Regiospecific Reductive Cleavage of the C(2)−N Bond of Aziridines Substituted with an Electron Acceptor Mediated by Mg/MeOH

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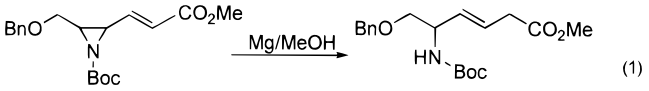
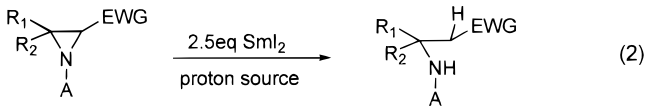
Introduction

In the preparation of α- and *β*-amino acid units, which can be utilized as building blocks for the synthesis of biologically important compounds, considerable efforts have been made to open aziridine rings activated by an adjacent carboxyl group.[1] By comparison to the numerous examples of nucleophilic addition reactions that result in the selective cleavage of the C(3)−N bond leading to an α-amino acid,[2] the methods used for the regiospecific cleavage of the C(2)−N bond that lead to *β*-amino acids are quite limited.[3] For that reason, the nonselective manner has usually been employed.[4] Until now, the only known ways to open the ring of aziridine-2-carboxylate in a regiospecific manner are the reductive cleavage reactions that use catalytic hydrogenation by Pd/EtOH for C(2)−N cleavage[3] or catalytic transfer hydrogenation that uses Pd/HCOOH/EtOH for C(3)−N cleavage.[5] It has been reported[6] that the C(2)−N bond of an aziridine tethered to an α,*β*-unsaturated ester can be opened selectively by using catalytic transfer hydrogenation conditions that afford various regioisomer mixtures of α,*β*- and *β*,*γ*-unsaturated *δ*-amino esters. We have previously demonstrated the regiospecific C(2)−N ring opening of an aziridine tethered to an α,*β*-unsaturated ester by using magnesium in methanol which gives the corresponding *β*,*γ*-unsaturated *δ*-amino ester as a single regioisomer (eq 1).[7] In other work done on the same kind of substrates, regiospecific C(2)−N bond cleavage was realized by adding a carbon nucleophile via the S_N2' reaction.[8]



(1)

Molander et al. have recently reported[9] the regiospecific reductive cleavage of the C(2)−N bond of 2-acyl or -(carboalkoxy) acylaziridines activated by *N*-Ts, Boc, and Tr groups by using SmI_2 in THF in the presence of a proton source such as methanol or *N*,*N*-dimethylaminoethanol. That reaction method affords the corresponding *β*-amino ester and ketone exclusively (eq 2).



(2)

R_1,R_2=alkyl,aryl

EWG=Ac,CO_2Et

A=Ts,Boc,Ac,CO_2Et,Tr

Cleavage of the C_α−heteroatom bond tethered to a ketone or ester group by using SmI_2[10] has been reported, but the same type of reaction is not known for magnesium in methanol since isolated electron acceptors such as ketones, esters, or nitriles are reported to be inert to magnesium in methanol.[11a] Because we have been interested to expand the synthetic utility of magnesium in methanol as a remarkably simple, convenient, and economic electron-transfer reagent[11] compared to SmI_2, it prompted us to study C(2)−N bond cleavage of aziridines substituted with various electron acceptors.

Results and Discussion

Aziridine substrates **1a**−**k**,**n**−**p** were prepared from the corresponding α,*β*-unsaturated ketones, esters, and

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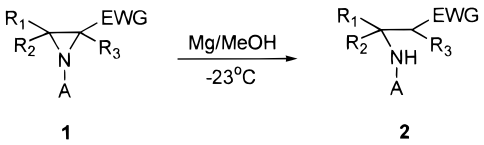
Table 1. Reductive Cleavage of Aziridines Substituted with Electron Acceptors

