





**2-Nitrocyclohexanol (6):**

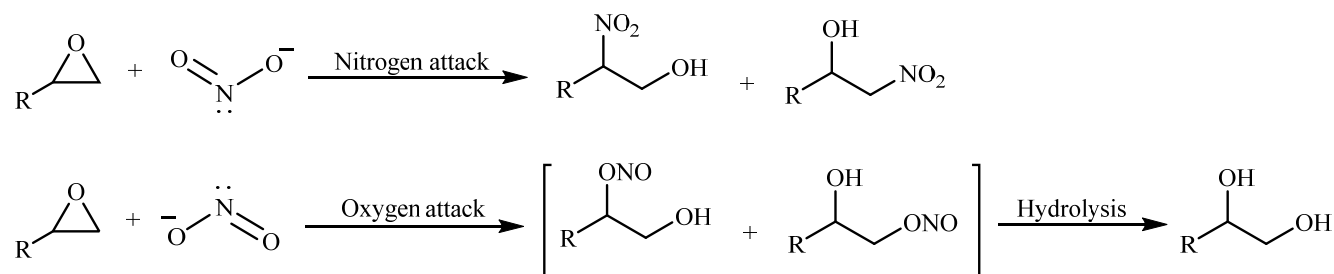
IR (neat):  $\bar{\nu} = 1378$  and  $1555$  ( $\text{NO}_2$ )  $\text{cm}^{-1}$ .  $^{13}\text{C}$ NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta = 89.4$  ( $\text{CHNO}_2$ ),  $72.1$  ( $\text{CHOH}$ ),  $32.5$  ( $\text{CH}_2$ ),  $28.3$  ( $\text{CH}_2$ ),  $25.1$  ( $\text{CH}_2$ ),  $24.4$  ( $\text{CH}_2$ ) ppm.

**3. Results and Discussion**

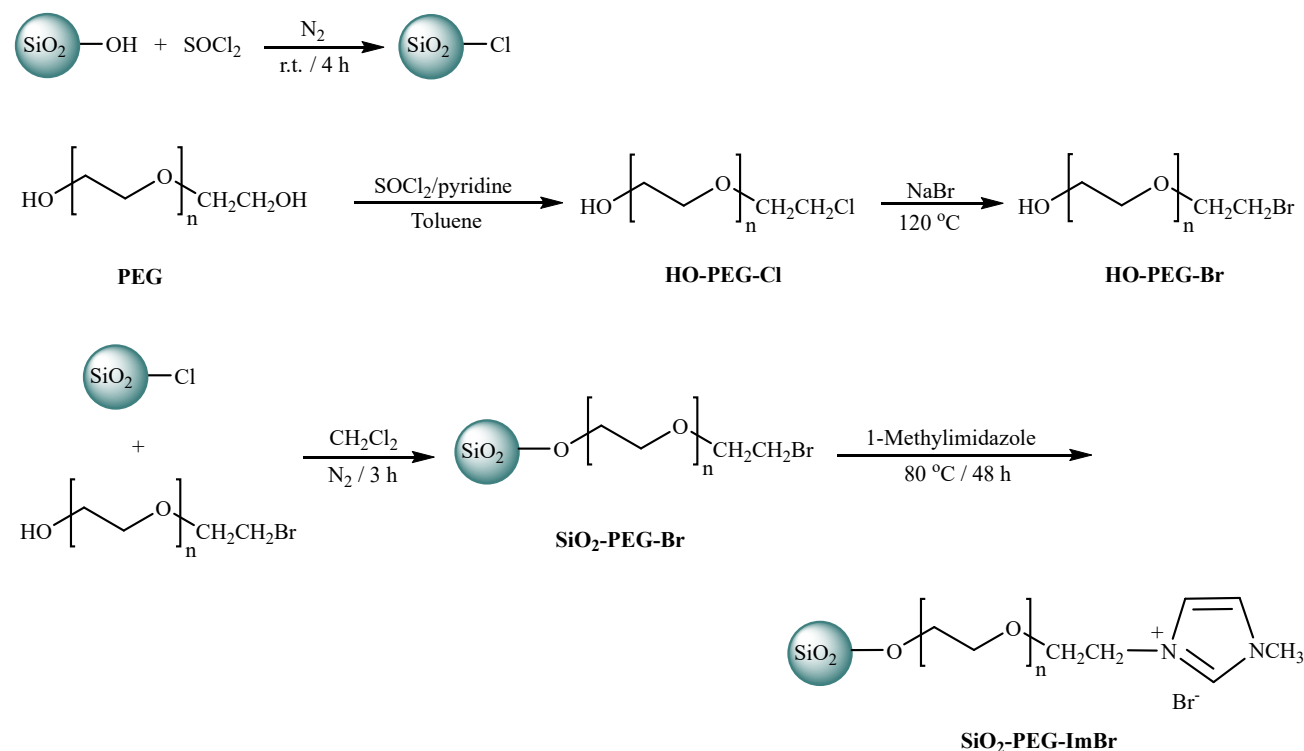
Nitrite anion is an ambident nucleophile and it can attack epoxides through its nitrogen or oxygen. Theoretically it can be expected four types of adducts as shown in Scheme 2. The formation of products depends on two types of regioselectivity: nitrogen or oxygen attack, and  $\alpha$ - or  $\beta$ -selectivity of the attack on the epoxide ring. Attack to the nitrogen can lead to the formation of 2-nitroalcohols, which are stable and can be

