# Oxidation of Ketone Acetals by Hydride Transfer

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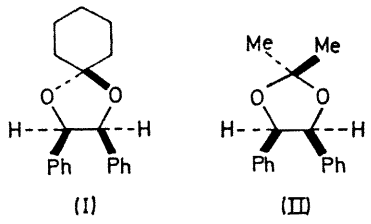
*Summary* Trityl fluoroborate is a useful reagent for the deacetalisation of ketone acetals, the glycol function being thereby smoothly oxidised to an α-ketol; the reaction has synthetic application especially in carbohydrate chemistry.

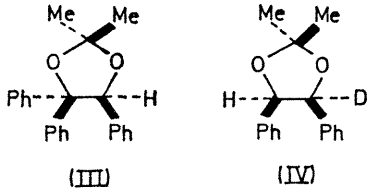
TRITYL carbonium ion is well documented[1] as a hydride ion acceptor and has found preparative use as in the dehydrogenation of cycloheptatriene to the tropylium ion.[2] Recently tertiary methylamines have been dehydrogenated to methyleneimmonium salts using trityl perchlorate.[3] It is also known that aldehyde acetals reduce the trityl carbonium ion by an intermolecular hydride process.[4] A similar reaction with ketone acetals has hitherto not been suspected.

Treatment of cyclohexanone ethylene acetal with trityl fluoroborate[5] in dichloromethane at room temperature followed by aqueous work up gave cyclohexanone (80%), and tritylmethane (100%). The ethylene acetal of benzophenone, on treatment with trityl fluoroborate, gave benzophenone (100%) and tritylmethane (100%). Cholestanone ethylene acetal gave cholestanone (80%) in 15 min and similarly 11α-hydroxyprogesterone bis(ethylene acetal)[6] gave 11α-hydroxyprogesterone (60%) when treated with trityl fluoroborate. To establish the nature of the oxidised ethylene glycol moiety the acetal (I) was prepared by transacetalisation with cyclohexanone ethylene dithioacetal and *meso*-dihydrobenzoin.[7-9] Treatment of the acetal (I) with trityl fluoroborate (3 h) gave cyclohexanone and benzoin (64%). Similarly the acetonide (II) gave

benzoin in good (65%) yield. The methyl groups in (II) appear at $\tau$ 8·75 and 8·56 as singlets. When the oxidation of compound (II) was carried out in an n.m.r. tube the methyl signals of (II) coalesced to a singlet (6H) at $\tau$ 8·25.



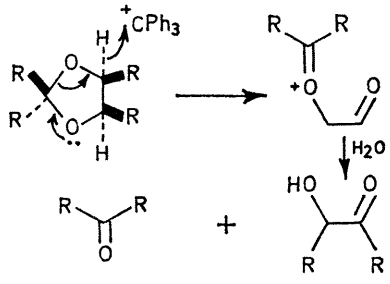
(I) (II)



(III) (IV)

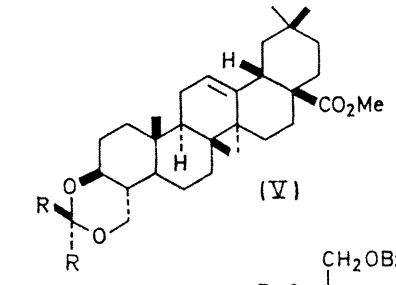
indicative of a symmetrical species. The acetonide (III) upon treatment with trityl fluoroborate (4 h), gave α-hydroxy-αα-diphenylacetophenone[10] (40%). Oxidation of the dioxolan (IV) with trityl fluoroborate gave benzoin and triphenylmethane. The $k_H/k_D$ ratio for this reaction was calculated as 4·2 and 4·9 for the benzoin and for the triphenylmethane respectively (analysed by mass spectrometry).

The ethylene dithioacetal of benzophenone was found to be inert to trityl fluoroborate, whereas the ethylene hemithioacetal gave benzophenone (100%). Presumably the thiocarbonyl group is of too high energy relative to the carbonyl group to be formed (see later).

