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Heterogenisation of ketone catalysts within mesoporous supports for asymmetric epoxidation†

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The synthesis of the first mesoporous silica (150 Å) anchored carbohydrate-derived chiral ketone is described. This new heterogeneous catalyst has been shown to be effective in the asymmetric epoxidation of olefins by oxone. The heterogeneous ketone catalyst has comparable activity to that of its homogeneous counterpart and returned enantioselectivities up to 90% *e.e.*

Introduction

Stereoselective catalytic transformations are of central importance in modern organic synthesis. Homogenous asymmetric catalysis affords many effective transformations[1] accelerating reactions with minimal energy input, however the removal of the catalyst can be challenging resulting in inefficient purifications and catalyst recovery and recycling. Separation of catalysts and reagents by heterogenisation overcomes some of these difficulties by offering simplified product isolation.[2] Furthermore, heterogenisation can facilitate implementation of continuous flow processes.[3] With respect to selectivity, it has been established that by anchoring a homogeneous catalyst within the pores of a suitable silica support reactivities and enantioselectivities can be conserved or even enhanced.[4] Mesoporous silicas, such as the M41S (*e.g.* MCM-41), can be synthesised with structurally ordered nanopores in a range sizes, with narrow pore size distributions. These solid supports can act as scaffolds for catalysis when modified with homogeneous catalysts and influence the yield, configuration or constitution of the final products.[5]

Asymmetric alkene epoxidation is one of the most useful synthetic transformations in the preparation of chiral building blocks for the synthesis of biologically active molecules.[6] Non racemic chiral ketones, which generate chiral dioxiranes *in situ* in the presence of an oxidising agent such as oxone, have been well documented to effectively promote asymmetric epoxidations.[7] Early reports from the Shi group described fructose-derived ketone **1a** as a successful epoxidation catalyst for *trans* 1,2-disubstituted and trisubstituted olefins (Fig. 1).[8] Subsequent studies from the same group showed that oxazolidinone-bearing ketone (catalyst **1b**) catalysed the epoxidation of a wide range of olefins with high enantioselectivities[9] and the lactam ketone **1c** could be utilised to epoxidise a variety of 1,1-disubstituted terminal olefins using oxone as the oxidant, giving up to 88% *e.e.*[10] However, it is known that these chiral ketones can undergo undesired Baeyer–Villiger side reactions leading to their inactivation, necessitating relatively high catalyst loadings (typically 20–30 mol%).[11]

It was envisaged that heterogenisation of optically pure chiral ketones **1b** within the interior of mesoporous silicas would afford asymmetric epoxidation catalysts with the potential benefits of ease of product separation, and catalyst recovery. Additionally, the environment within the pore structure could influence the reactivity and selectivity of the heterogeneous catalyst (Fig. 2). Indeed, Armstrong *et al.* showed that immobilisation of an α-fluorotropinone on silica gave a material with comparable catalytic efficiency and selectivity to the homogeneous system.[12]

Herein we describe the first successful application of a novel heterogeneous system based on an oxazolidinone catalyst to the asymmetric oxidation of a range of conjugated olefins to their corresponding epoxides in high yields and selectivities.

Results and discussion

Our study commenced by modifying a homogeneous chiral ketone with a linker that terminated in a suitable functionality for attachment on to a solid support, under immobilisation

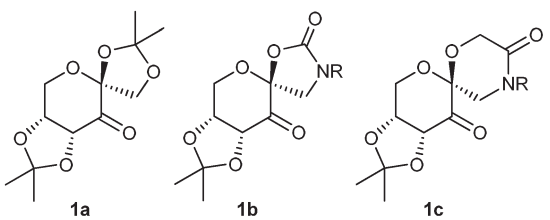

Fig. 1 Shi's chiral ketone catalysts

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† Electronic supplementary information (ESI) available: ^{1}H and ^{13}C NMR of compounds **2–7**, ^{1}H NMR and HPLC of epoxides and ^{13}C and ^{29}Si CP-MAS NMR of silicas **8a–10a**. See DOI: 10.1039/c2ra21837b

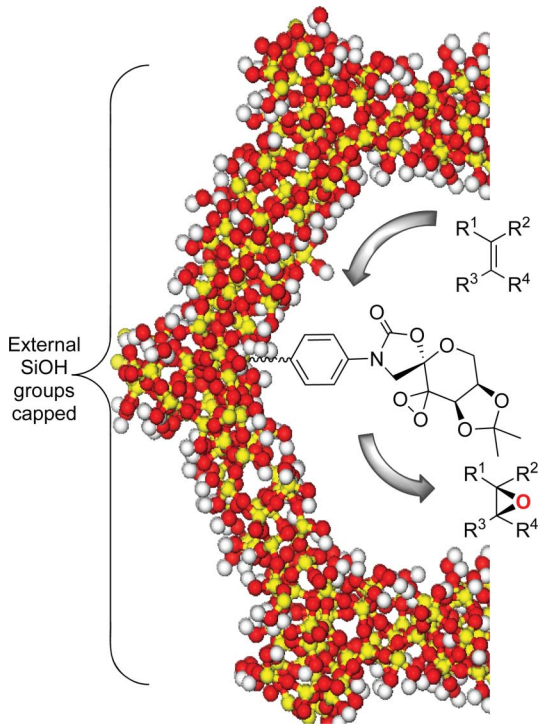
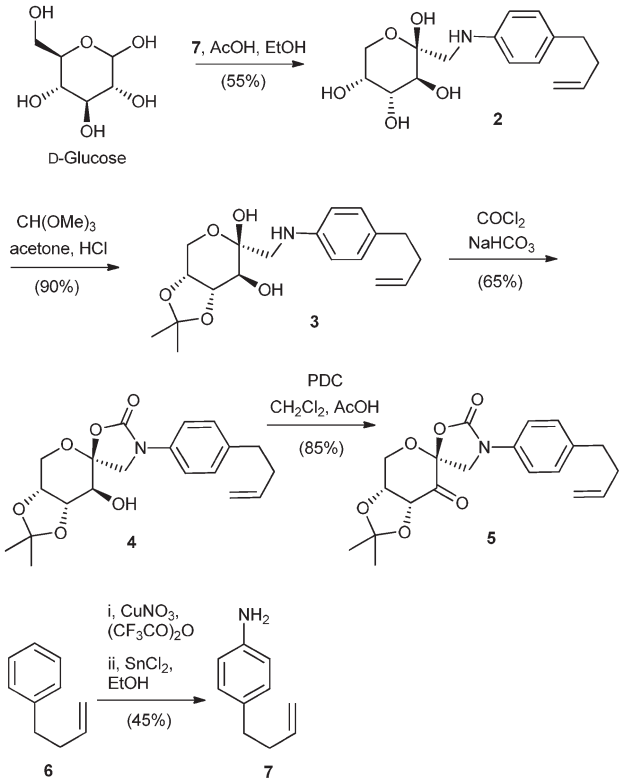


