Zeolite-catalysed rearrangements in organic synthesis

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Abstract

Results are presented on the use of zeolites as catalysts in organic rearrangements of interest in the synthesis of fine chemicals viz., the rearrangement of epoxides and α, β-epoxy ketones, the Claisen rearrangement of allyl aryl ethers and an intramolecular hydroxyalkylation of an aromatic with an epoxide. © 1998 Elsevier Science B.V. All rights reserved.

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1. Introduction

As part of an ongoing study of the use of solid acid catalysts in the synthesis of fine chemicals, we investigated the hydroxyalkylation of aromatics with epoxides [1]. The hydroxyalkylation of benzene with ethylene oxide (Fig. 1; R=H), for example, is employed industrially for the synthesis of 2-phenylethanol, an important fragrance chemical. The industrial process employs stoichiometric amounts of $AlCl_3$ and generates substantial amounts of $AlCl_3$-containing effluent. Hence, there is a definite need for a cleaner, catalytic alternative. As a model reaction, we chose the hydroxyalkylation of benzene with propylene oxide (Fig. 1; R=CH$_3$).

An initial screening of zeolites, clays and ion-exchange resins afforded, in the best cases, only small amounts ($< 2\%$) of the desired 2-phenyl-1-propanol. The major reaction was acid-catalysed oligomerisation of the propylene oxide, even when activated aromatics, such as anisole or mesitylene were used. Consideration of the reaction mechanism (Fig. 2) reveals the cause of the problem. The complex formed between the epoxide and the acid catalyst can react either with the aromatic substrate or another molecule of epoxide, giving an oligomer. In the classical homogeneous process, the concentration of free epoxide is maintained at a low level by employing a large excess of aromatic and more than one equivalent of $AlCl_3$. Clearly, the latter condition is not met in the case of heterogeneous catalysis. Moreover, adsorption experiments revealed that the epoxide is preferentially adsorbed by the hydrophilic catalyst. Adsorption experiments revealed an additional problem: the 2-phenyl-1-propanol product is not stable towards dehydration under the reaction conditions.

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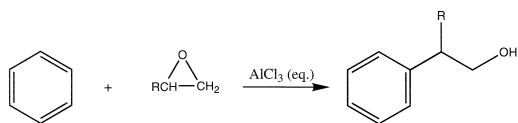[1] Present address: Department of Chemistry, University of York, Heslington, York YO1 5DD, UK.

Fig. 1. Hydroxyalkylation of benzene with epoxides.

Fig. 3. Rearrangement of 2,3-dimethyl-2,3-epoxybutane to pinacolone.

In order to circumvent the problem of oligomerisation, we performed experiments with a sterically hindered epoxide: 2,3-dimethyl-2,3-epoxybutane. Indeed no epoxide oligomers were formed. However, no hydroxyalkylation was observed; instead the epoxide underwent acid-catalysed rearrangement to pinacolone (Fig. 3). Since pinacolone is a valuable intermediate for the production of photographic and crop-protection chemicals and 2,3-dimethyl-2-butene is readily available from propene dimerisation, this is a commercially significant result.

This result prompted us to study the rearrangement of other epoxides in the presence of solid acid catalysts. In this paper we shall present results obtained in the above mentioned rearrangement and analogous rearrangements of α,β-epoxy ketones.

The results obtained in epoxide rearrangements also prompted us to study other acid-catalysed rearrangements. For example, we have explored the use of zeolites as catalysts in the Claisen rearrangement of allyl aryl ethers. The Claisen rearrangement of allyl aryl ethers to the corresponding *o*-allylphenols is a well-known reaction in organic chemistry [2]. It is generally performed by heating the ether at elevated tem-
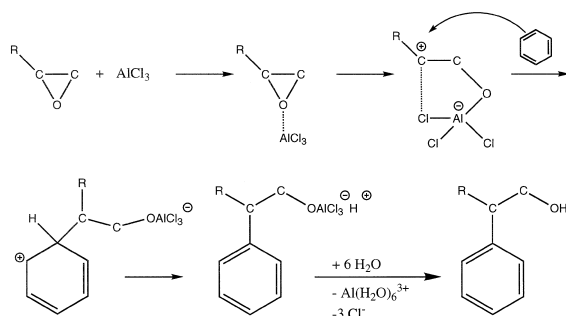
peratures ($> 200°C$) but has been reported to be susceptible to catalysis by Lewis and Brønsted acids [2,3].

