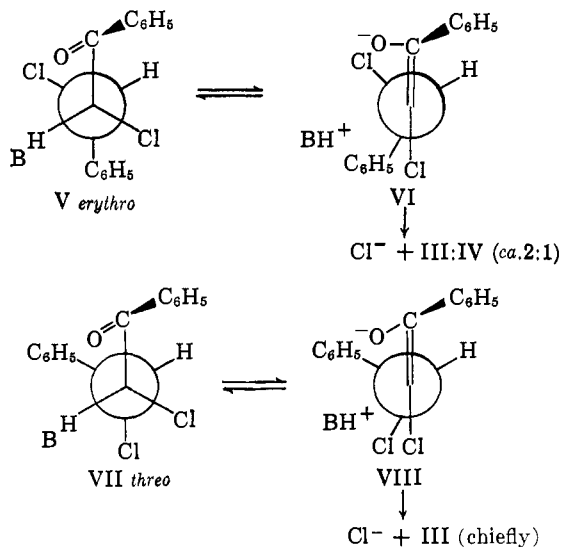


Fig. 2.—pH-rate profile (ethanol).

rise in rate at higher pH values. (Deuterium exchange of the acidic hydrogen atom of SHX would not be expected in this pH range since the reversal of the ionization step is much slower than the loss of chloride ion.) At pH 17, chloride production is complete in 2 sec., indicating that the expected leveling off of the rate, as step 1 becomes rapid and complete, has not commenced. This sets a lower limit of 70 min.⁻¹ for k_2 .

The measurements were made by ultraviolet spectrophotometry at 282 m μ , the isosbestic point of the products, the *trans* and *cis* chalcones III and IV. They are stable in the buffer solutions employed but are photochemically interconverted in diffuse light. Near pH 16, the rate of base consumption was observed by means of indicators.⁴

Preliminary experiments with the *threo* chalcone dichloride (II) point to kinetic behavior similar to the *erythro* form, but the k_1 values are higher. Since the course of the reaction is first order, there is at least no rapid conversion of the *threo* to the *erythro* form. The product contains a much higher proportion of *trans*-S. The relation of rate and products to the configuration of SHX is entirely in accord with a previously published study of the corresponding chalcone dibromides.⁵ The kinetic data here reported support the carbanion mechanism which was suggested for the *erythro* isomer but require modification of the concerted mechanism



(5) R. E. Lutz, D. F. Hinkley, and R. H. Jordan, *J. Am. Chem. Soc.*, **73**, 4647 (1951).

proposed.^{5,6} Possibly conformations related to those favored in the *erythro* and *threo* dichlorides, V and VII, persist in the very short-lived anions having the same, more stable enolate double bond configuration, VI and VIII. Group interferences coupled with solvent effects and ion pairing might contribute sufficiently to the energy barrier to rotation on the 2,3-dicarbon axis to direct return of the proton stereospecifically in the direction from which it had been abstracted. Subsequent irreversible separation of chloride ion from VI and VIII with attendant conformational adjustments could then bring about relatively nonstereospecific development of the α,β double bond in the end products III and IV. Thus the actually observed formation of different mixtures in the two cases of *trans* and *cis* products, with *trans* predominant, is understandable.

Acknowledgment.—We are grateful for the support of the National Science Foundation, Grant G-13292 (T. I. C.) and the U.S. Army Research Office (R. E. L.).

(6) E. S. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., Inc., New York, N. Y., 1959, p. 492.

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Trialkyl Phosphites: Novel Ring-Opening Reactions with Dimethylketene Dimers¹

Sir:

There have been numerous recent studies of reactions of trialkyl phosphites with carbonyl compounds, e.g.: α -diketones^{2a}; quinones^{2b,c}; α,β -unsaturated aldehydes, acids, and esters^{2d-f}; alkyl and aryl aldehydes^{2d}; diaryl ketones^{2g}; β -propiolactone^{2h}; and phthalic anhydride.²ⁱ Frequently, the product of reaction is an adduct. An example, the combination of diphenylketene with triethyl phosphite in 2:1 mole ratio, was described recently.³ Subsequent pyrolysis was reported to give triethyl phosphate, diphenylacetylene, and diphenylketene dimer.

