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# New enantioselective method for hydration of alkenes using cyclodextrins as phase transfer catalyst

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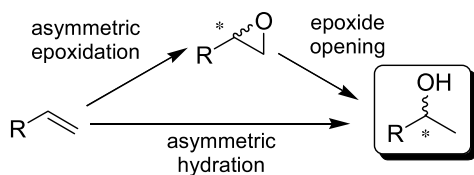
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**Abstract**—A new enantioselective/inverse phase transfer catalysis (IPTC) reaction for the Markovnikov hydration of double bonds by an oxymercuration–demercuration reaction with cyclodextrins as catalysts was disclosed. Moderate ee (up to 32%) and yields (14–60%) were obtained for allylic amines and protected allylic alcohols as starting materials.  
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## 1. Introduction

The enantioselective functionalization of alkenes is extremely important in synthetic organic chemistry and much effort has been expended for the development of new synthetic methods.<sup>1</sup> The epoxidation of allylic alcohols with titanium tartarate complexes (Sharpless) and of styrene-like olefins with porphyrin complexes (Katsuki–Jacobsen) are two prominent ways of asymmetric functionalization of olefins.<sup>1</sup> For asymmetric hydration of a terminal double bond, Sharpless or Jacobsen asymmetric epoxidation followed by hydride opening of the resulting epoxide ring might be a satisfactory solution (Scheme 1). However, the scope of this strategy is limited by the epoxidation step as the asymmetric epoxidation of some olefins cannot be accomplished.<sup>1</sup>



**Scheme 1.** Main synthetic strategies for asymmetric hydration of terminal double bonds.

Alternatively, Markovnikov-like hydration of double bonds may be performed by the classical oxymercuration–

demercuration process. The reaction of mercuric acetate with unsaturated substrates leads to the addition of a hydroxyl group to one side of the double bond and mercury to the other side, via a mercurinium ion intermediate. Reduction of the C–Hg bond with sodium borohydride in aqueous sodium hydroxide yields the alcohol corresponding to a Markovnikov addition of water to the double bond.<sup>2</sup> The enantioselective version of this reaction was achieved by the use of optically active mercuric salts but low yields and moderate ee were observed.<sup>3</sup> Another drawback of this method is that the mercuric salts are not readily available and have to be synthesized. Oxymercuration of (1:1) complexes of olefin– $\beta$ -cyclodextrin is also not a practical proposition.<sup>4</sup>

The present new method of hydration of alkenes using cyclodextrins was developed to overcome difficulties observed with some alkenes where the Sharpless/Jacobsen epoxidation failed to produce enantioselective epoxides.

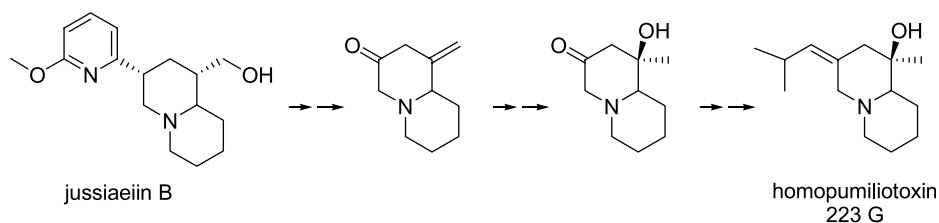
## 2. Results and discussion

To improve synthetic efficiency of the hemisynthesis of homopumiliotoxins<sup>5</sup> from jussiaeines<sup>6</sup> the enantioselective hydration of a double bond was needed (Scheme 2).

