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Reactivity of 2-halo-2*H*-azirines. Part 3:☆ Dehalogenation of 2-halo-2*H*-azirine-2-carboxylates

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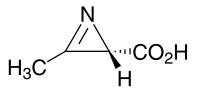
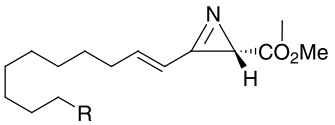
Abstract—The dehalogenation of 2-halo-3-phenyl-2*H*-azirine-2-carboxylates is described. Using sodium borohydride and tributyltin hydride 3-phenyl-2*H*-azirine-2-carboxylates were obtained in moderate yields. The synthesis of a new 2-bromo-2*H*-azirines with a chiral auxiliary, 10-phenylsulfonylisobornyl 2-bromo-3-phenyl-2*H*-azirine-2-carboxylate, is reported. Its dehalogenation led to 10-phenylsulfonylisobornyl 2*H*-azirine-2-carboxylate as single stereoisomer together with the formation of 10-phenylsulfonylisobornyl acetate.

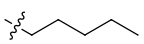
1. Introduction

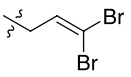
2*H*-Azirines are very important class of compounds not only due to their theoretical interest but also because they are versatile building blocks for organic synthesis.[2] Chiral derivatives bearing a carboxylic acid group or an ester group at C-2 are of particular interest since some of these substituted 2*H*-azirines are naturally occurring antibiotics. In fact azirinomycin (**1**), isolated from *Streptomyces auras* cultures, and its methyl ester exhibit antibiotic activity. Moreover, both enantiomers of (*R*)-(+)- and (*S*)-(−)-dysidazirine **2** and (*S*)-(+)-antazirine **3** were isolated from the marine sponge *Dysidea fragilis*. Therefore, the development of new asymmetric synthesis of 2*H*-azirine-2-carboxylates has recently attracted great attention.[3]



Azirinomycin **1**



R =  (*S*)-(-)-*Dysidazirine* **2**

R = 

(*S*)-(+)-*Antazirine* **3**

Chiral 2*H*-azirines have been prepared by elimination reaction of *N*-substituted aziridines namely dehydrochlorination of *N*-chloroaziridines,[3a] Swern oxidation of aziridines[3b] and elimination from *N*-sulphynilaziridines.[3d] The latest procedure has been used in the asymmetric synthesis of (*R*)-(+)- and (*S*)-(−)-*disydazirine*. These interesting methods involve nevertheless the use of high enantiopure aziridine esters as starting materials. A different approach has also been described consisting in an alkaloid-mediated Neber reaction (Scheme 1).[3c]

We have developed a very general route to 2-halo-2*H*-azirines starting from α-oxophosphorus ylides which allows the synthesis of a range of 2-iodo-, 2-bromo and 2-chloro-2*H*-azirines. The 2*H*-azirines, including 2-halo-2*H*-azirine-2-carboxylate derivatives, are obtained by our synthetic procedure as racemic mixtures.[4]

Our aim was to achieve the synthesis of chiral 2*H*-azirine-2-carboxylates by dehalogenation of these 2-halo-2*H*-azirine-2-carboxylates. The synthetic strategy should be a process involving an intermediate (carbocation or radical) with a chiral auxiliary to control the configuration of the new chiral center. Two reducing agents, which allow the formation of the referred intermediates are sodium borohydride and tributyltin hydride. The approach could be the synthesis of the chiral esters of 2-halo-2*H*-azirine-2-carboxylic acids followed by the dehalogenation reaction.

☆ See Ref. 1.

Keywords: dehalogenation; 2-halo-2*H*-azirine-2-carboxylates; chiral 2*H*-azirine-2-carboxylates.

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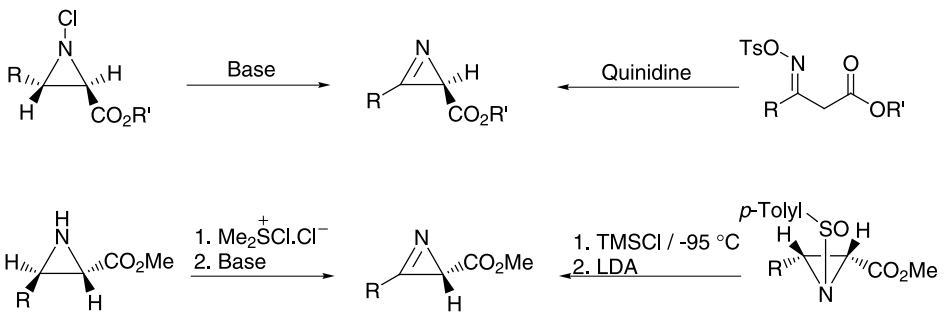
doi:10.1016/S0040-4020(03)00248-5



Scheme 1.

2. Results and discussion

The first objective was to determine, if tin hydrides and sodium borohydride could be used as reducing agents to promote dehalogenation of 2-halo-2*H*-azirine-2-carboxylates.

The reaction of 2-chloro-, 2-bromo- and 2-iodo-3-phenyl-2*H*-azirine-2-carboxylates[4] with sodium borohydride was studied (Table 1). It was known[3c] that 2*H*-azirine can be converted into the corresponding aziridine on reacting with $NaBH_4$/EtOH. For this reason, reaction conditions should be found to allow the selective formation of 3-phenyl-2*H*-azirine-2-carboxylates.