Fig. 2 Representation of heterogeneous epoxidation



Scheme 1 Synthesis of chiral ketone catalyst-linker conjugate **5**.

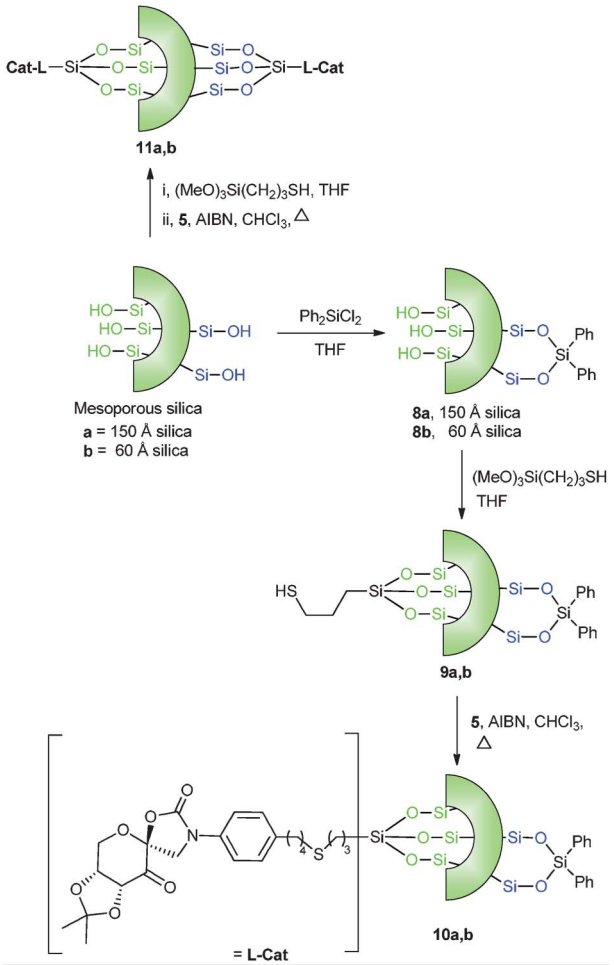
conditions compatible with the functionality present in the catalyst (Scheme 1).[12] In the present case a terminal alkene linker was selected, which would be coupled to a thiol functionalised support using a thiyl radical coupling process.[13] The synthesis of the catalyst-linker conjugate **5** was adapted from the method of Shi,[14] commencing with the Amadori rearrangement of D-glucose and aniline **7** to produce the tetraol **2**.[15] Ketalisation, oxazolidinone formation and oxidation of the resulting secondary alcohol **4** provided the desired ketone **5** with the appended linker.

In order to prepare the supported catalyst, dry calcined (T = 550 °C) mesoporous silica was first reacted with dichlorodiphenylsilane with the objective to preferentially cap the more accessible Si–OH functionality following a method previously described for capping external sites (Scheme 2).[16,17] This left the surface of the inner walls of the mesoporous silicas free for catalyst attachment, thus confining the ketone predominately within its interior pores. With the intent of securing the catalyst to the internal siloxyl functionality of the support, the silica was then reacted with 3-mercaptopropyl trimethoxysilane to provide thiol functionalisation ready for radical mediated addition to the olefin moiety of the ketone **5**.

Refluxing the thiol modified silica **9** in a $CHCl_3$ solution of catalyst **5** and AIBN in the dark completed the heterogenisation of the ketone catalyst.[12] Elemental analysis of both silicas **9a** and **10a** showed clear incorporation of the thiol, and from nitrogen analysis of **10a** the loading of the catalyst was estimated to be 0.20 mmol g^{-1} (entries 3 and 4, Table 1). IR spectroscopy confirmed the presence of the ketone (ν_{CO} 1770 cm^{-1}).

Confirmation of the immobilisation of the ketone catalyst within the pores of the supports, not just on the more accessible outer surface sites, came from nitrogen adsorption isotherms. Firstly, there was a clear drop in BET surface area from 263 m^2 g^{-1} for the underivatised mesoporous silica (entry 1, Table 1) to 210 m^2 g^{-1} after heterogenisation of the catalyst (entry 4, Table 1). The total pore volume showed no decrease after capping, when the linker was attached there was a small decrease in volume, however when the catalyst was attached there was a large decrease from 0.152 mL g^{-1} to 0.122 mL g^{-1}. These data provide strong evidence for the anchoring of the ketone catalyst within the pores of the support.

