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Study of conventional *versus* microwave-assisted reactions of 3,4-epoxyalcohols by $CeCl_3 \cdot 7H_2O$: Synthesis of tetrahydrofurans and 1-chloro-3-substituted-2-propanols

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Abstract

3,4-Epoxyalcohols undergo regioselective cyclization in the presence of $CeCl_3 \cdot 7H_2O$ in ref1uxing acetonitrile to afford tetrahydrofuran derivatives in good yields. On the other hand epoxyalcohols afforded 1-chloro-3-substituted-2-propanols under microwave irradiation using $CeCl_3 \cdot 7H_2O$ supported on SiO_2 under solvent-free conditions.

Keywords: Epoxyalcohols; Conventional; Microwave; Tetrahydrofurans; Chloro substituted propanols

1. Introduction

Epoxyalcohols are important precursors for the construction of oxygen-containing heterocycles. Intramolecular cyclization of epoxyalcohols is a useful reaction, which has been used for the synthesis of many natural products and other related biologically active compounds [1–5]. Cyclization of epoxyalcohols is reported using magnesium halide [6] but it requires longer reaction times (5–7 days) and reflux temperatures. Treatment of epoxyalcohols with base in 75% aqueous DMSO [7] produced four-membered ether, oxetane along with its hydrolysis products [8]. While treatment under anhydrous conditions in aprotic solvents led to formation of dimeric five-membered ether, oxolane or of a simple alcoholysis product [9].

Microwave-assisted organic synthesis [10–14] has gained popularity in recent years because microwave irradiation was found to accelerate remarkably a wide variety of reactions. Particularly, a solvent-free microwave-assisted reaction provide an opportunity to work with open vessels thus avoiding the development of high pressure and provides a possibility of up scaling the reaction on a preparative scale and helps the induction of the reaction under dry conditions. Recently, there has been increasing interest on the use of $CeCl_3$ in various organic transformations [15–18] because of its low toxicity, inexpensive, ready availability and moisture and air tolerance. Recently $CeCl_3 \cdot 7H_2O$/NaI system [19] was reported for the dehydration of β-hydroxy carbonyl compounds to give the corresponding (*E*)-enones and for the synthesis of (*S*)-pulegone [20]. In our continued interest on the study of epoxide opening [21,22], we herein report $CeCl_3 \cdot 7H_2O$ mediated ring opening reactions of epoxyalcohols for the synthesis of tetrahydrofuran and 1-chloro-3-substituted-2-propanols under conventional and microwave irradiation conditions (Schemes 1 and 2).

2. Results and discussion

The required epoxyalcohols **la–j** were prepared by known methods starting from ketones by allylation with allylbromide and Zn followed by epoxidation of double bond with *m*-chloroperbenzoic acid (*m*-CPBA). The reaction of epoxyalcohol, 1-(2,3-epoxypropyl)-1-cyclohexanol, **1a** in the presence of 0.5 equiv. of $CeCl_3 \cdot 7H_2O$ in refluxing acetonitrile afforded a spiro-hydroxytetrahydrofuran (**2a**) as the sole product in 75%

