Experiments on the Synthesis of Tetracycline. Part XI.† Oxidation of Ketone Acetals and Ethers by Hydride Transfer [1]

By D. H. R. Barton,* P. D. Magnus, G. Smith, G. Streckert, and D. Zurr, Department of Chemistry, Imperial College, London SW7 2AY

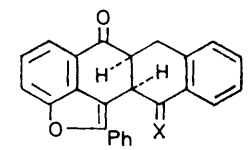
A method for oxidising a diol as its acetonide, or other acetal, by hydride transfer to the triphenyl carbonium ion, is described. Triphenylcarbonium ion oxidation is applied to the selective deprotection of benzyl and benzyloxycarbonyl ethers.

ATTEMPTS to convert the acetal (I; X = O·CH_2·CH_2·O) into the diketone (I; X = O) under the usual aqueous acid conditions led largely to decomposition; only 10% of the diketone was isolated.[2] We required a method of irreversible deacetalisation under neutral conditions. The mechanism of the hydrolysis of acetals is thought to involve the intermediate (II; R = H) [3] (Scheme 1). The first step, reversible when R = H, would be irreversible if R = alkyl or aryl, and would thus permit the desired transformation. The following experiments showed the feasibility of the scheme.

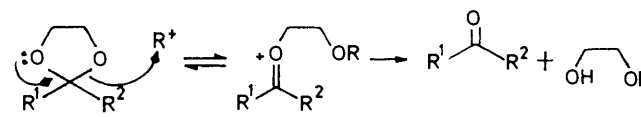
Pregnenolone ethylene acetal (III) [4] and 11α-hydroxyprogesterone ethylene acetal [5] (IV) were treated with triethyloxonium fluoroborate [6] (corresponding to R = Et in Scheme 1). Pregnenolone and 11α-hydroxyprogesterone were obtained after aqueous work-up in yields of 80 and 70%, respectively (reaction times of 8 and 20 min, respectively). Cholesterol tetrahydropyranyl ether [7] was converted into cholesterol with triethyloxonium fluoroborate in 64% yield.

To study the proposed mechanism (Scheme 1; R = Et), cyclohexanone ethylene acetal [8] was treated with triethyloxonium fluoroborate and the products were examined by g.l.c. The monoethyl ether of ethylene glycol was detected.

At this stage we examined a more bulky alkylating agent, trityl tetrafluoroborate,[9] hoping to isolate the



(I)



(II)

SCHEME 1

trityl ether of ethylene glycol. Treatment of the acetal (I; X = O·CH_2·CH_2·O) with trityl tetrafluoroborate in dichloromethane, followed by aqueous work-up,

† Part X, D. H. R. Barton, J. A. Challis, P. D. Magnus, and J. P. Marshall, *J. Chem. Soc.* (*C*), 1971, 2241.

[1] Preliminary communications, D. H. R. Barton, P. D. Magnus, G. Smith, and D. Zurr, *Chem. Comm.*, 1971, 861; D. H. R. Barton, P. D. Magnus, and G. Streckert, *ibid.*, p. 1109.

[2] D. H. R. Barton, D. L. J. Clive, P. D. Magnus, and G. Smith, *J. Chem. Soc.*, 1971, 2193.

[3] E. H. Cordes, *Progr. Phys. Org. Chem.*, 1967, **4**, 1.

[4] F. Sondheimer and Y. Klibansky, *Tetrahedron*, 1959, **5**, 15.

[5] G. Cooley, B. Ellis, D. N. Kirk, and V. Petrow, *J. Chem. Soc.*, 1957, 4112.

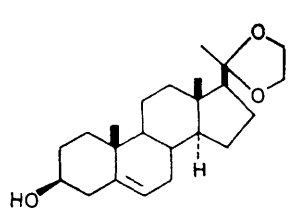
[6] H. Meerwein, P. Borner, O. Fuchs, H. Sasse, M. Schrodt, and J. Spille, *Chem. Ber.*, 1956, **89**, 2060.

[7] W. G. Dauben and H. L. Bradlow, *J. Amer. Chem. Soc.*, 1952, **74**, 559.

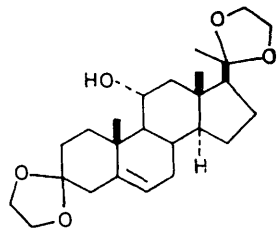
[8] M. Sulzbacher, E. Bergmann, and E. R. Pariser, *J. Amer. Chem. Soc.*, 1948, **70**, 2827.

[9] H. J. Dauben, jun., L. R. Honnen, and K. M. Harmon, *J. Org. Chem.*, 1960, **25**, 1442.

gave the diketone (I; X = O) in 65% yield. This was a vast improvement over conventional deacetalisation methods. No trityl ether of ethylene glycol was detected. Reaction of trityl tetrafluoroborate with cyclohexanone



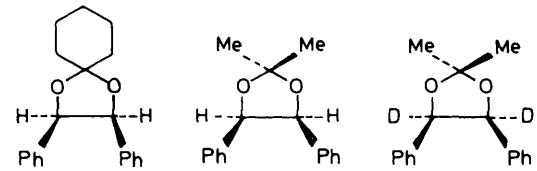
(III)



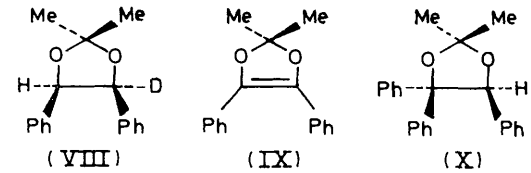
(IV)

ethylene acetal gave cyclohexanone (80%) and, again, no trityl ether of ethylene glycol. This reaction was followed by n.m.r. spectroscopy, which revealed the formation of triphenylmethane (τ 5·48);[10] indeed we were able to isolate triphenylmethane in quantitative yield. Evidently trityl tetrafluoroborate had abstracted a hydride ion from an ethylene acetal. Triphenylcarbonium ion is well documented[11] as a hydride ion acceptor and has found preparative use, for example in the dehydrogenation of cycloheptatriene to the tropylium ion.[12] It is known that aldehyde acetals reduce triphenylcarbonium ion by an intermolecular process,[1] but a similar reaction with ketone acetals has hitherto not been suspected.

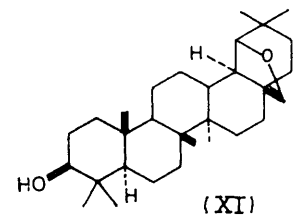
Treatment of benzophenone ethylene acetal with trityl tetrafluoroborate in dichloromethane at room temperature, gave, after aqueous work-up benzophenone (100%) and triphenylmethane (100%). Traces of triphenylmethanol present were formed from excess of reagent. To establish the nature of the oxidised ethylene glycol system the acetal (V) was prepared by transacetalisation between cyclohexanone ethylene dithioacetal and *meso*-1,2-diphenylethane-1,2-diol[14-16] (the usual acetalisation procedures result in pinacol rearrangement of *meso*-1,2-diphenylethane-1,2-diol). Treatment of the acetal (V) with trityl tetrafluoroborate (3 h) gave cyclohexanone and benzoin (64%). *meso*-1,2-Diphenylethane-1,2-diol acetonide (VI) was prepared by transacetalisation with 2,2-dimethoxypropane and the diol. The n.m.r. spectrum of the acetonide (VI) exhibited two singlets for the methyl groups at τ 8·75 and 8·6. When compound (VI) was oxidised at room temperature the methyl signals coalesced to a six-proton singlet at τ 8·25, indicative of a symmetrical species. *meso*-1,2-Diphenyl[1,2-$^2H_2$]ethane-1,2-diol acetonide (VII) (incorporation of deuterium 87%) was prepared from benzil by reduction with sodium borodeuteride, followed by transacetalisation with 2,2-dimethoxypropane. Treatment of the dideuterio-derivative (VII) with trityl tetrafluoroborate gave deuteriated benzoin (incorporation of ^2H 84%) and triphenylmethane (incorporation 71%). These results establish the occurrence of an intermolecular hydride abstraction from the ethylene acetal by the triphenylcarbonium ion. *meso*-1,2-Diphenyl[1-^2H]ethane-1,2-diol acetonide (VIII) (incorporation of ^2H 89%) was prepared by reduction of benzoin with sodium borodeuteride, followed by transacetalisation with 2,2-dimethoxypropane. Treatment of the product (VIII) with trityl



(V) (VI) (VII)



(VIII) (IX) (X)



(XI)

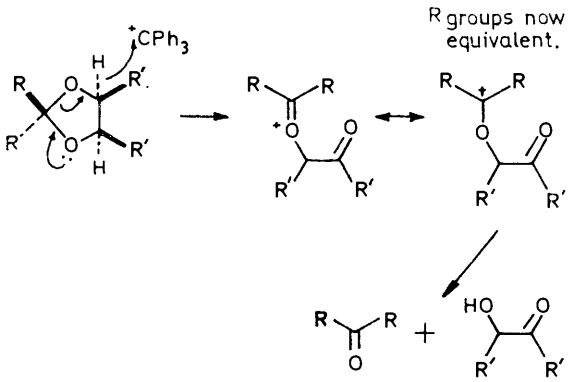
tetrafluoroborate gave benzoin (incorporation 75%) and triphenylmethane (incorporation 16·5%). Calculations based on the triphenylmethane–deuteriated triphenylmethane ratio gave $k_H/k_D = 4·2$, and those on the benzoin–deuteriated benzoin ratio gave $k_H/k_D = 4·9$ (the calculations were based on mass spectra and ignore the secondary isotope effect). The relatively high[17] isotope effect indicates that hydride abstraction is the rate-determining step in this reaction.