	aziridines						products							
entry	**1**	R_1	R_2	R_3	EWG	A	**2**	R_1	R_2	R_3	EWG	A	method[a]	yields[b] (%)
1	**1a**	H	H	H	COMe	Ts	**2a**	H	H	H	COMe	Ts	A	97
2	**1b**	Me	Me	H	COMe	Ts	**2b**	Me	Me	H	COMe	Ts	A	97
3	**1c**	Ph	H	Me	COMe	Ts	**2c**	Ph	H	Me	COMe	Ts	A	98[c]
4	**1d**	Ph	H	H	COMe	Ts	**2d**	Ph	H	H	COMe	Ts	B	75[d]
5	**1e**	Ph	H	H	COPh	Ts	**2e**						C	*e*
6	**1f**	Ph	H	Me	COPh	Ts	**2f**						C	*f*
7	**1g**	H	H	H	CO_2Me	Ts	**2g**	H	H	H	CO_2Me	Ts	D	96
8	**1h**	Me	H	H	CO_2Me	Ts	**2h**	Me	H	H	CO_2Me	Ts	D	94
9	**1i**	Et	H	Me	CO_2Me	Ts	**2i**	Et	H	Me	CO_2Me	Ts	D	95[c]
10	**1j**	Ph	H	H	CO_2Me	Ts	**2j**	Ph	H	H	CO_2Me	Ts	D	35[g]
11	**1k**	H	H	H	CO_2t-Bu	Ts	**2k**	H	H	H	CO_2t-Bu	Ts	D	85
12	**1l**	Ph	H	H	CO_2Et	Ph	**2l**						C	*h*
13	**1m**	H	H	H	CO_2Et	HC(Me)Ph	**2m**						C	*h*
14	**1n**	H	H	H	CN	Ts	**2n**	H	H	H	CN	Ts	D	83
15	**1o**	H	H	Me	CN	Ts	**2o**	H	H	Me	CN	Ts	D	85
16	**1p**	Ph	H	H	CN	Ts	**2p**	Ph	H	H	CN	Ts	D	80
17	**1q**	h	h	h	CH_2Br	Bn	**2q**	H	H	H	$=CH_2$	Bn	D	93
18	**1r**	H	H	H	CH_2Br	*p*-ClBn	**2r**	H	H	H	$=CH_2$	*p*-ClBn	D	95
19	**1s**	$BNOCH_2$	H	H	$PhSO_2CH$	Boc	**2s**	$BnOCH_2$	H	H	$=CH_2$	Boc	C	94

[a] See Experimental Section. [b] Isolated yield. [c] A mixture of 1:1 diastereoisomer is obtained. [d] Benzalacetone is obtained as a minor product. [e] α-*N*-Tosylamino chalcone is obtained in 65% yield. [f] Starting material is completely recovered. [g] Rest of the product is desulfonylated aziridine. [h] Only ester exchange occurs.

Scheme 1



1 **2**

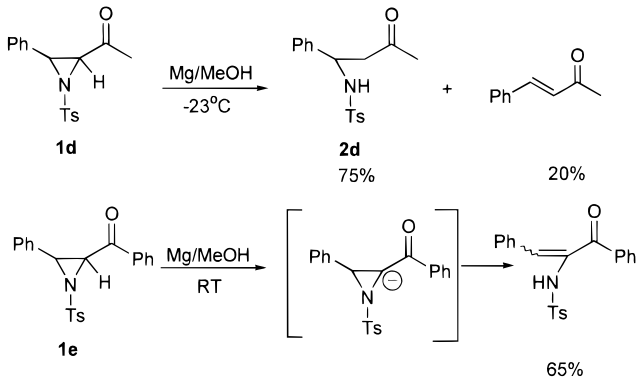
nitriles by employing Evans's aziridination procedure.[12] Other substrates, *N*-phenyl- and *N*-phenethylaziridine (**1l**,**m**),[13,14] bromomethylaziridines (**1q**,**r**),[15] and phenylsulfonylmethylaziridine (**1s**),[7] were obtained by applying published procedures.

Reductive cleavage of C(2)−N bonds of substituted aziridines by using magnesium in methanol is carried out as depicted in Scheme 1.

Various substituted aziridines were subjected to Mg/MeOH to provide the corresponding β-amino products. The results are summarized in Table 1.

Treatment of 2-acylaziridines **1a**−**c** with 3 equiv of magnesium powder (−50 mesh) in methanol at −23 °C provided the corresponding C(2)−N cleavage products, β-*N*-tosylamino ketones **2a**−**c** in excellent yields within 1 h (Table 1). According to ^{1}H and ^{13}CNMR analysis, a 1:1 diastereomeric mixture, which is difficult to separate, was obtained in the case of **1c**. The expected product **2d** was obtained from **1d** in somewhat lower yield (75%) along with benzalacetone as a minor product (20%) which resulted from elimination of tosyl group by $Mg(OMe)_2$ in solution. To minimize elimination reaction acid workup at 0 °C was necessary because cleavage product **2d** was completely changed into benzalacetone within 15 min when the temperature of the reaction mixture was raised at room temperature. Due to a solubility problem the reaction of 3-benzoylaziridine **1e** was run at room temperature. Surprisingly it afforded the unexpected ring opening product as shown in Scheme 2.

