

Zeolite β Induced Rearrangement of Alkoxybenzyl Allyl Ethers to Aldehydes and Ketones. Part IV.† Investigation of the Reaction Conditions

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The reaction conditions for the rearrangement of *p*-methoxybenzyl allyl ether **1** have been investigated with respect to catalysts and solvents. Zeolite β was the best catalyst but zeolite Y and mordenite were also effective. The Lewis acids $\text{BF}_3 \cdot \text{OEt}_2$, $(i\text{PrO})_2\text{TiCl}_2$ and AlMe_2Cl induced the rearrangement but were considerably less efficient than the solid catalysts. Protic acids were not very useful owing to the formation of too many products. Among the solvents tested dichloromethane and 1,1,2-trichloroethane were the most useful even though the rearrangement took place in several other solvents. Interestingly, **1** rearranged spontaneously on dissolution in 1,1,1,3,3,3-hexafluoropropan-2-ol (HFP).

As we earlier reported, certain substituted benzyl allyl ethers such as **1** rearrange to give 4-arylbutanals (**2**) under the influence of zeolite β (Scheme 1).¹ The reaction involves two steps: a 1,4-migration of the benzylic group in addition to a 1,2-hydride or 1,2-alkyl migration, and for simplicity reasons we call the overall reaction the BenzAll rearrangement (*benzyl allyl*). Previous results indicated that there were perhaps only a few reaction conditions that would promote the reaction. In order to better define these conditions we chose to investigate the rearrangement of **1** using different solvents, reaction times and amount and types of catalysts.

Results and discussion

Variation of the solvent. Solutions of **1** in ten different solvents, chosen with different properties based on the Carlson plot,² were stirred at room temperature in the presence of 125 mg of zeolite β . The progress of the rearrangement was monitored by GC analysis after 2 and 18 h, using phenylcyclohexane as an internal standard. As seen in Table 1 various degrees of conversion had occurred after 2 h, but the yields were very similar in most of these solvents after 18 h except for acetonitrile and 1,1,1,3,3,3-hexafluoropropan-2-ol (HFP). Apparently the rearrangement was slower in Et_2O , hexane and toluene than in CH_2Cl_2 and 1,1,2-trichloroethane (Tri). A by-product (**3**) was formed in substantial

amounts particularly in the chlorinated solvents, which, apart from this problem, gave very clean reaction mixtures, making it easy to purify **2** by chromatography. Even if the use of Et_2O gave the highest yields of **2** and thus seems to be the best solvent, numerous unidentified by-products in small amounts made the chromatographic purification of **2** very difficult. In acetonitrile the reaction was slower and the degree of conversion never exceeded 26%.

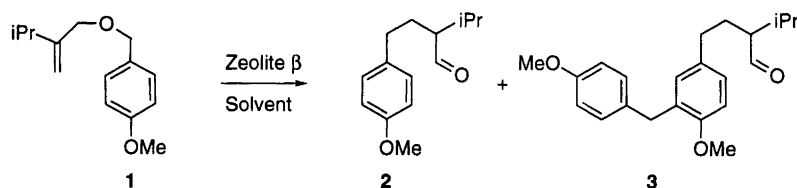
HFP has recently been reviewed as a solvent with extreme properties.³ It has a combination of low nucleophilicity, high hydrogen-bonding donor strength, low hydrogen-bonding acceptor strength, high ionizing power and high polarity, which makes it an exceptionally good solvent for cations and radical cations due to efficient solvation of the counter ions. Thus, it is used as solvent in EPR spectroscopy and mechanistic studies of radical

Table 1. Solvent effects in the rearrangement of **1** using 125 mg of zeolite β per mmol of **1**.

Entry	Solvent	1:2:3	
		2 h	18 h
1	CH_2Cl_2	5:69:9	0:70:19
2	Tri	9:66:10	0:67:24
3	Et_2O	38:47:0	6:72:2
4	Hexane	52:33:2	8:65:9
5	Toluene	11:53:7	0:66:12
6	CH_3CN	72:21:—	69:26:0
7	HFP	0:41:0	—

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† For Part III see Ref. 6.



Scheme 1.

cations. Indeed, carbocations, including various benzylic cations, have been shown to be remarkably long-lived in HFP.^{4,5} These facts may explain the spontaneous rearrangement of **1** on dissolution in HFP, since the mechanism probably involves charge separation in the transition state and perhaps also a more or less free benzylic carbocation.⁶

When HFP and **1** were combined the components seemed to be insoluble in each other but after a few seconds the reaction mixture became homogenous and turned wine-red just as in the zeolite-catalysed reactions. After approximately 5 min the colour had changed to yellow and then the HFP was removed under reduced pressure and replaced by CH_2Cl_2 . GC analysis showed that **2** was formed in 41% yield together with some higher molecular weight by-products. It is possible that the latter originated from the reaction of the benzylic cation with the substrate in an uncontrolled way.