The intervention of an intermediate such as (IX) was ruled out by the work just described, but was also excluded in an alternative manner. The acetonide (X) was prepared from triphenylethylene by performic acid oxidation[18] followed by exchange acetalisation with 2,2-dimethoxypropane. Treatment of the acetal (X) with trityl tetrafluoroborate gave triphenylmethane

[10] W. B. Smith and B. A. Shoulders, *J. Phys. Chem.*, 1965, **69**, 2022.
[11] C. D. Nenitzescu, 'Carbonium Ions,' eds. G. A. Olah and P. von R. Schleyer, Wiley–Interscience, New York, 1970, vol. 2, p. 484.
[12] H. J. Dauben, jun., F. A. Gadecki, K. M. Harman, and D. L. Pearson, *J. Amer. Chem. Soc.*, 1957, **79**, 4557.
[13] H. Meerwein, V. Hederick, H. Morshel, and K. Wunderlich, *Annalen*, 1960, **635**, 1.
[14] L. F. Fieser, *J. Chem. Educ.*, 1954, **31**, 291.
[15] D. L. MacDonnald and H. G. Fletcher, *J. Amer. Chem. Soc.*, 1959, **81**, 3719.
[16] H. A. Campbell and K. P. Link, *J. Biol. Chem.*, 1938, **122**, 635.
[17] J. Hine, 'Physical Organic Chemistry,' McGraw-Hill, New York, 1962, p. 71.
[18] H. Riviere, *Bull. Soc. chim. France*, 1964, 97.

and α-hydroxy-αα-diphenylacetophenone (40%),[19] a compound which cannot arise *via* an intermediate such as (IX).

These results are best explained by a mechanism involving a rate-determining hydride abstraction from the ethylene acetal with concerted formation of an oxonium ion (Scheme 2). This explains the n.m.r.



SCHEME 2

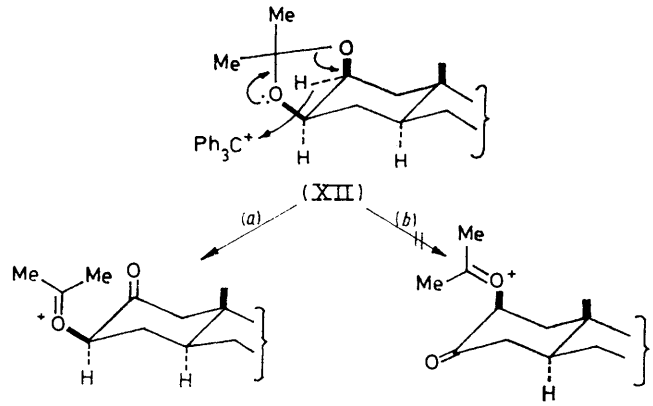
results (see before) and the fact that during the reaction an i.r. carbonyl absorption develops at 1700 cm^{-1} before aqueous work-up. The intermediate oxonium ion is quenched by aqueous work-up to give the observed products. Reduction of the oxonium ion with sodium borohydride gave the starting acetal as the only product. The concerted nature of the process is shown by the fact that ordinary ethers are dehydrogenated by triphenylcarbonium ion much more slowly than acetals. No reaction was observed when allobetulin[20] (XI) was treated with trityl tetrafluoroborate under the usual conditions (see Experimental section).

We then examined the synthetic scope of this reaction in two senses, first as a method of deprotecting masked ketone functions, and second as a way of oxidising a diol to a ketol.

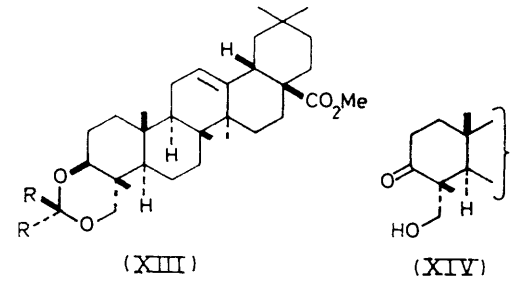
11α-Hydroxyprogesterone ethylene acetal (IV) and pregnenolone ethylene acetal (III) reacted with trityl tetrafluoroborate to give 11α-hydroxyprogesterone (70%) and pregnenolone (80%), respectively. No oxidation of the 3β- or 11α-hydroxy-groups was detected. Cholestanone ethylene acetal on treatment with trityl tetrafluoroborate gave cholestanone (80%).

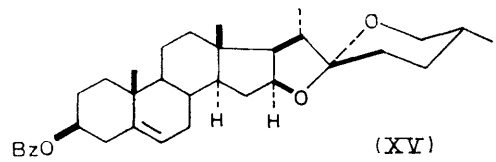
The ethylene dithioacetal of benzophenone was inert to trityl tetrafluoroborate, whereas the ethylene hemithioacetal gave benzophenone (100%). This selectivity can be interpreted on the basis of the lower stability of sulphonium[21] ion relative to that of oxonium ion (*cf.* siliconium ion *versus* carbonium ion).

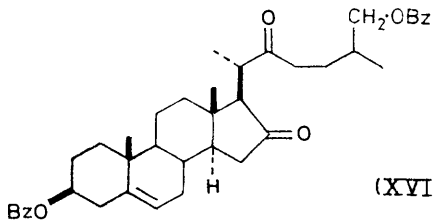
Cholest-2-ene was converted into the 2β,3β-diol.[22] The derived acetonide (XII) gave 3β-hydroxycholestan-2-one[23,24] (79%) on treatment with trityl tetrafluoroborate (4 h). The specific oxidation at position 2 can be explained (Scheme 3) in terms of abstraction of the equatorial 2α-hydrogen atom, resulting in an equatorial 3β-oxonium ion (*a*). The alternative abstraction of the



SCHEME 3







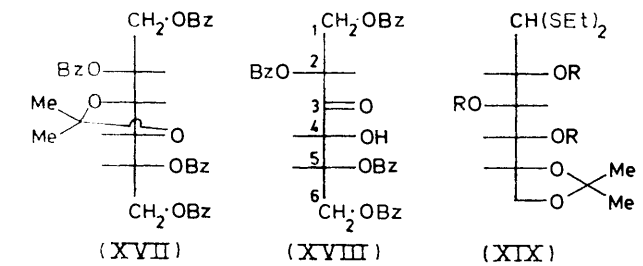
axial 3α-hydrogen atom would result in a sterically unfavourable axial 2β-oxonium ion (*b*).

Methyl hederagenin[25,26] readily afforded the acetonide (XIII; R = Me) on transacetalisation with 2,2-dimethoxypropane, and the diphenylmethylene acetal (XIII; R = Ph) by exchange with benzophenone

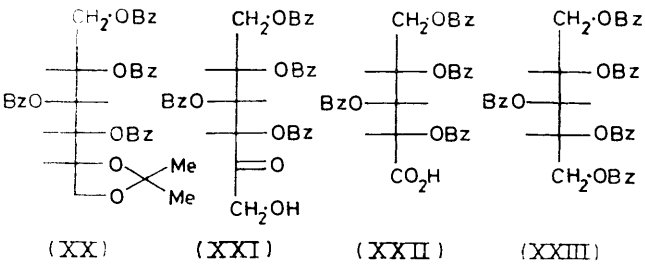
[19] Y. Iskander, Y. Riad, and R. Tewfik, *J. Chem. Soc.*, 1962, 3232.
[20] G. S. Davy, T. G. Halsall, and E. R. H. Jones, *J. Chem. Soc.*, 1951, 2696.
[21] D. Bethell and V. Gold, ' Carbonium Ions,' Academic Press, 1967, p. 305.
[22] P. S. Ellington, D. G. Hey, and G. D. Meakins, *J. Chem. Soc.*, 1966, 1327.
[23] J. C. Sheehan and W. F. Erman, *J. Amer. Chem. Soc.*, 1957 **79**, 6050.
[24] T. Cohen and T. Tsuji, *J. Org. Chem.*, 1961, **26**, 1681.
[25] W. A. Jacobs, *J. Biol. Chem.*, 1925, **63**, 631.
[26] D. H. R. Barton and P. de Mayo, *J. Chem. Soc.*, 1954, 887.

ethylene dithioacetal. Trityl tetrafluoroborate oxidation of the acetonide (XIII; R = Me) gave methyl hederagonate (XIV) (20%). Similarly the acetal (XIII; R = Ph) gave the ketone (XIV) (25%). The axial 3α-hydrogen atom is abstracted. The other mode of oxidation may occur, since the yield of the ketone (XIV) was low, although compared with the conventional oxidation of methyl hederagenin to methyl hederagonate [26] (<5%) it represents a substantial improvement. The structure of (XIV) was substantiated by its retro-aldol transformation into methyl hedragonate.[26]

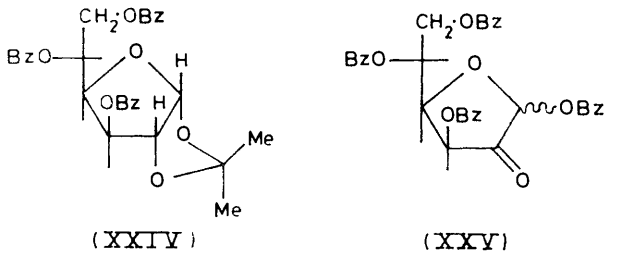
Treatment of diosgenin benzoate (XV) with trityl tetrafluoroborate gave, after benzoylation, kryptogenin



(XVII) (XVIII) (XIX)



(XX) (XXI) (XXII) (XXIII)



(XXIV) (XXV)

dibenzoate [27] (XVI) (35%), identical with an authentic sample. The tertiary 16α-hydrogen atom is abstracted by triphenylcarbonium ion.

