Studies of Organophosphorochloridates. Part VI.† Reactions of Steroid Phosphorochloridates with Amines and Some Alcohols

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Cholesteryl phosphorodichloridate is best prepared by the action of phosphoryl chloride on cholesterol in the presence of triethylamine. Chromatography and thermal decomposition of the phosphorodichloridate are briefly discussed. Cholesteryl, lanosteryl, and ergosteryl phosphorodichloridates have been treated with selected primary and secondary amines. In all cases nucleophilic substitution at the phosphorus atom took place; only with the ergosteryl derivative was there elimination at C-3.

trans-4-t-Butylcyclohexanol has been converted by phosphoryl chloride or pyrophosphoryl chloride into the phosphorodichloridate. With phosphoryl chloride and a larger proportion of the alcohol, bis-4-t-butylcyclohexyl phosphorochloridate was isolated.

A further study has been made of the reactions of some steroid phosphorodichloridates with alcohols; the mechanisms are briefly discussed.

CHOLESTERYL PHOSPHORODICHLORIDATE has previously been prepared [1,2] by the action of phosphoryl chloride on cholesterol in acetone–pyridine. Later work has shown that the yield and purity of the product are improved by performing the phosphorylation in ether–triethylamine. T.l.c. of cholesteryl phosphorodichloridate in benzene–ether has revealed [3] that the ester decomposes; t.l.c. in chloroform showed only one major spot, corresponding to cholesterol, and column chromatography on silica gel gave cholesterol (83%). In boiling tetrahydrofuran, cholesteryl phosphorodichloridate decomposes into a mixture of products, including cholesta-3,5-diene.

† Part V, R. J. W. Cremlyn, J. David, and N. Kishore, *J.C.S. Perkin I*, 1972, 583.

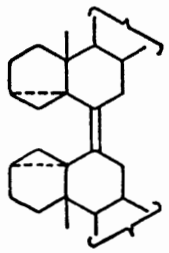
[1] H. Venner, *J. prakt. Chem.*, 1960, **12**, 59.

[2] R. J. W. Cremlyn and N. A. Olsson, *J. Chem. Soc.* (*C*), 1969, 2305.

[3] R. J. W. Cremlyn and N. A. Olsson, *J. Chem. Soc.* (*C*), 1971, 2023.

The steroid phosphorodichloridates melt to orange or red liquids. Even when they are impure the m.p. is sharp, indicating a strongly exothermic decomposition at the m.p. Subsequent examination by use of a differential thermal calorimeter revealed that a small endothermic change occurred at the m.p., immediately followed by a strongly exothermic reaction.

When cholesteryl phosphorodichloridate was maintained just above the m.p., mass spectral examination showed that it evolved phosphoryl chloride and some hydrogen chloride to give a steroid hydrocarbon and inorganic phosphate. The steroid is probably a dimer containing a tetrasubstituted double bond (no olefinic signals in the n.m.r. spectrum, but the compound gave an orange colour with tetranitromethane); the 6,6′-bis-3,5-cyclosteroid structure (I) is suggested since the mass



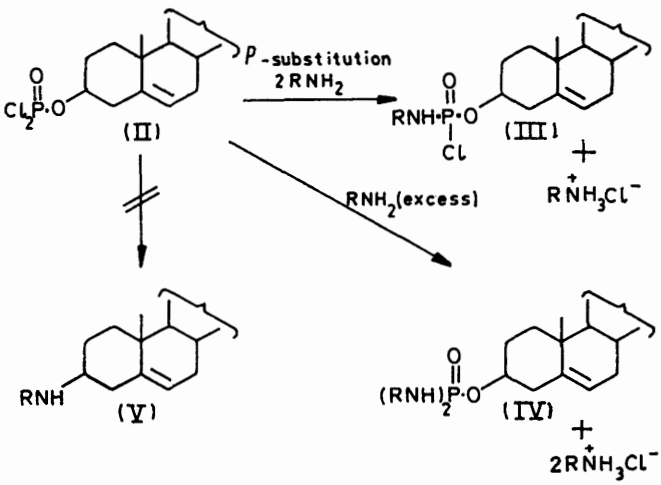
(I)

spectrum showed a major ion at *m/e* 736 and this ion has also been detected in the spectrum of cholesteryl dihydrogen phosphate.[4]

