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Synthesis of α-Substituted Vinylsulfonium Salts and Their Application as Annulation Reagents in the Formation of Epoxide- and Cyclopropane-Fused Heterocycles

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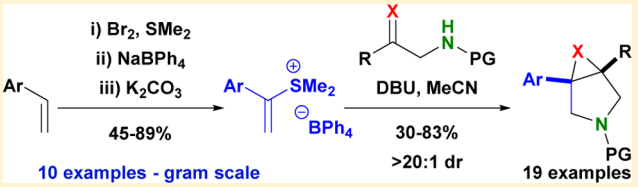
Supporting Information

ABSTRACT: The discovery of new methods for the synthesis of classes of potentially bioactive molecules remains an important goal for synthetic chemists. Vinylsulfonium salts have been used for the synthesis of a wide variety of small heterocyclic motifs; however, further developments to this important class of reagents has been focused on reaction with new substrates rather than development of new vinylsulfonium salts. We herein report the synthesis of a range of α-substituted vinylsulfonium tetraphenylborates (10 examples) in a 3 step procedure from commercially available styrenes. The important role of the tetraphenylborate counterion on the stability and accessibility of the vinylsulfonium salts is also detailed. The α-substituted vinylsulfonium tetraphenylborates gave good to excellent yields in the epoxyannulation of β-amino ketones (15 examples) and the cyclopropanation of allylic amines (4 examples). Hydrogenation of an epoxyannulation product proceeded with good diastereoselectivity.



INTRODUCTION

Saturated N-heterocycles are abundant in many drug-like molecules.[1] A recent review on the analysis of reactions used in the pursuit of drug candidates at GlaxoSmithKline, Pfizer and AstraZeneca, indicated that during a 1 year period a total of 7315 distinct reactions were published, and ca. 8% of these involved the formation of heterocycles. The authors of this review surmise that while new synthetic methods are required to access novel ring systems, the academic community is unlikely to pursue targets that lack evidence of biological activity.[2] Therefore, new methods for the synthesis of novel classes of potentially biologically active molecules remain an important goal for synthetic chemists.

Vinylsulfonium triflate **1** and its immediate precursor bromoethylsulfonium triflate **2** have been shown to be excellent annulation reagents in the synthesis of a wide variety of heterocyclic motifs (Scheme 1).[3−19] The development of this methodology has also proven a valuable tool for the preparation of novel bioactive compounds often encountered during the drug discovery process on scales ranging from >100 mg to <1 kg.[20−37] We have been interested in expanding the scope of this methodology to include more substituted vinylsulfonium salts. Previous work reported in the literature documents several examples of the annulation properties of β-substituted vinylsulfonium salts **3** and **4**;[28,38−50] however, to our knowledge, only two types of vinylsulfonium salt bearing α-substituents have been prepared (**5** and **6**) and only their use in the cyclopropanation of malonate derivatives and the aziridination of primary amines was explored (Scheme 1).[50−52] While sulfonium salts of type **6** can be prepared from commercially available styrenes according to the method first reported by Chow[51,53] and then extended by Chandrasekaran,[50] the scope of this transformation is still severely limited in terms of functional group tolerance. Herein, we report a general synthetic route to a series of functionally diverse α-substituted vinylsulfonium salts, which overcome the issues of functional group compatibility. We demonstrate their annulation properties, providing entry to heterocyclic ring systems with substitution patterns that are difficult to access using current literature procedures.

RESULTS AND DISCUSSION

Our initial strategy involved preparing a series of α-substituted vinylsulfonium salts utilizing the methodology reported by Chow et al. through the bromination of electron-rich alkenes, with bromodimethylsulfonium bromide.[53] We envisaged that through an extension of this methodology, a small library of α-substituted vinylsulfonium salts could be prepared quickly and simply from commerically available styrenes. Treatment of styrene **7a** with bromodimethylsulfonium bromide prepared in

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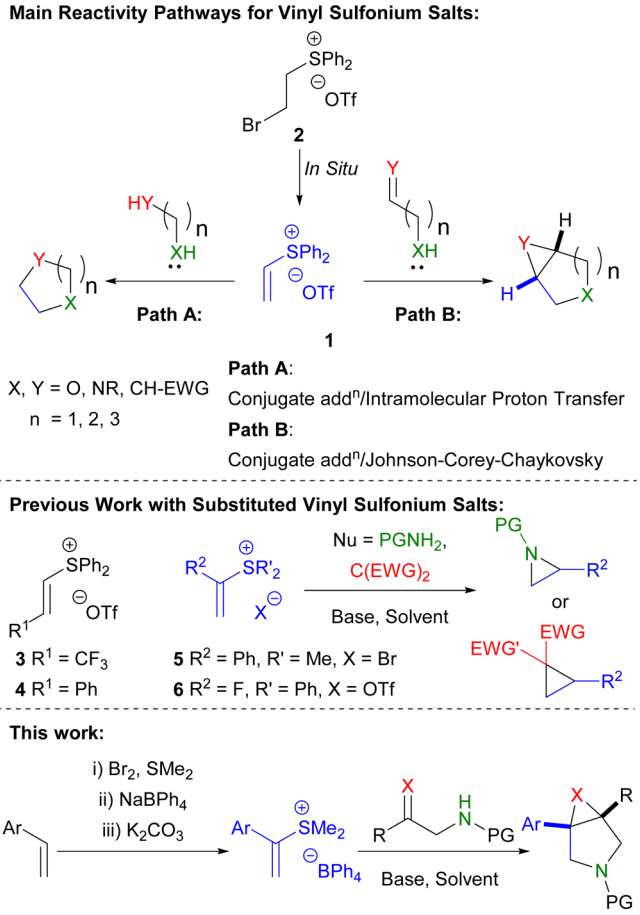
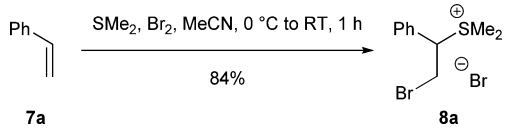
Scheme 1. Reactivity Pathways for Vinylsulfonium Salt 1 and Previous Work on Substituted Vinylsulfonium Salts



situ from dimethylsulfide and bromine gave the literature known sulfonium salt **8a** in good yield (Scheme 2).

The annulation properties of **8a** were tested in the epoxyannulation of β-amino ketone **9** (Table 1), which was easily prepared in one step by protection of the commercially available amine.[54] The 6-oxa-3-azabicyclo[3.1.0]hexane ring system was chosen as an initial target because the tetrasubstituted fused-epoxide pyrrolidine ring system that would be generated is difficult to access using current literature methods.[55−64] Commonly this type of structure is made through formation of the epoxide and pyrrolidine rings in

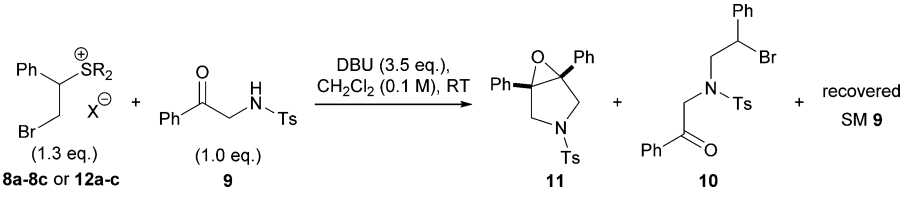
Scheme 2. Synthesis of α-Substituted Vinylsulfonium Bromide 8a



separate distinct steps, with limited examples for the formation of the fused-bicyclic system in one step. Under our standard annulation conditions,[5] with generation of vinylsulfonium salt in situ from **8a**, we isolated **10** as the main product of the reaction, along with recovered starting material **9** (Table 1, entry 1). The formation of **10** probably derives from initial protonation of the sulfur ylide intermediate and subsequent S_N2 displacement of the sulfonium group by the bromide counterion. Significant decomposition of **8a** was also observed under the reaction conditions which accounts for the recovery of starting material **9**. We hypothesized this decomposition was occurring as a result of demethylation of **8a**, which is supported by reports in the literature which highlight that sulfonium salts bearing one or more methyl groups are effective methylating reagents.[65,66]

We set out to improve the overall conversion of the β-amino-ketone starting material, so our attention turned to the synthesis of cyclic sulfonium salts derived from tetrahydrothiophene and pentamethylene sulfide, in order to avoid vinylsulfonium salt decomposition. We also attempted the reaction with more sterically demanding substrates such as diisopropylsulfide and the chiral isothiocineole; however, neither gave the corresponding sulfonium salts. The reaction of tetrahydrothiophene or pentamethylene sulfide with bromine in acetonitrile led to the formation of the desired electrophilic brominating reagents, as yellow precipitates.[67,68] Trapping with styrene **7a** gave the corresponding sulfonium salts **8b** and **8c**, respectively. The cyclic sulfonium groups increased the stability of the vinylsulfonium salts generated in situ, as demonstrated by the production of the desired 6-oxa-3-azabicyclo[3.1.0]-hexane **11** in reactions with **9** (Table 1, entries 2, 3). However, both **8b** and **8c** still generated small amounts of the undesired side product **10**, as well as recovered starting material **9**. In an effort to prevent the formation of **10** our attention turned to the nature of the counterion employed. Through exchange of the bromide anion in **8a** for various counterions (BF_4^-, BPh_4^- and OTf^-) we identified the tetraphenylborate counterion as optimum due to the stability/crystallinity of the desired

Table 1. Effect of Sulfonium Substituents and Counterions on Epoxyannulation Reactions



entry	sulfonium salt	R	X	**11** (%)	**10** (%)	recovered **9** (%)
1	**8a**	Me	Br	0	21	67
2	**8b**	$-(CH_2)_4-$	Br	10	10	54
3	**8c**	$-(CH_2)_5-$	Br	55	15	23
4	**12a**	Me	BPh_4	63	–	0
5	**12b**	$-(CH_2)_4-$	BPh_4	66	–	0
6	**12c**	$-(CH_2)_5-$	BPh_4	63	–	0

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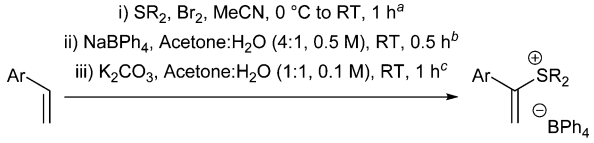
sulfonium salt. The tetraphenylborate vinylsulfonium salts **12a–c**, synthesized from **8a–c**, were also bench stable crystalline solids which could be stored for >6 months without decomposition. Pleasingly, treatment of **9** with **12a–12c** gave epoxide-fused pyrrolidine **11** in good yields and with complete consumption of starting material (Table 1, entries 4–6).

Encouraged by these initial results, the scope of substituents on the aromatic ring in the α-position was next investigated using a range of commercially available styrenes **7a–h**. A range of electron rich (Table 2, entries 1–3, 8, 9) and electron poor

Table 2. Synthesis of Substituted Vinylsulfonium Salts



7a-j **12a-j**

Entry	Sulfide	Styrene Derivative (Ar)	Yield / %[d]
1	SMe_2	**7a** Ph	**12a** 75
2		**7a** Ph	**12b** 79
3		**7a** Ph	**12c** 45
4	SMe_2	**7d** 4-BrC_6H_4	**12d** 80
5	SMe_2	**7e** 2-BrC_6H_4	**12e** 60
6	SMe_2	**7f** 4-FC_6H_4	**12f** 89
7	SMe_2	**7g** 4-$(CF_3)C_6H_4$	**12g** 56
8	SMe_2	**7h** 3,4-$(MeO)_2C_6H_3$	**12h** 84
9	SMe_2	**7i** 4-TBDMSOC_6H_4	**12i** 58
10	SMe_2	**7j** 4-MeO_2C-C_6H_4	**12j** 36

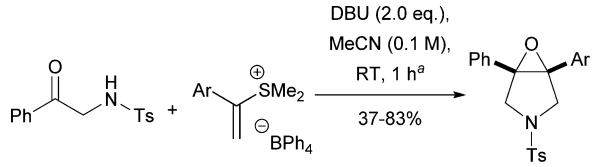
[a]Abbreviated procedure: Br_2 (1.0 equiv) treated with SMe_2 (3.5 equiv) at 0 °C in MeCN (0.5 M) for 10 min then styrene (2.0 equiv), warm to rt over 50 min. [b]$NaBPh_4$ (0.95 equiv) in acetone:H_2O (4:1, 0.5 M) at rt for 0.5 h. [c]K_2CO_3 (2.0 equiv) in acetone:H_2O (1:1, 0.1 M) at rt for 1 h. [d]All yields are isolated yields after recrystallization from acetone.

(Table 2, entries 4–7, 10) styrenes gave bromoethylsulfonium salts in good to excellent yields. Counterion exchange gave the tetraphenylborate salts in quantitative yields, before base-induced elimination of bromide gave the bench stable, crystalline solids **12a–j** in moderate to excellent yields over the three steps. Importantly, the bromide counterion analogues of **12h–j**, bearing reactive functionalities, could not be accessed using the previous methodology (Scheme 2), owing to their instability. However, using the counterion exchange/elimination procedure, we were able to isolate the tetraphenylborate salts **12h–j**.

We found that carrying out the counterion exchange/elimination procedure in one pot led to decreased isolated yields (~50%). In the one pot procedure, a decomposition pathway was evident from the diminishing yields as the reaction proceeded. By carrying out the counterion exchange first, followed by the elimination in a miscible, acetone:water solvent system, we found the decomposition pathway could be suppressed.

With a range of α-substituted vinylsulfonium salts in hand we tested each with the model epoxyannulation substrate **9**. Pleasingly, the majority of α-substituted vinylsulfonium salts underwent the desired transformation in good yields with both electron-rich and electron-deficient substituents to give tetrasubstituted 6-oxa-3-azabicyclo[3.1.0]hexanes (Table 3).

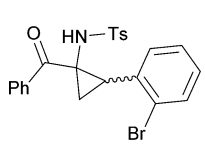
Table 3. Scope of Vinylsulfonium Salt Annulation



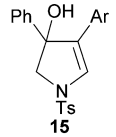
9 **12a-j** **11, 13d-j**

entry	sulfonium salt	Ar	yield (%)[b]
1	**12a**	Ph	**11** 63
2	**12d**	4-BrC_6H_4	**13d** 83
3	**12e**	2-BrC_6H_4	**13e** 0[c]
4	**12f**	4-FC_6H_4	**13f** 55
5	**12g**	4-$(CF_3)C_6H_4$	**13g** 71
6	**12h**	3,4-$(MeO)_2C_6H_4$	**13h** 67
7	**12i**	4-TBDMSO-C_6H_4	**13i**: 0[d]; 30[e]
8	**12j**	4-MeO_2C–C_6H_4	**13j** 69

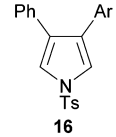
[a]Abbreviated procedure: **9** (1.0 equiv) and **12a** (1.3 equiv) in MeCN (0.1 M) treated with DBU (2.0 equiv) at rt for 1 h. [b]All yields are isolated yields. [c]Expected 6-oxa-3-azabicyclo[3.1.0]hexane **13e** was not formed, instead **14** was formed as the major product. [d]Conditions A: general procedure followed with citric acid workup gave **16**. [e]Conditions B: crude reaction mixture columned directly without workup to give **13i** and **15**.



14 43%[c] yield



15
A:[d] 0%
B:[e] 20%
Ar = 4-TBDMSO-C_6H_4



16
A:[d] 43%
B:[e] 0%
Ar = 4-OH-C_6H_4

The presence of a bromine substituent at the 2-position of **12e** led to the formation of cyclopropane **14**[44–46,49,69–73] as a 1:1 mixture of diastereomers, rather than the expected 6-oxa-3-azabicyclo[3.1.0]hexane **13e**. A proposed mechanism for the formation of **14** is shown in Scheme 3. We suggest that until the displacement of dimethylsulfide occurs, each step of the reaction is reversible. While **12e** was the only 2-aryl-substituted vinylsulfonium salt tested in the epoxyannulation, we propose that the pathway leading to the formation of the desired 3-azabicyclo[3.1.0]hexane **13e** is too sterically encumbered with 2-aryl-substituted salts and therefore the undesired pathway leading to the formation of **14** dominates.