The dehalogenation of ethyl 2-chloro-2*H*-azirine-2-carboxylate **4a** was carried out at room temperature and after 2 h two products were obtained: 2*H*-azirine **5a** in 5% yield and aziridine **7a** in 27% yield. When the reaction of 2-chloro-2*H*-azirine **4a** with sodium borohydride was carried out at 50°C for 15 min a mixture of two isomeric 2*H*-azirines was obtained: 3-phenyl-2*H*-azirine-2-carboxylate **5a** in 28% yield and 2-phenyl-2*H*-azirine-3-carboxylate **6** in 20% yield. The formation of 2*H*-azirine **6** can be rationalized considering a process involving an S_N2' mechanism. Alternatively, if an azacyclopropenyl cation was formed it could lead to the synthesis of the isomeric 2*H*-azirines **5a** and **6**. In fact azacyclopropenyl cation has been suggested as an intermediate in the thermal isomerization of 2-chloro-2,3-dimethyl-2*H*-azirine.[5]

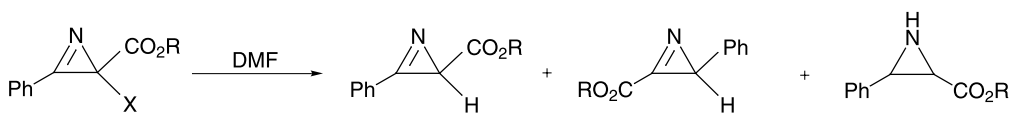
The 2-bromo-2*H*-azirine-2-carboxylate **4b** reacted with sodium borohydride at room temperature giving 2*H*-azirine **5a** (37%), 2*H*-azirine **6** (5%) and aziridine **7a** (8%). 2*H*-azirine **5a** was obtained as the sole product in 30% yield when the reaction was performed at 0°C for 24 h.

The conversion of 2-iodo-2*H*-azirine **4c** into 2*H*-azirine **5b** (17% yield) was also carried out at 0°C. The low yield can be explained by lower stability of the iodo-2*H*-azirine. The reaction of methyl 2-bromo-3-phenyl-2*H*-azirine-2-carboxylate **4d** with $NaBH_4$ at room temperature gave 2*H*-azirine **5b** in 22% yield and aziridine **7b** in 34% yield.

The dehalogenation of 2-bromo-2*H*-azirine **4b** with tributyltin hydride was also performed (Table 2). Different reaction conditions were studied and these include the use of radical initiators and also the use of triethylborane reported to act as catalyst in the reduction of alkyl bromides with tributyltin hydride.[6] These attempted improvements did not allow significant differences of yields. However, the reaction of 2-bromo-2*H*-azirine **4b** with tributyltin hydride and ACN performed at 80°C for 30 min led to 2*H*-azirine **5a** in an acceptable yield of 31%.

The results described above prove that 3-phenyl-2*H*-azirines can be obtained from dehalogenation of 2-halo-2*H*-azirine-2-carboxylates with tributyltin hydride and sodium borohydride. Low moderate yields obtained for these reactions are certainly a consequence of the competitive side reactions namely the reduction of the iminic bond or azirine isomerization when sodium borohydride was used or radical coupling reactions when tributyltin hydride was the reducing agent.

Table 1.



4a R = Et; X = Cl
4b R = Et; X = Br
4c R = Me; X = I
4d R = Me; X = Br

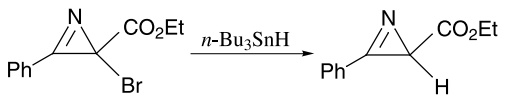
5a R = Et
5b R = Me

6 R = Et

7a R = Et
7b R =Me

2*H*-Azirine	Reagents	Temperature	Reaction time	Products (yield)		
4a	$NaBH_4$	rt	2 h	**5a** (5%)	–	**7a** (27%)
4a	$NaBH_4$	50°C	15 min	**5a** (28%)	**6** (20%)	–
4b	$NaBH_4$	rt	2 h	**5a** (37%)	**6** (5%)	**7a** (8%)
4b	$NaBH_4$	0°C	24 h	**5a** (30%)	–	–
4c	$NaBH_4$	−5/0°C	0.5 h	**5b** (17%)	–	–
4d	$NaBH_4$	rt	2 h	**5b** (22%)	–	**7b** (34%)

Table 2.



4b **5a**

Reagents	Temperature	Reaction time (h)	**5a** (Yield) (%)
–[a]	rt	24	15
–[b]	0°C	24	–
AIBN[a]	rt	1	12
AIBN[a]	0°C	24	13
ACN[a]	rt	2	27
ACN[b]	rt	2	18
ACN[b]	rt	24	19
ACN[c]	80°C	1/2	31
ACN[c]	80°C	1	18
Et_3B[d]	0°C	1/2	15
Et_3B[d]	0°C	1	13

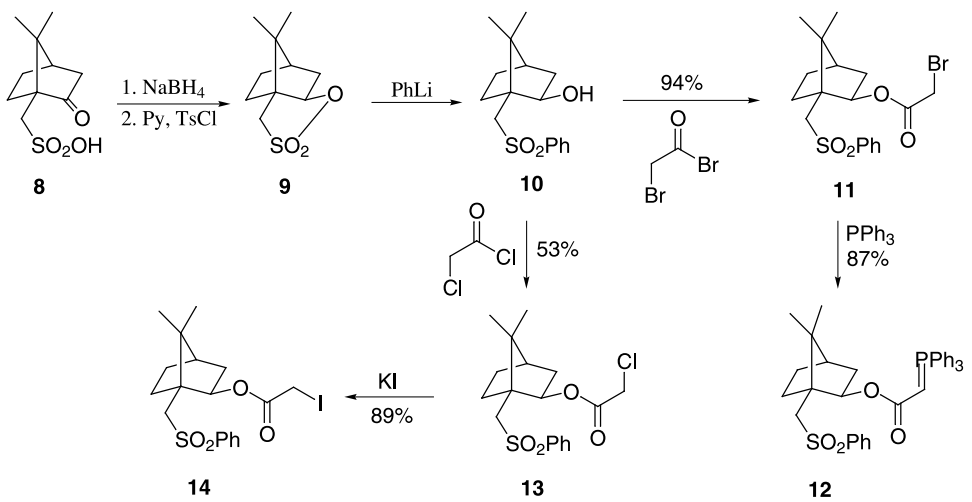
[a] In pentane.
[b] In ether.
[c] In DMF.
[d] In toluene.

