

the closely related 4-diphenylmethylene-2,5-cyclohexadienone, which lacks the potential cyclopropenium core of VII. Further evidence bearing on these and related points will be described subsequently.

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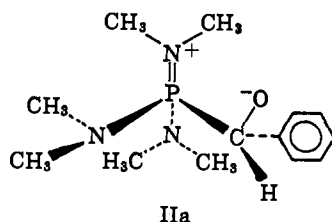
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Nucleophilic Reactions of Trivalent Phosphorus Compounds: A New Synthesis of Epoxides

Sir:

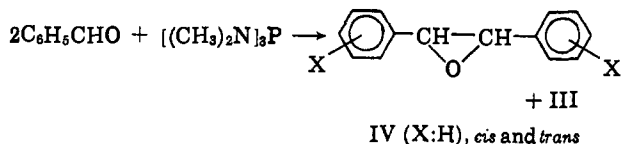
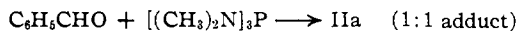
Continuing our investigation on the nucleophilic behavior of trivalent phosphorus compounds, we wish to describe the reaction of phosphorous triamides, $(R_2N)_3P$, (I) with aldehydes.

The addition of Ia ($R = CH_3$), to two moles of benzaldehyde yielded, after 70 hr. at room temperature, a slurry of white crystals in a pale yellow liquid. Analysis of the crystals (m.p. 118–119°; mol. wt. 266 ± 2%; C, 57.8; H, 8.8; P, 11.3) indicated the composition of a 1:1 adduct of benzaldehyde and Ia. Hydrogen n.m.r. [multiplets in the aromatic region (δ 7.14 to 7.55 p.p.m.; area 5.3), a doublet (δ 3.88; $J = 17.9$ c.p.s.; area 1.0) and a set of three doublets of equal areas (δ 2.77, $J = 9.3$; δ 2.33, $J = 0.7$ and δ 2.24 p.p.m., $J = 8.5$ c.p.s., total area 18.0)] indicated structure IIa for the adduct



The mother liquor of the crystals contained hexamethylphosphoramide, $[(CH_3)_2N]_3PO$, III ($\delta_{P^{31}}$ -23.4 p.p.m.), and two isomeric structures identified as *trans*- and *cis*-stilbene oxide, δ (H, oxirane) 3.78 and 4.23 p.p.m., respectively.

The following reactions of benzaldehyde with I are indicated



The reaction of I with aldehydes subsequently was found to be of a general nature. Aromatic aldehydes with electronegative substituents, especially in the *ortho* position, yield, in a highly exothermic and practically instantaneous reaction, predominantly epoxides. Electron releasing substituents on the benzene ring favor the formation of adducts, generally in a slow but noticeably exothermic reaction.

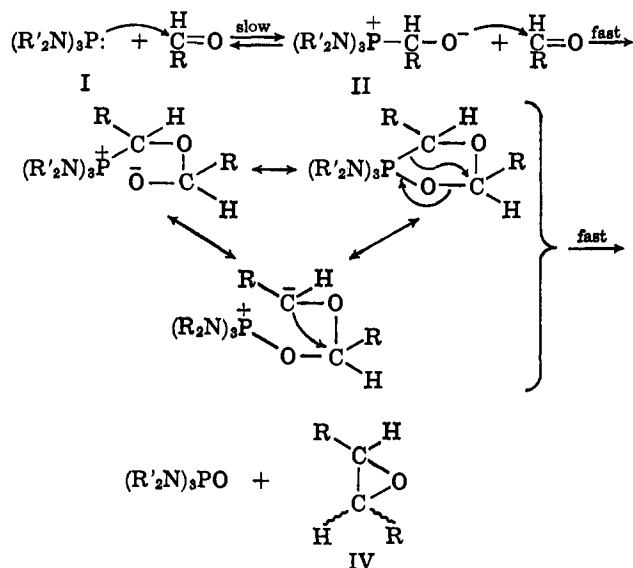
The H^1 and P^{31} n.m.r. characteristics of some adducts (II) are [X: ring substituent, δ_H (benzylic), J , δ_H (dimethylamino) p.p.m. (3 pairs), J (c.p.s.), $\delta_{P^{31}}$ (H_3PO_4) p.p.m.): *p*-F, 3.89, 17.5, 2.71, 8.98, 2.29, 0.8, 2.20, 8.2, -30.1; 3,4-(CH_3O)₂, —, —, 2.68, 8.8, 2.31, 0.8, 2.24, 8.2, -29.7; *m*- CH_3O , —, —, 2.70, 8.72, 2.29, 0.9, 2.21, 8.4, -29.8; *o*- CH_3O , 4.82, 18.1, 2.76, 8.92, 2.35, 0.7, 2.23, 8.42, -30.3; 3,4- CH_2O_2 , 3.89, 18.3, 2.75, 9.28, 2.32, 0.8, 2.30, 8.60, -30.7.

