structure of the cation itself? If so, **3** would become the first entirely organic sandwich compound.

In the absence of crystallographic data, cmr chemical shifts now appear to provide the most reliable criterion for achieving so subtle a distinction.[11] In Table I, those of **3** are compared with fluxional averages derived from reasonable models for **3a** ⇄ **3b**. The disagreement appears to be significant. (As expected, pmr shifts are less decisive.) Although suitable models for **3c** are more difficult to find, we note that $\delta_A$ is appropriate for an extensively delocalized trivalent cation (*e.g.*, benzhydryl, −5.6 ppm);[12] $\delta_C$ falls between that of the cyclopentadienyl anion (90 ppm) and of ferrocene (123 ppm).[13]

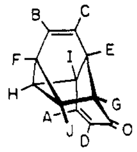
**Table I.** Estimated and Observed Nmr Chemical Shifts of **3**[a]

| Nucleus | Assigned location | Model estimates | | Mean | | |
|---|---|---|---|---|---|---|
| | | 5-Ring | 6-Ring | 5-Ring | 6-Ring | Obsd[b] |
| $^1$H | $A_1$ | $-1.26^{c,g}$ | $-0.25^c$ | | | |
| | $A_2$ | $4.35^e$ | $4.00^d$ | 2.29 | 2.80 | 1.91 |
| | $A_3$ | $7.69^d$ | $7.69^d$ | | | |
| | $B_1$ | $1.35^{c,g}$ | $1.68^c$ | 2.53 | 2.69 | 2.41 |
| | $B_2$ | $3.71^d$ | $3.71^d$ | | | |
| | $C_1$ | $7.30^d$ | $7.30^d$ | | | |
| | $C_2$ | $5.77^{c,g}$ | $6.19^c$ | 6.98 | 7.17 | 7.31 |
| | $C_3$ | $8.05^d$ | $8.05^d$ | | | |
| $^{13}$C | $A_1$ | $-24^c$ | $-41^c$ | | | |
| | $A_2$ | $63^e$ | $66^e$ | 50 | 42 | −4 |
| | $A_3$ | $184^f$ | $184^f$ | | | |
| | $B_1$ | $57^c$ | $48^c$ | 55 | 62 | 40 |
| | $B_2$ | $63^e$ | $66^e$ | | | |
| | $C_1$ | $165^f$ | $165^f$ | | | |
| | $C_2$ | $145^c$ | $160^c$ | 165 | 171 | 105 |
| | $C_3$ | $184^f$ | $184^f$ | | | |

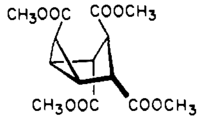
[a] Pmr shifts follow the τ scale; positive cmr shifts are upfield from $CS_2$. [b] Internal references: τ ($CDHCl_2$) 4.70, δ ($CH_2Cl_2$) 103. [c] Cyclopentenyl and cyclohexenyl cations relative to external $Me_4Si$: G. A. Olah, G. Liang, and Y. K. Mo, *J. Amer. Chem. Soc.*, **94,** 3544 (1972). [d] Ketone **4,** Table II. [e] Cyclopentene and cyclohexenes: D. E. Dorman, M. J. Jautelet, and J. D. Roberts, *J. Org. Chem.*, **36,** 2757 (1971). [f] Nortricyclane: G. A. Olah and A. M. White, *J. Amer. Chem. Soc.*, **91,** 3955 (1969). [g] Unimportant differences in the 5-ring means (2.51, 2.62, 7.02) result from the cyclopentenyl τ values of M. Saunders and R. Berger, *ibid.*, **94,** 4049 (1972).

Whether **3c** be indeed regarded as the structure of **3** or as that of its low-energy transition state, a new generic term seems appropriate. We suggest *armilene* (from the resemblance to an armillary sphere) and a numerical homologative specification. **3** is then called the [3.5.3]armilenium cation. It remains to be seen what significance might be drawn from previous failures to observe the [2.5.2]armilenium cation and related species.[8]

Least ambiguous of all is the gross structure of **3**. Aqueous quenching, followed by $MnO_2$ or $CrO_3$–pyridine oxidation, provides a ketone[14] whose pmr spectrum (Table II) and ozonolytic degradation to **5**[16] are consistent only with **4**.



