Catalysis of Ene Reactions by Lithium Perchlorate

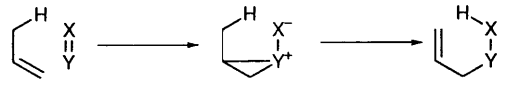
Alwyn G. Davies* and Wojciech J. Kinart
Chemistry Department, University College London, 20 Gordon Street, London, UK WC1H 0AJ

The ene reaction of some allylic hydrocarbons, and the metallo-ene reaction of some allyltin compounds, with 1,3,4-triazoline-2,5-diones or with diethyl azodicarboxylate as enophiles, in diethyl ether are strongly catalysed by lithium perchlorate. Azobenzene, on the other hand, reacts slowly with alkyltin compounds, undergoing hydrostannation. The reaction of cholesterol or of tributylallyltin with singlet oxygen is subject to a smaller catalysis.

A number of reactions have recently been shown to be surprisingly susceptible to catalysis by lithium perchlorate (typically 5 mol dm^{-3} in ether).[1,2] These include the rearrangement of allyl vinyl ethers[2] and of allyl stannanes,[3] Diels–Alder reactions,[4] the conjugate addition of silyl ketene acetals to α,β-unsaturated carbonyl compounds,[5] and the addition of allylstannanes to aldehydes.[6]

No clear picture of the mechanism of this catalysis has yet emerged, and it has variously been ascribed to a Lewis acid effect, to the ionic stabilisation of polar transition states, or to internal pressure created by the lipophobic medium.

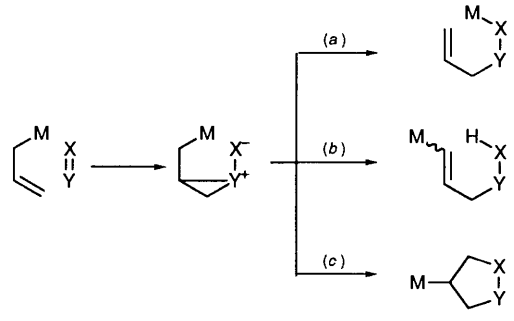
We have been interested in the hydrogen-ene reaction[7] (Scheme 1), and its organometallic equivalent, the metalloene



Scheme 1

reaction[8] [Scheme 2(*a*)], particularly when the (homopolar) enophile (X=Y) is singlet oxygen (O=O) or an azo compound (RN=NR). There is good evidence from stereochemical and hydrogen isotope studies that the hydrogen-ene reaction proceeds through an intermediate ene-enophile complex, which then undergoes internal hydrogen transfer.[9]

It is assumed that a similar complex is formed with allylmetallic compounds.[8] The reaction is then completed by transfer of the metal [Scheme 2(*a*)], but transfer of hydrogen [Scheme 2(*b*)], and migration of the metal to the central allylic carbon atom accompanied by ring closure [Scheme 2(*c*)] may compete.

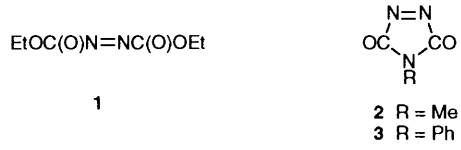


Scheme 2

Results

We now report the effect of lithium perchlorate on the reaction of allyl-hydrogen and allyl-tin enes with azo compounds and singlet oxygen as enophiles.

The reactions involving azo compounds were carried out with



1

2 R = Me
3 R = Ph

diethyl azodicarboxylate (**1**), *N*-methyltriazolinedione (**2**), *N*-phenyltriazolinedione (**3**), and azobenzene. The reactions can be followed visually by the fading of the red colour of the azo compound. The products were isolated and identified; compounds containing Sn–N bonds underwent hydrolysis during work-up, and were characterised as the corresponding protic compounds. The triazolinediones and the azodicarboxylate gave only hydrogen-ene products (Scheme 1) with the allylic hydrocarbons, and only metalloene products [Scheme 2(*a*)] with tributyl- and triphenyl-allyltin. The reactions were markedly accelerated by $LiClO_4$; the products, conditions, and times for complete reaction, are given in Table 1.

Azobenzene does not normally undergo a hydrogen-ene reaction, but we thought it possible that it might give a metalloene reaction with the more reactive allyltin compounds. A slow reaction did indeed occur between tributylallyltin and azobenzene in ether, but it took a surprising different course, and after 1 week, hydrazobenzene was isolated in 15% yield. If 5 mol dm^{-3} $LiClO_4$ was present, the yield was little changed (20%).

