the above was washed with water and dried, the solvents were removed under vacuum, and the residue was chromatographed on Woelm neutral alumina to give cholestan-3β-ol (32%) and cholestan-3-one (64%). The fractions were analyzed by melting point and tlc comparison and the infrared spectra were consistent with the assigned structures. Other fractions of small weight were not analyzed. Cholesteryl 3β-methylthiomethyl ether (III, R = OCH_2SCH_3) was identified from oxidations using unlabeled substrates.

DMSO–Acetic Anhydride Oxidation.—Cholestan-3β-ol was oxidized after the previously described procedure,[3] with the exception that *o*-xylene was found necessary for solubility purposes. In the absence of a cosolvent the reaction remains heterogeneous, and little (6%) oxidation product is formed, the majority of the substrate being recovered as cholesteryl 3β-methylthiomethyl ether (III, R = OCH_2SCH_3, 60%).

To a mixture of 1.23 g (3.17 mmoles) of cholestan-3β-ol, 6 ml (64 mmoles) of acetic anhydride, 9 ml (120 mmoles) of DMSO, and 15 ml of *o*-xylene was added 60 μl (55,800 counts/min) of the standard solution of cholestan-3α-H^3-3β-ol. The solution was allowed to stand at room temperature for 24 hr, and the DMS was collected as described previously. In this case, the volatile materials were passed through a column of finely ground potassium hydroxide, a process which removed two unidentified constituents, and resulted in recovery of only DMS and *o*-xylene. Cold water (100 ml) was added to the reaction mixture, and it was extracted with ethyl ether and the ether was dried and evaporated. Chromatography of the residue on Woelm neutral alumina yielded the following compounds which were characterized by melting point, infrared spectra, and tlc R_f values: cholestan-3β-ol acetate (33%), cholestan-3-one (21%), cholesteryl 3β-methylthiomethyl ether (39%).

DMSO–Collidine Oxidation.—This oxidation was carried out following the procedure of Jones and Saeed.[4] To 3.83 g (6.86 mmoles) of cholesteryl 3β-*p*-toluenesulfonate (specific activity, 7300 counts/min/mmole) was added 25 ml of DMSO and 0.75 ml (5.7 mmoles) of collidine. The solution was maintained at 95–100° for 3.5 hr. The temperature was lowered to 50° and the DMS was collected and analyzed as described previously. The reaction mixture was combined with 100 ml of water and extracted with ethyl ether, and the ether was extracted with 10% phosphoric acid, 5% sodium bicarbonate, and water, respectively. The ether was removed under vacuum and the residue was chromatographed on Woelm neutral alumina. The following compounds were recovered and characterized from their melting points, infrared spectra, and tlc R_f values: Δ^2-cholestene (21%), cholestan-3-one (43%), cholestan-3β-ol (32%), cholesteryl 3β-*p*-toluenesulfonate (3.3%).

Analysis of Aqueous Extracts.—To obtain a possible estimate of the amount of tritium label present as free H^{3+} at the end of the oxidation the DMSO–acetic anhydride, and the DMSO–collidine oxidations were extracted with small volumes of water (3 ml). The extracts were combined, 100 mg of dicyclohexylcarbodiimide (DCC) being added. After stirring for 48 hr, unreacted DCC was still present. Complete conversion to dicyclohexylurea was accomplished only after addition of dilute acid. The dicyclohexylurea formed was filtered, dried, and counted. Several drops of ethanol were found necessary to render the urea soluble in the scintillation solvent, toluene. The observed specific activities of the urea recovered are DMSO–acetic anhydride, 102 counts/minm/mole and DMSO–collidine, 8.38 counts/min/mmole.

DMSO–Oxygen Exchange.—Approximately 4 mmoles of tritiated dimethyl sulfide (specific activity 21,000 counts/min/mmole) was combined with 1 ml (14.5 mmoles) of dry DMSO alone, and in the presence of pyridine. After standing in a sealed tube for 48 hr, the dimethyl sulfide was removed under vacuum. The DMSO remaining was collected by distillation under vacuum, and was shown to be free of dimethyl sulfide by gas–liquid partition chromatography. The remaining samples were combined with scintillation fluid and counted. The specific activities were found to be negligible.

