Radical and Anionic Response of *N*-(Bromomethanesulfonyl)-Substituted α,α′-Bridged Piperidine Substrates

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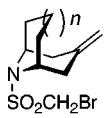
The *N*-(bromomethanesulfonyl) azabicyclic ketones **2a**−**c** and their *exo*-methylene analogues **1a**−**c** were prepared. Our examination of the radical-induced behavior of the latter triad provided experimental evidence for the propensity of the **b** and **c** systems to engage in 7-endo cyclization. For **1a**, only reductive debromination was observed. In no instance was ring closure by the 6-exo radical mode seen. As concerns ketones **2a**−**c**, all three showed a remarkable facility for engaging in intramolecular S_N2 displacement in the presence of KHMDS. Yields at the mid-80% level were realized irrespective of the value of *n*. Molecular mechanics calculations of the Monte Carlo type were performed on several conformational isomers and product classes in an effort to provide support for the explanatory conclusions offered as rationale for the collective experimental observations.

The development of α-halosulfonyl systems into synthetically useful building blocks has focused predominantly on their conversion into free radical intermediates and their ability to enter into nucleophilic displacement processes.[1] Recognized to receive insignificant stabilization by the flanking SO_2 group, C-centered α-sulfonyl radicals are highly electrophilic and enter readily into ring closure reactions.[2] These transient intermediates, when stereogenic at the halogen-bearing carbon, conform to the usual pattern of configurational instability.[3] Equally general is their kinetic preference to enter into 5-exo transition states whenever possible, a tendency that has recently been used to advantage in the synthesis of the first bridgehead bicyclic sultams.[4] Larger systems have been accorded much less attention. In the limited examples scrutinized, cyclization via the 7-endo option has been found to predominate over the 6-exo alternative.[5]

Although α-halosulfones are well recognized to be quite unreactive toward intermolecular nucleophilic displacement,[6] the situation can be improved by making recourse to DMF as solvent.[7] In contrast, intramolecular ring closures such as the Ramberg−Bäcklund rearrangement[8] occur readily, presumably because of a different topological arrangement of the atoms near the seat of reaction.[1]

The growing appreciation of steric and stereoelectronic effects in sulfone chemistry has caused us to seek out additional structural platforms that, by virtue of their unique conformational features and spatial orientations, can broaden the fundamental paradigms that have gained favor to the present time. Thus, to investigate systematically the degree of control that the size of a remote bridge can exert on the course of α-sulfonyl radical cyclization, we have constructed the series of molecules defined by **1** where *n* equals 0−2. We now also report a companion study in which a similar series of constraints was placed on **2** ($n = 0-2$) with a view to determining the susceptibility of the corresponding enolates to displace bromide ion and be converted to tricyclic keto sultams. The reactivity of enolates toward α-halosulfones has been examined only very infrequently.[9] Sulfonamide congeners appear not to have been accorded prior attention.



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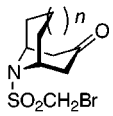

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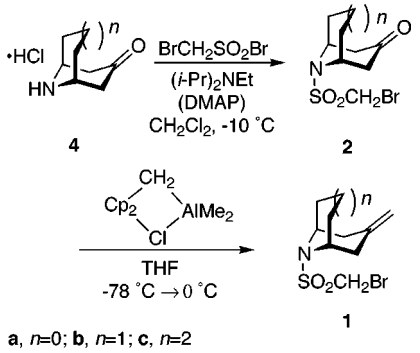
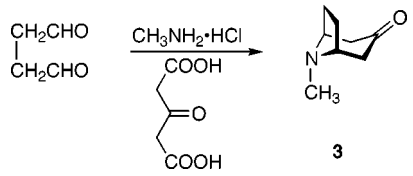
Scheme 1

