tyldimethylsilyl chloride and 2.2 mmol of imidazole. The reaction was stirred for 12 h at room temperature under a nitrogen atmosphere. The mixture was then diluted with ether, washed with saturated sodium bicarbonate and brine, and dried over magnesium sulfate. Purification by silica gel column chromatography (25% EtOAc–hexane) afforded silyl ethers **9a–d**.

To 1.0 mmol of silyl ether **9** in 2 mL of methylene chloride was added 1.0 mmol of NCS and the reaction stirred for 15 min. Filtration through a small plug of silica gel and concentration afforded chloramine **10**. This product was dissolved in 5 mL of ether; then 2.2 mmol of potassium superoxide and 5 mg of 18-crown-6 were added and the reaction was stirred at room temperature for 3–6 h. Filtration and concentration afforded the imine **11**, which was directly hydrolyzed to the aldehyde **7** by stirring in 1:1 saturated oxalic acid–pentane at room temperature for 12 h. The organic layer was separated, washed with sodium bicarbonate, dried ($MgSO_4$), and concentrated to afford the aldehyde **7**, which was purified by silica gel thin-layer chromatography (25% Et_2O–hexane). Conversion of the amino alcohols to the aldehydes was run on a 0.4–1.0-mmol scale with reagents scaled proportionately.

Catalytic Hydrogenation of Amino Alcohols 2a–l. General Procedure. To 5.0 mmol of the amino alcohol and 25 mL of absolute ethanol with 2.5 mL of pH 7 buffer in a Fisher–Porter hydrogenation bottle was added 200 mg of 5% palladium on charcoal. The bottle was pressurized with hydrogen to 50 psi and stirred at room temperature while monitoring for the disappearance of the amino alcohol by silica gel TLC. The flask was then depressurized, and the contents were filtered and taken up in methylene chloride, washed with water, 1 M HCl, and brine, dried ($MgSO_4$), and concentrated to give the toluene **12**. These reactions were run on a 3.3–5.0-mmol scale with the exception of **2i**, which was run on a 0.2-mmol scale with all reagents scaled proportionately.

Catalytic Hydrogenation of Amino Alcohols 4a–d. General Procedure. To 0.4 mmol of the amino alcohol was added 5 mL of 4.4% formic acid in methanol followed by 150 mg of 10% palladium on charcoal. The reaction was stirred at room temperature under a nitrogen atmosphere. Filtration, concentration, and purification by preparative layer chromatography using 15% ether–hexane afforded the toluene **12**.

Acknowledgment. Financial support from the National Institutes of Health is gratefully acknowledged.

Registry No. **1a**, 19312-06-2; **1b**, 57629-47-7; **1c**, 87306-63-6; **1d**, 53416-46-9; **1e**, 80762-49-8; **1f**, 85588-72-3; **1g**, 57598-40-0; **1h**, 75948-75-3; **1i**, 75934-10-0; **1j**, 87306-64-7; **1k**, 66464-27-5; **1l**, 87306-65-8; **2a**, 10250-27-8; **2b**, 87306-66-9; **2c**, 87306-67-0; **2d**, 25452-29-3; **2e**, 87306-68-1; **2f**, 87306-69-2; **2g**, 87306-70-5; **2h**, 87306-71-6; **2i**, 87306-72-7; **2j**, 87306-73-8; **2k**, 87306-74-9; **2l**, 87306-75-0; **3a**, 77250-60-3; **3b**, 87306-76-1; **3c**, 87306-76-1; **3d**, 87306-77-2; **4a**, 87306-78-3; **4b**, 87306-79-4; **4c**, 87306-80-7; **4d**, 87306-81-8; **7a**, 100-52-7; **7b**, 59059-42-6; **7b** semicarbazone, 69621-96-1; **7c**, 16358-79-5; **7c** semicarbazone, 16678-37-8; **7d**, 123-11-5; **7e**, 587-04-2; **7e** semicarbazone, 16678-40-3; **7f**, 120-57-0; **7f** semicarbazone, 16742-62-4; **7g**, 1203-68-5; **7g** semicarbazone, 2928-48-5; **7k**, 87306-82-9; **7k** semicarbazone, 87306-86-3; **7l**, 87306-83-0; **7l** semicarbazone, 87306-87-4; **7m**, 6630-33-7; **7n**, 529-20-4; **7o**, 87306-84-1; **7p**, 87306-85-2; **9a**, 87306-88-5; **9b**, 87306-89-6; **9c**, 87306-90-9; **9d**, 87306-91-0; **10a**, 87306-92-1; **10b**, 87306-93-2; **10c**, 87306-94-3; **10d**, 87306-95-4; **11a**, 87306-96-5; **11b**, 87306-97-6; **11c**, 87306-98-7; **11d**, 87306-99-8; **12b**, 1595-11-5; **12d**, 104-93-8; **12f**, 7145-99-5; **12g**, 643-58-3; **12i**, 52601-70-4; **12j**, 90-12-0; **12l**, 87307-00-4; **12m**, 38324-52-6; *o*-phenylbenzoic acid, 947-84-2; 1-benzoyl-8-methyl-1,2,3,4-tetrahydroquinone, 87307-01-5.

Palladium-Catalyzed Carbonylation. A New Synthesis of α-Methylene γ-, δ-, and ε-Lactams and -Lactones Including Bicyclic Lactams of Pyrrolizidine and Indolizidine Skeletons

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The insertion of carbon monoxide into vinyl halides bearing the secondary amine or alcohol with a catalytic amount of $Pd(OAc)_2$ and PPh_3 was realized to give five-, six-, and seven-membered lactams and lactones carrying α-methylene groups in fairly good yields. Bicyclic heterocycles, pyrrolizidine and indolizidine derivatives, were also synthesized from pyrrolidine and piperidine derivatives possessing vinyl halide groups in the side chain at the 2-position of the ring by means of palladium-catalyzed carbonylation.

Many biologically active substances possessing α-methylene carbonyl groups are found in natural sources,[1] and a number of synthetic methods for these compounds have been reported.[2] We now describe details of an efficient synthesis of α-methylene γ-, δ-, and ε-lactams and -lactones by utilization of palladium-catalyzed carbonylation, which was already successfully applied to the synthesis of α-methylene β-lactams, important precursors of 3-amino-nocardicinic acid (3-ANA),[3a] as an extension of syntheses of heterocycles with organometallic compounds developed in this laboratory.[3] The method proved to be potentially available for the synthesis of bicyclic lactams of pyrrolizidine and indolizidine skeletons also. In the meantime, several other groups have independently reported

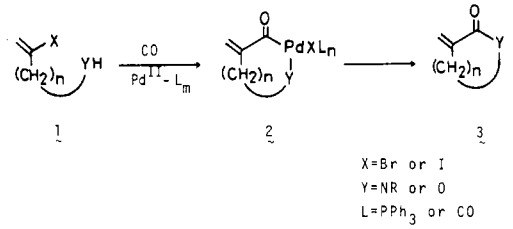
(1) Geissman, T. A.; Irwin, M. A. *Pure Appl. Chem.* **1970**, *21*, 167. Kupchan, S. M. *Ibid.* **1970**, *21*, 227. Lee, K.-H.; Piantadosi, C.; Huang, E.-S.; Pango, J. S.; Geissman, T. A. *Cancer Res.* **1971**, *31*, 1649.

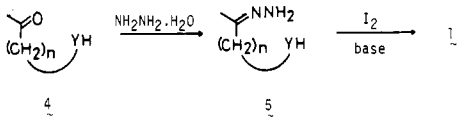
(2) (a) Grieco, P. *Synthesis* **1975**, 67. (b) Gammill, R. B.; Wilson, C. A.; Bryson, T. *Synth. Commun.* **1975**, *5*, 245. (c) Newaz, S. S. *Aldrichmica Acta* **1977**, *10*, 64.

(3) (a) Mori, M.; Chiba, K.; Okita, M.; Ban, Y. *J. Chem. Soc., Chem. Commun.* **1978**, 698. Chiba, K.; Mori, M.; Ban, Y. *Ibid.* **1980**, 770. (b) Mori, M.; Chiba, K.; Ban, Y. *J. Org. Chem.* **1978**, *43*, 1684. (c) Mori, M.; Chiba, K.; Ban, Y. *Heterocycles* **1977**, *6*, 1841. (d) Mori, M.; Chiba, K.; Inotsume, N.; Ban, Y., *Ibid.*, **1979**, *12*, 921. (e) Mori, M.; Chiba, K.; Ohta, N.; Ban, Y. *Ibid.* **1979**, *13*, 329. (f) Mori, M.; Ishikura, M.; Ikeda, T.; Ban, Y. *Ibid.* **1981**, *16*, 1491. Ishikura, M.; Mori, M.; Ikeda, T.; Terashima, M.; Ban, Y. *J. Org. Chem.* **1982**, *47*, 2456. Ishikura, M.; Mori, M.; Terashima, M.; Ban, Y. *J. Chem. Soc., Chem. Commun.* **1982**, 741.

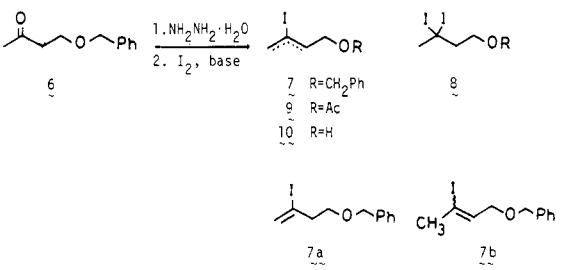
0022-3263/83/1948-4058$01.50/0

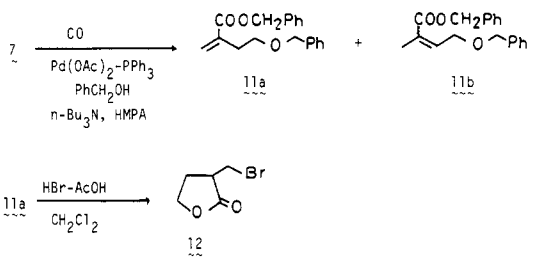
Scheme I





Scheme II





syntheses of α-methylene lactones from vinyl halides by means of transition-metal-catalyzed carbonylation.[4]

In the general scheme of the present method, the vinyl halides **1** bearing an amino or hydroxy group were subjected to carbonylation to afford five-, six-, and seven-membered lactams and lactones **3** through the acylapalladium complexes **2** (see Scheme I). 2,3-Dibromopropene was generally a useful starting material for the preparation of carbonylation substrates. In the other typical cases oxidation of hydrazone[5] or tosylhydrazone,[6] prepared from the corresponding ketone **4** on reaction with halogen in the presence of base, was effective for the synthesis of vinyl halide **1**. This reaction is attractive, because the ketone can be easily prepared by various methods and the halogen atom *regiospecifically* introduces carbon monoxide to the desired position.

