(2-Bromoethyl)sulfonium Trifluoromethanesulfonates in Stereoselective Annulation Reactions for the Formation of Fused Bicyclic Epoxides and Aziridines

by **Sven P. Fritz**[a]), **Zulfiquar Ali**[a]), **Matthew G. Unthank**[a]), **Eoghan M. McGarrigle**[a])[b]), and **Varinder K. Aggarwal***[a])

[a]) School of Chemistry, University of Bristol, Bristol, BS8 1TS, UK (phone: +44-117-9546315; fax: +44-117-9298611; e-mail: V.Aggarwal@Bristol.ac.uk)
[b]) Centre for Synthesis and Chemical Biology, UCD School of Chemistry and Chemical Biology, University College Dublin, Belfield, Dublin 4, Ireland

Dedicated to Professor *Dieter Seebach* on the occasion of his 75th birthday

A versatile and simple method is reported for the synthesis of bicyclic epoxide and aziridine–fused heterocycles (up to 98% yield, up to 96:4 er or up to 15:1 dr), using a tandem *Michael* addition/ *Johnson–Corey–Chaykovsky* annulation approach. A new chiral (2-bromoethyl)sulfonium reagent is described, based on an easily available chiral sulfide; it promotes or enhances stereoselectivity in the reaction.

Introduction. – The asymmetric synthesis of heterocycles continues to be of significant contemporary interest due to their prevalence in both natural products and pharmaceutical agents [1]. Strained, fused bicyclic systems are ideal starting points for the synthesis of functionalized heterocycles [2]. In particular, epoxide- and aziridine-fused five- and six-membered rings can be easily modified towards a broad range of more complex targets, as they are prone to ring-opening reactions [2][3]. Previous syntheses of these systems mostly relied on cyclic, olefin precursors, but subsequent asymmetric reactions (epoxidation [2c][2i][4], dihydroxylation [5], halogenation [6]) are often difficult to control.

We recently reported that bicyclic epoxide- or aziridine-fused heterocycles could be prepared using vinylsulfonium salt **1** or its chiral variant **2** [3][7][8], and also explored other modes of reactivity [9][10]. However, the diphenylvinylsulfonium salt **1** is a reactive oil, and the chiral salt **2** requires a lengthy synthesis [11]. We, therefore, decided to exploit recent advances in annulation reactions using (2-bromoethyl)sulfonium salts as precursors for the *in situ* generation of vinylsulfonium salts [9g] with the much more readily available chiral sulfonium salt **4** [12], which had the potential to render this work more practical (*Scheme 1*).

Results and Discussion. – (2-Bromoethyl)sulfonium salt **3** is, in contrast to vinylsulfonium salt **1**, a commercially available, air-stable, and crystalline compound that can be stored on the bench without precautions and weighed easily [9g]. Additionally, it often gives higher yields because the reactive vinylsulfonium salt

Scheme 1. *Context of Present Work*

Classic method [4 – 6]:

Previously published [3][7][8][10]:

X = O, NS(O)^{t}Bu
n = 1 or 2

This work:

Z = O, N-Ts
X = O, NS(O)^{t}Bu
n = 1 or 2
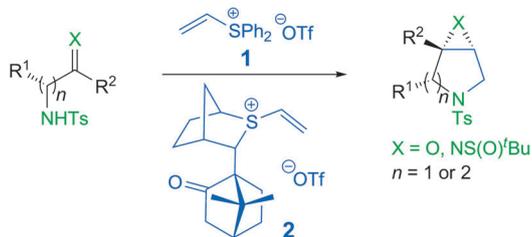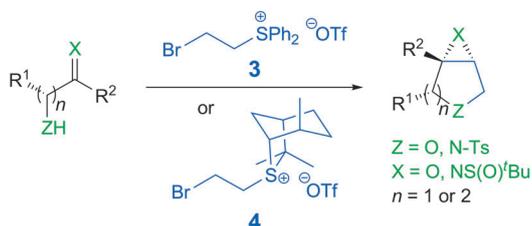
species is generated *in situ*, in lower concentrations. We also wanted to investigate the use of a novel (2-bromoethyl)sulfonium salt **4**, which in comparison to previously reported chiral sulfonium salt **2** (6 steps), was expected to be easily available from commercially sulfide **7** [12]. Indeed, chiral (2-bromoethyl)sulfonium salt **4** was readily prepared by alkylation of the corresponding triflate **6** (*Scheme 2*).

Scheme 2. *Synthesis of Sulfonium Salt* **4**
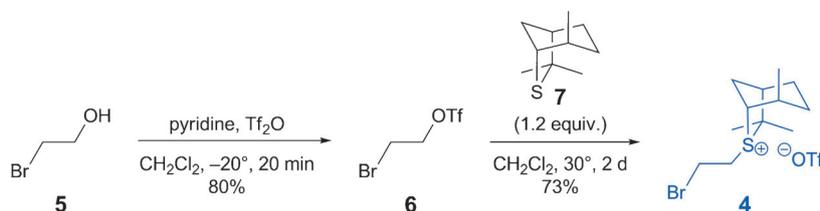
We first explored epoxy-annulation reactions, and inital results were promising, showing that we could achieve higher yields in the epoxy annulation reaction by using (2-bromoethyl)sulfonium salt **3** instead of vinylsulfonium salt **1** in almost every case (compare conditions *A* with *B*, *Table 1*). Furthermore, use of chiral (2-bromoethyl)-sulfonium salt **4** gave good yields with moderate to high enantioselectivity (*Table 1*,

Table 1. *Results and Scope of the Annulation Reactions Using Sulfonium Salts* **1** – **4** (DBU = 1,8-diaza-bicyclo[5.4.0]undec-7-ene)
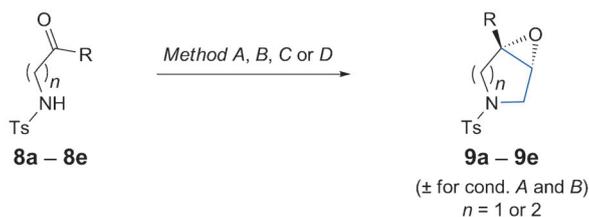
A: **3** (1.25 equiv.), DBU (3.5 equiv.), CH$_2$Cl$_2$ (0.1M), 0°, 2 – 4 h
B: **1** (1.20 equiv.); DBU (2.0 equiv.), CH$_2$Cl$_2$ (0.1M), 0°, 2 – 4 h
C: **4** (1.25 equiv.), DBU (3.5 equiv.), CH$_2$Cl$_2$ (0.015M), –20°, 1 – 3 d
D: **2** (1.00 equiv.), DBU (2.0 equiv.), CH$_2$Cl$_2$ (0.015M), –20°, 2 – 5 d
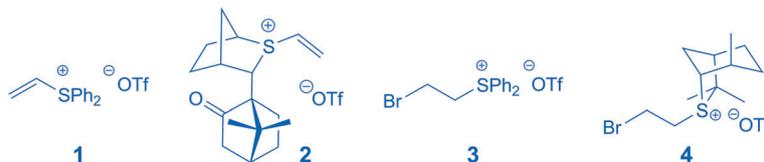
Entry	Substrate	R	*n*	Method	Product	Yield [%] (with **1** or **2**)[a]	ee [%] (ee with **2**)[b]
1	**8a**	Me	1	*A*/*B*	**9a**	94/(90)	–
				C/*D*		52/(76)	54/(97)
2	**8b**	Et	1	*A*/*B*	**9b**	99/(90)	–
				C/*D*		87/(65)	72/(99)
3	**8c**	Ph	1	*A*/*B*	**9c**	98/(96)	–
				C/*D*		88/(80)	68/(92)
4	**8d**	H	2	*A*/*B*	**9d**	71/(67)	–
				C/*D*		68/(67)	54/(98)
5	**8e**	Me	2	*A*/*B*	**9e**	72/(77)	–
				C/*D*		35/(30)	92/(86)

[a]) Isolated yields. Data in brackets are from [3]. [b]) Determined by chiral HPLC (for details, see *Exper. Part*).

conditions *C*). It should be noted that the lower yields observed with β-amino ketones/aldehydes **8d**/**8e** compared to those with the corresponding α-amino ketones/aldehydes **8a** – **8c** are a result of competing elimination of TsNH$_2$, leading to an enone (compare *Entries 4* and *5* with *Entries 1 – 3*, *Table 1*).