Piperidine model compounds were used as starting materials to develop the synthetic procedure. A piperidine ring containing an exocyclic double bond (**1**) was produced from a protected 3-hydroxymethylene piperidine, similar to the starting natural products. The enantioselective

**Keywords:** Reduction; IPTC; Oxymercuration; Cyclodextrin; Hydration.

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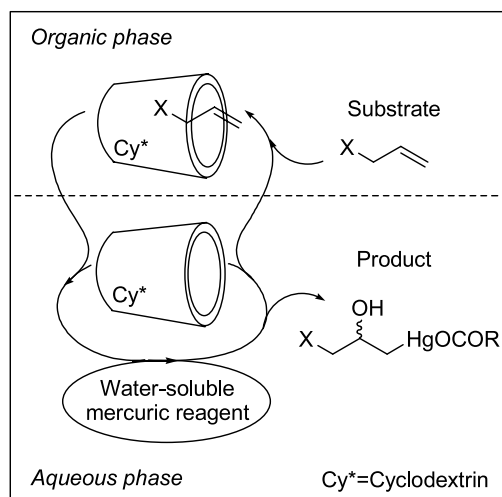
**Scheme 2.** Proposed pathway for the hemisynthesis of homopumiliotoxins from jussiaeines.

epoxidation/hydride opening by Sharpless and Jacobsen/Katsuky catalysts were assayed but both failed.

A new synthetic method for direct enantioselective hydration of the double bond was searched and an inverse phase transfer catalysis (IPTC) process with a chiral catalyst looked promising and therefore, investigated.

PTC reactions have been extensively applied to promote a variety of interfacial reactions with small molecules and several enantioselective methods have been developed (for example, Michael additions and reductions).<sup>4</sup> IPTC reactions—where a lipophilic reactant is transported to the aqueous phase by the catalyst—are still rare and only limited examples have been reported. We now report the first example of an enantioselective IPTC hydration reaction, promoting the hydration of alkenes via an oxymercuration–demercuration process.

The intermediate of the oxymercuration reaction results from the attack of the neutral alkene to the water soluble mercuric salt in the usual solvent system aqueous THF.<sup>8</sup> A two phase PTC reaction would allow to control the contact between the alkene and the mercuric salt, as the former will stay in the organic phase and the latter in the aqueous phase. A neutral PTC catalyst would be the right choice to carry the alkene to the aqueous phase and to create an asymmetric environment where the reaction would take place (Fig. 1).

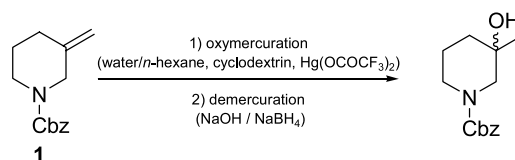


**Figure 1.** Simplified mechanism of an IPTC process mediated by cyclodextrins.

Neutral cyclodextrins were tested as phase transfer catalysts. They are cyclic polymeric sugars with a basket-like structure and are known to behave as chiral phase

transfer reagents.<sup>9</sup> Stereochemical (size of the hydrophobic cavity) and stereoelectronic effects may have strong influence on the behaviour of the cyclodextrin as IPTC catalyst.

Surprisingly or not, enantioselectivity was observed when the oxymercuration–demercuration process of **1** (Scheme 3) was conducted in a two phase water–*n*-hexane (1/1) system with  $\alpha$ - and  $\beta$ -cyclodextrin as IPTC catalyst (Table 1, entries 1,2).



**Scheme 3.** Enantioselective oxymercuration–demercuration of the piperidine derivative **1**.

Following this result, several other alkenes were tested. The alkenes were reacted with different molar quantities of mercuric salts in a water–*n*-hexane mixture (1/1) containing a phase transfer catalyst with formation of oxymercureals. These intermediates were not isolated but submitted to demercuration with alkaline borohydride.

Depending on the demercuration conditions the dihydroxylation product was also formed<sup>10</sup>. The demercuration reaction was conducted under inert atmosphere to increase the yield of monoalcohol product. The resulting alcohols were purified by preparative thin-layer chromatography and the ees were determined by HPLC on chiral stationary phase or by <sup>1</sup>H NMR experiments (using chiral shift reagents or Mosher's esters) (Tables 1 and 2).

Unfunctionalized alkenes like styrene failed to react under the IPTC conditions. However, hydration of allylic amines and allylic protected alcohols was successful and moderate enantioselectivity was observed. As usual, this reaction gave excellent chemoselectivity with formation of the more substituted alcohol.

