Preparation of Azetidines by 4-*endo trig* Cyclizations of *N*-Cinnamyl Tosylamides

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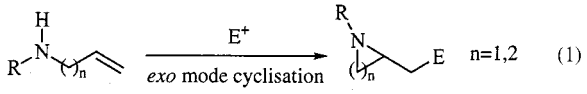
Formation of azetidines by electrophilic cyclizations have been reported, starting with homoallylic amines (4-*exo* mode cyclizations). We reported that the formation of these compounds can be carried out starting with allylic amines (4-*endo* mode cyclizations) using bis(collidine)bromonium(I) hexafluorophosphate as an electrophile. These cyclizations occur via a carbocation intermediate.

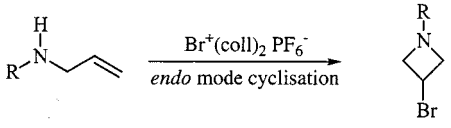
Introduction

The formation of aziridines and azetidines by electrophilic cyclizations remains until now a relatively unexplored reaction,[1,2] and literature reports have shown that ring closures proceed with *exo*-selectivity. Azetidines have been obtained from the cyclization of certain allylic amines, using electrophiles such as bromine[1a] or *N*-bromopyridinium tribromide.[1b] Recently, Taguchi and co-workers reported that the formation of aziridines was observed in the presence of iodide using metallic salts of *N*-allyl tosylamides.[1c] The formation of azetidines has also been reported to occur through the cyclization of homoallylic amines using *N*-bromosuccinimide[2a] or selenium salts[2b] as electrophiles (Equation 1).



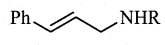
(1)

We recently reported that oxetanes can be obtained in moderate yields by the cyclization of allylic alcohols using bis(collidine)bromonium(I) hexafluorophosphate (BBH) as electrophile.[3] These reactions proceeded by a highly unfavourable 4-*endo* process. In the present paper we describe our results obtained for the preparation of azetidines by a similar reaction pathway (Equation 2).



(2)

In order to favour the 4-*endo* cyclization process, we chose cinnamyl amine derivatives **1** as substrates (Scheme 1). A preliminary study was carried out into the nature of the *N*-substituent which would favour such a process. Cinnamyl amine **1a** was prepared in two steps from cinnamyl bromide by reaction with sodium azide,[4] followed by catalytic hydrogenation using Lindlar's catalyst.[5] Subsequently, different nitrogen substituents were introduced using standard literature procedures. The cyclization reactions were carried out as follow: to a solution of amide **1a–d** in dichloromethane was added 1.3 equiv. of BBH in dichloromethane over a period of 6 hours using a push syringe. Subsequently the reaction mixture was concentrated and the final product purified by flash chromatography. Our results are reported Table 1.



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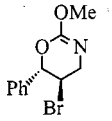
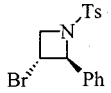
Scheme 1

Table 1. Reaction of cinnamyl derivatives **1** with $Br^+(collidine)_2\ PF_6^-$

Entry	N-Substituent on **1**	Product **2** (Yield, %)
a	—H	N.R.
b	—COMe	N.R.
c	—COOMe	 **2c** (44)
d	—SO_2—  —Me	 **2d** (71)

With amine **1a** and amide **1b** no reaction was observed. With carbamate **1c** we obtained the six-membered ring compound **2c**, formed by a 6-*endo* cyclization process. This compound was characterized by its NMR spectra; the *trans* stereochemistry was confirmed by the vicinal coupling constant between H-5 and H-6 (J = 9 Hz). Formation of this compound **2c** was not, in fact, surprising, since such cyclizations have already been reported.[6] With compound **1d**, we isolated the expected azetidine **2d** in good yield. Its

