

Zeolites for the Production of Fine Chemicals: Synthesis of the Fructose Frangency

M. J. Climent,^{*} A. Corma,^{*,1} A. Velty,^{*} and M. Susarte[†]

^{*}Instituto de Tecnología Química (UPV-CSIC), Universidad Politécnica de Valencia, Avda. de los Naranjos s/n, 46022 Valencia, Spain; and [†]ACEDESA, Carretera de Mazarrón, Km. 1.8, 30120 El Palmar, Murcia, Spain

Received May 4, 2000; revised August 10, 2000; accepted August 24, 2000

Fructose (ethyl 3,3-ethylenedioxybutyrate), a flavouring material, has been obtained by acetalization of ethyl acetoacetate with ethylene glycol using different microporous and mesoporous aluminosilicates as catalysts. Tridirectional zeolites (Y and Beta) are very effective and selective for carrying out this reaction. It has been found that a higher concentration of acid sites does not guarantee a better catalytic performance and the hydrophobic–hydrophilic properties of the material play a determinant role in this reaction due to the different polarity of the reactants. The coupling between the concentration of active sites and the adequate adsorption properties is achieved for Beta zeolites with a Si/Al ratio between 25 and 50. Optimisation of reaction conditions and the appropriate catalyst allow us to obtain fructose with conversions and selectivities close to 100%. © 2000 Academic Press

Key Words: fructose; zeolites; acetalization.

INTRODUCTION

The acetalization reaction is sometimes necessary to protect carbonyl groups in the presence of other functional groups when processing multifunctional organic molecules (1). Besides the interest in acetals as protecting groups, many of them have found direct applications as fragrances, in cosmetics, as food and beverage additives, in pharmaceuticals, in detergents, and in lacquer industries (2).

The most general method for the synthesis of acetals involves the reaction of carbonyl compounds with an alcohol or an orthoester in the presence of acid catalysts. A number of acetalization procedures include the use of protic acids, Lewis acids (zinc chloride) (3), alumina (4), montmorillonite (5), zeolites (6), and mesoporous aluminosilicates (7) and have had variable success. Acetalization of aldehydes can be performed in the presence of weak acids, while ketones generally need stronger conditions such as sulphuric, hydrochloric, or *p*-toluenesulfonic acids and larger amounts of catalyst than when reacting aldehydes. However, many

of the methods mentioned above present limitations due to the use of expensive reagents, the tedious work-up procedure, and the necessity of neutralisation (with the exception of solid catalysts) of the strong acid media producing undesired wastes. Consequently, there is a genuine need for an efficient heterogeneous catalytic procedure for these reactions. In this sense zeolites appear to be promising catalysts with the obvious advantages of easy separation, controlled acidity, shape selectivity, and reusability.

Preparation of fructose (ethyl 3,3-ethylenedioxybutyrate) (8), a flavouring material with apple scent, involves the acetalization of ethyl acetoacetate with ethylene glycol. This process is catalysed by strong acids such as *p*-toluenesulfonic acid. It is known that in homogeneous media a strong acid and the water formed during the acetalization can cause the hydrolysis of the ester, producing the corresponding 3,3-ethylenedioxy-butanoic acid. The formation of this product not only reduces the yield of fructose but also, when it is present in amounts $\geq 3\%$, can alter the organoleptic characteristic of the final product. Besides the formation of 3,3-ethylenedioxy-butanoic acid, the use of strong acid catalysts in liquid media presents the problem derived from the hydrolysis of the ethyl acetoacetate that results in a yield of fructose below 75%.

In the work described in this paper we have studied the possibilities of zeolites as catalysts for the synthesis of fructose from ethyl acetoacetate and ethylene glycol. It will be shown that by controlling the acidity, textural, and hydrophobic–hydrophilic properties of the zeolite, it is possible to design a successful catalyst that, when coupled with an adequate process design, maximises conversion and selectivity to fructose (9).

