Supporting Information
For

Electrophile dependent mechanisms in the asymmetric trapping of α-lithio-*N*-(*tert*-butoxythiocarbonyl)azetidine

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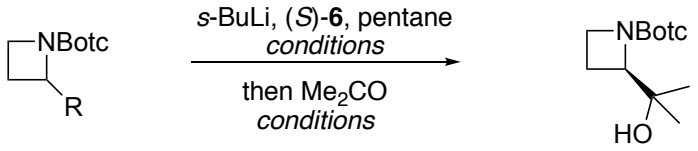
1. Additional results and discussion

(a) Full table of acetone trapping studies



5 R = H
(±)-**10** R = $SnMe_3$

(*R*)-**8**

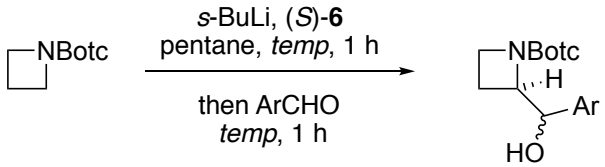
Entry[a]	5 or 10[b]	Metallation temp (time)	Trapping temp (time)	Yield (*R*)-8	er	Recovered 5
1	**5**	−78 °C (1 h)	−78 °C (1 h)	61%	89:11	21%
2	**10**	−78 °C (1 h)	−78 °C (1 h)	57%	90:10	30%
3	**10**	−78 °C (5 min)	−78 °C (1 h)	64%	85:15	25%
4	**10**	−78 °C (30min)	−78 °C (1 h)	45%	86:14	32%
5	**5**	−78 °C (1 h) −98 °C (10 min)	−98 °C (1 h)	55%	88:12	35%
6	**5**	−78 °C (1 min)	−78 °C (5 min)	28%	58:42	70%
7	**5** (0.5 equiv acetone)	−78 °C (1 h)	−78 °C (1 h)	29%	61:39	56%
8	**5** (0.1 equiv acetone)	−78 °C (1 h)	−78 °C (1 h)	2%	60:40	49%
9	**5**	−98 °C (1 h)	−98 °C (1 h)	38%	65:35	42%
10[c]	**5**	−98 °C (3 h)	−98 °C (1 h)	51%	86:14	45%
11	**5** (with $SnMe_4$)	−98 °C (1 h)	−98 °C (1 h)	38%	65:35	37%
12	**10**	−98 °C (1 h)	−98 °C (1 h)	41%	84:16	25%
13	**10** (0.5 equiv acetone)	−78 °C (1 h)	−78 °C (1 h)	19%	66:34	41%
14	**10** (0.1 equiv acetone)	−78 °C (1 h)	−78 °C (1 h)	7%	58:42	52%
15[d]	(*R*)-**10** (67:33 er)	−98 °C (1 min)	−98 °C (1 h)	39%	51:49	17%
16	**10**	Experimental procedure **C** (5 equiv)		1%	52:48	87% (**10**)

*[a] Unless noted, all reactions 0.25 mmol scale and trapped with 3 equiv of acetone. [b] All reactions with stannane (±)-**10** gave 0-7% recovered stannane **10** (determined to be racemic by HPLC) and 0-7% 2,4-substituted stannane **SI-1**. [c] Performed on a 0.35 mmol scale. [d] Performed on a 0.1 mmol scale with (±)-**6** DIANANE and gave 15 % recovered stannane **10** {enantioenriched}.*

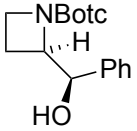
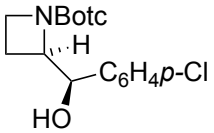
Table S1. Full table of acetone trapping studies.

(b) Partial configurational stability of α-Li 5 at −98 °C when trapping with aromatic aldehydes

Reduced enantioselectivities were observed for lithiation—electrophile trapping of *N*-Botc azetidine **5** with aromatic aldehydes after 1 h at −98 °C compared to at −78 °C (Table S2). If DKR was occurring an improvement in enantioselectivity would be expected at lower temperatures. Aromatic aldehydes are fast trapping electrophiles and therefore would be expected to trap the lithiated complexes at a rate faster than epimerisation. Reduced enantioselectivities at −98 °C suggest that the lithiated complexes have not fully equilibrated after 1 h (the same conclusion drawn with acetone in the main manuscript), again supporting partial configurational stability of the lithiated complexes at −98 °C.



5 **SI-2 or SI-3**

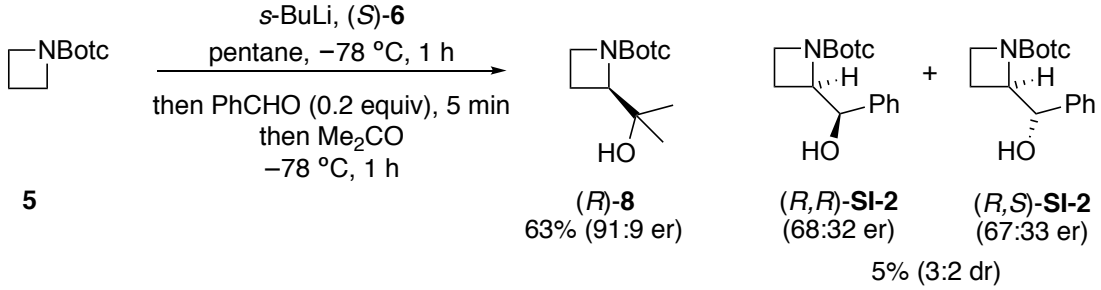
Entry[a]	Product (major diastereomer shown)	Lithiation temp	E^+ trapping temp	Yield (dr)	er[b]	% SM
1[1]		−78 °C	−78 °C	88% (60:40)	85:15	7
2	 **SI-2**	−98 °C	−98 °C	51% (71:29)	65:35	49
3		−78 °C	−78 °C	64% (69:31)	80:20	25
4	 **SI-3**	−98 °C	−98 °C	14% (64:36)	69:31	86

[a] *General procedure **A** was followed, on a 0.35 (entries 1 & 3) or 0.92 (entries 2 & 4) mmol scale.* [b] *Er of major diastereomer (er of minor diastereomer identical for entries 1 & 3; 60:40 and 65:35 for entries 2 & 4, respectively).*

Table S2. Partial configurational stability of α-Li 5 at -98 °C when trapping with aromatic aldehydes.

[1] D. M. Hodgson, C. L. Mortimer and J. M. McKenna, *Org. Lett*., 2015, **17**, 330.

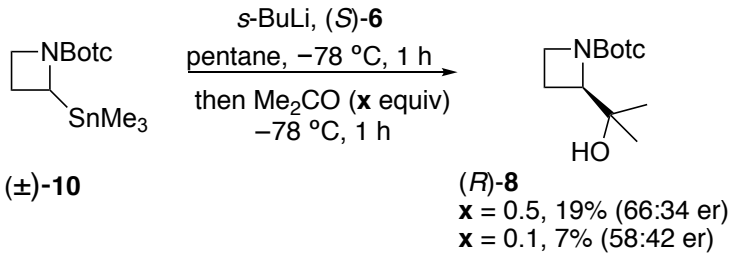
Further evidence for DTR with benzaldehyde was found when attempting to use it as a sacrificial electrophile in sub-stoichiometric amounts (0.2 equiv, Scheme S1). The reduction in er seen for both diastereomers of the benzaldehyde-trapped adduct **SI-2**, suggests that the reaction proceeds via DTR with the minor diastereomeric complex being the faster reacting intermediate.



Scheme S1. Benzaldehyde as a sacrificial electrophile.

(c) On the origin of lower configurational stability from anion generation via transmetallation compared to lithiation

A 'poor man's Hoffmann test' was undertaken on racemic stannane (±)-**10** in the presence of DIANANE (*S*)-**6**, to examine any potential differences between the intermediate organolithium complexes formed by transmetallation compared to deprotonation. Sn—Li exchange on stannane (±)-**10**, followed by trapping with substoichiometric amounts of acetone (0.5 equiv and 0.1 equiv) gave alcohol (*R*)-**8** in 19% (66:34 er) and 7% (58:42 er) respectively (Scheme S2). These results show the enantiodetermining step for reaction of the anion generated by Sn—Li exchange occurs by DTR and the 'minor' organolithium complex is the faster reacting species, i.e., like the direct deprotonation.

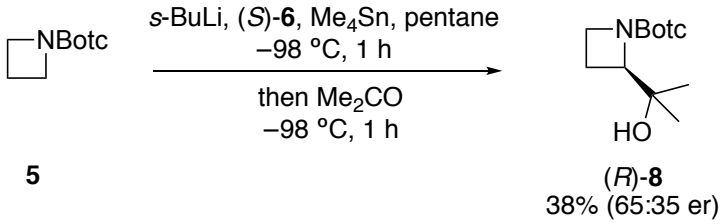


(±)-**10**

(*R*)-**8**
x = 0.5, 19% (66:34 er)
x = 0.1, 7% (58:42 er)

Scheme S2. 'Poor man's Hoffmann test' with stannane (±)-10.

To test if the tetraalkyltin generated during Sn—Li exchange could be influencing configurational stability of the anion, deprotonation was carried out in the presence of Me_4Sn (1 equiv) at −98 °C.[2] Following trapping with acetone, alcohol (*R*)-**8** was formed in 38% yield and 65:35 er (Scheme S3); this is the same level of enantioselectivity obtained from deprotonation in the absence of Me_4Sn at −98 °C and indicates the presence of a tetraalkyltin is not the origin of decreased configurational stability.



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(*R*)-**8**
38% (65:35 er)

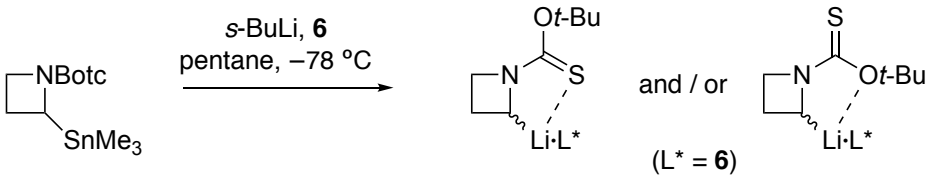
Scheme S3. Lithiation—electrophile trapping in the presence of Me_4Sn.

One speculative rationalisation for the difference in enantioselectivity through Sn—Li exchange could be the formation of oxygen-coordinated lithiated complexes from stannane **10** (Scheme S4). The rotamer ratio of stannane **10** is 2:1 (at rt) and rotamer interconversion does not occur on the reaction timescale at the low reaction temperatures used;[3]

[2] S. Thayumanavan, A. Basu and P. Beak, *J. Am. Chem. Soc.*, 1997, **119**, 8209.

[3] K. E. Jackson, C. L. Mortimer, B. Odell, J. M. McKenna, T. D. W. Claridge, R. S. Paton and D. M. Hodgson, *J. Org. Chem.*, 2015, **80**, 9838.

transmetallation could therefore lead to the formation of a sulfur-coordinated anion as well as an oxygen-coordinated anion. In contrast, as lithiation is directed by the thiocarbonyl group,[3] only the sulfur-coordinated lithiated complex would be expected from deprotonation. The possible oxygen-coordinated anion from Sn—Li exchange could possess less configurational stability and altered reactivity, due to the different nature of coordination at Li.



10

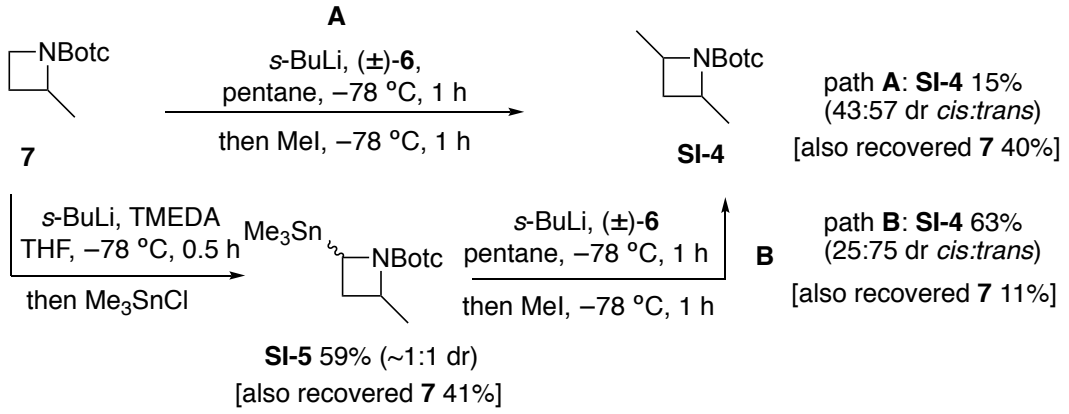
Scheme S4. Possible complexes from Sn—Li exchange.

Variations in configurational stability depending on the method of carbanion formation have been observed for 2-lithio-*N*-Boc piperidine,[4] which may arise due to different Li ligation/aggregation states formed by deprotonation or transmetallation. The authors did not investigate the origins further; however, rotamers in the starting 2-tributylstannyl-*N*-Boc piperidine may facilitate formation of different carbanionic species. The demonstration of a configurationally stable carbanion by Sn—Li exchange of *N*-Boc azetidine stannane **13** (Scheme 6 main paper), suggests that in this case both rotameric carbanionic species, if formed, are configurationally stable.

[4] (*a*) D. Stead, G. Carbone, P. O'Brien, K. R. Campos, I. Coldham and A. Sanderson, *J. Am. Chem. Soc.,* 2010, **132**, 7260. (*b*) T. K. Beng, W. S. Tyree, T. Parker, C. Su, P. G. Williard and R. E. Gawley, *J. Am. Chem. Soc.*, 2012, **134**, 16845.

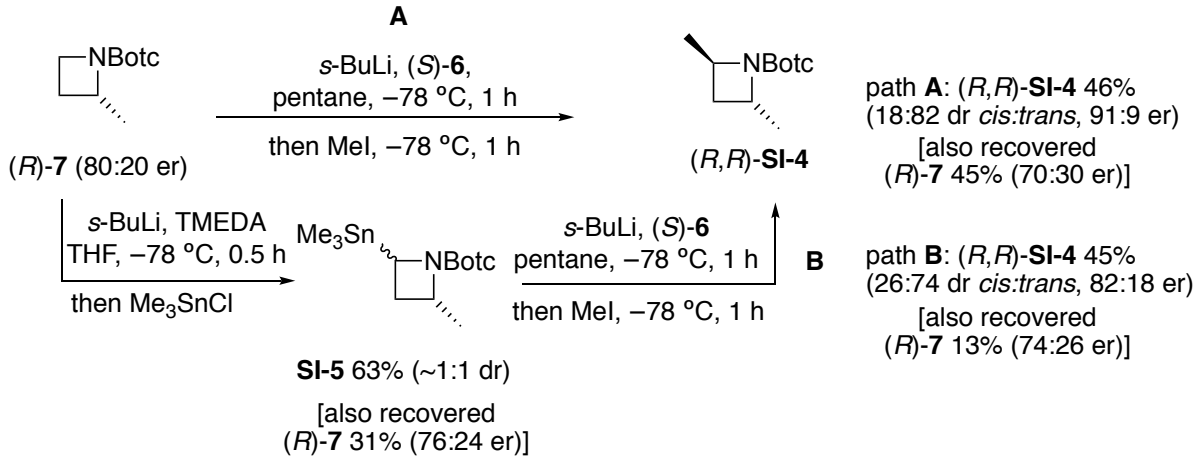
(d) Differing stereoselectivity in the syntheses of 2,4-dimethylazetidines via lithiation compared to transmetallation

Synthesis of 2,4-dimethylazetidine **SI-4** was achieved from α′-lithiation—electrophile trapping of 2-methylazetidine (±)-**7** (Scheme S5). Lithiation at −78 °C for 1 h in pentane with racemic DIANANE (±)-**6** then trapping with MeI gave 2,4-dimethylazetidine **SI-4** in 15% yield (43:57 dr *cis*:*trans*), with a slight preference for the *trans*-2,4-dimethylazetidine. Low diastereoselectivity is similarly observed when 2,4-dimethylazetidine **SI-4** was prepared in THF with TMEDA as the diamine ligand (1:1 dr).[3] These results indicate the steric and stereoelectronic influence of the pre-existing methyl group is minimal during α′-lithiation—electrophile trapping. However, when 2,4-dimethylazetidine **SI-4** was prepared by transmetallation from 4-methyl-2-stannylazetidine **SI-5**, different diastereoselectivity was observed (Scheme S5). 4-Methyl-2-stannylazetidine **SI-5** was prepared by α′-lithiation of racemic 2-methylazetidine **7** in THF with TMEDA, followed by trapping with Me_3SnCl; this gave an ~ 1:1 dr (inseparable) of stannane **SI-5** in 59% yield. Transmetallation of stannane **SI-5** in pentane in the presence of racemic DIANANE (±)-**6** at −78 °C for 1 h followed by trapping with MeI gave 2,4-dimethylazetidine **SI-4** in 63% yield (25:75 dr *cis*:*trans*). The major diastereomer is again the *trans*-2,4-dimethylazetidine **SI-4**, but interestingly the diastereoselectivity of the reaction via transmetallation was higher compared to lithiation. Although, the yield via α′-lithiation is low, if we assume that (like α-methylation) the reaction is proceeding via DKR, then the selectivity should not be influenced by the conversion. These results provide further evidence that the anion formed by transmetallation possesses slightly different characteristics compared to the anion formed by lithiation.



Scheme S5. Syntheses of 2,4-dimethylazetidine SI-4.

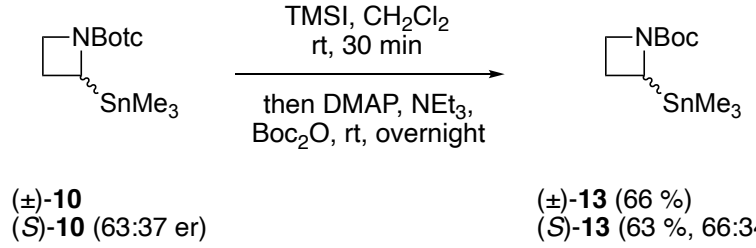
Further differences were observed between lithiation and transmetallation in the asymmetric synthesis of 2,4-dimethylazetidine (*R*,*R*)-**SI-4** (Scheme S6). Deprotonation of (*R*)-**7** (80:20 er) at −78 °C for 1 h before trapping with MeI, gave 2,4-dimethylazetidine (*R*,*R*)-**SI-4** in 46% yield (18:82 dr *cis*:*trans*, 91:9 er). Interestingly, starting material (*R*)-**7** 45% was recovered with reduced enantioenrichment (70:30 er). Restricted rotation of the thiocarbonyl group (1:2.5 *cis*:*trans* rotamers)[3] prevents complete α′-lithiation of (*R*)-**7** at the unsubstituted α-methylene site (from the *cis* rotamer) and prevents synthetically useful yields. An attempt to improve the yield of the overall transformation was examined via stannane **SI-5** as an intermediate (Scheme S6). Lithiation—stannylation of (*R*)-**7** (80:20 er) with TMEDA in THF, gave stannane **SI-5** in 63% yield (~1:1 dr). Transmetallation of stannane **SI-5** in the presence of DIANANE (*S*)-**6** gave 2,4-dimethylazetidine (*R*,*R*)-**SI-4** in 45% yield (26:74 dr *cis*:*trans*, 82:18 er). The reduced diastereo- and enantioselectivity from this approach again highlights differences in behaviour of the anionic complexes formed from deprotonation and transmetallation.



Scheme S6. Asymmetric syntheses of 2,4-dimethylazetidine (R,R)-SI-4.

(e) Synthesis of *N*-Boc stannane 13

Attempts to generate *N*-Boc stannane **13**, by deprotection of *N*-Botc stannane **10** under previously described acidic conditions[1] followed by Boc protection, resulted in significant proto-destannylation with only trace product formed. Gawley and co-workers previously described *N*-Boc deprotection of 2-stannyl pyrrolidines using TMSI.[5] Application of this procedure to *N*-Botc stannane **10** allowed clean removal of the directing group; subsequent trapping with Boc_2O gave *N*-Boc stannane **13** in moderate yield 66% (Scheme S7). Similarly, enantioenriched stannane (*S*)-**10** (63:37 er) gave enantioenriched *N*-Boc stannane (*S*)-**13** in 66:34 er (63% yield). This demonstrates a new 'milder' method for *N*-Botc deprotection and serves as a viable alternative when acid labile substituents are present.

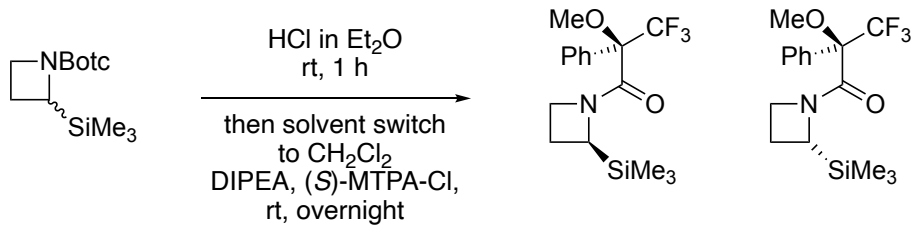


Scheme S7. Synthesis of N-Boc stannane 13 via deprotection of stannane 10 using TMSI.

[5] R. E. Gawley, S. Narayan and D. A. Vicic, *J. Org. Chem.*, 2005, **70**, 328.

(f) Determination of absolute configurations by conversion to Mosher amides

The absolute configuration of silane (−)-**12** was determined by conversion to the Mosher amide and analysis of the ^{1}H NMR spectra. Transformation of silane (±)-**12** to the diastereomeric chromatographically separable Mosher amides (*R,S*)-**SI-6** and (*R*,*R*)-**SI-6** was achieved by acidic deprotection of the *N*-Botc group,[1] followed by amide formation with (*S*)-MPTA-Cl (52%, 55:45 dr, Scheme S8).



	(*R*,*S*)-**SI-6**	:	(*R*,*R*)-**SI-6**
(±)-**12**	55	:	45
(*R*)-**12** (69:31 er)	26	:	74

Scheme S8. Conversion of silane 12 to Mosher amides (R,R)-SI-6 and (R,S)-SI-6.

For all the Mosher amides analysed, only single rotamers were observed. The rotamers for the two silyl amides (*R,S*)-**SI-6** and (*R*,*R*)-**SI-6** were assigned *cis* from 2D-NOSEY cross-peaks both between methoxy and a deshielded H of NCH_2, and between the shielded H of NCH_2 and the phenyl group (Fig. S1-S4); this is consistent with the previously established rotamer preference for an analogous 2-trimethylsilyl *N*-thiopivaloyl azetidine.[3] These cross-peaks allow assignment of the NCH_2 protons in both diastereomers. With the rotameric form established, the relative stereochemistry of the silyl group could then be assigned from NOE cross-peaks between either the methoxy or Ph group of the Mosher amide, depending on the diastereomer. Additional cross-peaks between the $SiMe_3$ group and the ring protons were used to establish relative configuration of the remaining ring protons (Fig. S1-S4). These

assignments were supported by vicinal proton-proton coupling constants around the ring: azetidines typically show larger values for mutually *cis* protons (~9-11 Hz) compared to *trans* protons (~5-7 Hz).[6]

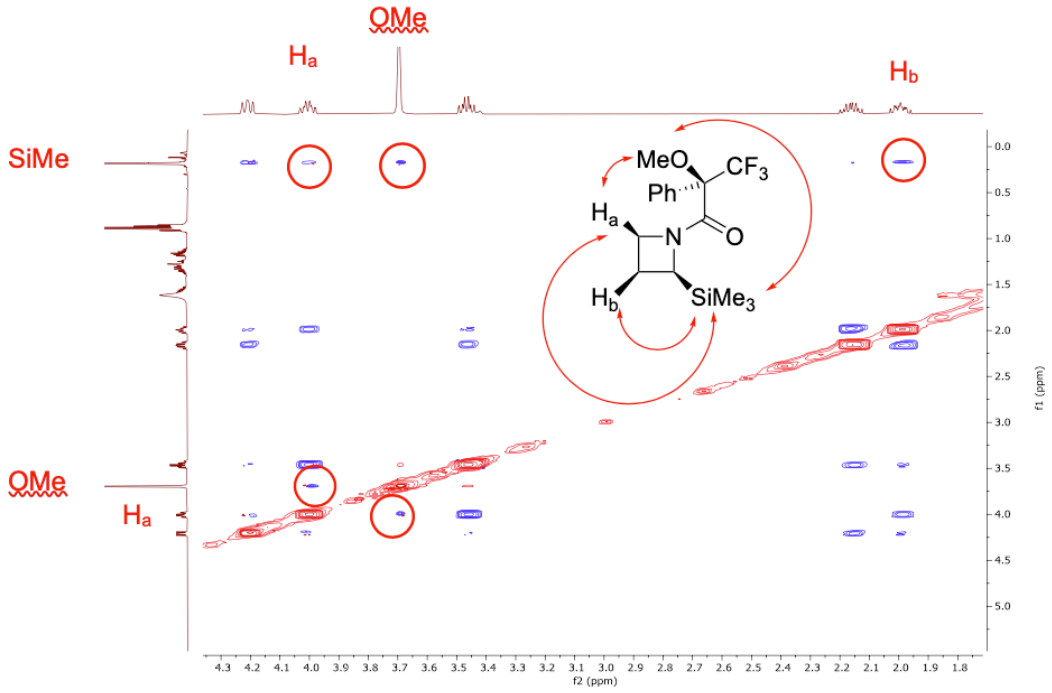


Figure S1. NOESY spectrum of minor diastereomer silane (R,S)-SI-6.

[6] D. C. G. A. Pinto, C. M. M. Santos and A. M. S. Silva, Advanced NMR techniques for structural characterization of heterocyclic structures, in *Recent Research Developments in Heterocyclic Chemistry*, ed. T. M. V. D. Pinho e Melo and A. M. R. Gonsalves, Research Signpost, Kerala, India, 2007, ch. 8, pp. 397–475.

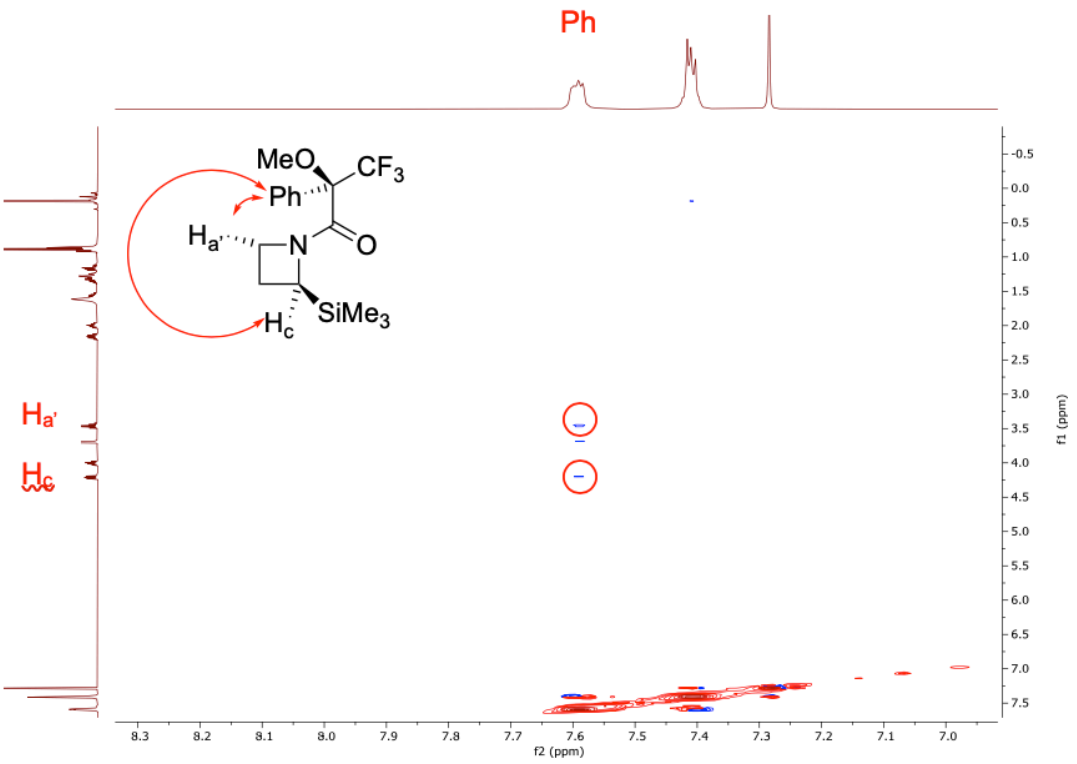


Figure S2. NOESY spectrum of minor diastereomer (aromatic region) silane (R,S)-SI-6.

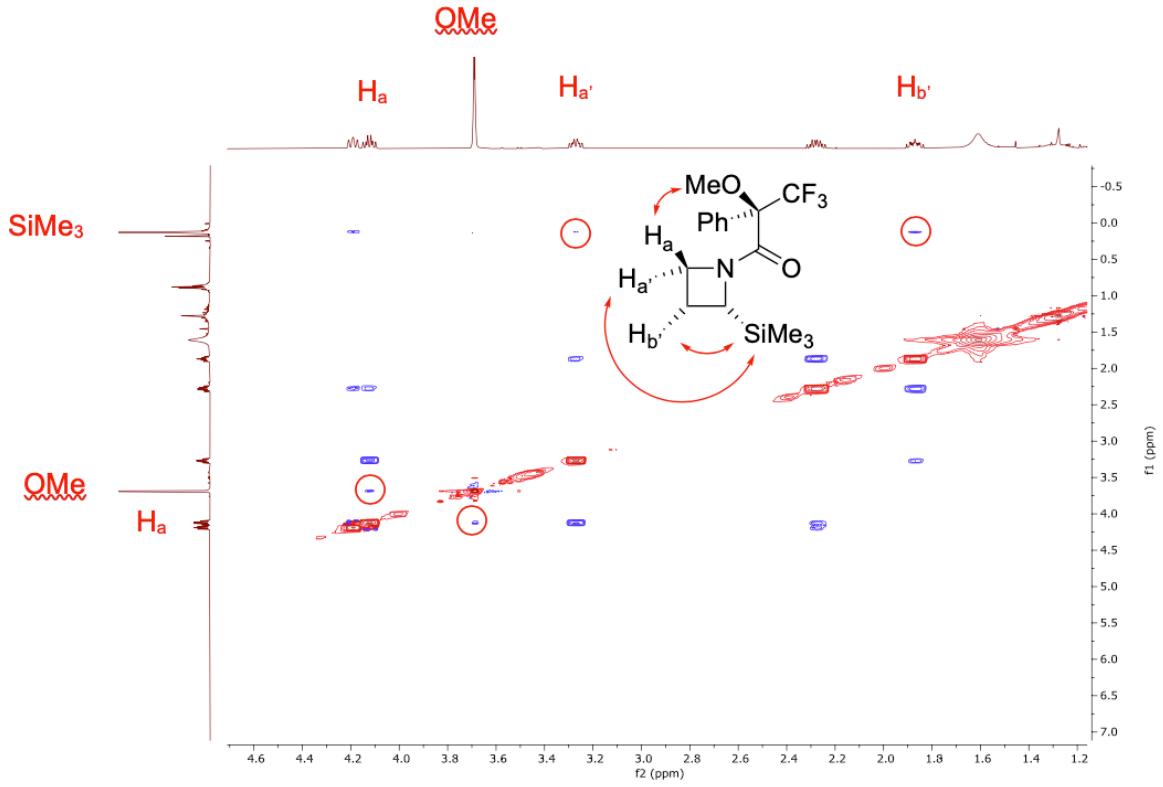


Figure S3. NOESY spectrum of major diastereomer silane (R,R)-SI-6.

