*Organic Letters*

# Supporting Information

## Addition Reactions of Iodomethyllithium to Imines. A Direct and Efficient Synthesis of Aziridines and Enantiopure Amino Aziridines

*José M. Concellón,* Humberto Rodríguez-Solla and Carmen Simal*

Departamento de Química Orgánica e Inorgánica. Facultad de Química, Universidad de Oviedo, C/ Julián Clavería, 8, 33006, Oviedo, Spain.

jmcg@uniovi.es

**GENERAL**

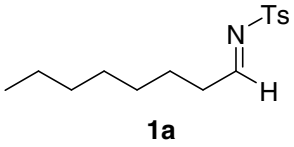
Reactions requiring an inert atmosphere were conducted under dry nitrogen, and the glassware was oven dried (120 °C). THF was distilled from sodium/benzophenone ketyl immediately prior to use. All reagents were purchased in the higher quality available and were used without further purification. Flash column chromatography was carried out on silica gel 230-400 mesh. Compounds were visualized on analytical thin layer chromatograms (TLC) by UV light (254 nm). $^{1}$H NMR spectra were recorded at 300 or 400 MHz. $^{13}$C NMR spectra and DEPT experiments were determined at 75 or 100 MHz. Chemical shifts are given in ppm relative to tetramethylsilane (TMS), which is used as an internal standard, and coupling constants (*J*) are reported in Hz. The diastereoisomeric ratio were obtained using $^{1}$H NMR analysis and GC-MS of crude products. GC-MS and HRMS were measured at 70 eV or using FAB conditions. When HRMS could not be measured on molecular ion the HRMS of a significant fragment is given. Only the most important IR absortions ($cm^{-1}$) and the molecular ions and/or base peaks in MS are given.

*Synthesis of sulfonylimines **1**:*

Sulfonylimines **1** were synthesized following the method reported in reference 17, see manuscript.

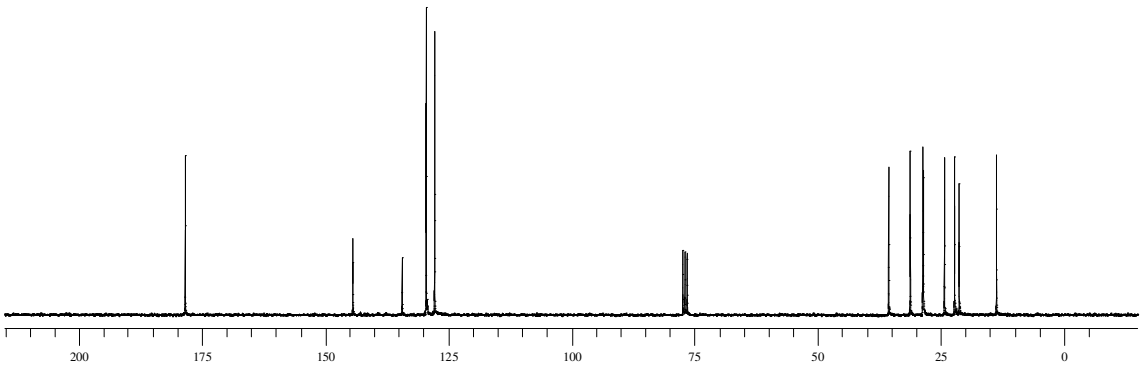
**_N_-Tosyloctan-1-imine (1a)**

$^{1}$H NMR (300 MHz, $CDCl_3$): δ = 8.60 (t, *J* = 4.55 Hz, 1 H), 7.81 (d, *J* = 8.22 Hz, 2 H), 7.34 (d, *J* = 8.22 Hz, 2 H), 2.51 (dt, *J* = 7.37, 4.59 Hz, 2 H), 2.43 (s, 3 H), 1.66-1.57 (m, 2 H), 1.39-1.14 (m, 8 H), 0.86 (t, *J* = 6.75 Hz, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 178.4 (CH), 144.4 (C), 134.4 (C), 129.5 (2xCH), 127.8 (2xCH), 35.6 ($CH_2$), 31.2 ($CH_2$), 28.7 ($CH_2$), 28.5 ($CH_2$), 24.3 ($CH_2$), 22.2 ($CH_2$), 21.3 ($CH_3$), 13.7 ($CH_3$); MS (70 eV): *m/z* (%): 281 [$M^+$] (4), 210 (19), 197 (24), 155 (49), 133 (51), 91 (100), 65 (28); HRMS calcd for $C_{15}H_{23}NO_2S$ 281,1449, found 281,1415; IR (neat): 3292, 1629, 1161, 1020, 737 cm$^{-1}$; $R_f$ = 0.40 (hexane:ethyl acetate 3:1)



