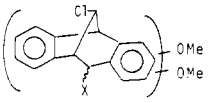
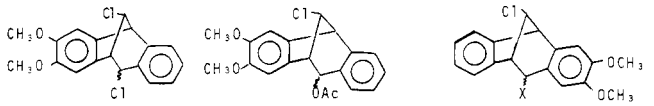
spectrum of the mixture with the ^1H NMR spectra of the authentic samples.

Irradiation of the Cis-Anti Isomer 16 at 300 nm. A solution of 2.9 mg of **16** (0.009 mmol) was dissolved in 1.0 mL of acetic acid-d_4 and placed in a Pyrex NMR tube. The solution was deoxygenated as described previously and sealed. The tube was irradiated at 300 nm for 1 h. Analysis of the ^1H NMR spectrum showed 70% conversion of starting material to products. The minor products (24%) were identified as **26**-Cl (endo:exo = 1:1) by comparison of the ^1H NMR spectrum to the ^1H NMR spectrum of an authentic sample of an epimeric mixture of **26**-Cl. The major products had the following type of [3.2.1] structure: **24-Cl**



X = Cl, OAc

and **24-OAc** are known compounds. The products were not **24** and,



therefore, must be **25** (of which 51% was **25**-Cl, endo:exo = 1.8, and 25% was **25**-OAc, endo:exo = 1:2.5).

"Dark Reactions" of 15, 16, and 17. "Dark reactions" were performed simultaneously with all three irradiations. Solutions were made up with similar concentrations, placed in similar tubes, wrapped in foil, and placed in the Rayonet beside the "light reactions". The "dark reactions" remained in the Rayonet for as long as the "light reactions". All "dark reactions" were worked up (if a workup was involved) in the same way as the "light reactions." For all three compounds, **15**, **16**, and **17**, no reaction was observed in the dark.

Acknowledgments. We are indebted to the National Science Foundation (Grant CHE80-11933) and to the Office of Basic Energy Sciences, U.S. Department of Energy (Contract DE-AC02-79ER10366), for support of this work. S.J.C. is indebted to the John Simon Guggenheim Memorial Foundation and to the Council on Research and Creative Work of the University of Colorado for fellowship support. The authors are also indebted to Dr. T. H. Bindel for technical aid.

Registry No. 12, 87567-71-3; **13**, 87637-73-8; **14**, 87637-74-9; **15**, 75920-61-5; **16**, 87637-75-0; **17**, 87637-76-1; *exo*-**18** (X = OH), 87567-74-6; *exo*-**18** (X = OAc), 87567-72-4; *exo*-**19** (X = OH), 87567-75-7; *exo*-**19** (X = OAc), 87567-73-5; **20**, 87567-76-8; **21**, 87567-77-9; **22** (X = O), 87637-60-3; *endo*-**22** (X = OH), 87637-58-9; *endo*-**22** (X = OAc), 87637-57-8; *exo*-**22** (X = OAc), 87637-56-7; *exo*-**22** (X = OH), 87637-59-0; **2** (X = O), 87637-65-8; *endo*-**23** (X = OH), 87637-63-6; *endo*-23 (X = OAc), 87637-61-4; *exo*-**23** (X = OH), 87637-64-7; *exo*-**23** (X = OAc), 87637-62-5; **24** (X = OAc), 87637-67-0; **24** (X = OH), 87637-68-1; **24** (X = Cl), 87637-69-2; **24** (X = O), 87637-70-5; *endo*-**25** (X = Cl), 87567-87-1; *endo*-**25** (X = OAc), 87637-71-6; *exo*-**25** (X = OAc), 87637-72-7; *exo*-**25** (X = Cl), 87637-77-2; **26** (X = 0), 87567-85-9; *endo*-**26** (X = Cl), 87567-86-0; *endo*-**26** (X = OAc), 87567-83-7; *exo*-**26** (X = OH), 87567-84-8; *exo*-**26** (X = Cl), 87637-66-9; **27** (X = O), 87567-82-6; *endo*-**27** (X = OAc), 87567-80-4; *endo*-27 (X = OH), 87567-81-5; 2-(2,3-dimethoxybenzyl)benzoic acid, 76250-92-5; 2-(2,3-dimethoxybenzyl)benzoic acid, 87567-78-0; 2,3-dimethoxy-9-anthrone, 87567-79-1; naphthacene, 92-24-0; *trans*-1,2-dichloroethene, 156-60-5; *cis*-1,2-dichloroethene, 156-59-2; silver acetate, 563-63-3; 2,3-dimethoxyanthracene, 51790-19-3; phthalic anhydride, 85-44-9; veratrole, 91-16-7.

Synthesis of β-Lactam Antibiotics by the Sulfeno-Cycloamination

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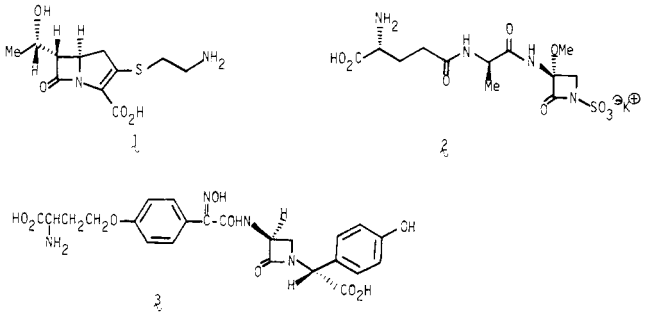
Abstract: A novel efficient β-lactam synthesis was achieved by two successive processes (sulfeno-cycloamination), addition of phenylsulfenyl chloride to α,β-unsaturated amides followed by base treatment. Key synthetic intermediates of monobactams and nocardicin derivatives were obtained via this method. Construction of the 1-carbapenam ring system by the sulfeno-cycloamination is also described.

The discovery of thienamycin (**1**), an unusually potent carbapenem antibiotic,[1,2] and the monobactams such as sulfazecin (**2**),[3,4] a family of monocyclic 2-oxoazetidine-*N*-sulfonic acids produced in bacteria, has led to intense activity in the synthesis of β-lactam antibiotics. These substances possess reactive β-lactam linkages, which show high antibacterial potency and a wide antibacterial spectrum. Among a variety of methods for the construction of the β-lactam ring,[5] the formation of the N–C_4 bond is known as a biomimetic process. Kishi first demonstrated this type of β-lactam formation by ring closure of β-halo amides,[6] and similar approaches were successfully extended by other workers.[7–13] Furthermore, β-hydroxy secondary amides were cyclized to β-lactams under the Mitsunobu reaction conditions.[14–17] We envisaged that a neighboring group effect would enhance β-lactam formation through addition of sulfenyl halides to α,β-unsaturated

Chart I



† Pharmaceutical Institute.
‡ Institute of Medicinal Chemistry.

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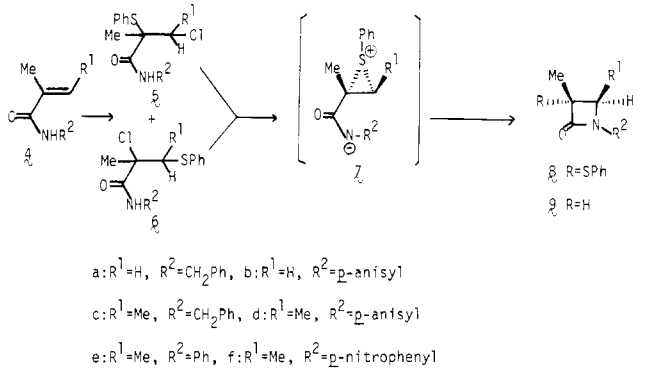
Scheme I



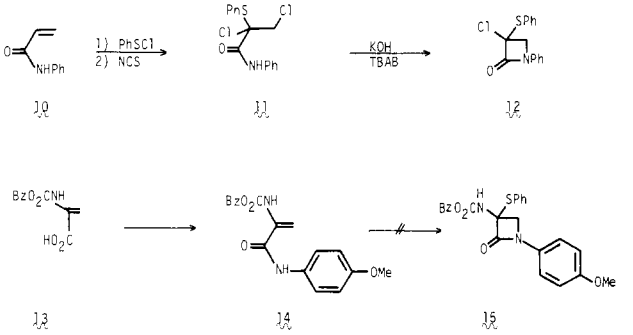
a: R^1=H, R^2=CH_2Ph, b: R^1=H, R^2=p-anisyl

c: R^1=Me, R^2=CH_2Ph, d: R^1=Me, R^2=p-anisyl

e: R^1=Me, R^2=Ph, f: R^1=Me, R^2=p-nitrophenyl

amides followed by intramolecular substitution. As shown in our preliminary communication,[18] several β-lactams were effectively synthesized by this strategy.[19] This ring formation reaction was further applied to olefinic amines, which led us to the efficient total synthesis of the necine bases (±)-retronecine and (±)-turneforcidine.[20] The cyclization, named "sulfeno-cycloamination", accomplished by two successive processes, addition of phenylsulfenyl chloride to the carbon–carbon double bond and base treatment, has the following distingushing characteristics. First, the reaction proceeds, most probably, via an episulfonium intermediate under mild conditions without the necessity for separation of the regioisomers of the adducts. Second, the resulting sulfenyl group is readily removable as well as useful for introduction of other functional groups. In this paper, we describe the β-lactam formation via sulfeno-cycloamination, including syntheses of key intermediates of monobactams and nocardicins (3) (Chart I) and the construction of the carbapenam ring system.

