

ON THE REACTIVITY OF SILYLPEROXIDES

OXIDATION OF THIOXANE AND OF N,N-DIMETHYL-PARA-ANISIDINE BY BIS(TRIMETHYLSILYL)PEROXIDE AND BY TERT-BUTYL(TRIMETHYLSILYL)PEROXIDE

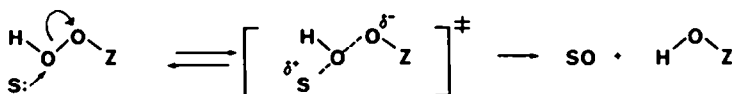
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Abstract - Rates and rate-laws have been determined for the oxidation of 1-thia-4-oxacyclohexane 5 by bis(trimethylsilyl)peroxide 1 and tert-butyl-(trimethylsilyl)peroxide 2 in CHCl_3 at 25.0° ; these are compared to the rates of oxidation of the same substrate by the more common oxidants, tert-butyl hydroperoxide 3 and di-tert-butyl peroxide 4 in the same solvent. The two silylperoxides give similar oxidations rates, which are over 50 times higher than that measured for $t\text{-BuOOH}$, while $t\text{-Bu}_2\text{O}_2$ is almost unreactive under the conditions adopted. Oxidation of N,N-dimethyl-p-anisidine 6, a nitrogen nucleophile, by silylperoxide 1 in CHCl_3 is ca. 1000 times slower than that of the sulphur nucleophile 5. The results are discussed in terms of a mechanism involving nucleophilic attack by the substrate on the peroxide, with the heterolysis of the O-O bond being assisted by the migration of the $\text{Me}_3\text{Si-}$ group.

Selective oxidations of organic substrates by peroxyacid compounds is one of the most important transformations in organic synthesis.^{1,2} In fact, inorganic and organic peroxyacids, as well as hydrogen peroxide and alkyl hydroperoxides, are widely employed to achieve selective, non-radical oxidations, either in catalytic or uncatalysed processes.¹⁻⁴ In many instances, it was shown the most plausible mechanism implies nucleophilic attack by the substrate at the weak O-O bond of the peroxide, according to a sequence amounting to electrophilic transfer of peroxide oxygen to the substrate (in Scheme 1 : S = substrate, SO = oxidized substrate, and Z = alkyl, acyl, or inorganic residue).¹⁻⁴

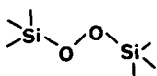


Scheme 1

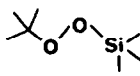
Several pieces of evidence have indicated that a key feature in these processes is that the energetically unfavoured charge separation, that is incipient in the t.s., be minimized by means of facile hydrogen atom transfers from the peroxide oxygen reaction centre to the -OZ leaving group. Thus, peroxyacids reach an intra-molecular H-bonded configuration (as, e.g., in the well

known "Bartlett's butterfly" t. s. for olefin epoxidation); and simple hydroperoxides require the intervention of protic molecule species.¹⁻⁵

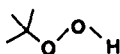
Although the potentiality of organosilicon reagents has been well developed in organic synthesis during the last few decades, the reactivity of organosilyl derivatives of peroxyacids and of hydroperoxides appears to have been little explored.⁶⁻⁸ It was pointed out bis(trimethylsilyl)peroxide 1 might be considered analogous to hydrogen peroxide in that oxidizes organic sulphides to sulfoxides and sulphones, phosphites to phosphates, and tertiary phosphines to phosphine oxides; tert-butyl(trimethylsilyl)peroxide 2 also oxidizes tertiary phosphines to phosphine oxides.⁹ Transition metals-catalysed epoxidations and oxidation of alcohols by silylperoxides 1 and 2, respectively, have been described.^{10,11}



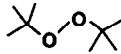
1



2



3



4

It was also reported that the bis(trimethylsilyl)derivative of Caro's acid $\text{Me}_3\text{SiO}-\text{SO}_2-\text{OOSiMe}_3$,¹² or 1 with Me_3SiOTf "catalyst",¹³ can convert ketones into esters, in a Bayer-Villiger type oxidation; this is likely to proceed *via* the preliminary addition of the silylperoxide to the carbonyl. These pieces of information contain the hint that substitution of the proton by the silyl group does not diminish either the electrophilicity or the nucleophilic character of the peroxide oxygen in silylperoxides with respect to their parent proton species.

