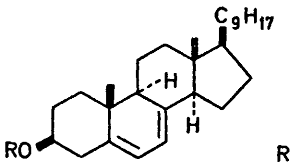
An Unusual Synthesis of Ergosterol Acetate Peroxide

By D. H. R. Barton,* G. Leclerc, P. D. Magnus, and I. D. Menzies
(*Chemistry Department, Imperial College, South Kensington, London* S.W.7)

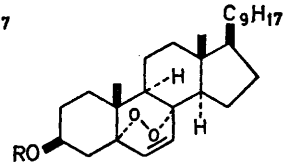
Summary Trityl tetrafluoroborate and tris-(*p*-bromophenyl)aminium cation-radical are exceptionally effective catalysts for oxygenation of ergosteryl acetate (I; R=Ac) to the peroxide (II; R=Ac); the trityl cation catalysed reaction is a photo-oxygenation, whilst the aminium cation-radical catalysed reaction is thermal.

During studies related to the use of trityl cation for the deprotection of masked steroidal alcohols[1] we treated ergosterol acetate with trityl tetrafluoroborate (0·3 equiv.) in dichloromethane without precautions to exclude oxygen. At −78 °C the peroxide[2] (II; R=Ac) was formed in quantitative yield. Ergosteryl benzoate (I; R=Bz) similarly gave the benzoate (II; R=Bz).

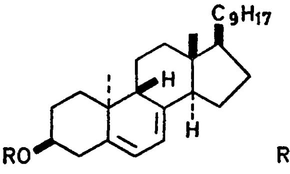
Further investigation showed that the acetate (I; R=Ac) (100 mg) in dry dichloromethane with a catalytic amount (10 mg) of trityl tetrafluoroborate at −78 °C with exposure to air and laboratory lighting gave the peroxide (II; R=Ac) quantitatively in 2·75 h. Irradiation of the above system with a tungsten lamp (500 W) gave the peroxide (II; R=Ac) in 30 min. Under pure oxygen (1·03 mol uptake) peroxide (II; R=Ac) formation was complete in 10 min at −78 °C, even on a preparative scale (>1 g). The trityl cation was isolated as tritylmethanol (86%) from aqueous work-up. Photo-oxygenation at −15 °C, 0 °C, or room temperature did not give clean reactions. Only at −15 °C was the peroxide formed in good yield.



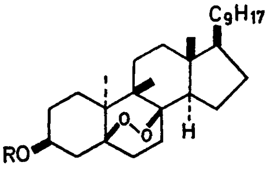
(I)



(II)



(III)



(IV)

$Ph_3C{-}N{=}N{-}CPh_3$

(V)

$X^-\dot{N}^+(C_6H_4Br\text{-}p)_3$

(VI)

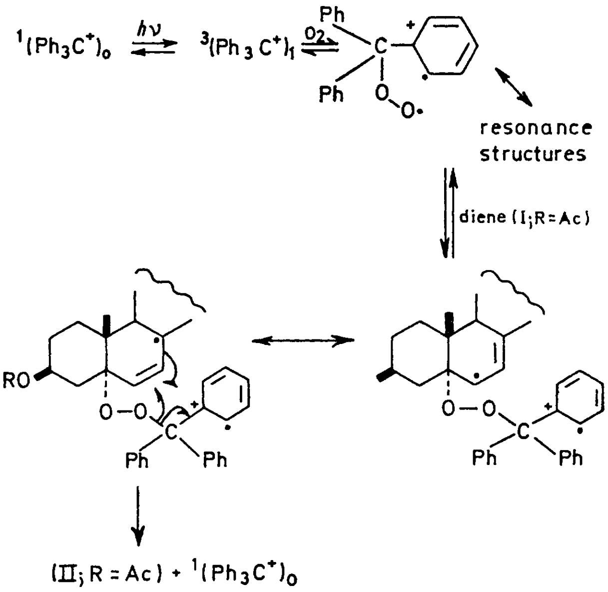
When trityl cation in dichloromethane at −78 °C in the presence of oxygen was irradiated (tungsten lamp) in the absence of ergosteryl acetate, no oxygen was consumed (*cf.* ref. 3).

TABLE

Substrate	Conditions	Time of oxygenation	Product (% yield)
(I; R=Ac)	Substrate (100 mg)/$Ph_3C^+BF_4^-$ (10 mg) CH_2Cl_2/−78 °C, O_2	2 min	(II; R=Ac) (100%)
(III; R=Ac)	Substrate (100 mg)/$Ph_3C^+BF_4^-$ (10 mg) CH_2Cl_2/−78 °C, O_2	10 h	5% conversion into (IV; R=Ac)
(I; R=Ac)	Substrate (50 mg)/Eosin (10·5 mg) $PhCN/CH_2Cl_2$(2:1), −15 °C, O_2	30 min	(II; R=Ac) (>95%)
(III; R=Ac)	Substrate (50 mg)/Eosin (10·5 mg) $PhCN/CH_2Cl_2$(2:1), −15 °C, O_2	100 min	(IV; R=Ac) (>95%)

To compare conventional singlet oxygen photo-oxygenation[4] and the trityl cation system the experiments summarised in the Table were carried out. The rate ratio k(I; R=Ac)/k(III; R=Ac) was *ca.* 6000 for the trityl system whereas the ratio for the eosin system was *ca.* 3·3. This dramatic difference in relative reactivity appears to discount the trityl cation acting merely as a triplet to singlet oxygen sensitiser.