The use of heterogeneous catalysts to effect the rearrangement at lower temperatures is of interest. In particular we envisaged that the use of zeolites might, because of steric restrictions imposed by the zeolite pores, promote the migration of the allyl group to the *para*-position. This would provide a cleaner alternative to the method currently employed for the synthesis of *p*-allylphenol, namely the low yield reaction of phenol with allyl bromide mediated by $ZnCl_2$ [4].

2. Experimental

2.1. Catalyst preparation

The zeolites (acidic form) and montmorillonite K10 were prepared and treated as described before [1,5,6]. Mordenite (sodium form, $Si/Al = 7.3$, $Al/Na = 1.0$) was obtained from PQ zeolites. Zeolite beta ($Si/Al = 12$) was synthesised according to a slightly modified method of Wadlinger et al. [7]. Zeolite NaY ($Si/Al = 2.7$, $Al/Na = 1.0$) was kindly donated by Akzo. Two different ZSM-5 samples were used ($Si/Al = 45$ and 85). The zeolites were converted to their ammonium forms by ion exchange with 1 M aqueous ammonium nitrate. Dealuminated mordenite ($Si/Al = 33$) was prepared by refluxing the mordenite in 6 M aqueous nitric acid according to a patent of Dow [8]. Montmorillonite K10 ($Si/Al = 5.1$, $Al/Na = 45$) was purchased from Fluka.

All zeolites and the clay were preactivated at 450°C for one night (including heating up with 1°C/min) prior to use in the catalytic reactions.

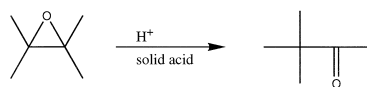Fig. 2. Postulated mechanism for the aluminium chloride catalysed hydroxyalkylation of aromatics with epoxides.

2.2. Synthesis of 2,3-dimethyl-2,3-epoxybutane and 2,3-dimethyl-3-buten-2-ol

The epoxide was prepared by epoxidation of 2,3-dimethyl-2-butene with *tert*-butyl hydroperoxide in refluxing pentane in the presence of $Mo(CO)_6$ as a catalyst, based on a method of Sharpless and Verhoeven [9].

A reference sample of 2,3-dimethyl-3-buten-2-ol was made by addition of methanesulfonic acid to a solution of the epoxide in dichloromethane, according to a method of Van Zon and Huis [10].

2.3. Catalytic reactions with 2,3-dimethyl-2,3-epoxybutane

H-mordenite (1 g) was suspended in a solution of 20 mmol epoxide and 2 mmol 1,3,5-tri-*tert*-butylbenzene (bulky internal standard) in 100 ml benzene. The reaction mixture was stirred at room temperature or reflux temperature. Aliquots were taken during the reaction and analysed by GC.

2.4. Synthesis of isophorone oxide

Isophorone oxide was synthesised by the epoxidation of isophorone with alkaline hydrogen peroxide according to a slightly modified method of House and Wasson [6,11–13].

2.5. Catalytic reactions with isophorone oxide

The homogeneous rearrangement of isophorone oxide was based on a method of House and Wasson [6,11,14]. To a solution of 32 mmol isophorone oxide in 100 ml benzene was added 32 mmol $BF_3 \cdot Et_2O$. The resulting solution was mixed by swirling and allowed to stand for 10 min. After work-up the solution was analysed by GC using an internal standard.

The solid catalysts (0.5 g) were suspended in a solution of 10 mmol isophorone oxide and 1 mmol 1,3,5-tri-*tert*-butylbenzene (bulky internal standard) in 50 ml solvent. The reaction mixture

was heated to the desired temperature with stirring at 1000 rpm. Aliquots were analysed by GC. Products were isolated by column chromatography and identified by NMR and GC/MS.

2.6. Synthesis of allyl aryl ethers

The synthesis was based on a general method of McKillop et al. [15] for the preparation of phenol ethers using phase-transfer catalysis.

2.7. Catalytic reactions with the allyl aryl ethers

The zeolites (1 g) were suspended in a solution of 15 mmol allyl aryl ether and 2 mmol 1,3,5-tri-*tert*-butylbenzene (bulky internal standard) in 100 ml solvent. The reaction mixture was heated to 80°C and stirred (1000 rpm) under nitrogen. Aliquots were analysed by GC. Products were isolated by column chromatography and identified by NMR and GC/MS.

2.8. Synthesis of 4,6-di-tert-butyl-2-methyldihydrobenzofuran

H-mordenite was suspended in a solution of 20 g allyl 3,5-di-*tert*-butylphenyl ether in 500 ml benzene. The reaction mixture was stirred at reflux temperature for 50 h and subsequently filtered. Evaporation of the solvent gave the crude product in 100% yield, which was purified by recrystallisation from ethanol/water, melting point: 62–64°C.

