order rate constant was found to be 7.09×10^{-3} l. mol^{-1} sec^{-1}; under the same conditions, the second-order rate constant for the reaction of alanylglycine with 2,4-dinitrofluorobenzene was 6.52×10^{-3} l. mole^{-1} sec^{-1}.

Kinetics of Benzimidazolone (17) Formation.—Aliquots (500 µl) of a solution of 2.091 mg of **14**-glycylalanine in 10 ml of ethanol were diluted to 5.00 ml with 0.2 *M* carbonate buffer at various pH values. Benzimidazolone formation was followed at 25°, by the decrease in optical density at 370 mµ. Observed first-order rate constants for benzimidazolone formation follow (pH, $k \times 10^3$ in sec^{-1}): 9.42, 0.36; 9.65, 0.54; 10.04, 1.41; 10.20, 1.96; 10.41, 3.52; 10.68, 5.70.

Registry No.—**8**, 18646-02-1; **11**, 18646-13-4; **12**, 18646-03-2; **14**-glycylalanine, 18646-04-3; **15**-glycine, 18646-05-4; **15**-alanine, 18646-06-5; **15**-isoleucine, 18646-07-6; **15**-valine, 18646-08-7; **15**-proline, 18646-09-8; **17**, 18646-10-1.

1,4 Additions of Phosphorus Trichloride to Cyclic α,β-Unsaturated Ketones[1a,b]

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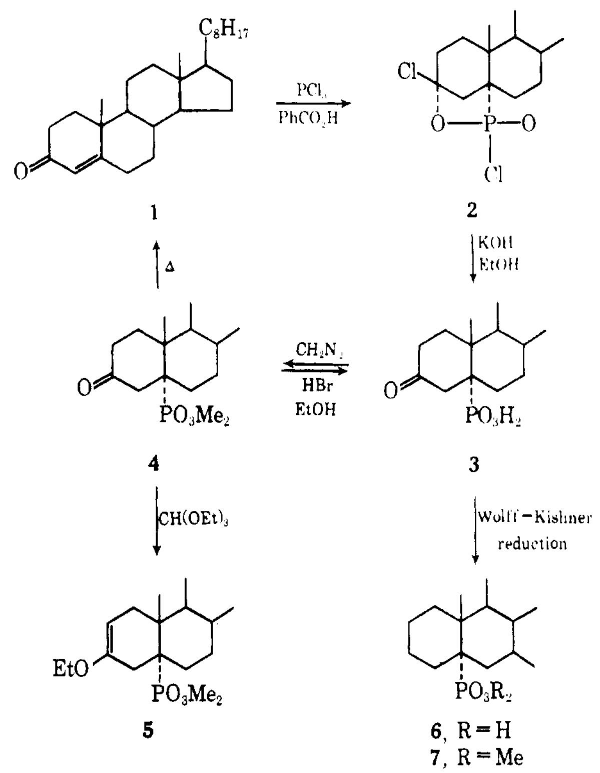
Phosphorus trichloride reacts with 4-cholesten-3-one in the presence of benzoic acid to provide a stable, crystalline intermediate in the normal 1,4-addition reaction of this reagent. Chemical and spectral evidence support the assignment of phostonyl chloride structure 2 to this intermediate with the phosphorus atom in the 5α position. An analogous product (**11**) is obtained from 2-keto-10-methyl-$\Delta^{1,9}$-octalin. A mechanism is proposed involving an initial electrophilic attack of the phosphorus atom on the carbonyl oxygen.

The reactions of phosphorus trichloride with ketones provide methods for forming carbon–phosphorus bonds which we have investigated for use in preparing steroidal phosphonic acids. We have found that the course of the reactions of this reagent with Δ^4-3-keto steroids is dependent upon the reaction conditions, thus the use of acetic acid as the solvent leads to 3-chloro-3,5-dienes, whereas acetic anhydride causes the formation of 3-acetoxy-3,5-dienes.[2] Substituting crystalline phosphorous acid for the acetic acid and using phosphorus trichloride in excess provides 3,5-dien-3-ylphosphonic acids by 1,2 addition of the phosphorus reagent.[3] We now report that the use of benzoic acid in phosphorus trichloride as the solvent allows the isolation of 1,4-addition products of 4-cholesten-3-one and 2-keto-10-methyl-$\Delta^{1,9}$-octalin which are the first fully characterized intermediates obtained from the normal 1,4-addition reaction of this reagent with α,β-unsaturated ketones to give γ-ketophosphonic acids. In addition to providing a route to steroidal C_5-phosphonic acids, therefore, these intermediates have significance in providing evidence about the mechanism of the reaction.

The nonhydrolytic work-up of a solution of 4-cholesten-3-one (**1**), phosphorus trichloride, and benzoic acid allows the isolation in 20–25% yield of a crystalline phosphorus-containing steroid, mp 206–208°, in addition to the major product, 3-chloro-3,5-cholestadiene. The elemental analysis and molecular weight of this new compound are consistent with the molecular formula $C_{27}H_{45}Cl_2O_2P$. On the basis of these and the following data, structure **2** is proposed for this compound (Scheme I).[4]

SCHEME I



(1) (a) Abstracted from the Ph.D. Dissertation of M. D. Martz, University of Missouri, Jan 1967. Presented in part at the First Midwest Regional Meeting of the American Chemical Society, Kansas City, Mo., Nov 1965. (b) Journal Series Paper No. 5457. Approved by the Director of the Missouri Agriculture Experiment Station. (c) To whom all correspondence should be addressed at the Department of Plant Pathology, University of Missouri, Columbia, Mo. 65201.

(2) J. A. Ross and M. D. Martz, *J. Org. Chem.*, **29**, 2784 (1964).

(3) J. A. Ross and S. S. Wasson, Abstracts of Papers Presented at the First Midwest Regional Meeting of the American Chemical Society, Kansas City, Mo., Nov 4–5, 1965, p 31.

