Bioglycerol-based Sulphonic Acid Functionalized Carbon: An Efficient and Recyclable, Solid Acid Catalyst for the Regioselective Azidolysis of Epoxides in Aqueous Acetonitrile

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Abstract: A convenient and efficient method was developed for the synthesis of 1,2-azidooxolcohols by ring opening of terminal epoxides with sodium azide employing glycerol-based sulphonic acid functionalized carbon as heterogeneous catalyst in aqueous acetonitrile. The reaction is highly regioselective and affords the corresponding products in excellent yields (78-100%) under mild reaction conditions. The catalyst exhibited efficient reusability without loosing its activity even after 5 cycles of azidolysis of methyl 10,11-epoxy undecanoate under optimized conditions within 2 h.

Key words: Glycerol-based Carbon Catalyst, Methyl 10,11-Epoxy Undecanoate; Azidolysis, Sodium Azide, Acetonitrile

1 INTRODUCTION

Glycerol is obtained as a by-product in fatty acid production, biodiesel production, and microbial fermentation. It can be prepared also by hydrogenolysis of glucose or other saccharides from propylene, but this route is at present economically unpleasant as a result of high crude oil prices. The rapid growth of the biodiesel industry has resulted in an oversupply of bioglycerol, which has become a burden until new markets are created for bioglycerol by the development of new products. Huge amounts of sulphuric acid as homogenous catalyst is being consumed worldwide for the production of industrially important chemicals. The acid-based processes involve high energy consumption, a difficult separation of the catalyst from the reaction mixture and are expensive as well as chemically wasteful. Recyclable heterogeneous acid catalysts have gained attention as replacement for liquid-acid catalysts with several intrinsic advantages over their homogeneous counterparts, such as ease of product separation and reusability. However, to maintain economic viability heterogeneous catalysts should exhibit activities and selectivity comparable to or superior to, existing homogeneous catalysts. This is a serious issue, particularly for the production of specialty chemicals, which require high product purity and versatile protocols. Thus, to find innovative and flexible systems is mandatory.

Epoxides plays a key role in organic synthesis as intermediates, the ring opening of epoxides by various nucleophiles yielding a broad range of valuable products. Among these, the azidolysis of epoxides enjoys a prominent position for the preparation of amino alcohols. The vicinal azido alcohols are precursors of amino alcohols which are well known as β-blockers and a common structural component in vast group of natural products. In particular β-azido alcohols can be obtained through the nucleophilic ring opening of epoxides with azide nucleophile. Even though the classic protocol uses sodium azide and ammonium chloride, the azidolysis reaction requires a long reaction time (12-48 h) and the azidoxydrin is often accompanied by isomerization, epimerization and rearrangement of products. However the azide opening is promoted by traditional homogeneous systems as metal chlorides, salts and alkyl metal azides. Some heterogeneous catalysts, relying on the use of traditional solid acids such as Amberlyst IRA-400 supported azide, Dowex resin grafted by poly ethylene glycol, oxone, sodium azide supported on Zeolite CaY, ammonium salt of a heteropoly acids, quaternized ammonium salt and quaternized amino functionalized cross linked polyacrylamide have been recently reported.
Given the low cost and simple protocols involved in their preparation, carbon-based solid acids could provide an appealing option to the sulphonic acid resins as heterogeneous catalysts for the azidolysis reaction. In recent years carbon-based solid acid catalysts\(^{47-49}\) have gained prominence due to their significant advantages over homogeneous liquid phase mineral acids such as increased activity and selectivity, longer catalyst life, negligible equipment corrosion, ease of product separation, and reusability. These carbon-based catalysts, obtained by the incomplete carbonization and sulphonation of aromatic hydrocarbons or sugars, consisting of small polycyclic aromatic carbon sheets with attached \(-\text{SO}_2\)H groups, have proven to be highly active in the esterification of fatty acids. Prabhavathi et al. reported a sustainable method for the preparation of similar sulphonic acid functionalized polycyclic aromatic carbon catalyst from bioglycerol (biodiesel by-product) and also from glycerol-pitch (waste from fat splitting industry) by \textit{in situ} partial carbonization and sulphonation\(^{41,42}\). Such catalysts have been shown to be inexpensive, highly stable, robust, recyclable, and easily produced from naturally available glycerol, and are demonstrated to be effective for the esterification of fatty acids to its methyl esters\(^{41}\), THP protection and deprotection of alcohols and phenols\(^{42}\), one-pot synthesis of highly substituted imidazoles\(^{40}\), 3,4-dihydropyrimidin-2-(1H)-ones\(^{46}\) and a mild and expeditious synthesis of amides from aldehydes\(^{45}\). In continuation of our efforts towards exploring the applications of the carbon-based catalysts, we are reporting a simple and highly efficient approach for the regioselective azidolysis of epoxides to azido alcohols under mild reaction conditions using glycerol-based sulphonic acid functionalized carbon as a recyclable catalyst.