Interestingly, when the electron-rich vinylsulfonium salt **12i**, bearing a silyl-protected ether, was submitted to the reaction conditions, desilylated pyrrole **16** was formed as the major product of the reaction (Table 3, entry 7, conditions A). To clarify when desilylation was occurring, the reaction was repeated without the citric acid workup, followed by direct purification by flash column chromatography (Table 3, entry 7, conditions B). This gave the desired 6-oxa-3-azabiyclo[3.1.0]-hexane **13i**, albeit in poor yield, and 2,3-dihydro-1*H*-pyrrol-3-ol **15** as the major side-product. Both **13i** and **15** contained the *tert*-butyldimethylsilyl ether suggesting that the formation of

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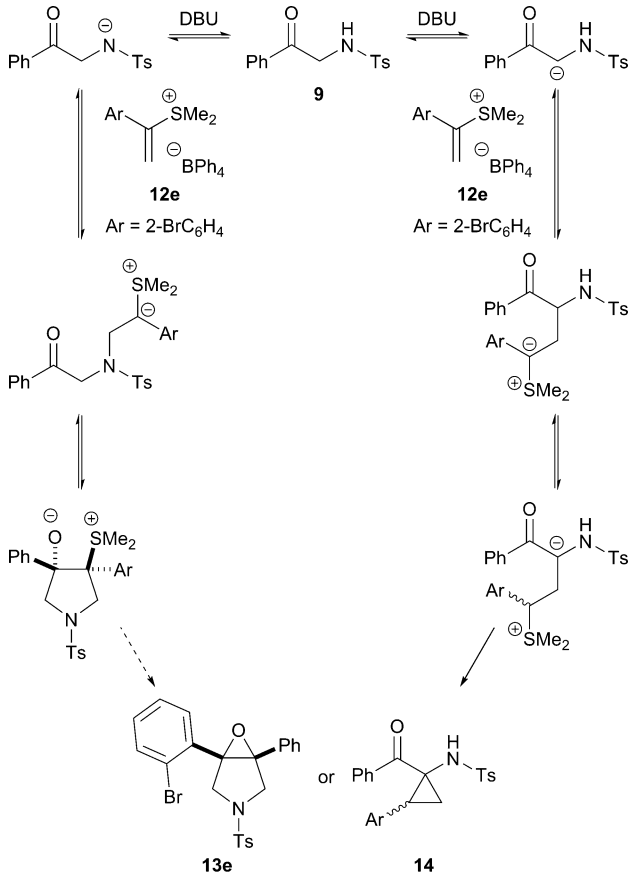
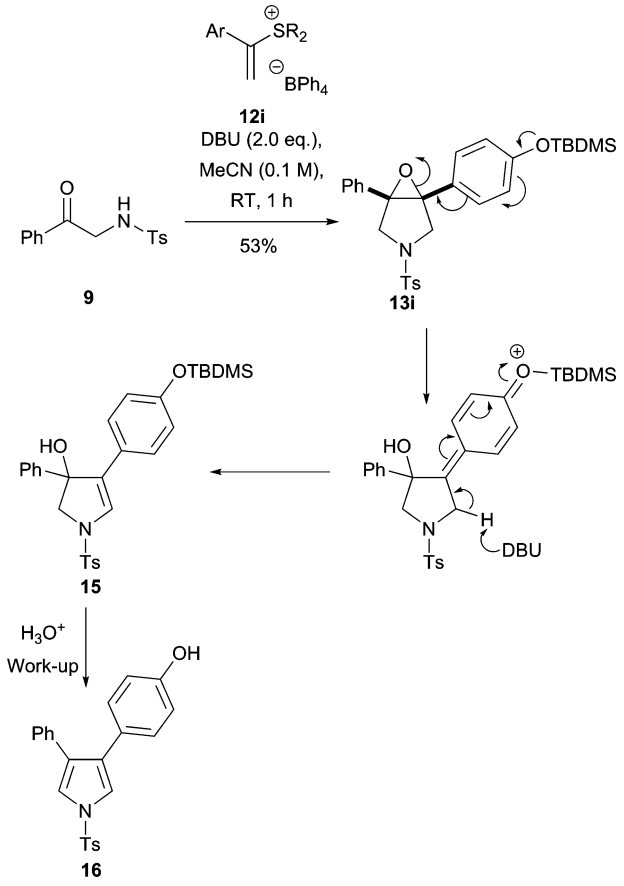
Scheme 3. Proposed Mechanism for the Formation of Cyclopropane 14 Rather than 13 in the Case of 2-Aryl-Substituted Vinylsulfonium Salts



Scheme 4. Proposed Mechanism for the Formation of Dihydropyrrole 15 and Pyrrole 16

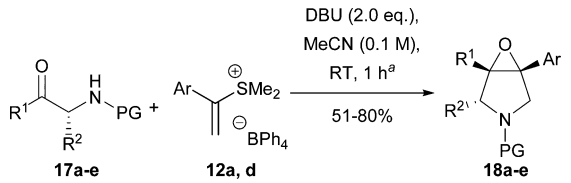


pyrrole **16** was partially occurring during the reaction pathway, but that desilylation was occurring during workup. We propose that the formation of **16** occurs through ring opening of the epoxide **13i**, promoted by the electron-rich nature of the aromatic ring. Base-promoted rearomatization then gives the intermediate 2,3-dihydro-1*H*-pyrrol-3-ol **15**, followed by desilylation and loss of water upon treatment with citric acid to give the observed pyrrole **16** (Scheme 4).

We have previously shown that vinylsulfonium salt annulations are compatible with a range of N-protecting groups.[5,6,74] We therefore wanted to demonstrate that vinylsulfonium salts bearing α-substituents were also compatible with various protecting groups. Both 4-nitrobenzenesulfonamide (Ns) and 2-(trimethylsilyl)ethyl sulfonamide (SES), which can be removed under mild conditions,[75] gave the desired pyrrolidines **18a** and **18b**, albeit, in slightly reduced yields in comparison to the tosyl protecting group (Table 4, entries 1, 2). As expected, attempts using carbamate-protected amines were unsuccessful.[74]

Expanding this methodology further, we were able to utilize a range of easily accessible β-amino ketones as starting materials for the cyclization (Table 4). Alkyl ketone **17c** readily underwent the desired transformation to give **18c** in good yield, demonstrating that this chemistry is not restricted to aromatic ketones such as **9** (Table 4, entry 3). We were also able to show that heteroaromatic ketones such as **17d** were compatible with the desired reaction to give pyrrolidine **18d** (Table 4, entry 4). Pleasingly, enantioenriched (>99:1 *er*) β-

Table 4. Scope of Annulation Substrate



Entry		R^1	R^2	PG	Sulfonium Salt / Ar			Yield / %[b]
1	**17a**	Ph	H	Ns	**12d**	4-BrC_6H_4	**18a**	54
2	**17b**	Ph	H	SES	**12d**	4-BrC_6H_4	**18b**	60
3	**17c**	Et	H	Ts	**12a**	Ph	**18c**	72
4	**17d**		H	Ts	**12a**	Ph	**18d**	66
5	**17e**	Ph	(*R*)-Ph >99:1 er	Ts	**12a**	Ph	**18e**	65 >95:5 dr 97:3 er[c]
6	**17f**	4-ClC_6H_4	H	Ts	**12d**	4-BrC_6H_4	**18f**	80
7	**17g**	4-ClC_6H_4	H	Ns	**12d**	4-BrC_6H_4	**18g**	51

[a]Abbreviated procedure: **17a** (1.0 equiv) and **12a** (1.3 equiv) in MeCN (0.1 M) were treated with DBU (2.0 equiv) at rt for 1 h. [b]All yields are isolated yields. [c]Diastereoselectivity and enantiomeric ratio varies with temperatures: 25 °C (65%, >95:5 dr, 86:14 er), −20 to 0 °C (62%, >95:5 dr, 97:3 er).

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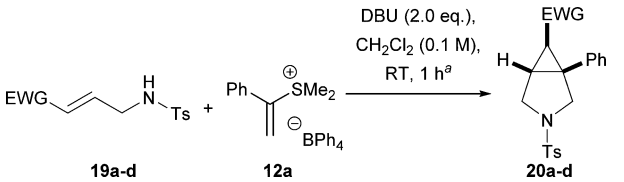
amino ketone **17e** generated the bicyclic ring system **18e** as a single diastereoisomer, with only a small erosion (97:3 *er*) of the stereochemistry (at a lower reaction temperature), with the relative stereochemistry determined by NOE analysis (Table 4, entry 5). The ability to incorporate orthogonal functional group handles on the aromatic rings is a useful feature of the chemistry described and is demonstrated by the use of 4-chloro-substituted aromatic ketone **17f** to give the diaromatic substituted pyrrolidine **18f** in good yield (Table 4, entry 6). We were again able to demonstrate that nosyl analogue **17g** was tolerant of the reaction conditions giving **18g** in moderate yield (Table 4, entry 7).

Our next goal was to expand the reactivity of this new class of annulation reagents to the intramolecular-Michael/cyclopropanation reaction of various allylic amines previously used with bromoethylsulfonium triflate **2**.[3] Taking allylic amines **19a–d**, bearing different Michael acceptors, we demonstrated that α-substituted vinylsulfonium salt **12a** behaved in an analogous manner to vinylsulfonium triflate **1**, generating 3-azabicyclo[3.1.0]hexanes **20a–d** in moderate to good yields as single diastereoisomers (Table 5, entries 1–4). An X-ray crystal structure of **20a** (see Supporting Information) showed that the COMe group is *cis* to the aromatic group introduced by the annulation reagent.

Table 5. Cyclopropanation Substrate Scope



19a-d **12a** **20a-d**

entry	allylic amine, EWG	*dr*	yield (%)[b]
1	**19a** COMe	>95:5	**20a** 72
2	**19b** CO_2Me	>95:5	**20b** 45
3	**19c** CO_2tBu	>95:5	**20c** 63
4	**19d** CN	>95:5	**20d** 53

[a]Abbreviated procedure: **19a** (1.0 equiv) and **12a** (1.3 equiv) in CH_2Cl_2 (0.1 M) were treated with DBU (2.0 equiv) at rt for 1 h. [b]All yields are isolated yields.

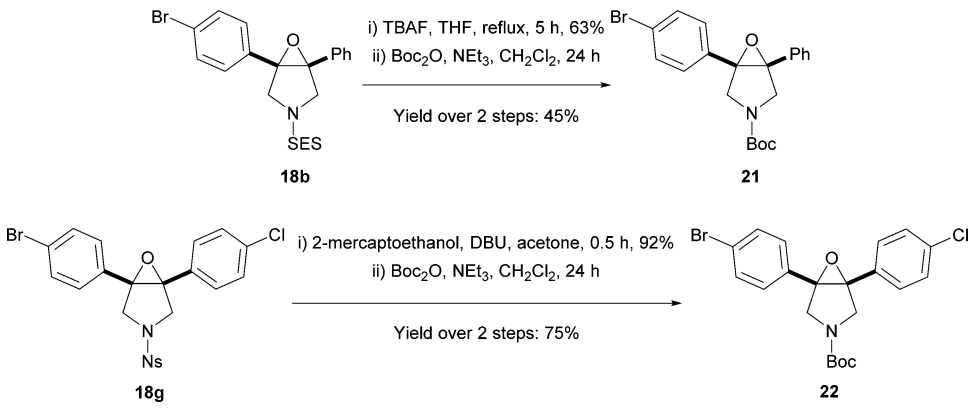
The deprotection of *N*-tosyl **18e**, using sodium naphthalenide conditions led to the decomposition of the material; however, we successfully deprotected the *N*-SES **18b** and *N*-nosyl **18g** epoxyannulation products without loss of the epoxide, generating the free amines, which were characterized as the *N*-Boc protected amines **21** and **22**, respectively (Scheme 5). The synthetic utility of the epoxide-fused pyrrolidines was demonstrated by submitting **11** to hydrogenation conditions (Scheme 6). Using H-cube hydrogenation flow apparatus we were able to isolate the tertiary alcohol *cis*-**23** in good yields and with good diastereoselectivity. Using more conventional batch hydrogenation conditions, we were able to show that a similar yield could be achieved with the same diastereocontrol, albeit requiring longer reaction times in comparison. We were also able to deoxygenate **11** using conditions reported by Nugent and RajanBabu to give dihydro-1*H*-pyrrole **24** in moderate yield.[76]

In summary, we have devised a high yielding synthesis of α-substituted vinylsulfonium tetrafluoroborates. These bench stable salts have enabled us to significantly expand the annulation protocol in the synthesis of more substituted fused-bicyclic pyrrolidines, a useful class of building blocks in the construction of bioactive molecules.

EXPERIMENTAL SECTION

General Information. Reactions requiring anhydrous conditions (General method **GP1** and where specified) were executed under dry nitrogen or argon atmospheres in glassware that was dried using either a combination of vacuum and heat-gun, oven, or flame drying. Reaction mixtures were stirred magnetically. Air- and moisture-sensitive liquids and solutions were transferred via syringe or cannula into the reaction vessels through rubber septa. All reagents were purchased (unless specified) at highest commercial quality and used as received. All solvents were either purchased at the highest commercial quality (anhydrous) and used as received or were obtained from a purification column composed of activated alumina (A-2).[77] Materials: 4-Methyl-*N*-(2-oxo-2-phenylethyl)benzenesulfonamide **9**, 4-nitro-*N*-(2-oxo-2-phenylethyl)benzenesulfonamide **17a**, *N*-(2-(4-chlorophenyl)-2-oxoethyl)-4-methylbenzenesulfonamide **17f** and *N*-(2-(4-chlorophenyl)-2-oxoethyl)-4-nitrobenzenesulfonamide **17g** were prepared according to the procedure reported by Magedov et al.[54] *N*-(2-Oxo-2-phenylethyl)-2-(trimethylsilyl)ethanesulfonamide **17b** was prepared according to the procedure reported by Miura et al.[78] 4-Methyl-*N*-(2-oxobutyl)benzenesulfonamide **17c** was prepared according to the procedure reported by Unthank et al.[8] 4-Methyl-*N*-(2-oxo-2-(thiophen-2-yl)ethyl)benzenesulfonamide **17d** was prepared according to the procedure reported by Harikrishna et al.[79] (*R*)-4-Methyl-*N*-(2-oxo-1,2-diphenylethyl)benzenesulfonamide **17e** was prepared according to the procedure reported by Unthank et al.[7] (*E*)-4-Methyl-*N*-(4-oxopent-2-en-1-yl)benzenesulfonamide **19a**, methyl (*E*)-4-((4-methylphenyl)sulfonamido)but-2-enoate **19b**, *tert*-butyl (*E*)-4-((4-methylphenyl)sulfonamido)but-2-enoate **19c** and (*E*)-*N*-(3-cyanoallyl)-4-methylbenzenesulfonamide **19d** were prepared according to the

Scheme 5. Deprotection of *N*-SES 18b and *N*-Nosyl 18g



18b **21**

18g **22**

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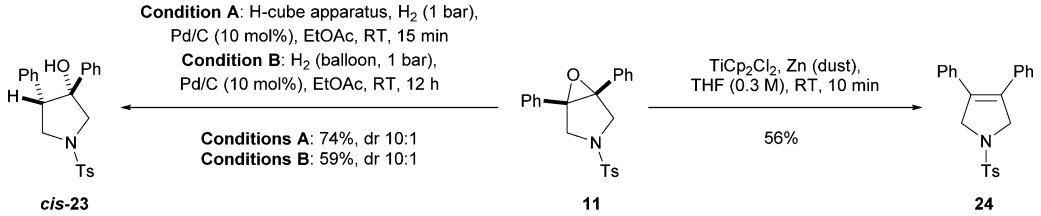
Scheme 6. Hydrogenation of Epoxide 11 to Give Tertiary Alcohol *cis*-23 and Radical Deoxygenation of Epoxide 11 to Give Dihydro-1*H*-pyrrole 24



procedure reported by Fritz et al.[3] Spectroscopic data were consistent with those reported in the literature for **9**,[78] **17a**,[78] **17b**,[78] **17c**,[8] **17d**,[79] **17e**,[7] **17f**,[80] **17g**,[54] **19a**,[3] **19b**,[3] **19c**[3] and **19d**.[3] Yields refer to spectroscopically pure compounds unless otherwise stated. Melting points were determined using a melting point apparatus and are uncorrected. Flash chromatography was performed on silica gel (Merck Kieselgel 60 F_{254} 230−400 mesh). TLC was performed on aluminum-backed silica plates (0.2 mm, 60 F_{254}). IR spectra were recorded on neat compounds using a FT-IR spectrometer (ATR sampling accessory). Only strong and selected absorbances (ν_{max} expressed in cm^{-1}) are reported. ^1H and ^{13}C NMR spectra were recorded on (100 and 400 MHz) and (125 and 500 MHz) instruments. Chemical shifts (δ_H, δ_C) are quoted in parts per million (ppm) and referenced to the appropriate NMR solvent peak(s) and are assigned ArH, C, CH, C*H*H or CH*H* (diastereotopic protons), CH_2, CH_3. COSY, HSQC and HMBC experiments were used in assigning NMR spectra and are included in the Supporting Information. Spin−spin coupling constants (J) are reported in Hz. Low and high resolution mass spectra were recorded in CI or ESI modes respectively on a FT-MS instrument. Optical rotations were measured using a polarimeter where c is given in g/100 mL. Chiral Supercritical fluid chromatography was performed using Chiralpak IA, IB and IC columns (4.6 × 250 mm, × 5 μm) or a Whelk O-1 column (4.6 × 250 mm, × 5 μm) on a SFC system and monitored by DAD (Diode Array Detector).