Syntheses of Five-Membered Lactones and Lactams (Schemes II and III). For the synthesis of five-membered lactones (**3**, n = 2, Y = O) and lactams (**3**, n = 2, Y = N), the vinyl halide (**1**, n = 2, Y = O or N) was required as a starting material and was prepared from the

Scheme III

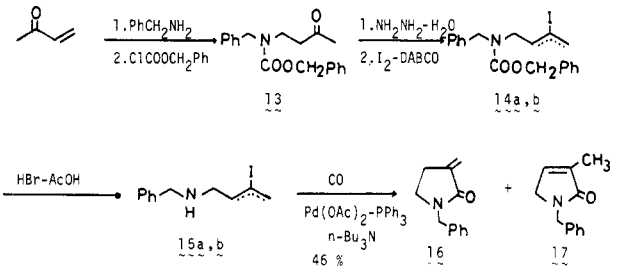


Table I. Treatment of the Hydrazone of Compound 6 with Iodine under Various Conditions

solvent	base (equiv)	yield of 7 + 8, %	7:8	7a:7b
ether	NEt_3 (10)	62	1:1	
benzene	NEt_3 (10)	58	1:1	
CCl_4	NEt_3 (10)	69	6:5	
ether	Dabco (10)	35	17:1	11:5
benzene	Dabco (10)	38	15:1	3:2
CH_2Cl_2	Dabco (10)	34	9:1	5:3
ether-CH_2Cl_2 (1:1)	Dabco (5)	54	1:0	13:8

hydrazone **5** of ketone **4** carrying a hydroxy or amino group at the terminal position. Thus, the ketone **6** was converted to the hydrazone in the usual manner and then treated with iodine and NEt_3 in tetrahydrofuran to give the desired vinyl iodide **7** and a significant amount of diiodide **8**. Other solvents such as benzene or carbon tetrachloride did not give any improved results. To abstract the methyl proton of the hydrazone stronger bases, such as 1,8-diazabicyclo[5.4.0]undecene (DBU), piperidine, and diazabicyclo[2.2.2]octane (Dabco), were used in place of NEt_3. Among these bases Dabco in methylene chloride–ether (1:1) gave the best results. The NMR spectrum of the crude product did not indicate generation of the undesired diiodide **8**, but a small amount of the inner olefin **7b** was obtained in rare cases. Treatment of the vinyl iodides **7a** and **7b** with HBr–AcOH gave the acetate **9**, but hydrolysis of the acetate did not afford the alcohol **10**. Therefore, a solution of the vinyl iodide **7**, benzyl alcohol, a catalytic amount of $Pd(OAc)_2$ and PPh_3 in hexamethylphosphoric triamide (HMPA) was warmed in the presence of n-Bu_3N under an atmosphere of carbon monoxide[7] to give the desired ester **11a** and **11b** in 48% yield. Debenzylation of the ester **11a** with HBr–AcOH gave 3-(bromomethyl)-2-furanone **12** (59.2%) (see Table I).

Ketone **13** was prepared by Michael addition of methyl vinyl ketone with benzylamine followed by protection of the secondary amino group with carbobenzyloxy chloride. The hydrazone of ketone **13** was treated in the same manner to produce vinyl iodide **14**, which was followed by treatment with HBr–AcOH to afford the secondary amine **15** in a good yield. Carbonylation of this amine **15** was carried out to afford the desired five-membered lactams **16** and **17** in a ratio of 10:1.

Syntheses of Six-Membered Lactones and Lactams (Schemes IV and V). For the synthesis of six-membered lactones and lactams (**3**, n = 3), the vinyl halide (**1**, n = 3) was prepared by alkylation of diethyl malonate[8] with 2,3-dibromopropene. Decarboethoxylation of **18** in dimethyl sulfoxide in the presence of sodium chloride[9] gave

(4) (a) Cowell, A.; Stille, J. K. *J. Am. Chem. Soc.* **1980**, *102*, 4193. (b) Semmelhack, M. F.; Brickner, S. J. *J. Am. Chem. Soc.* **1981**, *103*, 3945. (c) Matsuda, I. *Chem. Lett.* **1978**, 773.

(5) (a) Barton, D. H. R.; O'Brien, R. E.; Sternhell, S. *J. Chem. Soc.* **1962**, 470. (b) Pross, A.; Sternhell, S. *Aust. J. Chem.* **1970**, *23*, 989.

(6) Chambelin, A. R.; Stemke, J. E.; Bond, F. T. *J. Org. Chem.* **1978**, *43*, 147.

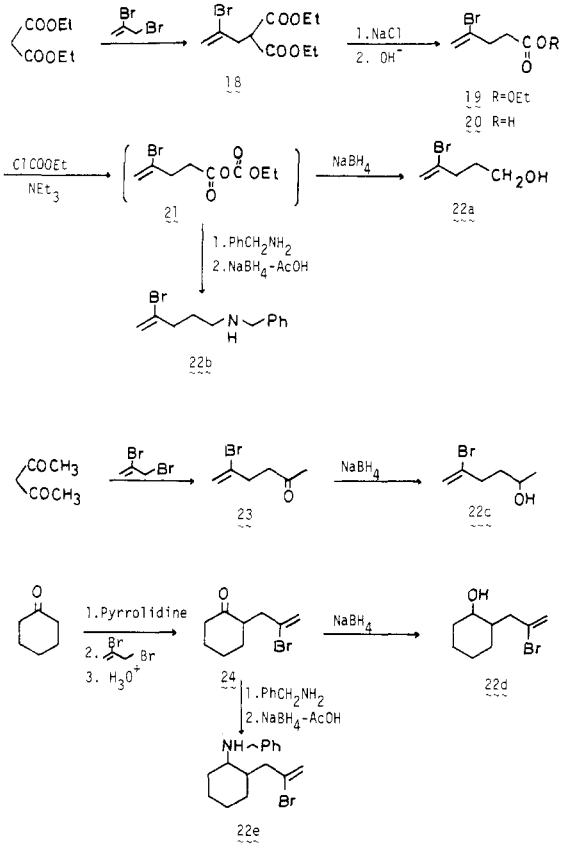
(7) Schoenberg, A.; Bartoletti, I.; Heck, R. F. *J. Org. Chem.* **1974**, *39*, 3318.

(8) Normant, H.; Cuvigny, T. *Bull. Soc. Chim. Fr.* **1965**, 1881.

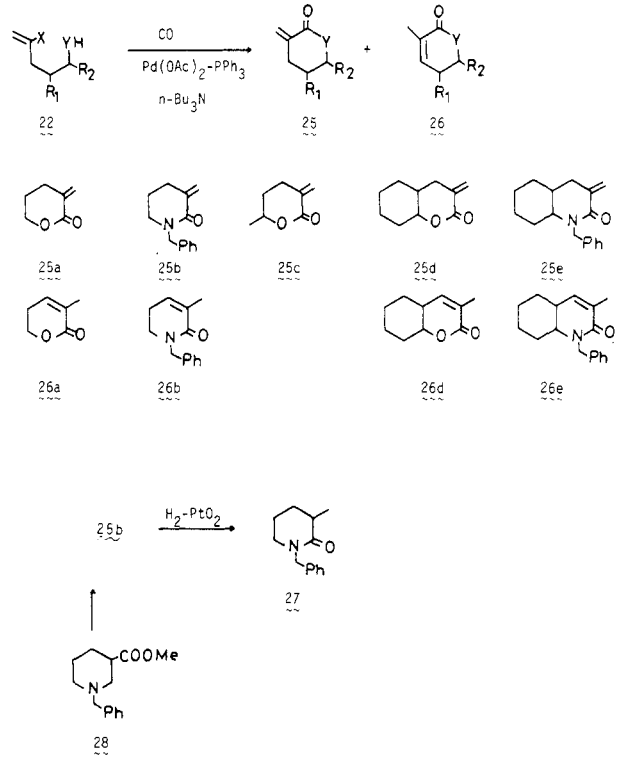
Table II. Insertion of Carbon Monoxide into the Vinyl Halide 22

entry	vinyl halide	R_1	R_2	YH	temp, °C	time, h	yield, % 25	yield, % 26
1	**22a**	H	H	OH	100	6	28	7
2	**22c**	H	CH_3	OH	100	3	31	
3	**22d**		$-(CH_2)_4-$	OH	100	3	50	13
4	**22d**		$-(CH_2)_4-$	OH	100	6	41	10
5	**22b**	H	H	$NHCH_2Ph$	100	5	61	
6	**22b**	H	H	$NHCH_2Ph$	120	3	25	4
7	**22e**		$-(CH_2)_4-$	$NHCH_2Ph$	100	2.5	75	7
8	**22e**		$-(CH_2)_4-$	$NHCH_2Ph$	90	5	80	2

Scheme IV



Scheme V



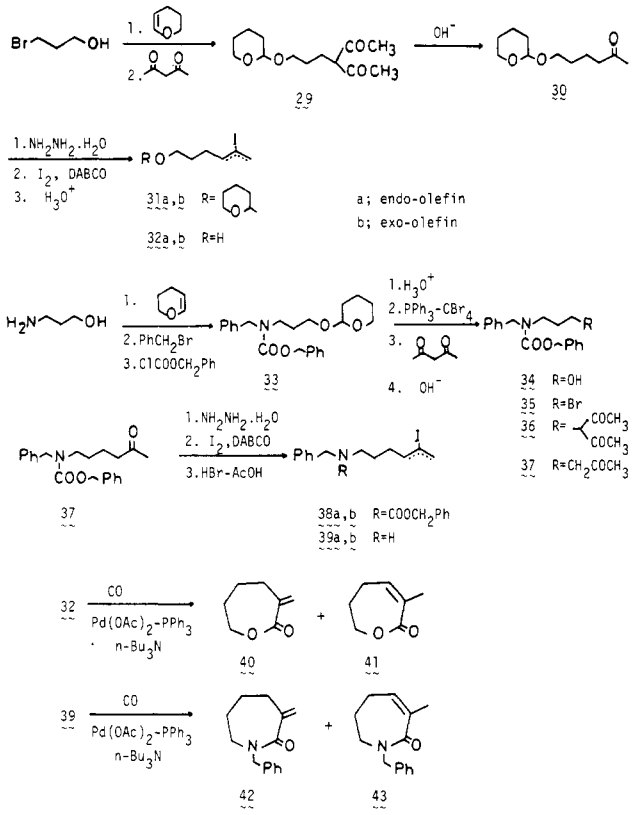
the monoester **19**. After hydrolysis of this ester, the carboxylic acid **20** was condensed with ethyl chloroformate in the presence of NEt_3 followed by reduction with $NaBH_4$ to produce 4-bromo-4-penten-1-ol (**22a**). On the other hand, benzylamine was added to this mixed anhydride **21** followed by reduction with $NaBH_4$ and acetic acid[10] to give *N*-benzyl-4-bromo-4-pentenylamine (**22b**). Palladium-catalyzed carbonylation of compounds **22a** and **22b** proceeded smoothly to afford α-methylene δ-lactone **25a** and -lactam **25b** along with generation of a small amount of **26a** and **26b**, respectively (Table II, entries 1 and 5).

To confirm this structure, compound **25b** was hydrogenated in the presence of PtO_2 in ethanol to give **27**. α-Methylene δ-lactam **25b** was alternatively synthesized from *N*-benzylnipecotinate (**28**) according to Rapoport's method.[11] The spectral data of the compound prepared by Rapoport's method were fully identical with those of the compound obtained by palladium-catalyzed carbonylation. The insertion of carbon monoxide into the secondary alcohol **22c**, which was prepared from acetylacetone and 2,3-dibromopropene followed by reduction with $NaBH_4$, was carried out under an atmosphere of carbon monoxide to afford α-methylene δ-lactone **25c** (Table II, entry 2). Subsequently, the pyrrolidine enamine of cyclohexanone was allowed to react with 2,3-dibromopropene followed by acid treatment to give **24**, which was reduced with $NaBH_4$ to give the alcohol **22d**. Condensation of **24** with benzylamine followed by reduction with $NaBH_4$ gave the secondary amine **22e**. Carbonylation of these compounds proceeded smoothly to give the bicyclic α-methylene δ-lactone **25d** and lactam **25e** in good yields along with small amounts of endo olefins **26d** and **26e**, respectively. These results are summarized in Table II. In this reaction, longer reaction time decreases the yield of the cyclized products (entry 4) and higher reaction temperature leads to an increase of the endo olefin **26** (entries 6 and 7). The ring junction of **25d** was considered to be cis because the C-8a proton signal of the trans compound has been reported to be δ 4.52[12] and that of the cis compound to be δ 3.80. The latter absorption is very close to the C-8a proton signal (δ 3.85) of this compound.