**4**



**5**

**Table II.** Pmr Spectrum of Ketone **4**[a]

| Assignment | $A^b$ | τ | $s^c$ | Appearance[d] |
|---|---|---|---|---|
| $H_A$ | 1.13 | 2.41 | −9.2 | dd (*J* = 9.8, 6.6) |
| $H_B$ | 1.01 | 3.71 | −4.8 | ddd (*J* = 8.0, 7.0, 1.5) |
| $H_C$ | 0.91 | 4.00 | −3.2 | ddd (*J* = 8.0, 8.0, 1.6) |
| $H_D$ | 1.12 | 4.08 | −32.8 | dd (*J* = 9.8, 1.7) |
| $H_E$ | 0.95 | 7.30 | −15.3 | d (*J* = 8.0) |
| $H_F$ | 0.93 | 7.69 | −6.4 | dtd (*J* = 7.0, 6.0, 1.6) |
| $H_G$ | 0.97 | 8.03 | −32.4 | s |
| $H_H$ | 1.07 | 8.05 | −12.3 | t (*J* = 6.0) |
| $H_I$ | 0.90 | 8.23 | −8.0 | d (*J* = 6.6) |
| $H_J$ | 1.05 | 8.51 | −18.7 | t (*J* = 6.0) |

[a] In $CDCl_3$ at 90 MHz. [b] Areas normalized to ten protons at optimal [Eu(fod)$_3$]. [c] Slope of τ *vs.* molar ratio [Eu(fod)$_3$]/[substrate]. [d] Reported *J* (Hz) are first-order splittings as observed at appropriate [Pr(fod)$_3$].

**Acknowledgment.** We are greatly indebted to M. A. Battiste, R. Hoffmann, P. v. R. Schleyer, and G. Schröder for their critical comments, to D. E. Goldstein, H. Caplan, and E. A. Matzner for linguistic suggestions, and to Public Health Service Research Grant No. 10495 (National Cancer Institute) for partial financial support.

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*Received August 2, 1972*

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[11] *Cf.* G. A. Olah, A. M. White, J. R. DeMember, A. Commeyras, and C. Y. Lui, *J. Amer. Chem. Soc.*, **92,** 4627 (1970).

[12] G. A. Olah, *ibid.*, **94,** 808 (1972), and references there cited.

[13] P. S. Pregosin and E. W. Randall in "Determination of Organic Structures by Physical Methods," Vol. 4, F. C. Nachod and J. J. Zuckerman Ed., Academic Press, New York, N. Y., 1971, p 263.

[14] *m/e* 158; ir ($CCl_4$) 5990, 4450 (ε(4450)/ε(5990) = 2.4),[15] 3048, 3032, 2950, 2925, 2312 (w?), 1680, 1617, and 1598 cm$^{-1}$; Raman ($CCl_4$) 3064, 3048, 2950, 1680, 1617, and 1598 cm$^{-1}$; uv max (isooctane) and ε 248 (3300), 304 (80), and 326 (117) nm. *Anal.* Found: C, 83.23; H, 6.68.

[15] *Cf.* H. Weitkamp and F. Korte, *Tetrahedron*, **20,** 2125 (1964).

[16] τ ($C_6D_6$) 4.83 (t, *J* = 7.3 Hz, 0.95), 5.83 (d, *J* = 7.3 Hz, 2.12), 6.38 (s, 2.93), 6.40 (s, 6.09), 6.54 (s, 2.89), 7.89 (d, *J* = 8.7 Hz, 1.91), and 8.26 (t, *J* = 8.7 Hz, 1.11) ppm.

[17] U. S. Public Health Service Fellow, 1967–1970, and Trainee, 1970–1971.

