

# Dioxirane mediated asymmetric epoxidations: stereochemical studies *via* isotopic labeling†‡

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A study, *via* isotopic labeling, of the stereoselective processes in a Shi-type epoxidation, has revealed that the chiral platform provided by the catalyst mediates the transfer of the pro-*S* “O” of the related dioxirane species to the alkene in a doubly stereoselective manner.

## Introduction

The asymmetric epoxidation of alkenes is a powerful route to chiral epoxides,<sup>1</sup> which are useful synthetic intermediates in the asymmetric synthesis of complex molecules<sup>2</sup> or chiral catalysts.<sup>3</sup> Amongst the wide repertoire of catalytic asymmetric epoxidation methods, chiral dioxiranes, which are generated *in situ* from chiral ketones and potassium peroxomonosulfate (KHSO<sub>5</sub>), are practically unrivalled for the epoxidation of unfunctionalized *trans*- and trisubstituted alkenes.<sup>1b,d,4</sup> Shi and co-workers have developed one of the most efficient of these methodologies based on carbohydrate-derived ketones<sup>4a-c</sup> as the chiral catalysts and KHSO<sub>5</sub> (Oxone<sup>®</sup>) as the stoichiometric oxidant. Shi's fructose derivative **1** is the most well-known of these catalysts (Fig. 1).<sup>5</sup> Diester-fructose derivative **2** is even more attractive in terms of robustness and substrate scope in the asymmetric epoxidation of alkenes: Shi and co-workers<sup>6</sup> have already reported its use in the epoxidation of  $\alpha,\beta$ -unsaturated esters and our group<sup>7</sup> has extended its use to unfunctionalized alkenes using low catalyst loadings.<sup>8</sup> Furthermore, we have developed a selective and efficient method for the preparation of diester **2** and its hydrate **3** and recently reported that hydrate **3** shows the same high catalytic activity as its parent compound **2** in epoxidation studies of a model *trans*-alkene.<sup>7</sup> Shi's model for epoxidations mediated by

the tricyclic system **1** is based on analysis of the stereochemistry of the produced epoxides. The chiral dioxirane derived from ketone **1**, adopting a chair conformation, has two diastereomeric oxygens and on the basis of sterical arguments the equatorial oxygen is likely to be the more accessible for approach by the olefin, with the major enantiomer being produced *via* a spiro transition state.<sup>5</sup> Singleton and Wang have recently studied the epoxidation of  $\beta$ -methylstyrene with Shi's ketone through the use of experimental kinetic isotope effects (KIE) and DFT calculations,<sup>9</sup> their results supporting Shi's earlier analysis. They predicted though, that the observed major enantiomeric product results from an asynchronous spiro transition state. At the same time the minor enantiomer arises from neither a planar nor a spiro transition state, but rather the plane of the developing epoxide is twisted, *ca.* 45°, from the plane of the dioxirane, thereby increasing the asynchronicity of the transition state.

We considered that a study *via* the chemoselective isotopic labeling of the dioxirane species derived from bicyclic chiral catalyst **2** or **3**,<sup>10</sup> could experimentally clarify the origin of the stereodifferentiating processes at hand in the organocatalyzed epoxidation of unfunctionalized alkenes mediated by these chiral catalysts.

## Results and discussion

Before carrying out the epoxidation with the labeled species, we first optimized the reaction conditions of the epoxidation of a model *trans*-alkene mediated by **3**. The epoxidations (Scheme 1)

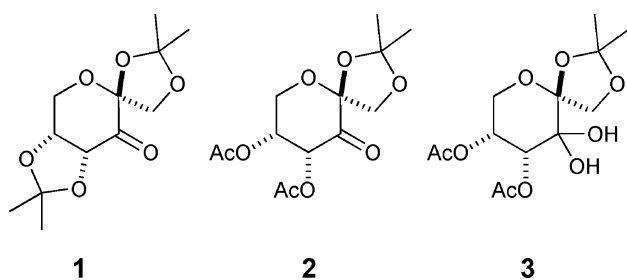


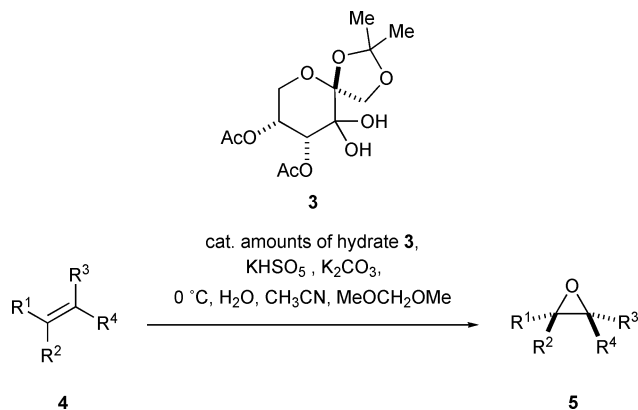
Fig. 1 Shi's standard catalyst (**1**), diester-fructose derivative (**2**) and its hydrate (**3**).

