

Comparative study of phenol alkylation mechanisms using homogeneous and silica-supported boron trifluoride catalysts

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Abstract

The application of silica-supported BF_3 as a mild solid acid catalyst to the C- and O-alkylation of various aryl alcohols is described. In the case of O-alkylation, the reactivity of the ether product in both heterogeneous and homogeneous systems is compared, and it is shown that the former can be used to affect selective C-alkylation of ethers, while in the latter system, ether rearrangement to ring poly-alkylated phenols also occurs. Ether rearrangement is thought to require coordination of the ether to an available Lewis acid site, which, in the case of the heterogeneous system, is apparently impossible. The difference between the homogeneous and the supported BF_3 may be attributed to steric restrictions and/or relatively weak Lewis acidity of the supported system. Effects of steric hindrance at the reaction centre are examined. Possible routes to ethers and ring-alkylated products are also discussed. © 2000 Elsevier Science B.V. All rights reserved.

Keywords: Supported BF_3 ; C-alkylation; O-alkylation; Solid acid catalysis

1. Introduction

C-alkylated phenols, in particular, *tert*-butyl-, *iso*-octyl-, and *iso*-decyl phenols, are widely used in the chemical industry as drilling oil additives, antioxidants, and polymer stabilizers [1]. The isomeric O-alkylated phenols also have numerous industrial applications, particularly in the production of dyes and agrochemicals [2]. The large-scale manufacturing of these compounds (over 2.5×10^5 tons in 1995 worldwide) is based on homogeneous acid-catalysis technologies, using HF, H_2SO_4 , AlCl_3 or BF_3 .

Although good yields and high turnover numbers are obtained, the production volume is such that the toxic aqueous waste resulting from the catalysts is a problem. The drive towards eco-friendly processes has advanced interest in solid acid catalysts, which can reduce the corrosiveness of the reaction mixture, and may be removed by simple filtration rather than the aqueous quench required in homogeneous processes. Among the heterogeneous systems examined to date are anion exchange resins [3,4], NaX and Y zeolites [5,6], heteropoly acids [7], acid-treated clays [8], and titania-supported AlPO_4 [9].

Recently, we reported the synthesis and catalytic properties of a novel, silica-supported BF_3 catalyst, $\text{BF}_3\text{:HL-SiO}_2$ [10]. This solid acid catalyst possesses tunable Brønsted and Lewis acidity through the use of various organic or

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inorganic ligands (HL). Initial experiments with this catalyst showed that it catalyses C- and O-alkylation of phenol with 1-octene.

In this paper, we examine the various reaction routes for phenol C- and O-alkylation using cyclohexene as a model-alkylating agent, and compare the activity of homogeneous and heterogeneous (silica-supported) BF_3 . Possible analogies between the reaction mechanisms of homogeneous BF_3 , heterogeneous BF_3 , and aluminum halides, are discussed.

2. Experimental

2.1. Materials and instrumentation

^1H and ^{13}C NMR spectra were measured on a JEOL EX 270 instrument at 270.05 and 67.92 MHz, respectively. GC analyses were performed using an HP-5890 gas chromatograph with an HP1 capillary column (25 m/0.25 mm). Unless stated otherwise, chemicals were purchased from commercial firms (> 98% pure) and used without further purification. Mesoporous silica (Merck K-100) of $310 \text{ m}^2 \text{ g}^{-1}$ surface area was dried for 24 h at 300°C before use. Cyclohexyl phenyl ether was synthesized through a modification of the literary procedure [11] (vide infra). Gradual addition of reagents was performed using a Watson-Marlow 505S peristaltic pump. Products were either isolated and identified by comparison of their ^1H NMR spectra to standard samples, or identified by MS data and comparison of their GC retention times with commercial reference samples. *n*-Dodecane was used as internal standard in all reactions.

2.2. General procedure for the preparation of supported BF_3 catalyst

Ten grams of silica was treated as above and then stirred with 100 ml of ethanol containing 4.2 g (400 mmol) of $\text{BF}_3(\text{H}_2\text{O})_2$ for 2 h at 30°C , under a nitrogen atmosphere. The slurry

was dried slowly on a rotary evaporator at 50°C . The typical loading obtained was $2\text{--}3 \text{ mmol g}^{-1}$ as determined by ICP-MS. Characterisation of the catalyst acid sites was performed as described previously [10].