Evidence to support covalent functionalisation of the mesoporous framework was provided by solid-state NMR spectroscopy; ^{29}Si CP-MAS (cross-polarized magic angle spinning) NMR spectra of the silica **8a** showed three signals: Q_2 signals (−92 ppm) derived from a low level of silandiol groups ($Si(OH)_2$), Q_4 signals (−102 ppm) from the siloxanes ($Si(OSi)_4$) and stronger Q_3 signals (−111 pm) from the silanol groups (Si–OH) (Fig. 3). The presence of Si environments due to the capping was below the detection levels of the experiment. The ^{29}Si NMR spectrum of silica **9a** containing the mercaptopropyl linker showed a decreased relative intensity of the Q_3 signal compared to silica **8a** and Q_2 almost disappeared, providing a clear indication that the 3-mercaptopropyl trimethoxysilane reacted with the available Si–OH groups. The presence of three new resonances in the ^{29}Si NMR spectrum of **9a** (−47 ppm T_1,



Scheme 2 Derivatisation of mesoporous silica.

functionality rather than disulfides or higher sulfur oxidation states. The ^{29}Si CP-MAS NMR spectra for the heterogeneous catalyst **10a** did not display any new signals as anticipated, whereas the ^{13}C NMR showed characteristic signals for the immobilised catalyst consistent with the presence of aromatic, C–O and aliphatic carbon signals. The ketone carbon signal was too weak to be observed due to its high anisotropic environment and splitting between a centre band and spinning sidebands under experimental conditions. However, the presence of the chiral ketone was strongly supported by IR spectroscopy and the ability of the modified silica to mediate the asymmetric epoxidation of olefins.

To enable us to probe the influence of pore size and application of the capping protocol upon the reactivity and selectivity of the heterogeneous chiral ketone catalysts, two uncapped silica supported catalysts **11a,b** were also prepared from KG-60 Å and KG-150 Å (Scheme 2).‡ The epoxidation of the chromene **12** was selected as a test reaction and the four heterogeneous catalysts, **10a**, **10b**, **11a** and **11b** were evaluated under these conditions. Our preliminary results (Table 2, entries 1–4) were obtained with low catalyst loadings (typically 2.5 mol%). Interestingly, a substantial drop in *e.e.* was observed for the epoxidations conducted in the presence of the heterogenised catalysts prepared without capping (entries 2 and 4, Table 2) relative to the capped catalysts (entries 1 and 3, Table 2). These results indicate that capping the more accessible Si–OH functionalities is a significant factor in gaining high enantioselectivities in this system, which could be due to confinement of the catalyst within the pores of the silica. It was possible that without capping there was a separate, unselective background epoxidation reaction occurring.[17]

Table 1 Physical data supporting heterogenisation of the catalyst into the internal pores of 150 Å silica

				Elemental analysis by combustion (%)				
Entry	Catalyst sample	S_{BET}/m^2 g^{-1}	Pore volume[a]/mL g^{-1}	C	H	N	S	Loading[b]/mmol g^{-1}
1	SG-150 Å silica	263	0.156	—	—	—	—	—
2	**8a**	266	0.158	—	—	—	—	—
3	**9a**	262	0.152	1.97	1.19	<0.10	2.78	—
4	**10a**	210	0.122	8.39	1.53	0.29	2.05	0.20

[a] Total pore volume was measured at P/Po = 0.410. [b] Loading based on N%.

(RSi(OSi)–(OH)$_2$), −57 ppm T$_2$, (RSi(OSi)$_2$–(OH)), −67 ppm, T$_3$, (RSi(OSi)$_3$)) further confirmed the incorporation of organic silanes on the silica surface.

Fig. 4 shows the ^{13}C CP-MAS NMR spectrum of **9a**, with three resonances (27.9, 22.8, 10.6 ppm) corresponding to the CH_2SH, CH_2 and CH_2Si methylene carbons of the propyl linker respectively. Oxidation of surface thiol groups to disulfides may occur in air under ambient conditions, however, the chemical shift data are consistent with the presence of thiol

Our results indicated that the KG-150 Å (**10a**) gave better conversions which may be due to enhanced site isolation of the catalyst molecules within this larger polymeric framework. Subsequent optimisation showed that using the KG-150 Å

‡ KG-60 Å: particle size 70-230 mesh; 63-200 μm; pore size 0.8 cm^3 g^{-1}; pore volume 60 Å; surface area 500 m^2 g^{-1}; pH 6.0-7.5 (10% in H_2O); bp 2230 °C; mp 1600 °C. KG-150 Å: particle size 100-200 mesh; 75-150 μm; pore size 1.15 cm^3 g^{-1}; pore volume 150 Å; surface area 300 m^2 g^{-1}; pH 7.0 (5% in slurry); bp 2230 °C; mp 1600 °C.