No reaction occurred in EtOH, *N,N*-dimethylformamide (DMF), tetrahydrofuran (THF) or 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidone (DMPU). It is likely that these solvents inactivated the zeolite by binding too strongly to the acidic sites, and they obviously did not have sufficiently strong solvating power to allow the rearrangement to proceed without the zeolite.

Amount of zeolite. Different amounts of zeolite β were used in the reaction of **1** for 18 h in CH_2Cl_2 . As seen in Fig. 1 there is an optimum around 100 mg mmol^{-1} of substrate. At lower levels a substantial amount of starting material was left. On the other hand, when larger

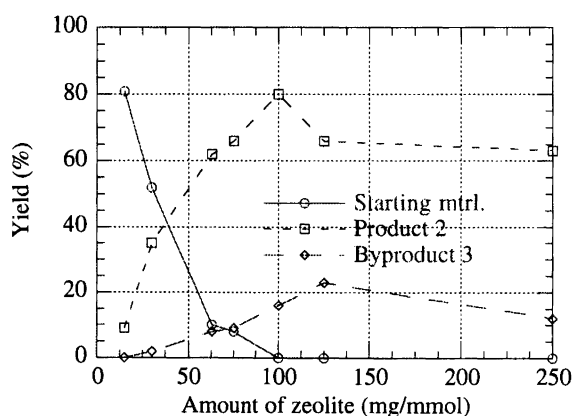


Fig. 1. Variation of the amount of zeolite in the rearrangement of **1** in dichloromethane; reaction time 18 h. The yields were determined by GC analysis using phenylcyclohexane as an internal standard.

amounts of zeolite were used the number and the amounts of by-products increased. Even at very low levels of zeolite some by-product **3** was formed and at the 250 mg mmol^{-1} level we also noticed the appearance of 14% of a higher molecular weight unidentified by-product, probably carrying several *p*-methoxybenzyl (PMB) groups. Compared with other cases of zeolite induced reactions the amount of zeolite needed in this rearrangement was quite low. In most other zeolite induced reactions recorded in the literature $0.5\text{--}3 \text{ g mmol}^{-1}$ were used.⁷⁻⁹

Variation of the reaction time. The development of the reaction versus time was investigated in dichloromethane with zeolite β at two levels: 100 and 125 mg mmol^{-1} of substrate. At the 125 mg level [Fig. 2(a)] the reaction was quite fast; after 2 h all of the starting material was consumed and the yield of **2** was 81%. At this point the yield of by-product **3** was 11%, but with an extended reaction time the ratio of **2**:**3** decreased, indicating degradation of **2**.

At the 100 mg level [Fig. 2(b)] the reaction was slow compared with the 125 mg case but after 10 h nearly all of the starting material was consumed. Despite the longer reaction time the yield of **2** was high (78%) and there was only a small amount of **3** (12%). The relatively large increase in rate caused by the modest increase of the amount of catalyst was unexpected and an explanation awaits further investigation. However, the initial reaction rates were not drastically different. In conclusion the reaction should be performed in CH_2Cl_2 at room temperature with either 100 mg mmol^{-1} zeolite with a long reaction time or 125 mg mmol^{-1} zeolite with a short reaction time. These findings are, of course, not directly transferable to other substrates and should be regarded as crude settings of the experimental conditions.

Different catalysts. A large number of catalysts were tested. The application of the strong Lewis acids TiCl_4 , SnCl_4 and FeCl_3 resulted in cleavage of the PMB-ether to give mixtures of the corresponding alcohols and halides, even though the reactions were run at a temperature interval between -78°C and -20°C and with short reaction times. AlCl_3 at -20°C did not give any conversion and degraded the starting material at room temperature. Also, the use of the milder Lewis acids ZnCl_2 and SnCl_2 resulted in degradation of the starting material and/or formation of several by-products. The weak Lewis acids LiCl , LiBr , LiClO_4 , CuBr , MgClO_4 and $\text{Ti}(\text{OiPr})_4$ were completely inefficient; no reaction

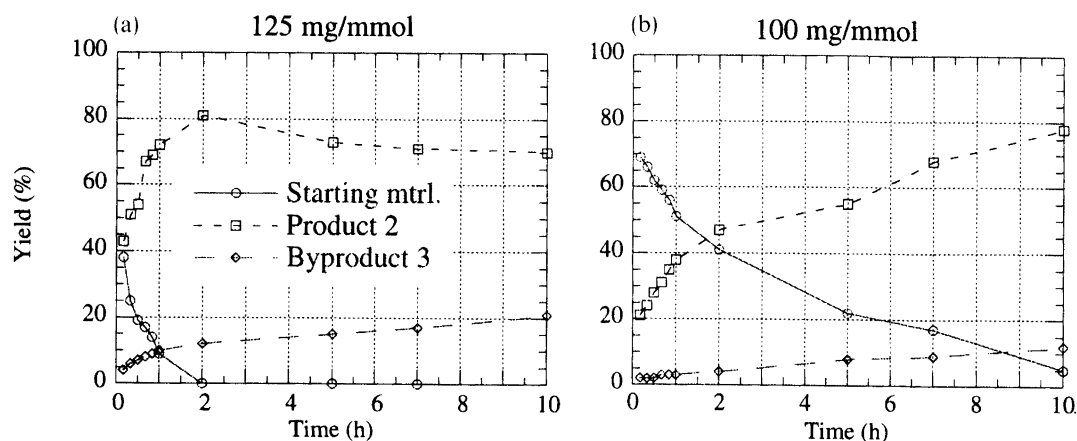


Fig. 2. Time development of the rearrangement of **1** in the presence of (a) 125 and (b) 100 mg mmol⁻¹ of zeolite β.

