Pergamon

Tetrahedron 56 (2000) 2967–2974

TETRAHEDRON

Synthesis of 2-(α-Substituted *N*-Tosylaminomethyl)-2,5-Dihydrofurans by Reaction of *N*-Sulfonylimines with Arsonium or Sulfonium 4-Hydroxyl-*cis*-2-butenylides

Wei-Ping Deng, An-Hu Li, Li-Xin Dai* and Xue-Long Hou

Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, People's Republic of China

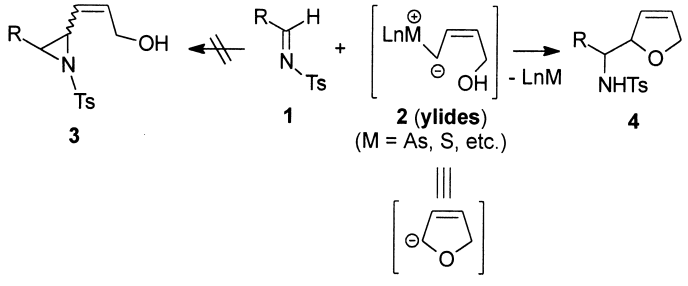
Received 18 November 1999; revised 14 February 2000; accepted 2 March 2000

Abstract—On treatment of *N*-tosylimines **1** and 4-hydroxyl-*cis*-butenyl arsonium salt **5** or sulfonium salt **11a** with KOH in acetonitrile at room temperature, 2-(α-substituted *N*-tosylaminomethyl)-2,5-dihydrofurans **4** were obtained in moderate yields through a new ylide cyclization process. Ylide **2** acts formally as an equivalent of the 2,5-dihydrofuran anion. However, the reaction of 4-hydroxyl-*trans*-butenyl sulfonium salt **11b** with *N*-tosylimine **1b** under the same conditions gave only the normal aziridination product **12**. A plausible mechanism was proposed for this new 5-membered cyclization reaction, and a high yield process for the synthesis of target molecules **4** is also recommended.

Introduction

The discovery of the Wittig reaction in 1953[1] symbolized the formal entering of ylides into the field of organic chemistry as an important synthetic tool. Over the past 46 years, three types of ylide reactions, i.e. olefinations, cyclizations to three-membered ring compounds (epoxidation, cyclopropanation, and aziridination), and rearrangements, have been developed and some of them have been successfully applied in the synthesis of complex molecules.[2] In our previous work on the reactivities of semi-stabilized and stabilized ylides, an efficient asymmetric[3] and a stereocontrolled[4] epoxidation, stereochemically tunable cyclopropanations,[5] and *N*-sulfonylimines-based aziridinations,[6a–d] including their asymmetric version,[6e,f] have been realized. In the study of ylide aziridinations, we found that, in contrast to common *N*-alkyl- or *N*-aryl-imines, *N*-sulfonylimines **1** showed unusually high reactivity towards either semi-stabilized allylic[6a–c] and propargylic[6e] sulfonium ylides or stabilized allylic ylides[6d] and even a carboxamide stabilized ylide.[6f] This encouraged us to further extend the application of ylide reagents.

We have reported in a preliminary communication that when functionalized arsonium or sulfonium 4-hydroxyl-*cis*-2-butenylides **2** were used to react with *N*-sulfonylimines **1**, instead of the expected aziridine **3**, a five-membered heterocyclic ring product **4** was obtained (Scheme 1).[6g] To our knowledge, this was the first example of the reaction of an imine with an ylide to form a five-membered ring compound. Herein, we report the full details about this reaction.

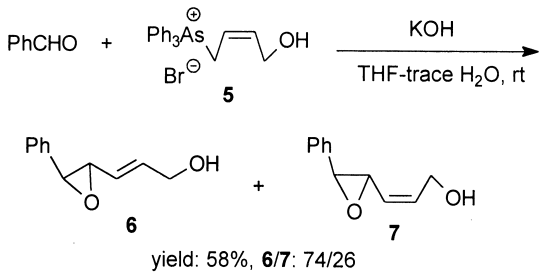


Scheme 1.

Keywords: dihydrofuran; ylide; aziridination; *N*-tosylimines.

* Corresponding author. Tel.: +86-21-6416-3300; fax: +86-21-6416-6128; e-mail: dailx@pub.sioc.ac.cn

0040–4020/00/$ - see front matter
PII: S0040-4020(00)00191-5



Scheme 2.

Results and Discussion

Reaction of *N*-tosylimines 1 with arsonium salt 5 in the presence of KOH under phase-transfer conditions

In 1991, Huang et al.[7] found that, similar to other semi-stabilized allylic arsonium ylides,[8] hydroxyl-substituted ylides produced in situ from *cis*-butenyl arsonium salt **5** react smoothly with benzaldehyde to form a 74:26 mixture of vinylepoxides **6** and **7** in 58% yield (Scheme 2). Besides the expected *cis*/*trans* product **7**, the *trans*/*trans* product **6** was also produced as a result of isomerization of the *cis*-double bond containing arsonium salts and/or the corresponding ylides.

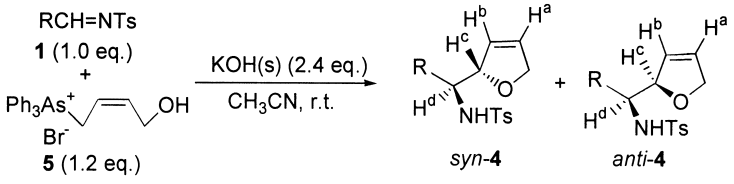
Based on our previous experiences in aziridination of *N*-sulfonylimines with allylic ylides,[6] we attempted to use *N*-tosylimines instead of benzaldehyde to perform the above reaction since hydroxyl-functionalized propenyl-substituted aziridines might be prepared. Therefore, we mixed imine **1** (R=Ph, 1.0 equiv.), arsonium salt **5** (1.2 equiv.), and powdered KOH (2.4 equiv.) in CH_3CN at room temperature. After completion of the reaction (5–12 min) and work-up, we obtained a product with complex NMR spectra, which could hardly be assigned the expected aziridination products but looked rather like an unexpected product, 2,5-dihydrofuran derivative **4a**, in consideration of the complex coupling patterns of this kind of compound[9] (Scheme 3).

To further confirm the structure of the product we obtained, a simple chemical transformation was performed, i.e. the oxidation of product **4a** with PCC. As expected, *N*-tosyl furyl-substituted benzylamine **8** was obtained, whose structure was unambiguously assigned based on its spectroscopic and microanalytical data (Scheme 4). The 2,5-dihydrofuran structure of product **4a** was therefore deduced and was also in good agreement with its characteristic spectroscopic data.

