Isomerization of eugenol and safrole over MgAl hydrotalcite, a solid base catalyst†

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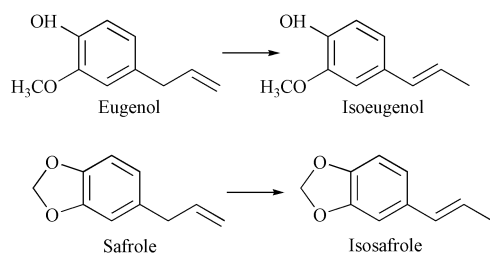*E-mail: salt@csir.res.in; Fax: +91-278-566970; Tel: +91-278-567760*

Isomerization of olefins, in particular eugenol and safrole, is an important reaction as the products, namely isoeugenol and isosafrole, find application in pharmaceuticals and fragrances. The catalyst employed to carry out this reaction is either a strong alkaline solution (KOH or KO*t*Bu) or precious metal catalysts under homogenous conditions, which pose severe environmental problems such as handling and effluent disposal as well as cost. The present paper discloses a new alternative route wherein hydrotalcite is used as a solid base catalyst, which is environmentally friendly as well as economical in obtaining good yields of the isomerized products.

Introduction

Isomerization of eugenol and safrole to the corresponding thermodynamically stable isomers namely isoeugenol and isosafrole (Scheme 1), is an important olefin isomerization reaction wherein the products find application in the fragrance and pharmaceutical industries.[1,2] Traditionally these reactions are catalyzed by alkalis such as KOH in alcoholic solutions (most often in higher alcohols) at high temperatures.[3,4] Alternatively, complexes of group VIII elements are used to catalyze these reactions.[5,6] Cerveny *et al.*[7] have studied isomerization of eugenol over both alcoholic alkali solution as well as on anhydrous RhCl$_3$. A high concentration of alkali was needed (nearly seven times the concentration of substrate) to achieve stoichiometric yield while a reduction in the concentration of alkali decreased the conversion of eugenol. Isomerization over RhCl$_3$ showed a strong negative influence when the reaction was carried out in the presence of water and the inherent activity of the catalyst decreased with time. Radhakrishna and coworkers[8,9] have carried out isomerization of eugenol and safrole on KF on neutral alumina in dry ethylene glycol and obtained around 75% yield at 150 °C. Conversion improved when they used 'dry media' without using any solvent. However, in these cases, the amount of base employed was 10–20 times (w/w ratio) more than the substrate. Very recently, Thach *et al.*[10,11] have employed a microwave batch reactor to facilitate these isomerization reactions in both dry media as well as under alkaline solutions. A conversion of 73% was obtained for eugenol and 86% was obtained for safrole at 220 °C for 15 min in the presence of NaOH. Replacement of conventional alkali based catalysts by solid base catalysts is one of the important tasks in view of easier process handling, effluent control, easy separation and in turn resulting in a cleaner environment.[12–14] Hydrotalcite-like (HT-like) compounds are one of such promising heterogeneous solid base catalysts, which have been exploited for various base catalyzed transformations such as aldol condensation,[15,16] double bond isomerization of alkenes[17] and dehydrogenation of 2-propanol.[18] They are layered materials with the general formula $[M(II)_{1-x}M(III)_x(OH)_2][A_{x/n}{}^{n-}]\cdot mH_2O$ where M(II) is a bivalent metal ion and M(III) is a trivalent metal ion, A is the interlayer anion and x can generally have the values between 0.2 and 0.35. Structurally, they possess a brucite-like (Mg(OH)$_2$) layered network wherein a partial substitution of bivalent ion by trivalent ion, say Al^{3+}, occurs, and the resulting excess positive charge in the layers is compensated by anions located in the interlayers.[19] Corma *et al.*[20] have explored these materials for the production of citronitril, a fine chemical used in the perfume industry through condensation of ethyl cyanoacetate and benzyl alcohol over calcined MgAl hydrotalcites and claimed highest activity for the catalyst with an Mg/Al atomic ratio of 3.0. Kaneda and coworkers[21] have exploited the basic character of hydrotalcites in the epoxidation of olefins using hydrogen peroxide in presence of nitriles. Common linear and cyclo olefins such as oct-1-ene and cyclohexene gave the corresponding epoxide as the sole product in excellent yield while for α,β-unsaturated ketones, such as cyclohex-2-en-1-one, epoxidation occurred exclusively without formation of Bayer–Villiger oxidation products. Very recently Kumbhar *et al.*[22] have carried

Scheme 1 Isomerization of eugenol and safrole.

