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Synthesis of 2,3-epoxy-1-phenyl-3-aryl-1-propanone by combination of phase transfer catalyst and ultrasound irradiation

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Abstract: Seven 2,3-epoxy-1-phenyl-3-aryl-1-propanones were synthesized *via* epoxidation of the corresponding 1-phenyl-3-aryl-2-propen-1-ones with 30% aqueous hydrogen peroxide in 74-99% yields using benzyldimethyltetradecylammonium chloride as phase transfer catalyst under ultrasound irradiation.

Keywords: Epoxidation; 2,3-epoxy-1-phenyl-3-aryl-1-propanone; phase-transfer catalysis; ultrasonic irradiation.

1. Introduction

Epoxy carbonyl compounds are very important synthetic intermediates[1] and can serve as versatile precursor in synthesis of many natural products and drug molecules,[2] which are usually prepared *via* epoxidation of α,β–unsaturated ketones .[3]

Epoxidation reaction has recently been the subject of numerous investigations and a number of useful methodologies involving different types of catalyst-reagent combinations have been elaborated.[4] Among these methodologies, the method utilizing phase-transfer catalysis occupies a unique place.[6] The use of phase-transfer catalysis is a technique by which reactions between substances located in mutually immiscible phases are brought about or accelerated. In the absence of a catalyst such reactions are often slow or do not occur at all. In comparison with traditional methods, the technique has the following advantages: no need for expensive aprotic solvent; simpler work-up; shorter reaction time and lower reaction temperature.[7] Hummelen and Wynberg[8] firstly reported epoxidation of 1,3-diphenyl-2-propen-1-one with sodium hypochlorite using phase-transfer catalyst (PTC) derived from cinchona alkaloid in toluene at 25 ^{o}C by stirring vigorously for 72 h in 1978, but the yield of 2,3-epoxy-1,3-diphenyl-1-propanone was only 66%, and needed a long reaction time and the excess of sodium hypochlorite.

Hydrogen peroxide has recently regained importance as an oxidant in both industrial and academic community. The main reason are related to ' regulatory forces causing the chemical industry to reduce, and in some instances eliminate environmental pollution', and to the fact that the chemical industry is now capable of employing H_2O_2 in a safer, more efficient and innovative manner.[9] In 1979, Marsman and Wynberg[10] reported that the epoxidation of 1,3-diphenyl-2-propen-1-one was carried out in 92% yield at 3 ^{o}C by stirring for 100 h. with 30% hydrogen peroxide solution and sodium

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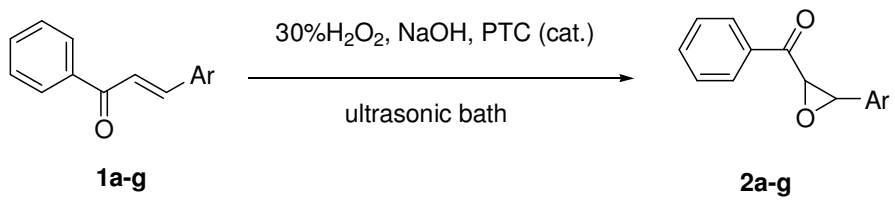
hydroxide in CCl_4 in the presence of quininiumbenzyl chloride. In 1998, Arai et al.[11] reported the epoxidation of

1,3-diphenyl-2-propen-1-one using a quaternaryammonium salt with 30% H_2O_2 in aqueous LiOH-dibutyl ether at 4 ^oC for 37 h to give epoxide in 97% yield. In 2003, Fioroni et al.[12] described the epoxidation of 1,3-diphenyl-2-propen-1-one catalyzed by cetyltrimethylammonium hydroxide with 30% H_2O_2 at 0-2 ^oC for 2 h to give in 85% yield. Recently, Lv et al. reported that epoxidation of 1,3-diphenyl-2-propen-1-one with cumylhydroperoxide was carried out in 90% yield at 0 ^oC in dichloromethane for 48 h by using polyethylene glycol-supported cinchona ammonium salt.[13] However, in spite of their potential utility, some of the reported methods suffer from drawbacks such as longer reaction times and/or lower yields.

Ultrasound irradiation has been considered as a clean and useful protocol in organic synthesis in the last three decades. Compared with traditional methods, the procedure is more convenient. A large number of organic reactions can be carried out in higher yield, shorter reaction time or milder conditions under ultrasonic irradiation.[14,15] In recent years, the combination of ultrasonic technique and phase transfer catalyst for the organic reactions have been reported.[16-18] Herein, we wish to report the synthesis of 2,3-epoxy-1-phenyl-3-aryl-1-propanones via epoxidation of 1-phenyl-3-aryl-2-propen-1-ones with aqueous hydrogen peroxide at room temperature in the presence of benzyldimethyltetradecylammonium chloride under ultrasound irradiation (**Scheme 1**).



