Selective hydration of dihydromyrcene in ionic liquids

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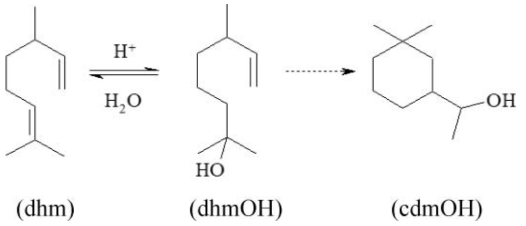
Acid catalysed direct hydration of dihydromyrcene to dihydromyrcenol proceeds selectively in ionic liquid media. By making use of the tuneable physicochemical properties of ionic liquids, and depending upon the process requirement, either biphasic or triphasic systems can be developed. The selectivity to dihydromyrcenol remains extremely high over a wide range of reaction conditions.

Introduction

'Dihydromyrcenol' (dhmOH; 2,6-dimethyl-7-octen-2-ol) has a powerful, fresh floral-muguet (lily of the valley) fragrance, and finds application mainly in soaps and detergents, and also in various functional products.[1] Dihydromyrcenol is traditionally prepared by the reaction of dihydromyrcene (dhm; 3,7-dimethyl-1,6-octadiene, citronellene) with concentrated sulfuric acid, followed by the hydrolysis of the sulfate adduct using dilute acid. This process, however, might be viewed as potentially polluting, as the diluted acid discharge has to be either neutralised or re-concentrated for recycle. Further, the corrosion and hazards associated with the use of mineral acids warrant an alternative route for preparing alcohols from olefins in general.[2]

Catalytic or direct hydration of olefins to alcohols can be viewed as a greener alternative to the current process. In the presence of an acid catalyst, olefinic carbocations undergo nucleophilic addition of water, obeying Markovnikov's rule, to produce the desired alcohol with 100% atom efficiency (Scheme 1).



Scheme 1 Acid catalysed hydration of dihydromyrcene (dhm = dihydromyrcene; dhmOH = dihydromyrcenol; cdmOH = 1-(3,3-dimethylcyclohexyl)ethanol, or Cyclademol).

There have been extensive investigations of the development of solid acid catalysts, mainly using zeolites,[3,4] heteropoly acids,[5] niobic acid,[6] or resins,[7] and there exists a commercial processes to produce cyclohexanol directly from cyclohexene using zeolite catalysis.[8] The yield per pass for such reactions is strongly influenced by solubility and by thermodynamics, as rates for the forward (hydration) and backward (dehydration) reactions are similar.[9] Further, due to the relatively high reactivity of terpenes, the use of stringent reaction conditions has to be avoided in order to achieve higher selectivity.[10] Hydration of dihydromyrcene using heteropoly acids was described by Kozhevnikov *et al.*, but found to be a less selective reaction due to a large amount of by-product formation.[5] Work from Corma's group reported high reactivity using a hydrophobic H-Beta catalyst when propanone was used as a solvent to homogenise dihydromyrcene and water (*ca.* 64% conversion after 24 h, with selectivity in excess of 90%). In the absence of the solvent, however, the biphasic system showed a reduced conversion to *ca.* 11% with only 50% overall selectivity.[3]

In this context, exploring the role of ionic liquids as potential solvents for the hydration reaction could be interesting. By making use of the large choice of cations and anions, a *designer solvent* can be created to suit a particular application.[11] We contend that if a reaction mechanism involves the generation of ionic intermediates or transition states, ionic media may well enhance, or at least may govern, the product selectivity for that reaction. We have shown previously that the use of ionic liquids not only influences the product selectivity,[12] but can also change the course of the reaction to form an entirely different product profile.[13] These merits of ionic liquids have been highlighted in many scientific reports, and have been reviewed comprehensively.[14] As the use of the acid form of zeolites in ionic liquid media is restricted due to the possibility of generating homogeneous acid catalysts *via* ion-exchange,[15] we have attempted the direct hydration of dihydromyrcene to dihydromyrcenol using trifluoromethanesulfonic acid (HOTf; CF_3SO_3H) as a catalyst in ionic liquids, and our initial results are presented here.

Experimental

Dihydromyrcene was obtained as a mixture of isomers with 93% purity (NMR and GC analysis) and used as received. Triflic acid (HOTf), methanesulfonic acid (CH_3SO_3H) and phosphotungstic acid ($H_3PW_{12}O_{40}$) were purchased from Aldrich. All

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Table 1 The performance of various ionic liquids and catalysts for the direct hydration of dihydromyrcene[a]