Green Context

The isomerisation of olefins is an important chemical transformation used in many industrial processes. Among the most valuable of these are the isomerisation of eugenol to isoeugenol and safrole to isosafrole. Like many other olefin isomerisations these are commonly carried out using conventional bases such as KOH in alcoholic solvents. Other catalysts have been reported but common problems are caustic waste streams and the need for very large quantities of base to give good substrate conversions. Here the benign solid base hydrotalcite is shown to be very active for these isomerisations. Waste streams can thus be avoided and the catalyst which is shown to be insensitive to the atmosphere, is easy and safe to handle. *JHC*

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out cyanoethylation of methanol over rehydrated hydrotalcites and claimed a very high activity in the liquid phase under mild reaction conditions. In the present paper, we report our first results on the isomerization of safrole and eugenol over MgAl hydrotalcite-like compounds. For completeness, end members of the series, namely $Mg(OH)_2$ and $Al(OH)_3$, are also synthesized and their activities are compared.

Results and discussion

Table 1 summarizes the physicochemical properties of the compounds synthesized. Elemental analysis showed no significant deviation between the input Mg/Al atomic composition and the final solid composition, except at higher Mg/Al atomic ratios where deviations are likely due to preferential precipitation,[23] ensuring the completion of precipitation. PXRD of the samples (Fig. S1, ESI†) showed a pure hydrotalcite-like phase for Mg/Al atomic ratios up to 6.0. With a further increase in the ratio, an additional phase, namely magnesium carbonate ($5MgO·4CO_2·5H_2O$, JCPDS 01-0168) was observed along with the HT-like phase. It is known in the literature, that the pure HT-like phase is obtainable for M(II)/M(III) atomic ratios in the range 1.5–5.7.[19] The lattice parameters of these samples were calculated ('c' was calculated from the position of the first basal peak appearing around $2\theta = 11°$ as $c = 3d_{(003)}$ and 'a' was calculated from the position of first peak of the doublet appearing around $2\theta = 60°$ as $a = 2d_{(110)}$), and are summarized in Table 1. An increase in the 'a' parameter was observed with an increase in Mg/Al atomic ratio, while the 'c' parameter increased up to Mg/Al atomic ratio of 6.0 and then was not altered significantly with a further increase in the ratio. The increase in the 'a' parameter is attributed to higher ionic radius of Mg^{2+} (0.72 Å) with respect of Al^{3+} (0.53 Å) while the increase in the 'c' parameter is rationalized by lower electrostatic interactions between layers and interlayers due to the lower concentration of aluminum (in turn on carbonate content in the interlayers). Further, with an increase in Mg/Al atomic ratio a continuous decrease in the surface area was noted.

Table 1 Physicochemical properties of the samples synthesized

| Catalyst | Mg/Al atomic ratio | | Lattice parameters | | Surface area/$m^2 g^{-1}$ |
	Solution	Solid	a	c	
MgAl-2HT	2.0	2.0	3.04	22.85	102
MgAl-3HT	3.0	2.7	3.06	23.20	80
MgAl-4HT	4.0	3.5	3.07	24.41	83
MgAl-6HT	6.0	4.2	3.08	23.85	61
MgAl-8HT	8.0	5.8	3.09	24.12	49
MgAl-10HT	10.0	6.4	3.10	24.19	44

Table 2 summarizes the isomerization activity of various MgAl hydrotalcites towards both safrole and eugenol. End members, namely $Mg(OH)_2$ and $Al(OH)_3$, are also included for comparison. It is clear from the Table that both end members are not active for eugenol and exhibited very low activity for safrole. The mixed hydroxycarbonates of Mg and Al crystallizing in the hydrotalcite-like phase showed considerable activity, which, however, varied with the Mg/Al atomic composition. In the case of eugenol an Mg/Al atomic ratio of 4.0 (MgAl-4HT) showed maximum activity with the conversion of around 73% with a *cis*:*trans* ratio of 17:83 while the catalyst with Mg/Al atomic ratio of 6.0 (MgAl–6HT) showed maximum activity for safrole, exhibiting around 75% conversion with a *cis*:*trans* ratio of 15:85. *Trans* isomers were formed predominantly in both cases due to their better thermodynamic stability. The activity of MgAl–2HT was lower compared to the catalysts mentioned above for both transformations, despite having maximum

Table 2 Isomerization activities of eugenol and safrole over various MgAl hydrotalcites

| Catalyst | Eugenol | | | Safrole | | |
| | Conv. (%) | Selectivity (%) | | Conv. (%) | Selectivity (%) | |
		cis	*trans*		*cis*	*trans*
MgAl-2HT	34	29	71	2	—	100
MgAl-3HT	48	23	77	1	—	100
MgAl-4HT	73	17	83	28	11	89
MgAl-6HT	45	27	73	75	15	85
MgAl-8HT	40	30	70	33	15	85
MgAl-10HT	23	—	100	54	15	85
$Mg(OH)_2$	—	—	—	0.3	—	100
$Al(OH)_3$	—	—	—	0.1	—	100
Blank	—	—	—	—	—	100