Having selected the reducing agents we went on to investigate the possibility of preparing 2-halo-2*H*-azirines with a chiral auxiliary. The synthetic strategy is outlined in Schemes 2 and 3.

The 10-phenylsulfonylisoborneol **10** was prepared from camphorsulfonic acid following a procedure described in the literature.[7] This alcohol reacted with bromoacetyl bromide to give ester **11** in 94% yield which on reacting with triphenylphosphine gave the new chiral phosphorus ylide **12** (87%). Esters **13** and **14** were also prepared and used as precursors of ylide **12**. However, the best result was obtained when compound **11** was used as the starting material (Scheme 2).

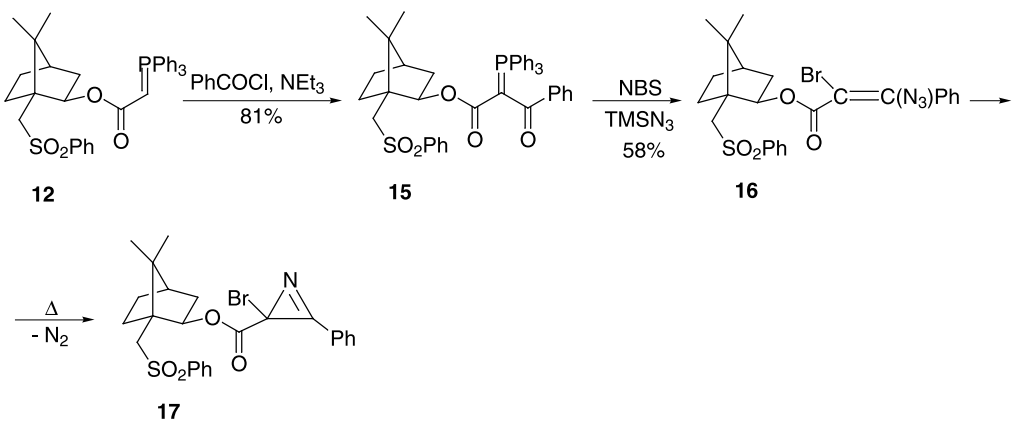
The reaction of compound **12** with benzoyl chloride allowed the synthesis of chiral ylide **15** in 81% yield. Using our synthetic methodology[8] ylide **15** reacted with *N*-bromosuccinimide in the presence of azidotrimethylsilane giving the corresponding haloazidoalkene **16** in 58% yield. Alkene was easily converted into the diastereoisomeric mixture of 10-phenylsulfonylisobornyl 2-bromo-3-phenyl-2*H*-azirine-2-carboxylate **17** on heating in heptane for 2–3 h. The reaction was followed by TLC and by IR by monitoring the disappearance of the band corresponding to the azido group (ν=2114 cm^{-1}) of the starting azidoalkene (Scheme 3).

The 10-phenylsulfonylisobornyl 2-bromo-3-phenyl-2*H*-azirine-2-carboxylate **17** was obtained as a diastereoisomeric mixture as shown by the complexity observed in



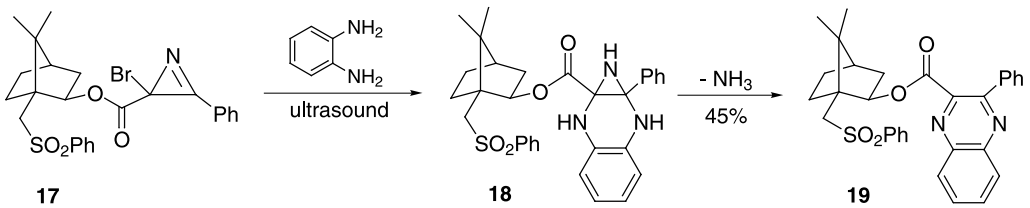
8 **9** **10** **11** **12** **13** **14**

Scheme 2.

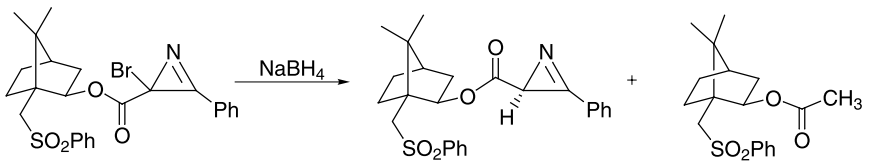


12 **15** **16** **17**

Scheme 3.



Scheme 4.



Scheme 5.

the ^{1}H NMR spectrum. However, the diastereoisomers could be separated by preparative TLC.