A study of the reaction conditions was carried out with the allylic alcohol **2** as starting material (Table 2). The use of ultrasound, previously applied to prepare the mercuric salt in situ,<sup>11</sup> increased significantly the reaction rate (entries 1–4). Even though Hg(OCOCH<sub>3</sub>)<sub>2</sub> gives better yields than Hg(OCOCH<sub>3</sub>)<sub>2</sub>, enantioselectivity was only achieved with the latter (entries 5 and 7). The yield of the process was increased using an excess of the mercuric compound (entries 8–11). For this substrate,  $\beta$ -cyclodextrin was a better catalyst (entries 5–9) and higher enantioselectivity

**Table 1.** Reaction conditions, yields and ee for IPTC oxymercuration–demercuration of allylic amines

Substrate	Entry	IPTC catalyst (cyclodextrin)	Time (h)	Yield (%)	ee (%)
<b>1</b>	1	$\beta$	4	58	25 <sup>a</sup>
	2	$\alpha$	4	36	32 <sup>a</sup>
	3	2,6-Di- <i>O</i> -methyl- $\beta$	4	36	18 <sup>a</sup>
	4	Random methyl- $\beta$	4	38	11 <sup>a</sup>
	5 <sup>b</sup>	$\beta$	0.7	60	15 <sup>a</sup>
	6 <sup>b</sup>	$\alpha$	0.7	27	17 <sup>a</sup>
	7 <sup>b</sup>	2,6-Di- <i>O</i> -methyl- $\beta$	0.7	53	11 <sup>a</sup>
	8 <sup>b</sup>	Random methyl- $\beta$	0.7	46	14 <sup>a</sup>
<b>4</b>	9	$\beta$	2	31	25 <sup>a</sup>
	10	$\alpha$	2	40	11 <sup>a</sup>
	11	2,6-Di- <i>O</i> -methyl- $\beta$	2	60	11 <sup>a</sup>
	12	Random methyl- $\beta$	2	43	10 <sup>a</sup>
<b>5</b>	13	$\beta$	3	40	30 <sup>c</sup>
	14	$\alpha$	3	42	11 <sup>c</sup>
	15	2,6-Di- <i>O</i> -methyl- $\beta$	3	25	28 <sup>c</sup>
	16	Random methyl- $\beta$	3	55	31 <sup>c</sup>
<b>6</b>	17	$\beta$	2	30	0 <sup>c</sup>
	18	$\alpha$	2	32	0 <sup>c</sup>
	19	2,6-Di- <i>O</i> -methyl- $\beta$	2	27	6 <sup>c</sup>
	20	Random methyl- $\beta$	2	14	0 <sup>c</sup>

<sup>a</sup> ee calculated by <sup>1</sup>H NMR experiment by addition of chiral shift reagent (Eu(hfpc)<sub>3</sub>).<sup>b</sup> Hg(OCOCH<sub>3</sub>)<sub>2</sub> as oxymercuration agent.<sup>c</sup> ee calculated by <sup>1</sup>H NMR experiment of the Mosher's esters.

was obtained by lowering the temperature of the reaction mixture (entry 12–14). The best conditions were found to be 3 mol equiv of mercuric acetate in H<sub>2</sub>O/*n*-hexane with  $\beta$ -cyclodextrin as IPTC catalyst, at 0 °C with ultrasound conditions. Moderate ees were observed. A non-catalyzed hydration process always operates and reduces the observed ee (entry 15, 19% yield at 0 °C obtained without PTC catalyst).

Allylic amines showed similar behaviour. The optimized

process for **2** was applied to four different allylic amines with four different cyclodextrins as catalysts. It looks like that an aromatic ring must be present in the substrate to achieve enantioselectivity (Table 1, entries 17–20). The best results are always obtained with  $\alpha$ - or  $\beta$ -cyclodextrin. Modified cyclodextrins (2,6-di-*O*-methyl and random methyl cyclodextrins) neither improve yield nor enantioselectivity. *N*-allyl-*N*-benzylmethanamine is an interesting example as the benzyl group may be removed by catalytic hydrogenation.

