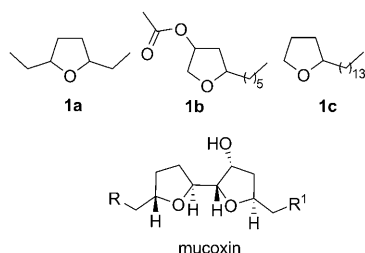


Zeolites Efficiently Promote the Cyclization of Nonactivated Unsaturated Alcohols

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Tetrahydrofurans are an important class of five-membered oxygen heterocycles often present in a great variety of natural products^[1] and as synthetic compounds exhibit biological activity.^[2] Among their industrial applications they are widely used in cosmetic formulations, perfumes and flavors.^[3] As examples, mucoxin is a natural product with high potential as specific antitumor agent against breast carcinoma.^[4] Furans **1a**, **1b** and **1c** are known as flavors^[5] and show insecticidal activity^[6] (Scheme 1).



Scheme 1. Tetrahydrofurans with biological activity.

The simplest synthetic strategies to prepare cyclic ethers consists of the intramolecular cyclization of suitable unsaturated alcohols or by dehydration of 1,4-diols.^[7] Both reactions take place in the presence of Brønsted acids often used in excess amounts. An alternative to the ring closure of unsaturated alcohols is the intramolecular oximercuration

recently applied to the synthesis of muxocin.^[4] In the Green Chemistry context, Coulombel et al.^[8] recently reviewed the use of trifluoromethane sulfonates, as Lewis superacids and environmental-friendly catalysts, for intramolecular cyclization of alcohols of nonactivated olefins, for example, TfOH, Al(TfO)₃ and Sn(TfO)₄. However, only a few examples of heterogeneous catalysts such as heteropolyacids in ionic liquids as solvents,^[9] metal(IV) phosphates^[10] and Amberlyst H-15^[11] have been reported up-to-now, not including zeolites as robust catalysts with modulable acidity, useful for production of Fine Chemicals.^[12] TS-1 has been used for the preparation of furans by epoxidation/cyclization of unsaturated alcohols in the presence of H₂O₂.^[13]

In this communication, we report on the intramolecular cyclization of *cis*-4-decenol (**2**), selected as model unsaturated alcohol, efficiently catalyzed by several zeolites. Zeolites offer the possibility of tailoring the appropriate size and connectivity of their pores and adjusting the concentration and strength of their active acid sites.^[14] Based on our experience, we selected H-BEA, H-MFI, H-FAU, and H-STF as catalysts but not H-MOR, which was completely inactive. Commercial clay, montmorillonite K-10, was used for comparison with zeolites in this study.

Table 1 shows textural and chemical parameters including type and concentrations of acid sites of zeolites. These zeolites were tested in the cyclization of *cis*-4-decenol (**2**) as shown in Scheme 2.

The cyclization of **2** in nitroethane as solvent at 358 K was catalyzed by the zeolites of our choice, affording compound **3** with yields in the range of 78–95 % (Table 2). In general, zeolites with 3D and 1D channel structure promote efficiently the cyclization of hydroxyl group to nonactivated C=C double bond yielding compound **3** with excellent yields. Furthermore, the reaction takes place with almost total selectivity, yield of pyran **4** being lower than 5 % in all cases. The ring closure provides the corresponding five-membered ring following the Markovnikov's rule, as expected. In a blank experiment it was shown that no cyclization of **2** was observed in the absence of catalyst.

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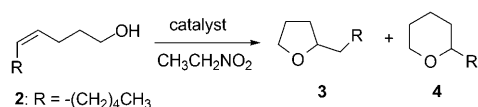
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Table 1. Structural and textural parameters of zeolites under study.

Catalyst	Origin	Channel structure	Si/Al ratio ^[a]	$S_{\text{BET}}^{\text{[b]}}$ [m ² g ⁻¹]	Channel diameter [nm]	$c_{\text{LC}}^{\text{[c]}}$ [mmol g ⁻¹]	$c_{\text{BC}}^{\text{[d]}}$ [mmol g ⁻¹]	Coke ^[e] [wt %]
H-BEA	Zeolyst	3D	12.5	674	0.64 × 0.70 0.55 × 0.55	0.40	0.32	–
H-MFI	Zeolyst	3D	15	395	0.51 × 0.56	0.13	0.25	1.29
H-FAU	Zeolyst	3D	15	769	0.74	0.18	0.12	2.67
H-STF	Chevron	1D	38.5	475	0.54 × 0.57	0.10	0.23	–
H-MOR	Zeolyst	2D	10	393	0.65 × 0.70 0.26 × 0.57	0.25	0.27	5.64

[a] Determined by ICP-MS. [b] S_{BET} , BET surface area. [c] c_{LC} = concentration of Lewis acid sites. [d] c_{BC} = concentration of Brønsted acid sites, both of them determined by FTIR using pyridine as probe molecule.^[15b] [e] Determined by a combustion analyzer EA 2000 (Analytikjena).