General Procedure for the Synthesis of α-Aryl Substituted Bromoethyl Sulfonium Bromides (GP1). A flask dried by heat gun under a vacuum was charged with bromine (1 equiv) in MeCN (2 mL/mmol) at 0 °C. To this was added dimethylsulfide (3.5 equiv) dropwise over 5 min leading to the formation of a yellow precipitate. The reaction mixture was stirred for 10 min before the addition of a styrene derivative (2 equiv) dropwise over 5 min. The reaction mixture was then warmed to rt generating a homogeneous solution (n.b., the yellow precipitate persists for longer time periods with increasingly electron deficient styrenes), followed by a subsequent precipitation of the sulfonium bromide. The reaction mixture was stirred for 30 min before being diluted with Et_2O (5 mL/mmol) to ensure full precipitation/removal of the excess reagents. The solid precipitate was isolated by removal of the ethereal supernatant by filtration and washed with a further portion of Et_2O (2.5 mL/mmol) before drying under a vacuum to yield the desired α-aryl substituted bromoethyl sulfonium bromide (n.b., all of these compounds are air stable for ∼24 h and can be isolated for analysis by ^1H and ^{13}C NMR in either D_2O or DMSO-d_6; however, some of the compounds rapidly decompose in D_2O/DMSO and the NMR data obtained reflect this).

General Procedure for the Synthesis of α-Aryl Substituted Bromoethyl Sulfonium Tetraphenylborates (GP2). Freshly prepared α-aryl substituted bromoethyl sulfonium bromide (1 equiv) was dissolved in acetone:H_2O (4:1, 0.5 M) followed by the addition of sodium tetraphenylborate (0.95 equiv). The reaction mixture was then stirred for 30 min before a second portion of H_2O (10 mL/mmol) was added followed by filtration of the solid precipitate. The isolated precipitate was washed with H_2O (3 × 10 mL/mmol) (n.b., The tetraphenylborate salts are soluble in acetone and precipitate in water, conversely the bromide salts are soluble in water and any excess is removed during the washing stage). The filtrate was then discarded and the residue was dried under high vacuum for 24 h with gentle heating (warm water bath) to give the corresponding α-aryl substituted bromoethyl sulfonium tetraphenylborates.

General Procedure for the Synthesis of α-Aryl Substituted Vinyl Sulfonium Tetraphenylborates (GP3). α-Aryl substituted bromoethyl sulfonium tetraphenylborate (1 equiv) was dissolved in acetone:H_2O (1:1, 0.1 M), followed by the addition of potassium carbonate (2 equiv). The reaction was then stirred for 1 h, before filtration and subsequent washing of the resultant precipitate with H_2O (3 × 10 mL/mmol). The filtrate was then discarded and the isolated solid recrystallized from hot acetone (5−6 crops, ∼50% by mass of pure compound is obtained per recrystallization) to give the desired α-aryl substituted vinyl sulfonium tetraphenylborates.

*(2-Bromo-1-phenylethyl)dimethylsulfonium bromide (**8a**).* Prepared according to general method GP1 and was used without further purification in the next step; 26 g, 80% yield; white solid; *Spectroscopic data were consistent with those reported in the literature.*[53]

(2-Bromo-1-phenylethyl)dimethylsulfonium tetraphenylborate. Prepared according to GP2 and was used in the next step without further purification; 24.6 g, 99% yield; white solid; An analytically pure sample was prepared by recrystallization from acetone; mp 167−168 °C (acetone); ν_{max} (film)/cm^{-1} 3053, 2984, 1477, 1421, 1215, 739, 699; δ_H (400 MHz, DMSO-d_6) 7.55−7.46 (5 H, m, ArH), 7.21−7.11 (8 H, m, ArH), 6.90 (8 H, t, J 7.3, ArH), 6.77 (4 H, t, J 7.3, ArH), 5.21 (1 H, dd, J 9.9, 5.8, CH), 4.36 (1 H, dd, J 10.8, 5.8, C*H*H), 4.32 (1 H, dd, J 10.8, 9.9, CH*H*), 2.85 (3 H, s, CH_3), 2.58 (3 H, s, CH_3); δ_C (100 MHz, DMSO-d_6) 163.8 (q, J_{B-C} 49, C), 136.0 (q, J_{B-C} 1, CH), 131.0 (CH), 130.3 (C), 130.0 (CH), 129.9 (CH), 125.8 (q, J_{B-C} 3, CH), 122.0 (CH), 59.3 (CH), 29.6 (CH_2), 24.4 (CH_3), 23.0 (CH_3); m/z (ESI$^+$) 245.0 [M(^{79}Br)−BPh_4]$^+$, 245.0 [M(^{81}Br)−BPh_4]$^+$; HRMS (ESI$^+$) $C_{10}H_{14}{}^{79}BrS^+$ [M−BPh_4]$^+$ requires 244.9994; found 244.9993. $C_{10}H_{14}{}^{81}BrS^+$ [M−BPh_4]$^+$ requires 246.9974; found 246.9973.

*Dimethyl(1-phenylvinyl)sulfonium tetraphenylborate (**12a**).* Prepared according to GP3; Crystals suitable for X-ray analysis (CCDC 1006749) were grown as described in the Supporting Information (SI); 17.95 g, 95% yield; white solid; mp 195−197 °C (acetone); ν_{max} (film)/cm^{-1} 3053, 3002, 1477, 1425, 769, 731, 703; δ_H (400 MHz, acetone-d_6) 7.60−7.49 (5 H, m, ArH), 7.41−7.32 (8 H, m, ArH), 6.94 (8 H, t, J 7.3, ArH), 6.79 (4 H, t, J 7.3, ArH), 6.43 (1 H, d, J 3.4, C*H*H), 6.31 (1 H, d, J 3.4, CH*H*), 2.93 (6 H, s, 2 × CH_3); δ_C (100 MHz, acetone-d_6) 164.9 (q, J_{B-C} 49, C), 137.4 (C), 137.0 (q, J_{B-C} 1, CH), 132.6 (C), 131.7 (CH), 130.3 (CH), 128.9 (CH), 128.2 (CH_2), 126.1 (q, J_{B-C} 3, CH), 122.3 (CH), 26.8 (CH_3); m/z (ESI$^+$) 165.1 [M−BPh_4]$^+$; HRMS (ESI$^+$) $C_{10}H_{13}S^+$ [M−BPh_4]$^+$ requires 165.0732; found 165.0738.

*1-(2-Bromo-1-phenylethyl)tetrahydro-1H-thiophen-1-ium bromide (**8b**).* Prepared according to general method GP1 and was used without further purification in the next step; 6.1 g, 87% yield; white solid; δ_H (400 MHz, D_2O) 7.63−7.54 (5 H, m, ArH), 5.02 (1 H, dd, J 9.0, 5.9, CH), 4.23 (1 H, dd, J 11.1, 5.9, CH*H*), 4.18 (1 H, dd, J 11.1, 9.0, C*H*H), 3.88−3.73 (2 H, m, CH_2), 3.39 (1 H, dt, J 14.2, 7.2, C*H*H), 3.05 (1 H, dt, J 13.2, 6.3, CH*H*), 2.32−2.22 (2 H, m, CH_2), 2.22−2.06 (2 H, m, CH_2); δ_C (100 MHz, D_2O) 131.0 (CH), 130.7 (C), 129.9 (CH), 129.2 (CH), 60.1 (CH), 44.5 (CH_2), 42.8 (CH_2), 29.7 (CH_2), 28.7 (CH_2), 28.4 (CH_2).

1-(2-Bromo-1-phenylethyl)tetrahydro-1H-thiophen-1-ium tetraphenylborate. Prepared according to GP2 and was used in the next step without further purification; 9.33 g, 98% yield; white solid; An analytically pure sample was prepared by recrystallization from

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acetone; mp 143−144 °C (acetone); ν_{max} (film)/cm^{-1} 3054, 1476, 1425, 1259, 962, 842, 745, 733; δ_H (400 MHz, DMSO-d_6) 7.71−7.57 (2 H, m, ArH), 7.57−7.48 (3 H, m, ArH), 7.29−7.18 (8 H, m, ArH), 6.96 (8 H, t, J 7.3, ArH), 6.83 (4 H, t, J 7.3, ArH), 5.14 (1 H, dd, J 9.5, 5.5, CH), 4.46−4.28 (2 H, m, CH_2), 3.77 (1 H, dt, J 12.8, 6.4, C*H*H), 3.59 (1 H, dt, J 13.5, 7.0, CH*H*), 3.34 (1 H, dt, J 13.5, 7.0, C*H*H), 2.97 (1 H, dt, J 12.8, 6.4, CH*H*), 2.15−1.92 (4 H, m, 2 × CH_2); δ_C (100 MHz, DMSO-d_6) 163.4 (q, J_{B-C} 49, C), 135.5 (CH), 131.5 (C), 130.5 (CH), 129.5 (CH), 129.3 (CH), 125.3 (q, J_{B-C} 3, CH), 121.5 (CH), 58.3 (CH), 43.5 (CH_2), 42.5 (CH_2), 30.5 (CH_2), 28.5 (CH_2), 28.3 (CH_2); m/z (ESI$^+$) 271.0 [M(^{79}Br)−BPh$_4$]$^+$, 273.0 [M(^{81}Br)−BPh$_4$]$^+$; HRMS (ESI$^+$) $C_{12}H_{16}{}^{79}BrS^+$ [M−BPh$_4$]$^+$ requires 271.0151; found 271.0153. $C_{12}H_{16}{}^{81}BrS^+$ [M−BPh$_4$]$^+$ requires 273.0130; found 273.0130.

*1-(1-Phenylvinyl)tetrahydro-1H-thiophen-1-ium tetraphenylborate (**12b**).* Prepared according to GP3; 7.47 g, 93% yield; white yield; mp 174−176 °C (acetone); ν_{max} (film)/cm^{-1} 3051, 2997, 1477, 1427, 966, 743, 729, 705, 698; δ_H (400 MHz, DMSO-d_6) 7.63−7.47 (5 H, m, ArH), 7.24−7.15 (8 H, m, ArH), 6.93 (8 H, t, J 7.3, ArH), 6.79 (4 H, t, J 7.3, ArH), 6.42 (1 H, d, J 3.6, C*H*H), 6.26 (1 H, d, J 3.6, CH*H*), 3.74−3.61 (2 H, m, 2 × CHH), 3.60−3.45 (2 H, m, 2 × CHH), 2.20−1.99 (4 H, m, 2 × CH_2); δ_C (100 MHz, DMSO-d_6) 163.3 (q, J_{B-C} 49), 135.5, 135.2, 133.1, 130.4, 129.3, 127.7, 125.9, 125.3 (q, J_{B-C} 3), 121.5, 45.0, 27.8; m/z (ESI$^+$) 191.1 [M−BPh$_4$]$^+$; HRMS (ESI$^+$) $C_{12}H_{15}S^+$ [M−BPh$_4$]$^+$ requires 191.0889; found 191.0892.

*1-(2-Bromo-1-phenylethyl)hexahydrothiopyrylium bromide (**8c**).* Prepared according to general method GP1 and was used without further purification in the next step; 3.66 g, 50% yield; white solid; δ_H (400 MHz, D_2O) 7.66−7.52 (5 H, m, ArH), 5.23 (1 H, dd, J 9.2, 5.5, CH), 4.24 (1 H, dd, J 11.0, 5.5, CH*H*), 4.16 (1 H, dd, J 11.0, 9.2, C*H*H), 3.79 (1 H, ddt, J 11.8, 5.6, 2.6, C*H*H), 3.36−3.26 (1 H, m, CH*H*), 3.14−3.04 (1 H, m, C*H*H), 2.93−2.83 (1 H, m, CH*H*), 2.36−2.23 (1 H, m, C*H*H), 2.21−2.09 (1 H, m, CH*H*), 2.00−1.86 (1 H, m, C*H*H), 1.85−1.72 (2 H, m, CH_2), 1.58−1.43 (1 H, m, CH*H*); δ_C (100 MHz, D_2O) 131.0 (CH), 129.8 (CH), 129.6 (C), 129.2 (CH), 59.0 (CH), 37.5 (CH_2), 36.0 (CH_2), 28.7 (CH_2), 22.2 (CH_2), 21.6 (CH_2), 21.5 (CH_2).

1-(2-Bromo-1-phenylethyl)hexahydrothiopyrylium tetraphenylborate. Prepared according to GP2 and was used in the next step without further purification; 4.92 g, 99% yield; white solid; An analytically pure sample was prepared by recrystallization from acetone; mp 164−165 °C (acetone); ν_{max} (film)/cm^{-1} 3051, 1478, 1426, 1148, 849, 744, 733, 701; δ_H (400 MHz, DMSO-d_6) 7.63−7.44 (5 H, m, ArH), 7.19 (8 H, m, ArH), 6.93 (8 H, t, J 7.3, ArH), 6.81 (4 H, t, J 7.3, ArH), 5.39 (1 H, dd, J 10.1, 5.0, CH), 4.36 (1 H, dd, J 10.7, 5.0, C*H*H), 4.30 (1 H, app. t, J 10.4, CH*H*), 3.84−3.72 (1 H, m, CH), 3.42−3.26 (1 H, m, CH), 3.08−2.95 (1 H, m, CH), 2.90−2.78 (1 H, m, CH), 2.25−2.13 (1 H, m, CH), 2.12−2.00 (1 H, m, CH), 1.86−1.56 (3 H, m, CH_2 and CH), 1.49−1.31 (1 H, m, CH); δ_C (100 MHz, DMSO-d_6) 163.4 (q, J_{B-C} 49, C), 135.5 (CH), 130.4 (CH), 130.2 (C), 129.4 (CH), 129.1 (CH), 125.3 (q, J_{B-C} 3, CH), 121.5 (CH), 57.3 (CH), 36.3 (CH_2), 35.5 (CH_2), 29.6 (CH_2), 22.2 (CH_2), 21.2 (CH_2), 21.1 (CH_2); m/z (ESI$^+$) 285.0 [M(^{79}Br)−BPh$_4$]$^+$, 287.0 [M(^{81}Br)−BPh$_4$]$^+$; HRMS (ESI$^+$) $C_{13}H_{18}{}^{79}BrS^+$ [M−BPh$_4$]$^+$ requires 285.0307; found 285.0311. $C_{13}H_{18}{}^{81}BrS^+$ [M−BPh$_4$]$^+$ requires 287.0278; found 287.0283.

*1-(1-Phenylvinyl)hexahydrothiopyrylium tetraphenylborate (**12c**).* Prepared according to GP3; 4.11 g, 91% yield; white solid; mp 163−165 °C (acetone); ν_{max} (film)/cm^{-1} 3053, 3000, 1478, 932, 737, 698; δ_H (400 MHz, DMSO-d_6) 7.63−7.47 (5 H, m, ArH), 7.23−7.14 (8 H, m, ArH), 6.92 (8 H, t, J 7.3, ArH), 6.79 (4 H, t, J 7.3, ArH), 6.59 (1 H, d, J 3.4, C*H*H), 6.35 (1 H, d, J 3.4, CH*H*), 3.75−3.63 (2 H, m, 2 × CHH), 3.41−3.27 (2 H, m, 2 × CHH), 2.10−1.96 (2 H, m, 2 × CHH), 1.88−1.73 (2 H, m, 2 × CHH), 1.71−1.48 (2 H, m, 2 × CHH); δ_C (100 MHz, DMSO-d_6) 163.3 (q, J_{B-C} 49), 135.5, 133.9, 132.3, 130.5, 129.4, 127.9, 127.4, 125.3 (q, J_{B-C} 3), 121.5, 37.9, 22.1, 21.1; m/z (ESI$^+$) 205.1 [M−BPh$_4$]$^+$; HRMS (ESI$^+$) $C_{13}H_{17}S^+$ [M−BPh$_4$]$^+$ requires 205.1045; found 205.1046.