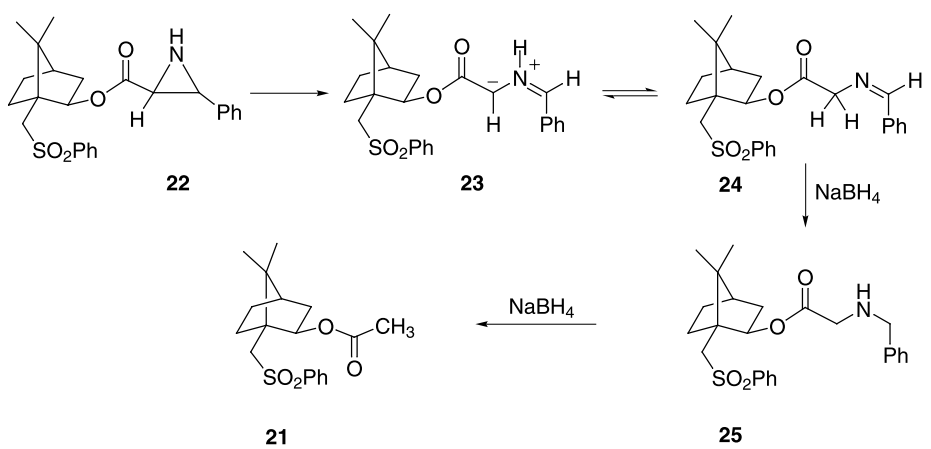
In order to confirm the structure of 2*H*-azirine **17** we promoted its reaction with 1,2-phenylenediamine. The reaction was carried out in an ultrasound bath leading to the synthesis of the chiral quinoxaline **19** which was completely characterized. In agreement with the reactivity previously observed for other 2-halo-2*H*-azirines[8] the process involved the halide displacement and addition to the iminic double bond of the 2*H*-azirine giving **18**. The opening of the aziridine ring followed by the elimination of ammonia led to quinoxaline **19** (Scheme 4).

The dehalogenation reactions of 2*H*-azirine **17** using sodium borohydride and tributyltin hydride as reducing agents were studied (Scheme 5). From the reaction with tributyltin hydride a complex mixture was obtained and the dehalogenated 2*H*-azirine **20** could only be obtained in very low yield. The dehalogenation of 2*H*-azirine **17** with sodium borohydride led to the synthesis of two products, the expected 10-phenylsulfonylisobornyl 3-phenyl-2*H*-azirine-2-carboxylate **20** in 24% yield and 10-phenylsulfonyl-isobornyl acetate **21** in 27% yield.

The ^{1}H NMR spectrum of dehalogenated 2*H*-azirine **20** suggested that the product was obtained as a single stereoisomer. A diastereoisomeric mixture should be easily detected. The assignment of the most relevant proton and carbon signals in the ^{1}H and ^{13}C spectra of 2*H*-azirine **20** was made on the basis of an HETCOR spectrum. The structural assignment was also achieved using a two-dimensional technique: the NOESY spectrum showed cross peaks between H-2 of the azirine ring with the *ortho*-protons of the C-3 phenyl group. This points to the proposed stereochemistry, *S* configuration at C-2, for 10-phenylsulfonyl-isobornyl 3-phenyl-2*H*-azirine-2-carboxylate **20**.

The diastereoselectivity observed in synthesis of (2*S*)-2*H*-azirine-2-carboxylate **20**, starting from a 2-bromo-2*H*-azirine **17** as a diastereoisomeric mixture, can only be explained considering that a S_N1 type mechanism is involved. In fact the already mentioned formation of 2*H*-azirine **6** in the dehalogenation of 2-chloro- and 2-bromo-2*H*-azirines **4a** and **4b** is in agreement with such mechanism. Although typical S_N2 reaction conditions were used, a S_N1 process may occur since it would lead to the formation of an aromatic 2π-electron system, an azacyclopropenyl cation. The presence of a chiral auxiliary in the intermediate allows asymmetric induction.

The unexpected formation of compound **21** can be



Scheme 6.

rationalized as resulting from ring opening of 10-phenylsulfonylisobornyl 3-phenylaziridine-2-carboxylate **22** followed by reduction reactions (Scheme 6). In fact, the reaction conditions used to promote the dehalogenation of 2*H*-azirine **17** should lead to a mixture of the corresponding dehalogenated 2*H*-azirine and aziridine as observed with 2*H*-azirines **4a** and **4d** (Table 1). However, from the reaction of 2*H*-azirine **17** with sodium borohydride the aziridine was not isolated and instead 10-phenylsulfonylisobornyl acetate **21** was obtained. The aziridine **22** leads to azomethine ylide **23**, which can be converted to the imine **24** through a 1,3-prototropic rearrangement. This compound undergoes a reduction reaction to give **25** which on reacting with sodium borohydride gives 10-phenylsulfonylisobornyl acetate **21**. Studies are underway to further clarify the mechanism for the synthesis of this chiral compound (**21**).

3. Conclusion

The work described proved that 3-phenyl-2*H*-azirine-2-carboxylates can be obtained in moderate yield from dehalogenation of 2-halo-3-phenyl-2*H*-azirine-2-carboxylates using sodium borohydride and tributyltin hydride as reducing agents.

The synthesis of a 2-bromo-2*H*-azirine with a chiral auxiliary was achieved and its dehalogenation reaction with sodium borohydride was promoted allowing the development of a diastereoselective synthesis of (2*S*)-2*H*-azirine-2-carboxylate **20**. In this reaction 10-phenylsulfonylisobornyl acetate was also formed.