Scheme 2



Deprotonation, instead of a cleavage, must have occurred by the use of $Mg(OMe)_2$ in solution. Thus the incipient carbanion undergoes rearrangement to an α-*N*-tosylamino chalcone (**2e**) in 65% yield without any trace of the expected cleavage product. A blank test with commercial $Mg(OMe)_2$ solution in methanol at room temperature afforded the same product. In an attempt to prevent deprotonation, the α-proton was substituted with the methyl group that gave **1f**. In contrast to **1c,** the reaction did not take place for **1f** as shown in Scheme 3.

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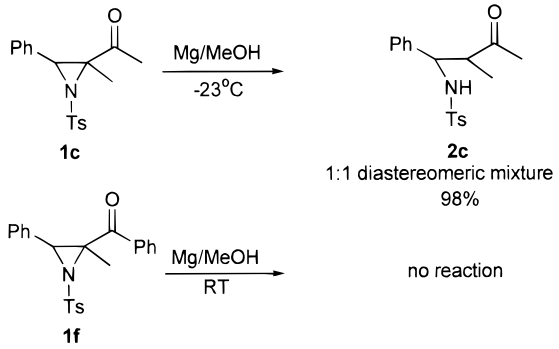
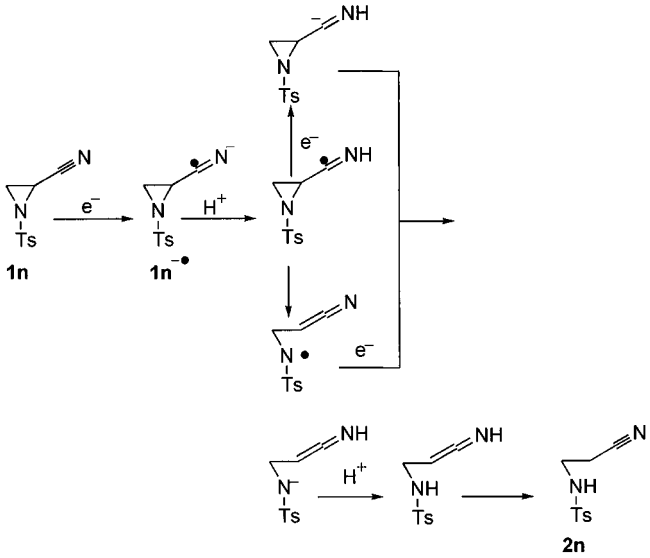
Scheme 3



Since aryl ketones have a higher electron affinity than alkyl ketones,[16] ketyls derived from aryl ketones **1e**,**f** are expected to be more stable than those from alkyl ketones **1c**,**d**. However, ketyl reactions of phenyl ketones using SmI_2 were known to be sluggish and resulted in poor yields compared to those of aliphatic ketones.[17] Probably due to these unfavorable characteristics, reactions of aryl ketones are rare in the literature in contrast to numerous examples of aliphatic ketones.[18] According to the electron-transfer mechanism studied for the enone system using the polarographic method presented by House et al.,[19] a fast equilibrium exists between the starting material and ketyl which has a suffcient half-life (ca. 10 min). Considering these precedents and in the absence of kinetic data, we may speculate that ketyls from **1c**,**f** are so stable that there may only be an equilibrium of fast electron transfer between ketyl and starting material so that no further reaction proceeds while magnesium is being consumed by methanol.

