Reductive Deprotection of *N*-Tritylaziridines

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Synthetic projects in our laboratory have encountered the need to deprotect *N*-tritylaziridines related to **1**, **3**, and **5** (Chart 1). There are several literature reports describing conventional acid-catalyzed detritylation of aziridinecarboxylates such as **1b.**[1,2] However, we could not deprotect the more sensitive aziridines **3** and **5** without extensive aziridine ring cleavage using formic acid/methanol[1a] or trifluoroacetic acid (TFA).[1b] After considerable experimentation, good results were obtained for a number of *N*-tritylaziridines using TFA together with a reducing agent capable of trapping trityl cation at 0 °C in dichloromethane or chloroform (Table 1). In most of the substrates tested, the combination of TFA and triethylsilane works well (method A).[3,4] However, an alternative procedure using methanesulfonic acid (MsOH) in place of TFA is best for the sensitive aziridine **3a** (method B). A third procedure (method C; TFA/Me_3N-BH_3)[5] is generally faster than method A, is also broadly applicable, and gives cleaner products in some cases. Thus, cleavage of **5**[5] using method A afforded the product **6**[5] contaminated with Et_3Si signals, apparently resulting from silyl ether exchange (entry 13). This complication is not a factor using method C (entry 14), and **6** was obtained in good yield and purity. In other examples, method C gave somewhat lower yields under the standard conditions, probably because TFA reacts rapidly with Me_3N-BH_3 to release hydrogen. This competing pathway deactivates the reagent and results in incomplete detritylation in some cases.

Chart 1

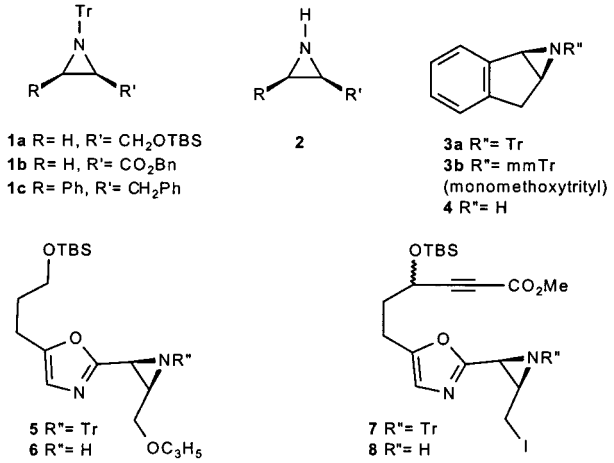

Table 1. Deprotection of *N*-Tritylaziridines[a]

entry	substrate	method	time	product (yield, %)
1	**1a**	A	1 h	**2a** (85)
2	**1a**	B	30 min	**2a** (<5)[b]
3	**1b**	A	30 min	**2b** (56)[c]
4	**1b**	B	30 min	**2b** (43)
5	**1c**	A	30 min	**2c** (82)
6	**1c**	B	25 min	**2c** (85)
7	**1c**	C	40 min	**2c** (61)
8	**3a**	A	30 min	**13** (37)
9	**3a**	B	30 min	**4** (63)[d]
10	**3a**	C	30 min	**4** (<5)[e]
11	**3b**	A	30 min	**4** (19)
12	**3b**	B	30 min	**4** (40)
13	**5**	A	1 h	**6** (86)[f]
14	**5**	C	5 min	**6** (85)
15	**7**	A	30 min	**8** (84)
16	**19**	A	30 min	**20** (72)
17	**21**	C	5 min	**22** (88)

[a] All experiments in dichloromethane at 0 °C, 4 equiv each of the acid and the reducing agent. Method A: TFA/Et_3SiH. Method B: methanesulfonic acid/Et_3SiH. Method C: TFA/trimethylamine−borane. Workup with diisopropylethylamine in all cases. [b] The alcohol from TBS cleavage was isolated (66%) with the trityl group intact, along with recovered **1a** (27%). [c] The crude product prior to workup contains NMR signals of protonated **2b** and triphenylmethane as the sole products. Material loss occurs due to partial decomposition under the conditions of the standard workup procedure. [d] TsOH in place of MsOH gave a 73% yield of **4**. [e] Ring opening to **13** was the major pathway. [f] Product contaminated with the Et_3SiO analogue, ≤3% on mg scale, but as much as 20% on 5 g scale.

To obtain good yields of aziridines, it is important to quench the crude products from methods A−C with a tertiary amine base. Diisopropylethylamine was used for this purpose as part of the standard procedure. The reasons why quenching with base is necessary were found to be substrate dependent, and were related to the details of the workup and to the relative ease of aziridine ring opening as discussed below.

