5-Hydroperoxycarbonylphthalimide: a new reagent for epoxidation

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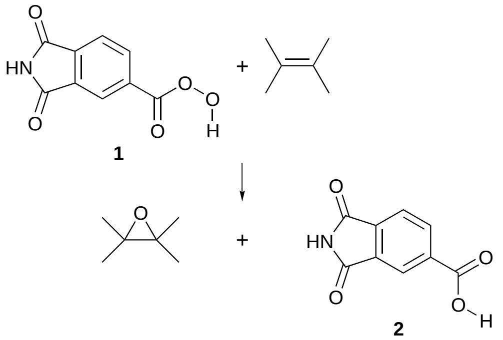
Peroxycarboxylic acids, widely used for epoxidation in industry and general research, have various drawbacks, such as difficulty of preparation in a pure state, cost and the possibly ring-opening of the product epoxides due to acid-catalysed reactions; a new reagent, 5-hydroperoxycarbonylphthalimide, overcomes these problems.

The formation of epoxides (oxiranes) from alkenes is a widely used reaction, either for the product epoxides themselves or for their preparation as intermediates in further synthesis.[1] The manufacture of epoxides ranges in scale from the small requirements of a research reaction to the huge tonnages of industrial epoxides and bis-epoxides. Hydrogen peroxide, a clean oxidant producing only water as a by-product, would be ideal if it could be used to produce epoxides directly. Although epoxidation can be effected with hydrogen peroxide through use of metal catalysts such as those of tungsten[2] or molybdenum,[3] titanium silicalites[4] and porphyrins,[5] these catalysts are not universally applicable for various reasons, including cost, lack of specificity, inability to selectively epoxidise without formation of serious quantities of by-products and lack of reactivity towards alkenes having electron-deficient double bonds. Such catalysts have not found general favour, except in some specialised instances. There is widespread use of hydrogen peroxide by first converting it into a suitably reactive form, such as *tert*-butyl peroxide and the popular peroxycarboxylic acids. Of the latter, although many are known, only a few are in general use.[6] Thus, peroxyformic, peroxyacetic, peroxybenzoic, peroxyphthalic (also as its magnesium salt), peroxytrifluoroacetic and *m*-chloroperoxybenzoic acids are the ones most frequently employed. Generally, the relatively cheap, lower molecular mass, liquid peroxyformic and peroxyacetic acids are used for large-scale industrial epoxidation and the higher molecular mass, solid *m*-chloroperoxybenzoic acid is widely employed for research or very small scale purposes. There are serious disadvantages to the use of peroxyformic and peroxyacetic acids, including their difficulty of synthesis in high concentration, their lack of stability, the need for buffering of a reaction medium to lessen acid-induced side reactions and the difficulty of recycling the parent acid. *m*-Chloroperoxybenzoic acid is not available commercially in large quantities or in pure form because of its easy thermal decomposition and sensitivity to mechanical shock;[7] the peroxyacid is also expensive because of the cost of the starting acid and the need to use methanesulfonic acid to catalyse its formation from hydrogen peroxide. Nevertheless, *m*-chloroperoxybenzoic acid does have desirable properties, in being capable of effecting many kinds of epoxidation and in giving a product acid that is relatively insoluble in non-polar solvents. The present research has shown that 5-hydroperoxycarbonylphthalimide **1** (5-PCP; 1,3-dioxo-1,3-dihydroisoindole-5-peroxycarboxylic acid; Scheme 1)[8] is an excellent, cheaper reagent for effecting epoxidation, ameliorating or overcoming many of the disadvantages listed above. Its preparation is described in a footnote to Table 1.

The alkenes shown in Table 1 were epoxidised at temperatures between 0 and 60 °C in various solvents (Scheme 1). The



Scheme 1

Table 1 Alkenes epoxidised with 5-hydroperoxycarbonylphthalimide **1** (5-PCP)[a]

Alkene	*T*/°C[b]	Solvent	*t*/h[c]
2,3-Dimethylbut-2-ene	20	CH_2Cl_2	2
Cyclohexene	20	CH_2Cl_2	6
1-Methylcyclohexene	20	CH_2Cl_2	2
	20	Toluene	3
Cyclooctene	20	CH_2Cl_2	2
α-Pinene	20	CH_2Cl_2	2
β-Pinene	20	CH_2Cl_2	2.5
Limonene	20	CH_2Cl_2	2 + 4[d]
Oct-1-ene	35	CH_2Cl_2	24
cis-Stilbene	35	CH_2Cl_2	24
trans-Stilbene	35	CH_2Cl_2	24
Allyl phenyl ether	60	$ClCH_2CH_2Cl$	113
Styrene	35	CH_2Cl_2	24
Diallyl maleate	60	$ClCH_2CH_2Cl$	150
6-Methylhept-5-en-2-one	0	CH_2Cl_2	7
1,2-Diallyloxyethane	55	EtOAc	70

