

Microwave-Accelerated Epoxidation of α,β -Unsaturated Ketones with Urea-Hydrogen Peroxide

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Abstract: The reaction time needed to perform the epoxidation of several α,β -unsaturated ketones with urea-hydrogen peroxide were substantially reduced by means of microwave irradiation. This environmental friendly protocol showed to be very useful, especially to effect the epoxidation of sterically hindered substrates.

Keywords: α,β -unsaturated ketones, urea-hydrogen peroxide, epoxidation, microwave irradiation.

Since epoxides are very important chemicals in synthetic organic chemistry [1-6] as well as in industry, great attention has been dedicated on the development of methodologies allowing the epoxidation of carbon-carbon double bonds. Epoxidation of α,β -unsaturated ketones, alkenes and allylic alcohols using Urea-Hydrogen Peroxide (UHP), has been described [7, 8].

UHP, a white crystalline solid, is formed when urea is recrystallized from aqueous hydrogen peroxide [9]. It has been employed as a solid substitute for liquid hydrogen peroxide. UHP has a quite high hydrogen peroxide content (36% w/w) and it is relatively stable. The application of UHP as a reagent in organic synthesis started to be described more recently [7,10], and it has the advantage of generating innocuous by-products.

The first applications of microwave (MW) irradiation in order to accelerate organic [11,12] organometallic [13,14] and solid state reactions [15] have paved the way for applying this technique in organic synthesis. Nowadays MW has been employed not only to decrease reaction times but also to improve yields. MWs constitute a very original procedure for heating materials, clearly different from the classical ways. The reduction on reaction times are attributed to be a result of both temperature and pressure effects and supposed specific effects of the radiation, such as improved homogeneity in temperature, a faster temperature rise, and possible modifications of activation parameters ΔH^\ddagger and ΔS^\ddagger [16,17]. Several reviews have been published covering various aspects of microwave-assisted chemistry [18-20]. MW irradiation has been reported to accelerate epoxidation of α,β -unsaturated ketones and alkenes [21,22].

Herein, we describe our results on the preparation of epoxides through an environmental friendly and time saving protocol, reacting α,β -unsaturated ketones with UHP under MW irradiation.

The epoxidation of all enones tested upon MW irradiation occurred within seconds, even for the compounds

more sterically hindered, such as isophorone whose epoxidation has been described to be troublesome [23] (entry 5) and for verbenone (entry 6), which had the reaction time dramatically reduced from more than 48 hours to 90 seconds and the product yield improved from 40 to 80%. As a result of the reaction conditions employed [7] carvone (entry 2) was epoxidized in completely regioselective way.

In all cases the reaction mixture was submitted to irradiation from 3 to 6 times (each time for 15-20 s with 5 min intervals). To avoid solvent loss the reaction was performed in a glass round-bottom flask, which was placed inside a modified domestic microwave oven [24, 25], which allowed the coupling between the reaction flask and a water condenser located completely outside the oven cavity.

In conclusion the epoxidation of α,β -unsaturated ketones were successfully carried out applying an environmental friendly and time saving protocol. The isolated yields of the products are good and usually higher than those achieved when the reactions were performed without MW irradiation, especially for sterically hindered compounds.

EXPERIMENTAL

MW induced reactions were carried out in a modified Panasonic domestic household oven (900 W) at 2450 MHz. In all cases the reaction mixtures were subjected to MW-irradiation for a period of 15 s with 5 min mixing intervals. Reactions were monitored by thin-layer chromatography (TLC; E. Merck, Type 5554 plates) and gas chromatography with a Varian 3800 GC (flame ionization detector) using a VA-5, 5% phenyl 95% methylpolysiloxane capillary column (30 m x 0.25 mm x 0.25 μ m). Mass spectra of all epoxides prepared were obtained on a Varian Saturn GC/MS/MS 2000 spectrometer using the same capillary column described for the GC analysis. FTIR spectra were recorded on a Hartmann & Braun spectrometer model B-100. Flash column chromatography was carried out with 230-400 mesh silica gel (E. Merck).

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Table 1. Epoxidation of α,β -Unsaturated Ketones with UHP under MW Irradiation

Entry	Substrate	Product	UHP/Substrate (mole ratio)	Microwave yield ^a (%), Time (s)	No microwave yield ^a (%), Time (h)
1			3	95 (45)	100 (5)
2			3	84 (90)	87 (3)
3			3	85 (75)	80 (2)
4			3	92 (45)	88 (1)
5			4	85 (120)	70 (>24)
6			4	80 (90)	40 (>48)
7			3	82 ^b (45)	74 ^b (1)
8			3	83 ^b (60)	76 ^b (1)
9			3	75 ^b (75)	68 ^b (1)
10			3	80 (120)	92 (6)

^aisolated yield, ^bGC yield. All products are known compounds and were identified by GC-MS and FTIR analysis.

TYPICAL PROCEDURE FOR EPOXIDATION OF α,β -UNSATURATED KETONES UNDER MW IRRADIATION

In a round-bottom flask containing chalcone (0.416g, 2 mmol) and UHP (36% w/w) (1.567 g, 6 mmol) dissolved in a mixture of 1,4-dioxane (10 mL) and water (4 mL), was added an aqueous solution of NaOH (1 Mol/L) (0.2 mL). The water condenser was adapted to the reaction flask, which was irradiated for 45 s (3 times, each time of 15 s with 5 min intervals). The reaction mixture was transferred to a separatory funnel with ether (100 mL), washed with water (3 x 30 mL) and dried over Na₂SO₄. The filtrate was concentrated in vacuo and purified by flash chromatography (hexane/ethyl ether 4:1 v/v) to give the corresponding epoxide (0.426 g, 95%).

All compounds were also reacted with UHP but without MW irradiation, at 25 °C.

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