Substrate: 0.5 g, solvent: DMF (20 ml), catalyst: 250 mg, reaction temp./time: 200 °C/6 h.

surface area, suggesting the necessity of appropriate basicity. For both series of catalysts, an increase in the conversion was noted with an increase in Mg/Al atomic ratio, however, conversion reached a maximum and decreased with a further increase in this ratio. This could probably be due to variation in the basicity of the catalysts. Although basicity correlation with the observed activity is underway, it is known in the literature that basicity varies in a similar trend with the Mg/Al atomic composition, in line with the activity trend depicted above.[18,24] Further, the catalysts possessing maximum activity for the two different substrates were different, suggesting a difference in basicity requirements for propagating the two reactions. To compare the activity of our catalysts with conventional catalysts, we have carried out isomerization of eugenol over KOH and KO*t*Bu in excess substrate:catalyst mole ratio (1:3 for KOH and 1:1.5 for KOtBu). A conversion of 9% and 5% of eugenol to isoeugenol was observed respectively, far less compared to our hydrotalcite-based catalysts, indicating their superior behavior in addition to their environmental benefits.

From the results above, we selected MgAl–4HT for eugenol and MgAl–6HT for safrole, as they showed maximum activity for the corresponding isomerization reactions, for further study. Table 3 shows the influence of catalyst:substrate mass ratio for eugenol and safrole over these catalysts. The conversion increased with an increase in catalyst:substrate ratio for both the series of catalysts. At equivalent mass ratio (which is nearly 1:3.6 catalyst:substrate mole ratio), a conversion of 85% of eugenol with a *cis*:*trans* ratio of 15:85 was observed. To our knowledge, this is the highest conversion for eugenol reported in the literature so far under conventional conditions. In the case of safrole, 88% conversion of safrole was obtained under equivalent substrate:catalyst mass ratio. Further in both cases, the mass balance of substrates were better than 95% suggesting selective isomerization without forming any additional or

Table 3 Isomerization activities of eugenol over MgAl-4HT and safrole over MgAl-6HT

| Sub:Cat mass ratio | Eugenol | | | Safrole | | |
| | Conv. (%) | Selectivity (%) | | Conv. (%) | Selectivity (%) | |
		cis	*trans*		*cis*	*trans*
10:1	30		100	20	25	75
5:1	45	22	78	45	18	82
3.3:1	60	17	83	53	15	85
2.5:1	65	15	85	56	14	86
2:1	73	16	84	75	15	85
1:1	85	15	85	88	13	87

Substrate: 0.5 g, solvent: DMF (20 ml), reaction temp./time : 200 °C/6 h

consecutive reaction products. High conversion with exceptionally good yields of isomerized products for both eugenol and safrole over these solid base catalysts, suggests their application for commercial exploitation.

Solvent variation studies showed that, among the various solvents screened, namely THF, DMF, DMSO, toluene, glycerol, acetonitrile and glycol, DMF was best for eugenol and DMSO was best for safrole isomerization, and hence were selected for further study. Variation in the reaction temperature for these isomerization reactions showed (Fig. 1A), in the case of eugenol, conversion was noticed above 160 °C (1.8%) and increased with an increase in the temperature. However, a sharp increase in the conversion was noticed when the temperature was raised to 200 °C (75%). However, in the case of safrole, a gradual increase was noted with an increase in reaction temperature, wherein 98% conversion was achieved at 200 °C with a *cis*:*trans* ratio of 10:90. These results show that, despite both the isomerization reactions being carried out over similar catalysts, the kinetics of the reaction varied with the nature of substrate. However, the influence of solvent in affecting the course of the reaction cannot be completely ruled out. The effect of reaction time substantiated the difference in kinetics (Fig. 1B) wherein more than 95% conversion of safrole to isosafrole was obtained in 1 h while a gradual increase in the conversion of eugenol was noticed with an increase in time, wherein more than 70% conversion was observed after 4 h. No significant change in the yield of isomeric products was noticed with a further increase in time suggesting the absence of consecutive reactions.

In an anticipation to find better catalysts, MgAl-4HT was calcined at various temperatures (200, 400, 600 and 800 °C) and tested for eugenol isomerization activity. Although recent interest has been in exploring the basic and/or redox properties of fresh hydrotalcites for various catalytic transformations, much of the earlier work involved using calcined hydrotalcites as base catalysts.[19] In our case, conversion decreased with an increase in the calcination temperature, however, reasonable conversion (~ 40% with a *cis*:*trans* ratio of 10:90) was shown

