methyl groups), and 3.54 ppm (doublet, J_{HP} = 11.5 Hz, OCH_3). Noteworthy ir bands (film) occur at 1745 (s), 1640 (w), and 1265 (s) cm^{-1}.

Quantitative elemental analysis and mass spectral data are consistent with the structures of the reaction products.

These results are consistent with a compound (Ia) having a very reactive, polarized carbon–phosphorus bond as indicated by the inclusion of the polar canonical structure. In fact, the carbanion-like reactivity of Ia suggests that perhaps a small equilibrium amount of a dipolar intermediate may be present. The high positive chemical shift in the P^{31} nmr is that expected for a pentacovalent species rather than a dipolar structure, although the effects of the carbonyl and olefinic groups on the P^{31} chemical shifts are difficult to predict. The apparent lack of coupling between phosphorus and the geminal methyls has led us to consider other possible structures for the phosphorane in which the geminal methyls are not adjacent to phosphorus; however, the chemical evidence lends considerable support to the structure assignment Ia.

We have successfully applied this synthesis to a broad range of cyclic and acyclic phosphites and phosphoramidites to show its generality (Ib–g). These phosphoranes undergo reactions analogous to those reported for Ia. These results will be reported in a full paper.

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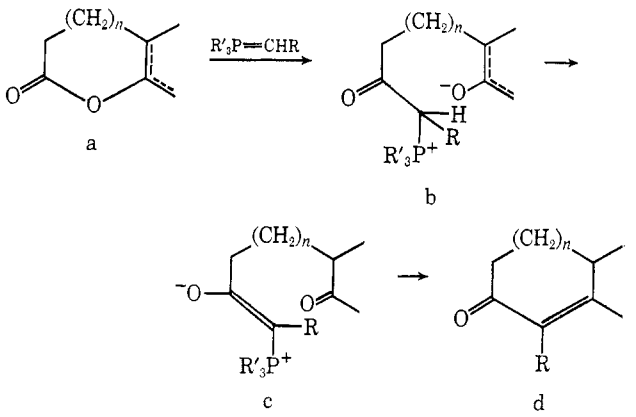
The Reaction of Phosphoranes and Phosphonate Anions with Enol Lactones. A New Method for the Preparation of Cyclic α,β-Unsaturated Ketones[1]

Sir:

The synthetic methods utilized for the preparation of cyclic α,β-unsaturated ketones from acyclic precursors often suffer from the disadvantage that alternate condensation reactions frequently occur which lead to isomeric unsaturated ketones or other undesirable products.[2] In principle, the unidirectional cyclization process depicted by the transformations a–d constitutes a useful general method for the synthesis of α,β-unsaturated ketones. Thus, attack of a phosphonium ylide on the cyclic enol lactone (a) should yield the ketophosphorane (c) after proton reorganization within the



initially formed phosphonium enolate salt (b). Cyclization could then proceed by an intramolecular Wittig reaction to yield the enone (d). This process would be expected to compete favorably with the intermolecular reaction which is known to be sluggish in the case of stabilized ylides.[3] In this communication we wish to report that both alkylidenetriphenylphosphoranes and dialkyl alkylphosphonate anions attack a variety of cyclic enol lactones according to the proposed scheme to yield in one step the desired cyclic α,β-unsaturated ketones.

Exposure of benzylidenephthalide (**1**) to 1.0 equiv of methylene–triphenylphosphorane (**2**) (prepared from methyltriphenylphosphonium bromide and butyllithium in tetrahydrofuran) for 24 hr at 23° afforded in 44% yield 3-benzylidenindan-1-one (**3a**)[4] [mp 104–105°; $\nu_{max}^{CCl_4}$ 1720, 1595 cm^{-1}; λ_{max}^{EtOH} 218, 235, 257, 263, 290, 301, 314 mμ (log ε 4.34, 4.20, 4.08, 4.07, 4.18, 4.20, 4.09); nmr 3.49 (d, J = 2 cps, 2-H), 7.18 (t, J = 2 cps, $C_6H_5CH{=}C<$), 7.1–7.9 ppm (m, aromatic H)][5] and 32% of starting material.