(4) The Chemical Abstracts name for **2** is (3β-chloro-3-hydroxy-5α-cholestan-5-yl)phosphonochloridic acid intramolecular ester. We shall refer to it as a "phostonyl chloride" following Conant's original suggestion: *cf.* A. Eberhard and F. H. Westheimer, *J. Amer. Chem. Soc.*, **87**, 253 (1965).

The infrared, ultraviolet, and nmr spectra of phostonyl chloride 2 corroborate the absence of hydroxyl, carbonyl, and olefinic groups. The infrared spectrum is quite complex with multiple bands centered at 1280 and 890 cm^{-1} assigned to the P–O and P–OR groups, respectively. Phostonyl chloride 2 is surprisingly stable to alcohols, amines, and aqueous acids. Treatment of the compound with ethanolic potassium hydroxide, however, provides the ketophosphonic acid 3, the normal 1,4-addition product expected from the reaction of phosphorus trichloride with cholestenone.

The 3-keto group of 3 is indicated by its infrared absorption at 1715 cm^{-1} and the formation of a 2,4-dinitrophenylhydrazone. Ketophosphonic acid 3 is smoothly converted into the dimethyl ester 4 by diazomethane. The complete esterification is shown by the doublet in its nmr spectrum at δ 3.71 (J_{PH} = 11 Hz) having an area corresponding to six protons. This ester can be completely hydrolyzed to the ketophosphonic acid 3 by refluxing in ethanolic hydrobromic acid. The 3-keto group of 4 reacts normally in the formation of a 2,4-dinitrophenylhydrazone and by reaction with ethyl orthoformate to give the enol ether 5.

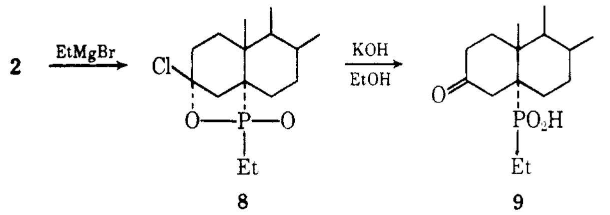
The absence of any deep-seated structural change during these reactions is shown by the pyrolysis of the dimethyl ketophosphonate 4 to 4-cholesten-3-one (1). This reaction, which is similar to the Cope elimination of amine oxides or the Kraft ester pyrolysis, is unusual for phosphonates and has been reported previously only in the case of certain α-phosphonoaldehydes.[5] The ease of the carbon–phosphorus cleavage in this case is apparently due to the presence of the acidic α-hydrogen (relative to the ketone) which allows the elimination of dimethylphosphonate.

The dimethyl ketophosphonate 4 proved to be resistant to Wolff–Kishner reduction, but the free acid 3 is readily reduced under these conditions to cholestan-5α-ylphosphonic acid (6). Reaction of this acid with diazomethane yields the dimethyl ester 7.

Although phostonyl chloride 2 is very stable to a number of nucleophilic reagents, it does react with an excess of ethylmagnesium bromide to give a new compound 8 in which one of the chlorine atoms is replaced by an ethyl group and the phostone ring is retained. The infrared spectrum of this product is very similar to that of the parent phostonyl chloride with complex bands in the 1300–600-cm^{-1} region. The phosphoryl oxygen absorption is found at 1265 cm^{-1}, a 20-cm^{-1} shift from that of 2. This is in fair agreement with the 38-cm^{-1} shift calculated for the substitution of an alkyl group for chlorine in this series.[6]

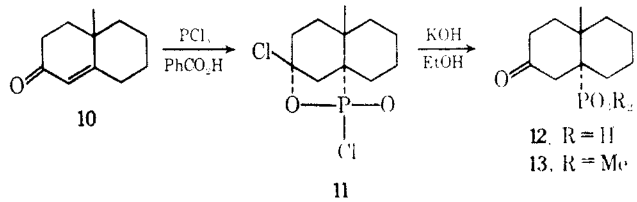
Basic hydrolysis of 8 opens the phosphorus ring to give a ketophosphinic acid 9 as shown by its infrared spectrum. This compound could not be obtained analytically pure, but its 2,4-dinitrophenylhydrazone gave acceptable analytical data to complete its characterization.

The stepwise removal of the chlorine atoms provides



conclusive evidence for their assignment at C_3 and on the phosphorus atom. The C_5 assignment of the phosphorus atom is based on the previously known mode of reaction of phosphorus trichloride with α,β-unsaturated ketones, the ease of elimination of dimethyl phosphonate from 4, and the spectral evidence described below.

The bicyclic analog of cholestenone, 2-keto-10-methyl-$\Delta^{1,9}$-octalin (10), was also found to form a phostonyl chloride (11) in low yields when allowed to react with phosphorus trichloride and benzoic acid. The spectral properties of 11 are similar to those of 2, and it is readily cleaved by basic hydrolysis to the ketophosphonic acid 12. When 12 was treated with diazomethane in a solution of chloroform, dioxane, and N,N-dimethylformamide and the solvents were subsequently evaporated under reduced pressure, a yellow oil was obtained which was shown by its infrared spectrum to be a mixture of the expected dimethyl ester 13 and the unsaturated ketone 10. The latter was probably a product of heating 13 during the



evaporation of the solvents. Distillation of the crude reaction mixture failed to achieve separation of the two compounds, and glpc analysis of the distillate showed that the ketophosphonate was contaminated with 5% of 10. Characterization of 13 was achieved by means of its 2,4-dinitrophenylhydrazone, which could be obtained free of contamination.

The 5α assignment of the phosphorus groups in compounds 2–9 and 10–13 is supported by their nmr data. Arguments can be advanced that there is no *a priori* assumption that the phosphorus atom must be at the angular position *trans* to the methyl group, and it is necessary, therefore, to exclude substitution at C_4 and C_6 (steroids) or at C_1 or C_8 (decalins). All other sites of substitution are excluded by the pyrolysis of the dimethyl ketophosphonate 4 to cholestenone.