With a view toward defining their reactivity, organosilicon peroxides such as 1 and 2 pose interesting questions as for the mechanism of their reduction by nucleophilic substrates. In fact, while the Me_3Si group might - at first sight - resemble the *t*-butyl group in hindering the attack at the O-O bond, the steric hindrance presented by the trimethylsilyl group should be considerably reduced due to the fact that the Si-O bond is significantly longer than the C-O bond (i. e., 1.63 Å *vs.* 1.43 Å).⁶⁻⁸ Also relevant to a mechanism of nucleophilic attack at the peroxide bond, the $\text{Me}_3\text{SiO}-$ group should behave as a better leaving group with respect to the $\text{Me}_3\text{CO}-$ or to the $\text{HO}-$ group, since silanols seem to be more acidic than alcohols having analogous structure.¹⁴ It is also relevant that the Me_3Si group might act as the "organic proton" also in these reactions;⁶⁻⁸ in fact, the availability of empty d-orbitals on silicon, and their possible interaction with filled π^* orbitals of the O-O bond, might effectively reduce charge separation in the t.s., thus favouring the oxidation process.

With this in mind we undertook the present study, that is aimed to determine the reactivity of silylperoxides 1 and 2, in comparison to the analogous organic peroxides 3 and 4.

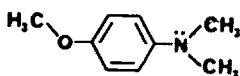
RESULTS AND DISCUSSION

To measure the reactivity of silylperoxides 1 and 2, thioxane 5 was chosen as a standard nucleophilic substrate. Previous studies, in fact, have demonstrated that organic sulphides can serve as useful model substrates to determine the general features of nucleophilic attack at the O-O bond of peroxides.^{1-3,5} Also, a good crop of kinetic data has been already collected concerning the oxidation of 5 by a variety of peroxide species in a number of solvents.^{2,5,15}

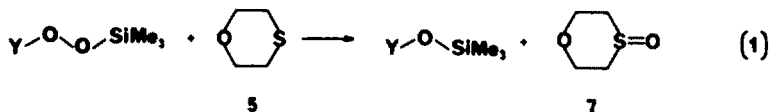
Organosilicon peroxides 1 and 2 were synthesized by following reported procedures. We find that the oxidation of the sulphide 5 by silylperoxides 1 and 2 occurs smoothly in CHCl_3 , dry ethanol, or dioxane at 25.0° . The 1:1 stoichiometry in eqn (1) was demonstrated by the nearly quantitative formation of the corresponding sulfoxide 7 (GLC analyses and product isolation). Only traces, if any, of sulphone could be detected.



5



6



(with $\text{Y} = -\text{SiMe}_3, -\text{CMe}_3$)

The nitrogen nucleophile *N,N*-dimethyl-*p*-anisidine 6 was employed in order to compare *N*-oxidation with sulfoxidation by silylperoxide 1; HPLC analyses showed that *N,N*-dimethyl(*p*-methoxyphenyl)-amine oxide is formed (yield 88-92%) in the reaction of 6 with 1 in CHCl_3 at 25.0° , again according to a one to one stoichiometry. The oxidation rates of the substrates by peroxides 1-4 were followed by monitoring the disappearance of the peroxide (iodometric titre) in reactions where the substrate was in large excess (from 20 to 200 fold) over peroxide. Integrated pseudo-first-

order plots were usually linear over two half-lives; pseudo-first-order rate constants were a linear function of excess substrate concentration and independent of the initial concentration of the peroxide (Table 1). Furthermore, a $\log k_1$ vs. $\log [\text{Thioxane}]_0$ plot is linear, with unit slope; as expected, therefore, the rate obeys a second-order-overall kinetic law, order one in each of the reagents. For 1 and 2, peroxide decomposition is too slow to compete with substrate oxidation under the given conditions.

