

Polymer-supported Oxone and *tert*-butyl hydroperoxide: new reagents for the epoxidation of α,β -unsaturated aldehydes and ketones

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Efficient, mild and selective epoxidation of α,β -unsaturated aldehydes and ketones was performed using polyvinylpyrrolidone-supported Oxone (Oxone/PVP) and Bu^tOOH/PVP.

Epoxidation of alkenes, especially electron-deficient carbon-carbon double bonds in α,β -enals and α,β -enones, is of great interest.¹ α,β -Unsaturated ketones are used in the production of perfumes and flavouring substances.^{1(c)} These compounds could be functionalized by nucleophilic ring-opening of the oxirane ring of the corresponding epoxide.² One recent example is reported for the synthesis of a novel class of C-10 halo-genated and C-12 oxygenated prostaglandin-A₂ derivatives.^{2(b)}

Peroxides are frequently used as oxidants in organic synthesis for the epoxidation of α,β -unsaturated carbonyl compounds.^{3,4} In the epoxidation of α,β -enones, peroxides are superior reagents to organic peracids with respect to their mildness, good yields and absence of by-products. Epoxidation of electron-deficient alkenes is normally sluggish with electrophilic oxidizing agents such as *m*-CPBA. Hydrolysis of produced oxirane ring and oxidation of aldehyde functional group are disadvantages of using organic peracids. Potassium peroxomonosulfate triple salt (Oxone) is an efficient reagent for this purpose, but it requires an aqueous reaction medium that can lead to extensive hydrolysis. The epoxidation of α,β -unsaturated ketones with hydrogen peroxide under basic conditions was discovered by Weitz and Scheffer, and it is one of the oldest applications of hydrogen peroxide as an oxidant in synthetic organic chemistry.⁵ It is generally known that hydrogen peroxide decomposes on prolonged storage, and a large number of stabilizers has been used for slowing down the decomposition.⁶ Other epoxidation methods have been developed for α,β -unsaturated carbonyl compounds, which involve sodium peroxide,⁷ Keggin heteropoly compounds with aqueous H₂O₂ in acetonitrile,⁸ hydrogen peroxide in the ionic liquid/water biphasic system,⁹ urea-hydrogen peroxide,¹⁰ dioxirane,¹¹ alkaline hydrogen peroxide in nonionic microemulsions in the presence or absence of a phase-transfer agent¹² and many asymmetric methods are well known.¹³

On the other hand, the development of new clean oxidation methods, which can supply the needs for improvements in epoxide synthesis, is of general interest. Selective epoxidation methods are implemented under heterogeneous conditions and with safe, clean, cheap and regenerable oxidants.¹⁴ Polymer-supported reagents are of considerable interest due to their selectivity, stability and easy handling.^{15–18} They could serve as heterogeneous, clean and regenerable reagents in epoxidation reactions. Recently, the epoxidation of α,β -enones and other double bonds with cross-linked polystyrene-supported *tert*-butyl hydroperoxide has been investigated, but it suffers from low yields, low selectivity and long reaction times.¹⁸ Asensio and co-workers have found that anhydrous potassium peroxomonosulfate supported on silica (SiO₂-KHSO₅) efficiently oxidizes a variety of acyclic

and cyclic ketones to the corresponding esters or lactones (Baeyer–Villiger oxidation) without hydrolysis of products.¹⁹

Recently, we reported the use of polyvinylpyrrolidone-supported hydrogen peroxide (H₂O₂/PVP)²⁰ as a stable solid oxidizing reagent in the presence of KI or I₂ for iodination of activated aromatic compounds²¹ and epoxidation of α,β -unsaturated carbonyl compounds.²² Now, we report the simple preparation of PVP-supported Oxone (Oxone/PVP) and *tert*-butyl hydroperoxide (Bu^tOOH/PVP) as new stable, safe and recyclable reagents. The peroxide contents of the supported reagents (as determined by iodometric titration) were 1.7 and 6.4 mmol g^{–1} for Oxone and Bu^tOOH, respectively. The reagents could be stored in a refrigerator for several months without noticeable loss of activity. In this work, we investigated an efficient method for the epoxidation of α,β -enones by using these reagents under heterogeneous conditions.[†]