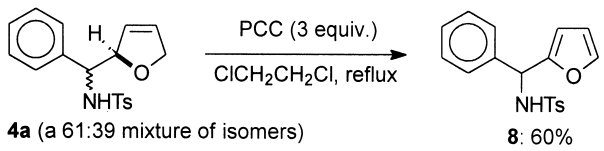
From the standpoints of both ylide chemistry and methodology for preparing 2,5-dihydrofuran derivatives, the above newly found reaction (Scheme 3) was noteworthy. Firstly, this reaction formally looks like a direct addition of a 2,5-dihydrofuran anion to an imine and ylide **2** acted as an equivalent of a 2,5-dihydrofuran anion (Scheme 1). Secondly, the present one-pot process may provide a simpler, mild, and direct entry to dihydrofuran derivatives.[10] Also, 2,5-dihydrofuran-derived amines **4** are expected to be a type of very useful synthetic intermediate. This is not only because they exist as a structural unit in antibiotics such as furanomycin[11] but also because they can undergo a variety of chemical transformations,[12] e.g. conversion into γ-butenolides,[13] and many synthetic applications have been reported.[14]

To explore the substrate scope of the above new reaction (Scheme 3), a series of imines were examined and some results are listed in Table 1. Table 1 shows that various aromatic (entries 1–4), heteroaromatic (entry 5), and α,β-unsaturated (entry 6) *N*-tosylaldimines are suitable substrates for this reaction. However, when aliphatic aldimines (*t*-BuCH=NTs, *c*-C_6H_{11}CH=NTs) and ketimine (Me_2C=NTs) were used, only carbonyl compounds from the hydrolysis of precursor imines were obtained. With *N*-aryl- or -alkyl-imines, no 2,5-dihydrofurans were obtained. Among several solvents and bases tried, CH_3CN and solid KOH were the most suitable solvent and base. In addition, the use of an excess amount of base (>2.0 equiv.) was necessary to keep ylides in high concentration, which could ensure that the ylide cyclization is more favored and therefore leads to high yields of 2,5-dihydrofurans, because the hydrolysis of imines to aldehydes and $TsNH_2$ is competitive with the ylide cyclization reaction. Under the above conditions, moderate yields were obtained in all cases but the ratios of *syn* and *anti* isomers (vide infra) were not satisfactory.

The ratio of *syn***4**:*anti***4** could be determined by the integral of NMR peak area of H^d, H^c, or two olefinic protons. But the assignment of each isomer was still pending. During the study of the mechanism of this reaction, we had compound **9a** with known geometry at hand. Fortunately, we found it is easy to deprotect the TBS group of **9a** and consequently open the aziridine ring to construct the 2,5-dihydrofurans **4**. In consideration of the mechanism of this reaction intramolecular S_N2 reaction, the stereoconfiguration of aziridines ring should dictate that of the product, i.e. *cis* aziridine affords *syn* product and *trans* aziridine affords *anti* product (Scheme 5). When a 3:7 mixture of *cis*/*trans* isomers were exposed to the reaction condition, a 3:7 mixture of product was obtained in quantitative yields. The *syn* and *anti* isomers were thus assigned and the ratio of *syn*/*anti* is equal to 3:7.



Scheme 3.



Scheme 4.

Table 1. Preparation of 2-(α-substituted *N*-tosylaminomethyl)-2,5-dihydrofurans **4** by the reaction of *N*-sulfonylimines **1** with arsonium salt **5** under solid–liquid phase-transfer condition (all reactions were carried out under solid–liquid phase-transfer conditions at 25°C in a ratio of imine/arsonium salt/KOH=1:1.2:2.4 at a 0.5-mmol scale in CH_3CN)

Entry	R (imine **1**)	Product	Yield of **4** (%)[a]	*anti*/*syn*[b]
1	Phenyl– (**1a**)	**4a**	54	61/39
2	*p*-ClC_6H_4– (**1b**)	**4b**	62	68/32
3	1-Naphthyl– (**1c**)	**4c**	60	57/43
4	2-$MeOC_6H_4$– (**1d**)	**4d**	68	61/39
5	2-Furyl– (**1e**)	**4e**	62	62/38
6	Cinnamyl– (**1f**)	**4f**	52	51/49

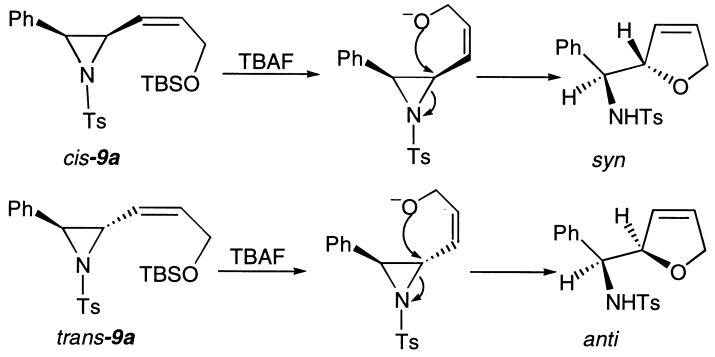
[a] Isolated yields based on imine (5–20%) of aldehydes from the hydrolysis of corresponding imine were also obtained in all cases.
[b] Determined by 300 MHz ^1H NMR analysis and *syn* or *anti* isomers were assigned by chemical transformation.

Reaction of *N*-tosylimines 1b with *cis* sulfonium salt 11a and *trans* sulfonium salt 11b in the presence of KOH under phase-transfer conditions

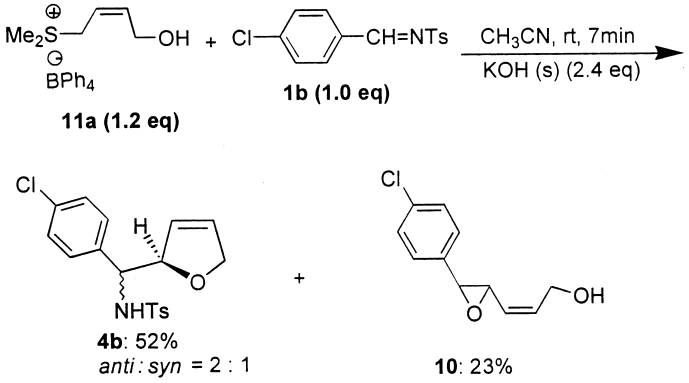
In our previous aziridination by using allylic ylides, we found that sulfonium ylides were better than the corresponding arsonium and telluronium ylides.[6b] Furthermore, arsonium ylides are relatively more toxic and expensive than sulfonium ylides. For these reasons, *cis* sulfonium salt **11a** and its *trans* analog **11b** were prepared[15] and used to replace arsonium salt **5** to react with imine **1b** in the presence of KOH (Scheme 6).