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## Effect of Divalent Metal Ions on the Intramolecular Nucleophilic Catalysis of Phosphate Diester Hydrolysis

*Sir:*

Recent investigations[1,2] have demonstrated that remarkable rate enhancements may be obtained in the hydrolysis of phosphate diesters by suitably positioning nucleophilic groups within the reacting molecule. Moreover, these reactions are thought to proceed *via* metastable pentacovalent intermediates owing to the magnitude of the rate enhancements ($10^4$–$10^6$), high sensitivity to changes in leaving group $pK_a$ ($\beta = -1.2$),

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[1] K. J. Schray and S. J. Benkovic, *J. Amer. Chem. Soc.*, **93,** 2532 (1971).

[2] (a) S. A. Khan, *et al.*, *J. Chem. Soc. B*, 1182 (1970); (b) D. M. Brown and D. A. Usher, *J. Chem. Soc.*, 6558 (1965).

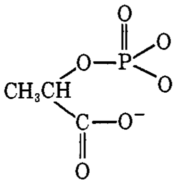
**Table I.** Rate Constants for the Uncatalyzed and Metal Ion Catalyzed Hydrolysis of I–III, 35°, $\mu$ = 0.20

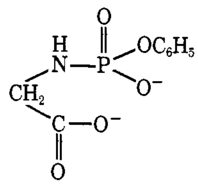
| | | Mg$^{2+}$ | | Zn$^{2+}$ | |
|---|---|---|---|---|---|
| Compd | $k_0$, min$^{-1}$ | $k_M$, min$^{-1}$ | $K$, $M^{-1}$ | $k_M$, min$^{-1}$ | $K$, $M^{-1}$ |
| I[a] | $0.89 \times 10^{-4}$ | $2.1 \times 10^{-3}$ | 13 | $2.7 \times 10^{-2}$ | 20 |
| II[b] | $1.22 \times 10^{-4}$ | $4.8 \times 10^{-3}$ | 13.5 | $3.6 \times 10^{-2}$ | 35 |
| III[c] | $0.88 \times 10^{-4}$ | | | $6.5 \times 10^{-3}$ | 30 |

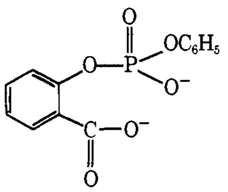
[a] 0.02 $M$ Pipes buffer, pH 6.9. [b] 0.002 $M$ acetate buffer, pH 5.5. [c] 0.02 $M$ Pipes buffer, pH 6.2.

and the marked preference (>90%) for exocyclic ligand loss. We wish to report that the rates for these intramolecular systems are significantly increased by biologically important divalent metal ions and include an important example of Mg$^{2+}$ ion catalysis. The data furthermore suggest that a major fraction of the metal ion catalysis may arise from a unique stabilizing interaction between the metal ion and the intermediate pentacovalent species.

The first-order rate coefficients for hydrolysis of compounds I–III[3] were measured by the addition of 1 $N$ NaOH to aliquots of the reaction mixture and determining the phenoxide liberated spectrophotometrically (287 m$\mu$). All compounds hydrolyze with exclusive expulsion of phenoxide at pH >6 where the observed rates become independent of pH. The hydrolytic rate coefficients for I–III are listed in Table I. The oxygen esters hydrolyze by a factor of >$10^7$ more rapidly than diphenyl phosphate,[4] whereas II hydrolyzes by at least $10^4$ more rapidly than phenyl phosphoramidate, but with P–O rather than P–N bond scission. That the hydrolyses of I–III proceed through nucleophilic addition of carboxylate to form transient cyclic acyl phosphates is supported by (a) the detection of cyclic acyl phosphates in hydroxylamine trapping experiments[5] with I and II where the observed rate of hydroxamate formation is identical within experimental error to the rate of phenoxide release in hydroxylamine buffer, pH 7.2, and (b) spectrophotometric observation of cyclic acyl phosphate formation and disappearance in the case of $m$-nitrophenyl salicylyl phosphate.[2]


I


II


III

The rates of hydrolysis of I–III are significantly accelerated in the presence of Zn$^{2+}$ ion, for which rate enhancements of 304-, 296-, and 74-fold were observed at saturating metal ion concentrations. Hydrolyses of I and II were also examined in the presence of Mg$^{2+}$, for which rate enhancements of 24- and 39-fold were found, respectively. The observed kinetics can be described in terms of preequilibrium formation of a reactive 1:1 ester–metal ion complex, ME, where [ME] ≪ [M$^{+2}$] according to eq 1.