It appeared that the reaction was analogous to that which we observed some years ago between alkylboranes and azo-compounds,[10] and involved the butyl rather than the allyl group (Scheme 3); the stannylhydrazine would undergo hydrolysis during the isolation procedure.

$$CH_3CH_2CH_2CH_2SnR_3 + PhN{=}NPh \longrightarrow CH_3CH_2CH{=}CH_2 + PhNHN(SnR_3)Ph$$

Scheme 3

Tetrabutyltin, tributyltin chloride, dibutyltin dichloride, and butyltin trichloride were therefore treated with azobenzene under the same conditions, and in each case, after one week, hydrazobenzene was obtained in about 20% yield.

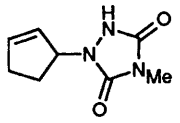
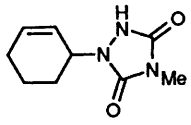
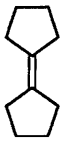
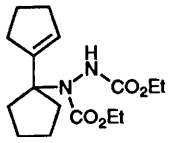
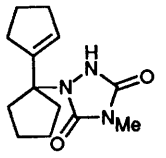
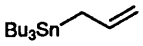
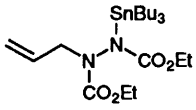
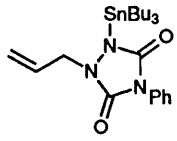
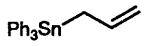
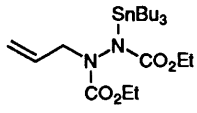
Diethyl azodicarboxylate reacts in the same way (Scheme 4)

$$CH_3CH_2CH_2CH_2SnR_3 + EtOCON{=}NCO_2Et \longrightarrow CH_3CH_2CH{=}CH_2 + EtOCONHN(SnR_3)CO_2Et$$

Scheme 4

though more slowly than it undergoes the metalloene reaction; with tetrabutyltin, tributyltin chloride, dibutyltin dichloride,

Table 1 Reactions of allyl-H and allyl-Sn compounds with azo compounds

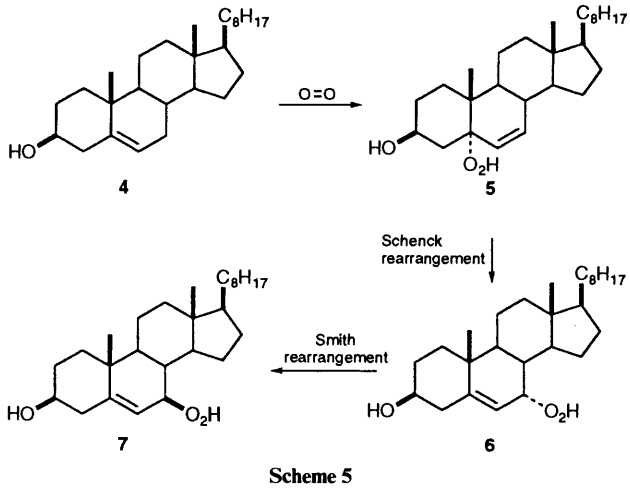
Ene	Enophile	Product	Solvent	$[LiClO_4]$/mol dm^{-3}	Time
	2		Et_2O	0	10 days
				5	1 h
	2		Et_2O	0	4 days
				5	4 h
	1		Et_2O	0	4 days
				5	4 h
			EtOAc	0	4 days
				2.35	1 day
	2		Et_2O	0	< 5 min
				5	< 5 min
	1		Et_2O	0	28 h
				5	12 min
	3		Et_2O	0	1 h
				5	< 5 min
	1		Et_2O	0	80 min
				2	< 5 min
				5	< 5 min

and butyltin trichloride the colour of the solution was bleached after 7, 5, 3, and 2.5 days respectively, and diethyl hydrazodicarboxylate was identified as the product. 2,6-Di-*tert*-butylphenol and 2,6-di-*tert*-butyl-4-methylphenol, as potential inhibitors of radical chain reactions, had no effect on the rates of the reactions.

The hydrogen-ene reaction involving singlet oxygen has been investigated most thoroughly with cholesterol (**4**) (Scheme 5);[7a,11,12] the 5α-hydroperoxycholest-6-ene (**5**) is formed as the initial product, but in a non-polar solvent this rearranges during about 1 day to the 7α-hydroperoxy-5-ene (**6**) (the Schenck rearrangement)[11] and then further, during about 1 week, to the 7β-hydroperoxy-5-ene (**7**) (the Smith rearrangement).[12] Both the Schenck and the Smith rearrangements are radical chain processes involving allylperoxyl radicals.[7a,b,11-14]

We have therefore studied the effect of lithium perchlorate on these reactions. Cholesterol has only a low solubility in ether, so our reactions were carried out in ethyl acetate as solvent, in which lithium perchlorate has adequate solubility; Grieco[1a,4] has shown that lithium perchlorate can show a positive catalytic effect (on Diels–Alder reactions) in ethyl acetate, though in other solvents (*e.g.* tetrahydrofuran) the effect can be negative.

