Mechanistic Aspects of the Zeolite β Induced Rearrangement of Alkoxybenzyl Allyl Ethers to Aldehydes and Ketones

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Dedicated to Professor Lennart Eberon on the occasion of his 65th birthday


The mechanism for the novel zeolite β catalyzed rearrangement of alkoxybenzyl allyl ethers to aldehydes and ketones has been investigated by use of cross reactions and deuterium labeling. The reaction is mainly intramolecular and may be described as a nucleophilic attack of the double bond on the electrophilic benzylic carbon of the ether–Lewis acid complex, followed by a 1,2-hydride (or alkyl) migration.

We recently found that alkoxybenzyl allyl ethers 1 rearranged under the influence of zeolite β or BF₃·OEt₂ to give aldehydes 2 in good yields (Scheme 1). Typical examples are p-methoxybenzyl (PMB) allyl ethers, although the parent benzyl allyl ether does not rearrange under these reaction conditions. This, together with the fact that only zeolite β and BF₃·OEt₂ were effective among several Lewis acids tested, may explain why the reaction has escaped attention although benzyl allyl ethers constitute a well known class of compounds. It has been observed that bis-allylic ethers may undergo a 1,4-Wittig rearrangement to give aldehydes and/or ketones as a minor pathway under strongly basic conditions.

The need for electron-donating substituents in the benzene ring indicates that a benzyl cation intermediate may be involved. In order to find out whether the mechanism is intramolecular or intermolecular cross experiments were performed. By mixing equimolar amounts of either compounds 1a and 1b or 1c and 1d and allowing them to rearrange under the influence of zeolite β we were able to show from the product distribution that the reaction was approximately 10% intermolecular (cross products) and 90% intramolecular (Scheme 2). The amounts of cross products could be suppressed to less than 5% by diluting the reaction mixture by a factor of about 500.

By-product 3 was formed in various amounts (up to 25%) when 1a was treated with larger portions of zeolite β. This by-product is most likely a result of a free benzyl cation attacking the aromatic ring either in the starting material or in the product.

The 1,2-hydride shift was demonstrated by using the deuteriated compound 4 as the starting material.
Deuterium was found to migrate from position 1 to 2 as shown by $^1$H and $^{13}$C NMR spectroscopy. Interestingly, the hydride and the deuteride migrated to the same extent according to NMR analysis (see Experimental), which was not totally unexpected since it is known that the H/D isotope effect in 1,2-migrations may be quite small. Further evidence for a 1,2-bond shift was the formation of 6 and 7 (1:2) when 5 was treated with zeolite β (Scheme 3). Here competition between a hydride shift and a methyl shift occurred.

Scheme 3.

Assuming that a Lewis acid–ether complex is the first formed reactive species the C–O bond length in model oxonium ions would indicate the rearrangement. Thus, calculations (3-21 G*) of the C–O bond length of 8a and 8b showed that 8a has the shorter bond length and corresponds to the benzyl allyl ether that did not rearrange. The C–O distance of 8b is longer and so 8b corresponds to the case that did rearrange. In several other cases there was a correlation between the tendency to rearrangement and increasing bond length, which will be reported elsewhere.

For a further indication of a cationic intermediate, the rearrangement of allyllysilane 9 was tested. With this substrate the intermediate tertiary carbocation was expected to undergo a β-elimination to give allylic alcohol 10. However, aldehyde 2c was the only product isolated, probably as a result of rearrangement of 10 under the reaction conditions. The alternative sequence involving a hydride migration or elimination of a proton next to the oxygen is not likely, since the putative product β-TMS aldehyde should be stable under the reaction conditions. Proto-desilylation of 9 to give 1c followed by the rearrangement would also produce 2c. These details were not further investigated, however.

From the data presented here the following events explain the results. Coordination of the Lewis acid, or possibly a proton in zeolite β, renders the benzyl carbon electrophilic and susceptible to attack by the π-electrons of the double bond (11). Subsequent or concomitant 1,2-bond migration followed by loss of the acid species gives the product aldehyde 2. Although carbocation 12 was not proved to be an intermediate, such species are frequently depicted in the pinacol rearrangement and the Lewis acid induced epoxide-to-aldehyde or ketone-rerarrangements.

The alkoxybenzyl allyl ethers were synthesised by allylation of the appropriate allylic alcohols with different benzyl chloride derivatives except for allyllysilane 9 which was synthesized from the corresponding allylic alcohol and 4-methoxybenzyl-2,2,2-trichloroacetimidate. The deuteriated ether 4 was prepared by reduction of 2-(2-propyl)propanol with sodium borodeuteride followed by allylation of the resulting allylic alcohol with 4-methoxybenzyl chloride.