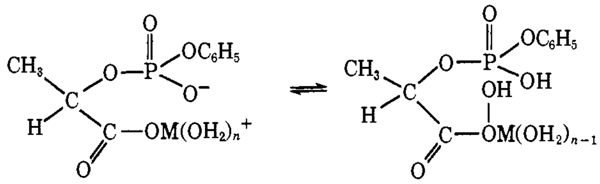
$$\begin{tikzcd} M^{+2} + E \arrow[r, shift left, "K"] \arrow[rr, bend right, "k_0"'] & ME \arrow[l, shift left] \arrow[r, "k_M"] & \text{products} \end{tikzcd} \qquad (1)$$

From eq 1, $k_{\text{obsd}}$ is given by

$$k_{\text{obsd}} = \frac{k_0 + K[M_T]k_M}{1 + K[M_T]} \qquad (2)$$

where [$M_T$] is the initial stoichiometric concentration of metal ion; $k_0$, $k_M$, and $K$ are defined above. The values of the kinetic parameters are given in Table I. Formation of a cyclic acyl phosphate intermediate has been observed spectrophotometrically in the Zn$^{2+}$ catalyzed hydrolysis of the $m$-nitrophenyl derivative of III. This finding in conjunction with continued P–O rather than P–N bond cleavage for II suggests that the nucleophilic mechanism described above is operative in the metal ion catalyzed hydrolyses.

*A priori*, the source of the metal ion catalysis may originate from simple electrostatic neutralization promoting carboxylate attack. The equivalence in $k_0$ for compounds I and III argues that the residual electrostatic term in these two systems is roughly constant. In fact, Kirby, *et al.*, have shown convincingly that the adverse factor due to electrostatic repulsion, known to affect the rates of intermolecular reactions between oxyanions and phosphate diester anions, is apparently absent in the intramolecular reactions associated with I–III.[6] This effect should be distinguished from polarization of the phosphoryl moiety by the electron deficient metal acting to increase the susceptibility of phosphorus to nucleophilic attack. Furthermore, the observation of catalysis of the same order of magnitude in I and II indicates that the primary metal ion interaction is not with the endocyclic ligand. Nucleophilic catalysis by metal-bound hydroxide, as in IVb, is unequivocally eliminated for the Zn$^{2+}$ catalyzed hydrolysis of $m$-nitrophenyl salicylyl phosphate where an intermediate cyclic acyl phosphate has been observed.


IVa IVb

A plausible rationale for our observations is the interaction of the divalent metal ion with the presumed pentacovalent intermediate as in V, where the exact position of the metal ion is only conjecture, or unusual

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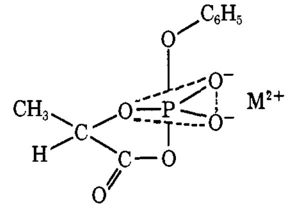
[3] I and II were prepared by phosphorylation of the ethyl esters of lactic acid and glycine, respectively, with diphenyl phosphorochloridate in anhydrous pyridine, followed by partial hydrolysis in dilute aqueous KOH solution. Spectral analysis of I showed nmr ($D_2O$) $\delta$ 1.97 (d, 3 H, $CH_3$), 5.2 (q, 1 H, $CH_3CH$), and 7.7 (multiplet, 5 H, $C_6H_5$). II showed nmr ($D_2O$) $\delta$ 3.48 (d, 2 H, $-NCH_2CO_2-$) and 7.33 (broad multiplet, 5 H, $C_6H_5$). Both I and II gave satisfactory elemental analyses. III and its $m$-nitrophenyl analog were prepared *in situ* by the method outlined in ref 2a.