Scheme II



Construction of the β-Lactam Linkage and Synthesis of Monobactam and Nocardicin Derivatives. Although the reaction between sulfenyl halides and olefins has been well studied,[21] there is no report concerning the addition to α,β-unsaturated amides. We observed that phenylsulfenyl chloride rapidly reacted with many kinds of α,β-unsaturated amides to produce two regioisomers. Thus, reaction of *N*-benzylmethacrylamide (**4a**) with 1.2 equiv mol of the sulfenyl chloride in methylene chloride at ambient temperature for 2 h gave 88% yield of two products in a ratio of 3:1. The major product (**5a**), the kinetically controlled adduct, was gradually converted into another one (**6a**) by allowing it to stand at ambient temperature or by column chromatography on silica gel. The adducts were cyclized by base treatments; the β-lactam formation was effectively conducted with alkalis in the presence of phase-transfer catalysts:[8,11,12] heating the former (**5a**) with 1 mol equiv of potassium hydroxide in the presence of a small amount of tetra-*n*-butylammonium bromide (TBAB) in a mixture of water and benzene at 40–50 °C for 16 h furnished azetidinone **8a** in 94% yield. The regioisomer (**6a**) also gave **8a** in a similar yield on treatment under the same conditions. This phenomenon could be reasonably explained by the episulfonium ion intermediate (**7a**) (Scheme I).[22] By a one-pot reaction without isolation of the adduct **8a** was obtained in 52% yield from **4a**. Purification of the mixture of adducts from the excess of the sulfenyl chloride by a short-column chromatography usually gave better results. Treatment of the mixture of adducts (**5a** and **6a**) with sodium hydride in dimethylformamide also produced β-lactam **8a** in good yield.

The corresponding 1-(*p*-methoxyphenyl)azetidin-2-one (**8b**) was synthesized in 75% yield from the 1:1 mixture of adducts (**5b** and **6b**) by the reaction with potassium hydroxide in the presence of TBAB at ambient temperature. The amides **4c–f** derived from tiglic acid also produced two adducts, **5c–f** and **6c–f**, respectively, by the action of the sulfenyl chloride. The slow transformation of the former (**5c–f**) into the latter (**6c–f**) was again observed. Single stereoisomers of β-lactams **8c–f** were obtained, respectively, from the mixture of adducts by treatment with potassium hydroxide and TBAB. The rate of cyclization was influenced by the acidity of the NH bond; the increased acidity led to easier formation of β-lactams. The phenylsulfenyl group was easily removed by treatment with Raney nickel. The stereochemistry of azetidinones **9c** and **9e** obtained in 85 and 95% yield was determined as cis on the basis of the coupling constant (J = 6–7 Hz) between the two hydrogens on the β-lactam ring. The spectral data of the former (**9c**) were fully consistent with the reported values.[23] The above observations strongly suggest that the two

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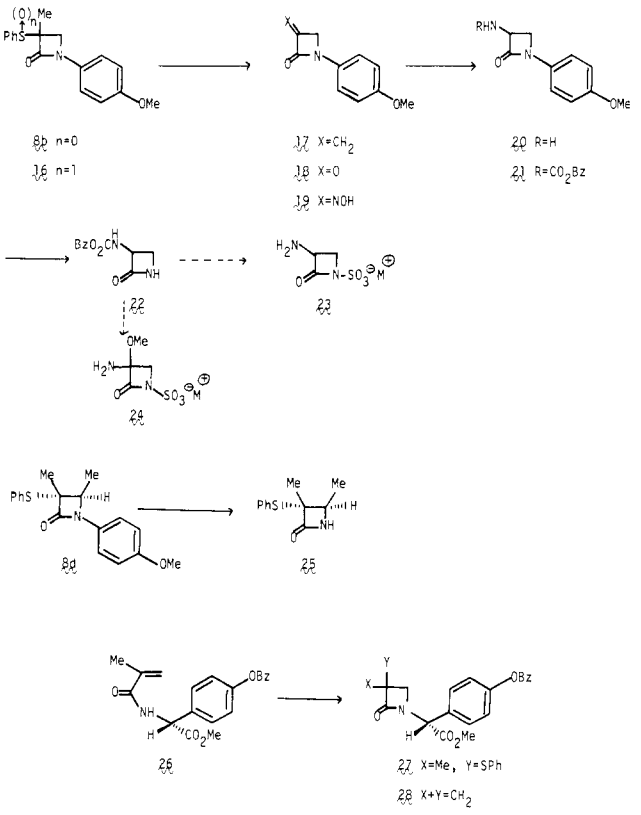
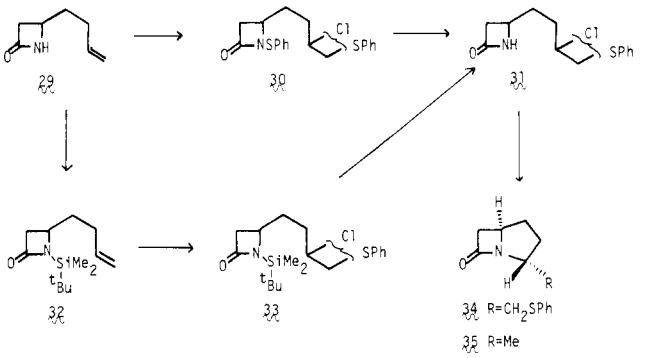
Scheme III



Scheme IV



adducts **5c–f** and **6c–f** are not stereoisomers but regioisomers and the cyclization proceeds via the episulfonium ion intermediate.

In order to prepare azetidin-2-ones having functional groups at the C_3 position other than the alkyl group, acrylanilide (**10**) was treated with the sulfenyl chloride and then *N*-chlorosuccinimide[24] to afford dichlorinated compound **11** (Scheme II). Cyclization of **11** under conditions similar to those above gave **12** in 35% yield. In studies aimed at the synthesis of intermediates leading to monobactams, the sulfeno-cycloamination of 2-(((benzyloxy)carbonyl)amino)acrylamide **14** was further examined. 2-(((Benzyloxy)carbonyl)amino)acrylic acid (**13**) prepared by a modification of the known method[25] was condensed with *p*-anisidine in the presence of dicyclohexylcarbodiimide to afford **14**. However reaction of **14** with phenylthio chloride, followed by cyclization was not successful, because dehydrochlorination of the adduct easily occurred giving olefinic compounds. Therefore our attention was directed toward the conversion of β-lactam **8b**, obtained by the above method, into **22**, the important synthetic intermediate of monobactams.[26]

Oxidation of the above azetidin-2-one (**8b**) with *m*-chloroperbenzoic acid in methylene chloride at −78 °C gave, quantitatively, sulfoxide **16**, which was then subjected to syn elimination by heating in toluene to afford exo methylene **17** in 78% yield (Scheme III). No formation of the corresponding endo olefin was observed. Ozonolysis of **17** in ethyl acetate at −78 °C followed by treatment with dimethyl sulfide furnished keto β-lactam **18**. Introduction of the amino group at the C_3 position was achieved by utilizing the method established by Ban and co-workers in their synthesis of 3-aminonocardicinic acid (3-ANA):[27] transformation of **18** into the oxime **19** followed by catalytic hydrogenation with rhodium on alumina under several atmospheres of pressure of hydrogen afforded amine **20**. After protection of the amino group as urethane **21**, oxidation of **21** with ceric ammonium nitrate[28] (CAN) in a mixture of water and acetonitrile at 0 °C for 15 min produced, in 59% yield, the desired secondary β-lactam **22**, mp 160–162 °C. The corresponding optically active compound had been synthesized from 6-APA and converted into 3-aminobactamic acid (3-AMA) (**23**) and its 3-methoxy derivative (**24**), key intermediates for the synthesis of monobactams by the Squibb group.[26]

The above oxidative deprotection was also applied to the sulfide **8d**. Treatment of **8d** with 2 equiv of CAN under the same conditions as above gave **25** in 72.2% with the intact sulfenyl group.

Following this, methacrylamide **26**, $[\alpha]_D$ −80.1° ($CHCl_3$), prepared from methyl D-((*p*-benzyloxy)phenyl)glycinate,[29] was subjected to sulfeno-cycloamination. Reaction of **26** with the sulfenyl chloride gave the adduct (95%), as a mixture of regio isomers, which was cyclized by treatment with sodium hydride in a mixture of benzene and dimethylformamide at 0 °C to afford β-lactam **27** as a diastereoisomeric mixture (52%). By oxidation with *m*-chloroperbenzoic acid followed by the syn elimination under the same conditions as above, **27** was transformed into exo methylene **28**, $[\alpha]_D$ −16.2° ($CHCl_3$). The corresponding benzyl ester had been converted, by Ban and co-workers,[27] into 3-ANA.[9,10,16,29,30]

The above results have thus demonstrated that sulfeno-cycloamination is a very useful method for the synthesis of monocyclic antibiotics.

Construction of the Carbapenam Ring System. The cyclization of 4-(3-butenyl)azetidin-2-one (**29**), initiated by electrophilic reagents, was studied by Aida and co-workers.[31] They reported the exclusive formation of the addition product in the anti-Markovnikov type manner by the reaction of **29** with phenylsulfenyl chloride. However in our case we observed a facile N-sulfenylation giving a mixture of regioisomers of adducts (**30**) (Scheme IV) even if the reaction was carried out with equimolar sulfenyl chloride in methylene chloride at −78 °C. Selective removal of the *N*-sulfenyl group to afford **31** was achieved by reduction with sodium borohydride in methanol. Adduct **31** was also synthesized from **29** in three steps as follows. After protection with the *tert*-butyldimethylsilyl group, the reaction of the resulting **32** with the sulfenyl chloride followed by deblocking with the fluoride ion furnished **31** in high yield. Cyclization was conducted by refluxing **31** with triethylamine and potassium carbonate in the presence of sodium iodide in acetonitrile to give carbapenam

