Stereoselective Addition of Sulfone Carbanions to C=N: A Critical Dependence on the Stability and Reactivity of the Amide Anions in MIRC Reactions[‡]

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A procedure was developed for the selective synthesis of functionalized 4-methylenepyrrolidines by tuning the electron-withdrawing group ($ArSO_2$, COOEt, ArSO) attached to the acceptor imine nitrogen atom during addition of allyl sulfone carbanions. Sulfone carbanion additions to 2*H*-azirines were also examined.

Introduction

Stereoselective 1,2-addition of nucleophiles to activated imino functions is a valuable method for the synthesis of primary and secondary amines, often in optically active forms.[2] Among the reactions of activated imino groups, their action as 1,3 dipolarophiles or in similar [3+2] additions has gained special attention since it can lead to functionalized pyrrolidines in one pot.[3a] One such reaction leading to pyrrolidines is the addition of TMM (trimethylenemethane) equivalents to an imine function under Pd-catalyzed reaction conditions.[3b]

Our interest in the area of [3+2] cycloaddition reactions involving 2-(halomethyl)-3-(phenylsulfonyl)-1-propene **1a** or **1b** and olefins bearing various electron-withdrawing groups, led to the discovery of a general synthesis of functionalized methylenecyclopentanes under basic conditions by a process called MIRC (Michael-initiated ring closure) reactions.[4] Furthermore, we reported the synthesis of chiral nonracemic 2-arylpyrrolines by [3+2] MIRC reactions using *N*-(arylmethylene)-sulfinamides **2** and 2-(bromomethyl)-3-(phenylsulfonyl)-1-propene (**1b**).[5] An inherent problem in these reactions is the isomerization of the *exo*-methylene group into an *endo* double bond under basic conditions, thus affording the pyrrolines **3** instead of the expected 4-methylenepyrrolidines **4** (Scheme 1).

We reasoned that the above phenomenon arose mainly because the weakly stabilized sulfinamide anion **5** (Scheme 2), generated by Michael addition, abstracts the labile α-sulfonyl proton in **5** forming **6**.[6] The new allylsulfonyl carbanion in **6** via its resonance form **7** can abstract the proton on the sulfinamide to generate amide **8** followed by intramolecular ring closure through the nitrogen atom leading to the pyrroline **3**. Alternatively, since only a catalytic amount of base is needed to convert an allylic sulfone into a vinylic sulfone, isomerization of **4** into **3** after the MIRC reaction cannot be ruled out.

Results and Discussion

The isomerization of allyl sulfone to vinyl sulfone leads to the loss of a chiral center in **5**. We intended to circumvent this problem by placing a different appropriate electron-withdrawing group on the imine nitrogen atom so that the anion on the nitrogen atom in the initially formed **5** is well stabilized, i.e. it becomes less basic before it undergoes ring closure. For this purpose we prepared a representative imine **9**[7] bearing the electron-withdrawing ethoxycarbonyl group. Indeed deprotonation of **1b** using LDA (lithium diisopropylamide) in THF at −95 °C followed by addition of a THF solution of **9** afforded a mixture of the desired 4-methylenepyrrolidine **10** (35%) and the open-chain adduct **11** (20%) which were easily separated by column chromatography [Equation (1)].

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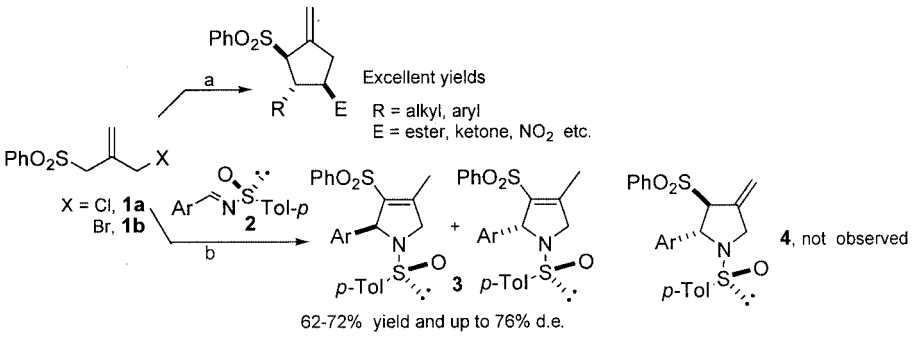
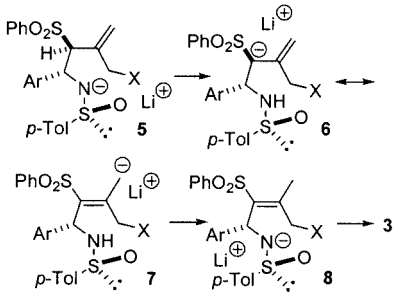
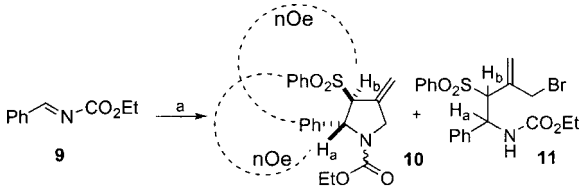


