resulting yellow solution was warmed to 0 °C and stirred at this temperature for 15 min. The solution, now colorless, was warmed to room temperature and partitioned between Et_2O (30 mL) and 1 M HCl (10 mL). The aqueous layer was removed, and the organic layer was washed with H_2O (1 × 10 mL), saturated $NaHCO_3$ solution (1 × 10 mL), and brine (1 × 10 mL). The solution was dried ($MgSO_4$), and the solvent was evaporated to give a white solid (282 mg, 104%). ^1H NMR analysis showed that this consisted of a cis–trans (40:60) mixture of the dimethyl compounds.

The dioxide **20a** was prepared by dissolving the crude solid in a solution of ca. 10 mg of Na in 70 mL of absolute EtOH and refluxing the solution for 4 h. Extractive workup and chromatography led to 152 mg (56%): mp 205–208 °C; ^1H NMR ($CDCl_3$) δ 7.52–7.45 (8 H, m), 4.00 (2 H, q, J = 7.0 Hz), 1.76 (6 H, d, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ 140.3, 132.3, 129.0, 128.8, 126.3, 56.4, 8.1; mass spectrum, m/z (intensity) 273 (1.84), 272 (1.03), 222 (1.81), 209 (8.24), 208 (47.93), 207 (8.59), 194 (19.96), 193 (100.00), 192 (7.36), 191 (7.82), 179 (25.45), 178 (57.59), 165 (12.60); mass spectrum, m/z 272.0875, calcd 272.0871 for $C_{16}H_{16}O_2S$.

Dioxide **20b** was prepared by substitution of CH_2OD for EtOH in the above procedure. Recrystallization from 95% EtOH gave white flakes: 48%, mp 212–214 °C; ^1H NMR ($CDCl_3$) δ 7.52–7.45 (8 H, m), 1.76 (6 H, s); ^{13}C NMR ($CDCl_3$) δ 140.3, 132.3, 129.9, 129.0, 128.1, 126.4, 56.1 (t, J = 21 Hz), 8.0; mass spectrum, m/z (intensity) 275 (0.26), 274 (0.55), 211 (6.99), 210 (41.79), 208 (11.0), 196 (15.51), 195 (100.00), 194 (6.44) 193 (10.01), 181 (8.68), 180 (52.53), 179 (11.81), 178 (5.27), 166 (7.77), 97 (5.58), 90 (6.07).

Pyrolysis of 20b at 737 °C. Pyrolysis of 101 mg (0.37 mmol) of **20b** at 737 ± 7 °C (0.12 Torr) produced 73 mg of a colorless oil. GC indicated that the mixture contained six components, although more than 90% of the peak area was due to two components. A, t_R 6.25 min, area 62.6% of total; B, t_R 9.17 min, area = 29.0% of total. GCMS was used to identify A as 9,10-dimethyl-9,10-dihydrophenanthrene-d_2 and B as phenanthrene-d_2. A: mass spectrum, m/z (intensity) 211 (2.4), 210 (20.0), 196 (12.6), 195 (100.0), 181 (12.6), 180 (79.8), 179 (16.3), 166 (10.2), 96 (10.2), 90 (17.5), 83 (17.9), 77 (12.6). B: mass spectrum, m/z (intensity) 181 (13.6), 180 (100.0), 179 (13.6), 178 (15.3), 90 (23.5), 89 (15.3), 77 (24.0). Since mass spectra of polycyclic species are known[16] to give fragment ions in which H atom scrambling has occurred, mass spectrometry could not be used to determine the location of the labels.

The ^1H NMR ($CDCl_3$) spectrum of the mixture clearly established that the labels were located on C9 and C10 of the 9,10-dihydro-9,10-dimethylphenanthrene; the spectrum had a slightly broadened methyl singlet at δ 1.052. The assignment was corroborated by its ^{13}C NMR spectrum ($CDCl_3$), which displayed a triplet at δ 40.156, and by ^2H NMR ($CHCl_3$), which exhibited a singlet at 2.876 ppm.

The location of the label on the phenanthrene-d_2 was established in an analogous manner. No signal for the protons on C9 or C10 was observed in the ^1H NMR of the mixture, but this region of the spectrum was partially obscured by aromatic resonances due to 9,10-dihydro-9,10-dimethylphenanthrene-*9,10-d_2*. However, the ^{13}C and ^2H NMR spectra provided convincing evidence that the label was located exclusively at C9 and C10. The C9–C10 resonance, in addition to being of low intensity due to the loss of NOE upon substitution by deuterium, was shifted upfield from 126.882 ppm (unlabeled phenanthrene) to 126.634 ppm. This isotope-induced chemical shift has been observed previously[24] in phenanthrene-*9,10-d_2*. A similar isotope-induced chemical shift, also previously observed was seen in the resonance due to C9a and C10a, which was shifted upfield from 131.986 (unlabeled) to 131.919. The aromatic region of the ^2H NMR contained only a major resonance at 7.851 pm (relative intensity 92.7). A smaller resonance at 7.693 ppm (relative intensity 7.3) is due to an impurity.

Pyrolysis of 5,7-Dimethyl-5,7-dihydrodibenzo[*c*,*e*]thiepin 6,6-Dioxide at 530 °C. The sulfone (102 mg, 0.37 mmol) was pyrolyzed (530 °C, 0.2 Torr) by using the usual procedure. A colorless oil (81 mg) was collected. Flash chromatography on a silica gel column with CCl_4 elution gave 68 mg of a colorless oil identified as 9,10-dimethyl-9,10-dihydrophenanthrene by analysis of its ^{13}C NMR spectrum and comparison of its ^1H NMR data with published data:[23] ^1H NMR ($CDCl_3$) δ 7.82–7.72 (2 H, m), 7.36–7.18 (6 H, m), 2.85 (2 H, q, J = 6.8 Hz), 1.08 (6 H, d, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$) δ 140.53, 132.19, 129.07, 127.76, 162.78, 123.61, 40.82, 21.81.

Supplementary Material Available: Improved procedures for the preparation of **2a**, **3a**, **4a**, and **1a** (3 pages). Ordering information is given on any current masthead page.

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Formation of Fused Tricyclic Azetidinones and Pyrrolidinones by Intramolecular S_H2 Processes[1]

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Treatment of a variety of suitably substituted sulfides of *N*-(*o*-halobenzyl)- or *N*-(*o*-halophenyl)azetidinone (e.g., **4** and **8**) and -pyrrolidinone (e.g., **12** and **14**) systems with either tributylstannane or tributyltin deuteride affords, by aryl radical substitution at the sulfur atom, the corresponding tricyclic azetidinones (**21** and **26**) and pyrrolidinones (**38** and **47**). The reactions with tributyltin deuteride give, in addition to the cyclized product, products arising through competing intramolecular hydrogen atom migration processes. The approximate rate constants, k_c for ring closure and $k_{1,x}$ (x = 5–7) for unimolecular hydrogen atom transfer, have been determined by comparison with either k_H or k_D, the rate constants for reactions of aryl radicals with tributylstannane or tributyltin deuteride, respectively.

Numerous recent examples[2] have illustrated the increasing importance of free-radical cyclization in synthetic chemistry. Most of them involve intramolecular homolytic addition processes as key steps in the synthesis of carbo-

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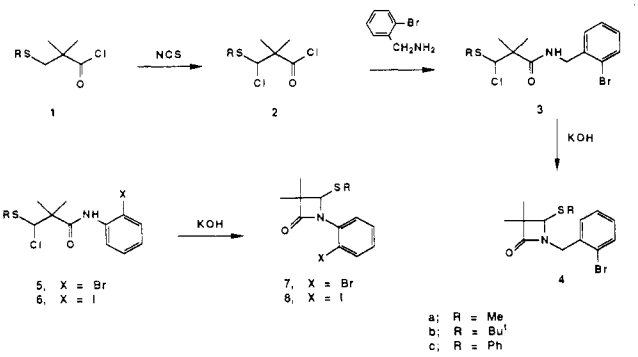
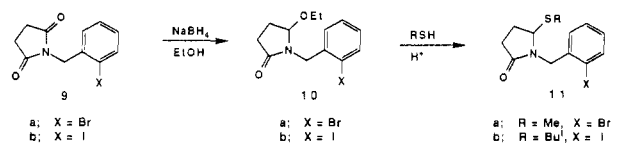
(1) Taken in part from: Boate, D. R. Ph.D. Thesis, Australian National University, 1986.

0022-3263/88/1953-4339$01.50/0

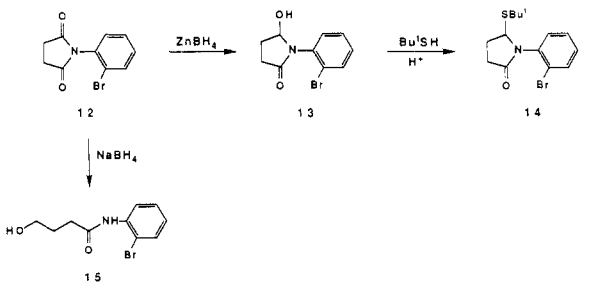
Scheme I



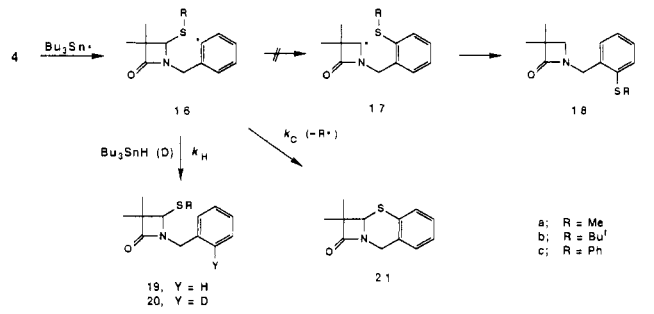
Scheme II



Scheme III



Scheme IV



cyclic or heterocyclic systems. The formation of heterocyclic systems by intramolecular homolytic substitution (S_H2) processes at suitably substituted heteroatoms has been less extensively explored. Except for the formation of a few cyclic peroxides,[3] sulfides,[4-6] and sulfoxides,[6b,7] very little is known about the potential of this method as a general route to mono and fused heterocyclic compounds.

In the present work[8] we have examined the feasibility of preparing fused heterocyclic systems containing either the azetidinone (**21** and **26**) or the pyrrolidinone (**38** and **47**) nucleus by free-radical cyclization of various suitably substituted *N*-(*o*-halobenzyl)- and *N*-(*o*-halophenyl)azetidinones (**4**, **7**, and **8**) and -pyrrolidinones (**11** and **14**) and have determined approximate values of the rate constants for these and other unimolecular reactions.

Results and Discussion

Precursors. The required azetidinone substrates **4a–c** were readily prepared from the appropriately substituted propanoyl chlorides **1a–c** (Scheme I). Thus, treatment of **1c** with *N*-chlorosuccinimide in carbon tetrachloride gave the unstable α-chloro sulfide **2c**, identified by its NMR spectrum, which showed a resonance at δ 5.44 for one proton. Treatment of crude **2c** with *o*-bromobenzylamine[9] gave the chloro amide **3c**, which was converted into the β-lactam **4c** in 78% yield by heating with powdered KOH in the presence of a catalytic amount of 18-crown-6 ether. The related benzyl amides **4a** and **4b** were similarly obtained as were the *N*-arylazetidinones **7a**, **7b**, and **8b**, except that the intermediate amides **5a**, **5b**, and **6b** were not isolated because of their instability but were used in situ immediately after their preparation.

