

often failed³; on the other hand there appear to be favorable nucleophiles and solvents which facilitate the steps a-b of eq. 1. For example, $C_6H_5C\equiv CP-(C_6H_5)_3^+Br^-$ and $C_6H_5C\equiv CP(C_4H_9)_3^+Br^-$ have been prepared from reactions in ether at room temperature. We are investigating the scope and rationale of these displacements involving nucleophiles containing sulfur, nitrogen, phosphorus, oxygen, etc., in detail.

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NEUTRON ACTIVATION AS A METHOD FOR LABELLING THE PHOSPHORUS OF NUCLEOTIDES¹

Sir:

Ribonucleotides and deoxyribonucleotides labelled with phosphorus-32 have been of great value in exploring the biochemistry of nucleic acids. The preparation of such compounds tends to be complex, however, involving as it does either biological methods or multi-step synthetic procedures with chromatographic purification of the final product.² These problems are particularly unfortunate, since the half-life of phosphorus-32 is comparatively short (14.3 days).

It was found recently that neutron activation could be used as a method for the preparation,³ from "cold" selenium-containing organic compounds, of the corresponding substances labeled with selenium-75; under these conditions only negligible decomposition occurred. It was of interest, therefore, to determine whether neutron activation could be applied to the phosphorus of nucleotides.

Samples (100 to 200 mg.) of 5'-adenosine monophosphate (AMP), 5' - adenosine diphosphate (ADP), 5'-adenosine triphosphate (ATP), 3'-adenosine monophosphate (3'-AMP), and 5'-deoxyadenosine monophosphate (dAMP) were irradiated in the water-cooled compartment of a graphite reactor at a neutron flux of 6.5×10^{11} neutrons/cm.²/sec. for 62 hours. After discharge, the samples were permitted to stand for 150 hours to permit decay of sodium-24 in those samples (ADP, ATP) that had been submitted as sodium salts. Gamma spectrometry showed traces of arsenic-76 and antimony-122 in dAMP, traces of antimony-122 in 3'-AMP, and traces of residual sodium-24 in ADP and ATP. All other radioactivity was attributable to phosphorus-32.

Seventeen days after discharge from the reactor,

(1) This work was supported, in part (H.G.M.), by grants from the National Science Foundation (G19329) and the U. S. Public Health Service (CY-3937).

(2) For instance, G. M. Tener, *J. Am. Chem. Soc.*, **83**, 159 (1961); J. M. Lowenstein and R. L. Metzberg in "Biochemical Preparations," Vol. 7, John Wiley & Sons, Inc., New York, N. Y., 1960, p. 5.

(3) K. P. McConnell, H. G. Mautner, and G. W. Leddicotte, *Biochim. Biophys. Acta*, in press.

the radioactivity of the samples was determined using a low background automatic counter (Nuclear-Chicago) with a counting efficiency of 45%. Aliquots of sample solutions were plated on stainless steel planchettes. Recovery of samples after activation was quantitative; no purification was carried out prior to counting.

These results were obtained:

Compound	Counts/ μ mole/min.
AMP	2.4×10^6
ADP	4.9×10^6
ATP	8.0×10^6
3'-AMP	2.0×10^6
dAMP	2.2×10^6

Chromatography of the activated compounds (isobutyric acid:concd. ammonium hydroxide: water; 66:1:33) yielded well-defined spots with R_f values identical with those of control material. Neutron activation did not reduce the ability of the ATP sample (Pabst Laboratories, lot no. 131A) to induce luminescence in the luciferin-luciferase assay which specifically requires the triphosphate.⁴ This assay was carried out in quadruplicate.

Use of a strip counter showed only negligible radioactivity outside the spots. On the basis of these findings, neutron activation appears to be a useful tool for the labelling of the phosphorus of nucleotides and presumably of other phosphorus-containing compounds.

(4) B. L. Strehler and J. R. Totter in D. Glick, "Methods of Biochemical Analysis," Vol. I, Interscience Publishers, New York, N. Y., 1954, p. 345.