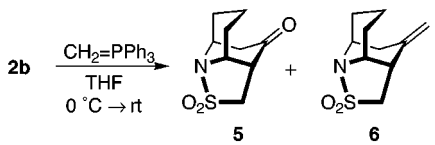


Access to **1** and **2** can be readily gained as a consequence of the general operability of the classical Robinson−Schöpf reaction.[10] In water under biogenetic-like conditions, an α,ω-dialdehyde undergoes decarboxylative double Mannich condensation with methylamine hydrochloride and acetonedicarboxylic acid.[11] The formation of tropinone (**3**) is illustrative. Alternative recourse to



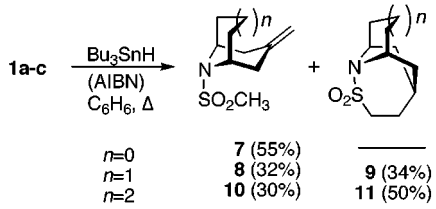
benzylamine hydrochloride as the source of the nitrogen atom delivers *N*-benzyl derivatives that have proven amenable to hydrogenolysis.[12] These amino ketones (**4**) have served as our starting materials.

Synthesis. The azabicyclic hydrochlorides **4a**−**c** were obtained following the procedure described by Momose et al.[12] Arrival at **2a**−**c** was readily accomplished, albeit in moderate yield, by treatment of the salts with bromomethanesulfonyl bromide[13] and Hunig's base in cold CH_2Cl_2 (Scheme 1). The successful conversion of **2a**−**c** to the *exo*-methylene analogues **1a**−**c**, respectively, was realized by making use of the Tebbe reagent.[14] Recourse to these conditions, which proved to be particularly conducive to clean homologation, was made when it was recognized that the Wittig olefination of **2b** with methylenetriphenylphosphorane gave rise to a mixture of **5** and **6**, without evidence for the generation of **1b**. We were therefore provided early in this study with an indication of the susceptibility of these keto sulfonamides to base-promoted cyclization.



Radical Cyclization. A systematic investigation of the reactivity of **1a**−**c** toward tri-*n*-butyltin hydride and

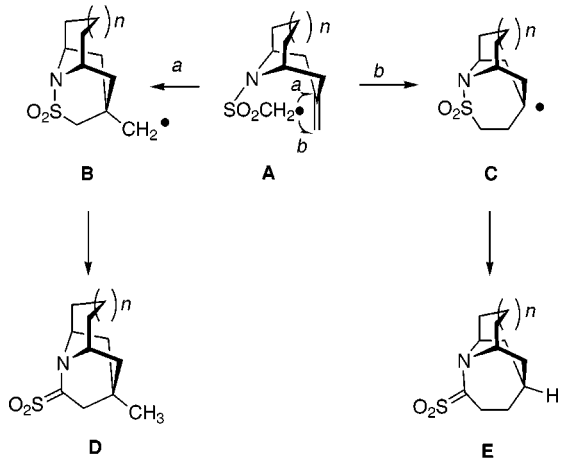
Scheme 2



AIBN in refluxing benzene was undertaken. Whereas **1a** is rapidly consumed under these conditions, only reductive debromination was observed with the isolation of **7** in 55% yield (Scheme 2).[15] In contrast, the comparable handling of **1b** gave rise to a 1:1 mixture of **8** and **9** with an overall efficiency of 66%. Still more fruitful results emerged from the $n = 2$ example **1c**, which smoothly cyclized to generate **11** predominantly.

In no instance was 6-exo cyclization as in **A** → **B** observed despite a very careful search for products of this type. This fact is notable since hydrocarbon networks are frequently seen to follow this particular pathway.[16] Since intermediate **B**, if formed, would be expected to be converted ultimately to the methyl derivative **D** by hydrogen atom transfer, its ready identification can be assured. However, no upfield ^{1}H NMR singlet was observed upon close inspection of the spectra of either crude or purified reaction mixtures.

Instead, the predominance of **9** and especially **11** serves as an indicator that adoption of a 7-endo reaction trajectory as defined by **A** → **C** is kinetically favored. The inability of **1a** to exhibit this capacity for cyclization can be traced to conformational and ring strain factors as discussed below. It is obvious that when $n = 0$, the ring closure of **A** by either trajectory is not able to compete at a reasonable level with reduction.