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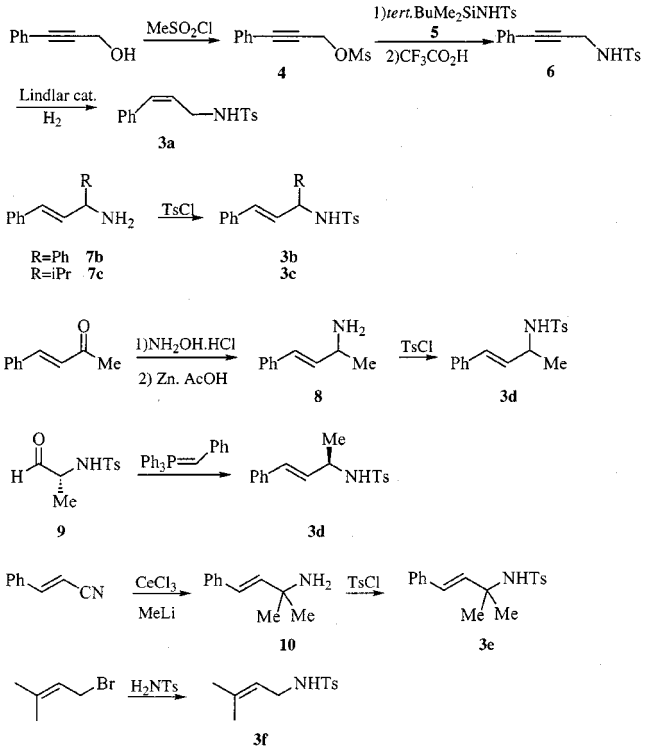
structure was deduced from its ^1H and ^{13}C NMR spectra. The stereochemistry between the hydrogens at C-2 and C-3 was assigned to be *trans*, based on the NOE observed between the C-2 proton and the phenyl protons. No NOE was observed between 2-H and 3-H.

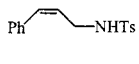
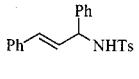
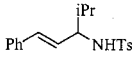
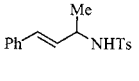
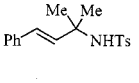
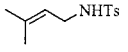
This easy cyclization of the tosylamide **1d** led us to study this reaction in detail. With this aim in mind, tosylamides **3a−f** were prepared as outlined in Scheme 2.



Scheme 2

Z-Cinnamyl tosylamide **3a** was obtained by the catalytic hydrogenation of acetylenic amide **6**, which in turn was obtained in moderate yield by alkylation of *tert*-butyldimethylsilyltosylamide (**5)** with mesylate **4**, followed by removal of the silyl protecting group. We observed that the reaction of the mesylate **4** with *p*-toluenesulfonamide led mainly to the dialkylated product. Tosylamides **3b** and **3c** were synthesized by tosylation of amines **7b** and **7c**, respectively, prepared according to the one-pot procedure described by Oh.[7] This method was not successful for the preparation of tosylamide **3d**. This latter was obtained in racemic form in three steps from benzylideneacetone by zinc reduction of the corresponding oxime,[8] followed by tosylation of the intermediate amine **8**. Tosylamide **3d** was also prepared in an enantiomerically enriched form by the Wittig reaction of *N*-tosyl-alaninal **9**[9] with benzylidenetriphenylphosphorane. Tosylamide **3e** was obtained by tosylation of the known amine **10**,[10] while tosylamide **3f** was prepared[11] by the reaction of 1-bromo-3-methyl-2-butene with *p*-toluenesulfonamide. The cyclizations of compounds **3a−3f** were carried out as described above. Our results are summarized in Table 2.

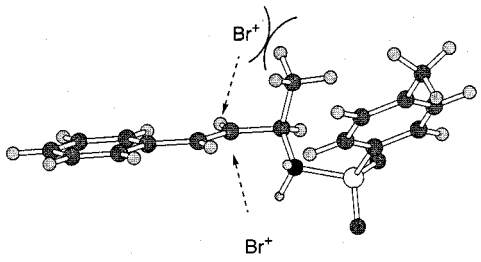
Table 2. Reaction of tosylamides **3a−f** with $Br^+(collidine)_2\ PF_6^-$

Entry	Substrate **3**	Product(s) **11** (Yield, %)	
a		 **11a** (52.5)	 **11a'** (9)
b		 **11b** (64)	
c		 **11c** (74)	 **11c'** (6.5)
d		 **11d** (66.5)	 **11d'** (16.5)
e		 **11e** (95)	
f		N.R.	

