Pergamon

SCIENCE DIRECT®

Tetrahedron Letters 44 (2003) 2677–2681

TETRAHEDRON LETTERS

On the lithiation of oxazolinylaziridines

Renzo Luisi, Vito Capriati, Saverio Florio* and Rosa Ranaldo

Dipartimento Farmaco-Chimico, Università di Bari, Via E. Orabona 4, I-70126, Bari C.N.R., Istituto di Chimica dei Composti OrganoMetallici 'ICCOM', Sezione di Bari, Italy

Received 29 January 2003; revised 3 February 2003; accepted 6 February 2003

Abstract—Lithiated *N*-sulfonyloxazolinylaziridines **6a** and **7a**, generated by deprotonation of the corresponding aziridines **6** and **7** with *sec*-BuLi/TMEDA at −98°C in THF, were found to be chemically and configurationally stable to be stereospecifically captured by electrophiles, while warming up to rt resulted in the formation of oxazolinylazirine **15**. In contrast, lithiation of *N*-phenyloxazolinylaziridines **8** and **9** led to oxazolinylenamine **18**. Tricyclic aziridines **10** and **11** resulted from an intramolecular addition of the aziridinyllithium **6a** to the phenyl ring of the benzenesulfonyl group.

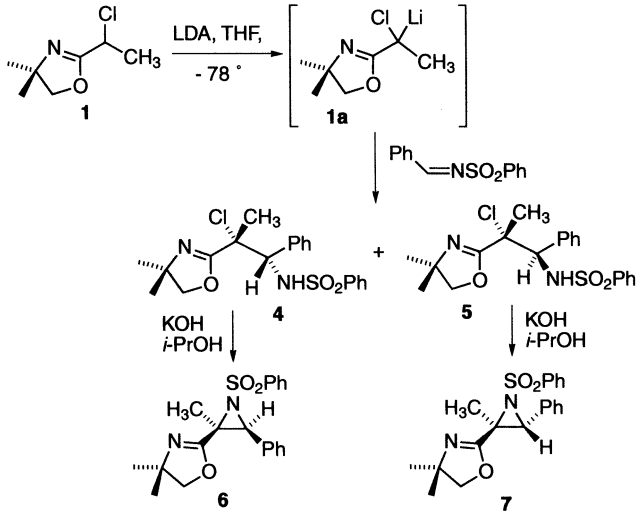
The oxiranyl and aziridinyl anion methodology,[1] conceived as a tool for making functionalized oxiranes and aziridines from simpler and easily available precursors, is undoubtedly a useful and convenient synthetic procedure. The synthesis of a number of target molecules of interest in several fields has been made possible by such a synthetic procedure.[1c]

As part of a research plan directed to the use of the oxiranyl[2] and aziridinyl anion methodology for synthetic purposes we reported some time ago that oxazolinyl aziridines can be easily lithiated and the resulting α-lithiated species proved to be rather stable and could be smoothly trapped with electrophiles.[3] The role of the oxazolinyl moiety was crucial as it provided stabilization to the lithiated species, as amply proved by the α and β lithiation reaction of oxazolinyloxiranes.[4]

Assuming that the oxazolinyl group could stabilize also β-lithiated oxazolinylaziridines, we decided to study the β-metalation reaction of certain trisubstituted oxazolinylaziridines.

The required aziridines were synthesized, as reported, from the 2-(1-chloroethyl)-4,4-dimethyl-2-oxazoline **1** and *N*-sulfonyl and *N*-phenylimines **2** and **3**.[5] The addition of *N*-benzylidenesulfonamide **2** to lithiated 2-(1-chloroethyl)-4,4-dimethyl-2-oxazoline **1a**, generated upon treatment of **1** with LDA (−98°C, THF), gave a mixture of diastereomeric chlorosulfonamides **4** and **5** (Scheme 1), which could be easily separated by column chromatography. Treatment of **4** and **5** with 10% w/w KOH in *i*-PrOH stereospecifically furnished oxazolinylaziridines **6** (64%) and **7** (30%), respectively.[6]