Table 1. Rates of oxidation of thioxane by bis(trimethylsilyl)peroxide in CHCl_3 at $25.00 \pm 0.05^\circ$

$[\text{Thioxane}]_0$ M	$10^2 [(\text{Me}_3\text{Si})_2\text{O}_2]_0$ M	$10^3 k_1$ s^{-1}	$10^3 k_2^a$ $\text{M}^{-1}\text{s}^{-1}$
0.205	1.15	0.48	2.34
0.230	1.42	0.56	2.43
0.480	1.38	1.15	2.40
0.480	1.38	1.18	2.46
0.510	1.12	1.17	2.29
0.960	1.15	2.30	2.40
0.960	3.05	2.20	2.34
1.18	1.40	2.95	2.50

^a Obtained as $k_2 = k_1 / [\text{Thioxane}]_0$.

In Table 2 kinetic data are collected that allow one to compare the reactivity of silylperoxide 1 and 2 with that of the

more common peroxide species 3 and 4. In CHCl_3 , actually, thioxane oxidation by tert-butyl hydroperoxide 3 fits better a pseudo-second-order kinetic law during the initial stages of the reaction. In fact, $1/(a-x)$ vs. time plots were linear up to the first 30–40% reaction, allowing one to obtain $k_2 = (0.27 \pm 0.02) \times 10^{-5} \text{ M}^{-1} \text{ s}^{-1}$, and $k_3 = k_2/[\text{Thioxane}]_0 = (0.45 \pm 0.03) \times 10^{-5} \text{ M}^{-2} \text{ s}^{-1}$. Consistent with the view that – in the case of hydroperoxides – protic co-solvent molecules can participate to the t.s. involving nucleophilic attack at the O–O bond,^{2,5} in the oxidation of 1 we find that, with $[\text{t-BuO}_2\text{H}]_0 = 0.01 \text{ M}$, addition of as little as 0.005 M methanol to dry CHCl_3 allows one to observe again clean pseudo-first-order kinetics up to 60–70% reaction. Then, addition of trifluoroacetic acid (TFA) to pure CHCl_3 has the effect of yielding both a marked increase in rates and regular pseudo-first-order kinetics up to over 80% reaction. On basis of a rate-law for acid catalysis of the type: $k_2^{\text{obs}} = k_2^0[\text{Thioxane}][\text{t-BuO}_2\text{H}] + k_3[\text{Thioxane}][\text{t-BuO}_2\text{H}][\text{TFA}]_0$,^{2,5} and performing kinetic runs at varying concentration of TFA catalyst, the value for the "uncatalyzed" second-order rate constant for thioxane oxidation by t-BuOOH in CHCl_3 could be estimated (see footnote on Table 2). Oxidation of thioxane 5 by bis(trimethylsilyl)peroxide 1 in CHCl_3 occurs about 700-fold faster than the oxidation of the arylamine 6 (Table 2); as this reflects well the order of nucleophilicity of sulphur and nitrogen substrates in attacking the peroxide O–O bond,^{2,5} there can be no doubt that silylperoxides act as electrophilic partners in the reaction studied. For silylperoxide 1, the thioxane oxidation rate increases on going from dioxane, to ethanol, to CHCl_3 ; this is also the solvent-effect trend observed in the oxidation of organic sulphides by peroxyacids.^{2,5b}

Table 2. Oxidation rates of thioxane and N,N-dimethyl-p-anisidine by silylperoxide 1 and 2 as compared to analogous peroxide species, in chloroform at $25.00 \pm 0.05^\circ$.^a

Substrate	Peroxide	Solvent	$10^4 k_2^b$ $\text{M}^{-1} \text{s}^{-1}$
Thioxane (5)	t-BuOOBu-t	CHCl_3	0.005
"	t-BuOOH	"	0.27 ± 0.02^c
"	"	"	0.30 ± 0.05^d
"	t-BuOOSiMe ₃	"	14.7 ± 0.6
"	Me ₃ SiOOSiMe ₃	"	24.0 ± 0.6
"	"	EtOH	0.80 ± 0.05
"	"	Dioxane	0.15 ± 0.03
p-MeO·C ₆ H ₄ ·NMe ₂ (6)	"	CHCl_3	0.034 ± 0.002

^aThe initial concentration of the peroxide was kept in the range $(0.95 - 1.8) \times 10^{-2} \text{ M}$ and that of the excess substrate in the range from 0.35 to 1.0 M in the great majority of runs.