[4] A. J. Kirby and M. Younas, *J. Chem. Soc. B*, 510 (1970).

[5] F. Lipmann and L. C. Tuttle, *J. Biol. Chem.*, **159**, 21 (1945).

[6] R. H. Bromilow, S. A. Khan, and A. J. Kirby, *J. Chem. Soc. B*, 1094 (1971); *J. Chem. Soc., Perkin Trans. 2*, 911 (1972).

polarization of the phosphoryl moiety. These effects may be combined to facilitate the breakdown of V, perhaps by complexation with the departing phenoxide and/or carboxylate. Thus, the two transition states leading to and from V would be of lower energy resulting in catalysis.



V

These results imply that divalent metal ions in biological phosphorylation reactions may in some cases be functioning mainly at the pentacoordinate level of the phosphoryl transfer reaction. We are continuing to explore a number of aspects concerning these model systems, including the effects of metal ions on intramolecular catalysis by neutral nucleophiles.

(7) N.I.H. Postdoctoral Fellow.

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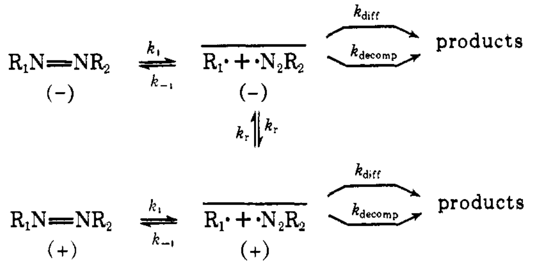
## Internal Return of Caged Geminate Radicals from 9-Azophenyl-2-bromo-9-methylfluorene. Viscosity-Dependent Rotation of Caged Radicals[1]

*Sir:*

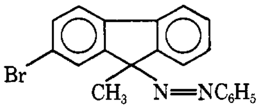
In a previous communication[2] direct evidence was reported for return ($k_{-1}$, eq 1) of caged geminate



(1)

radicals generated in the one bond thermolysis of an azo compound (I, $R_1 = C_6H_5CHCH_3$; $R_2 = CH_3$). The rate of loss of optical activity of a solution of (−)-I is faster than the rate of nitrogen evolution indicating rotation ($k_r$) of caged $\alpha$-phenylethyl radical with respect to its azomethyl partner radical. Decomposition of I in hexadecane at 162°[3] is accompanied by a relatively small amount of return which is in harmony with the notion that the predominant fate of the azomethyl radical is carbon–nitrogen bond rupture as suggested by previous kinetic isotope effect studies.[4a,b] Return in photochemical azo decomposition has also been demonstrated.[4c]

In an attempt to find a higher degree of return during azo compound thermolysis, a new compound, II,



II

expected[5] to lead to a more labile $R_1$–N bond and a more stable $N_2R_2$ radical, was synthesized in our laboratory.[6] First-order rate constants ($k_{N=N}$) for the disappearance of the azo chromophore at 410 nm due to (±)-II in paraffinic hydrocarbons were measured at 80° with a Datex-digitized Cary spectrophotometer.[7] Rate constants ($k_\alpha$) for the loss of optical activity of reactant (+)- or (−)-II were also measured under identical conditions with a Datex-digitized Bendix polarimeter, and these are all shown in Table I.