As expected, under the same conditions with the reaction using arsonium salt **5** (see Scheme 3), sulfonium ylides produced in situ from sulfonium salt **11a** reacted smoothly with imine **1b** to give 2,5-dihydrofuran **4b** in 52% yield, together with 23% of epoxide **10**, which came from the reaction of ylides with *p*-ClC_6H_4CHO (from the hydrolysis of imine **1b**). However aziridine **12** (50%), accompanied with epoxide **13** (26%), was produced instead of 2,5-dihydrofuran products when *trans* sulfonium salt **11b** was used (Scheme 7).

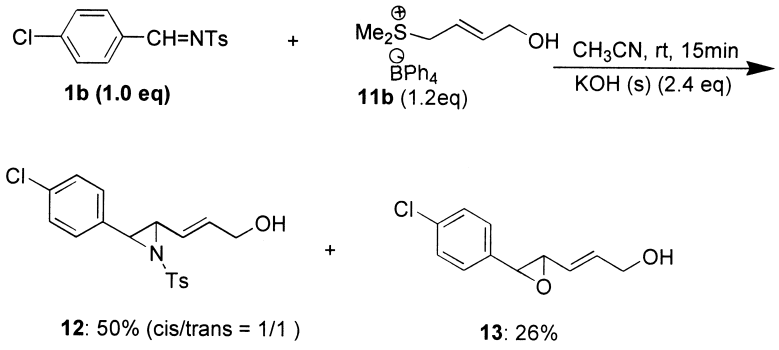
Although similar yields were achieved in preparing 2,5-dihydrofuran **4b** using arsonium **5** and sulfonium **11a** (comparing entry 2 in Table 1 and Scheme 6), the former was still more preferred in consideration of the easy work-up. In the former reaction, the main by-product was



Scheme 5.



Scheme 6.



Scheme 7.

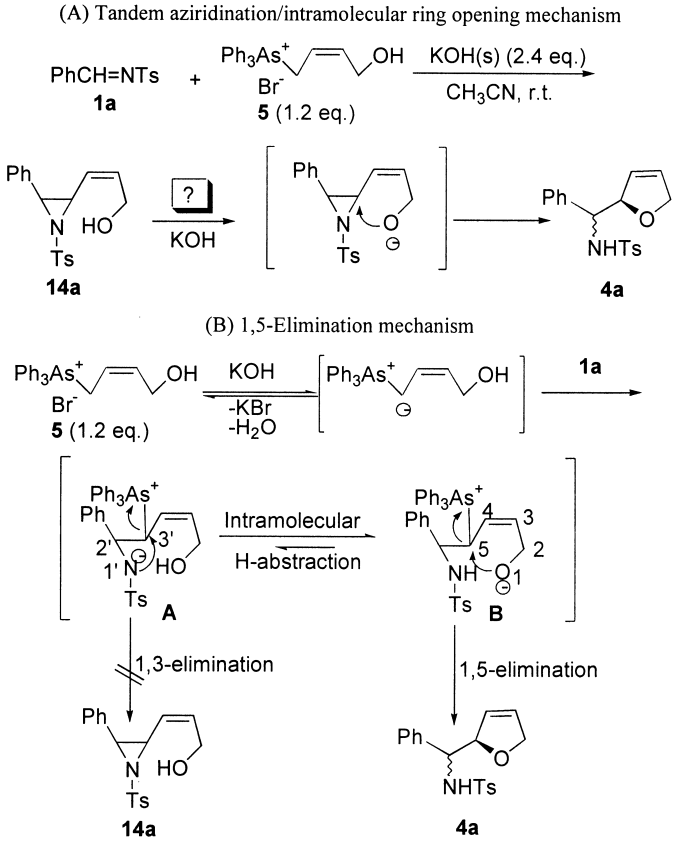
p-ClC_6H_4CHO and *N*-$TsNH_2$ from the hydrolysis of imine **1b**, which were easily separated from the product **4b**, but the main by-product in the latter reaction was epoxide **10**, which had similar R_f value to product **4b** and therefore a little difficulty might be encountered in the work-up process and careful handling was necessary.

Mechanistic interpretations for the reactions to produce 2,5-dihydrofuran derivatives

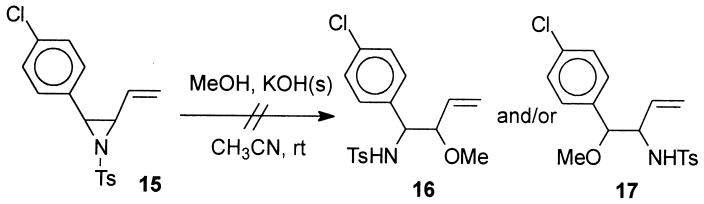
To explain the results, based on the known knowledge,[16] two possible ways may be speculated upon the production of 2,5-dihydrofuran derivatives in the reactions of *N*-tosyl-imines with *cis* 4-hydroxyl-butenylic ylides (Scheme 8).

In order to probe if product **4a** came from intramolecular ring-opening of aziridine **14a** (mechanism A) or not, vinyl-aziridine **15** was prepared according to our previous publications[6a,b] and used to react with MeOH in the presence of KOH at room temperature (the same conditions as those reactions in Schemes 3 and 6). However, neither ring-opening products **16** or **17** were obtained under such conditions (Scheme 9).

The failure of this model reaction demonstrated that conversion of **14a** into **4a** under such mild conditions was, at least, not easy. In addition, there are very few examples for aziridine ring-openings just with KOH/CH_3CN at room temperature.[17] Furthermore, an intramolecular ring-opening reaction will be easier than that of an intermolecular one. As shown in Scheme 5, ring opening of deprotected **9a** did afford the five-membered product under the same condition



Scheme 8.



Scheme 9.