Bromocyclization of the tosylamide **3a** possessing a *Z* carbon−carbon double bond resulted in a mixture of two diastereoisomers, **11a** and **11a′**. The major diastereoisomer, **11a**, was identical to the azetidine isolated from the cyclization of the tosylamide **2d** (Table 1). Tosylamide **3b** led to a cyclic product in which the two phenyl groups were in a *cis* position, as was deduced from ^1H and ^{13}C NMR spectra. In addition, from NOE experiments, we found that the bromine atom was in a *trans* position relative to the phenyl groups. Similar stereochemistries were found for the major diastereoisomers obtained from tosylamides **3c** and **3d**. However minor diastereoisomers **11c′** and **11d′** were also formed from the latter. Their stereochemistries were deduced from NOE experiments. The cyclization of the enantiomerically enriched tosylamide **3d** (*ee* = 80%) gave products **11d** and **11d′** with an *ee* identical to that of the starting material, as measured by chiral HPLC (OD-H column). With tosylamide **3e** the presence of a *gem*-dimethyl group appears to favour the cyclization, since a high yield was obtained (95%). Finally, no cyclized product was obtained from the amine **3f**. This result is in contrast to the one reported by Taguchi et al.[1c] who obtained an aziridine in good yield in the presence of iodine and a base. With our reagent, the formation of aziridine was never observed.

We have performed semi-empirical PM3 calculations using the Hyperchem program.[12] For the tosylamides **3b−3d**, it appeared that in the more stable conformation the allylic substituent is in a plane perpendicular to the plane of the carbon−carbon double bond (Scheme 3). With amide **3b**, steric hindrance (and possibly electronic effects) introduced by the phenyl in the 2 position directed the approach of the bromonium ion exclusively from the unhindered face. When the size of the substituent in position 2 was decreased (isopropyl and methyl) the approach of the bromonium ion from

the more hindered face became possible, leading to the formation of the minor products **11c′** and **11d′**. Since we obtained the same azetidine with tosylamide **3a** as with tosylamide **1d**, this result suggests that the bromocyclization proceeds via a carbocation intermediate.



Scheme 3

In conclusion we have shown, for the first time, that the formation of azetidines by a formal 4-*endo* cyclization is possible. Work is now in progress to apply these results to the preparation of natural products possessing an azetidine ring.

Experimental Section

General Remarks: ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$. Bis(collidine)bromonium(I) hexafluorophosphate (BBH) was prepared following a reported procedure.[3,13] The *ee*′s of the compounds **3d**, **11d**, **11d′** were measured by HPLC using an OD-H column (elution: 2-propanol/hexane).

Preparation of (*E*)-Cinnamylamines 1a−1c: The (*E*)-3-phenylallylamine (**1a**)[14] has been obtained from (*E*)-cinnamyl bromide, by substitution with sodium azide[4] followed by reduction with Lindlar′s catalyst.[5] (*E*)-*N*-(3-phenylallyl)acetamide (**1b**)[15] and (*E*)-*N*-(3-phenylallyl)carbamic acid methyl ester (**1c**) [16] were then obtained by standard procedures.