Scheme 1. Epoxidation of 1-phenyl-3-aryl-2-propen-1-ones with hydrogen peroxide

2. Results and Discussion

The effect of reaction conditions on epoxidation under ultrasound irradiation is summarized in Table 1. As shown in Table 1, the amount of phase transfer catalyst, the amount of NaOH and temperature had a significant effect on this reaction. We performed the experiment for the epoxidation of 1,3-diphenyl-2-propen-1-one (**1a,** 1 mmol) with 30% H_2O_2 (1.5 mmol) and NaOH (0.040g, 1 mmol) at 20 ^oC under ultrasonic irradiation for 2 h, in the absence of PTC, the yield of **2a** was only 13% (**Entry 6**). Increasing the amount of PTC to 0.01 mmol and 0.025 mmol, the yield of **2a** increased to 95 % and 98 % respectively. In the case of using 0.05 mmol PTC, the yield of **2a** was nearly quantitative (99%).

Table 1. The effect of reaction condition of epoxidation of 1,3-diphenyl-2-propen-1-one with hydrogen peroxide catalyzed by benzyldimethyltetradecylammonium chloride under ultrasound irradiation [a]

Entry	Substrate:H_2O_2 (mmol:mmol)	Amount of NaOH (mmol)	PTC (mmol)	T (^oC)	Isolated yield, (%)
1	1:1	1	0.05	20	92
2	1:1	1	0.05	30	85
3	1:1	1	0.05	40	70
4	1:1.2	1	0.05	20	96
5	1:1.5	1	0.05	20	99
6	1:1.5	1	0	20	13
7	1:1.5	1	0.01	20	95
8	1:1.5	1	0.025	20	98
9	1:1.5	0	0.05	20	8
10	1:1.5	0.25	0.05	20	78
11	1:1.5	0.50	0.05	20	92
12	1:1.5	0.75	0.05	20	97
13	1:1.5[b]	1	0.05	20	89
14	1:1.5[c]	40	0.05	20	70

aReaction time: 2 h; the frequency of ultrasonic cleaner is 40 kHz; T ± 2 ^oC.

[b] Stirred without ultrasound.

[c] Reacted in CH_2Cl_2–H_2O.

From the results given at Table 1, the most efficient reaction conditions were as follows: 1-phenyl-3-aryl-2-propen-1-one (**1**, 1 mmol), H_2O_2 (30%, 0.170 g, 1.5 mmol), NaOH (1 mmol), PTC (0.05 mmol), 20 ^oC, water (2 mL), and ultrasonic irradiation frequency (40 kHz). Using this reaction system, we did a series of experiments for the epoxidation of chalcones. The results were summarized in Table 2.

As shown in Table 2, epoxidation of 1-phenyl-3-aryl-2-propen-1-one was carried out in moderate to good yields with aqueous H_2O_2 catalyzed by benzyldimethyltetradecylammonium chloride under ultrasound irradiation. The dramatic improvement is observed with regard to reaction time. In reported methods [9, 11, 13] the reaction time of epoxidation were not less than 37 h and needed organic solvent(CCl_4, CH_2Cl_2 or toluene), whereas in the present procedure, the epoxidation of 1-phenyl-3-aryl-2-propen-1-ones **1a-g** was carried out in good yields within 2-3 h, and did not require organic solvent.

We also observed the epoxidation of 1,3-diphenyl-2-propen-1-one with 30% H_2O_2 catalyzed by cinchonidininumbenzyl chloride in CCl_4 at r.t. under ultrasound, the reaction was completed within 1.5 h to give product **2a** in 89% yield, which was similar to that by stirring for 100 h in the presence of quininiumbenzyl chloride.[10]

From these results, we can deduce that the yields are, in general, similar or higher than those described in literatures.[9-13] Compared with the previous procedures, the main advantages of the procedure are milder conditions and shorter reaction time.

In conclusion, we have found an efficient and practical procedure for the synthesis of some 2,3-epoxy-1-phenyl-3-aryl-1-propanones *via* the epoxidation of 1-phenyl-3-aryl-2-propen-1-ones with aqueous hydrogen peroxide by combination of phase transfer catalyst and ultrasound irradiation.

Table 2 Epoxidation of 1-phenyl-3-aryl-2-propen-1-ones with hydrogen peroxide by combination of benzyldimethyltetradecylammonium chloride and ultrasound irradiation [a]

Entry	Ar	Time (h)	Isolated Yield (%)	M.p (lit.) (^{o}C)
a	C_6H_5	2	)99	81-82 (82-85) [15]
b	4-ClC_6H_4	3	82	69-70 (68-71) [16]
c	3-$O_2NC_6H_4$	3	78	115-116 (115-116) [11]
d	4-$O_2NC_6H_4$	3	85	140-141 (140-142) [17]
e	4-$CH_3C_6H_4$	3	86	69-71 (70-71) [18]
f	2-$CH_3OC_6H_4$	3	84	89-90 (90-91) [18]
g	2, 4- $Cl_2C_6H_3$	3	74	109-110

[a] Reaction condition: H_2O_2, 1.5 mmol; NaOH, 1 mmol; PTC, 0.05 mmol; reaction temperature, 20 ± 2 ^{o}C.