While higher yields were obtained with the new conditions employing the (2-bromoethyl)sulfonium salt **3**, the enantioselectivities using the new chiral (2-bromoethyl)sulfonium salt **4** were generally lower than those we had obtained with the less easily accessible sulfonium salt **2** [3]. Alternative solvents and additives were explored, but no significant increase in enantioselectivity was observed (see *Exper. Part* for details). The enantioselectivity in ylide epoxidations is determined in the reaction of the ylide with the aldehyde to form a betaine [13]. We propose that the lower enantioselectivity obtained using salt **4** *vs.* salt **2** as ylide precursors is due to differences

in the populations of ylide conformers **Y1/Y2** *vs.* **Z1/Z2** (*Scheme 3*), which in turn leads to different enantiomers of the product being formed. In the case of ylide **Y**, conformer **Y1** is strongly favored over **Y2** due to the steric interactions between the bridgehead H-atoms and the ylide substitutents. Similar steric interactions are present in ylide conformer **Z2**, but conformer **Z1** suffers from *gauche* interactions from the neighboring geminal dimethyl moiety, not present in **Y**, making it less strongly favored. As a result lower enantioselectivity was observed (*Scheme 3*).

Use of enantiomerically enriched α-substituted aldehydes/ketones **10a – 10g** was also explored with the two new sets of conditions [8b]. Use of the achiral (2-bromoethyl)sulfonium salt **3** gave the epoxides in high yield and moderate diaster-

Scheme 3. *Proposed Reaction Pathway for Annulations Using Chiral Sulfur Ylides*
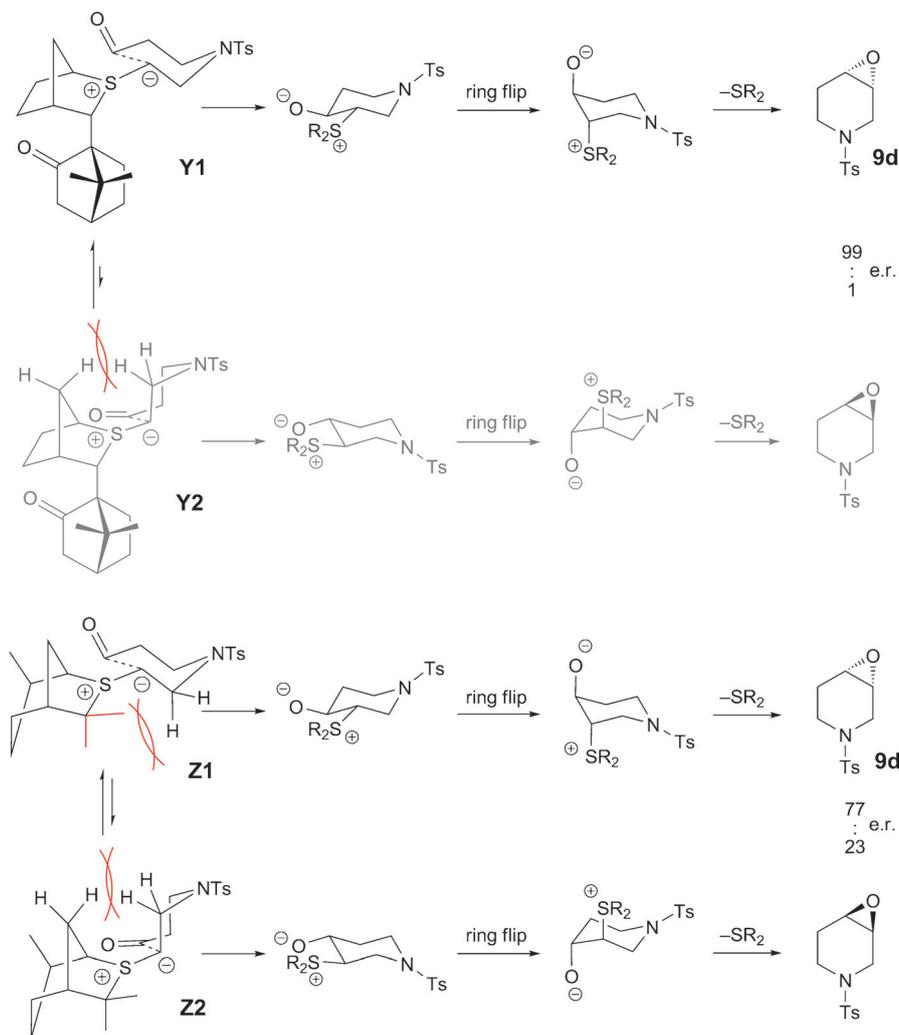
eoselectivity. Using the chiral sulfonium salt **4**, enhanced diastereoselectivity was observed, with the reagent contributing a *ca.* 2.5-fold increase (matched case) in selectivity (*Table 2*).

The issue of matched *vs.* mismatched double stereodifferentiation was explored with (+)- and (−)-amino ketone **10d/12**. Using the achiral salt **3**, a 4.2:1 ratio of epoxides *syn*-**11b**/*anti*-**11b** was obtained (*Scheme 4*), reflecting the extent of substrate

Table 2. *Results and Scope for α-Substituted Substrates*
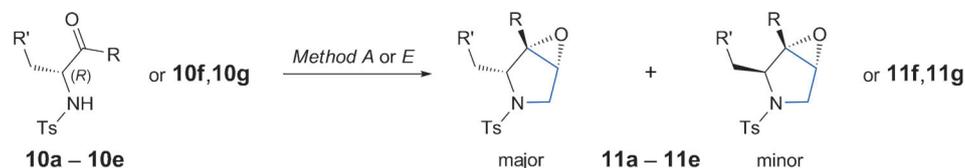
A: **3** (1.25 equiv.), DBU (3.5 equiv.), CH_2Cl_2 (0.1M), 0°, 2 – 4 h
E: **4** (1.40 equiv.), NaH (2.5 equiv.), CH_2Cl_2 (0.015M), 0°, 5 h
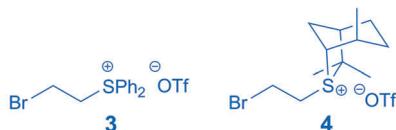
Entry	Substrate	R	R′	Method	Product	Yield [%][a]	d.r.[b]
1	**10a**	H	H	A	**11a**	47[c]	1:1.2
				E		No reaction	–
2	**10b**	Me	H	A	**11b**	98	4.2:1
				E		60	10:1
3	**10c**	Et	H	A	**11c**	89	3.8:1
				E		66	9.5:1
4	**10d**	Me	Ph	A	**11d**	88	6.6:1
				E		64	15:1
5	**10e**	Et	Ph	A	**11e**	98	7.2:1
				E		66	15:1
6	**10f**			A	**11f** *syn*	99	3.2:1
				E		No reaction	–
7	**10g**			A	**11g** *syn*	56	10:1
				E		No reaction	

[a]) Isolated yields. [b]) Determined from crude ^{1}H-NMR spectrum. [c]) From polymeric starting material.

Scheme 4. *Proposed Rationalization for Diastereoselectivity in the Annulation Reaction of* **8b** *with* **3**
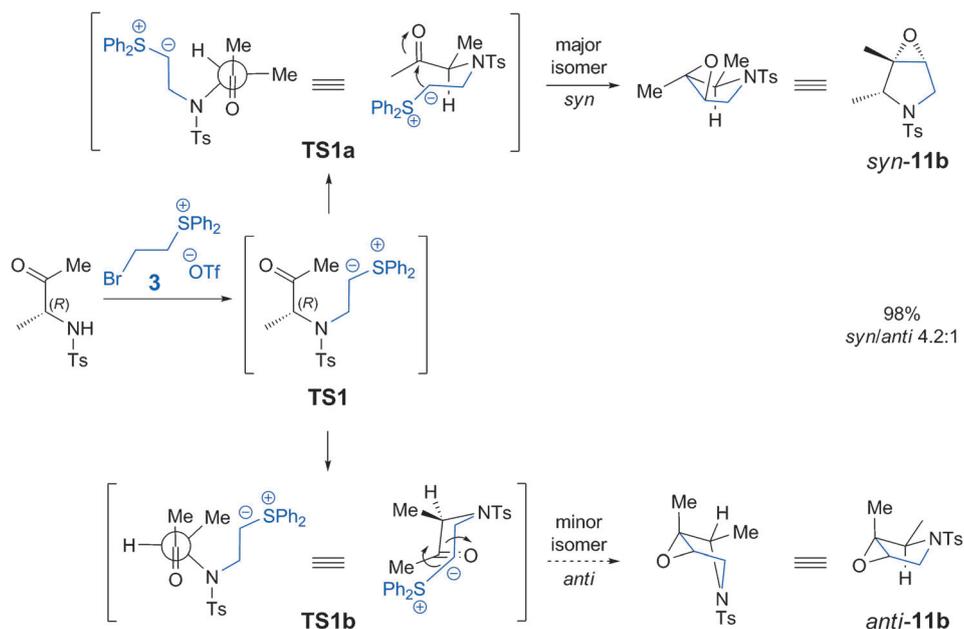
control. Using chiral sulfonium salt **4**, a 10 : 1 ratio was observed (matched), whereas, using the enantiomeric substrate **12** and the same chiral sulfonium salt **4**, a 1 : 1.4 ratio of diastereoisomers **13** was obtained (mismatched; *Scheme 5*). In the latter case, the major diastereoisomer is favored by the reagent (sulfide stereochemistry dominates) but disfavored by the substrate (pseudo-axial substituent, *anti-Felkin–Anh*-like), whereas the minor diastereoisomer is favored by the substrate (pseudo-equatorial substituent, *Felkin–Anh*-like) but disfavored by the reagent.