We find that trialkyl phosphites also give adducts (1:1) with the dimers of dimethylketene, I and VIII. These adducts are evidently of a different type than that isolated from reaction of triethyl phosphite with diphenylketene monomer, as structures III and IX could not be expected to give analogous pyrolysis products.³ In addition, these reactions are of interest in that: (1) distinctly different adducts result from reaction with the two dimer forms in contrast to the single product normally formed from ring opening of either the dione or lactone-form dimer under attack by nucleophiles⁴ and (2) ring opening is accompanied by an apparent alkoxy group migration in preference to the alkyl group displacement or migration which is common in the various phosphonate-forming Arbuzov-type reactions of tri-

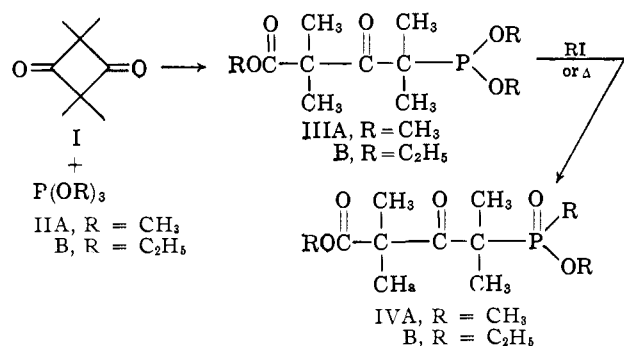
(1) Presented in part at the Southwest Regional Meeting of the American Chemical Society, Dallas, Texas, December, 1962.

(2) For references, see (a) F. Ramirez, N. Ramanathan, and N. B. Desai, *J. Am. Chem. Soc.*, **84**, 1317 (1962); (b) F. Ramirez, E. H. Chen, and S. Dershowitz, *ibid.*, **81**, 4338 (1959); (c) V. A. Kukhtin, N. S. Garif'yanov, and K. M. Orekhova, *Zh. Obshch. Khim.*, **31**, 1157 (1961); (d) V. A. Ginsberg and A. Ya. Yakubovich, *ibid.*, **30**, 3979, 3987 (1960); (e) G. Kamai and V. A. Kukhtin, *Dokl. Akad. Nauk SSSR*, **112**, 868 (1957); (f) G. Kamai and V. A. Kukhtin, *Zh. Obshch. Khim.*, **31**, 1735 (1961); (g) A. C. Poshkus and J. E. Herweh, Abstracts of Papers of the 141st National Meeting of the American Chemical Society, Washington, D. C., March, 1962, p. 17-O; (h) R. L. McConnell and H. W. Coover, Jr., *J. Am. Chem. Soc.*, **78**, 4453 (1956); (i) F. Ramirez, H. Yamanaka, and O. H. Basedow, *ibid.*, **83**, 173 (1961).

(3) T. Mukaiyama, H. Namku, and M. Okamoto, *J. Org. Chem.*, **27**, 3651 (1962).

(4) E.g., by amines and alkoxide ions, R. H. Hasek, E. U. Elam, and J. C. Martin, *ibid.*, **26**, 4340 (1961).

alkyl phosphites.⁵ With the dione dimer, tetramethyl-1,3-cyclobutanedione, the reaction is