A number of important oxidation procedures have been developed in the search for methods of preparing keto-sugars.[28-30] Trityl tetrafluoroborate oxidation of carbohydrate acetals was next examined. D-Mannitol was converted by standard procedures [31] into the 3,4-acetonide and benzoylated to give the ester (XVII). Treatment of the ester (XVII) with trityl tetrafluoroborate (0·5 h) gave the keto-sugar (XVIII) (65%). Since (XVII) is a symmetrical molecule with respect to hydrogen abstraction from the acetal, only one ketone is produced. The n.m.r. spectrum of compound (XVII) exhibited one D_2O-exchangeable proton and the C-4 proton signal appeared as a multiplet at τ 5·9 which on removal of the hydroxy-proton coupling (by D_2O) was transformed into a doublet ($J_{4,5}$ 10 Hz).

5,6-*O*-Isopropylidene-D-glucose diethyl dithioacetal (XIX; R = H) was prepared from D-glucose in 60% yield,[32] and was converted into its 2,3,4-tribenzoate (XIX; R = Bz). Treatment of the product (XIX; R = Bz) with mercury(II) chloride–mercury(II) oxide [33,34] followed by reduction with sodium borohydride and benzoylation gave 1,2,3,4-tetra-*O*-benzoyl-5,6-isopropylidene-D-glucitol (XX). Trityl tetrafluoroborate oxidation of the acetal (XX) (48 h) gave 3,4,5,6-tetra-*O*-benzoyl-L-sorbose (XXI), $\nu_{max.}$ 3500, 1720, and 1700 cm^{-1}, in 50% yield. The structure (XXI) was confirmed by the absence of an aldehyde signal in the n.m.r. spectrum and by periodate oxidation to the acid (XXII). Diborane reduction of the latter and benzoylation gave xylitol pentabenzoate (XXIII), identical with an authentic specimen. The process represents a partial synthesis of sorbose and hence of vitamin C which is not dependent on a microbiological transformation.[35] A recently reported synthesis of vitamin C uses direct oxidation of 1,2-*O*-isopropylidene-D-glucofuranose.[36]

1,2-*O*-Isopropylidene-D-glucofuranose [37] was benzoylated to give the tribenzoate (XXIV). Trityl tetrafluoroborate oxidation of the acetal (XXIV), followed by benzoylation, gave the ketone (XXV) (20%), $\nu_{max.}$ 1712 and 1705 cm^{-1}. No traces of lactones could be detected in the crude product (i.r. spectrum).

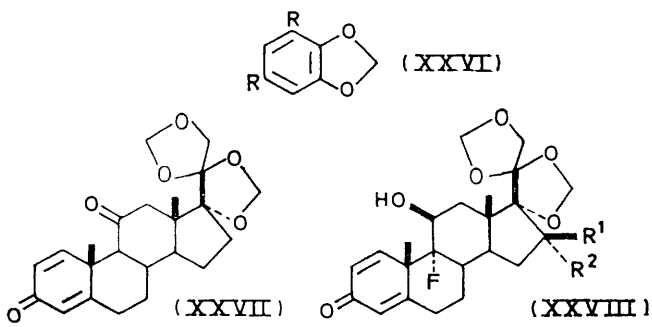
Implicit in the proposed mechanism of the oxidation of acetals by hydride transfer is the oxidation of methylenedioxy-, bismethylenedioxy-, benzyl, benzyloxycarbonyl, and tetrahydropyranyl hydroxy-protecting groups.

Treatment of the dioxole (XXVI; R = H) with trityl tetrafluoroborate (−20 to 20°) gave a complex mixture, probably resulting from electrophilic attack of triphenylcarbonium ion on the active aromatic nucleus. Similar treatment of compound (XXVI; R = Bu^t) with trityl tetrafluoroborate (1 min) gave, after work-up with aqueous sodium carbonate, 3,5-di-t-butylcatechol (80%).

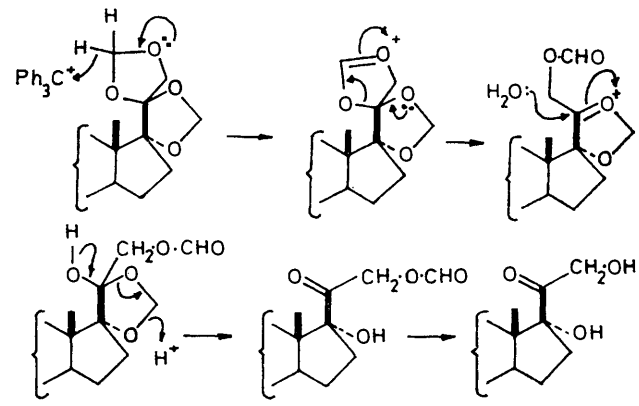
'Bismethylenedioxyprednisone' (XXVII) reacted

[27] G. Rosenkranz, S. T. Kaufmann, A. Landa, J. J. Corona, and A. Olalde, *J. Amer. Chem. Soc.*, 1948, **70**, 3518.
[28] K. E. Pfitzner and J. G. Moffat, *J. Amer. Chem. Soc.*, 1963, **85**, 3027.
[29] J. D. Albright and L. Goldman, *J. Org. Chem.*, 1965, **30**, 1107.
[30] B. J. Beynon, P. M. Collins, P. T. Doyanges, and W. G. Overend, *J. Chem. Soc.* (*C*), 1966, 1131.
[31] H. O. L. Fischer and H. Appel, *Helv. Chim. Acta*, 1934, **17**, 1574.
[32] P. A. J. Gormin, *Canad. J. Chem.*, 1965, **43**, 2078.
[33] N. L. Wolfrom, *J. Amer. Chem. Soc.*, 1929, **51**, 2188.
[34] J. English, jun., and P. H. Cariswold, jun., *J. Amer. Chem. Soc.*, 1945, **67**, 2039.
[35] (*a*) M. Kulhanek, *Chem. Listy*, 1953, **47**, 1081; (*b*) L. B. Lockwood, B. Tubenkin, and G. E. Ward, *J. Bacteriology*, 1941, **42**, 51; (*c*) T. Reichstein, A. Grussner, and R. Oppenauer, *Helv. Chim. Acta*, 1934, **17**, 311, 510.
[36] J. Bakke and O. Theander, *Chem. Comm.*, 1971, 175.
[37] W. N. Haworth and C. R. Porter, *J. Chem. Soc.*, 1929, 2796.

with trityl tetrafluoroborate to give, after hydrolysis of the 21-*O*-formate system, prednisone (40%). Although the 21-*O*-formate was not isolated, evidence for its intermediacy comes from n.m.r. data [τ 1·9 (1H, s)]



and the i.r. spectrum ($\nu_{max.}$ 1725 cm^{-1}). Formylation of prednisone [38] gave a compound with the same R_F value (t.l.c.) as the supposed 21-*O*-formate derived from 'bismethylenedioxyprednisone'. Similarly, 'bismethylenedioxydexamethasone' [39] (XXVIII; R^1 = H, R^2 = Me) and 'bismethylenedioxybetamethasone' (XXVIII; R^1 = Me, R^2 = H) gave dexamethasone



SCHEME 4

(30%) and betamethasone (40%), respectively, on treatment with trityl tetrafluoroborate (24 h). Mechanistically the removal of the protecting group can be be written as in Scheme 4.

[38] F. Cortese and L. Bauman, *J. Amer. Chem. Soc.*, 1935, **57**, 1393.

[39] R. E. Beyler, F. Hoffmann, R. M. Moriarty, and L. M. Sarett, *J. Org. Chem.*, 1961, **26**, 2421.

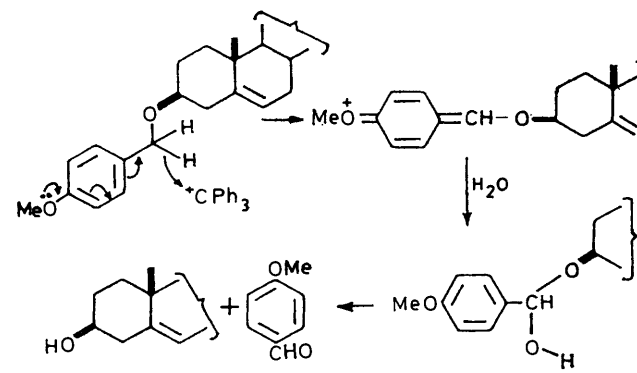
Oxidation of benzyl ethers with trityl tetrafluoroborate can be used either to prepare aromatic aldehydes or to cleave benzyl ethers of alcohols. A number of simple benzyl ethers were prepared and treated with trityl tetrafluoroborate. The results are shown in Table 1. Solvolytic reactions [40,41] show that *p*-methoxy-substitution of benzyl chloride increases the rate of solvolysis by factors of between 10^2 and 5×10^5. To study benzyl ethers for hydroxy-protection, three cholesterol derivatives were prepared (Table 1). The relative rates of debenzylation parallel the rates of hydrolysis of the corresponding benzyl chlorides.[40,41] Mechanistically the debenzylation process can be illustrated as in Scheme 5. 4-Methoxy-3,5-dimethylbenzyl cholesteryl ether appears to be the most suitable benzyl ether in terms of ease and yield of deprotection. (A reaction time of 5 min was found to be more convenient than very rapid reactions.)