Scheme 1. Stereoselective addition of allyl sulfone carbanions to various acceptors: a) alkene acceptor, base, THF, low temperature; b) **2**, base, THF, −100 °C



Scheme 2. A plausible pathway for the formation of the pyrroline **3**



(1)

As shown in Table 1 (Entry 2), warming of the reaction mixture to −60 °C after initial stirring at −95 °C for 1 h led only to a 3% increase in the chemical yield of **10**. Addition of DMPU did not improve the yield of either the pyrrolidine **10** or the open-chain adduct **11**. Addition of HMPA and warming of the reaction mixture to −50 °C increased the yield of both pyrrolidine and the open-chain adduct (Entry 4).

Table 1. MIRC reaction of **9** under various conditions

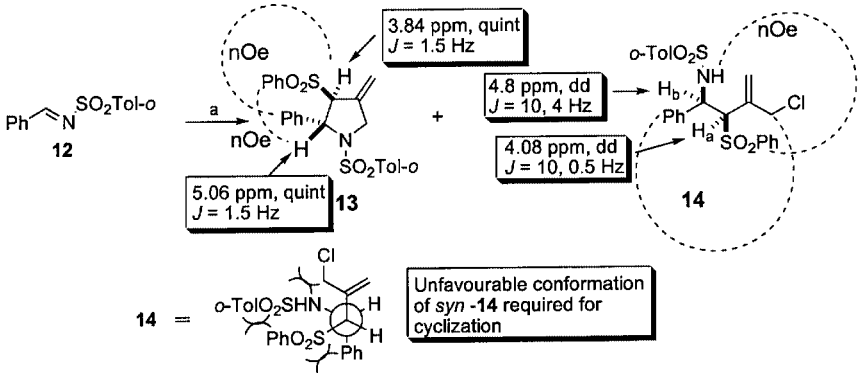
Entry	Conditions	**10**[a]	**11**[a]
1	1 h, −95 °C	35	20
2	1 h, −95 °C, 1 h, −60 °C	38	20
3	1 h, −95 °C, DMPU, −78 °C[b]	38	10
4	1 h, −95 °C, HMPA, −50 °C[b]	40	26

[a] Yield in %. [b] Stirred at this temperature for 1 h.

The structures of products **10** and **11** were unambiguously determined by ^{1}H and ^{13}C NMR spectroscopy. The pyrrolidine derivative **10** was found to exist as two amide rotamers in a ratio of 1:1. The relative stereochemistry of the 2-phenyl and the 3-(phenylsulfonyl) groups was established as *trans* because $J_{Ha,Hb} < 1$ Hz. Strong NOESY cross peaks between the *o*-protons of the phenylsulfonyl group and H_a as well as between H_b and the *o*-protons of the 2-phenyl group further corroborated the assigned stereochemistry. On the other hand, the relative stereochemistry of the aryl group with respect to the phenylsulfonyl group in the open-chain adduct **11** could not be ascertained either from the coupling constant $J_{Ha,Hb}$ (8.5 Hz) or from the NOESY cross peaks between the phenyl and the *o*-protons of the phenylsulfonyl group, since many conformers bearing gauche Ph and $PhSO_2$ groups are possible.