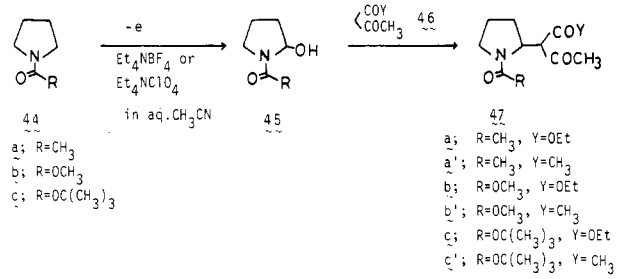
Syntheses of Seven-Membered Lactones and Lactams (Scheme VI). In order to synthesize the seven-membered lactones (**3**, $n = 4$, Y = O) and lactams (**3**, $n = 4$, Y = NR), vinyl halide (**1**, $n = 4$) was prepared from the

(9) Krapcho, A. P.; Lovey, A. J. *Tetrahedron Lett.* **1973**, 957.
(10) Umino, N.; Iwakuma, T.; Itoh, N. *Tetrahedron Lett.* **1976**, 763.
(11) Lee, D. L.; Morrow, C. J.; Rapoport, H. *J. Org. Chem.* **1974**, *39*, 893.
(12) Tanaka, T.; Nakata, T.; Yamashita, K. *Agric. Biol. Chem.* **1973**, *37*, 2365.

Scheme VI



Scheme VII



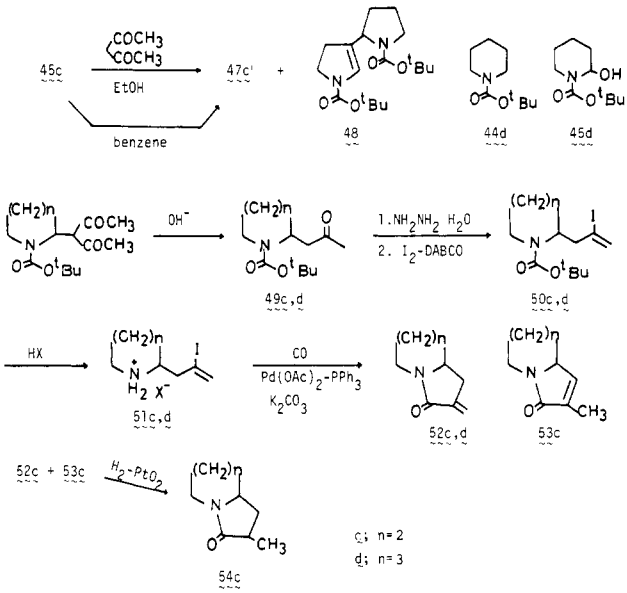
hydrazone of methyl ketone (**4**, $n = 4$) by iodine oxidation.

Commercially available 3-bromo-1-propanol was protected with 2,3-dihydropyran followed by condensation with acetylacetone in the presence of potassium iodide and potassium carbonate in methyl ethyl ketone to give compound **29** in a fairly good yield. Deacetylation of **29** with 5% NaOH–MeOH was followed by iodine oxidation to vinyl iodide **31**, which was treated with acid to give the alcohol **32** in good yield. Carbonylation of compound **32** was carried out to give the seven-membered lactones **40** and **41** in a moderate yield. To obtain the lactams, 3-amino-1-propanol was converted to **33**, which was deprotected with acid followed by treatment with CBr_4 and PPh_3[13] to give the bromide **35**. Conversion of **35** to vinyl iodide **38** by the above-mentioned method followed by deprotection of the amino group with HBr-AcOH gave the secondary amine hydrochloride **39**. Carbonylation of this compound **39** was also effected smoothly to afford the lactams **42** and **43** in fairly good yields.

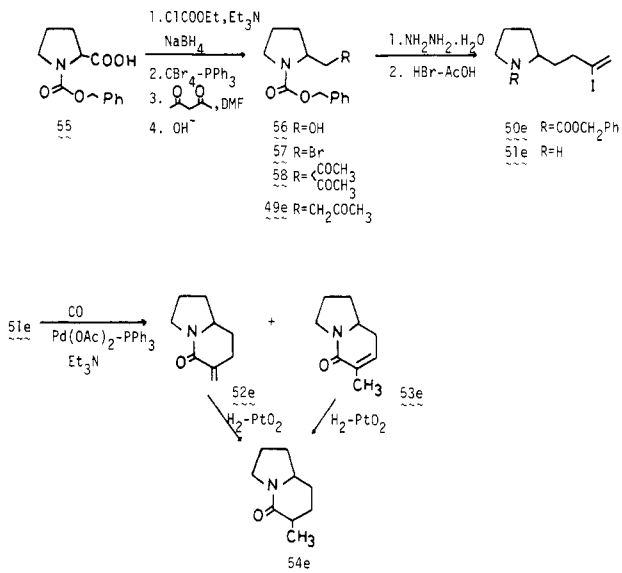
Syntheses of Pyrrolizidine and Indolizidine Derivatives (Schemes VII–IX). For the syntheses of pyrrolizidine and indolizidine derivatives, methyl ketones of

(13) Axelroad, E. H.; Milne, G. M.; van Tamalen, E. E. *J. Am. Chem. Soc.* **1970**, *92*, 2139.

Scheme VIII



Scheme IX



the general structure **49** were required. To obtain these intermediates, we made use of the electrochemical hydroxylation of lactams, previously reported by us,[14] followed by condensation with acetoacetic ester or acetylacetone.[15]

A solution of *N*-acetylpyrrolidine **44a** in aqueous acetonitrile was electrolyzed in an undivided cell to the hydroxylated compound **45a**, which was refluxed with active methylene compound **46** in the presence of a catalytic amount of piperidine in ethanol to give the condensation product **47a**. Various N-protected pyrrolidines **44** were electrolyzed under the same conditions followed by condensation with active methylene compounds **46** (Table III). Methoxycarbonyl and even *tert*-butoxycarbonyl were also suitable as protecting groups. Electrochemical oxidation of **44c** in aqueous medium proceeded smoothly to produce

(14) (a) Okita, M.; Wakamatsu, T.; Ban, Y. *J. Chem. Soc., Chem. Commun.* **1978**, 749. (b) Okita, M.; Wakamatsu, T.; Mori, M.; Ban, Y. *Heterocycles* **1980**, *14*, 1089.

(15) Recently, Speckamp reported that succinic imide was reduced with $NaBH_4$ to afford 2-hydroxy-5-oxopyrrolidine, which was considered to be an equilibrium with an aldehyde. deBoer, J. J. J.; Speckamp, W. N. *Tetrahedron Lett.* **1975**, 4039.

Table III. Electrochemical Oxidation of *N*-Acyl Cyclic Amine 44 and Condensation of the Hydroxylated Compound 45 with Active Methylene Compound 46

entry	starting material	R	46 (Y)	condensation reaction solvent	product	yield of 47 (from 44), %
1	44a	CH_3	OEt	EtOH	47a	26.8
2	44a	CH_3	CH_3	EtOH	47a′	21.4
3	44b	OCH_3	OEt	EtOH	47b	34.0
4	44b	OCH_3	CH_3	EtOH	47b′	46.6
5	44c	$OC(CH_3)_3$	OEt	EtOH	47c	62.9
6	44c	$OC(CH_3)_3$	CH_3	EtOH	47c′	26.3
7	44c	$OC(CH_3)_3$	CH_3	benzene	47c′	55.9
8	44d	$OC(CH_3)_3$	CH_3	benzene	47d	49.0

a hydroxylated compound, **45c**, but condensation with acetylacetone in ethanol led to a dimerization product, **48**, of **45c**[16] together with the desired compound **47c′**. Use of benzene as the solvent instead of ethanol gave the desired compound **47c′** as a sole product in a moderate yield.

Deacetylation of **47c′** gave the methyl ketone **49c**, whose hydrazone was treated with iodine followed by acid treatment to afford the vinyl iodide **51c**. Carbonylation of **51c** in the presence of excess potassium carbonate produced the desired pyrrolizidine derivatives **52c** and **53c** in 44% yield. In this reaction, shorter reaction time gave **52c** as a single product. To confirm these structures, a mixture of **52c** and **53c** was hydrogenated with PtO_2 in ethanol to give the saturated compound **54c** in quantitative yield.

Similarly, *N*-(*tert*-butoxycarbonyl)piperidine **44d** was electrochemically oxidized in aqueous acetonitrile to afford the hydroxylated compound **45d**, which was converted to **51d** in the same manner. Carbonylation of this secondary amine smoothly proceeded to give the indolizidine derivative **52d** (58%).

Indolizidine derivative **52** ($n = 3$, $m = 2$) was synthesized from L-proline. Benzyloxycarbonyl-L-proline (**55**) was reduced with $NaBH_4$ through the mixed anhydride to afford the alcohol **56**, which was converted to bromide **57** with CBr_4 and PPh_3 in acetonitrile.[13] Condensation of **57** with acetylacetone in dimethylformamide followed by base treatment afforded methyl ketone **49e**, which was converted to vinyl iodide **51e** in the usual manner. Carbonylation of this secondary amine **51e** proceeded smoothly to give the indolizidine derivatives **52e**[17] and **53e**, each in 27% yield. Compounds **52e** and **53e** were hydrogenated independently in the presence of PtO_2 under an atmosphere of hydrogen to afford the same compound, **54e**. These results suggest that bicyclic heterocycles, such as pyrrolizidine and indolizidine derivatives, can be easily prepared from the vinyl halide, which was prepared from the methyl ketone. Moreover, electrochemical oxidation of the *N*-acyl derivative of the cyclic amine **47** in aqueous medium was a useful synthetic method for the aldehyde having an amino group at the ω-position.

An important feature of these synthetic methods is that four-,[3] five-, six-, and seven-membered lactones and lactams can be easily prepared from the vinyl halide having the corresponding carbon chain. Moreover, since an atmosphere of carbon monoxide is usually satisfactory for these reactions, handling of chemicals is quite easy and the reaction apparatus is very simple.

Experimental Section

Melting points were measured with a hot stage microscope (Yanaco MP-J2) and with a melting point apparatus (Yanaco MP-1) and are uncorrected. ^1H NMR spectra were recorded in the indicated solvent on a Hitachi R-20B (60 MHz), a JEOL JNM-FX 100 (100 MHz), and a JEOL-FX 200 (200 MHz) spectrometers with Me_4Si as an internal standard. Splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad). Coupling constants are reported in hertz. A Jasco IRA-2 diffraction-grating infrared spectrophotometer and a Hitachi RMU-7M double-focusing mass spectrophotometer were used to determine IR and mass spectra, respectively. Electrochemical oxidation was carried out with Yanaco VE-8 controlled potential electrolyser.

N-Benzyl-N-((benzyloxy)carbonyl)-3-oxobutylamine (13). A solution of benzylamine (2.256 g, 21.1 mmol) and methyl vinyl ketone (1.647 g, 23.5 mmol) in ether (50 mL) was allowed to stand in an ice box for 21 h. To the ethereal solution a 2 N NaOH solution (50 mL) was added, and a solution of (benzyloxy)carbonyl chloride (4.318 g, 25.3 mmol) in ether (12 mL) was added dropwise to the solution at 0 °C. After the solution was stirred for 5 h, the ether layer was separated and the aqueous layer was extracted with ether. The combined ether layer was washed with 10% HCl solution, dried over Na_2SO_4, and evaporated. The residual oil was purified by chromatography on silica gel eluted with *n*-hexane–ethyl acetate (4:1) to give a colorless oil of **13** (3.692 g, 56.3%): IR ν_{max} (neat) 1700 cm^{-1}; NMR δ (CCl_4) 1.97 (s, 3 H, $COCH_3$), 2.27–2.81 (m, 2 H, CH_2CO), 3.41 (t, $J = 7$ Hz, 2 H, NCH_2), 4.47 (s, 2 H, $PhCH_2N$), 5.12 (s, 2 H, $PhCH_2O$), 7.21 (s, 5 H, aromatic), 7.28 (s, 5 H, aromatic).

Diethyl (2-Bromo-2-propenyl)malonate (18). To a suspension of NaH (60% in mineral oil, 5.00 g, 0.125 mol) in HMPA (50 mL) was added a solution of diethyl malonate (16.0 g, 0.10 mol) in HMPA (5 mL) at 0 °C under an atmosphere of argon. The mixture was stirred at 50 °C for 1 h. A solution of 2,3-dibromopropene (19.99 g, 0.10 mol) in HMPA (5 mL) was added to the diethyl malonate solution at 0 °C and the solution was warmed at 40 °C for 1 h. The reaction mixture was acidified with 10% HCl solution and the aqueous layer was extracted with ether. The organic layer was dried over $MgSO_4$ and concentrated to give a pale yellow oil of **18** (14.94 g, 53.5%): bp_{20} 130–140 °C; IR ν_{max} (neat) 1730, 1630 cm^{-1}; NMR δ (CCl_4) 1.25 (t, $J = 7$ Hz, 6 H, CH_3), 2.94 (d, $J = 8$ Hz, $=CCH_2$), 3.6 (m, 1 H, $COCHCO$), 4.14 (q, $J = 7$ Hz, 6 H, OCH_2), 5.42 (br s, 1 H, vinyl), 5.65 (m, 1 H, vinyl); mass spectrum, m/e 278 (M^+), 233, 205.