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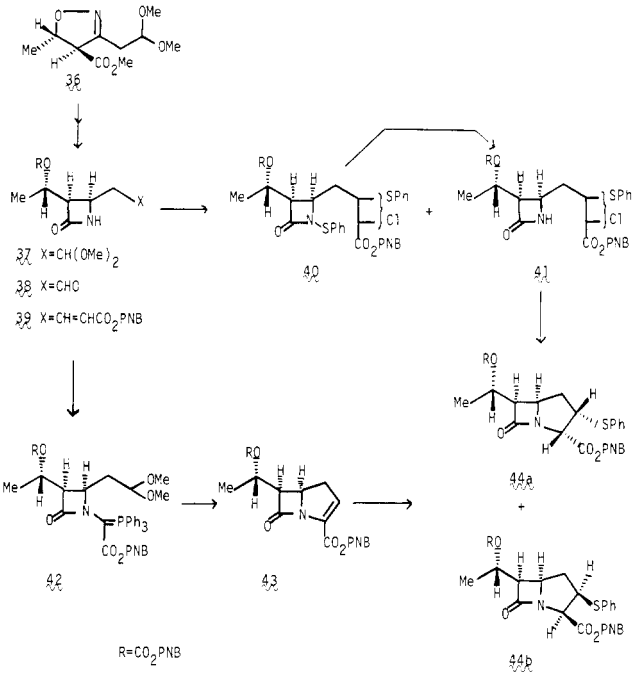
Scheme V



derivative **34** (82.1% based on the consumed **31**). The structure of the product was determined after desulfurization. Treatment of **34** with Raney nickel afforded 3-methylcarbapenem **35**, whose ^{1}H NMR spectrum ($CDCl_3$) showed the signal due to the methyl group at 1.45 ppm (doublet, J = 7 Hz). The spectral data were identical with those reported for the authentic sample.[32] Thus the relative stereochemistry of two hydrogens at the C_3 and C_5 position was determined as trans. The preferred formation of the five-membered ring to the six-membered one was also observed in the case of the sulfeno-cycloamination of olefinic amines.[20]

On the basis of the above results, we undertook to carry out a novel synthesis of the carbapenam derivative possessing the sulfenyl group at the C_2 position from an unsaturated ester such as **39** (Scheme V). According to our method,[33] the cis-substituted azetidinone **38**,[34] the synthetic intermediate of (±)-epithienamycins A and B, was prepared via acetal **37** and then subjected to the Wittig reaction. Treatment of unsaturated ester **39**, obtained as the *E* form, with the sulfenyl chloride gave *N*-sulfenyl compound **40** as a major product along with a small amount of adduct **41**. On treatment with sodium borohydride, compound **40** was converted into **41**. Cyclization of **41** under the same conditions as in the case of **35** produced in 6.9% yield the desired carbapenam derivative (**44**), whose structure was determined by direct comparison with the sample prepared by the alternative route outlined below.

Acetal **37** was transformed, by the established method,[33,35] into phosphoran **42**, which was subjected to the intramolecular Wittig reaction after deprotection.[33,35] Carbapenem **43** obtained was treated, according to the Beechams procedure,[36] with thiophenol and potassium carbonate in dimethylformamide to furnish the corresponding adduct, whose ^{1}H NMR spectrum showed the hydrogen at the C_3 position at 4.82 (d, J = 8 Hz) and 4.26 ppm (d, J = 8 Hz) in a ratio of 1:1, indicating a mixture of **44a** and **44b**[36] (homogeneous on TLC). A novel method for constructing the carbapenam system was thus developed via the sulfeno-cycloamination, although the above yield of **44** was not satisfactory.

Experimental Section

1-Benzyl-3-(phenylthio)-3-methylazetidin-2-one (8a). To a solution of *N*-benzylmethacrylamide (**4a**) (440 mg, 2.51 mmol) in dry CH_2Cl_2 (8 mL) was added dropwise a solution of PhSCl (440 mg, 3.05 mmol) in CH_2Cl_2 (2 mL), and the mixture was stirred for 2 h at ambient temperature. After addition of CH_2Cl_2 (30 mL), the resulting mixture was washed with a saturated $NaHCO_3$ solution and H_2O, dried (Na_2SO_4), and evaporated. The residue was subjected to chromatography on silica gel (15 g). Elution with AcOEt–benzene (3:97 v/v) gave **5a**[37] (529 mg, 66%) as a pale yellowish syrup: IR ($CHCl_3$) 3410 (NH), 1645 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 1.50 (3 H, s, Me), 3.50 and 3.86 (each 1 H, each d, J = 11 Hz, CH_2Cl), 4.36 (2 H, d, J = 6.2 Hz, NCH_2Ph); mass spectrum, m/z 319 and 321 (M^+). Further elution with the same solvent system afforded **6a**[37] (176 mg, 22%) as a pale yellowish syrup: IR ($CHCl_3$) 3450 (NH), 1650 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 1.83 (3 H, s, Me), 3.43 and 3.73 (each 1 H, each d, J = 14 Hz, CH_2SPh), 4.33 (2 H, d, J = 6.2 Hz, NCH_2Ph); mass spectrum, m/z 319 and 321 (M^+).

(A) A mixture of the above adducts (**5a** and **6a**) (295 mg, 0.923 mmol), KOH (51 mg 0.923 mmol), tetra-*n*-butylammonium bromide (TBAB) (150 mg), H_2O (0.13 mL), and benzene (20 mL) was stirred for 16 h at 40–50 °C. After dilution with benzene (30 mL), the organic layer was washed with H_2O and dried (Na_2SO_4). Evaporation of the solvent afforded a residue, which was purified by column chromatography on silica gel (6 g). Elution with AcOEt–benzene (1:49 v/v) gave β-lactam **8a**[37] as a syrup (243 mg, 93%): IR ($CHCl_3$) 1745 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 1.53 (3 H, s, Me), 3.03 (2 H, br s, C_4-H_2), 4.13 (2 H, s, NCH_2Ph); mass spectrum, m/z 283 (M^+); exact mass calcd for $C_{17}H_{17}NOS$ 283.1031, found 283.1041.

(B) A mixture of **5a** (50 mg, 0.157 mmol), KOH (8.8 mg, 0.158 mmol), TBAB (30 mg), H_2O (2 drops), and benzene (5 mL) was heated for 16 h at 40–50 °C and worked up as above to give **8a** (42 mg, 94%) as a syrup, whose spectral data and TLC behaviors were identical with those of the sample prepared by method A.

(C) A mixture of **6a** (50 mg) was converted into the β-lactam **8a** (41 mg, 92%), identical with the sample prepared by method A in all respects.

(D) To a solution of the mixture of **5a** and **6a** (29.5 mg, 0.092 mmol) in dry DMF (3 mL) was added 60% NaH (3.7 mg, 0.092 mmol) at 0 °C, and the mixture was stirred for 1 h at 0 °C and then for 3 h at ambient temperature. After dilution with benzene, the organic layer was washed with a saturated NH_4Cl solution and H_2O, dried (Na_2SO_4), and evaporated. The residue was purified by chromatography on silica gel as above to give **8a** (18.5 mg, 71%), identical with the above product in all respects. The following β-lactams (**8b–f**) were prepared in an analogous fashion of method A.

1-(*p*-Methoxyphenyl)-3-methyl-3-(phenylthio)azetidin-2-one (8b). Reaction of 1-(*p*-methoxyphenyl)methacrylamide (**4b**) [IR ($CHCl_3$) 3425 (NH), 1660 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 2.03 (3 H, s, Me), 3.77 (3 H, s, OMe), 5.38 and 5.73 (each 1 H, each br s, $=CH_2$), 6.81 (2 H, d, J = 9 Hz, 2 × ArH), 7.43 (2 H, d, J = 9 Hz, 2 × ArH), 7.28–7.62 (1 H, br s, NH); mass spectrum, m/z 191 (M^+).Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.33. Found: C, 68.73; H, 6.79; N, 7.44] with PhSCl gave a mixture of the corresponding adducts (**5b** and **6b**) as a yellowish syrup (91%): IR ($CHCl_3$) 3405 (NH), 1675 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 1.63 (1.5 H, s, Me), 1.93 (1.5 H, s, Me), 3.80 (3 H, s, OMe), 6.88 (2 H, d, J = 9 Hz, 2 × ArH), 7.00–7.63 (7 H, m, 7 × ArH), 8.47 (1 H, br s, NH); mass spectrum, m/z 335 and 337 (M^+). Anal. Calcd for $C_{17}H_{18}ClNO_2S$: C, 60.79; H, 5.40; N, 4.17. Found: C, 60.50; H, 5.17; N, 4.17. The mixture of the adducts was treated with KOH in the presence of TBAB for 24 h at ambient temperature to give β-lactam **8b** (75%) as colorless needles, mp 82–84 °C dec: IR ($CHCl_3$) 1750 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 1.62 (3 H, s, Me), 3.51 (2 H, s, C_4-H_2), 3.68 (3 H, s, OMe), 6.70 (2 H, d, J = 9 Hz, 2 × ArH), 7.00–7.67 (7 H, m, 7 × Ar); mass spectrum, m/z 299 (M^+). Anal. Calcd for $C_{17}H_{17}NO_2S$: C, 68.20; H, 5.72; N, 4.68. Found: C, 68.02; H, 5.90; N, 4.50.

(±)-1-Benzyl-3β,4β-dimethyl-3α-(phenylthio)azetidin-2-one (8c). The mixture of adducts **5c** and **6c** [IR ($CHCl_3$) 3420 (NH), 1660 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 1.33 (1.5 H, d, J = 7 Hz, Me), 1.45 (1.5 H, s, Me), 1.63 (1.5 H, d, J = 7 Hz, Me), 1.93 (1.5 H, s, Me), 3.80 (0.5 H, q, J = 7 Hz, C*H*SPh), 4.46 (0.5 H, q, J = 7 Hz, CHCl), 4.40 (2 H, d, J = 6 Hz, NCH_2Ph); mass spectrum, m/z 333 and 335 (M^+)] that was obtained in 93% yield from amide **4c** was converted, on treatment at 45–50 °C for 16 h, into β-lactam **8c**[37] (45%): IR ($CHCl_3$) 1747 cm^{-1}

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(37) The compound was homogeneous on analytical TLC.

(CO); ^{1}H NMR ($CDCl_3$) δ 1.16 (3 H, d, J = 7 Hz, Me), 1.30 (3 H, s, Me), 3.30 (1 H, q, J = 7 Hz, C_4-H), 3.90 and 4.47 (each 1 H, each d, J = 15 Hz, NCH_2Ph); mass spectrum, m/z 297 (M^+); exact mass calcd for $C_{18}H_{19}NOS$ 297.1188, found 297.1206.