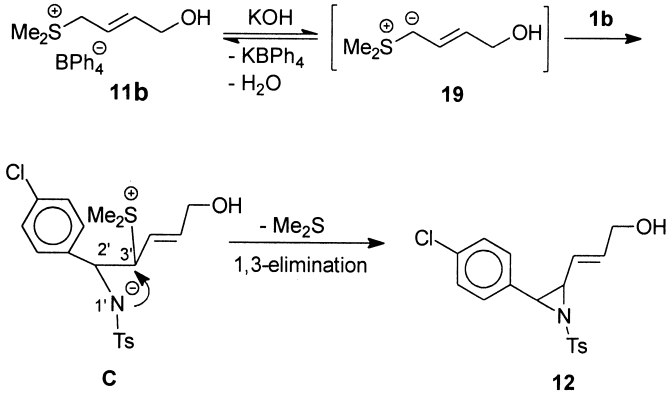
at last. At this moment, we are not able to discriminate which mechanism is more possible. If mechanism A is operative, it is possible to isolate **14a** during the reaction process. At first, we were not able to see any evidence of the presence of **14a** all the time, even with very careful manipulation, and mechanism B is favored by this phenomenon. On further consideration, we think, perhaps, compound **14a** is too susceptible in the reaction conditions. Therefore, we changed the reaction conditions by using NaOH aqueous solution and dichloromethane. Under these conditions, compound **14a** may enter the organic phase immediately on its formation and then is prevented from further reaction. Actually, compound **14a** was obtained as an impure product.[19] IR spectra showed a clear indication of a free hydroxyl group and ^{1}H NMR seemed to be a spectrum of **14a** and **4a**. On the other hand, by the analysis of ^{1}H NMR in DMSO-d_6, a multiple peak was found, but it disappears on treatment with D_2O. From this fact, the existence of a free hydroxyl group was further confirmed. Anyhow, on treatment of **14a** with KOH/THF, only a single product of **4a** was obtained in quantitative yield. So, mechanism A of this reaction is a very plausible one.

When *trans* sulfonium salt **11b** is used to replace *cis* sulfonium salt **11a**, the addition intermediate C is formed, which undergoes 1,3-elimination to construct aziridine **12**. However, it cannot undergo an intramolecular ring-opening reaction to form a five-membered ring product owing to the *trans* configuration of the double bond (Scheme 10).

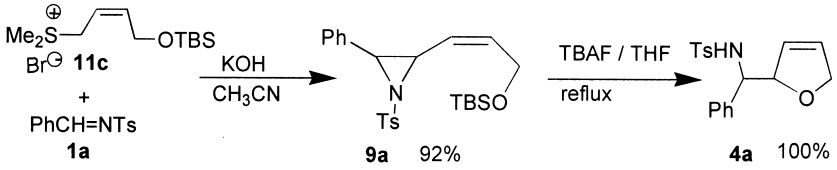
Upon this understanding, the dihydrofuran compound could also be synthesized in high yield. When ylide **11c** was reacted with *N*-tosylimines, as expected, corresponding aziridine compounds were derived in high yields under the same reaction condition, though the stereoselectivity is still not satisfactory, as shown in Scheme 11. The TBS protecting group of **9a** can be removed by treating with TBAF/THF, and the aziridine ring was opened immediately and 2,5-dihydrofuran compound **4a** was obtained in quantitative yields at refluxing temperature.

Conclusions

A simple and efficient one-pot process for the preparation of dihydrofuran-substituted *N*-tosyl amines through the reaction of *N*-tosylimines with arsonium or sulfonium 4-hydroxyl-*cis*-butenylides under very mild conditions was developed. Ylides produced from arsonium salt **5** or sulfonium salt **11a** may be formally regarded as the equivalents of 2,5-dihydrofuran anions. The products dihydrofuran-substituted amines may find applications in the synthesis of many complex molecules. Based on the results of comparative experiments, a tandem aziridination/



Scheme 10.



Scheme 11.

intramolecular ring opening reaction mechanism was proposed. An alternative tandem reaction is proposed for the synthesis of dihydrofuran derivatives **4** in high yield.

Experimental

Materials and general procedure

All reagents and solvents, unless otherwise specified, are commercially available and used without further purification. All *N*-sulfonylimines **1** were prepared according to literature methods in reasonable yields.[18] Arsonium salt **5** and sulfonium salts **11a** and **11b** were prepared by the reaction of corresponding 4-hydroxyl-2-butenyl bromides with Ph_3As or dimethylsulfide, and sulfonium salt **11c** was prepared by the reaction of corresponding bromide with dimethylsulfide in a little amount of acetone at room temperature with excellent yields.[7,15]

General procedure for the preparation of 2,5-dihydrofurans (method A). A 25-mL flask containing a magnetic stirring bar was charged with imine (**1**, 0.5 mmol), arsonium salt **5** (0.6 mmol), and acetonitrile (4 mL, reagent grade; it need not be dried before use). Powdered potassium hydroxide (2.0 mmol) was subsequently added under stirring. After the reaction was complete according to TLC, the reaction mixture was filtered on a short silica gel column to remove solid materials. The filtrate was concentrated and purified by chromatography on a preparative silica gel plate with a mixture of light petroleum (60–90°C) and ethyl acetate (3:1) as the eluent to give a white solid product **4**.

Oxidation of 2-(α-phenyl *N*-tosylaminomethyl)-2,5-dihydrofuran (4a). Compound **4a** (99 mg, 0.3 mmol) and PCC (65 mg, 0.3 mmol) were dissolved in anhydrous $ClCH_2CH_2Cl$ (3 mL) and stirred under reflux for 1 h. Two other portions of PCC (130 mg, 0.6 mmol) were then added to the reaction mixture at an interval of 1 h. After the reaction was complete according to TLC, the reaction mixture was filtered on a short silica gel column to remove solid materials. The filtrate was concentrated and chromatographed on a preparative silica gel plate with a mixture of light petroleum (60–90°C) and ethyl acetate (3:1) as the eluent to give a white solid product **8**, 60 mg, yield, 60%. Mp 160–161°C; IR (KBr pellet): 3269, 1599, 1458, 1444, 1322, 1161, 1095, 1057, 929, 811, 704, 666, 566; ^{1}H NMR ($CDCl_3$) δ 2.30 (s, 3H), 5.27 (d, J=7.7 Hz, 1H), 5.54 (d, J=7.7 Hz, 1H), 5.92 (d, J=2.9 Hz, 1H), 6.11 (dd, J=2.0, 3.2 Hz, 1H), 7.06–7.19 (m, 8H), 7.51 (dd, J=2.0, 8.3, 2H); MS *m/z* 250 (2.2), 172 (100), 157 (25.4), 143 (31.3), 128 (17.1), 91 (21), 77 (8.1), 43 (5.0); FAB-MS *m/z* 327 (M^+); Anal. Calcd for $C_{18}H_{17}NO_3S$: C, 66.05; H, 5.18; N, 4.25. Found: C, 66.01; H, 5.10; N, 3.98.