2 EXPERIMENTAL

2.1 Materials

Chemicals were purchased from S.d. Fine or Sigma Aldrich Chemical companies. All other reagents and solvents used were of analytical grade. Reactions were monitored on silica gel TLC plates (coated with TLC grade silica gel, obtained from Merck, India) employing iodine vapors for detection of spots and conversion\(^%\) was obtained from GC analysis on Agilent 6850 series GC system. Column chromatography was performed over silica gel (100-200 mesh) procured from Qualigens (India) using freshly distilled solvents. \(^1\)H and \(^13\)C NMR spectra were recorded on a 300 (Varian, Palo Alto, USA) spectrometer in CDCl\(_3\) solution with tetramethylsilane as the internal standard. Chemical shift values (\(\delta\)) are given in parts per million. Mass spectra were recorded using Waters, Micromass-Quattronico electron spray ionization (ESI-MS). IR spectra were recorded on a Perkin Elmer (model: spectrum BX) FT-IR Spectrometer using CHCl\(_3\).

2.2 Methods

2.2.1 Preparation of glycerol-based sulphonic acid functionalized carbon catalyst

A mixture of glycerol (10 g) and concentrated sulfuric acid (30 g) in a beaker (1 lt) was heated on electric heater from ambient temperature to 220°C for 20 min, to facilitate \textit{in situ} partial carbonization and sulphonation. The reaction mixture was allowed to remain at that temperature for about 20 min (until foaming ceased) to obtain solid carbon material and was cooled to ambient temperature and washed with hot water until the wash water becomes neutral to pH. The partially crystalline product was filtered and dried in an oven at 120°C for 2 h until it was moisture free to obtain the carbon acid catalyst in \(\sim 56\%\) yield (5.60 g). The catalyst was fully characterized by CHN analysis, XRD, XPS, IR, \(^{13}\)C MAS, and Raman spectroscopy. The methods are discussed in Supporting Information.

2.2.2 General procedure for the catalytic azidolysis of epoxides

In a typical azidolysis reaction, to a mixture of epoxide (1 mmol), carbon catalyst (10 wt. \% of epoxide), in 60:40 acetonitrile:water (1 mL/100 mg of epoxide) was added NaN\(_3\) (1.5 mmol). The suspension was magnetically stirred at 100°C for 2 h. The reaction was monitored by TLC. After separation of the catalyst by filtration, the reaction mixture was extracted with ethyl acetate, and the product mixture was analyzed by GC for separation of the catalyst by filtration, the reaction mixture was extracted with ethyl acetate, and the product mixture was analyzed by GC for determination of conversion and reusability.

2.2.3 Spectral data for selected compounds

Methyl 11-azido-10-hydroxyundecanoate; IR (neat) 3462, 2101 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 3.68-3.73 (m, 1H); 3.64 (s, 3H); 3.32 (dd, \(J = 2.9, 11.7\) Hz, 1H); 3.21 (dd, \(J = 6.8, 11.7\) Hz, 1H); 2.57 (bs, 1H); 2.27 (t, \(J = 7.8\) Hz, 2H); 1.58-1.63 (m, 2H); 1.41-1.48 (m, 2H); 1.26-1.37 (m, 10H). ESI-MS: m/z 280 [M + Na]\(^+\).

11-Azidoundecane-1,10-diol (Table 1, entry 8); IR (neat) 3350, 2100 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 3.66-3.72 (m, 1H); 3.59 (t, \(J = 6.7\) Hz, 2H); 3.31 (dd, 1H, \(J = 3.7, 12.08\) Hz); 3.20 (dd, 1H, \(J = 6.7, 12.08\) Hz); 2.15 (bs, 1H); 2.02 (s, 1H); 1.49-1.56 (m, 2H); 1.44 (m, 2H); 1.23-1.36 (bs, 12H). \(^{13}\)C-NMR (75 MHz, CDCl\(_3\)) \(\delta\) 70.56, 62.59, 56.83, 34.16, 32.47, 29.32, 29.26, 29.21, 25.55, 25.27. ESI-MS m/z 252 [M + Na]\(^+\).

2.2.4 Catalyst reusability

The recovered catalyst was washed with methanol, dried at 120°C in oven and reused for five cycles of azidolysis of methyl 10,11-epoxy undecanoate for determining its stability and activity.