Registry No.—Cholestan-3α-H^3-3β-ol, 7541-25-5; III (R = $OSO_2C_6H_4CH_3$), 7548-12-1; DMSO, 67-68-5; DCC, 538-75-0; pyridinium trifluoroacetate, 464-05-1; acetic anhydride, 108-24-7; DMS, 75-18-3.

The Reaction between Diphenylphosphinic Acid and Acetic Anhydride. Formation of Acetic Diphenylphosphinic Anhydride and Diphenylphosphinic Anhydride

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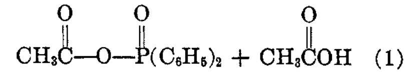
The general methods of preparing phosphinic anhydrides are based on the reaction of the appropriate phosphinic acid chloride with either an ester[1,2] or sodium salt[3] of a phosphinic acid, or with paraformaldehyde.[4] Other preparative methods of less utility have also been reported. Sodium azide mixed with phosphinic acid chloride and warmed to 40° yields the corresponding phosphinic anhydride.[3] Di(bromomethyl)phosphinic anhydride was reported as a product in the distillation of the residue obtained by mixing paraformaldehyde with bromomethylphosphonous dibromide.[5] Phosphinic anhydrides have also been prepared by the reaction of tetraalkyldiphosphine disulfides with mercury(II) oxide.[6] The preparation of phosphinic anhydrides by simple dehydration of the corresponding phosphinic acid has not yet been reported.

Anhydrides of aromatic and dibasic aliphatic carboxylic acids may be prepared by dehydration of the corresponding acid with acetic anhydride.[7,8] However, neither the reaction of phosphinic acids with acetic anhydride nor the isolation of mixed anhydrides formed between phosphinic acids and carboxylic acids has been reported. The present study was undertaken to determine the mode of reaction between diphenylphosphinic acid and acetic anhydride, and to isolate and identify intermediates and products formed in the reaction.

Results and Discussion

Diphenylphosphinic acid neither reacted with nor dissolved in acetic anhydride at room temperature. However, when the mixture was warmed to about 60°, and then cooled, acetic diphenylphosphinic anhydride was isolated in a 70% yield based on the acid (eq 1).



$$(C_6H_5)_2\overset{\overset{\large O}{\|}}{P}OH + (CH_3\overset{\overset{\large O}{\|}}{C})_2O \rightleftharpoons CH_3\overset{\overset{\large O}{\|}}{C}—O—\overset{\overset{\large O}{\|}}{P}(C_6H_5)_2 + CH_3\overset{\overset{\large O}{\|}}{C}OH \qquad (1)$$

At a temperature (about 140°) high enough to allow acetic acid to distil as it formed, both acetic diphenyl-

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[1] G. M. Kosolapoff and R. M. Watson, *J. Am. Chem. Soc.*, **73**, 4101 (1951).

[2] G. M. Kosolapoff and R. M. Watson, *ibid.*, **73**, 5466 (1951).

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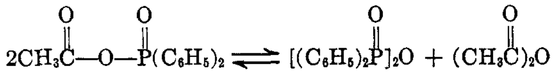
[6] W. Kuchen, K. Strolenberg, and H. Buchwald, *Ber.*, **95**, 1703 (1962).

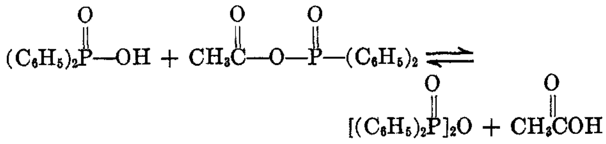
[7] A. I. Vogel, "Practical Organic Chemistry," Longmans, Green and Co., New York, N. Y., 1956, p 794.

[8] Reference 7, p 371.

phosphinic anhydride (29%) and diphenylphosphinic anhydride (42%) were isolated. Because acetic diphenylphosphinic anhydride decomposed quantitatively to diphenylphosphinic anhydride and acetic anhydride at 100° (eq 2), an equilibrium system (eq 3) was



$$2CH_3\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{P}}(C_6H_5)_2 \rightleftharpoons [(C_6H_5)_2\overset{O}{\overset{\|}{P}}]_2O + (CH_3\overset{O}{\overset{\|}{C}})_2O \quad (2)$$



$$(C_6H_5)_2\overset{O}{\overset{\|}{P}}-OH + CH_3\overset{O}{\overset{\|}{C}}-O-\overset{O}{\overset{\|}{P}}-(C_6H_5)_2 \rightleftharpoons [(C_6H_5)_2\overset{O}{\overset{\|}{P}}]_2O + CH_3\overset{O}{\overset{\|}{C}}OH \quad (3)$$

suggested at the higher reaction temperature. Accordingly, a 90% yield of the mixed anhydride was obtained when diphenylphosphinic acid was treated at about 140° with acetic anhydride containing 15 mole % of acetic acid. Since only the starting material was recovered when diphenylphosphinic acid was refluxed with acetic acid or with dry benzene, acetic diphenylphosphinic anhydride appears to be formed as an intermediate before diphenylphosphinic anhydride is produced.

