

SYNLETT Spotlight 130

This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Urea–Hydrogen Peroxide Complex

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Introduction

The hydrogen bonded urea–hydrogen peroxide complex [CO(NH₂)₂·H₂O₂, UHP] is a cheap and commercially available white crystalline solid (mp 84–86 °C, dec.) obtained by recrystallization of urea from commercially available 33% aqueous hydrogen peroxide.¹

Its stability at room temperature, high hydrogen peroxide content (36.2%) and the potential for releasing it in a controlled manner,² as well as its solubility in organic solvents (alcohols, dichloromethane) makes it a good and safe sub-

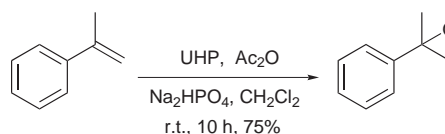
stitute for anhydrous hydrogen peroxide (not available anymore) in most oxidation reactions.

UHP has been used for the epoxidation of a wide range of alkenes.³ It is capable of oxidizing a number of functional groups: nitriles to amides,⁴ oximes to nitroalkanes,⁵ sulfides to sulfoxides⁶ or sulfones,⁷ aldehydes to acids,⁸ etc. UHP has also been found useful for heteroatom oxidation reactions,⁹ as well as to carry out Baeyer–Villiger¹⁰ and related reactions. In recent years, UHP has proved to be effective in solid state reactions, both under heating¹¹ or microwave irradiation,¹² so becoming an interesting eco-friendly reagent.

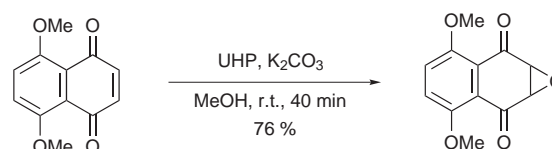
Abstracts

(A) In the presence of anhydrides, alkenes are epoxidized with UHP through the in situ formation of peroxyacetic acids.³ A large excess of UHP has to be used to avoid the build-up of high concentrations of diacyl peroxides.

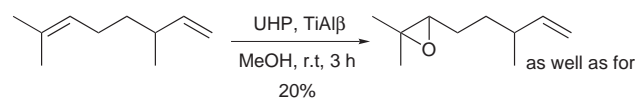
Phthalic anhydride supported on insoluble polystyrene-divinylbenzene (PS-DVB) and UHP allows the epoxidation of different alkenes in an efficient method where purification was limited to filtration, solvent change and evaporation.¹³



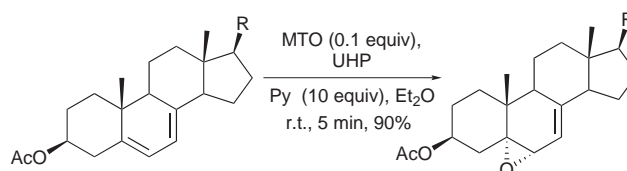
(B) Epoxidation of α,β -unsaturated ketones with UHP requires the presence of a base.^{3a,b} Quinones could also be epoxidized combining UHP and a base, using alcohols or dichloromethane as the solvent system.¹⁴ Asymmetric epoxidation of α,β -unsaturated aldehydes has been achieved with excellent yields and enantioselectivities.^{3c}



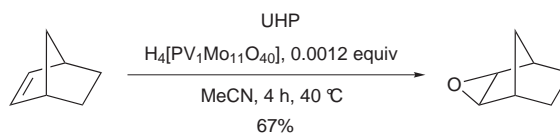
(C) Regioselective epoxidation of monoterpenes in the liquid phase using titanosilicates TS-1 and TiAlB combined with UHP as an oxidant has been achieved.¹⁵ Epoxidation occurs exclusively at the more electron-rich bond. Hutchings et al.¹⁶ have also studied the influence of the hydroxy group in the regioselectivity of the epoxidation in linalool, geraniol and citronellol.