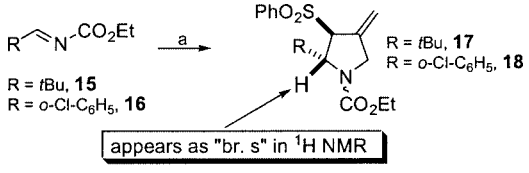
In order to study the scope of these reactions further we prepared imine **12**[8] bearing a more powerful electron-withdrawing phenylsulfonyl group. Reaction of **12** with **1b** under our previously described conditions yielded a series of ill-defined products. Further optimization with **1a** using *n*BuLi as the base at −78 to −50 °C gave a mixture of methylenepyrrolidine derivative **13** (11%) and the open-chain adduct **14** (65%) in a 1:6 ratio (Scheme 3). As before, the relative stereochemistry of the 2-phenyl and the 3-(phenylsulfonyl) groups in **13** was established as *trans*. The stereochemistry of the open-chain adduct was clearly established as *syn*[9] with respect to the 3-(phenylsulfonyl) and the 4-(*o*-tolylsulfamido) groups from the value of $J_{Ha,Hb}$ (10 Hz) and from a 2D NOESY spectrum. Strong NOESY cross peaks between the *o*-protons of the phenylsulfonyl group and the amido proton, and between the chloromethyl protons and the phenyl protons, strongly supported the assigned structure **14**.

Because these Michael additions led to both cyclized and uncyclized products, we surmised that the initial sulfone addition leads to the formation of both *syn* and *anti* diastereomeric adducts and the *anti* isomer undergoes rapid ring closure as there is less steric crowding in the transition state than for the *syn* isomer, in which all the bulky groups need to align in an unfavourable gauche relationship as in **14**, to bring about the required cyclization. In such a scenario, an appropriate R group that favours the formation of the *anti* over the *syn* isomer should lead to an MIRC reaction in high yield. In order to probe this we prepared imines **15**[10] and **16**[10] that bear bulky *tert*-butyl and 2-chloro-



Scheme 3. Addition of allyl sulfone **1a** to **12**: a) **1a**, *n*BuLi, THF, −78 to −50 °C

phenyl groups respectively. Remarkably, reaction of imine **15** with **1b** under our previously described conditions yielded only methylenepyrrolidine **17** in 73% yield [Equation (2), Table 2]. Similarly, imine **16** reacted with **1b** to afford the corresponding MIRC product **18** in 50% isolated yield with no trace of the open-chain adduct, thus suggesting that the success of the cyclization in these reactions depends entirely upon the stereoselectivity of the initial sulfone addition. The relative stereochemistry of the substituents in pyrrolidines **17** and **18** were established as before by a combination of 1D and 2D NMR experimental data. In all reactions studied, formation of polymeric side products was observed.



(2)

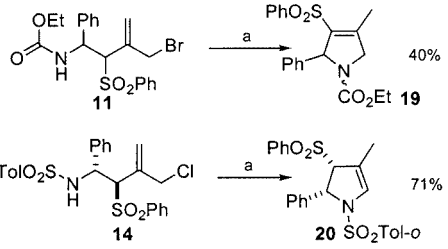
a) **1b**, LDA, THF, −95 °C

Table 2. Addition of **1b** to imines **15** and **16**

Entry	Conditions	Product	Yield
1	0.5 h, −95 °C	**17**	73%
2	0.5 h, −95 °C, HMPA	**18**	50%

A reasonable explanation of the *N*-substituent effect may be that in the case of the sulfonamide **12** addition of the allyl sulfones leads to a well-stabilized *N*-anion, which, being only weakly nucleophilic, affords more open-chain than cyclized product (cf. ratio **13/14**). By contrast, the sulfinamide anion (cf. **5**), being more basic, leads to complete isomerization before cyclization. The carbamate derived from **9** represents a balance between stability and reactivity leading to considerable ring closure (cf. **10**, **17**) and open-chain *syn* adduct (cf. **11**) without isomerization.

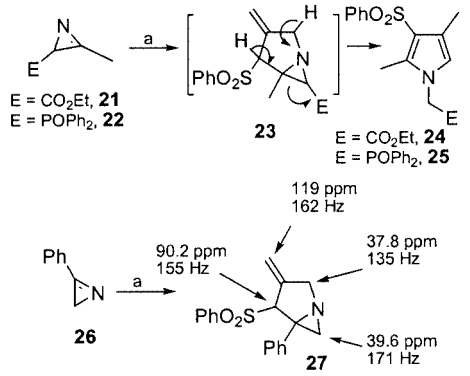
Our attempts to close the open-chain adducts **11** and **14** under a variety of reaction conditions using different bases



Scheme 4. Cyclization of open-chain adducts: a) K_2CO_3, DMF, room temp.

finally led us to employ K_2CO_3 in DMF at room temperature for 24 h as the best protocol (Scheme 4). Treatment of **11** under these reaction conditions led to pyrroline **19**, presumably by isomerization of the allyl sulfone to vinyl sulfone either before or after intramolecular ring closure. Stirring of **14** under the same reaction conditions led to the formation of **20** for reasons that are still obscure. The structure of **20** was derived from a systematic analysis of its ^1H NMR, ^{13}C NMR, COSY, NOESY, HMQC and HMBC spectra.