3 RESULTS AND DISCUSSION

3.1 Characterization of the carbon acid catalyst

The carbon catalyst prepared from glycerol by in situ partial carbonization and sulphonation was fully characterized by CHN analysis, XRD, XPS, IR, $^{13}$C MAS, and Raman spectroscopy. Elemental composition of the catalyst was found to be CH$_{0.74}$S$_{0.02}$O$_{0.51}$ with 1.6 mmol/g of acid density and surface area of 0.21 m$^2$/g. All the physico-chemical characterization studies indicates that the carbon catalyst is a partially crystalline material consisting of polycyclic aromatic carbon sheets with –SO$_3$H, –COOH and –OH functional groups as reported for similar carbon-based solid acid catalysts.

3.2 Azidolysis of methyl-10,11-epoxy undecanoate

Derivatives of vegetable oils and fatty esters with diethyl azidodicarboxylate, azides, aziridines and their N-substituted derivatives are gaining significance as biologically active compounds. 10-Undecenoic acid prepared from pyrolysis of castor oil is a potential intermediate for the production of several industrial products like nylon-11, perfumery compounds and other specialty chemicals.

Hence, in the present study 10-undecenoic acid methyl ester has been taken as a representative compound for the preparation of 1,2-azidoalcohols. Ring opening of methyl 10,11-epoxy undecanoate (1 mmol) with azide anion (1.2 mmol) was chosen as a model reaction employing glycerol-based carbon catalyst (Fig. 1).

Effect of various solvents is studied and no reaction is observed when using CH$_3$CN: H$_2$O (60:40). % conversion was determined by GC.

### Table 1: Azidolysis of Epoxides by Employing Glycerol-based Sulphonic Acid Functionalized Catalyst

<table>
<thead>
<tr>
<th>Entry</th>
<th>Epoxide</th>
<th>Product(s)</th>
<th>Time (h)</th>
<th>Conv. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image1" alt="Ph-O" /></td>
<td><img src="image2" alt="N$_2$-OH" /></td>
<td>1.0</td>
<td>84$^b$</td>
</tr>
<tr>
<td>2</td>
<td><img src="image3" alt="O" /></td>
<td><img src="image4" alt="OH" /></td>
<td>1.5</td>
<td>100</td>
</tr>
<tr>
<td>3</td>
<td><img src="image5" alt="Ph-O" /></td>
<td><img src="image6" alt="N$_3$" /></td>
<td>1.0</td>
<td>98</td>
</tr>
<tr>
<td>4</td>
<td><img src="image7" alt="Ph-O" /></td>
<td><img src="image8" alt="OH" /></td>
<td>2.5</td>
<td>78</td>
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<tr>
<td>5</td>
<td><img src="image9" alt="Ph-O" /></td>
<td><img src="image10" alt="N$_3$" /></td>
<td>4.0</td>
<td>89</td>
</tr>
<tr>
<td>6</td>
<td><img src="image11" alt="OH" /></td>
<td><img src="image12" alt="OH" /></td>
<td>1.5</td>
<td>98</td>
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<tr>
<td>7</td>
<td><img src="image13" alt="OH" /></td>
<td><img src="image14" alt="OH" /></td>
<td>5.0</td>
<td>80</td>
</tr>
<tr>
<td>8</td>
<td><img src="image15" alt="HO" /></td>
<td><img src="image16" alt="OH" /></td>
<td>3.5</td>
<td>100</td>
</tr>
</tbody>
</table>

$^a$ T = 100°C, 1.5 eq. NaN$_3$, 10 wt% Catalyst, 1 mL of CH$_3$CN: H$_2$O (60:40), % conversion was determined by GC.

$^b$ 16% of the other regioisomer was formed.
observed in case of solvents like chloroform, hexane, ethyl acetate, acetone, acetonitrile and water under reflux conditions even after 24 h of reaction time. However, reaction was observed in case of acetonitrile/H$_2$O system at reflux temperature in presence of carbon catalyst, whereas in the absence of catalyst no reaction was observed. It was investigated to optimize the reaction conditions like ratio of acetonitrile to H$_2$O, solvent ratio, amount of the catalyst and sodium azide and time of reaction for complete azidolysis of methyl 10,11-epoxy undecanoate to the corresponding azidohydrin under reflux temperature. Progress of the reaction was monitored by TLC and GC analysis. Based on the study, for the complete azidolysis of methyl 10,11-epoxy-undecanoate (0.46 mmol) to methyl 11-azido-10-hydroxy-undecanoate, the optimum reaction conditions are found to be 1.5 mol eq. of NaN$_3$, 10 wt.% of catalyst, 1 mL of CH$_3$CN:H$_2$O (60:40). Under these optimum conditions the effect of CH$_3$CN ratio with H$_2$O varying form 0-100% was studied and the results are depicted in Fig. 2. From this study, it is concluded that in 60:40 (CH$_3$CN:H$_2$O) system is optimum for obtaining $>99\%$ conversion in 2 h. Conversion of epoxide to azido alcohol increased with the decrease of water content by replacing with acetonitrile up to 60% and further increase of acetonitrile content, % of conversion was reduced. Even with 50:50 and 70:30 CH$_3$CN:H$_2$O solvent systems also resulted in more than 80% conversions within the same time.