2.3. General procedure for phenol alkylation

2.3 g (24 mmol) of phenol was stirred with 0.6 g $\text{BF}_3(\text{H}_2\text{O})_2/\text{SiO}_2$ at 85°C . After 2 min, 2.0 g (24 mmol) of cyclohexene was added gradually over a period of 30 min. Reaction progress was monitored by GC. Reactions using *o*-cresol, *p*-cresol, 2,6-dimethyl phenol and 2,6-di-*tert*-butyl phenol were carried out similarly. Reactions using homogeneous BF_3 were carried out under similar conditions but using 5 mol% of $\text{BF}_3(\text{H}_2\text{O})_2$ instead of the supported catalyst.

Ring-alkylation of phenoxy ethers (*n*-butyl phenyl ether, anisole, and phenetole) with cyclohexene were carried out according to the general procedure. Products were analysed by GCMS. Fragmentation analysis confirmed that no rearrangement of the ether took place in the presence of $\text{BF}_3(\text{H}_2\text{O})_2/\text{SiO}_2$. The *ortho/para* ratios were not determined for these products.

2.4. Synthesis of cyclohexyl phenyl ether

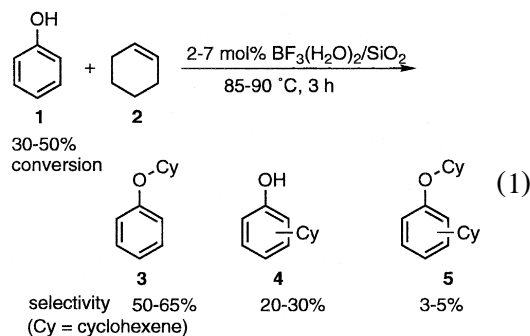
19.4 g (206 mmol) of phenol and 8.31 g (207 mmol) of NaOH were stirred in 10 ml of water at 25°C for 10 min, after which, the water was removed by rotary evaporator (a thin film of the phenoxide forms around the flask and is washed away in the next step). 50 ml of 2-propanol was added, and the mixture heated to reflux, after which, 13.3 g (81 mmol) of cyclohexyl bromide was added, and the reaction refluxed overnight. The cooled reaction mixture contains product, cyclohexene, and traces of phenol. Fifty milliliters of diethyl ether was then added, and the mixture was washed ($3 \times 20 \text{ ml}$) with 5% NaOH solution. The phases were separated, the organic phase dried over MgSO_4 , and the diethyl ether and cyclohexene removed by evaporation under reduced pressure. The yield of

cyclohexyl phenyl ether is 10.5 g (30% based on starting material). Analytical data agreed well with literature values [3]. δ_{C} (CDCl_3) 23.70, 25.56, 31.76, 75.20, 115.96, 120.37, 129.32, 157.69. δ_{H} (CDCl_3) 1.21–2.0 (10H, m); 4.21 (1H, tt); 6.90 (2H, d); 7.24 (2H, t).

3. Results and discussion

3.1. Phenol alkylation with cyclohexene

In a typical reaction (Eq. 1), one equivalent of phenol **1** was stirred at 85–90°C together with 0.6 g of $\text{BF}_3(\text{H}_2\text{O})_2/\text{SiO}_2$ catalyst (5 mol% of BF_3 relative to substrate). Cyclohexene **2** was added dropwise to this mixture using a peristaltic pump. Cyclohexyl phenyl ether **3** was found to be the major product, together with some ring-alkylated phenol **4** and small quantities (1–2%) of the ring-alkylated ether **5**.



The reaction ceased after 30–50% conversion of **1**, depending on reaction conditions. This may be attributed to catalyst deactivation, for the reaction resumed when a fresh batch of catalyst was introduced. The deactivation may be due to the formation of cyclohexene oligomers, which block the catalyst pores. Indeed, batch addition of cyclohexene hastened the deactivation process, and when a phenol:cyclohexene ratio of 1:2 was used, no reaction took place. We believe that catalyst deactivation, in this case, is not due to leaching

of BF_3 from the silica support. This is evidenced indirectly through the remarkable differences in reactivity shown by the homogeneous and the heterogeneous BF_3 systems (vide infra).

