12r}–B_{12s} couple must be approximately −0.59 V. From this estimate the equilibrium constant for the reaction

$$(Co^I) + H^+ \underset{\longleftarrow}{\overset{Pt,\ H_2O}{\longrightarrow}} (Co^{II}) + 0.5H_2 \qquad (4)$$

is calculated to be of the order of 10^{-10} atm$^{1/2}$ M^{-1}. Therefore, at pH 7, only about 0.1% of the vitamin B_{12} could be present as Co(I) (1 atm of H_2). However, in view of its high nucleophilicity, this amount of B_{12s} is sufficient to permit alkylation of the cobalt. Thus, when a 10^{-3} M solution of vitamin B_{12r} (which does not react with alkylating agents) is buffered at pH 7 and shaken with methyl iodide and a platinum catalyst under an atmosphere of pure hydrogen, the formation of methylcobalamin is complete after 2 hr of shaking (the rate-determining step in this reaction involves a reaction at the surface of the platinum catalyst).

The similarly high values of the nucleophilicities of various $cobaloxime_s$ derivatives, in comparison with vitamin B_{12s}, are in line with other vitamin B_{12}-like chemical properties of these compounds.[12] The experiments with the cobaloximes show that the nucleophilicity of $cobaloxime_s$ depends on the nature of the axial base component. This is expected in view of the effect of axial coordination upon the charge density on the cobalt atom. A detailed study of this effect in vitamin B_{12s} (and other Co(I) chelates) is underway.

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(10) D. H. Dolphin and A. W. Johnson, *J. Chem. Soc.*, 2174 (1965).
(11) Decomposition into B_{12r} and hydrogen also occurs at higher pH if no hydrogen is present (also see ref 2).
(12) See G. N. Schrauzer, *Accounts Chem. Res.*, **1**, 97 (1968), and references therein.
(13) National Institutes of Health Postdoctoral Fellow, 1967–1968 (Contract No. 7-F2-6M-29, 156-01A1).

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Evidence for a 1,5-Hydrogen Transfer in the Photochemistry of an Aroylaziridine[1]

Sir:

The molecular changes involved in the photochemistry of the 1-benzyl-2-phenyl-3-benzoylaziridine system have been shown to be markedly dependent on the initial stereochemistry.[2] To account for the products obtained from the *trans* isomer we suggested that the reaction proceeds by intramolecular hydrogen transfer from the benzyl carbon to the p_y orbital of oxygen of the n–π^* excited state. In contrast to the above scheme, irradiation of the *cis* isomer gave products derived from fission of the carbon–carbon bond of the heterocyclic ring. Because such strikingly different photobehavior was observed, a more thorough investigation of N-substituted 2-phenyl-3-benzoylaziridines seemed desirable. In particular, it was of interest to inspect the photochemistry of a related aziridine system in which the group attached to the nitrogen atom is devoid of α hydrogens. To this end *cis*- and *trans*-1-*t*-butyl-2-phenyl-3-benzoylaziridines (I and II) were studied.

The necessary syntheses were accomplished by treating a mixture of *trans*-benzalacetophenone and *t*-butylamine with iodine in ether.[3] Fractional crystallization gave I, mp 106–107°, and II, mp 69–70°. Spectral data and elemental analyses were in complete agreement with the structures.[4] Irradiation of the *trans* isomer II in moist pentane with a Pyrex filter gave a mixture of four components which could be separated by liquid–liquid partition chromatography. The two major products were identified as 2,5-diphenyloxazole (III) (38%) and (β-*t*-butylamino)-*trans*-benzalacetophenone (IV) (41%), mp 114–115°. The two minor components were shown to be N-*t*-butylbenzalimine (6%) and benzaldehyde (4%).

(1) Photochemical Transformations of Small Ring Carbonyl Compounds. XVII. For part XVI, see A. Padwa and E. Alexander, *J. Am. Chem. Soc.*, **89**, 6376 (1967).
(2) A. Padwa and L. Hamilton, *ibid.*, 89, 102 (1967); 87, 1821 (1965).
(3) P. L. Southwick and D. R. Christman, *ibid.*, **74**, 1886 (1952).
(4) All compounds analyzed satisfactorily. Complete synthetic and degradative details will be given in our full publication.