Lewis Acid Catalysed Oxygenation of Ergosteryl Acetate by Triplet Oxygen

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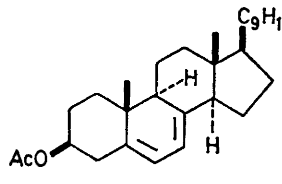
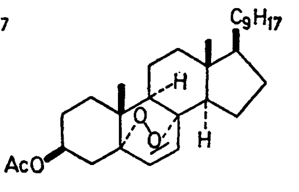
Summary Ergosteryl acetate can be converted into its peroxide by triplet oxygen in the presence of Lewis acids; mechanistic aspects have been discussed.

Previously[1,2] we have reported catalytic systems for the addition of triplet oxygen to cisoid 1,4-dienes. It has been suggested (by R. K. H.) that since cationic complexing of the diene was important, simple Lewis acids might also be effective catalysts and our results show this to be correct (Table).

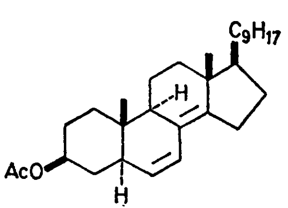
The systems using ferric chloride (as the etherate, acetonate or phosphorus oxychloride adduct), ferric bromide, molybdenum pentachloride, vanadium oxychloride, and tungsten hexachloride do not require irradiation. Diphenyl picrylhydrazyl (DPPH) which alone gives no peroxide,[2] induces a dark oxygenation with aluminium chloride–nitromethane, or stannic chloride. Antimony pentachloride is an oxygenation catalyst in the dark in the presence of certain polycyclic aromatic hydrocarbons. It is known that antimony pentachloride reacts with these particular hydrocarbons to give the corresponding radical cations.[3] Lumisteryl acetate is not converted to the corresponding *endo*-peroxide under any of the most favourable conditions in the Table. Indeed, competitive experiments with mixtures of ergosteryl and lumisteryl acetates showed complete conversion of the former to peroxide without any attack on the latter. This would appear to exclude any singlet oxygenation process.



(1)



(2)



(3)

Table

Lewis acid catalysts for the conversion of ergosterol (**1**) into its peroxide (**2**) [50 mg (**1**) and CH_2Cl_2 (25 ml) under O_2 at −78°]. Where illumination was used ($h\nu$) no oxygenation occurred in the dark. All irradiations were using a tungsten lamp.

Catalyst (equiv.)	Conditions (time/min)	Yield (%)[a] (**1**)	(**2**)	(**3**)
BF_3[b]	$h\nu$, (60)	10	90	
BCl_3 (0·2)	$h\nu$, (60)	30	70	
BBr_3 (0·2)	$h\nu$, (60)	10	65	25
$AlCl_3$ (0·2) CH_3NO_2 (0·22)	$h\nu$, (60)		*70*	
$AlCl_3$ (1·2) CH_3NO_2 (1·32)	$h\nu$, (60)	7	93	
$AlCl_3$ (0·2) CH_3NO_2 (0·22) DPPH (0·2)	dark, (20)		*95*	
$SnCl_4$ (0·2)	$h\nu$, (60)	4	*78*	4[d]
$SnCl_4$ $(1·2)_4$	$h\nu$, (5)	6[d]	*67*	5[d]
$SnCl_4$ (0·2), DPPH (0·22)	dark, (90)		*96*	
$VOCl_3$ (0·2)	dark, (60)		95[c,d]	
SbF_5 (0·2)	$h\nu$, (60)	3	97	
$SbCl_5$ (0·2)	$h\nu$, (60)	14	86[c]	
$SbCl_5$ (0·2) anthracene (0·2)[e]	dark, (5)	10	90	
$MoCl_5$ (0·2)	dark, (60)	3[c,d]	95	
WF_6 (0·2)	$h\nu$, (60)	5	95	
WCl_6 (0·2)	dark, (20)	5[c,d]	95	
$FeCl_3$ (0·7 suspension)	dark, (240)	10	90	
$FeCl_3$ (0·2) Et_2O or Acetone or $POCl_3$ (0·22)	dark, (60)	20	*76*	
$FeBr_3$ (0·2)	dark, (120)	10	90	
$FeBr_3$ (0·2), Et_2O (0·3)	dark, (120)	5	95	
Iodine (0·2)	$h\nu$, (30)		*90*	

[a] Estimated spectrophotometrically; italic figures are isolated yields. [b] BF_3 passed over solution until development of orange colour. [c] T.l.c. indicates small quantities of other materials. [d] Other products with λ_{max} ~ 275 nm also present in small quantities. [e] The same results were obtained using 9,10-diphenylanthracene and pyrene.

Although it would be premature to give a precise mechanism for these oxygenation reactions, the results of this and previous work[1,2] show that all effective catalysts are electrophilic in character and capable of forming a complex with a diene. For the dark reactions the electrophilic species must either be paramagnetic, or a suitable radical must be added to the electrophilic species. Cations which are not paramagnetic and radicals which are not (sufficiently electrophilic) cation radicals are ineffective (Scheme).

(a) Diene + Electrophilic (paramagnetic) species $\rightleftharpoons$ Complex A
Complex A + $^3O_2 \longrightarrow$ Complex A.$O_2 \longrightarrow$ Peroxide + Electrophilic (paramagnetic) species

(b) Diene + Electrophilic (diamagnetic) species $\rightleftharpoons$ Complex B
Complex B + Radical $\rightleftharpoons$ Complex B′
Complex B′ + $^3O_2 \longrightarrow$ Complex B′.$O_2 \longrightarrow$ Peroxide + Electrophilic (diamagnetic) species + Radical

(c) Diene + Electrophilic (diamagnetic) species $\rightleftharpoons$ Complex B $\xrightarrow{h\nu}$ Complex C (triplet) + $^3O_2 \longrightarrow$ Complex C.$O_2 \longrightarrow$ Peroxide + Electrophilic species

SCHEME

In route (a) the paramagnetic electrophilic species provides the mechanism for spin inversion by the exchange that we proposed earlier.[2] Similarly in route (b) the inversion process is made possible by the complex radical (Complex B′) and in route (c) by the triplet state (Complex C). In no case is singlet oxygen involved.

There are two compounds, $VOCl_3$ and WCl_6, which are exceptions to the above since both are diamagnetic. Both these compounds are very easily reduced to lower valent paramagnetic species and we suggest that this explains their catalytic activity in the dark.

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[1] D. H. R. Barton, R. K. Haynes, P. D. Magnus, and I. D. Menzies, unpublished observation.

[2] D. H. R. Barton, G. Leclerc, P. D. Magnus, and I. D. Menzies, *J.C.S. Chem. Comm.*, 1972, 447.

[3] D. W. Howarth and C. K. Fraenkel, *J. Chem. Phys.*, 1970, **52**, 6258, and references therein.