By comparison to the reaction conditions used for 2-acylaziridines, the 2-(carbomethoxy)aziridines, **1g**−**k**, required slightly more magnesium (4 equiv). The added magnesium provided the corresponding *β*-amino-*N*-tosyl esters in excellent yields. This result is in contrast to the use of SmI_2 in THF/EtOH[9] where C(3)−N bond cleavage and C(2)−N bond cleavage gave a mixture of α- and *β*-amino acids. Just as it was for **1c**, **1i** gave a 1:1 mixture of diastereoisomers. Although each diastereoisomer could be separated and identified, the relative stereochemistry of C(2) and C(3) was not determined. Under standard reaction conditions, ester **1j** provided a mixture of desulfonylated aziridine and the expected cleavage product **2j** in 60% and 35% yield, respectively. Attempts to desulfonylate **1j** by $Mg(OMe)_2$ in methanol failed. In this case the starting material was completely recovered. Because desulfonylation of arenesulfonamides by an electron-transfer reagent is known,[16] direct electron transfer may have caused desulfonylation instead of methanolysis catalyzed by $Mg(OMe)_2$. When modified reaction conditions[11c] (10 equiv of Mg, EtOH/THF, catalyst $HgCl_2$, room temperature) were employed, desulfonylation was avoided to provide ethyl ester of **2j** in excellent yield (95%). In the case of *t*-Bu ester **1k** ester exchange did not happen which contrasts with the case of the ethyl ester.[11d] When the nitrogen was substituted with a phenyl or a phenethyl group like **1l**−**m**, the expected reaction did not proceed. Only ester exchange was observed. As previously noted,[2k,5a] activation of a C−N bond by substitution with electron withdrawing group such as *N*-Ts or *N*-Boc seems to be necessary for ring opening reaction. The reductive cleavage of cyanoaziridine **1n**−**p** took place smoothly to afford *β*-amino-*N*-tosyl nitriles **2n**−**p** in excellent yield. Although isolated cyano groups are reported to be inert to magnesium in methanol,[11a] α,*β*-unsaturated nitriles were reduced to the saturated nitriles[21] and underwent intramolecular hydrodimerization via radical anion mechanism.[22] It reveals that the cyano group can play a role as electron acceptor if tethered to a proper functional group which can stabilize the resulting radical anion. By analogy of ketyl reaction mechanism,[9] electron transfer from magnesium metal to substrate will generate C═N radical anion from which subsequent ring cleavage will occur via the ketimine as shown in Scheme 4.

Scheme 4



Reaction of 2-(bromomethyl)aziridines **1q**,**r** was slow at −23 °C so the temperature was elevated to room temperature which produced the corresponding allylamine **2q**,**r** smoothly even though the C−N bond was not activated. The identical cleavage product was obtained in moderate yields (50−53%) by a sonochemical cleavage of the 2-(bromomethyl)aziridines in the presence of a zinc−copper couple.[15] As suggested by Kimpe et al.,[15] a radical anion generated by single electron transfer from magnesium to (bromomethyl)aziridines **1q**,**r** will lose bromide ion to give methyl radical which might undergo either radical cleavage or anionic cleavage by accepting another electron. We have previously reported the desulfonylation of alkyl sulfones[11h] and the reductive elimination of *β*-acetates or benzoate-substituted alkylsulfones[11c] which afford the corresponding olefins. In the case of

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sulfone **1s** the corresponding olefin **2s** was obtained as a sole product. Similar radical anion intermediate for (bromomethyl)aziridine can be assumed for reductive desulfonylation. Garst et al. have recently demonstrated[23] that radical species formed on the surface of Mg in Grignard reagent formation undergo mostly reduction on the surface to Grignard reagent, but at the same time a certain amount of it diffused into solvent is in an equilibrium with one on the surface so as to form a coupling product and hydrogen abstraction product. In the same context, we might assume that radical species formed on the surface of Mg in methanol undergo either further reduction to carbanion or ring cleavage to form aminyl radical. Although we could not detect any of C(2)−C(3) cleavage product in our cases, it has been reported that homolytic cleavage can occur both on the C(2)−N and C(2)−C(3) bond from aziridinylmethyl radical[15,24] or oxyranylmethyl radical[25] depending on the substituent at C(3). Thus, the cleavage reaction pathway can be explained either by a carbanionic or a radical species.

In summary, a remarkably simple, convenient, and economic method for highly regiospecific C(2)−N bond reduction of various 2-acyl-, (carboalkoxy)-, cyano-, (halomethyl)-, and (phenylsulfonylmethyl)aziridines has been established by employing magnesium in methanol as the electron-transfer reagent.

Experimental Section

Methanol was dried over magnesium powder. Magnesium powder, purchased from Aldrich (−50 mesh, 99+%), was used without any special activation. The reaction was routinely monitored by TLC using precoated silica gel plates (0.25 mm 60 F-254 E. Merck). Flash column chromatography was performed with Merck Kiesegel 60 (230−400 mesh ASTM) silica. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ at a specified magnetic field.