(±)-1-(*p*-Methoxyphenyl)-3β,4β-dimethyl-3α-(phenylthio)azetidin-2-one (8d). Cyclization of mixture of adducts **5d** and **6d** [IR ($CHCl_3$) 3400 (NH), 1675 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 1.37 (1.5 H, s, Me), 1.38 (1.5 H, d, J = 7 Hz, Me), 1.60 (1.5 H, d, J = 7 Hz, Me), 1.93 (1.5 H, s, Me), 3.67 (3 H, s, OMe), 3.80 (0.5 H, q, J = 7 Hz, C*H*SPh), 4.43 (0.5 H, q, J = 7 Hz, CHCl); mass spectrum, m/z 349 and 351 (M^+). Anal. Calcd for $C_{18}H_{20}ClNO_2S$: C, 61.80; H, 5.72; N, 4.01. Found: C, 61.33; H, 5.75; N, 3.84] prepared from amide **4d** in 95% yield was carried out at ambient temperature for 8 h to give β-lactam **8d**[37] (73%): IR ($CHCl_3$) 1740 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 1.50 (3 H, s, Me), 1.56 (3 H, d, J = 7 Hz, Me), 3.70 (3 H, s, OMe), 3.97 (1 H, q, J = 7 Hz, C_4-H); mass spectrum, m/z 313 (M^+); exact mass calcd for $C_{18}H_{19}NO_2S$ 313.1134, found 313.1122.

(±)-1-Phenyl-3β,4β-dimethyl-3α-(phenylthio)azetidin-2-one (8e). On the cyclization at ambient temperature for 5 h, adduct **5e**, mp 116–117 °C, (95%) [IR ($CHCl_3$) 3380 (NH), 1670 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 1.47 (3 H, s, Me), 1.70 (3 H, d, J = 7 Hz, Me), 4.50 (1 H, q, J = 7 Hz, CHCl); mass spectrum, m/z 319 and 321 (M^+)] was converted into β-lactam **8e**[37] (95%) as needles, mp 94–96 °C: IR ($CHCl_3$) 1743 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 1.57 (3 H, s, Me), 1.63 (3 H, d, J = 6 Hz, Me), 4.08 (1 H, q, J = 6 Hz, C_4-H); mass spectrum, m/z 383 (M^+); exact mass calcd for 283.1029, found 283.1028.

(±)-1-(*p*-Nitrophenyl)-3β,4β-dimethyl-3α-(phenylthio)azetidin-2-one (8f). By the treatment with the base at ambient temperature for 2 h, the mixture of adducts **5f** and **6f** (91%) [IR ($CHCl_3$) 3380 (NH), 1700 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 1.43 (0.75 H, d, J = 7 Hz, Me), 1.52 (2.25 H, s, Me), 1.70 (2.25 H, d, J = 6.8 Hz, Me), 2.00 (0.75 H, s, Me), 3.77 (0.25 H, q, J = 7 Hz, C*H*SPh), 4.43 (0.75 H, q, J = 6.8 Hz, CHCl); mass spectrum, m/z 364 and 366 (M^+)] was transformed into β-lactam **8f**[37] (97%) as needles, mp 105–106 °C: IR ($CHCl_3$) 1760 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$) δ 1.58 (3 H, s, Me), 1.73 (3 H, d, J = 7 Hz, Me), 4.16 (1 H, q, J = 7 Hz, C_4-H); mass spectrum, m/z 328 (M^+); exact mass calcd for $C_{17}H_{16}N_2O_3S$ 328.0880, found 328.0874.

3-Chloro-1-phenyl-3-(phenylthio)azetidin-2-one (12). Reaction of acrylanilide **10** (650 mg, 4.42 mmol) and PhSCl (650 mg, 4.51 mmol) in dry CH_2Cl_2 (20 mL) at room temperature for 2 h followed by purification by silica gel column chromatography gave the corresponding adducts (1.12 g, 87%) as a pale yellowish syrup: IR ($CHCl_3$) 3410 (NH), 1680 cm^{-1} (CO); mass spectrum, m/z 291 and 293 (M^+). The mixture of the adduct (303 mg, 1.04 mmol) and NCS (143 mg, 1.07 mmol) in dry CCl_4 (10 mL) was stirred at ambient temperature for 3 h. After filtration, the filtrate was evaporated to give a syrup, which was chromatographed on silica gel (8 g). Elution with benzene afforded dichloro compound **11**[37] (316 mg, 93%): IR ($CHCl_3$) 3410 (NH), 1693 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 3.77 and 4.36 (each 1 H, each d, J = 12 Hz, CH_2Cl).

A mixture of the above compound (**11**) (118 mg, 0.36 mmol), KOH (23.8 mg, 0.36 mmol), TBAB (110 mg), and H_2O (0.06 mL) in benzene (10 mL) was stirred at ambient temperature for 18 h and then washed with H_2O. The benzene extract was dried (Na_2SO_4) and evaporated to give a residue, which was subjected to chromatography on silica gel (3 g). Elution with *n*-hexane–benzene (1:4 v/v) afforded β-lactam **12**[37] as a syrup (36 mg, 35%): IR ($CHCl_3$) 1770 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 3.90 (2 H, s, C_4-H_2), 7.03–7.67 (10 H, m, 2 × Ph), mass spectrum, m/z 289 and 291 (M^+); exact mass calcd for $C_{15}H_{12}ClNOS$ 289.0328 and 291.0297, found 289.0293 and 291.0272.

(±)-1-Benzyl-3β,4β-dimethylazetidin-2-one (9c). A mixture of β-lactam **8c** (50 mg, 0.168 mmol) and W_2-Raney Ni (0.5 mL) in acetone (5 mL) was stirred at room temperature for 30 min and then filtered through celite. After evaporation of the solvent, the residue was taken up into CH_2Cl_2, washed with H_2O, and dried (Na_2SO_4). Evaporation of the solvent gave a yellowish oil, which was chromatographed on silica gel (1.5 g). Elution with AcOEt–benzene (1:9 v/v) afforded **9c**[37] (24 mg, 85%) as an oil: IR ($CHCl_3$) 1735 cm^{-1} (CO); mass spectrum, m/z 189 (M^+); exact mass calcd for $C_{12}H_{15}NO$ 189.1152, found 189.1132, whose ^{1}H NMR spectrum ($CDCl_3$) was consistent with the reported data.[23]

(±)-1-Phenyl-3β,4β-dimethylazetidin-2-one (9e). 3-(Phenylthio)azetidin-2-one (**8e**) (80 mg, 0.282 mmol) was treated with W_2-Raney Ni (1 mL) in acetone (10 mL) for 30 min and then worked up as above to give **9e**[37] (46 mg, 93%) as an oil: IR ($CHCl_3$) 1740 cm^{-1} (CO): ^{1}H NMR ($CDCl_3$) δ 1.18 (3 H, d, J = 8 Hz, Me), 1.33 (3 H, d, J = 7 Hz, Me), 3.17 (1 H, dq, J = 7 and 8 Hz, C_3-H), 4.16 (1 H, dq, J = 7 and 7 Hz, C_4-H); mass spectrum, m/z 175 (M^+); exact mass calcd for $C_{11}H_{13}NO$ 175.0987, found 175.0998.

2-(((Benzyloxy)carbonyl)amino)acrylic Acid (13). A solution of benzyl carbamate (1.23 g, 8.13 mmol), hydroquinone (20 mg), and pyruvic acid (3.32 g, 37.78 mmol) in benzene (65 mL) was refluxed for 6 h in a Dean–Stark apparatus. The resulting mixture was extracted with a saturated $NaHCO_3$ solution. The aqueous extract was acidified by 10% HCl under cooling with ice and then extracted with $CHCl_3$. The extract was washed with a saturated NaCl solution, dried (Na_2SO_4), and evaporated to give a residue, which was chromatographed on silica gel. Elution with $CHCl_3$ afforded acid **13** (0.862 g, 46%) as crystals, mp 98–100 °C dec [lit.,[25] mp 100–101 °C dec].

2-(((Benzyloxy)carbonyl)amino)-*N*-(*p*-methoxyphenyl)acrylamide (14). To a solution of the above acid (**13**) (416 mg, 1.88 mmol) and *p*-anisidine (231 mg, 1.88 mmol) in dioxane (15 mL) was added a solution of DCC (387 mg, 1.88 mmol) in dioxane (3 mL) at room temperature. The mixture was stirred for 16 h at the same temperature before addition of benzene (100 mL). After filtration, the filtrate was washed with 10% HCl, a saturated $NaHCO_3$ solution, and H_2O, dried (Na_2SO_4), and evaporated. The residue was subjected to column chromatography on silica gel eluting with AcOEt–benzene (1:19 v/v) to give amide (**14**) (502 mg, 82%), which was recrystallized from benzene affording colorless fine needles: mp 108–110 °C dec; IR ($CHCl_3$) 3370 (NH), 1730 (CO), 1665 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 3.77 (3 H, s, OMe), 5.15 (2 H, s, OCH_2Ph), 5.23 and 6.15 (each 1 H, each d, each J = 2 Hz, =CH_2), 6.83 (2 H, d, J = 9 Hz, 2 × ArH), 7.20–7.47 (7 H, m, 7 × ArH); mass spectrum, m/z 326 (M^+); exact mass calcd for $C_{18}H_{18}N_2O_2$ 326.1265, found 326.1262.

1-(*p*-Methoxyphenyl)-3-methyl-3-(phenylsulfinyl)azetidin-2-one (16). 1-(*p*-Methoxyphenyl)-3-methyl-3-(phenylthio)azetidin-2-one (**8b**) (1.08 g, 3.61 mmol) was dissolved in dry CH_2Cl_2 (20 mL) and to this solution was dropwise added a solution of MCPBA (0.672 g, 3.89 mmol) in dry CH_2Cl_2 (5 mL) at −78 °C. The mixture was stirred for 20 min at the same temperature before evaporation of the solvent. The residue was chromatographed on silica gel with AcOEt–benzene as eluent (3:17 v/v) to give sulfoxide **16** (1.15 g, 99%). Recrystallization from benzene afforded colorless needles: mp 110–113 °C; IR ($CHCl_3$) 1750 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 1.66 (3 H, s, C_3-Me), 3.65 (3 H, s, OMe), 6.73 (2 H, d, J = 9 Hz, 2 × ArH), 6.99 (2 H, d, J = 9 Hz, 2 × ArH), 7.23–7.72 (5 H, m, 5 × ArH); mass spectrum, m/z 315 (M^+). Anal. Calcd for $C_{17}H_{17}NO_3S{\cdot}0.25H_2O$: C, 63.83; H, 5.36; N, 4.44. Found: C, 63.64; H, 5.32; N, 4.33.