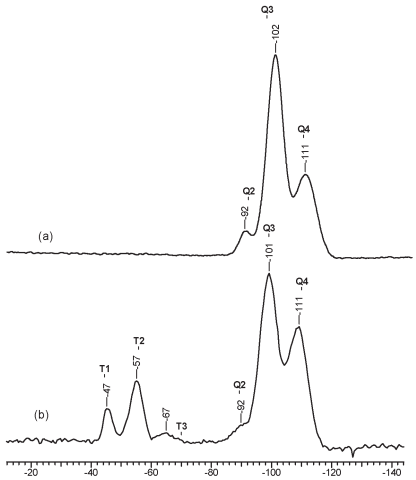


Fig. 3 ^{29}Si CP-MAS NMR of (a) silica **8a** (b) silica **9a**.

mesoporous silica with the more accessible sites capped (catalyst **10a**) with loadings of 20 mol% (Table 2 entry 5) gave excellent conversions in reasonable timescales and therefore all ensuing reactions were performed under these conditions. Comparing the heterogeneous catalyst **10a** to its homogeneous counterpart **5** (Table 2, entries 5 and 6) showed that the heterogeneous ketone gave improved conversion, with only a modest drop in *e.e*. This conversion required 20 mol% of the heterogeneous catalyst and was almost complete within 6 h, whereas but the homogeneous catalyst used 25 mol% and had not reached completion after 24 h. This was reflected in the improved turnover number (TON = moles of product/moles of catalyst). The conversion of *trans*-stilbene by heterogeneous

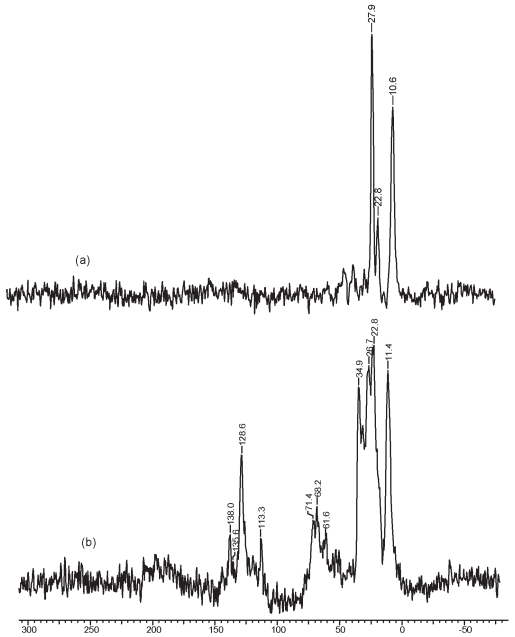
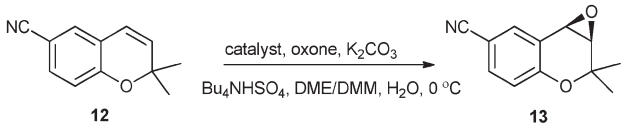


Fig. 4 ^{13}C CP-MAS NMR of (a) silica **9a** (b) catalyst **10a**.

Table 2 Effect of heterogenisation and capping on ketone catalyst



12 13

Entry	Catalyst	Pore size	Capping	conv (%)	*e.e*. (%)	TON
1	**10a**	150	✓	23[a]	65	9.2
2	**11a**	150	x	20[a]	32	8
3	**10b**	60	✓	16[a]	69	6.4
4	**11b**	60	x	8[a]	32	3.2
5	**10a**	150	✓	96[b]	88	4.8
6	**5**	—	—	80[c]	93	3.2

[a] Catalyst (2.5 mol%), oxone (2.7 equiv.), K_2CO_3 (10.5 equiv.), 0 °C to rt, 24 h. [b] Catalyst (20 mol%), oxone (2.7 equiv.), K_2CO_3 (10.5 equiv.), 0 °C to rt, 6 h. [c] Catalyst (25 mol%), oxone (2.7 equiv.), K_2CO_3 (10.5 equiv.), 0 °C to rt, 24 h.

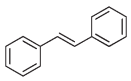
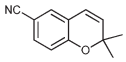
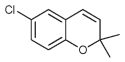
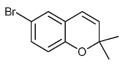
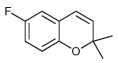
epoxidation was also comparable to that attained by the homogeneous equivalent, again with a small drop in enantioselectivity (homogeneous 74%, 93% *e.e*.; heterogeneous 70%, 86% *e.e*.).

The heterogeneous catalyst **10a** was employed in the epoxidation of a range of olefins and the conversions and *e.e.* were measured (Table 3). In all cases the epoxidation reactions were very efficient giving high conversions and good isolated yields. A major advantage of the heterogeneous catalyst was the ease of purification. Unlike its homogeneous equivalent which required separation from the product by chromatography, the supported catalyst was removed by simple filtration. The TON in all reactions ranged from 3.5 to 5.0 indicating that the heterogeneous catalyst was as effective as its homogeneous equivalent. The addition of the oxone was performed as described by Shi involving the simultaneous and separate addition of aqueous oxone and aqueous K_2CO_3 at 0 °C to buffer the effect of $KHSO_4$ and ensure that a mildly basic pH was maintained through the reaction.[18] With slower addition times, the *e.e.* values were typically higher whilst retaining good conversions. *trans*-Stilbene gave a slightly lower conversion than expected, which was attributed to its insolubility in the mixed aqueous/organic solvent medium.

The choice of epoxidation conditions has been noted to be substrate dependant[11] and a modified procedure where oxone and $NaHCO_3$ were added as solids proved advantageous raising the conversion to 70%.