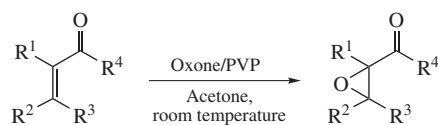
[†] *Preparation of Oxone/PVP.* To 6 g of polyvinylpyrrolidone K-30 (*M*_w 40000; from Fluka) a solution of Oxone[®] (from Fluka; 6.14 g) in 35 ml of distilled water was added with gently stirring in an ice bath. After 1 h, the solvent was vacuum evaporated at room temperature, and the resulting powder was dried in a vacuum to constant weight. The peroxide content of the supported reagent (as determined by iodometric titration) was 1.7 mmol peroxide g^{–1}. The reagent could be stored at 0 °C for several months without noticeable loss of activity.

Preparation of Bu^tOOH/PVP. An aqueous 70% solution of Bu^tOOH (6 ml) was added to 3 g of polyvinylpyrrolidone at 0 °C with gently stirring. After 2 h, the solvent was vacuum evaporated at room temperature, and the resulting solid was powdered and then dried in a vacuum to constant weight. The peroxide content of the supported reagent (as determined by iodometric titration) was 6.4 mmol Bu^tOOH g^{–1}. The reagent could be stored at 0 °C for several months without noticeable loss of activity.

Epoxidation of 3-phenyl-2-propenal with Oxone/PVP. Oxone/PVP (0.588 g, 1 mmol) was added to a solution of 3-phenyl-2-propenal (0.132 g, 1 mmol) in acetone (5 ml). The mixture was stirred at room temperature, and the progress of the reaction was monitored by TLC. After 4 h, the reaction mixture was filtered. Evaporation of the solvent followed by column chromatography on silica gel by using light petroleum–EtOAc (5:1) as an eluent gave 2,3-epoxy-3-phenylpropanal (0.124 g, 84% yield).

Epoxidation of 2-cyclohexen-1-one with Bu^tOOH/PVP. To a solution of 2-cyclohexen-1-one (0.096 g, 1 mmol) in dioxane (5 ml), Bu^tOOH/PVP (0.155 g, 1 mmol) and four drops of an aqueous solution of NaOH (0.1 M) were added. The mixture was refluxed, and the progress of the reaction was monitored by TLC. After 6.5 h, the reaction mixture was cooled and filtered. Then, dichloromethane (10 ml) was added to the filtrate, and the mixture was washed with distilled water (3×10 ml). The filtrate was dried over anhydrous magnesium sulfate. Evaporation of the solvent followed by column chromatography on silica gel using light petroleum–EtOAc (5:1) as an eluent gave 2,3-epoxycyclohexanone (0.110 g, 98% yield).

In our procedure, α,β -unsaturated carbonyl compounds reacted with Oxone/PVP in acetone at room temperature (Scheme 1). We first optimized the epoxidation reaction with 2-cyclohexen-1-one as a model (Table 1, entry 1) and then applied the conditions for other enones. Under these conditions, 2-cyclohexen-1-one was converted into 2,3-epoxycyclohexanone in 82% isolated yield after 3 h.

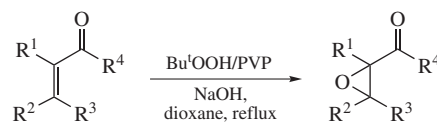


Scheme 1

Table 1 shows that α,β -unsaturated carbonyl compounds, including aldehydes and ketones, were efficiently converted into the corresponding epoxides with Oxone/PVP in acetone at room temperature in good to excellent yields. Under these conditions, cyclohexene was epoxidized slowly, and the corresponding epoxide was obtained in poor yield (Table 1, entry 12). During epoxidation of unsaturated aldehydes and alcohols with

Oxone/PVP, the hydroxyl and aldehyde groups were intact and double bonds were selectively converted to oxirane (Table 1, entries 8–11). Polyvinylpyrrolidone can be recycled by simple filtration after completion of the reaction.