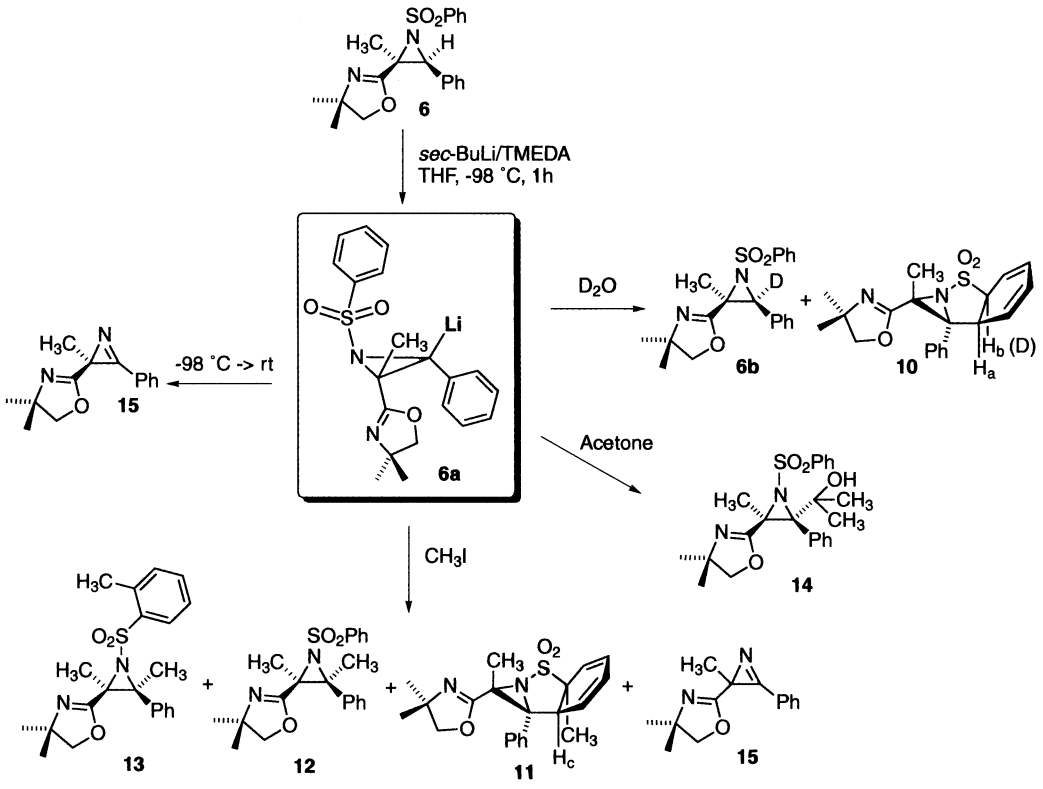
The diastereomeric oxazolinylaziridines were studied separately.[7] Treatment of oxazolinylaziridine **6** with *sec*-BuLi/TMEDA at −98°C in THF followed by quenching with D_2O after 1 h afforded a mixture of deuterated aziridine **6b** (41% yield, 95% D) retaining the configuration of the starting aziridine **6** and the tricyclic aziridine **10** (28% yield, 40% D) as a single stereoisomer.[8] The formation of both the aziridines **6b** and **10** can be accounted for with the intermediacy of the aziridinyllithium **6a** (Scheme 2).



Scheme 1.

* Corresponding author. Tel.: +39-080-5442749; fax: +39-080-5442231; e-mail: florio@farmchim.uniba.it

0040-4039/03/$ - see front matter
doi:10.1016/S0040-4039(03)00368-X



Scheme 2.