The Shi catalysts are well documented to undergo an undesirable Baeyer–Villiger side reaction resulting in their deactivation, thereby impeding a high number of catalytic cycles. Therefore the recyclability of the heterogeneous catalyst **10a** was investigated by the epoxidation of the chromene substrate **12**. It was observed that after two cycles there was only a minor reduction in catalytic ability and enantioselectivity. However, by the third cycle a significant drop in conversion was noted and a small drop in enantioselectivity due to the increased significance of the background reaction

Table 3 Epoxidation data for a range of olefins

Entry	Substrate	Add. time (h)[c]	Conv.(%)[d]	Yield[e] [Sel][f](%)	*e.e.*[g] (%)	Config[j]
1[a]		6[h]	100	79 [79][i]	90	(1*S*,2*R*)[20]
2[b]		3.5[h]	70	63 [90]	86	(*R*,*R*)[21]
3[a]		6	96	93 [97]	88	(3*R*,4*R*)[22]
4[a]		6	93	82 [88]	80	(3*R*,4*R*)[22]
5[a]		6	75	65 [86]	79	(3*R*,4*R*)[23]
6[a]		6	93	80 [86]	83	(3*R*,4*R*)[22]
7[a]		6	90	77 [86]	81	(3*R*,4*R*)[20]
8[a]		4	100	75 [75]	68	(1*R*,2*S*)[24]
9[a]		6	100	83 [83]	18	—[k]

[a] Typical procedure: olefin (0.2 mmol), silica supported ketone catalyst **10a** (200 mg, 0.04 mmol, 20 mol%, based on a calculated loading of 0.20 mmol g^{-1}), K_2CO_3 (0.84 M in aq. Na_2EDTA (4×10^{-4} M), 2.52 mL, 2.11 mmol, 10.5 equiv.), oxone (0.212 M in aq. Na_2EDTA (4×10^{-4} M), 2.52 mL, (0.53 mmol, 2.7 equiv.), Bu_4NHSO_4 (0.0015 mmol) in DME : DMM (3 : 1, v/v, 3.0 mL) and K_2CO_3–AcOH buffer (0.1 M, pH 9.3, 2.0 mL) at 0 °C. [b] Olefin (0.1 mmol), silica supported ketone catalyst **10a** (100 mg, 0.02 mmol, 20 mol%, based on a calculated loading of 0.20 mmol g^{-1}), $NaHCO_3$ (3.1 mmol, 30 equiv.), oxone (1.0 mmol, 10 equiv.), in DME : DMM (3 : 1, v/v, 1.5 mL) and Na_2EDTA buffer (4×10^{-4} M, 1.0 mL) at 0 °C. [c] Time allowed for complete simultaneous addition of the K_2CO_3 and oxone. [d] The conversions were determined by ^1H NMR. [e] Yields of isolated products. [f] (Yield/conv.) × 100. [g] Enantioselectivites were determined by chiral HPLC using a Chiralcel ODH or a Chiralcel OBH column. [h] Total reaction time 24 h. [i] Product isolated as a mixture of epoxide (54%) and diol (46%). [j] The absolute configurations were determined by comparing HPLC retention times and orders of elution with reported values. [k] The absolute configuration was not determined.

(racemic epoxidation by oxone alone) which becomes more apparent at lower conversions.[19]

Conclusion

In summary, we have synthesised and heterogenised a chiral ketone catalyst on the inner walls of mesoporous silica supports. Capping of the more accessible siloxyl groups, prior to catalyst immobilisation, was found to be advantageous in terms of enantioselectivities for the epoxidation of a number of olefin substrates. The heterogeneous catalyst has been applied to the epoxidation of a range of olefins with good conversions and enantioselectivities.

Experimental

General

All reagents were purchased from Sigma–Aldrich and used without further purification. All reactions were performed in dry glassware and in an atmosphere of nitrogen. Dichloromethane was dried by distillation from CaH_2. ^1H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ solution using Bruker AC300, AV300 (300 and 75 MHz respectively) or Bruker DPX400 (400 and 100 MHz respectively) spectrometers. Chemical shifts are reported in δ units using $CHCl_3$ as an internal standard (δ 7.27 ppm ^1H, δ 77.00 ppm ^{13}C respectively). Infrared spectra were recorded on a Nicolet 380 spectrometer fitted with a Diamond platform, as solids or neat liquids. Electrospray mass spectra were obtained using a Micromass platform mass analyser with an electrospray ion source. Chiral HPLC separations were performed on a Agilent 1120 Compact LC using a Chiralcel ODH or OBH column eluting with isopropanol : hexane mixtures monitored by UV detection at 220 or 254 nm. Elemental analyses were performed at Medac Ltd, Chobham Business Centre, Surrey, UK. BET-Nitrogen asorption isotherms were obtained with a Gemini 2375 volumetric gas adsorption apparatus (micromeritics) at 77 K.

(2*R*,3*S*,4*R*,5*R*)-2-(((4-(But-3-en-1-yl)phenyl)amino)methyl)tetrahydro-2*H*-pyran-2,3,4,5-tetraol (**2**). A solution of D-glucose (3.00 g, 16.7 mmol)

and aniline **7** (2.95 g, 20.0 mmol, 1.2 equiv.) in acetic acid (40.0 mg, 0.67 mmol, 0.04 equiv.) and H_2O (1.0 mL) was heated at 95 °C (bath temp.). After 10 min the reaction was dark red and after 1 h had formed a dark red solid. The heat was removed, EtOH (1.0 mL) added, and the reaction allowed to cool with stirring for 30 min. The reaction was then diluted with Et_2O and the resultant precipitate removed by filtration. The crude product remaining in the filtrate was purified by silica gel column chromatography eluting with 2 to 5% MeOH : CH_2Cl_2. The combined solids were dried *in vacuo* to give the title compound as an off white solid (2.58 g, 8.35 mmol, 50%). IR ν_{max}(neat)/cm^{-1} 3345 (s), 1616 (m); ^1H NMR (DMSO-d_6, 300 MHz): δ 6.89 (d, J = 7.9 Hz, 2H), 6.55 (d, J = 7.9 Hz, 2H), 5.69–5.93 (m, 1H), 5.47 (s, 1H), 5.01 (d, J = 17.2 Hz, 1H), 4.94 (d, J = 9.1 Hz, 2H), 4.24–4.56 (m, 3H), 3.84 (d, J = 12.1 Hz, 1H), 3.71–3.22 (m, 5H), 3.05–2.93 (m, 1H), 2.50 (t, J = 7.1 Hz, 2H), 2.32–2.18 (m, 2H); ^{13}C NMR (DMSO-d_6, 75 MHz): δ 147.2, 138.4, 128.6, 128.5, 114.9, 112.3, 98.1, 70.0, 69.2, 68.7, 63.3, 49.6, 35.6, 33.8; LRMS (ESI$^+$) m/z 310.2 ([M+H]$^+$).