The pyrrolidinones **11a** and **11b** were readily prepared from the corresponding *N*-(*o*-halobenzyl)succinimides (Scheme II). Thus, treatment of *o*-bromobenzyl bromide with potassium succinimide[10] afforded **9a** (74%), which, by selective reduction of one of the carbonyl groups with sodium borohydride[12] in ethanol, gave a mixture of the ethoxy compound **10a** with the corresponding alcohol. Separation of the mixture was not necessary, as its treatment with methanethiol in the presence of a catalytic amoung of *p*-toluenesulfonic acid[13] gave the required sulfide **11a** in good yield (88%). The *tert*-butyl sulfide **11b** was similarly prepared from **9b**.

The 2-pyrrolidinone derivative **14** was prepared in four steps from succinic anhydride and *o*-bromoaniline (Scheme III). The appropriate succinamic acid[14] was heated with sodium acetate and acetic anhydride to afford the succinimide **12** (93%), which was treated with sodium borohydride as described above in an attempt to bring about selective reduction of one of the carbonyl groups. The only

(2) For some recent examples of ring formation, see: Baldwin, J. E.; Li, C.-S. *J. Chem. Soc., Chem. Commun.* **1987**, 166. Newcomb, M.; Deeb, T. M. *J. Am. Chem. Soc.* **1987**, *109*, 3163. Snider, B. R.; Mohna, R.; Kates, S. A. *Tetrahedron Lett.* **1987**, *28*, 844. Curran, D. P.; Rakiewicz, D. M. *Tetrahedron* **1985**, *41*, 3943. Choi, J. K.; Hart, D. J. *Ibid.* **1985**, *41*, 3959. Beckwith, A. L. J.; Roberts, D. H. *J. Am. Chem. Soc.* **1986**, *108*, 5893. Beckwith, A. L. J.; Roberts, D. H.; Schiesser, C. H.; Wallner, A. *Tetrahedron Lett.* **1985**, *26*, 3349. Stork, G.; Kaku, M. *J. Am. Chem. Soc.* **1985**, *107*, 500. Moeller, K. D.; Little, R. D. *Tetrahedron Lett.* **1985**, *26*, 3417. Koreeda, M.; George, I. A. *J. Am. Chem. Soc.* **1986**, *108*, 8098 and references cited therein.

(3) Porter, N. A.; Funk, M. U.; Gilmore, D.; Isaac, R.; Nixon, J. *J. Am. Chem. Soc.* **1976**, *98*, 6000. Beckwith, A. L. J.; Wagner, R. D. *J. Chem. Soc., Chem. Commun.* **1980**, 485. Porter, N. A.; Nixon, J. R.; Gilmore, D. W. In *Organic Free Radicals*; Pryor, W. A., Ed.; ACS Symposium Series 69; American Chemical Society: Washington, DC, 1978; p 89. Ingold, K. U.; Roberts, B. P. In *Free Radical Substitution Reactions*; Wiley-Interscience: New York, 1971; p 180.

(4) Beckwith, A. L. J.; Boate, D. R. *Tetrahedron Lett.* **1985**, *26*, 1761.

(5) Beckwith, A. L. J.; Boate, D. R. *J. Chem. Soc., Chem. Commun.* **1985**, 797.

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(7) Beckwith, A. L. J.; Boate, D. R. *J. Chem. Soc., Chem. Commun.* **1986**, 189.

(8) This work has been published in a preliminary form.[4,5]

(9) *o*-Bromobenzylamine and *o*-iodobenzylamine were prepared from *o*-halobenzyl bromide and potassium phthalimide[10] by the Gabriel synthesis.[11]

(10) Sheehan, J. C.; Bolhofer, W. A. *J. Am. Chem. Soc.* **1950**, *72*, 2786.

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(12) Hubert, J. C.; Wijnberg, J. B. P.; Speckamp, W. N. *Tetrahedron* **1975**, *31*, 1437.

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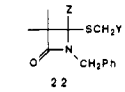
product, however, was the open-chain compound **15** (93%) thought to arise by base-catalyzed ring opening of the desired alcohol, **13**. Accordingly, zinc borohydride,[15] a milder reducing agent, was employed. With **12** it afforded **13**, which was not isolated but which was converted immediately into **14** by treatment with *tert*-butyl mercaptan and a catalytic amount of *p*-toluenesulfonic acid.

Cyclization of Azetidinone Substrates. When the *tert*-butyl thioether **4b** was treated with tributylstannane (0.03 M) and a catalytic amount of AIBN in boiling benzene, it afforded a separable mixture of unchanged starting material (17%) with the two products expected on the basis of the mechanism of Scheme IV, namely, the direct reduction product **19b** (17%) and the tricyclic β-lactam **21** (42%). The tricyclic compound **21** was identified by its spectral data. Thus the ^{1}H NMR spectrum contained (i) resonances for four aromatic protons (as indicated by integration), (ii) a pair of doublets (4.13 ppm, J = 17 Hz and 4.72 ppm, J = 17 Hz) assigned to the *N*-methylene protons, and (iii) a methine singlet α to sulfur at 4.70 ppm. The methine resonance is shifted downfield by about 0.5 ppm, relative to that for **4b**, due to the electron-withdrawing effect of the adjacent phenyl ring. The nonequivalence of the *N*-methylene protons (they are equivalent in **4b**) reflects the relative conformational rigidity of the cyclic system. The ^{13}C NMR spectrum displayed five upfield carbon resonances, all of which were expected for **21**. Neither spectrum contained resonances attributable to the *tert*-butyl group.

When **4b** was heated with Bu_3SnD (0.03 M), the cyclized product **21** (35%), unchanged starting material (4%), and only the directly reduced β-lactam **20b** (26%) were obtained. None of the possible products containing deuterium in either the *tert*-butyl or azetidinone moieties could be detected.

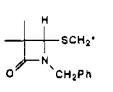
The methyl thioether **4a** gave, upon similar treatment with stannane (0.005 M), the same tricyclic product **21** but in less yield (21%). Also isolated were unchanged starting material (5%) and the directly reduced product **19a** (46%). Treatment of the phenyl thioether **4c** with stannane (0.015 M) afforded only unchanged starting material (42%) and the directly reduced product **19c** (40%). None of the cyclic product could be detected.

Repetition of the reaction of **4a** with tri-*n*-butyltin deuteride showed that some of the products were formed by intramolecular hydrogen atom transfer. Thus, treatment of **4a** with Bu_3SnD (0.03 M) gave **21** (21%) and an inseparable mixture of the deuteriated products **20a** (11%), **22a** (35%), and **22b** (15%). The sites of deuterium incorporation were determined by ^{2}H NMR, and the yields of the three reduced products were calculated from the known mass of the mixture and the product ratio deduced from the integrated ^{2}H NMR spectrum.

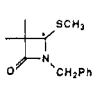


22

a; Y = D, Z = H
b; Y = H, Z = D



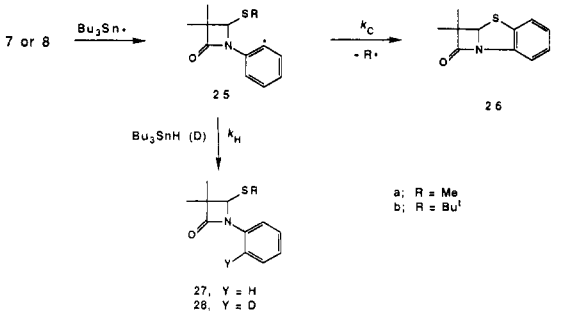
23



24

The formation of **20a** and **20b** in these reactions involves the direct reduction of the respective aryl radical with tributyltin deuteride (i.e., **16a,b** → **20a,b**). The formation of **22a** from **4a**, however, must proceed via the methylthio radical **23** and thus involves 1,7-hydrogen atom migration between the aryl radical and the methylthio moiety of **16a**, whereas the formation of **22b** proceeds via the radical **24** and involves 1,5-hydrogen atom transfer between the aryl radical and the C4 proton of the azetidinone ring of **16a**.

Scheme V



Many examples of 1,5-hydrogen atom transfer between carbon atoms have been reported, and such reactions have been extensively reviewed.[16,17] They occur through a distorted six-membered cyclic transition structure and often exhibit relatively large rate constants. Although hydrogen atom migrations between more remote carbon atoms have been recorded,[16,17] they proceed relatively slowly because of the adverse changes in strain energy and entropy associated with formation of transition structures larger than six-membered. It is not surprising, therefore, that no incorporation of deuterium into the *tert*-butyl group of **19b** occurs since this would involve 1,8-hydrogen atom transfer through a nine-membered cyclic transition structure.

However, the occurrence of both 1,5- and 1,7-hydrogen atom transfer in **16a** to give **22a** and **22b** respectively was unexpected. Both sites are activated toward hydrogen abstraction by the adjacent sulfur atom, but the nitrogen atom should provide additional driving force for loss of the ring hydrogen. However, in this case it appears that simple steric effects take precedence. Examination of molecular models indicates that the conformational rigidity associated with the presence of the azetidinone ring allows the methylthio hydrogens in **16a** to be brought into close juxtaposition with the aryl radical center, while disfavoring the formation of the six-membered cyclic transition structure required for transfer of the ring hydrogen atom.

A noteworthy feature of these reactions is their failure to afford aryl thioethers **18a,b** by intramolecular homolytic substitution at sulfur in **16a,b** to afford azetidinone radicals **17a,b**. If the reactions were under thermodynamic control, the formation of **17a,b** should be a favored process as the free spin would be stabilized by conjugative delocalization through the nitrogen lone pair and onto the carbonyl group, as predicted[18] by MNDO calculations. It appears therefore that the reaction is under stereoelectronic control and proceeds by interaction of the semioccupied orbital with a lobe of the σ* orbital of the bond undergoing fission.[6a,16,19] The collinear arrangement required for intramolecular S_H2 displacement is readily attainable for fission of the S–R bond in **16a,b** to afford **21**, but not for fission of the bond to the azetidinone moiety, which would lead to **17a,b**.

(15) Fieser, M.; Fieser, L. F. *Reagents for Organic Synthesis*; Wiley-Interscience: New York, 1972; Vol. 3, p 337. Corey, E. J.; Anderson, N. H.; Carlson, R. M.; Vedejis, P. E.; Vlattes, I.; Winter, R. E. K. *J. Am. Chem. Soc.* **1968**, *90*, 3245.

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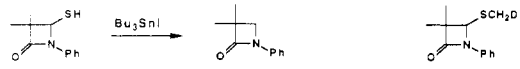
Within this constraint, the usual thermochemical factors appear to be operative. Thus, the data indicate that the S–Me bond undergoes cleavage a little less rapidly than the weaker S–*t*-Bu bond, while the essentially thermoneutral transformation **16c** → **21** involving fission of the relatively strong S–Ar bond[3d,20,21] does not occur.

Since five-membered rings are usually formed more readily than six in related homolytic ring closures,[16,19] it was expected that the radicals **25a,b** would behave similarly to their higher homologues and yield the tricyclic β-lactam **26** by an S_H2 displacement of R· from sulfur (Scheme V). However, when the methylthio azetidinone **7a** was heated with 1.1 molar equiv of stannane (0.015 M) in boiling benzene, only the reduced product **27a** (70%) and unchanged starting material (6%) were observed and none of the cyclized product **26** could be detected. In a similar experiment, the methyl sulfide **7a**, when treated with Bu_3SnD under identical conditions, gave only the *N*-phenylazetidinone **31** (95%) in which all of the deuterium resides in the thiomethyl group. This transformation clearly proceeds by 1,6-hydrogen atom transfer through the intermediacy of the *N*-phenyl analogue of the methylthio radical **23**.

Reactions of the *tert*-butyl sulfides **7b** and **8b** with Bu_3SnH, under identical conditions, followed a different course from those of **7a** and **8a**. Thus, **7b** gave the unexpected 4-mercaptoazetidinone **29** in 60% yield and unchanged starting material (10%), whereas **8b** furnished **29** (42%), the 4-unsubstituted β-lactam **30** (17%), and a trace (ca. 1%) of the tricyclic product **26**.