Experimental

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. NMR spectra were recorded at 300 MHz using CDCl$_3$ as an internal standard. Chromatographic separations were performed on Matrixx Amicon normal phase silica gel 60 (0.035–0.070 mm). TLC was performed on Merck precoated TLC plates (Silica gel 60 F-254, 0.25 mm). After elution the TLC plates were sprayed with a solution of p-methoxybenzaldehyde (2.6 ml), glacial acetic acid (1.1 ml), concentrated sulfuric acid (3.5 ml), and 95% ethanol (96 ml) and the compounds were visualized upon heating. Chemicals were reagent grade. Zeolite β was obtained from EKA Chemicals AB. THF was distilled under N$_2$ from sodium–benzophenone ketyl, and CH$_3$Cl was distilled from P$_2$O$_5$ prior to use.

1-Deuterio-2-(2-propyl)-2-propanol. NaBD$_4$ (155 mg, 3.70 mmol) was added in small portions to a solution of 2-(2-propyl)propanol (980 mg, 10.0 mmol) in methanol (5 ml) over 15 min at 0 °C. The mixture was stirred at room temperature for 30 min and the pH was then adjusted to 7 with 1 M HCl. Water (3 ml) was added and the resulting mixture was extracted with ether
Scheme 4. Mechanism of the rearrangement.

3-(4-Ethoxybenzylxoxy)-2-methyl-1-propene (1b). A solution of 2-methyl-2-propenol (289 mg, 4.00 mmol) in THF (2 ml) was slowly added to a suspension of NaH (176 mg, 4.40 mmol, 60% in mineral oil) in DMF (2 ml) at 0°C under argon and the mixture was stirred for 30 min. 4-Ethoxybenzyl chloride (700 mg, 4.10 mmol) in THF (2 ml) was then added and the mixture was stirred for 2 h. Water (0.5 ml) and ether (2 ml) were added and the mixture was washed with water (2 ml) and brine (2 ml), after which the organic extract was dried with MgSO₄. The solvent was removed under reduced pressure and the residue was chromatographed (heptane-EtOAc 8:2) to give 1b (590 mg, 72%). ¹H NMR (CDCl₃): δ 7.27, 6.88 (2 d, J 8.6 Hz, 2 H), 4.99, 4.92 (2 s, 1 H), 4.41 (s, 2 H), 4.03 (q, J 7.0 Hz, 2 H), 3.91 (s, 2 H), 1.77 (s, 2 H), 1.41 (t, J 7.0 Hz, 3 H). ¹³C NMR (CDCl₃): δ 158.5, 142.3, 130.4, 129.3, 114.3, 112.3, 73.8, 71.5, 63.4, 19.6, 14.9. IR (film cm⁻¹): 2960, 1615, 1520, 1240, 1170, 900, 820. Anal. HRMS Calcd. for C₁₃H₁₈O₂ (M⁺): 207.1385. Found 207.1382.

3-(4-Methoxybenzylxoxy)-2-methyl-1-propene (1c) was prepared as described above from 2-methyl-2-propenol (10.0 mmol) and 4-methoxybenzyl chloride. Chromatography (heptane-ethylacetate 8:2) gave 1c (1.87 g, 97%). ¹H NMR (CDCl₃): δ 7.28, 6.88 (2 d, J 8.7 Hz, 2 H), 5.02, 4.94 (2 s, 1 H), 4.43 (s, 2 H), 3.92 (s, 2 H), 3.81 (s, 3 H), 1.79 (s, 3 H). ¹³C NMR (CDCl₃): δ 159.1, 142.3, 130.5, 129.3, 113.8, 112.3, 73.8, 71.5, 55.3, 19.6. IR (film cm⁻¹): 2915, 1730, 1610, 1505, 1235, 1170, 1080, 820. Anal. HRMS Calcd. for C₁₄H₁₉O₂ (M⁺): 203.1228. Found 193.1227.

3-(4-Ethoxybenzylxoxy)-2-(2-propyl)-1-propene (1d) was prepared as described above from 2-(2-propyl)-2-propenol (4.00 mmol) and 4-ethoxybenzyl chloride. Chromatography (heptane-EtOAc 8:2) gave 1d (800 mg, 85%). ¹H NMR (CDCl₃): δ 7.27, 6.88 (2 d, J 8.7 Hz, 2 H), 5.03, 4.94 (2 s, 1 H), 4.40 (s, 2 H), 4.02 (q, J 7.0 Hz, 2 H), 3.95 (s, 2 H), 2.37 (m, 1 H), 1.40 (t, J 7.0 Hz, 3 H), 1.06 (d, J 6.8 Hz, 6 H). ¹³C NMR (CDCl₃): δ 158.5, 152.1, 130.4, 129.3, 114.3, 109.4, 72.1, 71.6, 63.4, 30.9, 21.7, 14.9. IR (film cm⁻¹): 2860, 1610, 1510, 1245, 1170, 820. Anal. HRMS Calcd. for C₁₅H₂₂O₂ (M⁺): 235.1698. Found 235.1699.