Proton nmr results (100 MHz) for acetic diphenylphosphinic anhydride in several solvents are given in Table I. The methyl protons are spin coupled to the phosphorus atom with $^4J_{PH} \simeq 1.3$ Hz, a reasonable value for a four-bond coupling.[9-12] A slight temperature dependence was observed in benzene-d_6 for δ_{CH_3} and $^4J_{PH}$. Spectra were also recorded at 60 MHz to confirm the spin-coupling nature of the methyl splitting. The aromatic region consists of two complex multiplets at δ 7.9 and 7.6 (in acetone-d_6) which had relative areas of 4 and 6, respectively. Integration of the entire spectrum gave the expected methyl proton-to-aromatic proton ratio of 3:10. Disproportionation of the acetic diphenylphosphinic anhydride to diphenylphosphinic anhydride and acetic anhydride was observed in the nmr spectra of the benzene and acetone solutions. A new acetyl methyl peak appeared and changes occurred in the aromatic multiplets as the disproportionation proceeded. No hydroxyl peak was observed. Heating the sample increased the rate of disproportionation.

TABLE I

NMR RESULTS FOR ACETIC DIPHENYLPHOSPHINIC ANHYDRIDE

		Chemical shifts[b]		
Solvent[a]	$^4J_{PH}$, Hz	δ_{CH_3}	δ_o[c]	$\delta_{m,p}$[c]
Acetic anhydride	1.4	2.26		
Acetone-d_6 (0.21 M)	1.3	2.30	7.9	7.6
Benzene-d_6 (0.16 M)	1.2	1.57	7.9	7.1

[a] Concentration of anhydride is given in parentheses. Ac_2O spectra were of samples taken from the reaction mixture after about half of the acetic acid and acetic anhydride had been removed at reduced pressure. [b] δ in parts per million from tetramethylsilane internal reference. [c] δ_o = center of multiplet. $\delta_{m,p}$ = position of most intense peak in the multiplet.

Pertinent infrared spectral data of acetic acid, acetic anhydride, acetic diphenylphosphinic anhydride, diphenylphosphinic anhydride, and diphenylphosphinic acid are shown in Table II. The infrared spectrum of acetic diphenylphosphinic anhydride is characterized by a single C═O stretching vibration at 1773 cm^{-1} which is absent in the spectrum of diphenylphosphinic anhydride. In the diphenylphosphinic acid spectrum, the hydrogen-bonded P═O stretching vibration occurs at 1181 cm^{-1}; however, the phosphoryl absorption is shifted to 1238 cm^{-1} in the spectra of diphenylphosphinic anhydride and acetic diphenylphosphinic anhydride. Shifts of 55 to 60 cm^{-1} between hydrogen-bonded and free phosphoryl groups have been reported.[13,14] In agreement with Thomas and Chittenden,[15] we find that the presence of several strong absorptions between 685 and 715 cm^{-1} prevents any P—O assigments to be made in this region. The strong absorptions at 1183 cm^{-1} in the acetic diphenylphosphinic anhydride spectrum and at 1134 cm^{-1} in the acetic anhydride spectrum are assigned to the C—O(—P) stretching and to the C—O(—C) stretching, respectively, of the open-chain anhydrides.[15]

In conclusion, diphenylphosphinic acid and acetic anhydride react to form acetic diphenylphosphinic anhydride and/or diphenylphosphinic anhydride in proportions which depend on the reaction conditions. A versatile and simple procedure for the synthesis of phosphinic anhydrides from the corresponding acid is suggested by the reported reaction.

Experimental Section

Because of their reactivity with moisture, all products were handled in a dry nitrogen atmosphere. To determine any shifts owing to the physical state of the sample, the infrared spectra were run as mineral oil mulls and as potassium bromide pellets. Perkin-Elmer Model 21 and Beckman IR-12 spectrometers were used for infrared measurements. Proton nmr spectra were run on Varian HA-100 and A-60 spectrometers. Tetramethylsilane was used as an internal reference.