was noted. Only three of the Lewis acids tested namely $\text{BF}_3 \cdot \text{Et}_2\text{O}$, $(i\text{PrO})_2\text{TiCl}_2$ and AlMe_2Cl (all at -20°C) gave the desired product **2**, but the yields were low and various amounts of by-products were formed. Essentially the same result was obtained with the protic acids TsOH and TFA, while the weaker pyridinium tosylate (PPTS) did not give any reaction at all.

Zeolite Y (Y-25, pore size $7.4 \times 7.4 \text{ \AA}$) and mordenite (M-82, pore size $6.5 \times 7.0 \text{ \AA}$) gave results similar to those obtained with zeolite β (b-52, pore size $7.4 \times 7.4 \text{ \AA}$), but somewhat larger amounts of by-products were formed. Zeolite ZSM-5 (pore size $5.1 \times 5.4 \text{ \AA}$) and molecular sieves 4 \AA did not give any conversion of the starting material, which may be due to their small pore size. It has recently been reported that a small amount of water in zeolites is critical for success in some reactions.¹⁰⁻¹² A drying temperature of 120°C is recommended. In contrast, the rearrangement of **1** was unsuccessful when we used zeolite β dried at this temperature. An activation at 400°C for at least 3 h seems necessary.

In summary, the best conditions for this rearrangement were to stir the substrate in CH_2Cl_2 at room temperature for 2 h in the presence of 125 mg of zeolite β per mmol of substrate, or for longer times (typically more than 10 h) with 100 mg mmol⁻¹ of substrate. With lower levels of the zeolite the reaction times were impractically extended. Other solvents such as Et_2O and other catalysts such as zeolite Y and mordenite may also be worth trying. Among the homogenous phase catalysts $\text{BF}_3 \cdot \text{OEt}_2$ was the best, but it was still inferior to zeolite β. However, $\text{BF}_3 \cdot \text{OEt}_2$ may be worth testing in cases where the substrates are too bulky to fit the pores of the zeolite, if this is where the reaction takes place. Preliminary results indicated a dependence between the size of the substrate and the pore size of the zeolite.

Experimental

Chemicals. Dichloromethane, 1,1,2-trichloroethane, toluene and hexane were distilled from P_2O_5 , THF and diethyl ether were distilled under N_2 from sodium-

benzophenone ketyl, DMF was dried over MS 4A and distilled under reduced pressure, CH_3CN and DMPU were dried over CaH_2 and distilled under normal and reduced pressure, respectively. HFP was of Merck Uvasol[®] quality. Lewis acids were of *puriss* or *p.a.* quality and were used as received. Zeolites were obtained from EKA Chemicals AB and were dried for 3 h at 400°C prior to use. Compound **1** was prepared according to the literature¹³ and data for compound **2** and **3** were as described previously.⁶

General techniques. Gas chromatographic analyses were performed on a DB wax (J&W Scientific) capillary column 30 m, 0.25 mm i.d., 0.25 mm stationary phase. Thin layer chromatography was performed on Merck precoated TLC plates with Silica gel 60 F-254, 0.25 mm. After elution the TLC plates were sprayed with a solution of *p*-methoxybenzaldehyde (26 ml), glacial acetic acid (11 ml), concentrated sulfuric acid (35 ml), and 95% ethanol (960 ml) and the compounds were visualized upon heating. The zeolites were activated at 400°C for 3 h prior to use and all glassware was dried at 120°C .

General procedure for the investigation of the effects of solvent, time and amount of zeolite on the rearrangement. Compound **1** (44 mg, 0.20 mmol) and a weighed amount of phenylcyclohexane (ca. 30 mg) in dichloromethane (0.5 ml) were added to a nitrogen-gas flushed 7 ml vial charged with the zeolite and a magnetic stirring bar. The mixture was stirred at room temperature for the time indicated in the text for the respective experiments. To monitor the reaction, samples were withdrawn at regular intervals, diluted with dichloromethane, filtered and analysed by GC.

General procedure for the investigation of different catalysts. Compound **1** (44 mg, 0.20 mmol) in dichloromethane (0.25 ml) was added to a nitrogen-gas flushed 7 ml vial, charged with a magnetic stirring bar and a mixture of the appropriate catalyst (0.20 mmol) in dichloromethane (0.25 ml). The mixture was stirred and samples were

withdrawn at regular intervals, diluted with ether, washed with aqueous saturated sodium hydrogencarbonate solution, dried over magnesium sulfate and analysed by TLC.

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