Scheme 2. Intramolecular cyclization of *cis*-4-decenol (**2**).

Table 2. Conversions for the cyclization of *cis*-4-decenol (**2**) over zeolites and montmorillonite K-10 at 358 K.

Catalyst	<i>t</i> [h]	Yield 3 [%]
H-BEA	1.5	95
H-MFI	2	90
H-FAU	4	89
H-STF	4	78
montmorillonite K-10	1.5	65

With these results in mind, we confirmed that the cyclization proceeds under milder reaction conditions than those reported for Al(TfO)₃ (374 K in nitromethane) affording compound **3** with quantitative yield during 90 min when using H-BEA. It is important to note that in none cases the corresponding dehydration product from **2** was isolated. H-BEA resulted in the most active catalyst. Figure 1 depicts the kinetic profiles for the reaction in each case. As shown in Figure 1A, the yield of compound **3** over H-MFI was slightly lower than for H-BEA at the shortest reaction times while this trend was inverted from the first 30 min of the reaction. H-FAU and H-STF were less efficient catalysts as compared with H-BEA and H-MFI. After 60 or 90 min, it can be clearly seen (Figure 1A) that the conversion order is H-BEA > H-MFI > H-FAU > H-STF. No activity of H-MOR in cyclization of the alcohol **2**, even at 373 K, was due to the highest acid strength of H-MOR and only one-type of accessible channels in comparison with other zeolite catalysts inducing fast deactivation due to coke formation (cf. Table 1 for other zeolites). Cyclization of **2** catalyzed by montmorillonite K-10, under the same experimental conditions, yielded furan **3** in 65 % during 90 min. It was observed a slight evolution of the cyclization reaction from the shortest reaction times. Thus, compound **3** was obtained in 58 % of yield in only 15 min while reaction times longer than 90 min did not produce increased yield of **3**. The results suggest that although the cyclization catalyzed by montmoril-

lonite K-10 takes place more rapidly than using zeolites for short reaction times, this clay is inactivated with increasing reaction time. This circumstance was not observed when using H-BEA and H-MFI zeolites as catalysts yielding the furan **3** in quantitative yield after 2 h.

Concentration of Lewis or Brønsted acid sites differs for zeolites under study (Table 1)

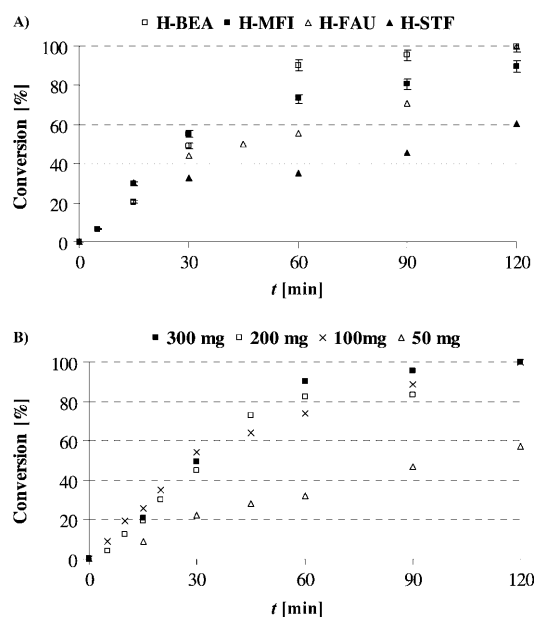


Figure 1. Kinetic profiles for the cyclization of *cis*-4-decenol (**2**) catalyzed by A) H-BEA (12.5), H-MFI (15), H-FAU (15) and H-STF (38.5) at 358 K (catalyst amount 300 mg). B) H-BEA (12.5). Influence of the catalyst amount.

but both of them could contribute to their catalytic activity in the cyclization of **2** as reported.^[8,11] In more detail, H-BEA and H-MFI exhibited the highest conversions; H-BEA being the most active zeolite showing the highest concentration of Lewis acid sites. This feature strongly suggests that the cyclization is predominantly promoted by the Lewis acid sites in zeolites. It is in accordance with the lower catalytic performance observed for H-FAU and H-STF. Although H-STF exhibited the lowest conversion of *cis*-4-decenol, this zeolite was rather active considering its 1D 10-ring channel system and low concentration of Lewis acid sites. This fact could be attributed to its special channel morphology with 18-ring STF cages as described for *p*-xylene alkylation.^[15]

Brønsted acid sites may also contribute to the catalytic activity of zeolites; thus, H-MFI with predominantly Brønsted acid sites is highly active. In contrast, having H-MOR as inactive catalyst in this cyclization reaction, one can assume that strong Brønsted acid sites are not sufficient to catalyze

this reaction even though the size of H-MOR channels is larger than of H-MFI or H-STF.