The adduct IIIA, b.p. 76–77° (0.03 mm.), formed on heating the dione with a three-mole excess of IIA for 30 days at 100° under nitrogen, is rapidly air-oxidized at room temperature, shows infrared absorption at 1685 and 1750 cm.⁻¹ (capillary film), an n.m.r. 3-H singlet at 6.37 τ (CO₂CH₃), 3-H doublet at 6.45 τ , $J_{\beta\text{H-P}} = 11.5$ c.p.s. (POCH₃), 6-H doublet at 8.87 τ , $J_{\beta\text{H-P}} = 10.5$ c.p.s. [$-\text{C}(\text{CH}_3)_2\text{P}<$], and a 6-H singlet at 8.73 τ [$-\text{C}(\text{CH}_3)_2\text{CO}_2-$]. *Anal.* Calcd. for C₁₁H₂₁O₅P: C, 50.0; H, 8.0; P, 11.7. Found: C, 50.0, 49.7; H, 8.1, 8.4; P, 11.3, 11.7. The phosphonite IIIA is converted to the phosphinate, IVA, by thermal isomerization, complete in a maximum of 8 hr. at 150–160°, and by methyl iodide-catalyzed Arbuzov rearrangement at room temperature as verified by infrared and n.m.r. spectral comparisons. Product IVA is also formed directly in 47% yield by a 120-hr. reaction of dione, I, with excess refluxing IIA, temperature 120–150°.

The structure of IVA, b.p. 96–97° (0.03 mm.), is based on the following: (1) *Anal.* Calcd. for C₁₁H₂₁O₅P: C, 50.0; H, 8.0; P, 11.7. Found: C, 50.1; H, 8.3; P, 11.5; (2) mass spectral parent peak, 264; (3) infrared absorption at 1755 and 1695 cm.⁻¹ (CCl₄); (4) ultraviolet spectrum $\lambda_{\text{max}}^{\text{cyclohexane}}$ 290 μ (ϵ 40); (5) n.m.r. spectrum with 3-H doublet at 6.34 τ , $J_{\beta\text{H-P}} = 10.5$ c.p.s. (POCH₃), 3-H singlet at 6.28 τ , (CO₂CH₃); (6) resistance to peracetic acid oxidation; (7) acid hydrolysis of IVA (1:1 HCl-H₂O, 72 hr., 100°) to diisopropyl ketone,⁶ 50% yield; (8) saponification of IVA with 10% aqueous KOH at room temperature to V, m.p. 119.4–120.0° (*Anal.* Calcd. for C₁₀H₁₉O₅P: C, 48.0; H, 7.6; P, 12.4. Found: C, 48.0, H, 7.4; P, 12.3), neut. equiv. 250 (252 calcd.), pK_a 3.3, infrared absorption strong at 1715 and 1695, broad at 2600–3300 cm.⁻¹ (CCl₄), n.m.r. 3-H doublet at 6.26 τ ($J_{\beta\text{H-P}} = 10.5$ c.p.s.) and 1-H singlet at -1.4 τ (CO₂H); (9) decarboxylation of V at 150° to a neutral, colorless liquid, VI, single infrared absorption (CCl₄) in 1700–1800 cm.⁻¹ region at 1701 cm.⁻¹, peak at 1225 cm.⁻¹ (phosphinate P=O)⁷ mass spectral parent peak, 206; (10) saponification of IVA in 8 hr. with refluxing aqueous KOH to the phosphinic acid, VII, m.p. 71.4–72.8° (*Anal.* Calcd. for C₈H₁₇O₃P: C, 50.0; H, 8.9; P, 16.1. Found: C, 49.8, 49.7; H, 8.9, 9.0; P, 16.1, 16.5), infrared absorption (CHCl₃) 2200–3100 cm.⁻¹ (POH), 1695 cm.⁻¹ (C=O), absence of 3-H doublet near 6.3 τ , presence of 1-H singlet at -2.3 τ (POH) in

(5) V. A. Kukhtin and A. N. Pudovik, *Usp. Khim.*, **28**, 96 (1960), reviews phosphonate-forming Arbuzov-type reactions.