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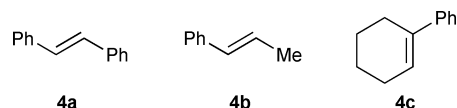


Scheme 1 Epoxidations of alkenes mediated by hydrate **3**.

**Table 1** Epoxidations mediated by hydrate **3**

Entry	Alkene <b>4</b>	Reaction conditions <sup>a</sup>	Yield (%) <sup>b</sup>	ee (%) <sup>c</sup>
1	<b>4a</b>	10 mol% <b>3</b> , 1.6 eq. Oxone <sup>®</sup> , 2.4 eq. K <sub>2</sub> CO <sub>3</sub>	55	89 ( <i>R,R</i> )- <b>5a</b>
2	<b>4a</b>	10 mol% <b>3</b> , 1.6 eq. Oxone <sup>®</sup> , 4.4 eq. K <sub>2</sub> CO <sub>3</sub>	39	95 ( <i>R,R</i> )- <b>5a</b>
3	<b>4a</b>	10 mol% <b>3</b> , 3.2 eq. Oxone <sup>®</sup> , 6.8 eq. K <sub>2</sub> CO <sub>3</sub>	63	93.5 ( <i>R,R</i> )- <b>5a</b>
4	<b>4a</b>	30 mol% <b>3</b> , 3.2 eq. Oxone <sup>®</sup> , 6.8 eq. K <sub>2</sub> CO <sub>3</sub>	95	95.5 ( <i>R,R</i> )- <b>5a</b>
5	<b>4b</b>	30 mol% <b>3</b> , 3.2 eq. Oxone <sup>®</sup> , 6.8 eq. K <sub>2</sub> CO <sub>3</sub>	83	89 ( <i>R,R</i> )- <b>5b</b>
6	<b>4c</b>	10 mol% <b>3</b> , 1.6 eq. Oxone <sup>®</sup> , 2.4 eq. K <sub>2</sub> CO <sub>3</sub>	82	92 ( <i>R,R</i> )- <b>5c</b>

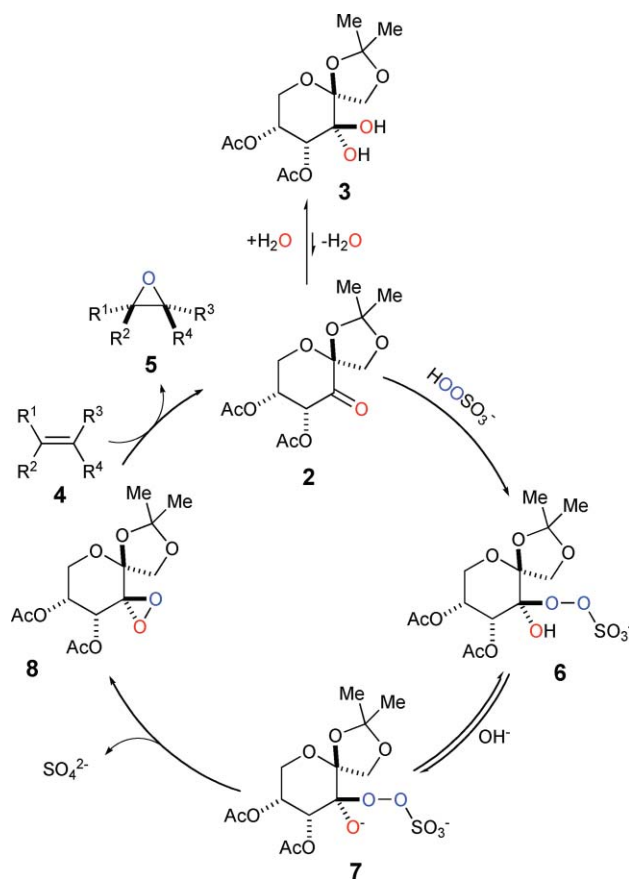
<sup>a</sup> Oxone<sup>®</sup> and base were simultaneously added over 2 hours. The reaction mixture was further stirred at 0 °C for 16 h. pH values increased throughout the addition period from 6 to *ca.* 9 when 2.4 eq. of K<sub>2</sub>CO<sub>3</sub> were used, and to *ca.* 10 in the other cases. <sup>b</sup> Isolated material. <sup>c</sup> Enantiomeric excesses.