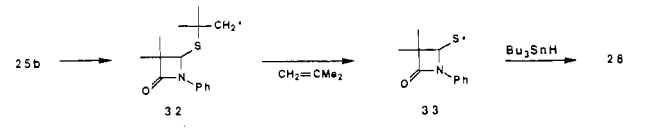


29 30 31

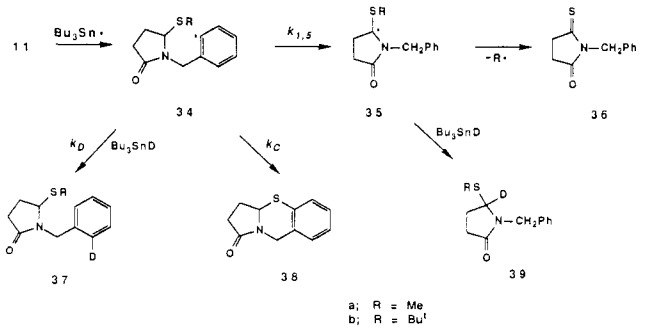
Unlike some 4-mercaptoazetidinones,[22] **29** (mp 50–58 °C) was found to be moderately stable and could be recrystallized from nonpolar solvents. It was fully characterized by its spectral and microanalytical data and by its *S*-benzoyl derivative[23] (mp 101–107 °C). Characteristic features of the ^1H NMR spectrum of **29** included doublets (J = 9 Hz) assigned to the coupled SH and β-lactam methine protons at δ 2.02 and 4.96 respectively. The ^{13}C NMR spectrum contained a carbonyl resonance at δ 169.7, the four aromatic carbon signals expected for a monosubstituted phenyl ring, and four upfield resonances consistent with the proposed structure. Neither spectrum contained signals attributable to the *tert*-butyl group. As expected, the IR spectrum displayed absorptions at 1755 and 2560 cm^{-1} associated with the β-lactam carbonyl and S–H stretching frequencies. The tricyclic lactam **26**, like its higher homologue **21**, was identified by its spectral data.

Since the reduced product **27b** was not detected in the reactions of either **7b** or **8b** with stannane, it is unlikely to be an intermediate in the formation of the thiol **29**. The tricyclic species **26** is also unlikely to lie on the pathway leading to **29** as attack of stannyl radicals at sulfur would be expected to result in fission of the bond to the azetidinone ring, the weaker of the two available C–S bonds. In addition, the stoichiometry of the reaction appears to preclude the intermediacy of either **26** or **27b** because 2 molar equiv of stannane would be required, whereas only 1.1 molar equiv was available.

Scheme VI



Scheme VII



We propose, therefore, that the formation of the thiol **29** involves 1,7-hydrogen atom migration between the aryl radical and the *tert*-butyl moiety of **25b** (Scheme VI), followed by rapid β-elimination of isobutylene to afford the thiyl radical **33**. The newly generated thiyl radical then undertakes hydrogen atom abstraction from stannane to afford **29** and a stannyl radical which maintains chain propagation. In support of this hypothesis, treatment of **7b** with Bu_3SnD afforded, after silica gel chromatography of the crude product, the thiol **29** (64%) in which no deuterium was incorporated into either the thiol or the aromatic ring. Also isolated was the tricyclic species **26** (ca. 1%). Any deuterium in the thiol moiety would undoubtedly have undergone proton exchange when **29** was subjected to column chromatography. The key byproduct in the β-elimination step (**32** → **33**), isobutylene, was isolated as its 1,2-dibromide upon passing of the effluent gas through a bromine–carbon tetrachloride solution when the mixture was purged with nitrogen, and was identified by comparison with an authentic sample by gas chromatography.

Since the dethiolated product **30** was obtained only when the iodoarene **8b** was used as substrate, we propose that the mechanism of its formation probably involves a reaction between thiol **29** and tributyltin iodide. Indeed, when **29** was treated consecutively with the latter (prepared in situ from tributylstannane and iodobenzene) and stannane, the only product obtained was **30** (88%).

Cyclization of Pyrrolidinone Substrates. Since the reactions of **4a,b**, **7a,b**, and **8a,b** with Bu_3SnD demonstrated the utility of this reagent for detecting the occurrence of intramolecular hydrogen atom transfer processes, we chose to employ similar methods for studying reactions of the pyrrolidinone substrates **11a,b** and **14**. When the *tert*-butyl sulfide **11b** was treated with Bu_3SnD (0.03 M) in boiling benzene, the major product isolated was the oxopyrrolidine-2-thione **36** in 65% yield. The reaction also afforded the product **37b** (4%) of direct reduction and the tricyclic compound **38** (25%). The (methylthio)-pyrrolidinone **11a**, upon similar treatment, gave the thione **36** (34%), the tricyclic product **38** (7%), and an inseparable mixture of the deuteriated compounds **37a** (7%), **39a** (36%), and **41** (8%) as determined by ^2H NMR. The thioimide **36** and the cyclized product **38** were also identified by their spectral data. The characteristic features

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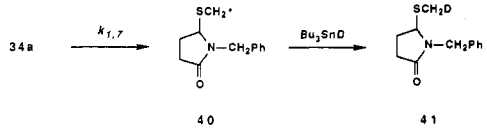
(21) Ingold, K. U. In *Free Radicals*; Kochi, J. K., Ed.; Wiley-Interscience: New York, 1973; Vol. 1, p 37.
(22) Baldwin, J. E.; Abraham, E. P.; Adlington, R. M.; Crimmin, M. J.; Field, L. D.; Jayatilake, G. S.; White, R. L.; Usher, J. J. *Tetrahedron* **1984**, *40*, 1907. Chung, S. K.; Shankaranarayan, R.; Scott, A. I. *Tetrahedron Lett.* **1983**, *24*, 2941. Brian, E. G.; Broom, N. J. P.; Hickling, R. I. *J. Chem. Soc., Perkin Trans. 1* **1981**, 982.
(23) The thiobenzoate was prepared by treating **25** with benzoyl chloride in dry carbon tetrachloride.

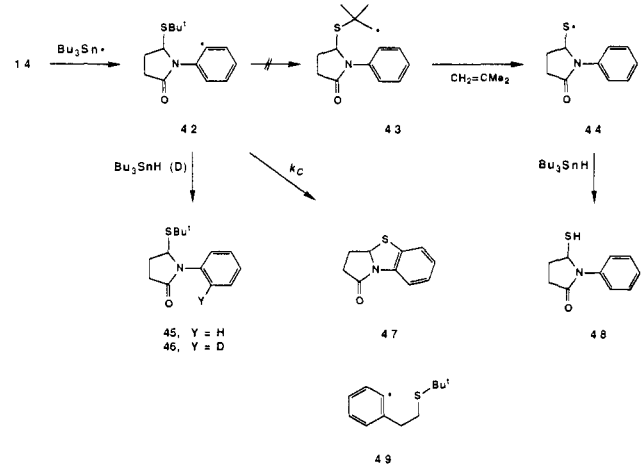
Table I. Yields of Products from Intramolecular S_H2 at Sulfur

reactants		products (yields, %)		
		cyclized	reduced	recovered, %
4a	Bu_3SnH	**21** (21)	**19a** (46)	5
4b	Bu_3SnH	**21** (42)	**19b** (16)	17
4c	Bu_3SnH		**19c** (40)	42
4a	Bu_3SnD	**21** (21)	**20a** (11), **22a** (35), **22b** (15)	–
4b	Bu_3SnD	**21** (35)	**20b** (26)	4
7a	Bu_3SnH		**27a** (70)	6
7b	Bu_3SnH		**29** (60)	10
8b	Bu_3SnH	**26** (1)	**29** (42), **30** (17)	–
7a	Bu_3SnD		**31** (95)	–
8b	Bu_3SnD	**26** (1)	**29** (64)	–
11a	Bu_3SnD	**38** (7)	**37a** (7), **36** (34), **39a** (35), **41** (3)	–
11b	Bu_3SnD	**38** (25)	**37b** (4), **36** (65)	–
14	Bu_3SnH	**47** (45)	**45** (21)	–
14	Bu_3SnD	**47** (89)		–

Scheme VIII



Scheme IX



of the ^{13}C NMR spectrum of **36** include an amide carbonyl at δ 178.6, a thiocarbonyl resonance at δ 210.3, and four aromatic carbon resonances indicative of a monosubstituted aromatic ring.

The formation of **37a** and **37b** must involve deuterium atom transfer to the respective aryl radicals (**34a,b**) from Bu_3SnD while the most likely route to the thione **36** appears to be by β-elimination of methyl or *tert*-butyl radical from **35a** or **35b**, the species generated by 1,5-intramolecular hydrogen atom transfer in **34a** and **34b** (Scheme VII). It is noteworthy that the yield of **36** from **11a** is lower than that from **11b**, while the former affords a deuteriated compound **39a**, whereas the latter does not afford its analogue, **39b**. These results are consistent with the expected effect of the strengths of the R–S bonds on the relative rates of the competing processes open to **35a** and **35b**, namely, β-fission or deuterium atom transfer from Bu_3SnD. In **35b**, the S–*t*-Bu bond is sufficiently weak to cause β-fission to be the kinetically dominant process, but in **35a** the rate of fission of the stronger S–Me bond is slow enough to allow deuterium atom transfer (**35a** → **39a**) to compete. The isolation of **39a** also provides evidence for the intermediacy of **35b** on the pathway to **36b**, while the formation of **41** clearly involves the intermediacy of the radical **40** generated by 1,7-hydrogen atom transfer (Scheme VIII).

N-(*o*-Bromophenyl)pyrrolidinone **14**, when treated with Bu_3SnD (0.03 M), behaved very differently from its higher homologue **11b**. Only the tricyclic product **47** (89%) was isolated, and no evidence was obtained for deuterium atom transfer either directly or after intramolecular hydrogen atom transfer, i.e., neither **46** nor the thiol **48** could be detected. In order to estimate the rate constant for the cyclization step **42** → **47**, we repeated the reaction with Bu_3SnH at higher concentration. When $[Bu_3SnH]$ = 0.5 M, the products obtained were **45** and **47** in yields of 21% and 45% respectively.

Kinetic Results. The results presented above show that the various radicals studied, although superficially similar in that they are all aryl radicals and all contain a sulfur atom available for S_H2 attack, in fact exhibit a wide range of behavior and reactivity. In an attempt to probe the underlying bases for the observed differences, we have made estimates of the rate constants for some of the reactions.

In all of the mechanisms outlined in Schemes IV, V, and VII–IX, unimolecular processes involving ring closure or intramolecular hydrogen atom transfer compete directly with atom transfer from Bu_3SnH or Bu_3SnD. Under these circumstances, the rate constant, k_1, for the unimolecular process is related to that, k_2, for the bimolecular transfer by the equation

$$k_1/k_2 = R/U \times [S]_m$$

where R/U is the ratio of yields of the rearranged and unrearranged products, and $[S]_m$ is the effective concentration of stannane, taken in this case to be equal to the mean stannane concentration.[24] It has thus been possible to derive from our data approximate values of k_r/k_H and k_r/k_D where k_r, k_H, and k_D are the respective rate constants for rearrangement by cyclization or by intramolecular atom transfer, for hydrogen atom transfer from Bu_3SnH to an aryl radical, and for deuterium transfer from Bu_3SnD to an aryl radical. The results are given in Table II. Also given is a list of relative rate constants based (i) on the known deuterium isotope effect for hydrogen atom transfer from stannane to aryl radicals, viz., k_H/k_D = 1.3,[26] (ii) on the assumption that k_H and k_D will not vary in value between the various aryl radicals, (iii) on the assumption that the methods used would have allowed the detection of *U*

(24) The approximate expression used here gives values of rate constants that do not differ appreciably from those obtained by means of the more accurate iterative method based on the appropriate integrated rate equation.[25]

(25) Beckwith, A. L. J.; Moad, G. *J. Chem. Soc., Chem. Commun.* **1974**, 472. Beckwith, A. L. J.; Giara, W. B. *J. Chem. Soc., Perkin Trans. 2* **1975**, 795.