The reasonably stable **1a** was deprotected smoothly using method A followed by workup with diisopropylethylamine or triethylamine (entry 1, 85% **2a** isolated). However, if the reaction was repeated without the tertiary amine workup, and was quenched with ice−water followed by rapid extraction with hexane, then **2a** was isolated in only 13% yield, together with detritylated

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(4) Prior work on *N*-trityl cleavage using TFA/silane reagents: Dinsmore, C. J.; MacTough, S. C.; Stokker, G. E.; Williams, T. M. *Chem. Abstr.* **1998**, *128*, 140700. Yang, L.; Morriello, G. *Tetrahedron Lett.* **1999**, *40*, 8197. Cleavage of the *N*-diphenylmethyl group with hot TFA/EtSiH: Neumann, W. L.; Rogic, M. M.; Dunn, T. J. *Tetrahedron Lett.* **1991**, *32*, 5865. Portner, J. R.; Wirschun, W. G.; Kuntz, K. W.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 2657.

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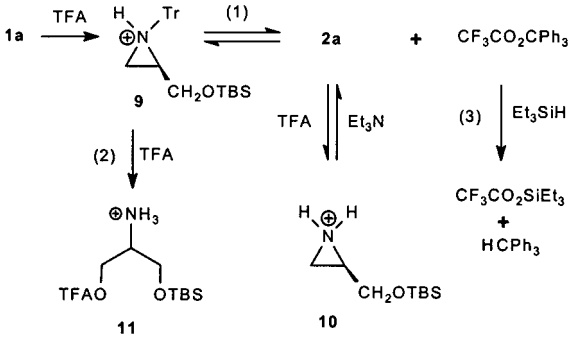
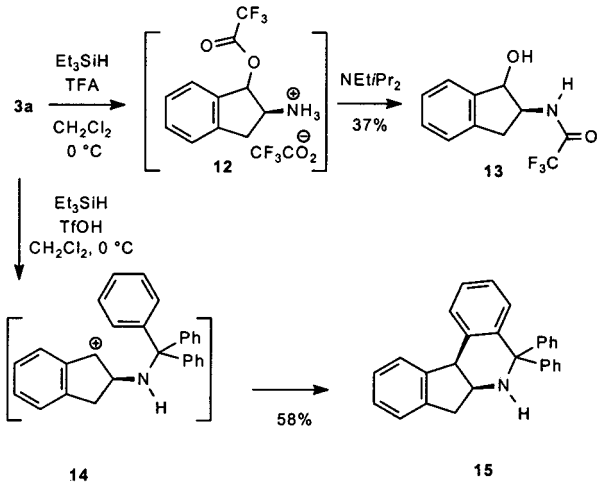
products of aziridine ring cleavage according to NMR assay. A similar experiment was then conducted in $CDCl_3$ solution in an NMR tube according to method A, but with no quench. Complete conversion was observed within 20 min at room temperature to the aziridinium salt **10** via an intermediate presumed to be **9**. Characteristic aziridinium C−H protons were observed at 2.85, 2.93, and 3.47 ppm, together with ^{13}C signals at 36.4 and 24.8 ppm that are consistent with the structure **10**. Furthermore, an identical NMR spectrum was obtained by mixing deprotected **2a** with 3 equiv of TFA in $CDCl_3$. The NMR signals of **10** did not change over 6 h at room temperature, indicating that ring opening of the deprotected aziridine to **11** or isomeric products does not take place on this time scale. Furthermore, addition of triethylamine to the solution of **10** obtained from **1a** in the NMR experiment resulted in conversion to **2a** in 77% isolated yield. Since the corresponding experiment quenched with ice−water and no base gave only 13% **2a**, the evidence indicates that ring opening of **10** is facile in the presence of water and TFA, but does not occur during the method A procedure in dichloromethane or chloroform. Thus, addition of the tertiary amine prevents aziridine ring cleavage by neutralizing residual TFA, as well as TFA released by hydrolysis of $Et_3SiOTFA$. The latter byproduct is derived from reaction of triethylsilane with the trityl trifluoroacetate that results from acid-induced *N*-trityl cleavage.

One additional experiment was performed starting with **1a** and TFA in $CDCl_3$, but without triethylsilane. Within 45 min at room temperature, the aziridine NMR signals attributed to **9** had disappeared and were replaced by complex downfield signals consistent with nucleophilic cleavage of the aziridine ring. Since the analogous cleavage is not a major pathway with triethylsilane present, the evidence is consistent with a scenario where the protonated *N*-tritylaziridine **9** is in equilibrium with **2a**, **10**, and trityl trifluoroacetate (eq 1). If a reducing agent such as Et_3SiH is present, the equilibrium is forced toward **2a** and **10** as the trityl trifluoroacetate is converted to triphenylmethane (eq 3). In the absence of a hydride donor, nucleophilic cleavage pathways such as eq 2 become competitive and products of aziridine cleavage are formed prior to aqueous workup.