4. Experimental

^{1}H NMR spectra were recorded on a Bruker AMX300 instrument operating at 300 MHz or on a Varian (400 MHz) instrument. ^{13}C spectra were recorded on a Bruker AMX300 instrument operating at 75.5 MHz or on a Varian (400 MHz) instrument operating at 100.6 MHz. The solvent is deuteriochloroform except where indicated otherwise. IR spectra were recorded on a Perkin–Elmer 1720X FTIR spectrometer. Mass spectra were recorded on a HP GC 6890/MSD5973 instrument or in a Trio 1000 GC mass spectrometer either under electron impact (EI) or under chemical ionization (CI) with ammonia by GC inlet or direct inlet for the thermally labile products Mass spectra were also recorded in a LCQ Advantage, Thermo Finnigan mass spectrometer under APCI+ where indicated. Optical rotations were measured on an Optical Activity AA-5 electrical polarimeter. Microanalyses were performed in the University of Coimbra using a EA 1108-CHNS-O Fisons instrument or in the University of Liverpool using a Carlo-Erba elemental analyser. Mp were recorded on a Reichert hot stage and are uncorrected. Flash column chromatography was performed with Merck 9385 silica as the stationary phase. 2-Halo-2*H*-azirines **4a**–**4d** were prepared as described in the literature.[4]

4.1. General procedures for the dehalogenation of 2-halo-3-phenyl-2*H*-azirine-2-carboxylates

(a) *Dehalogenation with sodium borohydride*. To a stirred solution of the 2-halo-2*H*-azirine (6.42 mmol) in DMF (90 mL), cooled to 0°C, sodium borohydride (0.53 g, 14.12 mmol) was cautiously added. The mixture was stirred using the reaction conditions indicated in Table 1 (temperature and reaction time). After addition of dichloromethane the solution was washed with water, dried ($MgSO_4$) and evaporated off. The product was purified by flash chromatography (ethyl acetate/hexane (1:2)).

(b) *Dehalogenation with tributyltin hydride*. To a stirred solution (10 mL) of 2-bromo-3-phenyl-2*H*-azirine-2-carboxylate **4b** (0.25 g, 0.93 mmol) cooled to 0°C and under N_2 atmosphere, tributyltin hydride (0.31 mL, 1.13 mmol) was slowly added. The mixture was stirred using the reaction conditions indicated in Table 2 (solvent, presence or absence of radical initiators, temperature, reaction time, etc.). After addition of dichloromethane the solution was washed with water, dried ($MgSO_4$) and evaporated off. The product was purified by flash chromatography (ethyl acetate/hexane (1:2)).

4.1.1. Ethyl 3-phenyl-2*H*-azirine-2-carboxylate 5a.[9] δ_H 1.31 (3H, t), 2.66 (1H, s), 4.23 (2H, q), 7.10–7.15 (1H, m, Ar-H), 7.31–7.38 (2H, m, Ar-H) and 7.50–7.57 (2H, m, Ar-H); *m/z* (EI) 190 (MH^+, 5), 176 (31), 161 (100) and 145 (43).

4.1.2. Methyl 3-phenyl-2*H*-azirine-2-carboxylate 5b.[3] δ_H 2.50 (1H, s), 3.51 (3H, s) and 7.06–7.53 (5H, m, Ar-H); *m/z* (CI) 178 [$(MH_3)^+$, 100], 177 [$(MH_2)^+$, 3], 139 (12) and 78 (1).

4.1.3. Ethyl 2-phenyl-2*H*-azirine-3-carboxylate 6. δ_H[10] 1.31 (3H, t), 3.46 (1H, s), 4.26 (2H, q), 7.12–7.14 (1H, m, Ar-H), 7.27–7.35 (2H, m, Ar-H) and 7.54–7.57 (2H, m, Ar-H); δ_C 14.0, 41.6, 61.8, 120.0, 124.5, 128.9, 137.4, 163.0 and 169.8; *m/z* (CI) 208 [$(MH+NH_4)^+$, 100], 207 [$(M+NH_4)^+$, 25] and 93 (22).

4.1.4. Ethyl 2-phenylaziridine-3-carboxylate 7a.[11] δ_H 0.85–1.03 (3H, m), 2.99–3.03 (1H, m), 3.46–3.48 (1H, m), 3.94–4.02 (2H, m) and 7.24–7.39 (5H, m, Ar-H); δ_C 14.3, 37.6, 61.5, 128.1, 128.3, 129.4, 130.1 and 162.8; *m/z* (CI) 209 [$(MNH_4)^+$, 1], 192 (MH^+, 100), 191 (M^+, 3), 139 (15) and 122 (17).

4.1.5. Methyl 2-phenylaziridine-3-carboxylate 7b. δ_H 3.27–3.33 (1H, m), 3.69 (3H, s), 3.79–3.82 (1H. m), 7.22–7.26 (2H, m, Ar-H) and 7.36–7.40 (3H, m, Ar-H); δ_C 44.6, 49.1, 53.5, 126.9, 129.0, 129.4, 129.5 and 165.6; *m/z* (CI) 195 [$(MNH_4)^+$, 2], 178 (MH^+, 100), 146 (3), 118 (5), 89 (30) and 60 (9); *m/z* (APCI+) 178 [ms/ms of 178:146 and 118].

4.1.6. 10-Isobornylsultone 9. This was prepared from *d*-10-camphorsulfonic acid **8** by a procedure described in the literature (65%).[7a] Mp 120.8–122.5°C (lit.,[7a] 114–116°C). (Found: C, 55.17; H, 7.51; S, 14.40. $C_{10}H_{15}O_3S$ requires C, 55.53; H, 7.46; S, 14.82). δ_H 0.94 (3H, s), 1.12 (3H, s),

1.22–1.33 (1H, m), 1.34–1.42 (1H, m), 1.88–1.98 (4H, m), 2.24–2.31 (1H, m), 3.18 (1H, d, J=13.7 Hz), 3.28 (1H, d, J=13.7 Hz), 4.38 (1H, dd, J=3.4, 7.8 Hz); δ_C 19.8, 19.9, 26.7, 29.0, 35.8, 44.3, 47.4, 49.0, 55.5, 87.9; m/z (EI) 216 (M^+, 100), 215 (65), 168 (15) and 152 (10).