Preparation of 4-Methyl-*N*-[(*E*)-3-phenylallyl]benzenesulfonamide (1d): A mixture of (*E*)-3-phenylallylamine (**1a**) (17.4 mmol, 2.32 g), triethylamine (17.4 mmol, 2.5 mL) and tosyl chloride (17.4 mmol, 3.35 g) in tetrahydrofuran (25 mL) was stirred overnight at room temperature. Ether (25 mL) was added and the organic layer was washed with an aqueous solution of HCl (1 M, 10 mL) and then a saturated solution of $NaHCO_3$ (10 mL). After drying (Na_2SO_4), the solvents were removed under reduced pressure. The crude residue was purified by liquid chromatography over flash silica gel (ether/pentane, 40:60) to give tosylamide **1d** (1.39 g, 4.44 mmol, 28%). Spectral data were in agreement with those already described.[17]

Preparation of 4-Methyl-*N*-[(*Z*)-3-phenylallyl]benzenesulfonamide (3a): 3-Phenyl-2-propyn-1-ol (7.6 mmol, 1 g), methanesulfonyl chloride (11.4 mmol, 900 μL), and triethylamine (11.4 mmol, 1.6 mL) were introduced successively into a round-bottomed flask at 0 °C containing ether (20 mL). The mixture was stirred for 12 h at room temp. The solid was filtered and solvent removed under reduced pressure to give the mesylate **4**. *N*-(*tert*-butyldimethylsilyl)-4-methylbenzenesulfonamide (**5**) was prepared by the method described for the preparation of 4-methyl-*N*-(phenyldimethylsilyl)-benzenesulfonamide (93%).[18] The crude mesylate **4** (1.5 mmol, 313.5 mg) was dissolved in acetone (45 mL) and heated overnight at reflux in the presence of *N*-(*tert*-butyldimethylsilyl)-4-methylbenzenesulfonamide (1.5 mmol, 427 mg) and potassium carbonate (1.5 mmol, 207 mg). Acetone was removed and an aqueous solution of HCl (1 M, 20 mL) was added. This aqueous phase was extracted with dichloromethane (3×20 mL). Silica gel (2 g) and four drops of CF_3CO_2H were added, and this heterogeneous mixture was stirred for 12 h. After filtration and concentration under reduce pressure, the residue was purified by flash liquid chromatography over silica gel (ether/pentane, 30:70). Tosylamide **6** (100.5 mg, 0.4 mmol, 24%) was isolated. **6** was reduced with Lindlar′s catalyst (343 mg) in 5 mL of MeOH in the presence of quinoline (30 μL) under hydrogen at atmospheric pressure. After absorption of 1 equiv. of hydrogen (1 night) the reaction mixture was filtered and concentrated under reduced pressure. The crude residue was diluted with HCl (1 N, 10 mL) and the aqueous phase was extracted with diethyl ether (3×10 mL). The organic phase was dried (Na_2SO_4) and the solvent removed under reduced pressure. (*Z*)-Tosylamide **3a** (339.7 mg, 1.2 mmol, 100% yield) was pure enough to be used without further purification. Spectral data were in agreement with those already described.[17]

Preparation of *N*-[(*E*)-1,3-Diphenylallyl]-4-methylbenzenesulfonamide (3b): *n*BuLi (1.31 M in hexane, 10 mmol, 7.64 mL) was added to a solution of dimethylphosphonate (10 mmol, 1.07 mL) in THF (30 mL) under nitrogen at −78 °C. Benzonitrile (10 mmol, 1.24 mL) was then added and the mixture was stirred at −5 °C for 1 h. Benzaldehyde (10 mmol, 1.01 mL) was added at room temp. over 30 min and the mixture was cooled again to −78 °C. Sodium borohydride (20 mmol, 757 mg) was added followed by MeOH (50 mL). The mixture was stirred at −78 °C for 1 h and warmed to room temp. An aqueous solution of HCl (3%, 30 mL) was added and the mixture was stirred for 1 h. The solution was made basic by the addition of NaOH pellets. The aqueous phase was extracted with EtOAc. The organic phase was dried (Na_2SO_4), and then concentrated under reduced pressure. Purification of the residue by flash liquid chromatography led to (*E*)-1,3-diphenylallylamine (**7b**) (1.23 g, 5.88 mmol, 59%). − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.88 (s broad, 2 H), 4.72 (d, *J* = 6.5 Hz, 1 H), 6.38 (dd, *J* = 15.9 and 6.5 Hz, 1 H), 6.62 (d, *J* = 15.9 Hz, 1 H), 7.15−7.49 (m, 5 H). The amine **7b** (1 g, 4.78 mmol), *p*-toluenesulfonyl chloride (9.6 mmol, 1.82 g), pyridine (9.6 mmol, 0.775 mL), and dichloromethane (10 mL) were introduced into a round-bottomed flask. The mixture was stirred for 1 day. Diethyl ether was then added and the organic layer was washed with aqueous HCl solution (1 N) and dried (Na_2SO_4). The solvent was evaporated under reduced pressure. The crude residue was purified by liquid chromatography over flash silica gel (eluent: Et_2O/pentane: 25:75) to afford *N*-[(*E*)-1,3-diphenyl-allyl]-4-methylbenzenesulfonamide (**3b**) (1.16 g, 3.19 mmol, 67%). Spectral data were in agreement with those already reported.[19]