Despite different channel sizes and dimensionality, zeolites H-BEA, H-MFI, H-FAU and H-STF catalyze cyclization of unsaturated alcohols with high conversions. It could be mostly due to the fact that 2-hexyltetrahydrofuran can fit into the channel structure of 10-ring zeolites without any severe steric restrictions. Simultaneously, size of the channels prevents the formation of more bulky products, which could block the channel system and decrease the rate of the reaction.

In addition, Figure 1B depicts the influence of the catalyst amount used in the cyclization reaction. This study was performed at 358 K when using the most active catalyst, H-BEA. As shown, the increased catalyst amount from 100 to 300 mg, in all cases, produced slightly increased conversions clearly detected after 60 or 90 min of the reaction becoming quantitative within less than 2 h. Lower amount of the catalyst (50 mg) yielded the compound **3** in 60% after 2 h.

Remarkably, the cyclization takes also place at lower reaction temperatures; as example, the yield of **3**, at 337 K were 92% (6 h) and 99% (24 h) catalyzed by H-BEA and H-MFI, respectively. In both cases the different catalytic behavior was notably observed maintaining the activity order. Obviously, when operating at higher temperatures the conversions were considerably increased and the reaction times reduced (Figure 2). At the highest temperatures no significant differences were found between H-BEA and H-MFI. However, yields of **3** when catalyzed by zeolite H-BEA at 337 or 313 K were 20% while almost negligible conversion was obtained over H-MFI. The differences in the conversion over zeolites H-BEA and H-MFI at low reaction temperatures can be explained either in terms of lower activation barrier for Lewis acid catalyzed reaction or by a slower diffusivity of reactants/products in 10-ring channel system of zeolite H-MFI.

Recyclability of studied zeolites should be stressed; particularly H-BEA can be reused for the preparation of compound **3** while maintaining its catalytic activity during at least three consecutive cycles.

In summary, in this communication we report on efficient zeolite catalysts to synthesize 2-hexyltetrahydrofuran (**3**) with almost total conversion and excellent selectivity. The yield of by-product pyran **4** was in all reactions lower than 5%. H-BEA and H-MFI zeolites were the best catalysts for the cyclization of *cis*-4-decenol (**2**). Probably, the reaction is catalyzed by both Brønsted and Lewis acid sites in these zeolites. Pore size and dimensionality in zeolites under study influence their catalytic activity. In the case of H-STF, lower conversion values to **3** are probably due to its special cage structure. Zeolites reported here were found reusable, effective and selective even more than the other heterogeneous catalysts reported earlier. This methodology finds its application in the synthesis of oxygen heterocycles with industrial importance.^[6,16]

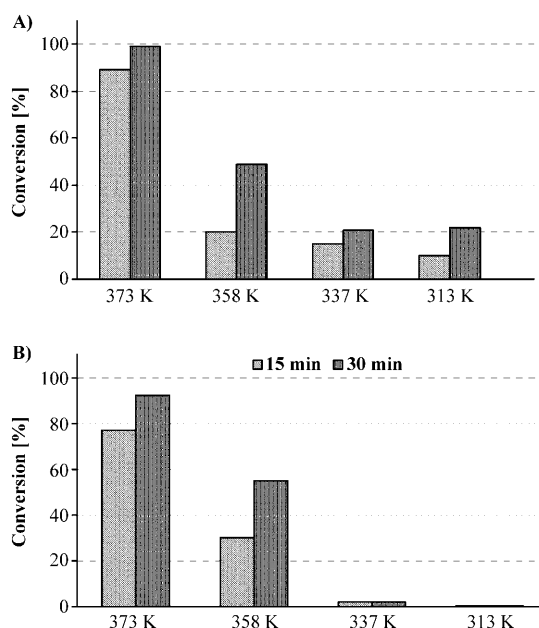


Figure 2. Temperature effect in the cyclization of *cis*-4-decenol (**2**) catalyzed by A) H-BEA and B) H-MFI.

Experimental Section

The surface areas and void volumes of the zeolites under study were determined from adsorption isotherms of nitrogen at 77 K applying the BET method using a static volumetric apparatus Micromeritics, ASAP 2020 (Table 1). Type and concentration of acid sites was determined by FTIR using pyridine as probe molecule with a FTIR Nicolet 6700.

NMR spectra were recorded with a Varian Mercury 300 spectrometer. ¹H chemical shifts (δ) in CDCl₃ are given from internal tetramethylsilane. MS spectra were recorded with a GS/MS ThermoElectron. The reactions were followed by GC, Agilent 6850 using mesitylene as internal standard. All the reagents and solvents were obtained from Aldrich.

Typical procedure: To a solution of *cis*-4-decenol (**2**) (2 mmol) in nitroethane (4 mL), at a given reaction temperature, the catalyst (300 mg) was added and the reaction mixture was stirred during the time shown in Table 2. Catalysts were activated at 723 K using a ramp of 283 K min⁻¹ during 90 min.

For the reutilization studies, catalyst was filtered from the reaction crude, washed with CH₂Cl₂ for three times and dried at 333 K during 1 h.

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