Base-Promoted Cyclization. The availability of triad **2a**−**c** brings into focus the desirability of scrutinizing the susceptibility of these ketones for intramolecular anionic displacement. The most probable pathway for S_N2 attack on an acyclic α-halosulfone RSO_2CH_2X is depicted in **F**.[6b] Note that the nucleophile is forced to approach at least one negatively charged oxygen center very closely, a major consequence of which is a strong disincentive to

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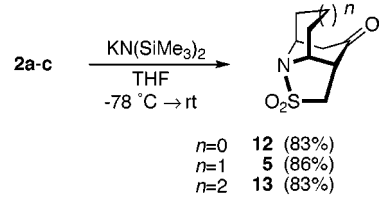
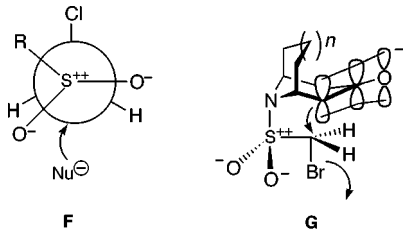
(14) Review: Pine, S. H. *Org. React.* **1993**, *43*, 1.
(15) In one experiment, approximately 5−10% of cyclized product was isolated. However, this result could not be duplicated.
(16) Curran, D. P.; Porter, N. A.; Giese, B. *Stereochemistry of Radical Reactions*; VCH: Weinheim, 1996.

Scheme 3



continue onward toward the halogen-substituted carbon. For the enolate anions of **2**, the transition state scenario is dramatically different despite the commonality of structural features. In this circumstance, geometric factors conspire to require orientation of the sulfonyl oxygens as remote as possible from the attacking enolate carbon (see **G**). No longer is a negative field effect serving as a deterrent to nucleophilic approach. In addition, the relative positioning of the bromine atom and the sulfonyl oxygens is well suited to the minimization of steric effects during structural preorganization for an intramolecular S_N2 process. Beyond this, the orientation of the nitrogen lone pair in the bisector of the O−S−O internuclear angle displayed for **G** conforms to the decided preference exhibited in many crystalline sulfonamides as seen by X-ray crystallography.[4,17]



The above analysis led us to anticipate significantly heightened reactivity on the part of **2a**−**c** following generation of their enolate anions with an appropriate base. Admixture of **2a** with potassium hexamethyldisilazide in THF at −78 °C to room temperature resulted in the isolation of **12** in 83% yield (Scheme 3). The conversion of **2b** and **2c** to **5** and **13**, respectively, proved to be equally rapid and efficient. The smooth formation of a new C−C bond was easily recognized as a consequence of the evolution of a chiral ketonic product with loss of a plane of symmetry. Diagnostic changes in the ^{1}H NMR spectra also manifest themselves. These include an upfield shift of the original $-SO_2CH_2Br$ singlet with enhancement of its multiplicity and a reduction in the number of α-carbonyl protons from four to three.

Discussion

Since the intramolecular free radical cyclization of **1** is required to pass through a transition state of type **A** in which the *exo*-methylene-substituted six-membered ring must adopt a boat geometry, the energetics associated with the **H** ⇄ **I** equilibrium as a function of *n* were assessed by the Monte Carlo conformational searching method and the MM3 force field. Recourse was made to *N*-methyl derivatives because parameters for the sulfonamide functionality are not available at this level of refinement. The local minima arrived at after 1000 iterations for each conformer were further minimized by the Full-Matrix Newton Raphson method in order to ensure accurate geometries and relative energies. The results are compiled in Table 1. In all three examples, the chair form **H** is more stable than **I** for the usual reasons. The small extent to which **I** is destabilized relative to **H** (5.38−7.79 kcal/mol) suggests that the barriers to their interconversion are not prohibitive at room temperature. Therefore, the inability of **1a** to undergo cyclization does not appear to originate at this level.