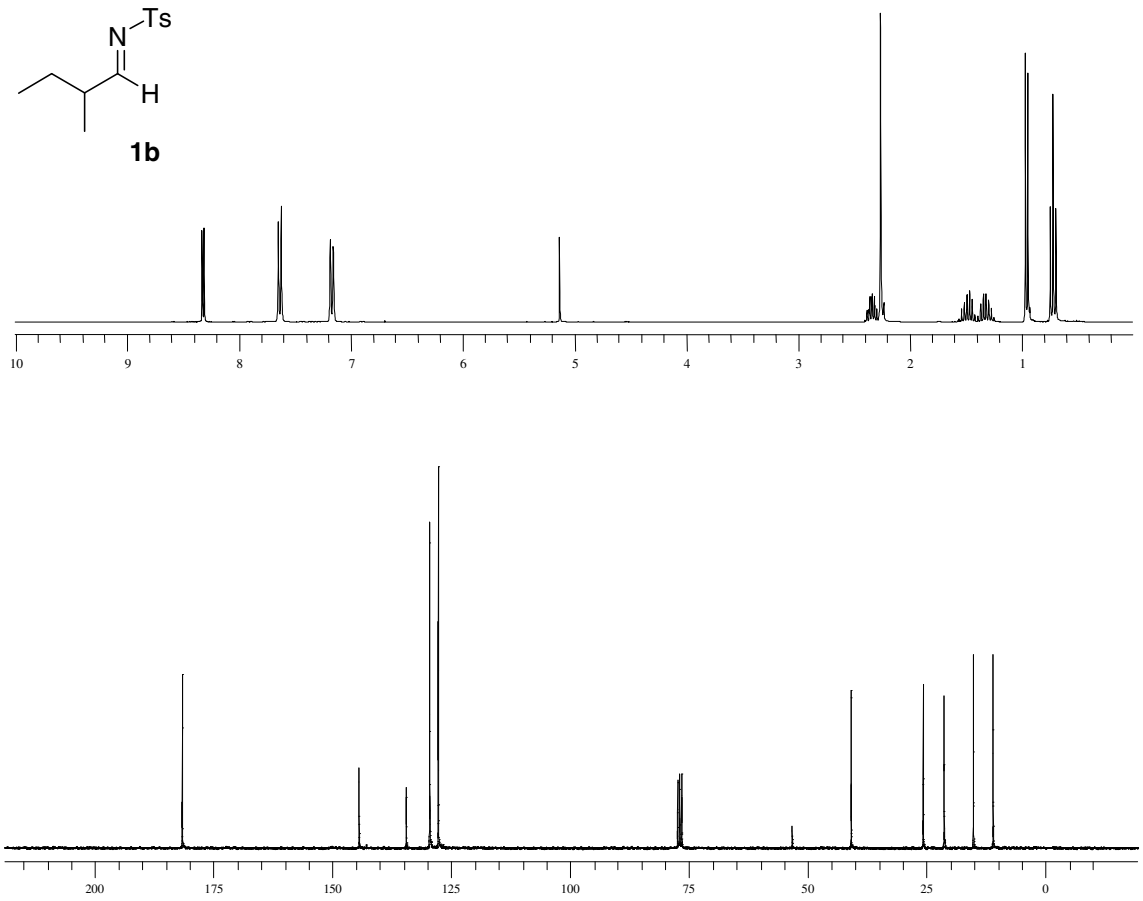

**1a**



**2-Methyl-*N*-tosylbutan-1-imine (1b)**

$^{1}$H NMR (300 MHz, $CDCl_3$): δ = 8.49 (d, *J* = 5.10 Hz, 1 H), 7.80 (d, *J* = 8.22 Hz, 2 H), 7.34 (d, *J* = 8.22 Hz, 2 H), 2.55-2.47 (m, 1 H), 2.43 (s, 3 H), 1.73-1.59 (m, 1 H), 1.56-1.41 (m, 1 H), 1.12 (d, *J* = 6.78 Hz, 3 H), 0.89 (t, *J* = 7.41 Hz, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 181.6 (CH), 144.4 (C), 134.5 (C), 129.6 (2xCH), 127.7 (2xCH), 40.9 (CH), 25.7 ($CH_2$), 21.3 ($CH_3$), 15.1 ($CH_3$), 11.0 ($CH_3$); MS (70 eV): *m/z* (%): 239 [$M^+$] (4), 193 (19), 190 (50), 169 (21), 119 (34), 91 (27), 69 (100); HRMS calcd for $C_{12}H_{17}NO_2S$ 239.0980, found 239.0946; IR (neat): 3326, 1631, 1266, 1008, 738 $cm^{-1}$; $R_f$ = 0.47 (hexane:ethyl acetate 3:1)