A series of benzyloxycarbonyl cholesteryl derivatives were made and treated with trityl tetrafluoroborate. The results are given in Table 2. The unsubstituted benzyloxycarbonylcholesterol did not react within 24 h, presumably because electron withdrawal by the carbonyl group induces an electron shift opposite to that required to stabilise a benzyloxonium ion. Reactions at 0° were generally cleaner. The *p*-methoxybenzyloxycarbonyl derivative reacts within 4 min

TABLE 1

Ether oxidations

Ether	T/°C	t	Product	Method	Yield (%)
$PhCH_2$·OMe	20	2 h	PhCHO	P.l.c.	75
p-MeO·C_6H_4·CH_2·OMe	20	10 min	*p*-MeO·C_6H_4·CHO	P.l.c.	25
$PhCH_2$·O·C_6H_4·NO_2-*p*	Reflux	5 days	*p*-HO·C_6H_4·NO_2	P.l.c.	50
$PhCH_2$·O·CH_2Ph	20	14 h	PhCHO	N.m.r.	>90
$PhCH_2$·O·Chol	20	4 h	Cholesterol	G.l.c.	60
			Cholest-4-enone	G.l.c.	20
p-MeO·C_6H_4·CH_2·O·Chol	20	30 s	Cholesterol	G.l.c.	75—85
4-MeO-3,5-$Me_2C_6H_2$·CH_2·O·Chol	20	5 min	Cholesterol	G.l.c.	85—90
Cholesterol	20	6 h	Cholest-4-enone	P.l.c.	50



SCHEME 5

because the formation of a stabilised oxonium ion is facilitated by the +*M* effect of the *p*-methoxy-group.

[40] W. H. Harting and R. Simonoff, *Org. Reactions*, 1953, **7**, 264.

[41] G. Baddeley, N. H. P. Smith, and M. A. Vickers, *J. Chem. Soc.*, 1956, 2455.

Optimal mesomeric stabilisation requires planarity; in the case of the 4-methoxy-3,5-dimethylbenzyloxycarbonyl group steric hindrance occurs and the deprotection is slower (16 min). A second methoxy-group, as in the 3,4-dimethoxybenzyloxycarbonyl derivative, facilitates oxonium ion formation [42] and,

TABLE 2

Oxidation of benzyloxycarbonyl derivatives

Ester	T/°C	t	Yield (%) *
$PhCH_2{\cdot}O{\cdot}CO{\cdot}O{\cdot}$Chol	20		No reaction
p-$MeO{\cdot}C_6H_4{\cdot}CH_2{\cdot}O{\cdot}CO{\cdot}O{\cdot}$Chol	20	4·5 min	60—80
	0	6 min	90
4-MeO-3,5-$Me_2C_6H_2{\cdot}CH_2{\cdot}O{\cdot}CO{\cdot}O{\cdot}$Chol	20	16 min	80
3,4-$(MeO)_2C_6H_3{\cdot}CH_2{\cdot}O{\cdot}CO{\cdot}O{\cdot}$Chol	20	1—2 min	
	0	15 min	90
	−20	2 h	
3,4,5-$(MeO)_3C_6H_2{\cdot}CH_2{\cdot}O{\cdot}CO{\cdot}O{\cdot}$Chol	20	1 h	70

* The product was cholesterol, determined by g.l.c.

as a consequence, the deprotection is rapid and efficient (90%). The 3,4,5-trimethoxybenzyloxycarbonyl derivative reacts slowly [41] (60 min). This method of deprotecting masked hydroxy-groups should be applicable to other functional groups (*e.g.* NH, CO_2H, OAr, *etc.*).

EXPERIMENTAL

The following general comments apply unless otherwise stated. M.p.s were measured on a Kofler hot-stage apparatus. I.r. spectra were taken for Nujol mulls with a Unicam SP 200 spectrometer. Mass spectra were taken with an A.E.I. MS9 high-resolution spectrometer. N.m.r. spectra were measured for solutions in deuteriochloroform with tetramethylsilane as internal standard using a Varian T-60 spectrometer. The quantitative n.m.r.[43] measurements on aldehydes were carried out by integration of the aldehyde proton signal in the reaction mixture after work-up. Comparison with a calibration curve obtained from standard samples (*c* about 100 mol. %) in dichloromethane gave the concentration of the aldehyde. Rotations were measured for samples in a 10 cm cell (0·5 ml) at the sodium D-line wavelength with a Perkin-Elmer 141 polarimeter for solutions in chloroform.

Dichloromethane was dried over calcium chloride, decanted, and distilled from powdered calcium hydride. Light petroleum refers to the fraction b.p. 40—100°.

Deacetalisation of Pregnenolone Ethylene Acetal (III).—Pregnenolone ethylene acetal [4] (III) (107 mg) in dry dichloromethane (25 ml) was treated with triethyloxonium fluoroborate (89 mg). After 8 min at room temperature, the stirred solution was poured into aqueous sodium hydrogen carbonate. The dichloromethane layer was separated, washed with water, dried (Na_2SO_4), and evaporated to give pregnenolone (80%), identical (m.p., mixed m.p., and i.r. spectrum) with an authentic sample.

Deacetalisation of 11α-Hydroxyprogesterone Ethylene Acetal (IV).—11α-Hydroxyprogesterone ethylene acetal [5] (IV) (94 mg) in dry dichloromethane (20 ml) was treated with triethyloxonium fluoroborate (359 mg). After 20 min the stirred solution was worked up as before and the residue was chromatographed on silica gel (20 × 20 cm) to give 11α-hydroxyprogesterone (52 mg, 70%), m.p. 165—167° (lit.,[44] 166—167°).

Reaction of Cholesterol Tetrahydropyranyl Ether with Triethyloxonium Fluoroborate.—Cholesterol tetrahydropyranyl ether [7] (129 mg) in dry dichloromethane (10 ml) was treated with triethyloxonium fluoroborate (60 mg) in dichloromethane (10 mg). After 0·5 h the solution was worked up as before and the residue was chromatographed on alumina [ether–benzene (1 : 1)] to give cholesterol (67 mg, 64%), m.p. 148—149°).

Reaction of Cyclohexanone Ethylene Acetal with Triethyloxonium Fluoroborate.—Triethyloxonium fluoroborate (1·59 g) in dry dichloromethane (10 ml) was treated with cyclohexanone ethylene acetal [8] (372 mg). After 2 h at room temperature the mixture was worked up as before and the aqueous phase was continuously extracted with ether (24 h). G.l.c. of the dichloromethane phase (Carbowax column) showed cyclohexanone ethylene acetal (62%) and a trace of mono-*O*-ethylethylene glycol. The ether extracts showed (g.l.c.) only the monoethyl ether of ethylene glycol.

General Procedure for Reactions with Trityl Tetrafluoroborate.—The acetal and trityl tetrafluoroborate in a dry flask were stirred under nitrogen (dry) and covered with dry dichloromethane (distilled directly into the flask). When the reaction was complete (t.l.c. control) an excess of aqueous sodium hydrogen carbonate was added and the two-phase mixture was stirred for 10 min. The organic phase was washed with water, dried (Na_2SO_4), and evaporated *in vacuo*. The residue was chromatographed over silica to separate triphenylmethane, triphenylmethanol (trace), and the product(s).

Trityl Tetrafluoroborate.[9]—Prepared from triphenylmethanol and hydrofluoroboric acid, the salt was dried under high vacuum for 45 h before use and had m.p. 200° (decomp.).

6aα,12aα-Dihydro-1-phenyl-7H-naphthaceno[1,12-bc]-*furan-6,12-dione* (I; X = O).—The acetal (I; X = $O{\cdot}CH_2{\cdot}CH_2{\cdot}O$) (97 mg) in dry dichloromethane (20 ml) was treated with trityl tetrafluoroborate (85 mg). The mixture was stirred for 5 h, more trityl tetrafluoroborate (85 mg) was added, and the mixture was stirred for 84 h. Work-up as described in the general procedure gave the diketone (I; X = O) (56 mg, 65%), m.p. 234—235° (from benzene) (lit.,[45] 234—235°).

Cyclohexanone from Cyclohexanone Ethylene Acetal.—Cyclohexanone ethylene acetal (149 mg) and trityl tetrafluoroborate (400 mg) in dichloromethane (10 ml) were stirred together for 30 min. Work-up in the standard manner gave cyclohexanone (80%), estimated by quantitative g.l.c. analysis.

A similar reaction in deuteriochloroform carried out in an n.m.r. sample tube showed the presence of triphenyl methane.[10] From a separate experiment, triphenylmethane (100%) was isolated (p.l.c.).

Benzophenone from Benzophenone Ethylene Acetal.—Benzophenone ethylene acetal (226 mg) and trityl tetrafluoroborate (330 mg) in dichloromethane (20 ml) reacted

[42] N. H. P. Smith, 'Steric Effects in Conjugated Systems,' ed. G. W. Gray, Butterworth, London, 1958, p. 113.

[43] J. W. Emsley, J. Feeney, and L. H. Sutcliffe, 'High Resolution Nuclear Magnetic Resonance Spectroscopy,' Pergamon, Oxford, vol. I, 1965, p. 234.

[44] O. Mancera, H. Romo, F. Sondheimer, G. Rosenkranz, and C. Djerassi, *J. Org. Chem.*, 1952, **17**, 1066.

[45] E. Aufderhaar, J. E. Baldwin, D. H. R. Barton, D. J. Faulkner, and M. Slaytor, *J. Chem. Soc.* (*C*), 1971, 2175.

for 15 min in the standard manner. Benzophenone (100%) and triphenylmethane (100%) were isolated (p.l.c.).

Cyclohexanone meso-1,2-*Diphenylethylene Acetal* (V).—Cyclohexanone ethylene dithioacetal (0·43 g) in dry tetrahydrofuran (50 ml) was mixed with *meso*-1,2-diphenylethane-1,2-diol (0·5 g) and mercury(II) oxide (2·7 g) (yellow) and stirred under reflux. Mercury(II) chloride in dry tetrahydrofuran (5% w/v; 40 ml) was added at such a rate as to maintain gentle reflux. After 15 h the hot mixture was filtered and mercury(II) oxide (0·1 g) was added to the filtrate. The mixture was concentrated *in vacuo*, diluted with dichloromethane, and filtered. The filtrate was washed with water, aqueous potassium iodide (10% w/v), and water, dried (Na_2SO_4), and evaporated. Chromatography of the residue over silica gel (with benzene) gave *cyclohexanone* meso-1,2-*diphenylethylene acetal* (V) (0·54 g), m.p. (from ethanol) 63°, $\nu_{max.}$ 1050 and 1110 cm^{-1}, τ 8·2 (10H, m), 4·35 (2H, s), and 3·1 (10H, s) (Found: C, 81·5; H, 7·6. $C_{20}H_{12}O_2$ requires C, 81·6; H, 7·5%).