Ethyl 4-Bromo-4-pentenoate (19).[18] A solution of **18** (5.04 g, 18.1 mmol), NaCl (1.32 g, 22.5 mmol), and water (1.21 g, 67 mmol) in Me_2SO (10 mL) was refluxed for 8 h. After the evolution of carbon dioxide ceased, water was added to the solution and the aqueous layer was extracted with ethyl acetate. The organic layer was washed with water, dried over Na_2SO_4, and concentrated. The residue was purified by chromatography on silica gel eluted with *n*-hexane–ethyl acetate (4:1) to give a pale yellow oil of **20** (2.5 g, 67%): IR ν_{max} (neat) 1730, 1630 cm^{-1}; NMR δ (CCl_4) 1.25 (t, 3 H, $J = 7$ Hz, CH_3), 2.25–2.95 (m, 4 H), 4.07 (q, 2 H, $J = 7$ Hz, OCH_2), 5.9 (br s, 1 H, vinyl), 5.62 (br s, 1 H, vinyl).

4-Bromo-4-pentenoic Acid (20). A solution of **19** (441 mg, 2.3 mmol) in 5% KOH–MeOH (50% aqueous MeOH, 5 mL) was allowed to stand overnight. Solvent was removed under reduced pressure, the residue was made acidic with concentrated HCl, and the aqueous layer was extracted with ethyl acetate. The organic layer was dried over $MgSO_4$ and concentrated to give pale yellow

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crystals of **20** (369 mg, 97%): IR ν_{max} (Nujol) 1630 cm^{-1}; NMR δ (CCl_4) 2.58–2.75 (m, 4 H), 5.41 (m, 1 H), 11.54 (s, 1 H, COOH).

4-Bromo-4-penten-1-ol (22a).[19] To a solution of **20** (493 mg, 2.75 mmol) in THF (3 mL) was added a solution of NEt_3 (367 mg, 3.48 mmol) in THF (3 mL) at −10 °C. After being stirred for 10 min, a solution of ClCOOEt (377 mg, 3.47 mmol) in THF (3 mL) was added to the solution at the same temperature and the whole solution was stirred at −10 °C for 45 min. Then a solution of $NaBH_4$ (354 mg, 9.35 mmol) in water (2 mL) was carefully added to the solution of mixed anhydride at the same temperature and the mixture was stirred at 0 °C for 50 min and at room temperature for 50 min. After the solvent was removed under reduced pressure, water was added and the aqueous layer was extracted with ether. The organic layer was dried over Na_2SO_4 and concentrated. To the residue was added a 5% HCl–MeOH solution (50% aqueous MeOH, 12 mL) and the solution was refluxed for 30 min. The solvent was removed and the residue was extracted with ethyl acetate. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by chromatography on silica gel eluted with *n*-hexane–ethyl acetate (1:1) to give a pale yellow oil of **22a** (205 mg, 45%): IR ν_{max} (neat) 3300, 1625 cm^{-1}; NMR δ (CCl_4) 1.63–1.90 (m, 2 H), 2.36–2.69 (m, 2 H, $=CCH_2$), 3.59 (t, 2 H, J = 7 Hz, OCH_2), 5.40 (br s, 1 H, vinyl), 5.61 (m, 1 H, vinyl).

***N*-Benzyl-4-bromo-4-pentenylamine (22b).** To a solution of **21**, which was prepared from **20** (503 mg, 2.8 mmol), NEt_3 (393 mg, 3.70 mmol), and ClCOOEt (383 mg, 3.53 mmol) in THF, was added a solution of benzylamine (359 mg, 3.36 mmol) in THF (3 mL) at −10 °C and the mixture was stirred at room temperature overnight. Solvent was removed under reduced pressure and the residue was extracted with ethyl acetate. The organic layer was washed with 10% HCl solution and saturated NaCl solution, dried over Na_2SO_4, and concentrated to give colorless needles of *N*-benzyl-4-bromo-4-pentenamide, which was purified by recrystallization from ethyl acetate and *n*-hexane (443 mg, 59%): mp 58.0–60.0 °C; IR ν_{max} (Nujol) 3250, 1630 cm^{-1}; NMR δ ($CDCl_3$) 2.20–2.70 (m, 4 H), 4.25 (d, 2 H, J = 6 Hz, NCH_2Ph), 5.35 (br s, 1 H, vinyl), 5.55 (br s, 1 H, vinyl), 6.40 (m, 1 H, NH), 7.15 (s, 5 H, aromatic).

Anal. Calcd for $C_{12}H_{14}BrNO$: C, 53.75; H, 5.26; N, 5.22. Found: C, 53.79; H, 5.14; N, 5.05.

To a suspension of $NaBH_4$ (1.10 g, 29.5 mmol) and *N*-benzyl-4-bromo-4-pentenamide (790 mg, 2.95 mmol) in THF (6 mL) was added a solution of acetic acid (1.77 g, 29.5 mmol) in THF (6 mL) at 10 °C and then the solution was refluxed for 3.5 h. Solvent was removed under reduced pressure and water was added carefully to the residue under water cooling. The aqueous layer was extracted with benzene and the organic layer was extracted with 10% HCl solution. The aqueous layer was made basic with K_2CO_3 and extracted with benzene. The organic layer was dried over Na_2SO_4 and concentrated to give a pale yellow oil, **22b** (352 mg). The benzene layer, which contained a neutral product, was dried over Na_2SO_4 and concentrated. To its residue was added a solution of 5% HCl–MeOH (50% aqueous MeOH, 8 mL), and the solution was refluxed for 1.5 h. Solvent was removed under reduced pressure, and the aqueous layer was made basic with K_2CO_3 and extracted with benzene. The organic layer was dried over Na_2SO_4 and evaporated to give a pale yellow oil (196 mg). The combined crude oil (548 mg) was purified by chromatography on aluminum eluted with benzene–ethyl acetate (2:1) to give a pale yellow oil, **22b** (364 mg, 49%): IR ν_{max} (neat) 3300, 1620 cm^{-1}; NMR δ (CCl_4) 1.30 (s, 1 H, NH), 1.65 (m, 2 H), 2.30–2.75 (m, 4 H), 5.32 (br s, 1 H, vinyl), 5.50 (br s, 1 H, vinyl), 7.20 (s, 5 H, aromatic).

6-Bromo-6-hepten-2-one (23). A solution of 2,3-dibromopropene (1.087 g, 5.43 mmol), K_2CO_3 (0.840 g, 6.08 mmol), and acetylacetone (0.600 g, 6.00 mmol) in EtOH (10 mL) was refluxed for 16 h. After the solvent was removed under reduced pressure, the residue was purified by chromatography on silica gel eluted with *n*-hexane–ethyl acetate (4:1) to give a colorless oil, **23** (0.407 g, 42.4%): IR ν_{max} (neat) 1720, 1630 cm^{-1}; NMR δ (CCl_4) 2.17 (s, 3 H, CH_3), 2.70 (m, 4 H), 5.45 (br s, 1 H, vinyl), 5.64 (br s, 1 H, vinyl).

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6-Bromo-6-hepten-2-ol (22c).[20] To a solution of **23** (0.407 g, 2.30 mmol) in EtOH (20 mL) was added $NaBH_4$ (0.364 g, 2.06 mmol) at 0 °C and the mixture was stirred at room temperature for 3 h. After removal of the solvent, water was added to the reaction mixture and the aqueous layer was extracted with ether. The organic layer was dried over Na_2SO_4 and evaporated. The residue was purified by chromatography on silica gel eluted with *n*-hexane–ethyl acetate (1:1) to give a colorless oil, **22c** (289 mg, 70.2%): IR ν_{max} (neat) 3320, 1630 cm^{-1}; NMR δ ($CDCl_3$) 1.24 (d, J = 7 Hz, 3 H, CH_3), 1.49–1.90 (m, 2 H), 1.90 (s, 1 H, OH), 2.68 (m, 2 H), 3.60–4.13 (m, 2 H), 5.45 (br s, 1 H, vinyl), 5.65 (br s, 1 H, vinyl); mass spectrum, m/e 99 (M^+ − Br), 81 (M^+ − Br − H_2O).

2-(2-Bromo-2-propenyl)cyclohexanone (24).[21] To a solution of 1-pyrrolidyl-1-cyclohexene (5 g, 0.033 mol) in anhydrous dioxane (20 mL) was added a solution of 2,3-dibromopropene (6.7 g, 0.033 mol) in anhydrous dioxane (10 mL) under an atmosphere of nitrogen at 0 °C. After being refluxed for 3 h, a 1% HCl solution (11 mL) was added to the reaction mixture and then the solution was refluxed for 3 h. Solvent was removed under reduced pressure and the aqueous layer was extracted with ether. The organic layer was washed with saturated NaCl solution, dried over Na_2SO_4, and concentrated. The residue was purified by distillation to give a colorless liquid, **24** (3.1 g, 42%): bp_3 96–99 °C; IR ν_{max} (neat) 1710, 1630 cm^{-1}; NMR δ (CCl_4) 1.0–3.2 (m, 11 H), 5.45 (br s, 1 H, vinyl), 5.62 (br s, 1 H, vinyl).

2-(2-Bromo-2-propenyl)cyclohexan-1-ol (22d). To a solution of **24** (1.005 g, 4.63 mmol) in MeOH (40 mL) was added $NaBH_4$ (175 mg, 4.63 mmol) by portions and the mixture was stirred at 0 °C for 1.5 h. Solvent was removed under reduced pressure and water was added to the residue. The aqueous layer was extracted with ether and the organic layer was dried over Na_2SO_4 and concentrated to give a pale yellow oil, which was purified by chromatography on silica gel eluted with *n*-hexane–ethyl acetate–EtOH (10:1:0.1) to afford a colorless oil, **22d** (659 mg, 65%): IR ν_{max} (neat) 3350, 1630 cm^{-1}; NMR δ (CCl_4) 5.40 (br s, 1 H, vinyl), 5.55 (br s, 1 H, vinyl); mass spectrum, m/e 201 (M^+ − H_2O).

***N*-Benzyl-2-(2-bromo-2-propenyl)cyclohexylamine (22e).** To a solution of **24** (979 mg, 4.5 mmol) in anhydrous benzene (20 mL) suspended with $MgSO_4$ was added a solution of benzylamine (580 mg, 5.4 mmol) in benzene (5 mL) and the mixture was stirred at room temperature overnight. After filtration of $MgSO_4$, benzene was evaporated to give a pale yellow oil of imine (1.39 g): IR ν_{max} (neat) 1660 cm^{-1}. The crude product was dissolved in MeOH (50 mL), and $NaBH_4$ (171 mg, 4.52 mmol) was added to the methanolic solution under ice cooling. After stirring at room temperature for 1.5 h, methanol was evaporated and water was added to the residue. The aqueous layer was extracted with ether and the ether layer was dried over Na_2SO_4 and concentrated. The residual oil was purified by chromatography on silica gel eluted with *n*-hexane–ether (2:1) to give a pale yellow oil, **22e** (869 mg, 62%): IR ν_{max} (neat) 3030, 3020, 1630 cm^{-1}; NMR δ (CCl_4) 1.2–2.8 (m, 10 H), 3.69 (s, 2 H, NCH_2Ph), 5.38 (br s, 1 H, vinyl), 5.50 (br s, 1 H, vinyl), 7.22 (s, 5 H, aromatic).