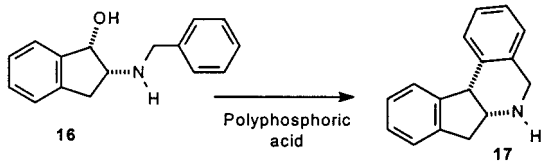
The implications of aziridine cleavage became more clear when the deprotection of **3a**[6] was investigated. In contrast to the reactions of **1a** or **1b**, **3a** gave no deprotected aziridine product **4** using method A. Instead, a ring-opened product, **13**, was obtained in 37% yield (one diastereomer isolated, stereochemistry not assigned)

Scheme 1



(Scheme 1). Structure **13** is the expected product from initial aziridine ring opening and *N*-detritylation to **12**, followed by neutralization and trifluoroacetyl migration from O to N.

In an attempt to prevent ring opening of **3a**, the experiment was repeated with the nonnucleophilic triflic acid in place of TFA. The reaction did produce some of the deprotected aziridine **4** (19%), but the tetracyclic amine **15** was formed as the major product (58%). Evidently, the *N*-tritylaziridinium triflate salt ring opens faster than the trityl group is cleaved in this sensitive system. The resulting benzylic carbocation **14** then undergoes intramolecular Friedel−Crafts cyclization, as in the closely analogous precedent from **16** to **17**.[7] The structure of **15** was deduced by NMR comparisons with **17**, and by the presence of 20 signals corresponding to aromatic carbons in the ^{13}C NMR spectrum.

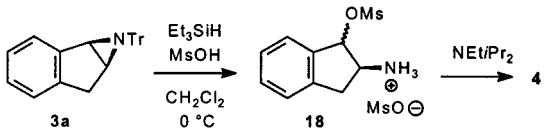


The Friedel−Crafts cyclization could be minimized by deprotecting **3a** using method B (methanesulfonic acid/triethylsilane). This procedure gave aziridine **4** in 63% yield after the usual quenching with diisopropylethylamine. Although this finding implies a simple acid-induced detritylation, NMR monitoring of the reaction revealed a more complicated sequence of events. Addition of MsOH to a solution of **3a** in $CDCl_3$ containing Et_3SiH gave a bright yellow solution, suggesting the release of trityl cation. The color faded within 5 min at room temperature, and the NMR signals of triphenylmethane appeared. The aziridine C−H signals at 2.81 and 2.5 ppm disappeared, and new signals were observed at 6.42 and 6.13 ppm (0.5H each), consistent with the formation of a diastereomer mixture of the ring-opened mesylate **18** as the ammonium salt. When diisopropylethylamine was added to this solution, the signals of **18** were replaced by signals of the aziridine **4**. In contrast to the analogous intermediate **12** in the TFA experiment, the ring-opened

(6) Chiu, I.-C.; Kohn, H. *J. Org. Chem.* **1983**, *48*, 2857.

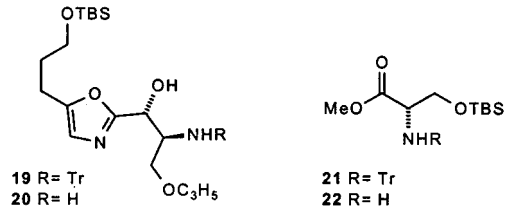
(7) Hagishita, S.; Shiro, M.; Kuriyama, K. *J. Chem. Soc., Perkin Trans. 1* **1984**, 1655.

18 undergoes reclosure to **4** upon neutralization with the tertiary amine, probably because the methanesulfonyl group is slow to undergo the internal O to N migration compared to trifluoroacetate.



The more labile *N*-monomethoxytrityl (*N*-mmt) substrate **3b** could be deprotected in low yield using method A (entry 11). Method B gave a small improvement in this case (entry 12, 40%). A detailed optimization was not carried out because we found it more difficult to prepare and purify **3b** due to its tendency to undergo deprotection and decomposition on silica gel. A prior report has described similar difficulties with an *N*-mmt-aziridine, although the protecting group survived an impressive range of experimental procedures.[8]

Since detritylation of **3a** using method B appears to involve a ring-cleaved intermediate rather than the starting aziridine, we briefly examined the deprotection of two simple *N*-tritylamines **19** and **21** (entries 17 and 18) under the reductive detritylation conditions to demonstrate generality. As expected, both **19**[5] and **21**[9] were converted easily into the parent amines **20** and **22**, respectively. In the absence of potential complications due to aziridine ring opening, the faster procedure using method C (entry 17) is probably best since the short reaction time minimizes potential problems with cleavage of other protecting groups for these amines.[10]



Summary

The acid-induced reductive aziridine detritylation procedures can take place by two distinct pathways. Relatively stable *N*-tritylaziridines such as **1a** are deprotected directly to the protonated aziridine, and quenching with a tertiary amine neutralizes the salts to give the free aziridine **2a**. Solvolytically sensitive aziridines such as **3** are deprotected under similar conditions, but the choice of acid is critical because the key intermediate is a ring-opened ammonium salt. If deprotection of the sensitive substrate is attempted with TFA as the acid source followed by the tertiary amine, then the ring-opened intermediate **12** rearranges to the *N*-trifluoroacetyl derivative **13**. With methanesulfonic acid as the proton source (method B), the corresponding intermediate **18** recloses to the aziridine.