Imines not bearing an activating group on N are usually inert towards nucleophilic attack. However, an imine function that is part of a strained ring has been shown to undergo a variety of interesting reactions leading to potentially important compounds in organic synthesis.[11] In this respect 2*H*-azirines with a ring-strain energy[12] of ca. 48 kcal·mol^{-1} have been shown to participate in a variety of nucleophilic addition reactions[11] and can also act as efficient dienophiles in Diels−Alder reactions.[13] Therefore, one may expect 2*H*-azirines to react with the anion of **1a** or **1b** to afford bicyclo[3.1.0] amines, which could be precursors for densely functionalized piperidines after selective opening of the strained bridging σ-bond. To demonstrate our plan we prepared azirine **21** accoding to a literature procedure.[14] Treatment of **21** with **1a** using either LDA or *n*BuLi at −78 °C afforded pyrrole derivative **24** in poor yield (Scheme 5, Table 3). Further, tuning the structure of the azirine by substituting a diphenylphosphoryl group for an ester group led to **22**.[15] Treatment of **22** with **1a** under the conditions described before yielded solely **25** in an acceptable yield. We inferred that the formation of unexpected **24** and **25** is the result of a synergistic influence of the acidic



Scheme 5. Addition of **1a** to 2*H*-azirines: a) **1a**, base, THF, −78 °C

Table 3. Addition of **1a** to azirines **21**, **22** and **26**

Entry	Base, time	Product	Yield
1	LDA, 2 h	**24**	10%
2	*n*BuLi, 2 h	**24**	30%
3	*n*BuLi, 2 h	**25**	41%
4	LDA, 4 h	**27**	13%

α-phenylsulfonyl proton and the ester group in the strained bicyclic intermediate **23**, which may promote facile ring opening. In an attempt to subdue this process we turned our attention to azirine **26**[16] not bearing any electron-withdrawing group on the ring. Reaction of **26** with **1a** at −78 °C in THF using LDA as the base afforded the desired azabicyclohexane **27** as the only product, albeit in only 13% yield. The structure of **27** was assigned based on ^{1}H NMR, ^{13}C NMR and mass spectra and $J_{C,H}$ coupling values obtained from a gated decoupling experiment. The observation of 171 Hz coupling for C-1 in **27** clearly indicated the increased s character as compared to other methylene groups, which is characteristic of an aziridinyl carbon atom involved in near sp^2 hybridization. The low yield can be attributed to the presence of the bulky phenyl group at the *ipso*-carbon atom in **26**, which greatly disfavours the attack of the sulfonyl carbanion thus leading instead to mostly polymeric products.

In conclusion we have developed a one-pot procedure for the selective synthesis of functionalized 4-methylenepyrrolidines selectively by tuning the electron-withdrawing group attached to the acceptor imine nitrogen atom. The success in obtaining pyrrolidine derivatives over pyrrolines in these MIRC reactions depends upon the critical balance between the stability and the reactivity of the anionic amide nitrogen atom, generated upon the initial addition of allyl sulfone carbanions.

Experimental Section

General: All air- and moisture-sensitive reactions were carried out in flame-dried, argon-flushed, two-necked flasks sealed with rubber septa, and the reagents were introduced with a syringe. Tetrahydrofuran was freshly distilled from sodium/benzophenone ketyl under argon, prior to every reaction. Chromatography was done on Merck silica gel 60 (230−400 mesh), and precoated Merck silica-gel plates (60F-254) were used for TLC. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ with a Bruker-600 MHz or Bruker AM-300 spectrometer. Mass spectra (CI in methane) were recorded at 60−70 eV.

General Procedure for the MIRC Reactions with Acceptors 9, 12, 15, 16 and Halo Sulfone 1a or 1b: A THF solution of the sulfone **1a** or **1b** (1 mmol) was added dropwise at −95 °C under Ar to a stirred solution of LDA prepared from diisopropylamine (0.17 mL, 1.2 mmol) and *n*BuLi (1.6 M in hexanes, 0.75 mL, 1.2 mmol) in THF (3 mL) (in cases where *n*BuLi was used as the base, *n*BuLi was added dropwise to a stirred solution of the halo sulfone in THF under Ar at −95 °C) and stirred for 10−15 min. The acceptor (1.1 mmol) dissolved in THF (2 mL) was added dropwise and stirred under the conditions described (Tables 1 and 2 with or without 2 equiv. of HMPA or DMPU). The reaction mixture was quenched with aq. NH_4Cl, poured into water, and extracted with CH_2Cl_2 (2 × 20 mL). The combined organic phase was washed with brine, dried ($MgSO_4$) and concentrated. Chromatographic purification of the residue gave the pure product as an oil or solid.