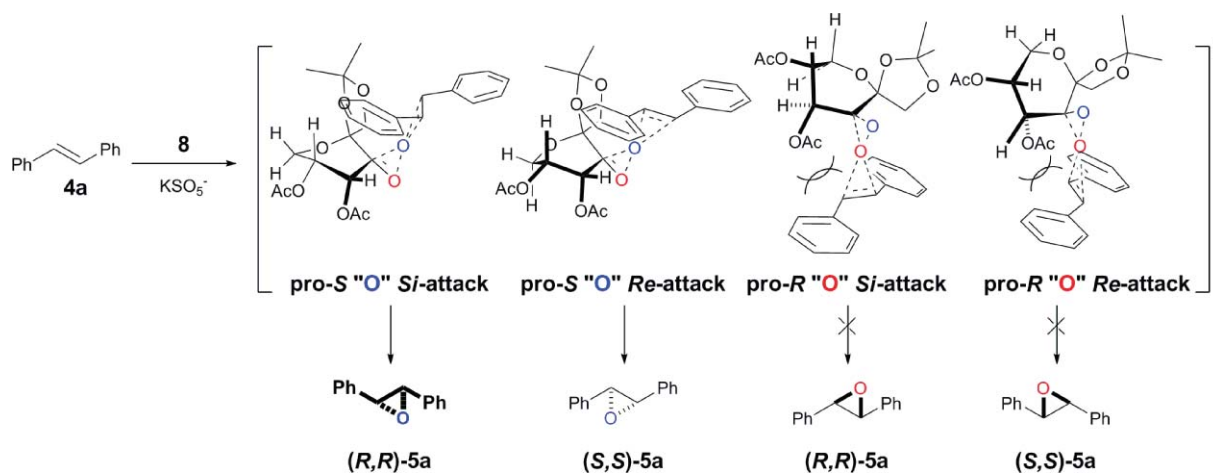
were carried out in organo-aqueous media with 10 mol% catalyst at 0 °C, as this temperature offers a good balance between conversion and selectivity.<sup>7</sup> pH is a key parameter in dioxirane-catalyzed epoxidations,<sup>5</sup> hence the optimal pH value for epoxidation with **3** was investigated using *trans*-stilbene as a test substrate. pH values from 9 to 10<sup>11</sup> were obtained by simultaneously adding aqueous K<sub>2</sub>CO<sub>3</sub> and a solution of Oxone<sup>®</sup> in pH 6 buffer (See Table 1). Lower conversion was observed at pH = 10 (entry 2, 39% yield) than at pH = 9, (entry 1, 55% yield). Conversely, enantioselectivity improved with higher pH. The lower stability of the oxidant at higher pH<sup>5</sup> values could account for the low conversion in entry 3. In order to overcome this problem, the amount of Oxone<sup>®</sup> was doubled while the pH value was fixed at 10. As expected, greater conversion was achieved (*cf.* entries 2 and 3). The best yield (95%) and enantioselectivity (95.5% ee) of all the epoxidation conditions tested was obtained by switching from catalytic to sub-stoichiometric amounts of hydrate **3** (30 mol%)<sup>8</sup> and doubling the amount of Oxone<sup>®</sup> while keeping the pH constant (entry 4). The epoxidation of two further alkenes was carried out straightforwardly (entries 5 and 6), thus indicating that these conditions were general enough for the study of alkene epoxidations mediated by **3** using isotopically labeled tracers.