3-Acetyl-6-((tetrahydro-2*H*-pyran-2-yl)oxy)-2-hexanone (29). A solution of 3-bromopropyl 2-tetrahydropyranyl ether[22] which was prepared from 3-bromopropanol (2.78 g, 20 mmol) and dihydropyran (1.68 g, 20 mmol), acetylacetone (4.14 g, 41.4 mmol), K_2CO_3 (2.877 g, 41.4 mmol), a small amount of potassium iodide, and 18-crown-6 in methyl ethyl ketone (60 mL) was refluxed overnight. After filtration of the undissolved material, solvent was removed under reduced pressure and the residue was purified by chromatography on silica gel eluted with *n*-hexane–ethyl acetate (4:1) to give a colorless oil, **29** (4.032 g, 80.5%): IR ν_{max} (neat) 1705, 1695, 1600 cm^{-1}; NMR δ ($CDCl_3$) 2.16 (s, 3 H, $COCH_3$), 2.28 (s, 3 H, $COCH_3$), 3.40–3.60 (m, 2 H, OCH_2), 3.60–4.0 (m, 2 H, OCH_2), 4.58 (s, 1 H, OCHO).

6-((Tetrahydro-2*H*-pyran-2-yl)oxy)-2-hexanone (30).[23] A solution of **29** (578 mg, 2.39 mmol) in 5% NaOH–EtOH (50%

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aqueous EtOH, 140 mL) was allowed to stand for 2 h. After the solvent was removed under reduced pressure, the residual oil was purified by chromatography on silica gel eluted with *n*-hexane–ethyl acetate (1:1) to give a colorless oil, **30** (362.6 mg, 75.9%): IR ν_{max} (neat) 1720 cm^{-1}; NMR δ ($CDCl_3$) 1.4–1.8 (m, 10 H), 2.14 (s, 3 H, $COCH_3$), 2.4–2.6 (m, 2 H, CH_2CO), 3.3–3.6 (m, 2 H, OCH_2), 3.6–3.9 (m, 2 H, OCH_2), 4.57 (s, 1 H, OCHO).

***N*-Benzyl-*N*-((benzyloxy)carbonyl)-3-((tetrahydro-2*H*-pyran-2-yl)oxy)propylamine (33).** To a solution of 3-aminopropanol (7.5 g, 0.1 mol) and *p*-toluenesulfonic acid (20.9 g, 0.11 mol) in CH_2Cl_2 (50 mL) was added a solution of dihydropyran (8.4 g, 0.1 mol) in CH_2Cl_2 (10 mL) at 0 °C, and the mixture was stirred at room temperature for 2 h. Solvent was removed under reduced pressure, the residue was dissolved in CH_3CN (100 mL) to which was added K_2CO_3 (16 g, 0.12 mol), and the solution was stirred vigorously. The white precipitates were filtered off and washed with acetonitrile. To the combined acetonitrile solutions, which contained K_2CO_3 (16 g, 0.12 mol) again, was added a solution of benzyl bromide (20.5 g, 0.12 mol) in acetonitrile (50 mL) and the solution was stirred at room temperature overnight. After filtration of undissolved material, the solvent was removed under reduced pressure and the residue was dissolved in acetone (200 mL). To the solution containing K_2CO_3 (16 g, 0.12 mol) was added a solution of (benzyloxy)carbonyl chloride (20 g, 0.12 mol) in acetone (20 mL) and the mixture was stirred overnight. After the solvent was removed under reduced pressure, water was added and the aqueous layer was extracted with ethyl acetate. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by chromatography on silica gel eluted with *n*-hexane–ethyl acetate (4:1) to give a colorless oil of **33** (14.47 g, 38.9%): NMR δ ($CDCl_3$) 1.3–2.0 (m, 8 H), 3.2–3.8 (m, 6 H), 4.48 (s, 2 H, NCH_2Ph), 5.12 (s, 2 H, OCH_2Ph), 7.20 and 7.27 (s, s, 10 H, aromatic).

3-(*N*-Benzyl-*N*-((benzyloxy)carbonyl)amino)-1-propanol (34). A solution of **33** (3.1 g, 8.3 mmol) and a catalytic amount of *p*-toluenesulfonic acid in methanol (100 mL) was allowed to stand at room temperature for 5 h. After removal of the solvent, the residue was dissolved in CH_2Cl_2 and the organic layer was washed with water, dried over Na_2SO_4, and concentrated. The residue was purified by chromatography on silica gel eluted with *n*-hexane–ethyl acetate (1:1) to give a colorless oil, **34** (2.4 g, 96.4%): NMR δ ($CDCl_3$) 1.4–1.8 (m, 2 H), 2.1 (m, 2 H), 3.3–3.6 (m, 2 H, OCH_2), 4.28 (s, 2 H, NCH_2Ph), 4.70 (s, 1 H, OH), 5.20 (s, 2 H, OCH_2Ph), 7.2–7.4 (10 H, aromatic).

***N*-Benzyl-*N*-((benzyloxy)carbonyl)-3-bromopropylamine (35).** To a solution of **34** (3.00 g, 10.0 mmol) and CBr_4 (4.00 g, 12.0 mmol) in CH_3CN (50 mL) was added PPh_3 (12.0 g, 8.48 mmol) by portions under ice cooling and the mixture was stirred at room temperature overnight. Undissolved material was filtered off and the solvent was removed under reduced pressure. The residue was purified by chromatography on silica gel eluted with *n*-hexane–ether (4:1) to give a colorless oil, **35** (3.350 g, 92.5%): IR ν_{max} (neat) 1700 cm^{-1}; NMR δ ($CDCl_3$) 1.9–2.3 (m, 2 H), 3.2–3.5 (m, 4 H), 4.52 (s, 2 H, NCH_2Ph), 5.20 (s, 2 H, OCH_2Ph), 7.2–7.5 (10 H, aromatic).

4-Acetyl-*N*-benzyl-*N*-((benzyloxy)carbonyl)-5-oxohexylamine (36). A solution of **35** (527 mg, 1.5 mmol), acetylacetone (303 mg, 3.0 mmol), K_2CO_3 (417 mg, 3.0 mmol), a catalytic amount of potassium iodide, and 18-crown-6 in methyl ethyl ketone (20 mL) was refluxed for 15 h. The undissolved material was filtered off and the solvent was removed under reduced pressure. The residue was purified by chromatography on silica gel eluted with *n*-hexane–ethyl acetate (4:1) to give a colorless oil, **36** (367.8 mg, 64.4%) with the starting material **35** (67.6 mg, 12.8%): IR ν_{max} (neat) 1700, 1695 cm^{-1}; NMR δ ($CDCl_3$) 3.1–3.4 (m, 2 H), 4.50 (s, 2 H, NCH_2Ph), 5.19 (s, 2 H, OCH_2Ph), 7.2–7.4 (10 H, aromatic).

6-(*N*-Benzyl-*N*-((benzyloxy)carbonyl)amino)-2-hexanone (37). A solution of **36** (367 mg, 0.96 mmol) in 5% NaOH–EtOH (50% aqueous EtOH, 20 mL) was allowed to stand at room temperature overnight. Solvent was removed under reduced pressure and the residue was dissolved in methylene chloride. The organic layer was washed with water, dried over K_2CO_3, and concentrated. The residual oil was purified by chromatography on silica gel eluted with *n*-hexane–ethyl acetate (1:1) to give a colorless oil of **37** (226.3 mg, 69.3%): IR ν_{max} (neat) 1700, 1695 cm^{-1}; NMR δ ($CDCl_3$) 1.3–1.7 (m, 4 H, CH_2CH_2), 2.06 (s, 3 H, $COCH_3$), 2.15–2.6 (m, 2 H, CH_2CO), 3.05–3.5 (m, 2 H, NCH_2), 4.53 (s, 2 H, NCH_2Ph), 5.22 (s, 2 H, OCH_2Ph), 7.31 and 7.38 (s, s, 10 H, aromatic); mass spectrum, *m/e* 339 (M^+), 248 ($M^+ - CH_2Ph$), 204 ($M^+ - CH_2Ph$), 91.

General Procedure for the Electrochemical Oxidation of *N*-Acyl Cyclic Amine 44 and the Condensation Reaction of 45 with Active Methylene Compound 46. A solution of N-acyl cyclic amine **44** and NEt_4BF_4 or NEt_4ClO_4 as electrolyte in aqueous CH_3CN ($CH_3CN:H_2O$ = 20:1) was electrochemically oxidized in an undivided cell using platinum plates as anode and cathode. After the solvent was removed under reduced pressure, the residue was dissolved in benzene. The undissolved material was filtered off and the filtrate was concentrated under reduced pressure. For removal of water, benzene was added, the solvent was removed, and the same treatment was repeated again. The residue was dissolved in benzene and the benzene layer was dried over K_2CO_3 and evaporated to give a hydroxylated amide **45**. A solution of **45**, active methylene compound **46**, and a catalytic amount of piperidine in benzene or EtOH was refluxed under an argon atmosphere overnight. Solvent was removed under reduced pressure and the residue was purified by chromatography on silica gel to give a desired condensation product **47**.

Ethyl 2-(*N*-acetylpyrrolidin-2-yl)-3-oxobutyrate (47a): yield, 26.8%; IR ν_{max} (neat) 1720, 1630 cm^{-1}; NMR δ ($CDCl_3$) 1.28 (t, 3 H, J = 7 Hz, CH_3), 1.94 (s, 3 H, $COCH_3$), 2.28 (s, 3 H, $COCH_3$), 4.20 (q, J = 7 Hz, 2 H, OCH_2); mass spectrum, *m/e* 241 (M^+), 198 ($M^+ - COCH_3$), 196, 156, 152, 102, 70.

3-(*N*-Acetylpyrrolidin-2-yl)-2,4-pentanedione (47a'):[24] yield, 21.4%; IR ν_{max} (neat) 1710, 1700 1620 cm^{-1}; NMR δ ($CDCl_3$) 2.04 (s, 3 H, $COCH_3$), 2.20 (s, 6 H, $COCH_3$), 3.50 (br t, 2 H), 4.53 (br s, 1 H, NCH); mass spectrum, *m/e* 211 (M^+), 168 ($M^+ - COCH_3$), 126, 112, 70.

Ethyl 2-(*N*-(methoxycarbonyl)pyrrolidin-2-yl)-3-oxobutyrate (47b): yield, 34.0%; IR ν_{max} (neat) 1700 cm^{-1}; NMR δ ($CDCl_3$) 1.29 (t, 3 H, J = 7 Hz, CH_3), 2.26 (s, 3 H, $COCH_3$), 3.72 (s, 3 H, OCH_3), 4.22 (q, J = 7 Hz, 2 H, OCH_2); mass spectrum, *m/e* 257 (M^+), 214 ($M^+ - COCH_3$), 212 ($M^+ - COCH_3$), 198 ($M^+ - COOMe$), 168, 128.

3-(*N*-(Methoxycarbonyl)pyrrolidin-2-yl)-2,4-pentanedione (47b'):[24] yield, 46.6%; IR ν_{max} (neat) 1700 cm^{-1}; NMR δ ($CDCl_3$) 2.19 (s, 3 H, $COCH_3$), 2.23 (s, 3 H, $COCH_3$), 1.5–2.1 (m, 4 H), 3.20–3.6 (m, 2 H), 3.60 (s, 3 H, OCH_3), 4.25 (m, 1 H).

Ethyl 2-(*N*-(*tert*-butoxycarbonyl)pyrrolidin-2-yl)-3-oxobutyrate (47c): yield, 62.9%; IR ν_{max} (neat) 1725, 1705 cm^{-1}; NMR δ ($CDCl_3$) 1.28 (t, J = 7 Hz, 3 H, CH_3), 1.46 [s, 9 H, $C(CH_3)_3$, 1.6–2.2 (m, 4 H), 2.22 (s, 3 H, $COCH_3$), 3.1–3.6 (m, 2 H), 4.20 (q, J = 7 Hz, 2 H, OCH_2); mass spectrum, *m/e* 299 (M^+), 243 ($M^+ - C_4H_8$), 242 ($M^+ - C_4H_9$), 226 ($M^+ - OC_4H_9$), 198 ($M^+ - COOC_4H_9$), 156, 104, 70, 57.