**Table 2.** Reaction conditions, yields and ee for IPTC oxymercuration–demercuration of allylic alcohol (**2**)

Entry	Mercuric salt	Solvent	Mixing	IPTC catalyst (cyclodextrin)	Temperature (°C)	Time (h)	Yield (%)	ee (%)
1	Hg(OCOCH <sub>3</sub> ) <sub>2</sub> (1 equiv)	H <sub>2</sub> O/THF	Magnetic stirring	—	20	6	41	0 <sup>a,b</sup>
2	Hg(OCOCH <sub>3</sub> ) <sub>2</sub> (1 equiv)	H <sub>2</sub> O/ <i>n</i> -hexane	Magnetic stirring	—	20	24	35	—
3	Hg(OCOCH <sub>3</sub> ) <sub>2</sub> (1 equiv)	H <sub>2</sub> O/THF	Ultra sound	—	20	1.5	52	—
4	Hg(OCOCH <sub>3</sub> ) <sub>2</sub> (1 equiv)	H <sub>2</sub> O/THF	Ultra sound	—	20	1.5	42	—
5	Hg(OCOCH <sub>3</sub> ) <sub>2</sub> (1 equiv)	H <sub>2</sub> O/ <i>n</i> -hexane	Ultra sound	$\beta$	20	0.5	52	0 <sup>a</sup>
6	Hg(OCOCH <sub>3</sub> ) <sub>2</sub> (1 equiv)	H <sub>2</sub> O/ <i>n</i> -hexane	Ultra sound	$\alpha$	20	0.75	38	0 <sup>a</sup>
7	Hg(OCOCH <sub>3</sub> ) <sub>2</sub> (1 equiv)	H <sub>2</sub> O/ <i>n</i> -hexane	Ultra sound	$\beta$	20	0.5	20	16 <sup>a</sup>
8	Hg(OCOCH <sub>3</sub> ) <sub>2</sub> (1 equiv)	H <sub>2</sub> O/ <i>n</i> -hexane	Ultra sound	$\alpha$	20	0.75	18	0 <sup>a</sup>
9	(2 equiv)	H <sub>2</sub> O/ <i>n</i> -hexane	Ultra sound	$\beta$	20	0.75	35	15 <sup>a</sup>
10	(3 equiv)	H <sub>2</sub> O/ <i>n</i> -hexane	Ultra sound	$\beta$	20	0.75	52	15 <sup>a</sup>
11	(4 equiv)	H <sub>2</sub> O/ <i>n</i> -hexane	Ultra sound	$\beta$	20	0.75	52	14 <sup>a</sup>
12	(3 equiv)	H <sub>2</sub> O/ <i>n</i> -hexane	Ultra sound	$\beta$	25	0.70	52	15 <sup>a</sup>
13	(3 equiv)	H <sub>2</sub> O/ <i>n</i> -hexane	Ultra sound	$\beta$	0	0.75	51	25 <sup>a,b</sup>
14	(3 equiv)	H <sub>2</sub> O/ <i>n</i> -hexane	Ultra sound	$\beta$	−75	5	0	—
15	(3 equiv)	H <sub>2</sub> O/ <i>n</i> -hexane	Ultra sound	—	0	0.75	19	—

<sup>a</sup> ee calculated by <sup>1</sup>H NMR experiment by addition of chiral shift reagent (Eu(hfpc)<sub>3</sub>).<sup>b</sup> ee calculated by HPLC on chiral stationary phase.

### 3. Experimental

Melting points were recorded on a Reichert-Thermovar hot stage apparatus and are reported uncorrected. Infrared (IR) spectra were recorded on Perkin Elmer Spectrum 1000 as KBr pellets or as film over NaCl plates.

Proton and carbon nuclear magnetic resonance spectra ( $^1\text{H}$  and  $^{13}\text{C}$  NMR) were recorded on Bruker ARX (400 MHz) spectrometer. Chemical shifts are expressed in ppm, downfield from TMS ( $\delta=0$ ) as an internal standard;  $J$  values are given in Hz. The exact attribution of NMR signals was preformed using two dimensional NMR experiments.