Procedures for Ring Cleavage of Aziridine. Method A. To 3.0 equiv of vacuum-dried magnesium powder, which was immersed in a dry ice/CCl_4 bath (−23 °C) and kept under a nitrogen atmosphere, a solution of the aziridine substrate in dry methanol (0.2 M) was added by syringe. After stirring of the mixture for 2 h, an equal volume of ethyl acetate was added to the gray colored reaction mixture. The whole mixture was then filtered through a silica gel pad and concentrated in vacuo. The residue was then purified by flash column chromatography (silica gel, 3/1 hexane/ethyl acetate) to give the desired product(s).

Method B. To 3.0 equiv of vacuum-dried magnesium powder, which was immersed in a dry ice/CCl_4 bath (−23 °C) and kept under a nitrogen atmosphere, a solution of the aziridine substrate (0.5 mmol) in dry methanol (3mL) was added by syringe. After being stirred for 4 h, the whole mixture was poured into ice cold 2 N HCl (1.6 mL). The mixture was extracted with EtOAc (3 × 10 mL), and the organic layer was dried with $MgSO_4$. After evaporation of the solvent, the residue was flash column chromatographed (silica gel, 3/1 hexane/ethyl acetate) to give the desired product(s).

Method C. Virtually the same procedure was used as method A except reaction temperature (room temperature).

Method D. Virtually the same procedure as method A was employed except amount of magnesium (4 equiv).

4-(*p*-Tosylamino)-4-phenyl-3-methyl-2-butanone (2c), Diastereomeric Mixture. Method A: yield 98%, oil; R_f 0.37 (4/1 hexane/EtOAc); ^{1}H NMR (300 MHz) δ 7.40−7.60 (m, 4 H), 6.90−7.25 (m, 14 H), 6.18 and 5.66 (two br d, J = 9.1, 8.6 Hz, 2 H), 4.49 (m, 2 H), 2.95 (m, 2 H), 2.33 and 2.30 (two s, 6 H), 2.00 and 1.80 (two s, 6 H), 1.15 and 1.07 (two d, J = 7.1, 7.1 Hz, 6 H); ^{13}C NMR (125.7 MHz) δ 212.3, 210.2, 143.1, 142.8, 138.9, 138.7, 137.7, 137.6, 129.2, 129.1, 128.3, 127.4, 127.3, 127.0, 126.9, 126.6, 60.3, 59.5, 52.5, 52.3, 29.6, 21.4, 15.1, 13.4. Anal. Calcd for $C_{18}H_{21}NO_3S$: C, 65.23; H, 6.39; N, 4.23; S, 9.67. Found: C, 65.53; H, 6.57;N, 4.09;S, 9.91.

4-(*p*-Tosylamino)-4-phenyl-2-butanone (2d). Method B: yield 75%, white solid, mp 104.5−105.5 °C; R_f 0.21 (2/1 hexane/EtOAc); ^{1}H NMR (500 MHz) δ 7.52 (d, J = 8.3 Hz, 2 H), 7.07−7.13 (m, 5 H), 7.00−7.05 (m, 2 H), 5.71 (d, J = 7.4 Hz, 1 H), 4.63 (m, 1 H), 2.97 (dd, J = 17.2, 5.8 Hz, 1 H), 2.83 (dd, J = 17.2, 6.2 Hz, 1 H), 2.31 (s, 3 H), 1.96 (s, 3 H); ^{13}C NMR (125.7 MHz) δ 206.6, 143.2, 139.7, 137.2, 129.4, 128.5, 127.6, 127.1, 126.5, 54.0, 49.6, 30.7, 21.4. Anal. Calcd: C, 64.33; H, 6.03; N, 4.41; S, 10.10. Found: C, 63.72; H, 6.23; N, 4.36; S, 9.85. HRMS (CI): calcd for $C_{17}H_{20}NO_3S$, m/e 318.1164; found, m/e 318.1167.

Benzalacetone: yield 20%, oil; ^{1}H NMR (200 MHz) δ 7.39−7.58 (m, 6 H), 6.73 (d, J = 16.2 Hz, 1 H), 2.40 (s, 3 H). ^{1}H NMR data are identical with the literature values.[26]

2-(*p*-Tosylamino)-1,3-diphenyl-2-propen-1-one (2e). Method C: yield 65%, oil; ^{1}H NMR (500 MHz) δ 6.80−7.90 (m, 16 H), 2.36 (s, 3 H); ^{13}C NMR (125.7 MHz) δ 193.6, 144.1, 139.1, 136.3, 136.2, 132.7, 132.3, 131.3, 130.8, 130.5, 129.5, 129.1, 128.6, 128.5, 128.3, 127.5, 21.5. Anal. Calcd for $C_{22}H_{19}NO_3S$: C, 70.01 H, 5.07; N, 3.71; S, 8.49. Found: C, 70.11; H, 5.12;N, 3.63;S, 8.37 HRMS: calcd for $C_{22}H_{19}NO_3S$, m/e 377.1086; found, m/e 377.1083.