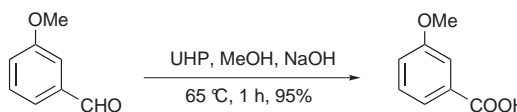
(D) Methyl trioxorhenium (MTO) has proved an efficient catalyst for regio- and stereospecific epoxidation of different substrates¹⁷ both in room temperature ionic liquids (based on *N,N'*-dialkylimidazolium or *N*-alkylpyridinium cations)¹⁸ and in non-protic solvents such as dichloromethane.¹⁹ Diethyl ether as solvent and pyridine as the ligand gives the optimal results for epoxidation of cholesterol.²⁰ α -Hydroxy and α -siloxy esters are obtained from methyl trimethylsilyl ketene acetals through the corresponding epoxide under similar conditions.²¹



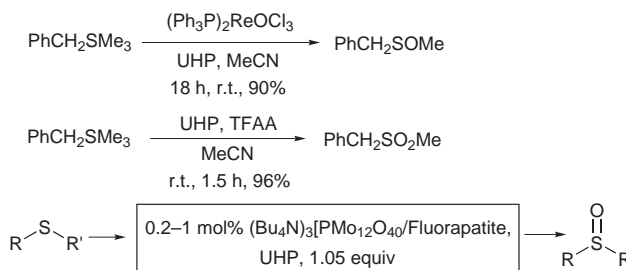
(E) *Exo* epoxidation of norbornene has been carried out over vanadium substituted phosphomolybdic acid catalysts with H₂O₂, UHP or TBHP. UHP shows similar conversion rates as H₂O₂, but better selectivities (97% of the epoxide achieved) due to the slow and controlled release of hydrogen peroxide and the less acidic character of the reaction medium.²²



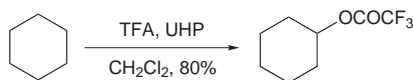
(F) Aromatic aldehydes are oxidized to the corresponding benzoic acids in good to excellent yields.⁸



(G) The oxidation of sulfide to sulfoxide has been achieved using rhenium catalysts in non-aqueous media. Triphenylphosphine ligands in the catalyst proved to be effective to stop the reaction at the sulfoxide stage in good yields.⁶ Using MTO-UHP the reaction proceeds further to the sulfone stage. A combination of UHP and trifluoroacetic anhydride in acetonitrile affords the sulfone in excellent yields.⁷ Solvent free oxidation of sulfides with UHP and tetrabutylammonium phosphomolybdate catalyst on fluorapatite was achieved at 4–25 °C giving the corresponding sulfoxides or sulfones selectively by controlling the amount of UHP employed.²³

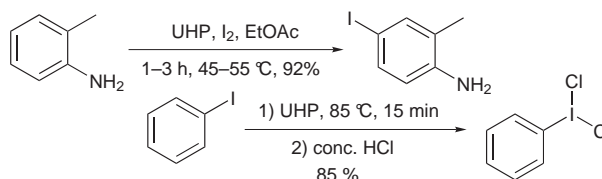


(H) The oxidation of unactivated C–H bonds with UHP has been reported. In the presence of catalytic amounts of a vanadium salt (Bu₄NVO₃) and pyrazine-2-carboxylic acid in acetonitrile, the hydroperoxide of cyclohexane was formed.²⁴ Substituted toluenes were selectively oxidized to aldehydes with UHP in the presence of cobalt(II) acetate, acetic acid and an inorganic bromide source.²⁵ Oxidation of cyclohexane with UHP in TFA gave the cyclohexyl trifluoroacetate in good yield.²⁶



(I) Oxidative halogenation of arenes with UHP and iodine in ethyl acetate has been reported.²⁷

Skulski et al. have also described an efficient solid state chlorination of iodoarenes with UHP affording dichloroiodoarenes in 64–98% yields after 15 minutes at 85 °C.²⁸



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