The half-height widths $W_{h/2}$ for the angular methyl group resonances were obtained according to the methods of Robinson[7] and of Williamson, Howell and Spencer[8] and are shown in Table I. All of the $\Delta W_{h/2}$

(5) R. H. Churi and C. E. Griffin, *J. Amer. Chem. Soc.*, **88**, 1824 (1966).

(6) J. V. Bell, J. Heisler, H. Tannenbaum, and J. Goldenson, *ibid.*, **76**, 5185 (1954).

(7) M. J. T. Robinson, *Tetrahedron Lett.*, 1685 (1965).

(8) K. L. Williamson, T. Howell, and T. A. Spencer, *J. Amer. Chem. Soc.*, **88**, 325 (1966).

TABLE I

NMR DATA OF ANGULAR METHYL GROUPS[a]

Compd	Chemical shift, ppm (Hz)	$\Delta W_{h/2}$ (rel to $W_{h/2}$ of TMS), Hz	Multiplicity
2	1.34 (80.4)	1.02	d (J = 0.8 Hz)
4	1.27 (76.2)	1.24	d (J = 0.8 Hz)
7	1.08 (64.8)	1.52	s
5	1.13 (67.8)	1.38	d (J = 0.8 Hz)
11	1.40 (84.0)	1.29	s
12	1.36 (81.5)	1.50	s

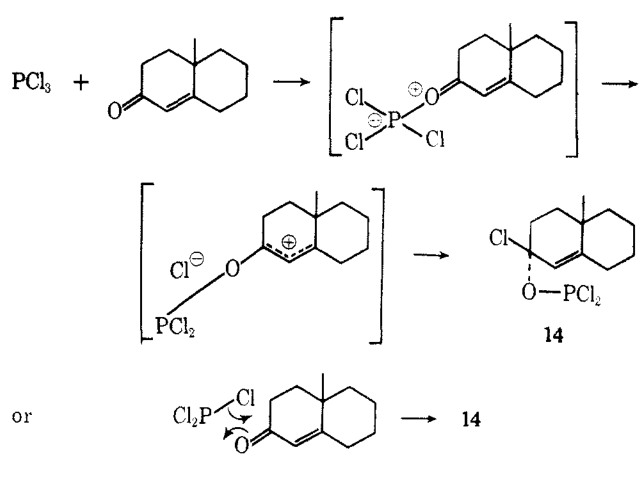
[a] The C_{19}-proton resonance of **3** disappeared into the methylene envelope.

values are larger than the average for *trans*-fused steroids (0.84 Hz[8]) or for *trans*-decalins (0.80 Hz[8]), and indicate a greater degree of coupling of the methyl protons than is found in the latter compounds. This coupling is further borne out by the splitting of the C_{19} proton resonances of **2**, **4** and **5** into doublets with coupling constants of 0.8 Hz. To our knowledge no other four-bond proton–phosphorus coupling through single bonds to carbon has been reported, but this coupling constant seems reasonable for these compounds. A phosphorus atom at C_4 or C_6 would require coupling through five σ bonds, and in neither case would the stereochemistry be so favorable.

The chemical shifts of the C_{19} protons are also in agreement with the 5α assignment. By use of the substituent additivity rules of Zürcher[9] the substituent effect of the dimethoxyphosphinyl group of **7** is calculated to be 18.3 Hz.[10] This value is consistent with the 10-Hz downfield shift of the 1α-dialkoxyphosphinyl group reported by Harvey, DeSombre, and Jensen.[11] The calculated chemical shift for the 3-keto derivative **4** is 79.3 Hz[12] whereas its observed value is 76.2 Hz, or 3.1 Hz higher field than calculated. This is similar to the 3.0 ± 0.5 Hz upfield shift, relative to the calculated values, observed for 5α-cyano steroids.[13] This deviation was explained in terms of a dipole–dipole interaction between the cyano group and the 3-keto group causing a distortion of ring A which in turn causes the C_{19} protons to be relatively shielded by the carbonyl group. The close agreement of the dimethoxyphosphinyl steroid value to the cyano steroid figure undoubtably is a result of the same kind of distortion effect.

Mechanism.—The reactions of phosphorus trichloride with carbonyl compounds have been widely used to prepare α-hydroxyphosphonic acids from saturated aldehydes or ketones and γ-ketophosphonic acids from α,β-unsaturated ketones.[14] Numerous mechanisms have been proposed for these reactions, based in part on proposed structures of labile, incompletely characterized intermediates obtained before the final hydrolysis to the isolated products.[15,16]

SCHEME II



Early workers, considering the unshared pair of electrons on the phosphorus atom, proposed nucleophilic addition of the reagent across the unsaturated system.[17] This same type of mechanism was proposed again recently to explain the reaction of phosphorus trichloride with dibenzoylethylene.[18]

Although such nucleophilic attack by phosphorus appears reasonable in view of the many well-known additions of nitrogen compounds and of trialkyl phosphines and phosphites to carbonyl derivatives, current knowledge about the reactions of halogen-containing trivalent phosphorus compounds indicates they have considerable electrophilic character due to the electronegativity of the halogens.[19] These compounds readily undergo reactions involving transition states which are stabilized by d-orbital interactions. Thus trivalent phosphorus chlorides undergo facile nucleophilic displacement of chlorine atoms by the oxygen atoms of water, alcohols and epoxides.[19] Similar nucleophilic attacks on the phosphorus atom have been proposed to explain the carbonyl reactions of phosphorus trichloride.[20–22] In these mechanisms the phosphorus atom is initially bonded to the carbonyl oxygen atom, and subsequent rearrangements leading to the carbon–phosphorus bond are proposed.