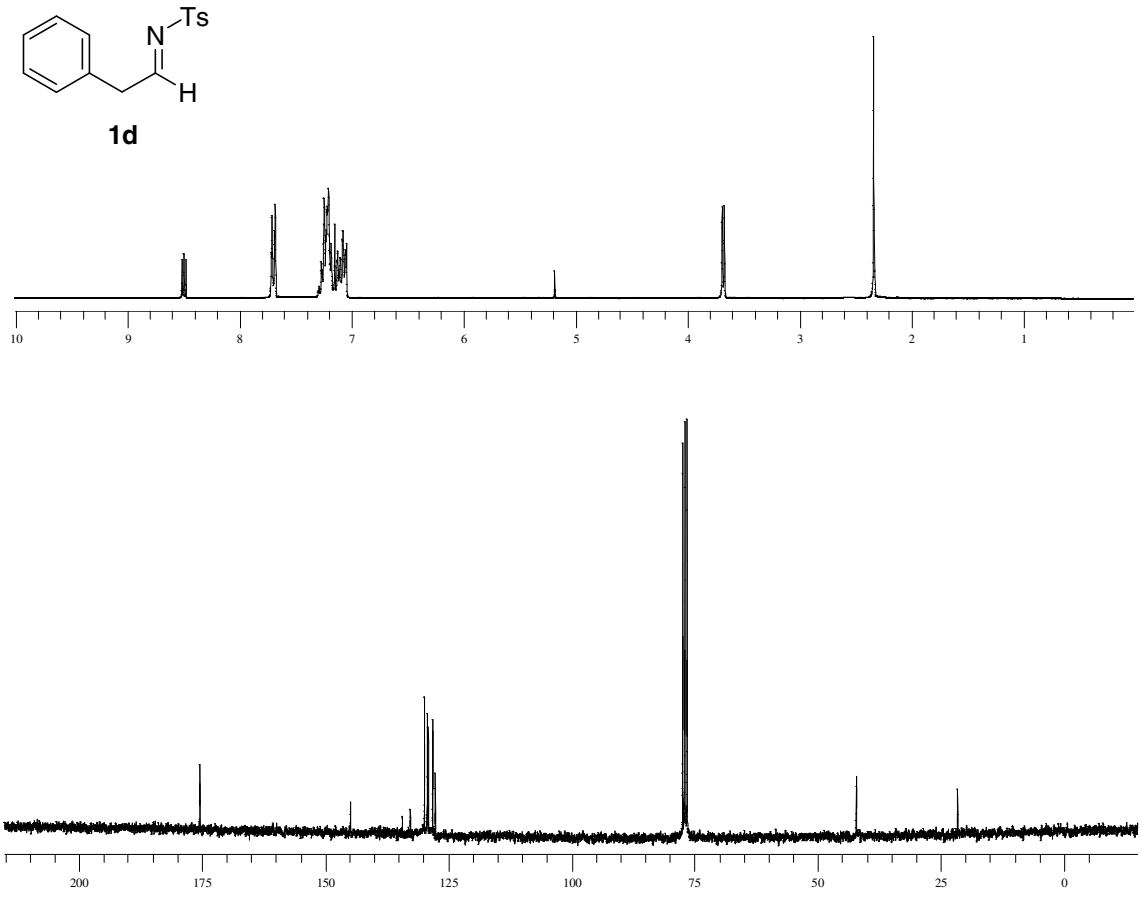


**Cyclohexyl-*N*-tosylmethanimine (1c)**

This compound displayed analytical data in accordance with the published values (Chemla, F.; Hebbe, V.; Normant J.-F. *Synthesis* **2000**, *1*, 75-77)

**2-Phenyl-*N*-tosylethanimine (1d)**

$^{1}$H NMR (300 MHz, $CDCl_3$): δ = 8.50 (t, *J* = 5.36 Hz, 1 H), 7.70 (d, *J* = 8.34 Hz, 2 H), 7.27-7.05 (m, 7 H), 3.68 (d, *J* = 5.37 Hz, 2 H), 2.34 (s, 3 H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 175.4 (CH), 144.8 (C), 134.3 (C), 132.7 (C), 129.8 (2xCH), 129.3 (2xCH), 129.1 (2xCH), 128.2 (2xCH), 127.6 (CH), 42.1 ($CH_2$), 21.6 ($CH_3$); MS (70 eV): *m/z* (%): 273 [$M^+$] (<1), 242 (16), 181 (47), 169 (46), 131 (48), 119 (18), 69 (100); HRMS calcd for $C_{15}H_{15}NO_2S$ 273.0823, found 273.0860; IR (neat): 3055, 1629, 1266, 1007, 739 $cm^{-1}$; $R_f$ = 0.55 (hexane:ethyl acetate 3:1)




**Phenyl-*N*-tosylmethanimine (1e)**

This compound displayed analytical data in accordance with the published values (Chemla, F.; Hebbe, V.; Normant J.-F. *Synthesis* **2000**, *1*, 75-77)

*General procedure for the synthesis of sulfonylaziridines **2**:*

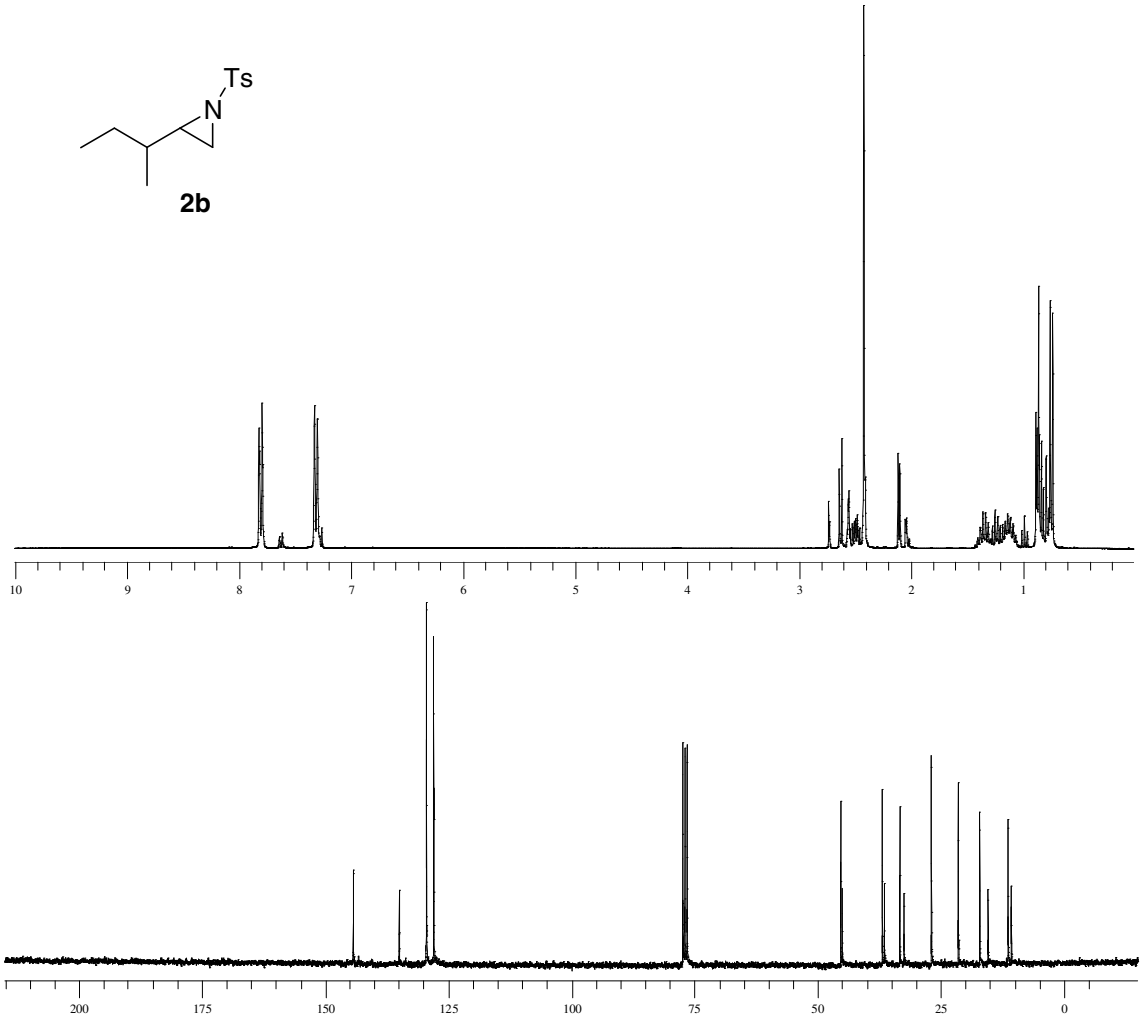
To a mixture of *N*-sulfonylimine **1** (0.4 mmol) and $CH_2I_2$ (0.6 mmol, 1.5 eq.) in dry THF (2 mL), a solution of MeLi in ether was added (1.5 M, 0.48 mmol, 1.2 eq.) at 0 ºC. The solution was stirred at the same temperature for 30 minutes and then was left at room temperature for an additional 30 minutes. The reaction mixture was then quenched with $NH_4Cl$ aq. and the organic layer was then extracted with diethyl ether (3 x 10 mL). The combined extracts were dried over $Na_2SO_4$ and concentrated under vacuum to yield crude *N*-sulfonylaziridines **2** which were purified by flash chromatography on silica gel (Hexane/EtOAc 10/1).