EXPERIMENTAL

Catalysts

Beta zeolite (β -1) and ZSM-5 were supplied by PQ Corp., in the acidic and in the ammonium form, respectively. The ZSM-5 sample was calcined at 823 K for 3 h to obtain the

¹ To whom correspondence should be addressed. Fax: 34 96 387 78 09. E-mail: acorma@itq.upv.es.

acid form. Zeolite Beta samples β -2, β -3, β -4, and β -5 were synthesised in our laboratory. The acid form of mordenite (MOR) was obtained by calcination of a commercial Conteka sample, followed by an acidic treatment to produce a sample with a final Si/Al ratio of 10.

The USY samples were obtained from PQ Zeolites B.V., and they were submitted to NH_4^+ exchange followed by calcination at 773 K for 3 h.

One sample of MCM-41 (pore diameter 3.5 nm and framework Si/Al = 15) was synthesised following the procedure given in Ref. (10) using hexadecyltrimethylammonium (Aldrich) cation as template, and pseudoboehmite (Capatal B, Vista) and Aerosil (Degussa) as the aluminum and silicon source, respectively. The sample was calcined in N_2 for 1 h and in air for 6 h at 813 K.

In order to measure the acidity of the samples, the infrared spectra were recorded at room temperature in a Nicolet 710 FTIR using self-supported wafers of $10 \text{ mg} \cdot \text{cm}^{-2}$. The calcined samples were outgased overnight at 673 K and 10^{-3} Pa dynamic vacuum; pyridine was then admitted into the cell at room temperature. After saturation, the samples were outgased at 523 K for 1 h under vacuum and cooled to room temperature, and the spectra were recorded.

Ethyl acetoacetate, ethylene glycol, and toluene (purity $\geq 99\%$) were purchased from Aldrich and were used without further purification.

Reaction Procedure

An ethyl acetoacetate (12 mmol) and ethylene glycol (24 mmol) solution was prepared and added onto the catalyst, which was previously activated at 353 K under vacuum (1 Torr) for 2 h in a batch reactor. The resultant suspension was heated to a defined temperature in a silicone oil bath with an automatic temperature control system with magnetically stirring.

In another series of experiments the same methodology was followed, but a defined amount of toluene (solvent) was added and a Dean-Stark instrument was adapted to remove the water formed *in situ*.

Finally, a third reaction procedure was carried out in the absence of toluene under vacuum (8 Torr) in order to distill the water formed during the reaction.

Samples were taken at regular time periods and analysed by gas chromatography (GC) using a FID detector and a capillary column (Trocar TR-Wax, $15 \text{ m} \times 0.32 \text{ mm} \times 0.25 \mu\text{m}$). At the end of the reaction the catalyst was filtered and washed with dichloromethane. The organic phase was washed with water in order to remove the excess ethylene glycol and dried over anhydrous sodium sulphate. The samples with solvent were previously distilled under reduced pressure. Finally, the products obtained were characterised by ^1H NMR (400 MHz Varian VXR-400S). After

reaction, the catalyst was submitted to continuous solid-liquid extractions with dichloromethane in a micro-Soxhlet apparatus. After removal of the solvent the residue was also weighed and analysed by GC-MS and ^1H NMR spectroscopy. In all the experiments the recovered material was greater than 95% (wt/wt). The reproducibility of the experiments has been measured by repeating three times the same experiment with three charges of catalyst (β -1). Thus the medium standard deviation calculated for the yield of fructose at each time of reaction was equal to 2.6, i.e., the relative error was equal to 4%.

RESULTS AND DISCUSSION

In order to determine the products formed and establish the reaction network, preparation of fructose **1** by acetalization of ethyl acetoacetate with ethylene glycol was carried out in the presence of 7.4% wt of zeolite β -1, with a volume ratio toluene/ethyl acetoacetate of 26.6 at 419 K. After 30 min reaction time a conversion of 95% with yields of 93% and 2% of fructose (**1**) and 3,3-ethylenedioxy-butanoic acid (**2**) was obtained. No other products were obtained, indicating that under the above reaction conditions the hydrolysis of ethyl acetoacetate and/or the transacetalization reactions do not occur.