Acetic Anhydride.—CP grade anhydride was redistilled; the middle fraction boiling at 130°[16] was collected and stored in a stoppered wash bottle. When needed, the reactant was dispensed by applying dry nitrogen to the mouthpiece of the bottle. Proton nmr and infrared spectral data of the purified anhydride indicated that hydroxyl-containing compounds were absent or below the limits of detection.

Diphenylphosphinic Acid.—This acid was prepared by the method of Amonoo-Neizer, Ray, Shaw, and Smith[17] from dimethyl sulfoxide and diphenylphosphinous chloride. Redistilled dimethyl sulfoxide (0.28 moles, 22.0 g) was slowly added to diphenylphosphinous chloride[18] (0.15 mole, 33.3 g) dissolved in 75 ml of methylene chloride. A dry nitrogen atmosphere was maintained in the system during the preparation. Refluxing of the reaction solution was maintained by the rate of dimethyl sulfoxide addition. After all of the dimethyl sulfoxide was added, the stirred solution became turbid within 1 hr. The insoluble material was filtered, washed with methylene chloride, and dried under reduced pressure. A 96% yield (29 g) of crude acid was isolated; the product was recrystallized from absolute ethanol (mp 195.0–196.1°).

Anal.[19] Calcd for $C_{12}H_{11}O_2P$: C, 66.06; H, 5.08; P, 14.19. Found: C, 65.77; H, 5.18; P, 13.64.

Acetic Diphenylphosphinic Anhydride. A.—Diphenylphosphinic acid (0.50 g, 2.3 mmoles) was dissolved in 25 ml of acetic anhydride by warming the stirred mixture to 60°. When

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[12] M. Gordon and C. E. Griffin, *ibid.*, **31**, 333 (1966).

[13] L. C. Thomas and R. A. Chittenden, *Spectrochim. Acta*, **20**, 467 (1964).

[14] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1958, pp 312–315.

[15] L. C. Thomas and R. A. Chittenden, *Spectrochim. Acta*, **20**, 489 (1964).

[16] All temperatures are uncorrected.

[17] E. H. Amonoo-Neizer, S. K. Ray, R. A. Shaw, and B. C. Smith, *J. Chem. Soc.*, 6250 (1965).

[18] Obtained from Stauffer Chemical Co., and used as received.

[19] Analysis performed by Aldridge Associates, Inc., Washington, D. C.

TABLE II

CHARACTERISTIC INFRARED SPECTRAL DATA OF ACETIC ACID, ACETIC ANHYDRIDE, ACETIC DIPHENYLPHOSPHINIC ANHYDRIDE, DIPHENYLPHOSPHINIC ANHYDRIDE, AND DIPHENYLPHOSPHINIC ACID

Infrared, cm^{-1}					
$CH_3C(O)OH$	$[CH_3C(O)]_2O$	$CH_3C(O)OP(O)$-$(C_6H_5)_2$	$[(C_6H_5)_2P(O)]_2O$	$(C_6H_5)_2P(O)OH$	Assignments
1718 (s)	$\left.\begin{matrix}1842\\1783\end{matrix}\right\}$ (s)	1773 (s)	...	...	COOH, C(O)OC(O), or C(O)OP(O): C═O stretching
...	1134 (s)	1183 (s)	...	...	COC or COP: CO stretching
...	...	1442 (s)	1441 (s)	1440 (s)	PC (aromatic)
1295 (s)	...	...			
...	...	1238 (s)	1238 (s)	1189 (sh) 1181 (s)	P(O)OC(O), P(O)OP(O), or P(O)OH: P═O stretching
...	...	916 (s)	966 (s)	962 (s)	POC, POP, or POH: PO stretching

the acetic anhydride was removed by flash evaporation, a crystalline material was isolated. After twice dissolving the solid in small amounts of benzene and removing the solvent by flash evaporation, the product was finally dried on a freeze drier under pressures of less than 1 μ. The dried product (0.41 g, 70% yield) melted between 93.0 and 97.3° in a sealed capillary tube; the melt heated above 100° produced a new solid (mp 144–148°) and a liquid on the cooler regions of the tube.

Anal. Calcd for $C_{14}H_{13}O_3P$: C, 64.62; H, 5.00; P, 11.92. Found: C, 64.81; H, 5.38; P, 11.51.