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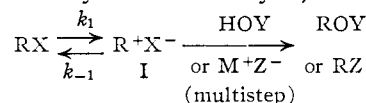
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THE QUESTION OF INTIMATE ION PAIRS¹

Sir:

Ion pairs (I) are intermediates in substitution reactions of triphenylmethyl (trityl) or benzhydryl compounds with hydroxylic reagents (solvolysis, hydrolysis, alcoholysis or acetolysis) or salts.³



Since certain rearrangement or racemization reactions of these compounds proceed even faster than substitution and also show a very large (but not identical) dependence of rate on solvent,⁴ these

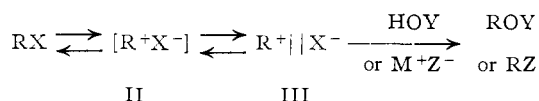
(1) Supported in part by the Atomic Energy Commission. We are grateful to Dr. W. v. E. Doering for information² in 1959 on trityl benzoate-carbonyl-O¹⁸.

(2) W. v. E. Doering, K. Okamoto and H. Krauch, *J. Am. Chem. Soc.*, **82**, 3579 (1960).

(3) R. F. Hudson and B. Saville, *Chem. and Ind.*, 1423 (1954); C. G. Swain and M. M. Kreevoy, *J. Am. Chem. Soc.*, **77**, 1122 (1955); E. D. Hughes, C. K. Ingold, S. F. Mok, S. Patai and Y. Pocker, *J. Chem. Soc.*, 1220, 1230, 1238, 1256, 1265 (1957); C. G. Swain and E. E. Pegues, *J. Am. Chem. Soc.*, **80**, 812 (1958).

(4) S. Winstein and J. S. Gall, *Tetrahedron Letters*, **2**, 31 (1960); S. Winstein, M. Hojo and S. Smith, *ibid.*, **22**, 12 (1960); S. Winstein, J. S. Gall, M. Hojo and S. Smith, *J. Am. Chem. Soc.*, **82**, 1010 (1960); Y. Pocker, *Proc. Chem. Soc.*, 140 (1961); S. Winstein, A. Ledwith and M. Hojo, *Tetrahedron Letters*, **10**, 341 (1961); H. L. Goering and J. F. Levy, *ibid.*, **18**, 644 (1961).

reactions must all have highly polar transition states. Unsettled questions are whether any *rearrangement* or *racemization* reaction has any intermediate,⁵ and, if so, whether it is the same as or different from the ion pair I involved in substitution. Special salt effects in these⁴ and other⁶ systems are consistent with but will be shown below not to require "intimate" ion pairs (II) as intermediates in rearrangement or racemization, preceding other "solvent-separated" ion pair intermediates (III) for substitution.



To improve the chance of capturing an intermediate in one of these rearrangements (if any exists), we used the relatively unhindered and strongly nucleophilic salt lithium azide, rather than the perchlorates and arenesulfonates used previously. As a simple rearrangement we chose the oxygen equilibration reaction of trityl benzoate-carbonyl-O¹⁸ (RX) in dry acetone at 60°.

Without LiN₃ the equilibration reaction has a rate constant (*k*₁) of 3.8 × 10⁻⁶ sec.⁻¹. With 0.020 *M* RX and 0.006 *M* LiN₃, the initial rate of equilibration dropped to zero. After 8.7 hours, when LiN₃ was 41% consumed, there was 0% equilibration (experimental error ~ 2%) in recovered RX *vs.* 11% without azide. After 20 hours there was 11% equilibration *vs.* 24% without

(5) By intermediate we mean a species between reactants and products or one in equilibrium with a species between them but not a transition state or activated complex nor a reversibly formed by-product formed from one or more of the reactants or products by an entirely separate path.

(6) S. Winstein, E. Clippinger, A. H. Fainberg and G. C. Robinson, *J. Am. Chem. Soc.*, **76**, 2597 (1954); S. Winstein and G. C. Robinson, *ibid.*, **80**, 169 (1958); S. Winstein and A. H. Fainberg, *ibid.*, **80**, 459 (1958); S. Winstein, P. E. Klinedinst, Jr. and G. C. Robinson, *ibid.*, **83**, 885 (1961); S. Winstein, P. E. Klinedinst, Jr., and E. Clippinger, *ibid.*, **83**, 4986 (1961).

azide. The rate constant ($-d \ln[\text{RX}]/dt$) from following the disappearance of ionic azide was 4.4 ± 0.4 × 10⁻⁶ sec.⁻¹ both initially and after 10 hours, but 6.3 ± 0.6 × 10⁻⁶ with 0.010 *M* LiN₃. After 5 days, 95% of pure trityl azide was isolated from 0.013 *M* RX in a saturated (0.02 *M*) solution of LiN₃.