When the yields of the different products were plotted versus the reaction time (Fig. 1), fructose appeared as the primary product, while the acid **2** appeared as a secondary product. According to the general reaction mechanism accepted for acetalization (Scheme 1), the first step in the

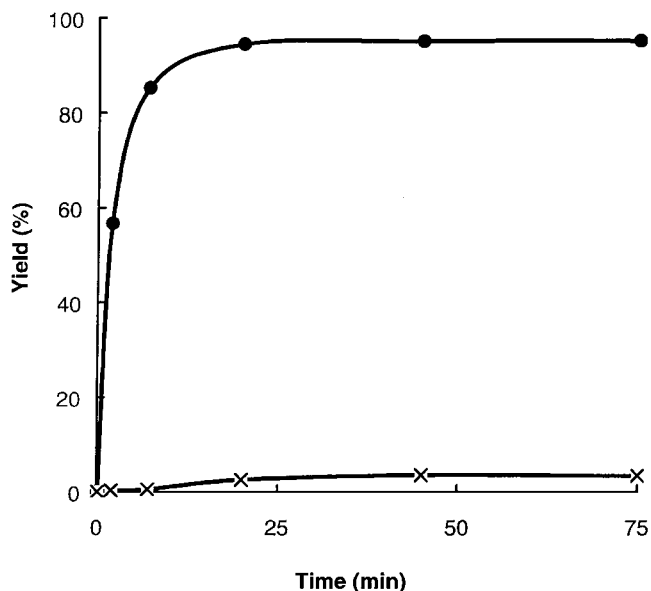


FIG. 1. Yield (%) of fructose **1** (●) and the corresponding ketal acid **2** (×) versus the reaction time; catalyst, β -1; volume ratio toluene/ethyl acetoacetate = 26.6; $T = 419 \text{ K}$.

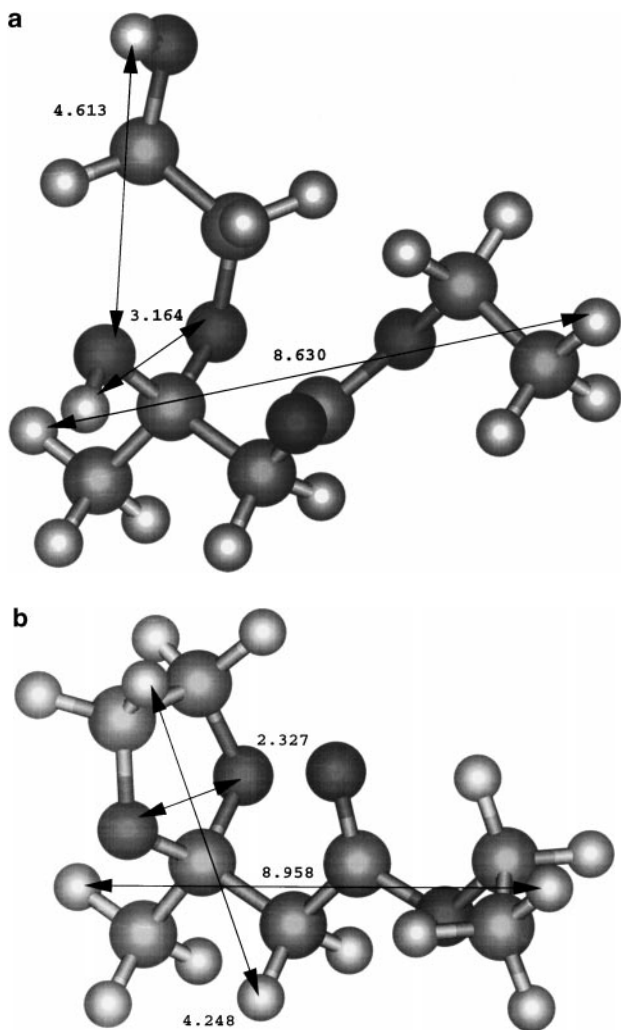


FIG. 2. Dimensions (Å) calculated with the Cerius 2 Visualizer Program: (a) hemiacetal and (b) fructose.