1-(*p*-Methodyphenyl)-3-methyleneazetidin-2-one (17). A solution of the above sulfoxide (**16**) (234 mg, 0.744 mmol) in dry toluene (15 mL) was refluxed for 20 h. After evaporation of the solvent, the residue was chromatographed on silica gel. Elution with benzene gave exo olefin **17** (110 mg, 78%), which was recrystallized from benzene to afford colorless needles: mp 108–109 °C (decomp); IR ($CHCl_3$) 1738 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 3.77 (3 H, s, OMe), 4.08 (2 H, dd, J = 1.5 and 2 Hz, C_4-H_2), 5.28 (1 H, dd, J = 1.5 and 2 Hz, =C*H*H), 5.80 (1 H, dd, J = 2 and 2 Hz, =CH*H*), 6.84 (2 H, d, J = 9 Hz, 2 × ArH), 7.30 (2 H, d, J = 9 Hz, 2 × ArH); mass spectrum, m/z 189 (M^+). Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.82; H, 5.86; N, 7.40. Found: C, 69.52; H, 5.77; N, 7.37.

1-(*p*-Methoxyphenyl)azetidine-2,3-dione (18). To a solution of the above olefin (**17**) (399 mg, 2.02 mmol) in AcOEt (20 mL), dry ozone was bubbled at −78 °C for 15 min and Me_2S (0.35 mL) was then added. The resulting mixture was stirred for 20 min at the same temperature before addition of AcOEt. The mixture was washed with H_2O, dried (Na_2SO_4), and evaporated to give a residue, which was purified by column chromatography on silica gel. Elution with benzene yielded keto β-lactam **18** (249 mg, 61%), which was recrystallized from benzene to afford yellowish needles: mp 160–161 °C dec; IR ($CHCl_3$) 1820 (CO), 1757 cm^{-1} (CO); ^{1}H NMR ($CDCl_3$) δ 3.85 (3 H, s, OMe), 4.28 (2 H, s, C_4-H_2), 6.95 (2 H, d, J = 9 Hz, 2 × ArH), 7.49 (2 H, d, J = 9 Hz, 2 × ArH); mass spectrum m/z 191 (M^+). Anal. Calcd for $C_{10}H_9NO_3$: C, 62.82; H, 4.75; N, 7.33. Found: C, 62.55; H, 4.61; N, 7.09.

1-(*p*-Methoxyphenyl)azetidin-2-one 3-Oxime (19). To a solution of the above keto β-lactam (**18**) (124 mg, 0.651 mmol) in MeOH (10 mL), $H_2NOH{\cdot}HCl$ (73 mg, 1.04 mmol) and pyridine (77 mg, 0.98 mmol) were added, and the mixture was stirred for 12 h at ambient temperature. After evaporation of the solvent, the residue was chromatographed on silica gel with $CHCl_3$ as eluent. Recrystallization of the product from MeOH afforded oxime **19**[37] (249 mg, 61%) as yellowish needles: mp 209–211 °C dec; IR ($CHCl_3$) 3320 (OH), 1740 cm^{-1} (CO); ^{1}H NMR (CD_3OD) δ 3.77 (3 H, s, OMe), 4.33 (2 H, s, C_4-H_2), 6.90 (2 H, d, J = 9 Hz, 2 × ArH), 7.37 (2 H, d, J = 9 Hz, 2 × ArH); mass spectrum, m/z 206 (M^+); exact mass calcd for $C_{10}H_{10}N_2O_3$ 206.0690, found 206.0679.

3-Amino-1-(*p*-methoxyphenyl)azetidin-2-one (20). A mixture of the above oxime (**19**) (82 mg, 0.34 mmol) and 5% rhodium–alumina (100 mg) in MeOH (15 mL) was shaken under 5.5 atm of H_2 at ambient temperature. After filtration followed by evaporation of the filtrate, the residue was taken up into CH_2Cl_2. The CH_2Cl_2 extract was washed with

a saturated $NaHCO_3$ solution and a saturated NaCl solution, dried (Na_2SO_4), and evaporated. Purification of the residue by column chromatography on silica gel eluting with $CHCl_3$ gave amine **20**[37] (57 mg, 75%) as a syrup: IR ($CHCl_3$) 3400 (NH), 1740 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 1.80 (2 H, br s, NH_2), 3.33 (1 H, dd, J = 3 and 6 Hz, C_4-H), 3.80 (3 H, s, OMe), 3.90 (1 H, t, J = 6 Hz, C_4-H), 4.33 (1 H, dd, J = 3 and 6 Hz, C_3-H), 6.83 (2 H, d, J = 9 Hz, 2 × ArH), 7.36 (2 H, d, J = 9 Hz, 2 × ArH); exact mass calcd for $C_{10}H_{12}N_2O_2$ 192.0898, found 192.0898.

3-(((Benzyloxy)carbonyl)amino)-1-(*p*-methoxyphenyl)azetidin-2-one (21). To a mixture of the above amine (**20**) (40 mg, 0.206 mmol), $NaHCO_3$ (35 mg, 0.414 mmol), H_2O (3 mL), and CH_2Cl_2 (3 mL), a solution of BzO_2CCl (46 mg, 0.267 mmol) in CH_2Cl_2 (2 mL) was added dropwise at ambient temperature and the mixture was stirred for 4 h at the same temperature. After addition of CH_2Cl_2, the organic layer was washed with H_2O, dried (Na_2SO_4), and evaporated to give a residue, which was chromatographed on silica gel. Elution with AcOEt–benzene (1:9 v/v) afforded urethane **21** (59 mg, 88%) as a powder: mp 153–155 °C dec; IR ($CHCl_3$) 3340 (NH), 1745 (CO), 1720 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 3.53 (1 H, dd, J = 3 and 6 Hz, C_4-H), 3.75 (3 H, s, OMe), 3.87 (1 H, t, J = 6 Hz, C_4-H), 4.88 (1 H, m, C_3-H), 5.08 (2 H, s, OCH_2Ph), 5.48 (1 H, m, NH), 6.78 (2 H, d, J = 9 Hz, 2 × ArH), 7.11–7.27 (7 H, m, 7 × ArH); mass spectrum, m/z 326 (M^+). Anal. Calcd for $C_{18}H_{18}N_2O_4 \cdot 0.25H_2O$: C, 65.34; H, 5.48; N, 8.46. Found: C, 65.71; H, 5.53; N, 8.46.

3-(((Benzyloxy)carbonyl)amino)azetidin-2-one (22). To a solution of urethane **21** (31 mg, 0.095 mmol) in CH_3CN (2 mL), a solution of ceric ammonium nitrate (160 mg, 0.292 mmol) in a mixture of CH_3CN (2 mL) and H_2O (2 mL) was added at 0 °C, and the mixture was stirred for 15 min at the same temperature. After addition of AcOEt, the organic layer was washed successively with a saturated $NaHCO_3$ solution, a saturated Na_2SO_3 solution, a saturated $NaHCO_3$ solution, and a saturated NaCl solution. Drying (Na_2SO_4), followed by evaporation of the solvent, gave a residue, which was subjected to silica gel column chromatography. Elution with MeOH–$CHCl_3$ (1:9 v/v) afforded β-lactam **22** (12 mg, 59%) as a colorless powder, which was recrystallized from benzene–$CHCl_3$ giving colorless fine needles: mp 160–162 °C dec; IR ($CHCl_3$) 3425 (NH), 3310 (NH), 1770 (CO), 1730 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 3.36 (1 H, dd, J = 3 and 9 Hz, C_4-H), 3.62 (1 H, t, J = 6 Hz, C_4-H), 4.84 (1 H, m, C_3-H), 5.10 (2 H, s, OCH_2Ph), 5.28 (1 H, m, NH), 5.74 (1 H, m, NH), 7.30 (5 H, s, 5 × ArH); mass spectrum, m/z 220 (M^+). Anal. Calcd for $C_{11}H_{12}N_2O_3 \cdot 0.5H_2O$: C, 57.63; H, 5.27; N, 12.22. Found: C, 58.11; H, 5.27; N, 12.34.

(±)-3β,4β-Dimethyl-3α-(phenylthio)azetidin-2-one (25). The β-lactam **8d** (83 mg, 0.265 mmol) was treated with ceric ammonium nitrate (290 mg, 0.530 mmol) under the same conditions as above and worked up to give **25**[37] (39 mg, 72.2%) as a syrup: IR ($CHCl_3$) 3410 (NH), 1765 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 1.40 (3 H, d, J = 7.5 Hz, C_4-Me), 1.43 (3 H, s, C_3-Me), 3.63 (1 H, q, J = 7.5 Hz, C_4-H), 7.03–7.60 (5 H, m, Ph); mass spectrum, m/z 207 (M^+); exact mass calcd for $C_{11}H_{13}NO$ 207.0716, found 207.0715.

Methyl D-α-Methylacrylamido-α-((*p*-benzyloxy)phenyl)acetate (26). To a solution of methacrylic acid (375 mg, 4.36 mmol) in CH_2Cl_2 (20 mL), $(COCl)_2$ (0.46 mL) and DMF (1 drop) were added, and the mixture was stirred for 2 h at room temperature. After the solvent and the reagent were distilled off, the residue was dissolved in CH_2Cl_2. A solution of methyl D-((*p*-benzyloxy)phenyl)glycinate[29] (582 mg, 2.15 mmol) in CH_2Cl_2 (15 mL) and then pyridine (0.43 mL) were added to it. The mixture was stirred for 2 h at room temperature before addition of CH_2Cl_2 (50 mL). Washing with a saturated $NaHCO_3$ solution and 10% HCl, followed by drying (Na_2SO_4) and evaporation of the solvent, yielded a residue, which was chromatographed on silica gel. Elution with AcOEt–benzene (1:19 v/v) afforded amide (**26**)[37] (537 mg, 74%) as a colorless powder: mp 134–136 °C dec; $[\alpha]^{15}_D$ −80.1° (c 0.76, $CHCl_3$); IR ($CHCl_3$) 3420 (NH), 1735 (CO), 1665 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 1.93 (3 H, br s, Me), 3.70 (3 H, s, OMe), 5.03 (2 H, s, OCH_2Ph), 5.37 and 5.75 (each 1 H, each br s, $=CH_2$), 5.55 (1 H, d, J = 6 Hz, CH), 6.63–7.50 (10 H, m, 9 × ArH and NH); mass spectrum, m/z 339 (M^+); exact mass calcd for $C_{20}H_{21}NO_4$ 339.1471, found 339.1483.