Preparation of *N*-[(*E*)-1-Isopropyl-3-phenylallyl]-4-methylbenzenesulfonamide (3c): Tosylamide **3c** was prepared following the procedure described above for **3b** with an overall yield of 10% from isobutyronitrile. **7c:** ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.94 (d, *J* = 6.3 Hz, 3 H), 0.98 (d, *J* = 6.3 Hz, 3 H), 1.73 (m, 1 H), 2.41 (bs, NH_2), 3.27 (dd, *J* = 8.4 and 6.3 Hz, 1 H), 6.17 (dd, *J* = 8.4 and 15.8 Hz, 1 H), 6.49 (d, *J* = 15.8 Hz, 1 H), 7.13−7.50 (m, 5 H). The subsequent tosylation was carried out as reported above for the preparation of **3b**. − **Tosylamide 3c:** white solid, m.p. 145.2 °C. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.90 (d, *J* = 7 Hz, 3 H), 0.93 (d, *J* = 7 Hz, 3 H), 1.82 (m, 1 H), 2.26 (s, 3 H), 3.73 (m, 1 H), 4.96 (d, *J* = 8.4 Hz, NH), 5.71 (dd, *J* = 7.8 and 15.9 Hz, 1 H), 6.09 (d, *J* = 15.9 Hz, 1 H), 7.0−7.37 (m, 7 H), 7.74 (d, *J* = 8.3 Hz, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 18.3, 18.4, 21.3, 33.1, 61.9, 126.2, 126.8,

127.2, 127.5, 128.2, 129.3, 132.1, 136.3, 138.0, 143.0. − MS (EI); (*m/z*,%): 65 (14), 91 (81), 115 (24), 130 (40), 155 (36), 286 (100), 329 (0.78). − $C_{19}H_{23}O_2NS$ (329.4554): calcd. C 69.27, H 7.04, N 4.25; found C 69.18, H 7.13, N 4.24.

Preparation of (±)-4-Methyl-*N*-[(*E*)-1-methyl-3-phenylallyl]-4-benzenesulfonamide (3d): Tosylamide **3d** was obtained using the method described by Bosnich[8] from *trans* 4-phenyl-but-3-en-2-one (2 g, 13.7 mmol). The oxime was reduced, without purification, with zinc/AcOH to give (*E*)-1-methyl-3-phenylallylamine (**8**) (678.4 mg, 4.6 mmol) which was purified by distillation under reduced pressure (120−180 °C at 15 Torr). Yield: 34% from the starting ketone. Tosylation using the method described above for the preparation of **3b** led to the tosylamide **3d** (60% yield). White solid, m.p. 81.5 °C. Spectral data were in agreement with those already described.[20]

