Computer-aided search for shape-selective zeolite catalysts for the synthesis of *p*-isobutylethylbenzene

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Molecular modelling studies show that the formation of *p*-isobutylethylbenzene is possible inside any 'large pore' zeolite, while mordenite is the most probable zeolite to achieve maximum selectivity.

p-Isobutylethylbenzene (*p*-IBEB) is the key intermediate in the production of α-(4-isobutylphenyl)propionic acid, which is the popular analgesic drug ibuprofen.[1] The conventional synthesis route for the production of *p*-IBEB involves the alkylation of isobutylbenzene (IBB) with ethene over Lewis-acid catalysts[2] in which the selectivity towards *p*-IBEB is typically 17.6%. Further, this process involves environmentally hostile catalyst materials such as mineral acids, aluminium chloride, zirconium chloride, *etc.*[2] Recently, the possibility of using zeolite catalysts for the production of *p*-IBEB by disproportionation of isobutylbenzene and a polyalkylbenzene over HY zeolite has been shown to lead to better selectivity (46.3%).[3] There are nearly twenty large-pore zeolites containing channels formed by 12-membered (12-m) rings, whose crystal structures have been reported in the literature.[4] Here, we describe how a combination of computer modelling techniques can be used to search the most viable zeolite catalyst for the selective synthesis of *p*-IBEB.

We studied the interaction between the mordenite zeolite framework and molecules such as ethylbenzene (EB), IBB and isomers of IBEB. The minimum energy configuration of the molecules was derived from force-field energy minimization procedures using CVFF parameters.[5] Conformational energy values were calculated for different conformers of the molecules by allowing cooperative motion of the alkyl groups. The dimensions of the molecules assumed were taken from measured values in three-dimensional space.[6] The interaction of the molecules with the mordenite zeolite framework was calculated by determining the long-range forces by classical electrostatic interactions and short-range interactions in terms of Lennard–Jones potentials.[5] The molecules were translated through the 12-m channel of mordenite in regular steps of 0.2 Å. A mordenite lattice was constructed which contained 1.7, 1.5 and 8 unit cells in the *a*, *b* and *c* directions, respectively, and forward and reverse diffusion of the interacting molecules was considered. After translating the molecule in each step, the most favourable orientation and configuration of the molecule was determined by minimising the energy of the molecule and the interaction energy. All computations were performed on a SiliconGraphics Indigo2 workstation using the 'catalysis software package', supplied by Biosym Technologies, USA.

The reactant molecules IBB and EB and the possible product molecules *o*-, *m*- and *p*-IBEB were generated as molecular models and their minimum energy configurations were determined. Indeed, the size and shape of the 'transition state' might be also a key factor in controlling the overall shape selectivity of the reaction. However, in this study we concentrated on the size, shape and diffusional characteristics of reactant and product molecules. A complete conformational search of the molecules by allowing free rotation of the ethyl and isobutyl groups in the three isomers of IBEB was performed. The relative flexibility of the isomers and the variation of the strain energy with respect to the conformational changes were calculated. These results also confirmed the equilibrium configuration for the molecules at the global minima. The dimensions of the molecules at their minimum energy configurations are given in Table 1. When correlating the dimensions of the molecules with the pore diameter of zeolites for molecular fitting purposes, it is customary to neglect the largest dimension (*a*) of the molecules. The molecules prefer to enter the cages *via* their smallest dimensions on the basis of interaction energy criteria. Thus by comparing the *b* and *c* dimensions of molecules in Table 1, it is observed that 'small' (with 8-membered rings) and 'medium' (with 10-membered rings) pore zeolites are too small to accommodate isomers of IBEB, while 'large' pore zeolites are suitable for the formation of IBEB.

Among the large-pore zeolites, the suitability of mordenite zeolite was probed by studying the diffusional characteristics of these molecules. Using the computer graphics method, it is possible to visualize how well the various reactant and product molecules fit into the pores of mordenite (pore dimensions 7.0 × 6.5 Å). This provides qualitative information while more quantitative data was obtained by calculating the interaction energy. During the calculation of the interaction energy, the ions in the zeolitic lattice were held fixed at their crystallographically determined geometries.[7] The simulation box contained the mordenite lattice generated based on its crystal structure determination[7] (space group $CmC2_1$, a = 18.09, b = 20.52, c = 7.52 Å). The actual dimensions of the simulation box are 30.8 × 30.8 × 60.2 Å in the *a*, *b* and *c* directions, respectively. The simulation box contains 3148 ions and a totally siliceous system was considered as the first approximation. The molecules were allowed to diffuse through three unit cells in the *c*-direction, which is the direction of the 12-m channel as shown in Fig. 1. The starting and final points of the diffusion path simulated are marked by +, although the interaction energy values are shown for only two unit cells. The interaction energy between the molecules and the mordenite framework was calculated using the force fields employed by Horsley *et al.*[8] who studied similar molecules. The cut-off for the van der Waals' energy calculation was 7.0 Å. The variation of the interaction energy as the *p*-IBEB diffuses through the 12-m channel of the mordenite is shown in Fig. 1. The diffusional energy characteristics of the other isomers, *o*- and *m*-IBEB are shown in Fig. 2(*a*). The molecule passes through energy maxima and minima when diffusing through a unit cell;

Table 1 Dimensions of different organic molecules as derived from the force-field calculations and their interaction energy with the mordenite lattice