Methyl 3-(*p*-Tosylamino)butanoate (2h). Method D: yield 94%, oil; ^{1}H NMR (300 MHz) δ 7.74 (d, J = 7.7 Hz, 2 H), 7.28 (d, J = 7.7 Hz, 2 H), 5.15 (br d, J = 8.6 Hz, 1 H), 3.68 (m, 1 H), 3.60 (s, 3 H), 2.41 (d, J = 5.3 Hz, 2 H), 2.40 (s, 3 H), 1.12 (d, J = 6.7 Hz, 3 H); ^{13}C NMR (75.4 MHz) δ 171.5, 143.3, 137.9, 129.6, 127.0, 51.6, 48.5, 40.5, 21.4, 21.0. Anal. Calcd for $C_{12}H_{17}NO_4S$: C, 53.12; H, 6.32; N, 5.16; S, 11.82. Found: C, 53.28; H, 6.41; N, 5.11; S, 11.78.

Methyl 3-(*p*-Tosylamino-2-methylpentanoate (2i). Method D: yield 95%, oil. Isomer A: R_f 0.39 (2/1 hexane/EtOAc); ^{1}H NMR (300 MHz) δ 7.65−7.85 (m, 2 H), 7.20−7.39 (m, 2 H), 5.03 (br d, J = 9.6 Hz, H), 3.60 (s, 3 H), 3.25−3.42 (m, 1 H), 2.52 (m, 1 H), 2.42 (s, 3 H), 1.20−1.58 (m, 2 H), 1.06 (d, J = 7.2 Hz, 3 H), 0.75 (t, J = 7.6 Hz, 3 H); ^{13}C NMR (75.4 MHz) δ 175.2, 143.1, 138.7, 129.5, 126.9, 57.7, 51.8, 41.8, 30.9, 27.0, 21.5, 14.4, 10.5. Anal. Calcd for $C_{14}H_{21}NO_4S$: C, 56.17; H, 7.07; N, 4.68; S, 10.71. Found: C, 56.28; H, 7.11; N, 4.59; S, 10.78. Isomer B: ^{1}H NMR (300 MHz) δ 7.65−7.85 (m, 2 H), 7.20−7.39 (m, 2 H), 5.35 (br d, J = 9.1 Hz, 1 H), 3.64 (s, 3 H), 3.25−3.42 (m, 1 H), 2.70 (m, 1 H), 2.42 (s, 3 H), 1.20−1.58 (m, 2 H), 1.07 (d, J = 7.2 Hz, 3 H), 0.78 (t, J = 7.4 Hz, 3 H); ^{13}C NMR (75.4 MHz) δ 174.3, 143.3, 138.3, 129.6, 127.0, 57.7, 51.8, 43.0, 29.7, 24.6, 21.5, 13.2, 10.4. HRMS (CI): calcd for $C_{14}H_{22}NO_4S$, m/e 300.1270; found, m/e 300.1289.

Methyl 3-(*p*-Tosylamino)-3-phenylpropanoate (2j). Method D: yield 35%, white solid, mp 102−102.5 °C; R_f 0.18 (3/1 hexane/EtOAc); ^{1}H NMR (500 MHz) δ 7.55−7.65 (m, 2 H), 7.05−7.25 (m, 7 H), 5.80 (d, J = 7.8 Hz, 1 H), 4.73 (m, 1 H), 3.54 (s, 3 H), 2.84 (dd, J = 9.6, 6.4 Hz, 1 H), 2.75 (dd, J = 9.6, 6.2 Hz, 1 H), 2.32 (s, 3 H); ^{13}C NMR (125.7 MHz) δ 171.0, 143.2, 139.4, 137.3, 129.4, 128.5, 127.7, 127.1, 126.4, 54.3, 51.8, 41.1, 21.4. HRMS (CI): calcd for $C_{17}H_{20}NO_4S$ (M + H$^+$), m/e 334.1113; found, m/e 334.1112.