We were also able to expand this methodology to indole-derived amino aldehydes and imines as substrates [7]. In the case of the aldehyde **14**, good yields were observed using salts **1** or **3** (*Scheme 6*).

Experiments with chiral sulfonium salts and indole **14** were limited by low yield and enantioselectivity [3][7]. However, the reaction of (2-bromoethyl)sulfonium salt **3** with the *Ellman* [14] sulfinimine **16** gave high diastereoselectivity for the fused aziridine **17**. This represents a short asymmetric route to the basic core of the mitomycin class of antibiotics [7][15] (*Scheme 7*).

Conclusions. – We have shown that the use of (2-bromoethyl)sulfonium salt **3** provides significantly improved yields and operational simplicity in epoxy-annulation reactions of α- and β-amino carbonyl compounds in the synthesis of epoxy-pyrrolidines and epoxy-piperidines. In the case of chiral α-substituted amino aldehydes and ketones, moderate diastereoselectivity was observed, which is easily enhanced using the chiral sulfonium salt **4**. The use of indole-derived imines in the annulation process leads to the core of mitomycins in good yield and high diastereoselectivity.

Scheme 5. *Proposed Rationalization for Diastereoselective Annulation with* **4**
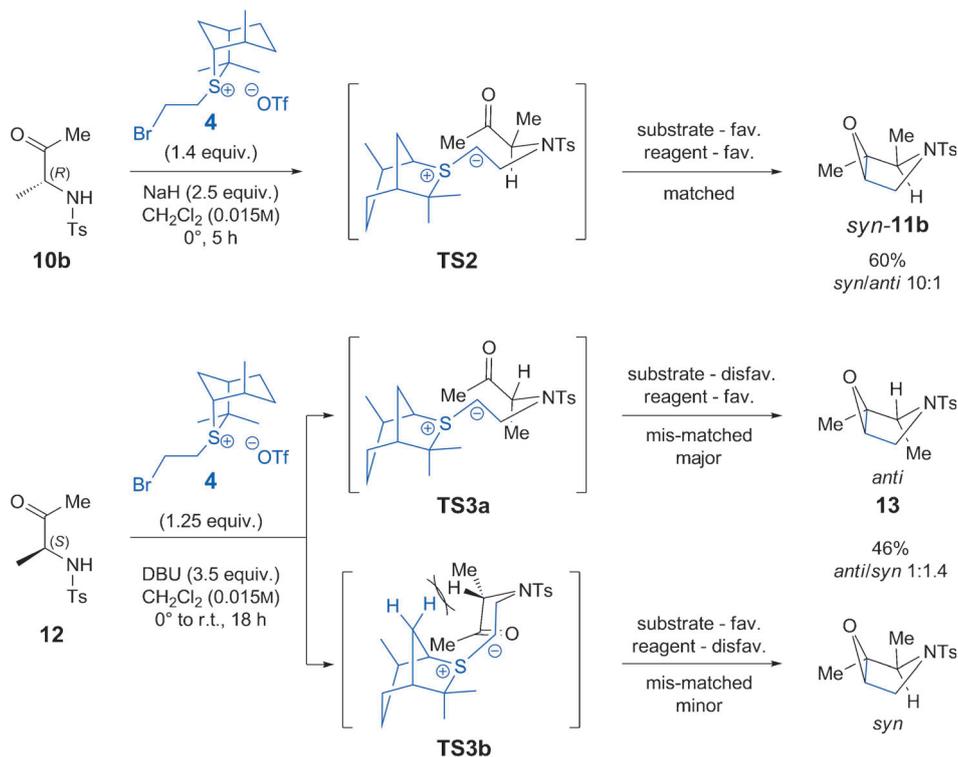
Scheme 6. *Reaction of Indole-2-aldehyde* **14** *with* **3**
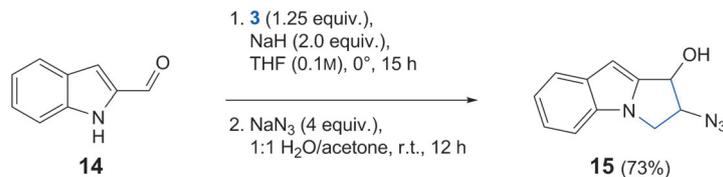
Experimental Part

1. *General.* All reagents and solvents were used as received. Anh. solvents (CH₂Cl₂, MeCN, THF) were obtained from a purification column composed of activated alumina (*A-2*) [7b][16]. Flash chromatography (FC): silica gel (*Merck Kieselgel 60 F₂₅₄*, 230–400 mesh). TLC: Aluminium backed silica-gel plates (0.2 mm, *60 F₂₅₄*); standard visualising agents: UV fluorescence (254 & 366 nm), I₂. M.p.: *Kofler* hotstage; uncorrected. Enantioselectivity: *Agilent 1100* series HPLC instrument using the described columns and solvent systems. All ratios of diastereoisomers were determined from the NMR of

Scheme 7. *Reaction of Sulfinimine* **16** *with* **3**

72%, > 20:1 d.r.,
after 4 × hexane wash,
from *ca.* 7:1 d.r. in crude

Mitomycin C
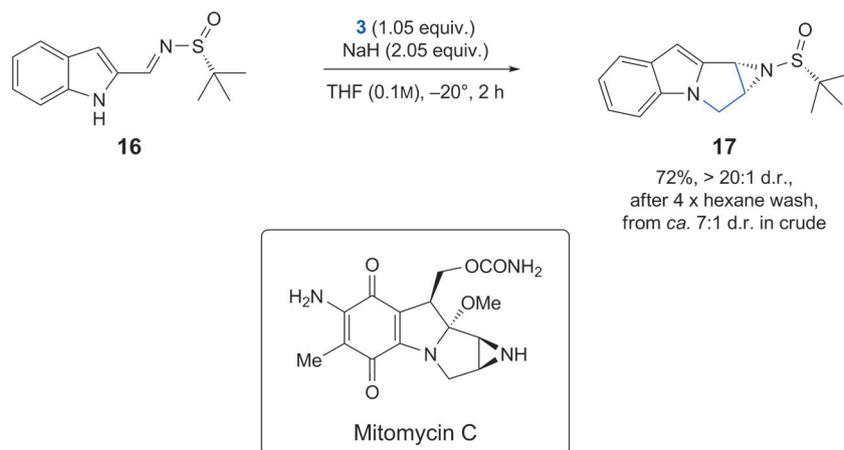
the crude reaction material, prior to isolation. Absolute configuration of the enantiomer was determined by comparison with previously reported literature data (same major, same minor, similar $[\alpha]_D$), for which X-ray crystallography was used [3]. Configuration of diastereoisomers (*syn/anti*) was determined by comparison with previously reported literature data (same ^{1}H- and ^{13}C-NMR), for which X-ray crystallography was used [8b]. IR Spectra: ATR sampling accessory on a *Perkin–Elmer Spectrum One* FT-IR spectrometer, neat compounds, only strong and selected absorbances ($\tilde{\nu}_{max}$) reported. ^{1}H-NMR Spectra: 300 or 400 MHz on *JEOL Delta GX* or *Eclipse ECP/400* instruments, resp.; $\delta(H)$ in ppm rel. to Me$_4$Si and/or the appropriate NMR solvent peak(s), J in Hz. ^{13}C-NMR Spectra: 100 MHz on *JEOL Delta GX* or *Eclipse ECP/400* instruments, resp.; $\delta(C)$ in ppm rel. to the appropriate solvent peak(s) and are assigned C, CH, CH$_2$, and Me. DEPT, COSY, HMBC and HMQC/HSQC were used where necessary in assigning NMR spectra. LR-MS: *VG Autospec* (CI) and a *Bruker Daltronics Apex 4e 7.0T* FT-MS (ESI), with only molecular ions (M^+ or $[M+H]^+$) and major peaks being reported; in m/z. HR-MS: *VG Autospec* (CI) and a *Bruker Daltronics Apex 4e 7.0T* FT-MS (ESI) spectrometer; in m/z.

