complex with a number of nucleophilic reagents. Other bases such as piperidine also act as catalysts. The rates then increase with increasing concentration of piperidine, though not in a simple fashion. The rates vary inversely with the concentration of added piperidinium ion when piperidine is used as a base, again not in a simple fashion. In all these cases first order kinetics are observed.

For a given concentration of catalyst, the rate of reaction is independent of the concentration of the nucleophilic reagent, for example, the nitrite ion. For a given concentration of catalyst the rate is the same for the three nucleophilic reagents, nitrite ion, thiocyanate ion and azide ion.

Allowing for the fact that acid-base reactions in non-aqueous solvents often do not yield simple equilibria, it is clear that the above observations are accounted for by the S_N1 CB mechanism

$$\mathrm{Co(en)_2NO_2Cl^+ + B \rightleftarrows Co(en)(en\text{-}H)NO_2Cl + BH^+} \quad (5)$$

$$\mathrm{Co(en)(en\text{-}H)NO_2Cl \longrightarrow Co(en)(en\text{-}H)NO_2^+ + Cl^-} \quad (6)$$

$$\mathrm{Co(en)(en\text{-}H)NO_2^+ + NO_2^- \longrightarrow Co(en)(en\text{-}H)(NO_2)_2} \quad (7)$$

$$\mathrm{Co(en)(en\text{-}H)(NO_2)_2 + BH^+ \longrightarrow Co(en)_2(NO_2)_2^+ + B} \quad (8)$$

In water the direct reaction with nucleophilic reagents generally does not occur for complexes of cobalt(III), chromium(III), rhodium(III), iridium(III) and platinum(IV). Therefore base catalysis of substitution reactions in non-aqueous media has important synthetic applications, since often the direct reactions are extremely slow in these media.

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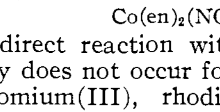
DEPARTMENT OF CHEMISTRY RALPH G. PEARSON
NORTHWESTERN UNIVERSITY HANS H. SCHMIDTKE
EVANSTON, ILL. F. BASOLO

RECEIVED JUNE 21, 1960

1-ALKOXYVINYL ESTERS OF PHOSPHORIC ACIDS AS PHOSPHORYLATING AGENTS

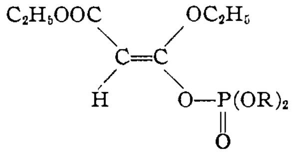
Sir:

Among the most successful methods for carrying out phosphorylation reactions is the use of carbodiimides as developed by Khorana and Todd.[1] It has, however, proved impossible to isolate the postulated intermediates (I) despite their obvious usefulness in synthesis. Thus, attempts to make unsymmetrical pyrophosphates using carbodiimides have invariably led to the formation of mixed products.[2] Cramer, making use of the *Perkow* reaction, obtained II[3] from the reaction of trialkyl phosphites with bromomalonic ester. This type of intermediate was shown to be a very reactive phosphorylating agent for carboxylic, sulfonic and phosphoric acids and, more recently, also adenylic acid.[4] However, this preparation of substituted ketene acylals (II) is limited by the restricted accessibility of triesters of phosphorous acid.



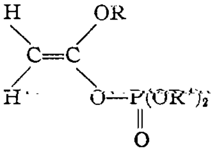
$$\mathrm{R{-}N{=}C(NHR){-}O{-}P(=O)(OR')_2}$$

I



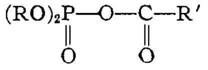
II

We now describe a general method for the preparation of 1-alkoxyvinyl phosphates (III) from esters of phosphoric acid in a manner similar to that described recently for the preparation of 1-alkoxyvinyl esters of carboxylic acids.[5,6,7] The formation of the alkoxyvinyl esters and their subsequent reactions can be followed by observing their infrared spectra (characteristic peaks at 5.96, 5.74μ). In this way, formation of compounds of the type III (R' = C_6H_5, $C_6H_5CH_2$, p-$NO_2C_6H_4$) has been demonstrated. These compounds can be obtained as oils which tend to polymerize on heating, but which, as described below, may be obtained in a pure state by cautious distillation in high vacuum. Thus, III (R = C_2H_5, R' = C_6H_5) has been isolated from the reaction of ethoxyacetylene with diphenylphosphoric acid in methylene chloride[8] solution at 0° in the presence of a mercuric acetate catalyst. After removal of solvent, III (R = C_2H_5, R' = C_6H_5) was obtained as a pale yellow liquid by molecular distillation (2 × 10^{-4} mm., 100° (Calcd. for $C_{16}H_{17}O_5P$: C, 60.0; H, 5.31; P, 9.68. Found: C, 59.9; H, 5.47; P, 9.67)).