**Table I.** Spectrophotometric and Polarimetric First-Order Rate Constants for the Disappearance of 9-Azophenyl-2-bromo-9-methylfluorene (II)[a]

| Compd | $10^3 \times$ concn, *M* | Solvent | $10^4k_{N=N}$, $\sec^{-1}$ | $10^4k_\alpha$, $\sec^{-1}$ | $k_{-1}/(k_{decomp} + k_{diff})$ |
|---|---|---|---|---|---|
| (+)-II | 3.49 | $n$-$C_7H_{16}$ | | 3.56 | |
| (±)-II | 9.63 | $n$-$C_7H_{16}$ | 3.40[b] | | 0.288 |
| (−)-II | 6.60 | $n$-$C_7H_{16}$ | | 3.82 | |
| (±)-II | 6.50 | $n$-$C_8H_{18}$ | 3.24[b] | | 0.352 |
| (±)-II | 6.50 | $n$-$C_{10}H_{22}$ | 3.05[b] | | 0.436 |
| (±)-II | 6.50 | $n$-$C_{12}H_{26}$ | 2.91[b] | | 0.505 |
| (±)-II | 4.9–10.6 | $n$-$C_{16}H_{34}$ | 2.41[b] | | 0.817 |
| (+)-II | 4.90 | $n$-$C_{16}H_{34}$ | | 2.99 | |
| (−)-II | 7.45 | $n$-$C_{16}H_{34}$ | | 3.18 | |
| (±)-II | 6.25 | $n$-$C_{18}H_{38}$ | 2.27[b] | | 0.930 |
| (+)-II | 6.80 | $n$-$C_{18}H_{38}$[c] | | 2.74 | |
| (+)-II | 6.15 | $n$-$C_{18}H_{38}$[c] | | 2.75 | |
| (±)-II | 8.62 | $n$-$C_{18}H_{38}$[d] | 2.46 | | |
| (±)-II | 6.5 | $n$-$C_{18}H_{38}$[c] | 2.26 | | |
| (±)-II | 7.23 | $n$-$C_{18}H_{38}$[e] | 2.21 | | |

[a] Rate constants measured in degassed systems at 80.22 ± 0.05°. Two separate thermostats were used but both were adjusted with the same thermocouple. [b] Average of three runs. Average deviations for these range between ±0.2 and ±1.9%. [c] Contained 0.50 *M* 1-octadecene. [d] Benzoyl peroxide (BPO) was present. Initial [BPO]/[II] = 0.13. [e] Contained same concentration of BPO as in *d* and 0.50 *M* 1-octadecene.

That these are true rate constants for unimolecular decomposition are shown by the last few entries of Table I. Addition of benzoyl peroxide (BPO) causes a 10% increase in azo decomposition rate presumably due to induced decomposition resulting from additional phenyl and benzoyl radicals. Addition of 0.50 *M* 1-octadecene to this solution brings the rate constant back to about the value observed in the absence of BPO. 1-Octadecene appears to be an efficient scavenger.[8] Moreover, in the absence of BPO, the

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[1] Research performed under the auspices of the U. S. Atomic Energy Commission.

[2] A. Tsolis, S. G. Mylonakis, M. T. Nieh, and S. Seltzer, *J. Amer. Chem. Soc.*, **94**, 829 (1972).

[3] The temperature at which kinetics can be easily measured.

[4] (a) S. Seltzer and F. T. Dunn, *J. Amer. Chem. Soc.*, **87**, 2628 (1965); (b) S. G. Mylonakis and S. Seltzer, *ibid.*, **90**, 5487 (1968); (c) N. A. Porter, L. J. Marnett, C. H. Lochmüller, G. L. Closs, and M. Shobataki, *ibid.*, **94**, 3664 (1972), and papers cited therein.

[5] S. G. Cohen, F. Cohen, and C. H. Wang, *J. Org. Chem.*, **28**, 1479 (1963).

[6] J. S. Fowler, *ibid.*, 37, 510 (1972).

[7] C. Santiago and S. Seltzer, *J. Amer. Chem. Soc.*, **93**, 4546 (1971).

[8] 1-Olefins have a 5–10% lower absolute viscosity than $n$-alkanes of the same chain length.[9] Assuming ideal behavior, a $n$-alkane containing 0.50 *M* of the corresponding 1-olefin might be expected to have its viscosity lowered by 1% or less than the pure alkane. The rate effect due solely to this change in viscosity is in most cases within experimental error of the rate measurements.