Similarly reaction of **1** with 1.1 equiv of *n*-butylenetriphenylphosphorane gave a 30% yield of 3-benzyl-2-*n*-propylindenone (**4**)[6] [yellow oil, $\nu_{max}^{CCl_4}$ 1710, 1605 cm^{-1}; λ_{max}^{EtOH} 236, 243, 315, 395 mμ (log ε 4.59, 4.62, 3.01, 2.76); nmr 0.92 (t, J = 7 cps, $CH_3CH_2CH_2$–), 1.50 (m, $CH_3CH_2CH_2$–), 2.33 (t, J = 7 cps, CH_3CH_2-CH_2), 3.93 (s, $C_6H_5CH_2$–), 6.7–7.5 ppm (m, aromatic H)] and 29% of 2-propyl-3-benzylidenindanone (**3b**) [mp 84–86°; ν_{max}^{film} 1715, 1610 cm^{-1}; λ_{max}^{EtOH} 221, 239, 296, 305, 318 (sh) mμ (log ε 4.26, 4.24, 4.29, 4.30, 4.16); nmr 0.72 (t, J = 7 cps, $CH_3CH_2CH_2$–), 3.7 (m, 2-H), 7.2–8.0 ppm (m, olefinic and aromatic H)].

The tetracyclic enol lactone (±)-3-methoxy-15-methyl-16-oxaestra-1,3,5(10),6,8,14-hexaen-17-one (**5**)[7] also reacts in tetrahydrofuran with **2** to give only the

(1) Publication No. 347 from the Syntex Institute of Steroid Chemistry. Publication No. 346: S. Kaufmann, L. Tökes, J. Murphy, and P. Crabbé, submitted for publication.

(2) For examples see S. Julia, *Bull. Soc. Chim. Fr.*, 780 (1954); K. D. Zwahlen, W. J. Horton, and G. I. Fujimoto, *J. Amer. Chem. Soc.*, **79**, 3131 (1957); W. S. Johnson, J. J. Korst, R. A. Clement, and J. Dutta, *ibid.*, **82**, 614 (1960); L. Velluz, G. Nominé, and J. Mathieu, *Angew. Chem.*, **72**, 725 (1960); L. J. Chinn and H. L. Dryden, *J. Org. Chem.*, **26**, 3904 (1961); J. A. Marshall and D. J. Schaeffer, *ibid.*, **30**, 3642 (1965); M. Ohashi, H. Kamachi, H. Kakisawa, and G. Stork, *J. Amer. Chem. Soc.*, **89**, 5460 (1967).

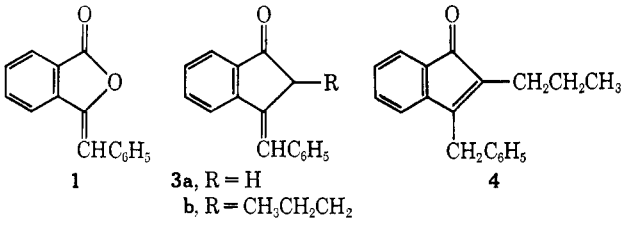
(3) (a) A. W. Johnson, "Ylid Chemistry," Academic Press, New York, N. Y., 1966, p 138; (b) see also E. E. Schweizer and J. G. Liehr, *J. Org. Chem.*, **33**, 583 (1968); H. G. Lehmann and R. Wiechert, *Angew. Chem. Intern. Ed. Engl.*, **7**, 300 (1968).

(4) 3-Benzylindenone, the initial product of this reaction, is isomerized to **3a** *via* the enolate anion in turn generated by the ylide **2**. When 1.8–2.0 equiv of ylide is used, **3a** is obtained in greater than 90% yield.

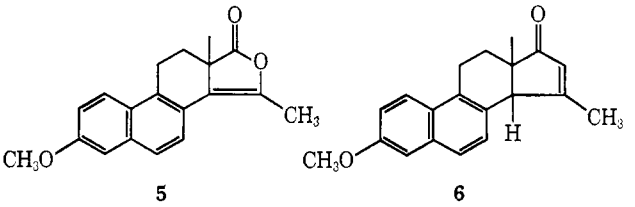
(5) Satisfactory analyses were obtained for all fully characterized compounds. Nmr spectra were obtained on Varian A-60 and HA-100 spectrometers in deuteriochloroform solutions (10% w/v) containing tetramethylsilane as internal reference. Chemical shifts are reported as parts per million on the δ scale. We thank Miss J. Tremble for these determinations. In the presentation of data d = doublet, t = triplet, and m = multiplet.