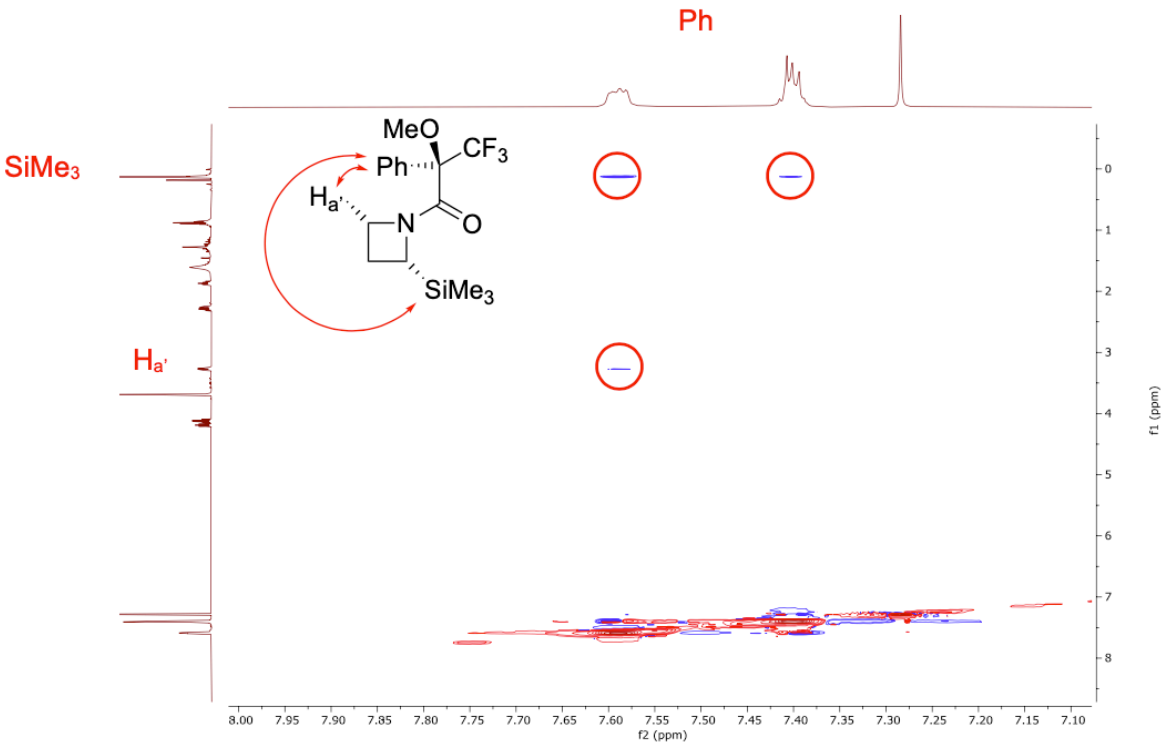


Figure S4. NOESY spectrum of major diastereomer (aromatic region) silane (R,R)-SI-6.

The silane diastereomers possessed distinctive chemical shift patterns, with the NCH_2 and $NCHCH_2$ protons showing significant Δδ ppm values (Fig. S5, Table S3). The lack of any significant Δδ ppm for the NCH proton (entry 5) further supports the previously *cis* rotamer assignment, with the C=O group pointing towards the substituted side of the azetidine ring.[7] The chemical shift patterns for the silanes indicate the phenyl group has a shielding effect on the NCH_2 and $NCHCH_2$ protons which occupy the same space below the ring ($H_{a'}$ & $H_{b'}$, as drawn). Additionally, the trimethylsilyl group influences chemical shift values; mutually *cis* protons being shielded relative to those that are *anti*. The latter is particularly apparent for H_b, which for (*R*,*S*)-**SI-6** is more shielded than the (*R*,*R*)-**SI-6** H_b proton (entry 3), despite being on the opposite side of the ring to the phenyl group. Importantly, these chemical shift

[7] T. R. Hoye and M. K. Renner, *J. Org. Chem.*, 1996, **61**, 2056; *corrigendum*, *J. Org. Chem.*, 2006, **71**, 1754.

patterns are observable with other substituted azetidines (see below) and therefore allow for assignment of relative/absolute configurations of other similarly substituted azetidines following conversion to Mosher amides.

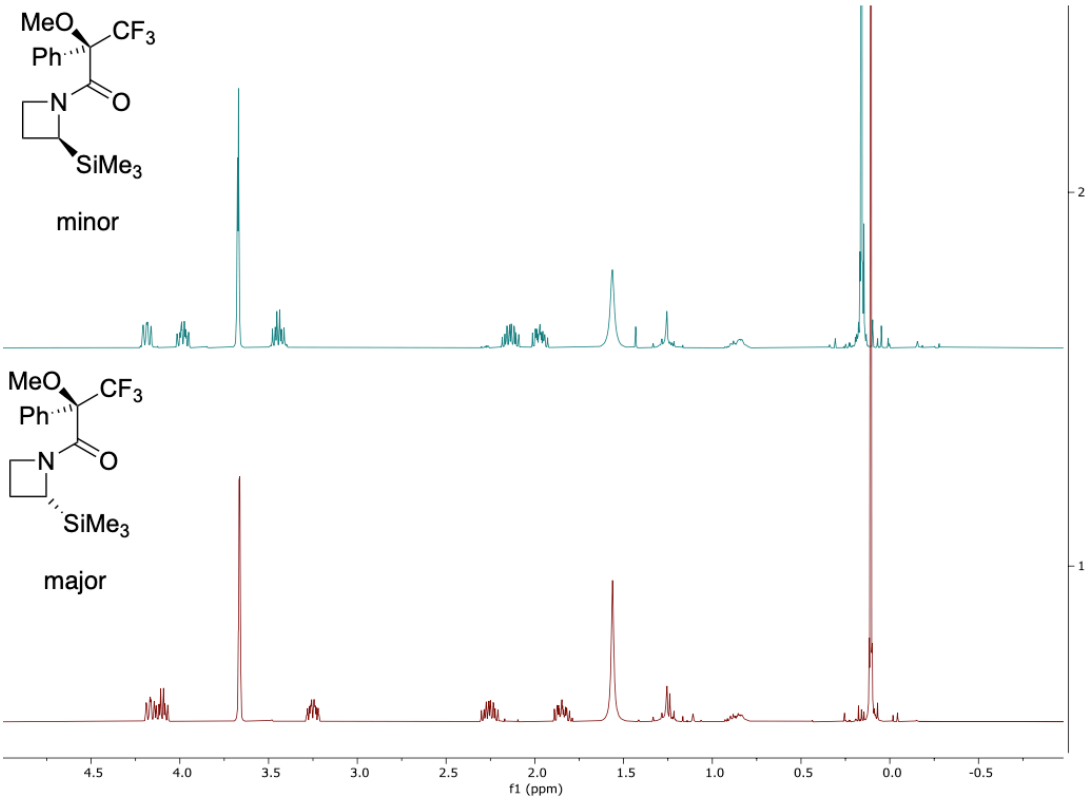
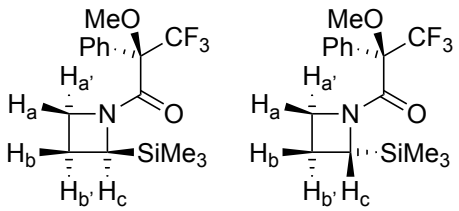


Figure S5. Overlapped ^{1}H NMR spectra of Mosher silanes (R,S)-SI-6 and (R,R)-SI-6.



(*R*,*S*)-**SI-6** (*R*,*R*)-**SI-6**

Entry	Proton	(*R*,*S*)-SI-6	(*R*,*R*)-SI-6	$\Delta\delta_{(\delta S-\ \delta R)}$
1	H_a	3.98	4.10	-0.12
2	$H_{a'}$	3.44	3.25	0.19

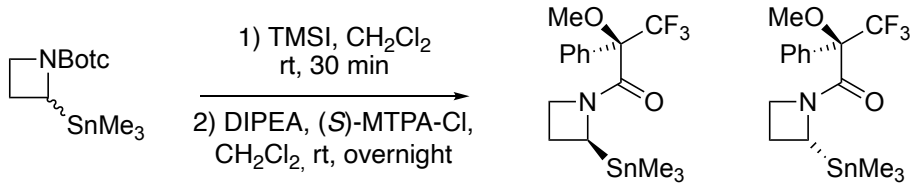
3	H_b	1.97	2.25	-0.28
4	$H_{b'}$	2.14	1.85	0.29
5	H_c	4.18	4.17	0.01
6	$SiMe_3$	0.16	0.11	0.05

Table S3. Chemical shifts differences between (R,S)-SI-6 and (R,R)-SI-6 silanes.

Having determined the relative and absolute configuration of the two diastereomeric Mosher silanes (*R*,*S*)-**SI-6** and (*R*,*R*)-**SI-6**, enantioenriched silane (−)-**12** (69:31 er) was converted to the Mosher silanes following the same deprotection/amide formation sequence (41%, 88:12 dr (isolated), Scheme S8). ^{19}F NMR analysis of the crude reaction mixture indicated a 74:26 dr, by integration of the corresponding CF_3 peaks, with (*R,R*)-**SI-6** being the major diastereomer; this result enables assignment of the absolute configuration of silane (−)-**12** as *R*.

Stannane **10** was converted to the corresponding stannyl Mosher amides (*R,R*)-**SI-7** and (*R,S*)-**SI-7** following a modified deprotection/amide formation protocol with (*S*)-MPTA-Cl (28%, 52:48 dr (isolated), Scheme S9). Deprotection was achieved using TMSI (p. S8-S9). The two diastereomers were formed in a 1:1 ratio, by ^{19}F NMR analysis of the crude. Following separation by column chromatography, the diastereomers were analysed by ^{1}H NMR and their absolute and relative configurations assigned by analogy to the corresponding silyl Mosher amides (*R,R*)-**SI-6** and (*R,S*)-**SI-6**, due to the observation of similar chemical shift patterns (Fig. S6 and Table S4, *cf* Fig. S5 and Table S3).[8]

[8] A single crystal suitable for X-ray crystallographic analysis of (*R*,*S*)-**SI-7** was grown by slow evaporation of an Et_2O solution. 2027137 CCDC contains the supplementary crystallographic data for (*R*,*S*)-**SI-7**, which confirms the configuration assigned by NMR. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. We thank Owen Smith (Oxford) for obtaining and processing this X-ray crystallography data.



	(*R*,*S*)-**SI-7**	:	(*R*,*R*)-**SI-7**
(±)-**10**	50	:	50
(*S*)-**10** (62:38 er)	59	:	41

Scheme S9. Conversion of stannane 10 to Mosher amides (R,R)-SI-7 and (R,S)-SI-7.

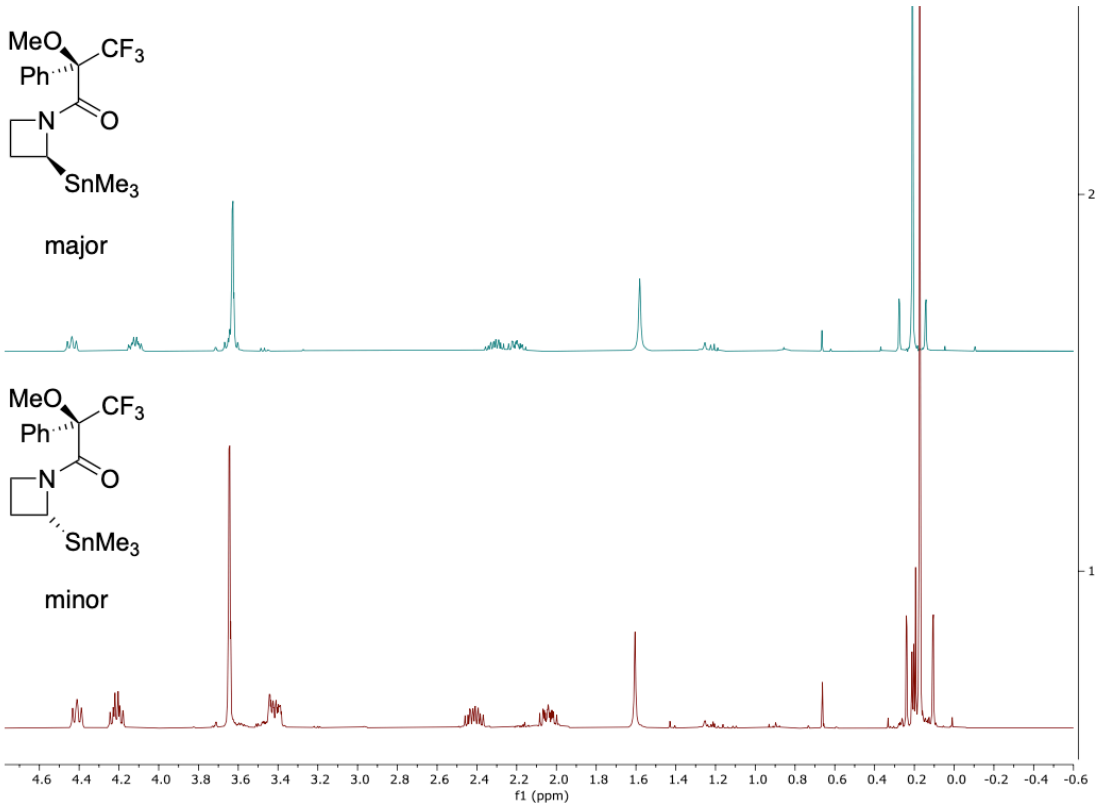
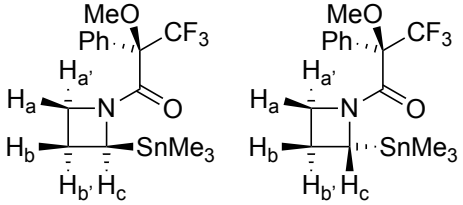


Figure S6. Overlapped ^{1}H NMR spectra of Mosher stannanes (R,S)-SI-7 and (R,R)-SI-7.



(*R*,*S*)-**SI-7** (*R*,*R*)-**SI-7**

Entry	Proton	(*R*,*S*)-SI-7	(*R*,*R*)-SI-7	$\Delta\delta_{(\delta S-\delta R)}$
1	H_a	4.12	4.21	-0.09
2	$H_{a'}$	3.64[a]	3.43[a]	0.21
3	H_b	2.20	2.41	-0.21
4	$H_{b'}$	2.31	2.04	0.27
5	H_c	4.44[a]	4.41	0.03
6	$SnMe_3$	0.21	0.17	0.04

[a] *For multiplets, peak position was determined as the mean of the multiplet range.*

Table S4. Chemical shifts differences between (R,S)-SI-7 and (R,R)-SI-7 stannanes.

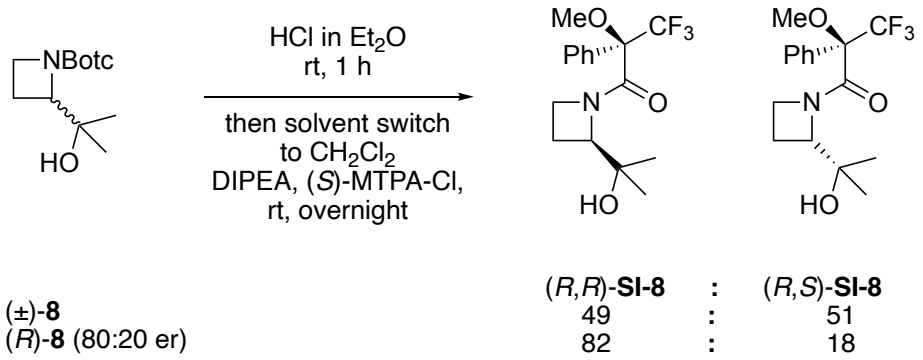
Enantioenriched stannane (+)-**10** (62:38 er) was converted to the corresponding Mosher amides following the previously developed route (51%, 54:46 dr (isolated), Scheme S9). Analysis of the crude by ^{19}F NMR gave a 59:41 dr, in good agreement with the enantioenrichment of the starting material. The major ^{19}F NMR peak corresponded to stannane (*R*,*S*)-**SI-7**, which was used to assign the absolute configuration of stannane (+)-**10** as *S*.

Further supporting evidence for absolute configuration of stannane (+)-**10** was obtained following conversion to *N*-Boc stannane (+)-**13** (Scheme S7) and subsequent lithiation—electrophile trapping with acetone to give enantioenriched alcohol (*R*)-**14** (main paper Scheme 6). The absolute configuration of alcohol (*R*)-**14** has been previously established.[9] Assuming Sn—Li exchange and trapping with acetone occur with retention of configuration, then the absolute configuration of the starting stannane (+)-**10** can be inferred as *S*. This matches the absolute configuration determined by conversion to the Mosher amide.

Additional evidence for the assignment of absolute configuration was achieved by converting alcohol (±)-**8** into the corresponding hydroxy Mosher amides (*R,S*)-**SI-8** and (*R,R*)-**SI-8** (Scheme

[9] P. K. Delany and D. M. Hodgson, *Org. Lett.*, 2019, **21**, 9981.

S10). With racemic alcohol (±)-**8** a 1:1 mixture of diastereomers was formed (confirmed by ^{19}F NMR analysis of the crude). Separation of the diastereomers and ^{1}H NMR analysis revealed chemical similar shift patterns (Fig. S7, Table S5), similar to those previously observed for the silyl and stannyl Mosher amides. Enantioenriched alcohol (*R*)-**8** (80:20 er) of known absolute configuration was subsequently converted into hydroxy Mosher amides (*R,S*)-**SI-8** and (*R,R*)-**SI-8** (^{19}F NMR analysis of crude gave 82:18 dr). Purification of the resulting hydroxy Mosher amides (*R,S*)-**SI-8** and (*R,R*)-**SI-8** showed the major diastereomer to have similar ^{1}H NMR shift patterns to the major stannyl Mosher amide (*R*,*R*)-**SI-7**.



(±)-**8**
(*R*)-**8** (80:20 er)

(*R*,*R*)-**SI-8**	:	(*R*,*S*)-**SI-8**
49	:	51
82	:	18

Scheme S10. Conversion of hydroxy 8 to Mosher amides (R,R)-SI-8 and (R,S)-SI-8.

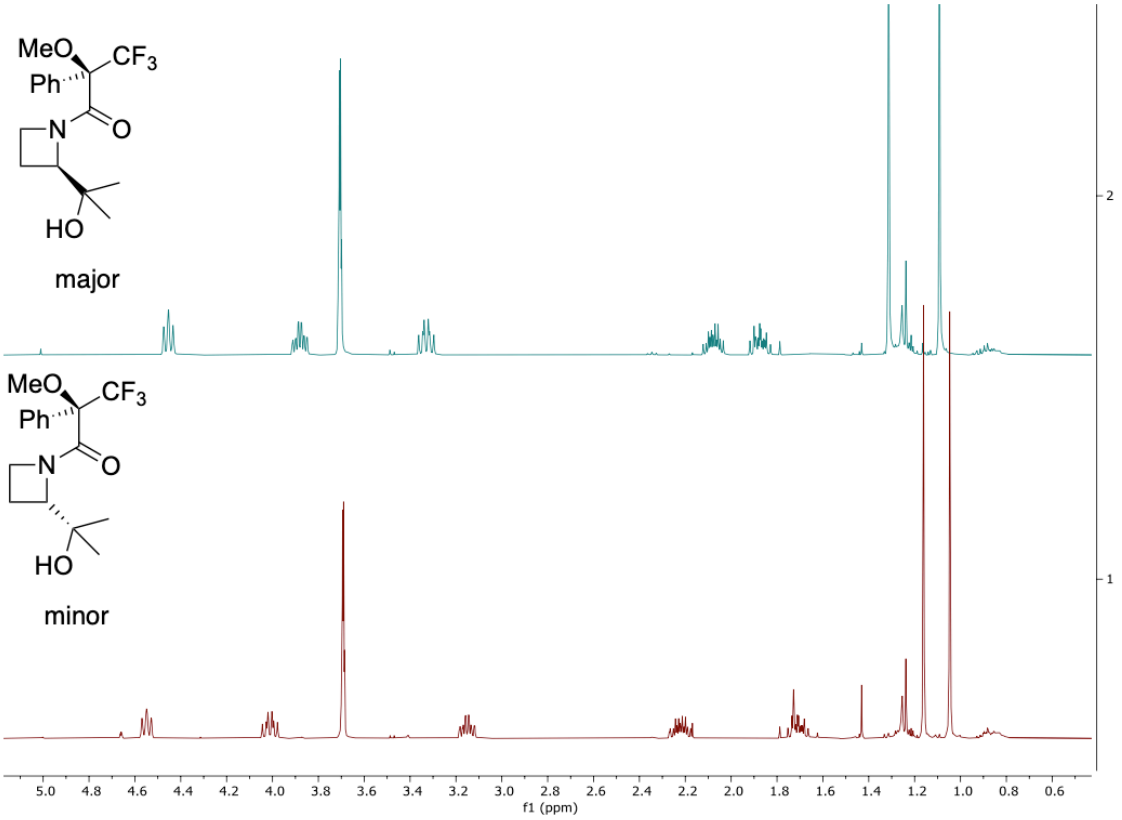
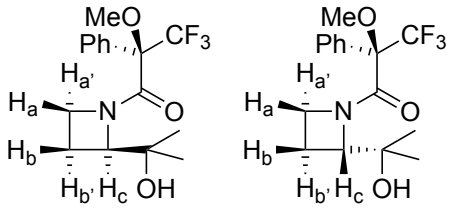


Figure S7. Overlapped ^{1}H NMR of Mosher alcohols (R,S)-SI-8 and (R,R)-SI-8.



(*R*,*R*)-**SI-8** (*R*,*S*)-**SI-8**

Entry	Proton	(*R*,*R*)-SI-8	(*R*,*S*)-SI-8	$\Delta\delta_{(\delta R-\delta S)}{}^{a}$
1	H_a	3.88	4.01	-0.13
2	$H_{a'}$	3.33	3.15	0.18
3	H_b	1.87	2.22	-0.35
4	$H_{b'}$	2.08	1.71	0.37
5	H_c	4.45	4.55	-0.10
6	Me	1.31	1.16	0.15
7	Me'	1.09	1.05	0.04

[a] δR-δS due to change in CIP priority assignment compared to amides in Tables S3-S4.

Table S5. Chemical shifts differences between (R,S)-SI-8 and (R,R)-SI-8 alcohols.

2. Experimental Conditions

(a) General Information

Commercially available chemicals/reagents were purchased from major suppliers and unless stated otherwise were used without further purification. TMEDA, TMSCl and Et_3N were distilled from CaH_2; TMSI was distilled from Cu powder; DIANANE (**6**)[10] was distilled under reduced pressure before use. All reactions were stirred using Teflon-coated magnetic stirrer bars. Where reactions are stated as under nitrogen atmosphere, glassware was flame-dried and solvents were degassed and dried using a Pure Solv-MD solvent purification system and transferred under nitrogen. The following cooling baths were used: –78 °C (dry ice/acetone) and –98 °C (liquid N_2/MeOH). Reactions were monitored by TLC using Merck silica gel 60 F254 (aluminium support) TLC plates, which were developed using standard visualising agents: UV fluorescence (254 nm), potassium permanganate /Δ or vanillin /Δ. Column chromatography was carried out on silica gel (43-63 μm) in the solvent system indicated. Petroleum ether refers to the fraction boiling between 40 °C to 60 °C. Melting points were measured in open capillaries using Stuart Scientific melting point apparatus and are uncorrected. Infra-red spectra were recorded neat and the intensity of the peaks are reported as s, m, w, br, denoting strong, medium, weak, and broad, respectively. NMR spectra were recorded on Brüker DPX200 (^{1}H = 200 MHz), Brüker AVF400 (^{1}H = 400 MHz, ^{13}C = 100 MHz), AVC 500 (^{1}H = 500 MHz, ^{13}C 125 MHz) machines in commercial, deuterated, TMS free solvents at 25 °C. Chemical shifts (δ) are given in ppm relative to TMS, calibrated using residual solvent peaks. Where rotamers/diastereomers are discernible, signals due to the minor rotamer/diastereomer are given in parentheses. ^{13}C NMR spectra were recorded using the UDEFT or PENDANT pulse sequences from the Brüker standard pulse program library. ^{13}C DEPT spectra and 2D COSY, HSQC and HMBC spectra were recorded so as to assist with assignment when required. Multiplicity is denoted in ^{1}H NMR by: s (singlet), d (doublet), t (triplet), q (quartet), quin (quintet), sext (sextet), hept (heptet), m (multiplet). Proton coupling constants *J* are reported to the nearest 0.1 Hz. NMR spectra were processed using MestReNova software. High resolution mass spectra were obtained by FI (Micromass GCT), or by ESI (LCT Premier reflectron TOF and Brüker MicroTOF) using tetraoctylammonium bromide or sodium dodecyl sulfate as lock mass; values are quoted as ratio of mass to charge in Daltons, and relative intensities of assignable peaks observed are quoted as a percentage value of the base peak. Chiral HPLC was performed on a Dionex UltiMate 3000 system comprising a Dionex LPG-3400A pump, WPS-3000SL autosampler, TCC-3000SD column compartment and DAD-3000 diode-array detector, fitted with the appropriate Daicel Chiralpak column (dimensions: 0.46 cm ø x 25 cm) and corresponding guard column (0.4 cm ø x 1 cm). Wavelengths (λ) are reported in nm, retention times (τ_R) are reported in mins and solvent flow rates are reported in mL min^{-1}.

[10] J. Praz, L. Guenée, S. Aziz, A. Berkessel and A. Alexakis, *Adv. Synth. Catal.*, 2012, **354**, 1780.

(b) General Procedures

Procedure A: Deprotonation—electrophile trapping (external trapping)

A solution of (1*S*,2*S*,4*S*,5*S*)-N^2,N^2,N^5,N^5-tetramethylbicyclo[2.2.1]heptane-2,5-diamine (*S*)-**6**[10] (1.3 equiv) and *N*-Botc azetidine (**5**) (1 equiv) in pentane (8 mL/mmol **5**) was cooled to (−78 °C or −98 °C) and *s*-BuLi (1.3 M in cyclohexane/hexane, 1.3 equiv) was added dropwise (~1 min). The reaction mixture was stirred for the time stated at (−78 °C or −98 °C) before addition of electrophile (**X** equiv) dropwise. The reaction mixture was stirred for the time stated at (−78 °C or −98 °C), then quenched with sat. aq NH_4Cl (20 mL /mmol **5**), and extracted with Et_2O (3 × 20 mL /mmol **5**). The combined organic extracts were washed with water (20 mL /mmol **5**), then brine (20 mL /mmol **5**), dried ($MgSO_4$) and concentrated under reduced pressure.

Procedure B: Sn–Li exchange—electrophile trapping (external trapping)

A solution of (1*S*,2*S*,4*S*,5*S*)-N^2,N^2,N^5,N^5-tetramethylbicyclo[2.2.1]heptane-2,5-diamine (*S*)-**6**[10] (1.3 equiv) and stannane **10** or **13** (1 equiv) in pentane (8 mL/mmol **5**) was cooled to (−78 °C or −98 °C) and *s*-BuLi (1.3 M in cyclohexane/hexane, 1.3 equiv) was added dropwise (~1 min). The reaction mixture was stirred for the time stated at (−78 °C or −98 °C) before addition of electrophile (**X** equiv) dropwise. The reaction mixture was stirred for the time stated at (−78 °C or −98 °C), then quenched with sat. aq NH_4Cl (20 mL /mmol **5**), and extracted with Et_2O (3 × 20 mL /mmol **5**). The combined organic extracts were washed with water (20 mL /mmol **5**), then brine (20 mL /mmol **5**), dried ($MgSO_4$) and concentrated under reduced pressure.

Procedure C: Sn–Li exchange—electrophile trapping (internal trapping)

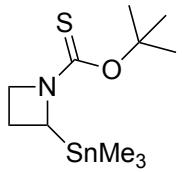
A solution of (1*S*,2*S*,4*S*,5*S*)-N^2,N^2,N^5,N^5-tetramethylbicyclo[2.2.1]heptane-2,5-diamine (*S*)-**6**[10] (1.3 equiv), stannane **10** (1 equiv) and electrophile (5 or 10 equiv) in pentane (8 mL/mmol **10**) was cooled to (−78 °C) and *s*-BuLi (1.3 M in cyclohexane/hexane, 1.3 equiv) was added dropwise (~1 min). The reaction mixture was stirred for 1 h at (−78 °C), then quenched with sat. aq NH_4Cl (20 mL /mmol **10**), and extracted with Et_2O (3 × 20 mL /mmol **10**). The combined organic extracts were washed with water (20 mL /mmol **5**), then brine (20 mL /mmol **10**), dried ($MgSO_4$) and concentrated under reduced pressure.

Procedure D: Formation of Mosher amides

To the 2-substituted *N*-Botc azetidine (1 equiv) was added HCl (2 M in Et_2O, 8 equiv) and the mixture was stirred for 1 h at rt. The reaction was concentrated under a stream of nitrogen and the crude dissolved in CH_2Cl_2 (0.1 M). DIPEA (2.2 equiv) and (*S*)-MTPA-Cl (1.2 equiv) was added and the reaction was stirred at rt overnight. The reaction mixture was concentrated under reduced pressure and to the crude was added sat. aq NH_4Cl (20 mL /mmol **8**/**12**), and extracted with CH_2Cl_2 (3 × 20 mL /mmol **8**/**12**). The combined organic extracts were washed with brine (20 mL /mmol **8**/**12**), dried ($MgSO_4$) and concentrated under reduced pressure.

(c) Specific experimental procedures and characterisation data

***O*-(*t*-Butyl) 2-(trimethylstannyl)azetidine-1-carbothioate 10**



A solution of *N*-Botc azetidine **5** (490 mg, 2.85 mmol) and TMEDA (1.00 mL, 6.7 mmol) in THF (14 mL) was cooled to −78 °C. *s*-BuLi (2.80 mL, 1.3 M in cyclohexane/hexane, 3.60 mmol) was added dropwise (~5 min). The reaction mixture was stirred for 1 h at −78 °C before addition of Me_3SnCl (5.3 mL, 1.0 M in pentane, 5.3 mmol) dropwise. The reaction mixture was stirred for a further 1 h at −78 °C, then quenched with sat. aq NH_4Cl (20 mL), and extracted with Et_2O (3 × 20 mL). The combined organic extracts were washed with water (20 mL), then brine (20 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give a pale-yellow oil. The crude material was purified by column chromatography (1% Et_2O/petroleum ether) to first give a colourless oil, stannane **10** (782 mg, 82%). Second eluted a colourless oil, *N*-Botc azetidine **5** (22 mg, 4%).

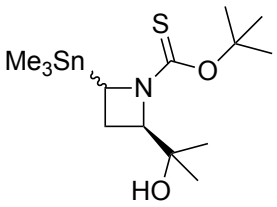
R_f 0.55 (20% TBME/*n*-hexane); IR (neat/cm^{-1}) 2924 m, 2855 w, 1490 m, 1455 s, 1365 m, 1266 m, 1229 w, 1137 m; δ_H (400 MHz, $CDCl_3$) (2:1 rotamer mixture by analysis of $C(CH_3)_3$ signals at 1.66 and 1.61) 4.4 6– 4.40 (1H, m, NCH), 4.17 – 4.09 (1H, m, NCH*H'*), 4.00 (4.25) (1H, dddd, *J* = 10.6, 8.9, 6.4, 1.8 Hz (ddd, *J* = 10.9, 9.5, 5.2 Hz), NC*H*H'), 2.56 – 2.39 (1H, m, NCH_2CHH'), 2.13 – 2.05 (1H, m, NCH_2CH*H'*), 1.61 (1.66) (9H, s, $C(CH_3)_3$), 0.20 (9H, s, $^2J_{^{119}Sn\,H}$ = 54 Hz, $^2J_{^{117}Sn\text{-}H}$ = 52 Hz, $SnMe_3$); δ_C (100 MHz, $CDCl_3$) (rotamer mixture) 182.1 (C=S), 83.9 (84.8) ($C(CH_3)_3$), 55.3 (54.9) (NCH), 50.9 (52.6) (NCH_2), 28.6 (28.9) ($C(CH_3)_3$), 17.9 (18.5) (CH_2), –8.2 (–9.5) ($J_{^{119}Sn\text{-}C}$ = 334 Hz, $J_{^{117}Sn\text{-}C}$ = 319 Hz, $SnMe_3$); HRMS (FI^+) calcd for [M+H] $C_{11}H_{23}NOS^{120}Sn$ 337.0522, found 337.0525.