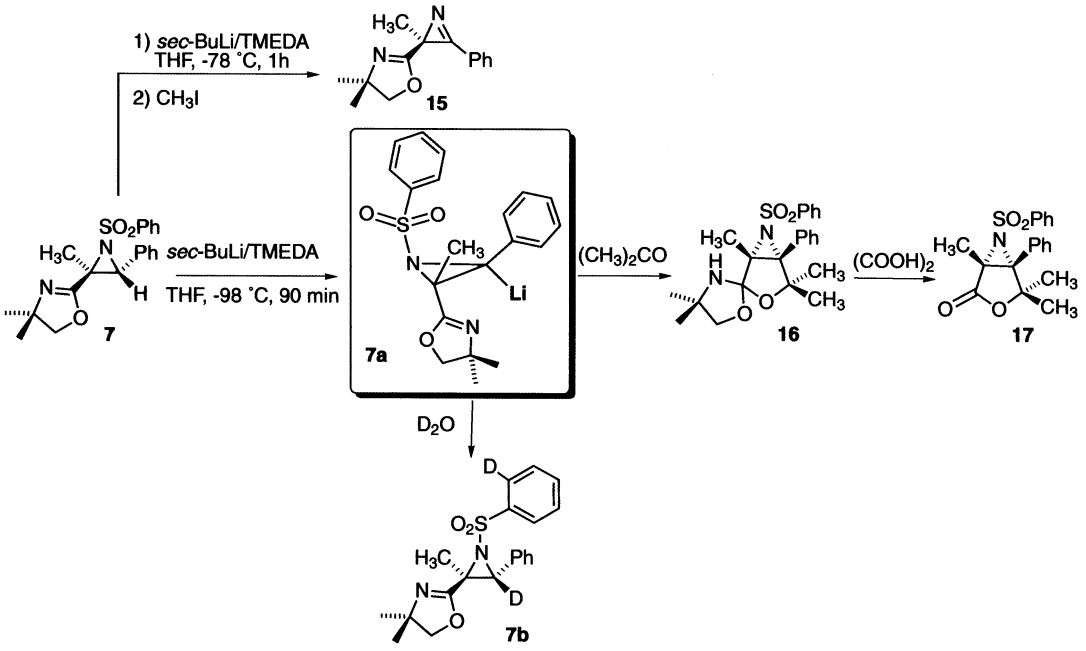
Specifically, aziridine **10** would result from the intramolecular attack of the aziridinyllithium **6a** to the *ortho* position of the benzenesulfonyl group. An analogous reaction was reported by Schaumann some years ago using 1-tosyl-2-phenylaziridine[9] and more recently by Aggarwal in the metalation of *C*-silylaziridines.[10]

Aziridinyllithium **6a**, therefore, turned out to be chemically and configurationally stable under these reaction conditions: so we felt encouraged to evaluate the possibility of using **6a** as an intermediate for synthetic purposes. Lithiation of **6** (*sec*-BuLi/TMEDA, THF, –98°C), followed by the addition of methyl iodide, gave a mixture of the 3-methylated aziridine **12** (21%), 2′,3-dimethylated aziridine **13** (69%), likely derived from a double lithiation (at the aziridine ring and *ortho* to the phenyl ring of the sulfonyl group), tricyclic aziridine **11** (8%)[8] and azirine **15** (<2%). Lithiation of **6** under the same conditions followed by quenching with acetone afforded the hydroxypropyl aziridine **14** (21%).[11]

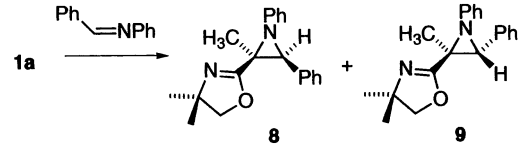
In contrast, treatment of **6** with *sec*-BuLi/TMEDA at –98°C and warm up to room temperature furnished a high yield of the azirine **15** (75% yield), which likely results from the elimination of lithium phenylsulfinate from **6a**.

