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A catalytic, environmentally benign method for the epoxidation of unsaturated terpenes with hydrogen peroxide

Georgia Grigoropoulou and James H. Clark*

Centre for Clean Technology, Chemistry Department, University of York, York YO10 5DD, UK

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Abstract—Various unsaturated terpenes were selectively oxidised to the corresponding epoxides in good yields using phosphate buffered hydrogen peroxide and catalytic amounts of tungstate under halide free conditions. The selectivity of the reaction to epoxides was significantly increased with respect to the ionic strength of the aqueous phase of the system.

The oxidation of terpenes is an important industrial application as their epoxides are used as starting materials in the synthesis of commercially important fragrance and flavour materials.[1] One of the most used epoxidation methods in the fine chemicals industry is the stoichiometric peracid route using acids such as peracetic acid and *m*-chloroperbenzoic acid.[2] The employment of peracids is not a clean method as equivalent amounts of acid waste are produced. The safety issues associated with handling peracids are also a matter for concern. Therefore, there is a strong need for catalytic epoxidation methods which employ safer oxidants and produce little waste. The employment of hydrogen peroxide is an attractive option both on environmental and economic grounds.[3] It is cheap, readily available and gives water as the only by-product.

Tungsten-based catalysts have been shown to be very effective in some epoxidations using hydrogen peroxide. Reactions are carried out under biphasic phase transfer catalysed conditions and require the employment of halogenated solvents[4] and the use of a preformed catalyst. An improved catalytic system under halide free conditions was developed by Noyori[5] but requires the use of aminomethyl phosphonic acid additive and fails to produce acid sensitive epoxides due to their hydrolytic decomposition under the acidic conditions.

We report here the synthesis of several acid labile epoxides from a range of terpenes (Scheme 1) under pseudo-Noyori conditions without expensive phosphonic acids and halo auxiliaries but optimised with respect to pH and ionic strength.

Limonene (**1**) was chosen as a model substrate. It has been oxidised to limonene oxide (**1a**) with hydrogen peroxide in the presence of catalytic amounts of sodium tungstate under various reaction conditions (Table 1).

The oxidation of **1** in the presence of a catalytic system which consists of sodium tungstate dihydrate, (aminomethyl)phosphonic acid and methyltri-*n*-octylammonium hydrogen sulfate[6] in a 2:1:1 ratio, resulted in high conversion but low selectivity to limonene oxide (45%), entry 1.

The use of a phosphate buffer solution of H_3PO_4/NaH_2PO_4 (0.1 M made in H_2O_2 solution) as a phosphate source increases significantly the selectivity of the reaction to epoxide. Addition of a 7:3 molar ratio of H_3PO_4/NaH_2PO_4 solution to the reaction mixture (initial pH of aqueous phase 2.5) results in high conversion and an increased selectivity to limonene oxide (66%), entry 2. The use of a 5:5 molar ratio of H_3PO_4/NaH_2PO_4 solution to the reaction mixture (initial pH of aqueous phase 3.0) is not beneficial to the selectivity of the reaction and it also results in a decrease of the reaction rate, entry 3.

The effect of the counter anion of the methyltri-*n*-octylammonium salt was investigated and it was found that dihydrogen phosphate[7] compared to hydrogen sulfate

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* Corresponding author. E-mail: jhc1@york.ac.uk

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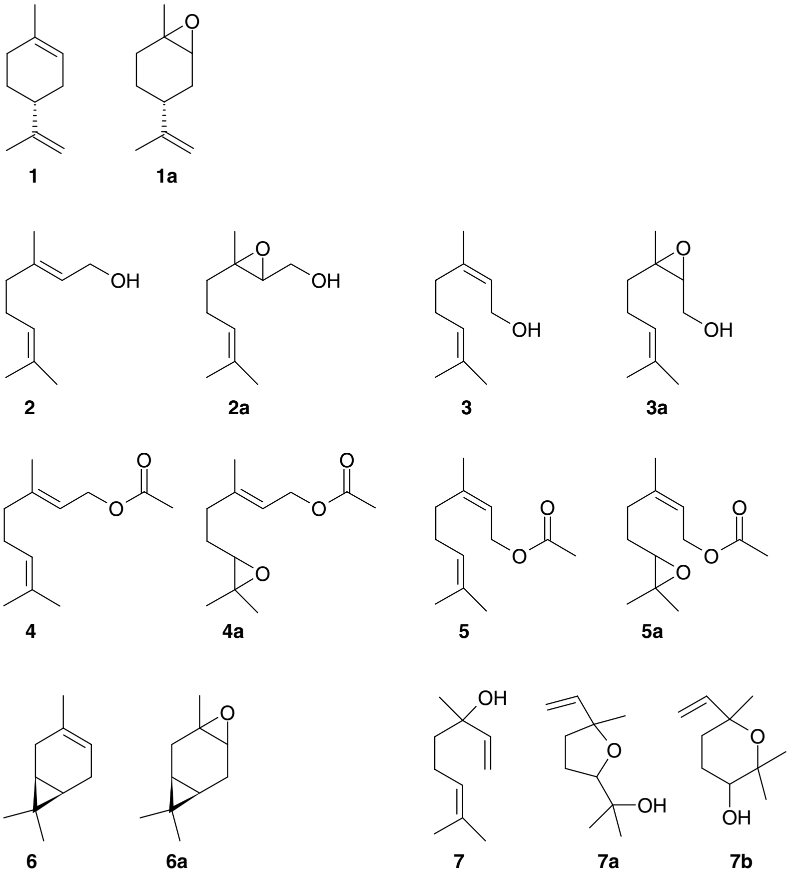