***O*-(*t*-Butyl) (*R*)-2-(trimethylstannyl)azetidine-1-carbothioate (*R*)-10**

The stannane was prepared following general procedure **A**, using *N*-Botc azetidine **5** (430 mg, 2.50 mmol) and DIANANE (*R*)-**6** (600 mg, 3.30 mmol), with a –78 °C lithiation temp (1 h). Me_3SnCl (4.5 mL, 1.0 M in pentane, 4.5 mmol) was then added dropwise at –78 °C (1 h). The crude material was purified by column chromatography (1% Et_2O/petroleum ether) to first give a colourless oil, stannane (*R*)-**10** (764 mg, 91%, 67:33 er by HPLC: ODH column; eluent: *n*-hexane/*i*-PrOH (99.9:0.01); flow rate = 1 mL min^{-1}; τ_R ((*S*) minor) = 6.09 min, τ_R ((*R*) major) = 7.44 min); $[\alpha]_D^{25}$–97.9 (*c* 1.03, $CHCl_3$); all other data as described for racemic stannane **10** (see above). Second eluted a colourless oil, recovered *N*-Botc azetidine **5**[1] (23 mg, 5%).

Disubstituted azetidine from transmetallation (Table S1)

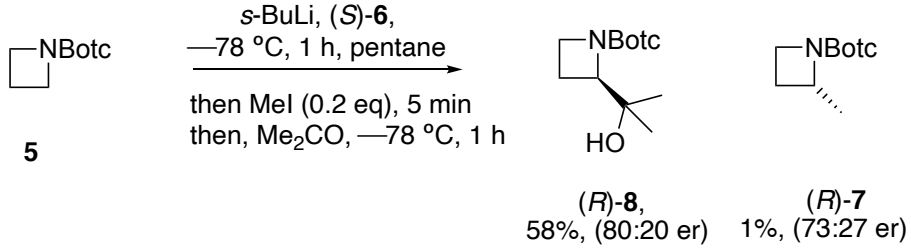
***O*-(*t*-Butyl) (*R*)-2-(2-hydroxypropan-2-yl)-4-(trimethylstannyl)azetidine-1-carbothioate SI-1**



R_f 0.28 (20% EtOAc/petroleum ether); IR (neat/cm^{-1}) 3323 br, 2974 m, 2916 m, 1472 s, 1446 s, 1367 s, 1270 s, 1148 s; δ_H (400 MHz, $CDCl_3$) (mixture of diastereomers and rotamers) 6.09 (3.59) (1H, s, OH), 4.37 (4.58) (1H, ddd, *J* = 8.5, 6.2, 1.9 Hz (*J* = 8.8, 7.3, 1.9 Hz) NC*H*), 4.25 – 4.15 (1H, m, Me_3SnCH), 2.25 – 2.00 (2H, m, $NCHCH_2$), 1.68 (1.64) (9H, s, $C(CH_3)_3$), 1.25 (1.31) (3H, s, $C(CH_3)_2$), 1.12 (1.08) (3H, s, $C(CH_3)_2$), 0.18 (0.20) (9H, s, $^2J_{119Sn\,H}$ = 54 Hz, $^2J_{117Sn\text{-}H}$ = 52 Hz, $SnMe_3$)); δ_C (125 MHz, $CDCl_3$) (mixture of diastereomers and rotamers) 182.5 (183.3) (C=S),

86.8 (86.1) ($C(CH_3)_3$), 74.5 (74.9) (NCH), 72.6 (72.3) ($C(CH_3)_2$), 53.2 (52.8) (Me_3SnCH), 28.6 (29.0) ($C(CH_3)_3$), 24.7 (25.0) ($C(CH_3)_2$), 23.2 (22.8) ($C(CH_3)_2$), 22.0 ($NCHCH_2$), –7.6 (–8.7) ($SnMe_3$); HRMS (FTMS) calcd for $[M+H]^+$ $C_{14}H_{30}O_2NS^{120}Sn$ 396.1011, found 396.1014.

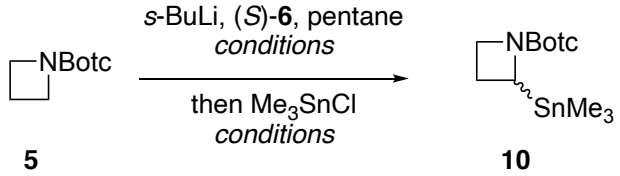
Methyl Iodide as a sacrificial electrophile[11]



The alcohol was prepared following general procedure **A**, using *N*-Botc azetidine **5** (43 mg, 0.25 mmol), with a −78 °C lithiation temp (1 h). MeI (3 µL, 0.05 mmol) was then added, and the reaction was stirred for 5 min at −78 °C before acetone (55 µL, 0.75 mmol) was added with a −78 °C trapping temp (1 h). The crude material was purified by column chromatography (1%-20% Et_2O/petroleum ether) to first give a colourless oil, 2-methylazetidine (*R*)-**7** (0.5 mg, 1%, 73:27 er by HPLC: IC column; eluent: *n*-hexane/*i*-PrOH (99:1); flow rate = 1 mL min^{-1}; τ_R ((*S*) minor) = 17.03 min, τ_R ((*R*) major) = 19.34 min); all other data described in Lit.[1] Second eluted a colourless oil, recovered *N*-Botc azetidine **5** (9 mg, 21% RSM). Third eluted a colourless oil, alcohol (*R*)-**8** (33 mg, 58%, 80:20 er by HPLC: column; eluent: *n*-hexane/*i*-PrOH (95:5); flow rate = 1 mL min^{-1}; τ_R ((*R*) major) = 12.20 min, τ_R ((*S*) minor) = 14.34 min); all other data as described in Lit.[1]

[11] A comparative sample of (*R*)-**7** was prepared following general procedure **A** (0.25 mmol scale), using MeI as the electrophile (lithiation −78 °C (1 h), trapping −78 °C (1 h)). This gave (*R*)-**7** in 77:23 er (36 % yield); all other data as described in Lit.[1]

Asymmetric stannylation



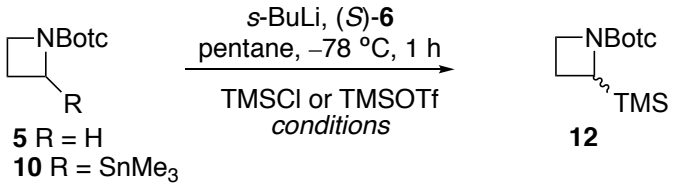
5 **10**

Entry[a]	Lithiation temp (time)	Stannylation temp (time)	Yield 10	er (*R*:*S*)	$[\alpha]_D^{25}$[b]	Recovered 5
1	−78 °C (1 h)	−78 °C (30 min) then rt (30 min)	90%	33:67	+166.3	0%
2	−78 °C (1 h)	−78 °C (30 min)	80%	39:61	+120.9	0%
3	−78 °C (5 min)	−78 °C (30 min) then rt (30 min)	62%	54:46	-42.3	38%
4	−98 °C (3 h)	−98 °C (30 min)	77%	36:64	+145.1	21%
5	−98 °C (1 h)	−98 °C (30 min)	70%	54:46	-32.2	24%

*[a] Reactions were performed following general procedure **A**, on a 0.46-0.92 mmol scale and trapping with 2 equiv of Me_3SnCl. [b] All at c = 0.92-1.19 in $CHCl_3$.*

Table S6. Asymmetric stannylation of N-Botc azetidine 5.

Asymmetric silylation



5 R = H
10 R = $SnMe_3$

12

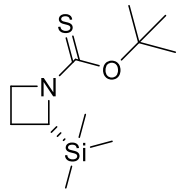
Entry[a]	Substrate 5 or 10	Exp Procedure	Electrophile (equiv)	Incubation time	Yield 12	er (*R*:*S*)
1	**5**	A	TMSCl (3)	1 h	52%	68:32
2	**5**	See below	TMSCl (10)	*In situ*	29%	70:30
3	**10**	C	TMSCl (10)	*In situ*	39%	70:30
4	**5**	A	TMSCl (0.5)	1 h	34%	69:31
4	**5**	A	TMSOTf (3)	1 h	28%	42:58

[a] All reactions 0.25 mmol scale.

Table S7. Asymmetric silylation of N-Botc azetidine 5

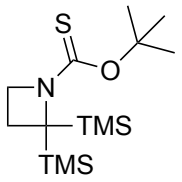
Internal trapping with TMSCl

***O*-(*t*-Butyl) 2-(trimethylsilyl)azetidine-1-carbothioate (*R*)-12**



A solution of (1*S*,2*S*,4*S*,5*S*)-N^2,N^2,N^5,N^5-tetramethylbicyclo[2.2.1]heptane-2,5-diamine (*S*)-**6** (60 mg, 0.33 mmol), *N*-Botc azetidine **5** (43 mg, 0.25 mmol) and TMSCl (0.32 mL, 2.5 mmol) in pentane (2 mL) was cooled to −78 °C. *s*-BuLi (0.25 mL, 1.3 M in cyclohexane/hexane, 0.33 mmol) was added dropwise (~1 min). The reaction mixture was stirred for 1 h at −78 °C, then quenched with sat. aq NH_4Cl (5 mL), and extracted with Et_2O (3 × 5 mL). The combined organic extracts were washed with water (5 mL), then brine (5 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give a yellow oil. The crude material was purified by column chromatography (1% Et_2O/petroleum ether) to first give a colourless oil, disilane **SI-9** (24 mg, 30%). Second eluted a colourless oil, silane (*R*)-**12** (18 mg, 29%, 70:30 er by HPLC: OD-H column; eluent: *n*-hexane/*i*-PrOH (99.9:0.01); flow rate = 1 mL min^{-1}; τ_R ((*S*) minor) = 5.97 min, τ_R ((*R*) major) = 6.51 min); $[\alpha]_D^{25}$ –60.0 (*c* 1.01, $CHCl_3$); all other data as described in Lit.[1] Third eluted a colourless oil, recovered *N*-Botc azetidine **5** (16 mg, 37%).

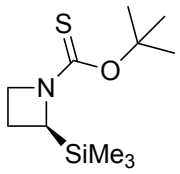
***O*-(*t*-Butyl) 2,2-bis(trimethylsilyl)azetidine-1-carbothioate SI-9**



All data as described in Lit.[3]

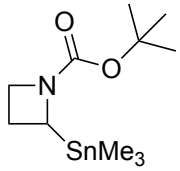
External trapping with TMSOTf

O-(*t*-butyl) 2-(trimethylsilyl)azetidine-1-carbothioate (*S*)-12



Prepared following general procedure **A**, using *N*-Botc azetidine **5** (43 mg, 0.25 mmol), with a −78 °C lithiation temp (1 h). TMSOTf (0.14 mL, 0.75 mmol) was then added with a −78 °C trapping temp (1 h). The crude material was purified by column chromatography (1% Et_2O/petroleum ether) to give eluted a colourless oil, silane (*S*)-**12** (17 mg, 28 %, 58:42 er by HPLC: ODH column; eluent: *n*-hexane/*i*-PrOH (99.9:0.01); flow rate = 1 mL min^{-1}; τ_R ((*S*) major) = 5.44 min, τ_R ((*R*) minor) = 5.82 min); $[\alpha]_D^{25}$+25.5 (*c* 0.86, $CHCl_3$); all other data as described in Lit.[1]

***t*-Butyl 2-(trimethylstannyl)azetidine-1-carboxylate (±)-13**

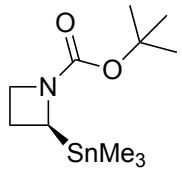


To a solution of stannane (±)-**10** (173 mg, 0.51 mmol) in CH_2Cl_2 (3 mL) was added TMSI (0.10 mL, 0.66 mmol) at rt. The reaction was stirred for 30 min and then concentrated under a stream of nitrogen. The residue was dissolved in CH_2Cl_2 (5 mL), then NEt_3 (0.1 mL, 0.77 mmol), DMAP (5 mg, 0.05 mmol) and Boc_2O (120 mg, 0.56 mmol) was added and the mixture was stirred overnight. The reaction mixture was then concentrated under reduced pressure and to the residue was added sat. aq NH_4Cl (10 mL), and the mixture extracted with CH_2Cl_2 (10 × 2 mL). The combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give a pale yellow oil. This crude material was

purified by column chromatography (5% Et_2O/petroleum ether) to give a colourless oil, stannane (±)-**13** (108 mg, 66%).

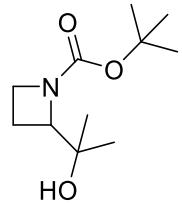
R_f 0.44 (20% Et_2O/petroleum ether); IR (neat/cm^{-1}) 2976 (w), 1687 (s), 1399 (s), 1365 (m), 1152 (m); δ_H (500 MHz, $CDCl_3$) 4.33 (1H, br, NCH), 4.14 – 4.02 (1H, m, NCH*H*'), 3.96 (1H, td, *J* = 9.0, 6.3 Hz, NC*H*H'), 2.47 (1H, qd, *J* = 10.0, 6.3 Hz, NCHCH*H*'), 2.18 – 2.08 (1H, m, NCHC*H*H'), 1.42 (9H, s, $C(CH_3)_3$), 0.14 (9H, s, $^2J_{119Sn-H}$ = 53 Hz, $^2J_{117Sn-H}$ = 51 Hz, $SnMe_3$); δ_C (125 MHz, $CDCl_3$) (rotamers) 156.5 (155.9) (C=O), 79.3 (78.8) ($C(CH_3)_3$), 52.8 (51.2) (NCH), 50.8 (49.6) (NCH_2), 28.7 ($C(CH_3)_3$), 19.7 ($NCHCH_2$), –10.1 ($J_{119Sn-C}$ = 325 Hz, $J_{117Sn-C}$ = 312 Hz, $SnMe_3$); HRMS (FTMS) calcd for [M+Na] $C_{11}H_{23}O_2NNa^{120}Sn$ 344.0644, found 344.0644.

_t_-Butyl (_S_)-2-(trimethylstannyl)azetidine-1-carboxylate (_S_)-13



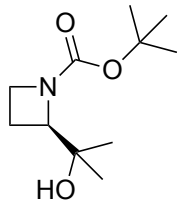
Prepared following the same procedure for racemic **13** (see above), but using stannane (*S*)-**10** (173 mg, 0.51 mmol, 63:37 er) to give stannane (*S*)-**13** (104 mg, 63%, 66:34 er by HPLC: ODH column; eluent: *n*-hexane/*i*-PrOH (99:1); flow rate = 1 mL min^{-1}; τ_R ((*S*) major) = 4.16 min, τ_R ((*R*) minor) = 4.53 min); $[\alpha]_D^{25}$ +57.9 (*c* 0.38, $CHCl_3$); all other data as described above.

_t_-Butyl 2-(2-hydroxypropan-2-yl)azetidine-1-carboxylate (±)-14



N-Boc alcohol (±)-**14** was prepared following general procedure **B**, using stannane (±)-**13** (80 mg, 0.25 mmol) and DIANANE (*S*)-**6**, with a −78 °C lithiation temp (1 h). Acetone (60 µL, 0.75 mmol) was then added with a −78 °C trapping temp (1 h). The crude material was purified by column chromatography (1%-10% Et_2O/petroleum ether) to first give a colourless oil, *N*-Boc azetidine (6 mg, 16%). Second eluted a colourless oil, *N*-Boc alcohol **14** (25 mg, 47%, 50:50 er by HPLC: ADH column; eluent: *n*-hexane/*i*-PrOH (95:5); flow rate = 1 mL min^{-1}; τ_R (*R*) = 9.42 min, τ_R (*S*) = 15.10 min); all other data as described in Lit.[12]

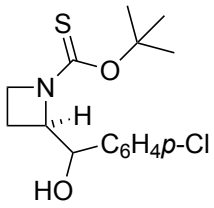
_t_-Butyl (*R*)-2-(2-hydroxypropan-2-yl)azetidine-1-carboxylate (*R*)-14



N-Boc alcohol (*R*)-**14** was prepared following general procedure **B**, using stannane (*S*)-**13** (80 mg, 0.25 mmol, 66:34 er) and racemic DIANANE (±)-**6**, with a −78 °C lithiation temp (1 h). Acetone (60 µL, 0.75 mmol) was then added with a −78 °C trapping temp (1 h). The crude material was purified by column chromatography (1%-10% Et_2O/petroleum ether) to first give a colourless oil, *N*-Boc azetidine (6 mg, 16%). Second eluted a colourless oil, *N*-Boc alcohol (*R*)-**14** (22 mg, 40%, 67:33 er by HPLC: ADH column; eluent: *n*-hexane/*i*-PrOH (95:5); flow rate = 1 mL min^{-1}; τ_R (*R*) major = 9.38 min, τ_R , (*S*) minor = 15.09 min); $[\alpha]_D^{25}$+14.6 (*c* 0.13, $CHCl_3$) (lit.,[7] $[\alpha]_D^{25}$+45.8 (*c* 0.62 in $CHCl_3$ for (*R*)-**14** of 89:11 er)); all other data as described in Lit.[12]

[12] D. M. Hodgson, C. Pearson and M. Kazmi, *Org. Lett*., 2014, **16**, 856.

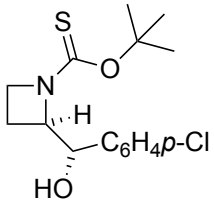
***O*-(*t*-Butyl) (2*R*)-2-((4-chlorophenyl)(hydroxy)methyl)azetidine-1-carbothioate (*R,R*)-SI-3 and (*R,S*)-SI-3**



The alcohol was prepared following general procedure **A**, using *N*-Botc azetidine **5** (60 mg, 0.35 mmol), with a −78 °C lithiation temp (1 h). 4-Chlorobenzaldehyde (146 µL, 1.04 mmol) was then added with a −78 °C trapping temp (1 h). The crude material was purified by column chromatography (5%-20% Et_2O/petroleum ether) to first give a colourless oil, recovered *N*-Botc azetidine **5** (15 mg, 25% RSM). Second eluted a colourless oil, alcohol minor diastereomer (*R,S*)-**SI-3** (22 mg, 20%, 80:20 er by HPLC: AD-H column; eluent: *n*-hexane/*i*-PrOH (95:5); flow rate = 1 mL min^{-1}; τ_R ((*S*,*R*) minor) = 11.74 min, τ_R ((*R*,*S*) minor) = 13.05 min). Third eluted a white solid, alcohol major diastereomer (*R,R*)-**SI-3** (48 mg, 44%, 80:20 er by HPLC: AD-H column; eluent: *n*-hexane/*i*-PrOH (96:4); flow rate = 1 mL min^{-1}; τ_R ((*S*,*S*) minor) = 8.34 min, τ_R ((*R*,*R*) major) = 19.70 min).

Absolute configurations were assigned by analogy to (*R,S*)-**SI-2** and (*R,R*)-**SI-2**.[9]

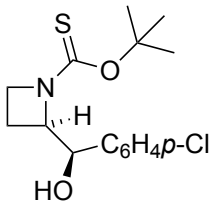
***O*-(*t*-butyl) (*R*)-2-((*S*)-(4-chlorophenyl)(hydroxy)methyl)azetidine-1-carbothioate (*R,S*)-SI-3 minor**



$[\alpha]_D^{25}$ +79.0 (*c* 0.90, $CHCl_3$); all other data described in Lit.[1]

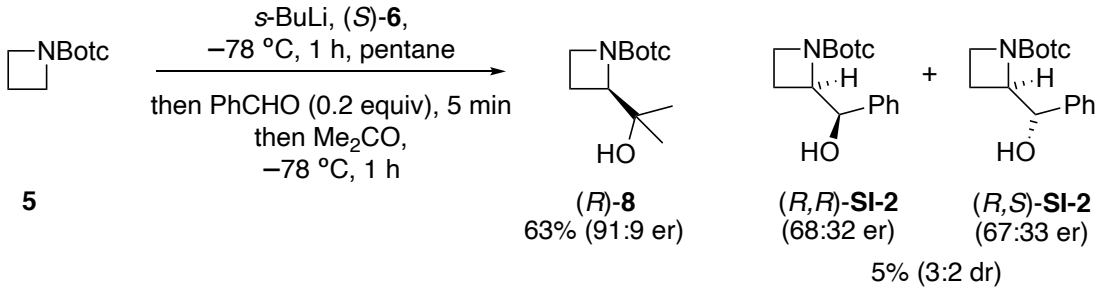
***O*-(*t*-butyl) (*R*)-2-((*R*)-(4-chlorophenyl)(hydroxy)methyl)azetidine-1-carbothioate (*R,R*)-SI-3**

major



$[\alpha]_D^{25}$ +23.2 (*c* 0.98, $CHCl_3$); all other data described in Lit.[1]

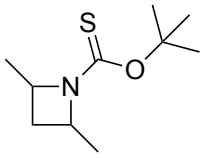
Benzaldehyde as sacrificial electrophile



The alcohol was prepared following general procedure **A**, using *N*-Botc azetidine **5** (43 mg, 0.25 mmol), with a −78 °C lithiation temp (1 h). Benzaldehyde (5 µL, 0.05 mmol) was then added, the reaction was then stirred for 5 min at −78 °C before acetone (55 µL, 0.75 mmol) was added with a −78 °C trapping temp (1 h). The crude material was purified by column chromatography (1%-20% Et_2O/petroleum ether) to first give a colourless oil, recovered azetidine **5** (12 mg, 29% RSM). Second eluted a colourless oil, a mixture of diastereomeric alcohols minor (*R,S*)-**SI-2** (2 mg, 2%, 67:33 er by HPLC: AD-H column; eluent: *n*-hexane/*i*-PrOH (96:4); flow rate = 1 mL min^{-1}; τ_R ((*S*,*R*) minor) = 10.54 min, τ_R ((*R*,*S*) major) = 11.31 min) and major (*R,R*)-**SI-2** (3 mg, 3%, 68:32 er by HPLC: AD-H column; eluent: *n*-hexane/*i*-PrOH (96:4); flow rate = 1 mL min^{-1}; τ_R ((*S*,*S*) minor) = 23.41 min, τ_R ((*R*,*R*) major) = 33.10 min). Third eluted a colourless oil, alcohol (*R*)-**8** (36 mg, 63%, 91:9 er by HPLC: AD-H column; eluent:

n-hexane/*i*-PrOH (95:5); flow rate = 1 mL min^{-1}; τ_R ((*R*) major) = 12.18 min, τ_R ((*S*) minor) = 14.17 min); all other data as described in Lit.[1]

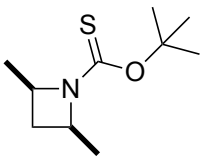
_O_-(_t_-Butyl) 2,4-dimethylazetidine-1-carbothioate SI-4



2,4-Dimethylazetidine **SI-4** was prepared following general procedure **A**, using 2-methylazetidine (±)-**7** (47 mg, 0.25 mmol) and DIANANE (±)-**6**, with a −78 °C lithiation temp (1 h). MeI (50 µL, 0.75 mmol) was then added with a −78 °C trapping temp (1 h). The crude material was purified by column chromatography (1%-5% Et_2O/petroleum ether) to first give a colourless oil, a mixture of diastereomers 2,4-dimethylazetidine **SI-4** (7 mg, 15%, 43:57 dr *cis:trans*). Second eluted a colourless oil, recovered methylazetidine **7** (19 mg, 40% RSM).

Analytically pure sample of diastereomers ***cis*-SI-4** and ***trans*-SI-4** was obtained following prep-TLC (5% Et_2O/petroleum ether).

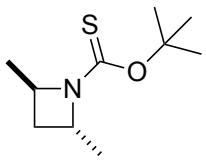
***cis*-*O*-(*t*-Butyl) (*R*,S**)-2,4-dimethylazetidine-1-carbothioate *cis*-SI-4**



R_f 0.37 (5% Et_2O/petroleum ether); IR (neat/cm^{-1}) 1469 s, 1434 s, 1390 m, 1269 s, 1224 m, 1142 s; δ_H (400 MHz, $CDCl_3$) (single rotamer) 4.37 (4.24) (2H, dquin, *J* = 8.6, 6.3 Hz (*J* = 8.6, 6.3 Hz), NC*H*), 2.54 (1H, dt, *J* = 11.2, 8.6 Hz, $NCHCH_{cis}\mathit{H}_{trans}$), 1.64 (9H, s, $C(C\mathit{H}_3)_3$), 1.56 (1.42) (6H, d, *J* = 6.3, $NCHC\mathit{H}_3$), 1.39 – 1.30 (1 H, m, $NCHC\mathit{H}_{cis}H_{trans}$); δ_C (100 MHz, $CDCl_3$) (single rotamer)

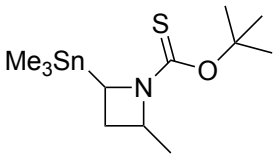
186.6 (C=S), 84.6 (*C*$(CH_3)_3$), 58.74 and 58.72 (2x NCH), 31.3 (NCH*C*H_2), 28.7 (C(*C*$H_3)_3$), 22.2 and 21.5 (2x CH*C*H_3); HRMS (FI^+) calcd for [M+H] $C_{10}H_{20}NOS$: 202.1260, found 202.1262.

_O_-(_t_-Butyl) (_R*_,_R*_)-2,4-dimethylazetidine-1-carbothioate _trans_-SI-4



R_f 0.35 (5% Et_2O/petroleum ether); IR (neat/cm^{-1}) 1427 m, 1390 s, 1365 m, 1270 s, 1226 m, 1139 s; δ_H (400 MHz, $CDCl_3$) (single rotamer) 4.56 – 4.45 (4.45 – 4.35) (2H, m, NC*H*), 1.99 – 1.87 (2H, m, NCHCH_2), 1.64 (9H, s, C(C$H_3)_3$), 1.55 (1.40) (6H, d, *J* = 6.3 Hz, NCHCH_3); δ_C (100 MHz, $CDCl_3$) (single rotamer) 184.4 (C=S), 84.7 (*C*$(CH_3)_3$) , 58.3 and 57.8 (2x NCH), 31.4 (NCH*C*H_2), 28.8 (C(*C*$H_3)_3$), 19.2 and 20.5 (2x CH*C*H_3); HRMS (FI^+) calcd for [M+H] $C_{10}H_{20}NOS$: 202.1260, found 202.1262.

_O_-(_t_-Butyl) 4-methyl-2-(trimethylstannyl)azetidine-1-carbothioate SI-5

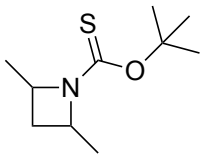


A solution of 2-methylazetidine **7** (240 mg, 1.30 mmol) and TMEDA (0.46 mL, 3.1 mmol) in THF (6.5 mL) was cooled to −78 °C. *s*-BuLi (1.30 mL, 1.3 M in cyclohexane/hexane, 1.70 mmol) was added dropwise. The reaction mixture was stirred for 30 min at −78 °C before addition of Me_3SnCl (2.40 mL, 1 M in pentane, 2.4 mmol) dropwise. The reaction mixture was stirred for a further 30 min at −78 °C, then quenched with sat. aq NH_4Cl (10 mL), and extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed with water (10 mL), then brine (10

mL), dried ($MgSO_4$) and concentrated under reduced pressure to give a pale-yellow oil. The crude material was purified by column chromatography (1% Et_2O/petroleum ether) to first give a colourless oil, stannane **SI-5** (270 mg, 59%, (~1:1 dr). Second eluted a colourless oil, recovered 2-methylazetidine **7** (84 mg, 41% RSM).

R_f 0.86 (5% Et_2O/petroleum ether); IR (neat/cm^{-1}) 2975 w, 1793 m, 1490 m, 1228 s, 1144 s; δ_H (400 MHz, $CDCl_3$) (mixture of diastereomers and rotamers) 4.70 – 4.24 (4H, m, NCH), 2.56 (2.70) (1H, ddd, *J* = 11.1, 10.1, 8.4 Hz, (td, *J* = 10.8, 8.6 Hz), NCHC*H*H' (*cis*)), 2.26 (1H, ddd, *J* = 11.0, 8.0, 6.3 Hz, NCHC*H*H' (*trans*)), 2.01 (1H, ddd, *J* = 11.1, 10.1, 5.9 Hz, NCHCH*H*' (*trans*)), 1.78 – 1.68 (1H, m, NCHCH*H*' (*cis*)), 1.61 (1.61) (1.65) (1.64) (18H, s, $C(CH_3)_3$), 1.26 (6H, pseudo t, *J* = 6.7 Hz, CHC*H*$_3$), 0.02 (0.00) (18H, s, $^2J_{119Sn\,H}$ = 27 Hz, $^2J_{117Sn\text{-}H}$ = 26 Hz, $Sn(CH_3)_3$); δ_C (100 MHz, $CDCl_3$) (mixture of diastereomers and rotamers)) 181.8 (C=S), 83.92 (83.86) ($C(CH_3)_3$), 60.14 (60.11) (N*C*HCH$_3$), 52.3 (51.8) (N*C*HSnMe$_3$), 28.74 (28.72) (28.9) (C(CH_3)$_3$), 26.5 (26.4) (NCH*C*H$_2$), 20.7 (20.4) (NCH*C*H$_3$), –7.9 (–8.3) ($SnMe_3$); HRMS not found.