α,β -Unsaturated carbonyl compounds reacted with Bu^tOOH/PVP in dioxane under reflux conditions (Scheme 2). In this case, the best results were obtained when the reaction was performed in the presence of NaOH in dioxane. Under these conditions, 2-cyclohexen-1-one was converted into 2,3-epoxycyclohexanone in 98% isolated yield after 6.5 h. As shown in Table 1, various α,β -unsaturated carbonyl compounds were efficiently converted into the corresponding epoxides with Bu^tOOH/PVP in dioxane under reflux conditions in good to excellent yields. During epoxidation of unsaturated aldehydes and alcohols with Bu^tOOH/



Scheme 2

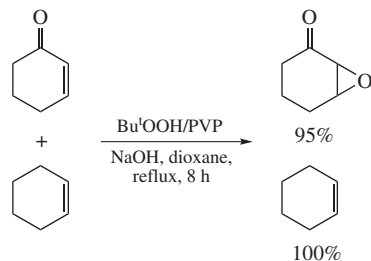
Table 1 Conversion of carbon–carbon double bonds to epoxides with Oxone/PVP and Bu^tOOH/PVP.

Entry	Substrate	Product ^a	Oxone/PVP		Bu ^t OOH/PVP	
			Time/h	Yield ^b (%)	Time/h	Yield ^b (%)
1			3	82	6.5	98
2			4	93	7	94
3			6.2	96	6	90
4	PhCH=CH-C(=O)Ph	PhHC(O)-CH-C(=O)Ph	12	88	24	85
5	PhCH=CH-C(=O)Me	PhHC(O)-CH-C(=O)Me	8	90	20	95
6	PhCH=CH-C(=O)OMe	PhHC(O)-CH-C(=O)OMe	24	60	28	70
7	MeHC=C(Me)C(=O)Me	MeC(O)-C(Me)-C(=O)Me	4.5	95	7.5	98
8	PhCH=C(Me)CHO	PhC(O)-C(Me)-CHO	9.5	90	48	90
9	MeHC=CH-CHO	MeC(O)-CH-CHO	5.5	88	25	80
10	PhHC=CH-CHO	PhC(O)-CH-CHO	4	84	8	92
11	Me ₂ C=CH-CH ₂ OH	Me ₂ C(O)-CH-CH ₂ OH	5	85	14	88
12			48	50	48	30

^aAll products are known compounds identified by comparison of their physical (mp or bp) and spectral data with those of authentic samples. ^bIsolated yield.

PVP, the aldehyde and hydroxyl groups were intact (Table 1, entries 8–11), and cyclohexene oxide was obtained in poor yield (Table 1, entry 12).

We also examined the selectivity of this method by using Bu^tOOH/PVP as a mild oxidizing reagent. We observed excellent selectivity in the epoxidation of a mixture of 2-cyclohexen-1-one and cyclohexene. 2,3-Epoxycyclohexanone was obtained with 95% yield in the presence of cyclohexene after 8 h in refluxing dioxane, while cyclohexene remained intact (Scheme 3).



Scheme 3

In conclusion, Oxone/PVP and Bu^tOOH/PVP are stable, mild, recyclable and environmentally friendly reagents for the selective, clean and safe epoxidation of α,β -unsaturated carbonyl compounds. Unsaturated aldehydes and alcohols are epoxidized without oxidation of their formyl or hydroxyl groups. Oxone/PVP is more reactive than Bu^tOOH/PVP, but the latter is more selective. Excellent selectivity was observed in the epoxidation of a mixture of 2-cyclohexen-1-one and cyclohexene with Bu^tOOH/PVP in refluxing dioxane. High reaction yields, mild reaction conditions, simple setup and workup procedure are additional merits of our protocol.

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