(6) Compare the reaction of benzylidenephthalide with phenylmagnesium bromide which yields 2,3-diphenylindenone. See "Organic Syntheses," Coll. Vol. III, R. N. Adams, Ed., John Wiley & Sons, Inc., New York, N. Y., 1955, p 353.

(7) W. R. J. Simpson, D. Babbe, J. A. Edwards, and J. H. Fried, *Tetrahedron Lett.*, 3209 (1967).



1 3a, R = H b, R = $CH_3CH_2CH_2$ 4



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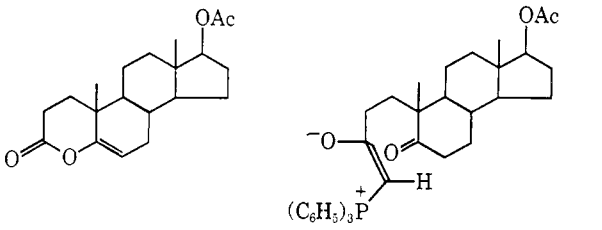

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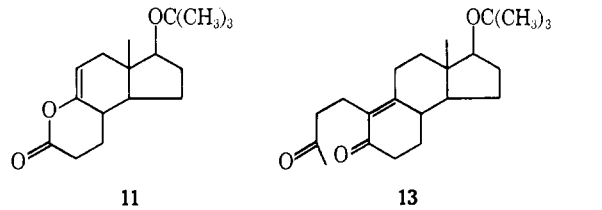

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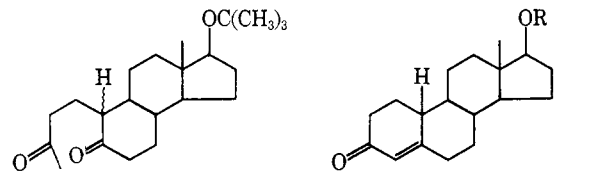

14 15a, R = H b, R = $C(CH_3)_3$

α,β-unsaturated ketone (±)-3-methoxy-15-methyl-14β-estra-1,3,5(10),6,8,15-hexaen-17-one (**6**) [mp 114–115°; $\nu_{max}^{CS_2}$ 1707, 1625 cm^{-1}; λ_{max}^{EtOH} 235, 268, 314, 322, 329, 336 mμ (log ϵ 4.94, 3.92, 3.25, 3.33, 3.25, 3.39); nmr 1.29 (18-H), 1.97 (t, $J_{14,15'}$ = 1.0 cps, $J_{15',16}$ = 1.5 cps, 15-CH_3), 3.75 (broad s, $J_{14,16}$ = 1.8 c.p.s., 14-H), 3.93 (methoxyl H), 5.95 (narrow m, $J_{14,16}$ = 1.8 cps, $J_{15',16}$ = 1.5 cps, 16-H), 7.1–7.9 ppm (m, aromatic H)] in 60% yield.

Mechanistic evidence for these ylide additions was obtained from the reaction of 17β-acetoxy-4-oxaandrost-5-en-3-one (**7**)[8] with methylenetriphenylphosphorane (**2**) (18 hr, 20° in tetrahydrofuran) which afforded a low yield of testosterone acetate (**8**) in addition to a good yield of the thermally unstable ylide (**9**) [oil; ν_{max}^{film} 1730, 1710, 1530 ("ylide carbonyl")[9] cm^{-1}; nmr 0.87 (18-H), 1.14 (19-H), 7.3–7.9 ppm (m, aromatic H); addition of 1 drop of HCl to the nmr solution gives the phosphonium salt; nmr 0.82 (18-H), 1.09 (19-H), 5.6 ppm (m, $(C_6H_5)_3P^+CH_2CO-$)]. The mass spectrum[10] of **9** shows molecular ions and fragments attributable to a mixture of testosterone acetate and triphenylphosphine oxide, suggesting decomposition of the ylide in the inlet chamber of the mass spectrometer. Pyrolysis of the ylide **9** in boiling xylene also affords testosterone acetate in modest yield. Efficient fragmentation of **9** is achieved by treatment with aqueous potassium hydroxide in methanol (16 hr at 23°) which furnishes testosterone in 50% over-all yield from **7**.