**2-Heptyl-1-tosylaziridine (2a)**

This compound displayed analytical data in accordance with the published values (Gao, G.-Y.; Harden, J. D.; Zang, X. P. *Org. Lett.* **2005**, *7*, 3191-3193)

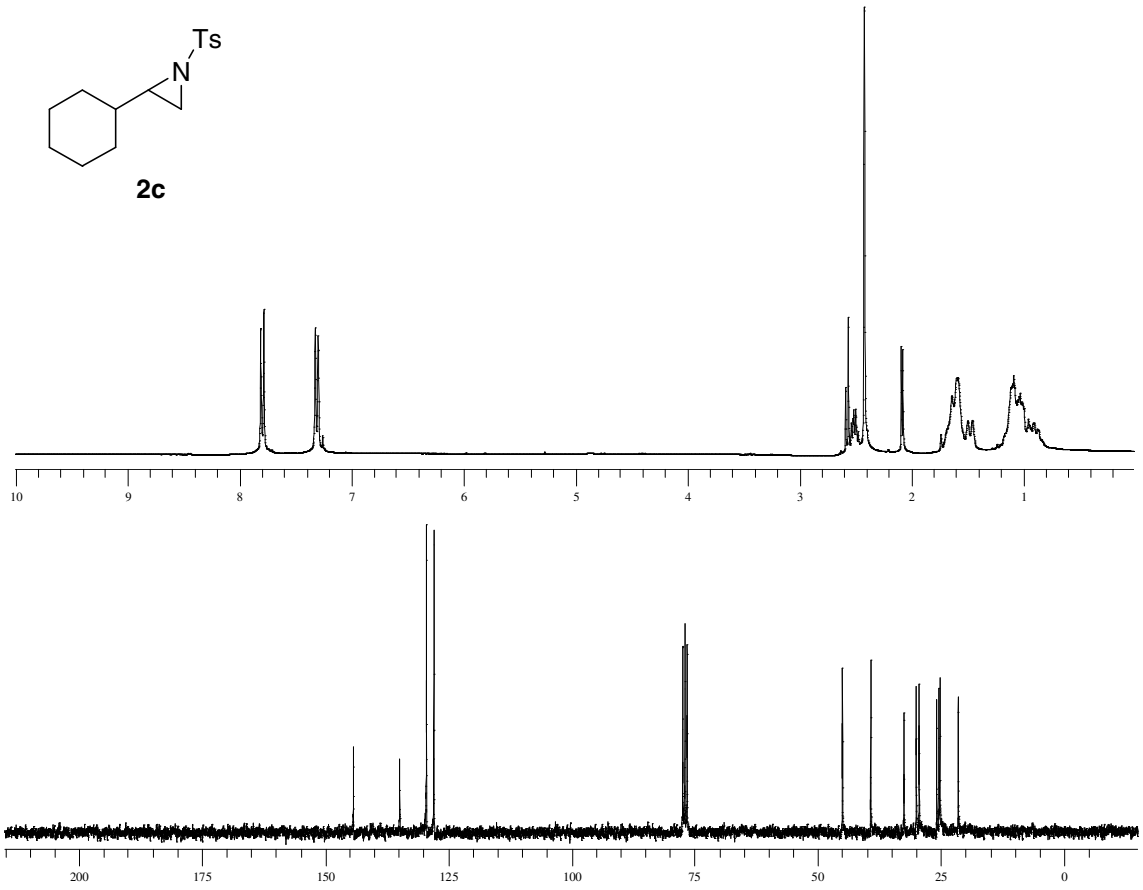
**2-*sec*-Butyl-1-tosylaziridine (2b)**

$^{1}$H NMR (300 MHz, $CDCl_3$): δ = major diastereoisomer, 87.81 (d, *J* = 8.19 Hz, 2 H), 7.31 (d, *J* = 8.19 Hz, 2 H), 2.63 (d, *J* = 7.05 Hz, 1 H), 2.57-2.46 (m, 1 H), 2.42 (s, 3 H), 2.11 (d, *J* = 4.50 Hz, 1 H), 1.40-1.06 (m, 3 H), 0.86 (t, *J* = 7.41 Hz, 3H), 0.74 (d, *J* = 6.48 Hz, 3 H); minor diastereoisomer, 7.63 (d, *J* = 8.19 Hz, 2 H), 7.32-7.28 (m, 2 H), 2.73 (d, *J* = 2.13 Hz, 1 H), 2.57-2.46 (m, 1 H), 2.41 (s, 3 H), 2.04 (d, *J* = 3.69 Hz, 1 H), 1.40-1.06 (m, 3 H), 0.88-0.73 (m, 6 H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ = major diastereoisomer, 144.3 (C), 135.0 (C), 129.5 (2xCH), 127.9 (2xCH), 45.3 (CH), 36.9 (CH), 33.3 ($CH_2$), 26.9 ($CH_2$), 21.5 ($CH_3$), 17.1 ($CH_3$), 11.4 ($CH_3$); minor diastereoisomer, 144.3 (C), 135.0 (C), 129.5 (2xCH), 127.9 (2xCH), 45.0 (CH), 36.5 (CH), 32.5 ($CH_2$), 26.9 ($CH_2$), 21.5 ($CH_3$), 15.4 ($CH_3$), 10.7 ($CH_3$); MS (70 eV): *m/z* (%): 253 [$M^+$] (<1), 155 (20), 98 (100), 91 (73), 69 (68), 56 (46), 42 (82); HRMS calcd for $C_{13}H_{19}NO_2S$ 253.1136, found 253.1154; IR (neat): 2972, 1324, 1162, 1005, 722 $cm^{-1}$; $R_f$ = 0.375 (hexane:ethyl acetate 3:1)