(2-Bromo-1-(4-bromophenyl)ethyl)dimethylsulfonium bromide. Prepared according to general method GP1 and was used without further purification in the next step; 1.05 g, 86% yield; white solid; *Spectroscopic data were consistent with those reported in the literature.*[50]

(2-Bromo-1-(4-bromophenyl)ethyl)dimethylsulfonium tetraphenylborate. Prepared according to GP2 and was used in the next step without further purification; 1.47 g, 95% yield; white solid; An analytically pure sample was prepared by recrystallization from acetone; mp 180−181 °C (acetone); ν_{max} (film)/cm^{-1} 1478, 1403, 1008, 825, 739, 730, 705; δ_H (400 MHz, DMSO-d_6) 7.81−7.73 (2 H, m, ArH), 7.53−7.46 (2 H, m, ArH), 7.26−7.17 (8 H, m, ArH), 6.95 (8 H, t, J 7.3, ArH), 6.81 (4 H, t, J 7.3, ArH), 5.26 (1 H, dd, J 9.9, 5.8, CH), 4.38 (1 H, dd, J 10.8, 5.8, C*H*H), 4.33 (1 H, ABX type br. t, J 10.5, CH*H*), 2.88 (3 H, s, CH_3), 2.63 (3 H, s, CH_3); δ_C (100 MHz, DMSO-d_6) 163.4 (q, J_{B-C} 49), 135.5 (q, J_{B-C} 1), 132.4, 131.7, 129.3, 125.3 (q, J_{B-C} 3), 124.2, 121.5, 57.9, 28.8, 23.9, 22.5; m/z (ESI$^+$) 322.9 [M(^{79}Br^{79}Br)−BPh$_4$]$^+$, 324.9 [M(^{79}Br^{81}Br + ^{81}Br^{79}Br)−BPh$_4$]$^+$, 326.9 [M(^{81}Br^{81}Br)−BPh$_4$]$^+$; HRMS (ESI$^+$) $C_{10}H_{13}{}^{79}Br^{79}BrS^+$ [M−BPh$_4$]$^+$ requires 322.9099; found 322.9102. $C_{10}H_{13}{}^{79}Br^{81}BrS^+$ + $C_{10}H_{13}{}^{81}Br^{79}BrS^+$ [M−BPh$_4$]$^+$ requires 324.9079; found 324.9073. $C_{10}H_{13}{}^{81}Br^{81}BrS^+$ [M−BPh$_4$]$^+$ requires 326.9059; found 326.9053.

*(1-(4-Bromophenyl)vinyl)dimethylsulfonium tetraphenylborate (**12d**).* Prepared according to GP3; 1.16 g, 98% yield; white solid; mp 204−206 °C (acetone); ν_{max} (film)/cm^{-1} 3055, 2998, 1479, 989, 827, 731; δ_H (400 MHz, DMSO-d_6) 7.78−7.69 (2 H, m, ArH), 7.56−7.47 (2 H, m, ArH), 7.24−7.14 (8 H, m, ArH), 6.93 (8 H, t, J 7.3, ArH), 6.79 (4 H, t, J 7.3, ArH), 6.58 (1 H, d, J 3.5, C*H*H), 6.41 (1 H, d, J 3.5, CH*H*), 3.02 (6 H, s, 2 × CH_3); δ_C (100 MHz, DMSO-d_6) 163.3 (q, J_{B-C} 49), 135.7, 135.5, 132.2, 131.6, 129.7, 127.7, 125.3 (q, J_{B-C} 3), 124.0, 121.5, 26.5; m/z (ESI$^+$) 243.0 [M(^{79}Br)−BPh$_4$]$^+$, 245.0 [M(^{81}Br)−BPh$_4$]$^+$; HRMS (ESI$^+$) $C_{10}H_{12}{}^{79}BrS^+$ [M−BPh$_4$]$^+$ requires 242.9838; found 242.9843; $C_{10}H_{12}{}^{81}BrS^+$ [M−BPh$_4$]$^+$ requires 244.9817; found 244.9821.

(2-Bromo-1-(2-bromophenyl)ethyl)dimethylsulfonium bromide. Prepared according to general method GP1 and was used without further purification in the next step; 2.6 g, 64% yield; white solid; We were unable to characterize this compound by NMR as the bromide salt due to decomposition in DMSO-d_6.

(2-Bromo-1-(2-bromophenyl)ethyl)dimethylsulfonium tetraphenylborate. Prepared according to general method GP2 and was used without further purification in the next step; 3.6 g, 95% yield; white solid; An analytically pure sample was prepared by recrystallization from acetone; mp 162−163 °C (acetone); ν_{max} (film)/cm^{-1} 1417, 1025, 745, 737, 706; δ_H (400 MHz, DMSO-d_6) 7.79 (1 H, dd, J 8.0, 1.1, ArH), 7.70 (1 H, br. d, J 7.4, ArH), 7.55 (1 H, br. t, J 7.4, ArH), 7.42 (1 H, td, J 8.0, 1.6, ArH), 7.29−7.06 (8 H, m, ArH), 6.90 (8 H, t, J 7.3, ArH), 6.76 (4 H, t, J 7.3, ArH), 5.56 (1 H, dd, J 9.9, 4.8, CH), 4.39−4.19 (2 H, m, CH_2), 3.00 (3 H, s, CH_3), 2.74 (3 H, s, CH_3); We were unable to obtain a ^{13}C spectrum due to decomposition of this material in DMSO-d_6; m/z (ESI$^+$) 322.9 [M(^{79}Br^{79}Br)−BPh$_4$]$^+$; 324.9 [M(^{79}Br^{81}Br + ^{81}Br^{79}Br)−BPh$_4$]$^+$; 326.9 [M(^{81}Br^{81}Br)−BPh$_4$]$^+$; HRMS (ESI$^+$) $C_{10}H_{13}{}^{79}Br^{79}BrS^+$ [M−BPh$_4$]$^+$ requires 322.9099; found 322.9098. $C_{10}H_{13}{}^{79}Br^{81}BrS^+$ + $C_{10}H_{13}{}^{81}Br^{79}BrS^+$ [M−BPh$_4$]$^+$ requires 324.9079; found 324.9075. $C_{10}H_{13}{}^{81}Br^{81}BrS^+$ [M−BPh$_4$]$^+$ requires 326.9059; found 326.9054.

*(1-(2-Bromophenyl)vinyl)dimethylsulfonium tetraphenylborate (**12e**).* Prepared according to GP3; 2.9 g, 99% yield; white solid; mp 204−205 °C (acetone); ν_{max} (film)/cm^{-1} 1471, 1427, 1215, 1030, 985, 766, 745, 733, 711; δ_H (400 MHz, DMSO-d_6) 7.83 (1 H, dd, J 8.0, 1.1, ArH), 7.58−7.46 (3 H, m, ArH), 7.24−7.15 (8 H, m, ArH), 6.93 (8 H, t, J 7.3, ArH), 6.80 (4 H, t, J 7.3, ArH), 6.75 (1 H, d, J 3.0, C*H*H), 6.49 (1 H, d, J 3.0, CH*H*), 3.06 (6 H, s, 2 × CH_3); δ_C (100 MHz, DMSO-d_6) 163.3 (q, J_{B-C} 49), 135.5, 135.2, 133.28, 133.25, 133.0, 132.6, 132.4, 128.4, 125.3 (q, J_{B-C} 3), 122.7, 121.5, 26.7; m/z (ESI$^+$) 243.0 [M(^{79}Br)−BPh$_4$]$^+$, 245.0 [M(^{81}Br)−BPh$_4$]$^+$; HRMS (ESI$^+$) $C_{10}H_{12}{}^{79}BrS^+$ [M−BPh$_4$]$^+$ requires 242.9838; found 242.9840; $C_{10}H_{12}{}^{81}BrS^+$ [M−BPh$_4$]$^+$ requires 244.9817; found 244.9821.

(2-Bromo-1-(4-fluorophenyl)ethyl)dimethylsulfonium bromide. Prepared according to general method GP1 and was used without further purification in the next step; 1.0 g, 97% yield; white solid; We

were unable to characterize this compound by NMR as the bromide salt due to decomposition in DMSO-d_6.

(2-Bromo-1-(4-fluorophenyl)ethyl)dimethylsulfonium tetraphenylborate. Prepared according to GP2 and was used in the next step without further purification; 1.65 g, 95% yield; white solid; An analytically pure sample was prepared by recrystallization from acetone. mp 175−176 °C (acetone); ν_{max} (film)/cm^{-1} 1508, 1422, 1215, 1162, 844, 739, 729, 705; δ_H (400 MHz, DMSO-d_6) 7.60 (2 H, dd, *J* 8.7, 5.3, ArH), 7.40 (2 H, t, *J* 8.7, ArH), 7.24−7.14 (8 H, m, ArH), 6.93 (8 H, t, *J* 7.3, ArH), 6.80 (4 H, t, *J* 7.3, ArH), 5.26 (1 H, dd, *J* 9.9, 5.9, CH), 4.39 (1 H, dd, *J* 10.8, 5.9, C*H*H), 4.34 (1 H, ABX type br. t, *J* 10.5, CH*H*), 2.88 (3 H, s, CH_3), 2.62 (3 H, s, CH_3); δ_C (100 MHz, DMSO-d_6) 163.3 (q, J_{B-C} 49), 163.1 (d, J_{F-C} 249), 135.5 (q, J_{B-C} 1), 132.0 (d, J_{F-C} 9), 126.2 (d, J_{F-C} 3), 125.3 (q, J_{B-C} 3), 121.5, 116.5 (d, J_{F-C} 22), 58.0, 29.1, 23.9, 22.4; δ_F (376 MHz, DMSO-d_6) −110.1 (1 F, m, CF); *m*/*z* (ESI$^+$) 263.0 [M(^{79}Br)−BPh$_4$]$^+$, 265.0 [M(^{81}Br)−BPh$_4$]$^+$; HRMS (ESI$^+$) $C_{10}H_{13}{}^{79}BrFS^+$ [M−BPh$_4$]$^+$ requires 262.9900; found 262.9903. $C_{10}H_{13}{}^{81}BrFS^+$ [M−BPh$_4$]$^+$ requires 264.9879; found 264.9887.

(1-(4-Fluorophenyl)vinyl)dimethylsulfonium tetraphenylborate ***(12f)****.* Prepared according to GP3; 1.24 g, 97% yield; white solid; mp 214−215 °C (acetone); ν_{max} (film)/cm^{-1} 1601, 1505, 1479, 1423, 1407, 1229, 1164, 835, 732, 703, 667; δ_H (400 MHz, DMSO-d_6) 7.68−7.59 (2 H, m, ArH), 7.38−7.35 (2 H, m, ArH), 7.23−7.10 (8 H, m, ArH), 6.92 (8 H, t, *J* 7.3, ArH), 6.79 (4 H, t, *J* 7.3, ArH), 6.54 (1 H, d, *J* 3.4, C*H*H), 6.39 (1 H, d, *J* 3.4, CH*H*), 3.03 (6 H, s, 2 × CH_3); δ_C (100 MHz, DMSO-d_6) 163.3 (q, J_{B-C} 49), 163.2 (d, J_{F-C} 249), 135.7, 135.5, 130.3 (d, J_{F-C} 9), 128.8 (d, J_{F-C} 3), 127.4, 125.3 (q, J_{B-C} 3), 121.5, 116.3 (d, J_{F-C} 22), 26.5; δ_F (376 MHz, DMSO-d_6) −110.2 (1 F, m, CF); *m*/*z* (ESI$^+$) 183.1 [M−BPh$_4$]$^+$; HRMS (ESI$^+$) $C_{10}H_{12}FS^+$ [M−BPh$_4$]$^+$ requires 183.0638; found 183.0644.

(2-Bromo-1-(4-(trifluoromethyl)phenyl)ethyl)dimethylsulfonium bromide. Prepared according to general method GP1 and was used without further purification in the next step; 0.71 g, 60% yield; white solid; We were unable to characterize this compound by NMR as the bromide salt due to decomposition in DMSO-d_6.

(2-Bromo-1-(4-(trifluoromethyl)phenyl)ethyl)dimethylsulfonium tetraphenylborate. Prepared according to GP2 and was used in the next step without further purification; 0.95 g, 95% yield; white solid; An analytically pure sample was prepared by recrystallization from acetone; mp 185−187 °C (acetone); ν_{max} (film)/cm^{-1} 1329, 1104, 1071, 729, 705; δ_H (400 MHz, DMSO-d_6) 7.94 (2 H, d, *J* 8.2 ArH), 7.77 (2 H, d, *J* 8.2, ArH), 7.21−7.14 (8 H, m, ArH), 6.92 (8 H, t, *J* 7.3, ArH), 6.79 (4 H, t, *J* 7.3, ArH), 5.36 (1 H, dd, *J* 9.7, 6.0, CH), 4.46−4.33 (2 H, m, CH_2), 2.93 (3 H, s, CH_3), 2.68 (3 H, s, CH_3); δ_C (100 MHz, DMSO-d_6) 163.4 (q, J_{B-C} 49, C), 135.5 (CH), 134.7 (C), 130.60 (CH), 130.55 (q, J_{F-C} 29, C), 126.4 (q, J_{F-C} 3, CH), 125.3 (q, J_{B-C} 3,CH), 121.5 (CH), 57.6 (CH), 28.7 (CH_2), 23.9 (CH_3), 22.8 (CH_3), CF_3 signal not observed; δ_F (376 MHz, DMSO-d_6) −61.0 (3 F, m, CF_3); *m*/*z* (ESI$^+$) 313.0 [M(^{79}Br)−BPh$_4$]$^+$, 315.0 [M(^{81}Br)−BPh$_4$]$^+$; HRMS (ESI$^+$) $C_{11}H_{13}{}^{79}BrF_3S^+$ [M−BPh$_4$]$^+$ requires 312.9868; found 312.9861. $C_{11}H_{13}{}^{81}BrF_3S^+$ [M−BPh$_4$]$^+$ requires 314.9847; found 314.9839.

(1-(4-(Trifluoromethyl)phenyl)vinyl)dimethylsulfonium tetraphenylborate ***(12g)****.* Prepared according to GP3; 0.64 g, 99% yield; white solid; mp 196−198 °C (acetone); ν_{max} (film)/cm^{-1} 1426, 1326, 1110, 1064, 847, 707, 733; δ_H (400 MHz, DMSO-d_6) 7.92 (2 H, d, *J* 8.2, ArH), 7.82 (2 H, d, *J* 8.2, ArH), 7.24−7.09 (8 H, m, ArH), 6.92 (8 H, t, *J* 7.3, ArH), 6.79 (4 H, t, *J* 7.3, ArH), 6.73 (1 H, d, *J* 3.6, C*H*H), 6.56 (1 H, d, *J* 3.6, CH*H*), 3.09 (6 H, s, 2 × CH_3); δ_C (100 MHz, DMSO-d_6) 163.4 (q, J_{B-C} 49, C), 136.5 (C), 135.5 (CH), 130.4 (q, J_{F-C} 31, C), 129.3 (CH_2), 128.7 (CH), 126.1 (q, J_{F-C} 4, CH), 125.3 (q, J_{B-C} 3, CH), 125.2 (C), 121.5 (CH), 121.1 (q, J_{F-C} 274, CF_3), 26.6 (CH_3); δ_F (376 MHz, DMSO-d_6) −61.3 (3 F, m, CF_3); *m*/*z* (ESI$^+$) 233.1 [M−BPh$_4$]$^+$; HRMS (ESI$^+$) $C_{11}H_{12}F_3S^+$ [M−BPh$_4$]$^+$ requires 233.0606; found 233.0605.

(2-Bromo-1-(3,4-(dimethoxyphenyl)ethyl)dimethylsulfonium bromide. Prepared according to general method GP1 and was used without further purification in the next step; 1.1 g, 93% yield; white solid; We were unable to characterize this compound by NMR as the bromide salt due to decomposition in DMSO-d_6.

(2-Bromo-1-(3,4-(dimethoxyphenyl)ethyl)dimethylsulfonium tetraphenylborate. Prepared according to GP2 however the tetraphenylborate salt was soluble in the solvent system used for counterion exchange, the addition of excess H_2O (100 mL) caused the *title compound* to precipitate which was then used in the next step without further purification; 1.61 g, 99% yield; white solid; We were unable to characterize this compound by NMR due to decomposition of the material over time.

