# Enantioselective synthesis of epoxides and aziridines by asymmetric methylidene transfer from a sulfimide to carbonyl compounds and imines

**Charlotte P. Baird and Paul C. Taylor ***

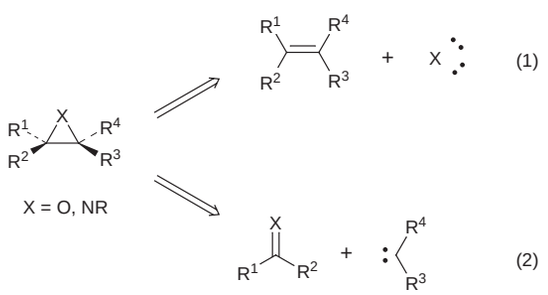
*Department of Chemistry, University of Warwick, Coventry, UK CV4 7AL*

***Received (in Cambridge) 10th July 1998, Accepted 18th August 1998***

The sodium salt of sulfimide **2** is a useful asymmetric methylidene transfer agent for the synthesis of enantiomerically enriched epoxides and aziridines. Moderate enantioselectivities are observed with a broad range of carbonyl compounds and with imines. An enantiomerically enriched β-adrenoreceptor agonist analogue was prepared using the new method.

## Introduction

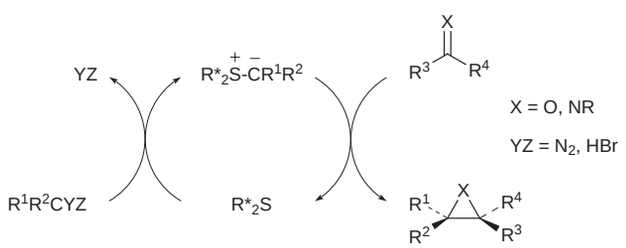
Asymmetric synthesis of epoxides and aziridines continues to attract a great deal of attention. The enantioselective methods can be classified retrosynthetically into two very different classes. Disconnections both to an alkene [eqn. (1)] and oxene/nitrene or to a carbon–heteroatom double bond and an alkylidene fragment [eqn. (2)] are conceivable (Scheme 1). The synthetic procedures corresponding to eqn. (1) are known as asymmetric epoxidation and asymmetric aziridination and, especially in the case of epoxidation, a great deal of progress has been made in achieving high enantioselectivities for a wide range of substrates.[1,2] The process corresponding to the disconnection shown in eqn. (2) could be described as an "asymmetric alkylidene transfer" reaction and is the subject of this paper.



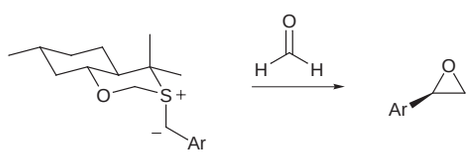

**Scheme 1**

In the synthesis of non-racemic epoxides by asymmetric alkylidene transfer reactions (to aldehydes/ketones), both the relative and absolute configuration of the product are established in a single step. A completely stereoselective method for this transformation, therefore, would be superior to asymmetric synthesis by epoxidation where alkenes of defined configuration are generally required but not always available.[3] Aggarwal and Dai, whose groups have both reported important advances in catalytic asymmetric alkylidene transfer, using ylides of chiral sulfides (Scheme 2), have recently reviewed the area.[4]

Despite the successes described above, asymmetric synthesis of monosubstituted and 2,2-disubstituted epoxides remains very challenging.[4,5] Typically, asymmetric epoxidations give low ees for these targets. Although Solladié-Cavallo has reported excellent enantioselectivities for asymmetric alkylidene transfer to formaldehyde (Scheme 3),[6] this method has the drawback that a different chiral sulfur ylide must be prepared for each given target, reducing the generality of the method.

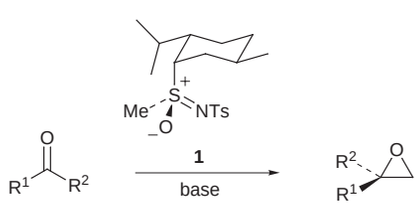



**Scheme 2**



**Scheme 3**

A more promising approach would appear to be asymmetric methylidene transfer to carbonyl compounds, but ees with methylidene sulfides have improved little since Trost's original report of 0% ee for the process in 1973![7] However, there are two classes of asymmetric methylidene transfer agents which yield epoxides with moderate ees. Chiral sulfoximide-stabilised anions were first employed by Johnson in 1973.[8] More recently, analogues derived from neomenthol and from camphor were studied by the group of Soman.[9] The best results were observed with sulfoximide **1** which reacted with aromatic aldehydes and ketones in 56–86% ee (Scheme 4). That the anions of chiral sulfimides behave analogously was communicated by ourselves in 1995[10] and our results are discussed in full herein.