Scheme 2 shows the reaction pathways that are believed to be involved in the catalytic cycle. An equilibrium is established between the ketone and the hydrate under the epoxidation conditions.<sup>12</sup> According to the commonly accepted mechanism,<sup>4,5</sup> chiral dioxirane **8** might thus be formed in three steps from ketone **2**. First, addition of KHSO<sub>5</sub> onto the carbonyl group would afford **6**. This intermediate would then evolve into dioxirane **8** by a base-catalyzed intramolecular dioxirane ring-closing reaction. The higher the pH value, the faster the dioxirane ring formation would proceed and the faster the active chiral catalytic species would be formed. The newly formed dioxirane would then transfer an oxygen atom to the olefin to form the corresponding epoxide, and consequently regenerate ketone **2**. The two diastereotopic oxygens of the catalyst-derived dioxirane have been colored in Scheme 2 according to their origin: those originating from the oxidizing agent have been marked in blue, and those already incorporated in the chiral platform provided by the catalyst before entering the catalytic cycle are marked in red.

The epoxidation has four possible stereochemical outcomes: each of the two diastereotopic oxygens of the chiral dioxirane

**Scheme 2** Asymmetric epoxidation catalysed by hydrate **3**.

**8** can be delivered onto either of the two enantiotopic faces of the alkene. The four possible diastereomeric transition states for the epoxidation of an alkene are depicted in Scheme 3. Shi has postulated that, for catalyst **1**, the major epoxide enantiomer observed results from attack of the least-hindered oxygen of the dioxirane by the *Si*-alkene face (pro-*S* “O” *Si*-attack). Accordingly, the minor enantiomer could be generated by a pro-*S* “O” *Re*-attack. Epoxidation *via* pro-*R* “O” attack is thought to be unfeasible because of steric interactions between the alkene and the dioxolane ring of the catalyst **1**.



Scheme 3 Possible stereochemical outcomes of the asymmetric epoxidation.

To experimentally clarify the origin of the stereodifferentiating processes at hand, in the case of hydrate **3**, we explored the epoxidation of *trans*-stilbene with  $\text{KSO}_5$ / $^{18}\text{O}$  using the previously optimized reaction conditions. The relative abundance of  $^{18}\text{O}$  :  $^{16}\text{O}$  isotopologues in the final epoxide were determined by mass spectrometry. This analysis showed that the epoxidation product  $^{18}\text{O}$ -*(R,R)*-*trans*-stilbene oxide had the same  $^{18}\text{O}$  :  $^{16}\text{O}$  proportion as that of the oxidizing agent ( $89.4 \pm 0.4\%$  experimental vs.  $90.0 \pm 0.3\%$  theoretical).<sup>14</sup> These results indicate that the epoxidation involves two stereoselective processes. The first comprises highly stereoselective attack of the  $\beta$  face of **2** by  $\text{HSO}_5^-$ . Subsequent dioxirane ring formation by intramolecular cyclization gives chiral dioxirane **8**, in which the oxygen marked in blue in Scheme 2 would be  $^{18}\text{O}$ . The second comprises oxygen transfer through approach of the *Si*-alkene face onto the  $\beta$  face of dioxirane **8** (pro-*S* "O" *Si*-attack). The fact that the final epoxide is fully  $^{18}\text{O}$ -labeled can only be accounted for by very high stereoselectivity in both processes. In an analogous way to this doubly stereoselective process, the methanolysis of hydrate **3** takes place in the absence of acidic or basic catalysis, with the stereoselective displacement of its pro-*S* hydroxyl group. Crystals of the methanolysis product of **3** could be isolated by slow evaporation of the solvent; the configuration of the carbon bearing the two oxygen functionalities in the methanolysis product of hydrate **3** (see Fig. 2 and ESI<sup>†</sup>) was determined by X-ray analysis<sup>‡</sup>, as the known configurations of the spiro carbon and the carbons bearing the acetoxy groups should remain unchanged with respect to the starting material (*D*-fructose).

Epoxidation of *trans*-stilbene with standard Oxone<sup>®</sup> in  $\text{H}_2^{18}\text{O}$  ( $10.2 \pm 0.3\%$   $^{18}\text{O}$  content) was then carried out, yielding unlabeled *(R,R)*-*trans*-stilbene oxide ( $^{18}\text{O}$  content  $<0.1\%$ ). Mass spectrometry revealed an exchange process between the gem-diol group of **3** and the solvent (experimental  $9.8 \pm 0.5\%$  vs.  $10.2 \pm 0.3\%$  theoretical  $^{18}\text{O}$  content), thus indicating that the  $^{18}\text{O}$ -label is incorporated into the catalyst. Assuming a preference for attack by the oxidant at the  $\beta$  face, this  $^{18}\text{O}$ -labeled species could evolve into the dioxirane **8**, in which the oxygen marked in red in Scheme 3 would be  $^{18}\text{O}$ . Attack of the most hindered face of **8** (pro-*R* "O" attack) by the alkene would thereby yield  $^{18}\text{O}$ -*(R,R)*-*trans*-stilbene oxide. As the final epoxide did not incorporate any  $^{18}\text{O}$ , we conclude that the facial selectivity of the oxygen transfer is also very high.