Fig. 1 shows the effect of the presence of a solvent and the effect of gradual addition of cyclohexene on phenol conversion. 1,2-Dichloroethane (DCE) was selected as a solvent based on the work of Espeel et al. [6] who showed that it is a suitable solvent for phenol alkylation over zeolites. Solvent influence on the reaction rate and selectivity was discerned to depend on competitive adsorption, rather than reflect a direct kinetic solvent effect. Similarly, our experiments using $\text{BF}_3(\text{H}_2\text{O})_2/\text{SiO}_2$ in the presence and absence of DCE show that two things occur in the presence of the solvent: the reaction is slower, and the final yield is lower. While the former may be attributed to lower reactant concentrations, the latter indicates that the solvent enhances catalyst deactivation, possibly by facilitating the approach of cyclohexene to the catalyst surface. Consequently, the best conver-

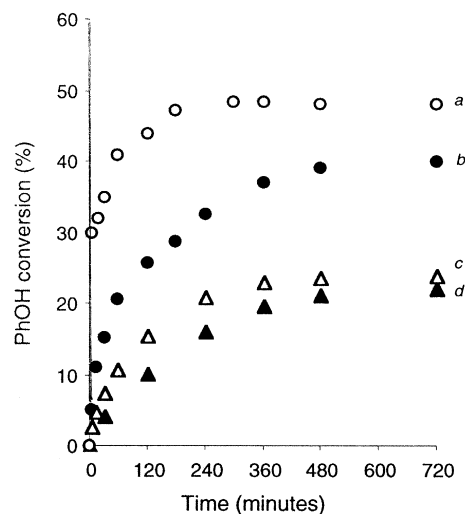


Fig. 1. Conversion profiles for **1** in alkylation catalyzed by supported BF_3 . Reaction conditions: 24 mmol PhOH, 48 mmol **2**, 85°C, 5 mol% $\text{BF}_3(\text{H}_2\text{O})_2/\text{SiO}_2$. (a) Solvent-free reaction, drip feed of cyclohexene. (b) Solvent free reaction, batch addition of 24 mmol **2**. (c) DCE solvent, drip feed of **2**. (d) DCE solvent, batch addition of 24 mmol **2**. Conversions are based on GC area, corrected by the presence of an internal standard.

sion (ca. 50%) was achieved by using no solvent and by dropwise addition of equimolar amounts of alkene to a suspension of the catalyst in the neat substrate.

3.2. Direct ring-alkylation vs. ether rearrangement

The acid-catalysed rearrangement of alkyl phenyl ethers to alkylphenols has been known for over a century [12]. Investigations show that this rearrangement can lead to ring-alkylation via both intra- and intermolecular routes [13–15], the extent of which depends on catalyst type and reaction media homogeneity [16]. In order to measure the extent of C- and O-alkylation, and compare it with the ether rearrangement, we examined the product distribution for both supported (Fig. 2, top) and homogeneous (Fig. 2, bottom) BF_3 .

Theoretically, it is possible to obtain **4** in our system either through direct ring-alkylation ($\mathbf{1} + \mathbf{2} \rightarrow \mathbf{4}$), or through etherification followed by rearrangement ($\mathbf{1} + \mathbf{2} \rightarrow \mathbf{3}$; $\mathbf{3} \rightarrow \mathbf{4}$). Similarly, **5** may form via direct ring-alkylation of phenol followed by etherification ($\mathbf{1} + \mathbf{2} \rightarrow \mathbf{4}$; $\mathbf{4} + \mathbf{2} \rightarrow \mathbf{5}$), or through etherification, followed by rearrangement and a second etherification ($\mathbf{1} + \mathbf{2} \rightarrow \mathbf{3}$; $\mathbf{3} \rightarrow \mathbf{4}$; $\mathbf{4} + \mathbf{2} \rightarrow \mathbf{5}$). In the analogous silica- and titania-supported aluminum halide catalysts, all of these routes were observed, and we therefore expected a similar outcome here. However, when ether **3** was used as the substrate instead of **1** (Eq. 2, the reaction conditions are identical to Eq. 1), no ether rearrangement took place when heterogeneous BF_3 was employed. On the other hand, homogeneous BF_3 , as could be expected from the literature [17], did catalyse ether rearrangement under the same conditions (Eq. 3). These results proved consistent, regardless of the ether used (R = cyclohexyl, Me, Et, or *n*-butyl). In the heterogeneous system, therefore, the only possible route to obtain the ring-alkylated products **4** and **5** would be via direct ring-alkylation. Note that according to this formulation, a Lewis acid is a prerequisite for ether