This competition experiment with LiN₃ proves rigorously that there is a capturable intermediate in this rearrangement distinct from RX, and that it is the same intermediate as for substitution by LiN₃. It is probably an ordinary ion pair I, (C₆H₅)₃C⁺-O₂CC₆H₅. Within some or perhaps all such ion pairs, the oxygens interchange or become equivalent before further reaction occurs. We attribute the slight increase in rate (3.8 to 4.4) to a salt effect of LiN₃ on *k*₁. Earlier (more intimate) partly or totally equilibrated ion pairs are disproved because rearrangement was suppressed completely early in the reaction. Although prior ion pairs in which the oxygens are not equilibrated may occur, our results neither require nor suggest involvement of two types of ion pairs.

Previous results may also be interpreted in this simpler way without the dual ion-pair hypothesis (without both intimate ion pairs and solvent-separated ion pairs). The faster rate of racemization than of solvolysis of 2-*p*-anisyl-1-alkyl arenesulfonates (RX) in acetic acid even with much lithium perchlorate⁶ can be due to reaction of R⁺ClO₄⁻ with LiX ion pairs to regenerate R⁺X⁻(I) and thence RX. The same kind of mechanism suffices for first-order exchange of benzhydryl chloride with radiochloride salts.⁴ The superimposed second-order exchange can be a one-step reaction.

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BOOK REVIEWS

Advances in Inorganic Chemistry and Radiochemistry. Volume 3. Editors, H. J. EMELÉUS and A. G. SHARPE, University Chemical Laboratory, Cambridge, England. Academic Press Inc., 111 Fifth Avenue, New York 3, N. Y. 1961. ix + 463 pp. 16 × 23.5 cm. Price, \$12.50.

The chapters in this volume are unrelated to each other and vary widely in length. They are reviews with numerous references and provide an excellent literature survey for those who are interested in the specialized subjects which were selected. It seems best to review each chapter separately. (1) "Mechanisms of Substitution Reactions of Metal Complexes" by F. Basolo and R. G. Pearson. The authors examine the results of numerous investigators, discuss the mechanisms for reactions and present many kinetic data in 33 tables (89 pp., 132 ref.). (2) "Molecular Complexes of Halogens" by L. J. Andrews and R. M. Keefer. After a historical introduction and a review of methods used for investigating complexes in solution, the authors discuss complex stabilities and the thermodynamics of the halogen complexes in a small number of organic solvents (40 pp.,

158 ref.). (3) "Structures of Interhalogen Compounds and Polyhalides" by E. H. Wiebenga, E. E. Havinga and K. H. Boswijk. Thermodynamic data and structural parameters are presented for 12 interhalogen, and 28 polyhalides with univalent cations. The discussion is limited mainly to their crystal structure and molecular dimensions, and an explanation of the nature of the bonds (36 pp., 121 ref.). (4) "Kinetic Behavior of the Radiolysis Products of Water" by C. Ferradini. There is a brief introduction concerning the primary action of ionizing radiation, the mechanism of radiolysis of water and the rates of formation of radicals and products. He discusses in detail the rates of reaction of the OH radical and the H atoms with numerous ions and compounds (34 pp., 104 ref.). (5) "Silanes and Their Derivatives" by A. G. MacDiarmid. The methods of preparation, and physical and chemical properties of a large number of silane derivatives are presented in which the silicon is bonded to carbon, halogen, pseudohalogen, oxygen, sulfur, selenium, nitrogen, phosphorus and arsenic. Silyl-metallic compounds containing alkali metals, germanium, tin, boron or iron are also discussed briefly (49 pp., 208 ref.). (6)