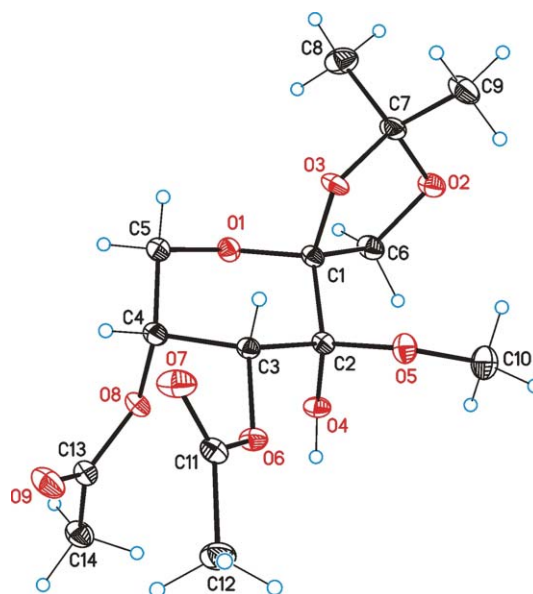


Fig. 2 ORTEP plot (thermal ellipsoids shown at 50% probability level) of the methanolysis product of **3**.

These results reveal several key aspects of the origin of the stereoinduction and these can be summarized as follows: i) the epoxidation process comprises a highly stereoselective attack of the  $\beta$  face of **2** by  $\text{HSO}_5^-$ ; ii) subsequent dioxirane ring formation renders the chiral dioxirane **8**, in which the oxygen marked in blue (Scheme 3) comes from the oxidant; iii) oxygen transfer from the dioxirane to the alkene proceeds predominately through approach of the *Si*-alkene face onto the  $\beta$  face of dioxirane **8** (pro-*S* "O" *Si*-attack); iv) attack of the most hindered face of **8** (pro-*R* "O" attack) by the alkene does not take place to any measurable extent. Although the two acetate groups have more conformational freedom with respect to the dioxolane ring in the standard Shi catalyst, they are bulky enough to prevent the pro-*R* "O" attack. Furthermore, while the participation of the pro-*R* "O" transition states has been discounted by computational studies on tricyclic catalysts<sup>9</sup> and on the basis of sterics, our labeling studies experimentally support the currently accepted model of dioxirane epoxidations by the chiral bicyclic platform provided by

the catalyst. One potential application of this methodology would be to use the labeled dioxiranes as a means of investigating oxygen transfer to some less-than-optimal substrates, with the extent of label transfer providing an efficient marker of  $\alpha$  vs.  $\beta$  face approach.

In terms of labeling efficiency in the preparation of non-racemic  $^{18}\text{O}$ -epoxides, the synthetic methodology described in this work is a very efficient one, as it ensures full isotopic labeling from the oxidizing agent to the alkene ( $89.4 \pm 0.4\%$  experimental vs.  $90.0 \pm 0.3\%$  theoretical).

## Experimental

### General procedure for the epoxidation of alkenes

The alkene (2.22 mmol) and the catalyst **3** (10–30 mol%) were dissolved in 1 : 2 v/v acetonitrile–dimethoxymethane (44 mL). A solution of pH = 6 buffer§ (8 mL) and tetrabutylammonium hydrogen sulfate (35 mg, 0.10 mmol) were then slowly added with stirring, and the mixture was cooled to the desired temperature. The flask was equipped with two syringe pumps: one was filled with  $\text{K}_2\text{CO}_3$  (5.33–15.10 mmol) in water (14 mL), and the other with the required amount of Oxone® (3.55–7.10 mmol) in the pH = 6 buffer (14 mL). The two solutions were added dropwise over a 2 h period by syringe pump. The reaction mixture was stirred at 0 °C for the corresponding time. The crude reaction mixture was quenched by the addition of water (40 mL) and pentane (10 mL), then extracted with an organic solvent (**5a** hexane,  $4 \times 40$  mL; **5b–c**:  $4 \times 40$  mL DCM). The combined organic extracts were washed with brine (50 mL), dried over sodium sulfate, filtered, and concentrated under reduced pressure. The crude material was purified by flash chromatography on silica gel. Enantioselectivity was determined by chiral chromatography and the configuration of epoxides **5** was established by comparison with either the reported elution order or optical rotation if reported data was available. For **5a**, HPLC, Chiralpak AD, (*R,R*)-**5a** elutes first.<sup>15</sup> For **5b**, GC, gamma dex, (*S,S*)-**5b** elutes first.<sup>5</sup> For **5c**, GC, gamma dex, (*S,S*)-**5c** elutes first.<sup>16</sup>