Preparation of 4-Methyl-*N*-[(1*S*)-(*E*)-1-methyl-3-phenylallyl]-4-benzenesulfonamide (3d): This amine was prepared by the reaction of 4-methyl-*N*-[(1*S*)-1-methyl-2-oxoethyl]benzenesulfonamide (**9**) [9] with benzylidenetriphenylphosphorane. A solution of phenyllithium in hexane (2 M, 2.5 mL, 5 mmol) was added at −40 °C under argon to a suspension of benzyltriphenylphosphonium chloride (1.6 g, 4 mmol) in THF. The mixture was stirred for 30 min at −40 °C and the aldehyde **9** (0.466 g, 2 mmol) in THF solution was added. After one night at room temp., water was added. The aqueous layer was extracted with dichloromethane (3×20 mL) and the organic phase was dried (Na_2SO_4). The solvent was evaporated under reduced pressure. The residue was purified by flash liquid chromatography over silica gel (ether/pentane, 25:75 to 50:50) to give tosylamide **3d** (0.268 g, 0.89 mmol, 22% yield). The enantiomeric excess measured by HPLC (chiracel OD-H column) was found to be 80%. − α_D = −103 (*c* = 1.25, $CDCl_3$).

Preparation of *N*-[(*E*)-1,1-Dimethyl-3-phenylallyl]-4-methylbenzenesulfonamide (3e): This amine was obtained by tosylation of (*E*)-1,1-dimethyl-3-phenylallylamine[10] following the conditions previously reported (74% yield). White solid, m.p. 75 °C. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.47 (s, 6 H), 2.35 (s, 3 H), 4.93 (bs, 1 H), 5.95 (d, *J* = 18 Hz, 1 H), 6.37 (d, *J* = 18 Hz, 1 H), 7.10−7.35 (m, 7 H), 7.75 (d, *J* = 6.0 Hz, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 21.3, 28.2 (2C), 56.7, 126.3 (2C), 127.0 (2C), 127.2, 127.4, 128.2 (2C), 129.3 (2C), 136.3, 139.7, 142.7, 142.8. − $C_{18}H_{21}NO_2S$: calcd. C 68.54, H 6.71, found C 68.65, H 6.88.

Preparation of 4-Methyl-*N*-(3-methylbut-2-enyl)benzenesulfonamide (3f): A mixture of 1-bromo-3-methylbut-2-ene[21] (2.7 g, 18 mmol), *p*-tolylsulfonamide (4.6 g, 27.1 mmol), potassium carbonate (3.75 g, 27.1 mmol) and acetone (100 mL) was heated overnight at reflux. The acetone was removed under reduced pressure and the residue was dissolved in an ether/water mixture. The aqueous layer was extracted with ether and the organic layers dried (Na_2SO_4). The solvent was evaporated under reduced pressure and the residue was purified by flash liquid chromatography over silica gel (ether/pentane, 25:75) to afford tosylamide **3f** (3.1 g, 12.9 mmol, 72% yield). Spectral data were in agreement with those already described.[22]

General Procedure for the Cyclization of Compounds 1a−1d, 3a−3f: A solution of BBH (0.374 g, 0.8 mmol) in dichloromethane (20 mL) was added at room temp. over 6 h to a solution of substrate **1** or **3** (0.6 mmol) in dichloromethane (20 mL). After complete addition, the mixture was stirred for 12 h. Silica gel (1 g) was added and the solvent removed under reduced pressure. The isolated powder was deposited on the top of a silica gel column. The product was then purified by elution with a ether/pentane mixture.

5-Bromo-5,6-dihydro-2-methoxy-6-phenyl-4*H*-1,3-oxazine (2c): White solid. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.65−3.90 (m, 2 H), 3.75 (s, 3 H), 4.20 (dq, *J* = 8.1, and 4.6 Hz, 1 H), 5.25 (d, *J* = 8.1 Hz, 1 H), 7.25−7.45 (m, 5 H). ^{13}C NMR ($CDCl_3$): δ = 44.8, 49.4, 54.9, 82.3, 126.7, 128.6, 128.7, 129.1, 136.6, 152.9.