**Scheme 4**

Asymmetric synthesis of aziridines by alkylidene transfer was first reported by Aggarwal's group in 1996, with very high ees for *trans* 2,3-diaryl products.[11] Dai and coworkers have also made a recent important contribution to this area.[12] However,

**Table 1** Reaction conditions, yields and ees for epoxides and aziridines **5**

| 5 | $R^1$ | $R^2$ | X | *T*/°C | *t*/h | Yield (%) | ee (%) | $[\alpha]_D$ (589 nm)[a] |
|---|---|---|---|---|---|---|---|---|
| **a** | Ph | H | O | −5 | 24 | 63 | 70 | +31 (26 °C, benzene) |
| **b** | Ph | Me | O | 20 | 160 | 60 | 45 | +31 (26 °C, acetone) |
| **c** | Cyclohexyl | H | O | 20 | 160 | 62 | *b* | +37 (26 °C, acetone) |
| **d** | $PhCH_2CH_2$ | Me | O | 66 | 140 | 64 | 21 | +8.3 (29 °C, acetone) |
| **e** | (*E*)-PhCH=CH | H | O | 20 | 90 | 62 | 42 | +11 (29 °C, acetone) |
| **f** | (*E*)-PhCH=CH | Ph | O | — | — | 0 | — | — |
| **g** | $^t$Bu | Me | O | — | — | 0 | — | — |
| **h** | Ph | H | NPh | 25 | 12 | 79 | 38 | −20 (26 °C, acetone) |
| **j** | Ph | H | $NC_6H_4Cl$-*p* | 25 | 8 | 73 | 18 | −23 (26 °C, acetone) |
| **k** | Ph | H | NTs | 24 | 25 | *c* | *c* | *c* |

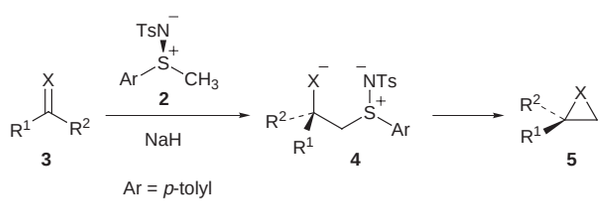
[a] Given in units of $10^{-1}$ deg $cm^2$ $g^{-1}$. [b] ee not determined. [c] 56% yield of racemic styrene oxide.

we are aware of only one report of asymmetric methylidene transfer to imines.[8] Johnson reported synthesis of aziridine **5h** using a chiral sulfoximide in what we calculate to be around 25% ee.

## Results and discussion

The asymmetric methylidene transfer reagent used in this study was (*S*)-*S*-methyl-*S*-(*p*-tolyl)-*N*-(*p*-tosyl)sulfimide **2**, which was prepared from commercially available (*R*)-methyl *p*-tolyl sulfoxide using Cram's method.[13] This reaction proved to be somewhat capricious, but when the Cram procedure was followed precisely with reagents and solvents of high purity, sulfimide of >90% enantiomeric purity, as determined by its optical rotation and its NMR spectrum in the presence of a chiral shift reagent, was obtained. It should be noted that an alternative method for preparing this and analogous sulfimides in high enantiomeric purity has very recently been published,[14] which should increase the utility of the chemistry described herein.

A representative range of carbonyl compounds and imines was selected (Scheme 5, Table 1); the imines were prepared from



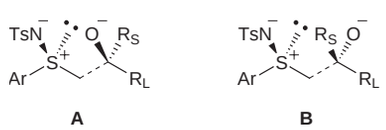

**Scheme 5**

the corresponding aldehydes using literature procedures.[15] Before attempting the asymmetric methylidene transfer reactions we reinvestigated the work from the groups of Tamura and of Johnson.[16] We felt sodium hydride in THF at room temperature to be the most promising reaction conditions, as both reasonable yields and high diastereoselectivities had been reported with this system. As, on repetition of the literature procedure, we found yields to be rather variable, we decided to attempt the reactions with inverse addition, *i.e.* substrate before sodium hydride.