Trityl Tetrafluoroborate Oxidation of the Acetal (V).—Cyclohexanone *meso*-1,2-diphenylethylene acetal (V) (300 mg) and trityl tetrafluoroborate (450 mg) in dry dichloromethane (15 ml) reacted for 4 h in the standard manner. Chromatography over silica gel [with acetone–light petroleum (1 : 9)] gave benzoin (145 mg), m.p. and mixed m.p. 134° (from ethanol), $\nu_{max.}$ 1680 and 3450 cm^{-1}.

Acetone 1,2-*Diphenylethylene Acetal* (VI).—*meso*-1,2-Diphenylethane-1,2-diol (0·4 g) in 2,2-dimethoxypropane (5 ml) was stirred at room temperature with toluene-*p*-sulphonic acid (10 mg) for 1 h. Chloroform (80 ml) was added to the mixture and the solution was washed successively with water, aqueous sodium hydrogen carbonate (5% w/v), and water. The organic phase was dried (Na_2SO_4) and evaporated to give the *acetonide* (VI) (0·41 g), m.p. (from ethanol) 58°, $\nu_{max.}$ 1060 cm^{-1}, τ 8·75 (3H, s), 8·6 (3H, s), 4·75 (2H, s), and 3·2 (10H, s) (Found: C, 80·5; H, 7·0. $C_{17}H_{18}O_2$ requires C, 80·3; H, 7·1%).

Trityl Tetrafluoroborate Oxidation of the Acetonide (VI).—The acetonide (VI) (250 mg) and trityl tetrafluoroborate (450 mg) in dichloromethane (15 ml) reacted for 4 h in the standard manner. Chromatography over silica gel [with acetone–light petroleum (1 : 9)] gave benzoin (135 mg), m.p. and mixed m.p. 134° (from ethanol).

Scrutiny of this reaction in an n.m.r. sample tube (at room temperature) showed that the two methyl signals at τ 8·75 and 8·6 coalesce to a singlet at τ 8·25 (6H) over the reaction period of 4 h.

Acetone meso-1,2-*Diphenyl*[1,2-$^2H_2$]*ethylene Acetal* (VII).—Benzil (0·45 g) in ethanol (5 ml) at reflux was treated with sodium borodeuteride (99·9%; 0·2 g). After 10 min, water (15 ml) was added and the mixture was cooled. The dideuteriated diol (0·38 g) crystallised out and was converted into its acetonide as previously described for (VI), and the product showed *m/e* 256 (M^+) (incorporation of deuterium 87%).

Acetone meso-1,2-*Diphenyl*[1-^2H]*ethylene Acetal* (VIII).—Benzoin (0·5 g) and sodium borodeuteride (0·1 g), treated as in the preceding experiment, gave the monodeuterio-diol, which was converted into its acetonide as for compound (VI); *m/e* 255 (M^+) (incorporated of deuterium 89%).

1,2-*Dihydroxy*-1,1,2-*triphenylethane*.—Triphenylethylene (256 mg) was treated with formic acid (99·9%; 4 ml) and hydrogen peroxide 30% (1 ml). The solution was held at 40° for 3 h and evaporated. The residue was treated with an excess of sodium hydroxide (3N; 15 ml) in methanol (15 ml) for 30 min. The solution was diluted with dichloromethane (50 ml) and the organic layer washed with water, dried, and evaporated to give the crude diol, $\nu_{max.}$ 3500 cm^{-1}.

1,2-O-*Isopropylidene*-1,2-*dihydroxy*-1,1,2-*triphenylethane* (X).—The crude 1,2-*dihydroxytriphenylethane* (250 mg) in 2,2-dimethoxypropane (15 ml) was treated with toluene-*p*-sulphonic acid monohydrate (15 mg). The mixture was stirred at room temperature for 1 h and after work-up in the usual way, chromatography over silica gel [with acetone–light petroleum (1 : 18)] gave the *acetonide* (X) (250 mg), m.p. (from ethanol) 113°, $\nu_{max.}$ 1100 cm^{-1}, τ 8·5 (3H, s), 8·2 (3H, s), 4·2 (1H, s), and 2·8 (15H, m) (Found: C, 83·6; H, 6·8. $C_{23}H_{22}O_2$ requires C, 83·6; H, 6·7%).

α-*Hydroxy*-αα-*diphenylacetophenone*.—The acetonide (X) (66 mg) and trityl tetrafluoroborate (100 mg) in dichloromethane (10 ml) reacted for 4 h in the standard manner. Chromatography over silica gel [with acetone–light petroleum (1 : 9)] gave α-hydroxy-αα-diphenylacetophenone [19] (40%), m.p. 89°, $\nu_{max.}$ 3400 and 1690 cm^{-1}.

Attempted Trityl Tetrafluoroborate Oxidation of Allobetulin (XI).—Allobetulin (XI) was treated with a large excess (5 equiv.) of trityl tetrafluoroborate in dichloromethane at room temperature for 5 days. Allobetulin was recovered in over 95% yield.

11α-*Hydroxyprogesterone from* 11α-*Hydroxyprogesterone Ethylene Acetal* (IV).—The acetal (IV) (209 mg) and trityl tetrafluoroborate (340 mg) in dichloromethane (15 ml) reacted for 30 min in the standard manner. The product was chromatographed over silica gel [with acetone–light petroleum (3 : 7)] to give 11α-hydroxyprogesterone (115 mg), m.p. and mixed m.p. 166—168° (from methanol), $[\alpha]_D^{23}$ +176° (*c* 1·0).

Pregnenolone from Pregnenolone Ethylene Acetal (III).—The acetal (III) (360 mg) and trityl tetrafluoroborate (450 mg) in dichloromethane (15 ml) reacted for 30 min in the standard manner. Chromatography over silica gel [double elution with acetone–light petroleum (1 : 9)] gave pregnenolone (255 mg), m.p. and mixed m.p. 193° (from ethanol), $[\alpha]_D^{23}$ +28° (*c* 1·1).

Cholestanone from Cholestanone Ethylene Acetal.—Cholestanone ethylene acetal (215 mg) and trityl tetrafluoroborate (165 mg) in dichloromethane (15 ml) reacted for 30 min in the standard manner. The product was chromatographed over silica gel [with acetone–light petroleum (1 : 9)] to give cholestanone (154 mg), m.p. and mixed m.p. 128—129°, $[\alpha]_D^{23}$ +43° (*c* 1·1).

Benzophenone Thiohemiacetal.—Benzophenone (1·0 g) in benzene (30 ml) was treated with β-mercaptoethanol (1 ml) and toluene-*p*-sulphonic acid monohydrate (5 mg). The mixture was heated at reflux for 12 h (water was removed by use of a Soxhlet packed with calcium hydride). The mixture was cooled to room temperature and poured into water and the benzene layer washed with aqueous sodium hydrogen carbonate (5% w/v; 40 ml). The organic phase was dried (Na_2SO_4) and evaporated. Chromatography of the residue over silica (with benzene) gave the thiohemiacetal (0·4 g), m.p. (from ethanol) 46°, τ 6·8 (2H, t, *J* 5 Hz), 5·8 (2H, t, *J* 5 Hz), and 2·8 (10H, m).

Benzophenone from Benzophenone Thiohemiacetal.—Benzophenone thiohemiacetal (240 mg) and trityl tetrafluoroborate (330 mg) in dichloromethane (10 ml) reacted for 15 min in the standard manner. Chromatography over silica (with benzene) gave benzophenone (175 mg), m.p. and mixed m.p. 49°.

3β-*Hydroxycholestan-2-one*.— 2β,3β-*O*-Isopropylidenecholestane [22] (XII) (110 mg) and trityl tetrafluoroborate (250 mg) in dichloromethane (10 ml) reacted for 2 h in the standard manner. Chromatography over silica gel (p.l.c.) (with benzene) gave 3β-hydroxycholestan-2-one [23,24] (80 mg), m.p. (from methanol) 107°, $[\alpha]_D^{23}$ +63° (*c* 1·3), $\nu_{max.}$ 1715 and 3500 cm^{-1} (Found: C, 80·8; H, 11·5. Calc. for $C_{27}H_{46}O_2$: C, 80·7; H, 11·5%).

Methyl Hederagenin Acetonide (XIII; R = Me).— Methyl hederagenin [26] (500 mg) in 2,2-dimethoxypropane (15 ml) was treated with toluene-*p*-sulphonic acid monohydrate (20 mg). After 3 h at room temperature the mixture was worked up in the usual way to give the acetonide (XIII; R = Me) (50 mg), m.p. (from methanol) 250—251°, $\nu_{max.}$ 1720 and 1185 cm^{-1}. τ 6·35 (2H, s), 6·5 (1H, s), and 4·65 (1H, m); other signals were due to methylene and methyl groups.