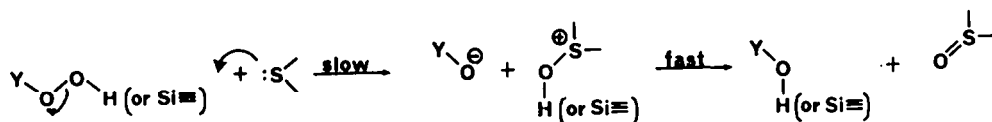
^bUnless noted otherwise k_2 values were obtained as $k_1/[\text{substrate}]_0$, with pseudo-first-order rate constant values k_1 calculated from first-order rate-law integrated plots.

^cExtrapolated at zero trifluoroacetic acid (TFA) initial concentration from runs carried out in CHCl_3 containing TFA catalyst; with thioxane initial concentration 0.598 M, and $10^2[\text{TFA}]_0 = 0.029, 0.233$, and 2.08 M, pseudo-first-order rate constants were, respectively, $10^4 k_1 = 0.22, 0.215$, and 6.65 s^{-1} .

^dEstimated from initial rates over the first 8–10% reaction.

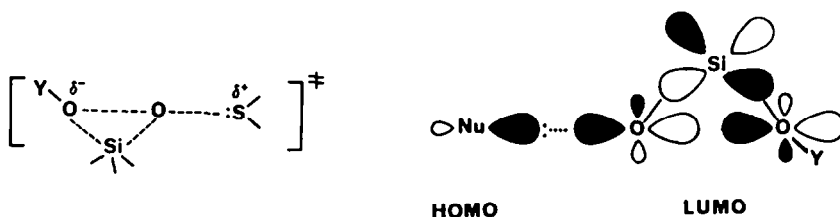
Inspection of data in Table 2 reveals that - in the oxidation of thioxane - bis(trimethylsilyl)-peroxide is more effective than *t*-BuOOH and *t*-BuOOBu-*t* by factors of *ca.* 10^2 and of over 5×10^{-3} , respectively. Reduced effective steric shielding by the -SiMe₃ with respect to the bulky -OMe₃ group might be invoked as one of the factors contributing to the drastic rate enhancement observed on going from 4 to 1 (see above). However, the finding that bis(trimethylsilyl)peroxide is almost 100 times more reactive than *t*-BuOOH suggests that the leaving group effect should be a major factor.¹⁶ In fact, based on the acidities of the proton species that are parent of the leaving groups (*i. e.*, Me₃SiOH $pK_a = 10$; ¹⁷ Me₃COH $pK_a = 17^{2,15}$), a Brønsted-type relationship predicts Me₃SiO- should be a leaving group more effective than Me₃CO-. This effect should be maximum if complete heterolysis occurs in the rate-determining step, and then transfer of either the proton or the Me₃Si- group takes place in a rapid, subsequent step (as in Scheme 2).

It is significant, however, that bis(trimethylsilyl)peroxide 1 reacts only 1.6 times faster than *tert*-butyl(trimethylsilyl)peroxide 2; the rates of the two species, in fact, would be



Scheme 2

quite close if one divides the rate constant of 1 by a statistical factor of two. This, in turn, suggests that a yet more relevant feature might consist in the ability of the Me₃Si- group to effectively minimize the charge separation in the transition state, by giving rise - *e.g.* - to bridged configurations as in Scheme 3. Then, silyl groups in silylperoxides might be able to assist the O-O bond cleavage, thus promoting the transfer of electrophilic peroxide oxygen to the substrate.