3. Experimental

3.1 General

1-Phenyl-3-aryl-1-propenones were prepared according to literature.[23] Melting points was uncorrected. Sonication was performed in Shanghai Branson BUG25-06 ultrasonic cleaner (with a frequency of 25 kHz, and a nominal power 250 W) and SK 250 LH ultrasonic cleaner (with a frequency of 40, 59 kHz and a nominal power 250 W; Shanghai Kudos ultrasonic instrument Co., Ltd.).The ^{1}H NMR spectra were recorded on a Bruker Avance 400 (400 MHz) spectrometer using TMS as internal standard and $CDCl_3$ as solvent. Heraeus (CHN-O-Rapid) analyzer.

3.2 Synthesis

The 1,3-diphenyl-2-propen-1-one (**1a)** (0.208 g, 1 mmol), aqueous 30% hydrogen peroxide (0.170 g, 1.5 mmol), benzyldimethyltetradecylammonium chloride (0.020 g, 0.05 mmol), water (2 mL), sodium hydroxide (0.040 g, 1 mmol) were added into a 50 mL Pyrex flask. The mixture was irradiated in the ultrasonic cleaning bath at 20 ^{o}C for 2 h (sonication was continued until benzalacetophenone had disappeared as indicated by TLC). The reaction mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were dried over anhydrous magnesium sulfate, filtered, and evaporated the solvent under reduced pressure. The crude product was purified by column chromatography on silica gel (200-300 mesh) eluting with petroleum ether or a mixture of petroleum ether and diethyl ether to afford the product **2a** (0.223g, 99%), The authenticity of the known compounds **2a-2f** was established by comparing their melting points and ^{1}H NMR data with data reported in literatures. [13, 20-22] The structure of **2g,** a new compound**,** was established by ^{1}H NMR and ^{13}C-NMR and elemental analysis.

2,3-Epoxy-1,3-diphenyl-1-propanone (**2a)**: colorless solid, m. p. 81-82 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.08 (d, 1H, J=1.6 Hz, 3- CH), 4.30 (d, 1H, J=1.6 Hz, 2-CH), 7.39-8.01 (m, 10H, Ph-H).

Synthesis of 2,3-epoxy-1-phenyl-3-aryl-1-propanone

2,3-Epoxy-1-phenyl-3-(4-chlorophenyl)-1-propanone (**2b)**: colorless solid, m.p.69-70 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.06 (d, 1H, J=1.6 Hz, 3-CH), 4.25 (d, 1H, J=1.6 Hz, 2-CH), 7.26-8.00 (m, 9H, Ph-H).

2,3-Epoxy-1-phenyl-3-(3-nitrophenyl)-1-propanone (2c): white solid, m.p.115-116 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.21 (d, 1H, J=1.2 Hz, 3-CH), 4.30 (d, 1H, J=1.2 Hz, 2-CH), 7.26-8.24 (m, 9H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 192.5, 149.2, 138.4, 135.7, 134.7, 132.1, 130.3, 129.4, 128.8, 124.3, 121.2, 61.1, 58.3.

2,3-Epoxy-1-phenyl-3-(4-nitrophenyl)-1-propanone (2d): yellow solid, m.p.140-141 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.21 (d, 1H, J=1.6 Hz, 3-CH), 4.27 (d, 1H, J=1.6 Hz, 2-CH), 7.51-8.28 (m, 9H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 192.4, 148.8, 143.2, 135.7, 134.7, 129.4, 128.8, 127.0, 124.5, 61.3, 58.3.

2,3-Epoxy-1-phenyl-3-(4-methylphenyl)-1-propanone (**2e)**: white solid, m.p.69-71 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.37 (s, 3H, CH_3), 4.03 (d, 1H, J=1.2 Hz, 3-CH), 4.30 (d, 1H, J=1.2 Hz, 2-CH,), 7.18-7.99 (m, 9H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 193.6, 139.4, 136.0, 134.3, 133.0, 129.9, 129.2, 129.0, 126.2, 61.5, 59.8, 21.6.

2,3-Epoxy-1-phenyl-3-(2-methoxyphenyl)-1-propanone (**2f)**: colorless solid, m.p. 89-90 ^{o}C, ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.84 (S, 3H, CH_3), 4.19 (d, 1H, J=1.6 Hz, 3-CH), 4.39 (d, 1H, J=1.6 Hz, 2-CH), 6.91-8.06 (m, 9H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 194.0, 158.7, 136.1, 134.1, 130.1, 129.1, 129.0, 126.0, 124.7, 121.2, 110.8, 60.9, 56.1, 55.8.

2,3-Epoxy-1-phenyl-3-(2,4-dichlorophenyl)-1-propanone (2g): colorless solid, m.p.109-110 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.14 (d, 1H, J=1.2 Hz, 3- CH), 4.33 (d, 1H, J=1.2 Hz, 2-CH), 7.26-8.03 (m, 8H, Ph-H). Anal. Calcd for $C_{15}H_{10}O_2Cl_2$: C 61.46, H 3.44; found C 61.67, H 3.77; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 192.8, 135.7, 135.5, 134.5, 134.4, 132.9, 129.7, 129.3, 129.3, 128.1, 127.5, 60.4, 57.0.

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