Mass spectra were taken with a Micromass GC-TOF (GCT) mass spectrometer. Microanalyses were performed on a Thermo Finnigan-CE Instruments Flash EA 1112 CHNS series microanalyser. The analyses were performed by the analytical services laboratory of REQUIMTE.

All reagents and solvents were reagent grade and were purified and dried by standard methods.

Organic extracts were dried over anhydrous sodium sulfate. Analytical thin-layer chromatography was performed on Merck Kieselgel 60, F254 silica gel 0.2 mm thick plates. For preparative TLC (PTLC) Merck Kieselgel 60, F254 silica gel 0.5, and 1 mm thick plates (20×20 cm) were used. Column chromatography was eluted over Merck Kieselgel 60 (240–400  $\mu\text{m}$ ) silica gel.

HPLC was performed on a system equipped with a Dionex P680 pump, UVD340S detector and Carolcel OD column.

#### 3.1. Synthesis of non commercial olefins

**3.1.1. 3-Methylenepiperidine-1-carboxylic acid benzyl ester (1).** 3-Hydroxymethylenepiperidine was treated with benzylchloroformate by standard method<sup>12</sup> to obtain the Cbz derivative: yellow oil, IV:  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ) 3436, 1678;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  7.40–7.26 (5H, m, ArH), 5.12 (2H, s,  $\text{CH}_2$ benzylic), 3.98–3.78 (2H, m,  $\text{N}(\text{Cbz})\text{C}_\alpha\text{H}_{\text{eq}}$ ), 3.48 (2H, m,  $\text{CH}_2\text{OH}$ ), 3.09–2.93 (2H, m,  $\text{N}(\text{Cbz})\text{C}_\alpha\text{H}_{\text{ax}}$ ), 1.81–1.65 (3, m,  $\text{CHCH}_2\text{OH}$ ,  $\text{N}(\text{Cbz})\text{C}_\beta\text{H}_{\text{eq}}$ ,  $\text{N}(\text{Cbz})\text{C}_\gamma\text{H}_{\text{eq}}$ ), 1.45 (1H, m,  $\text{N}(\text{Cbz})\text{C}_\beta\text{H}_{\text{ax}}$ ), 1.26–1.19 (1H, m,  $\text{N}(\text{Cbz})\text{C}_\gamma\text{H}_{\text{ax}}$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  155.0, 136.8, 128.6–126.9 (5C), 67.0, 64.3, 46.5, 44.8, 33.0, 26.8, 24.0. This compound was tosylated by standard method<sup>13</sup> to obtain the tosylated derivative: white solid, mp 60–62 °C, IV:  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ) 1694, 1354;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  7.76 (2H, d,  $J=7.48$  Hz, HTs), 7.38–7.26 (8H, m, ArH), 5.10 (2H, s,  $\text{CH}_2$ benzylic), 3.96–3.84 (4H, m,  $\text{N}(\text{Cbz})\text{C}_\alpha\text{H}_{\text{eq}}$ ,  $\text{CH}_2\text{OTs}$ ) 2.85 (1H, m,  $\text{N}(\text{Cbz})\text{C}_\alpha\text{H}_{\text{ax}}$ ), 2.68–2.60 (1H, m,  $\text{N}(\text{Cbz})\text{C}_\alpha\text{H}_{\text{ax}}$ ), 2.44 (3H, s,  $\text{CH}_3$ ), 1.89–1.84 (1H, m,  $\text{CHCH}_2\text{OTs}$ ), 1.75 (1H, m,  $\text{N}(\text{Cbz})\text{C}_\gamma\text{H}_{\text{eq}}$ ) 1.66–1.61 (1H, m,  $\text{N}(\text{Cbz})\text{C}_\beta\text{H}_{\text{eq}}$ ), 1.45–1.42 (1H, m,  $\text{N}(\text{Cbz})\text{C}_\beta\text{H}_{\text{ax}}$ ), 1.26–1.21 (1H, m,  $\text{N}(\text{Cbz})\text{C}_\gamma\text{H}_{\text{ax}}$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  155.2, 144.9, 136.7, 132.7, 129.9–127.9, 71.6, 67.1, 46.3, 44.3, 35.3, 26.6, 23.9, 21.6. Anal. Calcd for  $\text{C}_{21}\text{H}_{25}\text{NO}_5\text{S}$ : C, 62.51; H, 6.25; N, 3.47; S, 7.95 found C, 62.15; H, 6.17; N, 3.41; S, 7.75. This compound was treated with potassium *t*-butoxide (1.1 equiv) in DMSO (1.6 M) under inert atmosphere at room temperature for 2 h. Then the reaction