4.1.7. 10-Phenylsulfonylisoborneol 10. This was prepared from 10-Isobornylsultone **9** by a procedure described in the literature (64%).[7b] Mp 135.2–136.3°C (lit.[7b] 141.5–143.5°C). (Found: C, 65.29; H, 7.58. $C_{16}H_{22}O_3S$ requires C, 65.27; H, 7.53). δ_H 0.78 (3H, s), 1.05 (3H, s), 1.10–1.25 (1H, m), 1.54–1.86 (6H, m), 2.92 (1H, d, J=13.6 Hz), 3.49 (1H, d, J=13.6 Hz), 4.22–4.27 (1H, m), 7.57–7.63 (2H, m, Ar-H), 7.66–7.72 (1H, m, Ar-H), 7.95–7.99 (2H, m, Ar-H); δ_C 19.8, 20.4, 27.4, 30.4, 38.9, 44.1, 49.1, 51.1, 56.1, 76.3, 127.6, 129.3, 133.8, 140.5; m/z (CI) 312 [$(M+NH_4)^+$, 33], 294 (MH^+, 4) and 277 (100).

4.1.8. 10-Phenylsulfonylisobornyl bromoacetate 11. To a stirred solution of the alcohol **10** (8.01 g, 27.2 mmol) in dichloromethane bromoacetyl bromide (4.8 mL, 54.4 mmol) was added dropwise. The mixture was stirred under nitrogen at room temperature for 12 h. The solution was washed with water, dried ($MgSO_4$) and evaporated off giving **11** as an oil (10.6 g, 25.6 mmol, 94%). δ_H 0.87 (3H, s), 0.99 (3H, s), 1.20–1.25 (1H, m), 1.65–2.05 (6H, m), 2.99 (1H, d, J=13.9 Hz), 3.58 (1H, d, J=13.9 Hz), 3.79 (1H, d, J=12.8 Hz), 3.84 (1H, d, J=12.8 Hz), 4.97–4.99 (1H, m), 7.55–7.60 (2H, m, Ar-H), 7.64–7.69 (1H, m, Ar-H), 7.93–7.96 (2H, m, Ar-H); δ_C 19.8, 20.2, 26.2, 27.0, 29.7, 39.0, 43.9, 49.6, 49.9, 54.9, 79.5, 127.7, 129.2, 133.6, 141.0, 165.4; m/z (CI) 434 [$(M+NH_4)^+$, 54], 432 (40), 278 (18)) and 277 (88).

4.1.9. 10-Phenylsulfonylisobornyl chloroacetate 13. To a stirred solution of the alcohol **10** (2.5 g, 8.49 mmol) in dichloromethane chloroacetyl chloride (1.9 mL, 17 mmol) was added dropwise. The mixture was heated under reflux for 24 h. The solution was washed with water, dried ($MgSO_4$) and evaporated off. The product was purified by flash chromatography (ethyl acetate/hexane (3:1)) giving **13** as an oil in 53% yield (1.67 g, 4.5 mmol). δ_H 0.98 (3H, s), 1.29 (3H, s), 1.17–1.29 (1H, m), 1.64–2.04 (6H, m), 2.97 (1H, d, J=13.9 Hz), 3.57 (1H, d, J=13.9 Hz), 4.00 (1H, d, J=14.9 Hz), 4.06 (1H, d, J=14.9 Hz), 4.97–5.01 (1H, m), 7.25–7.59 (2H, m, Ar-H), 7.63–7.66 (1H, m, Ar-H), 7.91–7.94 (2H, m, Ar-H).

4.1.10. 10-Phenylsulfonylisobornyl iodoacetate 14. To a stirred solution of the ester **13** (0.3 g, 0.81 mmol) in acetone KI (0.135, 0.81 mmol) was added. The mixture was stirred under nitrogen at room temperature for 12 h. After addition of dichloromethane the solution was washed with water, dried ($MgSO_4$) and evaporated off giving **14** (0.302 g, 89%) as an oil. δ_H 0.85 (3H, s), 0.95 (3H, s), 1.14–1.24 (1H, m), 1.56–1.94 (6H, m), 1.97 (2H, s), 2.99 (2H, d, J=14.1 Hz), 3.56 (2H, d, J=14.1 Hz), 4.76 (2H, dd, J=3.2, 7.9 Hz), 7.53–7.59 (2H, m, Ar-H), 7.62–7.68 (1H, m, Ar-H), 7.89–7.93 (2H, m, Ar-H); δ_C 19.9, 20.3, 21.2, 27.1, 29.8, 39.6, 44.0, 49.2, 49.9, 55.2, 77.7, 127.7, 129.2, 133.6, 141.3, 196.5.

