4-Methyl-1-trifluoromethyl-2,6,7-trioxabicyclo[2.2.2]octane (I).—This starting material was prepared by a modification of the procedure described previously.[3] A solution of 60 g (0.50 mole) of 2-hydroxymethyl-2-methyl-1,3-propanediol, 57 g (0.50 mole) of trifluoroacetic acid, and 200 ml of benzene in a flask equipped with a Dean–Stark trap and a reflux condenser was heated under reflux until 1 equiv of water was collected in the Dean–Stark trap (*ca.* 24 hr). To the reaction mixture was added 1.0 ml of concentrated sulfuric acid, and heating was continued for 5 days. At the end of this time nearly the theoretical amount of water was found in the Dean–Stark trap. Removal of the solvent gave a white solid, which was washed with aqueous sodium carbonate solution and recrystallized from anhydrous benzene to give 55.7 g (56% yield) of compound I as a white powder, mp 152.5–153.5° (with sublimation; lit.[3] mp 145°). The fluorine nmr spectrum[4] of this material exhibits only a single resonance peak, which is a singlet at ϕ^* +84.9 (at 95° in benzene with benzotrifluoride as internal reference). The proton nmr spectrum shows two resonance peaks, both singlets, at τ +6.04 and at +9.12 in carbon tetrachloride at 25°. The former (and stronger) absorption is assigned to the methylene hydrogens, and the latter is assigned to the hydrogens of the methyl group.

1,4-Bis(trifluoromethyl)-2,6,7-trioxabicyclo[2.2.2]octane.—A suspension of 1.0 g of compound I (5.1×10^{-3} mole) in 75 ml of perfluorotributylamine[6] was placed in the fluorination apparatus above the sintered disk. The tube was cooled to 0° and flushed for 1 hr with dry nitrogen. Fluorine was then introduced into the nitrogen stream, and the fluorine–nitrogen mixture was passed into the reaction vessel. A total of 0.43 mole of fluorine was used as the fluorine concentration was increased stepwise from 2 to 25% over a period of 6 hr. The temperature of the reaction vessel was maintained at 0°. After the fluorine flow was discontinued, the cooling bath was removed, and the reaction vessel was purged with nitrogen for 2 hr to remove fluorine and to carry over the products of the reaction into the collection trap.

The contents of the trap were then subjected to fractional distillation–condensation on a vacuum line through traps at −5°, −78°, and −196°. The middle fraction was found to contain 0.3 ml of liquid product which was purified by gas chromatography on a column 2 m in length and 0.5 in. in diameter packed with poly(chlorotrifluoroethylene) oil (33%, commercially available from Minnesota Mining and Manufacturing Co. as Kel-F polymer oil KF-8126) coated on 30–60 mesh acid-washed Celite (67%, diatomaceous earth) and maintained at 70°. Helium was used as the carrier gas at a flow rate of 150 ml/min. Compound II was obtained as a colorless liquid having a vapor pressure of 53 mm at room temperature (*ca.* 23°). The yield of pure material obtained from chromatography was about 10% of the theoretical amount (*ca.* 0.5×10^{-3} mole) based on the amount of compound I used as starting material.

The structural formula of compound II was shown by the fluorine nmr spectrum, the infrared spectrum,[7] the mass cracking pattern, and the molecular weight.[8] The fluorine nmr spectrum in trichlorofluoromethane solution contains a singlet absorption at ϕ^* +84.8 (assigned by comparison with the singlet absorption at 84.9 in the starting material to the fluorines of the CF_3 group next to the carbon atom linked to three oxygen atoms), a fourfold absorption at +70.3 (assigned to the six fluorine atoms of the CF_2 groups), and a sevenfold absorption at 62.3 (assigned to the fluorines of the remaining CF_3 group). The coupling constant is 9.3 cps. The area ratios of the fluorine absorptions are consistent with the structure assignment. The mass cracking pattern shows fragments attributable to $C_4F_7^+$ (*m/e* 181), CF_3^+ (*m/e* 69, largest peak), and $C_7F_{11}O_3^+$ (*m/e* 341, the parent structure lacking one fluorine) in addition to many other peaks consistent with the structure. All peaks attributable to fragments containing more than four carbon atoms—for example, at mass numbers 225, 275, 294, and 341—appear at mass numbers attributable to fragments containing oxygen as well as carbon and fluorine. No peaks attributable to fragments containing hydrogen were observed. The molecular weight by the gas density method was found to be 350 (calcd 360). The infrared spectrum shows no absorption in the region 2.5–7.0 μ. The positions of the absorption peaks (wavelengths in μ) are as follows: 7.49 (s), 7.71 (vs), 7.82 (shoulder), 8.01 (s), 8.25 (m), 8.38 (m), 8.60 (m), 8.76 (m), 8.94 (s), 9.77 (s), 9.95 (s), 10.20 (m), 10.78 (w), 13.07 (m), and 14.74 (w).

