Soft and Hard Acidity in Ion-exchanged Y Zeolites: Rearrangement of 2-Bromopropiophenone Ethylene Acetal to 2-Hydroxyethyl 2-Phenylpropanoate

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The rearrangement of the cyclic ethylene acetal of 2-bromopropiophenone to 2-hydroxyethyl 2-phenylpropanoate is catalysed by zinc exchanged Y zeolites with higher activity than the conventional $ZnCl_2$; hydrolysis of the acetal moiety owing to the Brønsted acid sites is one of the major side reactions, while the competitive formation of 5-methyl-6-phenyl-2,3-dihydro-1,4-dioxine increases with the softness of the Lewis acid centres.

α-Arylalkanoic acids are an important class of organic compounds exhibiting potent antiinflammatory and analgesic activity.[1] One of the most general approaches for the synthesis of these compounds involves the rearrangement of acetals of aryl α-haloalkyl ketones.[2] It has been shown that this reaction can be catalysed by a variety of 'soft and borderline Lewis acids'.[3]

Zeolites are crystalline aluminosilicates characterized by strictly regular structures.[4] In particular, the large-pore Y zeolite basically consists of a tridimensional network of nearly spherical supercages of about 13 Å diameter connected through 8 Å windows. Each framework aluminium introduces a negative charge in the lattice that requires the presence of associate cations. These charge-compensating cations can be exchanged by other different cations from those directly introduced during the synthesis of the zeolite. In the present work, we report for the first time that transition metal ion exchanged zeolites can catalyse the rearrangement of the ethylene acetal of 2-bromopropiophenone to the corresponding α-phenylpropanoic ester. We have observed that the micro-environment provided by the zeolite framework strongly influences the activity and selectivity of the metal ion for this rearrangement.

The preparation of the HY sample was carried out by thermal decomposition of a NH_4Y zeolite following the experimental details described previously.[5] The ZnHY catalyst was obtained by stirring at 353 K for 2 h the HY zeolite with a 1 mol dm^{-3} aqueous solution of $ZnSO_4$ followed by drying and calcination at 773 K for 3 h. The ZnNaY was prepared by initially treating the NaY zeolite with a 0.5 mol dm^{-3} aqueous solution of $ZnNO_3$ using the same conditions as above, and then the resulting solid was neutralized by exchanging with a NaCl solution followed by a final exchange–calcination process using a 1 mol dm^{-3} aqueous solution of $ZnNO_3$. Likewise, the AgNaY and the HgNaY samples were prepared from NaY following the same ion exchange–neutralization protocol but using a 1 mol dm^{-3} solution of $AgNO_3$ (pH 7) or 0.1 mol dm^{-3} solution of $Hg(NO_3)_2$ (pH 1), respectively. The amount of active metal ion per unit mass for each catalyst is given in Table 1.

Treatment of the cyclic acetal[6] 1 in chlorobenzene at 403 K in the presence of the five ion exchange zeolites affords variable mixtures† of 2-bromopropiophenone 2, 2-hydroxyethyl 2-phenylpropanoate[6] 3 and 5-methyl-6-phenyl-2,3-dihy-

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† Trace amounts of propiophenone, 2-hydroxypropiophenone, 1-hydroxy-1-phenylpropanone and 2-phenylpropanoic acid could be also detected in some reaction mixtures.

Table 1 Results of the reaction of cyclic acetal **1** in chlorobenzene at 403 K for 20 h
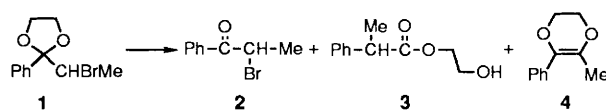
Catalyst	Transition metal content /mmol g^{-1}	Conversion (%)	Selectivity				k_{hydr} /h^{-1}g^{-1}	TON
			2	3	4	3/4		
HY	—	100	91	0	0	—	1.4	—
ZnHY	0.78	98	66	8	2	4.0	1.1	0.12
ZnNaY	1.87	86	23	38	19	2.0	0.14	0.23
ZnCl$_2$	7.34	89	15	56	14	4.0	7 × 10^{-3}	0.12
AgNaY	1.62	97.1	3	11	75	0.15	0.09	—
HgNaY	0.76	93.8	73	3	9	0.33	1.4	—
Hg$_2$Cl$_2$	4.23	6	—	71	28	2.5	—	—