(1-(3,4-(Dimethoxyphenyl)vinyl)dimethylsulfonium tetraphenylborate ***(12h)****.* Prepared according to GP3; 1.42 g, 92% yield; white solid; mp 174−175 °C (acetone); ν_{max} (film)/cm^{-1} 3053, 3005, 1515, 1423, 1261, 1244, 1142, 1022, 853, 706, 734; δ_H (400 MHz, DMSO-d_6) 7.22−7.13 (8 H, m, ArH), 7.15−7.04 (3 H, m, ArH), 6.92 (8 H, t, *J* 7.3, ArH), 6.79 (4 H, t, *J* 7.3, ArH), 6.49 (1 H, d, *J* 3.3, C*H*H), 6.27 (1 H, d, *J* 3.3, CH*H*), 3.82 (3 H, s, OCH_3), 3.81 (3 H, s, OCH_3), 3.03 (6 H, s, CH_3); δ_C (100 MHz, DMSO-d_6) 163.3 (q, J_{B-C} 49, C), 150.6 (C), 149.0 (C), 136.6 (C), 135.5 (CH), 125.3 (q, J_{B-C} 3, CH), 124.8 (CH_2), 124.5 (C), 121.5 (CH), 120.4 (CH), 111.8 (CH), 110.9 (CH), 55.71 (OCH_3), 55.67 (OCH_3), 26.4 (CH_3); *m*/*z* (ESI$^+$) 225.1 [M−BPh$_4$]$^+$; HRMS (ESI$^+$) $C_{12}H_{17}O_2S^+$ [M−BPh$_4$]$^+$ requires 225.0944; found 225.0941.

(2-Bromo-1-(4-((tert-butyldimethylsilyl)oxy)phenyl)ethyl)dimethylsulfonium bromide. Prepared according to general method GP1 and was used without further purification in the next step; (n.b., Upon warming to room temperature it was found to be important that the precipitate was isolated immediately (prolonged stirring at room temperature eventually lead to a homogeneous solution, the product could still be precipitated by the addition of Et_2O; however, this was at the expense of lower isolated yields)); 2.83 g, 62% yield; pale yellow solid; We were unable to characterize this compound by NMR as the bromide salt due to decomposition in DMSO-d_6.

(2-Bromo-1-(4-((tert-butyldimethylsilyl)oxy)phenyl)ethyl)dimethylsulfonium tetraphenylborate. Prepared according to GP2 and was used in the next step without further purification; (n.b., The precipitate formed during this reaction was difficult to manipulate; therefore, the residue isolated by filtration was used in the next step directly).

(1-(4-((tert-Butyldimethylsilyl)oxy)phenyl)vinyl)dimethylsulfonium tetraphenylborate ***(12i)****.* Prepared according to GP3; 1.25 g, 97% yield; pale yellow solid; (n.b., recrystallization from hot acetone was only effective on a small scale suitable for the preparation of a melting point sample); The rest of the data reported were obtained by analysis of the amorphous material; mp 182−183 °C (acetone); ν_{max} (film)/cm^{-1} 1602, 1505, 1286, 1271, 1258, 913, 836, 811, 743; δ_H (400 MHz, DMSO-d_6) 7.49 (2 H, d, *J* 8.6, ArH), 7.26−7.13 (8 H, m, ArH), 7.00 (2 H, d, *J* 8.6, ArH) 6.93 (8 H, t, *J* 7.3, ArH), 6.80 (4 H, t, *J* 7.3, ArH), 6.47 (1 H, d, *J* 3.3, C*H*H), 6.28 (1 H, d, *J* 3.3, CH*H*), 3.03 (6 H, s, 2 × CH_3), 0.97 (9 H, s, 3 × CH_3), 0.24 (6 H, s, 2 × CH_3); δ_C (100 MHz, DMSO-d_6) 163.4 (q, J_{B-C} 49, C), 157.0 (C), 136.4 (C), 135.5 (CH), 129.2 (CH), 125.4 (C), 125.3 (q, J_{B-C} 3, CH), 125.1 (CH_2), 121.5 (CH), 120.5 (CH), 26.5 (CH_3), 25.5 (CH_3), 17.9 (C), −4.6 (CH_3); *m*/*z* (ESI$^+$) 295.2 [M−BPh$_4$]$^+$; HRMS (ESI$^+$) $C_{16}H_{27}OSSi^+$ [M−BPh$_4$]$^+$ requires 295.1546; found 295.1544.

(2-Bromo-1-(4-(methoxycarbonyl)phenyl)ethyl)dimethylsulfonium bromide. Prepared according to general method GP1 and was used without further purification in the next step; 2.1 g, 55% yield; white solid; δ_H (400 MHz, DMSO-d_6) 8.09 (2 H, d, *J* 8.2, ArH), 7.74 (2 H, d, *J* 8.2, ArH), 5.56 (1 H, dd, *J* 9.7, 5.9, CH), 4.48−4.35 (2 H, m, CH_2), 3.88 (3 H, s, OCH_3), 3.02 (3 H, s, CH_3), 2.74 (3 H, s, CH_3); δ_C (100 MHz, DMSO-d_6) 166.1, 135.7, 131.7, 130.6, 130.4, 58.0, 52.9, 29.4, 24.5, 23.3.

(2-Bromo-1-(4-(methoxycarbonyl)phenyl)ethyl)dimethylsulfonium tetraphenylborate. Prepared according to GP2 and was used in the next step without further purification; (n.b., This material did not precipitate from the reaction solvent and instead a gum formed, which was difficult to manipulate. The reaction solvent was decanted to yield a sticky gum which was used in the next step directly).

(1-(4-(Methoxycarbonyl)phenyl)vinyl)dimethylsulfonium tetraphenylborate ***(12j)****.* Prepared according to GP3; 2.0 g, 66% yield; yellow solid; (n.b., recrystallization from acetone was only effective on

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a small scale suitable for the preparation of a melting point sample). The rest of the data reported were obtained by analysis of the amorphous material; mp 193−194 °C (acetone); ν_{max} (film)/cm^{-1} 1707, 1426, 1286, 1116, 741, 731, 706; δ_H (400 MHz, DMSO-d_6) 8.08 (2 H, d, *J* 8.3, ArH), 7.74 (2 H, d, *J* 8.3, ArH), 7.23−7.10 (8 H, m, ArH), 6.92 (8 H, t, *J* 7.3, ArH), 6.78 (4 H, t, *J* 7.3, ArH), 6.71 (1 H, d, *J* 3.5, C*H*H), 6.51 (1 H, d, *J* 3.5, CH*H*), 3.87 (3 H, s, CH_3), 3.06 (6 H, s, 2 × CH_3); δ_C (100 MHz, DMSO-d_6) 165.5 (C═O), 163.4 (q, J_{B-C} 49, C), 136.8 (C), 135.9 (C), 135.5 (CH), 131.0 (C), 129.9 (CH), 128.6 (CH_2), 127.9 (CH), 125.3 (q, J_{BC} 3, CH), 121.5 (CH), 52.5 (CH_3), 26.6 (CH_3); *m*/*z* (ESI$^+$) 223.1 [M−BPh_4]$^+$; HRMS (ESI$^+$) $C_{12}H_{15}O_2S^+$ [M−BPh_4]$^+$ requires 223.0787; found 223.0790.

General Procedure for the Synthesis of Epoxyannulation/Cyclopropanation-Annulation Products (GP4). A flask was charged with the amine substrate (1.0 equiv) and α-substituted vinylsulfonium salt (1.3 equiv) in anhydrous MeCN (0.1 M). Distilled DBU (2.0 equiv) was then added to the resulting solution at 0 °C under an atmosphere of nitrogen, before allowing the reaction mixture to stir for 1 h at room temperature. The reactions were then quenched with a sat. citric acid solution (15 mL per 0.5 mmol) unless otherwise stated and extracted with CH_2Cl_2 (3 × 20 mL per 0.5 mmol). The combined organic layers were dried over $MgSO_4$ or passed through a hydrophobic frit (SPE polyethylene) and concentrated under a vacuum. If applicable, NMR spectra of the resulting crude material to determine the diastereomeric ratio were measured before purification by flash column chromatography on silica gel, eluting with EtOAc/PE or Et_2O/PE, to yield the desired fused heterocycle.

*(1SR,5RS)-1,5-Diphenyl-3-tosyl-6-oxa-3-azabicyclo[3.1.0]hexane (**11**).* Prepared according to GP4 with **9**[54] and **12a**; 71 mg, 63% yield; with **9**[54] and **12b**; 89 mg, 66% yield; with **9**[54] and **12c**; 85 mg, 63% yield; white solid; R_f 0.2 (10% EtOAc/Cyclohexane); mp 175−177 °C (EtOAc); ν_{max} (film)/cm^{-1} 1340, 1161, 1096, 1008, 971, 811, 757, 694, 666; δ_H (400 MHz, $CDCl_3$) 7.76 (2 H, d, *J* 8.5, ArH), 7.35 (2 H, d, *J* 8.5, ArH), 7.27−7.12 (10 H, m, ArH), 3.99 (ABq, 4 H, $\Delta\delta_{AB}$ 0.05, *J* 12.2, 2 × CHH), 2.45 (3 H, s, $ArCH_3$); δ_C (100 MHz, $CDCl_3$) 143.8 (C), 135.1 (C), 131.6 (C), 129.9 (CH), 128.5 (CH), 128.4 (CH), 127.7 (CH), 126.8 (CH), 72.5 (C), 53.0 (CH_2), 21.8 (CH_3); *m*/*z* (ESI$^+$) 392.1 [M + H]$^+$; HRMS (ESI$^+$) $C_{23}H_{22}NO_3S^+$ [M + H]$^+$ requires 392.1315; found 392.1310.

*(±)-(1SR,5RS)-1-(4-Bromophenyl)-5-phenyl-3-tosyl-6-oxa-3-azabicyclo[3.1.0]hexane (**13d**).* Prepared according to GP4 with **9**[54] and **12d**; 127 mg, 78% yield; yellow solid; R_f 0.2 (10% EtOAc/Cyclohexane); mp 162−164 °C (EtOAc); ν_{max} (film)/cm^{-1} 1338, 1162, 1116, 1011, 822, 760, 695, 661; δ_H (400 MHz, $CDCl_3$) 7.82−7.74 (2 H, m, ArH), 7.42−7.31 (4 H, m, ArH), 7.27−7.15 (5 H, m, ArH), 7.11−7.04 (2 H, m, ArH), 4.05 (1 H, d, *J* 12.3, C*H*H), 4.04 (1 H, d, *J* 12.3, CH*H*), 3.98 (1 H, d, *J* 12.3, C*H*H), 3.97 (1 H, d, *J* 12.3, CH*H*), 2.48 (3 H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 143.8 (C), 134.9 (C), 131.5 (CH), 131.1 (C), 130.6 (C), 129.8 (CH), 128.6 (CH), 128.4 (CH), 128.3 (CH), 127.6 (CH), 126.6 (CH), 122.7 (C), 72.7 (CO), 71.9 (CO), 52.9 (CH_2), 52.6 (CH_2), 21.6 (CH_3); *m*/*z* (ESI$^+$) 492.0 [M(^{79}Br) + Na]$^+$, 494.0 [M(^{81}Br) + Na]$^+$; HRMS (ESI$^+$) $C_{23}H_{20}{}^{79}BrNNaO_3S^+$ [M + Na]$^+$ requires 492.0239; found 492.0222. $C_{23}H_{20}{}^{81}BrNNaO_3S^+$ [M + Na]$^+$ requires 494.0219; found 494.0209.

*cis- and trans-N-(1-Benzoyl-2-(2-bromophenyl)cyclopropyl)-4-methylbenzenesulfonamide (cis-**14**) and (trans-**14**).* Prepared according to GP4 with **9**[54] and **12e**; 141 mg, 43% yield, *cis*:*trans* 1:1; yellow solid; R_f 0.2 (40% Et_2O/*n*-Pentane); ν_{max} (film)/cm^{-1} 3284, 3236, 1673, 1652, 1416, 1322, 1156, 1021, 749, 658; δ_H (400 MHz, $CDCl_3$) 7.63 (1 H, dd, *J* 7.9, 1.3, ArH), 7.50 (2 H, d, *J* 8.3, ArH), 7.46−7.37 (6 H, m, ArH), 7.36−7.03 (14 H, m, ArH), 7.02−6.91 (2 H, m, ArH), 6.84 (1 H, dd, *J* 7.9, 1.3, ArH), 6.17 (1 H, s, NH), 5.04 (1 H, s, NH), 3.25 (1 H, br. t, *J* 9.3, CH), 2.94 (1 H, br. t, *J* 9.0, CH), 2.59 (1 H, dd, *J* 9.3, 6.3, C*H*H), 2.48 (1 H, dd, *J* 9.0, 6.1, C*H*H), 2.39 (3 H, s, CH_3), 2.37 (3 H, s, CH_3), 2.26 (1 H, dd, *J* 9.0, 6.1, CH*H*), 2.16 (1 H, dd, *J* 9.3, 6.3, CH*H*); δ_C (100 MHz, $CDCl_3$) 200.4 (C═O), 196.2 (C═O), 143.9 (C), 136.73 (C), 136.67 (C), 136.48 (C), 136.46 (C), 133.1 (C), 133.0 (CH), 132.6 (C), 132.5 (CH), 131.9 (CH), 131.7 (CH), 130.1 (CH), 129.71 (CH), 129.68 (CH), 129.67 (CH), 129.2 (CH), 129.0 (CH), 128.2 (CH), 128.1 (CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 127.5 (CH), 127.4 (CH), 127.2 (CH), 126.8 (C), 126.6 (C), 49.7 (C), 47.4 (C), 38.3 (CH), 37.2 (CH), 21.67 (CH_3), 21.64 (CH_3), 18.3 (CH_2), 17.5 (CH_2); *m*/*z* (ESI$^+$) 470.0 [M(^{79}Br) + H]$^+$, 472.0 [M(^{81}Br) + H]$^+$; HRMS (ESI$^+$) $C_{23}H_{21}{}^{79}BrNO_3S^+$ [M + H]$^+$ requires 470.0420; found 470.0408. $C_{23}H_{21}{}^{81}BrNO_3S^+$ [M + H]$^+$ requires 472.0400; found 472.0390.

*(±)-(1SR,5RS)-1-(4-Fluorophenyl)-5-phenyl-3-tosyl-6-oxa-3-azabicyclo[3.1.0]hexane (**13f**).* Prepared according to GP4 with **9**[54] and **12f**; 79 mg, 55% yield; white solid; R_f 0.2 (10% EtOAc/Cyclohexane); mp 141−142 °C (EtOAc); ν_{max} (film)/cm^{-1} 1515, 1335, 1165, 838, 813, 664; δ_H (400 MHz, $CDCl_3$) 7.84−7.73 (2 H, m, ArH), 7.42−7.35 (2 H, m, ArH), 7.26−7.12 (7 H, m, ArH), 6.96−6.84 (2 H, m, ArH), 4.06 (1 H, d, *J* 12.2, C*H*H), 4.03 (1 H, d, *J* 12.2, CH*H*), 3.98 (1 H, d, *J* 12.2, C*H*H), 3.97 (1 H, d, *J* 12.2, CH*H*), 2.49 (3 H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 162.6 (d, J_{F-C} 247, C), 143.9 (C), 135.0 (C), 131.4 (C), 129.9 (CH), 128.7 (d, J_{F-C} 2, CH), 128.6 (CH), 128.5 (CH), 127.7 (CH), 127.5 (d, J_{F-C} 3, C), 126.8 (CH), 115.5 (d, J_{F-C} 22, CH), 72.6 (C), 72.0 (C), 52.94 (CH_2), 52.90 (CH_2), 21.8 (CH_3); δ_F (376 MHz, $CDCl_3$) −112.7 (1 F, m, CF); *m*/*z* (ESI$^+$) 410.1 [M + H]$^+$; HRMS (ESI$^+$) $C_{23}H_{20}FNNaO_3S^+$ [M + Na]$^+$ requires 432.1040; found 432.1031.

*(±)-(1RS,5SR)-1-Phenyl-3-tosyl-5-(4-(trifluoromethyl)phenyl)-6-oxa-3-azabicyclo[3.1.0]hexane (**13g**).* Prepared according to GP4 with **9**[54] and **12g**; 112 mg, 71% yield; white solid; R_f 0.2 (10% EtOAc/Cyclohexane); mp 147−149 °C (EtOAc); ν_{max} (film)/cm^{-1} 1341, 1322, 1163, 1123, 1108, 673; δ_H (400 MHz, $CDCl_3$) 7.82−7.74 (2 H, m, ArH), 7.49−7.43 (2 H, m, ArH), 7.50−7.34 (2 H, m, ArH), 7.35−7.30 (2 H, m, ArH), 7.24−7.16 (5 H, m, ArH), 4.09 (1 H, d, *J* 12.3, C*H*H), 4.07 (1 H, d, *J* 12.3, CH*H*), 4.00 (1 H, d, *J* 12.3, C*H*H), 3.99 (1 H, d, *J* 12.3, CH*H*), 2.47 (3 H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 143.9 (C), 135.7 (C), 134.5 (C), 130.9 (C), 130.6 (q, J_{F-C} 33, C), 129.9 (CH), 128.8 (CH), 128.5 (CH), 127.7 (CH), 127.2 (CH), 126.7 (CH), 125.4 (q, J_{F-C} 4, CH), 123.9 (q, J_{F-C} 274, CF_3), 73.1 (C), 71.9 (C), 53.1 (CH_2), 52.7 (CH_2), 21.7 (CH_3); δ_F (376 MHz, $CDCl_3$) −62.8 (3 F, m, CF_3); *m*/*z* (ESI$^+$) 460.3 [M + H]$^+$; HRMS (ESI$^+$) $C_{24}H_{21}F_3NO_3S^+$ [M + H]$^+$ requires 460.1189; found 460.1180.