Benzophenone Methyl Hederagenin Acetal (XIII; R = Ph).—Benzophenone ethylene dithioacetal (128 mg) in dry tetrahydrofuran (40 ml) was treated with methyl hederagenin [26] (295 mg) and yellow mercury(II) oxide (2 g). The mixture was stirred under reflux and a solution of mercury(II) chloride in dry tetrahydrofuran (5% w/v; 30 ml) was added at such a rate as to maintain gentle reflux. After 15 h the hot mixture was filtered and mercury(II) oxide (1 g) was added to the filtrate. The mixture was concentrated *in vacuo*, diluted with dichloromethane, and filtered. The filtrate was washed successively with water, aqueous potassium iodide (10% w/v), and water. The organic phase was dried (Na_2SO_4) and evaporated. Chromatography of the residue over silica gel (with benzene) gave the *acetal* (XIII; R = Ph) (260 mg), m.p. (from methanol) 275—277°, $[\alpha]_D^{23}$ +31° (*c* 0·98), $\nu_{max.}$ 1725 cm^{-1} (Found: C, 81·2; H, 8·9. $C_{44}H_{58}O_4$ requires C, 81·3; H, 9·0%).

Methyl Hederagonate (XIV) *from the Acetonides* (XIII; R = Me) *and* (XIII; R = Ph).—Methyl hederagenin acetonide (XIII; R = Me) (250 mg) and trityl tetrafluoroborate (275 mg) in dichloromethane (15 ml) reacted for 15 h in the standard manner. Work-up in the usual way, followed by chromatography over silica gel (p.l.c.) [with benzene and acetone–light petroleum (1 : 9) successively] gave methyl hederagonate [26] (XIV) (50 mg), m.p. and mixed m.p. 217° (from methanol, $[\alpha]_D^{23}$ +78° (*c* 1·1) $\nu_{max.}$ 1680, 1722, and 3450 cm^{-1}.

Benzophenone methyl hederagenin acetal (XIII; R = Ph) (320 mg) and trityl tetrafluoroborate (300 mg) reacted for 15 h in the standard manner. Work-up in the usual way, followed by chromatography, as above, gave methyl hederagonate [26] (XIV) (49 mg).

Methyl Hedragonate.[26]—Methyl hederagonate (XIV) (10 mg) in methanol (7 ml) was treated with potassium hydroxide (400 mg) in water (3 ml) for 1 h. Work-up and chromatography over silica [with acetone–light petroleum (1 : 9)] gave methyl hedragonate [26] (7 mg), m.p. and mixed m.p. 203°, $[\alpha]_D^{23}$ +101° (*c* 1·0), $\nu_{max.}$ 1722 and 1680 cm^{-1}.

Kryptogenin Dibenzoate (XVI).—Diosgenin benzoate (XV) (100 mg) and trityl tetrafluoroborate (150 mg) in dichloromethane (15 ml) reacted for 15 h in the standard manner. Work-up in the usual way followed by chromatography over silica [with acetone–light petroleum (1 : 4)] gave crude kryptogenin monobenzoate (35 mg). This, in dry pyridine (7 ml), was treated with benzoyl chloride (0·3 ml) and left for 24 h. The mixture was poured into ice–water containing sodium hydrogen carbonate (1 g) and the mixture was extracted with chloroform. The chloroform layer was dried (Na_2SO_4) and evaporated. Chromatography of the residue over silica [with acetone–light petroleum (1 : 9)] gave kryptogenin dibenzoate (XVI) [27] (35 mg), m.p. and mixed m.p. 183° (from ethanol), $\nu_{max.}$ 1715, 1710, and 1700 cm^{-1}, τ 5·8 (2H, d, *J* 5 Hz), 5·0 (1H, m), 4·6 (1H, m), and 2·5 (10H, m); other signals were due to the methylene and methyl groups (Found: C, 77·2; H, 7·8. Calc. for $C_{41}H_{50}O_6$: C, 77·1; H, 7·9%).

1,2,5,6-*Tetra*-O-*benzoyl*-3,4-O-*isopropylidene*-D-*mannitol* (XVII).—3,4-*O*-Isopropylidene-D-mannitol [31] (200 mg) in dry pyridine (10 ml) was treated with freshly distilled benzoyl chloride (0·3 ml) at room temperature for 15 h. The mixture was poured into ice–water (150 ml) containing sodium hydrogen carbonate (1 g) and stirred for 1 h. Extraction with chloroform followed by drying (Na_2SO_4), evaporation, and chromatography of the residue over silica gel [with acetone–light petroleum (1 : 4)] gave the *tetrabenzoate* (XVII) (270 mg), m.p. (from ethanol) 101°, $[\alpha]_D^{23}$ +1·1° (*c* 1·0), $\nu_{max.}$ 1710, 1110, and 1290 cm^{-1}, τ 8·4 (6H, s), 5·3 (6H, m), 4·3 (2H, m), and 2·5 (20H, m) (Found: C, 69·7; H, 5·4. $C_{37}H_{34}O_{10}$ requires C, 69·6; H, 5·4%).

1,2,5,6-*Tetra*-O-*benzoyl*-4-*hydroxy*-D-*arabino*-3-*hexulose* (XVIII).—The acetonide (XVII) (314 mg) and trityl tetrafluoroborate (215 mg) in dichloromethane (15 ml) reacted for 4 h in the standard manner. Work-up in the usual way, followed by chromatography over silica gel [with acetone–light petroleum (1 : 4)] gave the *hydroxyketone* (XVIII) (190 mg), m.p. (from ethyl acetate–light petroleum) 103°, $[\alpha]_D^{23}$ +20·7° (*c* 0·3), $\nu_{max.}$ 1705, 1710, and 3500 cm^{-1}, τ 5·9 (2H, d, *J* 10 Hz), 5·2—4·3 (5H, m), 2·5 (20H, m), and 4·0 (1H, exchangeable with D_2O) (Found: C, 68·2; H, 4·9. $C_{34}H_{28}O_{10}$ requires C, 68·5; H, 4·7%).

2,3,4-*Tri*-O-*benzoyl*-5,6-O-*isopropylidene*-D-*glucose Diethyl Dithioacetal* (XIX; R = Bz).—The dithioacetal [32] (XIX; R = H) (250 mg) in dry pyridine (10 ml) was treated with freshly distilled benzoyl chloride (0·4 ml) at room temperature for 15 h. The solution was poured into ice–water (150 ml) containing sodium hydrogen carbonate (1 g) and stirred for 1 h, then extracted with chloroform (3 × 30 ml). The chloroform layer was dried (Na_2SO_4) and evaporated. Chromatography of the residue over silica gel [with acetone–light petroleum (1 : 4)] gave the tribenzoate (XIX; R = Bz) as an oil (318 mg), $\nu_{max.}$ 1710, 1110, and 1280 cm^{-1}, τ 8·9 (6H, t, *J* 6 Hz), 8·5 (6H, s), 7·5 (4H, q, *J* 6 Hz), 5·8—4·8 (7H, m), and 2·5 (15H, m).

1,2,3,4-*Tetra*-O-*benzoyl*-5,6-O-*isopropylidene*-D-*glucitol* (XX).—The tribenzoate (XIX; R = Bz) (200 mg) in aqueous acetone (1 : 9) was treated with yellow mercury(II) oxide (250 mg). The mixture was heated at reflux and mercury(II) chloride (250 mg) in acetone (5 ml) was added dropwise. After 4 h the hot solution was filtered and sodium hydrogen carbonate (0·3 g) was added to the filtrate. The filtrate was evaporated then diluted with chloroform. The chloroform solution was washed with water, aqueous potassium iodide (10% w/v; 30 ml), and water, dried (Na_2SO_4), and evaporated, and the residue was chromatographed over silica gel. Elution with acetone–light petroleum (1 : 4) gave 2,3,4-tri-*O*-benzoyl-5,6-*O*-isopropylidene-D-glucose as an oil, $\nu_{max.}$ 1710, 1100, and 1280 cm^{-1}, τ 8·6 (6H, d, *J* 2 Hz), 5·8—4·4 (6H, m), 2·5 (15H, m), and 1·0 (1H, s). Treatment of this aldehyde (100 mg) in methanol (20 ml) with sodium borohydride (20 mg) followed by the usual work-up gave an oil. Benzoylation of this oil gave 1,2,3,4-*tetra*-O-*benzoyl*-5,6-*isopropylidene*-D-*glucitol* (XX) (93 mg), m.p. (from ethyl acetate–light petroleum)

119—123°, $[\alpha]_D^{23}$ +24·8° (*c* 0·5), $\nu_{max.}$ 1710 and 1100 cm^{-1}, τ 8·6 (6H, s), 6·0—4·5 (8H, m), and 2·5 (20H, m) (Found: C, 69·5; H, 5·5. $C_{37}H_{34}O_{10}$ requires C, 69·6; H, 5·4%).

3,4,5,6-*Tetra*-O-*benzoyl*-L-*sorbose* (XXI).—The acetal (XX) (165 mg) and trityl tetrafluoroborate (250 mg) in dichloromethane (15 ml) reacted for 5 h in the standard manner. Work-up in the usual way, followed by chromatography over silica gel [with acetone–light petroleum (1 : 4)] gave 3,4,5,6-*tetra*-O-*benzoyl*-L-*sorbose* (XXI) (77 mg), m.p. (from ethyl acetate–light petroleum) 101—103°, $[\alpha]_D^{23}$ −8·6° (*c* 0·6), $\nu_{max.}$ 3500, 1710, and 1700 cm^{-1} (Found: C, 68·3; H, 4·2. $C_{34}H_{28}O_{10}$ requires C, 68·5; H, 4·7%).

Xylitol Pentabenzoate (XXII).—3,4,5,6-Tetra-*O*-benzoyl-L-sorbose (XXI) (150 mg) was added to a solution of potassium periodate (300 mg) in water–acetone (1 : 4; 7 ml) and the mixture was stirred at 5° for 15 min. Potassium permanganate (10 mg) in water–acetone (1 : 1; 2 ml) was added and the mixture was stirred at 5° for 24 h, then filtered. The filtrate was extracted with dichloromethane (3 × 30 ml); the extract was washed with water, dried (Na_2SO_4), and evaporated to give the crude acid. The crude acid in dry tetrahydrofuran (5 ml) was treated with diborane. After 1 h, water (5 ml) was added and the crude product (isolated in the usual way) was benzoylated (benzoyl chloride in pyridine). Work-up in the usual way gave a crystalline product which was chromatographed over silica gel [with acetone–light petroleum (1 : 9)] to give *xylitol pentabenzoate* (XXII) (10 mg), m.p. (from ethanol) 106—107°, identical (mixed m.p.) with a sample prepared from xylitol penta-acetate (Found: C, 71·4; H, 4·8. $C_{40}H_{32}O_{10}$ requires C, 71·4; H, 4·8%).