Under the conditions of method B, it is not necessary to anticipate whether the ring-fused aziridines undergo ring opening since the final product after tertiary amine quenching is still the same deprotected aziridine. This is because workup with a tertiary amine induces reclosure of the aminomesylate intermediates in the event that the ring is cleaved. Indeed, we did not test all of the substrates in Table 1 to prove whether the deprotection occurs with aziridine ring cleavage. However, the efficient detritylations using method A in entries 13 and 15 indicate that aziridine ring opening is not the dominant reaction pathway. Otherwise, these experiments should have resulted in the rearranged *N*-trifluoroacetyl alcohols as major products, as in the reactions of **3a** in the presence of TFA. By this criterion, the detritylation of **1c** using method A (entry 5) must also occur without aziridine ring opening even though structure **1c** resembles **3** in substitution. Of course, the geometric constraints that enforce orbital overlap between the benzylic C−N bond and the aromatic π-system in **3** are not present in **1c**, so the direct detritylation competes effectively with ring cleavage. The absence of cis/trans isomerization during deprotection of **1c**, **5**, and **7** (NMR assay) also argues against ring opening.

The reducing agent (triethylsilane or triethylamine−borane) does not appear to be involved in the process that breaks the *N*-trityl bond, but it plays an important role by trapping the trityl cation. This prevents reversal of the trityl cleavage step, and drives the equilibrium to completion. The method has been applied to other sensitive substrates in our laboratory, including examples in the aziridinomitosene series.[5] These results will be reported later in the context of total synthesis.

Experimental Section

N-Tritylaziridines **1b**[1d], **5**,[5] and **7**[5] and *N*-tritylamines **19**[5] and **21**[9] were prepared according to procedures described in the literature. The deprotected aziridines **2b**,[1d] **2c**,[11] and **4**[6] and the amines **20**[5] and **22**[9a] were identified by comparisons of spectroscopic data.

Preparation of Aziridine 1a. A solution of *N*-trityl-*O*-(*tert*-butyldimethylsilyl)-L-serinol[9,12] (1.04 g, 2.32 mmol) and PPh_3 (1.22 g, 4.65 mmol) in 14 mL of THF was cooled to 0 °C, and diethyl azodicarboxylate (Aldrich; 0.73 mL, 4.65 mmol) was added. The cooling bath was removed, and the reaction mixture was allowed to warm to rt. After being stirred at rt for 18 h, the yellow solution was poured into 50 mL of brine and extracted with 3 × 30 mL of ether. The combined organic extract was dried ($MgSO_4$), and after removal of solvent (aspirator), the residue was filtered through a 10 × 2.5 cm plug of silica, washing with 150 mL of 10:1 hexane/ether. After concentration by rotary evaporation, the residue was purified by flash chromatography on Whatman silica gel 60A (15 × 6 cm, 40:1 hexane/ether eluent, 20 mL fractions); fractions 15−22 gave 280 mg of the desired aziridine as a white foam. Fractions 12−14 and 23−25 were combined and, after concentration (rotary evaporation), repurified using flash chromatography on Whatman silica gel 60A (15 × 6 cm, 20 mL fractions, 400 mL of 99:1 hexane/ether and then 600 mL of 30:1 hexane/ether). Fractions 36−44 gave 362 mg of

(8) Moran, E. J.; Tellew, J. E.; Zhao, Z.; Armstrong, R. W. *J. Org. Chem.* **1993**, *58*, 7848.

(9) (a) Groneberg, R. D.; Regan, J. R.; Neuenschwander, K. W.; Scotese, A. C. *Chem. Abstr.* **1995**, 758641. (b) Vedejs, E.; Moss, W. O. *J. Am. Chem. Soc.* **1993**, *115*, 7.

(10) Method B was found to cleave the OTBS group in **1a** within 30 min.

(11) Landor, S. R.; Sonola, O. O.; Tatchell, A. R. *J. Chem. Soc., Perkin Trans. 1* **1974**, 1294. Kotera, K.; Okada, T.; Miyazaki, S. *Tetrahedron Lett.* **1968**, *9*, 5677.