(2*R,3*S**)-3-Bromo-1-(4-methylphenylsulfonyl)-2-phenylazetidine (11a or 2d):** White solid. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.48 (s, 3 H), 3.96 (dd, *J* = 7.0 and 7.5 Hz, 1 H), 4.17 (ddd, *J* = 7.0, 7.0, and 6.5 Hz, 1 H), 4.31 (dd, *J* = 7.0 and 7.5 Hz, 1 H), 4.99 (d, *J* = 6.5 Hz, 1 H), 7.3−7.5 (m, 7 H), 7.69 (d, *J* = 8.3 Hz, 2 H). − ^{13}C NMR: δ = 21.6, 38.9, 57.1, 75.9, 126.1, 127.8, 128.4, 128.7, 128.9, 131.4, 137.2, 144.6. − MS (EI); *m/z* (%): 51 (26), 65 (31), 77 (33), 91 (82), 103 (33), 118 (34), 130 (35), 155 (100), 184 (18), 222 (47), 286 (14). − $C_{16}H_{16}BrNO_2S$: calcd. C 52.47, H 4.40, N 3.82; found C 52.75, H 4.44, N 3.91.

(2*R,3*R**)-3-Bromo-1-(4-methylphenylsulfonyl)-2-phenylazetidine (11a′):** White solid. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.45 (s, 3 H), 3.94 (m, 1 H), 4.44 (dd, *J* = 9.7 and 7.3 Hz, 1 H), 4.57 (ddd, *J* = 7.3, 7.3 and 2.9 Hz, 1 H), 5.23 (d, *J* = 7.3 Hz, 1 H), 7.15−7.5 (m, 7 H), 7.69 (d, *J* = 8.3 Hz, 2 H). − ^{13}C NMR δ 21.6, 38.9, 57.3, 68.8, 127.5, 127.9, 128.3, 128.5, 129.8, 131.9, 136.0, 144.5.

(2*R,3*S**,4*S**)-3-Bromo-1-(4-methylphenylsulfonyl)-2,4-diphenylazetidine (11b):** White solid, m.p. 86.4 °C. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.48 (s, 3 H), 3.96 (dd, *J* = 6.8 Hz, 1 H), 5.0 (d, *J* = 6.8 Hz, 2 H), 7.25−7.57 (m, 7 H), 7.62 (d, *J* = 8.3 Hz, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 21.5, 47.6, 72.0, 126.4, 128.2, 128.7, 128.8, 129.6, 132.5, 137.3, 144.5. − MS (EI); *m/z* (%): 51 (12), 65 (13), 77 (17), 91 (31), 103 (26), 155 (10), 184 (100), 184 (98), 206 (22), 362 (22). − $C_{22}H_{20}BrNO_2S$: calcd. C 59.86, H 4.57, N 3.18; found C 59.61, H 4.51, N 2.94.

(2*R,3*S**,4*S**)-3-Bromo-2-isopropyl-1-(4methylphenylsulfonyl)-4-phenylazetidine (11c):** White solid, m.p. 96 °C. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.03 (d, *J* = 6.8 Hz, 3 H), 1.07 (d, *J* = 6.8 Hz, 3 H), 2.20 (m, 1 H), 2.46 (s, 3 H), 3.87 (dd, *J* = 6.4 and 6.4 Hz, 1 H), 4.04 (dd, *J* = 6.4 and 5.6 Hz, 1 H), 4.85 (d, *J* = 6.4 Hz, 1 H), 7.25−7.5 (m, 7 H), 7.65 (d, *J* = 8.3 Hz, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 16.5, 17.7, 21.5, 31.1, 40.8, 72.1, 75.1, 126.0, 128.2, 128.5, 128.6, 129.6, 132.2, 137.6, 144.3. − MS (EI); *m/z* (%): 41 (49), 57 (21), 65 (31), 77 (22), 91 (85), 103 (20), 130 (28), 155 (100), 182 (16), 260 (76), 284 (54), 328 (44), 409 (0.51).