of a given site will increase when there is a decrease in the number of aluminums in next-nearest-neighbour positions (NNN) of the aluminum atom which supports the acid site (13). A completely isolated aluminum tetrahedron will have zero NNN and will support the strongest type of framework Brønsted site. If a random distribution of aluminum in the zeolite framework is considered, one can expect in the case of Y and Beta zeolites to have all sites isolated when the framework Si/Al ratio is ≥ 9 . Then, if the synthesis of fructose could be catalysed by Brønsted sites of weak medium and strong acidities, a direct correlation between activity and framework Al or pyridine remaining adsorbed at 523 K should exist, regardless of whether zeolite Y or Beta is used as catalyst. On the other hand, if only the strongest acid sites present in the zeolites, i.e., those associated with 0 NNN, were active, then a maximum in activity for samples with a Si/Al ratio of ~ 9 should be observed.

When the second-order kinetic rate constant for the formation of fructose is plotted versus the Si/Al ratio of Y and

TABLE 2

Main Characteristics of Beta and USY Zeolite Catalysts

Catalysts	Si/Al	Brønsted acidity ^a		Crystallite size (μm)	Area (m^2/g)
		523 K	623 K		
β -1	13	42.4	22.4	0.15	666
β -2	15	33	15	0.50	518
β -3	25	36	28	0.25	503
β -4	50	19	8	0.50	452
β -5	100	11	10	0.20	463
USY-1	5	110	58	0.4–0.6	750
USY-2	13	80	32	0.4–0.6	730
USY-3	20	46	18	0.4–0.6	750
USY-4	40	39	15	0.4–0.6	720

^a Brønsted acidity (μmol of Py/g of catalyst) of the catalyst at 523 and 623 K.

Beta zeolites (Fig. 4), it can be seen that not only is there not a direct correlation between activity and total Al content or pyridine remaining adsorbed at 523 K (Table 2), but neither was a maximum in activity found at a Si/Al ratio close to 9. The results from Fig. 4 show that a maximum in

