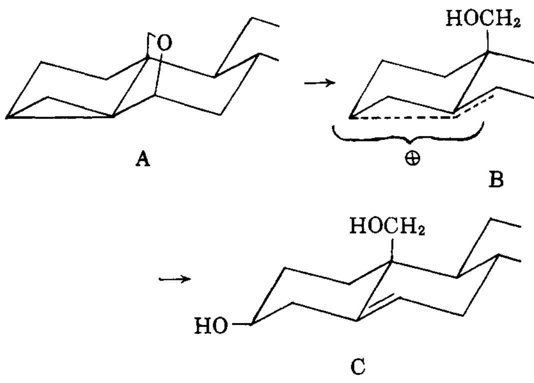
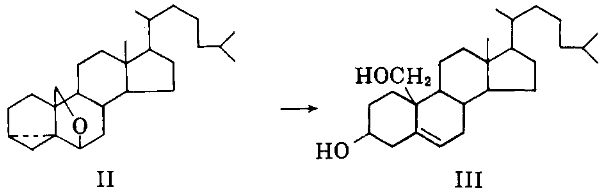


material, of 3α,5α-cyclo-6β,19-oxidocholestane (II).[1,5-7] The structural assignment is based upon composition, infrared and nuclear magnetic resonance spectra. The infrared spectrum (carbon tetrachloride) of II had a band at 11.08 μ which is characteristic of the 6β,-19-oxido bridge.[1] The n.m.r. spectrum[8] of the oxide lacked the C-19 methyl signal of starting *i*-steroid and was further characterized by the C-19 methylene multiplet centered at 6.23 τ,[9] J_{AB} = 12 c.p.s., δ_{AB}, 0.13 p.p.m. (2H); the unresolved C-6 multiplet at 6.68 τ (1H); and the cyclopropyl C-4 methylene centered at 9.75 τ (2H).

Treatment of 3α,5α-cyclo-6β,19-oxidocholestane (II) with a trace of sulfuric acid in aqueous acetone for two hours yielded Δ⁵-cholestene-3β,19-diol (II) in 80% yield. The identity of this material was proved by comparison with a known sample (melting point, mixture melting point, infrared) prepared by the method of Bowers.[1]



Experimental[10]

3α,5α-Cyclo-6β,19-oxidocholestane (II).—Lead tetraacetate 4.68 g. (0.107 mole) was recrystallized from benzene and dried *in vacuo* for 3 hr. It was dissolved in 250 ml. of dry benzene and 50 g. (0.5 mole) of anhydrous calcium carbonate was added. The resulting reaction mixture was kept at reflux for 1 hr. and then a solution of 3α,5α-cyclocholestan-6β-ol, 8.2 g. (0.021 mole) in 100 ml. of dry benzene was added in one portion. After 18 hr. at reflux the reaction was filtered and the benzene solution was washed with saturated potassium iodide solution. The resulting two-phase system was filtered from the insoluble lead oxide and the benzene layer was separated and washed with water. After drying, the benzene solution was concentrated *in vacuo*, yielding a gummy product weighing 4.24 g.

Chromatography was carried out using Merck neutral alumina. Elution with hexane–benzene yielded crystalline material which was recrystallized from acetone affording 600 mg., m.p. 79–80°, [α]D +65° (*c* 1.4).

Anal. Calcd. for $C_{27}H_{44}O$: C, 84.21; H, 11.53. Found: C, 84.48; H, 11.52.

Further elution with benzene–ether and pure ether yielded 3α,5α-cyclocholestan-6-one, cholesteryl acetate, and finally unchanged 3α,5α-cyclocholestan-6β-ol.

Δ⁵-Cholestene-3β,19-diol (III).—A solution of 3α,5α-cyclo-6β,19-oxidocholestane (0.10 g.) in 20 ml. of acetone was treated with 1.0 ml. of water and 0.5 ml. of 1 *N* sulfuric acid. After standing for 2 hr. at room temperature, the solution was neutralized with saturated sodium bicarbonate solution and extracted with ether. The combined ether extracts were washed with water and concentrated to dryness under reduced pressure.

Recrystallization of the crude product from methanol yielded 85 mg., m.p. 147–149°, [α]D −30° (*c* 1). This material was identical with an authentic sample prepared by the method of Bowers.[1]

Acknowledgment.—The authors wish to thank Professor Paul von R. Schleyer of Princeton University for supplying the nuclear magnetic resonance data. The generosity of Dr. James C. Orr of Syntex Company is acknowledged for supplying us with a reference sample of III.

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[5] M. S. Heller, H. Wehrli, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, **45**, 1261 (1962).

[6] The crude reaction product showed acetate bands in the infrared (carbon tetrachloride) at 5.78 and 8.20 μ. Presumably the acetate arises from acetolysis of either 3α,5α-cyclocholestan-6β-ol (I) or 3α,5α-cyclo-6β,19-oxidocholestane (II); the acetic acid forms as the oxidation proceeds. Calcium carbonate was used in the oxidizing system in order to minimize the solvolytic reaction by buffer action. Tanabe, *et al.*, (see ref. 3b) report a 25% yield in the formation of 6β,19-oxido-3α,5α-cycloandrostan-17-one by lead tetraacetate oxidation of 3α,5α-cycloandrostan-6β-ol-17-one without buffer. Although a control experiment in our system has not been carried out, the result of Tanabe indicates that buffering may not be necessary. This point is currently under investigation.