In an effort to prepare some model compounds for chemical reactivity comparisons with steroid phosphorodichloridates, *trans*-4-t-butylcyclohexanol was phosphorylated by phosphoryl chloride and by pyrophosphoryl chloride. *trans*-4-t-Butylcyclohexyl phosphorodichloridate could only be obtained as an impure oil, which decomposed on attempted distillation *in vacuo*. It was characterised as the monomorpholino derivative and as the *NN*′-dicyclohexylphosphorodiamidate; and by hydrolysis to the corresponding dihydrogen phosphate. Bis-*trans*-4-t-butylcyclohexyl phosphorochloridate was isolated as a crystalline solid, but it had different solubility properties from the cholesteryl phosphorochloridates; for instance the bis-*trans*-4-t-butyl compound was soluble in ethanol and ether. Attempted synthesis of tetrakis-*trans*-4-t-butylcyclohexyl pyrophosphate by selective hydrolysis (aqueous pyridine) of bis-*trans*-4-t-butylcyclohexyl phosphorochloridate was unsuccessful (*cf.* ref. 4).

In reactions of steroid phosphorodichloridates with nucleophiles attack may occur either at the electrophilic phosphorus atom or at C-3, since phosphorodichloridate can function as an effective leaving group. Previous studies[3] of the reactions of some steroid phosphorodichloridates with alcohols have shown that phosphate esters, ethers, or hydrocarbons can be obtained. We have now treated cholesteryl, lanosteryl, and ergosteryl phosphorodichloridates with amines (aniline, benzylamine, morpholine, and diethylamine) under various conditions to see if the reactions resemble those with alcohols.

Cholesteryl (II) and lanosteryl phosphorodichloridates gave exclusively the mono- and di-amidates (III) and (IV) derived from nucleophilic replacement at the phosphorus atom. T.l.c. gave no indication of the formation of the substituted cholesterylamine (V) by attack at C-3, nor was there any base-catalysed 1,2-elimination leading to cholesta-3,5-diene. However with ergosteryl phosphorodichloridate and aniline some elimination of phosphorodichloridate did occur to give



3,5-cycloergosta-6,8(14),22-triene (25%), although the major product was still that derived from substitution at phosphorus. With excess of morpholine only the phosphorodimorpholidate was isolated. Elimination would be more favoured in ergosteryl phosphorodichloridate owing to enhanced anchimeric assistance at C-3 by the π-electrons of the 5,6-double bond (*cf.* ref. 5).

These results differ from those reported[3] for the steroid phosphorodichloridates and alcohols, where the main reaction was generally C-3 substitution. In the reaction of ergosteryl phosphorodichloridate with methanol the only product was 3,5-cycloergosta-6,8(14),22-triene, though the dimethyl phosphate was obtained in the presence of a large excess of pyridine.[3]

This result suggests that the much greater tendency of amines to react by substitution at the phosphorus atom is probably due to their more powerful nucleophilic character. Substitution of the first chlorine atom generally occurred easily at room temperature, but replacement of the second chlorine atom, even in the presence of an excess of the amine, required heating (*cf.* ref. 6); solvent polarity was also an important factor in the preparation of the phosphorodiamidates. For instance cholesteryl phosphorodichloridate was con-

[4] R. J. W. Cremlyn and N. A. Olsson, *J. Chem. Soc.* (*C*), 1970, 1889.

[5] M. Simonetta and S. Winstein, *J. Amer. Chem. Soc.*, 1954, **76**, 18.

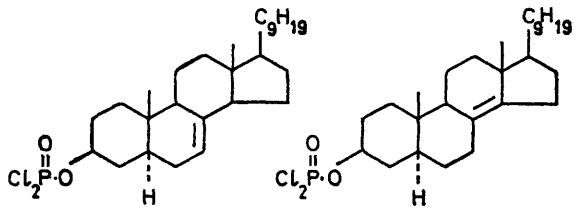
[6] R. J. W. Cremlyn, B. B. Dewhurst, and D. H. Wakeford, *J. Chem. Soc.* (*C*), 1971, 300.

verted into the dimorpholidate by boiling with an excess of morpholine in tetrahydrofuran or acetonitrile for a few minutes, but in benzene or light petroleum prolonged boiling was necessary.