2-(α-Phenyl *N*-tosylaminomethyl)-2,5-dihydrofuran (4a) (method A). A white solid, mp 107–108°C; IR (KBr pellet): 3280, 2840, 1600, 1500, 1440, 1320, 1165, 1080, 940, 815, 700, 680; *anti*-**4a**: ^{1}H NMR ($CDCl_3$) δ 2.34 (s, 3H), 4.46–4.58 (m, 3H), 5.03–5.06 (m, br., 1H), 5.27 (d, J=7.6 Hz, 1H), 5.56–5.59 (m, 1H), 5.86–5.89 (m, 1H), 7.07–7.18 (m, 7H), 7.56 (m, 2H); MS *m/z* 329 (M^+, 5.8), 281 (62.6), 260 (22), 249 (3), 221 (11.7), 207 (11), 178 (5), 155 (18.4), 147 (48), 133 (3.8), 117 (5.1), 91 (26), 73 (100), 69 (9.7), 57 (3.7), 44 (14); HRMS Calcd for ($C_{14}H_{14}NO_2S$, $M^+-C_4H_5O$) 260.0745, found 260.0745. *syn*-**4a**: ^{1}H NMR ($CDCl_3$) δ 2.36 (s, 3H), 4.37–4.41 (m, 3H), 4.90 (m, 1H), 5.38 (d, J=5.2 Hz, 1H), 5.47 (m, 1H), 5.94 (m, 1H), 7.07–7.18 (m, 7H), 7.51 (dd, J=1.5, 8.3 Hz, 2H).

2-[α-(*p*-Chlorophenyl) *N*-tosylaminomethyl]-2,5-dihydrofuran (4b) (method A). A white solid, mp 76–77°C; IR (KBr pellet): 3250, 1600, 1495, 1440, 1325, 1160, 1090, 1070, 1015, 890, 810,760, 690; *anti*-**4b**: ^{1}H NMR ($CDCl_3$) δ 2.36 (s, 3H), 4.44–4.54 (m, 3H), 5.00–5.04 (m, br., 1H), 5.30 (d, J=7.2 Hz, 1H), 5.53–5.57 (m, 1H), 5.83–5.86 (m, 1H), 7.00–7.14 (m, 6H), 7.52–7.56 (m, 2H); MS *m/z* 296 (17), 294 (43.7), 281 (0.8), 262 (1.2), 223 (4.9), 193 (11.7), 165 (1), 155 (61), 138 (16), 125 (4), 111 (5.7), 91 (100), 77 (9), 69 (78.4), 65 (27), 51 (6); HRMS Cacld for ($C_{14}H_{13}{}^{35}ClNO_2S$, $M^+-C_4H_5O$) 294.0356, found 294.0349; Calcd for ($C_{14}H_{13}{}^{37}ClNO_2S$, $M^+-C_4H_5O$) 296.0326, found 296.0323. *syn*-**4b**: ^{1}H NMR ($CDCl_3$) δ 2.36 (s, 3H), 4.27–4.36 (m, 3H), 4.85–4.87 (m, br., 1H), 5.34 (d, J=5.4 Hz, 1H), 5.46–5.49 (m, 1H), 5.90–5.93 (m, 1H), 7.00–7.14 (m, 6H), 7.52–7.56 (m, 2H).

2-[α-(*o*-Methoxyphenyl) *N*-tosylaminomethyl]-2,5-dihydrofuran (4c) (method A). A colorless oil; IR (KBr pellet): 3250, 1600, 1490, 1460, 1320, 1240, 1150, 1070, 1020, 820; *anti*-**4c**: ^{1}H NMR ($CDCl_3$) δ 2.27 (s, 3H), 3.72 (s, 3H), 4.32–4.49 (m, 3H), 4.60–4.72 (m, 1H), 4.93–4.96 (m, 1H), 5.49–5.52 (m, 1H), 5.62 (d, J=8.6 Hz, 1H), 5.86–5.89 (m, 1H), 6.63–6.72 (m, 2H), 6.92–7.10 (m, 4H), 7.50 (dd, J=1.3, 8.2 Hz, 2H); MS *m/z* 360 (M^++1, 0.4), 359 (M^+, 0.1), 342 (3.4), 290 (100), 274 (0.9), 262 (3), 223 (7.7), 203 (2.7), 189 (38), 187 (11.7), 175 (0.7), 155 (25.9), 134 (8.3), 121 (17.4), 104 (9), 91 (77.3), 77 (8.6), 69 (55), 65 (22), 51 (5.1); HRMS Calcd for ($C_{15}H_{16}NO_3S$, $M^+-C_4H_5O$) 290.0851, found 290.0844. *syn*-**4c**: ^{1}H NMR ($CDCl_3$) δ 2.27 (s, 3H), 3.74 (s, 3H), 4.20 (m, 1H), 4.32–4.49 (m, 1H), 4.60–4.72 (m, 1H), 4.98–5.02 (m, 1H), 5.58 (d, J= 8.6 Hz, 1H), 5.70–5.76 (m, 1H), 5.86–5.89 (m, 1H), 6.63–6.72 (m, 2H), 6.92–7.10 (m, 4H), 7.22 (m, 2H).

2-[α-(1-Naphthyl) *N*-tosylaminomethyl]-2,5-dihydrofuran (4d) (method A). A colorless oil; IR (KBr pellet): 3300, 3040, 1600, 1520, 1420, 1335, 1165, 1100, 1080, 915; *anti*-**4d**: ^{1}H NMR ($CDCl_3$) δ 2.25 (s, 3H), 4.45–4.70 (m, 2H), 5.05–5.27 (m, 2H), 5.44–5.61 (m, 2H), 5.88–5.93 (m, 1H), 6.86–7.97 (m, 11H); MS *m/z* 360 362 (1.8), 310 (41.8), 262 (1.9), 223 (4.4), 209 (18.5), 191 (1.9), 178 (2.2), 165 (3.2), 154 (46), 141 (4.8), 139 (5), 127 (26.3), 115 (2.6), 102 (2.7), 91 (46), 89 (9), 77 (5.2), 69 (100), 65 (20.5), 51 (4.3); HRMS Calcd for ($C_{18}H_{16}NO_2S$, $M^+-C_4H_5O$) 310.0902, found 310.0917. *syn*-**4d**: ^{1}H NMR ($CDCl_3$) δ 2.27 (s, 3H), 4.45–4.70 (m, 2H), 5.05–5.27 (m, 2H), 5.44–5.61 (m, 2H), 5.82–5.85 (m, 1H), 6.86–7.97 (m, 11H).