Methyl 3-Phenylaziridine-2-carboxylate (Desulfonylated Product). Method D: yield 60%, oil; R_f 0.47 (3/1 hexane/EtOAc); ^{1}H NMR (500 MHz) δ 7.20−7.40 (m, 5 H), 3.79 (s, 3 H), 3.26 (dd, J = 9.6, 2.3 Hz, 1 H), 2.58 (dd, J = 8.0, 2.3 Hz, 1 H), 1.85−2.00 (m, 1 H); ^{13}C NMR (125.7 MHz) δ 172.1, 137.7, 128.3, 127.7, 126.0, 52.6, 40.3, 39.2. HRMS (ESI): calcd for $C_{10}H_{12}NO_2$ (M + H$^+$), m/e 178.0868; found, m/e 178.0866.

Ethyl 3-(*p*-Tosylamino)-3-phenylpropanoate (Ethyl Ester of 2j). A solution of **1j** (25 mmol) in dry ethanol (1 mL) and THF (7 mL) mixture was added to magnesium powder (100 mmol). To the stirred reaction mixture, a few crystals of mercuric chloride were added. Stirring was continued under nitrogen

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atmosphere for 1.5 h at room temperature. The reaction mixture was poured into 0.2 N HCl (10 mL) and then extracted with ethyl acetate (40 mL × 2). The combined organic layer was washed with saturated aqueous $NaHCO_3$ solution, dried over anhydrous $MgSO_4$, filtered, and concentrated in vacuo. The residue was purified by silica gel flash column chromatography to give the desired product in 95% yield: ^{1}H NMR (300 MHz) δ 7.59 (d, J = 8.4 Hz, 2 H), 7.05−7.25 (m, 7 H), 5.99 (d, J = 7.9 Hz, 1 H), 4.74 (m, 1 H), 3.99 (q, J = 7.1 Hz, 2 H), 2.81 (dd, J = 15.7, 6.4 Hz, 1 H), 2.72 (dd, J = 15.7, 6.5 Hz, 1 H), 2.35 (s, 3 H), 1.11 (t, J = 7.1 Hz, 3 H); ^{13}C NMR (125.7 MHz) δ 170.5, 143.0, 139.3, 137.3, 129.3, 128.4, 127.5, 127.0, 126.7, 126.4, 107.7, 60.8, 54.4, 41.4, 21.4, 139. HRMS (CI): calcd for $C_{18}H_{21}NO_4S$ (M + H^+), *m*/*e* 348.1266; found, *m*/*e* 348.1269.

***tert*-Butyl 3-(*p*-Tosylamino)propanoate (2k). Method D:** yield 85%, oil; ^{1}H NMR (300 MHz) δ 7.75 (d, J = 8.2 Hz, 2 H), 7.30 (d, J = 8.2 Hz, 2 H), 5.20 (br s, 1 H), 3.05−3.20 (m, 2 H), 2.43 (t, J = 7.2 Hz, 2 H), 2.42 (s, 3 H), 1.40 (s, 9 H); ^{13}C NMR (75.4 MHz) δ 171.5, 143.4, 137.0, 129.7, 127.0, 81.6, 38.9, 34.9, 28.0, 21.5. Anal. Calcd for $C_{14}H_{21}NO_4S$: C, 56.17; H, 7.07; N, 4.68; S, 10.71. Found: C, 56.16; H, 7.06; N, 4.61; S 10.81.

3-(*p*-Tosylamino)propionitrile (2n). Method D: yield 83%, oil; ^{1}H NMR (500 MHz) δ 7.76 (d, J = 8.0 Hz, 2 H), 7.33 (d, J = 8.0 Hz, 2 H), 5.65 (br s, 1 H), 3.22 (t, J = 6.6 Hz, 2 H), 2.59 (t, J = 6.6 Hz, 2 H), 2.43 (s, 3 H); ^{13}C NMR (125.7 MHz) δ 144.0, 136.2, 129.9, 126.9, 117.5, 39.8, 21.4, 19.2. Anal. Calcd for $C_{10}H_{12}N_2O_2S$: C, 53.55; H, 5.39; N, 12.49; S, 14.30. Found: C, 53.42; H, 5.31; N, 12.38; S 14.30. HRMS: calcd for $C_{10}H_{12}N_2O_2S$, *m*/*e* 224.0619; found, *m*/*e* 224.0618.