Scheme 1. Unsaturated terpenes and the corresponding reaction products.

Table 1. Epoxidation of limonene with 30% H_2O_2[a]

Entry	Time (min)	Conversion (%)	Selectivity to **1a** (%)
1[b]	60	95	45
2	30	98	66
3	120	98	64
4[c]	120	39	69
5[d]	60	92	79
6[d,e]	120	94	81

[a] Reaction conditions: limonene (20 mmol), H_2O_2 (30 mmol), $Na_2WO_4 \cdot 2H_2O$ (0.4 mmol), $[(n\text{-}C_8H_{17})_3NCH_3]HSO_4$ (0.2 mmol), H_3PO_4/NaH_2PO_4 (0.2 mmol) in toluene (4 mL) at 70 °C.

[b] $NH_2CH_2PO_3H_2$ was used instead of H_3PO_4/NaH_2PO_4.

[c] $[(n\text{-}C_8H_{17})_3NCH_3]H_2PO_4$ was used instead of $[(n\text{-}C_8H_{17})_3NCH_3]HSO_4$.

[d] Addition of Na_2SO_4(1 mmol).

[e] 15 mL of toluene.

results in a significant decrease in the conversion of limonene but does not alter the selectivity of the reaction, entry 4. The low efficiency with dihydrogen phosphate is probably due to a higher initial pH value of the aqueous phase (pH 3.3).

The addition of sodium sulfate to increase the ionic strength of the aqueous phase results in a significant increase of the selectivity to epoxide, entry 5. The hydrolytic decomposition of epoxide slows down as the water content of the organic phase decreases[8] when large amounts of sodium sulfate are added to the system.

Furthermore, the increase of the volume of the solvent added to the reaction mixture is beneficial for both the conversion and selectivity of the reaction, entry 6.

Our optimised method was successfully expanded to other terpene substrates (Table 2).

It was found that both geraniol (**2**) and nerol (**3**) afforded the 2,3-epoxides (**2a**, **3a**) with high to moderate selectivities (81% and 47%, respectively). The observed regioselectivity in the oxidation of geraniol and nerol is not unexpected, as it has been demonstrated before[10] that in the presence of tungsten metal catalysts a complex is possibly formed involving the metal centre, the

Table 2. Epoxidation of a range of different terpenes under the optimum reaction conditions[9]

Substrate	Time (min)	Conversion (%)	Yield (%)	Selectivity to epoxide (%)
Geraniol **2**	30	98	80	81
Nerol **3**	30	99	47	47
Geranyl acetate **4**	120	90	71	80
Neryl acetate **5**	120	95	59	62
3-Carene **6**	240	93	88	95

oxidant and the substrate through OH coordination. The oxidation of geranyl acetate (**4**) and neryl acetate (**5**) gave the 6,7-epoxides **4a** and **5a** in good selectivities (80% and 62%, respectively). The epoxidation takes place preferably, as expected, at the C6–C7 double bond, which has higher electron density compared to the C2–C3 double bond.

Furthermore, the main product of the oxidation of 3-carene (**6**) was 3,4-epoxycarene (**6a**) with high selectivity (95%). Finally, linalool (**7**) was transformed with 91% conversion but no epoxide product was detected. Some of the identified reaction products were the tetrahydrofuran derivative **7a** with low selectivity (26%) and the tetrahydropyran derivative **7b** (14% selectivity).

In summary, a variety of terpenes were selectively oxidised with 30% H_2O_2 and a phosphotungstate catalytic system, to the corresponding epoxides in good yields under halide free conditions.

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