3-(*N*-(*tert*-Butoxycarbonyl)pyrrolidin-2-yl)-2,4-pentanedione (47c'). Method A: **51c'** (26.3%) and **52** (12.2%). Method B: **51c'** (55.9%). **51c'** IR ν_{max} (neat) 1695 cm^{-1}; NMR δ ($CDCl_3$) 1.49 (s, 9 H, $C(CH_3)_3$), 2.15 (s, 3 H, $COCH_3$), 2.20 (s, 3 H, $COCH_3$); mass spectrum *m/e* 170, 169 ($M^+ - COOC_4H_9$), 130, 114, 113, 96, 57. **52**: IR ν_{max} (neat) 1700 cm^{-1}; NMR δ ($CDCl_3$) 1.48 (s, 9 H, $C(CH_3)_3$); mass spectrum, *m/e* 269, 226, 212, 170, 169, 137, 126, 57.

3-(*N*-(*tert*-Butoxycarbonyl)piperidin-2-yl)-2,4-pentanedione (47d): yield, 49.0%; IR ν_{max} (neat) 1695 cm^{-1}; NMR δ ($CDCl_3$) 1.45 (s, 9 H, $C(CH_3)_3$), 2.14 (s, 3 H, $COCH_3$); mass spectrum, *m/e* 283 (M^+), 240 ($M^+ - COCH_3$), 227 ($M^+ - C_4H_8$), 226 ($M^+ - OC_4H_9$), 184, 168, 160 ($M^+ - COOC_4H_9$), 128, 84, 57.

***N*-(*tert*-Butoxycarbonyl)-2-(2-oxopropyl)pyrrolidine (49c).** A solution of **47c'** (530 mg, 1.97 mmol) in 5% NaOH–EtOH (50 mL, 50% aqueous EtOH) was allowed to stand at room temperature overnight. The solvent was evaporated, the residue was dissolved in CH_2Cl_2, and the organic layer was washed with water, dried over Na_2SO_4, and concentrated. The residual oil was purified by chromatography on silica gel eluted with *n*-hexane–ethyl acetate (1:1) to give a colorless oil of **49c** (422.2 mg, 98.9%): IR ν_{max} (neat) 1700 cm^{-1}; NMR δ ($CDCl_3$) 1.48 (s, 9 H, $C(CH_3)_3$),

(24) Shono, T.; Matsumura, Y.; Tsubata, K. *J. Am. Chem. Soc.* **1981**, *103*, 1172.

2.18 (s, 3 H, $COCH_3$), 3.2–3.5 (br t, 2 H), 3.9–4.4 (m, 1 H).

***N*-(*tert*-Butoxycarbonyl)-2-(2-oxopropyl)piperidine (49d).** A solution of **47d** (402.7 mg, 1.423 mmol) in 5% NaOH–EtOH (50% aqueous EtOH, 60 mL) was allowed to stand at room temperature for 4 h. Solvent was removed under reduced pressure and the residue was dissolved in ethyl acetate. The organic layer was washed with water, dried over Na_2SO_4, and concentrated. The residual oil was purified by chromatography on silica gel eluted with *n*-hexane–ethyl acetate (1:1) to give a colorless oil of **49d** (285.9 mg, 83.4%): IR ν_{max} (neat) 1695 cm^{-1}; NMR δ ($CDCl_3$) 1.45 (s, 9 H, $C(CH_3)_3$), 2.18 (s, 3 H, $COCH_3$); mass spectrum, *m/e* 241 (M^+), 184 ($M^+ - C_4H_9$), 168 ($M^+ - OC_4H_9$), 140 ($M^+ - COOC_4H_9$), 128, 98, 84, 57.

***N*-((Benzyloxy)carbonyl)-2-(hydroxymethyl)pyrrolidine (56).** To a solution of ((benzyloxy)carbonyl)-L-proline (**55**, 10.0 g, 0.04 mol) in THF (150 mL) was added a solution of NEt_3 (6.10 g, 0.06 mol) in THF (10 mL) at −10 °C. After 10 min, a solution of ClCOOEt (6.54 g, 0.06 mol) in THF (10 mL) was added to the solution at the same temperature and the mixture was stirred for 30 min. To the solution was added a solution of $NaBH_4$ (3.05 g, 0.08 mol) in H_2O (20 mL) at −10 °C and the solution was stirred at the same temperature for 50 min. A 10% HCl solution was added to the reaction mixture and the solvent was removed under reduced pressure. The residue was extracted with ethyl acetate and the organic layer was washed with water, dried over Na_2SO_4, and concentrated. The residual oil was purified by chromatography on silica gel eluted with *n*-hexane–ethyl acetate (3:1) to give a colorless oil of **56** (8.65 g, 92%): IR ν_{max} (neat) 3450, 1700 cm^{-1}; NMR δ ($CDCl_3$) 1.58–2.24 (m, 4 H), 3.25–3.65 (m, 2 H), 3.71–4.09 (m, 1 H), 5.12 (s, 2 H, OCH_2Ph), 5.38 (br s, 1 H, OH), 7.33 (s, 5 H, aromatic); mass spectrum, *m/e* 235 (M^+).

***N*-((Benzyloxy)carbonyl)-2-(bromomethyl)pyrrolidine (57).** To a solution of **56** (3.58 g, 15.2 mmol) and CBr_4 (5.06 g, 18.3 mmol) in CH_3CN (50 mL) was added PPh_3 (4.78 g, 18.3 mmol) by portions at 0 °C and the solution was stirred at room temperature overnight. The solvent was removed under reduced pressure and the residue was purified by chromatography on silica gel eluted with *n*-hexane–ethyl acetate (4:1) to give a colorless oil of **57** (2.71 g, 60%): IR ν_{max} (neat) 1700 cm^{-1}; NMR δ (CCl_4) 1.52–2.36 (m, 4 H), 3.10–3.70 (m, 3 H), 3.81–4.42 (m, 2 H), 5.07 (s, 2 H, OCH_2Ph), 7.27 (s, 5 H, aromatic); mass spectrum, *m/e* 299, 297 (M^+).

***N*-((Benzyloxy)carbonyl)-2-(2-acetyl-3-oxobutyl)-pyrrolidine (58).** A solution of **57** (3.43 g, 11.5 mmol), acetylacetone (1.72 g, 17.2 mmol), K_2CO_3 (3.28 g, 23 mmol), and a catalytic amount of potassium iodide in DMF (35 mL) was warmed at 60 °C under an atmosphere of argon for 24 h. Water was added to a reaction mixture and the solution was extracted with ethyl acetate. The organic layer was dried over Na_2SO_4 and concentrated. The residual oil was purified by chromatography on silica gel eluted with *n*-hexane–ethyl acetae (3:1) to give a colorless oil of **58** (2.15 g, 59%): IR ν_{max} (neat), 1700, 1580 cm^{-1}; NMR δ (CCl_4) 2.03 (s, $COCH_3$), 2.21 (s, $COCH_3$), 5.12 (s, 2 H, $PhCH_2O$), 7.31 (s, 5 H, aromatic); mass spectrum, *m/e* 317 (M^+).

***N*-((Benzyloxy)carbonyl)-2-(3-oxobutyl)pyrrolidine (49e).** A solution of **58** (2.15 g, 6.79 mmol) in 5% NaOH–EtOH (50% aqueous EtOH, 80 mL) was allowed to stand at room temperature for 3 h. After the solvent was removed under reduced pressure, the residue was extracted with ethyl acetate. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by chromatography on silica gel eluted with *n*-hexane–ethyl acetate (3:1) to give a colorless oil of **49e** (0.806 g, 43%): IR ν_{max} (neat) 1700 cm^{-1}; NMR δ (CCl_4) 1.19–1.95 (m, 6 H), 2.00 (s, 3 H, $COCH_3$), 2.18–2.61 (m, 2 H), 3.17–3.60 (m, 2 H), 3.60–4.15 (m, 1 H), 5.06 (s, 2 H, $PhCH_2O$), 7.32 (s, 5 H, aromatic); mass spectrum, *m/e* 275 (M^+).

General Procedure for the Synthesis of Vinyl Iodide 1 (X = I). A mixture of methyl ketone (1 equiv) and hydrazine hydrate (80%, 25 equiv) in ethanol was refluxed under an atmosphere of nitrogen for 2–12 h. After the solvent was evaporated under reduced pressure, the residue was extracted with ether, and the ether layer was dried over Na_2SO_4 and concentrated to give a hydrazone. To a solution of the crude hydrazone and Dabco (5 equiv) in CH_2Cl_2–ether (1:1) was slowly added a solution of iodine (2.4 equiv) in CH_2Cl_2–ether (1:1) under an atmosphere of argon. After being stirred at room temperature for 1 h, ether was added to the reaction mixture and the ether layer was washed with 20% sodium thiosulfate solution and saturated NaCl solution, dried over Na_2SO_4, and concentrated. The residue was purified by chromatography on silica gel to give the desired vinyl iodide **1**.

4-(Benzyloxy)-2-iodo-1-butene (7a) and 4-(Benzyloxy)-2-iodo-2-butene (7b). Compound **6** was prepared by a known method:[25] yield, 54.0% (**7a**:**7b** 13:8); IR ν_{max} (neat) 1620 cm^{-1}; NMR δ (CCl_4) for **7a**: 2.32–2.78 (m, 2 H, CH_2O), 3.50 (t, J = 7 Hz, 2 H, $=CICH_2$), 4.44 (s, 2 H, $PhCH_2O$), 5.74 (br s, 1 H, vinyl), 6.08 (br s, 1 H, vinyl), 7.25 (aromatic); for **7b**: 3.88–4.08 (m, 2 H, $=CCH_2O$), 4.42 (s, 2 H, OCH_2Ph), 6.21 (m, 1 H, vinyl), 7.25 (aromatic); mass spectrum, *m/e* 288 (M^+), 161 ($M^+ - I$), 121, 91; high-resolution mass spectrum calcd for $C_{11}H_{13}OI$, *m/e* 288.0011; found, 288.0011.

***N*-Benzyl-*N*-((benzyloxy)carbonyl)-3-iodo-3-butenylamine (14a) and *N*-benzyl-*N*-((benzyloxy)carbonyl)-3-iodo-2-butenylamine (14b):** yield, 42.8% (**14a**:**14b** = 9:4); IR ν_{max} (neat) 1700, 1615 cm^{-1}; NMR δ (CCl_4) for **14a**: 2.10–2.08 (m, 2 H, $=CICH_2$), 3.37 (t, J = 7 Hz, 2 H, NCH_2), 5.14 (s, 2 H, OCH_2Ph), 5.68 (br s, 1 H, vinyl), 5.96 (br s, 1 H, vinyl), 5.96 (br s, 1 H, vinyl), 7.23 and 7.29 (aromatic); for **14b**: 3.80 (t, 2 H, $NCH_2C=$), 4.41 (s, 2 H, OCH_2Ph), 7.23 and 7.29 (aromatic); mass spectrum, *m/e* 421 (M^+), 330 ($M^+ - CH_2Ph$), 294 ($M^+ - I$), 254, 210, 91; high-resolution mass spectrum calcd for $C_{19}H_{20}NO_2I$, *m/e* 421.0539; found, 421.0559.

2-(5-Iodo-5-hexenyloxy)tetrahydro-2*H*-pyran (31a) and 2-(5-iodo-4-hexenyloxy)tetrahydro-2*H*-pyran (31b): yield, 58.7% (**31a**:**31b** = 2:1); IR ν_{max} (neat) 1620 cm^{-1}; NMR δ (CCl_4) 1.3–1.8 (m, 10 H), 2.0–2.6 (m, 2 H, $=CCH_2$), 3.1–4.0 (m, 4 H, OCH_2), 4.52 (br s, 1 H, OCHO), 5.48 (br t, =CHI), 5.70 (br s, $CH_2=$), 6.05 (br s, $CH_2=$).