Methyl α-((*p*-Benzyloxy)phenyl)-α-(3-methyl-3-(phenylthio)-2-oxo-1-azetidinyl)acetate (27). To a solution of amide **26** (44 mg, 0.13 mmol) in dry CH_2Cl_2 (2 mL), a solution of PhSCl (37 mg, 0.26 mmol) in dry CH_2Cl_2 (2 mL) was added dropwise at 0 °C, and the mixture was stirred for 3 h at the same temperature under N_2. After addition of CH_2Cl_2 (20 mL), the mixture was washed with a saturated $NaHCO_3$ solution, 10% HCl, and H_2O and dried (Na_2SO_4). Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with benzene gave the corresponding adducts (60 mg, 95%) as a colorless syrup: IR ($CHCl_3$) 3350 (NH), 1730 (CO), 1650 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 3.67 (3 H, s, OMe), 4.97 (2 H, s, OCH_2Ph), 5.40 (1 H, d, J = 6 Hz, CH), 6.70–7.67 (15 H, m, 14 × ArH and NH); mass spectrum, m/z 483 and 485 (M^+); exact mass calcd for $C_{26}H_{26}ClNO_4S$ 483.1271 and 485.1242, found 483.1274 and 485.1293.

A solution of the above adduct (70 mg, 0.145 mmol) in dry benzene (2 mL) was added dropwise at 0 °C to a mixture of 60% NaH (6 mg, 0.15 mmol) and dry DMF (2 mL), and the resulting mixture was stirred for 1 h at 0 °C under N_2. After addition of benzene (20 mL), the mixture was washed with a saturated NH_4Cl solution and H_2O, dried (Na_2SO_4), and evaporated. The residue was chromatographed on silica gel with AcOEt–benzene as eluent (1:19 v/v) to give β-lactam **27**[37] (33.7 mg, 52%) as a colorless syrup: IR ($CHCl_3$) 1760 (CO), 1745 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 3.70 (3 H, s, OMe), 5.00 (2 H, s, OCH_2Ph), 5.33 (1 H, s, CH), 6.72–7.62 (14 H, m, 14 × ArH); mass spectrum, m/z 447 (M^+); exact mass calcd for $C_{26}H_{25}NO_4S$ 447.1504, found 447.1510.

Methyl α-(*p*-Benzyloxyphenyl)-1-(3-methylene-2-oxoazetidinyl)-acetate (28). To a solution of the above β-lactam **27** (27 mg, 0.06 mmol) in dry CH_2Cl_2 (2 mL) was added at −78 °C a solution of *m*-chloroperbenzoic acid (11 mg, 0.06 mmol) in dry CH_2Cl_2 (2 mL), and the mixture was stirred for 15 min at the same temperature. After dilution with CH_2Cl_2, the mixture was washed with a saturated $NaHCO_3$ solution, dried (Na_2SO_4), and evaporated. The residue was purified by chromatography on silica gel eluting with AcOEt–benzene (3:17 v/v) to afford the corresponding sulfoxide (23 mg, 82%) as a colorless syrup: IR ($CHCl_3$) 1760 (CO), 1745 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 3.70 (3 H, s, OMe), 5.00 (2 H, s, OCH_2Ph), 5.23 (1 H, s, CH), 6.73–7.87 (14 H, m, 14 × ArH); mass spectrum, m/z 463 (M^+); exact mass calcd for $C_{26}H_{25}NO_5S$ 463.1454, found 463.1472.

A solution of the above sulfoxide (20 mg, 0.04 mmol) in toluene (5 mL) was refluxed for 20 h. After evaporation of the solvent, the residue was subjected to column chromatography on silica gel. Elution with AcOEt–benzene (1:9 v/v) gave olefin **28**[37] (7.4 mg, 50%) as a pale yellowish syrup, $[\alpha]^{15}_D$ −16.2° (c = 0.15, $CHCl_3$); IR ($CHCl_3$) 1750 sh (CO), 1740 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 3.50–4.20 (1 H, m, C_4-H), 3.75 (3 H, s, OMe), 4.03–4.20 (1 H, m, C_4-H), 5.07 (2 H, s, OCH_2Ph), 5.13–5.23 (1 H, m, $=CHH$), 5.65 (1 H, s, CH), 5.70–5.80 (1 H, m, $=CHH$), 6.87–7.53 (9 H, m, 9 × ArH); mass spectrum, m/z 337 (M^+); exact mass calcd for $C_{20}H_{19}NO_4$ 337.1312, found 337.1309.

Reaction of 4-(3-Butenyl)azetidin-2-one (29) with PhSCl. To a solution of the olefinic β-lactam (**29**)[31] (107 mg, 0.86 mmol) in dry CH_3CN (10 mL) was added dropwise at 0 °C a solution of PhSCl (375 mg, 2.60 mmol) in dry CH_3CN (3 mL), and the mixture was stirred for 1 h at ambient temperature. After evaporation of the solvent, the residue was subjected to silica gel chromatography. Elution with AcOEt–benzene (3:97 v/v) gave *N*-phenylthio β-lactam **30** (151.9 mg, 47%) as a mixture of two regioisomers: IR ($CHCl_3$) 1760 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 7.35 (10 H, br s, 2 × SPh); mass spectrum m/z 377 and 379 (M^+). Anal. Calcd for $C_{19}H_{20}ClNOS_2$: C, 60.38; H, 5.33; N, 3.71. Found: C, 60.65; H, 5.33; N, 3.41.

1-(*tert*-Butyldimethylsilyl)-4-(3-butenyl)azetidin-2-one (32). To a solution of the olefinic β-lactam **29** (1.1 g, 8.71 mmol) and Et_3N (0.89 g, 8.71 mmol) in dry DMF (4 mL) was added slowly a solution of t-$BuMe_2SiCl$ (1.3 g, 8.71 mmol) in dry DMF (5 mL), and the mixture was stirred at ambient temperature for 1 h under N_2. After evaporation of the solvent, the residue was taken up into benzene, washed with H_2O, and dried (Na_2SO_4). Evaporation of the solvent, followed by chromatography on silica gel with AcOE–benzene as eluent (1:24 v/v) gave the silylated compound (**32**)[37] (1.8 g, 86%) as a colorless oil: IR ($CHCl_3$) 1720 cm^{-1} (CO); ^1H NMR (CCl_4) δ 0.39 (6 H, s, $SiMe_2$), 1.17 (9 H, s, Si-t-Bu), 1.56–2.32 (4 H, m, 2 × CH_2), 2.72 (1 H, dd, J = 3 and 14.4 Hz, C_3-H), 3.27 (1 H, dd, J = 5 and 14.4 Hz, C_3-H), 3.58–3.90 (1 H, m, C_4-H), 5.07–5.37 (2 H, m, $—CH=CH_2$), 5.65–6.30 (1 H, m, $—CH=CH_2$); mass spectrum, m/z 239 (M^+).

Reaction of 1-(*tert*-Butyldimethylsilyl)-4-(3-butenyl)azetidin-2-one (32) with PhSCl. To a solution of the above compound (**32**) (1.1 g, 4.65 mmol) in dry CH_2Cl_2 (10 mL) was added dropwise a solution of PhSCl (0.7 g, 4.65 mmol) in dry CH_2Cl_2 (10 mL) under N_2 at 0 °C, and the mixture was stirred for 2 h at ambient temperature. After evaporation of the solvent, the residue was subjected to column chromatography on silica gel. Elution with AcOEt–benzene (1:19 v/v) gave adduct **33** (1.5 g, 83%) as a mixture of two regioisomers: IR ($CHCl_3$) 1720 (CO); ^1H NMR (CCl_4) δ 7.33 (5 H, br s, SPh); mass spectrum, m/z 383 and 385 (M^+). Anal. Calcd for $C_{19}H_{30}ClNOSSi$: C, 59.42; H, 7.87; N, 3.65. Found: C, 58.95; H, 7.68; N, 3.67.

4-(3-Chloro-4-(phenylthio)butyl)azetidin-2-one and 4-(4-Chloro-3-(phenylthio)butyl)azetidin-2-one (31). (A) To a solution of the above N-silylated compound (**33**) (1.0 g, 2.62 mmol) in CH_3CN (10 mL) was added 1M n-Bu_4NF–THF (2.62 mL) under N_2, and the mixture was stirred for 1 h at 0 °C. After evaporation of the solvent, the residue was purified by column chromatography on silica gel eluting with AcOEt–benzene (3:17 v/v) to give secondary β-lactam **31** (576 mg, 82%) as a

mixture of two regioisomers: IR ($CHCl_3$) 3420 (NH), 1750 cm^{-1} (CO); ^1H NMR (CCl_4) δ 7.45 (1 H, br s, NH); mass spectrum, m/z 268 and 270 (M^+). Anal. Calcd for $C_{13}H_{16}ClNOS$: C, 57.88; H, 5.98; N, 5.19. Found: C, 57.44; H, 5.96; N, 5.25.

(B) To a solution of the above *N*-phenylthio β-lactam (**30**) (60 mg, 0.16 mmol) in a mixture of EtOH–CH_2Cl_2 (1:1 v/v) (5 mL) was added $NaBH_4$ (10 mg), and the mixture was stirred for 30 min at room temperature. After evaporation of the solvent, the residue was partitioned between benzene and H_2O. The organic phase was dried (Na_2SO_4) and evaporated to give a residue, which was purified by silica gel chromatography as above to afford **31** (19.2 mg, 44.5%) as a colorless syrup, whose spectral data and TLC behaviors were identical with those of the sample prepared by method A.