Ethyl (*trans*)-4-Methylene-2-phenyl-3-(phenylsulfonyl)pyrrolidine-1-carboxylate (10): Isolated as an oil by column chromatography in yields as reported in Table 1 under various reaction conditions, using 14% EtOAc in hexanes as eluent. ^{1}H NMR (600 MHz, $CDCl_3$, mixture of two rotamers): δ = 7.96 and 7.91 (dd, *J* = 8, 1.5 Hz, 2 H), 7.74−7.71 (m, 1 H from each rotamer), 7.63−7.58 (m, 2 H from each rotamer), 7.32−7.21 (m, 3 H from each rotamer), 7.11−7.09 and 7.04−7.02 (m, 2 H from each rotamer), 5.7 and 5.65 (2 s, 1 H from each rotamer), 5.47 and 5.41 (2 s, 1 H from each rotamer), 5.35 and 5.16 (2 s, 1 H from each rotamer), 4.14−4.12 (m, 1 H from each rotamer), 4.06−3.96 (m, 4 H from each rotamer), 1.21 and 1.12 (2 t, *J* = 8 Hz, 3 H from each rotamer) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.2 (2 C), 140.9 and 140.6, 137.3 and 136.7, 137 (2 C), 134.4 and 134.2, 129.6 (2 C), 129.2 (2 C), 128.4 (2 C), 127.5 (2 C), 125.4 (2 C), 117.6 (2 C), 77.7 and 76.4, 62.1 and 61.5, 61.46 (2 C), 50.9 (2 C), 14.6 (2 C) ppm. MS: *m/z* (%) = 372 (5) $[MH]^+$, 230 (100), 156.08 (50). HRMS: calcd. for $C_{20}H_{22}NO_4S$ $[M + H]^+$ 372.1270, found 372.1277.

Ethyl 3-Bromomethyl-1-phenyl-2-(phenylsulfonyl)but-3-enylcarbamate (11): Isolated as a solid by column chromatography in yields as reported in Table 1 under various reaction conditions, using 30% EtOAc in hexanes as eluent. M.p. 55−57 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.78 (dd, *J* = 9.1 Hz, 2 H), 7.61−7.59 (m, 1 H), 7.49−7.46 (m, 2 H), 7.26−7.2 (m, 5 H), 6.32 (br. s, 1 H), 5.6 (s, 1 H), 5.56 (q, *J* = 1 Hz, 1 H), 5.19 (dd, *J* = 8.5, 7.5 Hz, 1 H), 4.32 (br. d, *J* = 8.5 Hz, 1 H), 4.1−4.05 (m, 1 H), 4.04−4.0 (m, 1 H), 3.72 (dd, *J* = 11.5, 1 Hz, 1 H), 3.47 (d, *J* = 11.5 Hz, 1 H), 1.21 (br. t, *J* = 7 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 155.8, 139.1, 138.2, 136.4, 134.5, 129.8, 129.3, 128.8, 127.9, 124.2, 70.2, 61.6, 56.8, 52.3, 37.5, 14.9 ppm. MS: *m/z* (%) = 452 (10) $[MH]^+$, 230 (100), 218 (35). HRMS: calcd. for $C_{20}H_{23}BrNO_4S$ $[M + H]^+$ 452.0531, found 452.0563.

***(trans)*-4-Methylene-2-phenyl-3-phenylsulfonyl-1-(2-tolylsulfonyl)-pyrrolidine (13):** Isolated as an oil by column chromatography in 11% yield (50 mg) using 22% EtOAc in hexanes as eluent. M.p. 38−40 °C. ^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.81−7.79 (m, 2 H), 7.7−7.68 (m, 1 H), 7.58−7.55 (m, 4 H), 7.25−7.24 (m, 2 H), 7.22−7.21 (m, 3 H), 7.02−7.01 (m, 2 H), 5.4 (br. s, 2 H), 5.06 (quint, *J* = 1.5 Hz, 1 H), 4.18 (dt, *J* = 13, 2 Hz, 1 H), 4.07 (dq, *J* = 13, 2 Hz, 1 H), 3.84 (quint, *J* = 1.5 Hz, 1 H), 2.41 (s, 3 H)

ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143.6, 140.8, 136.34, 136.1, 134.8, 134.3, 129.5, 129.4, 129.2, 128.8, 128, 127.8, 125.9, 117.7, 77.1, 63.6, 52.8, 21.5 ppm. MS: *m*/*z* (%) = 454.12 (70) $[M]^+$, 312.11 (55), 168.99 (100), 130.99 (69).