^{1}H NMR ($CDCl_3$/TMS, 400 MHz): δ 1.29 (s, 9H, $-C-(CH_3)_3$); 1.34 (s, 9H, $-C-(CH_3)_3$); 1.47 (d, $J = 6.2$ Hz, 3H, $-CH-CH_3$); 2.93 (dd, $J = 8.3$ Hz, $J = 15.1$ Hz, 1H, $-CH_2-$); 3.44 (dd, $J = 8.5$ Hz, $J = 15.1$ Hz, 1H, $-CH_2-$); 4.78–4.88 (m, 1H, $-OCH-$); 6.71 (d, $J = 1.6$ Hz, 1H, $\varnothing$); 6.90 (d, $J = 1.8$ Hz, 1H, $\varnothing$).

^{13}C NMR ($CDCl_3$/TMS, 100 MHz): δ 21.7; 30.4; 31.4; 34.9; 35.7; 39.1; 78.8; 104.7; 114.7; 120.9; 146.8; 151.4; 160.3.

3. Results and discussion

3.1. Epoxide rearrangements

Rearrangement of 2,3-dimethyl-2,3-epoxybutane with H-mordenite in refluxing benzene afforded pinacolone as a single product. Already after 15 min, a conversion of nearly 100% was obtained with a selectivity (based only on the liquid phase of the reaction mixture) of 61%. Prolongation of refluxing increased the selectivity to 68% (60 min), after which it remained constant. The slow release of pinacolone and the relatively large amount of catalyst indicates that probably a substantial amount of pinacolone was adsorbed by the catalyst. The observed stability of pinacolone may preclude coke formation. The yield of pinacolone can probably be increased by using less catalyst.

When the rearrangement was performed at room temperature a conversion of 100% was obtained after 120 min. Interestingly, in this case a mixture of pinacolone (sel. 48%), 2,3-dimethyl-3-buten-2-ol (sel. 14%) and some dimeric product was observed. Heating of this reaction mixture to reflux temperature resulted in decomposition of the allyl alcohol and dimer with concomitant increase of the amount of pinacolone (sel. 64%).

The homogeneous acid catalysed rearrangement of 2,3-dimethyl-2,3-epoxy-butane has been extensively studied by Van Zon and Huis [10]. They found that small amounts of methanesulfonic acid and sulfuric acid are capable of catalysing the selective rearrangement to 2,3-dimethyl-3-buten-2-ol (conv. 100%, sel. > 80%). At higher amounts of sulfuric acid the formation of pinacolone and 2,3-dimethyl-1,3-butadiene was also observed, of which the latter compound polymerised on standing. They suggested a mechanism in which a rapidly and quantitatively formed epoxide-acid intermediate slowly decomposes into the allyl alcohol as the primary product. The similarities between this work and our results prompted us to study the effect of

temperature, amount of catalyst and type (acidity) of the catalyst on the rearrangement [13,16].

We have similarly investigated the rearrangement of various cyclic α,β-epoxy ketones in the presence of solid acid catalysts [6,13,17]. So far, the use of heterogeneous catalysts in the rearrangement of α,β-epoxy ketones has scarcely been reported. As a model compound, we chose isophorone oxide because it can be easily made from the cheap isophorone.

Rearrangement of isophorone oxide (**1**) with $BF_3 \cdot Et_2O$ or the heterogeneous catalysts gave as major products 3,5,5-trimethyl-1,2-cyclohexanedione (**2**) and 2-formyl-2,4,4-trimethylcyclopentanone (**3**). In some cases, deformylation of **3** to 2,4,4-trimethylcyclopentanone (**4**) was also observed. The reaction scheme is depicted in Fig. 4. The results of the reaction with the various catalysts are shown in Table 1.

In general, the three major product types are useful intermediates for organic synthesis [14,18]. The deformylation is normally realised by treatment of the ring-contracted keto aldehyde with a base.

Table 1 shows that the acidic form of the zeolites and montmorillonite K10 were able to rearrange **1** to **2** and **3** with high conversions and selectivities. The total selectivities to **2** and **3** ranged from 70 to 94% and are therefore comparable to or even better than those found for the homogeneously catalysed reaction with $BF_3 \cdot Et_2O$. In the case of H-beta substantial deformylation was observed. The turnover numbers (defined as ratio rearranged epoxide/bulk aluminium) were up to 20, but since they are a result of the choice of the reaction conditions
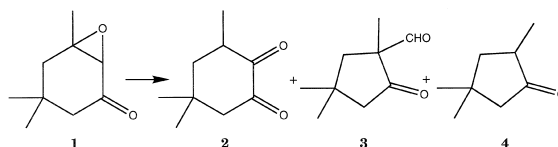

Fig. 4. Rearrangement of isophorone oxide to the three major products.