The isolation of stable intermediates **2** and **11** now provides strong evidence for initial electrophilic attack by the phosphorus atom on the carbonyl oxygen of the systems studied. We propose that the first step of the reaction is an electrophilic 1,2 addition of the reagent to the carbonyl group (Scheme II). Subsequent stages of the reaction must then involve the partial hydrolysis of the phosphorus substituent, the addition of this group to the double bond, and the protonation of C_4 to

(9) R. F. Zürcher, *Helv. Chim. Acta*, **46**, 2054 (1963)

(10) 18.3 Hz = 64.8 Hz (**7**) − [47.5 Hz ($5\alpha,14\alpha$-androstane)[9] − 1.0 Hz (17β-C_8H_{17})[9]].

(11) R. G. Harvey, E. R. DeSombre, and E. V. Jensen, *Steroids*, **9**, 101 (1967).

(12) 79.3 Hz = 64.8 Hz (**7**) + 14.5 Hz (3-oxo).[9]

(13) A. D. Cross and I. T. Harrison, *J. Amer. Chem. Soc.*, **85**, 3223 (1963).

(14) K. Sasse in Houben Weyl's "Methoden der organischen Chemie," E. Müller, Band XII/1, Georg Thieme, Stuttgart, Germany, 1963, pp 361–365.

(15) J. B. Conant and A. A. Cook, *J. Amer. Chem. Soc.*, **42**, 830 (1920).

(16) C. E. Griffin and J. T. Brown, *J. Org. Chem.*, **26**, 853 (1961).

(17) J. B. Conant and V. H. Wallingford, *J. Amer. Chem. Soc.*, **46**, 192 (1924), and references therein.

(18) F. Ramirez, O. P. Madan, and C. P. Smith, *J. Org. Chem.*, **30**, 2284 (1965).

(19) A. J. Kirby and S. G. Warren, "The Organic Chemistry of Phosphorus," Elsevier Publishing Co., Amsterdam, The Netherlands, 1967, Chapter 8.

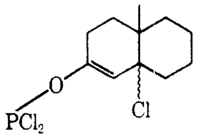
(20) H. J. Page, *J. Chem. Soc.*, **101**, 423 (1912).

(21) F. R. Atherton, V. M. Clark, and A. R. Todd, *Rec. Trav. Chim. Pays-Bas*, **69**, 295 (1950).

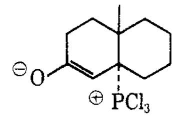
(22) M. I. Kabachnik and T. Ya. Medved, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 540 (1952); *Chem. Abstr.*, **47**, 4848 (1953).

yield 2 or 11. The exact sequence of these latter steps is not clear and a number of alternative routes can be written.

The initial 1,2 addition finds precedent in the mechanism proposed for the reaction of benzaldehyde with the reagent,[21] but differs from previously proposed 1,4 additions to α,β-unsaturated ketones.[20,22] In our examples initial 1,4 addition would lead to intermediates (*e.g.*, **15**) in which C_3 is planar, precluding ring closure in subsequent steps except by tortuous rearrangements or attack by another chlorinating agent. Similar reasoning argues against nucleophilic 1,4 addition leading to intermediates such as **16**.



15



16

This mechanism not only accounts for the products obtained in this investigation, but also for the partially characterized intermediates obtained from the reaction of phosphorus trichloride with benzalacetophenone.[15] In the latter case the initially formed phostonyl chloride would undergo facile elimination of hydrogen chloride to provide the observed unsaturated product.

Experimental Section[23]

(3β-Chloro-3-hydroxy-5α-cholestan-5-yl)phosphonochloridic Acid Intramolecular Ester (2).—A solution of 50.2 g (0.131 mol) of 4-cholesten-3-one (1) in 200 ml of phosphorus trichloride was allowed to stand at room temperature for 3 hr. Benzoic acid (16.5 g, 0.135 mol) was added to the solution with stirring, and the mixture was allowed to stand for an additional 26 hr. The excess phosphorus trichloride was then distilled under reduced pressure, and the resulting pasty residue was treated with 250 ml of ether. The mixture was cooled in an ice bath, filtered, and washed with ethanol to give 9.52 g of product, mp 204–206.5°. A second crop, mp 203–205°, was obtained to bring the total yield to 9.64 g (14.7%). Recrystallization of the crude product from chloroform–95% ethanol provided 8.95 g of pure **2**: mp 206.5–208.5°; $[\alpha]^{27}D$ +35.8° (*c* 1.59, $CHCl_3$); no absorption in the uv to 205 mμ; ir (Nujol) 1280 (≡PO), 1245, 1120, and 890 cm^{-1} (POC); nmr ($CDCl_3$) δ 1.35 (d, J_{PH} = 0.8 Hz, C_{19} protons), 3.4 (d, 1, J = 13 Hz).

Anal. Calcd for $C_{27}H_{45}Cl_2O_2P$: C, 64.40; H, 9.01; Cl, 14.08; P, 6.15; mol wt, 503. Found: C, 64.28; H, 9.07; Cl, 14.30; P, 6.24; mol wt, 496 (CCl_4, Cottrell boiling point apparatus).

Treatment of **2** with *p*-toluidine, N,N-diethylaniline, phenol, sodium methoxide in methanol, or aqueous acids resulted only in the recovery of the starting material.

The chilled filtrate from the second crop above was treated with methanol until the foaming had subsided. The solution was concentrated under reduced pressure, and the resulting crystalline solid was collected by filtration and washed successively with cold 95% ethanol, 5% aqueous $NaHCO_3$, and water. This material was recrystallized from ether–95% ethanol to give 21.2 g of crude 3-chloro-3,5-cholestadiene (identified by ir spectrum).

The yields of **2** varied from 10 to 21% in various experiments with the best yield being obtained by using 2 molar equiv of benzoic acid and allowing 48 hr to elapse before working up the reaction.