Table 1. Chair/Boat Energy Differences for the Conformersof the *N*-Methyl Derivatives of 1a−c[a]

compd	*n*	chair form **H**	boat form **I**	Δ*E*
1a	0	34.47	42.23	7.76
1b	1	28.79	36.58	7.79
1c	2	37.30	42.68	5.38

[a] The values for all global minima are given in kcal/mol.

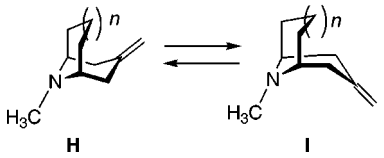
Table 2. Relative Strain Energies of Isomers D and E[a]

n	isomer D	isomer E	Δ*E*
0	35.36	36.75	1.39
1	29.95	31.26	1.31
2	39.17	39.51	0.34

[a] The values for all global minima are given in kcal/mol.

Table 3. Comparative Energies of J

n	*E* (kcal/mol)
0	23.16
1	19.43
2	26.31



The cyclizative options depicted in **A** feature a sulfonamide linkage embedded in either ring being generated. The bond lengths associated with this functionality are recognized to be longer than those associated with carboxamide prototypes.[18] However, because the MM3 force field is not parametrized for sulfonamides, we have evaluated instead the strain inherent in the products **D** and **E** by means of the MM2 software package (Table 2). The energy values hold relevance in pointing out the existence of a trend that indicates isomers **E** to be somewhat more strained than **D**. The longer sulfonamide bonds undoubtedly contribute to a diminution of the Δ**E** gaps. We conclude that strain effects are not the root cause of the noncyclizative behavior of **1a**. Rather, the reaction centers are more likely inappropriately aligned in **A** when $n = 0$, such that low energy trajectories of type **a** or **b** are not as easily accessible.

The strain energy differences calculated for **J** (Table 3) follow a pattern closely comparable to those compiled for **D** and **E**. Notwithstanding, the base-promoted cyclizations of **2a**−**c** proceed uniformly well. The ideality of the reaction trajectory **G** in all three examples contributes in an especially conducive way to the ready operation of these displacement processes. On this basis,

(17) Beddoes, R. L.; Dalton, L.; Joule, J. A.; Mills, O. S.; Street, J. D.; Watt, C. I. F. *J. Chem. Soc., Perkin Trans. 2* **1986**, 287.

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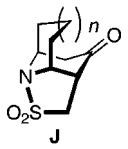
the ramifications of proper stereoelectronic alignment to the success of ring-forming reactions can be far-reaching.



J

Experimental Section

General. THF and ether were distilled from sodium benzophenone ketyl under nitrogen just prior to use. For CH_2Cl_2 and benzene, the drying agent was calcium hydride. All reactions were performed under a N_2 atmosphere. Analytical thin-layer chromatography was performed on E. Merck silica gel 60 F_{254} aluminum-backed plates. All chromatographic purifications were performed on E. Merck silica gel 60 (230−400 mesh) using the indicated solvent systems. Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on Bruker instruments at 300 and 75 MHz, respectively, with $CDCl_3$ as solvent. Elemental analyses were performed at Atlantic Microlab, Inc., Norcross, GA. The organic extracts were dried over anhydrous $MgSO_4$.The high-resolution mass spectra were obtained at The Ohio State University Campus Chemical Instrumentation Center.