isolated as final products, while attack to the oxygen causes unstable nitrite esters, which can be spontaneously hydrolyzed to their corresponding diols [25].

Because of the low nucleophilicity of nitrite anion, the ring opening of epoxides with this anion has not proceeded as desired, when only  $\text{NaNO}_2$  was used. These reactions can be sped up by the addition of a catalyst. We now wish to report the catalytic application of silica-bound 3-{2-[poly(ethylene glycol)]ethyl}-substituted 1-methyl-1H-imidazol-3-ium bromide,  $\text{SiO}_2$ -PEG-ImBr, as an efficient phase transfer catalyst in the regioselective preparation of nitrohydrins in aqueous media. A general synthetic route for the preparation of  $\text{SiO}_2$ -PEG-ImBr is presented in Scheme 3.



**Scheme 2.** Possible ring opening reactions of an epoxide with nitrite ion, depending on  $\alpha/\beta$  and N/O selectivity of the nucleophilic attack.



**Scheme 3.** Preparation of  $\text{SiO}_2$ -PEG-ImBr.

In the FT-IR spectrum of SiO<sub>2</sub>-PEG-ImBr (Fig. 1), the C–H stretching and bending bands can be observed at 2800–2950 cm<sup>-1</sup> and 1400–1500 cm<sup>-1</sup>, respectively. In addition, the presence of imidazolium unit was confirmed by the bands at 1619 cm<sup>-1</sup> (imidazole –C=N bending) and 1567 cm<sup>-1</sup> (imidazole ring stretching). Therefore, the successful introduction of PEG-ImBr onto silica surface was verified through the FT-IR spectra.

The thermogravimetric analysis (TGA) curve of the SiO<sub>2</sub>-PEG-ImBr showed the mass loss of the organic materials as they decompose upon heating (Fig. 2). The initial weight loss up to 126 °C is due to the removal of physically adsorbed water and surface hydroxyl groups. The weight loss of about 18 % between 150 and 420 °C may be associated to the thermal decomposition of PEG-ImBr. On the basis of this observation, the good grafting of PEG-ImBr on the SiO<sub>2</sub> surface was also verified.