(2*R,3*S**,4*R**)-3-Bromo-2-isopropyl-1-(4-methylphenylsulfonyl)-4-phenylazetidine (11c′):** White solid. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.20 (d, *J* = 6.8 Hz, 3 H), 1.25 (d, *J* = 6.8 Hz, 3 H), 2.37 (s, 3 H), 2.41 (m, 1 H), 4.47 (m, 1 H), 4.72 (dd, *J* = 7.8 Hz, *J* = 6 Hz, 1 H), 5.38 (d, *J* = 6 Hz, 1 H), 7.02−7.45 (m, 7 H), 7.67 (d, *J* = 8.3 Hz, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 18.3, 19.1, 21.4, 31.1, 45.5, 72.0, 76.0, 127.0, 128.3, 128.3, 128.9, 129.1, 134.2, 137.5, 142.8. − $C_{19}H_{22}BrNO_2S$ (**11c**−**11c′**): calcd. C 55.89, H 5.43, N 3.43; found C 55.28, H 5.47, N 3.22.

(2*R,3*S**,4*S**)-3-Bromo-2-methyl-1-(4-methylphenylsulfonyl)-4-phenylazetidine (11d):** White solid, m.p. 143.8 °C. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.52 (d, *J* = 6.2 Hz, 3 H), 2.46 (s, 3 H), 3.69 (dd, *J* = 6.7 and 6.7 Hz, 1 H), 4.11 (m, 1 H), 4.77 (d, *J* = 6.7 Hz, 1 H), 7.07−7.5 (m, 7 H), 7.67 (d, *J* = 8.3 Hz, 2 H). − ^{13}C NMR ($CDCl_3$): δ = 19.9, 21.5, 46.4, 66.6, 72.9, 126.3, 128.4, 128.7, 128.8, 129.8, 137.4, 144.6. − MS (EI); *m/z* (%): 41 (27), 57 (17), 83 (12), 91 (40), 103 (18), 132 (16), 145 (10), 155 (75), 182 (22), 195 (17), 224 (11), 259 (33), 260 (68), 299 (27), 300 (100), 301 (23), 379 (6), 381 (6).

(2*R,3*S**,4*R**)-3-Bromo-2-methyl-1-(4-methylphenylsulfonyl)-4-phenylazetidine (11d′):** White solid. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.67 (d, *J* = 6.2 Hz, 3 H), 2.36 (s, 3 H), 4.47 (dd, *J* = 6.9 and 6.9 Hz, 1 H), 4.71 (m, 1 H), 5.20 (d, *J* = 6.9 Hz, 1 H), 7.07−7.5 (m, 7 H), 7.67 (d, *J* = 8.3 Hz, 2 H). – ^{13}C NMR ($CDCl_3$): δ = 16.9, 21.3, 47.8, 63.7, 74.8, 127.0, 127.6, 128.5, 128.8, 129.3, 131.9, 136.0. – $C_{17}H_{18}BrNO_2S$ (**11d**−**11d′**): calcd. C 53.69, H 4.77, N 3.68; found C 53.43, H 4.77, N 3.56.

(3*R,4*R**)-3-Bromo-2,2-dimethyl-1-(4-methylphenylsulfonyl)-4-phenylazetidine (11e):** White solid, m.p. 51 °C. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.69 (s, 3 H), 1.73 (s, 3 H), 2.36 (s, 3 H), 4.03 (d, *J* = 8.5 Hz, 1 H), 4.95 (d, *J* = 8.5 Hz, 1 H), 7.10 (d, *J* = 7.5 Hz, 2 H), 7.20 (bs, 5 H), 7.46 (d, *J* = 7.5 Hz, 2 H). – ^{13}C NMR ($CDCl_3$): δ = 21.4, 22.33, 29.1, 54.5, 71.7, 72.7, 126.8, 127.7, 128.3, 128.6, 129.1, 135.8, 136.4, 143.5. – $C_{18}H_{20}BrNO_2S$: calcd. C 54.83, H 5.11; found C 54.86, H 5.32.

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