***N*-Benzyl-*N*-((benzyloxy)carbonyl)-5-iodo-5-hexenylamine (38a) and *N*-benzyl-*N*-((benzyloxy)carbonyl)-5-iodo-4-hexenylamine (38b):** yield, 63.4% (**38a**:**38b** = 4:1.5); IR ν_{max} (neat) 1700, 1615, 1595 cm^{-1}; NMR δ ($CDCl_3$) 3.05–3.45 (m, 2 H, NCH_2), 4.51 (s, 2 H, NCH_2Ph), 5.20 (s, 2 H, OCH_2Ph), 5.68 (br s, vinyl), 5.96 (br s, 2 H, vinyl).

***N*-(*tert*-Butoxycarbonyl)-2-(2-iodo-2-propenyl)pyrrolidine (50c):** yield, 23.8%; IR ν_{max} (neat) 1695, 1605 cm^{-1}; NMR δ ($CDCl_3$) 1.45 (s, 9 H, $C(CH_3)_3$, 5.78 (br s, 1 H, vinyl), 6.08 (br s, 1 H, vinyl); mass spectrum, *m/e* 264 ($M^+ - OC_4H_9$), 210 ($M^+ - I$), 170 ($M^+ - C_3H_4I$), 154, 114, 70, 57.

***N*-(*tert*-Butoxycarbonyl)-2-(2-iodo-2-propenyl)piperidine (50d):** yield, 17.6%; IR ν_{max} (neat) 1690, 1605 cm^{-1}; NMR δ ($CDCl_3$) 1.08 (s, 9 H, $C(CH_3)_3$), 5.79 (br s, 1 H, vinyl), 6.09 (1 H, vinyl); mass spectrum, *m/e* 295 ($M^+ - C_4H_8$), 294 ($M^+ - C_4H_9$), 278, 250 ($M^+ - C_3H_4I$), 128, 84, 57.

***N*-((Benzyloxy)carbonyl)-2-(3-iodo-3-butenyl)pyrrolidine (50e):** yield, 38.6%; IR ν_{max} (neat) 1700 cm^{-1}; NMR δ ($CDCl_3$) 1.27–2.11 (m, 6 H), 2.15–2.62 (m, 2 H), 3.10–3.60 (m, 2 H), 3.60–4.14 (m, 1 H), 5.08 (s, 2 H, OCH_2Ph), 5.67 (br s, 1 H, vinyl), 6.22 (s, 1 H, vinyl), 7.33 (aromatic); mass spectrum, *m/e* 386 (M^+), 91.

***N*-Benzyl-3-iodo-3-butenylamine (15).** To a solution of **14** (432.6 mg, 1.027 mmol, **15a**:**15b** = 11:5) in CH_2Cl_2 was added a solution of 25% HBr–AcOH (3 mL) at 0 °C. After being stirred for 4 h at the same temperature, water was added to the reaction mixture. The aqueous layer was washed with ether, made basic with K_2CO_3, and extracted with ether. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by chromatography on silica gel eluted with *n*-hexane–ethyl acetate to give a colorless oil of **15** (253.7 mg, 86.0%): IR ν_{max} (neat) 3300, 1610 cm^{-1}; NMR δ (CCl_4) for **16a**: 1.89 (s, 1 H, NH), 2.31–2.78 (m, 2 H, $CH_2CI=$), 3.05 (m, 2 H, NCH_2), 3.78 (s, 2 H, NCH_2Ph), 5.77 (br s, 1 H, vinyl), 6.13 (br s, 1 H, vinyl), 7.26 (s, 5 H, aromatic); for **16b**: 3.25 (t, 2 H, $NCH_2=$), 3.78 (s, 2 H, NCH_2Ph), 6.78–6.95 (m, 1 H, vinyl).

5-Iodo-5-hexen-1-ol (32a) and 5-Iodo-4-hexen-1-ol (32b). A methanolic solution of **31** (555.7 mg, 1.798 mmol) and a catalytic amount of *p*-toluenesulfonic acid was allowed to stand at room temperature for overnight. After the solvent was removed under reduced pressure, the residue was purified by chromatography on silica gel eluted with *n*-hexane–ether (1:1) to give a colorless

(25) Honingberg, I. L.; Goodson, L. H.; Burton, W. H. *J. Org. Chem.* **1961**, *26*, 2137.

oil of **32a** and **32b** (2:1, 377.9 mg, 93.8%): IR ν_{max} (neat) 3400, 1615 cm^{-1}; NMR δ ($CDCl_3$) 3.67 (t, 4 H, J = 7 Hz, OCH_2), 5.50 (br t, =CIH), 5.57 (br s, CH_2), 6.08 (br s, $=CH_2$).

***N*-Benzyl-5-iodo-5-hexenylamine (39a) and *N*-Benzyl-5-iodo-4-hexenylamine (39b).** To a solution of **38** (489.2 mg, 1.119 mmol) in CH_2Cl_2 (0.7 mL) was added a solution of 25% HBr–AcOH (0.7 mL) at 0 °C and the mixture was stirred at 0 °C for 1 h. Ether was added to the solution until the white precipitates appeared. The solids were collected by filtration and washed with ether to give colorless powders of **39a** and **39b** (8:3, 364.5 mg, 82.1%): NMR δ ($CDCl_3$) 2.6–3.0 (m, 2 H, CH_2C=), 4.13 (br t, 2 H, NCH_2), 5.43 (br t, =CHI), 5.72 (br s, CH_2=), 6.05 (br s, CH_2=); mass spectrum, m/e 315, 188, 120, 91; high-resolution mass spectrum calcd for $C_{13}H_{18}NI$, m/e 315.0480; found, 315.0440.

General Procedure for the Synthesis of Lactones and Lactams by Use of Palladium-Catalyzed Carbonylation.[3b] A mixture of vinyl halide (1 equiv), $Pd(OAc)_2$ (2 mol %), PPh_3 (2–10 mol %), and n-Bu_3N (1.2 equiv) in HMPA was heated under an atmosphere of carbon monoxide. To the reaction mixture was added ether or ethyl acetate and the organic layer was washed with a dilute HCl solution and water, dried over Na_2SO_4, and concentrated. The residue was purified by chromatography on silica gel to give the carbonylated product.

Benzyl 4-(Benzyloxy)-2-methylene-2-butenyrate (11a) and Benzyl 4-(Benzyloxy)-2-methyl-2-butenyrate (11b). 11a: yield, 44.4%; IR ν_{max} (neat) 1715, 1635 cm^{-1}; NMR δ (CCl_4) 2.60 (t, J = 7 Hz, 2 H, CH_2O), 3.55 (t, J = 7 Hz, 2 H, $=CCH_2$), 4.44 (s, 2 H, OCH_2Ph), 5.14 (s, 2 H, $COOCH_2Ph$), 5.65 (br s, 1 H, vinyl), 6.14 (br s, 1 H, vinyl), 7.25, 7.29 (10 H, aromatic); mass spectrum, m/e 296 (M^+), 205 ($M^+ - CH_2Ph$), 174, 157, 129, 91; high-resolution mass spectrum calcd for $C_{19}H_{20}O_3$, m/e 296.1407; found 296.1402. **11b**: yield, 4.2%; IR ν_{max} (neat) 1715, 1650 cm^{-1}; NMR δ (CCl_4) 1.94 (m, 3 H, CH_3), 4.38 (m, 1 H, CH_2O), 4.45 (s, 2 H, OCH_2Ph), 5.11 (s, 2 H, $COOCH_2Ph$), 6.15 (m, 1 H, vinyl), 7.25, 7.29 (10 H, aromatic); mass spectrum, m/e 205 ($M^+ - CH_2Ph$), 189, 171, 91.

1-Benzyl-3-methylene-2-pyrrolidone (16)[26] and 1-benzyl-3-methyl-3-azolin-2-one (17): yield, 45.9% (**16**:**17** = 10:1); IR ν_{max} (neat) 1680, 1650 cm^{-1}; NMR δ (CCl_4) for **16**: 2.47–2.87 (m, 2 H, CH_2C=), 3.06 (m, NCH_2), 4.45 (s, 2 H, NCH_2Ph), 5.28 (br s, 1 H, vinyl), 5.92 (br s, 1 H, vinyl), 7.23 (s, aromatic); for **17**: 1.80–1.93 (br s, 3 H, CH_3), 3.58–3.72 (m, 2 H, NCH_2), 4.52 (s, 2 H, NCH_2Ph), 6.64 (m, 1 H, vinyl), 7.23 (s, aromatic); mass spectrum, m/e 187 (M^+), 159, 96, 91; high-resolution mass spectrum calcd for $C_{12}H_{13}NO$, m/e 187.0994; found, 187.1003.

α-Methylene δ-Lactone 25a[27] and 2-Oxo-3-methyl-5,6-dihydro-2*H*-pyran (26a). 25a: yield, 27.6%; IR ν_{max} (neat) 1720, 1625 cm^{-1}; NMR δ (CCl_4) 1.76–2.12 (m, 2 H, CCH_2C), 2.50–2.82 (m, 2 H, $=CCH_2$), 4.31 (t, 2 H, J = 5 Hz), 5.46 (br s, 1 H, vinyl), 6.29 (m, 1 H, vinyl); mass spectrum, m/e 112 (M^+). **26a**: yield, 6.9%; IR ν_{max} (neat) 1720, 1625 cm^{-1}; NMR δ (CCl_4) 1.88 (m, 3 H, CH_3), 2.20–2.55 (m, 2 H, $=CCH_2$), 6.58 (m, 1 H, vinyl); mass spectrum, m/e 112 (M^+).

***N*-Benzyl-3-methylene-2-piperidone (25b)**:[11] yield, 61%; IR ν_{max} (neat) 1650, 1625 cm^{-1}; NMR δ (CCl_4) 1.63–1.98 (m, 2 H, CH_2), 2.40–2.67 (m, 2 H, CH_2), 3.24 (m, 2 H, NCH_2), 4.57 (s, 2 H, NCH_2Ph), 5.22 (br s, 1 H, vinyl), 6.19 (br s, 1 H, vinyl), 7.24 (s, 5 H, aromatic); mass spectrum, m/e 201 (M^+), 173, 172, 91.

***N*-Benzyl-3-methyl-5,6-dihydro-2-pyridone (26b)**: IR ν_{max} (neat) 1665, 1625 cm^{-1}; NMR δ (CCl_4) 1.86 (m, 3 H, CH_3), 2.00–2.40 (m, 2 H, $=CCH_2$), 3.25 (t, 2 H, J = 7 Hz, NCH_2), 4.53 (s, 2 H, NCH_2Ph), 6.20 (m, 1 H, vinyl), 7.24 (s, 5 H, aromatic); mass spectrum, m/e 201 (M^+), 186 ($M^+ - CH_3$), 110 ($M^+ - CH_2Ph$), 91.

6-Methyl-3-methylene-2-oxotetrahydro-2*H*-pyran (25c): yield, 31%; IR ν_{max} (neat) 1720, 1620 cm^{-1}; NMR δ ($CDCl_3$) 1.39 (d, 3 H, J = 6 Hz, CH_3), 1.52–2.02 (m, 2 H, CCH_2C); 2.55–2.81 (m, 2 H, $=CCH_2$), 4.25–4.85 (m, 1 H, vinyl); mass spectrum, m/e 126 (M^+), 121 ($M^+ - CH_3$), 92 ($M^+ - CO_2$).

3-Methyleneoctahydrocoumarin (25d)[12] and 3-Methyl-4a,5,6,7,8,8a-hexahydrocoumarin (26d). 25d: yield, 50%; IR ν_{max} (neat) 1720, 1625 cm^{-1}; NMR δ (CCl_4) 3.85 (m, 1 H, OCH), 5.40 (br s, 1 H, vinyl), 6.25 (m, 1 H, vinyl); mass spectrum, m/e 166 (M^+), 146, 91. **26d**: yield, 13%; mp 97.0–97.5% °C (colorless plates from n-hexane); IR ν_{max} (neat) 1705 cm^{-1}; NMR δ (CCl_4) 1.85 (m, 3 H, CH_3), 6.22 (m, 1 H, vinyl); mass spectrum, m/e 166 (M^+), 151 ($M^+ - CH_3$), 138 ($M^+ - CO$), 95.