#	Ionic liquid	Catalyst	No. of phases	dhm conv./wt%	Selectivity to dhmOH/wt%
1	None	HOTf	2	3	98
2	$[C_4mim][CH_3SO_3]$	CH_3SO_3H	2	2	100
3	$[P_{6\,6\,6\,14}]Cl$	$H_3PW_{12}O_{40}$	2	23	42
4	$[P_{6\,6\,6\,14}]Cl$	CH_3SO_3H	2	4	25
5	$[P_{6\,6\,6\,2}][OTf]$	CH_3SO_3H	2	24	13
6	$[P_{6\,6\,6\,2}][OTf]$	HOTf	2	33	10
7	$[C_2mim][OTf]$	HOTf	2	2	100
8	$[C_4mim][OTf]$	HOTf	2	3.4	100
9	$[C_4mim][OTf]$	HOTf[b]	2	11	100
10	$[C_6mim][OTf]$	HOTf	3	5	100
11	$[C_8mim][OTf]$	HOTf	3	5.5	100
12	$[C_8mim][OTf]$	HOTf[b]	3	15	100
13	$[C_{16}mim][HSO_4]$	H_2SO_4	1	5	73

[a] Conditions: dhm : water : catalyst = 1 : 10 : 0.2 mol; ionic liquid, 1 g; temperature, 90 °C; 1 h. [b] dhm added at the end after mixing ionic liquid, water and the acid catalyst.

the ionic liquids were prepared using well established published procedures.[16]

In a typical reaction, ionic liquid (1 g), dihydromyrcene (1.4 g; 10 mmol) and water (1.8 g; 100 mmol) were mixed in a round-bottomed flask (25 cm^3) – fitted with a reflux condenser – to which triflic acid (0.3 g; 2 mmol) was added while stirring. The flask was then heated to the desired temperature. In the case of the reaction at 120 °C, the reaction was carried out in an autoclave. After one hour, the reaction mixture was diluted with water (5 cm^3) and extracted with hexane (5×3 cm^3). The hexane layer was dried over anhydrous $MgSO_4$ and the sample was analysed by using a gas chromatograph fitted with a capillary column (25 m, 5% phenylmethylsilicone) and FID. The product identification and verification was carried out by ^1H NMR spectroscopy and by GC-MS. After correcting the GC relative peak area by response factors, the conversion of dihydromyrcene is reported as the percentage of dihydromyrcene reacted without considering its isomerisation. The errors in the yield measurements are estimated to be 3% for GC analysis and ^1H NMR analysis, and the yields were rounded to the nearest 1%.

Results and discussion

During the screening experiments, various acid catalysts were employed *e.g.* methanesulfonic acid, phosphotungstic acid ($H_3PW_{12}O_{40}$), trifluoromethanesulfonic acid, or sulfuric acid. A range of both hydrophilic and hydrophobic ionic liquids $[C_4mim]X$ or $[P_{6\,6\,6\,14}]X$ ($[C_4mim]^+$ = 1-butyl-3-methylimidazolium; $[P_{6\,6\,6\,14}]^+$ = trihexyltetradecylphosphonium; X^- = Cl^-, $[OTf]^-$, $[CH_3SO_3]^-$ or $[HSO_4]^-$) were used. After screening many ionic liquids and ruling out any tetrafluoroborate and hexafluorophosphate ionic liquids due to HF formation under the reaction conditions, it was found that trifluoromethanesulfonate ionic liquids gave the best results and hence were studied in detail. All but one of the ionic liquids were chosen to give biphasic or triphasic reaction conditions, to enable easy separation of the product from the ionic liquid and water by gravity separation. In the case of $[C_6mim]$ or $[C_8mim][OTf]$, these two hydrophobic ionic liquids allowed us to investigate reactions carried out under triphasic conditions. In general, it was observed that the reaction initially proceeded very quickly in under ten minutes, and had reached the ultimate yield after an hour.

Table 1 clearly indicates the superior performance of triflic acid in the imidazolium-based ionic liquids. The reactions when performed using phosphonium-based ionic liquids resulted mainly in the isomerisation of dihydromyrcene [entries 3–6]. In the case of imidazolium triflate ionic liquids, the overall conversion of dihydromyrcene increased as the alkyl chain length on the imidazolium cation increased [entries 7–12]. Although the reaction carried out in $[C_{16}mim][HSO_4]$ was monophasic [entry 13], it was not considered due to lower selectivity to dhmOH. The most pronounced effect was observed when the sequence of the addition of reagents was altered. When the dihydromyrcene was added to a preformed and heated mixture of ionic liquid, water and acid, the yield increased by almost two-fold without compromising the selectivity [entries 9 and 12]. This involved introducing the dihydromyrcene to the reaction mixture at the optimum reaction temperature, and is thought to be in part responsible for the increased yield.

A control experiment carried out without ionic liquid at 90 °C gave only 2.6% of product after one hour. Under similar conditions, control experiments carried in the absence of triflic acid gave no product and suggested (not surprisingly) that the ionic liquids do not catalyse this reaction, and also confirms the fact that there is no corresponding acid left during the syntheses of ionic liquids. Fig. 1 summarises the effect of temperature on the yield of dihydromyrcenol when the reaction was carried out under either biphasic or triphasic conditions. The overall yield of the hydration reaction increases as a function of temperature. It reached a maximum of 11% dhmOH maintaining the total selectivity. The reaction remains selective over a broad range of temperature. When the reactions were complete and above 100 °C, the yield dropped significantly, probably due to the removal of water. However, it should be noted that at 120 °C, a small amount of cdmOH {1-(3,3-dimethylcyclohexyl)ethanol; 0.8%} was also formed and hence the reaction was less selective. The effect of other process variables on the overall yield was investigated, and the key data are summarised in Table 2.