3,5,6-*Tri*-O-*benzoyl*-1,2-O-*isopropylidene*-D-*glucofuranose* (XXIV).—1,2-*O*-Isopropylidene-D-glucofuranose [37] (200 mg) in dry pyridine (20 ml) was treated with freshly distilled benzoyl chloride (0·3 ml). After 15 h at room temperature the mixture was worked up in the usual way to give, after chromatography over silica gel [with acetone–light petroleum (1 : 4)], the *tribenzoate* (XXIV) (380 mg), m.p. (from ethanol) 115°, $[\alpha]_D^{23}$ −99·7° (*c* 0·76), $\nu_{max.}$ 1710, 1110, and 1270 cm^{-1}, τ 8·65 (3H, s), 8·4 (3H, s), 3·9—5·2 (7H, m), and 2·4 (15H, m) (Found: C, 67·7; H, 5·3. $C_{30}H_{28}O_9$ requires C, 67·7; H, 5·1%).

Trityl Tetrafluoroborate Oxidation of the Acetal (XXIV).—The acetal (XXIV) (260 mg) and trityl tetrafluoroborate (200 mg) in dichloromethane (15 ml) reacted for 14 h in the standard manner. Work-up in the usual way, followed by chromatography over silica gel [with acetone–light petroleum (1 : 4)] gave the ketone as an oil, $[\alpha]_D^{23}$ −97·2° (*c* 0·9), $\nu_{max.}$ 3500, 1705, and 1712 cm^{-1}, τ 5·8—4·0 (6H, m) and 2·5 (15H, m). The oily product was benzoylated in the usual way to give the *ketone* (XXV) (37 mg), m.p. 150—151° (from ethyl acetate–light petroleum), $[\alpha]_D^{23}$ −61·4° (*c* 0·2), $\nu_{max.}$ 1712 and 1705 cm^{-1}, τ 5·8—4·0 (6H, m) and 2·5 (20H, m) (Found: C, 68·8; H, 4·7. $C_{34}H_{26}O_{10}$ requires C, 68·7; H, 4·4%).

3,5-*Di-t-butyl*-1,3-*benzodioxole* (XXVI; R = Bu^t).—Dry dichloromethane (2 ml) and dimethyl sulphoxide (10 ml) under nitrogen at 125—130° were treated with 3,5-di-t-butylcatechol (4 g) and sodium hydroxide (1·7 g) in portions during 2 h. Dichloromethane (2 ml) was added and the temperature was maintained at 130° for a further 1 h. The cooled mixture was diluted with water and extracted with chloroform (3 × 30 ml). The extract was washed with water, dried (Na_2SO_4), and evaporated to give an oil. Filtration of this oil through a short column of silica gel (with chloroform) gave the *dioxole* (XXVI; R = Bu^t) (3·2 g), b.p. 101° at 0·1 mmHg, τ 8·8 (18H, s), 4·2 (2H, s), and 3·3 (2H, s) (Found: C, 76·1; H, 9·1. $C_{15}H_{22}O_2$ requires C, 76·1; H, 9·4%).

3,5-*Di-t-butylcatechol*.—The dioxole (XXVI; R = Bu^t) (120 g) and trityl tetrafluoroborate (330 g) in dichloromethane (15 ml) reacted for 15 min in the standard manner. Work-up in the usual way gave 3,5-di-t-butylcatechol (95 mg), m.p. and mixed m.p. 98°.

A similar sequence with compound (XXVI; R = H) gave many products.

Prednisone from '*Bismethylenedioxyprednisone*' (XXVII).—'Bismethylenedioxyprednisone' (XXVII) (200 mg) and trityl tetrafluoroborate (300 mg) in dichloromethane (15 ml) reacted for 24 h in the standard manner. The product, in aqueous methanol (90% v/v; 40 ml) containing potassium hydrogen carbonate (0·5 g), was stirred for 15 h, and dichloromethane (50 ml) was added. The organic phase was washed with water, dried (Na_2SO_4), and evaporated. The residue was chromatographed over silica gel [with acetone–light petroleum (3 : 7)] to give prednisone (71 mg), m.p. and mixed m.p. (from chloroform–methanol) 233—235° (decomp.), $[\alpha]_D^{23}$ +172° (*c* 1·0 in dioxan), $\nu_{max.}$ 3500, 1703, 1660, and 1620 cm^{-1}.

Dexamethasone from '*Bismethylenedioxydexamethasone*' (XXVIII; R^1 = H, R^2 = Me).—'Bismethylenedioxydexamethasone' (XXVIII; R^1 = H, R^2 = Me) (150 mg) and trityl tetrafluoroborate (300 mg) in dichloromethane (15 ml) reacted for 24 h in the standard manner. The product in methanol (70 ml) was treated with aqueous potassium hydrogen carbonate (10% w/v; 30 ml) and the mixture was stirred for 5 h. Dichloromethane (50 ml) was added and the organic phase was washed with water, dried (Na_2SO_4), and evaporated. The residue was chromatographed over silica [with acetone–light petroleum (3 : 7)] to give dexamethasone (40 mg), m.p. and mixed m.p. 256°. $[\alpha]_D^{23}$ +86° (*c* 1·1).

'*Bismethylenedioxybetamethasone*' (XXVIII; R^1 = Me, R^2 = H).—Betamethasone (500 mg) in chloroform (25 ml) was stirred with aqueous formaldehyde (37%; 10 ml) and concentrated hydrochloric acid (*d* 1·19; 10 ml) for 24 h at room temperature. Chloroform (25 ml) was added, and the layers were separated. The chloroform layer was washed with saturated aqueous sodium hydrogen carbonate, dried (Na_2SO_4), and evaporated. Chromatography of the residue over silica gel [with acetone–light petroleum (3 : 7)] gave *product* (XXVIII; R^1 = Me, R^2 = H) (260 mg), m.p. (from dichloromethane–methanol) 300°, $\nu_{max.}$ 1650 and 1600 cm^{-1}, τ 2·9 (1H, d, *J* 5 Hz), 3·9 (1H, d, *J* 5 Hz), 4·15 (1H, s), 5·2 (4H, m), 6·0 (2H, q, *J* 4 Hz), and other signals (Found: C, 66·3; H, 7·3; F, 4·4. $C_{24}H_{31}O_5F$ requires C, 66·4; H, 7·3; F, 4·4%).

Betamethasone from '*Bismethylenedioxybetamethasone*'.—The bismethylenedioxy-derivative (XXVII; R^1 = Me, R^2 = H) (150 mg) and trityl tetrafluoroborate (300 mg) in dichloromethane (15 ml) reacted for 24 h in the standard manner. The product, in methanol (20 ml), was treated with aqueous potassium hydrogen carbonate (10% w/v; 30 ml) and the mixture was stirred for 5 h. Dichloromethane (50 ml) was added and the organic phase was washed with water, dried (Na_2SO_4), and evaporated. The residue was chromatographed over silica gel [with acetone–light petroleum (3 : 7)] to give betamethasone (55 mg), m.p. and mixed m.p. 233—235°, $[\alpha]_D^{23}$ +108° (*c* 1·1 in acetone).

Benzyl Ethers (*Table* 1).—Benzyl methyl ether [46] (1 mmol) was treated with trityl tetrafluoroborate (2 mmol) in dichloromethane (20 ml) under nitrogen at room temperature. After 2 h aqueous sodium hydrogen carbonate (5% w/v; 20 ml) was added. The organic layer was washed with water, dried (Na_2SO_4), and evaporated. Chromatography over silica gel [with acetone–light petroleum (2 : 78)] gave benzaldehyde (75%; characterised as its 2,4-dinitrophenylhydrazone, m.p. 235°). Anisyl methyl ether [47] was treated similarly to give anisaldehyde (25%), characterised as its 2,4-dinitrophenylhydrazone, m.p. 256°. Benzyl *p*-nitrophenyl ether [48] similarly (5 days) gave *p*-nitrophenol (50%), m.p. 113°. Dibenzyl ether [49] (14 h) gave benzaldehyde (100%) (determined by quantitative n.m.r.).

Benzyl cholesteryl ether [50] (1 mmol) was treated with trityl tetrafluoroborate (2 mmol) in dry dichloromethane (15 ml). After 4 h the mixture was worked up in the usual way. The yields of cholesterol and cholest-4-enone were determined by g.l.c. (60 and 20%, respectively) (Perkin-Elmer F11; glass column; 2·5 silicone E301 on Chromosorb G AW-DMGS, 80—100 mesh; length 2 ft, diam. ¼ in; temp. 230°, injection temp. 260°). Ergosterol was used as an internal standard (R_t 21 min); R_t for cholesterol 16 min.

Anisyl cholesteryl ether. Cholesterol (3 mmol) was treated with *p*-methoxybenzyl bromide (4 mmol) and sodium hydride (4 mmol) in dry benzene (30 ml). After 6 h at reflux the cooled mixture was filtered, and the filtrate was evaporated. The residue was chromatographed over silica gel [acetone–light petroleum (5 : 95)] to give *anisyl cholesteryl ether* (70%), m.p. (from methanol–light petroleum) 130°, $[\alpha]_D^{18}$ −22·2° (*c* 0·4), $\nu_{max.}$ 1040, 1085, and 1240 cm^{-1}, τ 3·37—2·8 (4H, A_2B_2), 5·63 (2H, s), 6·28 (3H, s), 4·8—4·6 (1H, m), and methylene and methyl signals (Found: C, 82·9; H, 10·9. $C_{35}H_{54}O_2$ requires C, 82·9; H, 10·7%).