dro-1,4-dioxine‡ **4**. In order to establish a valid comparison, this reaction was also carried out under the same experimental conditions using anhydrous ZnCl$_2$ and Hg$_2$Cl$_2$ as catalysts. The results are summarized in Table 1.§ Concerning the formation of the dioxine **4**, there are in the literature two precedents reporting that oxygen migration competitive to the 1,2-aryl shift can occur in the rearrangement of acetals of α-substituted propiophenones devoid of electron-donating groups on the aromatic ring.[7,8]

In order to get a deeper insight into the exact nature of the active sites responsible for the hydrolysis of the acetal, a characterization of the Brønsted and Lewis acidity of the centres was accomplished for the HY, ZnHY and ZnNaY samples by means of the pyridine adsorption method. Pyridine, when adsorbed on acidic solids, shows in the IR spectra specific bands assignable to the pyridinium ion (1540 cm^{-1}) and Lewis adducts (1450 cm^{-1}), respectively. The intensity of these absorptions is directly related to the population of both types of centres.[9] The IR spectra of the 1750–1350 cm^{-1} zone of pyridine adsorbed on these three ion exchanged zeolites are given in Fig. 1. They show in all cases the presence of both types of centres, i.e. Brønsted sites associated with protonic hydrogen from bridged structures Al(OH)Si, and Lewis acid sites associated with extra framework aluminium in the HY sample, and with zinc cations in the ZnHY and ZnNaY samples. From Fig. 1, a direct correlation between the ratio of 2/(3 + 4), i.e. hydrolysis to rearrangement, and the Brønsted to Lewis acid sites ratio, i.e. I_{1540}/I_{1450}, is obtained. Furthermore, and in order to explain the lack of activity of the Lewis acid sites associated with extraframework Al in the HY sample, the reaction was also carried out on γ-Al$_2$O$_3$ (Girdler, 180 m^2 g^{-1}) under the same experimental conditions. Then, only 4% conversion of **1** was obtained, with 81% selectivity to rearrangement. This result, together with the relatively much higher ratio of Brønsted to Lewis acid sites in sample HY, explain the catalytic results achieved with this sample. Therefore, it can be concluded that each type of acid site catalyses a different reaction, the presence of Brønsted centres being negative from the point of view of the catalyst selectivity for the 1,2-phenyl shift.