III

The active intermediates (III) will react *in situ* without purification, and in this way rapid phosphorylation of alcoholic, phenolic and nucleosidic hydroxyls, phosphoric acids, amines and carboxylic acids has been observed, the only other product being ethyl acetate. (Diphenyl N-cyclohexylphosphoroamidate, obtainable analytically pure, may be used as a method of estimating III (R = C_6H_5).) The mixed anhydride (IV) (R = $C_6H_5CH_2$, R' = C_6H_5), prepared in this manner reacted with cyclohexylamine to give the anticipated N-cyclohexylbenzamide and cyclohexylammonium dibenzyl phosphate.[9]



$$\mathrm{(RO)_2P(=O){-}O{-}C(=O){-}R'}$$

IV

Further reactions of these alkoxyvinyl phosphates, and the reactions of monoesters of phosphoric

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(1) H. G. Khorana and A. R. Todd, *J. Chem. Soc.*, 2257 (1953).

(2) See review by A. R. Todd, *Gazz. chim. ital.*, **89**, 126 (1959).

(3) F. Cramer, *Angew. Chem.*, **69**, 727 (1957).

(4) F. Cramer, *ibid.* **72**, 236 (1960).

(5) H. H. Wasserman and P. S. Wharton, *Tetrahedron*, **3**, 321 (1958).

(6) H. H. Wasserman and P. S. Wharton, THIS JOURNAL, **82**, 661 (1960).

(7) J. P. Arens and T. Doornbos (*Rec. trav. chim.*, **74**, 79 (1955)), prepared tetraethyl pyrophosphate by the reaction of diethyl phosphate with ethoxyacetylene without isolation of any intermediate.

(8) For III (R' = p-$NO_2C_6H_4$), di-p-nitrophenylphosphoric acid is dissolved in a dimethylformamide–methylene chloride mixture.

(9) Compare peptide synthesis by F. Cramer and K. G. Gärtner, *Ber.*, **91**, 1562 (1958).

acid with ethoxyacetylene in the presence of mercuric salt catalysts are under investigation. We have already shown that adenosine-5′ phosphate (as the pyridinium or triethylammonium salts) in methanol solution, reacts with ethoxyacetylene (in the presence of Hg^{++} catalyst) on standing overnight to give the monomethyl ester of AMP. This product, obtainable in quantitative yield, was characterized by comparison with a sample prepared by Khorana's dicyclohexylcarbodiimide technique[10] using two chromatographic systems (2-propanol–ammonia–water, 7:1:2; butanol–acetic acid–water, 5:2:3) and two paper electrophoretic systems (0.1 M K_2HPO_4: 0.1 M KH_2PO_4).

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[10] M. Smith, J. G. Moffatt and H. G. Khorana, THIS JOURNAL, **80**, 6204 (1958).

[11] This work was supported by U. S. Public Health Service Grant, RG-3789(C6).

CONTRIBUTION NO. 1630 FROM
THE STERLING CHEMISTRY LABORATORY[11]
YALE UNIVERSITY HARRY H. WASSERMAN
NEW HAVEN, CONN. DAVID COHEN

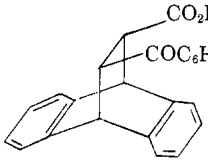
RECEIVED JUNE 27, 1960

ACCELERATION OF THE DIELS-ALDER REACTION BY ALUMINUM CHLORIDE

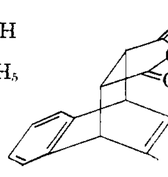
Sir:

Although catalysis of the Diels–Alder reaction by acids[1] has been reported, the influence of catalysts and condensing agents on the rate of this reaction has been held to be small.[2] Our observation of the acceleration by aluminum chloride of the rearrangement of a dicyclopentadien-8-one derivative to a dicyclopentadien-1-one derivative,[3] and the proposal that this type of reaction is related to the Diels–Alder reaction,[4] has led us to investigate the effect of aluminum chloride on the rate of the latter reaction. We have found that in appropriate cases (*vide infra*), the presence of one or more molar equivalents of aluminum chloride can bring about *remarkable acceleration of the Diels–Alder reaction.* The following cases are illustrative.