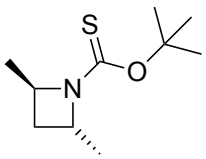
_O_-(_t_-Butyl) 2,4-dimethylazetidine-1-carbothioate SI-4



2,4-Dimethylazetidine **SI-4** was prepared following general procedure **B**, using stannane (±)-**SI-5** (88 mg, 0.25 mmol) and racemic DIANANE (±)-**6**, with a −78 °C lithiation temp (1 h). MeI (50 µL, 0.75 mmol) was then added with a −78 °C trapping temp (1 h). The crude material was purified by column chromatography (1%-5% Et_2O/petroleum ether) to first give a colourless oil, a mixture of diastereomers 2,4-dimethylazetidine **SI-4** (32 mg, 63%, 25:75 dr *cis:trans*); all

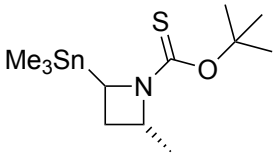
other data as described above. Second eluted a colourless oil, methylazetidine **7** (5 mg, 11%); all other data described in Lit.[1]

***O*-(*t*-Butyl) (2*R*,4*R*)-2,4-dimethylazetidine-1-carbothioate SI-4**



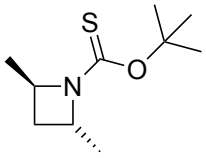
2,4-Dimethylazetidine (*R*,*R*)-**SI-4** was prepared following general procedure **A**, using 2-methylazetidine (*R*)-**7** (37 mg, 0.20 mmol, 80:20 er) with a −78 °C lithiation temp (1 h). MeI (40 µL, 0.60 mmol) was then added with a −78 °C trapping temp (1 h). The crude material was purified by column chromatography (1%-5% Et_2O/petroleum ether) to first give a colourless oil, (2*R*,4*R*)-2,4-dimethylazetidine (*R*,*R*)-**SI-4** (18 mg, 46%, 18:82 dr *cis:trans*, 91:9 er by HPLC: Chiralcel I-C column, eluent: *n*-hexane/*i*-PrOH (99:1), flow rate = 1 mL/min; τ_R ((*R*,*R*) major) = 11.8 min, τ_R (*cis*) = 13.0 min, τ_R ((*S*,*S*) minor) = 21.3 min); as an inseparable mixture of diastereomers; all other data as described above. Second eluted a colourless oil, recovered (*R*)-methylazetidine (*R*)-**7** (17 mg, 45% RSM, 70:30 er by HPLC: IC column; eluent: *n*-hexane/*i*-PrOH (99:1); flow rate = 1 mL min^{-1}; τ_R ((*S*) minor) = 17.38 min, τ_R ((*R*) major) = 21.20 min); all other data as described in Lit.[1]

***O*-(*t*-Butyl) (4*R*)-4-methyl-2-(trimethylstannyl)azetidine-1-carbothioate SI-5**



A solution of 2-methylazetidine (*R*)-**7** (290 mg, 1.50 mmol, 80:20 er) and TMEDA (0.55 mL, 3.7 mmol) in THF (7.7 mL) was cooled to −78 °C. *s*-BuLi (1.50 mL, 1.3 M in cyclohexane/hexane, 2.0 mmol) was added dropwise. The reaction mixture was stirred for 30 min at −78 °C before addition of Me_3SnCl (2.9 mL, 1.0 M in pentane, 2.9 mmol) dropwise. The reaction mixture was stirred for a further 30 min at −78 °C, then quenched with sat. aq NH_4Cl (10 mL), and extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed with water (10 mL), then brine (10 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give a pale-yellow oil. The crude material was purified by column chromatography (1% Et_2O/petroleum ether) to first give a colourless oil, stannane (4*R*)-**SI-5** (340 mg, 63%, 1:1 dr) as an inseparable mixture of diastereomers. Second eluted a colourless oil, recovered 2-methylazetidine (*R*)-**7** (90 mg, 31% RSM, 76:24 er by HPLC: IC column; eluent: *n*-hexane/*i*-PrOH (99:1); flow rate = 1 mL min^{-1}; τ_R ((*S*) minor) = 17.06 min, τ_R ((*R*) major) = 20.23 min); all other data as described in Lit.[1]

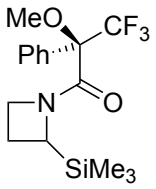
***O*-(*t*-Butyl) (2*R*,4*R*)-2,4-dimethylazetidine-1-carbothioate (*R*,*R*)-SI-4**



2,4-Dimethylazetidine (*R*,*R*)-**SI-4** was prepared following general procedure **B**, using enantioenriched stannanes (4*R*)-**SI-5** (70 mg, 0.20 mmol) and DIANANE (*S*)-**6** (48 mg, 0.26 mmol), with a −78 °C lithiation temp (1 h). MeI (40 µL, 0.60 mmol) was then added with a −78 °C trapping temp (1 h). The crude material was purified by column chromatography (1%-5% Et_2O/petroleum ether) to first give a colourless oil, a mixture of diastereomers 2,4-dimethylazetidine (*R*,*R*)-**SI-4** and ***cis*-SI-4** (18 mg, 45%, 26:74 dr *cis:trans*, 82:18 er by HPLC: Chiralcel I-C column, eluent: *n*-hexane/*i*-PrOH (99:1), flow rate = 1 mL/min; τ_R ((*S*,*S*) minor) =

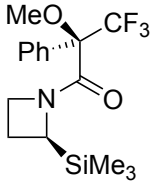
10.72 min, τ_R ((*R*,*R*) minor) = 18.30 min). Second eluted a colourless oil 2-methylazetidine (*R*)-**7** (5 mg, 13%, 74:26 er by HPLC: IC column; eluent: *n*-hexane/*i*-PrOH (99:1); flow rate = 1 mL min^{-1}; τ_R ((*S*) minor) = 17.09 min, τ_R ((*R*) major) = 20.75 min); all other data as described in Lit.[1]

(2*R*)-3,3,3-Trifluoro-2-methoxy-2-phenyl-1-(2-(trimethylsilyl)azetidin-1-yl)propan-1-one (*R*,*S*)-SI-6 and (*R*,*R*)-SI-6



Silyl Mosher amides (*R*,*S*)-**SI-6** and (*R*,*R*)-**SI-6** were prepared following general procedure **D**, using silane **12** (10 mg, 0.04 mmol). The crude material was purified by column chromatography (10%-20% Et_2O/petroleum ether) to first give a colourless oil, silyl Mosher amide (*R*,*S*)-**SI-6** (3 mg, 22%). Second eluted a colourless oil, silyl Mosher amide (*R*,*R*)-**SI-6** (4 mg, 30%).

(*R*)-3,3,3-Trifluoro-2-methoxy-2-phenyl-1-((*S*)-2-(trimethylsilyl)azetidin-1-yl)propan-1-one (*R*,*S*)-SI-6

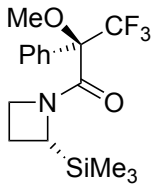


R_f 0.57 (50% Et_2O/petroleum ether); $[\alpha]_D^{25}$ +46.0 (*c* 0.05, $CHCl_3$); IR (neat/cm^{-1}) 2955 (w), 1656 (s), 1266 (m), 1251 (m), 1180 (s), 1165 (s), 841 (m); δ_H (500 MHz, $CDCl_3$) 7.60 – 7.53 (2H, m, *m*-Ph), 7.42 – 7.33 (3H, m, *o*-Ph & *p*-Ph), 4.18 (1H, ddd, *J* = 9.6, 7.4, 1.3 Hz, NCH), 3.98 (1H, dddd, *J* = 10.1, 9.2, 6.2, 1.3 Hz, NCH*H*'), 3.67 (3H, q, *J* = 1.9 Hz, OMe), 3.44 (1H, td, *J* = 10.1, 6.3

Hz, NC*H*H'), 2.14 (1H, dddd, *J* = 11.0, 10.1, 9.6, 6.2 Hz, NCHCH*H*'), 1.97 (1H, dddd, *J* = 11.0, 9.2, 7.4, 6.3, NCHC*H*H'), 0.16 (9H, s, $SiMe_3$); δ_C (125 MHz, $CDCl_3$) 164.5 (C=O), 133.6 (*i*-Ph), 129.3 (*p*-Ph), 128.4 (*o*-Ph), 127.1 (*m*-Ph), 123.5 (Q, *J* = 290 Hz, CF_3), 84.1 (q, *J* = 26 Hz *C*CF_3), 55.2 (NCH), 55.1 (q, *J* = 2 Hz, OMe), 52.6 (NCH_2), 18.2 (NCH*C*H_2), –3.1 ($SiMe_3$); δ_F (377 MHz, $CDCl_3$) –69.9 (s); HRMS (ESI^+) calcd for [M+H] $C_{16}H_{23}O_2NF_3{}^{28}Si$ 346.1445, found 346.1445.

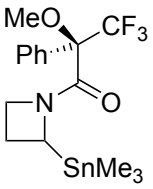
(*R*)-3,3,3-Trifluoro-2-methoxy-2-phenyl-1-((*R*)-2-(trimethylsilyl)azetidin-1-yl)propan-1-one

(*R*,*R*)-SI-6



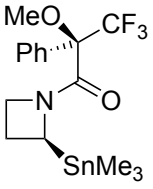
R_f 0.46 (50% Et_2O/petroleum ether); $[\alpha]_D^{25}$–13.8 (*c* 0.09, $CHCl_3$) IR (neat/cm^{-1}) 2981 (w), 1655 (s), 1268 (m), 1250 (m), 1178 (s), 1166 (s), 841 (m); δ_H (500 MHz, $CDCl_3$) 7.60 – 7.53 (2H, m, *m*-Ph), 7.40 – 7.35 (3H, m, *o*-Ph & *p*-Ph), 4.17 (1H, ddd, *J* = 11.0, 7.4, 1.6 Hz, NCH), 4.10 (1H, ddd, *J* = 10.3, 9.5, 6.3 Hz, NCH*H*'), 3.67 (3H, q, *J* = 1.7 Hz, OMe), 3.25 (1H, dddd, *J* = 10.3, 9.3, 6.1, 1.6 Hz, NC*H*H'), 2.25 (1H, tdd, *J* = 11.0, 9.5, 6.1 Hz, NCHCH*H*'), 1.85 (1H, dddd, *J* = 11.0, 9.3, 7.4, 6.3 Hz, NCHC*H*H'), 0.11 (9H, s, $SiMe_3$); δ_C (125 MHz, $CDCl_3$) 164.2 (C=O), 133.7 (*i*-Ph), 129.3 (*p*-Ph), 128.1 (*o*-Ph), 127.2 (*m*-Ph), 123.8 (Q, *J* = 289 Hz, CF_3), 83.9 (q, *J* = 26 Hz *C*CF_3), 55.2 (q, *J* = 3 Hz, OMe), 54.8 (NCH), 52.1 (NCH_2), 18.2 (NCH*C*H_2), –3.0 ($SiMe_3$); δ_F (377 MHz, $CDCl_3$) –70.6 (s); HRMS (ESI^+) calcd for [M+H] $C_{16}H_{23}O_2NF_3{}^{28}Si$ 346.1445, found 346.1445.

(2*R*)-3,3,3-Trifluoro-2-methoxy-2-phenyl-1-(2-(trimethylstannyl)azetidin-1-yl)propan-1-one (*R*,*S*)-SI-7 and (*R*,*R*)-SI-7



To a solution of stannane **10** (34 mg, 0.1 mmol) in CH_2Cl_2 (0.6 mL) was added TMSI (20 µL, 0.13 mmol) dropwise at rt. The reaction was stirred for 30 min and then concentrated under a stream of nitrogen. The crude was dissolved in CH_2Cl_2 (1.0 mL), then DIPEA (38 µL, 0.22 mmol) and (*S*)-MTPA-Cl (22 µL, 0.12 mmol) was added and the reaction was stirred overnight. The reaction mixture was then concentrated under reduced pressure and to the residue was added sat. aq NH_4Cl (2 mL), and extracted with CH_2Cl_2 (3 × 2 mL). The combined organic extracts were washed with brine (2 mL), dried ($MgSO_4$) and concentrated under reduced pressure to give a pale yellow oil. This was purified by column chromatography (5%-10% Et_2O/petroleum ether) to first give crystalline solid, stannyl Mosher amide (*R*,*S*)-**SI-7** (6 mg, 14%).[8] Second eluted a colourless oil stannyl Mosher amide (*R*,*R*)-**SI-7** (6 mg, 14%).

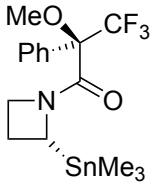
(*R*)-3,3,3-Trifluoro-2-methoxy-2-phenyl-1-((*S*)-2-(trimethylstannyl)azetidin-1-yl)propan-1-one (*R*,*S*)-SI-7



R_f 0.33 (5% Et_2O/petroleum ether); $[\alpha]_D^{25}$ +192.2 (*c* 0.25, $CHCl_3$); mp 115–116 °C; IR (neat/cm^{-1}) 2954 (w), 1813 (m), 1643 (m), 1165 (s); δ_H (400 MHz, $CDCl_3$) 7.58 – 7.52 (2H, m, *m*-Ph), 7.45 – 7.36 (3H, m, *o*-Ph & *p*-Ph), 4.50 – 4.37 (1H, m, NCH), 4.12 (1H, dddd, *J* = 10.5,

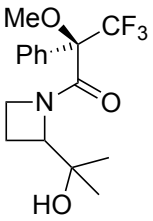
9.1, 5.8, 1.6 Hz, NCH*H*'), 3.67 – 3.60 (1H, m, NC*H*H'), 3.63 (3H, q, *J* = 1.9, OMe), 2.31 (1H, dddd, *J* = 11.2, 10.0, 9.3, 5.8 Hz, NCHCH*H*'), 2.20 (1H, dddd, *J* = 11.2, 9.1, 7.7, 6.5 Hz, NCHC*H*H'), 0.21 (9H, s, $^2J_{119Sn-H}$ = 54 Hz, $^2J_{117Sn-H}$ = 52 Hz, $SnMe_3$); δ_C (100 MHz, $CDCl_3$) 163.7 (C=O), 133.6 (*i*-Ph), 129.3 (*p*-Ph), 128.3 (*o*-Ph), 127.2 (*m*-Ph), 123.7 (Q, *J* = 290 Hz, CF_3), 84.2 (q, *J* = 26 Hz, *C*CF_3), 55.1 (q, *J* = 3 Hz, OMe), 53.3 (NCH_2), 52.5 (NCH), 20.6 (NCH*C*H_2), –9.76 ($J_{119Sn-C}$ = 331 Hz, $J_{117Sn-C}$ = 317 Hz, $SnMe_3$); δ_F (377 MHz, $CDCl_3$) –69.8 (s); HRMS (ESI^+) calcd for [M+H] $C_{16}H_{23}O_2NF_3{}^{120}Sn$ 438.0699, found 438.0691.

(*R*)-3,3,3-Trifluoro-2-methoxy-2-phenyl-1-((*R*)-2-(trimethylstannyl)azetidin-1-yl)propan-1-one (*R*,*R*)-SI-7



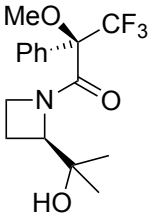
R_f 0.26 (5% Et_2O/petroleum ether); $[\alpha]_D^{25}$ –44.0 (*c* 0.13, $CHCl_3$); IR (neat/cm^{-1}) 2954 (w), 1814 (m), 1643 (m), 1230 (m), 1166 (s); δ_H (400 MHz, $CDCl_3$) 7.67 – 7.48 (2H, m, *m*-Ph), 7.46 – 7.28 (3H, m, *o*-Ph & *p*-Ph), 4.41 (1H, dddd, *J* = 10.1, 7.4, 1.5, 0.9 Hz, NCH), 4.21 (1H, dddd, *J* = 10.2, 9.3, 6.4, 0.9 Hz, NCH*H*'), 3.65 (3H, q, *J* = 1.8 Hz, OMe), 3.50 – 3.36 (1H, m, NC*H*H'), 2.41 (1H, dddd, *J* = 11.2, 10.1, 9.3, 5.9 Hz, NCHCH*H*'), 2.04 (1H, dddd, *J* = 11.2, 9.2, 7.4, 6.4 Hz, NCHC*H*H'), 0.17 (9H, s, $^2J_{119Sn-H}$ = 54 Hz, $^2J_{117Sn-H}$ = 52 Hz, $SnMe_3$); δ_C (100 MHz, $CDCl_3$) 163.9 (C=O), 133.6 (*i*-Ph), 129.3 (*p*-Ph), 128.2 (*o*-Ph), 127.2 (*m*-Ph), 124.0 (Q, *J* = 290 Hz, CF_3), 83.7 (q, *J* = 28 Hz, *C*CF_3), 55.1 (q, *J* = 2 Hz, OMe), 53.2 (NCH_2), 51.8 (NCH), 20.6 (NCH*C*H_2), –9.5 ($J_{119Sn-C}$ = 332 Hz, $J_{117Sn-C}$ = 318 Hz, $SnMe_3$); δ_F (377 MHz, $CDCl_3$) –70.2 (s); HRMS (ESI^+) calcd for [M+H] $C_{16}H_{23}O_2NF_3{}^{120}Sn$ 438.0699, found 438.0694.

(2*R*)-3,3,3-Trifluoro-1-(2-(2-hydroxypropan-2-yl)azetidin-1-yl)-2-methoxy-2-phenylpropan-1-one (*R*,*R*)-SI-8 and (*R*,*S*)-SI-8



Alcohol Mosher amides (*R*,*R*)-**SI-8** and (*R*,*S*)-**SI-8** were prepared following general procedure **D**, using alcohol **8** (10 mg, 0.04 mmol). The crude material was purified by column chromatography (40%-80% Et_2O/petroleum ether) to first give a crystalline solid, alcohol Mosher amide (*R*,*R*)-**SI-8** (1 mg, 8%). Second eluted a crystalline solid alcohol Mosher amide (*R*,*S*)-**SI-8** (1 mg, 8%).

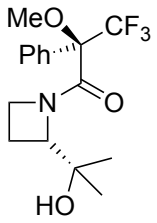
(*R*)-3,3,3-Trifluoro-1-((*R*)-2-(2-hydroxypropan-2-yl)azetidin-1-yl)-2-methoxy-2-phenylpropan-1-one (*R*,*R*)-SI-8



R_f 0.59 (100% Et_2O); $[\alpha]_D^{25}$ +136.5 (*c* 0.13, $CHCl_3$); mp 94 °C; IR (neat/cm^{-1}) 3363 (br), 2924 (m), 1639 (m), 1167 (m); δ_H (400 MHz, $CDCl_3$) 7.60 – 7.52 (2H, m, *m*-Ph), 7.45 – 7.39 (3H, m, *o*-Ph & *p*-Ph), 4.45 (1H, pseudo t, *J* = 8.2 Hz, NCH), 3.88 (1H, tdd, *J* = 9.9, 5.2, 1.3 Hz, NCH*H*'), 3.71 (3H, q, *J* = 1.9 Hz, OMe), 3.33 (1H, dddd, *J* = 9.9, 9.1, 7.2, 0.8, NC*H*H'), 2.08 (1H, dtd, *J* = 11.7, 9.1, 5.2 Hz, NCHCH*H*'), 1.87 (1 H, ddt, *J* = 11.7, 9.9, 7.2 Hz, NCHC*H*H'), 1.58 (1H, br s, OH), 1.31 (3H, s, CH_3), 1.09 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 167.8 (C=O), 132.9 (*i*-Ph), 129.7 (*p*-Ph),

128.6 (*o*-Ph), 127.0 (*m*-Ph), 123.4 (Q, *J* = 289 Hz, CF_3), 84.2 (q, *J* = 26 Hz, *C*CF_3), 73.8 (NCH), 71.3 (COH), 55.4 (q, *J* = 3 Hz, OMe), 49.8 (NCH_2), 24.2 (CH_3), 23.4 (CH_3), 20.4 (NCH*C*H_2); δ_F (377 MHz, $CDCl_3$) –69.9 (s); HRMS (ESI^+) calcd for [M+Na] $C_{16}H_{20}O_3NF_3Na$ 354.1287, found 354.1287.

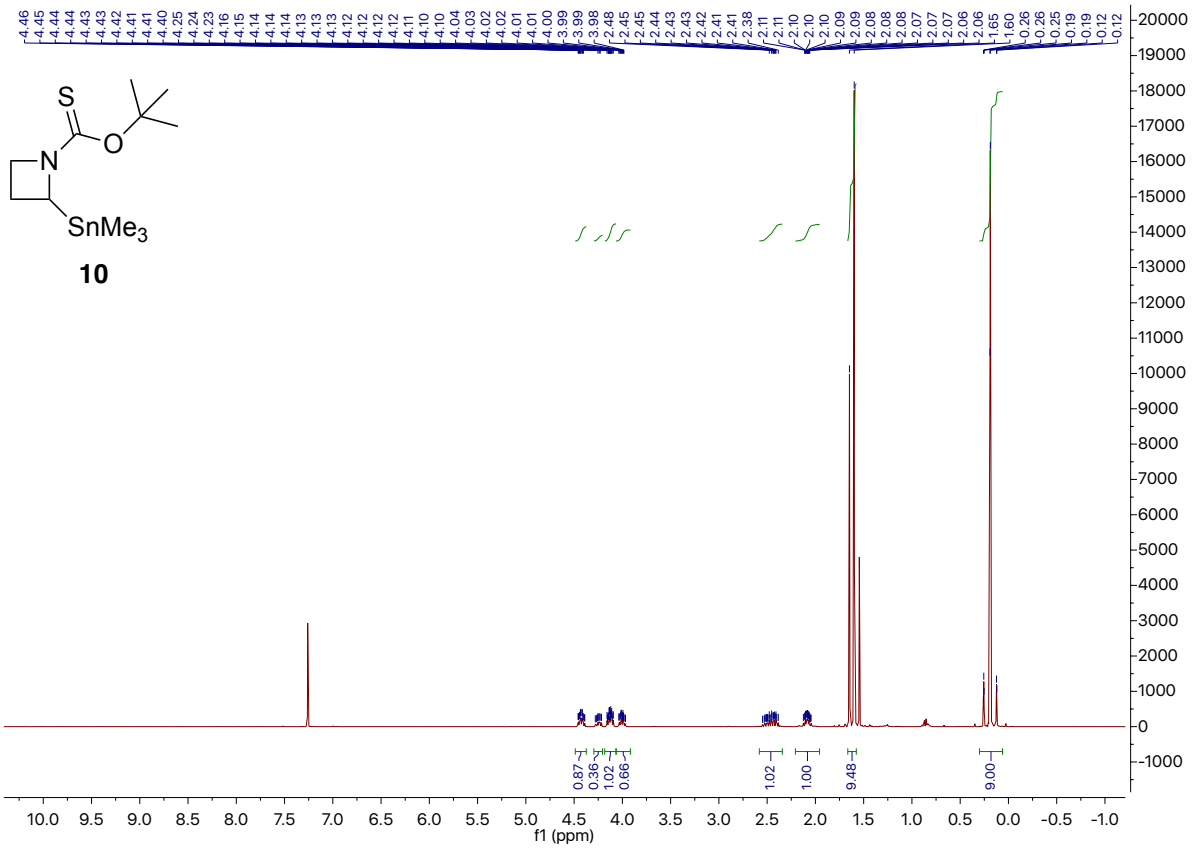
(*R*)-3,3,3-Trifluoro-1-((*S*)-2-(2-hydroxypropan-2-yl)azetidin-1-yl)-2-methoxy-2-phenylpropan-1-one (*R*,*S*)-SI-8



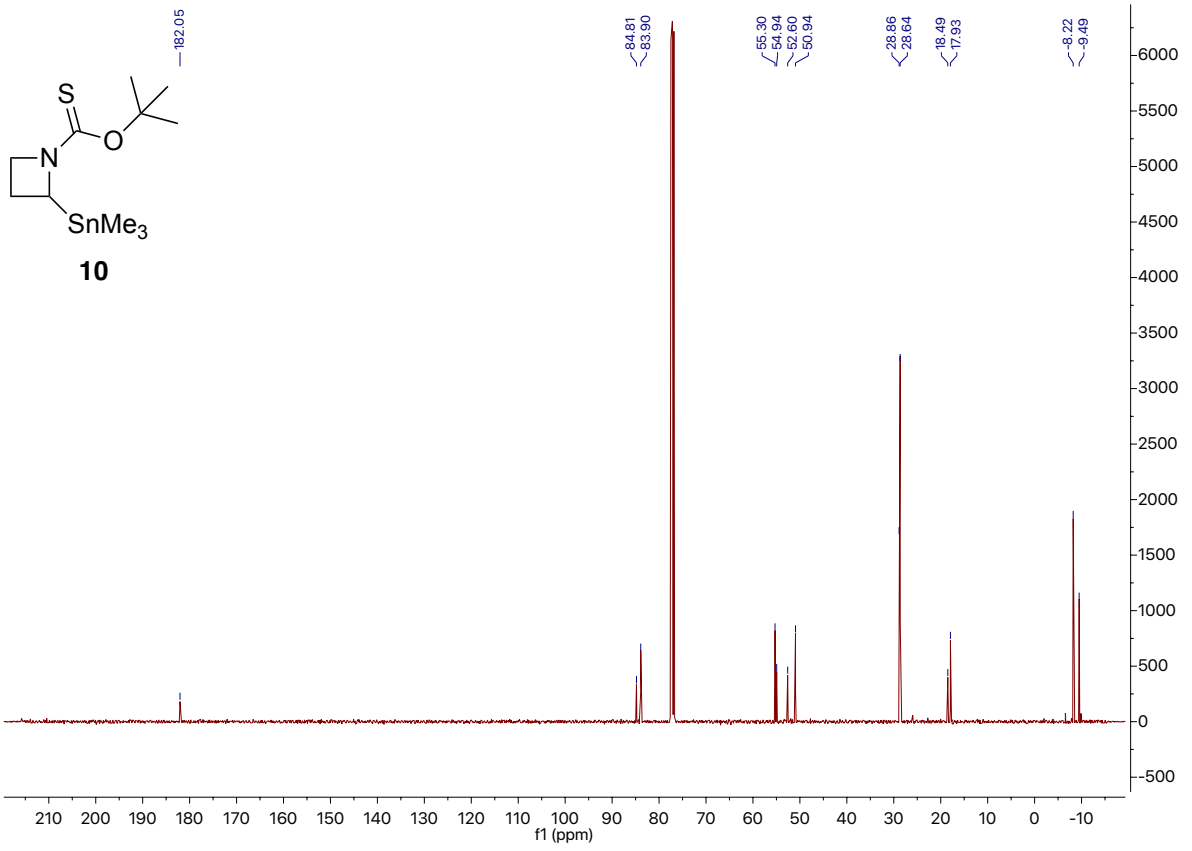
R_f 0.32 (100% Et_2O); $[\alpha]_D^{25}$ +32.6 (*c* 0.06, $CHCl_3$); mp 118–119 °C; IR (neat/cm^{-1}) 3362 (br), 2925 (m), 1635 (s), 1432 (m), 1168 (s); δ_H (500 MHz, $CDCl_3$ 7.61 – 7.57 (2H, m, *m*-Ph), 7.43 – 7.37 (3H, m, *o*-Ph & *p*-Ph), 4.55 (1H, pseudo t, *J* = 7.9 Hz, NCH), 4.01 (1H, dddd, *J* = 10.1, 9.2, 6.9, 0.8 Hz, NCH*H*'), 3.69 (3H, q, *J* = 1.7 Hz, OMe), 3.15 (1H, dddd, *J* = 10.1, 9.8, 5.6, 1.4 Hz, NC*H*H'), 2.22 (1H, dtd, *J* = 11.9, 9.2, 5.6 Hz, NCHCH*H*'), 1.71 (1H, ddt, *J* = 11.9, 9.8, 6.9 Hz, NCHC*H*H'), 1.16 (3H, s, CH_3), 1.05 (3H, s, CH_3); δ_C (125 MHz, $CDCl_3$) 167.2 (C=O), 132.7 (*i*-Ph), 129.7 (*p*-Ph), 128.4 (*o*-Ph), 127.1 (*m*-Ph), 123.5 (Q, *J* = 290 Hz, CF_3), 84.1 (q, *J* = 26 Hz, *C*CF_3), 73.7 (NCH), 71.4 (COH), 55.4 (q, *J* = 3 Hz, OMe), 49.6 (NCH_2), 24.2 (CH_3), 22.8 (CH_3), 20.3 (NCH*C*H_2); δ_F (377 MHz, $CDCl_3$) –70.5 (s); HRMS (ESI^+) calcd for [M+Na] $C_{16}H_{20}O_3NF_3Na$ 354.1287, found 354.1287.

3. ^{1}H, ^{13}C and ^{19}F NMR spectra

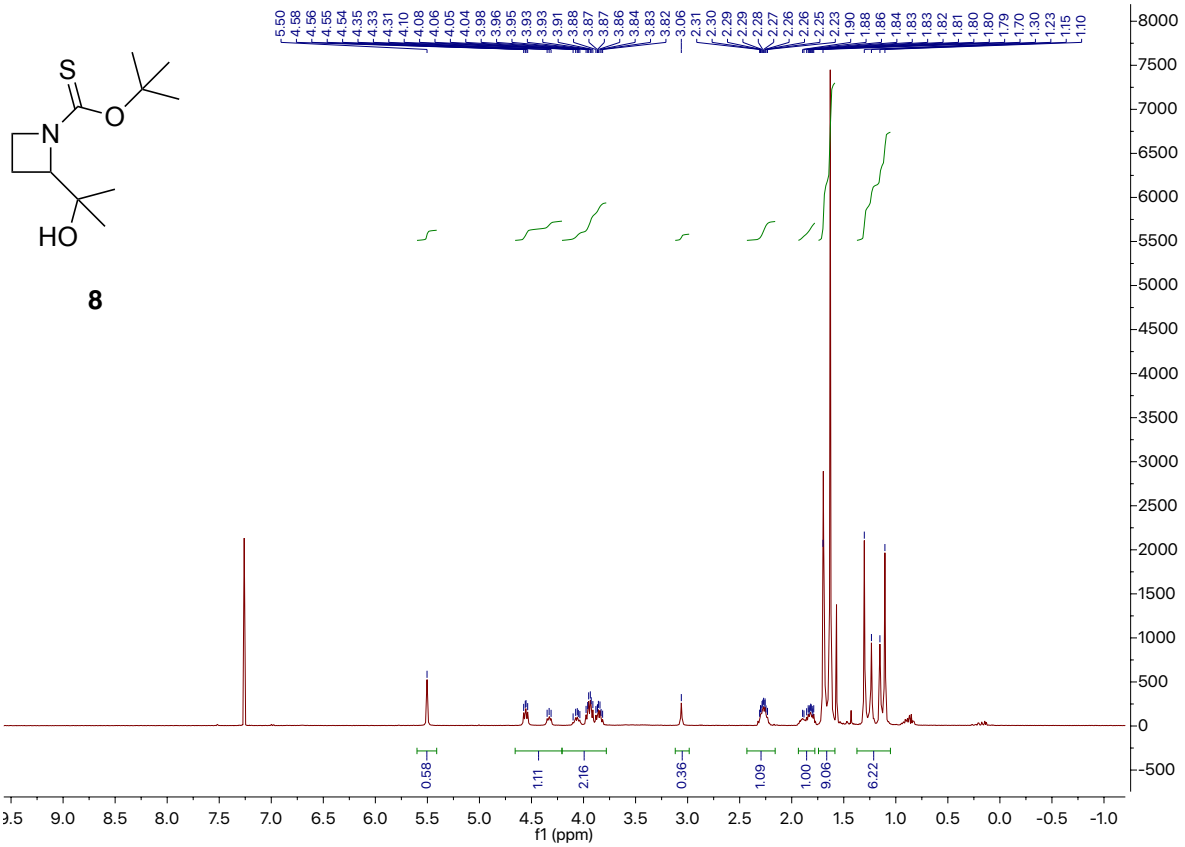
^{1}H NMR (400 MHz)



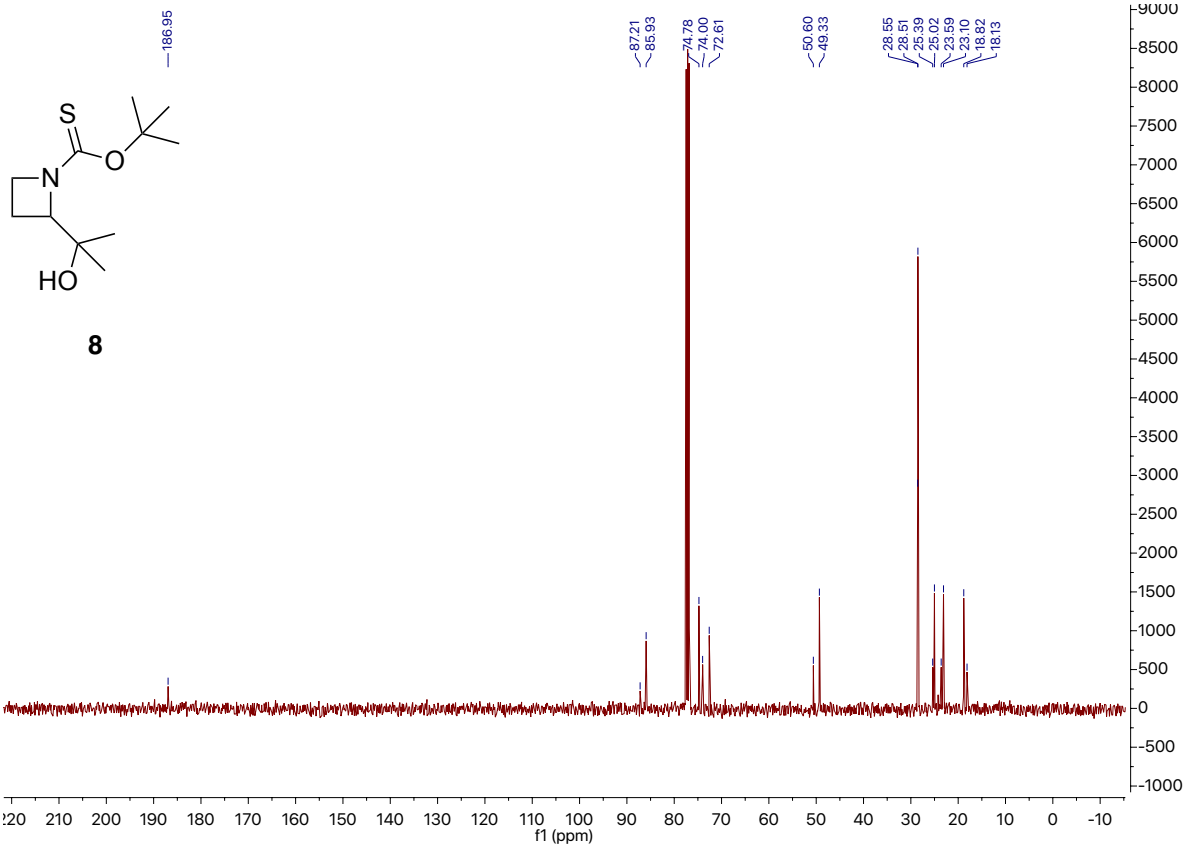
^{13}C NMR (100 MHz)