Under these conditions the reaction is highly repeatable for epoxides, with yields of 60–64% in all successful cases. The reaction only failed with the highly conjugated or sterically hindered examples **5f** and **5g**. However, when these conditions were applied to the imines as substrates, the yields were unsatisfactorily low. Inspired by related work on sulfoximide analogues,[8] we decided to use DMSO as solvent and good yields of aziridines were obtained, except with the *N*-tosyl imine **3k**, when the major product was *racemic styrene oxide*. We are unable to explain the formation of the epoxide product. However, we have excluded the possibility that the corresponding aldehyde is an intermediate. When the reaction was carried out in an NMR tube in $d_6$-DMSO, the resonances due to the imine were seen to disappear, but no resonances due to styrene oxide were observed. We therefore believe that the epoxide is formed in the work-up and that the aziridine is not formed due to the lower nucleophilicity of $X^-$ in intermediate **4** when X is *N*-tosyl than when X is *N*-aryl.

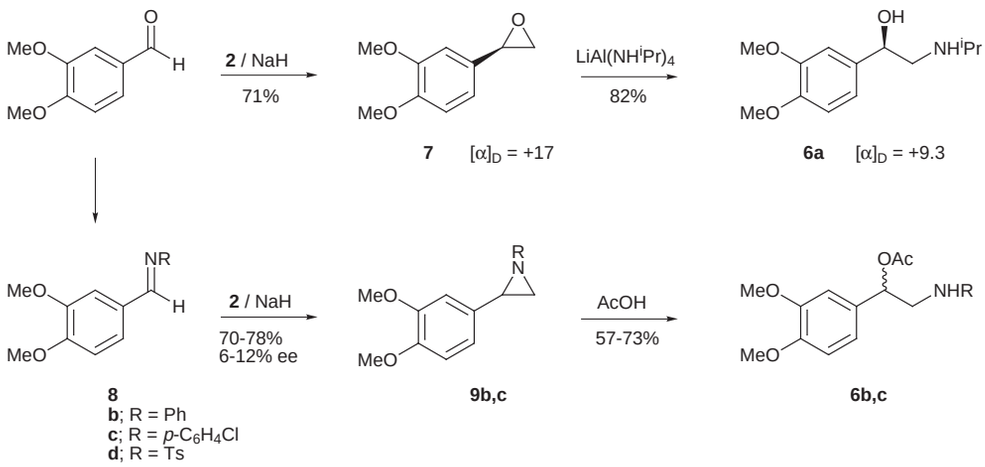
Ees for asymmetric methylidene transfer, as discussed above, are usually very low. Hence, the enantioselectivities of our reactions, listed in Table 1, are significant, though somewhat inferior to those of the Soman group using sulfoximides.[9] Since, with both the sulfimide and sulfoximide reagents, the chirality of the sulfur reagents is lost, the fact that **2** is synthetically much more accessible is important. One difference between the reactions of sulfimide and sulfoximide stabilised anions is that, as discovered by Johnson,[16c] sulfimide additions to enones are irreversible and always give the kinetically-favoured epoxide product; with aryl sulfoximides the more stable cyclopropane product is found. Hence, sulfimides appear to be the reagents of choice for targets such as **5e**. The ees of the aziridine products are lower, though the yields are higher. Nevertheless, the enantioselectivities do compare favourably with the one previous example of asymmetric methylidene transfer to an imine.[8]

The predictable sense of the asymmetric induction for the epoxides can be rationalised by means of an open chain model, similar to one proposed by Pearson for reaction of a sulfoximide analogue,[17] which is appropriate in the case of a sodium counterion. The model assumes that the largest groups in both the sulfimide and the carbonyl component will prefer an antiperiplanar relationship with respect to the newly forming chain, *i.e.* Ar antiperiplanar to the forming carbon–carbon bond and $R_L$ antiperiplanar to the $CH_2$–S bond. This assumption generates two transition states **A** and **B**. We propose that




the unfavourable electrostatic interaction between the highly negatively charged oxygen and nitrogen centres in **A** will lead to a preference for **B** in all cases. Increasing the size of the small group $R_S$ will raise the energy of **B** more than the energy of **A**, as in **B** there are unfavourable steric interactions between $R_S$ and TsN. The model thus predicts that (*S*)-sulfimide **2** will lead to (*R*)-epoxide **5** (*via* **B**) and that the enantiomeric excess will increase as the size of group $R_S$ decreases, as observed. Unfortunately, we have not been able to ascertain the absolute configurations of the product aziridines. Hence we are unable to test the validity of the model with imine substrates.

Finally, we wished to demonstrate the synthetic utility of our approach by preparing the more highly-functionalised targets **6**, which are analogues of β-adrenoreceptor agonists. Proceeding *via* the epoxide intermediate **7** and employing Solladié-




**Scheme 6**

Cavallo's regioselective epoxide-opening method,[18] we were able to synthesise enantiomerically enriched **6a**. However, we were unable to measure the ee by either chiral HPLC or NMR. An alternative path was to proceed *via* aziridines **9**. Three imines **8** were prepared using our usual methods.[15] As with **3k**, the *N*-tosyl imine **8d** led only to racemic epoxide **7**. However, with the *N*-aryl imines **8b**,**c**, good yields of aziridines **9b**,**c** resulted, though ees were very low. Unsurprisingly, regioselective conversion of aziridines **9** to the targets **6** using acetic acid led to racemic products. We were not able to satisfactorily purify these products.