3-(*p*-Tosylamino)-2-methylpropionitrile (2o). Method D: yield 85%, oil; ^{1}H NMR (300 MHz) δ 7.76 (d, J = 8.0 Hz, 2 H), 7.34 (d, J = 8.0 Hz, 2 H), 5.35 (t, J = 6.8 Hz, 1 H), 3.12 (m, 2 H), 2.86 (m, 1 H), 2.44 (s, 3 H), 1.30 (d, J = 7.1 Hz, 3 H); ^{13}C NMR (125.7 MHz) δ 207.8, 143.4, 137.0, 129.7, 129.0, 42.9, 38.0, 30.0, 21.5. Anal. Calcd for $C_{11}H_{14}N_2O_2S$: C, 55.44; H, 5.92; N, 11.76; S, 13.45. Found: C, 55.53; H, 5.98; N, 11.74; S, 13.42. HRMS: calcd for $C_{11}H_{14}N_2O_2S$, *m*/*e* 238.0775; found, *m*/*e* 238.0774.

3-(*p*-Tosylamino)-3-phenylpropionitrile (2p). Method D: yield 80%, oil; ^{1}H NMR (500 MHz) δ 7.65−7.75 (m, 2 H), 7.05−7.40 (m, 7 H), 5.07 (br s, 1 H), 4.57 (m, 1 H), 2.95 (m, 2 H), 2.42 (s, 3 H); ^{13}C NMR (75.4 MHz) δ 144.1, 137.1, 136.5, 129.8, 128.2, 128.0, 127.1, 126.2, 116.4, 54.1, 30.9, 26.2, 22.6, 14.2. Anal. Calcd for $C_{16}H_{16}N_2O_2S$: 63.98; H, 5.37; N, 9.33; S, 10.67. Found: C, 64.01; H, 5.42; N, 9.30; S, 10.65. HRMS: calcd for $C_{16}H_{16}N_2O_2S$, *m*/*e* 300.0932; found, *m*/*e* 300.0921.

***N*-Allyl-*N*-benzylamine (2q). Method D:** yield 93%, oil; ^{1}H NMR (300 MHz) δ 7.30−7.60 (m, 5 H), 5.85−6.05 (m, 1 H), 5.30−5.50 (m, 2 H), 4.02 (s, 2 H), 3.49 (m, 2 H); ^{13}C NMR (125.7 MHz) δ 133.4, 133.3, 130.4, 128.5, 121.5, 49.6, 48.8. Anal. Calcd for $C_{10}H_{13}N$: C, 81.59; H, 8.90; N, 9.51. Found: C, 81.62; H, 8.94; N, 9.44.

***N*-Allyl-*N*-*p*-chlorobenzylamine (2r). Method D:** yield 95%, oil; ^{1}H NMR (300 MHz) δ 9.65 (br s, 1 H), 7.40−7.70 (m, 4 H), 5.85−6.10 (m, 1 H), 5.30−5.55 (m, 2 H), 4.10 (s, 2 H), 3.55 (m, 2 H); ^{13}C NMR (125.7 MHz) δ 134.2, 132.2, 131.2, 129.1, 128.2, 122.1, 49.0. Anal. Calcd for $C_{10}H_{12}ClN$: C, 66.12; H, 6.66; N, 7.71. Found: C, 66.18; H, 6.69; N, 7.69.

Benzyl 3-(*N*-(*tert*-butoxycarbonyl)amino)-1-buten-4-yl Ether (2s). Method C: yield 94%, oil; ^{1}H NMR (300 MHz) δ 7.15−7.40 (m, 5 H), 5.70−5.95 (m, 1 H), 5.10−5.30 (m, 2 H), 4.85 (br s, 1 H), 4.51 (s, 2 H), 4.21−4.39 (m, 1H), 3.40−3.55 (m, 2 H), 1.42 (s, 9H); ^{13}C NMR (125.7 MHz) δ 155.4, 137.9, 136.4, 128.4, 127.7, 127.5, 115.6, 109.3, 79.5, 73.2, 72.1, 28.3. Anal. Calcd for $C_{16}H_{23}NO_3$: C, 69.29; H, 8.36; N, 5.05. Found: C, 69.42; H, 8.58; N, 5.11. HRMS (CI): calcd for $C_{16}H_{23}NO_3$ (M + H^+), *m*/*e* 277.1677; found, *m*/*e* 277.1659.

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Supporting Information Available: Text providing spectral data for the substrates **1a**−**s** and products **2a,b,g** (7 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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