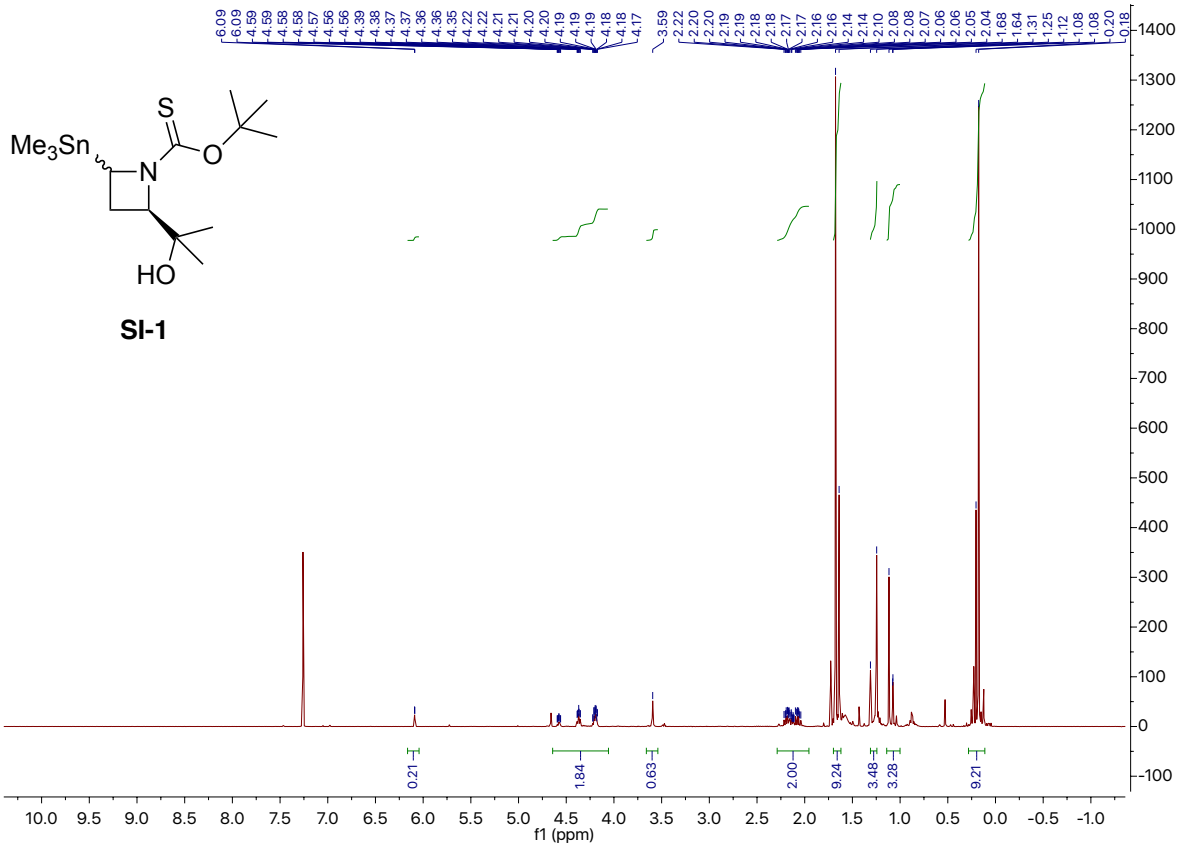
^{1}H NMR (400 MHz)



^{13}C NMR (100 MHz)

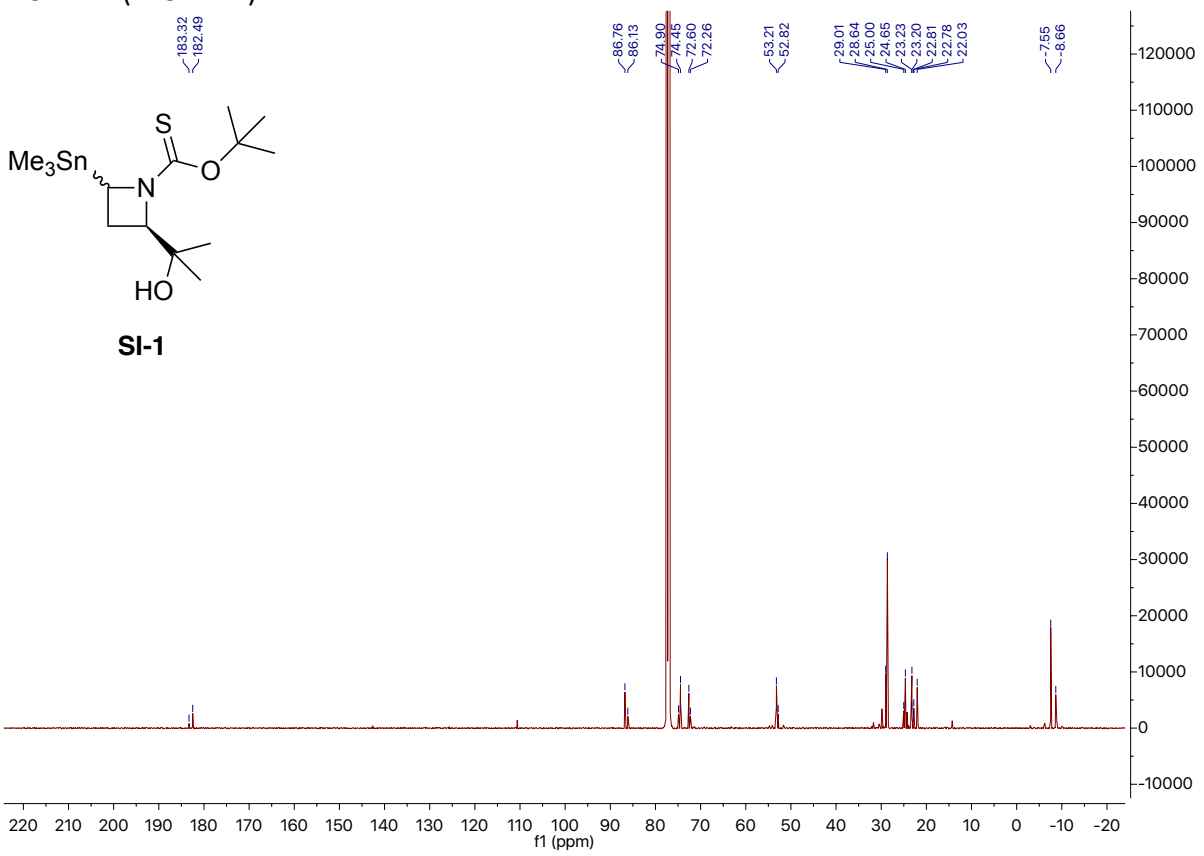


^{1}H NMR (400 MHz)



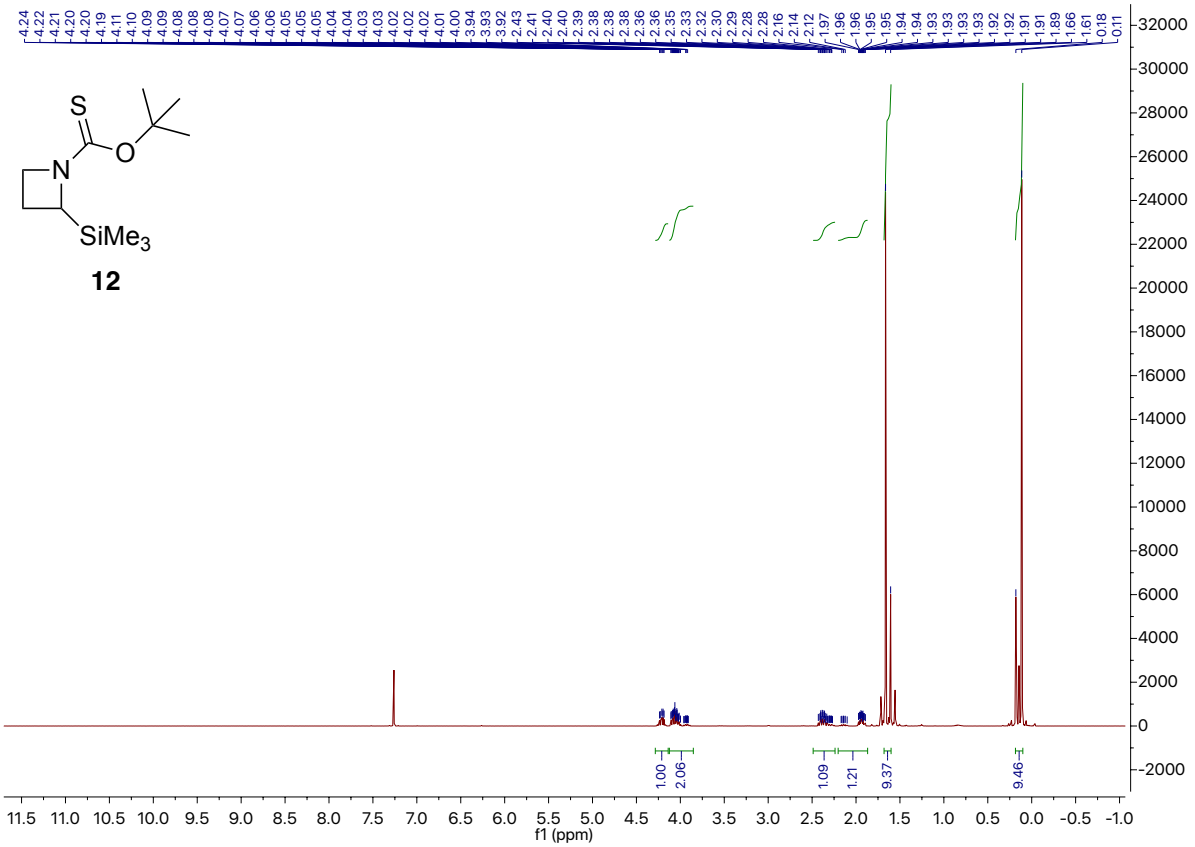
SI-1

^{13}C NMR (125 MHz)

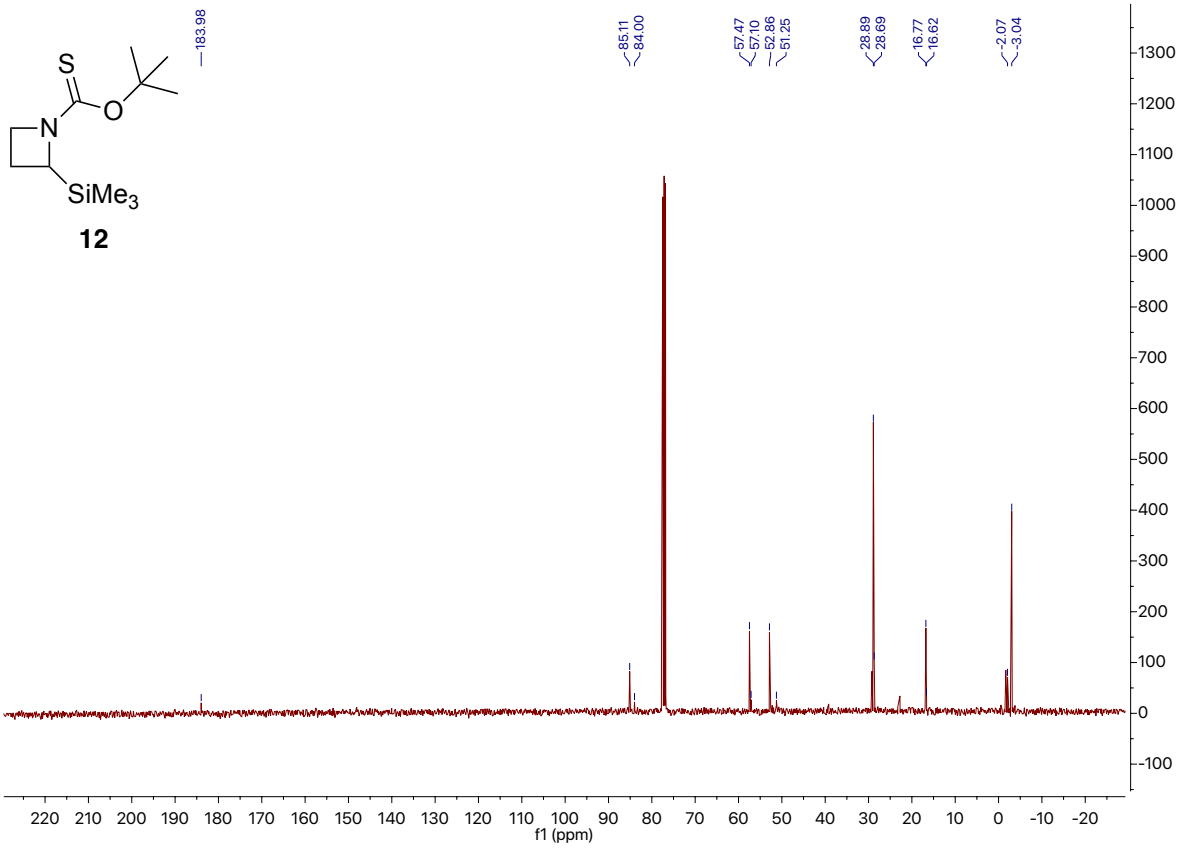


SI-1

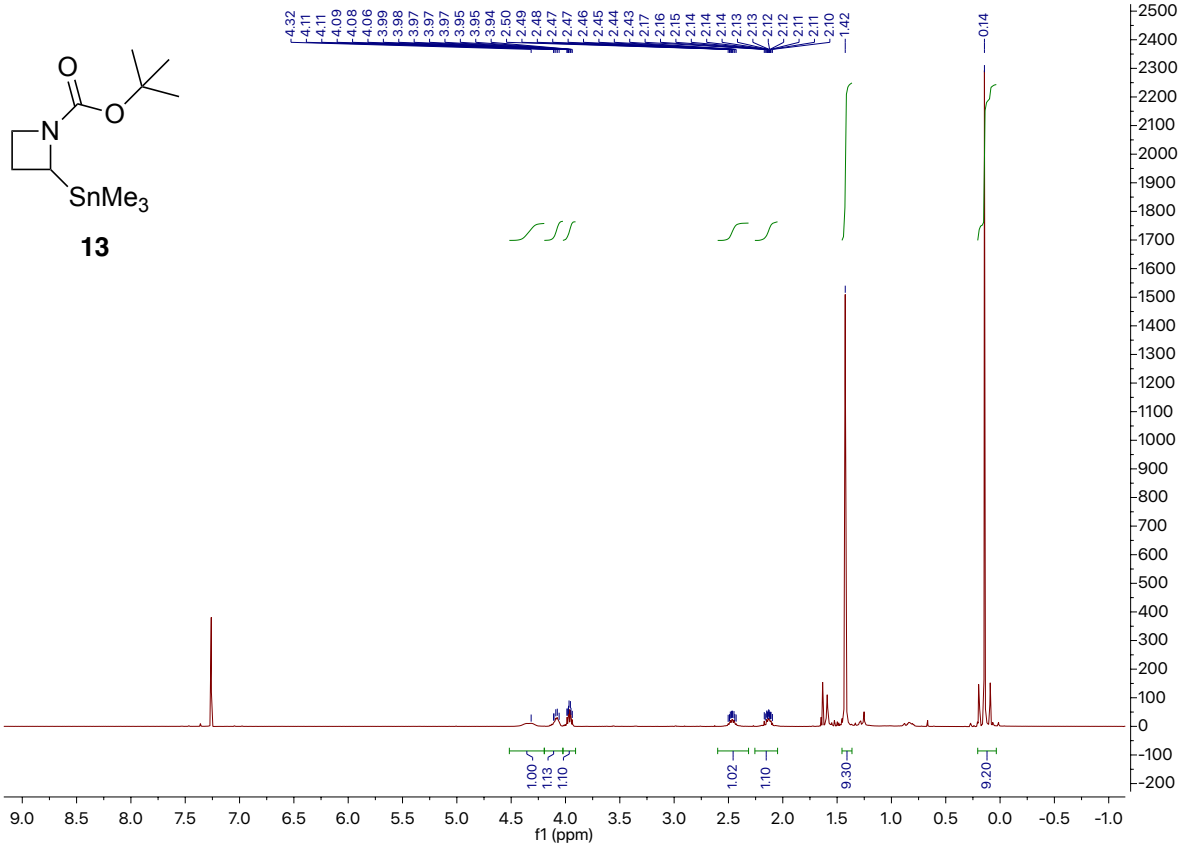
^{1}H NMR (400 MHz)



^{13}C NMR (100 MHz)

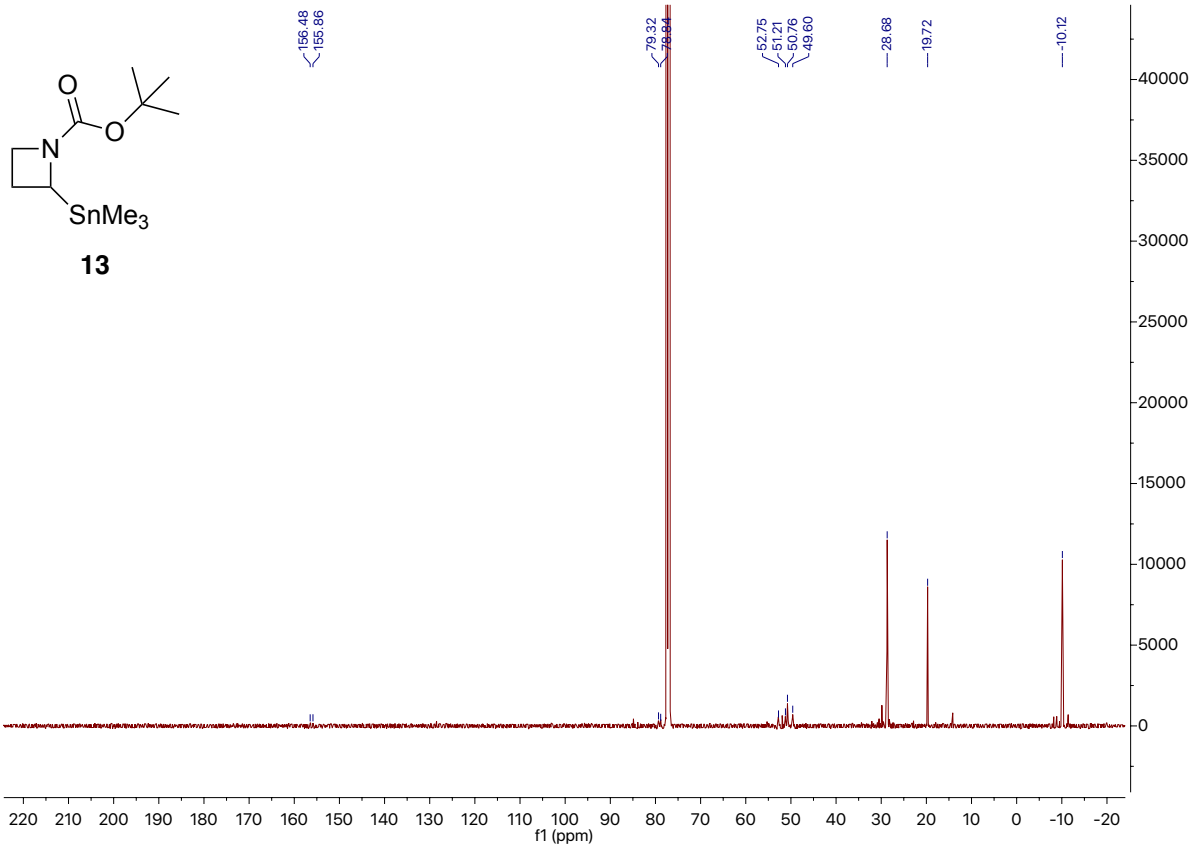


^{1}H NMR (500 MHz)



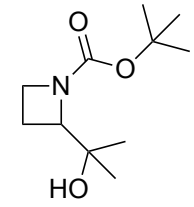
13

^{13}C NMR (125 MHz)



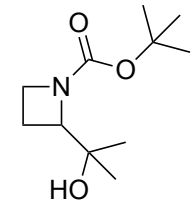
13

^{1}H NMR (400 MHz)



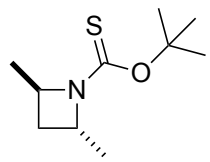
14

^{13}C NMR (100 MHz)



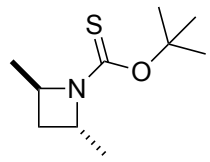
14

^{1}H NMR (400 MHz)



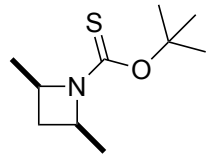
***trans*-SI-4**

^{13}C NMR (100 MHz)



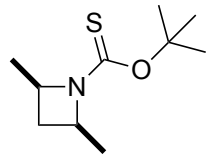
***trans*-SI-4**

^{1}H NMR (400 MHz)



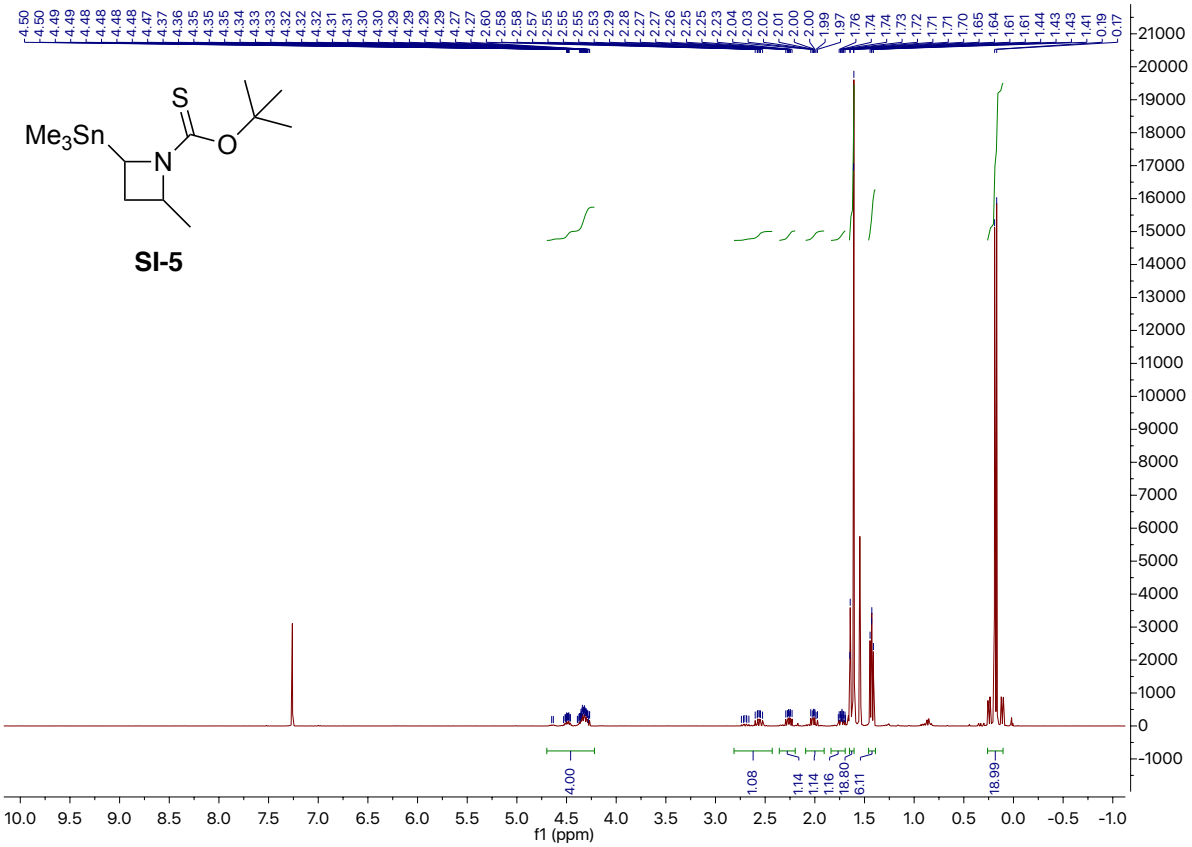
***cis*-SI-4**

^{13}C NMR (100 MHz)

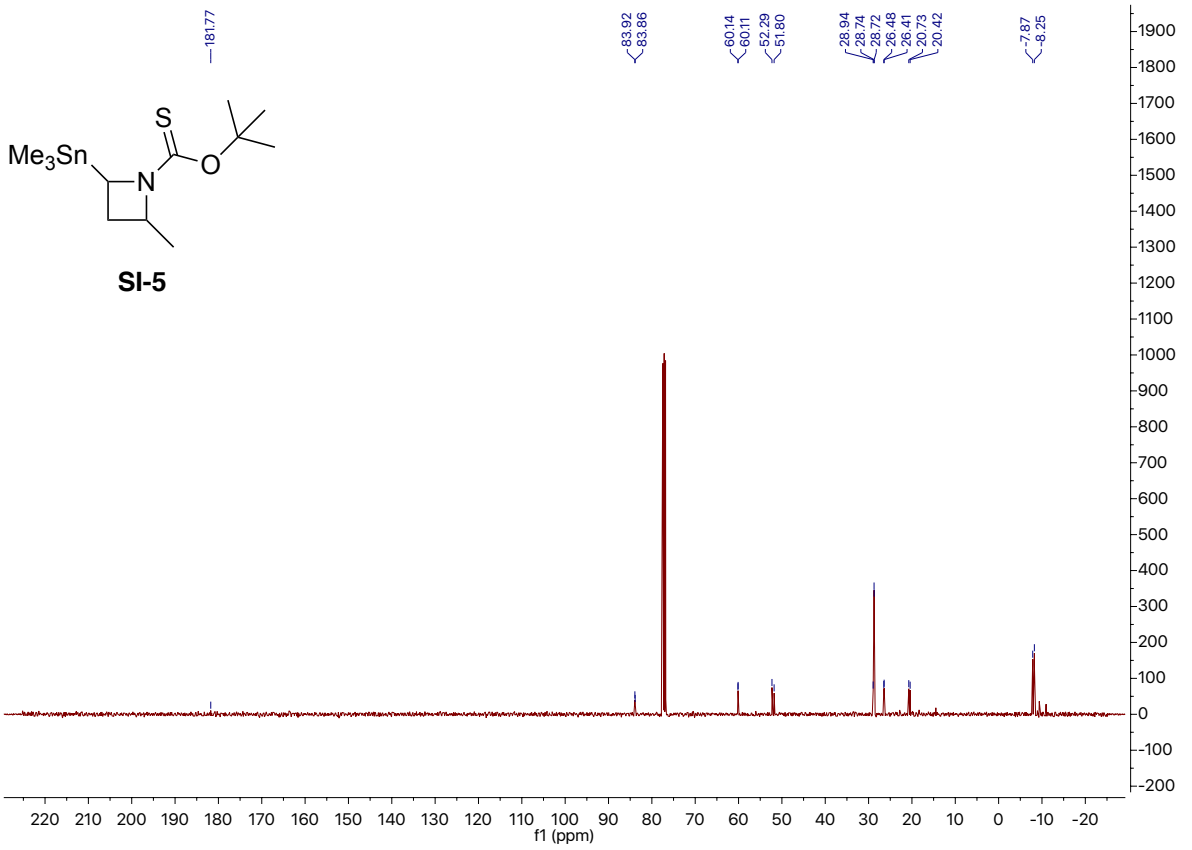


***cis*-SI-4**

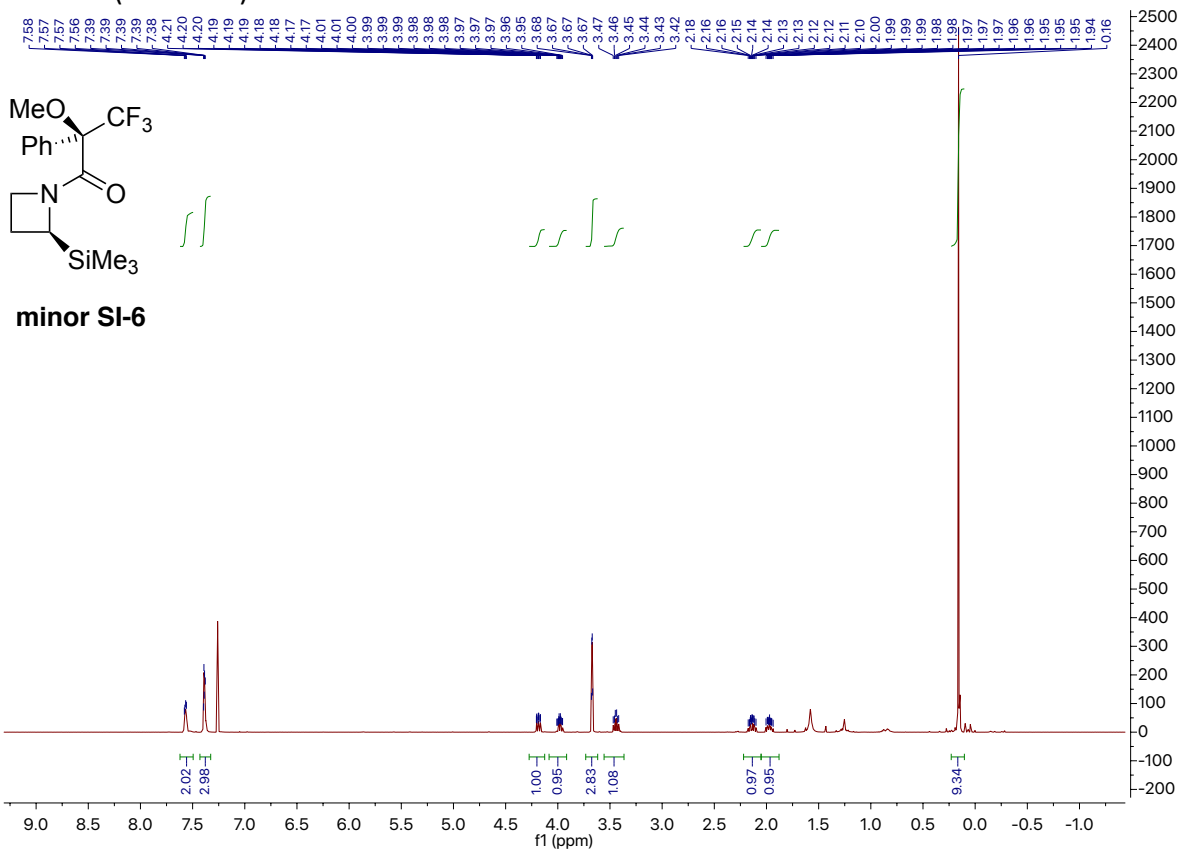
^{1}H NMR (400 MHz)



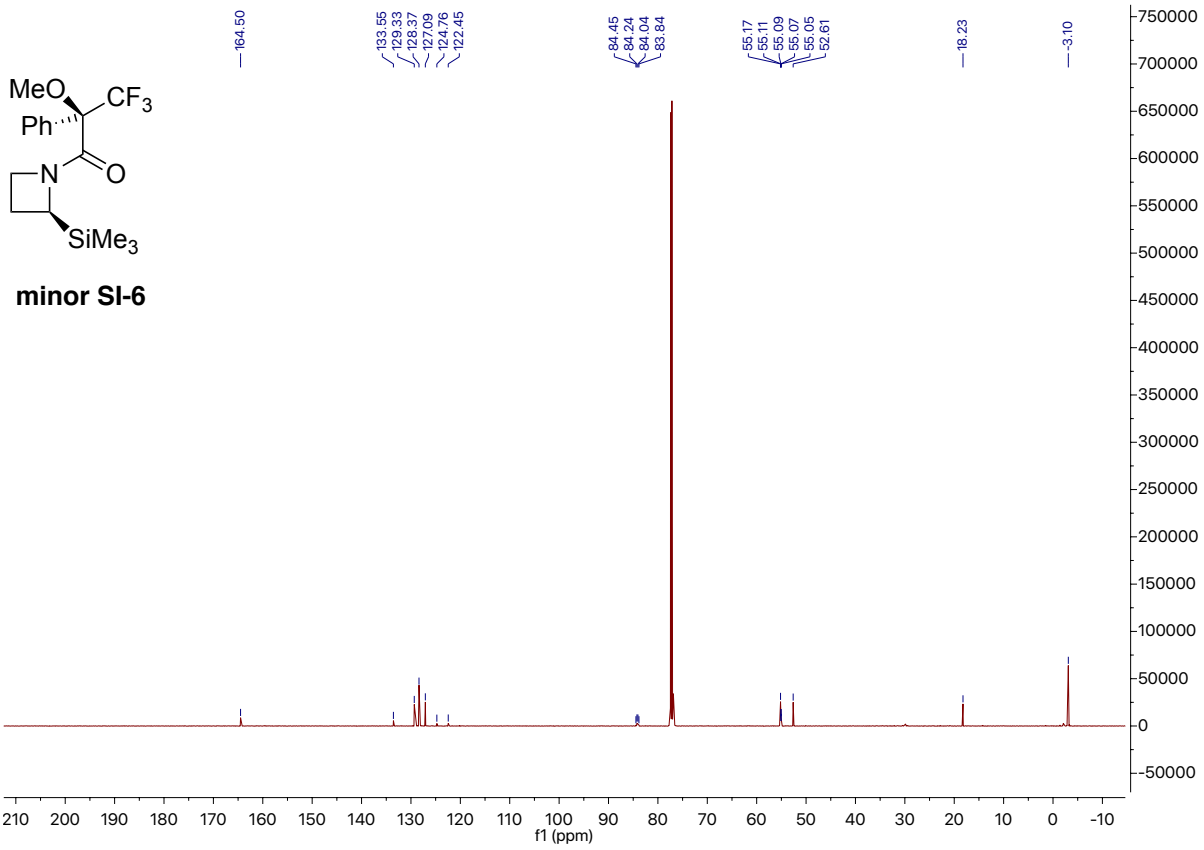
^{13}C NMR (100 MHz)