(3-Oxo-5α-cholestan-5-yl)phosphonic Acid (3).—A mixture of 2.00 g (3.98 mol) of **2** and 100 ml of 5% ethanolic KOH was refluxed for 2.5 hr under nitrogen. After the solution had cooled to room temperature, 100 ml of water was added to give a clear solution. This solution was acidified with 6 *N* hydrochloric acid, and the resulting white, crystalline precipitate was collected by filtration. Recrystallization of the crude product from acetonitrile–1 *N* hydrochloric acid provided 1.12 g (61%) of the ketophosphonic acid **3**: mp 237–240°; $[\alpha]^{27}D$ +35° (*c* 1.65, $CHCl_3$); ir (Nujol) 3530 (OH), 3380 (OH), 1715 (C=O), 1665 (C=O, not present in $CHCl_3$), 1225 (≡PO), 1185, and 1005 cm^{-1}.

Anal. Calcd for $C_{27}H_{47}O_4P$: C, 69.49; H, 10.15; P, 6.61; mol wt, 467. Found: C, 69.62; H, 10.31; P, 6.50; neut equiv, 468.

2,4-Dinitrophenylhydrazone had mp 150–163°.

Anal. Calcd for $C_{33}H_{51}N_4O_7P$: C, 61.28; H, 7.95; N, 8.66; P, 4.79. Found: C, 61.27; H, 8.24; N, 8.57; P, 4.65.

Dimethyl (3-Oxo-5α-cholestan-5-yl)phosphonate (4).—Diazomethane prepared from 3.05 g (14.2 mmol) of N-methyl-N-nitroso-*p*-toluenesulfonamide[24] was distilled into a slurry of 2.00 g (4.27 mmol) of ketophosphonic acid **3** in 70 ml of anhydrous ether. Enough chloroform was then added to dissolve the remaining solid, and the solution was washed successively with dilute hydrochloric acid, water, and saturated aqueous NaCl. The ether–chloroform solution was dried ($MgSO_4$), filtered, and evaporated under reduced pressure to give 1.56 g (73%) of the dimethyl ester **4**, mp 191–201°. Recrystallization from acetone (twice) and ethyl acetate (twice) provided an analytical sample: mp 204–209°; $[\alpha]^{27}D$ +30° (*c* 1.64, $CHCl_3$); ir (Nujol) 1720 (C=O), 1235 (≡PO), 1185 (POMe), 1055, 1010, 810 and 785 cm^{-1}; nmr ($CDCl_3$) δ 3.71 (d, 6, J_{PH} = 11 Hz, $POCH_3$), 1.27 (d, J_{PH} = 0.8 Hz, C_{19} protons).

Anal. Calcd for $C_{29}H_{51}O_4P$: C, 70.41; H, 10.39; P, 6.26. Found: C, 70.61; H, 10.58; P, 6.27.

2,4-Dinitrophenylhydrazone had mp 231–233°.

Anal. Calcd for $C_{35}H_{55}N_4O_7P$: C, 62.30; H, 8.22; N, 8.30; P, 4.59. Found: C, 62.36; H, 8.35; N, 8.32; P, 4.67.

Hydrolysis of Dimethyl (3-Oxo-5α-cholestan-5-yl)phosphonate (4).—A solution of 0.10 g (0.2 mmol) of the dimethyl ketophosphonate **4** in 13 ml of 95% ethanol and 11 ml of 42% hydrobromic acid was refluxed for 7 hr. Additional ethanol (*ca.* 5 ml) was added to dissolve the resulting precipitate, and the refluxing was continued for 1 additional hr. The slightly cloudy solution was allowed to cool to room temperature, and crystallization was completed at 15°. The resulting white solid was collected by filtration, washed with dilute hydrochloric acid, and dried over KOH to yield 0.09 g (96%) of crude ketophosphonic acid **3**, mp 229–236°. Recrystallization from acetone–6 *N* hydrochloric acid gave 0.06 g (67% recovery) of **3**: mp 235–239°; mmp with authentic **3** 235–240°; ir identical with that of authentic **3**.

Dimethyl (3-Ethoxy-5α-cholest-2-en-5-yl)phosphonate (5).—A mixture of 2.00 g (4.05 mmol) of dimethyl phosphonate **4**, 0.74 g (5.0 mmol) of triethyl orthoformate, 63 ml of absolute ethanol, and 10 drops of 8% ethanolic HCl was stirred at 80° for 1 hr. The clear, colorless solution was allowed to stand at room temperature for 11 hr and was then made alkaline with ethanolic NaOH. This solution was poured into 125 ml of water to give a heavy suspension of a white solid. This precipitate was collected by filtration, and a second crop was obtained by the addition of water to the filtrate. The ir spectrum of this crude product (1.72 g) indicated it was a mixture of starting material and the desired enol ether. This material was heated again for 40 min at 80° with 1.48 g (10 mmol) of redistilled triethyl orthoformate and 6 drops of 8% ethanolic HCl in 50 ml of absolute ethanol. Work-up as before provided 1.38 g (65%) of crude, waxy product, mp 139–145°. Recrystallization of this material from acetonitrile afforded a first crop of 0.93 g of enol ether **5**: mp 144–147°;

(23) All melting points and boiling points are uncorrected. Infrared spectra were determined on a Perkin-Elmer Model 237B Infracord spectrophotometer. Ultraviolet spectra were determined on a Beckman Model DB spectrophotometer. Nuclear magnetic resonance spectra were obtained on a Varian A-60 spectrometer with tetramethylsilane as the internal reference. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

(24) Th. J. de Boer and H. J. Backer in "Organic Syntheses," Coll. Vol. 4, N. Rabjohn, Ed., John Wiley & Sons, Inc., New York, N. Y., 1963, p 250.