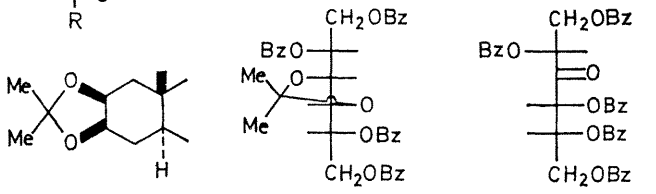


These results are explained by a mechanism involving a rate-determining hydride abstraction from the ethylene acetal with concerted formation of an oxonium ion (when the reaction is followed by i.r., a carbonyl absorption develops at 1700 $cm^{-1}$ before aqueous work-up). This ion is quenched by the aqueous work-up to give the observed products. Reduction of the oxonium ion with $NaBH_4$ gave the starting ethylene acetal as the only product. The concerted nature of the process is shown by the fact that ordinary ethers are dehydrogenated by trityl carbonium ion very much more slowly than acetals.

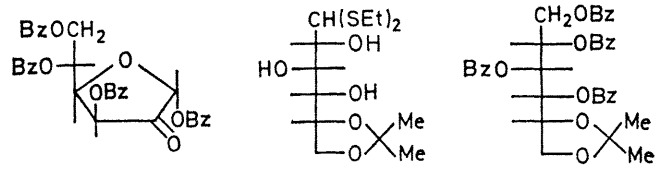
The acetonide (V; R = Me) of methyl hederagenin[11,12] was treated with trityl fluoroborate (18 h) to give methyl hederagonate (VI) (20%). Similarly the acetal (V; R=Ph) gave the ketone (VI) (20%). The structure of (VI) was substantiated by its retro-aldol transformation to methyl hederagonate.[12]



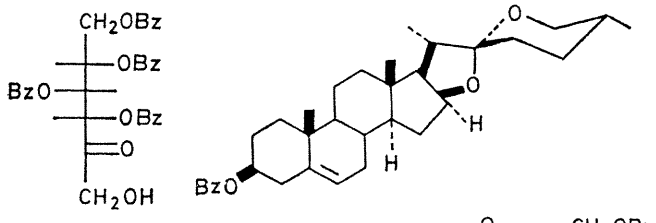
(V) (VI)



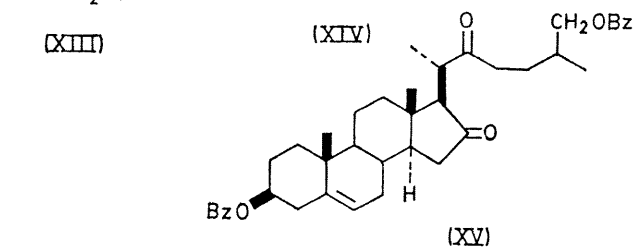
(VII) (VIII) (IX)



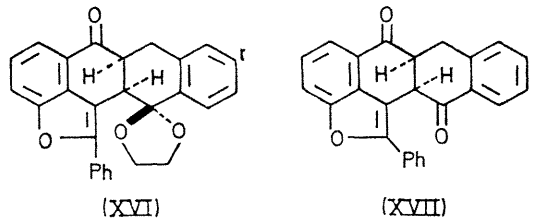
(X) (XI) (XII)



(XIII) (XIV)



(XV)



(XVI) (XVII)

Cholest-2-ene was converted into the 2β,3β-diol.[14] The derived acetonide (VII) gave 3β-hydroxycholestan-2-one[15] (79%) on treatment with trityl fluoroborate (4 h).

D-Mannitol was converted by standard procedures[16] into the 3,4-acetonide and benzoylated to give the ester (VIII). Treatment of (VIII) with trityl fluoroborate (0·5 h) followed by benzoylation gave the ketone (IX) (67%). Similarly

1,2-*O*-isopropylidene-D-glucofuranose[17] was benzoylated and on oxidation with trityl fluoroborate followed by benzoylation gave the ketone (X) (27%). 1,2,3,4-Tetra-*O*-benzoyl-5,6-*O*-isopropylidene-D-glucitol (XII) was prepared from D-glucose *via* 5,6-*O*-isopropylidene-D-glucose diethyl dithioacetal (XI).[18] Benzoylation of (XI) followed by treatment with mercuric chloride–mercuric oxide in aqueous acetone, reduction ($NaBH_4$),[19,20] and benzoylation gave the ester (XII). Reaction of (XII) with trityl fluoroborate (48 h) gave 3,4,5,6-tetra-*O*-benzoyl-L-sorbose (XIII). Its structure was confirmed by periodate oxidation followed by diborane reduction and benzoylation to xylitol pentabenzoate (authentic sample prepared from xylitol pentaacetate).† This process represents a partial synthesis of sorbose and hence of vitamin C which is not dependent on a microbiological transformation.[21]

Treatment of diosgenin benzoate (XIV) with trityl fluoroborate gave, after benzoylation, kryptogenin dibenzoate (XV) (35%), identical† with an authentic sample.[22]

These results illustrate a useful method of oxidising a diol, protected against the usual electron removal reagents, as an acetonide or other acetal.

