Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Sonochemical Formation of Iodohydrin and Epoxide from Cyclohexene

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To cite this article: Vanessa S. Fernandes, Jayne C. S. Barboza, & Antônio Aarão Serra (2007): Sonochemical Formation of Iodohydrin and Epoxide from Cyclohexene, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 37:9, 1433-1436

To link to this article: http://dx.doi.org/10.1080/00397910701226467

Synthetic Communications®, 37: 1433–1436, 2007
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ISSN 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910701226467

Sonochemical Formation of Iodohydrin and Epoxide from Cyclohexene

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Abstract: Ultrasonic irradiation substantially improves the reaction of cyclohexene with I_2 in aqueous dioxane in the presence of $Cu(OAc)_2 \cdot H_2O$ to generate the expected iodohydrin in high yield. The product undergoes cyclization to the epoxide by biphasic treatment with either Na_2CO_3 or KOH in a sonication-sensitive step.

Keywords: Epoxidation, iodohydrin, ultrasonic irradiation

INTRODUCTION

Halohydrins and epoxides are important intermediates in organic synthesis, and many methods are available for their preparations.[1–3] The two families of compounds are closely interconnected (i.e., one can be obtained from the other by ring closure or opening). Thus the oxidation of an olefin to the halohydrin followed by cyclization with base yields the epoxide; on the other hand, halohydrins can be prepared, inter alia, from cyclohexene by using a tin(II) halide–catalyzed process[4] under sonochemical activation. Thus, studies aimed at an improved access to one of the functionalities can have double effects. We have chosen to study the effect of ultrasounic irradiation[5] on the copper-mediated reaction of iodine with cyclohexene as a typical model (Scheme 1). Significant results are reported in this note.

Received in the USA October 2, 2006

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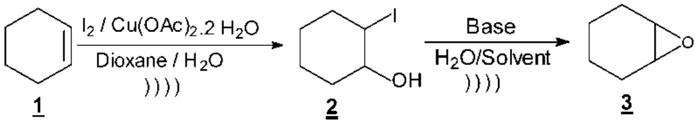

Scheme 1.

METHODS AND RESULTS

The purity of homemade cyclohexene (from cyclohexanol) was checked by usual methods (gas chromatography, ^1H and ^{13}C NMR, IR spectra). Cyclohexene preparation: cyclohexanol was added to phosphoric acid (85 wt.%), and cyclohexene was distilled off at 60–80°C. The product was redistilled at 74°C. Literature conditions[1] were applied to prepare standard samples of 1-iodo-2-hexanol 2. Cyclohexene oxide and n-octane (Aldrich) were used as the standard and internal standard respectively. Temperature was kept in the range of 23–25°C. GC analyses were performed on a CP3380 Varian gas chromatograph with FID using a CP-Sil 8 CD (silica capillary column, 30 m long, 0.32 mm ID, and 0.25 μm phase thickness, CP 8752) with N_2 as carrier gas. Oven temperature, initially at 50°C (5 min), rose to 110°C at a rate of $20°C \cdot min^{-1}$ and was kept constant at the final value for 8 min. The injector and detector temperatures were 230°C and 260°C, respectively. ^1H NMR and ^{13}C NMR were obtained on a Mercury 300-MHz and Varian spectrometers in $CDCl_3$ solutions with tetramethylsilane as internal standard. IR spectra were recorded on a Perkin-Elmer FT-IR Spectrum One.

A 50-mL Erlenmeyer flask was loaded with cyclohexene 1 (0.21 g, 2.60 mmol), Cu $(OAc)_2 \cdot 2H_2O$ (0.259 g, 1.30 mmol), n-octane 99 + % (0.31 g, 2.71 mmol), iodine (0.493 g, 1.95 mmol), dioxane (5.6 mL), and water (0.8 mL) (dioxane–H_2O ratio 7:1)[1]. The flask was closed with a rubber septum, and the heterogeneous mixture was sonicated in a laboratory cleaner (Kerry Pulsatron 60, 38 kHz) thermostated by running cold water in a steel coil placed inside the bath. Reaction temperature was 23–25°C. Samples (0.2 mL) were collected at the specified time, and solid materials were filtered off through Celite®. CH_2Cl_2 (3 mL) was added, and the resulting solution was treated with 2 mL of $NaBH_4$ in ethanolic suspension (1% w/v). The solutions were washed three times with water, and all the organic fractions were dried over anhydrous Na_2SO_4 followed by filtration through a cotton plug before GC analysis (0.1 μL). A purified sample 2 gave the following data: ^1H NMR: δ 4.12–3.95 (m, 1 H), 3.72–3.58 (m, 1 H), 2.55–2.40 (m, 1 H), 2.16–1.94 (m, 2 H), 1.92–1.78 (m, 1 H), 1.58–1.45 (m, 1 H), 1.44–1.15 (m, 4 H) ppm. ^{13}C NMR: δ 76.1, 43.0, 38.5, 33.5, 28.0, 24.2 ppm. IR: ν 3384, 2933, 2856, 1447, 1161, 1033, 952, 858, 657 cm^{-1}.