$[\alpha]^{29}D$ +83° (c 1.97, $CHCl_3$); ir (CCl_4) 1660 (C=C), 1240 (≡PO), 1200 (POMe), 1120, and 1060–1035 cm^{-1} (d); nmr ($CDCl_3$) δ 4.14 (d, 1, J = 3 Hz, C=CH), 3.77 (q, 2, J = 7 Hz, $COCH_2$), 3.70 (d, 6, J_{PH} = 10.5 Hz, $POCH_3$), 1.30 (t, J = 7 Hz, OCH_2CH_3), 1.13 (d, J_{PH} = 0.8 Hz, C_{19} protons).

A second crop, mp 140–145°, was obtained to bring the total recovery of **5** to 1.12 g (81%).

Anal. Calcd for $C_{31}H_{55}O_4P$: C, 71.22; H, 10.61; P, 5.93. Found: C, 71.23; H, 10.75; P, 6.00.

Pyrolysis of Dimethyl (3-Oxo-5α-cholestan-5-yl)phosphonate (4).—The dimethyl ketophosphonate **4** (0.50 g, 1 mmol) was heated at 225–231° (oil bath temperature) under vacuum (0.5 mm) using a Dry Ice trap for 6.5 hr. The resulting yellow melt was cooled to room temperature and dissolved in ether. A small amount of insoluble material was removed by filtration, and the ether filtrate was washed with 10% aqueous NaOH. This treatment caused the formation of an oil which was insoluble in ether and aqueous base and which was discarded. The ether solution was then washed with water and saturated aqueous NaCl, dried ($MgSO_4$), and evaporated to a yellow oil. The ir spectrum of this crude material showed it to be mainly 4-cholesten-3-one (**1**), but it could not be induced to crystallize. The 2,4-dinitrophenylhydrazone of **1** was then prepared from this product by the usual procedure. The final yield of this derivative was 0.03 g (23%): mp 230–232°; mmp with authentic 4-cholesten-3-one DNP 230–233°; uv max ($CHCl_3$) 286 mμ (log ε 4.38), 290 (4.02), 256 (4.20) [lit. mp 233–234°[25]; uv max ($CHCl_3$) 292 mμ (log ε 4.06), 281 (4.20), 256 (4.33)[26]].

From the Dry Ice trap was isolated 0.08 g (70%) of dimethyl phosphonate (identified by ir spectrum).

5α-Cholestan-5-ylphosphonic Acid (6).—The Huang-Minlon modification of the Wolff-Kishner reduction was used.[27] A mixture of 1.00 g (2.2 mmol) of ketophosphonic acid **3**, 5 ml of absolute ethanol, 70 ml of freshly distilled diethylene glycol, 8.0 g of KOH, and 10.5 ml (18 mmol) of 85% hydrazine hydrate was refluxed for 30 min. The temperature of the mixture was then raised to 204° over a 2-hr period by removing the condensate. The temperature was maintained at 204–208° for an additional 2 hr. The solution was allowed to cool to room temperature and was acidified with hydrochloric acid to give a white precipitate. This material was filtered, washed with water, and dried to give 0.92 g of crude product, mp 155–165° dec. Recrystallization from ether–methanol–concentrated hydrochloric acid yielded 0.69 g (71%) of phosphonic acid **6**: mp 242–247°; $[\alpha]^{28}D$ +21° (c 1.57, $CHCl_3$–MeOH); ir (Nujol) 1130 (broad, ≡PO), 1000–985 (broad), 950, and 920–900 cm^{-1} (d).

Anal. Calcd for $C_{27}H_{49}O_3P$: C, 71.64; H, 10.91; P, 6.84. Found: C, 71.65; H, 11.07; P, 6.73.

Dimethyl 5α-Cholestan-5-ylphosphonate (7).—Diazomethane prepared from 1.00 g (4.65 mmol) of N-methyl-N-nitroso-p-toluenesulfonamide[24] was distilled into a solution of 0.30 g (0.66 mmol) of phosphonic acid **6** in 200 ml of CH_2Cl_2–$CHCl_3$ (1:7, v/v). The resulting yellow solution was washed with dilute H_2SO_4, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl. The CH_2Cl_2–$CHCl_3$ solution was dried ($MgSO_4$) and evaporated under reduced pressure to a yellow-green oil which crystallized after standing at room temperature for several days. This crude product was chromatographed on 10 g of silica gel using $CHCl_3$ as the eluent to give 0.24 g (75%) of the dimethyl ester **7**: mp 95–100°; $[\alpha]^{27}D$ +23° (c 2.18, $CHCl_3$); ir (Nujol) 1240 (≡PO), 1185 (POMe), 1070–1030 (d), 810, 785, and 740 cm^{-1}; nmr ($CDCl_3$) δ 3.69 (d, 6, J_{PH} = 11 Hz, $POCH_3$) and 1.08 (s, C_{19} protons).

Anal. Calcd for $C_{29}H_{53}O_3P$: C, 72.46; H, 11.11; P, 6.44. Found: C, 72.55; H, 11.12; P, 6.26.

(3β-Chloro-3-hydroxy-5α-cholestan-5-yl)ethylphosphinic Acid Intramolecular Ester (8).—To a stirred mixture of 3.00 g (5.97 mmol) of phostonyl chloride **2** in 25 ml of anhydrous ether was added a solution of ethylmagnesium bromide prepared from 0.85 g (7.8 mmol) of ethyl bromide in 12 ml of anhydrous ether. As the addition proceeded, the slurry thickened and ether was added until the solid dissolved (final volume *ca.* 75 ml). This solution was stirred at room temperature for 3 hr and then refluxed for 4 hr. A colorless solid was deposited during the reflux period. After cooling, the mixture was filtered, and the filtrate was evaporated under reduced pressure to give a colorless dry foam. Trituration of this foam with 95% ethanol provided 1.15 g (39%) of crude **8**, mp 192–196°. Recrystallization of the crude product from methanol gave 0.92 g (80% recovery) of the intramolecular ester **8**: mp 202.5–205.5°; mmp with starting material 201–208.5°. Two additional recrystallizations provided an analytical sample: mp 206–209°; $[\alpha]^{27}D$ +23° (c 2.02, $CHCl_3$); ir (Nujol) 1265 (≡PO), 1230, 1050, and 900 cm^{-1}; nmr ($CDCl_3$) δ 4.21 (m, 0.6, J = 7 Hz, impurity[28]), 1.37 (s, broad, C_{19} protons).