2. *Synthesis of Precursors and Reagents. (2-Bromoethyl)(diphenyl)sulfonium trifluoromethanesulfonate* (**3**) [9g], 4-methyl-*N*-(3-oxopropyl)benzenesulfonamide [3], 4-methyl-*N*-(2-oxoethyl)benzenesulfonamide [3], 4-methyl-*N*-(2-oxopropyl)benzenesulfonamide [3], 4-methyl-*N*-(2-oxobutyl)benzenesulfonamide [3], 4-methyl-*N*-(2-oxo-2-phenylethyl)benzenesulfonamide [17], 4-methyl-*N*-(3-oxobutyl)-benzenesulfonamide [18], 4-methyl-*N*-[(2*R*)-1-methyl-2-oxopropyl]benzenesulfonamide [8b], 4-methyl-*N*-[(2*R*)-1-methyl-2-oxobutyl]benzenesulfonamide [8b], 4-methyl-*N*-(1-methyl-2-oxoethyl)benzenesulfonamide [8b], 4-methyl-*N*-[(2*R*)-3-oxo-1-phenylbutan-2-yl]benzenesulfonamide [19], and α-hydroxypropiophenone [20] were synthesized according to previously published procedures.

*(1*R,4R,5R,6R*)-6-(2-Bromoethyl)-4,7,7-trimethyl-6-thiabicyclo[3.2.1]octan-6-ium Trifluoromethanesulfonate* (**4**). A soln. of 2-bromoethyl trifluoromethanesulfonate (**6**) [9e] (5.00 g, 19.5 mmol, 1 equiv.) in CH$_2$Cl$_2$ was treated with (1*R*,4*R*,5*R*)-4,7,7-trimethyl-6-thiabicyclo[3.2.1]octane [12] (4.00 g, 23.4 mmol, 1.2 equiv.; er 99 :1) at r.t. and stirred for 3 d under N$_2$. The mixture was concentrated *in vacuo*, Et$_2$O was added to the crude oil, and the mixture was stirred vigorously until precipitation of a gray salt was complete. The salt was decanted from Et$_2$O and washed with additional Et$_2$O (3 × 50 ml), then dried *in vacuo* to afford pure **4** (6.73 g, 81%). White-to-pink salt. M.p. 68 – 71° (CH$_2$Cl$_2$/Et$_2$O). R_f (10% MeOH/CH$_2$Cl$_2$) 0.3. $[\alpha]_D^{23} = -45$ ($c = 4.2$, CHCl$_3$). IR (neat): 2932 – 2871, 1469, 1266, 1252, 1221, 1151, 1135, 1025. ^{1}H-NMR (400 MHz, CDCl$_3$): 4.30 – 4.22 (*m*, S–CH); 3.99 – 3.77 (*m*, 4 H); 2.56 – 2.31 (*m*, 4 H); 1.91 – 1.52 (*m*, 10 H); 1.17 (*d*, $J = 7.1$, Me). ^{13}C-NMR (100 MHz, CDCl$_3$): 120.4 (*q*, $J = 322$, CF$_3$); 73.2 (C); 68.1 (CH); 49.7 (CH); 41.5 (CH$_2$); 32.5 (CH$_2$); 31.7 (CH); 27.4 (CH$_2$); 26.4 (Me); 25.1 (CH$_2$); 23.0 (Me); 22.1

(CH$_2$); 17.7 (Me). ESI-MS: 277.1 (M^+(^{79}Br)), 279.1 (M^+(^{81}Br)). HR-ESI-MS: 277.0620 (M^+, C$_{12}$H$_{22}$BrS$^+$; calc. 277.0613).

*4-Methyl-*N-*[(2*R*)-3-oxo-1-phenylpentan-2-yl]benzenesulfonamide* (**10e**). The title compound was prepared from the corresponding *Weinreb* amide (300 mg, 0.82 mmol) [20], following literature procedure for similar compounds [8b] (182 mg, 68%). M.p. 94–96° (CH$_2$Cl$_2$/pentane). R_f (AcOEt/PE 1:1) 0.6. $[\alpha]_D^{24} = -30$ ($c = 2.66$, CHCl$_3$). IR (film): 3270 (arom. C–H), 3035 (C–H), 2941 (C–H), 1717 (C=O). ^{1}H-NMR (400 MHz, CDCl$_3$): 7.53–7.65 (*m*, 2 arom. H); 7.17–7.26 (*m*, 5 arom. H); 6.98–7.07 (*m*, 2 arom. H); 5.37 (*d*, *J* = 8.0, NH); 4.06–4.19 (*m*, COCH); 2.95 (*dd*, *J* = 14.0, 6.5, 1 H, PhCH$_2$); 2.87 (*dd*, *J* = 14.0, 6.5, 1 H, PhCH$_2$); 2.40 (*s*, Ar*Me*); 2.33 (*dq*, *J* = 18.4, 7.2, 1 H, MeCH$_2$); 2.18 (*dq*, *J* = 18.4, 7.2, 1 H, MeCH$_2$); 0.85 (*t*, *J* = 7.2, *Me*CH$_2$). ^{13}C-NMR (100 MHz, CDCl$_3$): 208.8 (C=O); 143.5 (C); 136.5 (C); 135.1 (C); 129.6 (CH); 129.1 (CH); 128.6 (CH); 127.1 (CH); 127.0 (CH); 61.8 (CH); 38.7 (CH$_2$); 33.8 (CH$_2$); 21.4 (Ar*Me*); 7.1 (Me). ESI-MS: 354.1 ([*M* + H]$^+$). HR-ESI-MS: 354.1134 ([*M* + Na]$^+$, C$_{18}$H$_{21}$NNaO$_3$S$^+$; calc. 354.1130).

3. Racemic and Enantioselective Epoxy-annulation Reactions. Method A (optimal achiral sulfonium salt conditions). A soln. of amino ketone (0.13 mmol, 1 equiv.) in anh. CH$_2$Cl$_2$ (1.5 ml) was treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (0.45 mmol, 3.5 equiv.) at 0° under inert atmosphere with stirring. *(2-Bromoethyl)(diphenyl)sulfonium triflate* (**3**; 0.16 mmol. 1.2 equiv.) was added, and the mixture was stirred for 2–4 h until complete consumption of starting material (HPLC or TLC). The reaction was then quenched with 10% aq. citric acid soln. (10 ml), and the aq. phase was extracted with CH$_2$Cl$_2$ (3 × 10 ml). The combined org. layers washed with brine (1 × 10 ml) and dried (MgSO$_4$). The crude mixture was purified by FC (AcOEt/petroleum ether (PE) or AcOEt/pentane) to give the desired epoxide after concentration under reduced pressure.

Method B (optimal chiral sulfonium salt conditions). A soln. of amino ketone or aldehyde (0.13 mmol, 1 equiv.) in CH$_2$Cl$_2$ (8.5 ml) was cooled to −20° by means of an ice/acetone/dry ice bath, under Ar with stirring. The mixture was then treated with DBU (0.45 mmol, 3.5 equiv.), followed by chiral (2-bromoethyl)sulfonium triflate (0.16 mmol. 1.2 equiv.). The mixture was placed in the freezer at −20° for 2–3 d until complete consumption of starting material was detected by HPLC or TLC, after which time the reaction was quenched with 10% aq. citric acid soln. (10 ml). The aq. phase was extracted with CH$_2$Cl$_2$ (3 × 10 ml), the combined org. layers washed with brine (1 × 10 ml), dried (MgSO$_4$), and concentrated *in vacuo*. The crude mixture was purified by FC (AcOEt/PE or AcOEt/pentane) to give the desired epoxide after concentration under reduced pressure. The ee was determined by chiral HPLC, with comparison to a racemic sample prepared by *Method A*.

Initial Screening of Conditions for the Enantioselective Reaction. Changes in conditions from standard *Method B*, using 4-methyl-*N*-(2-oxobutyl)benzenesulfonamide to prepare (1*S*,5*R*)-1-ethyl-3-[(4-methylphenyl)sulfonyl)]-6-oxa-3-azabicyclo[3.1.0]hexane:

Entry	Condition change	ee [%]
1	CH$_2$Cl$_2$	72
2	MeCN	70
3	THF	71
4	MeCN/LiCl (1 equiv.)	71
5	MeCN/LiOTf (1 equiv.)	70
6	MeCN/^{t}BuOH (9:1)	72
7	CH$_2$Cl$_2$/LiCl (1 equiv.)	70
8	CH$_2$Cl$_2$/LiOTf (1 equiv.)	69
9	CH$_2$Cl$_2$, 0°, 8 h	63
10	CH$_2$Cl$_2$, −40°, 5 d	72

We found the ee obtained in the reaction was not significantly affected by any of these changes, except that an increase of temp. eroded the ee. Further cooling of the reaction to −40° did not enhance enantioselectivity.