***N*-(Bromomethanesulfonamido) Ketones 2a−c.** A solution of **4a**[12] (400 mg, 2.12 mmol) in dry CH_2Cl_2 was treated with DMAP (13 mg, 0.11 mmol) and diisopropylethylamine (0.98 mL, 5.51 mmol) and cooled at 0 °C. Bromomethanesulfonyl bromide (940 mg, 3.95 mmol) dissolved in CH_2Cl_2 (3 mL) was introduced via cannula, and the solution was stirred for 18 h with slow warming to room temperature, washed with saturated $KHSO_4$ solution and brine, and then dried. Concentration and purification over silica gel (elution with 30% ethyl acetate in hexanes) gave **2a** (299 mg, 50%) as a white solid, mp 120−122 °C; IR (CH_2Cl_2, cm^{-1}) 1727, 1473, 1455, 1406; ^{1}H NMR δ 4.57−4.54 (m, 2H), 4.47 (s, 2H), 2.85 (dd, J = 16.6, 4.6 Hz, 2H), 2.43 (dd, J = 17.3, 1.5 Hz, 2H), 2.26−2.21 (m, 2H), 1.79 (d, J = 8.0 Hz, 2H); ^{13}C NMR δ 206.2, 57.2 (2C), 50.0 (2C), 42.9, 30.1 (2C); HRMS (EI) m/z (M^+) calcd 282.9700, obsd 282.9697. Anal. Calcd for $C_8H_{12}BrNO_3S$: C, 34.06; H, 4.29. Found: C, 34.33; H, 4.34.

For **2b** (55%): white solid, mp 122−124 °C; IR (CH_2Cl_2, cm^{-1}) 1713, 1469, 1440, 1412; ^{1}H NMR δ 4.43 (br s, 4H), 2.81 (dd, J = 16.8, 6.8 Hz, 2H), 2.42 (d, J = 16.8 Hz, 2H), 2.02−1.90 (m, 2H), 1.75−1.51 (m, 4H); ^{13}C NMR δ 207.2, 51.1 (2C), 46.1(2C), 42.2, 30.8 (2C), 15.6; HRMS (EI) m/z (M^+) calcd 294.9877, obsd 294.9897. Anal. Calcd for $C_9H_{14}BrNO_3S$: C, 36.50; H, 4.76. Found: C, 36.56; H, 4.82.

For **2c** (49%): white solid, mp 105−106 °C; IR (CH_2Cl_2, cm^{-1}) 1713, 1449, 1407; ^{1}H NMR δ 4.66 (br d, J = 4.4 Hz, 2H), 4.49 (s, 2H), 2.84 (dd, J = 15.2, 7.9 Hz, 2H), 2.34 (d, J = 15.2 Hz, 2H), 2.15−2.10 (m, 2H), 1.77−1.72 (m, 2H), 1.60−1.53 (m, 4H); ^{13}C NMR δ 206.5, 54.5, 45.6 (2C), 41.5 (2C), 35.1 (2C), 24.1 (2C); HRMS (EI) m/z (M^+) calcd 309.0034, obsd 309.0024. Anal. Calcd for $C_{10}H_{16}BrNO_3S$: C, 38.72; H, 5.20. Found: C, 39.00; H, 5.14.

Tebbe Olefination of 2a−c. Tebbe reagent (4.7 mL of 0.66 M, 3.12 mmol) was added to a cold (−78 °C) solution of a **2a** (293 mg, 1.04 mmol) in dry THF (25 mL), and the dark red mixture was stirred at this temperature for 1 h, warmed to 0 °C for 45 min, and slowly quenched with 15% sodium hydroxide solution until gas evolution ceased. After dilution with THF and an additional 2 h of stirring, the solids were removed by filtration through a plug of Celite. The filter cake was rinsed with CH_2Cl_2, and the combined filtrates were concentrated and purified over silica gel (elution with 5−15% ethyl acetate in hexanes) to give **1a** (222 mg, 76%) as a white solid, mp 84−86 °C; IR (CH_2Cl_2, cm^{-1}) 1469, 1453, 1421; ^{1}H NMR δ 4.90 (t, J = 2.1 Hz, 2H), 4.39 (s, 2H), 4.34−4.32 (m, 2H), 2.62 (br d, J = 13.4 Hz, 2H), 2.22−2.16 (m, 2H), 2.03−1.98 (m, 2H), 1.69 (d, J = 7.4 Hz, 2H); ^{13}C NMR δ 140.4, 114.7, 58.5 (2C), 42.8, 42.0 (2C), 29.3 (2C); HRMS (EI) m/z (M^+) calcd 278.9929, obsd 278.9926. Anal. Calcd for $C_9H_{14}BrNO_2S$: C, 38.58; H, 5.04. Found: C, 38.69; H, 5.08.