(3a*R*,6*R*,7*S*,7a*S*)-6-(((4-(But-3-en-1-yl)phenyl)amino)methyl)-2,2-dimethyltetrahydro-3a*H*-[1,3]dioxolo[4,5-*c*]pyran-6,7-diol (**3**). To a suspension of the tetraol **2** (0.34 g, 1.10 mmol) in dry acetone (11 mL) at 0 °C, under N_2, was added $CH(OCH_3)_3$ (0.29 mL, 2.64 mmol, 2.4 equiv.), followed by concentrated H_2SO_4 (96 μL, 1.79 mmol, 1.63 equiv.). After addition of the acid the reaction was clear but quickly became cloudy and thick and with vigorous stirring was complete within 15 min. The pH was adjusted to 8.9 by the addition of a few drops of NH_4OH solution and the reaction filtered through a pad of silica gel with suction to remove NH_4Cl, and washed through with acetone. Concentration *in vacuo* gave a yellow oil which was purified by silica gel column chromatography eluting with 2 to 3% MeOH : CH_2Cl_2 to give the title compound as a clear oil (383 mg, 1.10 mmol, 100%). IR ν_{max}(neat)/cm^{-1} 3393 (s), 2985 (m), 2932 (m), 1616 (m); ^1H NMR ($CDCl_3$, 300 MHz): δ 7.04 (d, J = 8.4 Hz, 2H), 6.73 (d, J = 8.4 Hz, 2H), 5.86 (ddt, J = 17.0, 10.3, 6.4 Hz, 1H), 5.11–4.92 (m, 2H), 4.33–4.10 (m, 3H), 4.01 (d, J = 13.0 Hz, 2H), 3.55–3.70 (m, 2H), 3.23 (d, J = 13.0 Hz, 1H), 2.56–2.69 (m, 2H), 2.25–2.39 (m, 2H), 1.57 (s, 3H), 1.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 145.9, 138.3, 132.9, 129.2, 114.7, 109.3, 96.3, 77.4, 73.6, 72.1, 59.5, 50.5, 35.8, 34.4, 28.1, 26.1; LRMS (ESI$^+$) m/z 350.2 ([M+H]$^+$), 332.2 ([M–OH]$^+$).

(3a*R*,5′*S*,7*S*,7a*S*)-3′-(4-(But-3-en-1-yl)phenyl)-7-hydroxy-2,2-dimethyltetrahydrospiro[[1,3]dioxolo[4,5-*c*]pyran-6,5′-oxazolin]-2′-one (**4**). Diol **3** (0.80 g, 2.29 mmol) was suspended in CH_2Cl_2 (3 mL), cooled to 0 °C and $NaHCO_3$ (1.16 g, 13.75 mmol, 6.0 equiv.) added followed by 20% phosgene in toluene (1.68 mL, 3.2 mmol, 1.4 equiv.) dropwise over 10 min. The reaction was stirred for a further 2 h at 0 °C and then triethylamine added (1.28 mL, 9.17 mmol, 4.0 equiv.). The reaction was filtered through a short pad of silica and eluted with EtOAc, and concentrated *in vacuo* to an orange oil. Purification by silica gel column chromatography eluting with 30 to 40% EtOAc : hexane gave the title oxazolidinone as a pale yellow foam (702 mg, 1.87 mmol, 82%). IR ν_{max}(neat)/cm^{-1} 3395 (w), 2985 (w), 2935 (w), 1754 (s), 1518 (m); ^1H NMR ($CDCl_3$, 300 MHz): δ 7.40 (d, J = 8.8 Hz, 2H), 7.17 (d, J = 8.8 Hz, 2H), 5.83 (ddt, J = 17.0, 10.3, 6.4 Hz, 1H), 5.08–4.94 (m, 2H), 4.38–4.24 (m, 4H), 4.18–4.10 (m, 1H), 3.85–3.74 (m, 2H), 3.05 (d, J = 7.7 Hz, 1H), 2.74–2.63 (m, 2H), 2.40–2.29 (m, 2H), 1.57 (s, 3H), 1.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 153.0, 138.1, 137.7, 135.3, 129.0, 118.6, 115.1, 109.8, 100.8, 76.4, 73.1, 71.4, 61.7, 53.0, 35.4, 34.6, 28.0, 26.0; LRMS (ESI$^+$) m/z 396.2 ([M+H]$^+$).