(1) One or both peaks are covered by the methoxyl frequencies.

The following examples are illustrative of the scope of the epoxide forming reaction (IV, X: ring substituent, δ (oxirane) *cis*, δ (oxirane) *trans*, yield % (total), *trans/cis* ratio): *o*-Cl, 4.49, 3.99 (m.p. 72–74°), 90, 1.38; *p*-Cl, 4.17, 3.65 (m.p. 123–125°), 40, 4.0; *m*-Br, 4.07, 3.56 (m.p. 84–86°), 53, 2.6; *o*-Br, 4.54, 4.05, 95, 1.45; *o*-F, 4.53, 4.20, 96, 1.54; 3,4- Cl_2 , 4.14, 3.63, 93, 1.50; 2,6- Cl_2 , 5.26, 4.67, 36, 8; *m*- O_2N , 4.58, 4.08 (m.p. 156–158°), 80, 2.8; *p*-NC, 4.46, 3.92, 95, 1.33; *p*-OCH, 4.48, 3.96, 80, 1.13; α -naphthaldehyde, 4.95, 4.40, 87, 1.13.

Ia reacts also with saturated and heterocyclic aldehyde and yields preferentially adducts (aldehyde, $\delta_{P^{31}}$ (p.p.m.): propionaldehyde, -31.8; 1,2,3,6-tetrahydrobenzaldehyde, -31.6; 2-furaldehyde, -28.2; 2-thiophenecarboxaldehyde, -28.4. The reaction of I with chloral takes a different course and yields the dichlorovinylphosphonium compound, $Cl_2C=CH-O-P^+(N(CH_3)_2)_3Cl^-$ (δ_{CH_3} , 2.94, $J_{PH} = 10.36$; $\delta_{HC} = 8.47$ p.p.m., $J_{PH} = 4.1$ c.p.s.; $\delta_{P^{31}} = -34.8$ p.p.m.).

The following mechanism is suggested for the transformations



When the carbonyl group is relatively a poor acceptor of nucleophile I, the 1:1 adducts are preferentially obtained.⁴ When R is an electronegative substituent and when I is added slowly to the aldehyde, IV is the major product.

The collapse of the postulated 2:1 adduct intermediate can be compared with the second step of the Wittig reaction: in both cases a carbon-phosphorus and a carbon-oxygen bond cleavage results in the formation of a phosphorus-oxygen and a carbon-carbon bond (π bond in the second case). An even closer analogy of the intramolecular SN_2 decay of the 2:1 adduct can be found in the recent work of Denney,⁵ Wadsworth⁶ and McEwen.^{7,8}

(2) Reported m.p. 123–124° (R. E. Lutz and R. S. Murphey, *J. Am. Chem. Soc.*, 71, 478 (1949)).

(3) The aldehydic hydrogen frequencies of IV, *p*-OCH, are at 9.88 p.p.m. for the *cis* and at 10.05 p.p.m. for the *trans* isomer.

(4) The solvation of the aldehyde by I probably explains the formation of II when no excess aldehyde is employed. The postulated mechanism is intended to apply to non-solvated aldehydes only.

(5) D. B. Denney, J. J. Vill and M. J. Boskin, *J. Am. Chem. Soc.*, 84, 3944 (1962).

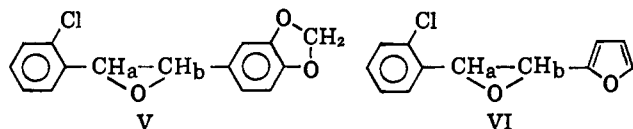
(6) W. S. Wadsworth and W. D. Emmons, *ibid.*, 83, 1733 (1961).

(7) W. E. McEwen, *et al.*, *ibid.*, 84, 676, 677 (1962).

