Preparation of Chiral Aziridines from Chiral Oxiranes with Retention of Configuration

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Chiral oxiranes are converted into chiral aziridines *via* β-hydroxyalkyl aryl sulfides and then β-tosylaminoalkyl aryl sulfides without loss of optical purity and with overall retention of configuration.

Recently, various procedures have been reported for the preparation of chiral aziridines with both biological[1] and chemical[2,3] interest. However, their preparations are still far from general as compared to those of chiral oxiranes.[4] We report herein that chiral oxiranes can be converted into chiral aziridines without loss of optical purity and with retention of configuration by the utilization of sulfur chemistry. Our procedure should be a good complement of the known procedure from oxiranes to aziridines with the inversion of configuration,[3] since it is not always possible to prepare both enantiomers of chiral oxiranes.

Our procedure is summarized in Scheme 1. Chiral oxiranes are converted into chiral β-hydroxyalkyl aryl sulfides (**2** and/or **3**) by a reported reaction.[5] The next stage is the key step of our procedure: *i.e.* the replacement of the hydroxy group by a tosylamino group with retention of configuration through the anchimeric assistance of the arylthio group **7**. The resulting β-tosylamino-substituted sulfides (**4** and/or **5**) were converted into the sulfonium salts, which were further treated with sodium hydride to afford tosyl protected chiral aziridines **6** in excellent yields. The regioselectivity of our procedure is noteworthy. A mixture of regioisomers was produced (in some cases) in two stages in Scheme 1, which then afforded one product in the next step without loss of optical purity (entries 2,3 and 4 in Table 1). Thus, one chiral aziridine was produced from each chiral oxirane.

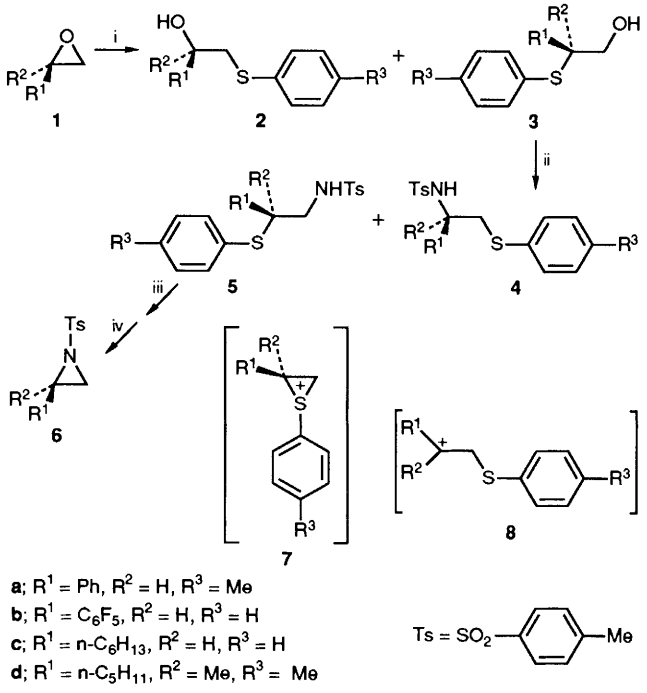
In the key step of our procedure, partial racemization (*ca.* 20%) was observed even in the reactions at −20 °C in some substrates where R^3 is H and R^1 and/or R^2 can stabilize an adjacent carbenium ion **8**. We minimized the partial racemization by the introduction of a methyl group into the arylthio group (R^3 = Me)(**2a** and **d** in Table 1). It is reasonable to assume that the episulfonium ion **7** would be stabilized effectively by the methyl group (R^3) on the benzene ring, while little stabilization would be expected on the (open chain) carbenium ion **8**, thus favouring the reaction with retention of configuration.

The use of sulfonamide as a nitrogen source is important for our aziridine formation, since sulfonium salts bearing the β-acylaminoalkyl substituent have been reported to afford oxazoline derivatives through cyclization by an oxygen atom.[6] To the best of our knowledge this transformation represents

Table 1 Chemical yields and enantiomeric excesses of sulfonamides and aziridines

			Step ii in Scheme 1							
Entry	Alcohol	E.e. (%)	Temp/°C	Time/h	Amide	Yield (%)	E.e. (%)	Aziridine	Yield (%)	E.e. (%)
1	**2a**	100	−20	2	**4a**	70	99[a]	**6a**	91	98[c]
2	**2b**	96	25	2	**4b**	94	96[a]	**6b**	92	95[c]
3	**3b**	97	25	96	**4b**	92	97[a]			
4	**2c**	91	25	24	**4c**	52	91[a]	**6c**	99	90[d]
					5c	33	92[a]			
5	**2d**	86	−20	2	**4d**	59	82[b]	**6d**	75	82[c]

[a–c] Determined by liquid chromatography using chiral column (Daicel,[a] Chiralcel OD,[b] Chiralpak AD, [c] Chiralcel AS). [d] Derivatised to *N*-[1-(2-methylpropyl)heptyl]toluene-*p*-sulfonamide by the reaction with isopropylmagnesium bromide and analysed by liquid chromatography using chiral column (Daicel, Chiralcel AS).



Scheme 1 *Reagents and conditions*: i, *p*-$R^3C_6H_4SH$, $NaBH_4$; ii, $BF_3{\cdot}OEt_2$, $TsNH_2$, CH_2Cl_2; iii, Me_3OBF_4, room temp. 4–6 h; iv, NaH, tetrahydrofuran, room temp., 24 h

the first example of the *N*-alkylation of sulfonamides by sulfonium salts. As the double alkylations proceeded stereospecifically, chiral *N*-tosylaziridines were produced. In principle our methodology would be applicable to various types of substituted oxiranes and our progress along this line will be reported in due course.

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