*(±)-(1SR,5RS)-1-(3,4-Dimethoxyphenyl)-5-phenyl-3-tosyl-6-oxa-3-azabicyclo[3.1.0]hexane (**13h**).* Prepared according to GP4 with **9**[54] and **12h**; 105 mg, 67% yield; white solid; R_f 0.2 (10% EtOAc/Cyclohexane); mp 155−156 °C (EtOAc); ν_{max} (film)/cm^{-1} 1339, 1162, 1115, 1011, 822, 760, 694, 661, 674; δ_H (400 MHz, $CDCl_3$) 7.81−7.71 (2 H, m, ArH), 7.37−7.31 (2 H, d, ArH), 7.21 (5 H, br. s, ArH), 6.78 (1 H, dd, *J* 8.3, 2.0, ArH), 6.69 (1 H, d, *J* 8.3, ArH), 6.56 (1 H, *J* 2.0, ArH), 4.06 (1 H, d, *J* 12.1, C*H*H), 4.01 (1 H, d, *J* 12.2, CH*H*), 3.96 (1 H, d, *J* 12.1, CH*H*), 3.94 (1 H, d, *J* 12.2, C*H*H), 3.77 (3 H, s, OCH_3), 3.63 (3 H, s, OCH_3), 2.44 (3 H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 149.2 (C), 148.7 (C), 143.8 (C), 135.1 (C), 131.8 (C), 129.9 (CH), 128.6 (CH), 128.4 (CH), 127.7 (CH), 127.0 (CH), 124.1 (C), 119.4 (CH), 110.9 (CH), 109.9 (CH), 72.6 (C), 72.0 (C), 55.9 (OCH_3), 55.8 (OCH_3), 53.2 (CH_2), 52.6 (CH_2), 21.8 (CH_3); *m*/*z* (ESI$^+$) 474.1 [M + Na]$^+$; HRMS (ESI$^+$) $C_{25}H_{25}NNaO_5S^+$ [M + Na]$^+$ requires 474.1346; found 474.1342.

*(±)-(1SR,5RS)-1-(4-((tert-Butyldimethylsilyl)oxy)phenyl)-5-phenyl-3-tosyl-6-oxa-3-azabicyclo[3.1.0]hexane (**13i**) and (±)-(RS)-4-(4-((tert-Butyldimethylsilyl)oxy)phenyl)-3-phenyl-1-tosyl-2,3-dihydro-1H-pyrrol-3-ol (**15**).* Prepared according to GP4 with **9**[54] and **12i** for the reaction setup; however, purification was altered. The reaction mixture was loaded directly and purified by flash column chromatography on silica gel (30% Et_2O/*n*-Pentane) **13i**; 80 mg, 30% yield; yellow solid; R_f 0.3 (30% Et_2O/*n*-Pentane); mp 148−150 °C (EtOAc); ν_{max} (film)/cm^{-1} 1514, 1333, 1254, 1163, 917, 763, 663; δ_H (400 MHz, $CDCl_3$) 7.76 (2 H, d, *J* 8.2, ArH), 7.35 (2 H, d, *J* 8.2, ArH), 7.23−7.11 (5 H, m, ArH), 7.02 (2 H, d, *J* 8.7, ArH), 6.65 (2 H, d, *J* 8.7, ArH), 4.02 (1 H, d, *J* 12.2, C*H*H), 4.00 (1 H, d, *J* 12.2, C*H*H), 3.95 (1 H, d, *J* 12.2, CH*H*), 3.94 (1 H, d, *J* 12.2, CH*H*), 2.46 (3 H, s, CH_3), 0.92 (9 H, s, CH_3), 0.12 (6 H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 155.9 (C), 143.8 (C), 135.0 (C), 131.8 (C), 129.9 (CH), 128.5 (CH), 128.3 (CH), 128.1 (CH), 127.7 (CH), 126.8 (CH), 124.3 (C), 120.0 (CH), 72.31 (C), 72.27 (C), 52.94 (CH_2), 52.92 (CH_2), 25.7 (CH_3), 21.8 (CH_3), 18.3 (C), −4.4 (CH_3); *m*/*z* (ESI$^+$) 544.2 [M + Na]$^+$;

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HRMS (ESI$^+$) $C_{29}H_{35}NNaO_4SSi^+$ [M + Na]$^+$ requires 544.1948; found 544.1945; and side-product **15**; 45 mg, 20% yield; yellow oil; R_f 0.2 (30% Et_2O/*n*-Pentane); ν_{max} (film)/cm^{-1} 1253, 1170, 1090, 907, 774, 669; δ_H (400 MHz, $CDCl_3$) 7.73 (2 H, d, *J* 8.2, ArH), 7.35 (2 H, d, *J* 8.2, ArH), 7.23−7.10 (5 H, m, ArH), 7.03 (1 H, s, C═CH), 7.02 (2 H, d, *J* 8.6, ArH), 6.60 (2 H, d, *J* 8.6, ArH), 3.87 (1 H, d, *J* 12.2, C*H*H), 3.69 (1 H, d, *J* 12.2, CH*H*), 2.46 (3 H, s, CH_3), 2.15 (1 H, s, OH), 0.93 (9 H, s, CH_3), 0.13 (6 H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 155.1 (C), 144.5 (C), 143.2 (C), 132.7 (C), 130.1 (CH), 129.0 (C), 128.4 (CH), 128.1 (CH), 127.8 (CH), 127.5 (CH), 127.4 (C═*C*H), 125.3 (CH), 124.2 (C), 120.2 (CH), 84.9 (C), 65.7 (CH_2), 25.7 (CH_3), 21.8 (CH_3), 18.3 (C), −4.3 (CH_3); *m*/*z* (ESI$^+$) 544.2 [M + Na]$^+$; HRMS (ESI$^+$) $C_{29}H_{35}NNaO_4SSi^+$ [M + Na]$^+$ requires 544.1948; found 544.1930.

*4-(4-Phenyl-1-tosyl-1H-pyrrol-3-yl)phenol (**16**).* Prepared according to GP4 with **9**[54] and **12i**; Purification by flash column chromatography on neutral alumina eluting nonpolar materials with 50% EtOAc/Petrol, followed by elution of the pyrrole with 10% MeOH/CH_2Cl_2. Further purification on silica gel eluting the *title compound* with 50% Et_2O/Petrol gave **16**; 116 mg, 43% yield; yellow solid; R_f 0.2 (50% Et_2O/*n*-Pentane); mp 54−55 °C (EtOAc); ν_{max} (film)/cm^{-1} 3461, 1365, 1166, 1088, 1050, 669; δ_H (400 MHz, $CDCl_3$) 7.86 (2 H, d, *J* 8.3, ArH), 7.35 (2 H, d, *J* 8.3, ArH), 7.31−7.24 (4 H, m, ArH), 7.24−7.17 (3 H, m, ArH), 7.07 (2 H, d, *J* 8.6, ArH), 6.75 (2 H, d, *J* 8.6, ArH), 2.45 (3 H, s, CH_3); Signal due to OH not observed; δ_C (100 MHz, $CDCl_3$) 155.0 (C), 145.2 (C), 135.9 (C), 133.6 (C), 130.1 (CH), 129.9 (CH), 128.6 (C), 128.5 (CH), 128.34 (C), 128.27 (CH), 127.1 (CH), 126.9 (CH), 125.8 (C), 118.8 (CH), 118.3 (CH), 115.3 (CH), 21.7 (CH_3); *m*/*z* (ESI$^+$) 412.1 [M + Na]$^+$; HRMS (ESI$^+$) $C_{23}H_{19}NNaO_3S^+$ [M + Na]$^+$ requires 412.0978; found 412.0979.

*(±)-Methyl 4-((1SR,5RS)-5-phenyl-3-tosyl-6-oxa-3-azabicyclo-[3.1.0]hexan-1-yl)benzoate (**13j**).* Prepared according to GP4 with **9**[54] and **12j**; 109 mg, 69% yield; white solid; R_f 0.32 (30% EtOAc/*n*-Pentane); mp 68−70 °C (EtOAc); ν_{max} (film)/cm^{-1} 1717, 1339, 1276, 1159, 1102, 1013, 773, 762, 698, 670, 663; δ_H (400 MHz, $CDCl_3$) 7.94−7.65 (4 H, m, ArH), 7.39−7.20 (4 H, m, ArH), 7.27−7.07 (5 H, m, ArH), 4.07 (1 H, d, *J* 12.2, C*H*H), 4.03 (1 H, d, *J* 12.5, C*H*H), 3.97 (1 H, d, *J* 12.2, CH*H*), 3.96 (1 H, d, *J* 12.5, CH*H*), 3.83 (3 H, s, OCH_3), 2.45 (3 H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 166.5, 143.9, 136.5, 135.0, 131.0, 130.2, 129.9, 129.6, 128.7, 128.4, 127.7, 126.8, 126.7, 73.1, 72.1, 53.0, 52.6, 52.2, 21.7; *m*/*z* (ESI$^+$) 450.1 [M + H]$^+$; HRMS (ESI$^+$) $C_{25}H_{24}NO_5S^+$ [M + H]$^+$ requires 450.1370; found 450.1363.

*(±)-(1SR,5RS)-1-(4-Bromophenyl)-3-((4-nitrophenyl)sulfonyl)-5-phenyl-6-oxa-3-aza bicyclo[3.1.0]hexane (**18a**).* Prepared according to GP4 with **17a**[54] and **12d**; 84 mg, 54% yield; white solid; R_f 0.3 (50% Et_2O/*n*-Pentane); mp 171−173 °C (EtOAc); ν_{max} (film)/cm^{-1} 1523, 1348, 1169, 973, 820, 735, 685; δ_H (400 MHz, $CDCl_3$) 8.45−8.38 (2 H, m, ArH), 8.07−7.99 (2 H, m, ArH), 7.37−7.28 (2 H, m, ArH), 7.25−7.19 (3 H, m, ArH), 7.17−7.08 (2 H, m, ArH), 7.06−6.96 (2 H, m, ArH), 4.12 (1 H, d, *J* 12.9, C*H*H), 4.11 (1 H, d, *J* 12.8, C*H*H), 3.98 (1 H, d, *J* 12.9, CH*H*), 3.97 (1 H, d, *J* 12.8, CH*H*); δ_C (100 MHz, $CDCl_3$) 150.3 (C), 143.8 (C), 131.6 (CH), 130.4 (C), 129.9 (C), 128.9 (CH), 128.7 (CH), 128.5 (CH), 128.2 (CH), 126.5 (CH), 124.4 (CH), 122.9 (C), 72.4 (C), 71.7 (C), 53.1 (CH_2), 52.8 (CH_2); *m*/*z* (ESI$^+$) 523.0 [M(^{79}Br) + Na]$^+$, 525.0 [M(^{81}Br) + Na]$^+$; HRMS (ESI$^+$) $C_{22}H_{17}{}^{79}BrN_2NaO_5S^+$ [M + Na]$^+$ requires 522.9934; found 522.9922. $C_{22}H_{17}{}^{81}BrN_2NaO_5S^+$ [M + Na]$^+$ requires 524.9913; found 524.9912.

*(±)-(1SR,5RS)-1-(4-Bromophenyl)-5-phenyl-3-((2-(trimethylsilyl)-ethyl)sulfonyl)-6-oxa-3-azabicyclo[3.1.0]hexane (**18b**).* Prepared according to GP4 with **17b**[78] and **12d**; 96 mg, 60% yield; orange solid; R_f 0.3 (25% EtOAc/Cyclohexane); mp 118−120 °C (EtOAc); ν_{max} (film)/cm^{-1} 1325, 1149, 1009, 820, 760, 695; δ_H (400 MHz, $CDCl_3$) 7.40−7.34 (2 H, m, ArH), 7.29−7.23 (5 H, m, ArH), 7.15 (2 H, m, ArH), 4.10 (1 H, d, *J* 12.9, C*H*H), 4.09 (1 H, d, *J* 12.9, C*H*H), 4.02 (1 H, d, *J* 12.9, CH*H*), 4.01 (1 H, d, *J* 12.9, CH*H*), 3.03 (2 H, *AA′XX′*, CH_2), 1.14 (2 H, *AA′XX′*, $SiCH_2$), 0.11 (9 H, s, 3 × CH_3); δ_C (100 MHz, $CDCl_3$) 131.6 (CH), 131.0 (C), 130.6 (C), 128.7 (CH), 128.5 (CH), 128.3 (CH), 126.7 (CH), 122.7 (C), 72.7 (C), 71.9 (C), 53.1 (CH_2), 52.8 (CH_2), 46.9 (CH_2), 10.2 ($SiCH_2$), 1.9 (3 × CH_3); *m*/*z* (ESI$^+$) 502.0 [M(^{79}Br) + Na]$^+$, 504.0 [M(^{81}Br) + Na]$^+$; HRMS (ESI$^+$) $C_{21}H_{26}{}^{79}BrNNaO_3SSi^+$ [M + Na]$^+$ requires 502.0478; found 502.0462. $C_{21}H_{26}{}^{81}BrNNaO_3SSi^+$ [M + Na]$^+$ requires 504.0458; found 504.0443.

*(±)-(1SR,5RS)-1-Ethyl-5-phenyl-3-tosyl-6-oxa-3-azabicyclo[3.1.0]-hexane (**18c**).* Prepared according to GP4 with **17c**[8] and **12a**; 10 mg, 71% yield; colorless oil; R_f 0.3 (10% EtOAc/*n*-Pentane); ν_{max} (film)/cm^{-1} 1339, 1159, 1093, 813, 762, 699, 666; δ_H (400 MHz, $CDCl_3$) 7.72 (2 H, d, *J* 8.2, ArH), 7.39−7.27 (7 H, m, ArH), 3.87 (1 H, d, *J* 12.0, C*H*H), 3.76 (2 H, app. t, *J* 11.9, 2 × CH), 3.55 (1 H, d, *J* 11.8, CH*H*), 2.44 (3 H, s, CH_3), 1.46 (1 H, dq, *J* 14.7, 7.7, C*H*H), 1.36 (1 H, dq, *J* 14.7, 7.7, CH*H*), 0.88 (3 H, t, *J* 7.7, CH_3); δ_C (100 MHz, $CDCl_3$) 143.6 (C), 134.9 (C), 132.3 (C), 129.7 (CH), 128.5 (CH), 128.4 (CH), 127.5 (CH), 126.6 (CH), 72.6 (C), 70.3 (C), 52.6 (CH_2), 51.0 (CH_2), 21.6 (CH_3), 20.9 (CH_2), 9.5 (CH_3); *m*/*z* (ESI$^+$) 344.1 [M + H]$^+$; HRMS (ESI$^+$) $C_{19}H_{22}NO_3S^+$ [M + H]$^+$ requires 344.1315; found 344.1303.

*(±)-(1RS,5SR)-1-Phenyl-5-(thiophen-2-yl)-3-tosyl-6-oxa-3-azabi-cyclo[3.1.0]hexane (**18d**).* Prepared according to GP4 with **17d**[79] and **12a**; 80 mg, 60% yield; pale yellow solid; R_f 0.2 (30% Et_2O/*n*-Pentane); mp 175−176 °C (EtOAc); ν_{max} (film)/cm^{-1} 1337, 1154, 1030, 806, 691, 666; δ_H (400 MHz, $CDCl_3$) 8.22 (2 H, d, *J* 8.1, ArH), 7.38 (2 H, d, *J* 8.1, ArH), 7.23−7.09 (5 H, m, ArH), 7.07 (1 H, dd, *J* 5.1, 1.0, ArH), 6.74 (1 H, dd, *J* 5.1, 3.7, ArH), 6.45 (1 H, dd, *J* 3.6, 1.0, ArH), 4.16 (1 H, d, *J* 10.4, C*H*H), 3.99 (1 H, d, *J* 11.2, C*H*H), 3.73 (1 H, d, *J* 11.2, CH*H*), 3.64 (1 H, d, *J* 10.4, CH*H*), 2.47 (3 H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 144.1 (C), 142.3 (C), 138.9 (C), 134.0 (C), 130.0 (CH), 128.3 (CH), 128.1 (CH), 127.8 (CH), 126.6 (CH), 125.9 (CH), 125.7 (CH), 124.9 (CH), 82.9 (C), 82.1 (C), 58.1 (CH_2), 57.4 (CH_2), 21.8 (CH_3); *m*/*z* (ESI$^+$) 398.1 [M + H]$^+$; HRMS (ESI$^+$) $C_{21}H_{20}NO_3S_2^+$ [M + H]$^+$ requires 398.0879; found 398.0878.