To determine the amount of imidazolium bromide in SiO<sub>2</sub>-PEG-ImBr, 0.01 g of the catalyst was immersed in 20 mL of 0.1 mol L<sup>-1</sup> aqueous HNO<sub>3</sub> solution. The bromide ions were determined by the Volhard's method. The amount of bromide equaled by imidazolium units was 2.85 mmol g<sup>-1</sup>. The amount of imidazolium units was also determined by the CHN analysis method (2.667 mmol g<sup>-1</sup>) (Fig. 3); this value is in good agreement with the obtained result from the Volhard's titration method.

In order to find the best experimental conditions, the catalytic activity of SiO<sub>2</sub>-PEG-ImBr in the ring opening of 3-phenyloxy-1,2-epoxypropane with NaNO<sub>2</sub> in water was tested. After a series of preliminary experiments, the best conversion was observed when 5 mmol NaNO<sub>2</sub> and 0.2 g PTC were added to the 1.0 mmol epoxide in 5 mL water and the mixture was stirred at 90 °C. In this condition, after 1.5 h the corresponding 2-nitroalcohol was obtained in 85% yield (Table 1, entry 3).

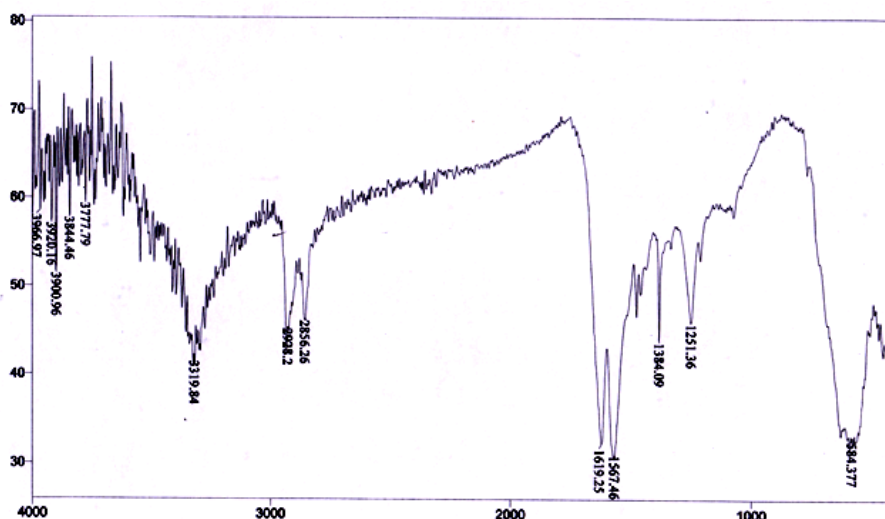


Fig. 1. The FT-IR spectrum of SiO<sub>2</sub>-PEG-ImBr.

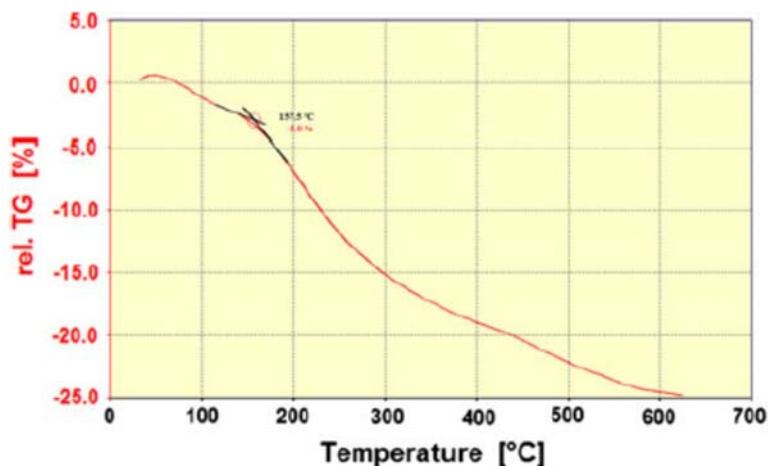


Fig. 2. TGA curve of SiO<sub>2</sub>-PEG-ImBr.