Increasing the water : alkene ratio resulted in enhanced yield and reached a maximum value, beyond which the yield started

Table 2 Effect of reagent concentration on the hydration of dihydromyrcene in [C_4mim][OTf] at 90 °C for 1 h

	Molar equivalents to dihydromyrcene				
Entry	Water	Acid	Ionic liquid	dhmOH (%)	Selectivity (%)
14	5	0.2	0.3	2	100
15	10	0.2	0.3	6	100
16	20	0.2	0.3	5	100
17	10	0.4	0.3	7	100
18	10	1	0.3	5	100
19	10	2	0.3	0	—
20	10	0.2	0.3	6	100
21	10	0.2	1	11	100

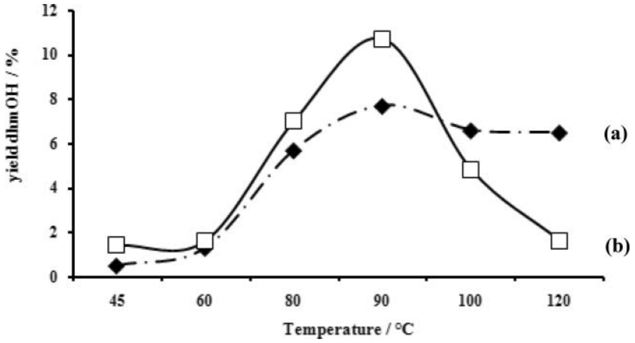

Fig. 1 The effect of temperature on the hydration of dhm using (a) [C_4mim][OTf] or (b) [C_8mim][OTf] ionic liquids to yield a biphasic and triphasic reaction mixture, respectively. Reaction conditions dhm : water : catalyst = 1 : 10 : 0.2 mol; ionic liquid, 1 g; 1 h.

to drop-off (presumably due to the dilution of the acid catalyst). At higher catalyst concentration, a reduced yield to dhmOH was observed suggesting that the reverse, dehydration reaction becomes significant. When the ionic liquid concentration was increased, an accelerated effect was observed. This effect was also well observed in the case of triphasic reaction systems, in which [C_8mim][OTf] ionic liquid was employed. The yield was also observed to increase as the hydrophobicity of the ionic liquid used increased as shown in entries 6 and 12, with the best yield observed in [P_{6662}][OTf]. In the case of [P_{6662}][OTf], this ionic liquid is mostly soluble in the organic phase. This would imply that the reaction proceeds most efficiently in the ionic phase. An increase in the overall reactivity with increasing ionic liquid concentration has also been observed previously.[17] A plausible explanation for this could be due to better solvation and stabilisation of the ionic transition state by the ionic liquid. A more detailed explanation of this was given by Yau and co-workers.[18]

At the end of a typical reaction, the top layer consists of unreacted dihydromyrcene containing dissolved dhmOH (5-10% by ^{1}H NMR), while the bottom layer contains [C_4mim][OTf], water and acid catalyst, along with around 8% product which upon equilibration gets extracted into the organic layer. Thus, the excess of dihydromyrcene can conveniently be distilled out of the product for recycle. Even when the reaction was performed with 10% product added at the beginning of the reaction, there was no significant reduction in the overall yields, suggesting the product does not inhibit the reaction. Under identical conditions, no dehydration of dhmOH was observed, suggesting that in the ionic liquid media, the desired forward reaction is favoured. This can be explained as follows: the presence of water has two effects. Acid catalysed dehydration of dhmOH gives a cation, which can either cyclise to cdmOH or react with water to reform dhmOH. Secondly, water moderates the acidity of the ionic liquid/catalyst combination, making dehydration of dhmOH less likely at the reaction temperatures used. The higher temperatures and anhydrous conditions required to dehydrate alcohols were investigated elsewhere by Atkins *et al.*[19,20]

Conclusions

The direct hydration reaction of dihydromyrcene in ionic liquid media has shown remarkable reactivity and selectivity for the production of dhmOH. As the protonation of a double bond of alkene is believed to be the first step, the resultant carbocation may well be stabilised by ionic liquid media. In [C_8mim][OTf], a hydrophobic ionic liquid, a ternary phase was obtained, while the reaction in [C_4mim][OTf] is biphasic in nature; optimum performance can be achieved by efficient mixing. It should be noted that the reaction remains totally selective over a wide range of process parameters. In the case of biphasic reactions, the product separates out in the dihydromyrcene layer leaving an aqueous ionic liquid layer containing the acid catalyst ready for subsequent runs.

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