was quenched with water and extracted with ethyl ether, the organic phase dried and concentrated to dryness under vacuum. The residue was chromatographed by column chromatography with ethyl acetate–*n*-hexane (1/2). Compound (1)<sup>14</sup> was obtained as a colourless oil, IV:  $\nu_{\text{max}}$  ( $\text{cm}^{-1}$ ) 1698, 1656;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  7.36–7.28 (5H, m, ArH), 5.13 (2H, s,  $\text{CH}_2$ benzylic), 4.84–4.77 (2H, m,  $\text{CCH}_2$ ), 3.96 (2H, s,  $\text{N}(\text{Cbz})\text{CH}_2\text{C}$ ), 3.52 (2H, t,  $J=5.6$  Hz,  $\text{N}(\text{Cbz})\text{CH}_2\text{CH}_2$ ), 2.27 (2H, t,  $J=5.6$  Hz,  $\text{CCH}_2\text{CH}_2$ ), 1.64 (2H, m,  $\text{CCH}_2\text{CH}_2$ );  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  155.1, 142.4, 136.9, 128.4–127.8, 110.2, 66.9, 50.5, 44.2, 32.6, 26.5.

**3.1.2. *N*-allyl-*N*-benzylmethylamine (4).**<sup>15</sup> To *N*-benzylmethylamine and NaH (1.1 equiv) in dry DMF (0.8 M) at 0 °C allylbromide (1.1 equiv) was added. The reaction was completed in 1 h at room temperature. Water was added and the mixture extracted 3× with ethyl acetate, the organic phases dried and concentrated to dryness under vacuum. Compound (4) was obtained as a colourless oil (76%),  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ) 7.36–7.26 (5H, m, ArH), 5.92 (1H, m, CH), 5.17 (2H, m,  $\text{CH}_2\text{CH}$ ), 3.50 (2H, s,  $\text{CH}_2$ benzylic), 3.03 (2H, d,  $J=6.3$  Hz,  $\text{NCH}_2\text{CH}$ ), 2.19 (3H, s,  $\text{NCH}_3$ ).

**3.1.3. *N*-allyl-*N*-cyclohexylmethylamine (6).**<sup>16</sup> This compound was prepared from cyclohexylmethylamine by the same procedure as compound (4). Compound (6) was purified by extraction to an acidic phase (HCl 10%), neutralization and recovered with dichloromethane. By evaporation of the dried organic phase the pure compound was obtained as a colourless oil (79%),  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ) 5.84 (1H, m,  $\text{CHallyl}$ ), 5.13 (2H, m,  $\text{CH}_2\text{CHallyl}$ ), 3.10 (2H, d,  $J=6.0$  Hz,  $\text{NCH}_2\text{CH}$ ), 2.37 (1H, m,  $\text{NCH}$ ), 2.22 (3H, s,  $\text{NCH}_3$ ), 1.78 (4H, m, H-cyclohexyl), 1.61 (1H, m, H-cyclohexyl), 1.21 (4H, m, cyclohexyl), 1.07 (1H, m, cyclohexyl).