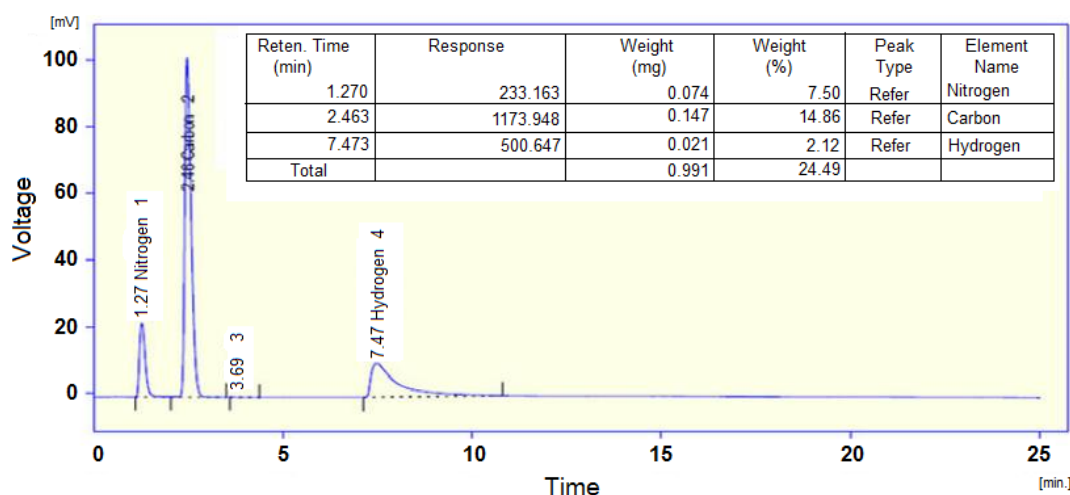


Fig. 3. CHN analysis of SiO<sub>2</sub>-PEG-ImBr.

After optimizing the reaction conditions, the generality and synthetic scope of this method for synthesizing a series of 2-nitroalcohols were demonstrated by the reaction of various epoxides with NaNO<sub>2</sub> under optimal conditions (Table 2). As shown in Table 2, yields of products are good to excellent for epoxides bearing both electron-donating and electron-withdrawing groups.

The direction of ring opening is characteristically observed for terminal epoxides under S<sub>N</sub>2 conditions and probably dictated by steric and electronic factors. Styrene oxide underwent cleavage with sodium nitrite in the presence of catalytic amount of SiO<sub>2</sub>-PEG-ImBr with the preferential attack at the benzylic position to give the corresponding 2-nitroalcohol in 80% yield (Table 2, entry 1). Except the reaction of styrene oxide, the reactions of other epoxides bears carrying electron withdrawing groups, it is the steric factor which predominates and the nucleophilic attack of nitrite anion

is strongly favored on the less substituted carbon atom of epoxides (Table 2, entries 2-5). Furthermore, the reactions with epoxides derived from cyclic olefins afforded exclusively *trans* isomers (Scheme 4 and Table 2, entries 6-8).

In the absence of the catalyst, the reactions were very slow in the water. The addition of SiO<sub>2</sub>-PEG-ImBr significantly improved the reaction rates and yields. This is probably due to the activation of the epoxide by the hydrogen bonding between silanol hydroxy groups on the silica gel surface and the oxygen of epoxide. In addition, polyethylene glycol units in PTC can encapsulate sodium cation, much like crown ethers, and this complex causes the nitrite anion to be activated. The 1-methylimidazol-3-ium units introduced ionic liquid property to the catalyst and the bromide to nitrite anion exchange can facilitate the rate of reaction (Scheme 5).