[7] Formation of the 6β,19-oxido bridge from a 3α,5α-cyclo-6β-ol is consistent with bond formation occurring directly between the axial hydroxyl group and C-19 methyl with retention of configuration at C-6.

[8] The n.m.r. spectrum was determined in carbon tetrachloride solution relative to tetramethylsilane as internal standard. A Varian A-60 spectrophotometer was used operating at 60.0 Mc.

[9] G. V. D. Tiers, *J. Chem. Phys.*, **62**, 1151 (1958).

[10] All melting points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer infracord spectrophotometer. N.m.r. spectra were determined on a Varian A-60 spectrophotometer operating at 60.0 Mc. using carbon tetrachloride with tetramethylsilane as internal standard. Optical rotations were obtained in chloroform solution. Microanalysis were carried out by George I. Robertson, Florham Park, N. J.

The Preparation of Chloromethyl Vinyl Ketones

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Halomethyl vinyl ketones have been prepared mainly by the direct halogenation of methyl vinyl ketones,[1] by the action of diazomethane on vinyl acyl halides,[2] and by the addition of halogenated acyl halides to acetylene and ethylene derivatives in the presence of aluminum trichloride.[3]

In view of the possible synthetic and biological use[4] of these compounds, we report our observations on the reaction of aldehydes[5] with triphenylchloracetonylphosphorane (I) (following).

$$\underset{\text{I}}{Ph_3P{=}CHCOCH_2Cl} + RCHO \longrightarrow Ph_3P{=}O + RCH{=}CH{-}COCH_2Cl$$

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[1] Ng. Ph. Buu-Hoï, *Experientia*, **2**, 310 (1946); P. L. Southwick, D. I. Sapper, and L. A. Pursglove, *J. Am. Chem. Soc.*, **72**, 4941 (1950).

[2] A. Rödig and R. Maier, *Chem. Ber.*, **86**, 1467 (1953); J. A. Moore, *J. Org. Chem.*, **20**, 1607 (1955).

[3] J. R. Catch, D. F. Elliott, D. H. Hey, and E. R. H. Jones, *J. Chem. Soc.*, 278 (1948); F. Bergmann and J. Klein, *J. Am. Chem. Soc.*, **75**, 4333 (1953).

[4] K. Kochetkov, A. N. Nesmeyanov, and N. A. Semenov, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 87 (1952); A. N. Nesmeyanov, N. K. Kochetkov, M. Karpeiskii, and G. V. Alexandrovna, *Dokl. Akad. Nauk SSSR*, **82**, 409 (1952); A. Arbusov, B. L. Dyatkin, and S. A. Shevelev, *ibid.*, **112**, 261 (1957); A. Arbusov and B. L. Dyatkin, *ibid.*, **111**, 1249 (1956).

[5] Reactions of this type have been reviewed by U. Schöllkopf, *Angew. Chem.*, **71**, 260 (1959).

TABLE I

PREPARATION OF CHLOROMETHYL VINYL KETONES, R—CH=CH—CO—CH_2Cl

		Reaction conditions			Products			Infrared stretching frequencies (cm.$^{-1}$)[c]	
	R	Equivalents of aldehyde used	Time, hr.	Temp., °C.	Yield,[a] %	M.p., °C.	B.p.,[b] °C. (mm.)	$\nu_{C=C}$	$\nu_{C=O}$
II	C_6H_5	5	72	80	30	60[d]	114 (0.001)	1600	1690
III	4-NO_2-C_6H_4	1.25	3	80	79	116[e]		1615	1670
IV	4-CH_3CONH-C_6H_4	2	3	100	33	232[f]		1580	1675 1656
V	n-C_3H_7	5	12	25	26		87–90 (10)	1620	1680
VI	Cl_3C	10	3	25	44		50–52 (0.01)	1620 1600	1740
VII	2-furyl	10	0.5	90	48	51–53[g]	100 (0.02)	1540	1690

[a] Yields after one distillation or crystallization. [b] Uncorrected. [c] Measured on "Infracord." [d] Lit. m.p. 62°, 138° (5 mm.); A. N. Nesmeyanov, M. I. Rybinskaya, and N. K. Kochetkov, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 1197 (1956). [e] Recrystallized in toluene. [f] Recrystallized in dimethylformamide. [g] Recrystallized in aqueous alcohol.

TABLE II

ANALYSES OF THE CHLOROMETHYL VINYL KETONES

	Calcd.						Found					
	C	H	Cl	N	O	Mol. wt.	C	H	Cl	N	O	Mol. wt.[b]
II	66.6	5.33	19.6			180.6	66.8	5.11	17.1[a]			150
III	53.2	3.59	15.75		21.3	225.6	53.6	3.60	15.28		21.6	208
IV	60.9	5.08	14.95	5.90			60.83	4.96	14.84	6.02		
V	57.3	7.55	24.2		10.9	146.6	57.7	7.83	23.5[a]		11.1	152
VI	27.2	1.82	63.9				27.21	1.95	63.74			
VII	56.40	4.13	20.80				56.47	4.07	20.87			

[a] Chlorine analysis was somewhat low due to the high reactivity of the compounds. [b] Determined by Rast method (in camphor).