(±)-3α-((Phenylthio)methyl)-1-carbapenam (34). A mixture of the above secondary β-lactam (**31**) (86.5 mg, 0.32 mmol), Et_3N (32.7 mg, 0.32 mmol), NaI (97 mg, 0.64 mmol), and K_2CO_3 (89 mg, 0.64 mmol) in CH_3CN (5 mL) was refluxed for 13 h. After evaporation of the solvent, the residue was taken up into CH_2Cl_2 and then filtered. Evaporation of the filtrate, followed by column chromatography on silica gel eluting with AcOEt–benzene (1:9 v/v), gave carbapenam **34** (32.4 mg, 82.1% based on the recovered starting material) as a syrup: IR ($CHCl_3$) 1740 (CO); ^1H NMR ($CDCl_3$) δ 1.25–4.12 (10 H, m), 7.18–7.40 (5 H, m, SPh); mass spectrum m/z 233 (M^+), whose ^{13}C NMR ($CDCl_3$) spectrum was consistent with reported ones.[31] Anal. Calcd for $C_{13}H_{15}NOS{\cdot}0.25H_2O$: C, 65.65; H, 6.58; N, 5.89. Found: C, 65.85; H, 6.37; N, 5.73.

Further elution with the same solvent system afforded starting material **31** (41.1 mg) as a mixture of two regioisomers.

(±)-3α-Methyl-1-carbapenam (35). A mixture of the above carbapenam (**34**) (47 mg, 0.2 mmol) and W_2-Raney Ni (2 mL) in EtOH (5 mL) was stirred for 2 h at ambient temperature. After filtration through Celite, the filtrate was evaporated to give a residue, which was taken up into benzene. The organic extract was washed with H_2O, dried (Na_2SO_4), and evaporated. Purification using column chromatography on silica gel eluting with AcOEt–benzene (1:9 v/v) afforded 3-methylcarbapenam **35**[37] (4.0 mg, 16%) as a syrup, whose IR and ^1H NMR spectra were well consistent with reported ones.[32]

(±)-3(*R)-(1(*S**)((((*p*-Nitrobenzyl)oxy)carbonyl)oxy)ethyl)-4-(*R**)-(3-(((*p*-nitrobenzyl)oxy)carbonyl)-2-propenyl)azetidin-2-one (39).** A mixture of aldehyde **38**[34] (331 mg, 1.03 mmol) and triphenylphosphine (((*p*-nitrobenzyl)oxy)carbonyl)methylene (467 mg, 1.03 mmol) in dry CH_2Cl_2 (10 mL) was refluxed for 1 h under N_2. After evaporation of the solvent, the residue was chromatographed on silica gel. Elution with AcOEt–benzene (1:9 v/v) gave unsaturated ester **39**[37] (507 mg, 96%) as a yellowish syrup: IR ($CHCl_3$) 3410 (NH), 1760 (CO), 1720 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 1.51 (3 H, d, J = 6 Hz, C_1-Me), 2.47–2.65 (2 H, m, C_4-CH_2), 3.29 (1 H, dd, J = 6 and 13 Hz, C_3-H), 3.65–3.87 (1 H, m, C_4-H), 4.98–5.09 (1 H, m, C_1-H), 5.19 (4 H, s, 2 × OCH_2Ar), 5.91 (1 H, d, J = 15.6 Hz, CH=C*H*CO_2PNB), 6.26 (1 H, br s, NH), 6.82 (1 H, dd, J = 7 and 15.6 Hz, C*H*=CHCO_2PNB), 7.48–8.14 (8 H, m, 8 × ArH); mass spectrum, m/z 513 (M^+).

Reaction of (±)-3(*R)-(1(*S**)-((((*p*-Nitrobenzyl)oxy)carbonyl)-oxy)ethyl)-4(*R**)-(3-(((*p*-nitrobenzyl)oxy)carbonyl)-2-propenyl)azetidin-2-one (39) with PhSCl.** To a solution of the above unsaturated ester (**39**) (662 mg, 1.3 mmol) in dry CH_3CN (10 mL) was added dropwise a solution of PhSCl (447 mg, 3.1 mmol) in dry CH_3CN (10 mL) at 0 °C under N_2. The mixture was stirred for 1 h at ambient temperature before evaporation of the solvent. Chromatography of the residue using silica gel eluting with AcOEt–benzene (1:19 v/v) gave **40** (511 mg, 65%) as a yellowish syrup: IR ($CHCl_3$) 1760 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 1.42 (3 H, d, J = 6 Hz, C_1-Me), 1.81–2.31 (2 H, m, C_4-CH_2), 3.29–4.16 (4 H, m, C*H*SPh, C*H*Cl, C_3-H, C_4-H), 4.95–5.02 (1 H, m, C_1-H), 5.16 (4 H, s, 2 × OCH_2Ar), 7.12–7.47 (14 H, m, 2 × SPh, 4 × ArH), 8.09 (4 H, d, J = 8 Hz, 4 × ArH). Anal. Calcd for $C_{36}H_{32}ClN_3O_{10}S_2$: C, 56.43; H, 4.21; N, 5.48. Found: C, 56.36; H, 4.15; N, 5.39.

Further elution with AcOEt–benzene (1:9 v/v) afforded adducts **41**[37] (27 mg, 4%) as a pale yellowish syrup: IR ($CHCl_3$) 3420 (NH), 1760 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 6.14 (1 H, br s, NH), 7.21–7.62 (9 H, m, SPh, 4 × ArH).

(±)-3(*R)-(1(*S**)-((((*p*-Nitrobenzyl)oxy)carbonyl)oxy)ethyl)-4-(*R**)-(3-(((*p*-nitrobenzyl)oxy)carbonyl)-3-chloro-2-(phenylthio)-propyl)azetidin-2-one and (±)-3(*R**)-(1(*S**)-((((*p*-Nitrobenzyl)oxy)-carbonyl)oxy)ethyl)-4(*R**)-(3-(((*p*-nitrobenzyl)oxy)carbonyl)-2-chloro-3-(phenylthio)propyl)azetidin-2-one (41).** To a solution of the compound (**40**) (303 mg, 0.396 mmol) in a mixture of MeOH–CH_2Cl_2 (1:1 v/v) (5 mL) was slowly added $NaBH_4$ (7.49 mg) at room temperature and the mixture was stirred for 45 min at the same temperature. The solvents were removed by a blow of N_2, and the residue was partitioned between CH_2Cl_2 and a phosphate buffer at pH 7. The organic extract was dried (Na_2SO_4) and evaporated to give a residue, which was chromatographed on silica gel. Elution with AcOEt–benzene (1:9 v/v) yielded adducts **41**[37] (156 mg, 60%), whose spectral data and TLC behaviors were identical with those of the above sample (**41**).

(±)-*p*-Nitrobenzyl 6(*R)-(1(*S**)-((((*p*-Nitrobenzyl)oxy)carbonyl)-oxy)ethyl)-1-carba-2-penem-3-carboxylate (43).** A mixture of acetal **37**[34] (250 mg, 0.66 mmol) and *p*-nitrobenzyl glyoxalate (438 mg, 2.1 mmol) in dry toluene (30 mL) was refluxed for 2 h in a Dean–Stark apparatus under N_2. After evaporation of the solvent, the residue was chromatographed on silica gel. Elution with AcOEt–benzene (3:17 v/v) gave (±)-1-(hydroxy-(((*p*-nitrobenzyl)oxy)carbonyl)methyl)-4(*R**)-(2,2-dimethoxyethyl)-3(*R**)-(1(*S**)-((((*p*-nitrobenzyl)oxy)carbonyl)oxy)-ethyl)azetidin-2-one (295 mg, 95%) as a mixture of two epimers: IR ($CHCl_3$) 1750 cm^{-1} (CO). Anal. Calcd for $C_{26}H_{29}N_3O_{13}$: C, 52.79; H, 4.94; N, 7.10. Found: C, 53.09; H, 5.01; N, 6.77.

To a solution of the above alcohol (295 mg, 0.5 mmol) in dry THF (5 mL) was added dropwise dry pyridine (83 mg, 1.0 mmol) and a solution of $SOCl_2$ (118 mg, 1.0 mmol) in dry THF (5 mL) at −20 °C under N_2. After the addition of benzene, the mixture was filtered and washed with dry benzene under N_2. Evaporation of the filtrate and washings gave a residue, which was dissolved in dry dioxane (5 mL). A mixture of PPh_3 (262 mg, 1.0 mmol) and 2,6-lutidine (107 mg, 1.0 mmol) in dry dioxane (5 mL) was dropwise added to the above mixture under N_2 and stirring. After stirring for 24 h at ambient temperature and then for 4 h at 50 °C, the mixture was filtered and washed with benzene. Evaporation of the filtrate and washings gave a yellow syrup, which was subjected to silica gel chromatography. Elution with AcOEt–benzene (1:4 v/v) afforded phosphorane **42**[37] (295 mg, 71%) as a gum: IR ($CHCl_3$) 1745 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 1.40 (3 H, d, J = 6.5 Hz, C_1-Me), 3.23 (6 H, s, 2 × OMe).

To a solution of the above phosphorane (**42**) (280 mg, 0.54 mmol) in dry THF (3 mL) was added a solution of *p*-TsOH (128 mg, 0.67 mmol) in dry THF (2 mL) under N_2 and stirring. After stirring for 1 h, Me_2CO (5 mL) was added and the mixture was further stirred for 6 h at ambient temperature. Evaporation of the solvent gave a residue, which was treated at ambient temperature for 30 min with a mixture of CH_2Cl_2 (10 mL) and a saturated $NaHCO_3$ solution (10 mL). The organic phase was dried (Na_2SO_4) and evaporated to give a yellowish syrup, which was chromatographed on silica gel. Elution with AcOEt–benzene (1:9 v/v) afforded carbapenem **43**[37] (62 mg, 36%) as a syrup: IR ($CHCl_3$) 1780 (CO), 1730 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 1.52 (3 H, d, J = 6 Hz, C_8-Me), 2.76–2.90 (2 H, m, C_1-H_2), 3.81 (1 H, dd, J = 6 and 9 Hz, C_6-H), 4.39 (1 H, dt, J = 6 and 9 Hz, C_5-H), 5.08 (1 H, m, C_8-H), 5.22 (4 H, s, 2 × OCH_2Ar), 6.60 (1 H, t, J = 2 Hz, C_2-H), 7.44–7.72 (4 H, m, 4 × ArH), 8.19 (4 H, d, J = 9 Hz, 4 × ArH).