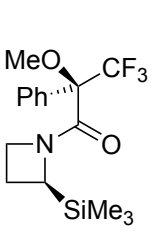
^{1}H NMR (500 MHz)



^{13}C NMR (125 MHz)

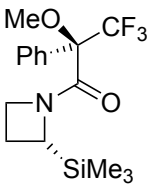


^{19}F NMR (377 MHz, $CDCl_3$)



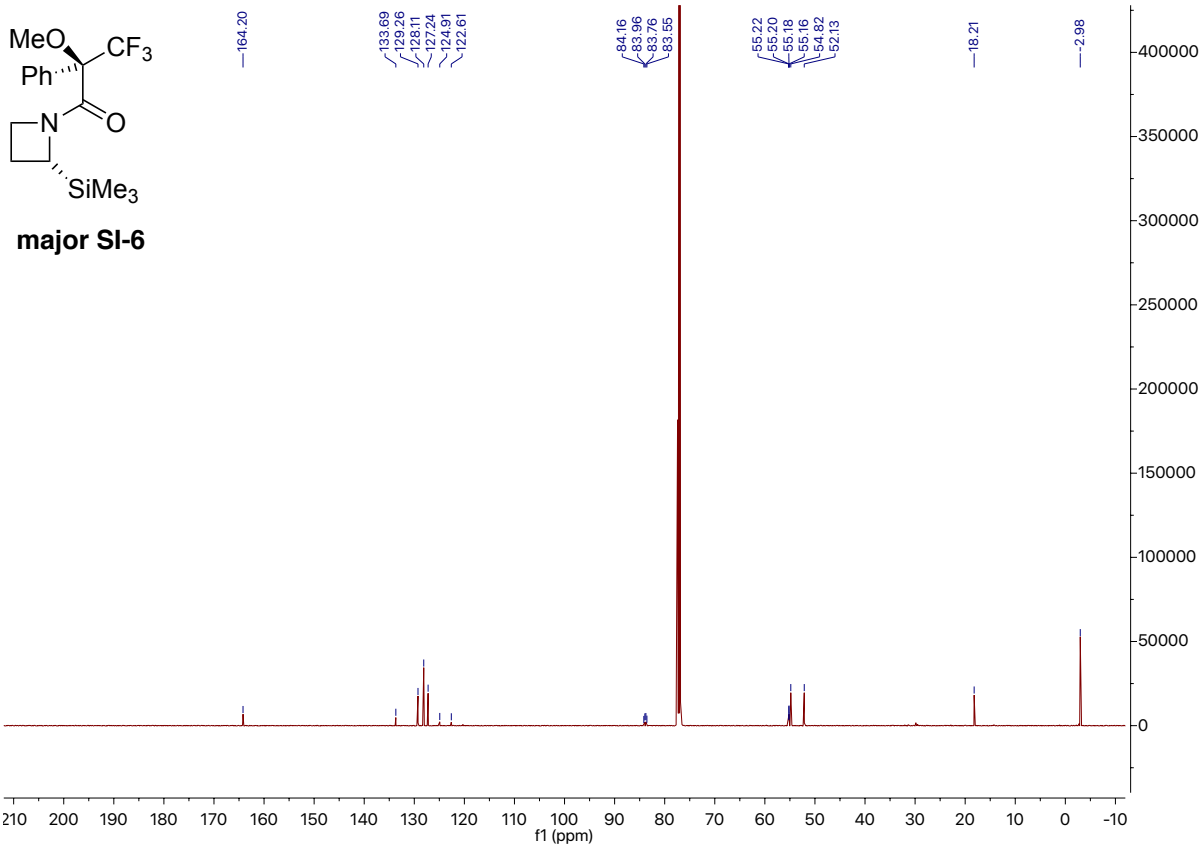
minor SI-6

^{1}H NMR (500 MHz)

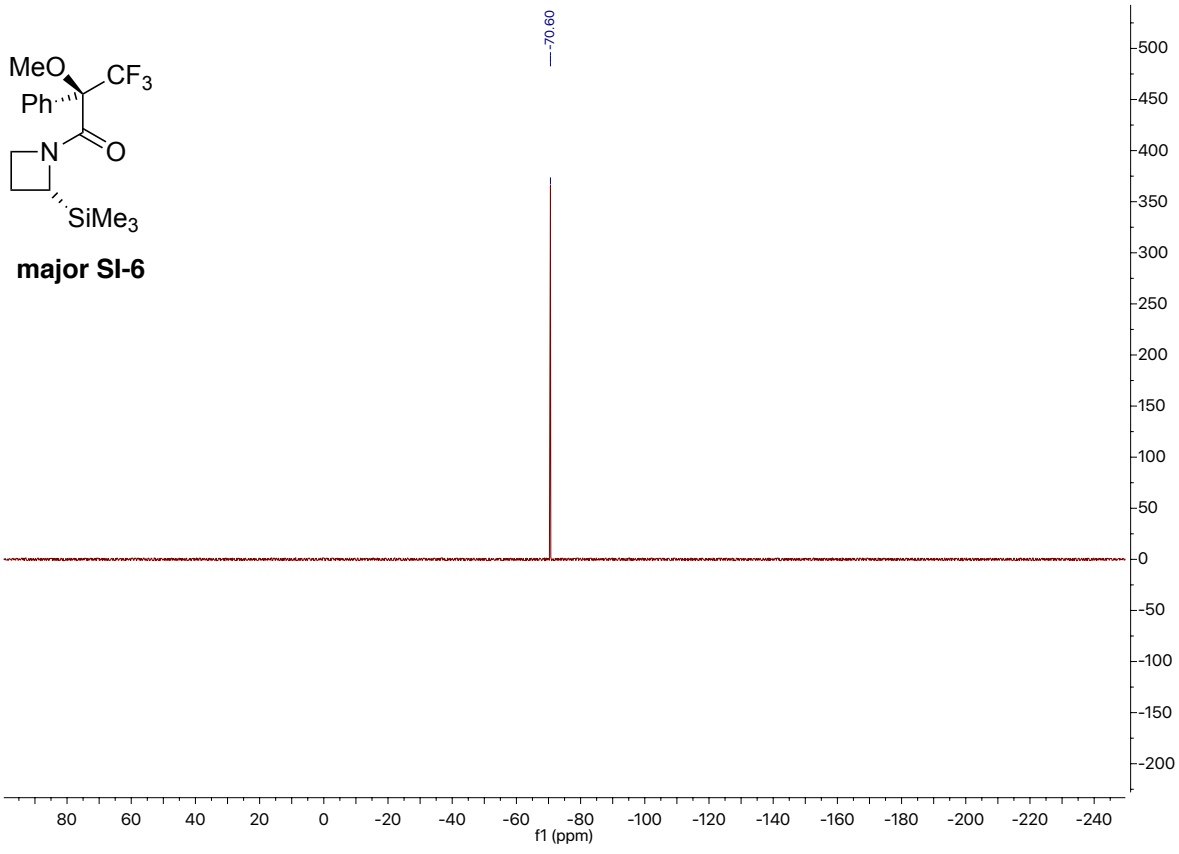


major SI-6

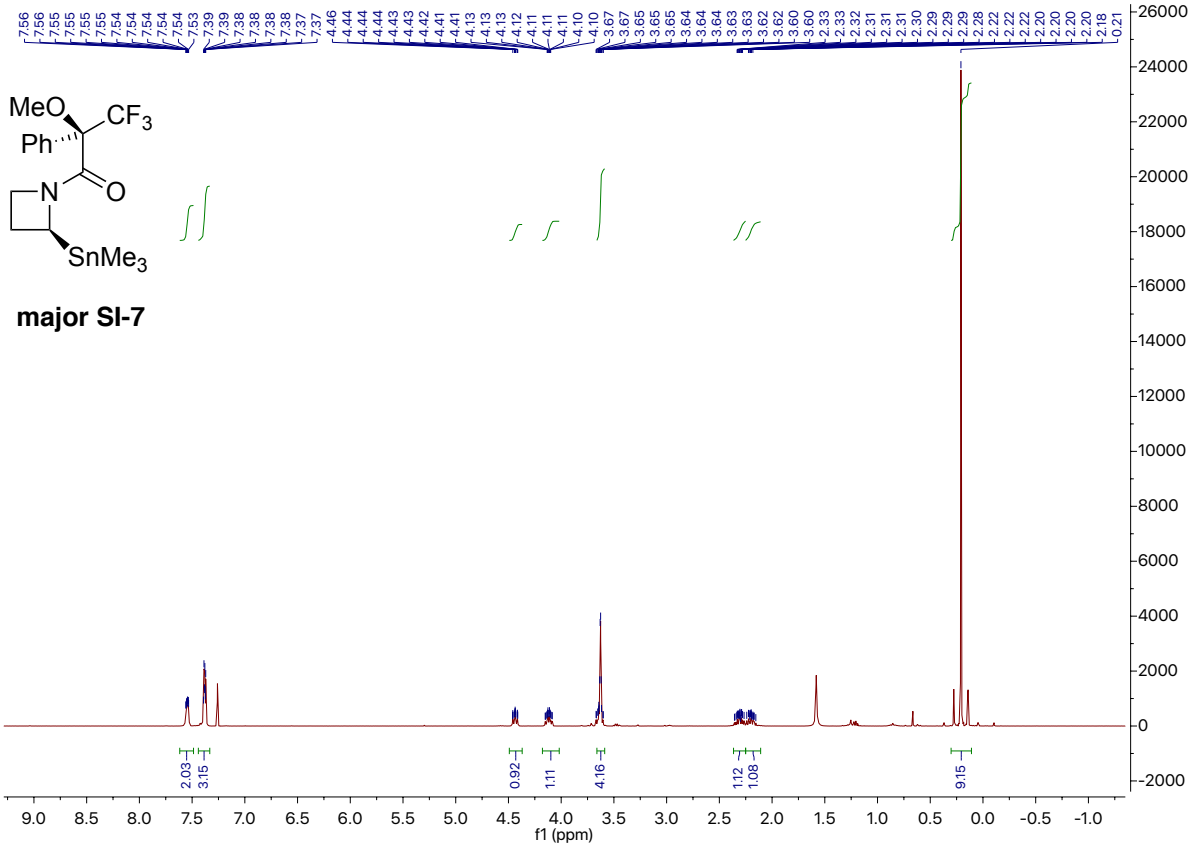
^{13}C NMR (125 MHz)



^{19}F NMR (377 MHz, $CDCl_3$)

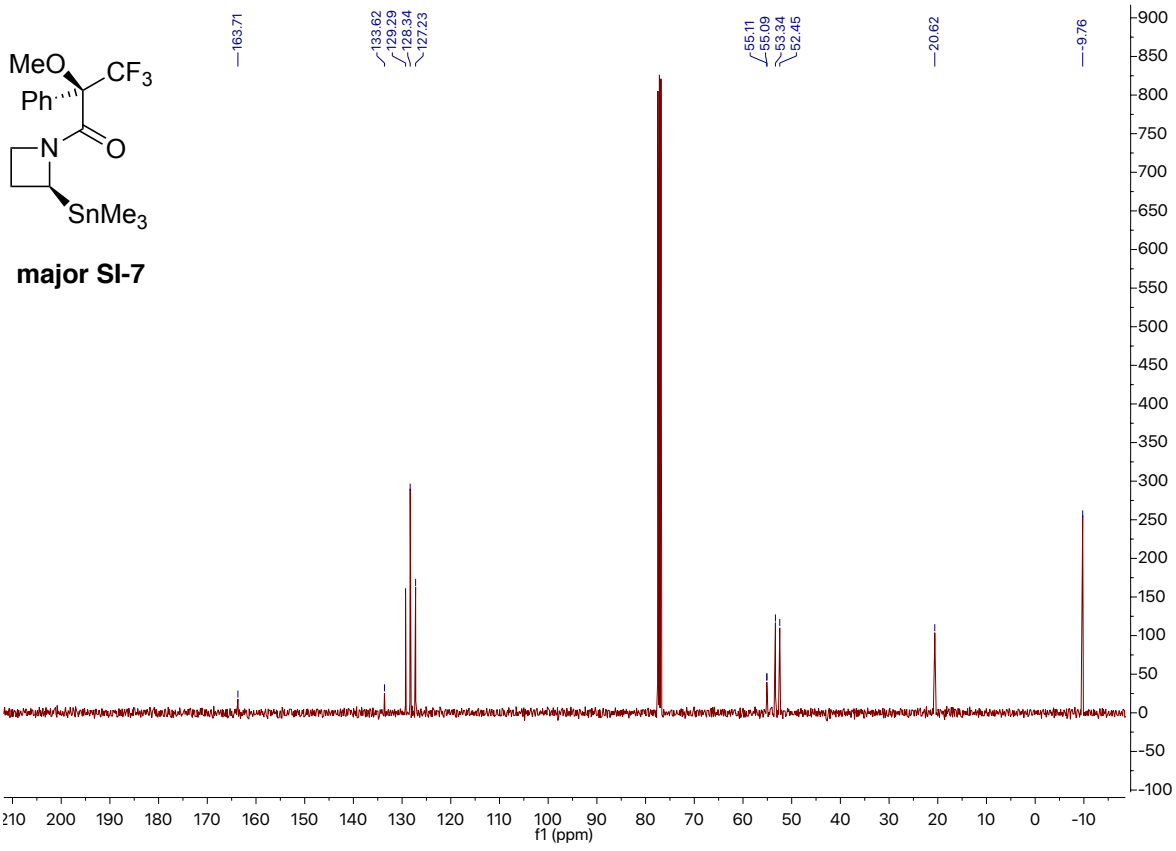


^{1}H NMR (400 MHz)



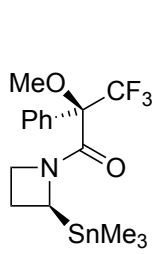
major SI-7

^{13}C NMR (100 MHz)



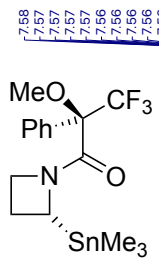
major SI-7

^{19}F NMR (377 MHz, $CDCl_3$)



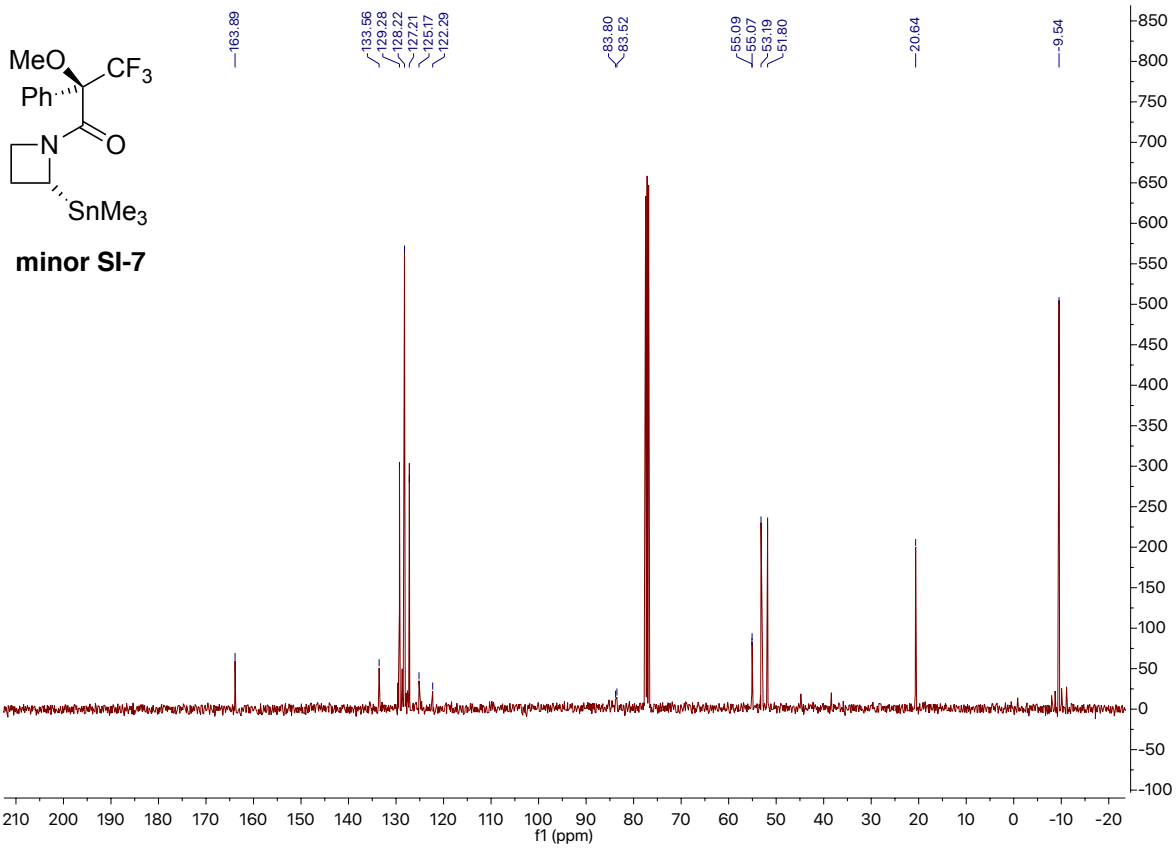
major SI-7

^{1}H NMR (400 MHz)

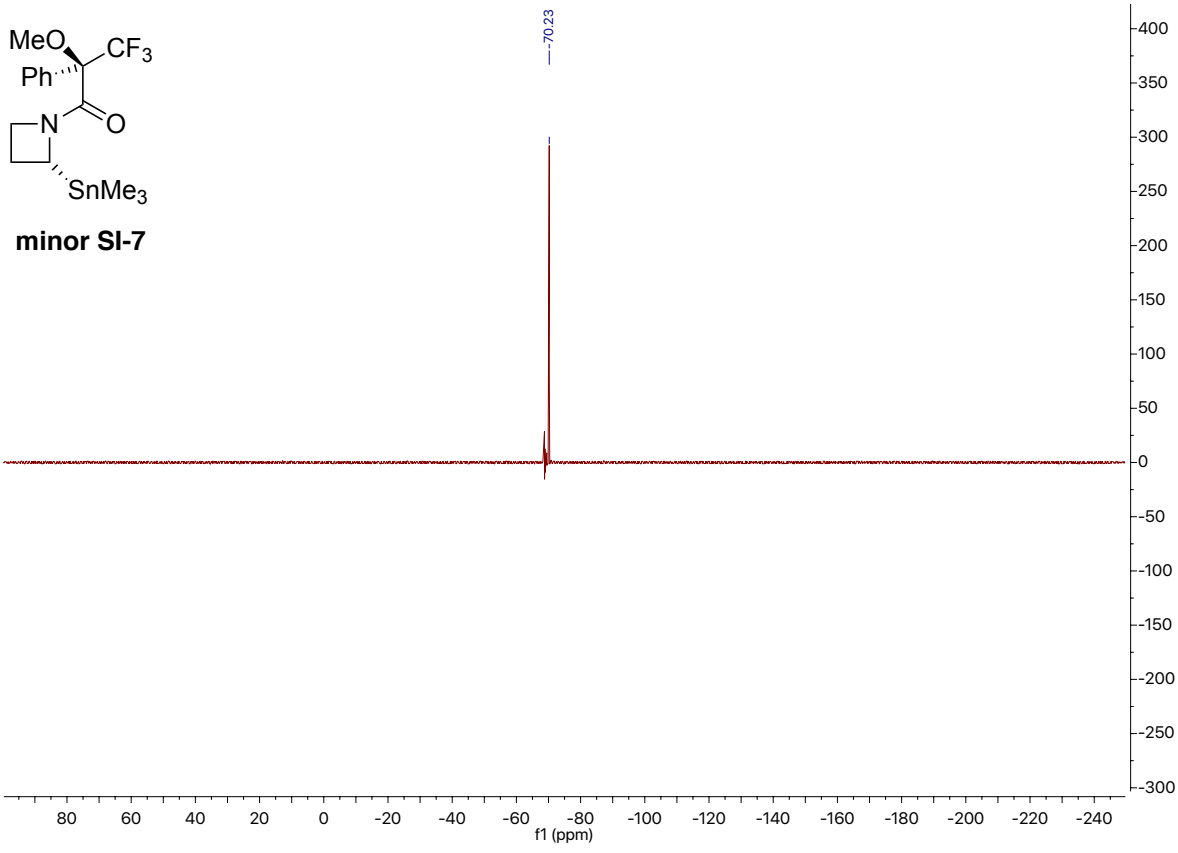


minor SI-7

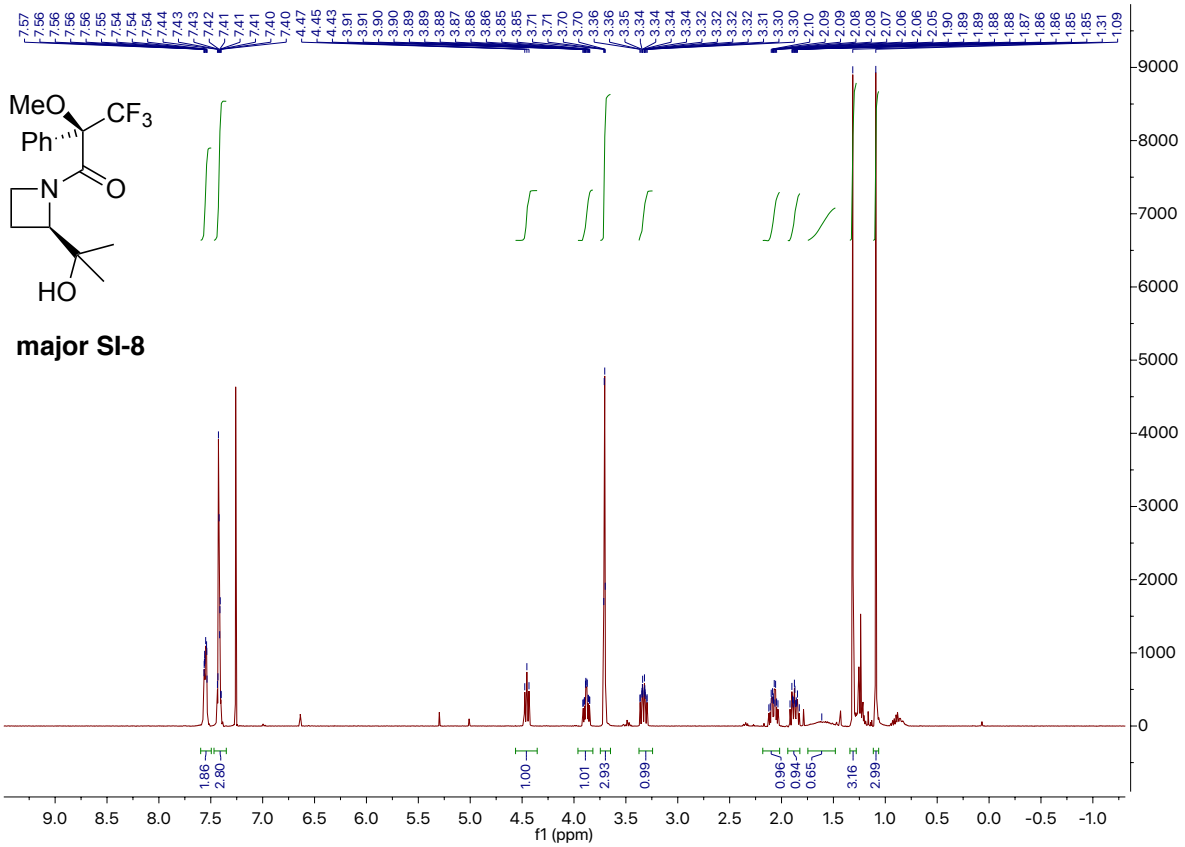
^{13}C NMR (100 MHz)



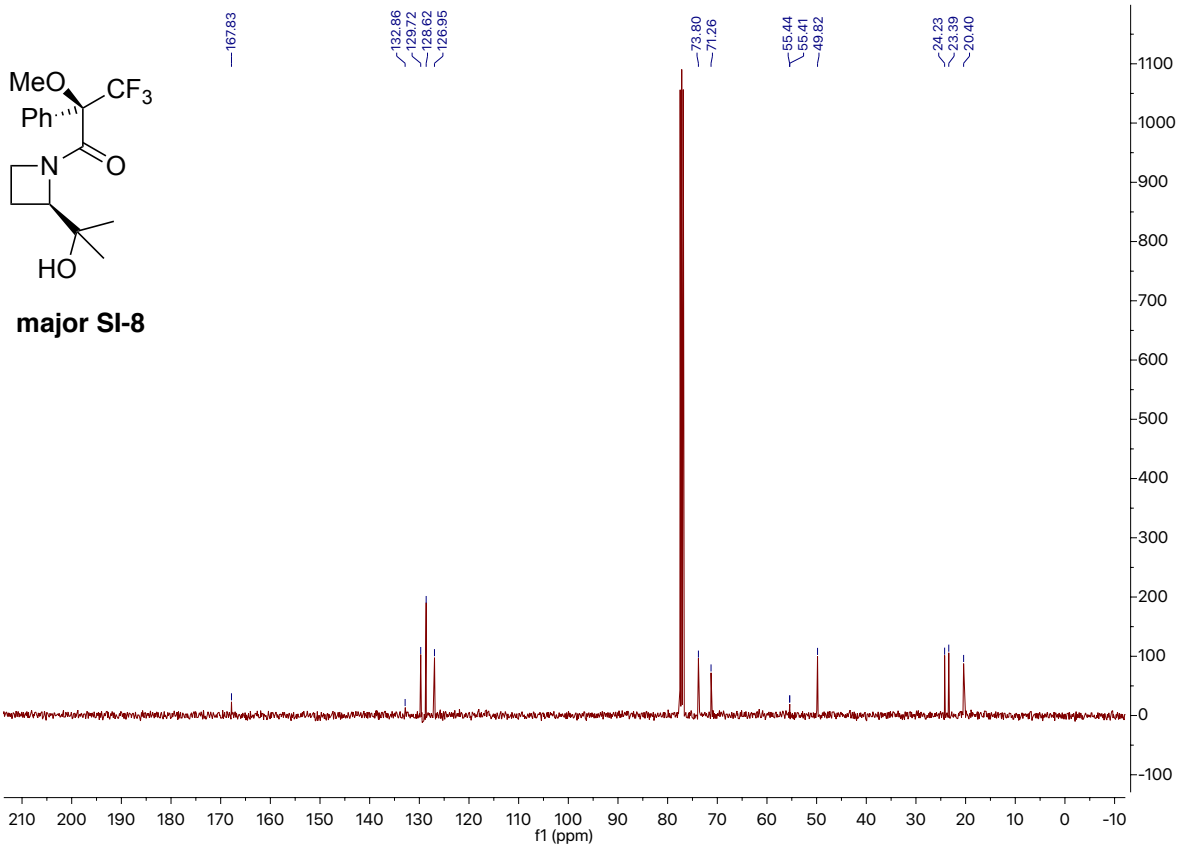
^{19}F NMR (377 MHz, $CDCl_3$)



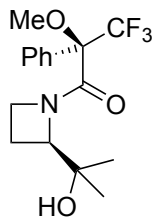
^{1}H NMR (400 MHz)



^{13}C NMR (100 MHz)



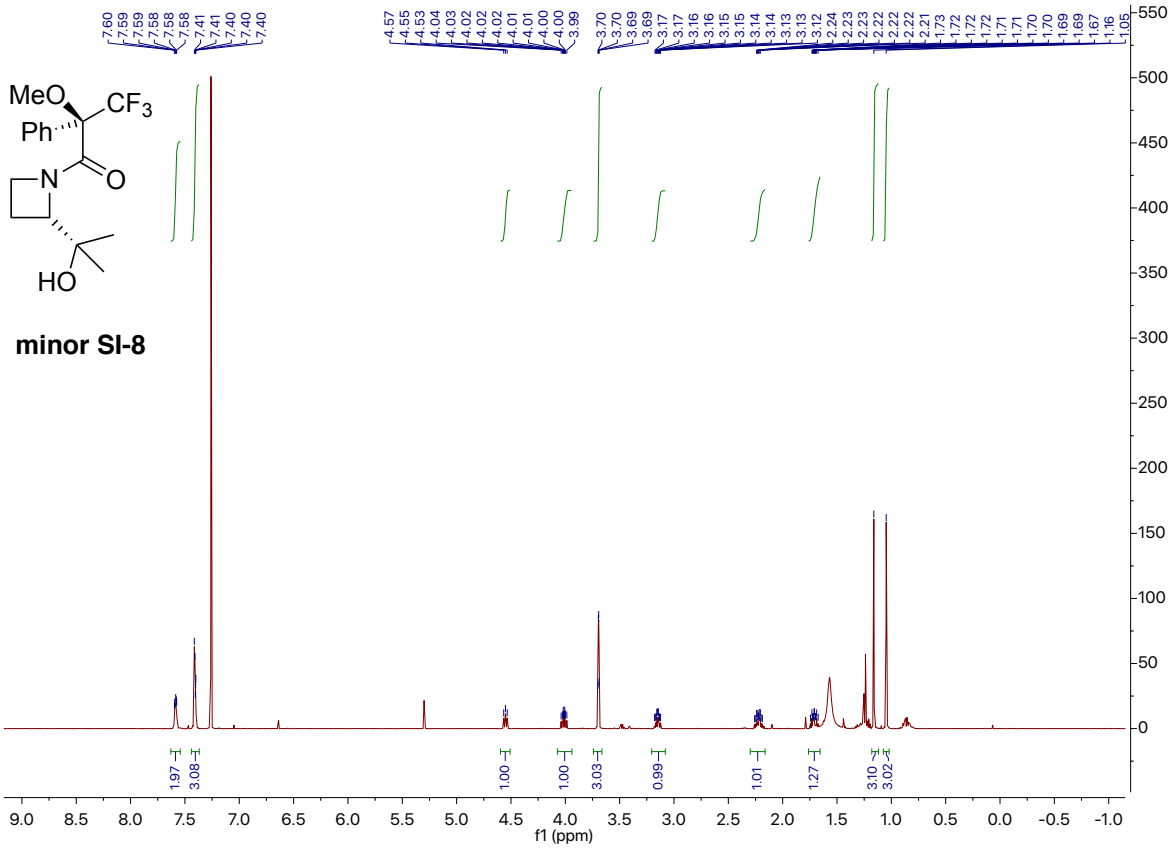
^{19}F NMR (377 MHz, $CDCl_3$)



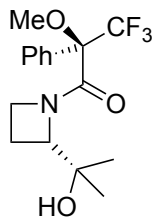
major SI-8

^{1}H NMR (500 MHz)

minor SI-8

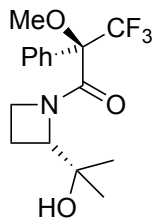


^{13}C NMR (125 MHz)



minor SI-8

^{19}F NMR (377 MHz, $CDCl_3$)

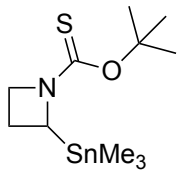


minor SI-8

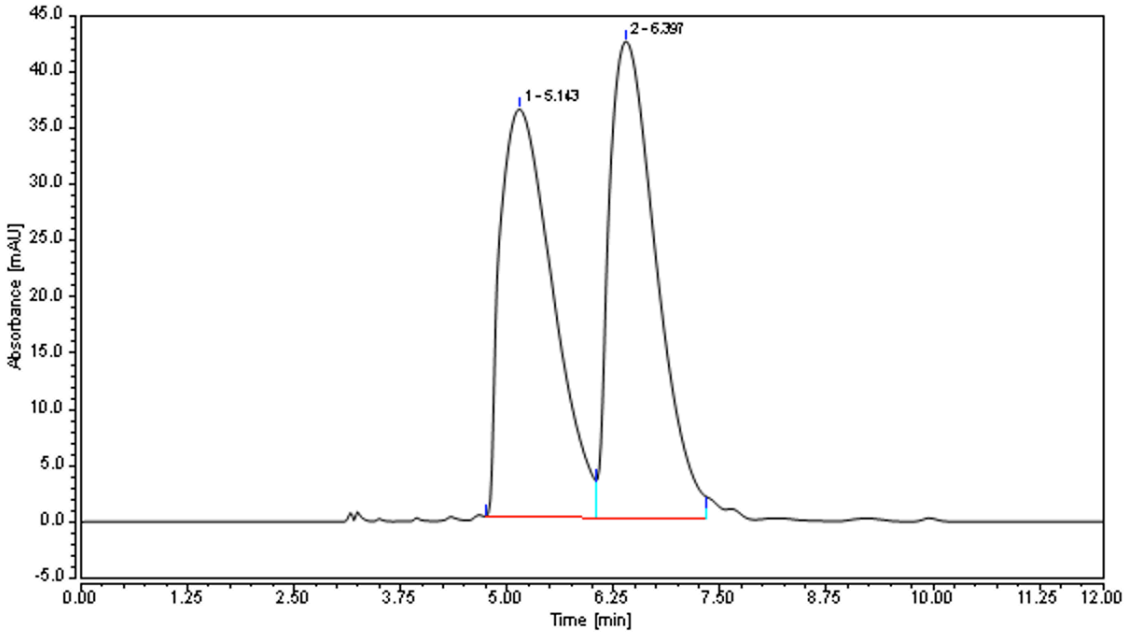
4. Chiral HPLC traces

Chiral HPLC for stannane 10: (Chiralpak ODH, 0.1% ^{i}PrOH, 99.9% hexane, 1.0 mL min^{-1}, λ = 254 nm, 10 μL injection) τ_R = 5.1 min, τ_R = 6.4 min.