(12) Prepared by diisobutylaluminum hydride reduction of **21**. Characterization data: analytical TLC on K6F silica gel 60A, 5:1 hexane/ether, R_f = 0.14; $[\alpha]_D$ = +14.1 (c = 0.34, CH_2Cl_2); HRMS: $C_{28}H_{37}NO_2Si$, M + H 448.2660, error 3 ppm, base peak 243 amu; IR (neat, cm^{-1}) 1596, C=C; 400 MHz NMR ($CDCl_3$, ppm) δ 7.59−7.53 (6 H, m) 7.30−7.24 (6 H, m) 7.22−7.16 (3 H, m) 3.42 (1 H, dd, J = 10.6, 2.9 Hz) 3.33 (1 H, dd, J = 9.9, 4.0 Hz) 3.05 (1 H, dd, J = 9.9, 5.9 Hz) 2.89 (1 H, dd, J = 10.6, 5.9 Hz) 2.78−2.72 (1 H, m) 2.35 (2 H, s) 0.85 (9 H, s) −0.03 (3 H, s) −0.04 (3 H, s); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 146.8, 128.7, 127.9, 126.4, 70.8, 64.9, 63.8, 53.7, 25.8, 18.1, −5.5, −5.5.

the desired aziridine as a white foam (642 mg, 64% combined yield): analytical TLC on K6F silica gel 60A, 20:1 hexane/ether, $R_f = 0.21$; $[\alpha]_D = +24.0$ ($c = 1.22$, CH_2Cl_2); no parent ion for $C_{28}H_{35}NOSi$, M + H^+ 430.2574, error 2 ppm, base peak 234 amu; IR (neat, cm^{-1}) 1596, C═C; 400 MHz NMR ($CDCl_3$, ppm) δ 7.51−7.48 (6 H, m) 7.29−7.17 (9 H, m) 3.97 (1 H, dd, $J = 10.6$, 5.0 Hz) 3.65 (1 H, dd, $J = 10.6$, 5.9 Hz) 1.68 (1 H, d, $J = 2.9$ Hz) 1.44−1.39 (1 H, m) 1.13 (1 H, d, $J = 6.2$ Hz) 0.87 (9 H, s) 0.04 (3 H, s) 0.02 (3 H, s); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 144.6, 129.5, 127.4, 126.5, 73.6, 65.9, 34.4, 25.9, 25.4, 18.3, −5.2.

Preparation of Aziridine 1c. The title compound was prepared according to the procedure for **3a** in 92% yield from **2c**:[11] analytical TLC on K6F silica gel 60A, 1:1 hexane/ether, $R_f = 0.80$; pure material was obtained by crystallization from ether/hexane, mp 149−151 °C, colorless, semitransparent; no parent ion for $C_{34}H_{29}N$, M + Na 474.2216, error 4 ppm, base peak 208 amu; IR (neat, cm^{-1}) 1598, C═C; 300 MHz NMR ($CDCl_3$, ppm) δ 7.60−7.00 (23 H, m) 6.61−6.57 (2 H, m) 3.07 (1 H, dd, $J = 14.3$, 3.8 Hz) 2.76 (1 H, dd, $J = 14.3$, 9.2 Hz) 2.42 (1 H, d, $J = 6.3$ Hz) 1.82−1.72 (1 H, m); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 144.4, 139.2, 137.6, 129.7, 128.7, 128.3, 128.0, 128.0, 127.4, 126.7, 126.7, 125.8, 75.8, 41.0, 39.3, 32.6.

***N*-Tritylindano[1,2-*b*]aziridine (3a).** To a solution of indano[1,2-*b*]aziridine (**4**)[6] (689 mg, 5.25 mmol) and NEt*i*Pr_2 (1.8 mL, 10.3 mmol) in 10 mL of anhydrous CH_2Cl_2 was added a solution of triphenylmethyl chloride (2.22 g, 7.96 mmol) in anhydrous CH_2Cl_2 (10 mL, including the cannula and flask washings) dropwise via cannula. After 30 min at rt, the pale tan solution was poured into ether and washed with water followed by brine. The organic phase was dried (Na_2SO_4) and concentrated by rotary evaporation, and the residue was purified by flash chromatography on silica gel (2.5 × 20 cm, 10:1 hexanes/ether eluent, 20 mL fractions). Fractions 5−10 gave 1.83 g (93%) of the product as white crystals: analytical TLC on silica gel 60 F_{254}, 10:1 hexane/EtOAc, $R_f = 0.44$; pure material was obtained by crystallization from hexanes, fine white crystals, mp 157−158 °C; molecular ion (M + H^+) calcd for $C_{28}H_{24}N$ 374.19088, found (DCI, NH_3) *m/e* 374.1922, error 4 ppm; IR (neat, cm^{-1}) 1594, C═C; 500 MHz NMR ($CDCl_3$, ppm) δ 7.48 (6H, d, $J = 7.3$ Hz) 7.38 (1H, d, $J = 6.6$ Hz) 7.28−7.25 (6H, m) 7.24−7.17 (6H, m) 3.31 (1H, d, $J = 17.1$ Hz) 2.99 (1H, dd, $J = 17.1$, 4.6 Hz) 2.81 (1H, d, $J = 4.6$ Hz) 2.50 (1H, dd, $J = 4.6$, 4.6 Hz); ^{13}C NMR (126 MHz, $CDCl_3$, ppm) δ 145.6, 145.1, 143.6, 129.4, 127.5, 127.0, 126.7, 125.9, 125.6, 124.2, 74.4, 43.1, 38.7, 35.5.