(±)-*p*-Nitrobenzyl 6(*R)-(1(*S**)-((((*p*-Nitrobenzyl)oxy)carbonyl)-oxy)ethyl)-2-(phenylthio)-1-carbapenam-3-carboxylate (44).** (A) A mixture of the above carbapenem (**43**) (12 mg, 0.023 mmol), PhSH (3.8 mg, 0.034 mmol), and K_2CO_3 (1.6 mg, 0.011 mmol) in dry DMF (1 mL) was stirred for 1 h at room temperature. After addition of benzene, the organic phase was washed with H_2O, dried (Na_2SO_4), and evaporated. Chromatography of the resulting residue on silica gel eluting with AcOEt–benzene (1:19 v/v) afforded a mixture of two carbapenams (**44a** and **44b**)[37] (5.0 mg, 35%): IR ($CHCl_3$) 1775 (CO), 1750 cm^{-1} (CO); ^1H NMR ($CDCl_3$) δ 1.41 (3 H, d, J = 6 Hz, C_8-Me), 2.12 (2 H, m, C_1-H_2), 3.41 (1 H, dd, J = 6 and 10 Hz, C_6-H), 3.62–4.14 (2 H, m, C_2-H and C_5-H), 4.26 (0.5 H, d, J = 8 Hz, C_3-H), 4.82 (0.5 H, d, J = 8 Hz, C_3-H), 5.08 (1 H, m, C_8-H), 5.23 (4 H, s, 2 × OCH_2Ar), 7.28–7.56 (9 H, m, 4 × ArH and SPh), 8.25 (4 H, d, J = 8 Hz, 4 × ArH); mass spectrum, m/z 621 (M^+).

(B) A mixture of adduct **41** (30.8 mg, 0.05 mmol), Et_3N (4.8 mg, 0.05 mmol), NaI (14.1 mg, 0.10 mmol), and K_2CO_3 (13.0 mg, 0.10 mmol) in CH_3CN (5 mL) was refluxed for 24 h. After evaporation of the solvent, the residue was taken up into CH_2Cl_2 and then filtered. Evaporation of the solvents gave a residue, which was subjected to chromatography on silica gel. Elution with AcOEt–benzene (1:19 v/v) afforded a syrup (2 mg, 6.9%), whose TLC behaviors under several solvent systems were identical with those of the sample prepared by method A.

Acknowledgment. We thank K. Mushiake, K. Koike, E. Kurosawa, K. Kawamura, and Y. Kobayashi, Pharmaceutical Institute, Tohoku University, for microanalyses and spectral measurements. We are also grateful to R. Kobayashi, K. Otomo, Y. Watanabe, and K. Itoh for help with the preparation of the manuscript and financial support from The Sendai Institute of Heterocyclic Chemistry.

Registry No. 4a, 3219-55-4; **4b**, 7274-71-7; (*E*)-**4c**, 83375-42-2; (*E*)-**4d**, 83375-43-3; (*E*)-**4e**, 17645-29-3; (*E*)-**4f**, 83375-44-4; (±)-**5a**, 87585-85-1; (±)-**5b**, 87568-26-1; **5c**, 83375-45-5; **5d**, 83375-46-6; **5e**,

83375-47-7; **5f**, 83375-48-8; (±)-**6a**, 87568-27-2; (±)-**6b**, 87568-28-3; **6c**, 83375-49-9; **6d**, 83375-50-2; **6f**, 83375-52-4; (±)-**8a**, 87568-29-4; (±)-**8b**, 87568-30-7; (±)-**8c**, 87568-31-8; (±)-**8d**, 87568-32-9; (±)-**8e**, 87568-33-0; (±)-**8f**, 87568-34-1; (±)-**9c**, 87568-35-2; (±)-**9e**, 87568-36-3; **10**, 2210-24-4; (±)-**10** PhSCl adduct (isomer 1), 87568-37-4; (±)-**10** PhSCl adduct (isomer 2), 87568-38-5; (±)-**11**, 87568-39-6; (±)-**12**, 87568-40-9; **13**, 39692-63-2; **14**, 87568-41-0; **16**, 87568-42-1; **17**, 69193-56-2; **18**, 87568-43-2; **19**, 87568-44-3; (±)-**20**, 87568-45-4; (±)-**21**, 87568-46-5; (±)-**22**, 87637-98-7; (±)-**25**, 87568-47-6; (*R*)-**26**, 87568-48-7; **26** PhSCl adduct (isomer 1), 87568-49-8; **26** PhSCl adduct (isomer 2), 87568-50-1; **27**, 87568-51-2; **27** sulfoxide, 87568-52-3; (*R*)-**28**, 87568-53-4; (±)-**29**, 81264-11-1; **30** (isomer 1), 87568-54-5; **30** (isomer 2), 87568-55-6; **31** (isomer 1), 87568-56-7; **31** (isomer 2), 74373-19-6; (±)-**32**, 87568-57-8; **33** (isomer 1), 87568-58-9; **33** (isomer 2), 87568-59-0; (±)-**34**, 87568-60-3; (±)-**35**, 87568-61-4; (±)-**37**, 77447-98-4; (±)-**38**, 77447-99-5; (*E*)-(±)-**39**, 87568-62-5; **40** (isomer 1), 87585-86-2; **40** (isomer 2), 87568-63-6; **41** (isomer 1), 87568-64-7; **41** (isomer 2), 87568-65-8; (±)-**42**, 87568-66-9; (±)-**43**, 87568-67-0; (±)-**44a**, 87568-68-1; (±)-**44b**, 87638-51-5; PhSCl, 931-59-9; benzyl carbamate, 621-84-1; pyruvic acid, 127-17-3; *p*-anisidine, 104-94-9; methacrylic acid, 79-41-4; methyl D-((*p*-benzyloxy)phenyl)glycinate, 71336-83-9; triphenylphosphine (((*p*-nitrobenzyl)oxy)carbonyl)methylene, 63760-39-4; *p*-nitrobenzyl glyoxalate, 64370-35-0; (±)-1-(hydroxy-(((*p*-nitrobenzyl)oxy)carbonyl)-methyl)-4(*R**)-(2,2-dimethoxyethyl)-3(*R**)-(1(*S**)-((((*p*-nitrobenzyl)-oxy)carbonyl)oxy)ethyl)azetidin-2-one (isomer 1), 87568-69-2; (±)-1-(hydroxy-(((*p*-nitrobenzyl)oxy)carbonyl)methyl)-4(*R**)-(2,2-dimethoxyethyl)-3(*R**)-(1(*S**)-((((*p*-nitrobenzyl)oxy)carbonyl)oxy)ethyl)azetidin-2-one (isomer 2), 87637-99-8.

Triquinane Sesquiterpenes. An Iterative, Highly Stereocontrolled Synthesis of (±)-Silphinene

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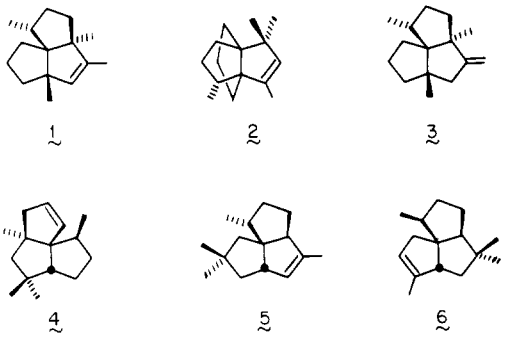
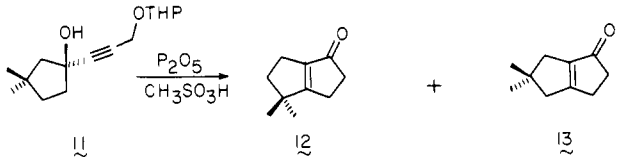
Abstract: A total synthesis of (±)-silphinene, a tricyclopentanoid sesquiterpene isolated from the roots of *Silphium perfoliatum* L., has been achieved. This structurally interesting triquinane was constructed in 15 steps and isolated in efficient overall yield. The key element of the synthesis was the implementation of an iterative cyclopentannulation scheme consisting of twofold conjugate addition of a functionalized organocopper reagent and subsequent aldol cyclization. This methodology is particularly serviceable for introducing vicinal quaternary carbon centers into polycyclic frameworks. A variety of other stereocontrolled chemical reactions were applied in the strategy that is outlined.

A variety of structurally interesting substances are produced by the roots of *Silphium perfoliatum* L.[2] The nonpolar extracts comprise a source, for example, of the previously characterized sesquiterpenes isocomene (**1**),[3,4] modhephene (**2**),[5,6] and β-isocomene (**3**).[6d,7] Also isolated was a fourth highly condensed tricyclopentanoid hydrocarbon for which the name silphinene was proposed. On the basis of NMR studies involving several oxidation products, silphinene was formulated as **4**.[2] The molecular array embodied in **4** is common to an increasingly widespread class of natural products that includes **1**, pentalenene (**5**),[8,9] and senoxydene (**6**).[10] As part of a program directed toward the synthesis of these fundamental triquinane[11] systems and their more highly oxygenated representatives, the construction of silphinene was viewed as a desirable undertaking.



Scheme I



From the outset, our interest in **4** as a synthetic target was prompted by the unique arrangement of its methyl substituents and double bond, which differs so extensively from those in **1**, **5**, and **6** as to require a radically altered protocol. In fact, no common synthetic thread has yet been found by which these tricyclic frameworks may be interwoven. An additional point of attraction was the close similarity of the silphinene nucleus to three of the four rings that form part of Nature's only fenestrane molecule, laurenene (**7**).[12] We therefore hoped to gain information on

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