For **1b** (70%): white solid, mp 68−70 °C; IR (CH_2Cl_2, cm^{-1}) 1385, 1349, 1324, 1312; ^{1}H NMR δ 4.80 (t, J = 2.5 Hz, 2H), 4.35 (s, 2H), 4.10 (br s, 2H), 2.76−2.70 (m, 2H), 2.38 (d, J = 15.1 Hz, 2H), 2.39−2.24 (m, 1H), 2.01−1.89 (m, 2h), 1.76−1.69 (m, 2H), 1.48−1.39 (m, 1H); ^{13}C NMR δ 144.0, 110.3, 50.4 (2C), 42.2, 38.9 (2C), 30.9 (2C), 17.3; HRMS (EI) m/z (M^+) calcd 295.0064, obsd 295.0069. Anal. Calcd for $C_{10}H_{16}BrNO_2S$: C, 40.83; H, 5.48. Found: C, 41.20; H, 5.42.

For **1c** (58%): white solid, mp 66−68 °C; IR (CH_2Cl_2, cm^{-1}) 1443, 1401, 1323, 1297; ^{1}H NMR δ 4.93 (t, J = 1.8 Hz, 2H), 4.40 (s, 2H), 4.32−4.26 (m, 2H), 2.64−2.57 (m, 2H), 2.14 (d, J = 13.7 Hz, 2H), 1.97−1.87 (m, 2H), 1.68−1.58 (m, 6H); ^{13}C NMR δ 140.1, 113.3, 53.6 (2C), 41.3, 39.4 (2C), 33.7 (2C), 24.4 (2C); HRMS (EI) m/z (M^+) calcd 307.0242, obsd 307.0242. Anal. calcd for $C_{11}H_{18}BrNO_2S$: C, 42.86; H, 5.89. Found: C, 43.31; H, 5.99.

Attempted Wittig Olefination of 2b. A suspension of methyltriphenylphosphonium bromide (711 mg, 1.99 mmol) in dry THF (10 mL) was added to a solution of potassium hexamethyldisilazide (3.98 mL of 0.50 M in THF, 1.99 mmol) in dry THF (4 mL) at 0 °C via cannula. The mixture was stirred for 1h, at which point a solution of **2b** (393 mg, 1.33 mmol) in THF (4 mL) was introduced. The reaction mixture was stirred at room temperature for 3 h, diluted with ether, and washed with saturated $NaHCO_3$ solution. The organic phase was dried and concentrated to leave a residue, purification of which on silica gel (elution with 15% ethyl acetate in hexanes) provided 101 mg (36%) of **5** and 127 mg (44%) of **6**.

For **5** (86%): white solid, mp 167−169 °C; IR (CH_2Cl_2, cm^{-1}) 1714, 1471, 1452, 1428; ^{1}H NMR δ 4.08−4.03 (m, 2H), 3.55 (ddd, J = 13.9, 7.1, 1.1 Hz, 1H), 3.22−3.14 (m, 2H), 3.06 (d, J = 13.9 Hz, 1H), 2.29 (d, J = 17.2 Hz, 1H), 2.26−2.14 (m, 1H), 1.98−1.86 (m, 2H), 1.85−1.76 (m, 1H), 1.62−1.43 (m, 2H); ^{13}C NMR δ 206.5, 58.2, 56.6, 56.1, 51.6, 40.5, 30.7, 24.7, 14.5; HRMS (EI) m/z (M^+) calcd 215.0616, obsd 215.0607. Anal. Calcd for $C_9H_{13}NO_3S$: C, 50.22; H, 6.09. Found: C, 50.48; H, 6.17.