Concerning the activity of the zinc exchanged zeolites, it is remarkable that the turnover frequency (TOF), measured as
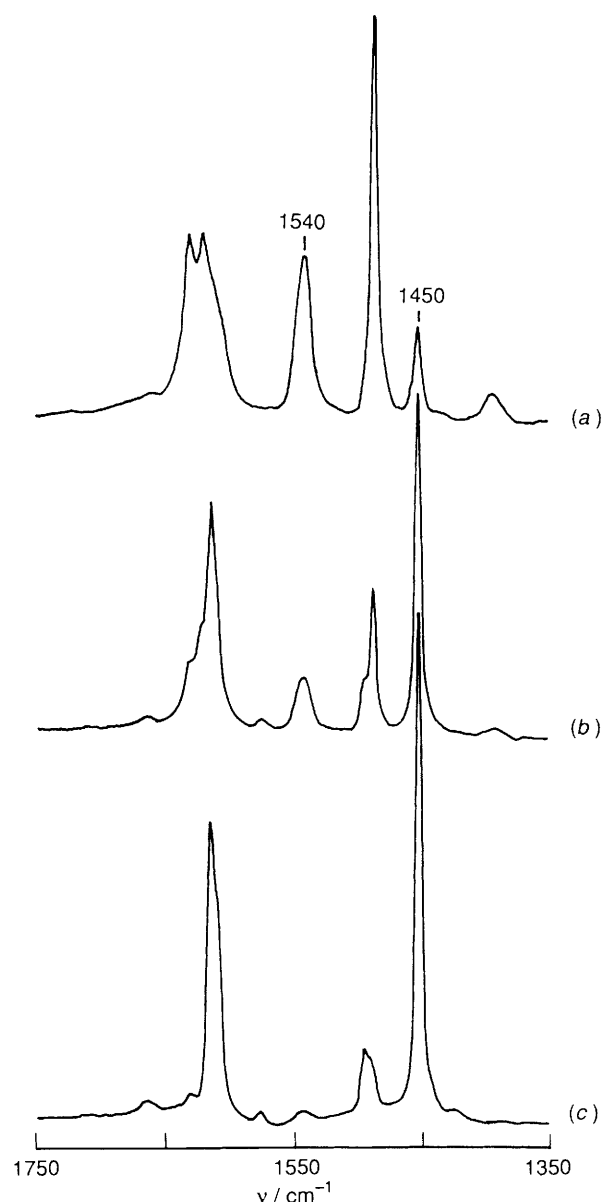
Fig. 1 IR spectra of pyridine retained on HY (a), ZnHY (b) and ZnNaY (c) zeolites after desorption at 523 K and 10^{-4} Torr (1 Torr = 133.3 Pa) for 1 h

‡ IR: v/cm^{-1} 3067w, 2976m, 2880m, 1678m, 1311m, 1228s, 1142m, 1054m, 914m, 760m and 696m; ^{1}H NMR: δ 7.75–6.95 (m, 5 H, C$_6$H$_5$), 4.05–3.15 (m, 4 H, CH$_2$CH$_2$) and 2.23 (s, 3 H, Me); MS: 176 (M$^+$, 25), 131 (1), 115 (4), 105 (100), 77 (31).

§ Analysis of the reaction mixtures was accomplished by GC-MS (HP 5988A spectrometer) and GC–FTIR (HP 5965A detector). Isolation of the reaction products was carried out by flash column chromatography using hexane–dichloromethane mixtures as eluent.

the molar ratio between the compound **2** formed and the zinc ions present in the catalyst, is almost twice for the ZnNaY sample than for the conventional ZnCl$_2$ catalyst. This clearly indicates that the activity of Zn^{2+} can be modified by
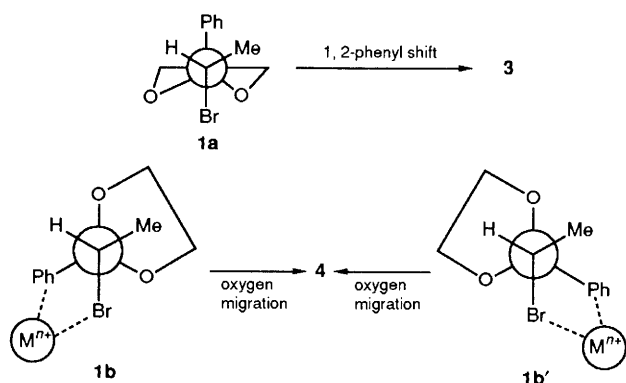
Fig. 2 Conformations of acetal **1** from which phenyl shift **1a** or alkoxy migration **1b** and **1b'** must occur

interaction with the zeolite framework. Since it has been shown[3] that the ability of Lewis acids to promote the 1,2-aryl migration increases with their softness, it can be concluded that the Zn^{2+} ions within the ZnNaY zeolite are softer than in the $ZnCl_2$ catalyst.