Next we studied the metalation of aziridine **7** (Scheme 3). Lithiation carried out at –78°C in THF followed by quenching with methyl iodide afforded the azirine **15** almost quantitatively. However, lithiation of **7** followed by quenching with D_2O after 90 min at –98°C provided a high yield of deuterated aziridine **7b** (85% yield, 95% D)[12] together with a small amount (9%) of **15** likely via aziridinyllithium **7a**. It is noteworthy that the intermediate aziridinyllithium **7a** too is configurationally stable (**7b** retains the configuration of starting aziridine **7**) and tricyclic aziridine of the kind of **10**, which was one of the products of the lithiation–deuteration of aziridine **6**, did not form. Also in this case, a slightly longer lithiation time is needed for complete deprotonation to occur. Such a different behavior of **6** towards lithiation in comparison with **7** could tentatively be accounted for by considering the structural features of **6** and **7**. Indeed, assuming that both the aziridines **6** and **7** are configurationally stable at the nitrogen stereocenter,[13] the formation of the tricyclic aziridines **10** and **11** from **6** and not from **7** can be explained with the fact that the benzenesulfonyl group and the aziridine ring hydrogen have a *cis* arrangement in **6** so that the relative aziridinyllithium **6a**, configurationally stable, is close enough to add to the phenyl ring of the sulfonyl group to give, upon quenching, the aziridines **10** and **11**. This is not the case of the aziridinyllithium **7a** were there is a *trans* arrangement between the ring hydrogen and the benzenesulfonyl group. The addition of acetone to **7a** resulted in the formation of the spirocyclic compound **16** that led to the α,β-aziridino-γ-butyrolactone **17** upon treatment with oxalic acid.[14]

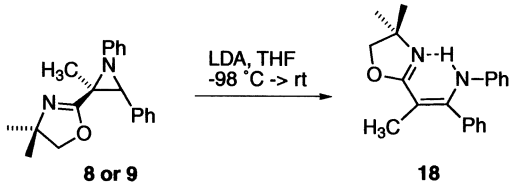
We suspected that the benzenesulfonyl group is also playing an important role in the deprotonation reaction of **6** and **7**. To prove this, we prepared the aziridines **8** and **9** from lithiated 2-(1-chloroethyl)-2-oxazoline **1a** and *N*-benylideneaniline **3** (Scheme 4) so obtaining a mixture of aziridines **8** (53%) and **9** (21%).[15]



Scheme 3.



Scheme 4.



Scheme 5.

With aziridines **8** and **9** in hand we subjected them to deprotonation under various conditions (LDA, *sec*-BuLi with and without TMEDA, THF, –98°C). In no case we observed the expected deuterated species upon quenching with D_2O at low temperature. The starting aziridines were recovered unchanged. The enamine **18** was obtained in high yield when the lithiation mixture was warmed to rt and then quenched with water (Scheme 5). Compound **18** likely stems from an E_2 ring strain promoted β-elimination taking place in the starting aziridine **8** (or **9**).[16] This result supports the hypothesis that the presence of the sulfonyl group on the nitrogen of the aziridine ring is crucial for the lithiation at the aziridine ring to occur.

In conclusion, *N*-sulfonylaziridines **6** and **7** can be lithiated to give products such as azirine **15**, more functionalized aziridines **6b**, **7b**, **12**–**14** and tricyclic aziridines **10** and **11**.[17] Whichever the starting aziridine (**6** or **7**), it is possible to tune the experimental conditions in order to favor the formation of the azirine **15**, which looks like a promising intermediate for the preparation of substituted oxazolinylaziridines. Tricyclic aziridines of the kind **10** and **11** form exclusively from **6**. The trapping of **7a** with acetone to give **16** and then **17** looks like a promising route to α,β-aziridino-γ-butyrolactones. Work is in progress to this end in our laboratory and results will be reported in due course.

Acknowledgements

This work was carried out under the framework of the National Project 'Stereoselezione in Sintesi Organica. Metodologie ed Applicazioni' supported by the Ministero dell'Istruzione, dell'Università e della Ricerca (MIUR, Rome), by the University of Bari and CNR (Rome) and by C.I.N.M.P.I.S. (Consorzio Interuniversitario Nazionale Metodologie e Processi Innovativi di Sintesi).

References

1. For reviews on oxiranyl and aziridinyl anion chemistry, see: (a) Satoh, T. *Chem. Rev.* **1996**, *96*, 3303–3325; (b) Mori, Y. *Reviews on Heteroatom Chemistry*; Oae, S., Ed.; Tokyo, 1997; Vol. 17, pp. 183–221; (c) Mori, Y.; Yaegashy, K.; Furukawa, H. *J. Org. Chem.* **1998**, *63*, 6200–6209; (d) Hodgson, D. M.; Gras, E. *Synthesis* **2002**, 1625–1642; (e) Florio, S. In *Oxiranyl and Aziridinyl Anions: Applications in Synthesis*. Seminars in Organic Synthesis. Società Chimica Italiana: Camerino (MC), 2001; pp. 199–225.
2. (a) Abbotto, A.; Capriati, V.; Degennaro, L.; Florio, S.; Luisi, R.; Pierrot, M.; Salomone, A. *J. Org. Chem.* **2001**, *69*, 3049–3058; (b) Capriati, V.; Florio, S.; Luisi, R.; Russo, V.; Salomone, A. *Tetrahedron Lett.* **2000**, *41*, 8835–8838.