4.1.11. 10-Phenylsulfonylisobornyl triphenylphosphoranylideneacetate 12. To a stirred solution of **11** (6.5 g, 15.65 mmol) in toluene triphenylphosphine (4.35 g, 14.43 mmol) was added. The mixture was heated under reflux for 12 h. Filtration of the solution gave the corresponding phosphonium salt which was dissolved in water (170 mL). The solution was neutralized by the addition of aqueous sodium hydroxide (10.9 g, 330 mL of water). The solid which resulted was collected by filtration and dried giving 8.16 g of **12** (13.7 mmol, 87%). Mp 201–202°C (from ethyl acetate–hexane). (Found: C, 71.9; H, 6.4. $C_{36}H_{37}O_4SP$ requires C, 74.5; H, 6.3%). δ_H 0.84 (3H, s), 0.94 (3H, s), 1.45–1.50 (1H, m), 1.65–1.93 (6H, m), 2.94 (1H, d, J=13.9 Hz), 3.79 (1H, d, J=13.9 Hz), 4.46 (1H, m), 7.25–7.30 (2H, m, Ar-H), 7.36–7.38 (1H, m, Ar-H), 7.44–7.51 (6H, m, Ar-H), 7.53–7.59 (3H, m, Ar-H), 7.64–7.72 (6H, m, Ar-H) and 7.93–7.96 (2H, m, Ar-H); m/z (CI) 597 (MH^+, 20%), 294 (19), 277 (100), 281 (61), 207 (97) and 73 (33). Accurate mass (ES+): 597.2228. $C_{36}H_{38}O_4SP$ $[MH]^+$ requires 597.2217. $[\alpha]_D^{25}$=+48.7 (c=0.1, CH_2Cl_2).

4.1.12. 10-Phenylsulfonylisobornyl 3-oxo-3-phenyl-2-triphenylphosphoranylidenepropanoate 15 (81%). A solution of ylide **11** (4.8 g, 8.04 mmol) and triethylamine (1.9 mL) in dry tetrahydrofuran (1.0 mL) was stirred at room temperature while a solution of benzoylchloride (8.04 mmol, 1.0 mL) in dry tetrahydrofuran was added dropwise to it. The mixture was stirred under nitrogen at room temperature for 12 h, filtered and the filtrate was washed with water, dried ($MgSO_4$) and concentrated under vacuum. The product was purified by flash chromatography [ethyl acetate/hexane (1:1)] giving **15** in 81% yield (4.58 g, 6.53 mmol). Mp 196.4–198.0°C. (Found: C, 73.62; H, 6.05. $C_{43}H_{41}O_5SP$ requires C, 73.69; H, 5.9%). δ_H 0.13 (3H, s), 0.63 (3H, s), 0.94–1.02 (1H, m), 1.25–1.72 (6H, m), 2.61 (1H, d, J=13.9 Hz), 3.04 (1H, d, J=13.9 Hz), 4.77 (1H, t, J=3.6 Hz), 7.18–7.22 (2H, m, Ar-H), 7.28–7.33 (1H, m, Ar-H), 7.44–7.59 (12H, m, Ar-H), 7.67–7.71 (2H, m, Ar-H) and 7.83–7.91 (8H, m, Ar-H); δ_C 19.45, 20.06, 26.92, 29.85, 36.94, 43.96, 49.07, 49.13, 54.50, 69.10 (d, $^1J_{CP}$=114 Hz), 125.40, 128.57 (d, $^3J_{CP}$=12.5 Hz), 131.65 (d, $^4J_{CP}$=2.7 Hz), 133.32 (d, $^2J_{CP}$=9.82 Hz), 141.56, 143.63 (d, $^3J_{CP}$=9.66 Hz), 167.07 (d, $^2J_{CP}$=15.4 Hz), 192.60 (d, $^2J_{CP}$=6.0 Hz); m/z (FAB) 701 (M^+, 66%), 551 (M^+, 6%), 460 (9%) and 407 (100). Accurate mass (ES+): 701.2491. $C_{43}H_{42}O_5SP$, $[M+H]^+$ requires 701.2506. $[\alpha]_D^{25}$=+47.6 (c=0.1, CH_2Cl_2).

4.1.13. 10-Phenylsulfonylisobornyl 3-phenylquinoxaline-2-carboxylate 19. The ylide **15** (3.15 g, 4.5 mmol) was dissolved in dichloromethane (50 mL) and a solution of azidotrimethylsilane (0.71 g, 6.5 mmol) and *N*-bromosuccinimide (1.15 g, 6.5 mmol) in dichloromethane (100 mL) was added. The reaction was complete after 5 min. The residue obtained upon removal of the solvent was purified by flash chromatography (ethyl acetate/hexane (3:1)) and gave 10-phenylsulfonylisobornyl 3-azido-2-chloro-3-phenylpropenoate **16** (58%). ν_{max} (film) 1738 and 2114 cm^{-1}; Accurate mass (ES+): 538.0675. $C_{25}H_{26}NO_4NaS^{79}Br$, $[MNa-N_2]^+$ requires 538.0664.

A solution of the vinyl azide **16** (1.0 g, 2.0 mmol) in heptane (10 mL) was heated under reflux for 2–3 h (the reaction was monitored by TLC). The reaction mixture was cooled and the solvent evaporated giving 10-phenylsulfonylisobornyl