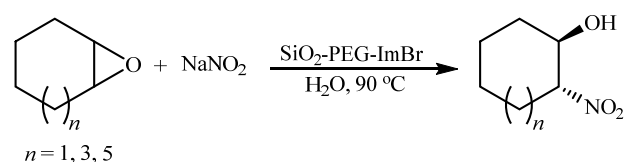
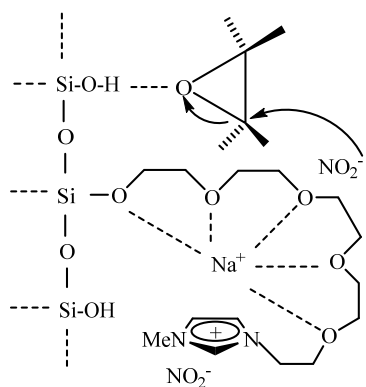
Table 1. Optimization of the reaction conditions for the ring opening of 3-phenyloxy-1,2-epoxypropane by NaNO<sub>2</sub>.

| Entry | NaNO <sub>2</sub> (mmol) | Catalyst (g) | Conditions              | Time (h) | Yields (%) <sup>a</sup> |
|-------|--------------------------|--------------|-------------------------|----------|-------------------------|
| 1     | 5                        | -            | H <sub>2</sub> O, 90 °C | 3        | trace                   |
| 2     | 5                        | 0.1          | H <sub>2</sub> O, 90 °C | 2.5      | 82                      |
| 3     | 5                        | 0.2          | H <sub>2</sub> O, 90 °C | 1.5      | 85                      |
| 4     | 5                        | 0.2          | H <sub>2</sub> O, r.t.  | 3        | 35                      |
| 5     | 5                        | 0.2          | H <sub>2</sub> O, 50 °C | 3        | 58                      |
| 6     | 5                        | 0.3          | H <sub>2</sub> O, 90 °C | 1.25     | 83                      |
| 7     | 4                        | 0.2          | H <sub>2</sub> O, 90 °C | 2.5      | 85                      |
| 8     | 5                        | 0.2          | MeCN, reflux            | 3        | 70                      |
| 9     | 5                        | 0.2          | EtOAc, reflux           | 3        | 65                      |
| 10    | 5                        | 0.2          | EtOH, 90 °C             | 3        | 69                      |

<sup>a</sup>Isolated yields.

**Table 2.** Synthesis of 2-nitroalcohols from epoxides in the presence of SiO<sub>2</sub>-PEG-ImBr in water at 90 °C.

| Entry | Substrate | Product | Time (h) | Yields (%) <sup>a</sup> |
|-------|-----------|---------|----------|-------------------------|
| 1     |           |         | 1        | 80                      |
| 2     |           |         | 1.5      | 85                      |
| 3     |           |         | 0.5      | 81                      |
| 4     |           |         | 0.5      | 75                      |
| 5     |           |         | 1.5      | 75                      |
| 6     |           |         | 1        | 75                      |
| 7     |           |         | 2.5      | 83                      |
| 8     |           |         | 1.5      | 82                      |

<sup>a</sup>Isolated yields.**Scheme 4.** Stereospecificity in ring opening of cycloalkyl epoxide.**Scheme 5.** The catalytic activity of SiO<sub>2</sub>-PEG-ImBr.

Because of the importance of the catalyst reusability in the large-scale operation and industrial point of view, the recovery and reusability of SiO<sub>2</sub>-PEG-ImBr were examined. After performing the reaction of styrene oxide under the reaction conditions, the catalyst was recovered by filtration, washed with water and methanol and dried at 70 °C, and then reused for a consecutive run under the same reaction conditions. Thus, after the first run, which gave the corresponding 2-nitroalcohol in 100% conversion and 80% isolated yield, after recovery, the catalyst was subjected four times to the same reaction from which it also gave the corresponding product in 78%, 79%, 80% and 78% yield, respectively.

The superiority of using SiO<sub>2</sub>-PEG-ImBr as the catalyst for the synthesis of 2-nitroalcohols by the ring opening of epoxides with nitrite anion is shown by comparing with those of the previously reported methods in the literature (Table 3).