***N*-[3-Chloromethyl-1-phenyl-2-(phenylsulfonyl)but-3-enyl]-2-methylbenzenesulfonamide (14):** Isolated as a solid by column chromatography in 65% yield (318 mg) using 40% EtOAc in hexanes as eluent. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.86 (dd, *J* = 8, 1.5 Hz, 2 H), 7.66 (tt, *J* = 8, 1 Hz, 1 H), 7.5 (dd, *J* = 8.5, 9 Hz, 2 H), 7.37 (d, *J* = 8 Hz, 2 H), 7.04−7.0 (m, 7 H), 6.75 (d, *J* = 4 Hz, 1 H), 5.34 (q, *J* = 1.5 Hz, 1 H), 5.24 (br. s, 1 H), 4.8 (dd, *J* = 10, 4 Hz, 1 H), 4.08 (dd, *J* = 10, 0.5 Hz, 1 H), 3.54 (dd, *J* = 13, 1 Hz, 1 H), 2.33 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 143, 137.1, 136.4, 135.9, 135.1, 134.5, 130, 129.1, 129, 128.7, 128.1, 128, 127.2, 123.6, 69.5, 58.7, 48.2, 21.5 ppm. MS: *m*/*z* (%) = 490.09 (14) $[MH]^+$, 260 (100), 129.07 (45). HRMS: calcd. for $C_{24}H_{25}ClNO_4S_2$ $[M + H]^+$ 490.0914, found 490.0928.

Ethyl (*trans*)-2-*tert*-Butyl-4-methylene-3-(phenylsulfonyl)pyrrolidine-1-carboxylate (17): Isolated as a solid by column chromatography in 73% yield (256 mg) using 12% EtOAc in hexanes as eluent. M.p. 118−120 °C. ^1H NMR (600 MHz, $CDCl_3$, mixture of two rotamers): δ = 7.91 and 7.85 ppm (dd, *J* = 9.1.5 Hz, 2 H from each rotamer), 7.7−7.65 (m, 1 H from each rotamer), 7.6−7.54 (m, 2 H from each rotamer), 5.55 and 5.37 (2 br. s, 1 H from each rotamer), 5.44 and 5.35 (2 br. s, 1 H from each rotamer), 4.41 and 4.39 (2 s, 1 H from each rotamer), 4.16−4.1 (m, 1 H from each rotamer), 4.05−3.98 (m, 1 H from each rotamer), 3.97−3.93 (m, 2 H from each rotamer), 3.84 (dt, *J* = 15, 2 Hz, 1 H from each rotamer), 1.3 and 1.17 (2 t, *J* = 7 Hz, 3 H from each rotamer), 0.85 and 0.8 (2 s, 9 H from each rotamer) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 156.2 and 155.8, 139.9 and 139.8, 136.9 and 136.6, 134.6 and 134.2, 130.1 and 129.8, 129.4 and 129.3, 115.9 and 115.8, 71.7 and 71.2, 67.8 and 67.4, 61.9 and 61.7, 52.2 and 52, 37.3 and 37.1, 26.8 and 26.7, 15 and 14.9 ppm. MS: *m*/*z* (%) = 352.16 (90) $[MH]^+$, 306 (100), 154.09 (48).