Scheme 3

Silicon bridging in organosilyl peroxides has been proposed¹⁸ and other 1,2-migrations of silyl groups are known (*e. g.*, from carbon to carbon and from carbon to oxygen) that may proceed *via* bridged transition states akin to that depicted in Scheme 3.^{6,7} In organosilicon peroxides, the availability of empty d orbitals on silicon and their interaction with filled π^* orbitals

of the O-O bond might be such as to favour silicon-bridged t.s. structures; for nucleophilic attack, then, the proper interaction of the nucleophile HOMO should be with a LUMO of the bridged peroxide specie, having the features of a σ^*-d_{xz} , or better of a σ^*-d_{xy} orbital (Scheme 3).¹⁹

In conclusion, we believe the rate data presented illustrate well the potential of silylperoxides in oxidation reactions. With respect to the more commonly employed simple alkyl hydroperoxides or hydrogen peroxide, they bear the obvious advantages of a much higher solubility in aprotic solvents, yielding easily separable reduction products, *e.g.* $(\text{Me}_3\text{Si})_2\text{O}$ or ROSiMe_3 . Furthermore, silylperoxides appear to be from 50 to 100 times more effective than analogous alkyl hydroperoxide species in performing electrophilic peroxide oxygen transfer to sulphur substrates in CHCl_3 at 25°; and this according to an uncomplicated rate-law, which does not require acid catalysis.^{2,5}

Thus, further studies in this area are warranted.

EXPERIMENTAL

Boiling and melting points are not corrected. The NMR spectra were obtained by using a Varian E360A or XL200 instrument. IR spectra were run on a Perkin-Elmer 681 spectrophotometer. GLC analyses were performed employing a capillary column DANI 3800 equipped with a C-RIA Shimadzu integrator; analytical HPLC was executed by using a Perkin-Elmer 3B chromatograph and LC-85B, detector and autocontrol.

Materials. Bis(trimethylsilyl)peroxide 1 was prepared on reaction of trimethylsilyl chloride (Aldrich) with the complex $\text{DABCO} \cdot (\text{H}_2\text{O}_2)_2$ ²⁰ according to a reported procedure:²¹ b.p. 42°/30 mm, NMR (CHCl_3 , Me_4Si): δ 0.16 (s). Starting with 98% t-butyl hydroperoxide 3, t-butyl(trimethylsilyl)peroxide 2 was obtained by following the method given by Bouncel and Davies:²² b.p. 44°/35 mm (lit.²²: b.p. 30°/25 mm); NMR (CHCl_3 , Me_4Si): δ 0.12(9H,s, SiCH_3), 1.16(9H,s, CCH_3). Commercial (Schuchardt) t-butyl hydroperoxide 3 (b.p. 39°/20 mm) and di-t-butyl peroxide 4 (b.p. 50-52°/90 mm) were purified by careful fractional distillations in vacuo. Thioxane (1-thia-4-oxacyclohexane) 5 and thioxane oxide 7 were obtained as previously described.⁵ N,N-dimethyl-p-anisidine 6 was prepared on reacting commercial (Aldrich) p-anisidine with Me_2SO_4 : b.p. 124-126°/21 mm;²³ an oxidation method described in the literature^{24,25} was adopted to convert 6 into dimethyl(p-methoxyphenyl)amine oxide: m.p. 131°(dec); NMR(CD_3OD , MeSi_4): δ 3.53(6H,s, $\text{CH}_3-\text{N}-\text{O}$), 3.77(3H,s, OCH_3), 6.7-8.3(4H,m,AA'XX' system, ArH); IR ν_{max} (nujol) cm^{-1} : 1260 ($\text{N}-\text{O}$ stretch). Other materials and solvents were purified by following standard procedures.⁵

Stoichiometry. Reaction stoichiometries were determined on reacting equimolar amounts (*e.g.*, 2.5 mmol in 10 ml of CHCl_3) of the substrate (5 or 6) with the silylperoxide (1 or 2). The nearly quantitative yield of sulphoxide 7 was established by GLC analyses (0.25 μM SE-30, 30 M x 0.25 nm i.d. capillary column, temp program); the formation of N,N-dimethyl-p-anisidine N-oxide (in 88-97% yield) was monitored by HPLC (10 μM C18, 25 cm x 4.6 mm i.d. analytical column, $\text{MeCN}/\text{H}_2\text{O}$ 60:40 mobile phase, 1 ml/min flow rate).

Kinetics. Oxidation rates were determined by following the disappearance of the peroxide (iodometric titre) with time according to techniques already described in detail.⁵ Rate constants listed on Table 2 are averages of values from at least three independent runs.

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