3. Florio, S.; Troisi, L.; Capriati, V.; Ingrosso, G. *Tetrahedron Lett*. **1999**, *40*, 6101–6104.
4. (a) Capriati, V.; Florio, S.; Luisi, R.; Salomone, A. *Org. Lett*. **2002**, *4*, 2445–2448; (b) Capriati, V.; Degennaro, L.; Favia, R.; Florio, S.; Luisi, R. *Org. Lett*. **2002**, *4*, 1551–1554.
5. Capriati, V.; Degennaro, L.; Florio, S.; Luisi, R.; Tralli, C.; Troisi, L. *Synthesis* **2001**, *15*, 2299–2306.
6. General procedure for the preparation of oxazolinylaziridines **6** and **7**. To a precooled (–98°C, with a methanol–liquid nitrogen bath) solution of LDA (1.3 mmol) in dry THF (10 mL) was added dropwise a solution of 2-(1-chloroethyl)-4,4-dimethyl-2-oxazoline (1.0 mmol) in dry THF (5 mL), under nitrogen and magnetic stirring. After 30 min at this temperature, a solution of imine **2** (1.0 mmol) in 5 mL of dry THF was added dropwise and the resulting mixture was slowly allowed to warm to room temperature under magnetic stirring and then quenched with saturated aq. NH_4Cl. The aqueous layer was extracted with AcOEt (3×10 mL) and the combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo. The crude product so obtained was purified by flash chromatography (silica gel, petroleum ether/AcOEt 6/4) affording chlorosulfonamides **4** and **5**. To a solution of **4** or **5** (1.0 mmol) in *i*-PrOH (5 mL) was added dropwise an aqueous solution of KOH (5 mL, 10% w/w) and the resulting mixture was stirred at room temperature for 2 h. After this time, the mixture was poured in water, extracted with AcOEt (3×10 mL) and the combined organic extracts were dried (Na_2SO_4) and evaporated in vacuo to give a slurry which was purified by flash chromatography (silica gel, petroleum ether/AcOEt 6/4) affording oxazolinylaziridines **6** and **7**. **6**: white solid (64%), ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.86 (s, 3H), 1.03 (s, 3H), 2.16 (s, 3H), 3.51–3.67 (2×d, AB system, $J=8.1$ Hz, 2H), 4.17 (s, 1H), 7.08–7.12 (m, 2H), 7.16–7.26 (m, 3H), 7.50–7.55 (m, 2H), 7.58–7.64 (m, 1H), 8.03–8.06 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 17.7 (q, $^1J_{CH}=135.0$ Hz, $^3J_{CH}=3.2$ Hz), 27.9, 51.3, 52.7, 67.5, 79.1, 127.0, 127.5, 127.9, 128.9, 132.7, 134.0, 161.1. FT-IR (film) cm^{-1}: 2972, 1661 (C=N), 1450, 1326, 1163, 1125, 1090, 907, 738, 701, 640, 622, 542. MS (ESI) m/z: 393 (100) $[M+Na]^+$, 229 (18). **7**: see Ref. 5.
7. Diastereomeric aziridines **6** and **7** were assigned the relative configuration on the basis of the long-range $^3J_{CH}$ coupling constant between the aziridine β-hydrogen (with respect to the oxazolinyl ring) and the methyl group on the α-carbon, as reported in Ref. 5.
8. Structure and configuration of tricyclic aziridines **10** and **11** were unambiguously established using extensive ^{1}H and ^{13}C NMR studies involving selective homonuclear decoupling experiments and 2D-NOESY Phase-sensitive experiments. Strong NOE interactions between the two bridge-head protons H_a and H_b in the case of **10** and between H_c and the bridge-head methyl in the case of **11** (see Scheme 2) suggest a *cis* configuration between the central five-membered ring and the cyclohexadienic ring. Moreover, weak NOE interactions between both H_a and H_c and the phenyl ring (obviously due to the *ortho* hydrogens) and between the α-methyl groups (with respect to the oxazolinyl moiety) and the olefinic protons are also diagnostic of a close proximity relationship between the aziridine and the cyclohexadienic rings as depicted in Scheme 2. **10**: colorless