Table 1
Conversion of isophorone oxide (**1**) and selectivities to 3,5,5-trimethyl-1,2-cyclohexanedione (**2**), 2-formyl-2,4,4-trimethylcyclopentanone (**3**) and 2,4,4-trimethylcyclopentanone (**4**)

Catalyst	Temperature (°C)	Time (min.)	Converted (%)	Selectivity (%)			Ratio $(\mathbf{3}+\mathbf{4})/\mathbf{2}$
				2	**3**	**4**	
No	80	120	0.0	0.0	0.0	0.0	−
$BF_3 \cdot Et_2O$	rT	10	100	2.1	76.3	0.0	35.8
NaM	80	1200	25.7	14.0	62.9	0.0	4.5
HM	80	120	100	8.0	80.6	0.3	10.1
HM	80	1320	100	13.1	80.8	0.4	6.2
HM (p)	80	120	30.0	3.6	80.0	0.7	22.3
HM (d)	80	120	100	4.9	84.7	0.9	17.6
HM (s)	80	1500	99.4	9.5	77.8	0.0	8.2
H β	80	120	100	14.6	56.2	24.9	5.6
H β (p)	80	120	100	11.0	70.7	9.0	7.2
NaHY	80	1380	97.1	20.9	68.5	0.5	3.3
Montmorillonite K10	rT	1350	39.6	10.0	63.3	0.0	6.3
Montmorillonite K10	80	120	100	14.2	78.0	0.0	5.5

(p) = poisoned with triphenylphosphine; (d) = dealuminated; (s) = silylated.

they are probably amenable to further improvement.

When zeolite NaHY was used as the catalyst, a relatively large amount of **2** was formed, but **3** was still the major product. This relatively high selectivity to the dione was also observed for other cyclic α,β-epoxy ketones, affording a convenient synthesis of various 1,2-diones albeit in moderate yields [13,17].

Because the external surface of zeolites may contribute to their reactivity (see also Section 3.3), it was interesting to investigate the effect of some external surface treatments on the product distribution in the rearrangement of **1**. The investigated treatments were poisoning with triphenylphosphine, silylation with tetraethyl orthosilicate and dealumination [6,13,19]. However, despite the fact that the treatments drastically decreased the external surface activity, only a limited effect on the ratio $(\mathbf{3}+\mathbf{4})/\mathbf{2}$ was found. In contrast, poisoned H-beta showed a significant decrease in deformylation, suggesting that deformylation primarily takes place on the external surface.

The heterogeneous approach to the rearrangement of **1** is an excellent alternative to the classic homogeneous system because of the ex-

cellent yields and the easy work-up. The use of zeolites and clays also proved to be useful in the rearrangement of other cyclic α,β-epoxy ketones. Especially the rearrangement of terpenoid α,β-epoxy ketones leads to interesting results and products [13,17].

3.2. Zeolite-catalysed Claisen rearrangement

As a model system for screening of the use of zeolites in the Claisen rearrangement the simplest substrate, allyl phenyl ether, was chosen [5,13]. Reactions with several zeolites were conducted in refluxing benzene. Although H-ZSM-5 proved to be inactive, product formation was observed with H-mordenite and H-beta. Both catalysts gave as major products 2-allylphenol, 2-methyldihydrobenzofuran and to a lesser extent 2-propenylphenol (Fig. 5; R=H). 2-Methyldihydrobenzofuran and 2-propenylphenol are formed by acid-catalysed isomerisation of the initial rearrangement product, 2-allylphenol, and caused the decline of the selectivity to 2-allylphenol during prolongation of the reaction. Furthermore, dimers and higher oligomers were formed, apparently from 2-propenylphenol, which caused strong deactivation
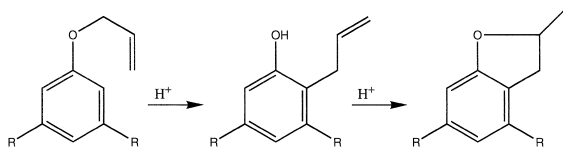
Fig. 5. Rearrangement of allyl phenyl ether (R = H) to 2-allylphenol, and cyclisation of the latter to 2-methyldihydrobenzofuran.

of the catalysts. H-beta was the most active catalyst (conv. 95% after 2 h, sel. 2-allylphenol 3%, sel. ring 40%) and H-mordenite the most selective (conv. 45% after 5 h, sel. 2-allylphenol 36%, sel. ring 29%).