A sample of compound II which had been stored in the gas phase at room temperature for nearly 3 years showed no evidence for decomposition.

Other products of the reaction were low molecular weight fragmentation products (carbon tetrafluoride, carbonyl fluoride, and carbon dioxide) and partially fluorinated hydrogen-containing materials which were not further identified.

Registry No.—1,4-Bis(trifluoromethyl)-2,6,7-trioxabicyclo[2.2.2]octane, 7492-72-0; I, 878-60-4.

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(4) The nmr spectra were obtained on a Varian V-4300-2 nmr spectrometer operated at 40.00 Mcps. Positions of the fluorine absorptions are expressed in ϕ^* units[5] relative to the absorption of $CFCl_3$.

(5) G. Filipovich and G. V. D. Tiers, *J. Phys. Chem.*, **63**, 761 (1959).

(6) Commercially available as FC-43, Minnesota Mining and Manufacturing Co.

(7) The infrared spectra were obtained on a Perkin-Elmer Model 21 double-beam infrared spectrophotometer on gas samples. The mass cracking pattern was obtained on a Consolidated Electrodynamics Corp. mass spectrometer, Type 21-103C, with an ionization potential of 70 v and an ionization chamber temperature of 250°.

(8) Elemental analyses for carbon and fluorine were attempted by the procedure developed in these laboratories for highly fluorinated compounds[9] by combustion of the samples in moist oxygen at 1100–1200°. Repeated attempts gave erratic results even with portions of the same sample, apparently because of incomplete combustion and formation of carbon tetrafluoride in the combustion reaction. The results of three determinations with the same sample are as given. *Anal.* Calcd for $C_7F_{12}O_3$: C, 23.3; F, 63.3. Found: C, 22.8, 22.4, 22.6; F, 60.5, 61.7, 60.9.

(9) H. E. Freier, B. W. Nippoldt, P. B. Olson, and D. G. Weiblen, *Anal. Chem.*, **27**, 146 (1955).

Dimethyl Sulfoxide Oxidations[1a]

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The use of dimethyl sulfoxide (DMSO) as a reactant in the oxidation of a variety of functional groups to carbonyl compounds has received a good deal of attention in recent years.[2-8] One of the most studied of these techniques is that involving an alcohol substrate, dicyclohexylcarbodiimide (DCC), and a proton source

(1) (a) This research has been supported by National Science Foundation Grant G. P. 5787, and Research Grant NB-04313 from the National Institute of Neurological Diseases and Blindness. (b) Abstracted from a portion of the thesis of F. W. Sweat submitted in partial fulfillment of the requirements for the Ph.D. degree.

(2) (a) K. E. Pfitzner and J. G. Moffatt, *J. Am. Chem. Soc.*, **87**, 5661 (1965); (b) K. E. Pfitzner and J. G. Moffatt, *ibid.*, **87**, 5670 (1965); (c) A. H. Fenselau and J. G. Moffatt, *ibid.*, **88**, 1762 (1966).

(3) J. D. Albright and L. Goldman, *ibid.*, **87**, 4214 (1965).

(4) D. N. Jones and M. A. Saeed, *J. Chem. Soc.*, 4657 (1963).

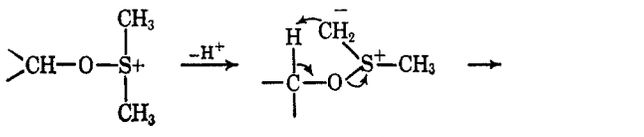
(5) H. R. Nace and J. J. Monagle, *J. Org. Chem.*, **24**, 1792 (1959); N. Kornblum, J. W. Powers, G. J. Anderson, W. J. Jones, H. O. Larson, O. Levand, and W. M. Weaver, *J. Am. Chem. Soc.*, **79**, 6562 (1957); R. N. Iacona, A. T. Rowland, and H. R. Nace, *J. Org. Chem.*, **29**, 3495 (1964); I. M. Hunsberger and J. M. Tien, *Chem. Ind.* (London), 88 (1959).

(6) W. Kornblum, W. J. Jones, and G. J. Anderson, *J. Am. Chem. Soc.*, **81**, 4113 (1959); A. P. Johnson and A. Pelter, *J. Chem. Soc.*, 520 (1964).