4-(4-Methoxyphenyl)-2-(2-propyl)butan-1-ol (2a) and 4-[3-(4-methoxybenzyl)-4-methoxyphenyl]-2-(2-propyl)butan-1-ol (3). A solution of 1a (220 mg, 1.00 mmol) in dichloromethane (2 ml) was added to zeolite β (100 mg, activated at 400°C for 3 h), under an argon atmosphere and then the resulting slurry was stirred for 8 h. When the reaction was complete the orange-red mixture was filtered through Celite. The Celite was washed with dichloromethane (2 × 5 ml) and the combined organic extracts were concentrated under reduced pressure. Chromatography of the residue (heptane-EtOAc 95:5) gave 2a (166 mg, 74%) together with variable amounts of 3 (0–25%).

2a: ¹H NMR (CDCl₃): δ 9.68 (s, 1 H), 7.13, 6.82 (2 d, J 8.7 Hz, 2 H), 3.79 (s, 3 H), 2.67–2.39 (m, 2 H), 2.16–1.89 (m, 3 H), 1.78–1.65 (m, 1 H). ¹³C NMR (CDCl₃): δ 205.7, 157.9, 133.7, 129.3, 113.8, 57.5, 55.3, 32.9, 28.3, 28.0, 20.2, 19.7. IR (film cm⁻¹): 2940, 1715, 1610, 1510, 1240, 1030, 820. Anal. HRMS Calcd. for C₁₅H₂₂O₂: 220.1463. Found 220.1464.

3: ¹H NMR (CDCl₃): δ 9.63 (s, 1 H) 7.14–6.75 (m, 7 H), 3.88 (s, 2 H), 3.79, 3.78 (2 s, 3 H), 2.61–2.33 (m, 2 H), 2.2–1.54 (m, 5 H), 0.96–0.91 (2 d, J 6.9 Hz, 3 H). ¹³C NMR (CDCl₃): δ 205.8, 157.7, 155.7, 133.4, 133.2, 130.3, 129.9, 129.8, 127.0, 113.7, 110.5, 57.5, 55.5, 55.2, 35.0, 33.1, 28.3, 27.9, 20.2, 19.7. IR (film cm⁻¹): 2920, 2915, 1715, 1500, 1240, 1160, 1030, 805. Anal. HRMS Calcd. for C₁₅H₂₂O₂: 340.2038. Found 340.2037.

4-(4-Ethoxyphenyl)-2-methylbutan-1-ol (2b). Zeolite β treatment of 1b (1.00 mmol) as above followed by chromatography (heptane-EtOAc 95:5) gave 2b (144 mg, 65%). ¹H NMR (CDCl₃): δ 9.63 (s, 1 H), 7.09, 6.82 (2 d, J 8.7 Hz, 2 H), 4.02 (q, J 7.0 Hz, 2 H), 2.66–2.56 (m, 2 H), 2.41–2.32 (m, 1 H), 2.10–1.96 (m, 1 H), 1.70–1.57 (m, 1 H), 1.41 (t, J 7.0 Hz, 3 H), 1.14 (d, J 7.0 Hz, 3 H). ¹³C NMR (CDCl₃): δ 205.0, 157.3, 133.2, 129.3, 114.4, 63.4, 45.6, 32.2, 32.2, 14.9, 13.3. IR (film cm⁻¹): 2920, 2915, 1720, 1505, 1240, 1040, 820. Anal. HRMS Calcd. for C₁₈H₂₄O₇: 206.1307. Found 206.1310.

4-(4-Methoxyphenyl)-2-methylbutan-1-ol (2c). Route 1. Compound 1c (192 mg, 1.00 mmol) was treated with zeolite β as described above to give 2c (160 mg, 83%).
after chromatography (heptane–EtOAc 95:5). 1H NMR (CDCl3): δ 8.96 (s, 1 H), 7.13, 6.84 (2 d, J 8.7 Hz, 2 H), 3.79 (s, 3 H), 2.66–2.57 (m, 2 H), 2.43–2.31 (m, 1 H), 2.30–1.97 (m, 1 H), 1.70–1.57 (m, 1 H), 1.15 (d, J 7.0 Hz, 3 H). 13C NMR (CDCl3): δ 204.9, 158.0, 133.4, 129.3, 113.9, 55.3, 45.6, 32.4, 32.1, 13.4. IR (film) cm⁻¹: 2910, 1715, 1505, 1235, 1035, 820. Anal. HRMS Calcd. for C14H12O2: 212.1526. Found 221.1529.