In an extension of previous studies [2,3] cholesteryl phosphorodichloridate has been treated with propanol to give cholesteryl dipropyl phosphate (66%), cholesteryl propyl ether (18%), and cholesta-3,5-diene (8%). The diene (20%) was obtained [3] in an analogous reaction with methanol–acetonitrile, and probably arises as a result of a thermal (*cis*) elimination process (*cf.* ref. 2). When cholesteryl phosphorodichloridate was treated with propanol in the presence of sodium propoxide, only the dipropyl phosphate (70%) was isolated, as expected (*cf.* ref. 1). Treatment of lanosteryl phosphorodichloridate with propanol gave the dipropyl phosphate (72%); similarly t-butyl alcohol gave the corresponding di-t-butyl phosphate (60%).

Ergosteryl phosphorodichloridate with ethanol–sodium ethoxide gave the diethyl phosphate (64%), though with propanol and a smaller proportion of sodium propoxide this dichloridate gave 3,5-cycloergosta-6,8(14),22-triene [7a] (68%) as the only isolated product. This may be compared with the change from triene to phosphate product observed [3] in the reaction of ergosteryl phosphorodichloridate with methanol in the presence of increasing amounts of pyridine.

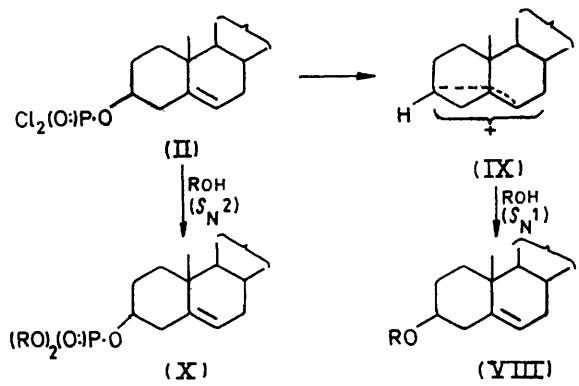
Ergost-7-enol [7b] was converted into the phosphorodichloridate (VI) by phosphoryl chloride–pyridine–light



(VI) (VII)

petroleum (attempted phosphorylation in acetone or with pyrophosphoryl chloride was unsuccessful). Treatment of the phosphorodichloridate (VI) with t-butyl alcohol gave the corresponding di-t-butyl phosphate (52%). Ergost-8(14)-enol [7b] was similarly phosphorylated to give the dichloridate (VII), and the latter, with t-butyl alcohol, gave the corresponding phosphate (60%).

The steroid alkyl ethers (VIII) arise from an S_N1-type reaction involving attack of the alcohol at C-3 of the homoallylic cation (IX), whereas the dialkyl phosphates (X) are formed by the competing S_N2 reaction in which the alcohol attacks the electrophilic phosphorus atom. The formation of the ether should therefore be favoured by the use of sterically hindered alcohols. Experimental results are in general agreement with this observation. For instance, cholesteryl phosphorodichloridate (II) with isopropyl alcohol gave cholesteryl isopropyl ether (54%) (ref. 3) (*cf.* 18% from n-propyl alcohol); t-butyl alcohol afforded 56% of the corresponding cholesteryl ether, and cyclohexanol 64% of the ether.



EXPERIMENTAL

I.r. spectra were measured for Nujol mulls with a Perkin-Elmer 257 spectrometer. N.m.r. spectra were determined with a Varian A60A spectrometer (tetramethylsilane as internal standard). Mass spectra were determined with an A.E.I. MS9 spectrometer at 70 eV. M.p. determinations were made with a Kofler hot-stage apparatus. T.l.c. plates were made up with silica gel G and the compounds located with a phosphomolybdic acid spray.

Cholesteryl Phosphorodichloridate.—Cholesterol (25·8 g) and triethylamine (6·8 g) in dry ether (400 ml) were added dropwise to a stirred solution of phosphoryl chloride (10·2 g) in dry ether (150 ml) at 0°. After 2 h at 0°, the precipitate was filtered off and washed with water to give cholesteryl phosphorodichloridate (28·5 g, 87%), m.p. 123° (lit.,[2] 122°) (Found: C, 64·2; H, 9·0; Cl, 14·0; P, 6·4. Calc. for $C_{27}H_{45}Cl_2O_2P$: C, 64·4; H, 8·9; Cl, 14·1; P, 6·2%), $\nu_{max.}$ 1300 (P=O), 1020 (P–O–C), and 536 and 429 (P–Cl) cm^{-1}.