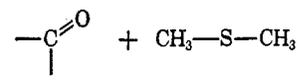
(7) T. Cohen and T. Tsuji, *J. Org. Chem.*, **26**, 1681 (1961).

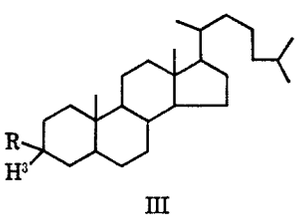
(8) D. H. R. Barton, B. J. Garner, and R. H. Wightman, *J. Chem. Soc.*, 1855 (1964).

plus the DMSO.[2] The work of Pfitzner, Fenselau, and Moffat[2] has established that in the DMSO–DCC oxidation an alkoxysulfonium salt (I) is converted into an ylid (II) which undergoes an intramolecular hydrogen transfer to give the observed carbonyl product plus dimethyl sulfide (DMS). Even in light of this work, it is not reasonable to assume that other oxidations involve the same ylid intermediate because of the notable difference in reaction conditions, *i.e.*, time, temperature. Our results using tritium-labeled substrates suggest that the primary pathway in the oxidation reactions studied is that involving the proposed intermediate (II) substantiating previous work[2c] and extending the generality of the proposed mechanism[2a] to other related oxidations. However, it is likely that a small, but as yet quantitatively undetermined, portion of the various oxidations proceeds by direct proton abstraction from I rather than the intramolecular hydrogen-transfer step. In our experiments, cholestan-



I II





III

3α-H^3-3β-ol (III, R = OH) was oxidized to cholestane-3-one by DMSO, DCC, and pyridinium trifloroacetate,[2b] and also by DMSO and acetic anhydride.[3] In addition, cholesteryl-3α-H^3 3β-*p*-toluenesulfonate (III, R = $OSO_2C_6H_4CH_3$) was oxidized by DMSO in the presence of collidine.[4] In each oxidation the resulting dimethyl sulfide was isolated by a nonequilibrium distillation and characterized by its gas–liquid partition chromatography retention time and by conversion to its mercuric chloride complex, mp 157–158°.[9] No attempts were made to obtain optimum yields since we wished to recover starting material to check specific activities (counts per min/mmole) before and after oxidation, for a possible indication of an isotope effect.[10] After removal of the DMS from the reaction mixtures the starting substrates and the other products were isolated by chromatography on alumina. The yields of these products are recorded in the Experimental Section. Specific activity comparisons of starting substrate, recovered substrate, and recovered DMS are shown in Table I.

(9) F. Challenger and M. I. Simpson, *J. Chem. Soc.*, 1591 (1948).

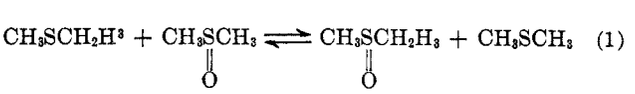
(10) L. Melander, "Isotope Effects on Reaction Rates," The Ronald Press, New York, N. Y., 1960, pp 46–64.

TABLE I

Method	Substrate	Specific activities, cpm/mmole: Starting substrate	Recovered DMS	Recovered substrate
DCC + DMSO	III, R = OH	24,900	7,300	26,000
Ac_2O + DMSO	III, R = OH	30,700	7,000	32,400
		17,600	3,930	...
Collidine + DMSO	III, R = OTs	7,300	1,970	7,000
		12,300	2,700	...

If the oxidation proceeds in accord with the proposed mechanism, the specific activities of the recovered DMS should be comparable in magnitude to the specific activities of the starting substrates. The low specific activity of the DMS (see Table I) as compared to that of the substrates, thus, requires some explanation or interpretation.[11]

An explanation involving a large primary isotope effect in the intramolecular hydrogen-transfer step[10] was negated by a comparison of the specific activities of the starting and recovered substrates. The possibility of oxygen exchange[12] (eq 1) followed by proton



(1)

equilibration of the resultant tritium-labeled DMSO[13] either in the work-up or in the reaction media itself was studied and found to be unimportant in contributing to the low specific activity of the DMS.

We have found that a standard DMSO–DCC oxidation using 5 ml of DMSO, but no alcohol substrate, will produce 0.24 mmole of DMS as determined by isolation of the mercuric chloride derivative. This observation is compatible with other labeling studies[2c] as well as the data concerning the decomposition and disproportionation of DMSO.[13–16] In the absence of suitable substrates, detectable amounts of DMS were also found for the other oxidations studied. These experiments show that DMS can be formed in reactions other than those involving formation of carbonyl compounds and suggests that the primary cause for the low specific activity of the DMS is due to additional pathways for the formation of DMS not involving oxidation.