(3a*R*,5′*S*,7a*R*)-3′-(4-(But-3-en-1-yl)phenyl)-2,2-dimethyldihydrospiro[[1,3]dioxolo[4,5-*c*]pyran-6,5′-oxazolidine]-2′,7-(7a*H*)-dione (**5**). To a suspension of the alcohol **4** (0.2 g, 0.53 mmol) and crushed 3 Å molecular sieves (dried, 1.00 g) in dry CH_2Cl_2 (5 mL) was added PDC (0.35 g, 1.6 mmol, 3.0 equiv.) portionwise over 20 min. Glacial acetic acid (30 μL) was added and the reaction stirred at room temperature overnight. The reaction was filtered through short pad of silica gel eluting with 40% EtOAc : hexane the resultant off white foam was recrystallised from hot Et_2O to give the title ketone as a white solid (168 mg, 0.45 mmol, 85%). IR ν_{max}(neat)/cm^{-1} 1755 (s), 1518 (m); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.43 (d, J = 8.5 Hz, 2H), 7.21 (d, J = 8.5 Hz, 2H), 5.83 (ddt, J = 16.9, 10.3, 6.5 Hz, 1H), 5.08–4.93 (m, 2H), 4.87 (d, J = 5.5 Hz, 1H), 4.75 (d, J = 10.3 Hz, 1H), 4.57–4.68 (m, 2H), 4.27 (d, J = 13.6 Hz, 1H), 3.76 (d, J = 10.3 Hz, 1H), 2.75–2.63 (m, 2H), 2.36 (q, J = 7.2 Hz, 2H), 1.49 (s, 3H), 1.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 195.0, 151.2, 138.7, 137.7, 134.8, 129.3, 118.7, 115.1, 111.1, 99.1, 77.5, 75.5, 60.9, 49.8, 35.3, 34.6, 27.0, 25.9; LRMS (EI$^+$) m/z 398 ([M+Na]$^+$).

4-(But-3-en-1-yl)aniline (**7**).[25,26]. To a stirred solution of trifluoroacetic anhydride (75 mL) at 0 °C containing 4-phenyl-1-butene (10.0 g, 75.6 mol) was added copper(II) nitrate (9.1 g, 37.7 mol) portionwise. After 30 min at 0 °C, the reaction was allowed to warm to room temperature and stirred for 2 h becoming dark green. The reaction was poured onto ice and extracted with Et_2O (x 3) the combined organics were washed with sat. $NaHCO_3$, brine and dried ($MgSO_4$) and concentrated *in vacuo* to a brown crude oil (14.5 g) which was used directly in the next step.

1-(But-3-en-1-yl)-4-nitrobenzene (14.5 g, *ca.* 75.6 mol) was dissolved in EtOH (300 mL), $SnCl_2{\cdot}2H_2O$ (85.0 g, 0.38 mol, 5.0 equiv.) was added and the reaction allowed to stir for 2 days. The reaction was poured onto water (250 mL) and the pH raised to 9 with 1 M NaOH, the cloudy mixture was extracted with EtOAc (x 3), Rochelle's salt was added to aid separation. Combined organics were washed with brine and dried ($MgSO_4$) and concentrated *in vacuo* to a brown oil which was purified by silica gel column chromatography eluting with 25 to 30% EtOAc : hexane gave the title *para*-isomer as a pale oil (6.40 g, 43.5 mmol, 58%) and the undesired *ortho*-isomer as a pale oil (2.10 g, 14.30 mmol, 19%). Data consistent with reported values[27] IR ν_{max}(neat)/cm^{-1} 1640 (m), 1515 (s), 1342 (s); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.01 (d, J = 8.0 Hz, 2H), 6.65 (d, J = 8.0 Hz, 2H), 5.88 (ddt, J = 16.9, 10.3, 6.7 Hz, 1H), 5.11–4.93 (m, 2H), 3.50 (br s, 2H), 2.68–2.55 (m, 2H), 2.35 (q, J = 7.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 101 MHz): δ 144.2, 138.4, 132.0, 129.1, 115.2, 114.6, 35.8, 34.5; LRMS (ESI$^+$) m/z 464.2 ([3M+Na]$^+$).

Derivitisation of 150 Å silica

Capping of external Si–OH functionalities (**8a**). To dry (heated at 550 °C) calcined 150 Å silica (Grace-Davidson 644, BET surface area 262.79 m^2 g^{-1}, pore volume 0.156 mL g^{-1}

determined by N_2 adsorption, 1.50 g) in dry THF (25 mL) was added dichlorodiphenylsilane (51 μL, 0.2 mmol) and turned slowly§ for 1 h at room temperature.

Activation of the internal surfaces of silica (**9a**). To the above solution was added 3-mercaptopropyl trimethoxysilane (1.50 mL, 8.00 mmol) and the reaction was turned gently for 24 h§. The resultant solution was filtered and washed with CH_2Cl_2 (×5), Et_2O (×5) and then purified by Soxhlet extraction with Et_2O for 4 h and dried *in vacuo* at room temperature. Elemental analysis found (%): C 1.97, H 1.19, S 2.78; BET surface area 266.97 $m^2\ g^{-1}$, pore volume 0.152 mL g^{-1}.

Immobilisation of (3a*R*,5′*S*,7a*R*)-3′-(4-(but-3-en-1-yl)phenyl)-2,2-dimethyldihydrospiro[[1,3]dioxolo[4,5-*c*]pyran-6,5′-oxazolidine]-2′,7(7a*H*)-dione (**10a**). The activated 150 Å silica (**9a**, 600 mg), α,α′-azoisobutyronitrile (AIBN, 131 mg, 0.80 mmol), and ketone catalyst (**5**, 300 mg, 0.8 mmol) were heated at reflux, in the dark, in dry, degassed $CHCl_3$ under nitrogen for 16 h. After this time the silica was removed by filtration and washed with CH_2Cl_2 (×5), Et_2O (×5) and then purified by Soxhlet extraction with Et_2O for 4 h and dried *in vacuo* at room temperature. ATR-IR ν_{max} 1770 cm^{-1}; Elemental analysis found (%): C 8.39, H 1.53, N 0.29, S 2.05; BET surface area 210.00 $m^2\ g^{-1}$, pore volume 0.122 mL g^{-1}.