***N*-Methoxytritylindano[1,2-*b*]aziridine (3b).** The title compound was prepared according to the procedure for **3a** in 74% yield from **4**: Analytical TLC on K6F silica gel 60A, 5:1 hexane/ether, $R_f = 0.26$ (plate pretreated with NEt_3); FAB HRMS for $C_{29}H_{25}NO$, M + Na 426.1838, error 1 ppm, base peak 273 amu; IR (neat, cm^{-1}) 1605, C═C; 400 MHz NMR ($CDCl_3$, ppm) δ 7.51−7.46 (4 H, m) 7.40−7.33 (3 H, m) 7.29−7.24 (5 H, m) 7.23−7.16 (4 H, m) 6.81 (2 H, d, $J = 9.2$ Hz) 3.79 (3 H, s) 3.31 (1 H, d, $J = 17.2$ Hz) 3.00 (1 H, dd, $J = 17.2$, 4.6 Hz) 2.80 (1 H, d, $J = 4.6$ Hz) 2.49 (1 H, dd, $J = 4.6$, 4.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$, ppm) δ 158.2, 145.6, 143.6, 130.8, 129.2, 127.5, 127.0, 126.6, 126.6, 125.9, 125.7, 124.2, 112.7, 74.0, 63.5, 55.2, 43.1, 38.7, 35.5.

Representative Procedures. Method A. A solution of the aziridine **1c** (110 mg, 0.243 mmol, 1 equiv) in 5.0 mL of anhydrous CH_2Cl_2 was cooled to 0 °C, and triethylsilane (155 μL, 0.973 mmol, 4 equiv) was added followed by trifluoroacetic acid (74 μL, 0.973 mmol, 4 equiv). The reaction flashed yellow upon addition of the acid, and became colorless within 2 min. Stirring was continued at 0 °C for 30 min, and then NEt*i*Pr_2 (210 μL, 1.21 mmol, 5 equiv) was added via syringe. After 10 min of stirring, the colorless solution was poured into 25 mL of ether and washed with brine. The combined organic extract was dried ($MgSO_4$) and concentrated by rotary evaporation, and the residue was purified by preparative TLC (20 × 10 × 0.2 cm, 1:1 hexanes/ether eluent) to give 41 mg (82%) of aziridine **2c**[11] as a white solid.

Deprotection of the Aziridine 3a with Triethylsilane and Methanesulfonic Acid (Method B). A solution of the aziridine **3a** (682 mg, 1.83 mmol) in 10 mL of CH_2Cl_2 was cooled to 0 °C, and triethylsilane (1.2 mL, 7.51 mmol) was added followed by methanesulfonic acid (0.49 mL, 7.55 mmol). The yellow color of the resulting solution gradually faded over 5 min. After 30 min at 0 °C, NEt*i*Pr_2 (2.0 mL, 11.5 mmol) was added. The colorless solution was stirred at 0 °C for 30 min, poured into 50 mL of ether, and washed with 2 × 20 mL of brine. The combined organic extract was dried (Na_2SO_4) and concentrated by rotary evaporation, and the residue was purified by flash chromatography on silica gel (2 × 15 cm, 1:1 hexanes/acetone eluent, 7 mL fractions). Fractions 11−25 gave 152 mg (63%) of the aziridine **4**.[6]

Method C. A solution of the aziridine **1c** (155 mg, 0.343 mmol, 1 equiv) in 1.0 mL of anhydrous CH_2Cl_2 was cooled to 0 °C, and a solution of trimethylamine−borane (Aldrich; 32.6 mg, 0.446 mmol, 1.3 equiv) in dry CH_2Cl_2 (2 mL, including the cannula and flask washings) was added via cannula. Trifluoroacetic acid (100 μL, 1.37 mmol, 4 equiv) was added dropwise via syringe. The reaction flashed bright yellow and quickly became colorless. Stirring was continued at 0 °C for 40 min, and then methanesulfonic acid (31 μL, 0.48 mmol, 1.4 equiv) was added dropwise to quench excess trimethylamine−borane (gas evolution!). The addition of methanesulfonic acid is not required for substrates that do not coelute with excess trimethylamine−borane. After 5 min, NEt*i*Pr_2 (0.42 mL, 2.40 mmol, 7 equiv) was added via syringe. The colorless solution was poured into 25 mL of ether and washed with 25 mL of water and 25 mL of brine. Purification as for method A gave 46 mg (61%) of aziridine **2c** as a white solid.