**2-Cyclohexyl-1-tosylaziridine (2c)**

$^{1}$H NMR (300 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 8.22 Hz, 2 H), 7.31 (d, *J* = 8.22 Hz, 2 H), 2.58 (d, *J* = 7.02 Hz, 1 H), 2.54-2.48 (m, 1 H), 2.42 (s, 3 H), 2.08 (d, *J* = 4.41 Hz, 1 H), 1.77-1.43 (m, 5 H), 1.25-0.80 (m, 6 H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 144.3 (C), 134.9 (C), 129.4 (2xCH), 127.9 (2xCH), 45.0 (CH), 39.2 (CH), 32.5 ($CH_2$), 30.0 ($CH_2$), 29.5 ($CH_2$), 25.8 ($CH_2$), 25.4 ($CH_2$), 25.2 ($CH_2$), 21.5 ($CH_3$); MS (70 eV): *m/z* (%): 155 [$M^+$- Ts] (24), 124 (99), 95 (100), 65 (42), 55 (33), 42 (85); HRMS calcd for $C_{15}H_{21}NO_2S$ 279.1293, found 279.1281; IR (neat): 2928, 1322, 1266, 1162, 1010 $cm^{-1}$; $R_f$ = 0.50 (hexane:ethyl acetate 3:1)




**2-Benzyl-1-tosylaziridine (2d)**

This compound displayed analytical data in accordance with the published values, see reference 18.

**2-Phenyl-1-tosylaziridine (2e)**

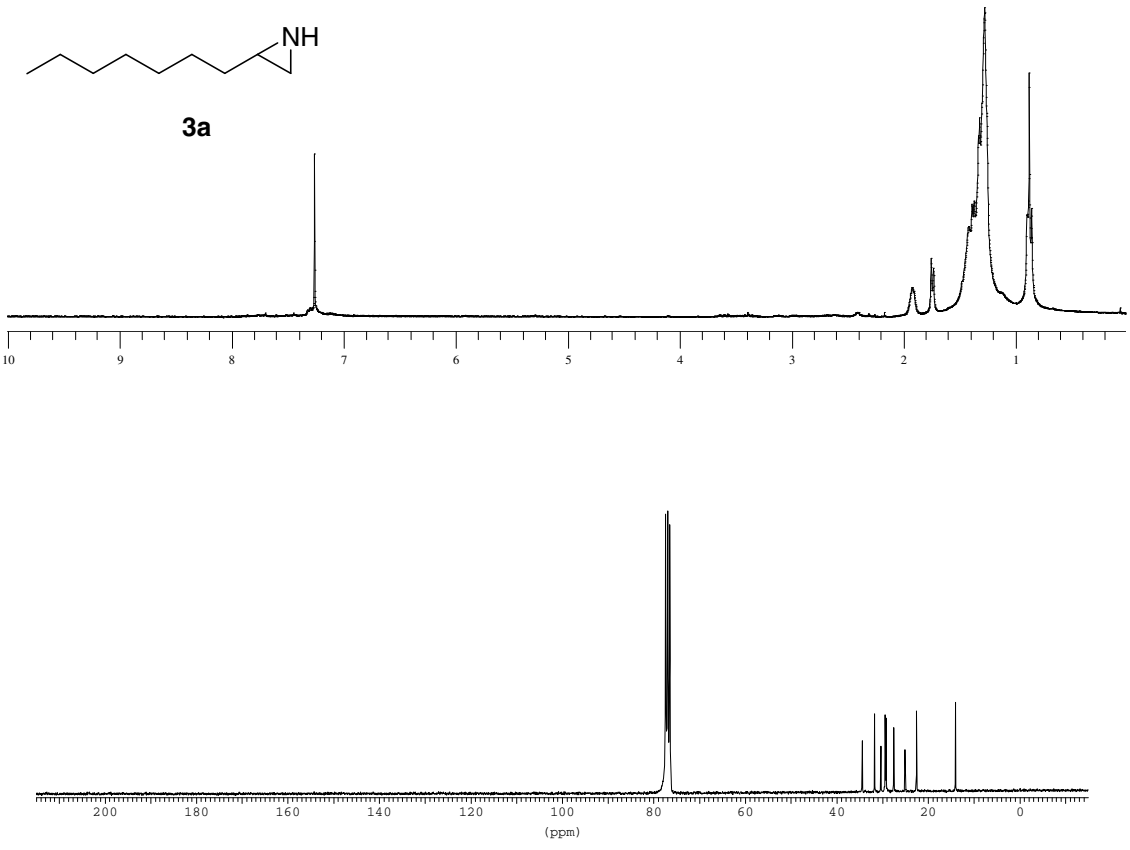
This compound displayed analytical data in accordance with the published values, see reference 18.