[a] To conc. H_2SO_4 (29.4 g; 98% w/w) was added water (1.7 g; demineralised), with stirring and cooling, followed by hydrogen peroxide (3.66 g; 85% w/w; 0.0915 mol), maintaining the reaction temperature below 15 °C. After addition had been completed, the mixture was warmed to 40 °C, at which stage 1,3-dihydro-1,3-dioxoisoindole-5-carboxylic acid (ref. 10) (5-carboxyphthalimide **2**; 5 g) was added. The mixture was stirred at 40 °C for 45 min, after which it was cooled and quenched by addition of ice–water. 5-Hydroperoxycarbonylphthalimide **1** (5-PCP) crystallised out. The product was filtered off, washed normally with water to pH 3 and air-dried to give the pure compound in > 90% yield, mp 175 °C. [b] In a typical reaction (Scheme 1), 1-methylcyclohexene (48 mg; 0.5 mmol) in CH_2Cl_2 (2 ml) was stirred with 5-PCP (0.12 g; 0.6 mmol) at room temperature for 2 h. The course of the reaction was monitored by GC and by GC–MS. At the end of reaction, the precipitated 5-carboxyphthalimide **2** was filtered off, the solvent was evaporated and the product was weighed and examined by ^1H NMR spectroscopy. All the epoxides are known and authentic materials were used for comparison with the epoxides produced with 5-PCP. Yields were between 98–100%. [c] Approximate time to complete reaction, as revealed by the disappearance of the starting alkene. [d] With 1 equiv. of 5-PCP, only the 1,2-*mono*(epoxide) was isolated after 2 h. Addition of a further 1 equiv. of 5-PCP at this stage gave the 1,2 : 9,10 *bis*(epoxide) after a further 4 h.

alkenes were chosen to explore the general suitability of 5-PCP for epoxidation. Thus, the reactivity of the alkenes towards electrophilic oxygen ranged from the electron-rich 2,3-dimethylbut-2-ene (containing a tetraalkyl-substituted double bond) to the electron-deficient allyl phenyl ether (containing a monosubstituted, oxygen-deactivated double bond). Other alkenes were chosen to demonstrate the stability of the resulting epoxide under the reaction conditions (styrene, α-pinene, 1,2-diallyloxyethane), the stereo integrity of reaction (*cis*- and *trans*-stilbene) or the selectivity of reaction (limonene, having two different double bonds).

In each case, epoxidation proceeded to give virtually a 100% yield of very pure product epoxide. Reaction rates were as expected from the known mechanism of epoxidation with peroxyacids.[1,6] Thus, at room temperature, reaction of 2,3-dimethylbut-2-ene, 1-methylcyclohexene, cyclohexene, cyclooctene and α- and β-pinene with 5-PCP was fast in CH_2Cl_2. For the less reactive alkenes, such as oct-1-ene, allyl phenyl ether, 1,2-diallyloxyethane and diallyl maleate, higher temperatures were needed to achieve reaction in a reasonable time. Such reactions could be carried out in CH_2Cl_2 under reflux (35 °C), 1,2-dichloroethane (at 50 °C), EtOAc (at 55 °C) and toluene (at 50 °C). When the epoxidation was carried out at higher temperatures than these, reaction was faster and a clean product was still obtained, but there was some small loss of active oxygen over long periods of time. In these cases, somewhat more than a 1 equiv. of peroxyacid to each double bond was needed. Thus, after a period of about 100 h at 60 °C with 2 equiv. of 5-PCP, epoxidation of the two allylic bonds in diallylmaleate ceased at about 60–70% because of depletion of the peroxyacid; addition of a further 1 equiv. (0.5 equiv. for each bond) caused the reaction to proceed to completion and to give a very pure product.

In all of the reactions, the product acid (5-carboxyphthalimide **2**) was almost totally insoluble in the solvent. This behaviour is highly advantageous in two ways. First, the product acid can be filtered off easily from the reaction medium and re-used; this potentially low-cost acid can be recycled with hydrogen peroxide to give little or no environmentally disadvantageous by-product. Second, the insolubility of the acid, due to extensive strong intermolecular hydrogen-bonding,[9] means that the hydrogen ion concentration in solution is extremely low. In turn, this means that acid-catalysed changes in the epoxide, when formed, are reduced to a very low level, enabling the isolation of even acid-sensitive epoxides in high yield and purity. 5-PCP itself is partly soluble in the solvents described here. This implies it has all of the kinetic advantages of a homogeneous reaction but, being a very weak acid, does not produce a significant hydrogen ion concentration in the reaction medium. Thus, there is little or no effect from acid-catalysed decomposition of the product epoxide. In the most sensitive epoxides prepared in this work (*e.g.* styrene oxide), reaction proceeded to virtually 100% yield with no evidence for acid-catalysed rearrangement products (phenylacetaldehyde in the case of styrene oxide). Until full hazard information is available, 5-PCP should be treated with caution, as with any peroxy compound.

Notes and References

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