## Conclusion

The sodium salt of sulfimide **2** is a useful asymmetric methylidene transfer agent. Moderate enantioselectivities were observed with a broad range of carbonyl compounds and with imine substrates. No products were observed for highly hindered or highly conjugated substrates and *N*-tosyl imines led to racemic epoxides rather than aziridines.

## Experimental

### General

Melting points were determined on a Stuart scientific SMP1 melting point apparatus and are uncorrected. Optical rotations were recorded on an Optical Activity Ltd. model AA-1000 polarimeter at 546 nm with a path length of 2 dm and are given in units of $10^{-1}$ deg cm$^2$ g$^{-1}$. Microanalyses were performed at the University of Warwick. Mass spectra were recorded on a Kratos MS90 spectrometer. Infra-red spectra were recorded neat on a Perkin-Elmer 1720X Fourier transform spectrometer. NMR spectra were recorded on Bruker ACF 250 or Bruker ACP 400 instruments. The ees of **2**, **5a**, **5h** and **5j** were determined from their $^1$H NMR spectra in $C_6D_6$ on a Bruker ACP 400 spectrometer using one equivalent of the chiral shift reagent (*R*)-(−)-(9-anthryl)-2,2,2-trifluorethanol (98% purity). Flash chromatography was performed on silica gel (Merck Kieselgel 60$F_{254}$, 230–400 mesh). The ees of all other products were determined by chiral HPLC recorded in hexane on a column APS-Hypersil (120 Å, 5 μm) coated with 20% cellulose dimethylphenyl carbamate (CDMPC); the mobile phase was (90 : 10) hexane–propan-2-ol at a flow rate of 0.5 ml min$^{-1}$ and the product was detected by UV absorption at $\lambda_{max}$ 250 nm.

### General procedure for synthesis of epoxides

To a solution of (*S*)-*S*-methyl-*S*-tolyl-*N*-tosylsulfimide **2**[13] (0.33 mmol) in dry THF (15 ml) was added carbonyl compound (0.33 mmol) then hexane-washed sodium hydride (2.3 mmol) and the mixture was stirred under nitrogen (see Table 1 for reaction temperatures and times). The solvent was removed *in vacuo* and water (15 ml) and pentane (15 ml) were added. The organic phase was separated and the aqueous phase was further extracted with pentane (2 × 15 ml). The organic extracts were dried over magnesium sulfate and concentrated *in vacuo*. Purification was achieved by flash chromotography on silica gel using ethyl acetate–petroleum ether mixtures as eluants. Yields and ees are listed in Table 1. Other analytical data are given below.

**(*R*)-(+)-Styrene oxide**[16a] **5a.** Found: C, 79.98; H, 0.82 ($C_8H_8O$ requires C, 79.97; H 0.84%); $[\alpha]_D$ = +31 (26 °C, *c* = 3.33, benzene); 70% ee from $\delta_H$ 2.36 (1H, dd).

**(+)-2-Methyl-2-phenyloxirane**[16a] **5b.** Found: C, 80.66; H, 7.50 ($C_9H_{10}O$ requires C, 80.56; H, 7.51%); $[\alpha]_D$ = +31 (26 °C, *c* = 2.98, acetone); 45% ee from HPLC 4.2 min (+), 4.6 min (−).

**(+)-Cyclohexyloxirane**[16a] **5c.** Found: C, 76.19; H, 11.08 ($C_8H_{13}O$ requires C, 76.14; H, 11.18%); $[\alpha]_D$ = +37 (26 °C, *c* = 2.38, acetone).

**(+)-2-Methyl-2-(2-phenylethyl)oxirane**[19] **5d.** Found: C, 81.04; H, 8.64 ($C_{11}H_{14}O$ requires C, 81.44; H, 8.70%); $[\alpha]_D$ = +8.3 (29 °C, *c* = 2.08, acetone); 21% ee from HPLC 6.2 min (+), 6.8 min (−).

**(+)-[(*E*)-Styryl]oxirane**[20] **5e.** Found: C, 82.14; H, 6.84 ($C_{10}H_{10}O$ requires C, 82.16; H, 6.89%); $[\alpha]_D$ = +11 (29 °C, *c* = 3.56 acetone) 42% ee from HPLC 5.9 min (+), 6.6 min (−).