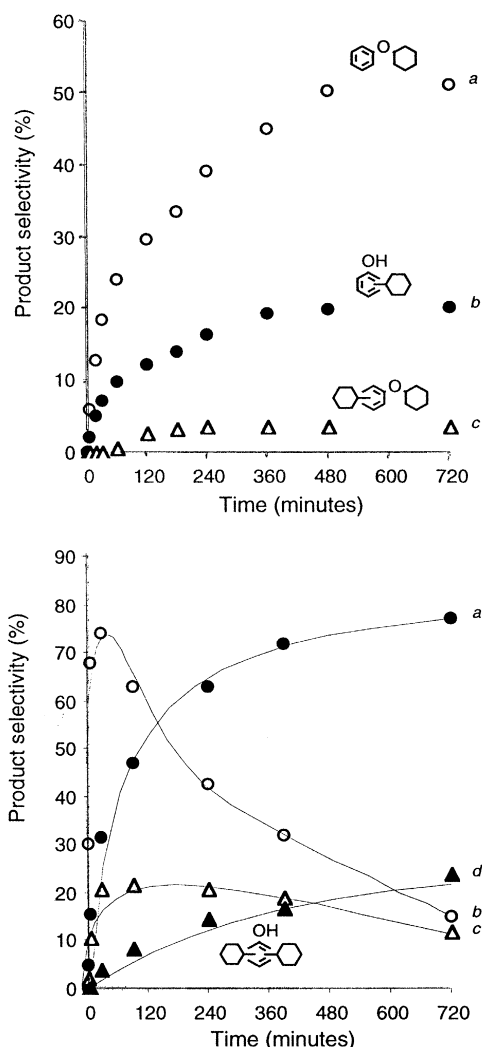
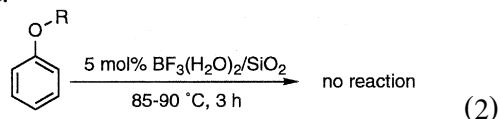
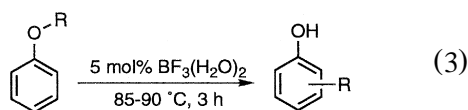


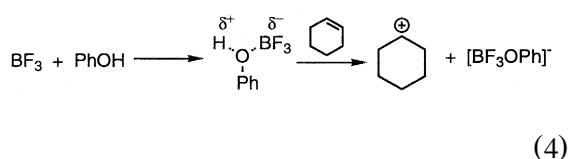
Fig. 2. Yields of C- and O-alkylation products catalysed by supported (top) and homogeneous (bottom) BF_3 . Reaction conditions: 24 mmol **1**, 24 mmol **2**, 85°C, solvent-free reaction, batch addition of **2**. (top) 7 mol% $\text{BF}_3(\text{H}_2\text{O})_2/\text{SiO}_2$. (bottom) 5 mol% $\text{BF}_3(\text{H}_2\text{O})_2$. (a) (empty circles) **3**. (b) (filled circles) **4**. (c) (empty triangles) **5**. (d) (filled triangles) Dialkylated ether. All yields based on GC area, corrected by the presence of an internal standard.

rearrangement to occur. Indeed, when *n*-butyl phenyl ether was heated to 80°C for 8 h with 5 mol% of triflic acid ($\text{CF}_3\text{SO}_3\text{H}$, a strong Brønsted acid), no ether rearrangement was observed.

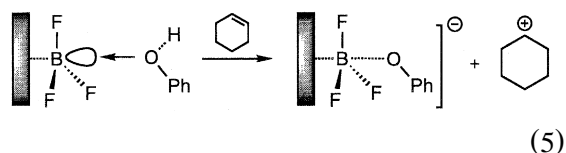




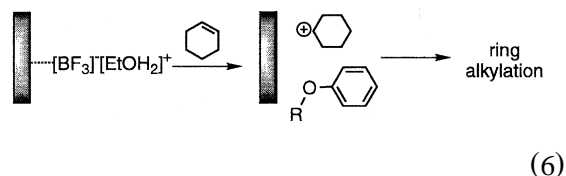
The above findings may be rationalized as follows: homogeneous BF_3 , in the presence of phenol, is known to easily undergo complexation with **1** [18], and the resulting complex can donate a proton to an alkene, e.g., **2** (Eq. 4). The cyclohexyl carbocation can then attack a phenol molecule to give the ring-alkylated product. Similarly, ether rearrangement in the homogeneous system can occur via complexation of the ether to BF_3 , followed by C–O bond scission and formation of a π -complex, or alternatively, a metastable ion-pair [19–21], which will collapse to give the rearranged product.