2-[α-(2-Furyl) *N*-tosylaminomethyl]-2,5-dihydrofuran (4e) (method A). A white solid, mp 98–99°C; IR (KBr pellet): 3250, 3000, 1600, 1500, 1440, 1330, 1160, 1080, 1010, 815; *anti*-**4e**: ^{1}H NMR ($CDCl_3$) δ 2.41 (s, 3H), 4.46–4.61 (m, 3H), 5.04–5.11 (m, 2H), 5.68–5.73 (m, 1H), 5.92–6.00 (m, 1H), 6.13–6.17 (m, 1H), 6.24–6.25 (m, 1H), 7.15–7.30 (m, 3H), 7.60–7.66 (m, 2H); MS *m/z* 250 (59.2), 238 (1.1), 223

(22.3), 180 (8.3), 171 (13), 155 (56.3), 139 (3.5), 107 (9.7), 95 (7.9), 91 (100), 77 (4.6), 69 (23.5), 65 (20), 51 (3.7); HRMS Calcd for ($C_{12}H_{12}NO_3S$, $M^+-C_4H_5O$) 250.0498, found 250.0488. *syn*-**4e**: ^{1}H NMR ($CDCl_3$) δ 2.39 (s, 3H), 3.99–4.18 (m, 3H), 5.04–5.11 (m, 2H), 5.57–5.60 (m, 1H), 5.80–5.86 (m, 1H), 6.07 (m, 1H), 6.24–6.25 (m, 1H), 7.15–7.30 (m, 3H), 7.60–7.66 (m, 2H).

2-[α-(*trans*-Phenylvinyl) *N*-tosylaminomethyl]-2,5-dihydrofuran (4f) (method A). A white solid, mp 42–43°C; IR (KBr pellet): 3250, 2980, 1600, 1500, 1430, 1325, 1150, 1080, 960, 820; *anti*-**4f**: ^{1}H NMR ($CDCl_3$) δ 2.33 (s, 3H), 3.73–3.77 (m, 1H), 3.86–3.93 (m, 1H), 4.15–4.20 (m, 2H), 4.57–4.61 (m, 1H), 4.74 (d, J=9.2 Hz, 1H), 5.65–5.70 (m, 1H), 5.79–6.01 (m, 2H), 6.58 (d, J=16.1 Hz, 1H), 7.10–7.31 (m, 7H), 7.69–7.75 (m, 2H); MS *m/z* 286 (66.6), 277 (3.8), 260 (1.6), 223 (54.8), 207 (2.9), 184 (1.7), 171 (3.6), 155 (60.8), 130 (35.2), 115 (23.3), 103 (8.2), 91 (100), 77 (10.5), 69 (18.7), 51 (4); HRMS Calcd for ($C_{16}H_{16}NO_2S$, $M^+-C_4H_5O$) 286.0876, found 286.0881. *syn*-**4f**: ^{1}H NMR ($CDCl_3$) δ 2.31 (s, 3H), 3.95–4.02 (m, 1H), 4.10–4.23 (m, 2H), 4.79–4.83 (m, 1H), 4.95 (d, J=7.1 Hz, 1H), 5.65–5.70 (m, 1H), 5.79–6.01 (m, 2H), 6.30 (d, J=16.0 Hz, 1H), 7.10–7.31 (m, 7H), 7.69–7.75 (m, 2H).

The preparation of compound 4a from method B. A 25-mL flask containing a magnetic stirring bar was charged with imine (**1a**, 0.5 mmol), arsonium salt **5** (0.6 mmol), dichloromethane (4 mL) and potassium hydroxide aqueous (1 M, 1 mL) was subsequently added under stirring at 0°C. After the reaction was complete according to TLC, organic phase was extracted by dichloromethane (10 mL), then was concentrated and chromatographed on a preparative silica gel plate with a mixture of light petroleum (60–90°C) and ethyl acetate (2:1) as the eluent to give product **14a** as a colorless oil (yield: 52%), then **14a** was treated with KOH in THF at room temperature. After the reaction was complete according to TLC, the reaction mixture was filtered on a short silica gel column to remove KOH. The filtrate was concentrated and gave a solid product **4a** in quantitative yield. The analytical data are the same as before.

The reaction of imine 1b with sulfonium salt 11a. A 25-mL flask containing a magnetic stirring bar was charged with imine (**1b**, 0.5 mmol), sulfonium salt **11a** (0.6 mmol), and acetonitrile (4 mL, reagent grade). Powdered potassium hydroxide (2.0 mmol) was subsequently added under stirring. After the reaction was complete according to TLC, the reaction mixture was filtered on a short silica gel column to remove solid materials. The filtrate was concentrated and chromatographed on a preparative silica gel plate with a mixture of light petroleum (60–90°C) and ethyl acetate (3:1) as the eluent to give a white solid **4b** (52%) containing a little amount of unknown compound, which can not be separated by chromatography on a preparative silica gel plate and an epoxide **10** (23%). The analytical data of **4b** are the same as before, *anti*/*syn*=2:1. Epoxide **10** was isolated as a colorless oil, *cis*/*trans*=2:1; IR (KBr pellet): 3417, 1598, 1492, 1086, 1014, 840, 689; *cis*-**10**: ^{1}H NMR ($CDCl_3$) δ 3.06 (br., 1H), 4.52 (d, J=6.8 Hz, 1H), 4.60–4.86 (m, 2H), 5.50–5.55 (m, 1H), 5.95–6.03 (m, 1H), 7.24–7.45 (m, 4H); MS *m/z* 210 (M^+, 0.67), 193 (100.0), 141 (18.3), 125 (29.1), 77 (17.3), 69 (53.1); HRMS Calcd for ($C_{11}H_{11}O_2Cl$) 210.0445, found 210.0439. *trans*-**10**: ^{1}H NMR ($CDCl_3$) δ 2.75 (br., 1H), 4.60–4.86 (m, 2H), 4.98 (m, 1H), 5.55–5.62 (m, 1H), 5.95–6.03 (m, 1H), 7.24–7.45 (m, 4H).