Although the above discussion provides a rationale for the low specific activity of the DMS, the possibility that an alternate mechanism is also operative should not be discounted. In this sense nonlabeled DMS could be formed by direct base abstraction of the hydrogen on the carbon being oxidized rather than formation of II, and would result in the tritium label being present in the reaction mixture as a proton. In the DMSO–DCC oxidation dicyclohexylurea whose formation is accompanied by removal of two protons from the reaction media was isolated and purified under con-

(11) It should be noted that in other labeling studies[2c] unlabeled DMS was also recovered but no comment or explanation was given for this observation.

(12) S. Searles and H. R. Hays, *J. Org. Chem.*, **23**, 2028 (1958).

(13) E. Buncel, E. A. Symons, and A. W. Zabel, *Chem. Commun.*, 173 (1965).

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(15) V. J. Traynelis and W. L. Hergenrother, *J. Org. Chem.*, **29**, 221 (1964).

(16) H. R. Davis, Jr., and D. P. Sorensen, U. S. Patent 2,870,215 (Jan 20, 1959); *Chem. Abstr.*, **53**, 11416*i* (1959).

ditions where further proton exchange would be minimized. The isolated dicyclohexylurea was found to possess small but real amounts of radioactivity (68 counts/min/mmole) (total counts isolated as the urea: 610 counts/min accounting for less than 1% of the total counts added). In other cases, the oxidations were terminated by water extraction and the extracts were treated with DCC to give dicyclohexylurea which also contained small amounts of radioactivity. It seems likely in view of the small amount of tritium isolable from the aqueous extracts of the oxidations that the primary pathway in each of the oxidation reactions involves the proposed intermediate II. The presence of radioactivity in the isolated dicyclohexylurea, even though a small amount, must be considered as evidence for some of the reaction proceeding by direct proton abstraction on species I.

We also found side product III, R = OCH_2SCH_3, previously reported in the DMSO–DCC[2b] and the DMSO–Ac_2O oxidations[3] to be typical of these oxidations; however, this compound was never detected as a side-product in the DMSO oxidation of the sulfonate ester (III, R = $OSO_2C_6H_4CH_3$). There is also a notable absence of any report of this methylthiomethyl ether being formed as a side product in oxidations where DMSO is necessarily displacing a leaving group (in this case OTs) leading directly to formation of intermediate I.[4,5,17] It has been postulated that this side product arises by rearrangement of II.[2a,18] Since III, R = OTs is converted, at least in part, to II before oxidation and yet does not form III (R = OCH_2SCH_3), a different mechanism seems necessary. A mechanism involving attack of the activated species, $CH_3\overset{+}{S}{=}CH_2$, on the free alcohol has been suggested,[2a,3] and would better fit these data.

Experimental Section

Materials.—DMSO was distilled under vacuum from calcium hydride prior to use in the oxidations. Collidine and pyridine were distilled and stored over potassium hydroxide. Trifluoroacetic acid, acetic anhydride, and DCC (all obtained from Matheson Coleman and Bell) were used without further purification. All other reagents were distilled prior to use. The sodium borotritiide is a commerical product of New England Nuclear Co. Melting points were determined on a Fisher-Johns apparatus and are uncorrected. All melting points assigned conformed with the literature values.[19] Infrared spectra were recorded on a Beckman IR 5A instrument. Gas liquid partition chromatography was performed on a F and M Scientific Corp. Model 500 instrument. A Packard liquid scintillation spectrometer was used in the determination of all specific activities. Quenching effects were considered, and found to be negligible for all samples. Background radiation was determined for each counting of samples with an external standard. All samples were counted for a length of time commensurate with the radioactivity present. Solid samples were recrystallized to a constant specific activity, and dried under vacuum prior to weighing. All products isolated were further characterized by thin layer chromatography using silica gel G as an adsorbant.

Procedure.—Each oxidation was carried out in a Claisen distillation apparatus modified so that the distillate would be trapped in a standard scintillation bottle maintained at −70°. After the oxidation was near completion, the reaction solution was heated to a temperature of 50° with a small stream of nitrogen bubbled through the mixture to facilitate the collection of the dimethyl sulfide, bp 38°. Following the collection bottle were five additional traps: two Dry Ice, one saturated mercuric chloride in ethanol, one acidic, and one alkaline trap to ensure complete capture of radioactive volatiles. The nitrogen sweep was maintained for a period of 45 min and a sample of the collected volatiles (DMS and *o*-xylene) was taken for gas liquid partition chromatographic analysis. From the areas of the respective curves, the weight per cent of DMS in the mixture was readily calculated by multiplying the areas by the square root of the molecular weight of the component and calculating the percentage contribution of each compound in the mixture.[20] The accuracy of this method is estimated to be 10%.[20] Scintillation fluid was added to the known weight of sample remaining, and the amount of tritium label was promptly determined. From these data the specific activity of the DMS was calculated (Table I).