(8) Referee I suggested an alternate mechanism, consisting of a nucleophilic attack by phosphorus on carbonyl oxygen followed by an attack on carbonyl carbon by the resultant 1:1 adduct (which is not identical with the isolated betaine) and concluded by displacement on carbon by oxide [*cf.* Ramirez and co-workers, *ibid.*, 84, 1317 (1962), and references therein]. The data presented above do not exclude a similar interpretation.

The stereochemistry of IV is preferentially *trans*. A high *trans/cis* ratio is favored by bulky *ortho* and *meta* substituents (*cf.* 2,6-dichlorobenzaldehyde), by moderate reaction conditions and by moderately reactive (hence more selective) reaction partners (*cf.* *p*-chlorobenzaldehyde).

The proposed mechanism is supported and the scope of the reaction is considerably extended also by the synthesis of mixed epoxides. The addition of I, a powerful nucleophile, to a mixture of aldehydes, in which the less reactive aldehyde predominates, yields, in addition to the symmetrical epoxide derived from the more reactive aldehyde, also varying proportions of the mixed epoxides. For instance, the addition of Ia to a mixture of *o*-chlorobenzaldehyde and piperonal (excess) yielded V (*trans*, δ_{Ha} 4.06, δ_{Hb} 3.56, p.p.m., $J = 1.9$ c.p.s.). Similarly, *o*-chlorobenzaldehyde and 2-furaldehyde yielded VI (δ_{Ha} 4.48, δ_{Hb} 3.73 p.p.m. $J = 2.18$ c.p.s.).



The often high yields and the simple, one step, preparative procedure render the present reaction of some interest in synthetic organic chemistry. The mild reaction conditions allow the preparation of epoxides with sensitive structural features, for which some of the most generally used epoxide syntheses (*e.g.*, *via* the olefins by peroxides) are not applicable. For instance, 2-thiophenecarboxaldehyde and Ib ($R = \text{ethyl}$) yielded IV ($R = 2\text{-thenyl}$: δ_{H} (oxirane) *trans* 4.24, *cis* 4.44 p.p.m.; ratio *trans/cis* 1.1). Similarly, 2-pyridinecarboxaldehyde and Ia gave a 90% yield of a reaction mixture, IV ($R = 2\text{-pyridyl}$), which comprised 75% of the *trans* epoxide [m.p. 95–97°; δ_{H} (oxirane) 4.51] and 25% of the *cis* epoxide [δ_{H} (oxirane) 4.73 p.p.m.].

(9) Pennsalt Chemicals Corporation, P. O. Box 4388, Philadelphia 18, Pa.

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Deuterium Isotope Effect in Intramolecular Insertion

Sir:

We here report the first example of isotopic discrimination in liquid phase CH insertion,¹ a reaction presumed to be characteristic of carbene intermediates² and heretofore characterized by unprecedented insensitivity to CH bond strengths.^{2a} We also note that only isotopic discrimination excludes the possibility of ground-state conformational control,³ notorious in intramolecular reactions of low ΔF^\ddagger .

Addition of precooled methylene chloride in tetrahydrofuran to 1,1-di(methyl-*d*₃)ethyl lithium (I) in the same solvent, at -65°, produced deuterated 1,1-dimethylcyclopropane, separated from other products by distillation and gas chromatography.⁴ Analysis by

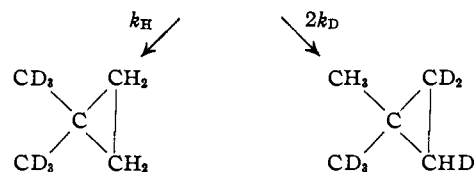
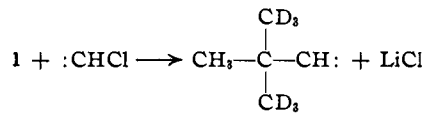
(1) Since the submission of our first draft, J. W. Simons and B. S. Rabino-vitch, *J. Am. Chem. Soc.*, **85**, 1023 (1963), have described deuterium isotope effects of 1.96 and 1.55 for *intermolecular* insertion of ketene-generated CH₂ into allylic and vinylic CH bonds, determined in the gas phase by *intermolecular* competition.