(26) Abeywickrema, A. N.; Beckwith, A. L. J. *J. Chem. Soc., Chem. Commun.* **1986**, 464.

Table II. Kinetic Data[a] for Radical Cyclizations and H· Transfers

entry	substrate	reaction	type	yield,[b] % R	yield,[b] % U	k_r/k_H	k_r/k_D	k_{rel}[c]
1	**4b**	**16b** → **21**	1,6-S-*t*-Bu	42	16	4×10^{-2}		3
2	**4a**	**16a** → **21**	1,6-SMe	21	11		3×10^{-2}	2
3	**11b**	**34b** → **38**	1,6-S-*t*-Bu	25	4		9×10^{-2}	6
4	**11a**	**34a** → **38**	1,6-SMe	7	7		1.5×10^{-2}	1
5	**8b**	**25b** → **26**	1,5-S-*t*-Bu	1	0		$>8 \times 10^{-3}$	>0.5
6	**14**	**42** → **47**	1,5-S-*t*-Bu	89	0		$>7 \times 10^{-1}$	>40
7	**14**	**42** → **47**	1,5-S-*t*-Bu	45[d]	21[d]	5×10^{-1}		40
8	**4b**	**16b** → *e*	1,5-H	0	26		$<1 \times 10^{-3}$	<0.07
9	**4a**	**16a** → **24**	1,5-H	15	11		2×10^{-2}	1
10	**4a**	**16a** → **23**	1,7-H	35	11		5×10^{-2}	1
11	**11b**	**34b** → **35b**	1,5-H	65	4		2.5×10^{-1}	16
12	**11a**	**34a** → **35a**	1,5-H	70	7		1.5×10^{-1}	10
13	**11a**	**34a** → **40**	1,7-H	8	7		1.7×10^{-2}	0.4
14	**7b**	**25b** → **32**	1,7-H	64	0		$>5 \times 10^{-1}$	>3
15	**7a**	**25a** → *f*	1,6-H	95	0		$>7 \times 10^{-1}$	>15

[a] $[Bu_3SnH]_{mean}$ or $[Bu_3SnD]_{mean}$ = 0.015 M except where otherwise specified. [b] R = rearranged; U = direct reduction product. [c] Corrected for statistical factors where appropriate; rate constants are relative to that for **34a** → **38**. [d] $[Bu_3SnH]_{mean}$ = 0.25 M in this experiment. [e] *S*-tert-Butyl analogue of **24**. [f] *N*-Phenyl analogue of **23**.

(direct reduction product) whenever it was formed in >1% yield, and (iv) on the application of a statistical factor in intramolecular transfer reactions to allow for the number of equivalent available hydrogen atoms. The resultant values of k_{rel} have been set on a scale in which the rate constant for the reaction **34a** → **38** has been arbitrarily set at 1. Since the rate constants have been derived from isolated yields and not from accurate analyses of product mixtures, they are subject to large uncertainties. However, even in the "worst case" situation where unrecovered material is attributed solely to decomposition of just one of the products during workup, the uncertainty in calculated rate constants is <100%. Consequently the large differences in relative rate constants given in Table II are authentic; they reveal some interesting and significant trends.

Consider first the various intramolecular transfer processes. Although simple comparison of the yields of **22a** and **22b** (see Table I) isolated from reactions of **4a** suggest that radical **23** is formed from **16a** more readily than is **24**, the statistically corrected data shows the relative rate constants to be approximately equal (cf. entries 9 and 10). Nevertheless, this is an unexpected observation[16,19] as 1,5-hydrogen atom transfers usually proceed much more readily than 1,7, and it appears, therefore, that in this case the effect of the azetidinone ring on molecular architecture is of prime importance. Despite NMR evidence to the contrary,[27] the general view, based on X-ray crystallographic studies,[28] is that the N atom in azetidinones lies very close to the plane of its substituents. In the case of radical **16a**, planarity of the nitrogen center prevents the molecule from attaining a strain-free transition structure for 1,5-hydrogen atom transfer, but has little effect on that for the 1,7-process. Examination of models indicates that similar impediments do not apply to the radical **34a**, in which the presence of the pyrrolidinone system allows the ring proton and the aryl radical center to be brought into close juxtaposition. In this case the normal entropic effects apply, and 1,5-hydrogen atom transfer occurs more rapidly than 1,7 (cf. entries 12 and 13).

Only lower limits could be estimated for the rates of the 1,7- and 1,6-transfers undergone by the radicals **25b** and **25a** respectively (entries 14 and 15) because the yields of unrearranged products were below detection limits. However, it is clear that these reactions are relatively fast. Once again, inspection of models reveals that the required disposition of reactive centers can be readily attained, although it is not clear why 1,7-transfer should occur more readily in **25b** (entry 14) than it does in **16a** (entry 10). A significant consequence of the rapidity of these reactions is that they dominate the behavior of radicals **25a** and **25b** and so virtually preclude the formation of other types of products. Thus the very low yield of the cyclized product **26** obtained from **8b** is not so much an indication of the sluggishness of the transformation **25b** → **26** as of the rapidity of **25b** → **32**.

Of the cyclization reactions, those involving radicals containing a pyrrolidinone ring system conform to expectation in that 1,5-ring closure is more rapid than 1,6 (cf. entries 7 and 3). Also, the value of k_r/k_H for the former is similar in magnitude to those for more simple aryl radicals.[7,29] Similarly, in all of the systems studied, cyclizations involving fission of a S–*t*-Bu bond occurred more rapidly than those involving S–Me bond fission. This is as expected on the basis of the relative stabilities of the alkyl radicals formed and has precedent in other intramolecular substitutions at sulfur.[29,30]

Although it has not been possible to obtain an accurate figure for cyclization to give a five-membered ring fused to the azetidinone system (**25b** → **26**), it seems probable that this process is much slower than the analogous reaction in the pyrrolidinone series (**42** → **47**). As in the case of atom transfer, this low reactivity is attributable to the effect of the β-lactam ring on molecular architecture, since models show that the collinear arrangement required for S_H2 displacement[7] cannot be attained unless the ring nitrogen is deformed from its planar configuration. This source of strain energy in the transition structure does not apply to the *N*-benzyl systems **16a** and **16b**, in which the flexibility associated with the methylene group allows the aryl radical center and the S–R bond to readily attain the required disposition.

Because of doubts raised about the accuracy of published values of k_H,[31] it is not possible to give firm values for the rate constants of the various unimolecular processes

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(29) Beckwith, A. L. J.; Best, W.; Boate, D. R.; Munaweera, S., unpublished observations.
(30) Franz, J. A.; Roberts, D. H.; Ferris, K. F. *J. Org. Chem.* **1987**, *52*, 2256.
(31) We have been informed by Prof. Ingold that the values for k_H given in ref 32 are probably in error.

set out in Table II. However, recent work in these laboratories[33] indicates that k_H at 80 °C is about 3×10^8 s^{-1}, in which case k_r for the cyclization **42** → **47** is about 1.5×10^8 s^{-1} at 80 °C. The close similarity of this value to that for ring closure of the more simple system **49**[7,29] is consistent with the conclusion, based upon inspection of models, that the presence of the pyrrolidinone ring in **42** imposes no particular impediment to the formation of the transition structure for cyclization. We have been unable to make a more precise estimate of the strain energies of the various transition structures[34] because of the unavailability of necessary force-field data. However, the usual MM2 calculations[34] indicate that the increase in strain energy accompanying ring formation is relatively small, e.g., about 6 kcal/mol for the changes **42** → **47** and **34b** → **38**.

Conclusion

The tricyclic pyrrolidinones **38** and **47** and the fused azetidinone **21** can be readily prepared in fair to good yield from suitable sulfides of various *N*-(*o*-haloaryl)- or *N*-(*o*-halobenzyl)azetidinones and -pyrrolidinones by treatment with Bu_3SnH or Bu_3SnD. The latter reagent allows the occurrence of various intramolecular hydrogen atom transfers to be detected. In the case of the *N*-(*o*-haloaryl)azetidinones **7a,b** and **8b**, such transfers dominate the behavior of the intermediate radicals **25a** and **25b**. The differences in relative rate constants can be rationalized on steric grounds. In particular, both 1,5-ring closure and 1,6-atom transfer are disfavored in the azetidinone systems, in which the required transition structures cannot be attained without deformation of the ring nitrogen from its preferred planar configuration. Rate constants for ring closure and atom transfer in the pyrrolidinone systems appear to be similar in value to those observed for related aryl radicals.

Experimental Section

Melting points were determined on a Reichert hot-stage microscope. Melting and boiling points are uncorrected. IR spectra were measured on a Perkin-Elmer 683 spectrophotometer. ^1H and ^{13}C NMR spectra were recorded on a JEOL FX 200 spectrometer operating at 200 and 50 MHz respectively. ^2H NMR spectra were measured on a Bruker CXP 200 spectrometer operating at 30.7 MHz. GLC analyses were carried out on a Varian 6000 chromatograph equipped with a Hewlett-Packard 3390A electronic integrator. The columns used were as follows: A, 2.0 m × 3.2 mm SE-30 (3%) on Chromosorb W (100–120 mesh); B, 2.0 m × 3.2 mm Carbowax (5%) on Chromosorb W (60–80 mesh); and C, 2.0 m × 3.2 mm Apiezon L (10%) on Chromosorb W (60–80 mesh). Merck Kieselgel 60 was used for flash chromatography and Merck LiChroprep Si60 (40–63 μm) columns were used for MPLC (medium-pressure liquid chromatography) separations. Benzene was washed with sulfuric acid and with water, then dried, distilled, and stored over molecular sieves. Tributyltin hydride (Aldrich) was stored under nitrogen in the freezer. Tributyltin deuteride, prepared by LAD reduction of Bu_3SnCl, was similarly stored and handled. Zinc borohydride was prepared as previously described.[35] *o*-Bromobenzylamine and *o*-iodobenzylamine were prepared from the corresponding *o*-halobenzyl bromides and potassium phthalimide[10] by the Gabriel synthesis.[11]

The *N*-(*o*-bromobenzyl)- and *N*-(*o*-halophenyl)azetidinones **4**, **7**, and **8** were prepared from the respective chloro amides **3**, **5**, and **6** by similar methods. The synthesis of **4c** (from **1c** via **3c**) is described in detail. Any deviations from this general route are detailed under the specific chemical heading.

***N*-(*o*-Bromobenzyl)-3-chloro-2,2-dimethyl-3-(phenylthio)propanamide (3c).** *N*-Chlorosuccinimide (NCS) (163 mg, 1.22 mmol) was added to a solution of **1c** (267 mg, 1.02 mmol, prepared from 2,2-dimethylpropanoic acid[23]) in CCl_4 (8 mL). The mixture was stirred for 4 h at 60 °C, then cooled to room temperature, and filtered. The precipitate of succinimide was washed with CCl_4 (2 × 10 mL) and the solvent removed under vacuum to afford the α-chloro sulfide **2c**: ^1H NMR ($CDCl_3$) δ 1.46 (3 H, s, Me), 1.50 (3 H, s, Me), 5.44 (1 H, s, CHCl), 7.20–7.75 (5 H, m, Ar H). Without further purification, **2c** was dissolved in dry CCl_4 (20 mL) and added to a cooled (0 °C) mixture of *o*-bromobenzylamine (232 mg, 1.25 mmol) and triethylamine (124 mg, 1.25 mmol). The cooled mixture was stirred for 0.5 h, filtered, and then concentrated to afford **3c** as an oil (380 mg, 92%): ^1H NMR ($CDCl_3$) δ 1.42 (6 H, s, 2Me), 4.51 (2 H, d, J = 6 Hz, NCH_2), 5.71 (1 H, s, CHCl), 6.84 (1 H, br s, NH), 7.00–7.53 (9 H, m, Ar H); exact mass calcd for $C_{18}H_{19}BrClNOS$ m/z 411.0059, found 411.0047.