**(+)-(3,4-Dimethoxyphenyl)oxirane**[21] **7.** Yield 71%; Found: C, 66.70; H, 6.72 ($C_{10}H_{12}O_3$ requires C, 66.65; H, 6.71%); $[\alpha]_D$ = +17.0 (25 °C, *c* = 1.44, acetone); $\nu_{max}$(Nujol)/cm$^{-1}$ 1160 (C–O), 1027, 804; $\lambda_{max}$(hexane)/nm 234; $\delta_H$(250 MHz; $CDCl_3$) 2.76 (1H, dd, *J* = 2.6, 5.5 Hz, H-3), 3.08 (1H, dd, *J* = 4.1, 5.5 Hz, H-2), 3.79 (1H, dd, *J* = 2.6, 4.1 Hz, H-1), 3.95 (3H, s, MeO), 3.97 (3H, s, MeO), 6.75 (1H, d, *J* = 1.8 Hz, Ar), 6.87 (2H, m, Ar); $\delta_C$(62.9 MHz; $CDCl_3$) 50.96 (C-2), 52.29 (C-1), 55.76 (MeO), 55.85 (MeO), 107.73, 109.82, 110.93, 118.29, 129.85, 148.97 (Ar); *m*/*z* (CI) 181 (30, MH$^+$).

### General procedure for synthesis of aziridines

To a solution of (*S*)-*S*-methyl-*S*-tolyl-*N*-tosylsulfimide[13] **2** (0.16 mmol) in dry DMSO (10 ml) was added imine (0.16 mmol) then hexane-washed sodium hydride (1.2 mmol) and the mixture was stirred under nitrogen (see Table 1 for reaction temperatures and times). Work-up was as for epoxides, except that dichloromethane–ether mixtures were used for chromotography. Yields and ees are listed in Table 1. Other analytical data are given below.

**(−)-1,2-Diphenylaziridine[8] 5h.** Found: C, 86.20; H, 6.77; N, 7.18 ($C_{14}H_{13}N$ requires C, 86.25; H, 6.71; N, 7.18%); $[a]_D = -20$ (26 °C, $c = 2.05$, acetone); 38% ee from $\delta_H$ 3.48 (1H, dd).

**(−)-1-(*p*-Chlorophenyl)-2-phenylaziridine[22] 5j.** Yield 73%; 18% ee from $\delta_H$ 2.31 (1H, dd); Found: C, 73.23; H, 5.21; N, 5.98 ($C_{14}H_{12}NCl$ requires C, 73.20; H, 5.27; N, 6.01%); $[a]_D = -23$ (26 °C, $c = 1.66$, acetone); $\nu_{max}$(neat)/cm$^{-1}$ 1282, 1222, 742; $\lambda_{max}$(hexane)/nm 240; $\delta_H$(250 MHz; $CDCl_3$) 2.42 (2H, m, H-3, H-1), 3.08 (1H, dd, $J = 3.2$, 6.4 Hz, H-2), 7.00 (2H, BB′ of AA′BB′, $J = 8.7$ Hz, *p*-$C_6H_4Cl$), 7.21 (2H, AA′ of AA′BB′, $J = 8.7$ Hz, *p*-$C_6H_4Cl$), 7.35 (5H, m, Ph); $\delta_C$(100.6 MHz; $CDCl_3$) 41.74 (C-2), 60.71 (C-1), 121.75, 126.706, 127.39, 128.43, 128.89, 129.68, 138.82, 153.03 (Ar); *m*/*z* (CI, $NH_3$) 230 (100, $MH^+$ [$^{35}$Cl]).

**(−)-2-(3,4-Dimethoxyphenyl)-1-phenylaziridine 9b.** Yield 78%; 12% ee from HPLC 6.6 min (+), 7.7 min (−); $[a]_D = -13.0$ ($c = 0.86$, acetone); $\nu_{max}$(neat)/cm$^{-1}$ 2999 (C=C–H), 2956 (C–H), 2834 ($CH_3O$), 1490 (Ph), 1463 (C–H), 1333 (Ph–N), 1268 (C–N) 1144 (C–O), 1027, 810; $\lambda_{max}$(hexane)/nm 241; $\delta_H$(250 MHz; $CDCl_3$) 2.37 (1H, dd, $J = 1.2$, 3.4 Hz, H-1), 2.44 (1H, dd, $J = 1.2$, 6.4 Hz, H-3), 3.08 (1H, dd, $J = 3.4$, 6.4 Hz, H-2), 3.89 (3H, s, MeO), 3.90 (3H, s, MeO), 6.87 (2H, m, Ar), 6.91 (1H, d, $J = 1.7$ Hz, Ar), 7.05 (3H, m, Ph), 7.26 (2H, m, Ph); $\delta_C$(62.9 MHz; $CDCl_3$) 37.52 (C-2), 41.33 (C-1), 55.78 (MeO), 55.89 (MeO), 108.48, 110.92, 118.50, 120.45, 122.40, 128.95, 131.92, 148.24, 149.09, 154.44 (Ar); *m*/*z* (EI) 255 (72, $M^{\bullet+}$), 77 (100, $Ph^{\bullet+}$); satisfactory elemental analysis data were not obtained.