Dimethyl methylphosphonate anion (**10**)[11] reacts efficiently with the enol lactones **5** and **7** in tetrahydrofuran at −78° (nitrogen atmosphere) to yield directly **6** and testosterone acetate in 80 and 50% yields, respectively.[12] The strongly nucleophilic β-ketophosphonate anion intermediate obviously facilitates ring closure to the tetracyclic enone in the case of **7**.[13]

The reaction of suitably modified Wittig and phosphonate reagents with the appropriate enol lactones provides new and useful methodology for the synthesis of steroids. Thus, treatment of the (+) tricyclic enol lactone **11**[14] with a slight excess of the anion of diethyl 4-cycloethylenedioxypentylphosphonate[17] (**12**) affords a mixture of the unconjugated and conjugated tricyclic ketones which is converted by sequential treatment with dilute sodium hydroxide and aqueous acetic acid (1.5 hr at 80°) into the unsaturated diketone **13** [mp 94–95°; $\nu_{max}^{CCl_4}$ 1715, 1665, 1600 cm^{-1}; λ_{max}^{EtOH} 247 mμ (log ϵ 4.06); $[\alpha]^{CHCl_3}D$ −14°; nmr 0.88 (18-H), 1.13 (*t*-butyl), 2.13 (CH_3CO)]. Hydrogenation of **13** over 5% palladized carbon in aqueous ethanol containing 0.2% triethylamine gave **14** [oil; ν_{max}^{film} 1710 cm^{-1}] which on acid-catalyzed cyclization (10% hydrochloric acid in boiling aqueous ethanol) gave 19-nortestosterone (**15a**) identical with an authentic sample. Base-catalyzed cyclization of **14** gave 19-nortestosterone *t*-butyl ether (**15b**) [mp 146–147°; $[\alpha]^{CHCl_3}D$ +54°; $\nu_{max}^{CCl_4}$ 1675, 1615 cm^{-1}; λ_{max}^{EtOH} 239 mμ (log ϵ 4.18); nmr 0.78 (18-H), 1.13 (*t*-butyl), 3.40 (t, 17α-H), 5.84 (m, 4-H)] identical with a sample prepared by the procedure of Beyerman[16] from **15a**.

We are continuing to evaluate the scope of the reactions reported herein by further examination of the structural requirements of both the ylide and the enol lactone components.

(8) (a) R. B. Turner, *J. Amer. Chem. Soc.*, **72**, 579 (1950); (b) G. I. Fujimoto, *ibid.*, **73**, 1856 (1951).

(9) See ref 3a, p 68.

(10) The mass spectrum was obtained with an Atlaswerke CH-4 spectrometer equipped with a direct inlet system. Spectra were measured at an ionizing potential of 70 eV and an acceleration voltage of 3 kV. We thank Mr. J. Smith and Dr. L. Tökes for assistance with this measurement.

(11) E. J. Corey and G. T. Kwiatkowski, *J. Amer. Chem. Soc.*, **88**, 5654 (1966).

(12) The conversion of the enol lactone 7 to testosterone by sequential treatment with 1 equiv of methyl Grignard and base proceeds in 25–50% yield.[8b] The potential utility of the phosphonate approach for the synthesis of 4-^{14}C steroids should be noted.

(13) W. S. Wadsworth and W. D. Emmons, *J. Amer. Chem. Soc.*, **83**, 1733 (1961). See also ref 3a, p 203.

(14) This substance was prepared by treating (+)-1β-hydroxy-4-(2′-carboxyethyl)-5-oxo-7aβ-methyl-3aβ,4β,5,6,7,7a-hexahydroindan[15] with isobutylene in methylene dichloride containing 93% sulfuric acid[16] followed by alkaline hydrolysis to the corresponding *t*-butoxy acid and enol lactonization with sodium acetate–acetic anhydride (reflux for 4 hr).

(15) L. Velluz, G. Nominé, G. Amiard, V. Torelli, and J. Cérède, *Compt. Rend.*, **257**, 3086 (1963).

(16) H. C. Beyerman and G. J. Heiszwolf, *Rec. Trav. Chim.*, **84**, 203 (1965).

(17) G. Sturtz, *Bull. Soc. Chim. Fr.*, 2340 (1964).

(18) Syntex postdoctoral Fellow: (a) 1967–1968; (b) 1966–1967.

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