### Asymmetric epoxidation of *trans*-stilbene with $^{18}\text{O}$ -labeled tracers

#### Preparation of $\text{KSO}_2^{18}\text{O}^{18}\text{OH}$

$^{18}\text{O}_2$ -Hydrogen peroxide (Cambridge Isotope Laboratories, 0.93 g, 2.5%  $\text{H}_2\text{O}_2$  content in water, 23 mg, 0.60 mmol,  $90 \pm 0.3\%$   $^{18}\text{O}$ -content) was carefully concentrated *in vacuo* (70 °C, 90 mbar) by eliminating 0.84 g of distillate through a 5 cm Vigreux column. The residue was cooled to  $-5$  °C and fuming sulfuric acid (20% as free  $\text{SO}_3$ , 0.49 g, 1.22 mmol of  $\text{SO}_3$ ) was added carefully (10 min). The mixture was allowed to reach 0 °C and was stirred for a further 2 h.  $\text{K}_2\text{CO}_3$  (0.65 g) in 1 mL water was added dropwise (10 min) to the solution, which was stirred for a further 15 min. The suspension, which contained  $\text{KSO}_2^{18}\text{O}^{18}\text{OH}$  (0.60 mmol theoretical amount), was stored at 4 °C and used in the next step without any further work-up.

#### Epoxidation of *trans*-stilbene with $\text{KSO}_2^{18}\text{O}^{18}\text{OH}$ .<sup>13</sup>

*trans*-Stilbene (65 mg, 0.35 mmol) and hydrate **3** (34 mg, 0.10 mmol) were dissolved in acetonitrile–dimethoxymethane

(6 mL, 1 : 2 v/v). A pH = 6 buffer§ solution (1.3 mL) and tetrabutylammonium hydrogen sulfate (5 mg, 0.015 mmol) were added slowly with stirring and the mixture was cooled to 0 °C. The flask was equipped with two syringe pumps; one filled with a solution of  $\text{KSO}_2^{18}\text{O}^{18}\text{OH}$  (0.60 mmol theoretical amount, reaction mixture from the previous step) in the pH = 6 buffer (2.3 mL) and the other one with a solution of  $\text{K}_2\text{CO}_3$  (0.11 g, 0.83 mmol) in water (2.3 mL). The two solutions were added dropwise over a 2h period (syringe pump). The solution was stirred at 0 °C for 18 h. The reaction mixture was extracted with hexanes ( $4 \times 6$  mL), the combined organic fractions were washed with saturated  $\text{NaCl}_{(\text{aq})}$  (10 mL) and then dried over  $\text{Na}_2\text{SO}_4$ .  $^{18}\text{O}$ -(*R,R*)-*trans*-stilbene oxide was obtained, together with starting material, after filtration and removal of the hexanes *in vacuo*. No isolation of  $^{18}\text{O}$ -(*R,R*)-*trans*-stilbene oxide was attempted: chiral HPLC of the raw material (Chiralpak AD, see general procedure) indicated a 94% ee;  $^1\text{H}$ -NMR and MS-CI analysis of the raw material provided the yield of the epoxidation (7  $\mu\text{mol}$ , 2% yield) and the relative abundance of the  $^{16}\text{O}$  :  $^{18}\text{O}$  isotopologues.