*General procedure for the synthesis of aziridines **3**:*

To a cooled (-78 ºC) suspension of Li powder (1.44 mmol) and naphthalene (1.62 mmol) in dry THF (4 mL) previously stirred for 1h at r.t., the corresponding *N*-sulfonylaziridine (0.36 mmol) was added under $N_2$ atm. The mixture was then stirred, for an additional 1 h, at the same temperature, and then was quenched with brine (10 mL). The corresponding pure aziridine was obtained in a good yield after a acid-base extraction.

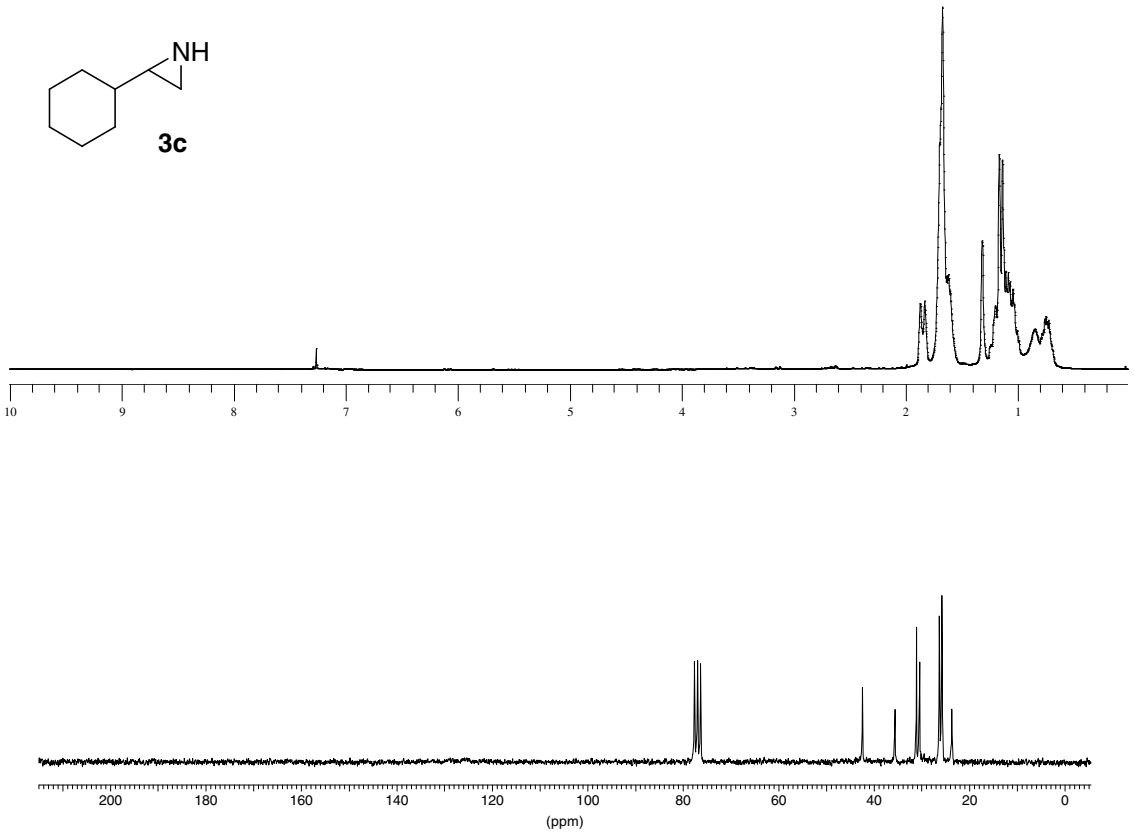
**2-Heptylaziridine (3a)**

$^1$H NMR (300 MHz, $CDCl_3$): δ = 1.97-1.87 (m, 1 H), 1.74 (d, *J* = 5.70 Hz, 1 H), 1.60-1.05 (m, 14 H), 0.88 (t, *J* = 6.75 Hz, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 34.4 ($CH_2$), 31.8 ($CH_2$), 30.3 (CH), 29.4 ($CH_2$), 29.2 ($CH_2$), 27.5 ($CH_2$), 25.1 ($CH_2$), 22.6 ($CH_2$), 14.0 ($CH_3$); MS (70 eV): *m/z* (%): 140 [$M^+$-1] (100), 122 (21), 91 (17), 69 (43); HRMS calcd for $C_9H_{19}N$ 141.1517, found 141.1487; IR (neat): 1581, 1265, 1002, 739, 705 cm$^{-1}$; $R_f$ = 0.32 (acetone)



**2-Cyclohexylaziridine (3c)**

$^{1}$H NMR (300 MHz, $CDCl_3$): δ = 1.85 (br d, *J* = 12.78 Hz, 1 H), 1.73-1.52 (m, 6 H), 1.31-0.96 (m, 6 H), 0.88-0.67 (m, 2 H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 42.4 (CH), 35.6 (CH), 31.1 ($CH_2$), 30.4 ($CH_2$), 26.3 ($CH_2$), 25.8 ($CH_2$), 25.7 ($CH_2$), 23.7 ($CH_2$); MS (70 eV): *m/z* (%): 124 [$M^+$-1] (12), 112 (100), 95 (17), 107 (22); HRMS calcd for $C_8H_{15}N$ 125.1204, found 125.1167; IR (neat): 1449, 1265, 1010, 786, 737 cm$^{-1}$; $R_f$ = 0.37 (acetone)