**(−)-1-(4-Chlorophenyl)-2-(3,4-dimethoxyphenyl)aziridine 9c.** Yield 70%; 6% ee from HPLC 6.7 min (+), 7.5 min (−); Found: C, 66.23; H, 5.55; N, 4.95 ($C_{16}H_{16}ClNO_2$ requires C, 66.32; H, 5.57; N, 4.83%); $[a]_D = -13.0$ (25 °C, $c = 1.87$, acetone); $\nu_{max}$(neat)/cm$^{-1}$ 2837 ($CH_3O$), 1464, 1376, 1269 (C–N), 1158, 1027, 810; $\lambda_{max}$(hexane)/nm 250; $\delta_H$(250 MHz; $CDCl_3$) 2.39 (2H, m, H-1, H-3), 3.03 (1H, dd, $J = 3.5$, 6.4 Hz, H-2), 3.88 (3H, s, MeO), 3.89 (3H, s, MeO), 6.84 (2H, m, Ar), 6.91 (1H, d, $J = 1.7$ Hz, Ar), 6.97 (2H, BB′ of AA′BB′, $J = 8.7$ Hz, *p*-$C_6H_4Cl$), 7.20 (2H, AA′ of AA′BB′, $J = 8.7$ Hz, *p*-$C_6H_4Cl$); $\delta_C$(100.6 MHz; $CDCl_3$) 41.57 (C-2), 55.76 (MeO), 55.85 (MeO), 67.82 (C-1), 108.57, 110.04, 116.31, 118.07, 129.24, 129.58, 133.79, 143.97 148.69, 149.08, (Ar); *m*/*z* (CI, $NH_3$) 290 (33, $MH^+$).

**(+)-2-(Isopropylamino)-1-(3,4-dimethoxyphenyl)ethanol[23] 6a.** To a 1 M solution of $LiAlH_4$ in ether (0.8 ml) was added dropwise isopropylamine (0.20 ml, 1.28 mmol) at room temperature. A white precipitate was formed, and stirring maintained for one hour. A solution of epoxide **7** (25 mg, 1.38 mmol) in ether (1 ml) was added, and the mixture was stirred overnight. The reaction was quenched with water (0.5 ml), 10% aqueous sodium hydroxide (0.5 ml), and water (1.5 ml), resulting in a new precipitate which was stirred until it became white and powdery. After filtration, evaporation of the solution gave a crude yellow oil which was purified by chromatography over silica gel pre-treated with 5% diethylamine in ether (ethyl acetate–methanol 9:1), affording a yellow powder (27 mg, 82%); mp 126–128 °C; Found: C, 62.30; H, 7.99; N, 6.90 ($C_{13}H_{21}O_3N$ requires C, 65.25; H, 8.84; N, 5.85%); $[a]_D = +9.3$ (25 °C, $c = 2.9$, acetone); $\nu_{max}$(Nujol)/cm$^{-1}$ 3392 (N–H) and (O–H), 1596 (N–H), 1464, 1167 (C–N), 1027 (C–O), 810, 735; $\lambda_{max}$(hexane)/nm 226; $\delta_H$(250 MHz; $CDCl_3$) 1.32 (6H, d, $J = 6.4$ Hz, $CH_3$), 2.78 (1H, B of ABX, $J = 9.8$, 12.0 Hz, H-2), 3.00 (1H, A of ABX, $J = 3.2$, 12.0 Hz, H-2), 3.13 (1H, br s, OH), 3.49 (1H, septet, CH), 3.91 (3H, s, MeO), 3.94 (3H, s, MeO), 4.81 (1H, dd, X of ABX, $J = 3.2$, 9.8 Hz, H-1), 6.87 (1H, d, $J = 2.0$ Hz, Ar), 7.14 (1H, dd, $J = 2.0$, 8.4 Hz, Ar), 7.41 (1H, d, $J = 2.0$ Hz, Ar); $\delta_C$(100.6 MHz; $CDCl_3$) 21.93 ($CH_3$), 22.07 ($CH_3$), 49.29 (CHN), 55.76 (MeO), 55.82 (MeO), 61.43 (C-2), 71.04 (C-1), 108.75, 109.99, 110.81, 122.65, 149.10, 157.80 (Ar); *m*/*z* (CI, $NH_3$) 240 (100, $MH^+$), 167 (17.6, ArCH=$OH^+$), 72 (84, $CH_2$=NHCH$(CH_3)_2^+$).