3-(4-Methoxybenzylxozy)-2,3-dimethyl-1-propene (5) was prepared from 3-methyl-3-butene-2-ol (10.0 mmol) and 4-methoxybenzyl chloride as described for 1b. Chromatography (heptane–EtOAc 95:5) gave 5 (1.17 g, 58%). 1H NMR (CDCl3): δ 7.28, 6.89 (2 d, J 8.7 Hz, 2 H), 4.87 (s, 2 H), 4.42 (d, J 11.4 Hz, 1 H), 4.21 (d, J 11.4 Hz, 1 H), 3.86 (q, J 6.5 Hz, 1 H), 3.81 (s, 1 H), 1.74 (s, 3 H), 1.28 (d, J 6.5 Hz, 3 H). 13C NMR (CDCl3): δ 159.0, 146.2, 130.9, 129.3, 113.8, 112.4, 78.4, 69.5, 55.3, 20.3, 16.9. IR (film) cm⁻¹: 1610, 1590, 1510, 1305, 1250, 820. Anal. HRMS Calcd. for C13H10O2 (M+H): 207.1385. Found 207.1385.

5-(4-Methoxybenzyl)-3-methyl-2-pentane (6) and 4-(4-methoxybenzyl)-2,2-dimethylbutanal (7). Compound 5 (1.00 mmol) was treated with zeolite β as described. Chromatography of the crude product (heptane–EtOAc 8:2) gave 6 (99 mg, 45%) and 7 (48 mg, 23%).

6: 1H NMR (CDCl3): δ 7.10 (d, J 8.7 Hz, 2 H), 6.84 (d, J 8.7 Hz, 2 H), 3.80 (s, 3 H), 2.53 (m, 3 H), 2.13 (s, 3 H), 1.99 (m, 1 H), 1.62 (m, 1 H), 1.14 (d, J 7.0 Hz, 3 H). 13C NMR (CDCl3): δ 212.6, 157.9, 133.7, 129.3, 113.8, 55.3, 46.4, 34.7, 32.5, 28.1, 16.3. IR (film) cm⁻¹: 1720, 1620, 1590, 1525, 830. Anal. HRMS Calcd. for C13H12O2: 206.1307. Found 206.1311.

7: 1H NMR (CDCl3): δ 9.98 (s, 1 H), 7.09 (d, J 8.6 Hz, 2 H), 6.83 (d, J 8.6 Hz, 2 H), 3.79 (s, 3 H), 2.48 (m, 2 H), 2.16 (m, 2 H), 1.14 (s, 6 H). 13C NMR (CDCl3): δ 206.0, 157.9, 133.9, 129.2, 113.9, 55.3, 45.9, 39.6, 29.9, 21.4. IR (film) cm⁻¹: 2910, 1730, 1605, 1580, 1510, 1300, 1240, 820. Anal. HRMS Calcd. for C14H11O2 (M+H): 207.1385. Found 207.1393.

3-(4-Methoxybenzylxozy)-2-(trimethylsilylmethyl)-1-propene (9). 4-Methoxybenzyl-2,2-trichloroacetimidate, prepared according to the literature10 from trichloroacetonitrile (317 ml, 3.13 mmol) and 4-methoxybenzyl alcohol (433 mg, 3.13 mmol), was dissolved in cyclohexane (5 ml). A solution of 2-(trimethylsilylmethyl)-2-propan-1-ol (purchased from Aldrich, 288 mg, 2.00 mmol) in dichloromethane (2.5 ml) was then added. The resulting solution was cooled to 0°C and treated with BF3·OEt2 (5 µL). The reaction mixture was warmed to room temperature and stirred overnight. The white precipitate was then removed by filtration through Celite and the residue was washed with a 1:2 mixture of dichloromethane and cyclohexane (2 x 5 ml). The filtrate was washed with saturated aqueous NaHCO3 (5 ml), dried over MgSO4 and concentrated under reduced pressure. Chromatography of the residue (heptane–EtOAc 8:2) gave 9 (295 mg, 56%). 1H NMR (CDCl3): δ 7.28 (d, J 8.7 Hz, 2 H), 6.88 (d, J 8.7 Hz, 2 H), 4.42 (s, 2 H), 3.84 (s, 2 H), 3.78 (s, 3 H), 0.15 (s, 2 H), 0.03 (s, 9 H). 13C NMR (CDCl3): δ 159.1, 143.9,
129.3, 129.2, 113.7, 109.2, 73.9, 71.5, 55.3, −0.4, −1.4. IR (film) cm⁻¹: 2950, 1610, 1510, 840. Anal. HRMS Calcd. for C₁₃H₂₄O₂Si: 264.1545. Found 264.1546.

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References

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