#### 3.2. Oxymercuration–demercuration reactions

**Standard homogeneous conditions.** To 10 ml of  $\text{H}_2\text{O}$ –THF mixture (1/1) the mercuric reagent was added followed by the addition of the alkene (0.4 mmol). After alkene consumption, 4 ml of NaOH (3 M) were added under inert atmosphere followed by the addition of  $\text{NaBH}_4$  (1 equiv) in 2 ml of NaOH (3 M). The mixture was stirred until complete flocculation of  $\text{Hg}^0$ . The THF was evaporated, the aqueous phase extracted with ethyl acetate, the organic phase dried and concentrated to dryness under vacuum. The resulting alcohol was purified by plate chromatography.

**Heterogeneous conditions.** The alkene (0.4 mmol) was dissolved in 5 ml of *n*-hexane followed by the addition, at the pretended temperature, of cyclodextrin (0.04 mmol), 5 ml of water and the mercuric reagent. After alkene consumption, 4 ml of NaOH (3 M) were added under inert atmosphere followed by the addition of  $\text{NaBH}_4$  (1 equiv) in 2 ml of NaOH (3 M). The mixture was stirred until complete flocculation of  $\text{Hg}^0$  and then extracted with ethyl acetate, the organic phase dried and concentrated to dryness under vacuum. The resulting alcohol was purified by plate chromatography.

By the above procedures the following compounds were prepared. The spectral data were in accordance with



literature: 1-benzyloxypropan-2-ol (**3**),<sup>17</sup> 1-(benzylmethylamino)-propan-2-ol,<sup>18</sup> 1-imidazol-1-yl-propan-2-ol,<sup>19</sup> 3-hydroxy-3-methylpiperidine-1-carboxylic acid benzyl ester.<sup>20</sup>

**3.2.1. 1-(Cyclohexylmethylamino)-propan-2-ol.** The alcohol was obtained as a colourless oil, <sup>1</sup>H NMR (CDCl<sub>3</sub>) 3.71 (1H, m, CHOH), 2.82 (1H, br l, OH), 2.38–2.34 (2H, m, CH<sub>2</sub>N), 2.25 (3H, s, NCH<sub>3</sub>), 2.22 (1H, m, NCH), 1.80 (3H, m, H-cyclohexyl), 1.65 (2H, m, H-cyclohexyl), 1.61 (1H, m, H-cyclohexyl), 1.33–1.01 (5H, m, cyclohexyl), 1.11 (3H, d, *J*=6.1 Hz, CH<sub>3</sub>CH); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 63.5, 62.4 (CHOH, CHN), 61.2 (CH<sub>2</sub>N), 37.2 (CH<sub>2</sub>N), 29.7, 29.3, 28.2, 26.3, 26.0, 19.9 (CH<sub>3</sub>C).

### 3.3. Methods for ee determination

*By the addition of a chiral shift reagent.* To a CDCl<sub>3</sub> solution of the alcohol ( $4.7 \times 10^{-2}$  mmol), Eu(hfpc)<sub>3</sub> (0.2 equiv) was added and the resulting solution was analysed by <sup>1</sup>H NMR.

*By HPLC on a chiral column.* A mixture of **2** and **3** was eluted with *n*-hexane–isopropanol (99/1) resulting on the retention times: 14 min for **2**, and 38, 42 min for each enantiomer of **3**.

*By formation of Mosher's esters.* The Mosher's esters were prepared by the addition of 1 equiv of Mosher's acid chloride to the alcohol in a CH<sub>2</sub>Cl<sub>2</sub> solution in the presence of base (K<sub>2</sub>CO<sub>3</sub>). The diastereomer pair was purified by thin-layer chromatography and analysed by <sup>1</sup>H NMR.

## 4. Conclusions

A completely new and simple method of asymmetric hydration of terminal double bonds of allylic amines and protected allylic alcohols was discovered. The readily available α- and β-cyclodextrins were able to induce enantioselectivity to the hydration method via an IPTC process. Moderate yields and ees were obtained. Results were found to be dependent on the starting alkene and on reaction conditions. Although there were previously reported methods for enantioselective hydration of allylic alcohols, no equivalent method was up-to-date available for the direct enantioselective functionalization of allylic amines. The present method was able to induce enantioselectivity to the direct hydration of allylic amines. Further developments to improve this new method (yields and enantioselectivity) are underway and will be reported.

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