(a) *Decomposition on silica gel.* The phosphorodichloridate (5 g) was dissolved in the minimum volume of anhydrous chloroform and poured on to a column of silica gel (200 g). Elution with benzene–ether (9 : 1; 1 l) and ether (1 l) gave cholesterol (3·2 g, 83%), m.p. and mixed m.p. 145—147°. No further material was eluted. T.l.c. of a solution of cholesteryl phosphorodichloridate in chloroform and development with chloroform gave one major spot corresponding (R_F) to cholesterol. Thus chloroform causes rapid decomposition of the phosphorodichloridate to cholesterol (single spot) on t.l.c.; development with benzene–ether resulted in slower decomposition, as shown by tailing (*cf.* ref. 3).

(b) *Thermal decomposition.* The phosphorodichloridate (1 g) was heated at 130° for 5 min; it evolved acidic vapour * and gave a red oil which solidified on cooling. T.l.c. ($CHCl_3$) showed one spot (R_F 0·95). Column chromatography (silica gel) and recrystallisation from ethyl acetate gave a white solid (0·6 g), m.p. 140—146° (Found: C, 87·7; H, 11·9. Calc. for $C_{54}H_{88}$: C, 88·0; H, 11·9%). The i.r. spectrum showed only C–H bands, and the n.m.r. indicated the absence of olefinic protons; the mass spectrum showed highest mass peaks at *m/e* 736, 738, and 740; $\lambda_{max.}$ (cyclohexane) 212 (ε 15,000), 230 (10,600), and 239 nm (8500).

Phosphorylation of trans-4-*t-Butylcyclohexanol.*—(a) *With phosphoryl chloride.* *trans*-4-t-Butylcyclohexanol (15·6 g)

* Mass spectral analysis indicated that this was mainly phosphoryl chloride with some hydrogen chloride.

[7] L. F. Fieser and M. Fieser, ' Steroids,' Reinhold, New York 1959, (*a*) p. 318; (*b*) p. 112; (*c*) p. 265.

and triethylamine (10·1 g) in ether (150 ml) were added dropwise to a stirred solution of phosphoryl chloride (15·3 g) in ether (65 ml) at 0°. Triethylamine hydrochloride (13·7 g) was filtered off and the filtrate was evaporated to give the phosphorodichloridate as an unstable oil (13·6 g), $\nu_{max.}$ 1315 (P=O) and 1030 (P–O–C) cm^{-1}. Decomposition occurred on attempted distillation under reduced pressure.

(b) *With pyrophosphoryl chloride.* The cyclohexanol (0·75 g) was gradually added to stirred pyrophosphoryl chloride [8] (6 ml) at 0°. After 40 min, the mixture was poured on ice–water (400 ml) and stirred for 1 h. The precipitate was filtered off, and on warming formed an oil identical to that from method (a).

trans-4-*t*-*Butylcyclohexyl Dihydrogen Phosphate.*—The phosphorodichloridate (1 g) was boiled under reflux with water (100 ml) for 8 h. Evaporation under reduced pressure and treatment with hot sodium carbonate solution gave 4-*t*-*butylcyclohexyl disodium phosphate* as a white powder (0·7 g, 55%), m.p. 268—270° (Found: C, 42·6; H, 6·9; P, 10·7. $C_{10}H_{19}Na_2O_4P$ requires C, 42·9; H, 6·8; P, 11·1%).

trans-4-*t*-*Butylcyclohexyl Morpholinophosphorochloridate.*—The phosphorodichloridate (400 mg) was gently warmed with morpholine (400 mg) in acetonitrile (20 ml) for 5 min. After 48 h at 0°, the *morpholinophosphorochloridate* (180 mg) was filtered off; m.p. 117—119° (Found: C, 51·6; H, 8·8; N, 4·0; P, 9·3. $C_{14}H_{27}ClNO_3P$ requires C, 51·9; H, 8·4; N, 4·3; P, 9·6%).

trans-4-*t*-*Butylcyclohexyl NN'-Dicyclohexylphosphorodiamidate.*—The phosphorodichloridate (500 mg) was boiled with cyclohexylamine (1 g) in acetonitrile (25 ml) for 5 min. Cooling gave the NN'-*dicyclohexylphosphorodiamidate* (450 mg), m.p. 134—137° (Found: C, 65·9; H, 10·5; N, 7·1; P, 8·3. $C_{22}H_{43}N_2O_2P$ requires C, 66·3; H, 10·8; N, 7·0; P, 7·8%), $\nu_{max.}$ 1215 (P=O) and 1030 (P–O–C) cm^{-1}.