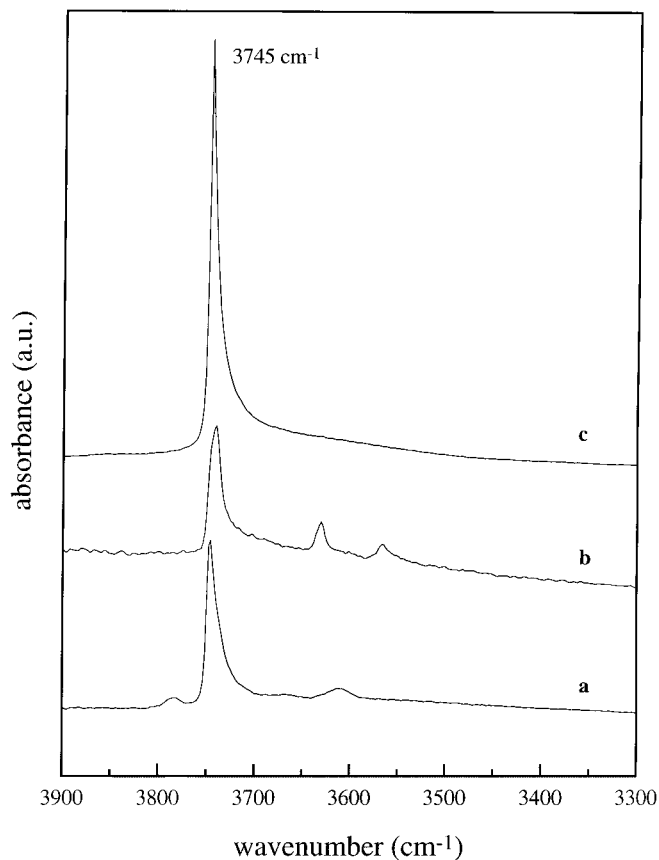


FIG. 3. IR spectra in the OH stretching region for Beta (a) and Y (b) zeolites and MCM-41 (c). The band at 3745 cm^{-1} corresponds to external silanols (sample treatment, 773 K and vacuum).

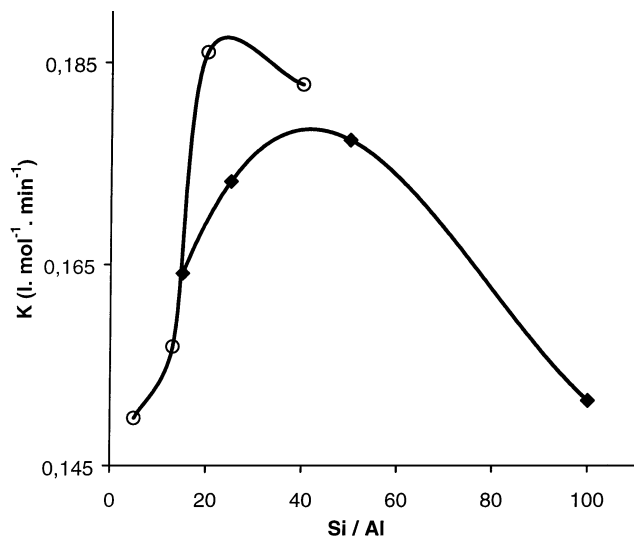


FIG. 4. Second-order kinetic rate constant (K) of USY (○) and H β (◆) zeolites with different Si/Al ratios at 1 h, when the reaction was carried out at 419 K; catalyst amount, 7.4% wt/wt (of ethyl acetoacetate amount); volume ratio toluene/ethyl acetoacetate = 26.6.

activity was found at Si/Al ratios of ~ 20 and 25–50 for Y and Beta zeolite, respectively.

It becomes clear at this point that factors other than acidity are playing an important role during the synthesis of fructose with zeolite catalysts. We have considered that for the synthesis of fructose a highly hydrophilic reactant (ethylene glycol) and a less hydrophilic reactant (ethyl acetoacetate) have to diffuse through the pores and adsorb on the acid sites of the zeolite. Thus, in the case of hydrophilic zeolites, the ethylene glycol will be preferentially adsorbed and the reaction will become limited by diffusion and adsorption of ethyl acetoacetate. In other words, it appears that besides the concentration of the adequate Brønsted acid sites, the adsorption properties of the zeolite and more specifically their hydrophobicity–hydrophilicity should play an important role in the activity and selectivity of the zeolites. In order to study the influence of the hydrophobicity of the zeolites on the synthesis of fructose, the catalytic activity of the commercial Beta zeolite (β -1) was then compared with that obtained with a more hydrophobic Beta zeolite synthesised in fluoride media (β -2) and so which does not have any internal silanols (14). The second-order kinetic rate constant obtained was similar in both cases, 0.168 and $0.167 \text{ l} \cdot \text{mol}^{-1} \cdot \text{min}^{-1}$ for β -1 and β -2, respectively, despite the fact that the total as well as the strong acidity measured by pyridine desorption at 523 and 623 K respectively is clearly higher in the more hydrophilic β -1 sample (Table 2).