The success of the first set of experiments using glycerol-based sulphonic acid functionalized carbon as a catalyst encouraged us to increase the scope of the reaction to other epoxides as given in Table 1. Excellent yields of the desired $\beta$-azido alcohols are obtained with a reversal of regioselectivity indicating attack at the less substituted carbon of the aliphatic epoxides, while styrene oxide (entry 1, Table 1) as an aryl epoxide formed the product by attack at the benzylic position. In all cases, a very clean reaction is observed and careful examination of the $^1$H NMR spectra of the crude products clearly indicated the formation of only one regioisomer in each case (except in entry 1, Table 1). The probable reason may be that, in styrene oxide, the positive charge on oxygen appears to be localized on the more highly substituted benzylic carbon leading to the major product, whereas in the case of aliphatic epoxides, steric factors predominate over electronic factors, thereby

Table 2

<table>
<thead>
<tr>
<th>Entry</th>
<th>Epoxide</th>
<th>Product(s)</th>
<th>Conditions</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph (\bigcirc)</td>
<td>Ph (\bigcirc)</td>
<td>A</td>
<td>1.0</td>
<td>84 (16)$^a$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>N$_3$OH</td>
<td>B</td>
<td>20.0</td>
<td>73 (20)</td>
</tr>
<tr>
<td>2</td>
<td>(\bigcirc)OH</td>
<td>(\bigcirc)N$_3$</td>
<td>A</td>
<td>1.5</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>B</td>
<td>36.0</td>
<td>90</td>
</tr>
<tr>
<td>3</td>
<td>Ph (\bigcirc)OH</td>
<td>Ph (\bigcirc)N$_3$OH</td>
<td>A</td>
<td>1.0</td>
<td>98</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>B</td>
<td>12.0</td>
<td>93 (1)</td>
</tr>
</tbody>
</table>

(A). Epoxide (1 eq), NaN$_3$ (1.5 eq), Catalyst (10 wt.%), CH$_3$CN:H$_2$O (60:40) (1 mL), 100$^\circ$C, yields of the product was determined by GC. (B). Epoxide (1 eq), NH$_4$Cl (2.3 eq), NaN$_3$ (5 eq), MeOH:H$_2$O (8:1), reflux (data reproduced from Ref. 23). $^a$ Other regioisomer.
facilitating attack at the less hindered carbon atom of the epoxide ring. In case of cyclohexene oxide also the reaction was completely antisterioselective, thus resulting in trans isomer only (entry 2, Table 1). All the products were characterised by ESI, MS, IR, $^1$H NMR data and are in comparison with authentic samples.

Comparative study of the carbon acid catalyzed protocol for the azidolysis of different epoxides (entries 1, 2, 3, Table 1) with that of classical procedure are summarized in Table 2. Carbon acid catalyzed azidolysis of styrene oxide (entry 1, Table 2) was found to be completed with in 1 h against 20 h of standard protocol with 16 and 20% of other regioisomer. In the case of remaining epoxides namely cyclohexene oxide, 2-(phenoxymethyl) oxirane (entries 2, 3, Table 2) reaction was completed within 1.5 h and 1 h with 95% and 98% yields respectively, where as the classical procedure resulted the corresponding azidoalcohols in 90% and 94% yields after 36 and 12 h. This study clearly indicates the superiority of our protocol employing glycerol-based carbon acid catalyst in terms of regioselectivity, yields, and reaction times.

3.3 Catalyst reusability and stability

After the reaction the product was extracted in to EtOAc and the catalyst from aqueous layer was separated by simple filtration, washed with MeOH, dried and reused. The reusability study of the catalyst for the azidolysis of methyl 10, 11-epoxy undecanoate under optimized conditions for five catalytic runs resulted complete reaction with in 2 h with 94-92% conversions against 95% of fresh catalyst.

4 CONCLUSIONS

In conclusion, we have demonstrated a simple, efficient and ecofriendly protocol for the synthesis of vicinal azidohydrins from epoxides employing a novel glycerol-based sulphonic acid functionalized carbon as a heterogeneous green catalyst. After isolating the products in to the organic phase, the catalyst from the aqueous phase is recovered by simple filtration for reuse without any pre-treatment. Environmental acceptability, high yields, easy work-up, cleaner reaction profiles and recyclability of the catalyst are the important features of this protocol.

Supporting Information

This material is available free of charge via the Internet at http://dx.doi.org/10.5650/jos.62. 849

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