**2-Benzylaziridine (3d)**

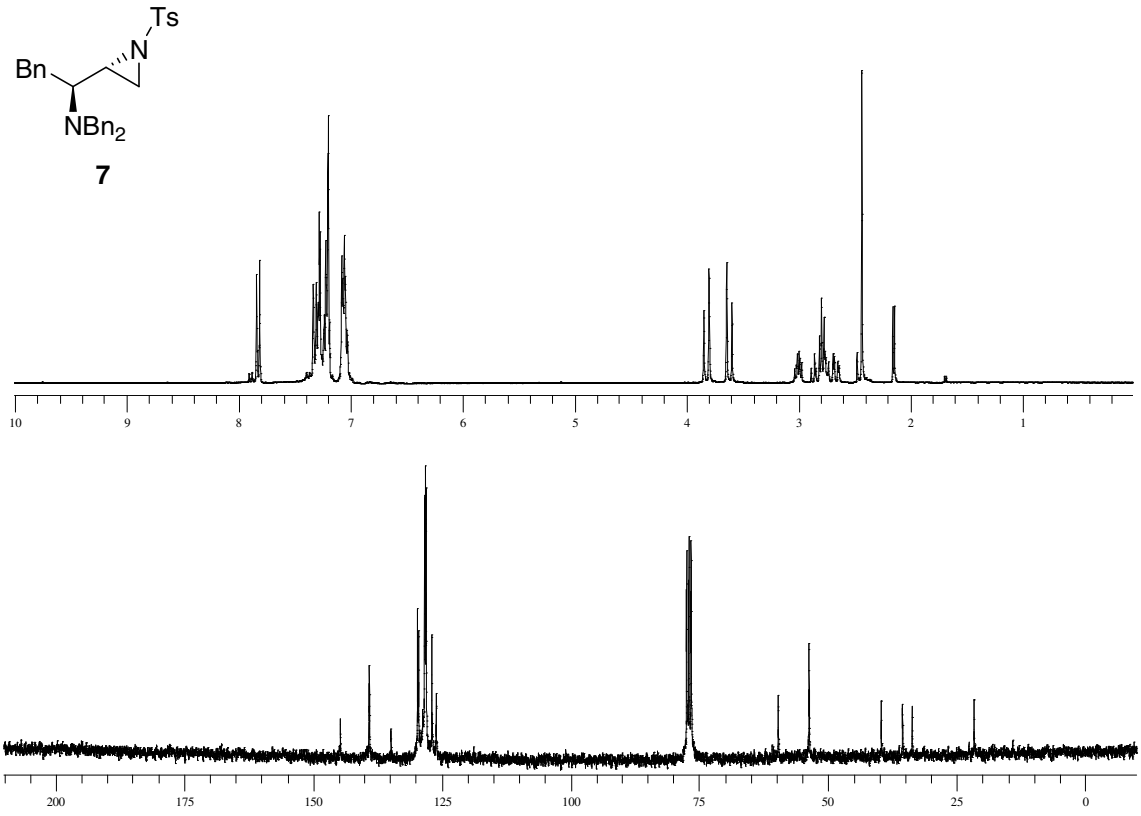
This compound displayed analytical data in accordance with the published values, see reference 18.

*Synthesis of (+)-(2R,1´S)-1-Tosyl-2-[1´-(dibenzylamino)-2´-phenylethyl]aziridine* (**7**)*:*

α-Aminoimine **6** were prepared using the method described by Weinreb (see reference 21). However no isolation of **6** was carried out due to its instability. Therefore, after applying the Weinreb conditions, $CH_2Cl_2$ was removed and THF (5 mL) was added. The reaction mixture was cooled to –78ºC and $CH_2I_2$ (1.6 mmol, 4 eq.) was added followed by a solution of MeLi in ether (1.5 M, 1.6 mmol, 4 eq.). The reaction mixture was stirred for 30 minutes and then warmed to room temperature and left to stir for an additional 30 minutes. The reaction mixture was then quenched with $NH_4Cl$ aq. and the organic layer was then extracted with diethyl ether (3 x 10 mL). The combined extracts were dried over $Na_2SO_4$ and concentrated under vacuum to yield crude aminoaziridine **7** which was purified by flash chromatography on silica gel (Hexane/EtOAc 10/1).

**(+)-(2*R*,1´*S*)-1-Tosyl-2-[1´-(dibenzylamino)-2´-phenylethyl]aziridine (7)**

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 8.22 Hz, 2 H), 7.31-7.18 (m, 12 H), 7.08-7.02 (m, 5 H), 3.82 (d, *J* = 13.89 Hz, 2 H), 3.62 (d, *J* = 13.89 Hz, 2 H), 3.00 (td, *J* = 7.11, 4.74 Hz, 1 H), 2.89-2.73 (m, 3 H), 2.66 (dd, *J* = 12.63, 3.45 Hz, 1 H), 2.43 (s, 3 H), 2.15 (d, *J* = 4.59 Hz, 1 H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 144.6 (C), 139.1 (C), 139.0 (2xC), 134.8 (C), 129.6 (2xCH), 129.5 (2xCH), 128.3 (4xCH), 128.1 (4xCH), 128.0 (4xCH), 126.8 (2xCH), 126.0 (CH), 59.6 (CH), 53.6 ($2xCH_2$), 39.6 (CH), 35.5 ($CH_2$), 33.6 ($CH_2$), 21.5 ($CH_3$); MS (70 eV): *m/z* (%): 497 [$M^+$+1] (100), 300 (14), 121 (24); HRMS calcd for $C_{31}H_{32}N_2O_2S$ 496.2184, found 496.2189; IR (neat): 3028, 1495, 1455, 1325, 1163 cm$^{-1}$; $[\alpha]_{20}$ = +23.6 (c= 0.85, $CHCl_3$), $R_f$ = 0.35 (hexane:ethyl acetate 5:1)