**Table 3.** Comparison of the ring opening of epoxides with nitrite ion in the presence of different catalysts.

| Entry  | Epoxides         | Reagent systems   | Solvent                            | Temp. (°C)                            | Time (min) | Yield (%) | Ref. |
|--|------------------|---|------------------------------------|---------------------------------------|------------|-----------|------|
| 1 <sup>a</sup>                                 |                  | NaNO <sub>2</sub> , MgSO <sub>4</sub>   | MeOH                               | 65                                    | 270        | 0:75      | [6]  |
|  |                  | Amberlit IRA-400, NO <sub>2</sub> <sup>-</sup>                                | EtOH                               | 50                                    | 120        | 32:48     | [7]  |
|  |                  | NaNO <sub>2</sub> , SDS <sup>b</sup> , Ce(OTf) <sub>4</sub>                   | H <sub>2</sub> O                   | 25                                    | 5          | 90:0      | [8]  |
|  |                  | NaNO <sub>2</sub> , QPA <sup>c</sup>  | MeCN                               | 25                                    | 60         | 85:8      | [9]  |
|  |                  | NaNO <sub>2</sub> , LaCl <sub>3</sub> ·7H <sub>2</sub> O, Bu <sub>4</sub> NBr | Et <sub>2</sub> O-H <sub>2</sub> O | 25                                    | 480        | 79:10     | [10] |
|  |                  | NaNO <sub>2</sub> , PNBA <sup>d</sup>   | H <sub>2</sub> O                   | 25                                    | 90         | 80:10     | [11] |
| 2  |                  | NaNO <sub>2</sub> , MgSO <sub>4</sub>   | MeOH                               | 65                                    | 180        | 86        | [6]  |
|  |                  | Amberlit IRA-400, NO <sub>2</sub> <sup>-</sup>                                | EtOH                               | 50                                    | 120        | 80        | [7]  |
|  |                  | NaNO <sub>2</sub> , QPA   | MeCN                               | 25                                    | 66         | 94        | [9]  |
|  |                  | NaNO <sub>2</sub> , PNBA  | H <sub>2</sub> O                   | 25                                    | 60         | 85        | [11] |
|  |                  | NaNO <sub>2</sub> , SiO <sub>2</sub> -PEG-ImBr                                | H <sub>2</sub> O                   | 90                                    | 90         | 85        | -    |
|  |                  | 3   |                                    | NaNO <sub>2</sub> , MgSO <sub>4</sub> | MeOH       | 65        | 420  |
| Amberlit IRA-400, NO <sub>2</sub> <sup>-</sup> | EtOH             |   |                                    | 50                                    | 120        | 80        | [7]  |
| NaNO <sub>2</sub> , SDS, Ce(OTf) <sub>4</sub>  | H <sub>2</sub> O |   |                                    | 25                                    | 10         | 78        | [8]  |
| NaNO <sub>2</sub> , QPA                        | MeCN             |   |                                    | 25                                    | 60         | 91        | [9]  |
| NaNO <sub>2</sub> , SiO <sub>2</sub> -PEG-ImBr | H <sub>2</sub> O |   |                                    | 90                                    | 60         | 75        | -    |

<sup>a</sup>The yield percentage for this epoxide has been shown as the percentage of PhCH(NO<sub>2</sub>)CH<sub>2</sub>OH and PhCH(OH)CH<sub>2</sub>NO<sub>2</sub>, respectively.

<sup>b</sup>SDS: Sodium dodecyl sulfate.

<sup>c</sup>QPA: Poly[N-(2-aminoethyl)acrylamido]trimethyl ammonium chloride resin.

<sup>d</sup>PNBA: Poly (N-bromoacrylamide).

<sup>e</sup>Present procedure.

#### 4. Conclusions

In conclusion, in this study, we have introduced a simple and efficient procedure for the regioselective synthesis of 2-nitroalcohols using catalytic amounts of SiO<sub>2</sub>-PEG-ImBr as an effective and recyclable phase transfer catalyst. The advantages of the present procedure, such as relatively short reaction times, simplicity in operation, high yield of products, excellent regioselectivity, and recyclability of the catalyst make this new process an attractive alternative to current methodologies.

#### Acknowledgments

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