**(±)-2-Acetoxy-2-(3,4-dimethoxyphenyl)-*N*-phenylethylamine 6b.** Aziridine **9b** (25 mg, 0.10 mmol) was dissolved in acetic acid and stirred under nitrogen overnight. The solvent was evaporated, and the product purified by column chromatography on silica (ether–dichloromethane 7:3), affording a yellow solid (22.5 mg, 73%) mp 53–55 °C; $\nu_{max}$(neat)/cm$^{-1}$ 3389 (N–H), 2837 ($CH_3O$), 1738 (C=O), 1549 (N–H), 1515 (Ph), 1464, 1158 (C–N), 1027 (C–O); $\lambda_{max}$(hexane)/nm 243; $\delta_H$(250 MHz; $CDCl_3$) 1.64 (1H, br s, NH), 3.80 (3H, s, H-4), 3.87 (3H, s, MeO), 3.88 (3H, s, MeO), 4.12 (1H, B of ABX, $J = 4.5$, 12.3 Hz, H-2), 4.78 (1H, A of ABX, $J = 4.5$, 9.0 Hz, H-2′), 5.89 (1H, dd, X of ABX, $J = 9.0$, 12.3 Hz, H-1), 6.75 (2H, m, Ar), 6.85 (1H, d, Ar), 6.95 (3H, m, Ph), 7.18 (2H, m, Ph); $\delta_C$(100.6 MHz; $CDCl_3$) 48.75 (C-4), 55.83 (MeO), 55.85 (MeO), 65.78 (C-2), 74.25 (C-1), 109.09, 110.96, 111.28, 113.05, 117.82, 119.45, 129.07, 130.59, 148.79, 149.17 (Ar), 170.39 (C-3); *m*/*z* (CI, $NH_3$) 316 (20, $MH^+$), 167 (100, ArCH=$OH^+$), 106 (35, $CH_2$=NH–$Ph^+$); satisfactory elemental analysis data were not obtained.

**(±)-2-Acetoxy-2-(3,4-dimethoxyphenyl)-*N*-(*p*-chlorophenyl)-ethylamine 6c.** Aziridine **9c** (25 mg, 0.09 mmol) was dissolved in acetic acid and stirred under nitrogen overnight. The solvent was evaporated, and the product purified by column chromatography on silica (ether–dichloromethane 7:3), affording a yellow solid (17 mg, 57%); mp 93–94 °C; $\nu_{max}$(Nujol)/cm$^{-1}$ 3392 (N–H), 1738 (C=O), 1596 (N–H), 1464, 1167 (C–N), 1027 (C–O), 810, 735; $\lambda_{max}$(hexane)/nm 253; $\delta_H$(250 MHz; $CDCl_3$) 1.79 (1H, br s, N–H), 3.80 (3H, s, $CH_3CO$), 3.82 (3H, s, MeO), 3.84 (3H, s, MeO), 3.86 (1H, B of ABX, $J = 9.0$, 12.0 Hz, H-2), 3.89 (1H, A of ABX, $J = 2.9$, 12.0 Hz, H-2′), 5.34 (1H, dd, X of ABX, $J = 2.9$, 9.0 Hz, H-1), 6.78 (2H, dd, $J = 1.8$, 7.3 Hz, Ar), 6.92 (1H, d, $J = 1.8$ Hz, Ar), 7.35 (2H, BB′ of AA′BB′, $J = 8.7$ Hz, *p*-$C_6H_4Cl$), 7.51 (2H, AA′ of AA′BB′, $J = 8.7$ Hz, *p*-$C_6H_4Cl$); $\delta_C$(100.6 MHz; $CDCl_3$) 49.05 (C-4), 55.84 (MeO), 56.34 (MeO), 60.84 (C-2), 73.95 (C-1), 109.61, 110.98, 111.29, 114.36, 119.81, 128.91, 129.68, 130.24, 132.66, 148.96 (Ar), 170.39 (C-3); *m*/*z* (CI) 350 (24.4, $MH^+$), 167 (80, ArCH=$OH^+$); satisfactory elemental analysis data were not obtained.

## References


1 Asymmetric epoxidations: R. A. Johnson and K. B. Sharpless, in *Catalytic Asymmetric Synthesis*, ed. I. Ojima, VCH, Weinheim, 1993, Section 4.1; E. N. Jacobsen, in *Catalytic Asymmetric Synthesis*, ed. I. Ojima, VCH, Weinheim, 1993, Section 4.2.