*(1*S*,5*R*)-1-Methyl-3-[(4-methylphenyl)sulfonyl]-6-oxa-3-azabicyclo[3.1.0]hexane* (**9a**). The title compound was synthesized from 4-methyl-*N*-(2-oxopropyl)benzenesulfonamide. *Method A* (racemic): **9a** as a white solid (34 mg, 94% yield); *Method B* (asymmetric): **9a** as a white solid (23 mg, 72% yield, 54% ee) after 3 d. M.p. 94–96° (AcOEt/PE). R_f (MeOH/CH$_2$Cl$_2$ 1 : 99) 0.4. Chiral HPLC (*OD-H*, 0.9 ml/min, 23°, 8% ^{i}PrOH/hexane): major (shown) t_R 27.2 min, minor t_R 31.30 min, 54% ee. ^{1}H-NMR (400 MHz, CDCl$_3$): 7.58 (*d*, *J* = 8.0, 2 arom. H); 7.24 (*d*, *J* = 8.0, 2 arom. H); 3.60 (*d*, *J* = 12.0, 1 H, NCH$_2$); 3.50 (*d*, *J* = 12.0, 1 H, NCH$_2$); 3.21–3.38 (*m*, 1 H, NCH$_2$, O–CH); 3.21 (*d*, *J* = 12.0, 1 H, NCH$_2$); 2.34 (*s*, Ar*Me*); 1.38 (*s*, *Me*C(O)CH). ^{13}C-NMR (100 MHz, CDCl$_3$): 143.6 (C); 135.0 (C); 129.7 (CH); 127.5 (CH); 63.1 (C); 60.8 (CH); 51.8 (CH$_2$); 49.3 (CH$_2$); 21.6 (Ar*Me*); 15.3 (Me). Spectroscopic data are in accordance with those reported in [3].

*(1*S*,5*R*)-1-Ethyl-3-[(4-methylphenyl)sulfonyl]-6-oxa-3-azabicyclo[3.1.0]hexane* (**9b**). The title compound was synthesized from 4-methyl-*N*-(2-oxobutyl)benzenesulfonamide; *Method A* (racemic): **9b** as a white solid (42 mg, 99% yield) after 5 h; *Method B* (asymmetric): **9b** as a white solid (38 mg, 87% yield, 72% ee) after 3 d. M.p. 79–81° (AcOEt/PE). R_f (AcOEt/PE 3 : 7) 0.3. Chiral HPLC (*OD-H*, 0.8 ml/min, 23°, 8% ^{i}PrOH/hexane): major (shown) t_R 42.8 min, minor t_R 52.5 min; 72% ee. ^{1}H-NMR (400 MHz, CDCl$_3$): 7.64 (*d*, *J* = 8.0, 2 arom. H); 7.21 (*d*, *J* = 8.0, 2 arom. H); 3.61 (*d*, *J* = 12.0, 1 H, NCH$_2$C(Et)); 3.54 (*d*, *J* = 12.0, 1 H, NCH$_2$C(Et)); 3.33 (br. *d*, *J* = 1.5, O–CH); 3.32 (*dd*, *J* = 12.0, 1.5, 1 H, NCH$_2$C(O)H); 3.23 (*d*, *J* = 12.0, 1 H, NCH$_2$); 2.38 (*s*, Ar*Me*); 1.78 (*dq*, *J* = 14.5, 7.5, 1 H, MeCH$_2$); 1.65 (*dq*, *J* = 14.5, 7.5, 1 H of MeCH$_2$); 0.83 (*t*, *J* = 7.5, *Me*CH$_2$). ^{13}C-NMR (100 MHz, CDCl$_3$): 143.4 (C); 134.8 (C); 129.5 (CH); 127.4 (CH); 67.1 (C); 59.0 (CH); 50.5 (CH$_2$); 49.0 (CH$_2$); 22.1 (CH$_2$); 21.5 (Ar*Me*); 9.0 (Me). Spectroscopic data are in accordance with those reported in [3].

*(1*S*,5*R*)-1-Phenyl-3-[(4-methylphenyl)sulfonyl]-6-oxa-3-azabicyclo[3.1.0]hexane* (**9c**). The title compound was synthesized from 4-methyl-*N*-(2-oxo-2-phenylethyl)benzenesulfonamide (**8c**). *Method A* (racemic): **9c** as a white solid (45 mg, 98% yield); *Method B* (asymmetric): **9c** as a white solid (41 mg, 88% yield, 68% ee) after 3 d. M.p. 77–80° (AcOEt/PE). Chiral HPLC (*OD-H*, 0.9 ml/min, 23°, 8% ^{i}PrOH/hexane): major (shown) t_R 38.9 min, minor t_R 47.5 min; 68 % ee. ^{1}H-NMR (400 MHz, CDCl$_3$): 7.64 (*d*, *J* = 8.0, 2 arom. H); 7.10–7.33 (*m*, 7 arom. H); 3.86 (*d*, *J* = 12.0, 1 H, NCH$_2$C(Ph)); 3.81 (*d*, *J* = 12.0, 1 H, NCH$_2$C(Ph)); 3.71 (*d*, *J* = 12.0, 1 H, NCH$_2$CH(O)); 3.60 (*d*, *J* = 1.2, O–CH); 3.45 (*dd*, *J* = 12.0, 1.2, 1 H, NCH$_2$CH(O)); 2.31 (*s*, Ar*Me*). ^{13}C-NMR (100 MHz, CDCl$_3$): 143.7 (C); 134.6 (C); 131.0 (C); 129.7 (CH); 128.8 (CH); 128.7 (CH); 127.5 (CH); 126.0 (CH); 65.8 (C); 63.2 (CH); 50.1 (CH$_2$); 49.4 (CH$_2$); 21.6 (Ar*Me*). Spectroscopic data are in accordance with those reported in [3].

*(1*R*,6*S*)-3-[(4-Methylphenyl)sulfonyl]-7-oxa-3-azabicyclo[4.1.0]heptane* (**9d**). The title compound was synthesized from *4-methyl-*N*-(3-oxopropyl)benzenesulfonamide* (**8d**). *Method A* (racemic): **9d** as a white solid (33 mg, 71% yield); *Method B* (asymmetric): **9d** as a white solid (31 mg, 68% yield, 54% ee) after 3 d. R_f (CH$_2$Cl$_2$) 0.2. Chiral HPLC (*OD-H*, 0.9 ml/min, 23°, 2% ^{i}PrOH/hexane): major (shown) t_R 61.6 min, minor t_R 72.3 min; 54 % ee. ^{1}H-NMR (400 MHz, CDCl$_3$): 7.64 (*d*, *J* = 8.0, 2 arom. H); 7.31 (*d*, *J* = 8.0, 2 arom. H); 3.81 (*ddd*, *J* = 13.5, 4.0, 1.5, 1 H, NCH$_2$); 3.32 (*dtd*, *J* = 11.5, 4.5, 1.5, 1 H, NCH$_2$); 3.22–3.25 (*m*, 2 O–CH); 3.10 (*d*, *J* = 13.5, 1 H, NCH$_2$); 2.53 (*m*, 1 H, 1 H, NCH$_2$CH$_2$); 2.41 (*s*, Ar*Me*); 2.11 (*m*, NCH$_2$CH$_2$CH). ^{13}C-NMR (100 MHz, CDCl$_3$): 143.7 (C); 132.8 (C); 129.8 (CH); 127.6 (CH); 50.4 (CH); 49.8 (CH); 44.2 (CH$_2$); 39.2 (CH$_2$); 25.3 (CH$_2$); 21.5 (Ar*Me*). Spectroscopic data are in accordance with those reported in [3].

*(1*R*,6*S*)-6-Methyl-3-[(4-methylphenyl)sulfonyl]-7-oxa-3-azabicyclo[4.1.0]heptane* (**9e**). The title compound was synthesized from *4-methyl-*N*-(3-oxobutyl)benzenesulfonamide* (**8e**). *Method A* (racemic): **9e** as a white solid (35 mg, 72% yield); *Method B* (asymmetric): **9e** as a white solid (17 mg, 35% yield, 92% ee) after 3 d. M.p. 95–97° (from AcOEt/hexane). Chiral HPLC (*IB* column, 0.7 ml/min, 23°, 15% ^{i}PrOH/hexane): major (shown) t_R 20.0 min, minor t_R 21.8 min, 92% ee. ^{1}H-NMR (400 MHz, CDCl$_3$): 7.52 (*d*, *J* = 8.0, 2 arom. H); 7.21 (*d*, *J* = 8.0, 2 arom. H); 3.82 (*ddd*, *J* = 13.5, 4.5, 1.5, 1 H, NCH$_2$); 3.34–3.37 (*m*, 1 H, NCH$_2$); 3.03 (*d*, *J* = 4.5, O–CH); 2.87 (*d*, *J* = 13.5, 1 H, NCH$_2$); 2.38 (*td*, *J* = 11.0, 3.0, 1 H, NCH$_2$); 2.31 (*s*, Ar*Me*); 1.97 (*ddd*, *J* = 14.5, 11.0, 5.0, 1 H of NCH$_2$CH$_2$); 1.88 (*dt*, *J* = 14.5, 3.0, 1 H, NCH$_2$CH$_2$); 1.26 (*s*, *Me*C(O)). ^{13}C-NMR (100 MHz, CDCl$_3$): 143.6 (C); 133.7 (C); 129.7 (CH); 127.6 (CH); 56.7 (C); 56.6 (CH); 44.4 (CH$_2$); 40.1 (CH$_2$); 30.4 (CH$_2$); 22.4 (Me); 21.6 (Me). Spectroscopic data are in accordance with those reported in [3].