	Dimensions/Å			Maximum energy/	Minimum energy/	Energy barrier/
Molecule	*a*	*b*	*c*	$kJ\ mol^{-1}$	$kJ\ mol^{-1}$	$kJ\ mol^{-1}$
EB	6.32	4.97	2.74	−137.57	−144.31	6.74
IBB	7.93	5.07	3.88	−53.22	−63.35	10.13
p-IBEB	10.47	5.22	4.46	−93.55	−99.99	6.44
m-IBEB	8.45	5.95	5.55	−74.60	−92.55	17.95
o-IBEB	7.50	6.85	4.64	1.76	−93.93	95.69

the variation of interaction energy values symmetrically repeats in the second unit cell also as seen in Figs. 1 and 2. Similar plots for the diffusion of EB and IBB are shown in Fig. 2(*b*). These results indicate that the energy minimisation parameters and the size of the system considered are suitable for realistic prediction of diffusional behaviour. Although, there is no significant variation in the sizes of these molecules their diffusional energy barriers are significantly different, as shown in Table 1. It is observed that the diffusion of the reactant molecules, *viz*. IBB and EB, have energy barriers of 10.13 and 6.74 kJ mol^{-1}, respectively. The energy barrier for the diffusion of *p*-IBEB is also of the same order (6.44 kJ mol^{-1}). However, there is an energy barrier of 17.95 kJ mol^{-1} for *m*-IBEB and a significantly large energy barrier of 95.69 kJ mol^{-1} for *o*-IBEB. The considerable increase in the diffusion barrier for *o*-IBEB can be related to its inflexibility as deduced from conformational energy analysis.

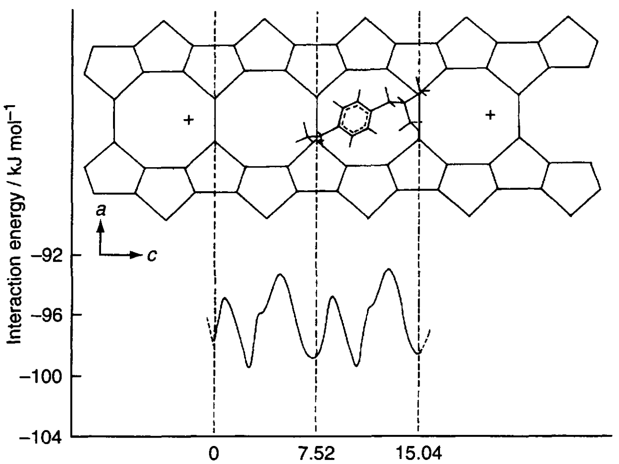

Fig. 1 Variation of interaction energy between *p*-IBEB and the mordenite framework as the molecule diffuses through the 12-m channel. The energy gradient symmetrically repeats in every unit cell. The cross-section of 12-m channel in the *ac* plane as viewed through 8-m windows is shown to illustrate the location of minima and maxima. Among the several locations and configurations for the molecule, a typical configuration at a minimum energy location is shown.

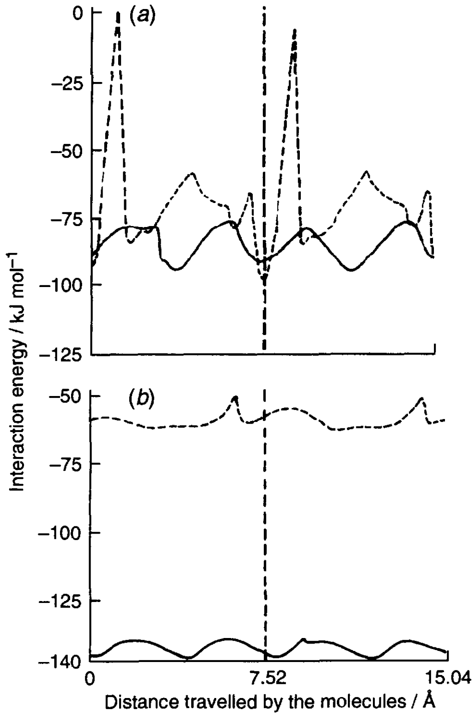

Fig. 2 Variation of interaction energy between the molecules and the mordenite framework as they diffuse through the 12-m channel in the *c*-direction. The end of a unit cell at 7.52 Å in the *c*-direction is also shown: *m*-IBEB (—), *o*-IBEB (-----) (*a*); EB (—), IBB (-----) (*b*).

These results also provide information on the nature of sites inside mordenite where the molecules have favourable and unfavourable interactions. The molecule passes through two maxima and two minima when crossing each 8-m ring as shown in Fig. 1. The 8-m ring can be divided into four quarters. It is observed that when the phenyl ring of the molecule is at the beginning (0), centre (0.5) or end (1) of the 8-m ring, the interaction of the molecule with the framework is most favourable while the unfavourable interaction corresponds to a configuration in which the phenyl ring is 0.25 or 0.75 through the 8-m ring. It is also observed that the favourable orientations of all the molecules inside the 12-m ring are those in which the plane of the phenyl ring is parallel to the 8-m channel opening.

The large-pore zeolites are suitable for the synthesis of isomers of IBEB. The detailed analysis of the diffusion characteristics of the isomers of IBEB inside the channel of mordenite predicts high selectivity for the production of *p*-IBEB. The ease of diffusion of different isomers of IBEB in the 12-m channel of mordenite is in the order *p*-IBEB > *m*-IBEB > *o*-IBEB, in accord with their dimensions and conformational flexibility.

A detailed report comprising the comparative diffusion behaviour of these molecules in different large-pore zeolites, size of the transition state, the orbital interaction and the electron distribution in the minimum energy configurations and the influence of various Si/Al ratios will be given elsewhere.[9]

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