The reaction of imine 1b with sulfonium salt 11b. A 25-mL flask containing a magnetic stirring bar was charged with imine (**1b**, 0.5 mmol), sulfonium salt **11b** (0.6 mmol), and acetonitrile (4 mL, reagent grade; it need not be dried before use). Powdered potassium hydroxide (2.0 mmol) was subsequently added under stirring. After the reaction was complete according to TLC, the reaction mixture was filtered on a short silica gel column to remove solid materials. The filtrate was concentrated and chromatographed on a preparative silica gel plate with a mixture of light petroleum (60–90°C) and ethyl acetate (3:1) as the eluent to afford an aziridine **12** (50%), and an epoxide **13** (26%). For compound **12**: a colorless oil; *trans*/*cis*=1:1; IR (KBr pellet): 3360, 1598, 1494, 1326, 1160, 1091, 1014, 815, 687; *trans*-**12**: ^{1}H NMR ($CDCl_3$) δ 1.8 (br., OH) 2.41 (s, 3H), 3.34 (dd, J=7.6, 1.8 Hz, 1H), 3.75 (d, J=1.8 Hz, 1H), 3.96–4.04 (m, 2H), 5.62 (ddt, J=15.7, 7.6, 1.6 Hz, 1H), 6.05 (dt, J=15.7, 5.0 Hz, 1H), 7.00–7.41 (m, 6H), 7.82 (d, J=8.3 Hz, 2H); MS *m/z* 364 ($M+1^+$, 6.51), 346 (14.6), 294 (29.7), 190 (22.4), 155 (70.5), 139 (27.4), 91 (100.0); HRMS Calcd for ($C_{18}H_{18}NO_3SCl$) 363.0692, found 363.0730. *cis*-**12**: ^{1}H NMR ($CDCl_3$) δ 1.8 (br., OH) 2.44 (s, 3H), 3.66 (t, J=7.7 Hz, 1H), 3.96–4.04 (m, 1H), 4.22 (m, 2H), 5.15 (ddt, J=15.5, 7.7, 1.7 Hz, 1H), 6.10 (dt, J=15.5, 5.0 Hz, 1H), 7.00–7.41 (m, 6H), 7.88 (d, J=8.2 Hz, 2H); For compound **13**: a colorless oil; *trans*/*cis*=1:1; IR (KBr pellet): 3412, 1698, 1218, 1024, 1014, 969; *trans*-**13**: ^{1}H NMR ($CDCl_3$) δ 2.5–2.9(br., 1H) 3.35 (dd, J=8.1, 1.8 Hz, 1H), 3.75 (d, J=1.8 Hz, 1H), 4.15 (d, J=4.6 Hz, 2H), 5.58 (ddt, J=15.7, 7.8, 1.5 Hz, 1H), 6.00–6.18 (m, 1H), 7.15–7.41 (m, 4H); MS *m/z* 210 (M^+, 2.43), 193 (100.0), 141 (28.3), 125 (35.1), 77 (19.5), 69 (48.1); HRMS Calcd for ($C_{11}H_{11}O_2Cl$) 210.0445, found 210.0451. *cis*-**13**: ^{1}H NMR ($CDCl_3$) δ 2.5–2.9(br., 1H) 3.70 (dd, J=8.6, 4.2 Hz, 1H), 4.00 (dd, J=5.2, 1.3 Hz, 2H), 4.20 (d, J=4.2 Hz, 1 H), 5.20 (ddt, J=15.7, 8.6, 1.5 Hz, 1 H), 6.00–6.18 (m, 1 H), 7.15–7.41 (m, 4H).

The preparation of aziridines 9a. A 25-mL flask containing a magnetic stirring bar was charged with imine (**1a**, 0.5 mmol), sulfonium salt **11c** (0.6 mmol), and acetonitrile (4 mL, reagent grade; it need not be dried before use). Powdered potassium hydroxide (2.0 mmol) was subsequently added under stirring. After the reaction was complete according to TLC, the reaction mixture was filtered on a short silica gel column to remove inorganic salts. The filtrate was concentrated and chromatographed on a silica gel column with a mixture of light petroleum (60–90°C) and ethyl acetate (10:1) as the eluent to give pure product. A colorless oil, yield 92%. *trans*/*cis*=7/3. IR (KBr pellet): 3244, 2966, 1759, 1461, 1337, 1328, 1168, 1090, 938, 920, 820, 811, 705, 677, 657; ^{1}H NMR ($CDCl_3$/TMS): *trans*: δ −0.01 (s, 6H), 0.08 (s, 9H), 2.29 (s, 3H), 3.35 (m, 1H), 3.96 (d, J=4.1 Hz, 1H), 4.1–4.4 (m, 2H), 5.93 (m, 2H), 7.0–7.3 (m, 7H), 7.74 (d, J=8.1 Hz, 2H). *cis*: δ 0.00 (s, 6H), 0.09 (s, 9H), 2.32 (s, 3H), 3.80 (t, J=7.6 Hz, 1H), 3.97 (d, J=7.4 Hz, 1H), 4.1–4.4 (m, 2H), 4.78 (td, J=9.6, 1.5 Hz, 1H), 5.59 (m, 1H), 7.0–7.3 (m, 7H),

7.79 (d, J=8.2 Hz, 2H). MS m/z 386 (6.3), 288 (14.2), 228 (11.3), 156 (69.2), 115 (22.4), 89 (77.8), 73 (100). Anal. Cacld for $C_{18}H_{17}NO_3Si$: C, 64.97; H, 7.50; N, 3.16. Found: C, 65.13; H, 7.81; N, 3.12.

The preparation of 2,5-dihydrofuran 4a from 9a. Aziridine compound **9a** (0.5 mmol) was dissolved in THF(4 mL), then a THF solution of TBAF (1 M, 0.5 mL) was added and heated to refluxing temperature. After the reaction was complete according to TLC, the reaction mixture was filtered on a short silica gel column. The filtrate was concentrated and chromatographed on a preparative silica gel plate with a mixture of light petroleum (60–90°C) and ethyl acetate (2:1) as the eluent to give a solid product **4a** in quantitative yield. The ratio of *anti* to *syn* is equal to 7:3. The analytical data are the same as before.

Acknowledgements

Financial support from the National Natural Science Foundation of China and Chinese Academy of Sciences is gratefully acknowledged.