4. *Diastereoselective Epoxy-annulation Reactions. Method A* (achiral reagent conditions). A soln. of α-amino ketone (0.13 mmol, 1 equiv.) in anh. CH_2Cl_2 (0.09M) was treated with DBU (0.46 mmol, 3.5 equiv.) at 0° under Ar with stirring. Salt **3** (0.16 mmol, 1.2 equiv.) was added, and the mixture was stirred for 2–4 h until complete consumption of starting material (HPLC or TLC). The reaction was then quenched with 10% aq. citric acid soln. (10 ml), the aq. phase was extracted with CH_2Cl_2 (3 × 10 ml), and the combined org. layers were washed with brine (1 × 10 ml), dried ($MgSO_4$), and concentrated *in vacuo*. The crude mixture was then purified by FC (AcOEt/PE or AcOEt/pentane) to give the desired epoxide after concentration under reduced pressure.

Method E (chiral reagent conditions). A soln. of α-amino ketone (0.13 mmol, 1 equiv.) in anh. CH_2Cl_2 (0.015M) was treated with NaH (60% in mineral oil, 2.5 equiv.) at 0° under Ar with stirring. The mixture was then treated with chiral salt **4** (1.4 equiv.) and stirred for 15 h until complete consumption of starting material (HPLC or TLC). The reaction was then quenched with 10% aq. citric acid soln. (10 ml), the aq. phase was extracted with CH_2Cl_2 (3 × 10 ml), and the combined org. layers were washed with brine (1 × 10 ml) dried ($MgSO_4$), and concentrated *in vacuo*. At this point, diastereoisomer ratio was determined by crude NMR. The crude mixture was then purified by FC (AcOEt/PE or AcOEt/pentane) to give the desired epoxide after concentration under reduced pressure.

*(1*S*,2*R*,5*R*)-2-Methyl-3-[(4-methylphenyl)sulfonyl]-6-oxa-3-azabicyclo[3.1.0]hexane* (**11a**). The title compound was synthesized from *4-methyl-*N*-[(2*R*)-1-oxopropan-2-yl]benzenesulfonamide* (**10a**; polymeric). *Method A* yielded the **11a** as a white gum (26 mg, 47% yield; dr 1.2:1). R_f (AcOEt/PE 1:3) 0.3. Reported as a mixture of two diastereoisomers: ^{1}H-NMR (400 MHz, $CDCl_3$): 7.70 (*d*, *J* = 8.0, 2 arom. H); 7.65 (*d*, *J* = 8.0, 2 arom. H); 7.32 (*d*, *J* = 8.0, 2 arom. H); 7.29 (*d*, *J* = 8.0, 2 arom. H); 3.98 (*q*, *J* = 7.0, MeC*H*N); 3.75 (*d*, *J* = 11.5, 1 H, NC*H*₂CH(O)); 3.47–3.67 (*m*, 6 H, NCH₂C*H*(O), NCH₂C*H*(O), MeC*H*N, 1 H of NC*H*₂CH(O), 1 H of NC*H*₂CH(O), C*H*(O)CHCH₂); 3.31 (*dd*, *J* = 9.5, 1.5, NC*H*CH(O)); 3.29 (br. *s*, C*H*(O)CHCH₂); 2.43 (*s*, Ar*Me*); 2.42 (*s*, Ar*Me*); 1.50 (*d*, *J* = 6.5, Me); 1.32 (*d*, *J* = 7.0, Me). ^{13}C-NMR (100 MHz, $CDCl_3$): 143.6 (C); 143.3 (C); 135.7 (C); 135.5 (C); 129.7 (CH); 129.5 (CH); 127.5 (CH); 127.4 (CH); 60.4 (CH); 59.2 (CH); 56.5 (CH); 55.9 (CH); 54.8 (CH_2); 54.2 (CH_2); 50.6 (CH); 47.9 (CH); 21.7 (Ar*Me*); 21.6 (Ar*Me*); 18.0 (Me); 16.5 (Me). Spectroscopic data are in accordance with those reported in [8b].

*(1*S*,2*R*,5*R*)-1,2-Dimethyl-3-[(4-methylphenyl)sulfonyl]-6-oxa-3-azabicyclo[3.1.0]hexane* (**11b**): The title compound was synthesized from *4-methyl-*N*-[(2*R*)-3-oxobutan-2-yl]benzenesulfonamide* (**10b**). *Method A* (achiral reagent): **11b** as a white solid (98% yield; dr 4.2:1 (*syn/anti*)); *Method E* (chiral reagent): **11b** as a white solid (60%; dr 10:1, determined from MeC(O)). R_f (AcOEt/PE 3:7) 0.3. Data for major (*syn*) stereoisomer: ^{1}H-NMR (400 MHz, $CDCl_3$): 7.68 (*d*, *J* = 8.0, 2 arom. H); 7.30 (*d*, *J* = 8.0, 2 arom. H); 3.66 (*d*, *J* = 12.0, 1 H, NC*H*₂); 3.41 (*d*, *J* = 1.5, O–CH); 3.40 (*q*, *J* = 6.5, NC*H*(Me)); 3.27 (*dd*, *J* = 12.0, 1.5, 1 H, NC*H*₂); 2.42 (*s*, Ar*Me*); 1.42 (*d*, *J* = 6.5, *Me*CHN); 1.36 (*s*, *Me*C(O)). ^{13}C-NMR (100 MHz, $CDCl_3$): 143.5 (C); 134.9 (C); 129.6 (CH); 127.4 (CH); 66.5 (C); 60.1 (CH); 58.3 (CH_2); 49.9 (CH); 21.5 (Ar*Me*); 14.8 (Me); 14.7 (Me). Spectroscopic data are in accordance with those reported in [8b].

*(1*S*,2*R*,5*R*)-1-Ethyl-2-methyl-3-[(4-methylphenyl)sulfonyl]-6-oxa-3-azabicyclo[3.1.0]hexane* (**11c**). The title compound was synthesized from *4-methyl-*N*-[(2*R*)-3-oxopentan-2-yl]benzenesulfonamide* (**10c**). *Method A* (achiral reagent): **11c** as a white solid (33 mg, 89% yield, dr 3.8:1 (*syn/anti*)); *Method E* (chiral reagent): **11c** as a white solid (37 mg, 66%, dr 9.5:1, determined from *Me*CH₂). R_f (AcOEt/PE 3:7) 0.5. Data for major (*syn*) stereoisomer: ^{1}H-NMR (400 MHz, $CDCl_3$): 7.65 (*d*, *J* = 8.0, 2 arom. H); 7.29 (*d*, *J* = 8.0, 2 arom. H); 3.65 (*d*, *J* = 11.5, 1 H of NC*H*₂CH(O)); 3.45 (*q*, *J* = 6.5, MeC*H*N); 3.43 (*d*, *J* = 2.0, O–CH); 3.23 (*dd*, *J* = 11.5, 2.0, 1 H, NC*H*₂CH(O)); 2.43 (*s*, Ar*Me*); 1.72 (*dq*, *J* = 15.0, 7.5, 1 H, MeC*H*₂); 1.64 (*dq*, *J* = 15.0, 7.5, 1 H, MeC*H*₂); 1.34 (*d*, *J* = 6.5, *Me*CHN); 0.75 (*t*, *J* = 7.5, *Me*CH₂). ^{13}C-NMR (100 MHz, $CDCl_3$): 143.5 (C); 135.0 (C); 129.6 (CH); 127.4 (CH); 70.5 (C); 58.0 (CH); 57.4 (CH); 49.9 (CH_2); 21.5 (Ar*Me*); 20.9 (CH_2); 15.0 (Me); 8.4 (Me). Spectroscopic data are in accordance with those reported in [8b].