A solution of cholesterol in ethyl acetate, together with tetraphenylporphin as a photosensitizer, was stirred vigorously under an atmosphere of oxygen, with irradiation with sodium



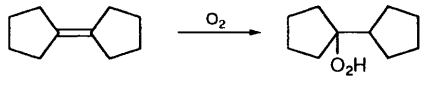
Scheme 5

light. The results are shown in Table 2. Pure 5α-hydroperoxide **5** was isolated, and its rearrangement in ethyl acetate was followed by NMR spectroscopy. The effect of lithium perchlorate was negligible: after 6 h in the absence of the salt, the composition **5**:**6**:**7** was 67:30:3, and in its presence was 61:32:7.

Results are also given in Table 2 for the oxidation of cyclopentylidenecyclopentane (**8**; Scheme 6), which is the most

Table 2 Reaction of allyl-H and allyl-Sn compounds with singlet oxygen

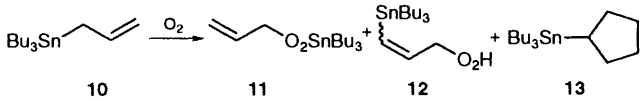
Ene	Solvent	$[LiClO_4]$/mol dm^{-3}	Time	Yield (%)	Product (%)
4	EtOAc	0	2 h	40	**5** (84) **6** (16) **7** (0)
		0	5 h	78	**5** (21) **6** (29) **7** (0)
		2.35	2 h	65	**5** (69) **6** (22) **7** (9)
8	Et_2O	0	10 min	39	**9** (100)
		5	10 min	47	**9** (100)
10	Et_2O	0	3 h	12	**11** (44) **12** (54) **13** (2)
		5	3 h	55	**11** (23) **12** (72) **13** (5)
	EtOAc	0	4.5 h	68	**11** (73) **12** (25) **13** (2)
		2.35	2 h	60	**11** (73) **12** (25) **13** (2)



8 **9**

Scheme 6

reactive ene towards singlet oxygen we have handled,[7f] and for tributylallyltin (**10**; Scheme 7).



10 **11** **12** **13**

Scheme 7

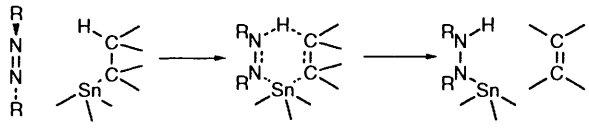
Discussion

The ene reactions of cyclopentene, cyclohexene, and cyclopentylidenecyclopentane, tributylallyltin, triphenylallyltin with azo enophiles are strongly accelerated by lithium perchlorate (Table 1); thus the time for complete reaction between cyclopentene and *N*-methyltriazolinedione in ether, is reduced by a factor of *ca.* 240 by 5 mol dm^{-3} lithium perchlorate, and that between tributylallyltin and diethyl azodicarboxylate is similarly reduced by a factor of *ca.* 140. This catalytic effect could be exploited in organic synthesis. None of the three models which have been suggested for the mechanism can be excluded: it is conceivable that the azo compound could have its HOMO lowered by association with the lithium, the formation of the polar intermediate (Scheme 1) could be facilitated by the ionic medium, and some ene reactions have been shown to have negative volumes of activation.[15]

Accurate comparisons between the rates of ene reactions of singlet oxygen under different conditions are not easy to make because of possible variations in the concentration of $^3O_2$ under the heterogeneous conditions, of the quantum yield of $^1O_2$, and of its lifetime. With that proviso, lithium perchlorate does show a catalytic effect on the reaction of cholesterol, cyclopentylidenecyclopentane, and tributylallyltin (Table 2), though the effect does not appear to be large enough to be preparatively useful. In the reaction of tributylallyltin with singlet oxygen in diethyl ether, the presence of lithium perchlorate accelerates all three of the reactions which are normally observed (metalloene, hydrogen-ene, and cyclisation), but the effect is greatest on the hydrogen-ene and cyclisation reactions.

No effect is apparent on the rates of the Schenck and Smith rearrangements of the 5α-hydroperoxide derived from cholesterol.