oil (28%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.81 (s, 3H), 0.98 (s, 3H), 1.79 (s, 3H), 3.40 (d, $J=7.9$ Hz, 1H), 3.60 (d, $J=7.9$ Hz, 1H), 3.87 (dd, $J=17.5$ and 2.4 Hz, 1H), 4.72 (ddd, $J=17.5$, 3.6 and 2.7 Hz, 1H), 5.89 (ddq, $J=9.7$, 3.6 and 0.91 Hz, 1H), 6.07–6.12 (m, 2H), 6.17–6.23 (m, 1H), 7.30–7.36 (m, 3H), 7.40–7.50 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.9, 27.8, 27.9, 41.8, 61.5, 67.2, 79.5, 116.4, 121.7, 122.7, 125.3, 127.5, 128.0, 128.5, 137.4, 162.0. FT-IR (film) cm^{-1}: 2963, 1652, 1343, 1261, 1090, 800. MS (ESI) m/z: 371 (21) $[M+H]^+$, 229 $[M^+-PhSO_2$, 100].
9. Breternitz, H. J.; Schaumann, E.; Adiwidjaja, G. *Tetrahedron Lett*. **1991**, *32*, 1299–1302.
10. Aggarwal, V. K.; Alonso, M.; Ferrara, M.; Spey, S. E. *J. Org. Chem*. **2002**, *67*, 2335–2344.
11. Starting material was also recovered in this reaction. Compound **14** could be isolated following the general procedure reported in Ref. 17 by quenching the reaction mixture with acetone. **14**: colorless oil (21%), ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.82 (s, 3H), 0.95 (s, 3H), 1.76 (s, 3H), 1.99 (s, 3H), 2.32 (s, 3H), 4.05 (s, 1H, exchanges with D_2O), 3.1–3.5 (2×d, AB system, $J=8.1$ Hz, 2H), 7.02–7.22 (m, 5H), 7.45–7.56 (m, 3H), 8.15–8.17 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 26.6, 27.7, 28.0, 28.6, 30.8, 53.2, 67.4, 69.5, 72.3, 77.2, 126.5, 127.3$_6$, 127.3$_8$, 127.4, 127.6, 128.7, 130.4, 132.7, 137.9, 163.6. FT-IR (film) cm^{-1}: 3283, 2972, 1737, 1662 (C=N), 1448, 1197, 1164, 974, 847, 758, 621, 554. MS (ESI) m/z: 451 (100) $[M+Na]^+$, 429 (5) $[M+H]^+$, 393 (17), 229 (15).
12. Compound **7b** showed a 30% of deuteration *ortho* to the phenyl ring of benzenesulfonyl group.
13. *N*-Benzenesulfonylaziridines **6** and **7** were also proved to be configurationally stable at the nitrogen atom. An attempt to provoke inversion at the nitrogen center failed. Warming in an NMR tube up to 160°C gave only decomposition. For hindered inversion of the nitrogen stereogenic center depending on the nature of the substituents and its detection, see: Gunther, H. *NMR Spectroscopy: Basic Principles Concepts and Application in Chemistry*, 2nd ed.; John Wiley: UK, 1995; Chapter 9, pp. 358–359.
14. Compound **16** could be isolated following the general procedure reported in Ref. 17 by quenching the reaction mixture with acetone. **16**: colorless oil (31%), ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.97 (s, 3H), 1.03 (s, 3H), 1.25 (s, 3H), 1.33 (s, 3H), 1.75 (s, 3H), 3.60–3.73 (2×d, AB system $J=7.7$ Hz, 2H), 7.29–7.69 (m, 8H), 7.98–8.14 (m, 2H). ^{13}C NMR (300 MHz, $CDCl_3$) δ: 8.7, 23.2, 25.3, 27.2, 28.6, 56.4, 59.7, 66.9, 78.2, 81.8, 119.6, 128.2, 128.4, 128.8, 129.1, 129.9, 130.4, 133.2, 141.4. FT-IR (film) cm^{-1}: 3376, 2975, 1738, 1448, 1380, 1323, 1160, 757, 599, 540. Hydrolysis of **16** with oxalic acid (Ref. 4b) gave **17** as a white solid: mp 197°C (hexane), ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.12 (s, 3H), 1.68 (s, 3H), 1.72 (s, 3H), 7.40–7.57 (m, 6H), 7.60–7.65 (m, 2H), 7.90–7.96 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 8.9, 21.9, 26.4, 52.6, 65.7, 85.9, 127.6, 128.1, 128.8, 129.2, 129.7, 129.8, 133.8, 140.1, 170.5. GC–MS m/z (rel. int.): 216 $[M^+-SO_2Ph$, 7], 147 (14), 119 (100), 91 (14), 77 (19). FT-IR (film) cm^{-1}: 2925, 1766 (C=O), 1449, 1319, 1166, 1089, 935, 752, 621, 597.
15. Compounds **8** and **9** were prepared as reported in Ref. 5. **8**: colorless oil (53%), ^{1}H NMR (300 MHz, $CDCl_3$) δ:

1.23 (s, 3H), 1.36 (s, 3H), 1.44 (s, 3H), 3.60 (s, 1H), 3.84–3.90 (2×d, AB system, $J=8.2$ Hz, 2H), 7.21–7.27 (m, 3H), 7.46–7.56 (m, 5H), 7.69–7.71 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 17 (q, $^1J_{CH}=129.5$ Hz, $^3J_{CH}=3.7$ Hz), 28.0, 45.7, 51.9, 67.1, 79.0, 120.3, 122.5, 127.4, 127.7, 128.7, 135.7, 148.3, 163.0. FT-IR (film) cm^{-1}: 2968, 1669 (C=N), 1489, 1116, 697, 618, 519. GC–MS m/z (rel. int.): 306 (M^+, 7), 174 (18), 118 (100), 77 (21). **9**: colorless oil (21%), ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.29 (s, 3H), 1.50 (s, 3H), 1.54 (s, 3H), 3.66–3.74 (2×d, AB system, $J=8.0$ Hz, 2H), 4.50 (s, 1H), 7.23–7.28 (m, 3H), 7.48–7.51 (m, 2H), 7.59–7.68 (m, 4H), 7.75–7.77 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 16.3 (q, $^1J_{CH}=129.0$ Hz), 27.9, 28.2, 45.2, 49.1, 67.1, 78.6, 119.5, 122.3, 127.4, 127.7, 128.1, 128.4, 135.8, 149.8, 162.3. FT-IR (film) cm^{-1}: 2970, 1793, 1651 (C=N), 1490, 1123, 757, 696, 633, 502. GC–MS m/z (rel. int.): 306 (M^+, 9), 174 (20), 118 (100), 77 (21).