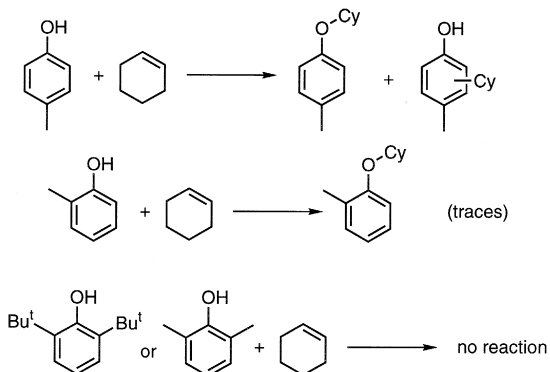
On the other hand, the heterogeneous system should contain both $>(\text{Si})_2\text{O} \cdots \text{BF}_3$ (Lewis) and $>\text{SiO} \cdots \text{BF}_3^-[\text{EtOH}_2]^+$ (Brønsted) acid sites [10], and complexation of **1** to one of the Lewis sites of the catalyst may be envisaged (Eq. 5). Attack of **2** on the complexed phenol may result in O–H cleavage, with subsequent formation of a cyclohexyl carbocation and ring-alkylation. Conversely, complexation of the ether to the Lewis site is apparently not possible, presumably due to strong steric effects of the ether alkyl chain. In fact, Rowsell et al. [22] have recently shown that when BF_3 is complexed as a Lewis acid, all three B–F bonds are lengthened and distorted out-of-plane so that a near-tetrahedral structure is formed. This distortion would force a longer B–O bond to the coordinating molecule, again making ether bonding unlikely.



It should also be noted that supported BF_3 is a weak Lewis acid, as the empty orbital on the boron atom is partially filled through coordination to the silica (see Ref. [10] for spectroscopic characterisation of Lewis and Brønsted sites). Thus, the relatively weak Lewis acidity of the supported catalyst may not suffice to facilitate O–C bond cleavage. In the presence of an olefin, however, the direct ring-alkylation of ethers may still occur, through the coordination of an olefin to one of the catalyst's Brønsted acid sites, followed by the attack of the resulting carbocation on a nearby ether molecule (Eq. 6).



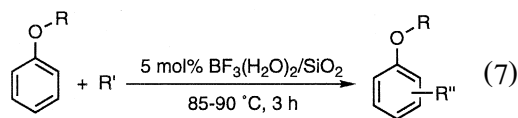
Under the conditions employed in these experiments, the supported BF_3 catalyst differs from its homogeneous counterpart in two main points: (a) C–O cleavage cannot occur (no ether rearrangement, *vide supra*), and (b) steric effects, as could be expected, play a major role. In fact, control experiments showed (Scheme 1)



Scheme 1. Effect of hindering groups near the reaction centre on the alkylation of substituted phenols. Reaction conditions: 5 mol% $\text{BF}_3(\text{H}_2\text{O})_2/\text{SiO}_2$, 85–90°C, 3 h. Cy = cyclohexene.

that, while *p*-cresol **6** evidenced a similar reactivity to **1**, alkylation of *o*-cresol **7** gave only traces of the ether, and no reaction at all was observed when 2,6-dimethyl phenol or 2,6-di-*t*-butyl phenol were used as substrates.

The fact that heterogeneous BF_3 catalyses the direct ring-alkylation of phenoxy ethers without rearranging them suggests that this system may be applied to selective ring-alkylation. Indeed, we found that **3** reacts with 1-octene [10], to give only octyl ring-alkylated ether products. Selective ring-alkylation (Eq. 7) was also observed when *n*-butyl phenyl ether, anisole, and phenetole, were reacted with **2** (cf. Section 2).



4. Conclusions

Silica-supported BF_3 is a new mild solid acid catalyst that can effect both C- and O-alkylations of various phenols. In contrast to homogeneous BF_3 , it does not catalyse the rearrangement of alkylphenyl ethers, and can therefore be used in the selective ring-alkylation of aromatic ethers.

Acknowledgements

Support of this research through an EPSRC grant, and an RSC journals grant for international authors (to GR) are gratefully acknowledged. One of us (JHC) also thanks the

RAEng-EPSRC for a Clean Technology fellowship.

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