The reduction of azobenzene and of diethyl azodicarboxylate by butyltin compounds was unexpected, but the known reaction of organoboranes provides an established model.[10] *trans*-Diethyl- and *trans*-di-*tert*-butyl azodicarboxylate, and *cis*- (but not *trans*-) azobenzene react very rapidly with trialkylboranes to give hydroboration of the azo group, with *cis*-elimination of alkene. The reactions of the azodicarboxylates were approximately first order in each reagent, and were accompanied by a radical chain component which could be quenched with a radical inhibitor. The corresponding reactions of alkyltin compounds show no evidence of a radical component, which is compatible with their relative reluctance to take part in radical chain reactions. It was suggested that the reactions of the organoboranes involved a six-centred cyclic transition state, and the same mechanism probably holds for the reaction of organotin compounds, as shown in Scheme 8.



Scheme 8

Experimental

General.—NMR spectra were recorded using a Varian XL200 spectrometer, and mass spectra on a VG 7070F instrument. The alkenes and allyltin compounds were obtained as described in refs. 7(*h*) and 8(*e*).

Ene reactions.—Typical examples of the ene reactions were as follows:

(1) Cyclopentylidenecyclopentane (28 mg, 0.21 mmol) and 4-methyl-1,2,4-triazolin-3,5-dione (23 mg, 0.20 mmol) were added to a 5 mol dm^{-3} solution of $LiClO_4$ in diethyl ether (1 cm^3). The colour of the azo compound was discharged within 5 min. The solution was washed with water, the ether was removed, and the product was isolated by chromatography on alumina.

(2) Diethyl azodicarboxylate (34.8 mg, 0.2 mmol) was added to a solution of tributylallyltin (68 mg, 0.2 mmol) in diethyl ether (1 cm^3). The progress of the reaction was monitored by TLC and by NMR spectroscopy, which showed that only diethyl *N*-allyl-*N'*-tributylstannylhydrazodicarboxylate was formed. Isolation of the product by gradient chromatography (light petroleum–ethyl acetate) gave diethyl *N*-allylhydrazodicarboxylate as an oil.

(3) A solution of tributylallyltin (68 mg, 0.2 mmol) and tetraphenylporphin (3 mg) in diethyl ether (1 cm^3) was vigorously stirred under oxygen while being irradiated with light from a 200 W sodium lamp. The solvent was removed and the products in the mixture were identified by NMR as reported previously.

The NMR spectra of most of the products from the ene reactions have been described in our previous papers, and provided the basis of the identifications reported in this work. Details of compounds which we have not reported before are as follows.

1-*Cyclopent-2-enyl-4-methyl*-1,2,4-*triazoline*-3,5-*dione*.—M.p 113–116 °C (lit.,[16] 118.5–119.5 °C). $\delta_H(CDCl_3)$ 1.74 (1 H, m), 2.20 (1 H, m), 2.43 (2 H, m), 3.08 (3 H, s, NMe), 5.26 (1 H, m), 5.66 (1 H, dm, *J* 2 and 5.6), 6.15 (1 H, dm, *J* 1.6 and 3.6) and 6.88 (1 H, br, NH).

1-*Cyclohex-2-enyl-4-methyl*-1,2,4-*triazoline*-3,5-*dione*.—M.p. 149–150 °C (lit.,[16] 149.0–149.6 °C). $\delta_H(CDCl_3)$ 1.76 (2 H, m), 1.86 (2 H, m), 2.04 (2 H, m), 3.08 (3 H, s, NMe), 4.74 (1 H, m), 5.52 (1 H, dm, *J* 9.8 and 2, –CH=), 6.04 (1 H, dm, *J* 9.8 and 2, =CH–) and 8.10 (1 H, br, NH).

Diethyl N-*Allylhydrazodicarboxylate*.—Oil. $\delta_H(CDCl_3)$ 1.23 (6 H, t, *J* 7.4, CH_2CH_3), 4.10 (2 H, d, CH_2), 4.17 (4 H, q, *J* 7.4, CH_2CH_3), 5.12 (1 H, d, *J* 1.1, H_2C=), 5.22 (1 H, dd, *J* 1.1 and 5, H_2C=), 5.8 (1 H, m, =CH–) and 6.52 (1 H, br s, NH).

Acknowledgements

This work was carried out during the tenure of a Commission of the European Communities Research Fellowship by W. J. K., on leave from the Department of Organic Chemistry, University of Lodz, Poland.