#### Mass spectrometric determination of the relative abundance of $^{16}\text{O}$ : $^{18}\text{O}$ isotopologues from the epoxidation of *trans*-stilbene with $\text{KSO}_2^{18}\text{O}^{18}\text{OH}$

A time-of-flight mass (TOF) mass spectrometer (Waters GCT) coupled to a gas chromatograph (Agilent 6890 N) was used to determine the relative abundance of  $^{16}\text{O}$  :  $^{18}\text{O}$  labeled  $^{18}\text{O}$ -(*R,R*)-*trans*-stilbene oxide. The GC conditions were as follows: a DB-XLB (Agilent) column, 30 m  $\times$  0.18 mm  $\times$  0.18  $\mu\text{m}$ ; GC analysis time 30 min ( $^{18}\text{O}$ -(*R,R*)-*trans*-stilbene oxide retention time 21 min); inlet temperature 250 °C (1 ng of sample injected, split ratio 100 : 1); oven temperature program, 40 °C held for 3 min, then a (10 °C  $\text{min}^{-1}$ ) ramp to 340 °C; GC carrier gas He; constant flow 0.6 mL  $\text{min}^{-1}$ . The mass spectrometer was operated in positive ion mode, using  $\text{CH}_4$  as the chemical ionization reagent gas at a source pressure of  $2 \times 10^{-4}$  mbar. The ion source temperature was 165 °C with an electron energy of 70 eV and an emission current of 100  $\mu\text{A}$ . Spectra were acquired at 25 000 Hz using an integration time of 0.45 s and a delay of 0.05 s (2 integrated spectra  $\text{s}^{-1}$ ).

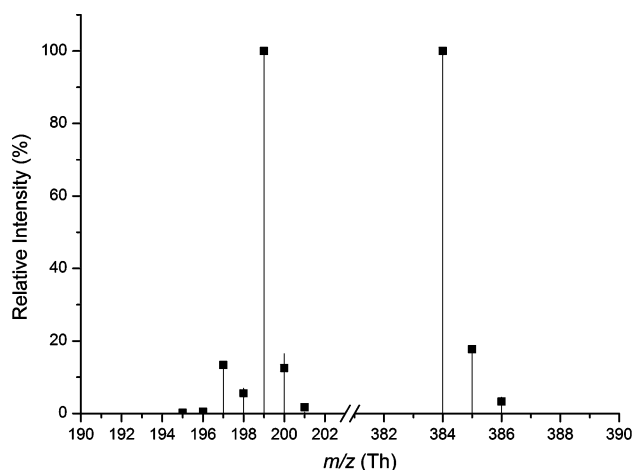
The  $^{16}\text{O}$  :  $^{18}\text{O}$  isotopologues were not separated using the GC method applied in this work. Rather the GC sample introduction provided an accurate means of background ion subtraction, facilitating subsequent  $^{16}\text{O}$  :  $^{18}\text{O}$  determination by comparison with a simulated mixed isotopologue mass spectrum. The simulation is generated by convolution of the respective  $^{16}\text{O}$  :  $^{18}\text{O}$  isotopologue  $m/z$  channel intensities, as determined experimentally using a pure, unlabeled standard (Sigma Aldrich). The relative intensities in each  $m/z$  channel are assumed to be identical for the two isotopologues. The  $^{16}\text{O}$  :  $^{18}\text{O}$  proportion, the only free parameter in the simulation, is obtained from a least squares fit of the observed intensities as a function of the intensities in the calculated spectrum.

After the epoxidation the catalyst **3** was analyzed for  $^{16}\text{O}$  :  $^{18}\text{O}$  content using a time-of-flight (TOF) mass spectrometer equipped with an electrospray ionization (ESI) source (Waters LCT premier) applying the following conditions: capillary voltage

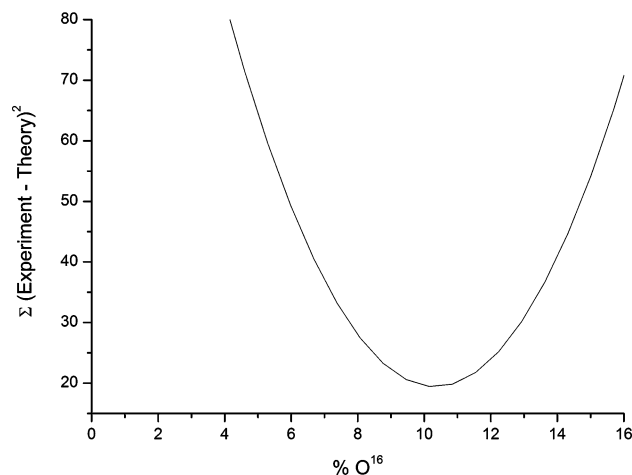
§ The pH = 6 buffer consisted of 6.8 g of  $\text{KH}_2\text{PO}_4$  and 5 mL of 1M  $\text{KOH}$   $\text{L}^{-1}$ .