Dimethyl Sulfide Characterization.—To the DMS collection bottle, containing DMS and *o*-xylene, 2 ml of a saturated solution of mercuric chloride in absolute ethanol was added, and an immediate precipitate was formed. Recrystallization from benzene gave the complex, $3HgCl_2 \cdot 2CH_3SCH_3$, mp 158°.[9] This compound was decomposed under benzene with dilute sodium hydroxide.[9] The benzene, along with several washings, was decanted into a scintillation bottle and the radioactivity was counted. Tritium-labeled DMS was isolated in this manner for each of the three oxidations.

Cholestan-3α-H³-3β-ol (III, R = OH).—To 330 mg (0.85 mmole) of cholestan-3-one in 100 ml of 95% ethanol was added 2 mg (0.053 mmole) of sodium borohydride. The solution was allowed to stir at room temperature for 30 min, and 12.9 mg (0.28 mmole) of sodium borotritiide (102 mcuries/mmole) was added. The reaction was stirred for 3.5 hr and 2 mg more of sodium borohydride was added. The reduction was allowed to proceed for 30 min more. The reaction was judged to be complete from pilot reductions using only sodium borohydride. Saturated ammonium chloride (20 ml) was slowly added, then 20 ml of cold water. The precipitated cholestan-3α-H³-3β-ol was filtered and recrystallized from methanol to yield 278 mg (84%) of product, mp 145°. The observed specific activity was 4550 counts/min/μg. A small fraction of this material was employed to make a standard solution in *o*-xylene with an experimentally determined activity of 929.7 counts/min/μl. Desired volumes of this standard were employed in the following oxidations.

Cholesteryl-3α-H³ 3β-*p*-toluenesulfonate (III, R = $OSO_2C_6H_4CH_3$).—To 5.0 g (12.9 mmoles) of cholestan-3β-ol and 160 μl (148,500 counts/min) of the standard solution of cholestan-3α-H³-3β-ol in 20 ml of anhydrous pyridine was added 2.8 g (14.7 mmoles) of *p*-toluenesulfonyl chloride. The solution was stirred for 12 hr at room temperature, and the reaction was terminated with the addition of 80 ml of cold water. The mixture was extracted with chloroform which was subsequently extracted thoroughly with 10% phosphoric acid, 5% sodium bicarbonate, and water, respectively. The chloroform layer was dried over anhydrous magnesium sulfate and evaporated. Recrystallization of the residue from acetone resulted in recovery of 4.37 g (61%) of cholesteryl-3α-H³ 3β-*p*-toluenesulfonate, mp 133–134°, specific activity, 13,290 counts/min/mmole.

DMSO–DCC–Pyridinium Trifluoroacetate Oxidation.—The oxidation of cholestan-3β-ol was run according to a previously described procedure,[2b] with the exception that benzene was replaced by the less volatile *o*-xylene.

To a mixture of 1.16 g (2.99 mmoles) of cholestan-3β-ol, 1.85 g of DCC (8.98 mmoles), 0.24 ml of pyridine (3 mmoles), 5 ml of DMSO (74 mmoles), and 0.12 ml of trifluoroacetic acid (1.5 mmoles) in the described apparatus was added 80 μl (74,400 counts/min) of the standard solution of cholestan-3α-H³-3β-ol. The reaction was allowed to proceed for 5 hr at room temperature and the dimethyl sulfide was collected along with a considerable amount of *o*-xylene. Gas liquid partition chromatographic analysis indicated only *o*-xylene and dimethyl sulfide to compose the collected volatiles. The weight per cent of dimethyl sulfide was determined as described above. Addition of dry ethyl acetate to the reaction solution resulted in the precipitation of DCC, mp 234°,[2b] which was filtered, washed with dry benzene, and dried prior to specific activity determination. The filtrate from

(17) F. X. Jarreau, B. Tchovbar, and R. Goutarel, *Bull. Soc. Chim. France*, 887 (1962).

(18) J. Bryan Jones and D. C. Wigfield, *Tetrahedron Letters*, 4103 (1965).

(19) L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1950.

(20) W. W. Epstein, E. Aoyagi, and P. W. Jennings, *Comp. Biochem. Physiol.*, **18**, 225 (1966).

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).

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

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

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