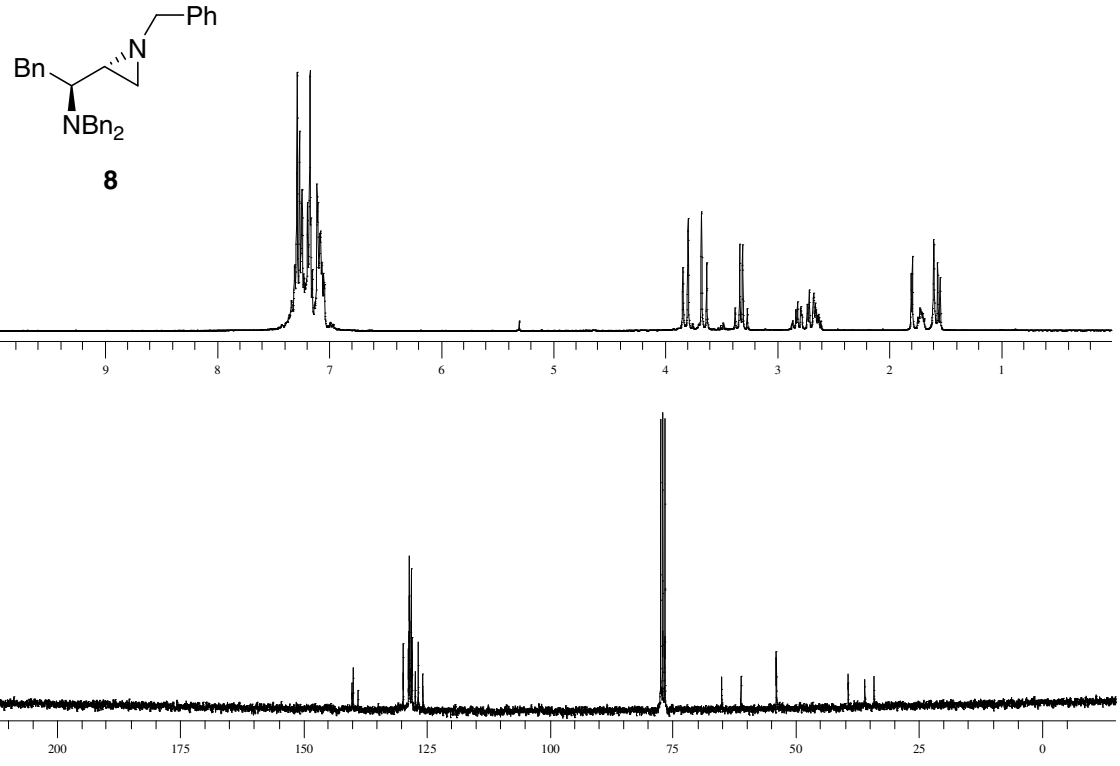


*Deprotection/Benzylation protocol of **7** towards the synthesis of compounds **8** and **9***

To a cooled (-78 ºC) suspension of Li powder (1.44 mmol) and naphthalene (1.62 mmol) in dry THF (4 mL) previously stirred for 1h at r.t., the corresponding *N*-sulfonylaziridine (0.36 mmol) was added under $N_2$ atm. The mixture was stirred, for an additional 1 h, at the same temperature, and then benzyl bromide (1.44 mmol) was added. The reaction was stirred overnight and quenched with $NaHCO_3$ subsequently. The organic layer was extracted with diethyl ether (3 x 10 mL) and the combined extracts were dried over $Na_2SO_4$ and concentrated under vacuum. The *N*-benzylaziridine crude was purified by flash chromatography on silica gel (Hexane/EtOAc 20/1) to afford the pure products **8** and **9**.

**(+)-(2*R*,1´*S*)-1-Benzyl-2-[1´-(dibenzylamino)-2´-phenylethyl]aziridine (8)**

$^1$H NMR (300 MHz, $CDCl_3$): δ = 7.36-7.07 (m, 20 H), 3.84 (d, *J* = 13.89 Hz, 2 H), 3.67 (d, *J* = 13.89 Hz, 2 H), 3.37 (d, *J* = 12.63 Hz, 1 H), 3.30 (d, *J* = 12.63 Hz, 1 H), 2.88-2.80 (m, 1 H), 2.75-2.63 (m, 2 H), 1.81 (d, *J* = 3.48 Hz, 1 H), 1.76-1.62 (m, 1 H), 1.57 (d, *J* = 6.30 Hz, 1 H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ = 140.1 (C), 139.8 (2xC), 138.8 (C), 129.6 (2xCH), 128.6 (2xCH), 128.4 (4xCH), 128.3 (2xCH), 128.0 (4xCH), 127.8 (2xCH), 127.2 (CH), 126.6 (2xCH), 125.7 (CH), 65.0 ($CH_2$), 61.1 (CH), 53.9 (2x$CH_2$), 39.3 (CH), 35.9 ($CH_2$), 34.0 ($CH_2$); MS (70 eV): *m/z* (%): 432 [$M^+$] (<1), 300 (10), 196 (22), 91 (100); HRMS calcd for $C_{31}H_{32}N_2$ 432.2565, found 432.2571; IR (neat): 3028, 1495, 1455, 1325, 1163 $cm^{-1}$; $[\alpha]_{20}$ = +25.0 (c= 0.85, $CHCl_3$), $R_f$ = 0.38 (hexane:ethyl acetate 5:1)




**(-)-(2*S*,1´*S*)-1-Benzyl-2-[1´-(dibenzylamino)-2´-phenylethyl]aziridine (9)**

This compound displayed analytical data in accordance with the published values, see reference 6f.