*(1*S*,2*R*,5*R*)-2-Benzyl-1-methyl-3-[(4-methylphenyl)sulfonyl]-6-oxa-3-azabicyclo[3.1.0]hexane* (**11d**). The title compound was synthesized from *4-methyl-*N*-[(2*R*)-3-oxo-1-phenylbutan-2-yl]benzenesulfonamide* (**10d**); *Method A* (achiral reagent): **11d** as a white solid (30 mg, 88% yield; dr 6.6:1 (*syn/anti*)); *Method E* (chiral reagent): **11d** as a white solid (34 mg, 64%; dr 15:1, determined from Me). M.p.

134–136° (CH$_2$Cl$_2$/pentane). R_f (Et$_2$O/pentane 1:1) 0.6. $[\alpha]_D^{24} = -70$ ($c = 0.923$, CHCl$_3$; from 15:1 mixture of diastereoisomers). IR (film): 3020 (arom. C–H), 2859 (aliph. C–H), 1337 (C–O). Data for major (*syn*) stereoisomer: ^{1}H-NMR (400 MHz, CDCl$_3$): 7.76 (*d*, $J = 8.3$, 2 arom. H); 7.20–7.39 (*m*, 7 arom. H); 3.79 (*dd*, $J = 10.5$, 3.5, NCHC); 3.63 (*d*, $J = 11.5$, 1 H, NC*H$_2$*); 3.55 (*dd*, $J = 13.5$, 3.5, 1 H, PhC*H$_2$*); 3.43 (*dd*, $J = 11.5$, 2.0, 1 H, NC*H$_2$*); 3.34 (*d*, $J = 2.0$, O–CH); 2.96 (*dd*, $J = 13.5$, 10.5, 1 H, PhC*H$_2$*); 2.45 (*s*, Ar*Me*); 0.86 (*s*, Me). ^{13}C-NMR (100 MHz, CDCl$_3$): 143.7 (C); 137.8 (C); 135.3 (C); 129.8 (CH); 129.6 (CH); 128.5 (CH); 127.4 (CH); 126.6 (CH); 66.7 (C); 64.1 (CH); 61.9 (CH); 49.5 (CH$_2$); 37.6 (CH$_2$); 21.5 (Ar*Me*); 17.1 (Me). ESI-MS: 366.1 ($[M + Na]^+$). HR-ESI-MS: 366.1134 ($[M + Na]^+$, C$_{19}$H$_{21}$NNaO$_3$S$^+$; calc. 366.1145).

*(1*S*,2*R*,5*R*)-2-Benzyl-1-ethyl-3-[(4-methylphenyl)sulfonyl]-6-oxa-3-azabicyclo[3.1.0]hexane* (**11e**). The title compound was synthesised from *4-methyl-*N*-[(2*R*)-3-oxo-1-phenylpentan-2-yl]benzenesulfon-amide* (**10e**). *Method A* (achiral reagent): **11e** as a white solid (35 mg, 98% yield; dr 7.2:1 (*syn/anti*)); *Method E* (chiral reagent): **11e** as a white solid (39 mg, 66%, dr 15:1, determined from Me). M.p. 91–93° (CH$_2$Cl$_2$/pentane). R_f (Et$_2$O/pentane 4:6) 0.4. $[\alpha]_D^{24} = -85.5$ ($c = 0.72$, CHCl$_3$; *syn/anti* 15:1). IR (film): 3020 (arom. C–H), 2972 (aliph. C–H), 1338 (C–O). Data for major (*syn*) stereoisomer: ^{1}H-NMR (400 MHz, CDCl$_3$): 7.77 (*d*, $J = 8.3$, 2 arom. H); 7.19–7.38 (*m*, 7 arom. H); 3.87 (*dd*, $J = 10.5$, 3.5, NCH); 3.65 (*d*, $J = 12.2$, 1 H, NC*H$_2$*); 3.52 (*dd*, $J = 13.5$, 3.5, 1 H, PhC*H$_2$*); 3.37–3.43 (*m*, 1 H, NC*H$_2$*, O–CH); 2.99 (*dd*, $J = 13.5$, 10.5, 1 H, PhC*H$_2$*); 2.44 (*s*, Ar*Me*); 1.20 (*dq*, $J = 15.0$, 7.5, 1 H of MeC*H$_2$*); 1.03 (*dq*, $J = 15.0$, 7.5, 1 H, MeC*H$_2$*); 0.50 (*t*, $J = 7.5$, *Me*CH$_2$). ^{13}C-NMR (100 MHz, CDCl$_3$): 143.7 (C); 137.9 (C); 135.2 (C); 129.7 (CH); 129.4 (CH); 128.4 (CH); 127.3 (CH); 126.6 (CH); 71.0 (C); 62.7 (CH); 59.4 (CH); 49.6 (CH$_2$); 37.7 (CH$_2$); 22.7 (CH$_2$); 21.5 (Me); 8.5 (Me). ESI-MS: 380.1 ($[M + Na]^+$). HR-ESI-MS: 380.1291 ($[M + Na]^+$, C$_{20}$H$_{23}$NNaO$_3$S$^+$; calc. 380.1301).

(±)-1,2-Diphenyl-3,6-dioxabicyclo[3.1.0]hexane (**11f**). The title compound was synthesized from *2-hydroxy-1,2-diphenylethanone* (**10f**). *Method A* (achiral reagent): **11f** as a clear oil (101 mg, 98% yield; dr 3.2:1 (*syn/anti*)). R_f (AcOEt/pentane 1:4) 0.3. IR (neat): 3021 (arom. C–H), 2966 (aliph. C–H), 1354 (C–O). Data for major (*syn*) stereoisomer: ^{1}H-NMR (400 MHz, CDCl$_3$): 7.04–7.50 (*m*, 10 arom. H); 4.26–4.38 (*m*, 1 H, OC*H$_2$*, OCHPh); 4.02 (*dd*, $J = 11.0$, 0.5, 1 H, OC*H$_2$*); 3.85 (*d*, $J = 0.5$, O–CH). ^{13}C-NMR (100 MHz, CDCl$_3$): 135.9 (C); 133.2 (C); 128.4 (CH); 128.3 (CH); 128.2 (CH); 128.0 (CH); 127.9 (CH); 126.4 (CH); 80.1 (C); 68.8 (CH); 67.8 (CH); 64.5 (CH$_2$). ESI-MS: 261.1 ($[M + Na]^+$). HR-ESI-MS: 261.0886 ($[M + Na]^+$, C$_{16}$H$_{14}$NaO$_2^+$; calc. 261.0895).

*(1*S*,4*S*,6*R*)-5,5-Dimethyl-4-(4-nitrophenyl)-3,7-dioxabicyclo[4.1.0]heptane* (**11g**). *Method A* with *(3*S*)-3-hydroxy-2,2-dimethyl-3-(4-nitrophenyl)propanal* (**10g**), prepared according to *Ley et al.* [9j] [21], afforded **11g** as a clear oil (32 mg, 58%; dr 10:1). R_f (AcOEt/pentane 2:8) 0.6. Data for major (*syn*) stereoisomer: ^{1}H-NMR (400 MHz, CDCl$_3$): 8.17 (*d*, $J = 8.8$, 2 arom. H); 7.40 (*d*, $J = 8.8$, 2 arom. H); 4.37 (*s*, CHOCH$_2$); 4.31 (*d*, $J = 13.5$, 1 H, C*H$_2$*); 4.07 (*d*, $J = 13.5$, 1 H, C*H$_2$*); 3.40 (*d*, $J = 4.0$, CHOC*H*CH$_2$); 3.10 (*d*, $J = 4.0$, C*H*OCHCH$_2$); 1.03 (*s*, Me); 0.86 (*s*, Me). ^{13}C-NMR (100 MHz, CDCl$_3$): 147.3 (C); 145.9 (C); 128.4 (CH); 122.7 (CH); 78.4 (CH); 65.4 (CH$_2$); 60.9 (CH); 52.7 (CH); 35.3 (C); 22.9 (Me); 17.9 (Me). Spectroscopic data are in accordance with those reported in [9j].

*(1*S*,2*S*,5*R*)-1,2-Dimethyl-3-[(4-methylphenyl)sulfonyl]-6-oxa-3-azabicyclo[3.1.0]hexane* (**13**). The title compound was synthesized from *(*S*)-3-{[(4-methylphenyl)sulfonyl]amino}butan-2-one* (**12**) using *Method E*. White solid (46% yield, dr 1:1.4 (*anti/syn*)). Minor diastereoisomer (*anti*): ^{1}H-NMR (400 MHz, CDCl$_3$): 7.64 (*d*, $J = 8.0$, 2 arom. H); 7.29 (*d*, $J = 8.0$, 2 arom. H); 3.82 (*q*, $J = 6.5$, NC*H*(Me); 3.59 (*d*, $J = 12.0$, 1 H, NC*H$_2$*); 3.51 (*d*, $J = 12.0$, 1 H, NC*H$_2$*); 3.30 (*s*, O–CH); 2.41 (*s*, Ar*Me*); 1.36 (*s*, *Me*C(O)); 1.35 (*d*, $J = 6.5$, Me). ^{13}C-NMR (100 MHz, CDCl$_3$): 143.2; 135.4; 129.4; 127.5; 65.6; 60.4; 59.1; 48.0; 21.0; 18.8; 14.2. Major diastereoisomer (*syn*) has identical data to those of enantiomeric **11b**. Spectroscopic data are in accordance with those reported in [8b].