(6) Carbon-phosphorus bond cleavage in acid hydrolysis where the phosphoryl group is located β to a ketone carbonyl is reported for diethyl 2-oxopropylphosphonate by N. Kreutzkamp and H. Kayser, *Chem. Ber.*, **89**, 1614 (1956), is alluded to by A. N. Pudovik and B. A. Arbuzov, *Dokl. Akad. Nauk SSSR*, **73**, 327 (1950), and is mentioned in the review of L. D. Freedman and G. O. Doak, *Chem. Rev.*, **57**, 479 (1957).

(7) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 312.

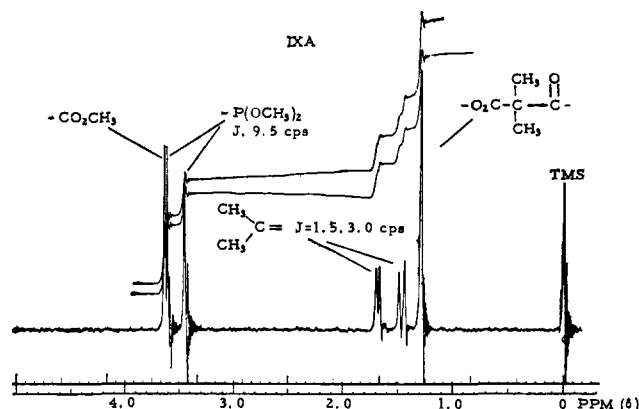
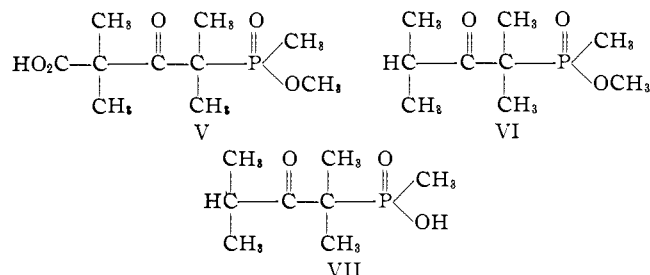
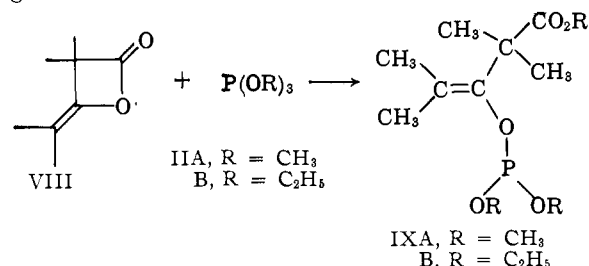


Figure 1.

the n.m.r. spectrum otherwise identical with that for VI, *i.e.*, 1-H multiplet at 6.69 τ and 6-H doublet at 8.98 τ (isopropyl group), $J_{\text{HX}} \sim 7$ c.p.s., 3-H doublet ($J_{\alpha\text{H-P}} = 13.5$ c.p.s.) at 8.65 τ (P-CH₃) and 6-H doublet ($J_{\beta\text{H-P}} = 15$ c.p.s.) at 8.61 τ [$\text{C}(\text{CH}_3)_2\text{P}=\text{O}$]. Satisfactory assignments based on structures shown can also be made for all other peaks in the n.m.r. spectra of IV and V. Compounds V–VII are assigned the structures

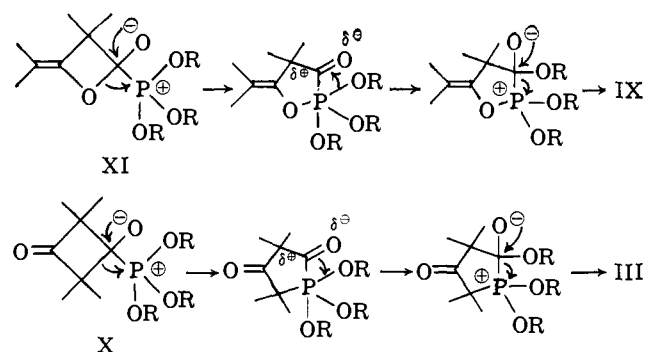


The lactone form of dimethylketene dimer, VIII, under attack by trialkyl phosphites undergoes a similar ring-opening rearrangement involving apparent alkoxy migration.