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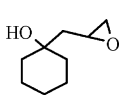
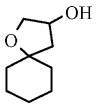
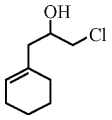
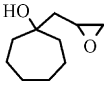
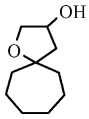
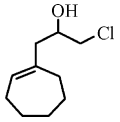
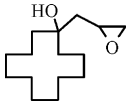
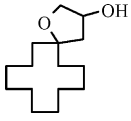
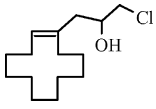
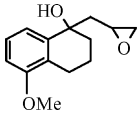
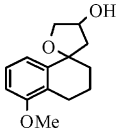
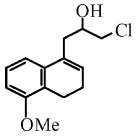
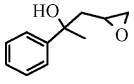
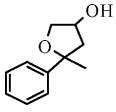
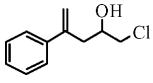
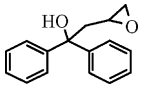
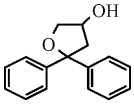
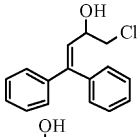
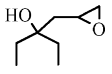
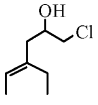
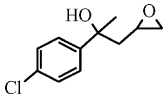
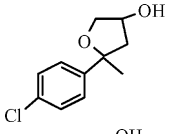
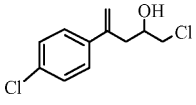
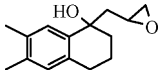
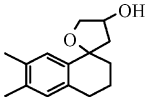
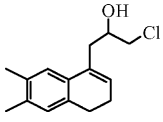
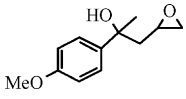
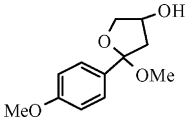
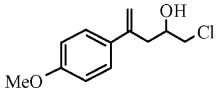
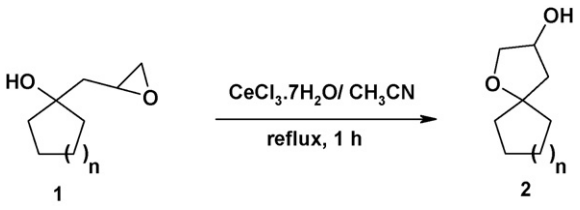
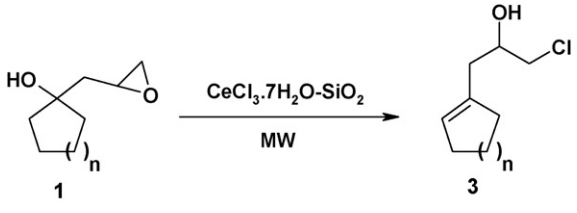
Table 1
Synthesis of tetrahydrofuran derivatives and 1-chloro-3-substituted-2-propanols from epoxyalcohols

Entry	Product[a]			Reaction time	Yield (%)[b]
	Epoxyalcohols **1**	Conventional **2**	Microwave **3**		
a				1.5 h (8 min)[c]	75 (60)[c]
b				1 h (7.5 min)	70 (55)
c				1 h (8 min)	73 (55)
d				1.2 h (6 min)	80 (60)
e				1 h (8 min)	74 (50)
f				1 h (8 min)	76 (65)
g				1.5 h (8 min)	65(55)
h				1.5 h (8 min)	65 (50)
i				1 h (7 min)	70 (60)
j				1 h (7 min)	74 (50)

[a] Products were characterised by spectral data.
[b] Yields refer to pure products after chromatography.
[c] Time and yields reported in parenthesis were obtained under microwave heating.



Scheme 1.



Scheme 2.

yield, after purification by silica gel column chromatography. The structure of the product was assigned based on ^{1}H NMR and mass spectral data. The reaction probably proceeds via regioselective opening of the epoxide to furnish a chlorohydrin, which undergoes cyclization to afford **2**. To examine the generality of the reaction, several epoxyalcohols were subjected to the same conditions and the results are summarized in Table 1. All the substrates afforded products arising from a formal 5-endo opening of epoxide.

To accelerate the cyclization of epoxyalcohols, reactions were carried out under microwave irradiation using solid supported $CeCl_3{\cdot}7H_2O$ catalyst. When epoxyalcohol, **1a** was exposed to microwave irradiation in the presence of $CeCl_3{\cdot}7H_2O$ supported on silica gel under solvent-free conditions l-chloro-3-(1-cyclohexenyl)-2-propanol (**3a**) was obtained as a sole product in 60% yield, after column chromatography. Dehydration of the $\mathbf{3}^0$ alcohol and epoxide opening had occurred under microwave irradiation, complete conversion being observed within 8 min. The structures of these products were deduced from their spectral data. Mass spectrum showed $M^{+\bullet}$, $M^{+\bullet}+2$ peaks in a ratio of 3:1 indicating the presence of Cl group. Formations of new products along with reduced reaction times are observed in this transformation employing microwave irradiation. The novelty and generality of the procedure is illustrated in Table 1.