at 200 and 400 °C. With a further increase in the temperature, conversion drastically decreased (3%) probably due to loss in specific surface area and phase transformation of HT-like network to mixed metal oxides (Fig. S2, ESI†). Constantino and Pinnavaia[25] have earlier observed this for the reaction of 2-methyl-3-butyn-2-ol over MgAl hydrotalcite, wherein they claimed thermal activation below the structural decomposition point (< 250 °C) resulted in higher activities compared to amorphous metal oxides formed by thermal activation at 450 °C. To determine the influence of the reaction atmosphere, eugenol isomerization was carried out over MgAl-4HT under nitrogen. The conversion decreased (44% with *cis*:*trans* ratio of 20/80) under inert conditions, suggesting the non-influence of atmosphere on the basic sites of these materials in catalyzing the reaction. This is advantageous in view of the general hurdle posed by basic catalysts prone to CO_2 and/or H_2O poisoning, forcing operation under inert conditions. Further, when the same catalyst was externally calcined at 200 °C for 5 h and tested for the reaction, the conversion of eugenol (39% conversion with *cis*:*trans* ratio of 10:90) was less than for the fresh catalyst subjected to 200 °C for the reaction, suggesting the superior nature of basic sites generated *in situ* under reaction conditions. This is our first report on the use of hydrotalcite-derived solid base catalysts for isomerization reactions. A further detailed investigation of various parameters such as influence of bivalent and trivalent metal ions, substrate concentration and basicity correlations with observed activity is underway.

Experimental

MgAl hydrotalcites with different Mg/Al atomic ratio (2.0, 3.0, 4.0, 6.0, 8.0 and 10.0) were synthesized by coprecipitation under low supersaturation.[19] A typical synthesis involves simultaneous addition of two solutions: Solution-A containing appropriate concentration of magnesium nitrate and aluminum nitrate solutions and Solution-B containing NaOH and Na_2CO_3 solutions as precipitants while maintaining the pH around 9–10 under vigorous stirring at room temperature. The precipitate was aged in the mother-liquor at 65 °C for 18 h, filtered off, washed thoroughly with distilled water (until total absence of nitrates and sodium in the filtrate) and dried at 110 °C for 12 h. The solids obtained here are referred as MgAl-*x*HT where *x* is the Mg/Al atomic ratio. Powder X-ray diffraction of the samples were recorded in a Philips Xpert MPD System using Cu-Kα radiation (λ = 1.5406 Å) with a step size of 0.02° and step time of 1 s. Specific surface area of these samples was measured by nitrogen adsorption at 77 K using a sorptometer (ASAP-2010, Micromeritics). The samples were degassed at 120 °C for 4 h prior to measurements.

Isomerization of eugenol and safrole was conducted in a batch reactor (50 ml), wherein the substrate, solvent and catalyst were charged all at once and raised to the reaction temperature, and the products were withdrawn using a syringe at definite time intervals and analyzed (using authentic samples) by gas chromatography (Shimadzu-14B, OV-17) using FID. Quantification of the products was done using isopropanol as internal standard. Identification of the products was also further verified using GC-MS (HP-5890-II GC connected to HP-5971 mass selective detector) as well as ^{1}H NMR (Bruker, Avance-200).
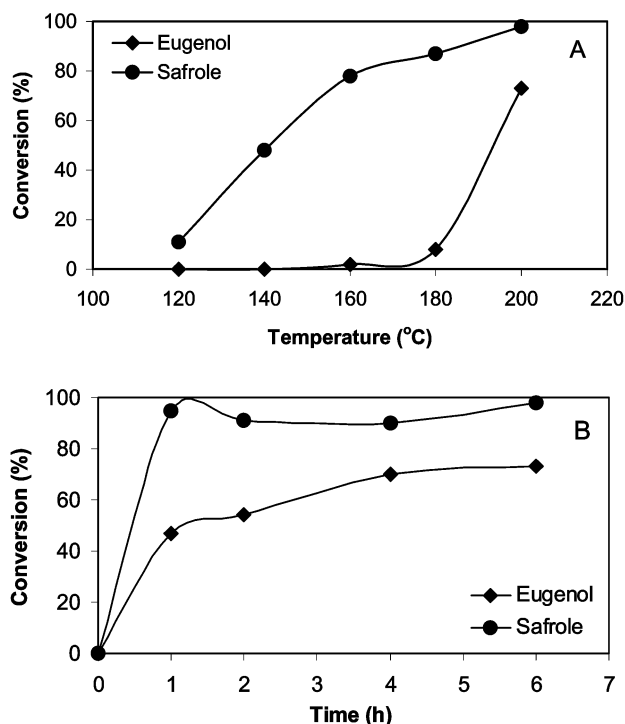

Fig. 1 A. Influence of reaction temperature (reaction time; 6 h) B. Influence of reaction time (reaction temperature; 200 °C) on the isomerization activities of eugenol and safrole over MgAl-4HT and MgAl-6HT, respectively—substrate: 0.5 g, catalyst: 250 mg, solvent: DMF, 20 ml for eugenol and DMSO, 10 ml for safrole.

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