2 Asymmetric aziridinations: D. A. Evans, M. M. Faul, M. T. Bilodeau, B. A. Anderson and D. M. Barnes, *J. Am. Chem. Soc.*, 1993, **115**, 5328; Z. Li, K. R. Conser and E. N. Jacobsen, *J. Am. Chem. Soc.*, 1993, **115**, 5326; P. Müller, C. Baud and Y. Jacquier, *Tetrahedron*, 1996, **52**, 1543; M. J. Södergren, D. A. Alonso and P. G. Andersson, *Tetrahedron: Asymmetry*, 1997, **8**, 3563.

3 S. E. Kelly, in *Comprehensive Organic Synthesis*, ed. B. M. Trost and I. Fleming, Pergamon, Oxford, 1991, Section 3.1.

4 A-H. Li, L.-X. Dai and V. K. Aggarwal, *Chem. Rev.*, 1997, **97**, 2341.

5 M. Tokunaga, J. F. Larrow, F. Kakiuchi and E. N. Jacobsen, *Science*, 1997, **277**, 936.

6 A. Solladié-Cavallo and A. Diep-Vohuule, *J. Org. Chem.*, 1995, **60**, 3494.

7 B. M. Trost and R. F. Hammen, *J. Am. Chem. Soc.*, 1973, **95**, 962.

8 C. R. Johnson, R. A. Kirchoff, R. J. Reischer and G. F. Katekar, *J. Am. Chem. Soc.*, 1973, **95**, 4287. There is an error in the structure labelled as 4-(*R*) in this paper since the molecule shown is of (*S*) configuration.

9 S. S. Taj, A. C. Shah, D. Lee, G. Newton and R. Soman, *Tetrahedron: Asymmetry*, 1995, **6**, 1731; S. S. Taj and R. Soman, *Tetrahedron: Asymmetry*, 1994, **5**, 1513.

10 C. P. Baird and P. C. Taylor, *J. Chem. Soc., Chem. Commun.*, 1995, 893.

11 V. K. Aggarwal, A. Thompson, R. V. H. Jones and M. C. H. Standen, *J. Org. Chem.*, 1996, **61**, 8368.

12 A.-H. Li, Y.-G. Zhou, L.-X. Dai, X.-L. Hou, L.-J. Xia and L. Lin, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 1317.

13 D. J. Cram, J. Day, D. R. Rayner, D. M. von Schrilz, D. J. Duchamp and D. C. Garwood, *J. Am. Chem. Soc.*, 1970, **92**, 7369.
14 G. Celentano, S. Colonna, N. Gaggero and C. Richelmi, *Chem. Commun.*, 1998, 701.
15 L. A. Bigelow and H. Eatough, *Org. Synth.*, 1941, **1**, 80; W. B. Jennings and C. J. Lovely, *Tetrahedron Lett.*, 1988, **29**, 3725.
16 (*a*) Y. Tamura, H. Matsushima and M. Ikeda, *Synthesis*, 1976, 35; (*b*) Y. Tamura, S. M. Bayomi, K. Sumoto and M. Ikeda, *Synthesis*, 1977, 693; (*c*) C. R. Johnson, K. Mori and A. Nakanishi, *J. Org. Chem.*, 1979, 2065.
17 A. J. Pearson, S. L. Blystone, H. Nar, A. A. Pinkerton, B. A. Roden and J. Y. Yoon, *J. Am. Chem. Soc.*, 1989, **111**, 134.
18 A. Solladié-Cavallo and M. Bencheqroun, *J. Org. Chem.*, 1992, **57**, 5831; we used a modified procedure described by the same group in Solladié-Cavallo, ref. 6 above.
19 S. K. Taylor, G. H. Hockerman, G. L. Karrick, S. B. Lyle and S. B. Schramm, *J. Org. Chem.*, 1983, **48**, 2449.
20 N. Krause and D. Seebach, *Chem. Ber.*, 1988, **121**, 1315.
21 M. Alvarez, R. Granados, R. Lavilla and M. Salas, *J. Heterocycl. Chem.*, 1985, **22**, 745.
22 E. Liepins, V. A. Pestunovich, A. V. Eremeev, D. A. Tikhomirov and N. P. Gaidarova, *Khim. Geterotsikl. Soedin.*, 1977, 906 (*Chem. Abstr.*, 1977, **87**, 183795b).
23 US 3281468 (*Chem. Abstr.*, 1967, **67**, 11329y).

*Paper 8/05405C*