Ethyl (*trans*)-2-(2-Chlorophenyl)-4-methylene-3-(phenylsulfonyl)-pyrrolidine-1-carboxylate (18): Isolated as an oil by column chromatography in 50% yield (203 mg) using 15% EtOAc in hexanes as eluent. ^1H NMR (600 MHz, $CDCl_3$ at 305 K, mixture of two rotamers): δ = 8.0 and 7.94 (d, *J* = 8 Hz, 2 H from each rotamer), 7.69 (t, *J* = 8 Hz, 1 H from each rotamer), 7.6−7.55 (br. q, *J* = 8 Hz, 2 H from each rotamer), 7.32−7.31 and 7.26−7.24 (2 m, 2 H from each rotamer), 7.2−7.16 (m, 1 H from each rotamer), 7.01−6.98 (m, 1 H from each rotamer), 5.98 and 5.94 (2 br. s, 1 H from each rotamer), 5.46 and 5.42 (2 s, 1 H from each rotamer), 5.31 and 5.15 (2 s, 1 H from each rotamer), 4.3 and 4.21 (2 br. d, *J* = 17 Hz, 2 H from one rotamer), 4.19−4.1 and 4.11 (m, dq, *J* = 11, 7 Hz, 5 H, 1 H, 4 H from one rotamer and 2 H from the other rotamer), 3.96 and 3.93 (2 s, 1 H from each rotamer), 1.26 and 1.12 (t, *J* = 7 Hz, 3 H from each rotamer) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.4 and 154.0, 137.9 and 137.4, 136.9, 136.6 and 136.2, 134.3 and 134.2, 131.9 and 131.8, 130.1 and 130.0, 129.9 and 129.6, 129.54, 129.5 and 129.1, 127.2 and 127.1, 126.7 and 126.6, 118.3, 118.2, 75.7 and 74.7, 61.8 and 61.7, 60.1 and 59.3, 14.7 and 14.5 ppm. MS: *m*/*z* (%) = 406 (11) $[MH]^+$, 264.07 (100), 212.04 (32). HRMS: calcd. for $C_{20}H_{21}ClNO_4S$ $[M + H]^+$ 406.0880, found 406.0904.

General Procedure for the Cyclization of Open-Chain Adducts 11 and 14: Solid K_2CO_3 (6 mmol) was added in one portion to a solution of the substrate (2 mmol) in DMF (6 mL). The solution was stirred at room temp. under N_2 for 24 h. Analysis by TLC indicated the complete consumption of the starting material while showing a nonpolar spot. Water (5 mL) was added to quench the reaction and the product was extracted with 50 mL of diethyl ether. The organic phase was washed with brine, dried ($MgSO_4$) and concentrated. Purification by flash column chromatography on silica afforded the cyclized product.

Ethyl 4-Methyl-2-phenyl-3-(phenylsulfonyl)-2,5-dihydropyrrole-1-carboxylate (19): Isolated as an oil by column chromatography in 40% yield (297 mg) using 15% EtOAc in hexanes as eluent. ^1H NMR (300 MHz, $CDCl_3$, mixture of two rotamers): δ = 7.47−7.0 (m, 10 H), 5.77−5.76 (m, 1 H), 4.55−4.38 (m, 2 H), 4.15−3.88 (m, 2 H), 2.33 (s, 3 H), 1.19 and 0.98 (2 t, *J* = 7 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 154.1, 148.4 and 148.2, 140.8, 139.2 and 138.8, 136, 133 and 132.9, 130, 53, 129, 128.1, 127.2, 127, 69.2 and 68.7, 61.4, 59.3 and 58.9, 14.6 and 14.2, 13.3 ppm. MS: *m*/*z* (%) = 371 (100) $[M]^+$, 342 (45), 294 (78), 200 (59). HRMS: calcd. for $C_{22}H_{21}NO_4S$ $[M]^+$ 371.1191, found 371.1165.

4-Methyl-1-[(2-methylphenyl)sulfonyl)]-2-phenyl-3-(phenylsulfonyl)-2,3-dihydro-1*H*-pyrrole (20): Isolated as an oil by column chromatography in 71% yield (643 mg) using 20% EtOAc in hexanes as eluent. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.72−7.71 (m, 2 H), 7.58−7.54 (m, 5 H), 7.28−7.27 (m, 2 H), 7.21−7.18 (m, 1 H), 7.16−7.14 (m, 2 H), 6.81−6.79 (m, 2 H), 6.57 (quint, *J* = 1.5 Hz, 1 H), 5.03 (br. d, *J* = 4 Hz, 1 H), 3.99 (dquint, *J* = 4, 1 Hz, 1 H), 2.44 (br. s, 3 H), 1.86 (dd, *J* = 1.5, 1 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 144.6, 139.6, 136.9, 134.3, 132.3, 130.7, 129.7, 129.4, 129.1, 128.8, 128.3, 127.6, 125.5, 111.1, 80.8, 64.1, 21.7, 13.1 ppm. MS: *m*/*z* (%) = 454.11 (10) $[MH]^+$, 311.10 (37), 156.07 (100). HRMS: calcd. for $C_{24}H_{24}NO_4S$ $[M + H]^+$ 454.1146, found 454.1117.