*2-Azido-2,3-dihydro-1*H*-pyrrolo[1,2-a]indol-1-ol* (**15**). Prepared according to the Method by *Jimenez* and co-workers [7], using *1*H*-indole-2-carbaldehyde* (**14**; 342 mg, 2.0 mmol). Orange oil (316 mg, 74%). ^{1}H-NMR (400 MHz, CDCl$_3$): 7.65 (*dt*, $J = 8.0$, 1.0); 7.27 (*ddd*, $J = 8.0$, 2.0, 1.0, 1 H); 7.23 (*ddd*, $J = 8.0$, 7.0, 1.0, 1 H); 7.13 (*ddd*, $J = 8.0$, 7.0, 1.0, 1 H); 6.55 (*s*, 1 H); 4.88 (*dd*, $J = 3.0$, 1.0, 1 H); 4.76–4.84 (*m*, 1 H); 4.42 (*dd*, $J = 11.0$, 5.5, 1 H); 4.01 (*dd*, $J = 11.0$, 3.0, 1 H); 2.34 (br. s, OH). ^{13}C-NMR (100 MHz, CDCl$_3$): 137.0; 133.0; 132.0; 122.3; 121.6; 120.0; 109.9; 96.7; 80.1; 64.7; 50.4. Spectroscopic data are in accordance with those reported in [7].

(R)-N-[(E)-1H-Indol-2-ylmethylidene]-2-methylpropane-2-sulfinamide (**16**). A stirred soln. of indole-2-carboxaldehyde (0.44 g, 3.0 mmol, 1 equiv.) in anh. CH_2Cl_2 (50 ml) was treated with $(EtO)_4Ti$ (*ca.* 20% soln. in EtOH; 7.0 ml; *ca.* 6.1 mmol, 2 equiv.) under Ar at r.t. The soln. was then treated with (*R*)-2-methylpropane-2-sulfinamide (0.40 g, 3.3 mmol, 1.1 equiv.) in a single portion. The mixture was heated to reflux for 4 h under Ar, then allowed to cool to r.t. before quenching the reaction with an equal volume of brine (*ca.* 50 ml). The resulting slurry was filtered through *Celite®*, washed with an excess of CH_2Cl_2 (300 ml), and the filtrate was partitioned between brine and CH_2Cl_2. The aq. phase was further extracted with CH_2Cl_2 (3 × 75 ml), and the combined org. layers were dried ($MgSO_4$) and concentrated under reduced pressure to give **16** as a yellow solid (0.73 g, 98%) of sufficient purity to be used in the next step. M.p. 140 – 142° (directly from procedure). R_f (AcOEt/PE 3 : 7) 0.2. $[\alpha]_D^{20} = +12$ ($c = 1.0$, CH_2Cl_2). IR (film): 3251 (NH), 1586 (HC=N), 1063 (S=O). ^{1}H-NMR (400 MHz, CDCl$_3$): 8.87 (br. *d*, *J* = 1.5, NH); 8.53 (*s*, CH=N); 7.62 (*dd*, *J* = 8.0, 1.0, H–C(4)); 7.35 (*dd*, *J* = 8.5, 1.0, H–C(7)); 7.26 (*ddd*, *J* = 8.5, 7.0, 1.0, H–C(6)); 7.08 (*ddd*, *J* = 8.0, 7.0, 1.0, H–C(5)); 6.98 (*d*, *J* = 1.5, H–C(3)); 1.21 (*s*, ^{t}Bu). ^{13}C-NMR (100 MHz, CDCl$_3$): 153.0 (N=CH); 137.8 (C); 133.4 (C); 128.0 (C); 126.0 (CH); 122.6 (CH); 120.9 (CH); 111.9 (CH); 111.6 (CH); 57.9 (C); 22.5 (3 Me). CI-MS: 249 (100, $[M + H]^+$), 192 (52, $[M + H - {}^tBu]^+$). HR-CI-MS: 249.1055 ($[M + H]^+$, $C_{13}H_{17}N_2OS^+$; calc. 249.1062).

(1aR,8bR)-1-[(R)-(tert-Butyl)sulfinyl]-1,1a,2,8b-tetrahydroazireno[2′,3′:3,4]pyrrolo[1,2-a]indole (**17**): A soln. of **16** (200 mg, 0.81 mmol) in anh. THF (9 ml, 0.09M) was cooled to $-20°$ and treated with NaH (60% in mineral oil; 64 mg, 1.7 mmol, 2.05 equiv.). The mixture was then treated with a soln. of **3** (377 mg, 0.85 mmol, 1.05 equiv.) in THF (3 ml) dropwise over 10 min, then allowed to stir for 2 h at $-20°$. The mixture was poured onto sat. NH$_4$Cl soln. (200 ml) and extracted with Et$_2$O (3 × 50 ml), then the org. layers were combined, washed with H$_2$O (3 × 75 ml), and dried (MgSO$_4$). After concentration under reduced pressure, the crude product was obtained as a yellow oil as a 7 : 1 mixture of diastereoisomers (major shown) containing Ph$_2$S as the only impurity detected by ^{1}H-NMR spectrum. The crude mixture was triturated with hexane (4 ×) to give **17** (160 mg, 72; > 20 : 1 diastereoselectivity). Pale-yellow solid. M.p. 139 – 141° (dec.). R_f (AcOEt/PE 3 : 7) 0.3. $[\alpha]_D^{20} = +8$ ($c = 1.00$, CH_2Cl_2). IR (film): 3053 (arom. C–H), 2954 (aliph. C–H), 1072 (S=O). ^{1}H-NMR (400 MHz, CDCl$_3$): 7.56 (*d*, *J* = 8.0, H–C(4)); 7.13 – 7.20 (*m*, H–C(6,7)); 7.06 (*ddd*, *J* = 8.0, 6.0, 2.0, H–C(5)); 6.41 (*s*, H–C(3)); 4.25 (*d*, *J* = 5.5, C*H*(NSO^{t}Bu)CHCH$_2$N); 4.24 (*d*, *J* = 11.0, 1 H, NC*H*$_2$CH); 4.19 (*dd*, *J* = 11.0, 3.5, 1 H, NC*H*$_2$CH); 3.75 (*dd*, *J* = 5.5, 3.5, NCH$_2$C*H*(N-SO^{t}Bu)CH); 1.23 (*s*, ^{t}Bu). ^{13}C-NMR (100 MHz, CDCl$_3$): 139.2 (C); 133.9 (C); 132.2 (CH); 121.9 (CH); 121.5 (CH); 119.7 (CH); 109.3 (CH); 95.4 (C); 57.9 (C); 46.5 (CH); 42.9 (CH); 32.9 (CH$_2$); 22.8 (3 Me). CI-MS: 275 (60, $[M + H]^+$), 217 (100, $[M - {}^tBu]^+$). HR-CI-MS: 275.1207 ($[M + H]^+$, $C_{15}H_{19}N_2OS^+$; calc. 275.1218). Anal. calc. for $C_{15}H_{18}N_2OS$ (274.38): C 65.66, H 6.61, N 10.21; found: C 65.27, H 6.37, N 10.00.

Personal Reminiscences

I first met *Dieter Seebach* at Sheffield University in 1992, where he received one of the highest honours the University has to offer, the '*Firth Lectureship and Medal*'. As a young lecturer, I discussed with him about our work on the synthesis and reactions of 1,3-dithiane-1,3-dioxide. I related some of the issues we had with this compound, and the first question *Dieter* asked me was 'What is the melting point of the bis-sulfoxide?' Well, we had measured it of course, but I could not recall what it was because I had not attached any importance to the number. *Dieter* did. He told me that in discussions with his group he would ask a co-worker about the compound with a melting point of (say) 128°. They would not remember which one he was talking about so would have to look up the relevant compound to continue the discussion. The co-workers were astonished that he could remember everyone's melting points but often, they could not remember their own. *Dieter* taught me a valuable lesson, as melting points have an impact on solubility, an issue we were struggling with at the time. Obvious, when you think about it. I learnt not only from this exchange but also from his many papers, which have been an important source of teaching for me.

Thank you *Dieter* for your help and insight. I wish you a very happy birthday.

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