3 kV, cone voltage 30 V, desolvation gas temperature 150 °C, source temperature 100 °C. The sample solution (1 ng  $\mu\text{L}^{-1}$  in sodium acetate doped  $\text{CH}_3\text{CN}$ ) was introduced into the spectrometer by direct infusion at 10  $\mu\text{L min}^{-1}$ . Spectra were acquired at 25 000 Hz using an integration time of 0.9 s and a delay of 0.1 s (1 integrated spectrum  $\text{s}^{-1}$ ).

Fig. 3 shows the calculated and observed isotopic patterns for compounds  $^{18}\text{O}$ -(*R,R*)-*trans*-stilbene oxide and **3**. In the case of compound  $^{18}\text{O}$ -(*R,R*)-*trans*-stilbene oxide excellent agreement is found using the least squares determined  $^{16}\text{O} : ^{18}\text{O}$  proportion, 10.6%, whilst for compound **3** the experimental mass spectrum is perfectly reproduced by the pure  $^{16}\text{O}$  isotopologue calculated intensities. Fig. 4 demonstrates the reliability of the derived  $^{16}\text{O} : ^{18}\text{O}$  proportion value for compound  $^{18}\text{O}$ -(*R,R*)-*trans*-stilbene oxide; a sharp minimum least squares difference is evident at around 10–11%  $^{16}\text{O}$ .



**Fig. 3** Mass spectra and simulated isotopic profiles (squares) of the mixed  $^{16}\text{O} : ^{18}\text{O}$  isotopologue ( $\text{M} + \text{H}$ ) ion of  $^{18}\text{O}$ -(*R,R*)-*trans*-stilbene oxide (monoisotopic masses 197 and 199) and the ( $\text{M} + \text{Na} + \text{CH}_3\text{CN}$ ) ion of **3** (monoisotopic masses 384 and 386).



**Fig. 4** Least squares fitting of the observed isotopic profile of  $^{18}\text{O}$ -(*R,R*)-*trans*-stilbene oxide as a function of a simulated mixed  $^{16}\text{O} : ^{18}\text{O}$  isotopologue profile.

## Epoxidation of *trans*-stilbene with $\text{H}_2^{18}\text{O}$

This transformation was carried out at 0 °C as described in the general procedure using: *trans*-stilbene (20 mg, 0.11 mmol), hydrate **3** (10 mg, 0.032 mmol) and tetrabutylammonium hydrogen sulfate (2 mg, 0.005 mmol) and pH = 6 buffer¶ (0.4 mL) in 1 : 2 v/v acetonitrile–dimethoxymethane (2 mL), Oxone® (0.11 g, 0.17 mmol) in pH = 6 buffer§ (0.7 mL) and  $\text{K}_2\text{CO}_3$  (0.35 g, 0.25 mmol) in  $\text{H}_2^{18}\text{O}$  (0.7 mL,  $10.2 \pm 0.3\%$   $^{18}\text{O}$  content). The reaction was quenched as described in the general procedure after stirring for 18 h at 0 °C. (*R,R*)-*trans*-stilbene oxide was obtained after extraction, together with starting material. No isolation of (*R,R*)-*trans*-stilbene oxide was attempted:  $^1\text{H}$ -NMR and MS-CI analysis of the raw material provided the yield of the epoxidation (0.08 mmol, 72% yield) and the relative abundance of the  $^{16}\text{O} : ^{18}\text{O}$  isotopologues. In the case of the recovered catalyst **3** excellent agreement is found using the least squares determined  $^{18}\text{O} : ^{16}\text{O}$  proportion,  $9.8 \pm 0.5\%$   $^{18}\text{O}$  content, whilst for compound (*R,R*)-*trans*-stilbene oxide the experimental mass spectrum is perfectly reproduced by the pure  $^{16}\text{O}$  isotopologue calculated intensities ( $^{18}\text{O}$  content <0.1%).

## Conclusions

In summary, we have described a study of the stereoselective processes in the organocatalytic epoxidation of alkenes, based on  $^{18}\text{O}$ -labeling experiments, which has revealed that the chiral platform provided by the catalyst mediates the transfer of the pro-*S* “O” of the related dioxirane species to the alkene in a doubly stereoselective manner. Current efforts are directed at exploiting this phenomenon to develop new epoxidation-related asymmetric transformations.

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## Notes and references

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¶ The pH = 6 buffer solution was prepared with  $\text{H}_2^{18}\text{O}$  ( $10.2 \pm 0.3\%$   $^{18}\text{O}$  content).

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