An important item related to the hardness and softness of the active sites is the change in the relative selectivity of the products arising from phenyl or ethyleneoxy migration. Thus, while for the $ZnCl_2$ and ZnHY samples the ratio **3** to **4** is the same, the use of the ZnNaY sample favours the formation of the dioxine **4**. Assuming that the rearrangement step follows a S_N2-like mechanism, where the migrating group and the bromine leaving atom must be in a disposition *anti* periplanar, the conformation required for the phenyl shift **1a** must be different to that leading to the dioxine **1b**, **1b'**. Therefore, an increase in the relative selectivity of compound **4** indicates a preferential stabilization of conformations **1b**, **1b'** (or the transition states arising from them) over **1a**, by interaction with the Lewis acid centres of the ZnNaY catalyst. In this context, a recent X-ray study of the crystal structure of complexes of aryl α-bromoalkyl ketones with Lewis acids has established that the softness and hardness determines the position where the acid is bound to the organic molecule, soft metal ions can be coordinated to Br atoms and the π-system of phenyl rings.[10] On the other hand, unimolecular effects resulting from conformational restrictions imposed on guest molecules by adsorption within the voids of zeolites are already well known.[11]

In order to obtain more clear evidence for the influence of the softness of the Lewis acid centres on the regioselectivity of the rearrangement, the reaction of **1** was carried out in the presence of AgNaY and HgNaY zeolites. The results included

in Table 1 show that, in fact, the softness of the active centres modifies the ratio **3** to **4**, softer sites increasing dramatically the alkoxy migration and the formation of the dioxine **4**, in agreement with the hypothesis of a conformational control of the transposition. The high yields of **2** that have been obtained with the HgNaY sample are probably owing to the particular exchange conditions required to introduce the Hg^{2+} in the zeolite (pH = 1), and which generates a high concentration of adventitious Brønsted sites in the HgNaY sample.

In conclusion, zinc-exchanged Y zeolites are promising catalysts for the rearrangement of acetals of α-bromopropiophenone to 2-phenylpropanoic acid derivatives. The best materials must have no Brønsted acid sites to avoid the competitive hydrolysis of the acetal moiety. Lewis acid centres are responsible for the rearrangement pathway, but their softness had to be controlled since alkoxy migrations are preferred using soft centres. In this way, a zinc-exchanged faujasite has been prepared with an activity per zinc ion twice as high as the conventional zinc dichloride. It is then deduced that the softness–hardness of the cations is strongly modified when in a zeolite owing to the framework interaction. Current work is in progress in order to determine the influence of the framework composition on the hardness–softness of the borderline Lewis acid metal ions of the zeolite.

References

1 S. H. Ferreira and J. R. Wayne, *Antiinflammatory Drugs*, Springer-Verlag, New York, 1979, p. 321.
2 J.-P. Rieu, A. Boucherle, M. Cousse and G. Mouzin, *Tetrahedron*, 1986, **42**, 4095.
3 G. Castaldi, A. Belli, F. Uggeri and C. Giordano, *J. Org. Chem.*, 1983, **48**, 4658.
4 A. Dyer, *Zeolite Molecular Sieves*, Wiley, New York, 1988.
5 M. J. Climent, A. Corma, H. García and J. Primo, *Appl. Catal.*, 1989, **51**, 113.
6 S. Uemura, S.-i. Fukuzawa, T. Yamauchi, K. Hattori, S. Mizukati and K. Tamaki, *J. Chem. Soc., Perkin Trans. 1*, 1986, 1983.
7 G. Castaldi, C. Giordano and F. Uggeri, *Synthesis*, 1985, 505.
8 H. R. Sonowane, B. S. Nanjundiah, D. G. Kulkarni and J. R. Ahuja, *Tetrahedron*, 1988, **23**, 7319.
9 For a discussion of the pyridine adsorption–desorption method to measure the acidity of the solids, see: A. Corma, C. Rodellas and V. Fornés, *J. Catal.*, 1984, **88**, 374.
10 T. Laube, A. Weidenhaupt and R. Hunziker, *J. Am. Chem. Soc.*, 1991, **113**, 2561.
11 D. R. Corbin, D. F. Eaton and V. Ramamurthy, *J. Org. Chem.*, 1988, **53**, 5386; D. R. Corbin, D. F. Eaton and V. Ramamurthy, *J. Am. Chem. Soc.*, 1989, **110**, 4848.