Anisyl cholesteryl ether (10 g) was treated with trityl tetrafluoroborate (10 g) in dichloromethane (5 ml). After 30 s work-up in the usual way gave cholesterol (75—85% by g.l.c.).

Cholesteryl 4-methoxy-3,5-dimethylbenzyl ether. Cholesterol (2·5 g) in dry benzene (50 ml) was treated with sodium hydride (1 g) and 4-methoxy-3,5-dimethylbenzyl bromide [51] (1 g). The mixture was heated at reflux for 15 h, cooled to room temperature, and filtered. The filtrate was evaporated and the residue chromatographed over silica gel [acetone–light petroleum (5 : 95)] to give the *ether* (1·5 g), m.p. (from methanol–light petroleum) 130°, $[\alpha]_D^{18}$ −21·6° (*c* 0·83), $\nu_{max.}$ 1220, 1140, and 1030 cm^{-1}, τ 3·17 (2H, s), 4·88—4·72 (1H, m), 5·7 (2H, s), 6·43 (3H, s), 7·48 (6H, s), and methylene and methyl signals (Found: C, 83·1; H, 10·8. $C_{37}H_{58}O_2$ requires C, 83·1; H, 10·9%).

4-Methoxy-3,5-dimethylbenzyl cholesteryl ether (1 mmol) was treated with trityl tetrafluoroborate (2 mmol) in dichloromethane (15 ml) for 5 min. Work-up in the usual way gave cholesterol (85—90% by g.l.c.).

Reaction of cholesterol with trityl tetrafluoroborate. Cholesterol (1 mmol) was treated with trityl tetrafluoroborate (2 mmol) in dichloromethane (30 ml) for 6 h. Work-up in the usual way with chromatography over silica gel [with acetone–light petroleum (1 : 4)] gave cholest-4-enone (50%) m.p. and mixed m.p. 81°.

Benzyloxycarbonyl Groups (*Table* 2).—Cholesteryl chloroformate was prepared by the method of Wieland; [52] m.p. 118°, $\nu_{max.}$ 1762 cm^{-1}.

Benzyloxycarbonylcholesterol. Cholesterol (2 g) in dry dioxan (20 ml) was treated with sodium hydride (1 g) followed by benzyl chloroformate (2 g). The mixture was stirred for 3 h, filtered, and evaporated. Chromatography of the residue over neutral alumina (G3) (with light petroleum) gave *benzyloxycarbonylcholesterol* (80%), m.p. (from methanol–dichloromethane) 110°, $[\alpha]_D^{22}$ −24·6° (*c* 1·6), $\nu_{max.}$ 1725, 1265, and 1250 cm^{-1}, τ 2·7 (5H, s), 4·75—4·58 (1H, m), 4·89 (2H, s), and methylene and methyl signals (Found: C, 80·6; H, 10·0. $C_{35}H_{52}O_3$ requires C, 80·7; H, 10·1%).

Benzyloxycarbonylcholesterol (1 mmol) was treated with trityl tetrafluoroborate (2 mmol) in dichloromethane (20 ml). After 24 h only starting material was present.

p-*Methoxybenzyloxycarbonylcholesterol.* Anisyl alcohol (1·4 g) and sodium hydride (0·5 g) in dry benzene (50 ml) were treated with cholesteryl chloroformate (4·5 g) for 15 h at room temperature. The mixture was filtered and the filtrate evaporated. The residue was chromatographed over silica gel [with acetone–light petroleum (1 : 4)] to give p-*methoxybenzyloxycarbonylcholesterol* (80%), m.p. (from methanol–dichloromethane) 124°, $[\alpha]_D^{22}$ −22·3° (*c* 1·49), $\nu_{max.}$ 1725, 1520, 1280, and 1260 cm^{-1}, 2·63—3·22 (4H, A_2B_2), 4·67—4·52 (1H, m), 4·92 (2H, s), 6·2 (3H, s), and methylene and methyl signals (Found: C, 78·3; H, 9·8. $C_{36}H_{54}O_4$ requires C, 78·5; H, 9·9%).

Reaction of p-*methoxybenzyloxycarbonylcholesterol with trityl tetrafluoroborate.* *p*-Methoxybenzyloxycarbonylcholesterol (1 mmol) was treated with trityl tetrafluoroborate (2 mmol) in dichloromethane (15 ml) for 4—5 min. Work-up in the usual way gave cholesterol (60—80% by g.l.c.). Conducting the reaction at 0° gave cholesterol (6 min; 90% by g.l.c.).

3,4-*Dimethoxybenzyloxycarbonylcholesterol.* Veratryl alcohol (1·7 g) in dry benzene (50 ml) was treated with sodium hydride (0·5 g) and cholesteryl chloroformate (4·5 g) and the mixture was stirred for 15 h. Work-up in the usual way gave 3,4-*dimethoxybenzyloxycarbonylcholesterol* (80%), m.p. (from methanol–dichloromethane) 113—114°, $[\alpha]_D^{22}$ −22·2° (*c* 0·68), $\nu_{max.}$ 1725, 1265, 1240, and 1160 cm^{-1}, τ 3·17—3·12 (3H, d), 4·7—4·6 (1H, m), 4·92 (2H, s), 6·1 (6H, s), and methylene and methyl signals (Found: C, 76·8; H, 9·9. $C_{37}H_{56}O_5$ requires C, 76·5; H, 9·7%).

Reaction of 3,4-*dimethoxybenzyloxycarbonylcholesterol with trityl tetrafluoroborate.* 3,4-Dimethoxybenzyloxycarbonylcholesterol (1 mmol) was treated with trityl tetrafluoroborate (2 mmol) in the standard manner. After 1·5—2·0 min, work-up in the usual way gave cholesterol (90% by g.l.c.). Conducting the reaction at 0° consumed the starting material after 12—15 min (90% yield), and at −20° it took 2 h for complete reaction.

4-*Methoxy*-3,5-*dimethylbenzyloxycarbonylcholesterol.* 4-Methoxy-3,5-dimethylbenzyl alcohol (1·7 g) and cholesteryl chloroformate (450 mg) in dry benzene (20 ml) were left for 15 h at room temperature. The mixture was worked

[46] F. Suitenis, *Annalen*, 1872, **161**, 329.
[47] S. Cannizzaro, *Annalen*, 1866, **137**, 244.
[48] G. Kumpf, *Annalen*, 1884, **224**, 96.
[49] G. M. Bennett and G. H. Willis, *J. Chem. Soc.*, 1928, 2306.
[50] J. H. Beynon, I. M. Heilbron, and F. S. Spring, *J. Chem. Soc.*, 1936, 967.
[51] E. Bamberger, *Ber.*, 1913, **36**, 2000.
[52] H. Wieland, *Z. physiol. Chem.*, 1923, **130**, 326.

up in the usual way to give 4-*methoxy*-3,5-*dimethylbenzyloxycarbonylcholesterol* (350 mg), m.p. (from methanol–dichloromethane) 115°, $[\alpha]_D^{22}$ −22·4° (*c* 0·94), $\nu_{max.}$ 1740, 1260, 1250, and 1140 cm^{-1}, τ 2·8 (2H, s), 4·72—4·54 (1H, m), 4·99 (2H, s), 6·3 (3H, s), 7·73 (6H, s), and methylene and methyl signals (Found: C, 78·8; H, 10·3. $C_{38}H_{58}O_4$ requires C, 78·8; H, 10·1%).

Reaction of 4-*methoxy*-3,5-*dimethylbenzyloxycarbonylcholesterol with trityl tetrafluoroborate.* 4-Methoxy-3,5-dimethylbenzyloxycarbonylcholesterol (1 mmol) was treated with trityl tetrafluoroborate (2 mmol) in dichloromethane (10 ml) in the standard manner. Work-up after 16 min gave cholesterol (80% by g.l.c.).

3,4,5-*Trimethoxybenzyloxycarbonylcholesterol.* 3,4,5-Trimethoxybenzyl alcohol (200 mg) was treated with sodium hydride (200 mg) and cholesteryl chloroformate (450 mg) in dry benzene (50 ml) at room temperature for 15 h. Work-up in the usual way gave 3,4,5-*trimethoxybenzyloxycarbonylcholesterol* (300 mg), m.p. (from methanol–dichloromethane) 104—105°, $[\alpha]_D^{22}$ −21·4° (*c* 1·3), $\nu_{max.}$ 1730, 1690, and 1150 cm^{-1}, τ 3·5 (2H, s), 4·8—4·6 (1H, m), 5·0 (2H, s), 6·17 (9H, s), and methylene and methyl signals (Found: C, 74·9; H, 9·5. $C_{38}H_{58}O_6$ requires C, 74·7; H, 9·6%).

Reaction of 3,4,5-*trimethoxybenzyloxycarbonylcholesterol with trityl tetrafluoroborate.* 3,4,5-Trimethoxybenzyloxycarbonylcholesterol (1 mmol) was treated with trityl tetrafluoroborate (2 mmol) in dichloromethane (20 ml) for 1 h. Work-up in the usual way gave cholesterol (70% by g.l.c.).

We thank Professor L. N. Owen for advice and for samples of xylitol penta-acetate, 1,2-*O*-isopropylidene-D-glucofuranose, and other carbohydrates, and Dr. George Rosenkranz for an authentic specimen of kryptogenin. We are grateful to the Schering Corporation (U.S.A.) for supplies of steroids.

[1/1836 *Received*, 8*th October*, 1971]