For **6**: white solid, mp 91−93 °C; IR (CH_2Cl_2, cm^{-1}) 1462, 1439, 1422, 1326; ^{1}H NMR δ 4.84 (d, J = 2.0 Hz, 1H), 4.77 (d, J = 2.0 Hz, 1H), 3.82−3.78 (m, 2H), 3.50 (dd, J = 13.2, 6.8 Hz, 1H), 3.25 (dd, J = 6.7, 2.4 Hz, 1H), 3.10 (dt, J = 16.3, 3.6 Hz, 1H), 2.98 (d, J = 13.2 Hz, 1H), 2.29−1.80 (series of m, 6H), 1.44−1.35 (m, 1H); ^{13}C NMR δ 146.0, 109.7, 58.6, 56.7, 51.4, 51.1, 31.7, 31.6, 25.3, 15.3; HRMS (EI) m/z (M^+) calcd 213.0824, obsd 213.0813. Anal. Calcd for $C_{10}H_{15}NO_2S$: C, 56.31; H, 7.09. Found C, 56.51; H, 7.11.

Free-Radical Reductions of 1a−c. A solution of tri-*n*-butyltin hydride (0.12 mL, 0.44 mmol) and AIBN (6 mg, 0.04 mmol) in dry benzene (10 mL) was added over 2 h to a refluxing solution of **1a** (103 mg, 0.37 mmol) in the same solvent (40 mL), heated for an additional 3 h after completion of the transfer, cooled to room temperature, and concentrated. Purification of the residue over silica gel (elution with 5−30% ethyl acetate in hexanes) provided **7** (40 mg, 55%) as a white solid, mp 89−90 °C; IR (CH_2Cl_2, cm^{-1}) 1469, 1447, 1425, 1332; ^{1}H NMR δ 4.88 (t, J = 2.0 Hz, 2H), 4.28−4.26 (m, 2H), 2.91 (s, 3H), 2.56 (br d, J = 13.7 Hz, 2H), 2.20−2.15 (m, 2H), 1.99−1.91(m, 2H), 1.71−1.64 (m, 2H); ^{13}C NMR δ 140.7, 114.5, 57.2 (2C), 42.1 (2C), 40.5, 28.9 (2C); HRMS (EI) m/z (M^+) calcd 201.0824, obsd 201.0825.

For **8** (32%): white solid, mp 72−73 °C; IR (CH_2Cl_2, cm^{-1}) 1440, 1383, 1330; ^{1}H NMR δ 4.81 (t, J = 2.5 Hz, 2H), 4.15 (br s, 2H), 2.92 (s, 3H), 2.72−2.67 (m, 2H), 2.40 (d, J = 14.8 Hz, 2H), 2.39−2.29 (m, 1H), 1.95−1.82 (m, 2H), 1.76−1.70 (m, 2H), 1.49−1.42 (m, 1H); ^{13}C NMR δ 144.5, 110.2, 49.2 (2C), 41.7, 38.8 (2C), 30.9 (2C), 17.6; HRMS (EI) m/z (M^+) calcd 215.0980, obsd 215.0980.

For **9** (34%): white solid, mp 75−76 °C; IR (CH_2Cl_2, cm^{-1}) 1475, 1453, 1438, 1424; ^{1}H NMR δ 4.02−3.99 (m, 2H), 3.26−3.22 (m, 2H), 2.26 (br t, J = 5.3 Hz, 1H), 1.98−1.48 (series of m, 12H); ^{13}C NMR δ 48.3, 46.3 (2C), 31.1 (2C), 31.0 (2C), 28.4, 25.5, 12.9; HRMS (EI) m/z (M^+) calcd 215.0980, obsd 215.0973.

Anal. Calcd for $C_{10}H_{17}NO_2S$: C, 55.78; H, 7.96. Found: C, 55.93; H, 8.04.