It is known that upon increasing the framework Si/Al ratio of zeolites, besides the changes in acidity explained above, the hydrophobicity of the material increases. Therefore, since a compromise between the number of active sites

and the hydrophobicity of the zeolite has to be reached for the synthesis of fructose, one should expect a maximum in the curve activity versus framework Si/Al ratio, and this maximum should be shifted toward Si/Al ratios higher than 9. This is indeed observed in Fig. 4, where the maximum activity is obtained for USY-3 and β -4 with Si/Al ratios of ~ 20 and ~ 25 –50, respectively, even if their acidities are much lower than those of samples USY-1 and USY-2 or β -1, β -2, and β -3 (Table 2).

Optimisation of the Reaction Process

During the acetalization reaction, water is formed with the corresponding negative effect on the yield of fructose due to the shift of the thermodynamic equilibrium toward the reactants, and to the hydrolysis of fructose to give 3,3-ethylenedioxy-butanoic acid. It appears then mandatory to remove the water formed in the reaction media in order to achieve high yield and selectivity of the desired product. The simplest operational method to achieve this would involve the use of highly hydrophobic zeolites as catalysts, with the hope that water will be very rapidly desorbed from the catalyst and its concentration in the pores would be much lower than that in the reaction media. If this occurs, the equilibrium would be shifted toward the formation of fructose, while avoiding its hydrolysis. The reaction was carried out using β -1 and β -3 as catalysts, ethylene glycol and ethyl acetoacetate in a molar ratio of 2 : 1, 333 K reaction temperature, and 5% wt/wt of catalyst in the absence of solvent, and the results are given in Fig. 5. Thus it is interesting to notice that the more hydrophobic β -3 gives a better conversion than the less hydrophobic β -1 (Fig. 5).

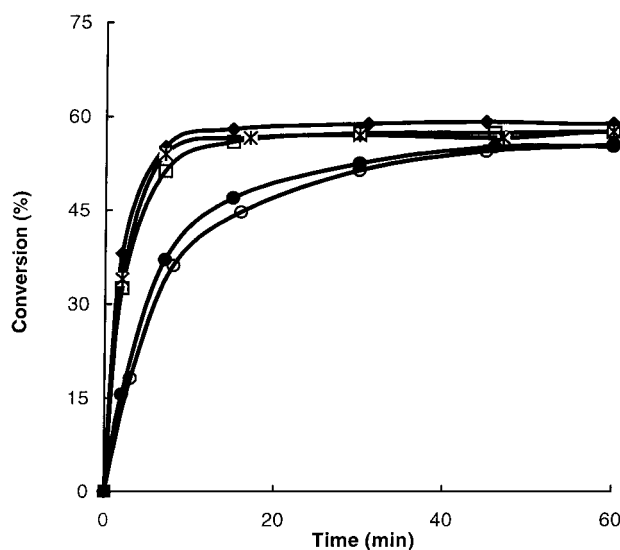


FIG. 5. Ethyl acetoacetate conversion to **1** versus reaction time in the presence of β -1 (○), β -2 (●), β -3 (◆), β -4 (*), and β -5 (□). Reaction conditions: $T = 333 \text{ K}$; catalyst amount, 5% wt/wt (of ethyl acetoacetate amount); $P = 760 \text{ Torr}$.