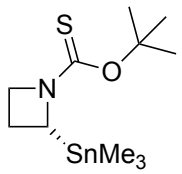
Racemic
(±)-10



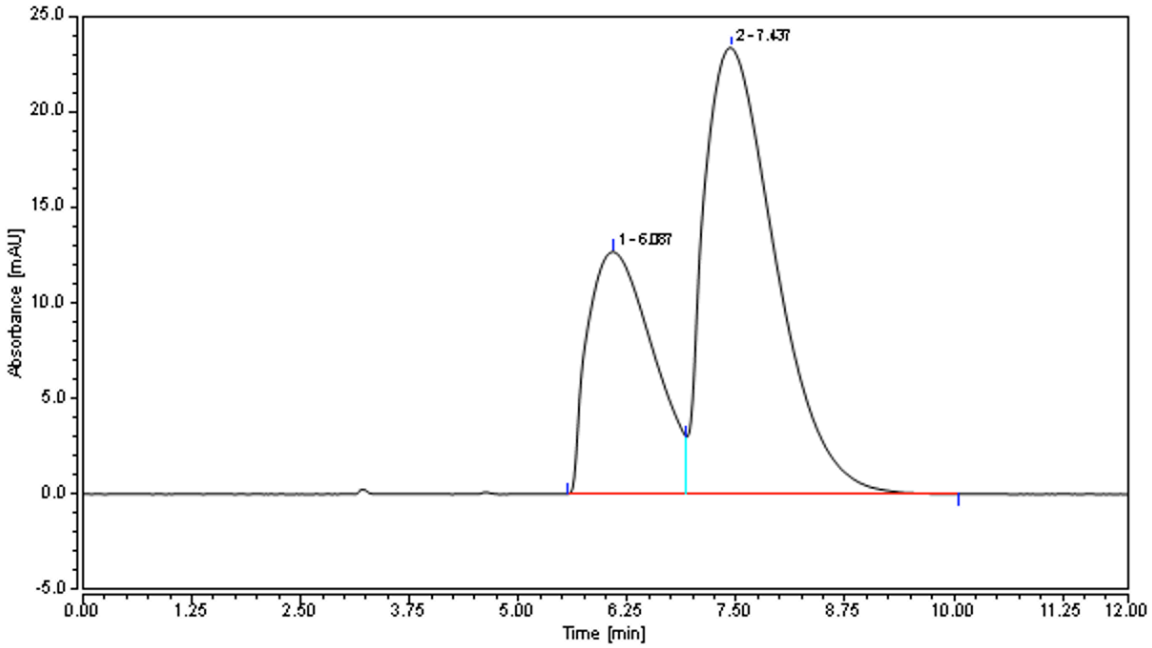
No.	Peak Name	Retention Time	Area	Height	Relative Area
		min	mAU*min	mAU	%
1		5.143	25.902	36.336	48.79
2		6.397	27.187	42.529	51.21
Total:			53.089	78.865	100.00



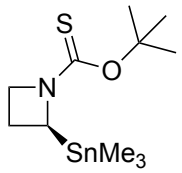
Enantioenriched
(*R*)-10



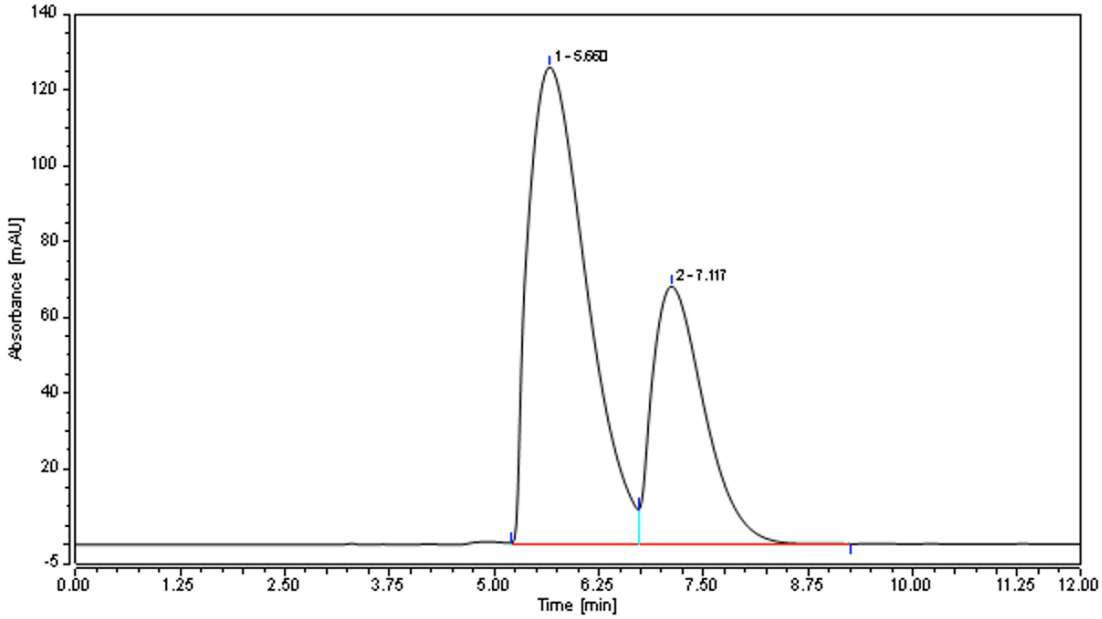
No.	Peak Name	Retention Time	Area	Height	Relative Area
		min	mAU*min	mAU	%
1		6.087	10.974	12.699	33.07
2		7.437	22.210	23.386	66.93
Total:			33.184	36.085	100.00



Enantioenriched
(*S*)-10

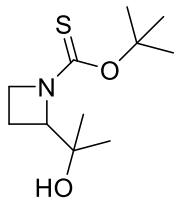


No.	Peak Name	Retention Time	Area	Height	Relative Area
		min	mAU*min	mAU	%
1		5.660	100.736	125.963	67.42
2		7.117	48.683	68.077	32.58
Total:			149.420	194.040	100.00

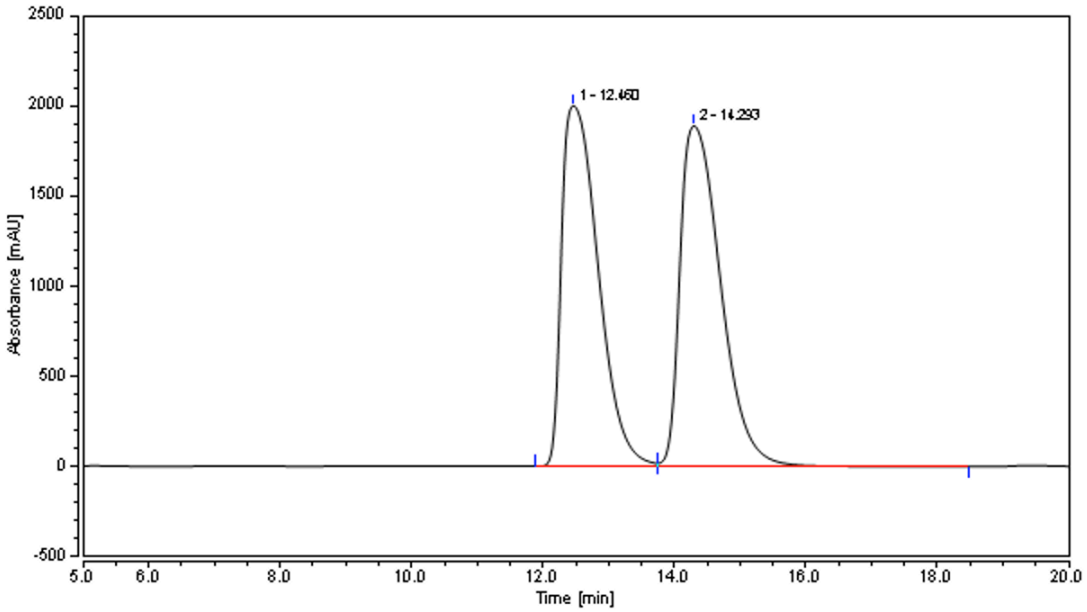


Chiral HPLC for alcohol 8: (Chiralpak ADH, 5% ^{i}PrOH, 95% hexane, 1.0 mL min^{-1}, λ = 254 nm, 25 µL injection) τ_R = 12.5 min, τ_R = 14.3 min.

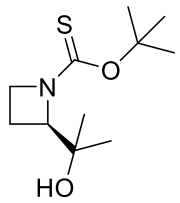
Racemic
(±)-8



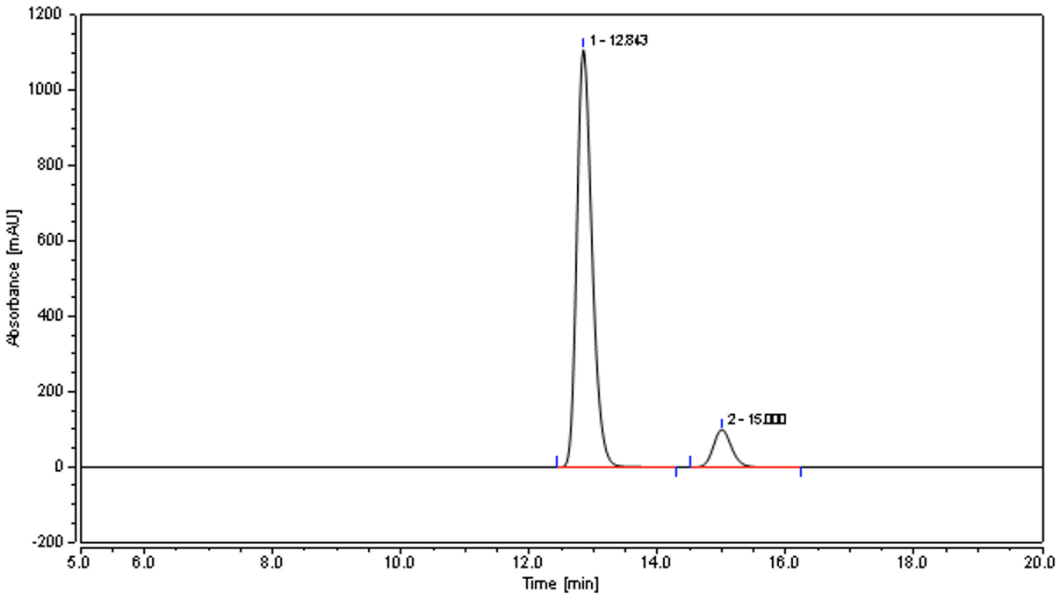
No.	Peak Name	Retention Time	Area	Height	Relative Area
		min	mAU*min	mAU	%
1		12.460	1290.733	2003.531	48.87
2		14.293	1350.631	1890.896	51.13
Total:			2641.363	3894.427	100.00



Enantioenriched
(*R*)-8

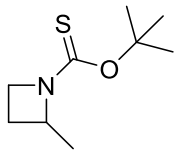


No.	Peak Name	Retention Time	Area	Height	Relative Area
		min	mAU*min	mAU	%
1		12.843	304.447	1109.391	90.29
2		15.000	32.749	99.916	9.71
Total:			337.196	1209.308	100.00

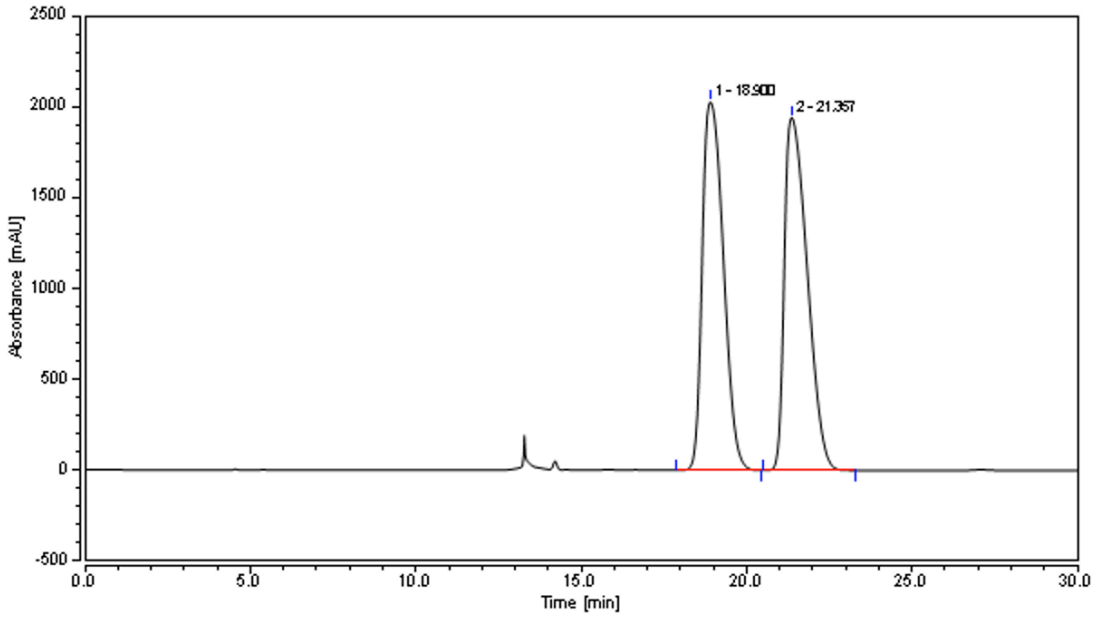


Chiral HPLC for 2-methylazetidine 7: (Chiralpak IC, 1% ^{i}PrOH, 99% hexane, 1.0 mL min^{-1}, λ = 258 nm, 50 μL injection) τ_R = 18.9 min, τ_R = 21.4 min.

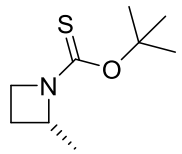
Racemic
(±)-7



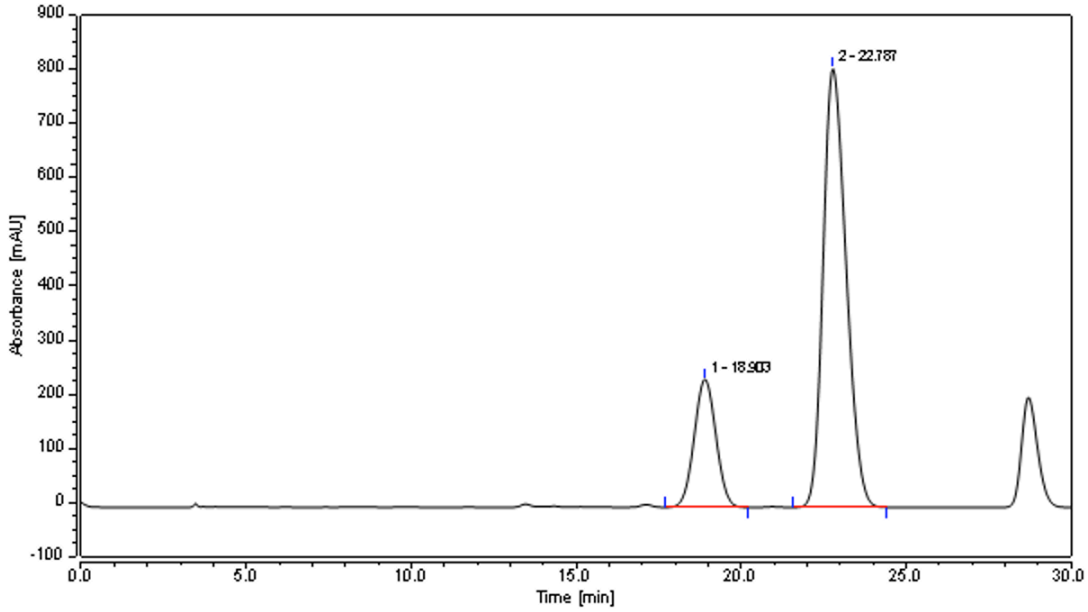
No.	Peak Name	Retention Time	Area	Height	Relative Area
		min	mAU*min	mAU	%
1		18.900	1498.102	2030.911	49.13
2		21.357	1551.000	1945.040	50.87
Total:			3049.101	3975.951	100.00



Enantioenriched
(*R*)-7

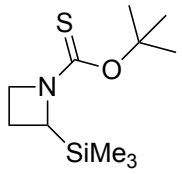


No.	Peak Name	Retention Time	Area	Height	Relative Area
		min	mAU*min	mAU	%
1		18.903	181.113	236.890	21.67
2		22.787	654.624	810.985	78.33
Total:			835.738	1047.875	100.00

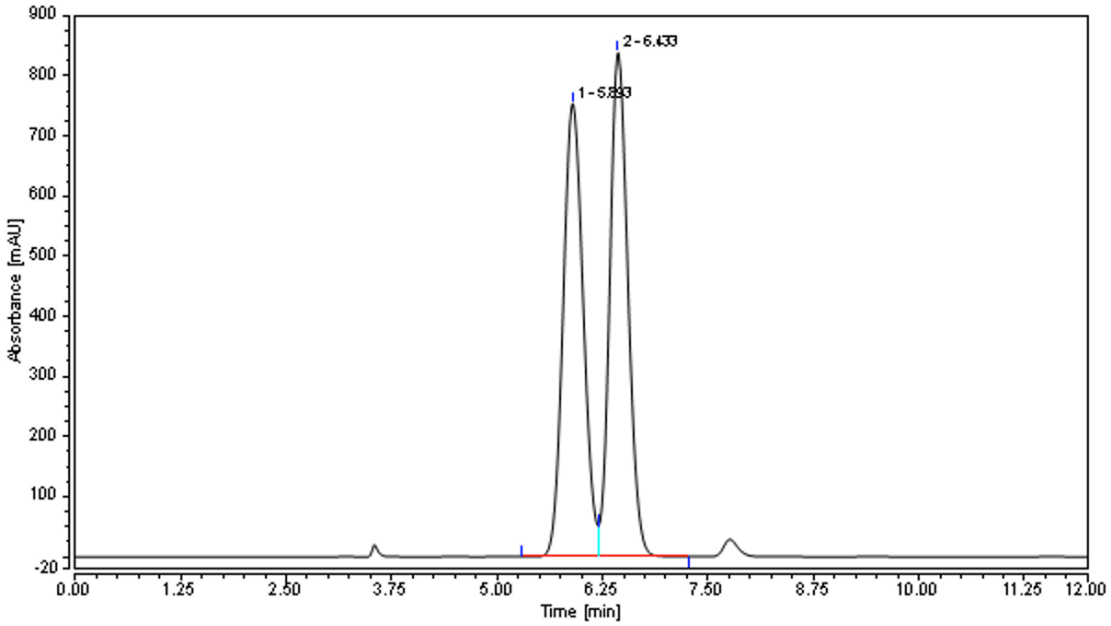


Chiral HPLC for silane 12: (Chiralpak ODH, 0.1% ^{i}PrOH, 99.9% hexane, 1.0 mL min^{-1}, λ = 254 nm, 10 μL injection) τ_R = 5.9 min, τ_R = 6.4 min.

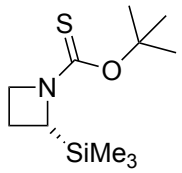
Racemic
(±)-12



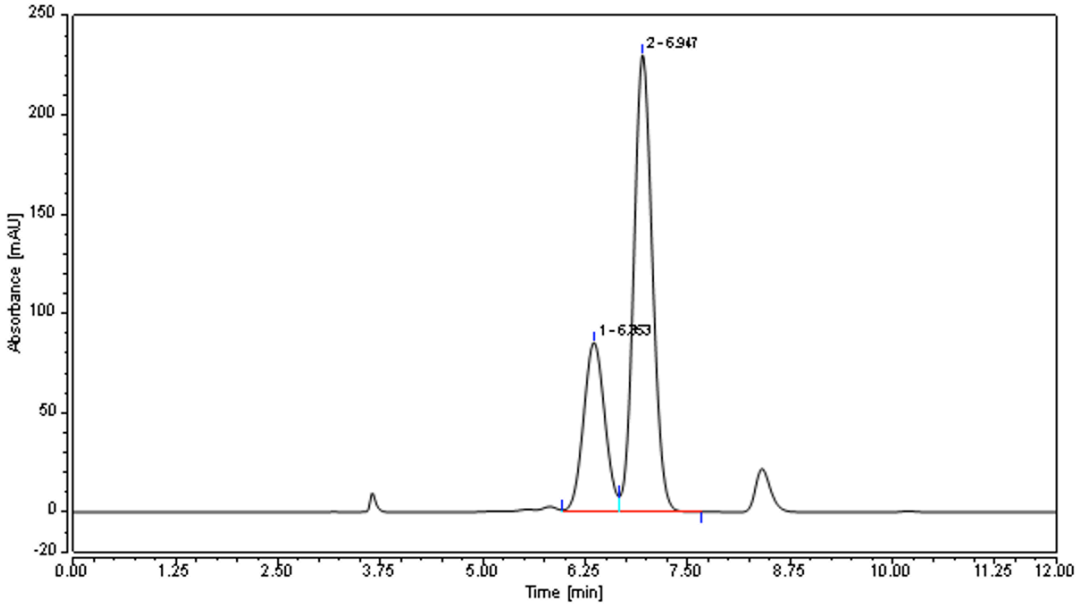
No.	Peak Name	Retention Time	Area	Height	Relative Area
		min	mAU*min	mAU	%
1		5.893	207.092	753.880	49.85
2		6.433	208.340	838.482	50.15
Total:			415.433	1592.362	100.00



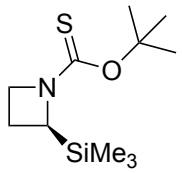
Enantioenriched
(*R*)-12



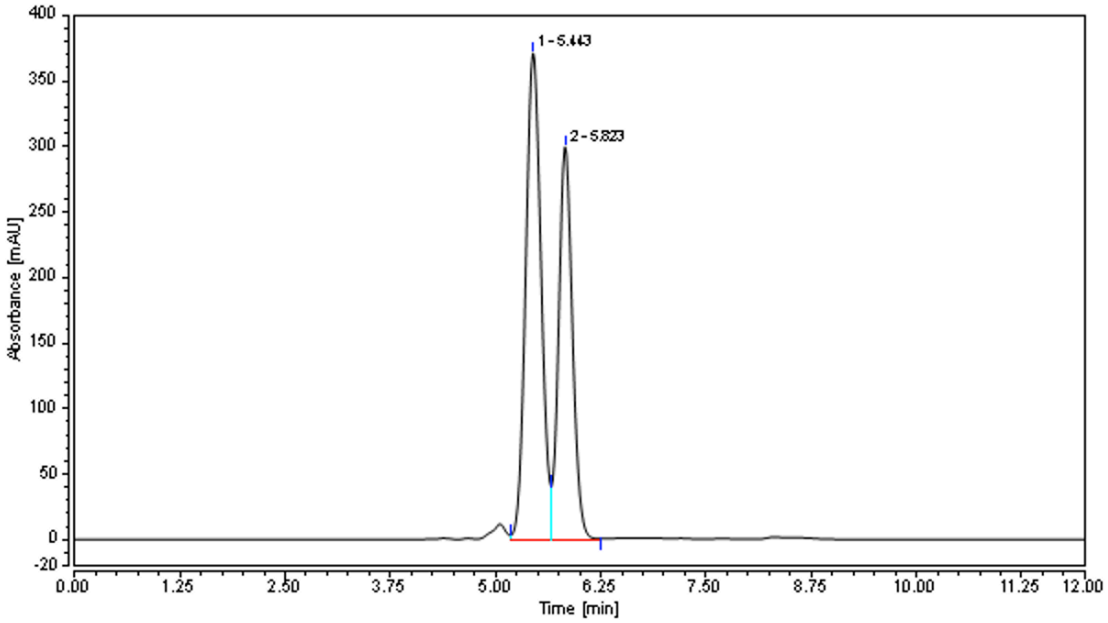
No.	Peak Name	Retention Time	Area	Height	Relative Area
		min	mAU*min	mAU	%
1		6.353	25.771	85.502	29.80
2		6.947	60.721	230.218	70.20
Total:			86.492	315.721	100.00



Enantioenriched
(*S*)-12

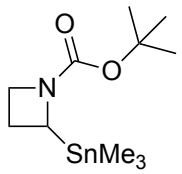


No.	Peak Name	Retention Time	Area	Height	Relative Area
		min	mAU*min	mAU	%
1		5.443	78.373	371.110	57.94
2		5.823	56.903	299.682	42.06
Total:			135.276	670.792	100.00

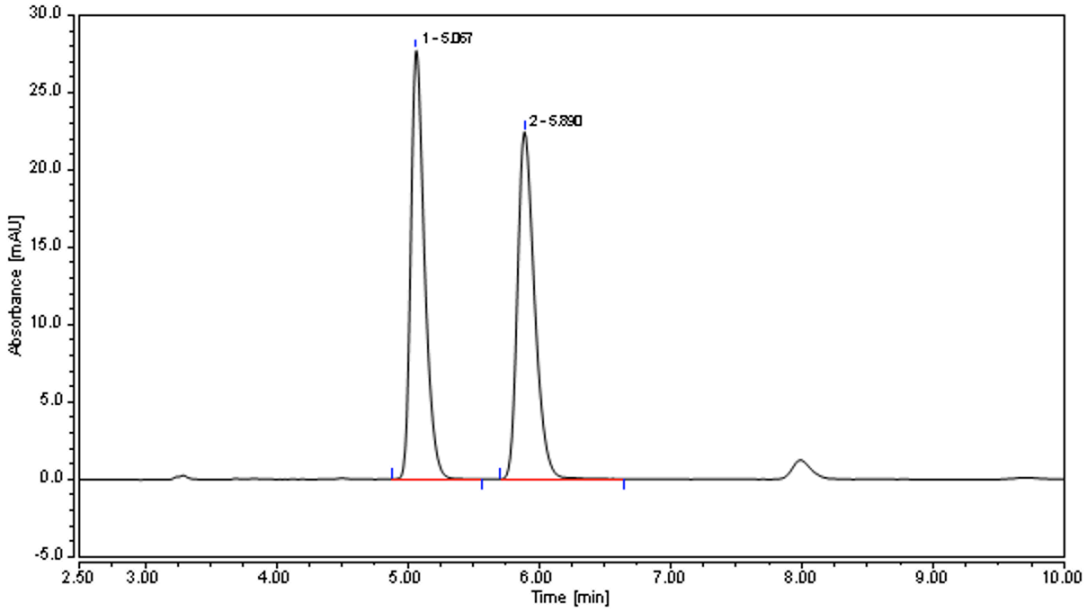


Chiral HPLC for stannane 13: (Chiralpak ODH, 1% ^{i}PrOH, 99% hexane, 1.0 mL min^{-1}, λ = 254 nm, 10 μL injection) τ_R = 5.1 min, τ_R = 5.9 min.