*(+)-(1S,2R,5R)-1,2,5-Triphenyl-3-tosyl-6-oxa-3-azabicyclo[3.1.0]-hexane (**18e**).* Prepared according to GP4 with **17e**[7] (er (*R*:*S*) >99:1) and **12a**; however, the reaction was carried out at −20 to 0 °C over 4 h to minimize epimerization of the stereocenter *α*- to nitrogen, (^{1}H NMR of the crude dr >95:5). Purification by flash column chromatography (25% EtOAc/Cyclohexane) gave **18e**; 61 mg, 65% yield, er (*R*:*S*) 97:3; white solid; R_f 0.4 (4:6, Et_2O/PE); mp 185−187 °C (EtOAc); ν_{max} (film)/cm^{-1} 2256, 1310, 1146, 1091, 723, 697; δ_H (400 MHz, $CDCl_3$) 7.49 (2 H, d, *J* 8.5, ArH), 7.23−7.06 (15 H, m, ArH), 7.01−6.96 (2 H, m, ArH), 5.15 (1 H, s, C*H*Ph), 4.38 (1 H, d, *J* 11.5, C*H*H), 4.17 (1 H, d, *J* 11.5, C*H*H), 2.41 (3 H, s, $ArCH_3$); δ_C (100 MHz, $CDCl_3$) 143.7 (C), 135.8 (C), 135.1 (C), 132.2 (C), 131.2 (C), 129.5 (CH), 128.7 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.2 (CH), 1278.1 (CH), 127.9 (CH), 127.7 (CH), 127.4 (CH), 126.6 (CH), 77.3 (C), 71.3 (C), 67.6 (CH), 53.4 (CH_2), 21.7 (CH_3); *m*/*z* (ESI$^+$) 468.2 [M + H]$^+$; HRMS (ESI$^+$) $C_{29}H_{26}NO_3S^+$ [M + H]$^+$ requires 468.1628; found 468.1625; $[\alpha]_D^{20}$ = +20 (*c*. 1.00, $CHCl_3$). Chiral supercritical fluid chromatography (Chiralpak IA column (4.6 × 250 mm × 5 *μ*m), 125 bar CO_2, 40 °C, 4 mL/min, 20% cosolvent (MeOH); t_R = 3.86 min (major enantiomer), 4.51 min (minor enantiomer), *er* 97:3.

*(±)-(1SR,5RS)-1-(4-Bromophenyl)-5-(4-chlorophenyl)-3-tosyl-6-oxa-3-azabicyclo[3.1.0]hexane (**18f**).* Prepared according to GP4 with **17f**[54] and **12d**; 124 mg, 80% yield; white solid; R_f 0.2 (30% EtOAc/*n*-Pentane); mp 139−140 °C (EtOAc); ν_{max} (film)/cm^{-1} 1328, 1162, 1092, 1006, 825, 759, 667; δ_H (400 MHz, $CDCl_3$) 7.77−7.70 (2 H, m, ArH), 7.38−7.28 (4 H, m, ArH), 7.19−7.13 (2 H, m, ArH), 7.13−7.07 (2 H, m, ArH), 7.06−7.00 (2 H, m, ArH), 3.99 (2 H, d, *J* 12.3, CH_2), 3.92 (2 H, d, *J* 12.3, CH_2), 2.44 (3 H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 144.0 (C), 134.9 (C), 134.7 (C), 131.7 (CH), 130.3 (C), 129.9 (CH), 129.8 (C), 128.8 (CH), 128.4 (CH), 128.1 (CH), 127.6 (CH), 122.9 (C), 72.22 (C), 72.17 (C), 52.71 (CH_2), 52.65 (CH_2), 21.7 (CH_3); *m*/*z* (ESI$^+$) 526.0 [M(^{79}Br^{35}Cl) + Na]$^+$, 528.0 [M(^{79}Br^{37}Cl + ^{81}Br^{35}Cl) + Na]$^+$, 530.0 [M(^{81}Br^{37}Cl) + Na]$^+$; HRMS (ESI$^+$) $C_{23}H_{19}{}^{79}Br^{35}ClNNaO_3S^+$ [M + Na]$^+$ requires 525.9850; found 525.9846. $C_{23}H_{19}{}^{79}Br^{37}ClNNaO_3S^+$ + $C_{23}H_{19}{}^{81}Br^{35}ClNNaO_3S^+$ [M + Na]$^+$ requires 527.9829; found 527.9825.

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$C_{23}H_{19}{}^{81}Br^{37}ClNNaO_3S^+$ [M + Na]$^+$ requires 529.9800; found 529.9806.

*(±)-(1SR,5RS)-1-(4-Bromophenyl)-5-(4-chlorophenyl)-3-((4-nitrophenyl)sulfonyl)-6-oxa-3-azabicyclo[3.1.0]hexane (**18g**).* Prepared according to GP4 with **17g**[54] and **12d**; 77 mg, 51% yield; white solid; R_f 0.3 (50% Et_2O/*n*-Pentane); mp 200−201 °C (EtOAc); ν_{max} (film)/cm^{-1} 1527, 1352, 1168, 975, 821, 735, 685; δ_H (400 MHz, $CDCl_3$) 8.48−8.39 (2 H, m, ArH), 8.08−8.00 (2 H, m, ArH), 7.41−7.33 (2 H, m, ArH), 7.24−7.18 (2 H, m, ArH), 7.13−7.06 (2 H, m, ArH), 7.06−7.00 (2 H, m, ArH), 4.11 (2 H, d, *J* 12.8, 2 × C*H*H), 3.97 (2 H, d, *J* 12.8, 2 × CH*H*); δ_C (100 MHz, $CDCl_3$) 150.4 (C), 143.8 (C), 135.1 (C), 131.9 (CH), 129.7 (C), 129.1 (C), 129.0 (CH), 128.8 (CH), 128.3 (CH), 128.0 (CH), 124.6 (CH), 123.3 (C), 72.1 (C), 72.0 (C), 53.0 (CH_2), 52.9 (CH_2); *m*/*z* (ESI$^+$) 557.0 [M($^{79}Br^{35}Cl$) + Na]$^+$, 559.0 [M($^{79}Br^{37}Cl$ + $^{81}Br^{35}Cl$) + Na]$^+$, 561.0 [M($^{81}Br^{37}Cl$) + Na]$^+$; HRMS (ESI$^+$) $C_{22}H_{16}{}^{79}Br^{35}ClN_2NaO_5S^+$ [M + Na]$^+$ requires 556.9544; found 556.9536. $C_{22}H_{16}{}^{79}Br^{37}ClN_2NaO_5S^+$ + $C_{22}H_{16}{}^{81}Br^{35}ClN_2NaO_5S^+$ [M + Na]$^+$ requires 558.9524; found 558.9522. $C_{22}H_{16}{}^{81}Br^{37}ClN_2NaO_5S^+$ [M + Na]$^+$ requires 560.9495; found 560.9511.

*(±)-1-((1RS,5RS,6RS)-1-Phenyl-3-tosyl-3-azabicyclo[3.1.0]hexan-6-yl)ethan-1-one (**20a**).* Prepared according to GP4 with **19a**[3] and **12a** in CH_2Cl_2; 100 mg, 72% yield, dr >95:5; white solid; Crystals suitable for X-ray analysis (CCDC 1006748) were grown as described in the SI; R_f 0.2 (30% EtOAc/*n*-Pentane); mp 107−109 °C (EtOAc); ν_{max} (film)/cm^{-1} 1698, 1345, 1162, 1099, 700, 664; δ_H (400 MHz, $CDCl_3$) 7.71−7.63 (2 H, m, ArH), 7.34−7.27 (2 H, m, ArH), 7.34−7.15 (3 H, m ArH), 7.14−7.04 (2 H, m, ArH), 4.08 (1 H, d, *J* 9.7, C*H*H), 3.74 (1 H, d, 9.4, CH*H*), 3.23−3.16 (1 H, m, C*H*H), 3.06 (1 H, d, *J* 9.7, CH*H*), 2.64−2.60 (2 H, m, 2 × CH), 2.41 (3 H, s, CH_3), 2.04 (3 H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 202.7 (C═O), 144.0 (C), 134.0 (C), 133.0 (C), 130.0 (CH), 128.9 (CH), 128.5 (CH), 127.9 (CH), 127.7 (CH), 55.4 (CH_2), 50.0 (CH_2), 43.4 (C), 37.2 (CH), 31.9 (CH), 28.3 (CH_3), 21.7 (CH_3); *m*/*z* (ESI$^+$) 356.1 [M + H]$^+$; HRMS (ESI$^+$) $C_{20}H_{21}NNaO_3S^+$ [M + Na]$^+$ requires 378.1134; found 378.1126.

*(±)-Methyl (1RS,5RS,6RS)-1-phenyl-3-tosyl-3-azabicyclo[3.1.0]-hexane-6-carboxylate (**20b**).* Prepared according to GP4 with **19b**[3] and **12a** in CH_2Cl_2; 62 mg, 45% yield, dr >95:5; colorless oil; The stereochemistry was assigned in analogy to **20a**; R_f 0.2 (50% Et_2O/*n*-Pentane); ν_{max} (film)/cm^{-1} 1728, 1347, 1160, 1102, 1031, 1015, 699, 662; δ_H (400 MHz, $CDCl_3$) 7.72−7.62 (2 H, m, ArH), 7.34−7.29 (2 H, m, ArH), 7.30−7.23 (3 H, m, ArH), 7.19−7.12 (2 H, m, ArH), 3.99 (1 H, d, *J* 9.6, C*H*H), 3.77 (1 H, d, *J* 9.5 C*H*H), 3.42 (3 H, s, CH_3), 3.27 (1 H, dd, *J* 9.5, 3.5, CH*H*), 3.07 (1 H, d, *J* 9.6, CH*H*), 2.53 (1 H, app. t, *J* 3.6, CH), 2.42 (3 H, s, CH_3), 2.32 (1 H, d, *J* 3.8, CH); δ_C (100 MHz, $CDCl_3$) 170.1 (C═O), 144.0 (C), 134.6 (C), 133.2 (C), 129.9 (CH), 129.0 (CH), 128.5 (CH), 128.0 (CH), 127.7 (CH), 55.5 (CH_2), 51.8 (CH_3), 50.0 (CH_2), 40.9 (C), 29.1 (CH), 28.1 (CH), 21.7 (CH_3); *m*/*z* (ESI$^+$) 394.1 [M + Na]$^+$; HRMS (ESI$^+$) $C_{20}H_{21}NNaO_4S^+$ [M + Na]$^+$ requires 394.1083; found 394.1078.

*(±)-tert-Butyl (1RS,5RS,6RS)-1-phenyl-3-tosyl-3-azabicyclo[3.1.0]-hexane-6-carboxylate (**20c**).* Prepared according to GP4 with **19c**[3] and **12a** in CH_2Cl_2; 83 mg, 63% yield, dr >95:5; The stereochemistry was assigned in analogy to **20a**; R_f 0.1 (20% Et_2O/*n*-Pentane); mp 121−123 °C (EtOAc); ν_{max} (film)/cm^{-1} 1732, 1343, 1161, 1147, 1106, 788, 701, 663; δ_H (400 MHz, $CDCl_3$) 7.66 (2 H, d, *J* 8.2, ArH), 7.31 (2 H, d, *J* 8.2, ArH), 7.27−7.03 (5 H, m, ArH), 3.97 (1 H, d, *J* 9.6, C*H*H), 3.74 (1 H, d, *J* 9.4, C*H*H), 3.25 (1 H, dd, *J* 9.4, 3.7, CH*H*), 3.05 (1 H, d, *J* 9.6, CH*H*), 2.46 (1 H, app. t, *J* 3.7, CH), 2.41 (3 H, s, CH_3), 2.20 (1 H, d, *J* 3.7, CH), 1.12 (9 H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 168.6 (C═O), 143.9 (C), 134.9 (C), 133.3 (C), 129.9 (CH), 129.3 (CH), 128.4 (CH), 127.8 (CH), 127.6 (CH), 80.8 (C), 55.4 (CH_2), 50.0 (CH_2), 40.5 (C), 30.3 (CH), 27.8 (CH_3), 27.3 (CH), 21.6 (CH_3); *m*/*z* (ESI$^+$) 436.2 [M + H]$^+$; HRMS (ESI$^+$) $C_{23}H_{27}NNaO_4S^+$ [M + Na]$^+$ requires 436.1553; found 436.1549.

*(±)-(1RS,5RS,6RS)-1-Phenyl-3-tosyl-3-azabicyclo[3.1.0]hexane-6-carbonitrile (**20d**).* Prepared according to GP4 with **19d**[3] and **12a** in CH_2Cl_2; 76 mg, 53% yield; dr >95:5; The stereochemistry was assigned in analogy to **20a**; R_f 0.1 (50% Et_2O/*n*-Pentane); ν_{max} (film)/cm^{-1} 2240, 1346, 1162, 1095, 1026, 698, 665; δ_H (400 MHz, $CDCl_3$) 7.68 (2 H, d, *J* 8.2, ArH), 7.42−7.29 (5 H, m, ArH), 7.25−7.17 (2 H, m, ArH), 4.03 (1 H, d, *J* 9.8, C*H*H), 3.82 (1 H, d, *J* 10.0, C*H*H), 3.23 (1 H, dd, *J* 10.0, 3.6, CH*H*), 3.14 (1 H, d, *J* 9.8, CH*H*), 2.45 (1 H, app. t, *J* 3.6, CH), 2.43 (3 H, s, CH_3), 2.11 (1 H, d, *J* 3.6, CH); δ_C (100 MHz, $CDCl_3$) 144.5 (C), 133.1 (C), 132.7 (C), 130.1 (CH), 129.1 (CH), 128.8 (CH), 128.3 (CH), 127.7 (CH), 117.9 (CN), 53.8 (CH_2), 49.4 (CH_2), 39.0 (C), 29.0 (CH), 21.7 (CH_3), 13.3 (CH); *m*/*z* (ESI$^+$) 361.1 [M + Na]$^+$; HRMS (ESI$^+$) $C_{19}H_{18}N_2NaO_2S^+$ [M + Na]$^+$ requires 361.0981; found 361.0975.

*(±)-tert-Butyl (1SR,5RS)-1-(4-bromophenyl)-5-phenyl-6-oxa-3-azabicyclo[3.1.0]hexane-3-carboxylate (**21**).* To a solution of **18b** (25 mg, 50 μmol) in THF (0.4 mL) was added tetrabutylammonium fluoride (27 mg, 100 μmol) at rt and the resulting reaction mixture stirred at reflux for 5 h, monitoring by TLC, until consumption of the starting material was observed. The crude reaction mixture was purified directly by flash column chromatography (10% MeOH/CH_2Cl_2) to give (±)-(1*SR*,5*RS*)-1-(4-bromophenyl)-5-phenyl-6-oxa-3-azabicyclo[3.1.0]hexane; 10 mg, 63% yield; yellow solid; R_f 0.2 (10% MeOH/CH_2Cl_2); *m*/*z* (ESI$^+$) 316.0 [M(^{79}Br) + H]$^+$, 318.0 [M(^{81}Br) + H]$^+$; HRMS (ESI$^+$) $C_{16}H_{15}{}^{79}BrNO^+$ [M + H]$^+$ requires 316.0332; found 316.0330. $C_{16}H_{15}{}^{81}BrNO^+$ [M + H]$^+$ requires 318.0312; found 318.0311. n.b., For ease of characterization the free amine was protected as the *N*-Boc protected compound. To a solution of (±)-(1*SR*,5*RS*)-1-(4-bromophenyl)-5-phenyl-6-oxa-3-azabicyclo-[3.1.0]hexane (13 mg, 41 μmol) and di-*tert*-butyl dicarbonate (10 mg, 45 μmol) in CH_2Cl_2 (0.3 mL) was added triethylamine (6 μL, 45 μmol) at rt and the reaction was left to stir overnight. The crude reaction mixture was purified directly by flash column chromatography (100% CH_2Cl_2) to give the *title compound* **21** (1:1 mixture of rotamers); 12 mg, 72% yield; white solid; R_f 0.3 (100% CH_2Cl_2); mp 76−78 °C (CH_2Cl_2); ν_{max} (film)/cm^{-1} 1694, 1391, 1167, 1119, 823, 762, 696; δ_H (500 MHz, $CDCl_3$) 7.38−7.32 (2 H, m, ArH), 7.30−7.22 (5 H, m, ArH), 7.19−7.12 (2 H, m, ArH), 4.13 and 4.12 (1 H, d, *J* 12.9; d, *J* 12.9, C*H*H), 4.06 and 4.05 (1 H, d, *J* 12.8; d, *J* 12.8, C*H*H), 3.96 and 3.95 (1 H, d, *J* 12.9; d, *J* 12.9, CH*H*), 3.93 and 3.91 (1 H, d, *J* 12.8; d, *J* 12.8, CH*H*), 1.49 and 1.48 (9 H, 2 × s, CH_3); δ_C (125 MHz, $CDCl_3$) 154.9 (C═O), 132.13 (C), 132.09 (C), 131.7 (C), 131.61 (C), 131.57 (CH), 128.6 (CH), 128.53 (CH), 128.51 (CH), 128.48 (CH), 126.9 (CH), 126.8 (CH), 122.5 (C), 80.3 (C), 73.4 (C), 72.8 (C), 72.5 (C), 71.9 (C), 52.2 (CH_2), 51.8 (CH_2), 51.5 (CH_2), 51.2 (CH_2), 28.6 (CH_3); *m*/*z* (ESI$^+$) 438.1 [M(^{79}Br) + Na]$^+$, 440.1 [M(^{81}Br) + Na]$^+$; HRMS (ESI$^+$) $C_{21}H_{22}{}^{79}BrNNaO_3^+$ [M + Na]$^+$ requires 438.0675; found 438.0665. $C_{21}H_{22}{}^{81}BrNNaO_3^+$ [M + Na]$^+$ requires 440.0665; found 440.0648.