References

1. Wittig, G.; Geissler, G. *Justus Liebigs Ann. Chem.* **1953**, *580*, 44.
2. (a) Huang, W.-F. *Ylide Chemistry*; Central China Normal University Press: Wuhan, 1993 (in Chinese). (b) Trost, B. M.; Melvin, L. S., Jr. *Sulfur Ylides*; Academic Press: New York, 1975. (c) Stirling, C. J. M. S., Patai, Eds., *Chemistry of the Sulfonium Group*; Wiley, 1981. (d) Shi, L. L.; Xiao, W. J.; Ge, Y.-T.; Huang, Y.-Z. *Acta Chimica Sinica* **1986**, *44*, 421.
3. Li, A.-H.; Dai, L.-X.; Hou, X.-L.; Huang, Y.-Z.; Li, F.-W. *J. Org. Chem.* **1996**, *61*, 489.
4. Zhou, Y.-G.; Li, A.-H.; Hou, X.-L.; Dai, L.-X. *Chem. Commun.* **1996**, 1353.
5. (a) Tang, Y.; Huang, Y.-Z.; Dai, L.-X.; Chi, Z.-F.; Shi, L.-P. *J. Org. Chem.* **1996**, *61*, 5762. (b) Tang, Y.; Huang, Y.-Z.; Dai, L-X.; Sun, J.; Xia, W. *J. Org. Chem.* **1997**, *62*, 954.
6. (a) Li, A.-H.; Dai, L.-X.; Hou, X.-L. *Chem. Commun.* **1996**, 491. (b) Li, A.-H.; Dai, L.-X.; Hou, X.-L.; Chen, M.-B. *J. Org. Chem.* **1996**, *61*, 4641. (c) Li, A.-H.; Dai, L.-X.; Hou, X.-L. *J. Chem. Soc., Perkin Trans. 1* **1996**, 867. (d) Li, A.-H.; Dai, L.-X.; Hou, X.-L. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2725. (e) Li, A.-H.; Zhou, Y.-G.; Dai, L.-X.; Hou, X.-L.; Xia, L.-J.; Lin, L. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1317. (f) Zhou, Y.-G.; Li, A.-H.; Hou, X.-L.; Dai, L.-X. *Tetrahedron Lett.* **1997**, *38*, 7225. (g) Li, A.-H.; Deng, W.-P.; Dai, L.-X.; Hou, X.-L. *Chin. J. Chem.* **1999**, *3*, 300.
7. Wang, W.-B.; Shi, L.-L.; Li, Z.-Q.; Huang, Y.-Z. *Tetrahedron Lett.* **1991**, *32*, 3999.
8. (a) Huang, Y.-Z.; Shen, Y.-C. *Adv. Organomet. Chem.* **1982**, *20*, 115. (b) Huang, Y.-Z.; Shi, L.-L.; Yang, J.-H.; Xiao, W.-J.; Li, S.-W. Wang, W.-B. In *Heteroatom Chemistry*; Block, E., Ed., VCH: New York, 1990; pp 189–206. (c) Huang, Y.-Z.; Shi, L.-L.; Yang, J.-H.; Xiao, W.-J. *Youji Huaxue* **1988**, *8*, 10.
9. A review on the structure of 2,5-dihydrofurans: (a) Dean, F. M., Sargent, M. V. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Charles, W. R., Eds., Pergamon Press: Oxford, 1984; Vol. 4, pp 531–597. A leading paper on the NMR study of 2,5-dihydrofurans: (b) Barfield, M.; Spear, R. J.; Sternhell, S. *J. Am. Chem. Soc.* **1975**, *97*, 5160.
10. Other than typical methods for preparing 2,5-dihydrofurans, the reaction of α,β-unsaturated ketones with dimethylsulfonium methylide (Bravo, P.; Ticozzi, C. *J. Chem. Soc., Chem. Commun.* **1979**, 438) or the intramolecular cyclization of allenic alcohols (Olsson, L.-I.; Claesson, A. *Synthesis* **1979**, 743) are also available.
11. (a) Semple, J. E.; Wang, P. C.; Lysenko, Z.; Joullié, M. M. *J. Am. Chem. Soc.* **1980**, *102*, 7505. (b) Masamune, T.; Ono, M. *Chem. Lett.* **1975**, 625.
12. A discussion on the reactivities of 2,5-dihydrofurans: Sargent, M. V.; Dean, F. M. In *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Charles, W. R., Eds., Pergamon Press: Oxford, 1984; Vol. 4, pp 599–656.
13. (a) Bloch, R.; Seck, M. *Tetrahedron Lett.* **1987**, *28*, 5819. (b) Bonadies, F.; Fabio, R. D. *J. Org. Chem.* **1984**, *49*, 1647.
14. Recent publications on the synthetic applications of 2,5-dihydrofurans: (a) Kang, S. H.; Lee, S. B. *J. Chem. Soc., Chem. Commun.* **1995**, 1017. (b) McDonald, F. E.; Gleason, M. M. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 350. (c) Paolucci, C.; Mazzini, C.; Fava, A. *J. Org. Chem.* **1995**, *60*, 169. (d) Ceré, V.; Paolucci, C.; Pollicino, S.; Sandri, E.; Fava, A. *Tetrahedron Lett.* **1989**, *30*, 6737.
15. Li, A.-H. Ph.D. Thesis, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, 1996.
16. Ruano, J. L. G.; Fernandez, I.; Hamdouchi, C. *Tetrahedron Lett.* **1995**, *36*, 295. (b) Mosset, P.; Greé, R. *Synth. Commun.* **1985**, *15*, 749. (c) Tewari, R. S.; Awasthi, A. K; Awasthi, A. *Synthesis* **1983**, 330. (d) Elmes, B. C. *Tetrahedron Lett.* **1971**, 4139. (e) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1353. (f) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1962**, *84*, 3782. (g) Franzen, V.; Driesen, H.-E. *Chem. Ber.* **1963**, *96*, 1881. (h) Hortmann, A. G.; Robertson, D. A. *J. Am. Chem. Soc.* **1967**, *89*, 5974. (i) Hortmann, A. G.; Robertson, D. A. *J. Am. Chem. Soc.* **1972**, *94*, 2758. (j) Johnson, C. R.; Janiga, E. R. *J. Am. Chem. Soc.* **1973**, *95*, 7692. A recent review on the aziridination reaction: (k) Li, A.-H.; Dai, L.-X. *Chemistry (The Chinese Chem. Soc., Taipei)* **1996**, *54* (4), 157–168 (in Chinese).
17. (a) Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599. (b) Tanner, D. *Pure Appl. Chem.* **1993**, *65*, 1319.
18. (a) Love, B. E.; Raje, P. S.; Williams, T. C., II *Synlett* **1994**, 493. (b) Jennings, W. B.; Lovely, C. J. *Tetrahedron Lett.* **1988**, *29*, 3725.
19. Due to the susceptibility of compound **14a** to ring closure, pure **14a** is very difficult to obtain. It is stable in dichloromethane, at room temperature, but the aziridine ring can be opened to produce compound **4a**, when the solvent is evaporated, even at −78°C.