Bis-4-*t*-*Butylcyclohexyl Phosphorochloridate.*—*trans*-4-*t*-Butylcyclohexanol (31·2 g) and triethylamine (22·2 g) in ether (300 ml) were dropped into a stirred solution of phosphoryl chloride (15·3 g) in ether (300 ml) at 0°. After 24 h, the filtrate was evaporated under reduced pressure to leave a white solid. Rapid recrystallisation from ethanol gave the *phosphorochloridate* (29 g), m.p. 127—128° (Found: C, 61·5; H, 10·0; P, 7·5. $C_{20}H_{38}ClO_3P$ requires C, 61·1; H, 9·7; P, 7·9%), $\nu_{max.}$ 1300 (P=O) and 1045 or 1005? (P–O–C) cm^{-1}.

Reactions of Cholesteryl Phosphorodichloridate with Amines.—(a) *Aniline.* (i) 2 *Mol. equiv.* The phosphorodichloridate (1 g) was warmed with aniline (0·38 g) in tetrahydrofuran (25 ml) at 40° for 5 min. After 1 h the amine hydrochloride was filtered off and the filtrate evaporated under reduced pressure to a cream solid. This was washed with water and recrystallised from tetrahydrofuran–acetonitrile to give *cholesteryl* N-*phenylphosphoramidic chloride* (0·8 g), m.p. 175° (Found: C, 70·7; H, 9·3; Cl, 5·9; N, 2·5. $C_{33}H_{51}ClNO_2P$ requires C, 70·8; H, 9·2; Cl, 6·3; N, 2·5%), $\nu_{max.}$ 3150 (NH), 1260 (P=O), and 1040 (P–O–C) cm^{-1}, τ ($CDCl_3$) 2·6—3·05 (6H, Ph and NH) and 7·5—9·8 (45H); t.l.c. ($CHCl_3$) R_F 0·70.

(ii) *Excess.* The phosphorodichloridate (1 g) was boiled with aniline (1 g) in tetrahydrofuran (25 ml) for 10 min to give a solid showing two spots on t.l.c. Column chromatography (silica gel) and elution with 10% benzene–chloroform gave cholesteryl *N*-phenylphosphoramidic chloride (0·3 g), m.p. 173—175° (mixed m.p. 175°). Elution with chloroform gave *cholesteryl* NN'-*diphenylphosphorodiamidate* (0·7 g), m.p. 180—182° (Found: C, 75·5; H, 9·2; N, 4·5. $C_{39}H_{57}N_2O_2P$ requires C, 75·9; H, 9·3; N, 4·5%); t.l.c. ($CHCl_3$) R_F 0·20.

(b) *Morpholine.* (i) 2 *Mol. equiv.* Use of 0·35 g of amine in tetrahydrofuran (25 ml) for 5 min at 60° gave cholesteryl morpholinophosphorochloridate (0·75 g), m.p. 147° (lit.,[2] 147°), $\nu_{max.}$ 1280 (P=O), 1260 (C–N), 1120 (C–O–C), and 1030 (P–O–C) cm^{-1}; t.l.c. ($CHCl_3$) R_F 0·80.

(ii) *Excess.* Use of excess (1 g) of amine in boiling acetonitrile (25 ml) for 1 min gave cholesteryl phosphorodimorpholidate (1 g, 85%), m.p. 159° (lit.,[2] 159—160°), $\nu_{max.}$ 1210 (P=O), 1260 (C–N), 1120 (C–O–C), and 1030 (P–O–C) cm^{-1}; t.l.c. ($CHCl_3$) R_F 0·35.

Repetition of this experiment in tetrahydrofuran (25 ml) gave the dimorpholidate (80%). In boiling benzene (0·25 h) t.l.c. indicated the major product was cholesteryl morpholinophosphorochloridate, with only a small amount of the dimorpholidate; after boiling for 12 h however the latter was the main product.