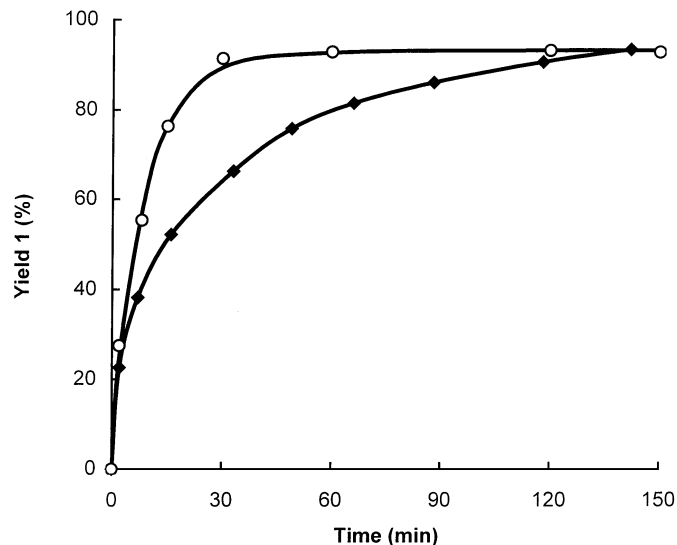


FIG. 6. Yield of **1** versus reaction time in the presence of β -3 zeolite: (○) experiment performed in toluene media (toluene/ethyl acetoacetate = 26.6), 7.4% wt/wt (with respect to ethyl acetoacetate), 419 K; (◆) experiment performed in vacuum ($P = 8$ Torr), 5% wt/wt (with respect to ethyl acetoacetate), $T = 313$ K.

Notice, however, that even with the most hydrophobic zeolites conversion does not exceed 60%. Better results are obtained when the water formed in the reaction is removed by azeotropic distillation using toluene, in this case the total conversion being 97% with 99% selectivity to fructose (Fig. 6).

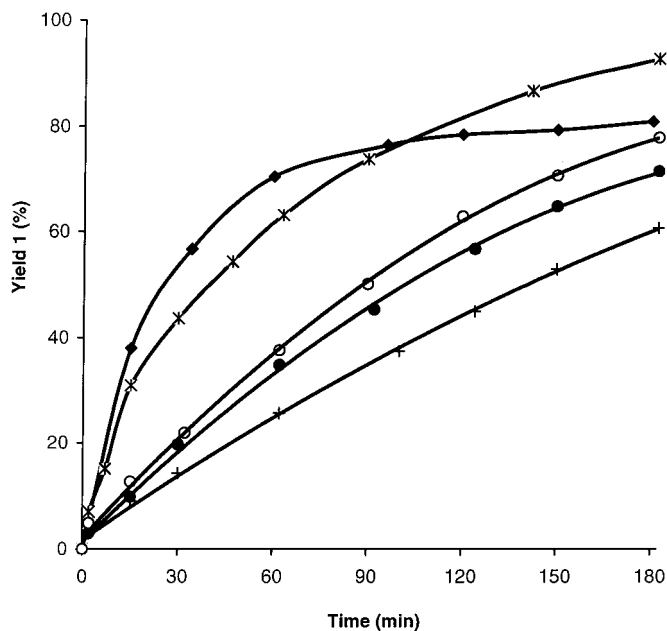


FIG. 7. Study of reuse of the catalyst β -1: first use (*); first recycle (○); second recycle (+); third recycle after extraction with a Soxhlet apparatus (●); fourth recycle after calcination (◆).

There is another possibility to remove the water formed in the reaction that does not require the use of toluene. This is to carry out the reaction under reduced pressure (8 Torr) in order to take advantage of the different boiling points of reactants and water which would be easily to distill. The results obtained show (Fig. 6) that by this procedure it is also possible to obtain conversions and yields close to 100%.

Catalyst Deactivation and Regeneration

During the acetalization reaction the products formed remain strongly adsorbed on the zeolite and/or they can react further to give larger molecules that may block the diffusion of reactants into the pores as has been observed in our case. So, the amount of remaining adsorbed organic in the zeolite after the first use (reaction at 60°C for 3 h) (Fig. 7) was determined by thermogravimetric analysis (TG, Mettler Toledo Star^e System) to be ~3% (wt/wt) of the catalyst. In order to see the effect of the adsorbed products on the reusability of the catalyst, the Beta sample used in the reaction was filtered, washed with acetone, and reused three times. In this case an important decrease in activity was observed (Fig. 7). In order to check if the decrease in activity was due to the reaction product (fructose) remaining adsorbed, the catalyst was subjected to a Soxhlet extraction with dichloromethane. The resultant sample was again reused, and only a fraction of activity was recovered, indicating that products bulkier than fructose have been built inside of the pores, and they cannot be extracted by dichloromethane. In this case full regeneration was achieved by calcining the catalyst at 773 K for 3 h in the presence of air.