2-bromo-3-phenyl-2*H*-azirine-2-carboxylate **17** as a diastereoisomeric mixture. ν_{max} (film) 1752 and 2956 cm^{-1}. Accurate mass (ES+): 538.0641 $C_{25}H_{26}NO_4NaS^{79}Br$, $[MNa]^+$ requires 538.0664. The diastereoisomers were separated by preparative TLC (ethyl acetate/hexane (1:3)) giving in order of elution: (i) δ_H 0.84 (3H, s), 0.88 (3H, s), 1.24–1.26 (1H, m), 1.61–2.05 (6H, m), 2.91 (1H, d, *J*=13.7 Hz), 3.64 (1H, d, *J*=13.7 Hz), 5.03 (1H, dd, *J*=3.1, 7.9 Hz), 7.56–7.63 (4H, m, Ar-H), 7.66–7.73 (2H, m, Ar-H) and 8.02–8.09 (4H, m, Ar-H); δ_C 19.7, 20.2, 27.1, 29.7, 39.1, 44.0, 44.5, 49.9, 50.0, 54.9, 80.8, 119.7, 127.9, 129.3, 129.6, 131.1, 133.6, 135.0, 141.1, 164.5, 165.4; (ii) δ_H 0.83 (3H, s), 0.95 (3H, s), 1.24–1.28 (1H, m), 1.77–2.04 (6H, m), 2.88 (1H, d, *J*=13.9 Hz), 3.40 (1H, d, *J*=13.9 Hz), 4.97 (1H, dd, *J*=2.9, 7.7 Hz), 7.50–7.56 (2H, m, Ar-H), 7.59–7.67 (3H, m, Ar-H), 7.72–7.78 (1H, m, Ar-H), 7.81–7.85 (1H, m, Ar-H) and 7.97–8.00 (2H. m, Ar-H); δ_C 19.9, 20.2, 27.0, 29.6, 39.3, 43.9, 44.6, 49.6, 50.0, 54.7, 80.5, 119.8, 127.8, 129.3, 129.7, 131.1, 133.6, 135.1, 140.9, 164.6, 165.0.

The diastereoisomeric mixture 2*H*-azirine **17** (0.143, 0.28 mmol) was dissolved in DMF (10 mL) and 1,2-phenylenediamine (32 mg, 0.28 mmol) was added. The reaction mixture was agitated in an ultrasound bath for 2 h. The solvent was evaporated and the residue was subjected to flash chromatography (with hexane/ethyl acetate (1:2)) giving the quinoxaline **19** as an oil (66 mg, 45%). δ_H 0.59 (3H, s), 0.81 (3H, s), 1.24–1.29 (1H, m), 1.61–2.05 (6H, m), 2.86 (1H, d, *J*=13.8 Hz), 3.44 (1H, d, *J*=13.8 Hz), 5.29 (1H, dd, *J*=3.3, 7.9 Hz), 7.29–7.40 (3H, m, Ar-H), 7.46–7.60 (4H, m, Ar-H), 7.81–7.95 (6H, m, Ar-H) and 8.20–8.27 (1H, m, Ar-H); δ_C 19.4, 20.3, 27.2, 29.4, 38.4, 44.1, 49.7, 49.8, 54.5, 79.8, 127.7, 128.8, 128.9, 129.2, 129.4, 129.5, 129.9, 130.5, 131.6, 133.4, 137.3, 137.4, 140.0, 141.2, 142.2, 146.1, 151.9 and 165.3; *m/z* (APCI+) 529 (M+2, 10%), 528 (M+1, 34), 527 (M, 100) and 277 (5). Accurate mass (ES+): 527.2019. $C_{31}H_{31}N_2O_4S$, $[M+H]^+$ requires 527.2005.

4.1.14. 10-Phenylsulfonylisobornyl (2*S*)-3-phenyl-2*H*-azirine-2-carboxylate 20 and 10-phenylsulfonylisobornyl acetate 21. To a stirred solution of azirine **17** (0.68 g, 1.32 mmol) in DMF (30 mL), cooled to 0°C, sodium borohydride (0.1 g, 2.64 mmol) was cautiously added. The mixture was stirred under nitrogen at room temperature for 2 h. After addition of dichloromethane the solution was washed with water, dried ($MgSO_4$) and evaporated off. The product was purified by flash chromatography (ethyl acetate/hexane (1:2)) giving the dehalogenated azirine **20** (0.14 g, 24%) and **21** (0.12 g, 27%).

10-Phenylsulfonylisobornyl 3-phenyl-2H-azirine-2-carboxylate **20** (24%). δ_H 0.84 (3H, s), 0.89 (3H, s), 1.21–1.29 (1H, m), 1.65 (1H, s), 1.66–2.02 (6H, m), 2.91 (1H, d, *J*=13.7 Hz), 3.65 (1H, d, *J*=13.7 Hz), 5.03 (1H, dd, m), 7.59–7.63 (4H, m, Ar-H), 7.67–7.69 (2H, m, Ar-H) and 8.03–8.09 (4H, m, Ar-H); δ_C 19.7, 20.2, 27.1, 29.7, 39.1, 44.0, 44.5, 49.9, 50.0, 54.8, 80.8, 119.7, 127.9, 129.3, 129.6, 131.1, 133.6, 135.0, 141.1, 164.5 and 165.4. $[\alpha]_D^{25}$=+48.1 (*c*=0.1, CH_2Cl_2).

10-Phenylsulfonylisobornyl acetate **21**. δ_H 0.86 (3H, s), 0.96 (3H, s), 1.18–1.28 (1H, m), 1.60–1.99 (9H, m), 3.00 (1H, d, *J*=14.1 Hz), 3.57 (1H, d, *J*=14.1 Hz), 4.78 (1H, dd, *J*=3.2, 7.9 Hz), 7.54–7.68 (3H, m, Ar-H) and 7.90–7.94 (2H, m, Ar-H); δ_C 19.7, 20.0, 21.0, 26.9, 29.6, 39.4, 43.8, 49.1, 49.7, 55.0, 77.5, 127.5, 129.1, 133.5, 141.1 and 169.4; *m/z* (CI) 354 $[(M+NH_4)^+$, 78], 337 (MH^+, 1), 294 (8) and 277 (100). Accurate mass (ES+): 359.1291. $C_{18}H_{24}O_4NaS$, $[M+Na]^+$ requires 359.1293.

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