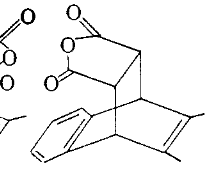
(i) Equimolar amounts of anthracene, maleic anhydride and aluminum chloride were dissolved in dichloromethane at room temperature to give a solution 0.0625 M in each; the progress of the reaction was followed by infrared spectroscopy, which showed that reaction was complete in 1.5 minutes. The reaction mixture was then poured onto ice, giving a quantitative yield of the Diels–Alder adduct.[5] From extrapolation of the rate curve for the reaction under equivalent conditions of temperature and concentration in the absence of aluminum chloride it is estimated that 4800 hours would be required for 95% completion.[6]



I



II



III

(ii) Reaction of equimolar amounts of anthracene, dimethyl fumarate and aluminum chloride dissolved in dichloromethane at room temperature was complete in less than two hours. When the relative molar concentration of aluminum chloride was increased to two, reaction was complete in less than 5 minutes. A quantitative yield of the Diels–Alder adduct[9] was obtained in each case. The reaction in the absence of aluminum chloride when carried out in boiling dioxane requires 2–3 days[9] and affords a less pure product.

(iii) Reaction of equimolar amounts of anthracene, p-benzoquinone and aluminum chloride dissolved in dichloromethane at room temperature was complete in less than 15 minutes, giving the 1:1 adduct[10] in 90% yield. When the relative molar concentration of anthracene was increased to two, there was obtained in 90% yield the previously unknown bis-adduct, m.p. 230° dec.,$\lambda_{\max}^{CH_2Cl_2}$ 5.90 μ, identified by its oxidation to the corresponding quinone.[10] Formation of the bis-adduct did not occur in boiling xylene in the absence of aluminum chloride.

(iv) Reaction of equimolar amounts of 2,3-dimethylnaphthalene, maleic anhydride and aluminum chloride in dichloromethane at room temperature was complete in *ca.* 4 hours. A 1:1 adduct m.p. 175–178° dec., was obtained in 40% yield; this is assigned structure II, since on treatment with boiling methanol it was converted to an acid ester, $C_{17}H_{18}O_4$, m.p. 184–185°, $\lambda_{\max}^{CH_2Cl_2}$ 5.75, 5.85 μ, which gave with bromine and aqueous sodium carbonate a bromolactonic ester, $C_{17}H_{17}O_4Br$, m.p. 191.5–192°, $\lambda_{\max}^{CH_2Cl_2}$ 5.60, 5.75 μ.[11] The same adduct has been obtained previously by heating 2,3-dimethylnaphthalene (1 mole) and maleic anhydride (30 moles) in a sealed tube at 100° for 24 hours.[12] Infrared spectral examination of the crude product formed under either set of reaction conditions indicated the presence of another adduct, presumably III; this was formed to a greater extent in the absence of aluminum chloride.

In addition to the cases cited in detail above, evidence has been obtained for the acceleration by aluminum chloride of the following Diels–Alder reactions: anthracene and diethyl maleate, diethyl fumarate, citraconic anhydride, or dichloromaleic anhydride (in dichloromethane); cyclopentadiene and p-benzoquinone (in carbon tetra-

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[1] A. Wassermann, *J. Chem. Soc.*, 618, 623 (1942); W. Rubin, H. Steiner and A. Wassermann, *ibid.*, 3046 (1949); A. Rodgman and G. F. Wright, *J. Org. Chem.*, **18**, 465 (1953); L. E. Gast, E. W. Bell and H. M. Teeter, *J. Am. Oil Chemists' Soc.*, **33**, 278 (1956).

[2] K. Alder in "Newer Methods of Preparative Organic Chemistry," Interscience Publishers, Inc., New York, N.Y., 1948, p. 404; C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 720.

[3] P. Yates and P. Eaton, *Tetrahedron Letters*, No. 11, 5 (1960).

[4] R. B. Woodward and T. J. Katz, *Tetrahedron*, **5**, 70 (1959).

[5] E. Clar, *Ber.*, **64**, 2194 (1931).

[6] The reaction of anthracene, maleic anhydride and aluminum chloride in benzene solution at 60–70° has been reported to yield β-(9-anthroyl)-acrylic acid.[7] We have found that this compound should be reformulated[8] as $C_{24}H_{18}O_3$ and that it has structure I, formed *via* an initial Diels–Alder reaction followed by a Friedel–Crafts condensation with the solvent.

[7] H. G. Oddy, THIS JOURNAL, **45**, 2156 (1923).

[8] Satisfactory elementary analyses for this compound and all new compounds here reported have been obtained.

[9] W. E. Bachmann and L. B. Scott, *ibid.*, **70**, 1458 (1948).

[10] E. Clar, *Ber.*, **64**, 1676 (1931).

[11] *Cf.* K. Alder and G. Stein, *Ann.*, **504**, 216 (1933); **514**, 1 (1934).

[12] M. C. Kloetzel and H. L. Herzog, THIS JOURNAL, **72**, 1991 (1950).