***N*-(*o*-Bromobenzyl)-4-(phenylthio)-3,3-dimethyl-2-azetidinone (4c).** A mixture of the preceding amide (350 mg, 0.85 mmol), powdered potassium hydroxide (74 mg, 1.32 mmol), 18-crown-6 ether (84 mg, 0.32 mmol), and dry benzene (25 mL) was stirred at ambient temperature for 4 h, filtered, and then concentrated. The residue was subjected to MPLC (CH_2Cl_2/ethyl acetate, 19:1) to afford **4c** as an oil, which crystallized from hexane (249 mg, 78%): mp 62–64 °C; ^1H NMR ($CDCl_3$) δ 1.40 (6 H, s, 2Me), 4.30 (1 H, d, J = 16 Hz, NCH), 4.59 (1 H, s, CHS), 4.68 (1 H, d, J = 16 Hz, NCH), 7.05–7.32 and 7.48–7.54 (9 H, 2 m, Ar H); ^{13}C NMR ($CDCl_3$) δ 18.7 (Me), 21.7 (Me), 43.9 (CH_2), 56.6 (quat), 73.7 (CH), 123.2, 127.4, 129.1, 130.1, 131.7, 132.8, 133.6, 134.3 (Ar), 171.9 (carbonyl); IR (Nujol) ν_{max} 1755 cm^{-1}. Anal. Calcd for $C_{18}H_{18}BrNOS$: C, 57.4; H, 4.8; N, 3.7. Found: C, 57.3; H, 4.8; N, 4.0.

***N*-(*o*-Bromobenzyl)-3-chloro-2,2-dimethyl-3-(methylthio)propanamide (3a).** A solution of 3-chloro-2,2-dimethylpropanoic acid[36] (20 g, 147 mmol) in dry dimethylformamide (50 mL) was added dropwise to a cooled (0 °C) mixture of methanethiol (11 g, 229 mmol), powdered sodium hydroxide (23.4 g, 585 mmol), and dry dimethylformamide (55 mL). The mixture was stirred for 9 h at 0 °C and then overnight at ambient temperature. It was then diluted with water, acidified (pH 1–2) with dilute sulfuric acid, and extracted with hexane. The extract was dried, the hexane evaporated, and the residue distilled to afford 2,2-dimethyl-3-(methylthio)propanoic acid (10.5 g, 48%): bp 134–136 °C (14 mm); ^1H NMR ($CDCl_3$) δ 1.26 (6 H, s, 2Me), 2.13 (3 H, s, SMe), 2.73 (2 H, s, CH_2S), 10.83 (1 H, br s, COOH); exact mass calcd for $C_6H_{12}O_2S$ m/z 148.0558, found 148.0556.

The preceding acid was converted into its acid chloride, **1a**, by treatment with thionyl chloride in the usual way. Consecutive treatment of **1a** (194 mg, 1.17 mmol) with NCS (187 mg, 1.40 mmol) for 1.5 h at 40 °C and then with *o*-bromobenzylamine (257 mg, 1.39 mmol) as described above gave **3a** as an oil (318 mg, 85%): ^1H NMR ($CDCl_3$) δ 1.38 (6 H, s, 2Me), 2.29 (3 H, s, SMe), 4.50 (2 H, d, J = 6 Hz, NCH_2), 5.45 (1 H, s, CHCl), 6.76 (1 H, br s, NH), 7.05–7.57 (4 H, m, Ar H); exact mass calcd for $C_{13}H_{17}BrClNOS$ m/z 348.9903, found 348.9889.

***N*-(*o*-Bromobenzyl)-3,3-dimethyl-4-(methylthio)-2-azetidinone (4a).** Lactamization of **3a** (268 mg, 0.76 mmol) with potassium hydroxide (91 mg, 1.63 mmol) and 18-crown-6 ether (77 mg, 0.29 mmol) gave **4a** as an oil (148 mg, 62%): ^1H NMR ($CDCl_3$) δ 1.28 (3 H, s, Me), 1.36 (3 H, s, Me), 1.97 (3 H, s, SMe), 4.29 (1 H, s, CHS), 4.35 (1 H, d, J = 16 Hz, NCH), 4.72 (1 H, d, J = 16 Hz, NCH), 7.00–7.40 and 7.45–7.63 (4 H, 2 m, Ar H); ^{13}C NMR ($CDCl_3$) δ 15.2 (SMe), 18.2 (Me), 21.9 (Me), 43.7 (CH_2), 56.3 (quat), 72.5 (CH), 123.7, 127.7, 129.4, 130.2, 133.0, 134.6 (Ar), 172.4 (carbonyl); IR (neat) ν_{max} 1755 cm^{-1}; exact mass calcd for $C_{13}H_{16}BrNOS$ m/z 313.0136, found 313.0139.

***N*-(*o*-Bromobenzyl)-3-[(1,1-dimethylethyl)thio]-3-chloro-2,2-dimethylpropanamide (3b).** A solution of 3-chloro-2,2-dimethylpropanoic acid[36] (12.0 g, 88 mmol) in dry

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dimethylformamide (10 mL) was added to a mixture of *tert*-butyl mercaptan (7.9 g, 88 mmol), powdered sodium hydroxide (7.1 g, 177 mmol), and dimethylformamide (30 mL). The mixture was stirred at 60 °C for 16 h, diluted with water, then acidified (pH 2) with dilute hydrochloride acid, and extracted with hexane. The extract was washed with water, dried, and then concentrated to afford 3-[(1,1-dimethylethyl)thio]-2,2-dimethylpropanoic acid (11.4 g, 68%), which crystallized from petroleum ether (bp 80–100 °C): mp 65–70 °C; ^{1}H NMR ($CDCl_3$) δ 1.29 (6 H, s, 2Me), 1.31 (9 H, s, M_3C), 2.75 (2 H, s, CH_2) 10.43 (1 H, br s, CO_2H). Anal. Calcd for $C_9H_{18}O_2S$: C, 56.8; H, 9.5. Found: C, 57.0; H, 9.7.

The preceding acid was converted into its acid chloride, **1b**, in the usual way. Consecutive treatment of **1b** (208 mg, 3.60 mmol) with NCS (525 mg, 3.95 mmol) for 40 min at 0 °C and then with *o*-bromobenzylamine (732 mg, 3.93 mmol) gave **3b** as an oil (1.0 g, 88%): ^{1}H NMR ($CDCl_3$) δ 1.33 (12 H, s, Me and Me_3C), 1.44 (3 H, s, Me), 4.53 (2 H, d, J = 6 Hz, NCH_2), 5.56 (1 H, s, CHCl), 6.37 (1 H, br s, NH), 7.10–7.60 (4 H, m, Ar H); exact mass calcd for $C_{16}H_{23}ClBrNOS$ m/z 391.0372, found 391.0380.

***N*-(*o*-Bromobenzyl)-4-[(1,1-dimethylethyl)thio]-3,3-dimethyl-2-azetidinone (4b).** Treatment of **3b** (800 mg, 2.04 mmol) with KOH (572 mg, 10.2 mmol) and 18-crown-6 ether (108 mg, 0.41 mmol) gave **4b** as an oil (242 mg, 33%): ^{1}H NMR ($CDCl_3$) δ 1.17 (9 H, s, Me_3C), 1.26 (3 H, s, Me), 1.39 (3 H, s, Me), 4.28 (1 H, s, CHS), 4.29 (2 H, d, J = 16 Hz, NCH), 4.68 (2 H, d, J = 16 Hz, NCH), 7.10–7.23, 7.30–7.36, and 7.53–7.60 (4 H, m, ArH); ^{13}C NMR ($CDCl_3$) δ 19.5 (Me) 21.5 (Me), 31.3 (3Me), 42.7 (CMe_3), 42.9 (CH_2), 56.2 (CMe_2), 67.3 (CH), 123.1, 127.5, 129.1, 129.9, 132.9, 134.8 (Ar), 172.6 (carbonyl); IR (neat) ν_{max} 1755 cm^{-1}; exact mass calcd for $C_{16}H_{22}BrNOS$ m/z 355.0605, found 355.0605.

***N*-(*o*-Bromophenyl)-3-chloro-2,2-dimethyl-3-(methylthio)propanamide (5a).** Consecutive treatment of **1a** (483 mg, 2.91 mmol) with NCS (426 mg, 3.20 mmol) for 1.5 h at ambient temperature and then with *o*-bromoaniline (509 mg, 2.96 mmol) for 3 h gave the required amide as an oil. Due to its instability, the amide was not isolated, but was used immediately.

***N*-(*o*-Bromophenyl)-3,3-dimethyl-4-(methylthio)-2-azetidinone (7a).** Treatment of the preceding amide with KOH (447 mg, 7.97 mmol) and 18-crown-6 (91 mg, 0.34 mmol) gave **7a** as an oil (243 mg, 28%): ^{1}H NMR ($CDCl_3$) δ 1.40 (3 H, s, Me), 1.54 (3 H, s, Me), 2.02 (3 H, s, SMe), 5.17 (1 H, s, CHS), 7.00–7.66 (4 H, m, Ar H); IR (neat) ν_{max} 1760 cm^{-1}; exact mass calcd for $C_{12}H_{14}BrNOS$ m/z 298.9979, found 298.9980.

***N*-(*o*-Bromophenyl)-3-[(1,1-dimethylethyl)thio]-3-chloro-2,2-dimethylpropanamide (5b).** Consecutive treatment of **1b** (514 mg, 2.47 mmol) with NCS (360 mg, 2.71 mmol) for 40 min at 0 °C and then with *o*-bromoaniline (436 mg, 2.53 mmol) for 5 h at reflux gave **5b** as an oil, which was not isolated, but was used immediately.

***N*-(*o*-Bromophenyl)-4-[(1,1-dimethylethyl)thio]-3,3-dimethyl-2-azetidinone (7b).** The preceding amide upon treatment with KOH (430 mg, 7.66 mmol) and 18-crown-6 (113 mg, 0.43 mmol) afforded **7b** (394 mg, 47%): mp 82–82 °C; ^{1}H NMR ($CDCl_3$) δ 1.41 (9 H, s, Me_3C), 1.33 (3 H, s, Me), 1.48 (3 H, s, Me), 5.15 (1 H, s, CHS), 7.20–7.32 and 7.46–7.62 (4 H, 2 m, ArH); IR (CH_2Cl_2) ν_{max} 1763 cm^{-1}; exact mass calcd for $C_{15}H_{20}BrNOS$ m/z 341.0449, found 341.0421.

3-[(1,1-Dimethylethyl)thio]-3-chloro-2,2-dimethyl-*N*-(*o*-iodophenyl)propanamide (6b). Consecutive treatment of **1b** (1.79 g, 8.60 mmol) with NCS (1.26 g, 9.46 mmol) for 40 min at 0 °C and then with *o*-iodoaniline (1.89 g, 8.63 mmol) for 5 h at reflux gave **6b**, which was not isolated.