Anal. Calcd for $C_{29}H_{50}ClO_2P$: C, 70.06; H, 10.14; Cl, 7.13; P, 6.23. Found: C, 69.75; H, 10.22; Cl, 6.90; P, 6.21.

(3-Oxo-5α-cholestan-5-yl)ethylphosphinic Acid (9).—A mixture of 0.50 g (1.0 mmol) of intramolecular ester **8** and 25 ml of 5% ethanolic KOH was flushed with nitrogen for 10 min and refluxed under nitrogen for an additional 15 min. The hot yellow solution was acidified with 25 ml of dilute hydrochloric acid and allowed to stand at room temperature for 24 hr. Since no crystallization occurred during this period, the mixture was extracted with $CHCl_3$. The $CHCl_3$ extract was dried ($MgSO_4$) and evaporated under reduced pressure to a dry foam. Addition of methanol to the foam caused the formation of a white precipitate which was collected by filtration. This solid (0.10 g), mp 139–220°, appeared to be a mixture of starting material and the desired product by its ir spectrum. The methanol filtrate was evaporated under reduced pressure, and the residue was crystallized over a period of 3 months from ethyl acetate–acetonitrile to give 0.12 g (25%) of the ketophosphinic acid **9**: mp 190–205°; $[\alpha]^{27}D$ +35° (c 2.02, $CHCl_3$); ir (CCl_4) 3450–3390 (OH), 2670–2630 (=PO_2H), 1720 (C=O), 1685–1650 (=PO_2H), 1175 (broad, ≡PO), 1040, and 960 cm^{-1}; nmr ($CDCl_3$) δ 7.41 (s, 1.5, OH), 4.10 (m, 1.3, J = 7 Hz), 2.15 (s, 1), 1.29 (s, C_{19} protons).

No satisfactory analysis could be obtained for this material, but the residue obtained by evaporation of the ethyl acetate–acetonitrile filtrate above provided a satisfactory 2,4-dinitrophenylhydrazone, mp 150–152°.

Anal. Calcd for $C_{35}H_{55}N_4O_6P$: C, 63.81; H, 8.42; N, 8.50; P, 4.70. Found: C, 63.58; H, 8.06; N, 8.47; P, 4.58.

***trans*-[3-Chlorooctahydro-3-hydroxy-8a-methyl-4a(2H)-naphthyl]phosphonochloridic Acid Intramolecular Ester (11).**—A solution of 21.5 g (0.131 mol) of 2-keto-10-methyl-$\Delta^{1,9}$-octalin (**10**)[29] in 125 ml of phosphorus trichloride was allowed to stand at room temperature for 3 hr. Benzoic acid (16.5 g, 0.135 mol) was added, and the solution was allowed to stand at room temperature for an additional 2 days. The excess phosphorus trichloride was evaporated under reduced pressure, and the residue consisting of an oil and a solid was treated with 50 ml of anhydrous ether to give a colorless precipitate. After filtration the colorless solid became yellow. The material was slurried in ether and kept at ice-bath temperature overnight. Filtration then provided 6.95 g of the product, mp 152–157°, in the first crop and 2.35 g, mp 146–152°, in the second crop (total yield 25%). Recrystallization of the first crop from $CHCl_3$–petroleum ether (bp 60–70°) and the second crop from cyclohexane provided 8.57 g (92% recovery) of the phostonyl chloride **11**: mp 147–152°; ir (Nujol) 1310, 1300, 1285 (≡PO), 1200, 1125, 1025, 940–935 (d), 910, 895–885 (d), 865 and 775 cm^{-1}; nmr ($CDCl_3$) δ 3.32 (d, 1, J_{PH} = 13 Hz, C_1-β proton?) and 1.40 (s, 3, CCH_3).

Anal. Calcd for $C_{11}H_{17}Cl_2O_2P$: C, 46.66; H, 6.05; Cl, 25.04; P, 10.94; mol wt, 283. Found: C, 46.56; H, 6.34; Cl, 25.16; P, 10.92; mol wt, 290 (CCl_4, Cottrell boiling point apparatus).

***trans*-[Octahydro-8a-methyl-3-oxo-4a(2H)-naphthyl]phosphonic Acid (12).**—Phostonyl chloride **11** (2.00 g, 7.07 mmol) was stirred in 100 ml of 5% ethanolic KOH under nitrogen for 100

(25) E. Josephy and F. Radt, Ed., "Elsevier's Encyclopedia of Organic Chemistry," Series III, Vol. 14, Elsevier Publishing Co., Inc., Amsterdam, The Netherlands, 1940, p 121.

(26) F. Radt, Ed., "Elsevier's Encyclopedia of Organic Chemistry," Series III, Vol. 14 supplement, Springer-Verlag, Berlin, Germany, 1956, p 2434s.

(27) Huang-Minlon, *J. Amer. Chem. Soc.*, **71**, 3301 (1949).

(28) This impurity is apparently the product of displacement of the phosphoryl chlorine of **2** by OC_2H_5 formed by oxidation of the Grignard reagent. The appearance and chemical shift of the δ 4.21 band are similar to the methylene proton resonances of other phosphorus ethyl esters. The presence of this impurity is also indicated in the mass spectrum of **8** by a small one-chlorine isotopic cluster at m/e 512–514, 16 mass units above the molecular ion cluster of **8**. A striking feature of this mass spectrum and the mass spectrum of **2** is a high abundance one-chlorine cluster at m/e 402–404 formed by loss of H_2PO_2Et and H_2PO_2Cl, respectively.