Ergosteryl acetate in dichloromethane (−78 °C) containing trityl tetrafluoroborate was oxygenated in the light (tungsten lamp). The formation of the peroxide (II; R=Ac) terminated at once in darkness but resumed on irradiation. This would appear to invalidate a photochemically initiated radical chain mechanism. Oxygenation of (I; R=Ac) with trityl tetrafluoroborate *in the dark* proceeded if diphenylpicrylhydrazyl was present in slightly greater amounts than trityl tetrafluoroborate to give the peroxide (II; R=Ac) quantitatively. Oxygenation of (I; R=Ac) with diphenylpicrylhydrazyl in the dark gave *no* peroxide (II; R=Ac).



SCHEME

Hydrazotriphenylmethane[5] on treatment with bromine at −78 °C gave azotriphenylmethane (V) which decomposed to nitrogen and triphenylmethyl radicals at −20 °C. Azotriphenylmethane (V) in dichloromethane at −78 °C with ergosteryl acetate (I; R=Ac) was oxygenated under irradiation. Warming the mixture to −15 °C gave no peroxide (II; R=Ac), only triphenylmethyl peroxide.[6] Trityl radicals are not, therefore, the catalytic oxygenation species.

Tris-(*p*-bromophenyl)aminium hexachloroantimonate[7] (VI; X=$SbCl_6$) catalysed the formation of ergosterol acetate peroxide (II; R=Ac) *in the dark* at −78 °C. Indeed, tris-(*p*-bromophenyl)aminium fluoroborate† (VI; X=BF_4) (10 mg) in dichloromethane catalysed the oxygenation of ergosteryl acetate (I; R=Ac) (100 mg) in a *dark* reaction to give quantitatively the peroxide (II; R=Ac) (5 min). Higher temperatures did not give clean products. Lumisteryl acetate (III; R=Ac) did not react under these conditions either at −78 °C or at room temperature.

To explain these reactions we discount singlet oxygen because of the comparative rate data (Table). In the dark

---

† Prepared from tribromotriphenylamine, silver tetrafluoroborate, and iodine at −30 °C.[7] All new compounds were characterised by the usual spectroscopic techniques and microanalysis.

reactions there would appear to be no way in which singlet oxygen could be generated.

The Scheme shows a possible mechanism for trityl tetrafluoroborate catalysed photo-oxygenation.

The dark reaction with the aminium cation-radical follows a similar course, a reversible adduct with oxygen being postulated. There is the alternative that the aminium cation-radical oxidises the diene to a cation-radical (in the manner suggested for the reaction with certain styrenes),[7] which then proceeds to the peroxide (II; R=Ac). But this would not explain why lumisteryl acetate (III; R=Ac) gives only very slow reactions. A bulky oxygen delivering species $(Ar_3NO_2)^{+\cdot}$ might impart the observed selectivity.

α-Terpinene on exposure to oxygen–trityl cation in dichloromethane at −78 °C gave rapidly ascaridole[8] in high yield. Similar treatment of tetraphenylfuran gave quantitatively *cis*-dibenzoyldiphenylethylene.[9]

These experiments demonstrate a previously unknown reaction, namely the insertion of triplet oxygen into certain dienes under exceptionally mild conditions, in excellent yields.

(*Received*, 3*rd February* 1972; *Com.* 165.)

---

[1] D. H. R. Barton, P. D. Magnus, G. Smith, and D. Zurr, *Chem. Comm.*, 1971, 861; D. H. R. Barton, P. D. Magnus, G. Streckert, and D. Zurr, *ibid.*, p. 1109; D. H. R. Barton, P. D. Magnus, G. Smith, G. Streckert, and D. Zurr, *J.C.S. Perkin I*, 1972, 542.

[2] V. Prelog and P. Wieland, *Helv. Chim. Acta*, 1947, **30**, 1028.

[3] E. E. van Tamelen and T. M. Cole, jun., *J. Amer. Chem. Soc.*, 1971, **93**, 6158; D. M. Allen and E. D. Owen, *Chem. Comm.*, 1971, 848.

[4] K. Gollnick and G. O. Schenk, 'Oxygen as a Dienophile', in 1,4-Cycloaddition Reactions: The Diels–Alder Reaction in Heterocyclic Syntheses, ed. J. Hamer, Academic Press, New York, 1967, p. 255; C. S. Foote, *Accounts Chem. Res.*, 1968, **1**, 104; D. R. Kearns, *Chem. Rev.*, 1971, **71**, 395; K. Gollnick, *Adv. Photochem.*, 1968, **6**, 1.

[5] H. Wieland, *Ber.*, 1909, **42**, 3020.

[6] M. Gomberg, *Ber.*, 1900, **33**, 3150; *Chem. Rev.*, 1924. **1**, 91.

[7] F. A. Bell, A. Ledwith, and D. C. Sherrington, *J. Chem. Soc.(C)*, 1969, 2719.

[8] G. O. Schenk and K. Ziegler, *Naturwiss.*, 1944, **32**, 157.

[9] G. O. Schenk, *Z. Electrochem.*, 1960, **64**, 997.