General Procedure for the Reaction of Sulfone 1a with 2*H*-Azirines 21, 22 and 26: *n*BuLi (0.9 mL, 1.44 mmol) was added dropwise at −78 °C under N_2 to a solution of the sulfone **1** (1.2 mmol) in THF (12 mL) [when LDA was used as the base, sulfone (1.2 mmol) in THF (3 mL) was added to LDA solution prepared freshly from *n*BuLi (1.44 mmol) and diisopropylamine (1.6 mmol) in THF (3 mL) at −40 °C]. After stirring at −78 °C for 10 min, azirine (1.2 mmol) in THF (5 mL) was added dropwise and stirred for the time indicated in Table 3. The reaction was quenched with water (2 mL) and the mixture extracted with diethyl ether (2 × 25 mL). The combined organic phases were washed with brine, dried ($MgSO_4$) and concentrated under reduced pressure. Chromatographic purification of the residue on silica afforded the pure material.

Ethyl [2,4-Dimethyl-3-(phenylsulfonyl)pyrrol-1-yl]acetate (24): Isolated as an oil by column chromatography in yields as reported in Table 3 under different reaction conditions, using 16% EtOAc in hexanes as eluent. ^1H NMR (600 MHz, $CDCl_3$): δ = 7.85 (dd, *J* = 9, 1.5 Hz, 2 H), 7.51 (tt, *J* = 7.5, 1 Hz, 1 H), 7.46 (dd, *J* = 9, 7.5 Hz, 2 H), 6.32 (d, *J* = 10 Hz, 1 H), 4.48 (s, 2 H), 4.22 (q, *J* = 7 Hz, 2 H), 2.48 (s, 3 H), 2.13 (d, *J* = 10 Hz, 3 H), 1.27 (t, *J* = 7 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.9, 144.8, 135.3, 132.5, 129.3, 126.6, 120.9, 119.7, 118.5, 62.4, 48.6, 14.5, 11.6, 11 ppm. MS: *m*/*z* (%) = 322 (100) $[MH]^+$, 291 (10).

1-[(Diphenylphosphoryl)methyl]-2,4-dimethyl-3-phenylsulfonyl-1*H*-pyrrole (25): Isolated as a solid by column chromatography in 41% yield (221 mg) using 12% EtOAc in hexanes as eluent. M.p. 68−70 °C. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.8−7.76 (m, 2 H), 7.6−7.36 (m, 13 H), 6.37 (br. d, *J* = 1 Hz, 1 H), 4.56 (d, *J* = 6.5 Hz, 2 H), 2.09 (s, 3 H), 2.03 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ =

144.5, 134.6, 132.8, 132.0, 131.2 (d, $J_{C,P}$ = 9 Hz), 131.1, 128.1 (d, $J_{C,P}$ = 100 Hz), 128.9 (d, $J_{C,P}$ = 12 Hz), 128.8, 126.2, 120.7, 119.4, 118.1, 47.4 (d, $J_{C,P}$ = 73 Hz), 11.2, 10.3 ppm. MS: *m/z* (%) = 449 (39) $[M]^+$, 340 (71), 303 (51), 202.05 (100), 125 (90). $C_{25}H_{24}NO_3PS$ (449.29): calcd. C 66.82, H 5.34, N 3.12; found C 66.62, H 5.43, N 2.98.

3-Methylene-5-phenyl-4-(phenylsulfonyl)-1-azabicyclo[3.1.0]hexane (27): Isolated as an oil by column chromatography in 13% yield (55 mg) using 25% EtOAc in hexanes as eluent. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.83 (m, 2 H), 7.47 (m, 1 H), 7.3 (m, 2 H), 7.22 (m, 5 H), 5.55 (ddd, *J* = 10, 3, 2.5 Hz,, 2 H), 4.55 (br. d, *J* = 1.5 Hz, 1 H), 3.03 (br. d, *J* = 16 Hz, 1 H), 2.82 (br. d, *J* = 16 Hz, 1 H), 2.17 (br. d, *J* = 1.5 Hz, 1 H), 1.75 (s, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 180, 136, 133, 130, 128.8, 128.1, 127.1, 126.4, 119.3, 90.2, 51, 39.6 (t, $J_{C,H}$ = 171 Hz), 37.8 ppm. MS: *m/z* (%) = 310 (10) $[M^+ - H]$, 247 (24), 170 (100). MS (CI; butane): *m/z* (%) = 312 (97) $[MH^+ - H]$, 171 (12), 170 (100).

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