4-[(1,1-Dimethylethyl)thio]-3,3-dimethyl-*N*-(*o*-iodophenyl)-2-azetidinone (8b). The titel compound was prepared from the preceding amide, KOH (600 mg, 10.7 mmol), and 18-crown-6 (581 mg, 2.20 mmol) as described above. The residue was subjected to flash chromatography (hexane/CH_2Cl_2, 3:2) to afford **8b** as an oil (2.01 g, 60%): ^{1}H NMR ($CDCl_3$) δ 1.13 (9 H, s, Me_3C), 1.35 (3 H, s, Me), 1.54 (3 H, s, Me), 5.18 (1 H, s, CHS), 6.80–7.18, 7.20–7.32, and 7.67–7.83 (4 H, m, Ar H); ^{13}C NMR ($CDCl_3$) δ 19.3 (Me)8 21.3 (Me), 31.6 (3Me), 43.2 (CMe_3), 56.2 (CMe_2), 70.0 (CH), 122.3, 126.4, 128.9, 130.1, 130.9, 139.3 (Ar), 171.1 (carbonyl); IR (neat) ν_{max} 1760 cm^{-1}; exact mass calcd for $C_{15}H_{20}INOs$ m/z 389.0310, found 389.0309.

***N*-(*o*-Bromobenzyl)succinimide (9a).** Succinimide (3.7 g, 37 mmol) was added to a cooled (0 °C) mixture of KOH (2.3 g, 41 mmol) and DMF (40 mL). The cooled mixture was stirred for 1.75 h, and then a solution of *o*-bromobenzyl bromide (9.3 g, 37 mmol) in DMF (2 mL) was added over 2 min. The resultant mixture was stirred at ambient temperature for 5 h, then poured into water, and extracted with diethyl ether. The extract was washed with 2 N sodium hydroxide, saturated aqueous ammonium chloride, and water, then dried, and concentrated. The residue was subjected to MPLC (CH_2Cl_2) to afford **9a**, which crystallized from CH_2Cl_2/hexane (7.4 g, 74%): mp 98–100 °C; ^{1}H NMR ($CDCl_3$) δ 2.73 (4 H, s, CH_2CH_2), 4.67 (2 H, s, NCH_2), 6.89–7.53 (4 H, m, Ar H). Anal. Calcd for $C_{11}H_{10}BrNO_2$: C, 49.3; H, 3.8; N, 5.2. Found: C, 49.2; H, 3.7; N, 5.2.

***N*-(*o*-Iodobenzyl)succinimide (9b).** The title compound was prepared from succinimide (1.8 g, 18 mmol), KOH (12.2 g, 21 mmol), and *o*-iodobenzyl chloride (4.5 g, 18 mmol) as described above. The residue isolated from the extract was recrystallized from CH_2Cl_2/hexane to afford **9b** (3.6 g, 64%): mp 142–145 °C; ^{1}H NMR ($CDCl_3$) δ 2.81 (4 H, s, CH_2CH_2), 4.73 (2 H, s, NCH_2), 6.77–7.48 and 7.72–7.90 (4 H, 2 m, Ar H). Anal. Calcd for $C_{11}H_{10}INO_2$: C, 41.9; H, 3.2; N, 4.5. Found: C, 41.7; H, 3.2; N, 4.5.

***N*-(*o*-Bromobenzyl)-5-ethoxy-2-pyrrolidinone and *N*-(*o*-Bromobenzyl)-5-hydroxy-2-pyrrolidinone.** Sodium borohydride (960 mg, 25.4 mmol) and *N*-(*o*-bromobenzyl)succinimide (760 mg, 2.8 mmol) were added to cooled (dry ice/CCl_4) absolute ethanol (250 mL). The cooled mixture was stirred for 4.5 h, during which time two or three drops of 2 N hydrochloric acid (in methanol) were added every 15 min. The temperature of the mixture was allowed to fluctuate between −20 and −10 °C during the addition of the hydrochloric acid. After the mixture had been stirred for 4.5 h, 2 N hydrochloric acid was added until the mixture reached pH 3. The resultant mixture was sitrred for an additional 1 h at 5 °C, then poured into water, and extracted with CH_2Cl_2. The extracts were dried and concentrated to afford a mixture of the title compounds, which was not separated but was used to prepare **11a**.

5-Ethoxy-*N*-(*o*-iodobenzyl)-2-pyrrolidinone and 5-Hydroxy-*N*-(*o*-iodobenzyl)-2-pyrrolidinone. The title compounds were prepared from *N*-(*o*-iodobenzyl)succinimide (420 mg, 1.3 mmol), sodium borohydride (720 mg, 19.1 mmol), and absolute ethanol (130 mL) as described above. The crude product mixture was not separated but was used to prepare **11b**.

***N*-(*o*-Bromobenzyl)-5-(methylthio)-2-pyrrolidinone (11a).** A solution of the mixture of **10a** and the corresponding alcohol in dry CH_2Cl_2 (10 mL) was added to a solution of *p*-toluenesulfonic acid (17 mg, 0.09 mmol) and methanethiol (890 mg, 18.5 mmol) in CH_2Cl_2 (6 mL). The mixture was stirred for 0.5 h at ambient temperature and then concentrated, and the residue was chromatographed [MPLC (CH_2Cl_2/ethyl acetate, 4:1)] to afford **11a** as an oil (1.1 g, 88%): ^{1}H NMR ($CDCl_3$) δ 1.96 (3 H, s, MeS), 2.18–2.32 and 2.41–2.63 (4 H, 2 m, CH_2CH_2), 4.37 (1 H, d, J = 15 Hz, NCH), 4.48 (1 H, m, NCHS), 5.01 (1 H, d, J = 15 Hz, NCH), 7.06–7.21, 7.26–7.31, and 7.50–7.61 (4 H, 3 m, Ar H); ^{13}C NMR ($CDCl_3$) δ 10.5 (SMe), 26.0 (CH_2CH), 2.95 (CH_2CO), 43.6 (NCH_2), 63.4 (CH), 123.3, 127.3, 128.9, 129.6, 132.8, 134.9 (Ar), 173.9 (carbonyl). Anal. Calcd for $C_{12}H_{14}BrNOS$: C, 48.0; H, 4.7; N, 4.5. Found: C, 48.0; H, 4.7; N, 4.7.

5-[(1,1-Dimethylethyl)thio]-*N*-(*o*-iodobenzyl)-2-pyrrolidinone (11b). The title compound was prepared from *tert*-butyl mercaptan (650 mg, 7.2 mmol) and the mixture of **10b** with the corresponding alcohol as described above, to afford **11b** (356 mg, 70%): mp 107–109 °C; ^{1}H NMR ($CDCl_3$) δ 1.21 (9 H, s, Me_3C), 2.18–2.76 (4 H, m, $COCH_2CH_2$), 4.28 (1 H, d, J = 16 Hz, NCH), 4.47 (1 H, d, J = 7 Hz, CHS), 4.87 (1 H, d, J = 16 Hz, NCH), 6.88–7.15, 7.27–7.40, and 7.77–7.86 (4 H, 3 m, Ar H); ^{13}C NMR ($CDCl_3$) δ 28.8 (CH_2CH), 30.6 (CH_2CO), 31.2 (3Me), 43.5 (quat), 48.5 (NCH_2), 61.4 (CH), 128.0, 128.1, 128.9, 137.8, 138.6, 139.6 (Ar), 174.3 (carbonyl). Anal. Calcd for $C_{15}H_{20}INOS$: C, 46.3; H, 5.2; N, 3.6. Found: C, 46.2; H, 5.3; N, 3.5.

***N*-(*o*-Bromophenyl)succinimide (12).** A solution of succinic anhydride (3.0 g, 30 mmol) and *o*-bromoaniline (4.3 g, 25 mmol) in toluene (60 mL) was stirred under reflux for 2.5 h, cooled, and filtered to give crude succinamic acid (6.2 g, 92%). A mixture of this acid (6.2 g, 232 mmol), sodium acetate (6.2 g, 76 mmol), and acetic anhydride (60 mL) was stirred at 70–80 °C for 4.5 h, then poured into water, and extracted with CH_2Cl_2. The extracts

were washed with saturated ammonium chloride, dried, and concentrated to afford **12**, which was recrystallized from CH_2Cl_2/hexane (5.4 g, 93%): mp 112–114 °C (lit.[37] mp 112–113 °C); ^1H NMR ($CDCl_3$) δ 2.90 (4 H, s, CH_2CH_2), 7.00–7.72 (4 H, m, Ar H).

Reduction of 12 with Sodium Borohydride. A mixture of **12** (520 mg, 2.1 mmol), sodium borohydride (820 mg, 21.7 mmol), and absolute ethanol (250 mL) was heated and then worked up as described above. The residue isolated from the CH_2Cl_2 extracts was subjected to MPLC (ethyl acetate) to afford **15**, which was recrystallized from CH_2Cl_2/hexane (500 mg, 93%): mp 65–67 °C; ^1H NMR ($CDCl_3$) δ 1.87–2.00 (2 H, m, CH_2CH_2OH), 2.57 (2 H, t, J = 7 Hz, CH_2CON), 3.12 (1 H, br s, OH), 3.72 (2 H, t, J = 6 Hz, CH_2OH), 6.89–7.01, 7.20–7.32, 7.46–7.55, and 8.12–8.25 (4 H, 4 m, Ar H), 7.90 (1 H, br s, NH). Anal. Calcd for $C_{10}H_{12}BrNO_2$: C, 46.5; H, 4.7; N, 5.4. Found: C, 46.6; H, 4.6; N, 5.6.

***N*-(*o*-Bromophenyl)-5-[(1,1-dimethylethyl)thio]-2-pyrrolidinone (14).** A solution of **12** (2.5 g, 9.9 mmol) in dry benzene (15 mL) was added to an ethereal solution of zinc borohydride (0.4 M, 248 mL, 99 mmol). The solution was stirred at ambient temperature for 24 h, and the excess of borohydride was then destroyed with dilute acetic acid. The aqueous solution was extracted with CH_2Cl_2, and the extract was washed with saturated sodium chloride, dried, and concentrated. The residue (presumably **13**) in CH_2Cl_2 (5 mL) was then added to a solution of *tert*-butyl mercaptan (2.2 mg, 0.1 mmol) in CH_2Cl_2 (10 mL). The solution was stirred for 0.5 h at room temperature and then washed with 2 N sodium hydroxide and water. The extract was dried and then concentrated, and the residue was subjected to flash chromatography (ethyl acetate/hexane, 11:9) to afford **14** as an oil (1.1 g, 34%), which crystallized on standing: mp 96–98 °C; ^1H NMR ($CDCl_3$) δ 1.07 (9 H, s, Me_3C), 2.20–2.97 (4 H, m, CH_2CH_2), 5.18 (1 H, dd, J = 4 and 7 Hz, CHS), 7.13–7.45 and 7.58–7.69 (4 H, 2 m, Ar H); ^{13}C NMR ($CDCl_3$) δ 29.8 (CH_2CH), 31.1 (CH_2CO), 31.2 (3Me), 43.9 (quat), 63.9 (CH), 122.9, 127.9, 129.8, 132.9, 133.3, 135.7 (Ar), 174.0 (carbonyl); exact mass calcd for $C_{14}H_{18}BrNOS$ m/z 327.0292, found 327.0297.

Free-Radical Cyclizations: General Procedure. A mixture of the halide, azobis(isobutyronitrile) (0.05 molar equiv), and either Bu_3SnH or Bu_3SnD (1.2 molar equiv) as a benzene solution of appropriate molarity (in each cyclization, the concentration of Bu_3SnH or Bu_3SnD was chosen so as to maximize the formation of cyclized product without sacrificing experimental convenience) was deaerated and refluxed under N_2 until the reaction was deemed to be complete (usually 4–18 h). The solvent was then removed in a rotary evaporator to afford crude product, which was purified or separated into its components by flash chromatography or MPLC with ethyl acetate/hexane or ethyl acetate/CH_2Cl_2 mixtures as eluants.