References

1 (*a*) H. Waldmann, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 1306; (*b*) P. A. Grieco, *Aldrichim. Acta*, 1991, **24**, 59.
2 P. A. Grieco, J. D. Clark and C. T. Jagoe, *J. Am. Chem. Soc.*, 1991, **113**, 5488.
3 Y. Nishigaichi, A. Takuwa, K. Iihama and N. Yoshida, *Chem. Lett.*, 1991, 693.
4 P. A. Grieco, J. J. Nunes and M. D. Gaul, *J. Am. Chem. Soc.*, 1990, **112**, 4595.
5 P. A. Grieco, R. J. Cooke, K. J. Henry and J. M. VanderRoest, *Tetrahedron Lett.*, 1991, **32**, 4665.
6 K. J. Henry, P. A. Grieco and C. T. Jagoe, *Tetrahedron Lett.*, 1992, **33**, 1817; Y. Nishigaichi, N. Nakano and A. Takuwa, *J. Chem. Soc., Perkin Trans. 1*, 1993, 1203.
7 (*a*) A. G. Davies, I. G. E. Davison, A. Maccoll, M. H. Mruzek and A. L. J. Beckwith, *J. Chem. Soc., Perkin Trans. 2*, 1989, 815; (*b*) A. G. Davies and I. G. E. Davison, *J. Chem. Soc., Perkin Trans. 2*, 1989, 825; (*c*) A. G. Davies and C. H. Schiesser, *Tetrahedron Lett.*, 1989, **30**, 7099; (*d*) A. G. Davies and W. J. Kinart, *J. Chem. Res. (S)*, 1989, 22; (*e*) H.-S. Dang, A. G. Davies and C. H. Schiesser, *J. Chem. Soc., Perkin Trans. 1*, 1990, 789; (*f*) H.-S. Dang, A. G. Davies, I. G. E. Davison and C. H. Schiesser, *J. Org. Chem.*, 1990, **55**, 1432; (*g*) A. G. Davies and C. H. Schiesser, *Tetrahedron*, 1991, **47**, 1707; (*h*) H.-S. Dang and A. G. Davies, *J. Chem. Soc., Perkin Trans. 2*, 1991, 721.
8 (*a*) H.-S. Dang and A. G. Davies, *Tetrahedron Lett.*, 1991, **32**, 1745; (*b*) H.-S. Dang and A. G. Davies, *J. Chem. Soc., Perkin Trans. 2*, 1991, 2011; (*c*) H.-S. Dang and A. G. Davies, *J. Organomet. Chem.*, 1992, **430**, 287; (*d*) H.-S. Dang and A. G. Davies, *J. Chem. Soc., Perkin Trans. 2*, 1992, 1095; (*e*) J. Cai and A. G. Davies, *J. Chem. Soc., Perkin Trans. 2*, 1992, 1743; (*f*) J. Cai and A. G. Davies, *J. Chem. Soc., Perkin Trans. 1*, 1992, 3383; (*g*) J. Cai, H.-S. Dang and A. G. Davies, *Frontiers of Organo-Germanium, -Tin, and -Lead Chemistry*, eds. E. Lukevics and L. Ignatovich, Riga, 1993, p. 197.
9 References are given in ref. 7(*h*).
10 A. G. Davies, K. G. Foot, B. P. Roberts and J. C. Scaiano, *J. Organomet. Chem.*, 1971, **31**, C1; A. G. Davies, B. P. Roberts and J. C. Scaiano, *J. Chem. Soc., Perkin Trans. 2*, 1972, 803.
11 G. O. Schenck, O.-A. Neumüller and W. Eisfeld, *Annalen*, 1958, **618**, 202.
12 J. I. Teng, M. J. Kulig, L. L. Smith, G. Kan and J. E. van Lier, *J. Org. Chem.*, 1973, **38**, 119.
13 W. F. Brill, *J. Chem. Soc., Perkin Trans. 2*, 1984, 621.
14 N. Porter and P. Zuraw, *J. Chem. Soc., Chem. Commun.*, 1985, 1472; N. Porter and J. S. Wujek, *J. Org. Chem.*, 1987, **52**, 5085; N. A. Porter, J. K. Kaplan and P. H. Dussault, *J. Am. Chem. Soc.*, 1990, **112**, 1266; K. A. Mills, S. E. Caldwell, G. R. Dubay and N. A. Porter, *J. Am. Chem. Soc.*, 1992, **114**, 9689; S. L. Boyd, R. J. Boyd, Z. Shi, L. R. C. Barclay and N. A. Porter, *J. Am. Chem. Soc.*, 1993, **115**, 687.
15 N. S. Isaacs, L. Maksimovic, G. B. Rintoul and D. J. Young, *J. Chem. Soc., Chem. Commun.*, 1992, 1749.
16 W. H. Pirkle and J. C. Stickler, *J. Chem. Soc., Chem. Commun.*, 1967, 760.

Paper 3/03687A
Received 28*th June* 1993
Accepted 2*nd August* 1993