Cyclization to cyclohexene oxide 3 was effected in a similar manner. A 50-mL Erlenmeyer flask was loaded with iodohydrin (0.34 g, 1.50 mmol), Na_2CO_3 (0.22 g, 2.10 mmol), water (5.6 mL), and C_2H_5OH (1.4 mL), with decane (0.079 g) as an internal standard. The flask was closed with a rubber septum and sonicated for 60 min at 23–25°C. Samples (0.1 mL) were collected at 15-min intervals and diluted with CH_2Cl_2 (2 mL); the organic phase was washed with water (3x), dried (anhydrous Na_2SO_4), filtered through a cotton plug, and analyzed by GC (0.1 μL).

Alternatively, using potassium hydroxide (0.062 g, 1.10 mmol), the mixture of iodohydrin (0.20 g, 0.90 mmol), water (1.6 mL), pentane (2.6 mL), and Et_2O (2.6 mL) in a 50-mL Erlenmeyer flask, with decane (0.062 g) as an internal standard, was sonicated for 40 min at 23–25°C. Samples (0.1 mL) were collected at intervals of 10 min and worked up as before, prior to GC analysis. Spectra of purified samples agree with published data.

From the results summarized in Tables 1 and 2, the sonication-induced acceleration of both process appears clearly. Higher yields were obtained using equimolar amounts of $Cu(OAc)_2 \cdot 2H_2O$, in contrast with the twofold excess required in published procedures (Table 1). Amounts lower than stoichiometrc give poor results, as normally expected because the copper salt acts as a source of acetate ions. The effect of the water percentage was considered in a second step, as shown in Table 2. Even when the amount of the organic phase decreased (different ratios of dioxane and water), good results were still achieved (Table 2).

Alkaline treatment of 2 produced cyclohexene oxide 3 with 70% yield within 60 min in a sonication step (59%, 24 h, different systems, under agitation[2]) when Na_2CO_3 was used and 100% (40 min) with KOH (83%, 50 min[1]).

Table 1. Reaction yields for the sonochemical and conventional systems to generate iodohydrin

Time (h)	Yield (%) agitation[a]	Yield (%) sonication $Cu(OAc)_2 \cdot 2H_2O$[b]	$Cu(OAc)_2 \cdot 2H_2O$[c]
0.5		7.8	36.3
1.0		24.0	66.5
1.5		29.5	76.2
2.0		34.8	79.2
2.5		45.0	83.5
3.0		48.0	86.7
18	89.0		

[a] Conditions reported in literature[1]: Ratio of alkene to $Cu(OAc)_2 \cdot 2H_2O$: 2 to 1.

[b] Sonochemical reaction with. ratio alkene to $Cu(OAc)_2 \cdot 2H_2O$: 2 to 1.

[c] Ratio of alkene to $Cu(OAc)_2 \cdot 2H_2O$: 1 to 1.

Table 2. Influence of solvent composition on the sonochemical reaction yields (%) of the iodohydrin

Time (h)	Dioxane–water[a,b] (7:1)	Dioxane–water[b] (1:1)	Dioxane–water[b] (1:3)
0.5	36.3	42.9	10.3
1.0	66.5	62.0	20.2
1.5	76.2	64.4	21.0
2.0	79.2	68.5	26.0
2.5	83.5	60.0	39.4

[a] Sonochemical formation of iodohydrin with solvent conditions reported in literature[1].

[b] Ratio alkene to $Cu(OAc)_2 \cdot 2H_2O$: 1 to 1.

This procedure proves to be convenient for the synthesis of iodohydrin and epoxide from cyclohexene under ultrasound irradiation. Extension to various classes of olefins, now under study, will determine the application of the procedure.

ACKNOWLEDGMENTS

Financial support by the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) and Conselho Nacional de Desenvolvimento Científicoe Tecnológico (CNPq) is greatly acknowledged. Thanks are also due to H. F. de Castro (Department of Chemical Engineering/Faculdade de Engenhoria Química de Lorena (DEQUI/FAENQUIL)) and J.-L. Luche (France) for fruitful discussions.

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