In order to check the possible influence of external surface passivation (see also Section 3.3) on the formation of by-products, we investigated the effect of dealumination and poisoning [5,13,19]. No dimers and oligomers were observed in the liquid phase of the reaction mixture with triphenylphosphine-poisoned H-mordenite and H-beta. The activity of poisoned H-mordenite was strongly reduced. Poisoning of H-beta improved the selectivity to 2-allylphenol and 2-propenylphenol but the activity was also somewhat reduced. Dealumination of H-mordenite reduced the external surface activity to 7% of the initial value. Interestingly, a similar product distribution was observed to that found for untreated H-mordenite (including dimers and oligomers), indicating improved accessibility to the acid sites.

In a continuation of this study we are currently optimising the surface treatment procedure with a view to further suppressing the undesirable oligomerisation. We are also investigating solvent effects and the influence of substituents in the ring and allyl group. These results will be reported elsewhere [13].

3.3. A mechanistic probe for external surface acidity

In acid-catalysed reactions zeolites also often show shape selectivity because of their unique pore structure. It is clear, however, that the shape-selective potential of zeolites cannot be exploited if the nonselective external surface is responsible for a substantial proportion of the total activity.

The work on the Claisen rearrangement offered the possibility to construct a bulky homologue of allyl phenyl ether. The derivative chosen was allyl 3,5-di-*tert*-butylphenyl ether, which, because of its dimensions (11.0 Å × 10.8 Å × 5.8 Å), cannot enter the pores of a large-pore zeolite.

The rearrangement of the probe in the presence of untreated H-mordenite and H-beta leads predominantly to the formation of 2-allyl 3,5-di-*tert*-butyl-phenol and 4,6-di-*tert*-butyl-2-methyldihydrobenzofuran (Fig. 5; R = *tert*-butyl), consistent with reaction taking place on the external surface. The *o*-allylphenol intermediate is converted rapidly to the ring product. The conversion proceeds so well that the procedure constitutes a convenient synthesis of the latter compound (sel. > 96%).

The probe has proven to be very valuable for the study of the effectiveness of different surface passivation methods [13,19–21]. For example, we have found that treatment of H-mordenite and H-beta with triphenylphosphine gave a total deactivation of the external surface. Treatment of H-mordenite with triphenylamine reduced the external surface to approximately half its previous level.

3.4. Intramolecular hydroxyalkylation

The preceding results show that zeolites and clays often give good results in intramolecular reactions, such as rearrangements. A reasonable explanation might be that in intramolecular reactions a potentially difficult simultaneous contacting of reactants with a marked difference in polarity is circumvented. These facts prompted us to study an intramolecular version of the hydroxyalkylation of aromatics with epoxides. By combining both reactants in a single
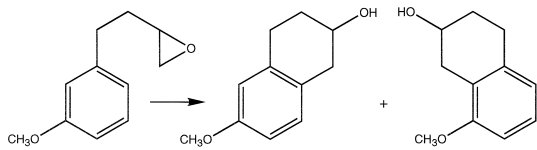
Fig. 6. Intramolecular hydroxyalkylation of 4-(3-methoxyphenyl)-1-butene oxide to 6-methoxy-1,2,3,4-tetrahydro-2-naphthol and 8-methoxy-1,2,3,4-tetrahydro-2-naphthol.

molecule, it can be elegantly demonstrated if solid (Brønsted) acid catalysed hydroxyalkylation is in principle possible. An example of such an attempt is shown in Fig. 6.

Indeed, we found that the reaction of the epoxide in refluxing benzene or chlorobenzene gave the desired tetrahydronaphthols, in a truly catalytic reaction (TON 6) and in yields of around 30–40% with the best catalysts [1]. Intramolecular hydroxyalkylation (cyclialkylation) in the presence of solid acids was also obtained with several other arylalkyl epoxides [13,22].

4. Conclusions

We have shown that solid acids, in particular zeolite beta and mordenite, are effective catalysts for the rearrangement of epoxides and α,β-epoxy ketones and the Claisen rearrangement of allyl aryl ethers. The principle of zeolite-catalysed hydroxyalkylation of aromatics was demonstrated for an intramolecular example of this reaction.

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