(2) (a) Reviewed by W. Kirmse, *Angew. Chem.*, **73**, 161 (1961); (b) H. E. Simmons and R. D. Smith, *J. Am. Chem. Soc.*, **81**, 4256 (1959); (c) G. L. Closs and J. J. Coyle, *ibid.*, **84**, 4350 (1962).

(3) *Cf.* J. H. Ridd, *Quart. Rev. (London)*, **15**, 418 (1961); A. Streitwieser, Jr., *J. Org. Chem.*, **22**, 861 (1957).

(4) *Cf.* G. L. Closs, Abstracts of papers presented at the 138th National Meeting of the American Chemical Society, September, 1960, p. 9P; *J. Am.*

n.m.r.: (a) excluded the presence of >3% 1,1-di-methylethyl-*d*₃ chloride in the alkyl lithium precursor; (b) excluded the presence of >0.8% isomeric alkenes in the purified product; and (c) established the magnitude of the isotope effect. The area ratio, (CH₂ + CH)/CH₃ = 1.47 ± 0.04,⁵ unchanged by resubmission of isolated products to reaction conditions, requires that $k_{\text{H}}/k_{\text{D}} = 1.71 \pm 0.06$.



Although similar in magnitude to the low "primary" isotope effects often noted in intramolecular⁶ (and intermolecular) hydride transfer, this result suffers from none of the ambiguities necessarily associated with similar interpretations in the latter reactions.^{6a} Since we have employed intramolecular competition we need not obtain independent kinetic evidence relating the hydrogen migration and rate-determining steps.^{6b,d,7} Since the solvent can play no significant role in the insertion step, no new hydrogen mass-dependent vibrational modes may be acquired by the transition state. The introduction of such modes has been considered the most general source of low $k_{\text{H}}/k_{\text{D}}$ values.⁸

With an unusually meaningful experimental value in hand, we are pleased to discover that it may be derived by the use of only two assumptions, introduced solely for purposes of simplification, but following logically from mechanistic preconception.



(1) Since the reaction is unusually exothermic,⁹ we first assume that the necessarily identical dimensions of the isotopically isomeric transition states, H and D, differ insignificantly from that of their common precursor.¹⁰ The product rule then requires that $3\pi^{\text{D}} \nu_{\text{H}}^{\text{H}}/\nu_{\text{H}}^{\text{D}} = 1$ and since H and D must at least differ in their unbound frequencies, ν_{L}

$$\frac{k_{\text{H}}}{k_{\text{D}}} = \frac{\sinh h\nu^{\text{D}}/2kT}{\sinh h\nu^{\text{H}}/2kT}$$

where ν^{D} is that frequency in D corresponding to $\nu_{\text{L}}^{\text{H}}$ and ν^{H} is that in H corresponding to $\nu_{\text{L}}^{\text{D}}$.

Chem. Soc., **84**, 809 (1962), W. Kirmse and W. von E. Doering, *Tetrahedron*, **11**, 266 (1960). The mechanism outlined is that proposed by these authors.

(5) Mean and standard deviation of results from three independent experiments using a Varian A-60 instrument.

(6) (a) E. S. Lewis and M. C. R. Symons, *Quart. Rev. (London)*, **12**, 230 (1958), and previous examples cited; (b) S. Winstein and J. Takahashi, *Tetrahedron*, **2**, 316 (1958); (c) C. J. Collins, W. T. Rainey, W. B. Smith and I. A. Kaye, *J. Am. Chem. Soc.*, **81**, 460 (1959); (d) W. B. Smith, R. E. Bowman and J. J. Kmet, *ibid.*, **81**, 997 (1959); (e) D. J. Cram and J. Tadanier, *ibid.*, **81**, 2737 (1959).

(7) L. Melander, "Isotope Effects on Reaction Rates," Ronald Press Co., New York, N. Y., 1960, pp. 103–105, discusses the relative merits of *inter vs. intramolecular* competition in isotope effect determinations.

(8) (a) F. H. Westheimer, *Chem. Rev.*, **61**, 265 (1961); (b) R. P. Bell, "The Proton in Chemistry," Cornell University Press, Ithaca, N. Y., 1959, pp. 190–193; (c) *ref.* 6, pp. 24–32.

(9) We estimate $-\Delta H^\ddagger = 58 \pm 3$ kcal./mole for "cold" ethyl carbene \rightarrow cyclopropane.

(10) G. S. Hammond, *J. Am. Chem. Soc.*, **77**, 334 (1955).