(2*S*,3*R*)-2-[5-[(3*R*) and (3*S*)-3-[(*tert*-Butyldimethylsilyl)-oxy]-5-(methoxycarbonyl)-4-pentynyl]oxazol-2-yl]-3-(iodomethyl)aziridine (8). A solution of the aziridine **7** (420 mg, 0.562 mmol; prepared according to the method of ref 5) and triethylsilane (0.36 mL, 2.25 mmol) in 10 mL of anhydrous CH_2Cl_2 was cooled to 0 °C, and trifluoroacetic acid (170 μL, 2.21 mmol) was added dropwise. The yellow color of the resulting solution gradually faded over 5 min. After 30 min at 0 °C, NEt*i*Pr_2 (0.48 mL, 2.75 mmol) was added. The colorless reaction mixture was poured into 50 mL of brine and extracted with 2 × 50 mL ether. The organic extract was dried (Na_2SO_4) and concentrated by rotary evaporation, and the residue was purified by flash chromatography on silica gel (2.5 × 15 cm, 3:1 hexane/acetone eluent, 15 mL fractions). Fractions 8−13 gave 239 mg (84%) of the desired aziridine (ca. 1:1 mixture of diastereomers) as a tan oil: analytical TLC on silica gel 60 F_{254}, EtOAc, $R_f = 0.59$; molecular ion (M + H^+) calcd for $C_{19}H_{30}IN_2O_4Si$ 505.10196, found (FAB) *m/e* 505.1007, error 2 ppm; IR (neat, cm^{-1}) 3234, N−H; 2239, C≡C; 1718, C═O. Preparation of the NMR sample: ca. 2 mg of powdered 4 Å molecular sieves was suspended in a solution of the aziridine **8** in an NMR tube: 500 MHz NMR ($CDCl_3$, ppm) δ 6.73 (1H, s) 4.56−4.50 (1H, m) 3.78 (3H, s) 3.53−3.47 (1H, m) 3.41−3.35 (0.6H, m) 3.29−3.21 (1.4H, m) 2.98−2.91 (0.6H, m) 2.86−2.79 (2H, m) 2.79−2.71 (0.4H, m) 2.10−2.02 (2H, m) 1.77 (0.6H, dd, $J = 8.9$, 8.9 Hz) 1.25−1.18 (0.4H, m) 0.91 (9H, s) 0.16 (3H, s) 0.12 (3H, s); the NMR spectrum displayed four sets of signals due to a 1:1 mixture of diastereomers and slow inversion at the aziridine nitrogen, a 3:2 ratio of invertomers according to integration of the N−H signals at 1.77 and 1.25−1.18 ppm; ^{13}C NMR (126 MHz, $CDCl_3$, ppm) δ 159.13, 153.69, 152.72, 152.63, 152.06, 123.25, 122.84, 122.74, 87.74, 76.27, 61.34, 52.81, 40.87, 40.84, 39.11, 35.38, 35.31, 34.80, 34.78, 25.68, 21.04, 18.10, 4.11, 1.74, −4.54, −5.12.

Reaction between the Aziridine 3a and Methanesulfonic Acid Monitored by NMR. A solution of the aziridine **3a** (48 mg, 0.129 mmol) in 0.6 mL of anhydrous $CDCl_3$ was cooled to 0 °C, and methanesulfonic acid (32 μL, 0.493 mmol) was added. The resulting dark yellow solution was immediately transferred via cannula into a nitrogen-flushed NMR tube capped with a rubber septum. After 5 min at rt, the 300 MHz NMR spectrum displayed a major set of the following selected signals assigned to the intermediate **18**, a ca. 1:1 mixture of diastereomers: δ 6.42 (0.5H, d, $J = 5.2$ Hz) 6.13 (0.5H, d, $J = 5.5$ Hz) 4.28−4.16 (1H, br m), 3.55 (0.5H, dd, $J = 16.5$, 8.2 Hz) 3.44−3.29 (1H, m) 3.28 (1.5H, s) 3.22 (0.5H, dd, $J = 16.5$, 7.2 Hz) 3.14 (1.5H, s) ppm. The solution gradually turned dark green after 5 h at rt although the 300 MHz NMR spectrum changed only a little.

Reaction between the Aziridine 3a, Triethylsilane, and Methanesulfonic Acid Monitored by NMR. A solution of the aziridine **3a** (55 mg, 0.147 mmol) in 0.6 mL of anhydrous $CDCl_3$ was cooled to 0 °C, and triethylsilane (48 μL, 0.300 mmol) was

added followed by methanesulfonic acid (38 μL, 0.586 mmol). The resulting yellow solution was immediately transferred via cannula into a nitrogen-flushed NMR tube capped with a rubber septum. The yellow color faded over 1 min at rt. After 10 min at rt, a 300 MHz NMR spectrum of the colorless solution displayed the same characteristic set of signals as reported for the previous experiment as well as a signal corresponding to triphenylmethane, δ 5.54 (1H, s) ppm.