(c) *Cyclohexylamine.* (i) Use of 2 mol. equiv. (0·4 g) in tetrahydrofuran (40 ml) for 0·25 h at room temperature gave *cholesteryl* N-*cyclohexylphosphoramidic chloride* (1 3 g), m.p. 190—192° (Found: C, 69·9; H, 10·0; N, 2·5; P, 5·2. $C_{33}H_{57}ClNO_2P$ requires C, 70·0; H, 10·1; N, 2·5; P, 5·5%), $\nu_{max.}$ 3190 (NH), 1255, 1240 (P=O), and 1045 (P–O–C) cm^{-1}; t.l.c. ($CHCl_3$) R_F 0·75.

(ii) Use of excess (1·2 g) of amine in tetrahydrofuran (40 ml) for 0·25 h at 60°, followed by dissolution in the minimum volume of chloroform, chromatography on a silica gel column, elution with benzene–chloroform (4 : 1), and recrystallisation from ethyl acetate gave *cholesteryl* NN'-*dicyclohexylphosphorodiamidate* (1·4 g), m.p. 146° (Found: C, 74·2; H, 11·0; N, 4·7. $C_{39}H_{69}N_2O_2P$ requires C, 74·5; H, 11·1; N, 4·5%), $\nu_{max.}$ 3200 (NH), 1220 (P=O), and 1040 (P–O–C) cm^{-1}; t.l.c. ($CHCl_3$) R_F 0·22.

(d) *Diethylamine.* (i) Use of 2 mol. equiv. (0·3 g) in tetrahydrofuran (25 ml) at room temperature gave *cholesteryl* NN-*diethylphosphoramidic chloride* (0·8 g), m.p. 115° (from acetonitrile) (Found: C, 68·5; H, 10·3; N, 2·5; P, 5·2. $C_{31}H_{55}ClNO_2P$ requires C, 68·9; H, 10·3; N, 2·6; P, 5·7%), $\nu_{max.}$ 1280 (P=O) and 1030 (P–O–C) cm^{-1}.

(ii) Use of excess (1 g) of amine in tetrahydrofuran (25 ml) at room temperature also gave the phosphoramidic chloride.

(e) *Benzylamine.* (i) Use of 2 mol. equiv. (0·5 g) in tetrahydrofuran (40 ml) for 0·25 h at room temperature gave *cholesteryl* N-*benzylphosphoramidic chloride* (1·2 g), m.p. 158—160° (Found: C, 70·8; H, 9·1; N, 2·5. $C_{34}H_{53}ClNO_2P$ requires C, 71·1; H, 9·3; N, 2·4%), $\nu_{max.}$ 3200 (NH), 1260 (P=O), and 1025 (P–O–C) cm^{-1}.

(f) *Piperidine.* Use of an excess (1·5 ml) of piperidine in acetonitrile (40 ml) for 10 min at 40° gave *cholesteryl phosphorodipiperidate* (700 mg), m.p. 106° (Found: C, 73·5; H, 10·9; N, 4·6; P, 4·9. $C_{37}H_{65}N_2O_2P$ requires C, 73·9; H, 10·9; N, 4·7; P, 5·2%), $\nu_{max.}$ 1240 (P=O), 1020 (P–O–C), and 730 (P–N) cm^{-1}.

Reactions of Lanosteryl Phosphorodichloridate with Amines.—(a) *Aniline.* The phosphorodichloridate (1 g) was warmed with aniline (0·38 g, 2 mol. equiv.) in tetrahydrofuran (25 ml) for 5 min at 40° then for 1 h at room temperature. Filtration of a chloroform solution of the product through a column of silica gel gave *lanosteryl* N-*phenylphosphoramidic chloride* (1·0 g), m.p. 135—140°

[8] H. Grunze and W. Koransky, *Angew. Chem.*, 1959, **71**, 407.

(Found: C, 71·9; H, 9·2; N, 2·4. $C_{36}H_{55}ClNO_2P$ requires C, 72·0; H, 9·2; N, 2·3%), $\nu_{max.}$ 3150 (NH), 1240 (P=O), and 1020 (P–O–C) cm^{-1}.

(b) *Morpholine.* (i) Use of 2 mol. equiv. (0·4 g) in tetrahydrofuran (30 ml) for 10 min at 40° gave lanosteryl morpholinophosphorochloridate as plates (850 mg) (from ethanol), m.p. 122° (lit.,[2] 120—122°), $\nu_{max.}$ 1280 (P=O), 1120 (C–O–C), and 1050 (P–O–C) cm^{-1}.