(29) N. C. Ross and R. Levine, *J. Org. Chem.*, **29**, 2341 (1964).

min at room temperature (the temperature increased slightly during the initial mixing). Water was added until the mixture was homogeneous, and the solution was poured into 80 ml of 6 N hydrochloric acid. When no crystallization occurred in 7 hr, the solution was adjusted to pH 2 and was extracted with four 65-ml portions of $CHCl_3$. Drying ($MgSO_4$) and evaporation of the combined extracts under reduced pressure gave a thick syrup. This material was crystallized from CH_2Cl_2–cyclohexane (1:1, v/v) to provide 0.70 g of product, mp 225–232° dec [second crop, 0.16 g, mp 217–226° dec (49% total)]. Recrystallization of the combined crude product from CH_2Cl_2–methanol gave 0.56 g (65% recovery) of ketophosphonic acid **12**: mp 224–230° dec; ir (Nujol) 1700 (C=O), 1200 (very broad, ≡PO), 1000, and 925 cm^{-1}; nmr (MeOH) δ 1.36 (s, CCH_3).

Anal. Calcd for $C_{11}H_{19}O_4P$: C 53.65; H, 7.78; P, 12.58; mol wt, 246. Found: C, 53.47; H, 7.86; P, 12.50; neut equiv, 252.

2,4-Dinitrophenylhydrazone had mp 203–208°.

Anal. Calcd for $C_{17}H_{23}N_4O_7P$: C, 47.89; H, 5.44; N, 13.14; P, 7.26. Found: C, 47.70; H, 5.60; N, 12.92; P, 7.19.

Dimethyl *trans*-[Octahydro-8a-methyl-3-oxo-4a(2H)-naphthyl]-phosphonate (13).—Diazomethane prepared from 5.80 g (27.2 mmol) of N-methyl-N-nitroso-*p*-toluenesulfonamide[24] was distilled into a solution of 2.00 g (8.12 mmol) of ketophosphonic acid **12** in 75 ml of a $CHCl_3$–dioxane–DMF mixture. The resulting solution was washed successively with dilute H_2SO_4, water, and saturated aqueous NaCl. Drying ($MgSO_4$) and evaporation of the solution under reduced pressure gave a yellow oil, the ir spectrum of which indicated was a mixture of the desired dimethyl ester and **10**. Distillation of this oil gave 0.65 g of product: bp 145–150° (1 mm); ir (neat) 1720 (C=O), 1675, 1620, 1235 (≡PO), 1180 (POMe), 1055–1035 (d, PO-alkyl), 815, and 775 cm^{-1}. Glpc analysis (Micro-Tek GC 2000-R, twin SE 30 columns, column temperature 210°, flame ionization detector) indicated that the product was contaminated with *ca.* 5% of the unsaturated ketone **10**.

Since no satisfactory separation of these compounds could be accomplished, the 2,4-dinitrophenylhydrazone, mp 124–127°, of **13** was prepared from the mixture by the usual procedure.

Anal. Calcd for $C_{19}H_{27}N_4O_7P$: C, 50.22; H, 5.99; N, 12.33; P, 6.82. Found: C, 50.02; H, 6.12; N, 12.12; P, 6.54.

Registry No.—**2**, 18554-19-3; **3**, 18554-20-6; **3** (2,4-dinitrophenylhydrazone derivative), 18554-21-7; **4**, 18554-22-8; **4** (2,4-dinitrophenylhydrazone derivative), 18554-23-9; **5**, 18554-24-0; **6**, 18554-25-1; **7**, 18554-26-2; **8**, 18554-27-3; **9**, 18554-28-4; **9** (2,4-dinitrophenylhydrazone derivative), 18554-29-5; **11**, 18554-30-8; **12**, 18554-31-9; **12** (2,4-dinitrophenylhydrazone derivative), 18554-32-0; **13**, 18554-33-1; **13**, (2,4-dinitrophenylhydrazone derivative), 18554-34-2; phosphorus trichloride, 7719-12-2.

Photochemical Reactions of Resin Acids. Photochemically Initiated Addition of Methanol to Abietic Acid[1a]

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Irradiation of abietic acid or methyl abietate in methanol or benzene–methanol mixture gave rise to two epimeric ethers **6** and **7** along with products of decarboxylation, disproportionation, isomerization and polymerization. The structures of the two photoadducts **6** and **7** were proved by chemical degradation and nmr and mass spectra. The addition is nonstereospecific at C_{13} and seems to be a bimolecular process,[2c] in which a photoexcited polar species abstracts a proton from methanol to give an intermediate carbonium ion, which then coordinates with solvent. No bicyclobutane intermediate could be isolated under the conditions used for photolysis.

Photochemical transformations of the diene systems in the steroids have been extensively studied[2] but only a few reports have been made on the diterpene resin acids. Photolytic valence isomerizations of levopimaric and palustric acids have been reported.[3,4] Irradiation of abietic acid in ethanol has been reported to give hydroxy acids.[5] The purpose of the present investigation was to study the photolysis of abietic acid and methyl abietate in methanol.

In contrast to the results in ethanol,[5] irradiation (2537 Å) of abietic acid or methyl abietate in absolute methanol or in benzene–methanol gave little if any alcoholic product. The major monomeric products (35% by glpc) were two ethers, photoadducts I and II, obtained in a 9:1 ratio. Isomerization, disproportionation, and, in the case of the acid, decarboxylation products were also obtained. Both ethers could be isolated by preparative glpc of the methyl esters. Thick layer or column chromatography separated the methyl esters of the adducts from the other products but not from each other. Fractional crystallization of the mixed ethers gave pure photoadduct I.

Reduction of photoadduct I with lithium aluminum hydride followed by dehydrogenation with palladium

(1) (a) Presented at the 156th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 8–13, 1968. (b) Resident Postdoctoral Research Associate under the auspices of the National Academy of Sciences, National Research Council. (c) One of the laboratories of the Southern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

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