1-Hydroxy-2-(trifluoroacetamido)indan (13). A solution of the aziridine **3a** (171 mg, 0.458 mmol) in 5 mL of anhydrous CH_2Cl_2 was cooled to 0 °C, and triethylsilane (0.30 mL, 1.88 mmol) was added followed by trifluoroacetic acid (0.14 mL, 1.82 mmol). The yellow color of the resulting solution gradually faded over 5 min. After 30 min at 0 °C, NE*t*iPr_2 (0.40 mL, 2.30 mmol) was added. The colorless reaction mixture was stirred at 0 °C for 1 min, poured into 20 mL of saturated aqueous $NaHCO_3$, and extracted with CH_2Cl_2. The combined organic extract was dried (Na_2SO_4) and concentrated by rotary evaporation, and the residue was purified by flash chromatography on silica gel (1.5 × 15 cm, 3:1 hexanes/acetone eluent, 10 mL fractions). Fractions 7−15 were concentrated, and the residue was purified by preparative TLC on silica gel (20 × 20 × 0.1 cm, 2:1 hexanes/ethyl acetate eluent) to give 42 mg (37%) of the product as white crystals: analytical TLC on silica gel 60 F_{254}, 1:1 hexane/EtOAc, R_f = 0.62; pure material was obtained by crystallization from CH_2Cl_2, fine white crystals, mp 111−112 °C; molecular ion (M + NH_4^+) calcd for $C_{11}H_{14}F_3N_2O_2$ 263.10074, found (CI, NH_3) *m*/*e* 263.1007, error 0.2 ppm; IR (neat, cm^{-1}) 3482, N−H; 3308, O−H; 1698, C=O; 500 MHz NMR ($CDCl_3$, ppm) δ 7.41 (1H, d, J = 7.3 Hz) 7.33 (1H, ddd, J = 7.3, 7.3, 1.2 Hz) 7.29−7.22 (3H, m) 5.07 (1H, dd, J = 4.8, 4.8 Hz) 4.59−4.53 (1H, m) 3.34 (1H, dd, J = 16.0, 7.5 Hz) 2.94 (1H, dd, J = 16.0, 7.5 Hz) 2.46 (1H, d, J = 4.8 Hz); ^{13}C NMR (126 MHz, $CDCl_3$, ppm) δ 157.4 (q, J = 37.1 Hz), 141.2, 140.5, 129.8, 127.6, 125.4, 125.1, 115.8 (q, J = 287.9 Hz), 74.0, 53.2, 36.3; ^{19}F NMR (376 MHz, $CDCl_3$, ppm) δ −76.3.

(6a*S,11b*S**)-5,5-Diphenyl-6,6a,7,11b-tetrahydro-5*H*-indeno[2,1-*c*]isoquinoline (15).** A solution of the aziridine **3a** (107 mg, 0.286 mmol) and triethylsilane (180 μL, 1.13 mmol) in 2 mL of CH_2Cl_2 was cooled to 0 °C, and trifluoromethanesulfonic acid (52 μL, 0.588 mmol) was added dropwise, causing brief flashes (ca. 5 s) of a transient yellow color. After the solution was stirred for 30 min at 0 °C, NE*t*iPr_2 (150 μL, 0.861 mmol) was added. The cooling bath was removed, and the reaction mixture was allowed to warm to rt. After 2 h, the resulting light green solution was poured into brine and extracted with ether. The combined organic extract was dried (Na_2SO_4) and concentrated by rotary evaporation, and the residue was purified by flash chromatography on silica gel (1.5 × 15 cm, 2:1 hexane/acetone eluent, 5 mL fractions). Fractions 11−15 gave 7.0 mg (19%) of the deprotected aziridine **4** as a colorless oil. Fractions 3−7 were concentrated by rotary evaporation, and the residue was purified by another flash chromatography on silica gel (1.5 × 15 cm, 20:1 hexane/ether eluent, 5 mL fractions). Fractions 7−10 gave 62 mg (58%) of **15** as a pale pink oil: analytical TLC on silica gel 60 F_{254}, 10:1 hexane/EtOAc, R_f = 0.38; molecular ion (M + H^+) calcd for $C_{28}H_{24}N$ 374.19088, found (CI, NH_3) *m*/*e* 374.1894, error 4 ppm; IR (neat, cm^{-1}) 3327, N−H; 1598, C=C; 500 MHz NMR ($CDCl_3$, ppm) δ 7.53 (1H, d, J = 7.1 Hz) 7.37−7.26 (6H, m) 7.23−7.17 (4H, m) 7.14−7.09 (4H, m) 7.01−6.97 (2H, m) 6.75 (1H, dd, J = 7.8, 1.1 Hz) 4.07 (1H, d, J = 4.6 Hz) 3.71 (1H, dd, J = 5.6, 4.6 Hz) 3.20 (1H, dd, J = 16.1, 5.6 Hz) 2.73 (1H, d, J = 16.1 Hz) 2.13 (1H, s); ^{13}C NMR (126 MHz, $CDCl_3$, ppm) δ 148.6, 146.1, 144.4, 141.7, 140.4, 135.8, 130.4, 130.3, 129.1, 128.8, 127.9, 127.7, 126.8, 126.7, 126.5, 126.4, 126.2, 125.5, 125.1, 124.5, 67.6, 53.7, 47.9, 40.2.

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Supporting Information Available: NMR spectra of the new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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