*(±)-tert-Butyl (1SR,5RS)-1-(4-bromophenyl)-5-(4-chlorophenyl)-6-oxa-3-azabicyclo[3.1.0]hexane-3-carboxylate (**22**).* To a solution of **18g** (25 mg, 50 μmol) in acetone (0.4 mL) was added 2-mercaptoethanol (7 μL, 100 μmol) and 1,8-diazabicycloundec-7-ene (15 μL, 100 μmol) at rt and the resulting reaction mixture stirred for 0.5 h, monitoring by TLC, until consumption of the starting material was observed. The crude reaction mixture was purified directly by flash column chromatography (10% MeOH/CH_2Cl_2) to give (±)-(1*SR*,5*RS*)-1-(4-bromophenyl)-5-(4-chlorophenyl)-6-oxa-3-azabicyclo[3.1.0]hexane; 16 mg, 92% yield; yellow solid; R_f 0.2 (10% MeOH/CH_2Cl_2); *m*/*z* (ESI$^+$) 350.0 [M($^{79}Br^{35}Cl$) + H]$^+$, 352.0 [M($^{79}Br^{37}Cl$ + $^{81}Br^{35}Cl$) + H]$^+$, 354.0 [M($^{81}Br^{37}Cl$) + H]$^+$; HRMS (ESI$^+$) $C_{16}H_{14}{}^{79}Br^{35}ClNO^+$ [M + H]$^+$ requires 349.9942; found 349.9930. $C_{16}H_{14}{}^{79}Br^{37}ClNO^+$ + $C_{16}H_{14}{}^{81}Br^{35}ClNO^+$ [M + H]$^+$ requires 351.9921; found 351.9910; $C_{16}H_{14}{}^{81}Br^{37}ClNO^+$ [M + H]$^+$ requires 353.9892; found 353.9882; (n.b., For ease of characterization the free amine was protected as the *N*-Boc protected compound). To a solution of (±)-(1*SR*,5*RS*)-1-(4-bromophenyl)-5-(4-chlorophenyl)-6-oxa-3-azabicyclo[3.1.0r (16 mg, 46 μmol) and di-*tert*-butyl dicarbonate (11 mg, 50 μmol) in CH_2Cl_2 (0.3 mL) was added triethylamine (7 μL, 50 μmol) at rt and the reaction was left to stir overnight. The crude reaction mixture was purified directly by flash column chromatography (100% CH_2Cl_2) to give the *title compound* **22** (1:1 mixture of rotamers); 17 mg, 82% yield; white solid; R_f 0.3 (100% CH_2Cl_2); mp 134−135 °C (CH_2Cl_2); ν_{max} (film)/cm^{-1} 1696, 1392, 1167, 1121,

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824; δ_H (500 MHz, $CDCl_3$) 7.43−7.35 (2 H, m, ArH), 7.26−7.17 (4 H, m, ArH), 7.18−7.12 (2 H, m, ArH), 4.12 (1 H, d, *J* 12.9, C*H*H), 4.05 (1 H, d, *J* 12.8, C*H*H), 3.93 (1 H, d, *J* 12.9, CH*H*), 3.91 (1 H, d, *J* 12.8, CH*H*), 1.49 (9 H, s, CH_3); δ_C (125 MHz, $CDCl_3$) 154.8 (C=O), 134.6 (C), 131.7 (CH), 131.3 (C), 131.2 (C), 130.72 (C), 130.69 (C), 128.8 (CH), 128.51 (CH), 128.45 (CH), 128.21 (CH), 128.16 (CH), 122.8 (C), 80.4 (C), 72.8 (C), 72.7 (C), 72.21 (C), 72.16 (C), 51.9 (CH_2), 51.8 (CH_2), 51.3 (CH_2), 51.2 (CH_2), 28.6 (CH_3); *m*/*z* (ESI^+) 472.0 [M($^{79}Br^{35}Cl$) + Na]$^+$, 474.0 [M($^{79}Br^{37}Cl$ + $^{81}Br^{35}Cl$) + Na]$^+$, 476.0 [M($^{81}Br^{37}Cl$) + Na]$^+$; HRMS (ESI^+) $C_{21}H_{21}{}^{79}Br^{35}ClNNaO_3{}^+$ [M + Na]$^+$ requires 472.0286; found 472.0297. $C_{21}H_{21}{}^{79}Br^{37}ClNNaO_3{}^+$ + $C_{21}H_{21}{}^{81}Br^{35}ClNNaO_3{}^+$ [M + Na]$^+$ requires 474.0266; found 474.0274. $C_{21}H_{21}{}^{81}Br^{37}ClNNaO_3{}^+$ [M + Na]$^+$ requires 476.0236; found 476.0259.

*(±)-(3RS,4SR)-3,4-Diphenyl-1-tosylpyrrolidin-3-ol (cis-**23**) and (±)-(3RS,4RS)-3,4-Diphenyl-1-tosylpyrrolidin-3-ol (trans-**23**).* Conditions A: A solution of (1*RS*,5*SR*)-1,5-diphenyl-3-tosyl-6-oxa-3-azabicyclo[3.1.0]hexane **11** (87 mg, 0.22 mmol) in ethyl acetate (11 mL) was hydrogenated on a H-cube (settings: 25 °C, 1 mL/min flow rate, 1 bar) using a 10% Pd/C CatCart 30 as the catalyst. The resulting organic solution was concentrated under a vacuum (^{1}H NMR of the crude *dr* 10:1 *cis*-**23**:*trans*-**23**) and purified by preparative HPLC to give the *title compounds* ***cis*-23**; 58 mg, 67% yield; white solid; and *trans*-**23**; 6 mg, 7% yield; white solid. Conditions B: To a flame-dried flask containing (1*RS*,5*SR*)-1,5-diphenyl-3-tosyl-6-oxa-3-azabicyclo-[3.1.0]hexane **11** (100 mg, 0.26 mmol) in ethyl acetate (13 mL) under nitrogen was added Pd/C (28 mg, 10 mol % Pd). The atmosphere was then evacuated and replaced with hydrogen gas in a three cycle vacuum/hydrogen exchange procedure via balloon. The reaction was then left to stir vigorously overnight at rt connected to a balloon of hydrogen. The catalyst was then filtered off under an inert atmosphere washing with ethyl acetate (3 × 14 mL) ensuring that the catalyst remains wet with solvent at all times. The resulting filtrate was concentrated under a vacuum (^{1}H NMR of the crude *dr* 10:1 *cis*-**23**:*trans*-**23**) and purified by preparative HPLC to give the *title compounds* ***cis*-23**; 55 mg, 54% yield; white solid; and *trans*-**23**; 5 mg, 5% yield; white solid; Crystals suitable for X-ray analysis of the major (CCDC 1006746) and minor diastereoisomers (CCDC 1006747) were grown as reported in the SI. *cis*-**23** major diastereomer; R_f 0.3 (30% EtOAc/*n*-Pentane); mp 118−120 °C (EtOAc); ν_{max} (film)/cm^{-1} 3485, 1323, 1314, 1147, 1101, 1054, 811, 772, 756, 695, 669; δ_H (400 MHz, $CDCl_3$) 7.92−7.78 (2 H, m, ArH), 7.44−7.38 (2 H, m, ArH), 7.36−7.13 (8 H, m, ArH), 6.93−6.88 (2 H, m, ArH), 3.99 (1 H, dd, *J* 9.4, 7.6, C*H*H), 3.89 (1 H, dd, *J* 11.6, 1.4, C*H*H), 3.86 (1 H, dd, *J* 11.2, 9.4, CH*H*), 3.74 (1 H, dd, *J* 11.2, 7.6, CH), 3.72 (1 H, d, *J* 11.6, CH*H*), 2.50 (3 H, s, CH_3), 1.69 (1 H, d, *J* 1.4, OH); δ_C (100 MHz, $CDCl_3$) 143.8 (C), 141.3 (C), 134.3 (C), 133.4 (C), 129.9 (CH), 128.8 (CH), 128.7 (CH), 128.6 (CH), 128.1 (CH), 127.84 (CH), 127.81 (CH), 125.3 (CH), 81.9 (C), 62.5 (CH_2), 55.0 (CH), 50.9 (CH_2), 21.8 (CH_3); *m*/*z* (ESI^+) 416.1 [M + Na]$^+$; HRMS (ESI^+) $C_{23}H_{23}NNaO_3S^+$ [M + Na]$^+$ requires 416.1291; found 416.1282. *trans*-**23** minor diastereomer; R_f 0.3 (30% EtOAc/*n*-Pentane); mp 186−187 °C (EtOAc); ν_{max} (film)/cm^{-1} 3490, 1338, 1161, 1115, 1071, 1040, 1011, 822, 760, 695, 674; δ_H (400 MHz, $CDCl_3$) 7.85 (2 H, d, *J* 8.2, ArH), 7.39 (2 H, d, *J* 8.2, ArH), 7.20−6.99 (6 H, m, ArH), 6.99−6.90 (2 H, m, ArH), 6.78−6.69 (2 H, m, ArH), 4.17 (1 H, d, *J* 11.1, C*H*H), 3.95 (1 H, dd, *J* 9.9, 7.2, C*H*H), 3.80 (1 H, dd, *J* 9.9, 4.6, CH*H*), 3.54 (1 H, d, *J* 11.1, CH*H*), 3.37 (1 H, dd, *J* 7.2, 4.6, PhCH), 2.48 (3 H, s, CH_3), 1.84 (1 H, s, OH); δ_C (100 MHz, $CDCl_3$) 143.9 (C), 139.7 (C), 137.6 (C), 134.3 (C), 130.0 (CH), 128.3 (CH), 128.2 (CH), 128.1 (CH), 128.0 (CH), 127.8 (CH), 127.2 (CH), 126.0 (CH), 83.3 (C), 57.9 (CH_2), 56.0 (CH), 52.3 (CH_2), 21.8 (CH_3); *m*/*z* (ESI^+) 416.1 [M + Na]$^+$; HRMS (ESI^+) $C_{23}H_{23}NNaO_3S^+$ [M + Na]$^+$ requires 416.1291; found 416.1285.

*3,4-Diphenyl-1-tosyl-2,5-dihydro-1H-pyrrole (**24**).* A flame-dried flask was charged with zinc dust (38 mg, 0.57 mmol) under nitrogen. Anhydrous Et_2O (1 mL) was then added followed by distilled chlorotrimethylsilane (72 μL, 0.57 mmol). The suspension was then stirred under nitrogen for 15 min at rt, before removal of solvent and volatiles under a vacuum. The activated zinc was then dried under high vacuum for 1 h. To the activated zinc was added bis(cyclopentadienyl) titanium dichloride (114 mg, 0.46 mmol) and the flask was purged with three cycles of nitrogen/vacuum. Anhydrous degassed THF (0.6 mL) was then added and the reaction stirred under nitrogen for 10 min at rt. The green titanium solution was then added quickly via syringe to a second flame-dried flask containing **11** (75 mg, 0.19 mmol) in anhydrous degassed THF (1.9 mL). The reaction mixture was then stirred for 10 min before the addition of 10% H_2SO_4 (5 mL) to quench the reaction. The reaction was then extracted with CH_2Cl_2 (3 × 10 mL) and the combined organic phases dried over $MgSO_4$, with the collected filtrate concentrated under a vacuum. Purification by flash column chromatography (20% Et_2O/Pentane) gave the title compound **24**; 40 mg, 56% yield; white solid; *Spectroscopic data were consistent with those reported in the literature.*[81]

*N-(2-Bromo-2-phenylethyl)-4-methyl-N-(2-oxo-2-phenylethyl)-benzenesulfonamide (**10**).* The tentatively assigned *title compound* **10** formed as a side product when using 4-methyl-*N*-(2-oxo-2-phenylethyl)benzenesulfonamide[54] **9** and α-substituted vinyl sulfonium salts with a bromide counterion. We were unable to separate this compound from product **11** and the characterization data reflects this; R_f 0.2 (10% EtOAc/Cyclohexane); ν_{max} (film)/cm^{-1} 1704 (deduced by subtraction). Signals from **10**: δ_H (400 MHz, $CDCl_3$) 7.72−7.63 (4 H, m, ArH), 7.61−7.54 (1 H, m, ArH), 7.47−7.38 (4 H, m, ArH), 7.33−7.24 (5 H, m, ArH), 5.30 (1 H, br. t, *J* 7.7, CH), 4.93 (1 H, d, *J* 19, C*H*H), 4.27 (1 H, d, *J* 19, CH*H*), 4.00 (1 H, dd, *J* 15.7, 7.7, C*H*H), 3.82 (1 H, dd, *J* 15.7, 7.7, CH*H*), 2.42 (3 H, s, CH_3); see ref 82 for explanation of large observed geminal coupling constants. δ_C (100 MHz, $CDCl_3$) 193.7 (C), 143.9 (C) 139.5 (C), 136.5 (C), 134.7 (C), 134.0 (CH), 129.7 (CH), 129.07 (CH), 129.04 (CH), 129.0 (CH), 128.1 (CH), 127.9 (CH), 127.7 (CH), 56.0 (CH_2), 54.7 (CH_2), 52.7 (CH), 21.75 (CH_3); *m*/*z* (ESI^+) 494.0 [M(^{79}Br) + Na]$^+$, 496.0 [M(^{81}Br) + Na]$^+$; HRMS (ESI^+) $C_{23}H_{22}{}^{79}BrNNaO_3S^+$ [M + Na]$^+$ requires 494.0396; found 494.0389. $C_{23}H_{22}{}^{81}BrNNaO_3S^+$ [M + Na]$^+$ requires 496.0376; found 496.0363. Signals from **11** for reference: ν_{max} (film)/cm^{-1} 1340, 1161, 1096, 1008, 971, 811, 757, 694, 666; δ_H (400 MHz, $CDCl_3$) 7.76 (2 H, d, *J* 8.5, ArH), 7.35 (2 H, d, *J* 8.5, ArH), 7.27−7.12 (10 H, m, ArH), 3.99 (ABq, 4 H, $\Delta\delta_{AB}$ 0.05, *J* 12.2, 2 × CHH), 2.45 (3 H, s, $ArCH_3$); δ_C (100 MHz, $CDCl_3$) 143.8 (C), 135.1 (C), 131.6 (C), 129.9 (CH), 128.6 (CH), 128.4 (CH), 127.7 (CH), 126.8 (CH), 72.5 (C), 53.0 (CH_2), 21.8 (CH_3);

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H NMR and ^{13}C NMR spectra and where appropriate HPLC traces/NOESY 1D/^{19}F/COSY/HSQC/HMBC NMR spectra for compounds **8a−c**, **12a−j**, **11**, **13d−g**, **14−16**, **18a−g**, **20a−d**, **21**, **22**, *cis*-**23**, *trans*-**23**, **24**, **10**. X-ray crystallography data (CIF) for **12a**, **20a**, *cis*- and *trans*-**23**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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