CONCLUSIONS

Solid acid catalysts and more specifically large-pore tridirectional zeolites are very effective for the preparation of the 1,3-dioxalane fragrance (fructose). Zeolites present clear advantages over the conventional homogeneous acid catalysts used commercially from the point of view of activity, selectivity, and waste production.

Starting from ethylene glycol and ethyl acetoacetate, the zeolites Beta and USY give the best results and an optimum in activity was found for samples in which a compromise between the number of acid sites and hydrophobicity was achieved. This corresponds to an optimum in the framework Si/Al ratio between 25 and 50 for Beta and ~20 for USY.

The thermodynamic equilibrium can be shifted by removing the water formed either by azeotropic distillation with toluene or by working in a vacuum of 8 Torr. With the optimised catalyst and conditions it is possible to obtain high conversion with 99% selectivity to fructose.

ACKNOWLEDGMENTS

The authors acknowledge financial support from the Dirección General de Investigación Científica y Técnica of Spain (Project MAT97-1016-C02-01) and ACEDESA.

REFERENCES

1. Green, T. W., and Wuts, P. G. M., "Protective Groups in Organic Synthesis," 2nd Ed., Vol. 4, p. 212. Wiley, New York, 1991.
2. Bauer, K., Garbe, D., and Surburg, H., "Common Fragrances and Flavors Materials," 2nd Ed., VCH, New York, 1990.
3. Ashton, M. J., Lawrence, C., Karlsson, J. A., Stuttle, K. A. J., Newton, C. G., Vacher, B. Y. J., Webber, S., and Withnall, M. J., *J. Med. Chem.* **39**, 4888 (1996).
4. Vu Thuy, V., and Maitte, P., *Bull. Soc. Chim. Fr.* 9 (1975).
5. Tong-Shuang, L., Sheng-Hui, L., Ji-Tai, L., and Hui-Zhang, L., *J. Chem. Res. Synop.* (1) 26 (1997); Csiba, M., Cleophax, J., Loupy, A., Malthete, J., and Gero, S. D., *Tetrahedron Lett.* **34**, 1787 (1993).
6. Corma, A., Climent, M. J., García, H., and Primo, J., *Appl. Catal.* **59**, 333 (1990); Ballini, R., Bosica, G., Frullanti, B., Maggi, R., Sartori, G., and Schroer, F., *Tetrahedron Lett.* **39**, 1615 (1998); Jiang, W., Tian, Y., Dao Ma, Y. D., and Wang, Q. L. W., *Chinese Chem. Lett.* **8**, 377 (1997).
7. Climent, M. J., Corma, A., Iborra, S., Navarro, M. C., and Primo, J., *J. Catal.* **161**, 783 (1996); Tanaka, Y., Sawamura, N., and Iwamoto, M., *Tetrahedron Lett.* **39**, 9457 (1998).
8. Ford, R. A., and Letizia, C., *Food Chem Toxicol.* **26**, 315 (1988).
9. Corma, A., Climent, M. J., Susarte, M., and Vely, A., Patent SP 9902439, 1999.
10. Beck, J. S., Chu, C., Johnson, J. D., Kresge, C. T., Leonowicz, M. E., Roth, W. J., and Vartuli, J. C., Patent WO 9111390, 1992.
11. Molecular dimensions of the hemiacetal and Fructose were calculated with the Cerius 2 Visualizer Program, Version 3.8, Molecular Simulations Inc., San Diego, 1999.
12. Corma, A., *Chem. Rev.* **95**, 559 (1995).
13. Pine, L. A., Maher, P. J., and Wachter, W. A., *J. Catal.* **85**, 466 (1984).
14. Cambor, M. A., Corma, A., Iborra, S., Miguel, S., Primo, J., and Valencia, S., *J. Catal.* **172**, 76 (1997).