B.—Diphenylphosphinic acid (0.50 g, 2.3 mmoles) was dissolved in acetic anhydride (25 ml) by warming to 60°. The reaction solution was brought to reflux and approximately 2.5 ml of distillate was collected between 110 and 125°. Although the reaction solution was maintained at approximately 140°, the distillation head was warmed with a heat gun to facilitate removal of the distillate. Using the method of Fernandez, *et al.*,[20] we found approximately 2.5 mmoles of acetic acid (theoretical, 2.3 mmoles) in the acetic anhydride–acetic acid distillate. After removing the acetic anhydride by flash evaporation, the white, hygroscopic residue was washed several times with dry carbon tetrachloride and twice dissolved in dry benzene and flash evaporated to dryness, and the residue was finally dried on the freeze drier. The solid (0.17 g, 29% yield based on the acid) melted between 99.0 and 100.0°.

Anal. Found: C, 64.44; H, 5.07; P, 12.00.

Carbon tetrachloride, which was used to wash the acetic diphenylphosphinic anhydride, was flash evaporated to dryness. The solid isolated (0.20 g, 42% yield) was found by spectral data to be diphenylphosphinic anhydride containing a trace of acetate group impurity.

C.—A mixture of diphenylphosphinic acid (0.50 g, 2.3 mmoles) and acetic anhydride (25 ml) containing approximately 15 mole % acetic acid (determined by proton nmr) was refluxed for several hours. An approximately 90% yield (0.53 g) of acetic diphenylphosphinic anhydride was obtained when the acetic anhydride–acetic acid mixture was removed by flash evaporation at low temperatures. The anhydride was identified by its infrared spectrum and its melting point.

D.—When diphenylphosphinic acid (0.50 g, 2.3 mmoles) was refluxed either with glacial acetic acid (25 ml) or with dry benzene (25 ml), only unreacted acid (infrared spectral data) was isolated after the solvents were removed by flash evaporation.

Diphenylphosphinic Anhydride. A.—A flask having an adaptor with a stopcock and containing approximately 0.1 g of acetic diphenylphosphinic anhydride was attached to the freeze drier. Moisture was excluded from the flask by sealing the products under reduced pressure or under dry nitrogen. After evacuating the system and cooling the traps with liquid nitrogen, the flask containing the mixed anhydride was heated in boiling water until the acetic diphenylphosphinic anhydride melted and resolidified. The resulting solid was heated at 100° for an additional 3 hr to ensure complete reaction, cooled to room temperature under reduced pressure, and transferred to the drybox for analysis. In a sealed capillary tube, the product melted at 148.0 to 148.5°.

Anal. Calcd for $C_{24}H_{20}O_3P_2$: C, 68.99; H, 4.78; P, 14.03. Found: C, 68.91; H, 5.25; P, 14.48.

B.—Reaction C for the preparation of acetic diphenylphosphinic anhydride was repeated. After removal of the acetic anhydride–acetic acid mixture from the reaction solution, the residual oil was heated above 100° until a crystalline product was obtained. This *in situ* decomposition of the mixed anhydride yielded 0.15 g (31%, based on the acid) of diphenylphosphinic anhydride (infrared spectrum).

Registry No.—Diphenylphosphinic acid, 1707-03-5; acetic anhydride, 108-24-7; acetic diphenylphosphinic anhydride, 7594-78-7; diphenylphosphinic anhydride, 5849-36-5.

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Reductions in Potassium Hydroxide–Ethylene Glycol Solution[1]

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The two 3-phenyl-2-norbornanols with *endo*-phenyl substituents (I and II) are readily available in quite respectable yields by hydroboration of 2-phenylnorbornene[2] and hydride reduction of 3-*endo*-phenyl-2-norbornanone.[3,4] In contrast, the two 3-phenyl-2-norbornanols with *exo*-phenyl substituents (III and IV) are obtained in comparatively low yields as a mixture, with some of II, from hydride reduction of the ketone mixture obtained *via* the Nef reaction on 3-*exo*-phenyl-2-*endo*-nitronorbornane.[5] The over-all yield of III and IV obtainable as a 4:1 mixture from 3-*exo*-phenyl-2-*endo*-nitronorbornane is *ca.* 8–10%.[6]

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(1) This research was supported in part by a grant from the National Science Foundation.

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