Compound I was obtained easily by the quaternization of triphenylphosphine with dichloroacetone in tetrahydrofuran and subsequent treatment of the quaternary salt with aqueous base. When the quaternization is performed in chloroform with two equivalents of the phosphine, both halogen atoms can be displaced.[6] The structure of compound I was confirmed from the infrared and n.m.r. spectra. It was highly stable and the chloride ion was not displaced by thiosulphate in water–alcohol mixtures at the boiling point.

Table I summarizes the compounds obtained from various aldehydes. In all cases more than 80% of the calculated yield of the phosphine oxide was obtained. The lower yields of the other products were probably due to polymerization, as the liquid vinyl ketones were unstable at room temperature. The compound obtained from benzaldehyde, chloromethyl styryl ketone (II), was converted to the corresponding quaternary salt and betaine ($Ph_3PCHCOCHCHPh$) by reaction with triphenylphosphine.

Experimental

Preparation of Triphenylchloracetonylphosphonium Chloride.—A mixture of triphenylphosphine (100 g., 0.38 mole) and 1,3-dichloroacetone (48.2 g., 0.38 mole) in 200 ml. of tetrahydrofuran was heated under reflux for 4 hr. Colorless crystals (127 g., 85%), m.p. 177–178°, were obtained from the cold reaction mixture. These were purified by three precipitations with ethyl acetate from warm methanol solutions, m.p. 210–212° dec.

Anal. Calcd. for $C_{21}H_{19}Cl_2OP$: C, 64.45; H, 4.92; Cl, 18.24; P, 7.96. Found: C, 64.45; H, 4.94; Cl, 17.91; P, 7.74.

The phosphonium salt easily formed a hydrate, m.p. 174°.

Anal. Calcd. for $C_{21}H_{21}Cl_2O_2P$: C, 62.1; H, 5.32; Cl, 17.4; P, 7.6. Found: C, 62.5; H, 5.21; Cl, 17.2; P, 6.8.

Triphenylchloracetonylphosphorane (I).—A solution of sodium carbonate (35 g., 0.31 mole) in water (200 ml.) was added rapidly and with stirring to triphenylchloracetonylphosphonium chloride (260 g., 0.62 mole) in methanol (300 ml.). The mixture was then diluted with two to three volumes of water and allowed to stand for 20–30 min. The white precipitate (215 g., 92%) was then collected and dried in air, m.p. 179–180°.

Anal. Calcd. for $C_{21}H_{18}ClOP$: C, 71.5; H, 5.1; Cl, 10.1; P, 8.8; mol. wt., 352.5. Found: C, 71.8; H, 5.2; Cl, 10.1; P, 8.5; mol. wt., 359. The infrared spectrum showed maxima at 1550, 1575, and 1430 cm.$^{-1}$. The n.m.r. spectrum showed a band at τ 2.49 of relative intensity 15 corresponding to the phenyl protons, a doublet centered at τ 5.64 at a separation of 22.6 c.p.s. of unit relative intensity, and a sharp singlet at τ 6.02 of relative intensity 2. This spectrum is in complete agreement with the proposed structure.

Chloromethyl Vinyl Ketones.—The phosphorane (I) reacted with the aldehydes according to the conditions defined in Table I. No solvent was used in the case of the volatile aldehydes, and in other cases benzene or toluene was used. After completion of the reaction, the solvent was removed and the phosphine oxide precipitated by the addition of cyclohexane. The precipitate was extracted repeatedly with cyclohexane, and the product was distilled from the extracts. Compounds III and IV crystallized from the cold reaction mixture.

Triphenylcinnamoylphosphonium Chloride.—Triphenylphosphine (5.2 g., 0.02 mole) and chloromethyl styryl ketone (3.6 g., 0.02 mole) in 25 ml. of tetrahydrofuran were heated under reflux for 3 hr. Most of the solvent was removed, and the crude phosphonium chloride (2.8 g., 32%), m.p. 184–186°, was precipitated with ethyl acetate. This was recrystallized from a mixture of ethanol (5%) and ethyl acetate (95%), m.p. 200–202°.

Anal. Calcd. for $C_{28}H_{24}ClOP$: Cl, 8.02; P, 7.00. Found: Cl, 8.69; P, 7.14.

Triphenylcinnamoylmethylenephosphorane was prepared in the same way as compound I, and recrystallized twice from ethylene glycol dimethyl ether (yield 0.8 g., 32%), m.p. 99–102°.

Anal. Calcd. for $C_{28}H_{23}OP$: P, 7.63. Found: P, 7.66.

Acknowledgment.—We wish to thank Dr. E. A. C. Lucken for interpreting the n.m.r. spectrum and Mr. G. Salvadori for technical assistance.

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[6] J. A. Ford and C. V. Wilson, *J. Org. Chem.*, **26**, 1433 (1961).