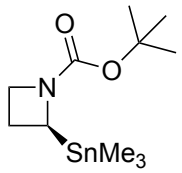
Racemic
(±)-13



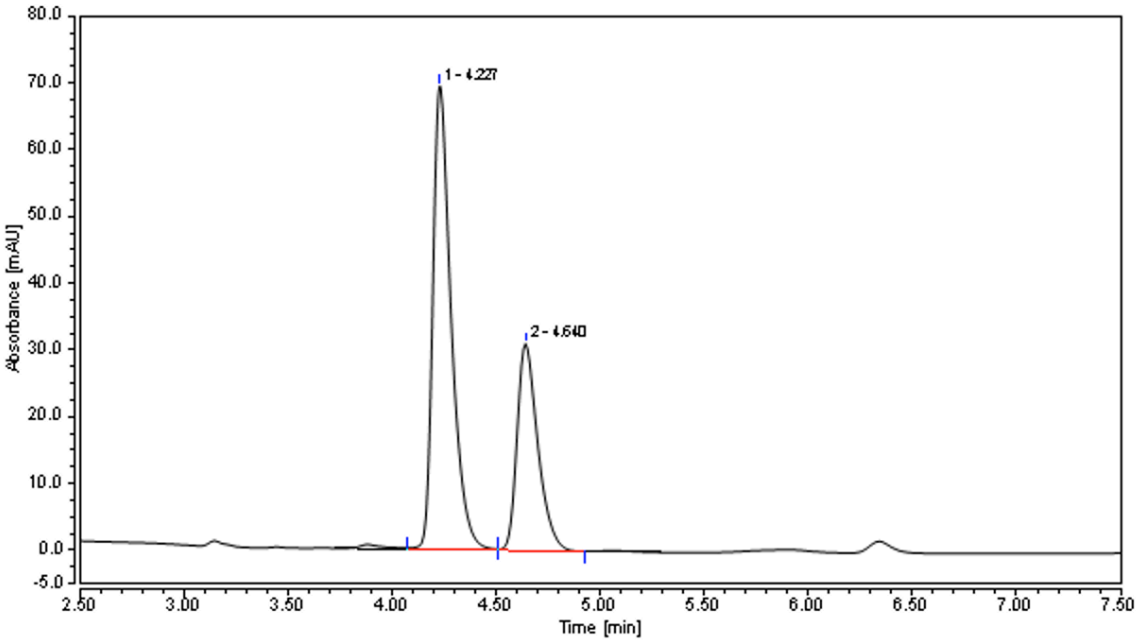
No.	Peak Name	Retention Time	Area	Height	Relative Area
		min	mAU*min	mAU	%
1		5.067	3.356	27.726	49.80
2		5.890	3.383	22.475	50.20
Total:			6.739	50.200	100.00



Enantioenriched
(*S*)-13

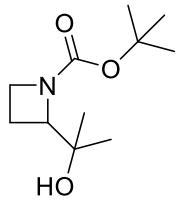


No.	Peak Name	Retention Time	Area	Height	Relative Area
		min	mAU*min	mAU	%
1		4.227	7.107	69.434	66.49
2		4.640	3.582	31.038	33.51
Total:			10.689	100.472	100.00

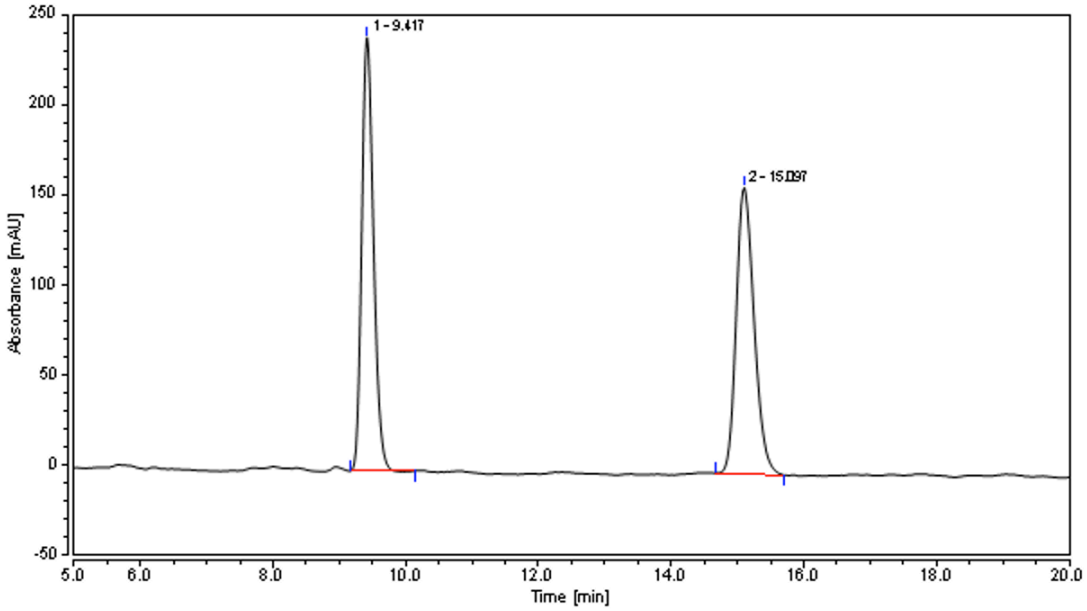


Chiral HPLC for alcohol 14: (Chiralpak ADH, 5% ^{i}PrOH, 95% hexane, 1.0 mL min^{-1}, λ = 205nm, 25 µL injection) τ_R = 9.4 min, τ_R = 15.1 min.

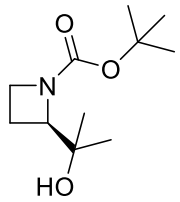
Racemic
(±)-14



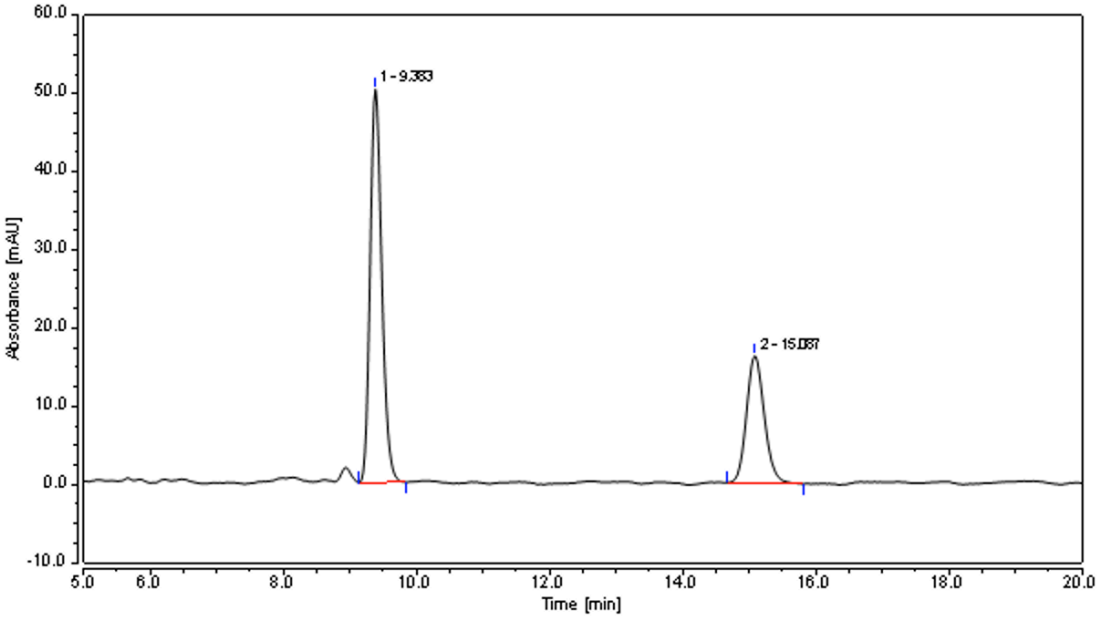
No.	Peak Name	Retention Time	Area	Height	Relative Area
		min	mAU*min	mAU	%
1		9.417	49.182	240.919	49.71
2		15.097	49.746	159.326	50.29
Total:			98.928	400.244	100.00



Enantioenriched
(*R*)-14

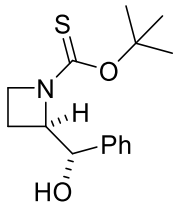


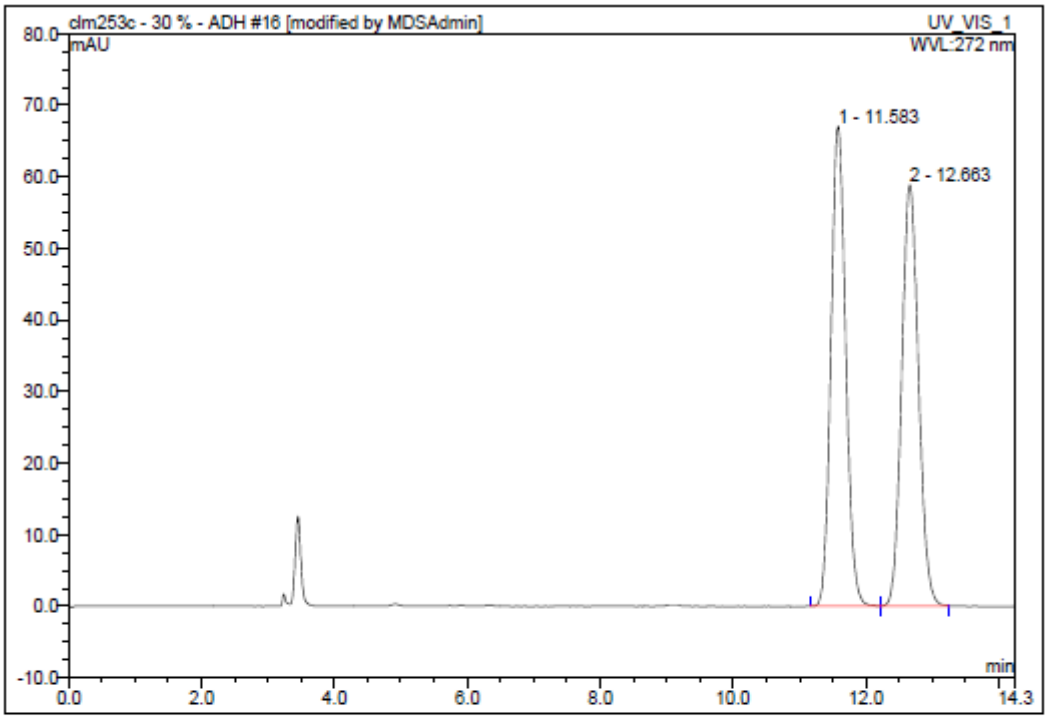
No.	Peak Name	Retention Time	Area	Height	Relative Area
		min	mAU*min	mAU	%
1		9.383	10.175	50.313	66.69
2		15.087	5.082	16.304	33.31
Total:			15.257	66.617	100.00



Chiral HPLC for alcohol (*R*,S)-SI-2:** (Chiralpak ADH, 4% ^{i}PrOH, 96% hexane, 1.0 mL min^{-1}, λ = 272 nm, 25 μL injection) τ_R = 11.6 min, τ_R = 12.7 min.

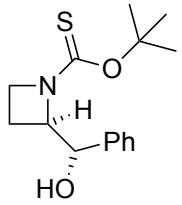
Racemic
(*R*,S)-SI-2**



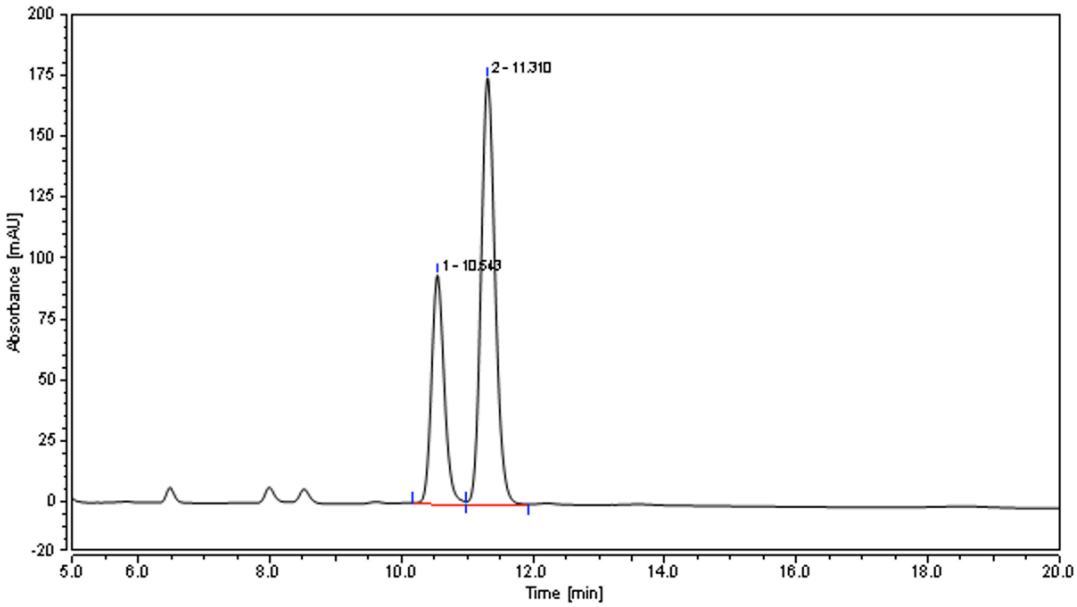


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	11.58	n.a.	67.093	17.305	50.06	n.a.	BM
2	12.66	n.a.	58.827	17.265	49.94	n.a.	MB
Total:			125.920	34.569	100.00	0.000	

Enantioenriched
(*R*,*S*)-SI-2

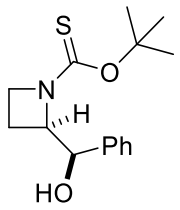


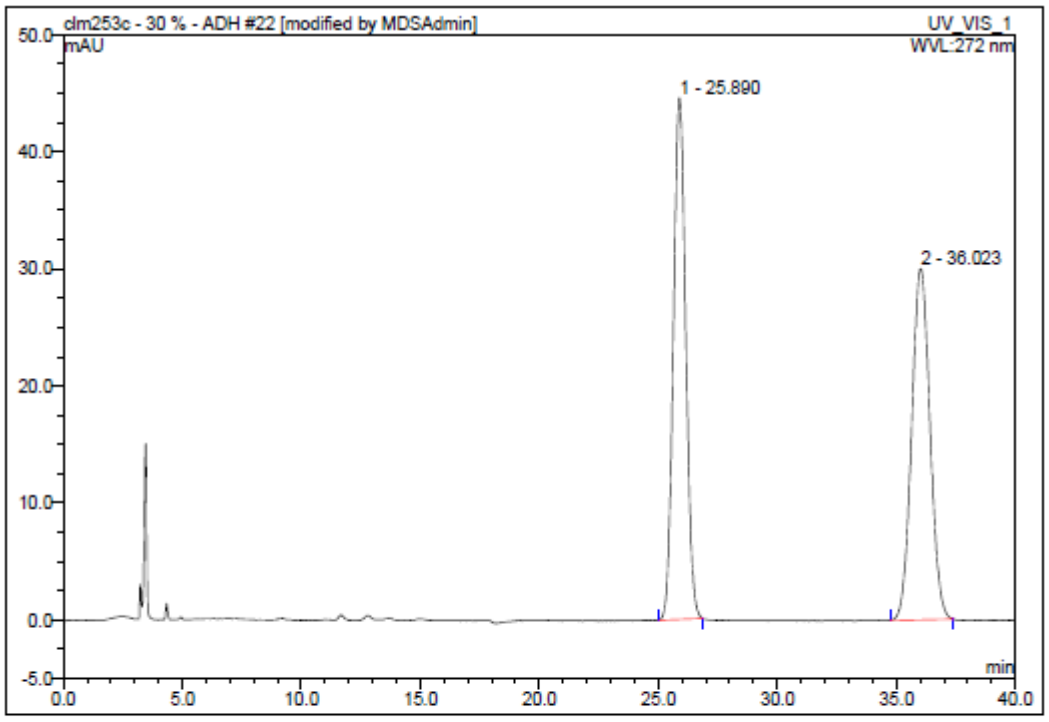
No.	Peak Name	Retention Time	Area	Height	Relative Area
		min	mAU*min	mAU	%
1		10.543	21.255	94.087	32.91
2		11.310	43.322	175.171	67.09
Total:			64.577	269.258	100.00



Chiral HPLC for alcohol (*R*,R)-SI-2:** (Chiralpak ADH, 4% ^{i}PrOH, 96% hexane, 1.0 mL min^{-1}, λ = 272 nm, 25 μL injection) τ_R = 25.9 min, τ_R = 36.0 min.

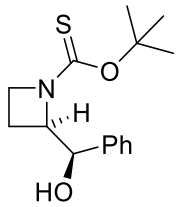
Racemic
(*R*,R)-SI-2**



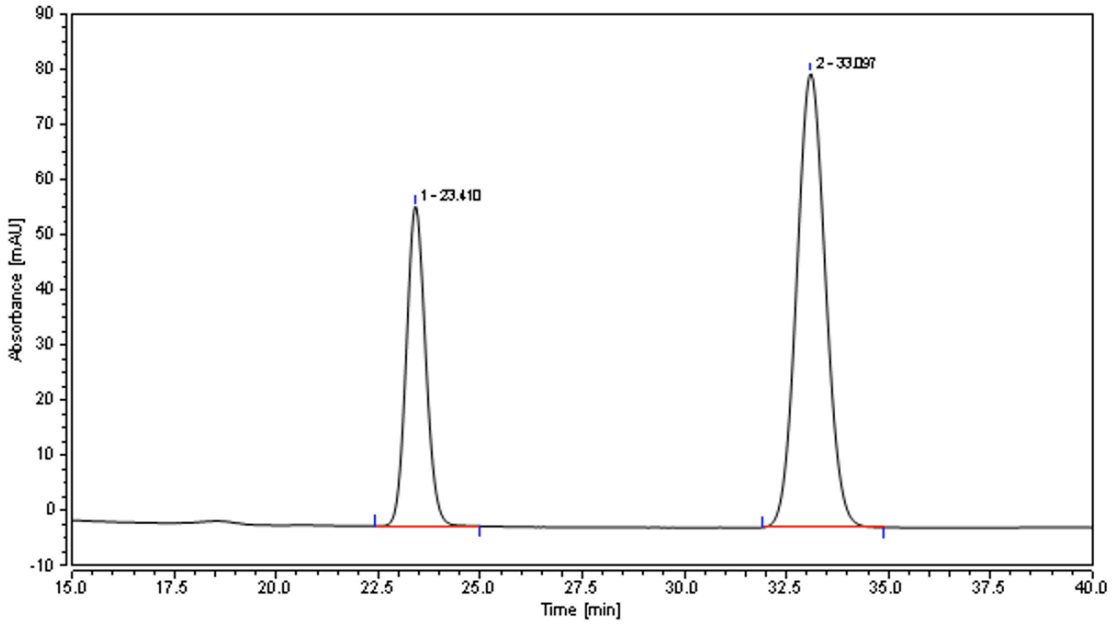


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	25.89	n.a.	44.569	26.750	50.08	n.a.	BMB
2	36.02	n.a.	29.998	26.667	49.92	n.a.	BMB
Total:			74.567	53.417	100.00	0.000	

Enantioenriched
(*R*,*R*)-SI-2

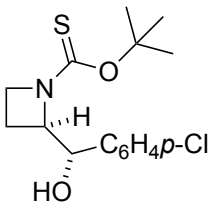


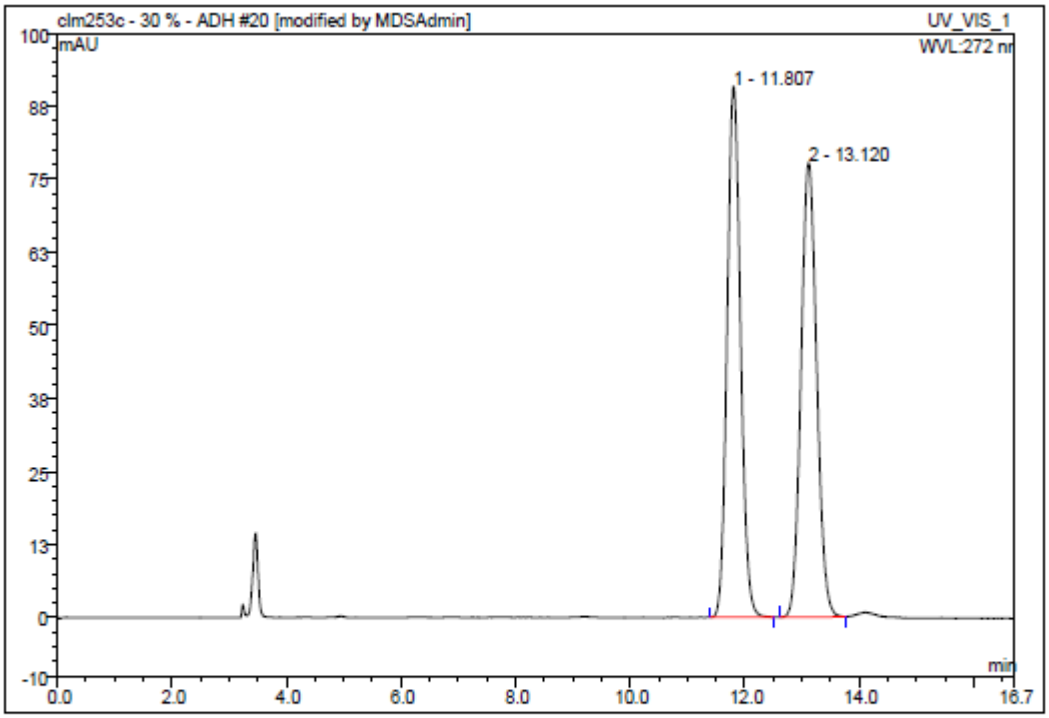
No.	Peak Name	Retention Time	Area	Height	Relative Area
		min	mAU*min	mAU	%
1		23.410	31.697	57.996	32.12
2		33.097	66.984	82.217	67.88
Total:			98.681	140.213	100.00



Chiral HPLC for alcohol (*R*,S)-SI-3:** (Chiralpak ADH, 4% ^{i}PrOH, 96% hexane, 1.0 mL min^{-1}, λ = 272 nm, 25 μL injection) τ_R = 11.8 min, τ_R = 13.1 min.

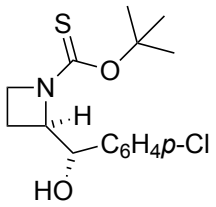
Racemic
(*R*,S)-SI-3**

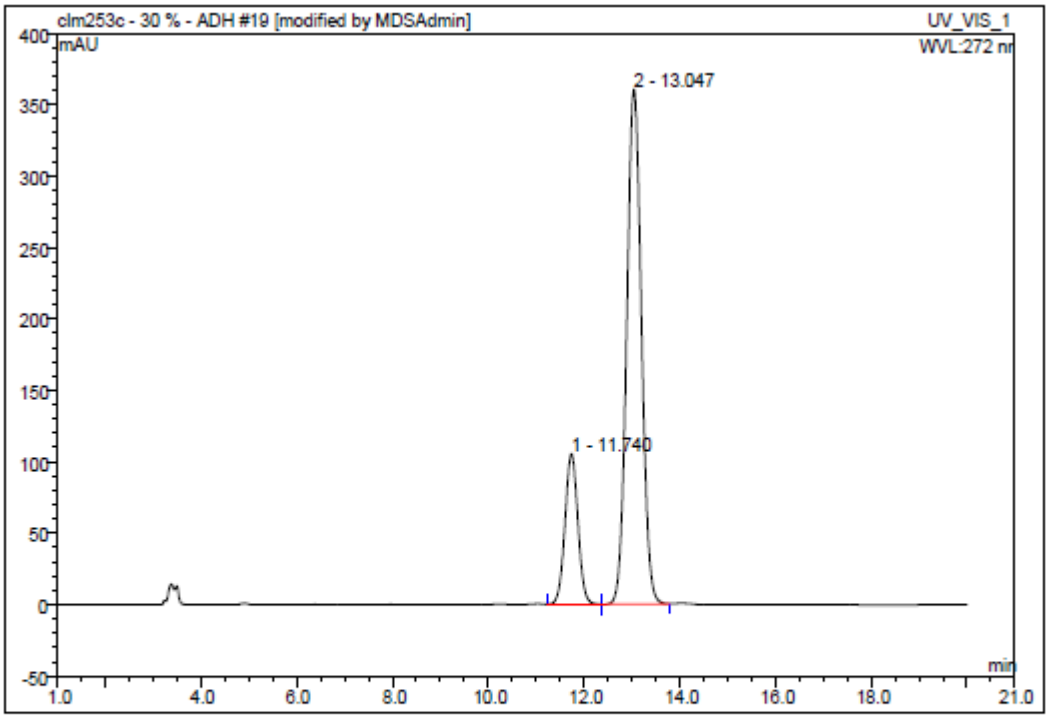




No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	11.81	n.a.	90.787	24.676	50.02	n.a.	BMB
2	13.12	n.a.	77.713	24.660	49.98	n.a.	BMB*
Total:			168.500	49.336	100.00	0.000	

Enantioenriched
(*R*,*S*)-SI-3

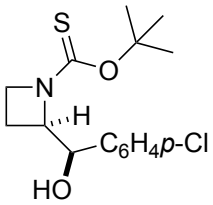


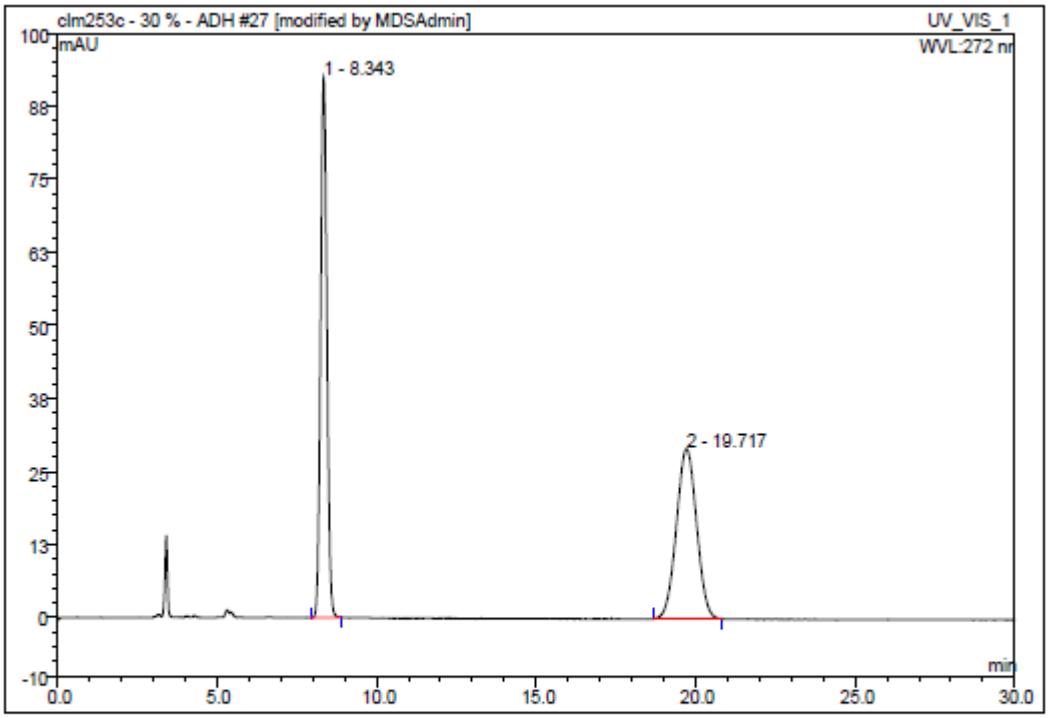


No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	11.74	n.a.	105.172	32.985	20.49	n.a.	BMB
2	13.05	n.a.	360.125	127.982	79.51	n.a.	BMB*
Total:			465.297	160.966	100.00	0.000	

Chiral HPLC for alcohol (*R*,R)-SI-3:** (Chiralpak ADH, 4% ^{i}PrOH, 96% hexane, 1.0 mL min^{-1}, λ = 272 nm, 25 μL injection) τ_R = 8.3 min, τ_R = 19.7 min.

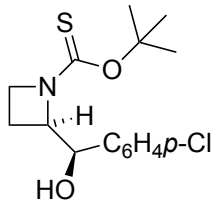
Racemic
(*R*,R)-SI-3**

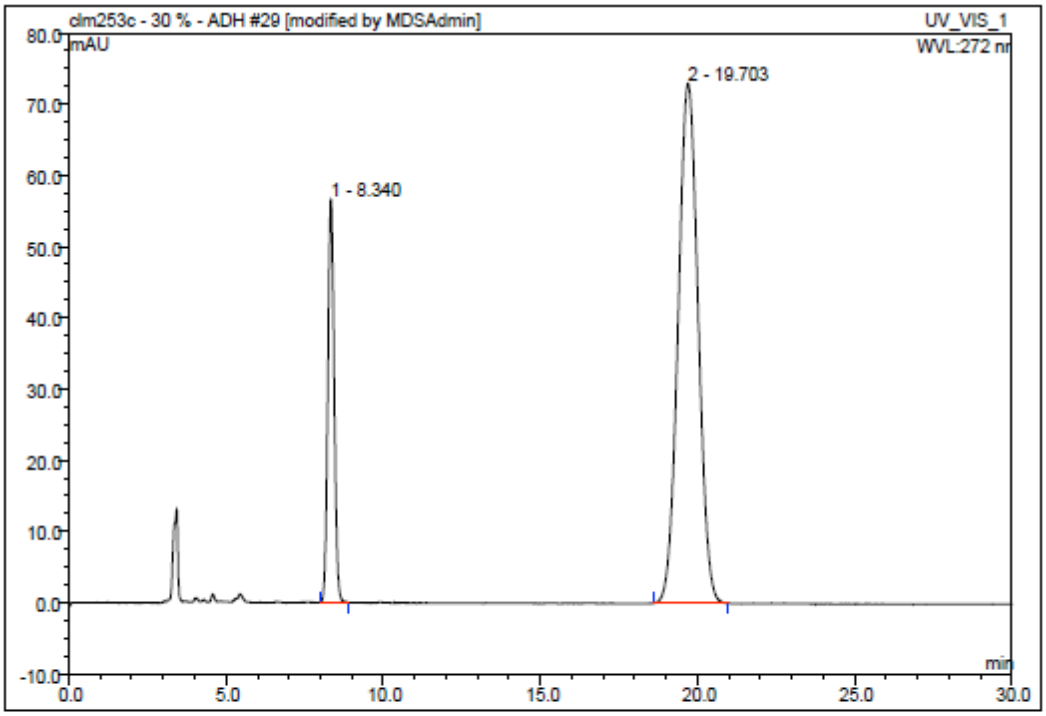




No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	8.34	n.a.	92.532	21.306	49.99	n.a.	BMB
2	19.72	n.a.	29.092	21.310	50.01	n.a.	BMB
Total:			121.624	42.616	100.00	0.000	

Enantioenriched
(*R*,*R*)-SI-3

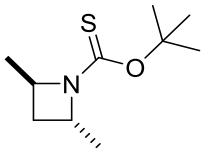




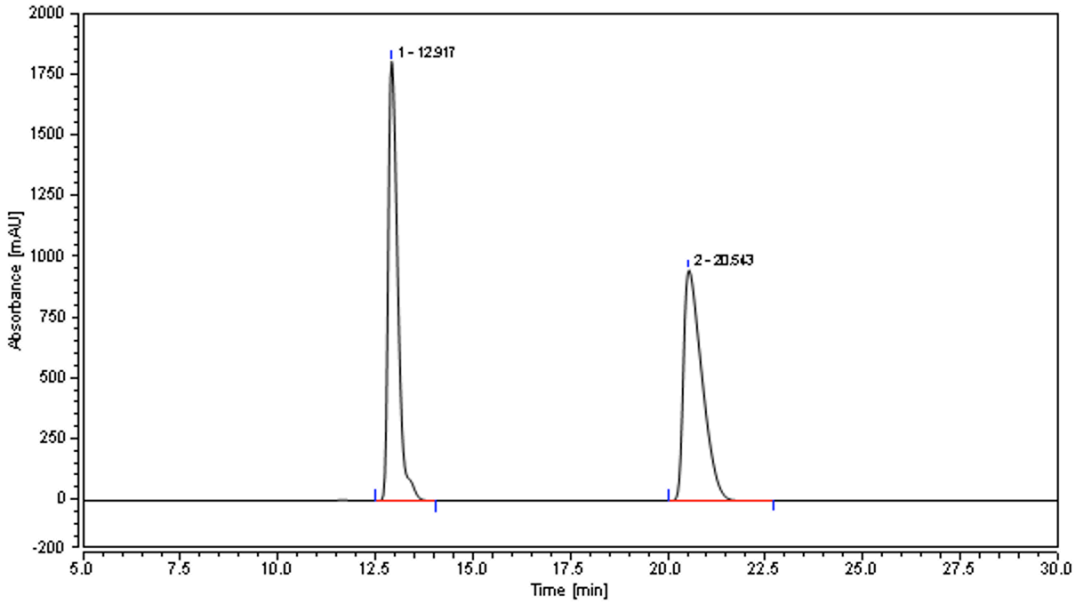
No.	Ret.Time min	Peak Name	Height mAU	Area mAU*min	Rel.Area %	Amount	Type
1	8.34	n.a.	56.623	13.213	19.73	n.a.	BMB
2	19.70	n.a.	72.967	53.755	80.27	n.a.	BMB
Total:			129.591	66.968	100.00	0.000	

Chiral HPLC for 2,4-dimethylazetidine SI-4: (Chiralpak IC, 1% ^{i}PrOH, 99% hexane, 1.0 mL min^{-1}, λ = 260 nm, 20 μL injection) τ_R = 12.9 min, τ_R = 20.5 min.

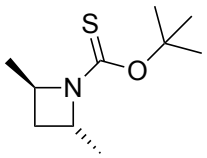
Racemic
(*R,*R**)-SI-4**



No.	Peak Name	Retention Time	Area	Height	Relative Area
		min	mAU*min	mAU	%
1		12.917	513.135	1808.372	49.62
2		20.543	521.055	950.119	50.38
Total:			1034.190	2758.491	100.00



Enantioenriched
(*R*,*R*)-SI-4



No.	Peak Name	Retention Time	Area	Height	Relative Area
		min	mAU*min	mAU	%
1		12.777	25.689	183.715	8.00
2		18.200	295.403	822.491	92.00
Total:			321.092	1006.206	100.00