Cyclization of 4b with Bu_3SnH. Heating of **4b** (47 mg, 0.13 mmol) with Bu_3SnH (0.03 M) in benzene gave a separable mixture of unchanged starting material (8 mg, 17%) and *N*-benzyl-4-[(1,1-dimethylethyl)thio]-3,3-dimethyl-2-azetidinone (**19b**) (6 mg, 16%): ^1H NMR ($CDCl_3$) δ 1.19 (9 H, s, Me_3C), 1.24 (3 H, s, Me), 1.32 (3 H, s, Me), 3.98 (1 H, d, J = 15 Hz, NCH), 4.23 (1 H, s, CHS), 4.75 (1 H, d, J = 15 Hz, NCH), 7.27–7.42 (5 H, m, Ar H); ^{13}C NMR ($CDCl_3$) δ 19.5 (Me), 21.3 (Me), 31.5 (3Me), 42.4 (CH_2), 42.8 (CMe_3), 56.3 (CMe_2), 66.8 (CH), 127.5, 128.1, 128.7, 136.1 (Ar), 172.8 (carbonyl); IR (CH_2Cl_2) ν_{max} 1753 cm^{-1}; exact mass calcd for $C_{16}H_{23}NOS$ m/z 277.1500, found 277.1476.

Further elution of the column afforded 3,4-benzo-7,7-dimethyl-8-oxo-5-thia-1-azabicyclo[4.2.0]octane (**21**) (12 mg, 42%): ^1H NMR ($CDCl_3$) δ 1.27 (3 H, s, Me), 1.45 (3 H, s, Me), 4.13 (1 H, d, J = 16 Hz, NCH), 4.70 (1 H, s, CHS), 4.72 (1 H, d, J = 16 Hz, NCH), 7.10–7.38 (4 H, m, Ar H); ^{13}C NMR ($CDCl_3$) δ 16.8 (Me), 22.2 (Me), 41.7 (CH_2), 56.4 (quat), 62.8 (CH), 126.0, 127.9, 128.2, 129.5, 130.5, 131.3 (Ar), 173.5 (carbonyl); IR (neat) ν_{max} 1755 cm^{-1}; exact mass calcd for $C_{12}H_{13}NOS$ m/z 219.0718, found 219.0719.

Cyclization of 4a with Bu_3SnH. Heating of **4a** (41 mg, 0.13 mmol) with Bu_3SnH (0.005 M) in benzene gave unchanged starting material (2 mg, 5%) and *N*-benzyl-3,3-dimethyl-4-(methylthio)-2-azetidinone (**19a**) (14 mg, 46%): ^1H NMR ($CDCl_3$) δ 1.29 (3 H, s, Me), 1.32 (3 H, s, Me), 1.98 (3 H, s, SMe), 4.04 (1 H, d, J = 16 Hz, NCH), 4.15 (1 H, s, CHS), 4.77 (1 H, d, J = 16 Hz, NCH), 7.22–7.46 (5 H, m, Ar H); ^{13}C NMR ($CDCl_3$) δ 15.1 (SMe), 18.1 (Me), 21.7 (Me)8 43.3 (CH_2), 56.2 (quat), 71.6 (CH), 127.7, 128.1, 128.8, 135.5 (Ar), 172.4 (carbonyl); IR (neat) ν_{max} 1750 cm^{-1}; exact mass calcd for $C_{13}H_{17}NOS$ m/z 235.1048, found 235.1048. Further elution afforded **21** (6 mg, 21%).

Attempted Cyclization of 4c with Bu_3SnH. Heating of **4c** (57 mg, 0.15 mmol) with Bu_3SnH (0.015 M) in benzene gave only unchanged starting material (24 mg, 42%) and *N*-benzyl-3,3-dimethyl-4-(phenylthio)-2-azetidinone (**19c**) (18 mg, 40%) as an oil: ^1H NMR ($CDCl_3$) δ 1.34 (3 H, s, Me), 1.39 (3 H, s, Me), 3.97 (1 H, d, J = 15 Hz, NCH), 4.56 (1 H, s, CHS), 4.73 (1 H, d, J = 15 Hz, NCH), 6.95–7.08 and 7.10–7.41 (10 H, 2 m, Ar H); ^{13}C NMR ($CDCl_3$) δ 18.5 (Me), 21.5 (Me), 43.5 (CH_2), 56.7 (quat), 72.8 (CH), 127.5, 127.6, 128.1, 128.7, 129.2, 131.8, 133.9, 135.5 (Ar), 172.1 (carbonyl); IR (CH_2Cl_2) ν_{max} 1755 cm^{-1}; exact mass calcd for $C_{18}H_{19}NOS$ m/z 297.1187, found 297.1177.

Cyclization of 4b with Bu_3SnD. Heating of **4b** (73 mg, 0.21 mmol) with Bu_3SnD (0.026 M) in benzene gave **20b** (15 mg, 26%): ^1H NMR ($CDCl_3$) as for **19b** above; ^2H NMR (CH_2Cl_2) δ 7.32. Further elution afforded unchanged starting material (3 mg, 4%) and **21** (16 mg, 35%).

Cyclization of 4a with Bu_3SnD. Heating of **4a** (104 mg, 0.33 mmol) with Bu_3SnD (0.03 M) in benzene gave an inseparable mixture of *N*-benzyl-3,3-dimethyl-4-[(monodeuteriomethyl)-thio]-2-azetidinone (**22a**) (27 mg, 35%), *N*-(*o*-deuteriobenzyl)-3,3-dimethyl-4-(methylthio)-2-azetidinone (**20a**) (9 mg, 11%), and *N*-benzyl-4-deuterio-3,3-dimethyl-4-(methylthio)-2-azetidinone (**22b**) (12 mg, 15%): ^1H NMR ($CDCl_3$) δ (upfield region only) 1.28 (3 H, s, Me), 1.32 (3 H, s, Me), 1.96 (2 H, 1:1:1 t, J = 2 Hz, SCH_2D), 1.98 (3 H, s, SMe); ^2H NMR (CH_2Cl_2) δ 1.98, 4.17, 7.31 in a ratio of 3.5:1:1.5. Further elution afforded **21** (15 mg, 21%).

Attempted Cyclization of 7a with Bu_3SnH. Heating of **7a** (53 mg, 0.18 mmol) with Bu_3SnH (0.015 M) in benzene gave 3,3-dimethyl-4-(methylthio)-*N*-phenyl-2-azetidinone (**27a**) (28 mg, 70%): ^1H NMR ($CDCl_3$) δ 1.40 (3 H, s, Me), 1.44 (3 H, s, Me), 2.16 (3 H, s, SMe), 4.71 (1 H, s, CHS), 7.08–7.19, 7.27–7.41, and 7.52–7.61 (5 H, 3 m, Ar H); ^{13}C NMR ($CDCl_3$) δ 1.41 (SMe), 17.9 (Me), 22.6 (Me), 56.2 (quat), 70.1 (CH), 117.7, 124.3, 129.0, 137.1 (Ar), 170.4 (carbonyl); IR (neat) ν_{max} 1755 cm^{-1}; exact mass calcd for $C_{12}H_{15}NOS$ m/z 221.0874, found 221.0872. Further elution afforded only unchanged starting material (3 mg, 6%); none of the cyclized product **26** was detected.

Attempted Cyclization of 7b with Bu_3SnH: Formation of 3,3-Dimethyl-4-mercapto-*N*-phenyl-2-azetidinone (29). Heating of **7b** (87 mg, 0.25 mmol) with Bu_3SnH (0.015 M) in benzene and chromatography of the product gave **29** (31 mg, 60%): mp 50–58 °C; ^1H NMR ($CDCl_3$) δ 1.39 (3 H, s, Me), 1.44 (3 H, s, Me), 2.02 (1 H, d, J = 9 Hz, SH), 4.96 (1 H, d, J = 9 Hz, CHS), 7.09–7.20, 7.31–7.42, and 7.46–7.56 (5 H, 3 m, Ar H); ^{13}C NMR ($CDCl_3$) δ 18.1 (Me), 21.8 (Me), 55.7 (quat), 62.6 (CH), 117.7, 124.3, 129.1, 136.4 (Ar), 169.7 (carbonyl); IR ($CDCl_3$) ν_{max} 1755, 2560 cm^{-1}. Anal. Calcd for $C_{11}H_{13}NOS$: C, 63.7; H, 6.3; N, 6.8. Found: C, 63.7; H, 6.4; N, 6.7. Further elution yielded unchanged starting material (9 mg, 10%).

Cyclization of 8b with Bu_3SnH. Heating of **8b** (818 mg, 2.10 mmol) with Bu_3SnH (0.015 M) in benzene afforded, after removal of the solvent, a residue, which was dissolved in ether and stirred vigorously with an excess of 60% aqueous potassium fluoride[35] for 2 h. The tributyltin fluoride precipitate was removed by filtration, and the two layers were separated. The aqueous layer was extracted with ehter. The combined organic layers were washed with brine, dried, filtered, and concentrated, and the residue was subjected to MPLC (CH_2Cl_2/ethyl acetate, 46:1) to afford a mixture of **26** and **29**. Further elution afforded 3,3-dimethyl-*N*-phenyl-2-azetidinone (**30**) as an oil (64 mg, 17%): ^1H NMR ($CDCl_3$) δ 1.39 (6 H, s, 2Me), 3.42 (2 H, s, CH_2), 7.00–7.12 and 7.20–7.48 (5 H, 2 m, Ar H); ^{13}C NMR ($CDCl_3$) δ 21.3 (2Me), 49.7 (quat), 53.0 (CH_2), 116.2, 123.5, 129.0, 138.5 (Ar), 170.9 (carbonyl); IR ($CDCl_3$) ν_{max} 1745 cm^{-1}; exact mass calcd for $C_{11}H_{13}NO$ m/z 175.0997, found 175.0993.

The mixture of **26** and **29** was resubjected to MPLC (CH_2Cl_2) to afford 2,3-benzo-6,6-dimethyl-7-oxo-4-thia-1-azabicyclo-[3.2.0]heptane (**26**) (4 mg, 1%): ^1H NMR ($CDCl_3$) δ 1.48 (3 H, s, Me), 1.58 (3 H, s, Me), 5.58 (1 H, s, CHS), 7.02–7.30 (4 H, m,

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Ar H); ^{13}C NMR ($CDCl_3$) δ 19.7 (Me), 22.9 (Me), 59.0 (quat), 74.1 (CH), 117.7, 122.4, 125.4, 126.3, 136.7, 137.5 (Ar), 178.3 (carbonyl); IR ($CDCl_3$) ν_{max} 1778 cm^{-1}; exact mass calcd for $C_{11}H_{11}NOS$ m/z 205.0561, found 205.0538. Further elution yielded **29** (181 mg, 42%).

Attempted Cyclization of 7a with Bu_3SnD. Heating of **7a** (81 mg, 0.27 mmol) with Bu_3SnD (0.018 M) in benzene gave only 3,3-dimethyl-4-[(monodeuteriomethyl)thio]-*N*-phenyl-2-azetidinone (**31**) as an oil (57 mg, 95%): ^1H NMR ($CDCl_3$) δ (upfield region only) 1.40 (3 H, s, Me), 1.44 (3 H, s, Me), 2.14 (2 H, 1:1:1 t, J = 2 Hz, SCH_2D); ^2H NMR (CH_2Cl_2) δ 2.14.

Reaction of 8b with Bu_3SnD. The reaction of **8b** with Bu_3SnD described above was repeated on a smaller scale. Also, the effluent gas, under a positive pressure of N_2, was bubbled through a solution of bromine in CCl_4. The reaction mixture was concentrated and subjected to MPLC (CH_2Cl_2) to afford **26** (1%) and **29** (64%). None of the sulfide **28b** with deuterium incorporated in the phenyl ring was detected.