With a two-mole excess of trimethyl phosphite under nitrogen at 100° for 160 hr., a 67% yield of adduct IXA results, b.p. 61.7° (0.05 mm.) (*Anal.* Calcd. for C₁₁H₂₁O₅P: C, 50.0; H, 8.0; P, 11.7. Found: C, 49.9, 49.8; H, 8.2, 8.4; P, 11.3, 11.5), infrared absorption at 1730 (CO₂CH₃) and 1660 cm.⁻¹ (C=C). Acid-catalyzed methanolysis of IXA gives only two products, the expected trimethyl phosphite and methyl 2,2,4-trimethyl-3-oxovalerate, identified by gas-liquid phase chromatography on an Apiezon L on firebrick column at 200°. Room temperature hydrolysis of IXA with dilute HCl in MeOH-H₂O gave the valerate (g.p.c.). The structure shown is also supported by the n.m.r. spectrum of IXA, Fig. 1.

Completely analogous reactions of I and VIII occur with triethyl phosphite. These ring openings and concomitant alkoxy migration may be understood by the following possible mechanism for reaction of intermediates X and XI which could result initially from nucleophilic attack by phosphorus at carbonyl carbon.



Here, ring expansion predominates over the alternative reactions: possible Arbuzov-type displacement by oxygen on alkyl carbon to give the phosphonate⁵ or reverse aldol-type ring opening, which then would lead to identical products from either I or VIII as with amines and alkoxide ions.⁴ Likely, neutralization of the positive charge developed on phosphorus and release of four-membered ring strain are the reaction driving forces.

Further work, *e.g.*, determination of migrational selectivity in reaction of mixed phosphites, is in progress.

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Acid- and Base-Catalyzed Hydrogen Exchange in Methyl-Substituted Indoles¹

Sir:

The exchange of isotopic hydrogen on the indole nucleus was first reported by Koizumi² for the heterogeneous system of molten indole and aqueous solutions containing some deuterium. These early studies established the position and number of hydrogen atoms ex-

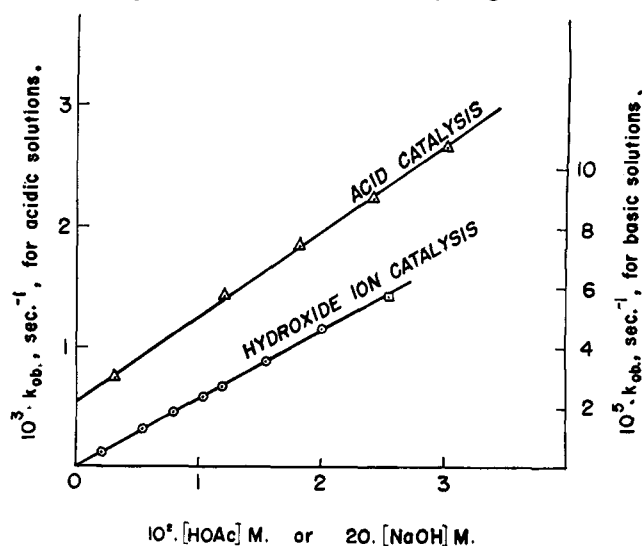


Figure 1.

changed, but not the mechanism of the process. More recently Hinman and Whipple³ studied the position of protonation to form the conjugate acid in several substituted indoles and reported the rates of homogeneous exchange with deuterated solvents for various positions of the heterocyclic ring. Their nuclear magnetic resonance technique required relatively high acid con-

centrations, which complicates the elucidation of the reaction mechanism.