(ii) Use of an excess (1·0 g) of amine in boiling acetonitrile (30 ml) for 1 min gave lanosteryl phosphorodimorpholidate as needles (0·75 g) (from ethanol), m.p. 159° (lit.,[2] 159°), $\nu_{max.}$ 1240—1220 (P=O), 1130 (C–O–C), and 1030 (P–O–C) cm^{-1}.

(c) *Cyclohexylamine.* Use of 2 mol. equiv. (0·4 g) in tetrahydrofuran (30 ml) for 5 min at 40° gave *lanosteryl N-cyclohexylphosphoramidic chloride* (0·8 g) (from methanol–methylene chloride), m.p. 180—181° (Found: C, 71·2; H, 10·2; N, 2·4; P, 4·7. $C_{36}H_{61}ClNO_2P$ requires C, 71·3; H, 10·1; N, 2·3; P, 5·1%), $\nu_{max.}$ 3200 (NH), 1260, 1250 (P=O), and 1045 (P–O–C) cm^{-1}.

Reactions of Ergosteryl Phosphorodichloridate with Amines.—(a) *Aniline.* The phosphorodichloridate (1 g) was warmed with aniline (0·36 g, 2 mol. equiv.) in tetrahydrofuran (25 ml) for 5 min at 40°. Chromatography on silica gel and elution with light petroleum (b.p. 60—80°)–benzene (1 : 1) gave 3,5-cycloergosta-6,8(14),22-triene (0·15 g), m.p. 99—101° (lit.,[7a] 102°), $\lambda_{max.}$ (cyclohexane) 260 nm (ε 24,000). Elution with benzene–chloroform (5 : 1) gave *ergosteryl N-phenylphosphoramidic chloride* (0·75 g), m.p. 150—153° (Found: C, 71·4; H, 8·4; N, 2·7. $C_{34}H_{49}ClNO_2P$ requires C, 71·6; H, 8·7; N, 2·5%), $\nu_{max.}$ 3260 (NH), 1275 (P=O), and 1035 (P–O–C) cm^{-1}.

(b) *Morpholine.* Ergosteryl phosphorodichloridate was treated with excess of morpholine in acetonitrile, as previously described,[2] to give ergosteryl phosphorodimorpholidate (70%), m.p. 146—147° (lit.,[2] 145—147°). T.l.c. of the filtrate indicated the absence of 3,5-cycloergosta-6,8(14),22-triene.

Cholesteryl Dipropyl Phosphate.—Method 1. Cholesteryl phosphorodichloridate [2] (2 g) was warmed with propyl alcohol at 60° for 20 min and left at room temperature for 1 week. The solution was evaporated under reduced pressure and the residue chromatographed on silica gel (300 g). Elution with light petroleum (b.p. 60—80°; 250 ml) gave cholesta-3,5-diene (0·1 g, 8%), m.p. 76—78° (lit.,[7c] 80°) (Found: C, 88·45; H, 11·7. Calc. for $C_{27}H_{44}$: C, 88·0; H, 12·0%); i.r. spectrum showed no P=O or P–O–C bands. Elution with light petroleum (b.p. 60—80°)–benzene (1 : 1; 500 ml) gave *cholesteryl propyl ether* (0·3 g, 18%), m.p. 96° (Found: C, 83·7; H, 12·2. $C_{30}H_{52}O$ requires C, 84·05; H, 12·2%), $\nu_{max.}$ 1100 (C–O–C) cm^{-1}. Elution with chloroform (500 ml) gave *cholesteryl dipropyl phosphate* (0·9 g, 66%), m.p. 65° (Found: C, 71·6; H, 11·0. $C_{33}H_{59}O_4$ requires C, 71·9; H, 10·8%), $\nu_{max.}$ 1320 (P=O) and 1005 (P–O–C) cm^{-1}.

Method 2. Cholesteryl phosphorodichloridate (1 g) was heated with a solution of sodium (0·7 g) in propyl alcohol (40 ml) until all the solid had dissolved. Evaporation *in vacuo* gave a solid residue, and recrystallisation from acetone gave cholesteryl dipropyl phosphate (0·6 g, 70%), m.p. 64°.