This oxidative deacetalisation was discovered in our attempt to convert the tetracyclic compound (XVI) to the diketone (XVII), a transformation required in our tetracycline work.[23] Treatment of (XVI) with trityl fluoroborate gave the diketone (XVII) (65%). Conventional deacetalisation procedures (aqueous acid) gave low yields of (XVII) (<10%).

All new compounds gave satisfactory spectral and microanalytical data. Yields refer to pure, crystalline products. The structures of compounds (IX), (X), and (XIII) were also established as follows: compound (IX) by i.r., n.m.r., mass spectrum, microanalysis and method of synthesis (symmetrical precursor), compound (X) by i.r. (no lactone band), n.m.r., mass spectrum and microanalysis, and compound (XIII) by i.r., n.m.r. (no aldehyde proton), mass spectrum, microanalysis and structure of precursor.

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[1] C. D. Nenitzescu, 'Carbonium Ions', eds G. A. Olah and P. von R. Schleyer, Wiley-Interscience, 1970, vol. 2, p. 484.
[2] H. J. Dauben, Jun., F. A. Gadecki, K. M. Harman, and D. L. Pearson, *J. Amer. Chem. Soc.*, 1957, **79**, 4557.
[3] H. Volz and H. H. Kiltz, *Tetrahedron Letters*, 1970, 1917.
[4] H. Meerwein, V. Hederick, H. Morschel, and K. Wunderlich, *Annalen*, 1960, **635**, 1.
[5] H. J. Dauben, Jun., L. R. Honnen, and K. M. Harmon, *J. Org. Chem.*, 1960, **25**, 1442.
[6] G. Cooley, B. Ellis, and D. Kirk, *J. Chem. Soc.*, 1957, 4112.
[7] L. F. Fieser, *J. Chem. Educ.*, 1954, **31**, 291.
[8] D. L. MacDonnald and H. G. Fletcher, *J. Amer. Chem. Soc.*, 1959, **81**, 3719.
[9] H. A. Campbell and K. P. Link, *J. Biol. Chem.*, 1938, **122**, 635.
[10] Y. Iskander, Y. Riad, and R. Tewfik, *J. Chem. Soc.*, 1962, 3232.
[11] W. A. Jacobs, *J. Biol. Chem.*, 1925, **63**, 631.
[12] D. H. R. Barton and P. de Mayo, *J. Chem. Soc.*, 1954, 887.
[13] L. F. Fieser, *J. Amer. Chem. Soc.*, 1954, **76**, 1945.
[14] P. S. Ellington, D. G. Hey, and G. D. Meakins, *J. Chem. Soc.*, 1966, 1327.
[15] J. C. Sheehan and W. F. Erman, *J. Amer. Chem. Soc.*, 1957, **79**, 6050.
[16] H. O. L. Fischer and H. Appel, *Helv. Chim. Acta*, 1934, **17**, 1574.
[17] W. N. Haworth, and C. R. Porter, *J. Chem. Soc.*, 1929, 2796.
[18] P. A. J. Gormin, *Canad. J. Chem.*, 1965, **43**, 2078.
[19] N. L. Wolfrom, *J. Amer. Chem. Soc.*, 1929, **51**, 2188.
[20] J. English, Jun., and P. H. Cariswold, Jun., *J. Amer. Chem. Soc.*, 1945, **67**, 2039.
[21] (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. Grüssner, and R. Oppenauer, *Helv. Chim. Acta*, 1934, **17**, 311, 510.
[22] G. Rosenkranz, S. T. Kaufmann, A. Landa, J. J. Corona, and A. Olalde, *J. Amer. Chem. Soc.*, 1948, **70**, 3518.
[23] D. H. R. Barton, D. L. J. Clive, P. D. Magnus, and G. Smith, *J. Chem. Soc.* (*C*), 1971, 2193.