16. Lithiation of aziridines **8** or **9** with LDA at −98°C in THF followed by warming up to rt gave quantitatively compound **18** as a colorless oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.39 (s, 6H), 1.77 (s, 3H), 3.94 (s, 2H), 6.37–6.63 (m, 2H), 6.66–6.87 (m, 1H), 6.89 (m, 2H), 7.17–7.59 (m, 5H), 11.56 (br. s, 1H, exchanges with D_2O). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 28.9, 67.0, 77.2, 120.6, 120.9, 128.1, 128.2, 128.3, 129.7, 135.8, 142.1, 149.8, 165.6. FT-IR (film) cm^{-1}: 3057, 3027, 2965, 1626, 1599, 1574, 1490, 1296, 1108, 1018, 786, 749, 705, 609, 501. GC–MS m/z (rel. int.): 306 (M^+, 64), 305 (100), 291 (25), 234 (9), 180 (61), 77 (30).
17. **General procedure for the lithiation of aziridines 6 (or 7); preparation of compounds 11, 12, 13 and 15**. To a pre-cooled solution (−98°C) of aziridine **6** (or **7**) (1 mmol) and TMEDA (1.5 mmol) in dry THF (5 mL), *sec*-BuLi (1.2 mmol) was added dropwise under nitrogen and magnetic stirring and the resulting mixture stirred at this temperature for 1 h (1.5 h in the case of **7**). After this time, MeI (1.5 mmol) was added and the mixture warmed up to rt and quenched with saturated aq. NH_4Cl. The aqueous layer was extracted with AcOEt (3×10 mL) and the combined organic extracts dried (Na_2SO_4). Volatiles were removed under reduced pressure and the crude mixture of products was subjected to flash chromatography (silica gel, petroleum ether/AcOEt 6/4) affording the above-named compounds. **11**: colorless oil (8%), ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.82 (s, 3H), 0.95 (s, 3H), 1.76 (s, 3H), 1.99 (s, 3H), 2.32 (s, 3H), 3.1–3.5 (2×d, AB system, $J=8.1$ Hz, 2H), 3.45 (dd, $J=4.8$ and 1.8 Hz, 1H), 5.86–5.89 (m, 1H), 6.07–6.18 (m, 1H), 6.21–6.28 (m, 2H), 7.3–7.53 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.5, 27.6, 29.6, 51.5, 63.8, 65.0, 67.2, 79.2, 120.9, 122.3, 122.9, 123.8, 128.4, 128.5, 137.9, 162.1. MS (ESI) m/z: 407 (83) [M+Na]$^+$, 385 (100) [M+H]$^+$, 343 (11), 251 (74), 229 (54). **12**: colorless oil (21%), ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.78 (s, 3H), 0.92 (s, 3H), 2.06 (s, 3H), 2.07 (s, 3H), 3.2–3.5 (2×d, AB system, $J=8.2$ Hz, 2H), 7.15–7.19 (m, 5H), 7.49–7.64 (m, 3H), 8.11–8.13 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.3, 17.6, 27.7, 57.6, 60.3, 67.3, 78.8, 126.6, 127.3, 127.4, 127.7, 128.9, 133.0, 139.8, 141.2, 162.7. MS (ESI) m/z: 407 (100) [M+Na]$^+$, 243 (27), 145 (22). FT-IR (film) cm^{-1}: 2971, 1653 (C=N), 1447, 1324, 1161, 994, 723, 616, 542. **13**: colorless oil (69%), ^{1}H NMR (500 MHz, $CDCl_3$) δ: 0.77 (s, 3H), 0.94 (s, 3H), 2.00 (s, 3H), 2.06 (s, 3H), 2.88 (s, 3H), 3.15–3.54 (2×d, AB system, $J=7.9$ Hz, 2H), 7.04–7.15 (m, 5H), 7.29–7.51 (m, 3H), 8.01–8.10 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 14.5, 17.8, 20.4, 27.8, 27.9, 51.6, 57.9, 67.4, 76.7, 126.0, 126.6, 127.2, 127.7, 129.0, 132.4, 133.2, 139.1, 139.4, 140.2, 163.0. MS (ESI) m/z: 421 (100) [M+Na]$^+$, 243 (21). **15**: white solid, (2%). Compound **15** could be obtained in higher yield performing the lithiation reaction at −78°C in the case of **7** (95%) or warming up to rt the reaction mixture in the case of **6** (75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.25 (s, 3H), 1.27 (s, 3H), 1.64 (s, 3H), 3.78–3.85 (2×d, AB system $J=7.9$ Hz, 2H), 7.5–7.6 (m, 3H), 7.78–7.83 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 19.0, 28.2, 28.3, 67.9, 79.3, 123.3, 129.2, 129.7, 133.4, 166.2, 167.2. FT-IR (film) cm^{-1}: 2968, 1751, 1652 (C=N), 1450, 1329, 1164, 906, 738, 621, 552. GC–MS m/z (rel. int.): 228 (M^+, 60), 213 (33), 173 (33), 104 (100), 77 (17).