General catalysis procedure

A mixture of the olefin (0.2 mmol), silica supported ketone catalyst **10a** (200 mg, 0.04 mmol), Bu_4NHSO_4 (1.00 mg, 0.003 mmol) in DME : DMM (3 : 1, v/v, 3.0 mL) were stirred at room temperature for 5 min and then cooled to 0 °C. K_2CO_3–AcOH buffer (0.1 M in aq. Na_2EDTA (4×10^{-4} M), pH 9.3, 2.0 mL) was added and the mixture stirred for a further 10 min at 0 °C. K_2CO_3 (0.84 M in aq. Na_2EDTA (4×10^{-4} M), 2.52 mL, 2.11 mmol, 10.5 equiv.) and oxone (0.212 M in aq. Na_2EDTA (4×10^{-4} M), 2.52 mL, 0.53 mmol, 2.7 equiv.) were then added simultaneously through separate syringes using a syringe pump. Addition times and final reaction times were as denoted in Table 3. The reaction was then diluted with Et_2O (20 mL) and water (20 mL), and extracted further with Et_2O (20 mL, ×2). Combined organics were washed with brine, dried ($MgSO_4$) and concentered *in vacuo* and then purified by silica gel column chromatography using the eluents described below.

(1*S*,2*R*)-1,2-Dihydronaphthalene oxide. (Table 3, entry 1):[28] Eluent: 10% Et_2O : pentane. White solid (yield 43% epoxide; 36% diol, *e.e.* 90%). Chiral HPLC: Chiralcel OBH column, eluent 1% IPA : hexane, UV 254 nm, flowrate: 1.0 mL min^{-1} (peak 1 15.59 min, 95.16%; peak 2 19.63 min, 4.84%).

(*R*,*R*)-*trans*-stilbene oxide. (Table 3, entry 2):[28] Eluent: 40% CH_2Cl_2 : hexane. Pale yellow oil (yield 63%, *e.e.* 86%). Chiral HPLC: Chiralcel ODH column, eluent 2% IPA : hexane, UV 254 nm, flowrate: 1.0 mL min^{-1} (peak 1 8.05 min, 6.90%; peak 2 8.77 min, 93.10%).

(3*R*,4*R*)-2,2-Dimethy-6-cyano-chromene oxide. (Table 3, entry 3):[20] Eluent: 25% EtOAc : hexane. White solid (yield 93%, *e.e.* 88%). Chiral HPLC: Chiralcel ODH column, eluent 10% IPA : hexane, UV 220 nm, flowrate: 1.0 mL min^{-1} (peak 1 10.96 min, 94.01%; peak 2 13.31 min, 5.94%).

(3*R*,4*R*)-2,2-Dimethylchromene oxide. (Table 3, entry 4):[22] Eluent: 10% EtOAc : hexane. Off white solid (yield 82%, *e.e.* 80%). Chiral HPLC: Chiralcel ODH column, eluent 10% IPA : hexane, UV 220 nm, flowrate: 1.0 mL min^{-1} (peak 1 5.62 min, 89.91%; peak 2 6.34 min, 10.09%).

(3*R*,4*R*)-2,2-Dimethy-6-chloro-chromene oxide. (Table 3, entry 5):[22] Eluent: 10% EtOAc : hexane. White solid (yield 65%, *e.e.* 79%). Chiral HPLC: Chiralcel ODH column, eluent 10% IPA : hexane, UV 220 nm, flowrate: 1.0 mL min^{-1} (peak 1 5.36 min, 89.25%; peak 2 5.83 min, 10.75%).

(3*R*,4*R*)-2,2-Dimethy-6-bromo-chromene oxide. (Table 3, entry 6):[22] Eluent: 10% EtOAc : hexane. Pale yellow oil (yield 80%, *e.e.* 83%). Chiral HPLC: Chiralcel ODH column, eluent 10% IPA : hexane, UV 220 nm, flowrate: 1.0 mL min^{-1} (peak 1 5.41 min, 87.79%; peak 2 6.15 min, 8.29%).

(3*R*,4*R*)-2,2-Dimethy-6-fluoro-chromene oxide. (Table 3, entry 7):[22] Eluent: 10% EtOAc : hexane. Pale yellow oil (yield 77%, *e.e.* 81%). Chiral HPLC: Chiralcel ODH column, eluent 10% IPA : hexane, UV 220 nm, flowrate: 1.0 mL min^{-1} (peak 1 5.28 min, 90.65%; peak 2 5.95 min, 9.35%).

(1*R*,2*S*)-Indene oxide. (Table 3, entry 8):[29] Eluent: 20% EtOAc : hexane. Pale yellow oil (yield 75%, *e.e.* 68%). Chiral HPLC: Chiralcel OBH column, eluent 0.5% IPA : hexane, UV 220 nm, flowrate: 1.0 mL min^{-1} (peak 1 20.63 min, 16.06%; peak 2 32.18 min, 83.94%).

1-Phenylcyclohexene oxide. (Table 3, entry 9):[28] Eluent: 5% Et_2O : pentane. Colourless oil (yield 83%, *e.e.* 18%). Chiral HPLC: Chiralcel ODH column, eluent 1% IPA : hexane, UV 220 nm, flowrate: 1.0 mL min^{-1} (peak 1 6.45 min, 59.18%; peak 2 6.98 min, 40.82%).

§ The silica was turned slowly in a round bottom flask attached to a rotary evaporator (without vacuum).

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