The CCl_4 solution was analyzed by GLC on three different columns (A, B, and C) and found to contain isobutylene dibromide. The retention times of the 1,2-dibromide from the reaction were identical with those of an authentic sample prepared from isobutylene and bromine. The program used for all three columns was 40 °C (5 min), 10 °C/min, 100 °C (5 min), and the retention times for the dibromide on each column were as follows: A, 6.77 min; B, 7.59 min; and C, 9.11 min.

Cyclization of 11a with Bu_3SnD. Heating of **11a** (111 mg, 0.37 mmol) with Bu_3SnD (0.029 M) in benzene gave, after flash chromatography (CH_2Cl_2), *N*-benzyl-5-thioxo-2-pyrrolidinone (**36**) (26 mg, 34%) as an oil: ^1H NMR ($CDCl_3$) δ 2.68–2.77 (2 H, m, CH_2CS), 3.09–3.18 (2 H, m, CH_2CO), 5.08 (2 H, s, NCH_2), 7.22–7.36 and 7.38–7.50 (5 H, 2 m, Ar H); ^{13}C NMR ($CDCl_3$) δ 28.8 (CH_2CS), 38.8 (CH_2CO), 45.5 (NCH_2), 127.9, 128.4, 129.1, 135.1 (Ar), 178.6 (C=O), 210.3 (C=S); exact mass calcd for $C_{11}H_{11}NOS$ m/z 205.0561, found 205.0544.

The residue isolated by flushing of the flash column with ethyl acetate was rechromatographed [MPLC (CH_2Cl_2/ethyl acetate, 3:1)] to afford an inseparable mixture of *N*-benzyl-5-deuterio-5-(methylthio)-2-pyrrolidinone (**39a**) (30 mg, 35%), *N*-(*o*-deuteriobenzyl)-5-(methylthio)-2-pyrrolidinone (**37a**) (6 mg, 7%), and *N*-benzyl-5-[(deuteriomethyl)thio]-2-pyrrolidinone (**41**) (7 mg, 3%): ^1H NMR (**39a**, $CDCl_3$) δ 1.94 (3 H, s, MeS), 2.10–2.30 (1 H, m, $COCH_2CH$), 2.34–2.65 (3 H, $COCH_2CH$), 4.07 (1 H, d, J = 15 Hz, NCH), 5.09 (1 H, d, J = 15 Hz, NCH), 7.30 (5 H, m, Ar H); ^1H NMR (**37a**, $CDCl_3$) δ same as for **39a** except for δ 4.30 (1 H, m, NCHS); ^2H NMR (CH_2Cl_2) δ 1.89, 4.38, 7.27 in a ratio of 1.2:5.5:1.0; chemical ionization exact mass calcd for $C_{12}H_{15}DNOS$ (M + 1) m/z 223.1015, found 223.1014.

Further elution gave 3,4-benzo-9-oxo-5-thia-1-azabicyclo-[4.3.0]nonane (**38**) (5 mg, 7%) as an oil: ^1H NMR ($CDCl_3$) δ 1.96–2.20 (1 H, m, $COCH_2CH$), 2.40–2.70 (3 H, m, $COCH_2CH$), 4.30 (1 H, d, J = 17 Hz, NCH), 5.09 (1 H, d, J = 17 Hz, NCH), 5.16 (1 H, m, CHS), 7.12 and 7.28 (4 H, 2 s, Ar H); ^{13}C NMR ($CDCl_3$) δ 24.4 (CH_2CH), 29.1 (CH_2CO), 42.6 (NCH_2), 59.2 (CH), 125.6, 127.1, 127.9, 128.5, 131.3, 136.4 (Ar), 173.9 (carbonyl); exact mass calcd for $C_{11}H_{11}NOS$ m/z 205.0561, found 205.0568.

Cyclization of 11b with Bu_3SnD. Heating of **11b** (100 mg, 0.26 mmol) with Bu_3SnD (0.028 M) in benzene afforded, after flash chromatography (CH_2Cl_2), **36** (35 mg, 65%). The residue isolated by flushing of the column with ethyl acetate was rechromatographed [MPLC (CH_2Cl_2/ethyl acetate, 3:1)] to afford *N*-(*o*-deuteriobenzyl)-5-[(1,1-dimethylethyl)thio]-2-pyrrolidinone (**37b**) (3 mg, 4%): ^1H NMR ($CDCl_3$) δ 1.26 (9 H, s, Me_3C), 2.20–2.70 (4 H, m, $COCH_2CH_2$), 4.02 (1 H, d, J = 14 Hz, NCH), 4.46 (1 H, d, J = 5 Hz, CHS), 5.09 (1 H, d, J = 14 Hz, NCH), 7.22–7.46 (4 H, m, Ar H); ^2H NMR (CH_2Cl_2) δ 7.26. Further elution gave **38** (13 mg, 25%).

Cyclization of 14 with Bu_3SnD. Heating of **14** (117 mg, 0.36 mmol) with Bu_3SnD (0.030 M) in benzene gave as the only product 2,3-benzo-8-oxo-4-thia-1-azabicyclo[3.3.0]octane (**47**), which was recrystallized from CH_2Cl_2/hexane (61 mg, 89%): mp 111–114 °C; ^1H NMR ($CDCl_3$) δ 2.35–2.94 (4 H, m, CH_2CH_2), 6.01 (1 H, dd, J = 6 and 8 Hz, NCHS), 6.95–7.20 and 7.53–7.68 (4 H, 2 m, Ar H); ^{13}C NMR ($CDCl_3$) δ 28.4 (CH_2CH), 34.3 (CH_2CO), 68.9 (CH), 116.6, 122.5, 125.4, 125.6, 133.1, 135.3 (Ar), 172.3 (carbonyl); exact mass calcd for $C_{10}H_9NOS$ m/z 191.0405, found 191.0415.

Cyclization of 14 with Bu_3SnH. When the preceding experiment was repeated with a benzene solution of Bu_3SnH (0.50 M), chromatography afforded **47** (23 mg, 45%) and 5-[(1,1-dimethylethyl)thio]-*N*-phenyl-2-pyrrolidinone (**45**) (14 mg, 21%): ^1H NMR ($CDCl_3$) δ 1.23 (9 H, s, Me_3C), 2.23–2.93 (4 H, m, $COCH_2CH_2$), 5.16 (1 H, dd, J = 2 and 7 Hz, NCHS), 7.20–7.30 and 7.32–7.47 (5 H, 2 m, Ar H); ^{13}C NMR ($CDCl_3$) δ 30.3 (CH_2CH), 31.2 (CH_2CO), 31.4 (Me_3C), 43.7 (quat), 64.9 (CH), 125.3, 126.6, 128.0, 147.2 (Ar), 173.8 (carbonyl); exact mass calcd for $C_{14}H_{19}NOS$ m/z 249.1187.found 249.1196.

3,3-Dimethyl-*N*-phenyl-2-azetidinone (30): Reaction of 29 with Bu_3SnI and Bu_3SnH. AIBN (4 mg, 0.02 mmol) was added to a deaerated benzene (3.6 mL) solution of **29** (22 mg, 0.11 mmol), Bu_3SnH (64 mg, 0.22 mmol; 0.06 M), and tributyltin iodide. The tributyltin iodide was prepared in situ by heating of a solution of iodobenzene (23 mg, 0.11 mmol), Bu_3SnH (35 mg, 0.12 mmol), and AIBN (3 mg, 0.02 mmol) in dry benzene (3.6 mL) for 1 h. The resultant solution was stirred under reflux for 22 h and then concentrated. The residue when subjected to MPLC (dichloromethane/ethyl acetate, 46:1) gave only **30** (17 mg, 88%).

4-(Benzoylthio)-3,3-dimethyl-*N*-phenyl-2-azetidinone. A solution of **29** (38 mg, 0.18 mmol) in dry CCl_4 (1 mL) was added to a cooled (0 °C) solution of benzoyl chloride (28 mg, 0.20 mmol) and triethylamine (28 mg, 0.28 mmol) in CCl_4 (3 mL). The cooled mixture was stirred for 0.5 h, filtered, and then concentrated. The residue was subjected to MPLC (CH_2Cl_2) to afford 4-(benzoylthio)-3,3-dimethyl-*N*-phenyl-2-azetidinone (29 mg, 52%), which crystallized from hexane, mp 101–107 °C: ^1H NMR ($CDCl_3$) δ 1.41 (3 H, s, Me), 1.57 (3 H, s, Me), 5.82 (1 H, s, CHS), 7.03–7.18, 7.20–7.70, and 7.89–8.07 (10 H, 3 m, Ar H); ^{13}C NMR ($CDCl_3$) δ 19.2 (Me), 21.9 (Me), 56.3 (quat), 66.0 (CH), 117.6, 124.5, 127.5, 128.9, 129.2, 134.2, 136.3, 136.4 (Ar), 169.8 (NC=O), 190.4 (S-C=O); IR (Nujol) ν_{max} 1770, 1665 cm^{-1}. Anal. Calcd for $C_{18}H_{17}NO_2S$: C, 69.4; H, 5.5; N, 4.5. Found: C, 69.8; H, 5.7; N, 4.7.

Registry No. **1a**, 37695-37-7; **1b**, 115363-85-4; **1c**, 64287-65-6; **2a**, 115363-83-2; **2b**, 115363-90-1; **2c**, 115363-96-7; **3a**, 115363-84-3; **3b**, 115363-97-8; **3c**, 115363-93-4; **4a**, 97249-44-0; **4b**, 97249-43-9; **4c**, 97249-45-1; **7a**, 99314-05-3; **7b**, 99314-07-5; **8b**, 99314-07-5; **9a**, 115363-86-5; **9b**, 115364-00-6; **10a**, 115363-87-6; **10b**, 115364-01-7; **11a**, 115363-88-7; **11b**, 115383-43-2; **12**, 115363-89-8; **14**, 115363-91-2; **15**, 115363-92-3; **19a**, 97249-48-4; **19b**, 97249-46-2; **19c**, 97249-49-5; **20a**, 115363-94-5; **20b**, 115364-07-3; **21**, 97249-47-3; **22a**, 115363-95-6; **22b**, 115364-09-5; **26**, 115363-98-9; **27a**, 99314-06-4; **29**, 99314-08-6; **29** (*S*-benzoyl deriv), 99314-10-0; **30**, 27983-93-3; **31**, 115363-99-0; **36**, 95141-59-6; **37a**, 115364-03-9; **37b**, 115383-44-3; **38**, 115364-04-0; **39a**, 115364-05-1; **41**, 115364-06-2; **45**, 115364-08-4; **47**, 34735-50-7; 1,2-dibromo-2-methylpropane, 594-34-3; *N*-(*o*-bromobenzyl)-5-hydroxy-2-pyrrolidinone, 115383-45-4; *o*-bromobenzyl bromide, 3433-80-5; *o*-bromobenzylamine, 3959-05-5; 3-chloro-2,2-dimethylpropanoic acid, 13511-38-1; 2,2-dimethyl-3-(methylthio)propanoic acid, 37695-38-8; 3-[(1,1-dimethylethyl)thio]-2,2-dimethylpropanoic acid, 115364-10-8; *o*-bromoaniline, 615-36-1; *o*-iodoaniline, 615-43-0; succinimide, 123-56-8; *o*-iodobenzyl chloride, 59473-45-9; 5-hydroxy-*N*-(*o*-iodobenzyl)-2-pyrrolidinone, 115364-11-9; succinic anhydride, 108-30-5; *N*-(*o*-bromophenyl)succinamic acid, 62134-47-8.