For **10** (30%): white solid, mp 63−64 °C; IR (CH_2Cl_2, cm^{-1}) 1438, 1320; ^1H NMR δ 4.93 (t, J = 1.7 Hz, 2H), 4.32−4.27 (m, 2H), 2.92 (s, 3H), 2.43 (dd, J = 13.9, 6.8 Hz, 2H), 2.14 (d, J = 13.9 Hz, 2H), 1.91−1.84 (m, 2H), 1.67−1.59 (m, 6H); ^{13}C NMR δ 140.5, 113.4, 52.1 (2C), 40.8, 39.2 (2C), 32.8 (2C), 24.1 (2C); HRMS (EI) m/z (M^+) calcd 229.1137, obsd 229.1137.

For **11** (50%): white solid, mp 144−145 °C; IR (CH_2Cl_2, cm^{-1}) 1461,1317; ^1H NMR δ 4.33−4.24 (m, 2H), 3.35−3.30 (m, 2H), 2.38−2.32 (m, 1H), 2.17−2.05 (m, 2H), 2.03−1.88 (m, 4H), 1.81−1.46 (series of m, 8H); ^{13}C NMR δ 50.7, 50.0 (2C), 36.2 (2C), 33.1 (2C), 26.0, 25.24, 25.17 (2C); HRMS (EI) m/z (M^+) calcd 229.1137, obsd 229.1136. Anal. Calcd for $C_{11}H_{19}NO_2S$: C, 57.61; H, 8.35. Found: C, 57.34; H, 8.27.

For **12**: white solid, mp 160−162 °C; IR (CH_2Cl_2, cm^{-1}) 1723, 1350, 1328; ^1H NMR δ 4.31−4.27 (m, 1H), 4.16 (t, J = 5.7 Hz, 1H), 3.63 (ddd, J = 14.0, 7.0, 0.8 Hz, 1H), 3.41 (ddd, J = 16.8, 5.4, 2.1 Hz, 1H), 3.24 (ddd, J = 7.0, 3.3, 1.0 Hz, 1H), 3.19 (d, J = 14.2 Hz, 1H), 2.43−2.16 (m, 3H), 1.92−1.80 (m, 2H); ^{13}C NMR δ 205.0, 63.8. 59.2, 58.6, 56.3, 43.6, 30.9, 24.7; HRMS (EI) m/z (M^+) calcd 201.0460, obsd 201.0461. Anal. Calcd for $C_8H_{11}NO_3S$: C, 47.75; H, 5.51. Found: C, 48.13; H, 5.69.

Base-Promoted Cyclizations of 2a−c. Potassium hexamethyldisilazide (0.78 mL of 0.52 M, 0.40 mmol) was added to a cold (−78 °C) solution of **2a** (95 mg, 0.34 mmol) in THF (6 mL), the reaction mixture was allowed to warm slowly to room temperature over 2 h, and the resulting yellow solution was diluted with CH_2Cl_2 and washed with brine. The organic phase was dried and concentrated, and the residue was chromatographed on silica gel (elution with 15−25% ethyl acetate in hexanes). There was isolated 56 mg (83%) of **12**, identical in all respects with the material described above.

For **13** (83%): white solid, mp 155−157 °C; IR (CH_2Cl_2, cm^{-1}) 1714, 1338, 1322; ^1H NMR δ 4.52−4.46 (m, 1H), 4.31−4.24 (m, 1H), 3.56 (dd, J = 13.8, 7.5 Hz, 1H), 3.18−3.09 (m, 2H), 2.89 (dd, J = 19.3, 10.5 Hz, 1H), 2.41−2.30 (m, 2H), 2.04−1.20 (series of m, 7H); ^{13}C NMR δ 206.5, 60.0, 55.2, 54.1, 52.2, 37.9, 33.6, 30.0, 25.5, 23.7; HRMS (EI) m/z (M^+) calcd 229.0773, obsd 229.0777. Anal. Calcd for $C_{10}H_{15}NO_3S$: C, 52.38; H, 6.59. Found: C, 52.12; H, 6.57.

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