3. Conclusions

In conclusion, we have demonstrated an efficient and novel method for the synthesis of tetrahydrofuran derivatives and l-chloro-3-(cyclohexenyl)-2-propanols using $CeCl_3{\cdot}7H_2O$ as a catalyst. The present method has advantage of improved yields, greater regioselectivity, simple experimental procedure, in comparatively less reaction time in excellent yields using less toxic and inexpensive reagent.

4. Experimental

4.1. Typical experimental procedure for the synthesis of tetrahydrofurans (conventional method)

A mixture of epoxyalcohol **1** (1 mmol) and $CeCl_3{\cdot}7H_2O$ (0.5 mmol) was refluxed in acetonitrile (5 mL) for 1–1.5 h. The reaction was monitored by TLC. After complete conversion, the solvent was evaporated and the residue was purified by silica gel column chromatography to afford pure tetrahydrofuran **2**.

4.2. Typical experimental procedure for the synthesis of 1-chloro-3-substituted-2-propanols (microwave method)

Epoxyalcohol **1** (1 mmol), $CeCl_3{\cdot}7H_2O$–SiO_2 (0.5 mmol) were mixed in a test tube, and the mixture was irradiated in laboratory microwave (Ethos 1600, 650 W) at 240 °C for appropriate minutes. After complete conversion, as indicated by TLC, the mixture was purified by silica gel column chromatography to afford the pure product **3**.

The spectral (^{1}H NMR, ^{13}C NMR and mass) data of some representative compounds are given below.

*4.2.1. 1-Oxaspiro [4.5] decan-3-ol (**2a**)*

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.20–1.80 (m, 12H), 3.0 (brs, 1H, OH), 3.40 (d, J = 8 Hz, 2H), 4.16 (m, 1H). ^{13}C NMR (75 MHz $CDCl_3$): δ 22.8, 27.0, 36.2, 44.0, 69.7, 72.3, 83.3. LCMS: m/z 179 ($M^{+\bullet}$ + Na).

*4.2.2. 1-Chloro-3-(1-cyclohexenyl)-2-propanol (**3a**)*

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.50–2.15 (m, 8H), 2.16–2.25 (m, 2H), 3.51 (2dd, J = 3.77, 10.57, 15.10 Hz, 2H), 3.80–4.00 (m, 1H), 5.52 (brs, 1H). ^{13}C NMR (75 MHz $CDCl_3$): δ 23.8, 26.0, 26.3, 30.4, 48.7, 56.9, 68.2, 118.6, 138.3. EIMS: m/z 174 ($M^{+\bullet}$), 176 ($M^{+\bullet}$ + 2).

*4.2.3. 1-Oxaspiro [4.11] hexadecane-3-ol (**2c**)*

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.15–1.60 (m, 22H), 1.65–1.85 (dd, J = 4.16 Hz, 2H), 3.38–3.68 (dd, J = 8, 16 Hz, 2H), 4.18 (m, 1H). EIMS: m/z 240 ($M^{+\bullet}$).

*4.2.4. 1-Chloro-3-(1-cyclododecenyl)-2-propanol (**3c**)*

^{1}H NMR (200 MHz, $CDCl_3$): δ 1.20–1.60 (m, 22H), 2.0–2.21 (m, 2H), 3.4–3.6 (dd, J = 4, 8 Hz, 2H), 3.84 (m, 1H), 5.22 (t, J = 8 Hz, 1H). EIMS: m/z 258 ($M^{+\bullet}$), 260 ($M^{+\bullet}$ + 2).

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