The detritiation of 2-methylindole-3-*t* in a homogeneous aqueous solution proceeds with a convenient rate at 25° in the pH range from 4 to 6. The reaction is catalyzed by the hydronium ion and general acids. This is illustrated by the data of the accompanying figure, where the observed first-order rate coefficient k_{ob} ($v = k_{ob}[2\text{-methylindole-3-}t]$) is plotted against the concentration of acetic acid for reaction in acetic acid-sodium acetate buffers at a pH of 5.01 and at an ionic strength of 0.1. The rate law of the exchange reaction is

$$k_{ob} = 42[\text{H}_3\text{O}^+] + 0.071[\text{HOAc}]$$

Similar studies for other carboxylic acids lead to a value of 0.58 for the Brønsted α factor. A more extensive Brønsted plot, embracing a series of acids extending to the hydronium ion, is not linear, indicating that the acid type, as well as its strength, is important in determining the degree of catalysis.

The acid-catalyzed detritiation of 1,2-dimethylindole-3-*t* in acetic acid-sodium acetate buffer solutions follows a similar rate law to that observed for 2-methylindole-3-*t*

$$k_{ob} = 72.4[\text{H}_3\text{O}^+] + 0.176[\text{HOAc}]$$

The greater reactivity of the disubstituted indole, compared to 2-methylindole-3-*t*, is in accord with the reported basicity^{4,5} of the 3-position for the two compounds.

The observed general acid catalysis strongly suggests that the exchange process in acidic solutions occurs *via* the A-SE2 mechanism recently proposed for the isotopic hydrogen exchange of azulene⁶ and 1,3,5-trimethoxybenzene.⁷

A point of considerable interest is that the detritiation of 2-methylindole-3-*t* is also catalyzed by hydroxide ion. A plot of the observed first-order rate coefficient (k_{ob}) against the hydroxide ion concentration, at a constant ionic strength of 0.1, is linear, as shown in the figure. The value of k_{OH^-} ($v = k_{OH^-}[2\text{-methylindole-3-}t][\text{OH}^-]$) at 25° is 4.5×10^{-4} mole⁻¹ sec⁻¹. In contrast to the results for acid catalysis, the rate of detritiation of 1,2-dimethylindole-3-*t* in alkaline solutions is much slower than that observed for 2-methylindole-3-*t*. Thus for a hydroxide ion concentration of 0.126 M the rate of tritium exchange for 1,2-dimethylindole-3-*t* is only 1.41×10^{-7} sec⁻¹, which approximates closely to the rate expected for the "spontaneous" catalysis by the aqueous medium itself. We therefore conclude that, within the limits of experimental error, there is no catalysis by hydroxide ion.

It is unlikely that the base-catalyzed exchange stems from a direct attack of hydroxide ion on the isotopic hydrogen attached to the 3-carbon, since for both the 1,2-dimethyl and 2-methyl derivatives this site is known to be basic, rather than acidic. The striking reversal of relative reactivity of the two compounds, on going from acidic to basic solutions, suggests that the strong base catalysis observed for 2-methylindole-3-*t* requires the presence of a labile aminohydrogen atom. An attack of hydroxide ion on the indolenine tautomer is ruled out because the tautomerism itself would lead to rapid exchange of the tritium label. The most probable explanation, then, is an attack of water, acting as a general acid, on the anion of 2-methylindole-3-*t* formed by proton loss from the nitrogen. 1,2-Dimethylindole-3-*t* is unable to form a comparable anion, and the ex-

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(7) A. J. Kresge and Y. Chiang, *J. Am. Chem. Soc.*, **81**, 5509 (1959); **83**, 2877 (1961).

(1) Work supported by a grant from the Atomic Energy Commission.

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(3) R. L. Hinman and E. B. Whipple, *J. Am. Chem. Soc.*, **84**, 2534 (1962).