Lanosteryl Dipropyl Phosphate.—Lanosteryl phosphorodichloridate [2] (1 g) was warmed with propyl alcohol (40 ml) at 60° for 20 min and left for 1 week at room temperature to give *lanosteryl dipropyl phosphate* (0·8 g, 72%), m.p. 168° (from acetone) (Found: C, 72·9; H, 10·5; P, 4·9. $C_{36}H_{63}O_4P$ requires C, 73·2; H, 10·7; P, 5·25%), $\nu_{max.}$ 1310 (P=O) and 1010 (P–O–C) cm^{-1}.

Lanosteryl Di-t-butyl Phosphate.—Lanosteryl phosphorodichloridate (1 g), on similar treatment with t-butyl alcohol, afforded *lanosteryl di-t-butyl phosphate* (0·9 g, 60%), m.p. 142° (Found: C, 73·6; H, 11·0; P, 4·8. $C_{38}H_{67}O_4P$ requires C, 73·8; H, 10·8; P, 5·0), $\nu_{max.}$ 1290 (P=O) and 1005 (P–O–C) cm^{-1}.

Ergosteryl Diethyl Phosphate.—Ergosteryl phosphorodichloridate [2] (1 g) was boiled under reflux with a solution of sodium (0·6 g) in absolute ethanol (50 ml) for 2 h to give *ergosteryl diethyl phosphate* (0·6 g, 64%), m.p. 86° (from acetonitrile) (Found: C, 73·7; H, 10·4. $C_{32}H_{53}O_4P$ requires C, 74·1; H, 10·2%).

3,5-Cycloergosta-6,8(14),22-triene.—Ergosteryl phosphorodichloridate (1 g) was boiled under reflux with a solution of sodium (0·2 g) in propyl alcohol (50 ml) for 2 h to give 3,5-cycloergosta-6,8(14),22-triene (0·6 g, 68%), m.p. 95—97° (lit.,[7a] 102°); i.r. spectrum showed no P=O or P–O–C bands.

7-Ergosteryl Phosphorodichloridate (VI).—Ergost-7-enol [7b] (1·5 g) dissolved in pyridine (15 ml) was added dropwise during 3 h to a stirred solution of phosphoryl chloride (2 ml) in light petroleum (20 ml) at 0°. After 1 h the mixture was filtered and evaporated. The solid residue was washed with water and acetone to give the *phosphorodichloridate* (1·2 g, 69%), m.p. 125—127° (Found: C, 65·4; H, 9·0; Cl, 13·5; P, 5·8. $C_{28}H_{45}Cl_2O_2P$ requires C, 65·2; H, 8·7; Cl, 13·8; P, 6·0%), $\nu_{max.}$ 1300 (P=O) and 1030 (P–O–C) cm^{-1}.

7-Ergosteryl Di-t-butyl Phosphate.—Ergost-7-enyl phosphorodichloridate (0·2 g) was heated with t-butyl alcohol (20 ml) for 0·5 h and left overnight at room temperature to give the *di-t-butyl phosphate* (0·13 g, 52%), m.p. 173—175° (from benzene) (Found: C, 73·4; H, 10·8; P, 5·1. $C_{36}H_{63}O_4P$ requires C, 73·2; H, 10·7; P, 5·25%), $\nu_{max.}$ 1300 (P=O) and 1060 (P–O–C) cm^{-1}.

Ergost-8(14)-enyl Phosphorodichloridate (VII).—Ergost-8(14)-enol [7b] (1·8 g) was treated with phosphoryl chloride (2 ml) in pyridine–ether as previously described to give the *phosphorodichloridate* (1·2 g, 69%), m.p. 144—146° (Found: C, 65·0; H, 8·5; Cl, 14·0; P, 6·2. $C_{28}H_{45}Cl_2O_2P$ requires C, 65·2; H, 8·7; Cl, 13·8; P, 6·0%), $\nu_{max.}$ 1305 (P=O) and 1030 (P–O–C) cm^{-1}.

Ergost-8(14)-enyl Di-t-butyl Phosphate.—Ergost-8(14)-enyl phosphorodichloridate (0·4 g) was heated with t-butyl alcohol to give the *di-t-butyl phosphate* (0·3 g, 60%), m.p. 160—162° (Found: C, 73·0; H, 11·0; P, 5·4. $C_{36}H_{63}O_4P$ requires C, 73·2; H, 10·7; P, 5·25%), $\nu_{max.}$ 1280 (P=O) and 1050 (P–O–C) cm^{-1}.

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