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.94. Found: C, 72.16; H, 8.55.

***N*-Benzyl-3-methyleneoctahydro-2-quinolone (25e) and *N*-Benzyl-3-methyl-4a,5,6,7,8,8a-hexahydro-2-quinolone (26e). 25e**: yield, 80%; IR ν_{max} (neat) 1655, 1610 cm^{-1}; NMR δ ($CDCl_3$) 1.0–3.4 (m, 12 H), 4.04, 5.37 (dd, J = 15 Hz, NCH_2Ph), 5.32 (m, 1 H, vinyl), 6.32 (m, 1 H, vinyl), 7.28 (s, 5 H, aromatic); mass spectrum, m/e 255 (M^+), 212, 198, 164 ($M^+ - CH_2PH$), 91. **26e**: yield, 2%; IR ν_{max} (neat) 1660, 1620 cm^{-1}; NMR δ ($CDCl_3$) 1.95 (m, 3 H, CH_3), 5.98 (m, 1 H, vinyl); mass spectrum, m/e 255 (M^+), 212, 164 ($M^+ - CH_2Ph$), 91.

2-Methylene-6-hexanolide (40) and 2-methyl-3-hexen-6-olide (41): yield 35.8% (**40**:**41** = 2:1); IR ν_{max} (neat) 1730 cm^{-1}; NMR δ ($CDCl_3$) for **40**: 2.2–2.5 (m, 2 H, $=CCH_2$), 4.1–4.3 (m, 2 H, OCH_2), 5.42 (br s, 1 H, vinyl), 5.63 (br s, 1 H, vinyl); for **41**: 6.20 (br t, vinyl); mass spectrum, m/e 126 (M^+); high-resolution mass spectrum calcd for $C_7H_{10}O_2$, m/e 126.0678; found, 126.0680.

1-Benzyl-3-methylenehexahydroazepin-2-one (42) and 1-Benzyl-3-methyl-5,6,7,8-tetrahydro-2*H*-azepin-2-one (43). 43: yield, 23.0%; IR ν_{max} (neat) 1640, 1605 cm^{-1}; NMR δ ($CDCl_3$) 1.70 (q, J = 3.6 Hz, CCH_2C), 1.95 (br s, 3 H, CH_3), 1.9–2.3 (m, 2 H, $=CCH_2$), 3.23 (t, J = 3.6 Hz, 2 H, NCH_2), 4.67 (s, 2 H, NCH_2Ph), 5.98 (br t, 1 H, vinyl); mass spectrum, m/e 215 (M^+), 91; high-resolution mass spectrum calcd for $C_{14}H_{17}NO$, m/e 215.1306; found, 215.1313. **42**: yield, 28.4%; IR ν_{max} (neat) 1640 cm^{-1}; NMR δ ($CDCl_3$) 1.3–1.9 (m, 4 H), 2.2–2.5 (m, 2 H, NCH_2), 4.61 (s, 2 H, NCH_2Ph), 5.28 (br s, 1 H, vinyl), 5.56 (br s, 1 H, vinyl); mass spectrum, m/e 215 (M^+), 91; high-resolution mass spectrum calcd for $C_{14}H_{17}NO$, m/e 215.1306; found, 215.1306.

2-Methylene-3-oxo-1*H*-hexahydropyrrolizine (52c): yield, 36.0%; IR ν_{max} (neat) 1680, 1650 cm^{-1}; NMR δ ($CDCl_3$) 5.32 (t, J = 2 Hz, 1 H, vinyl), 5.95 (t, J = 2 Hz, 1 H, vinyl); mass spectrum, m/e 137 (M^+), 109 ($M^+ - CO$), 81, 78; high-resolution mass spectrum calcd for $C_8H_{11}NO$, m/e 137.0838; found, 137.0837.

1-Oxo-2-methyleneoctahydroindolizine (52d): yield, 58.7%; IR ν_{max} (neat) 1690, 1655 cm^{-1}; NMR δ ($CDCl_3$) 2.5 (m, 1 H), 2.7–3.0 (m, 1 H), 3.0–4.0 (m, 1 H), 4.1–4.5 (br d, 1 H), 5.32 (t, 1 H, vinyl), 6.00 (t, 1 H, vinyl); mass spectrum, m/e 151 (M^+), 136, 122, 86, 84; high-resolution mass spectrum calcd for $C_9H_{13}NO$, m/e 151.0994; found, 151.0987.

5-Oxo-6-methyleneoctahydroindolizine (52e) and 5-Oxo-6-methyl-Δ^6-hexahydroindolizine (53e). 52e: yield, 26.4%; mp 68–71 °C (from n-hexane–ethyl acetate); IR ν_{max} (Nujol) 1650, 1600 cm^{-1}; NMR δ ($CDCl_3$) 1.66–2.92 (m, 8 H), 3.30–3.77 (m, 3 H), 5.28 (s, 1 H, vinyl), 6.24 (br s, 1 H, vinyl); mass spectrum, m/e 151 (M^+).

Anal. Calcd for $C_9H_{13}NO$: C, 71.52; H, 8.61; N, 9.27. Found: C, 71.50; H, 8.63; N, 9.20. **53e**: yield, 26.8%; mp 53.0–54.0 °C (from ether); IR ν_{max} (Nujol) 1650, 1600 cm^{-1}; NMR δ ($CDCl_3$) 1.89 (s, 3 H, CH_3), 1.91–2.57 (m, 6 H), 3.27–3.90 (m, 3 H), 6.20 (s, 1 H, vinyl); mass spectrum, m/e 151 (M^+).

3-Bromomethyl-2-furanone (12).[28] To a solution of **11a** (95.9 mg, 0.324 mol) in CH_2Cl_2 (1 mL) was added a solution of 25% HBr–AcOH (1 mL) at 0 °C. After being stirred for 4.5 h at the same temperature, CH_2Cl_2 was added to the reaction mixture and the organic layer was washed with saturated $NaHCO_3$ solution and saturated NaCl solution, dried over Na_2SO_4, and concentrated. The residue was purified by chromatography on silica gel eluted with n-hexane–ether (2:1) to give a colorless oil of **12** (34.3 mg, 59.2%): IR ν_{max} (neat) 1760 cm^{-1}; NMR δ ($CDCl_3$) 2.28–2.67 (m, 2 H), 2.72–3.23 (m, 1 H, COCHC), 3.48–3.72 (m, 2 H, CH_2O), 4.10–4.57 (m, 2 H, CH_2Br); mass spectrum, m/e 180, 178 (M^+), 152, 150 ($M^+ - CO$), 98 ($M^+ - HBr$), 55.

***N*-Benzyl-3-methyl-2-oxopyrrolidone (27).** A solution of **25b** (59.8 mg, 0.30 mmol) and PtO_2 (3 mg) in EtOH (3 mL) was stirred under an atmosphere of hydrogen overnight. After the catalyst was filtered off, the solvent was removed under reduced pressure. The residue was purified by chromatography on alu-

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minum eluted with *n*-hexane–ethyl acetate (1:1) to give a colorless oil of **27** (54 mg, 90%): IR ν_{max} (neat) 1635 cm^{-1}; NMR δ (CCl_4) 1.25 (d, 3 H, J = 6 Hz, CH_3), 1.40–2.20 (m, 2 H), 2.20–2.70 (m, 1 H), 3.00–3.40 (br t, 2 H, NCH_2), 4.45 (s, 2 H, $PhCH_2N$), 7.15 (s, 5 H, aromatic); mass spectrum, m/e 203 (M^+), 198 ($M^+ - CH_3$), 112 ($M^+ - CH_2Ph$), 91; high-resolution mass spectrum calcd for $C_{13}H_{17}NO$, m/e 203.1306; found, 203.1306.

2-Methyl-3-oxohexahydropyrrolizine (54c). A solution of **52c** and **53c** (49 mg) and PtO_2 (2.5 mg) in EtOH (12 mL) was stirred under an atmosphere of hydrogen at room temperature for 3 h. Solvent was removed under reduced pressure and the residue was purified by chromatography on silica gel eluted with ethyl acetate to give a colorless oil of **54c** (50 mg, quantitative): IR ν_{max} (neat) 1660 cm^{-1}; NMR δ ($CDCl_3$) 1.18 (d, J = 7 Hz, 3 H, CH_3), 1.1–1.7 (m, 2 H), 1.7–2.3 (m, 4 H), 2.3–3.3 (m, 2 H), 3.3–4.0 (m, 2 H).

5-Oxo-6-methyloctahydroindolizine (54e). From **52e**: A solution of **52e** (12.0 mg, 0.080 mmol) and PtO_2 (2 mg) in EtOH (10 mL) was stirred under an atmosphere of hydrogen at room temperature overnight. After the catalyst was filtered off, the solvent was removed under reduced pressure and the residue was purified by chromatography on silica gel eluted with ethyl acetate to give a colorless oil of **54e** (10.7 mg, 88%): IR ν_{max} (neat) 1620 cm^{-1}; NMR δ ($CDCl_3$) 1.35–2.63 (m, 10 H), 1.15 (d, J = 7 Hz, CH_3), 3.14–3.72 (m, 2 H); mass spectrum, m/e 153 (M^+). From **53e**: A solution of **53e** (12.3 mg, 0.815 mmol) and PtO_2 (2 mg) in EtOH (10 mL) was hydrogenated in the same manner as **52e** to give **54e** (11.2 mg, 86.0%).

Registry No. **6**, 6278-91-7; **6** hydrazone, 86953-35-7; **7a**, 86968-38-9; **7b**, 86953-36-8; **11a**, 86953-37-9; **11b**, 86953-38-0; **12**, 86953-39-1; **13**, 86953-40-4; **13** hydrazone, 86953-41-5; **14a**, 86953-42-6; **14b**, 86953-43-7; **15a**, 86953-44-8; **15b**, 86953-45-9; **16**, 86953-46-0; **17**, 27610-96-4; **18**, 86953-47-1; **19**, 35804-44-5; **20**, 86953-48-2; **22a**, 64180-78-5; **22b**, 86953-49-3; **22c**, 86953-50-6; **22d**, 86953-51-7; **22e**, 86953-52-8; **22e** imine derivative, 86953-53-9; **23**, 50775-03-6; **24**, 53626-84-9; **25a**, 42023-19-8; **25b**, 50586-10-2; **25c**, 86953-54-0; **25d**, 52961-97-4; **25e**, 86953-55-1; **26a**, 72649-02-6; **26b**, 86953-56-2; **26d**, 86953-57-3; **26e**, 86953-58-4; **27**, 37672-46-1; **29**, 86953-59-5; **30**, 64841-39-0; **30** hydrazone, 86953-60-8; **31a**, 86953-61-9; **31b**, 86953-62-0; **32a**, 86953-63-1; **32b**, 86953-64-2; **33**, 86953-65-3; **34**, 86953-66-4; **35**, 86953-67-5; **36**, 86953-68-6; **37**, 86953-69-7; **38a**, 86953-71-1; **38b**, 86953-72-2; **39a**, 86953-73-3; **39b**, 86953-74-4; **40**, 86953-75-5; **41**, 86953-76-6; **42**, 86953-77-7; **43**, 86953-78-8; **44a**, 4030-18-6; **44b**, 56475-80-0; **44c**, 86953-79-9; **44d**, 75844-69-8; **37** hydrazone, 86953-70-0; **45a**, 86968-39-0; **45b**, 86953-80-2; **45c**, 84766-91-6; **45d**, 86953-81-3; **46** (Y = OEt), 141-97-9; **46** (Y = CH_3), 123-54-6; **47a**, 86953-82-4; **47a'**, 86953-83-5; **47b**, 86953-84-6; **47b'**, 76460-90-7; **47c**, 86953-85-7; **47c'**, 86953-86-8; **47d**, 86953-87-9; **48**, 86953-88-0; **49c**, 86953-89-1; **49c** hydrazone, 86953-90-4; **49d**, 63459-12-1; **49d** hydrazone, 86953-91-5; **49e**, 86953-92-6; **49e** hydrazone, 86968-40-3; **50c**, 86953-93-7; **50d**, 86953-94-8; **50e**, 86953-95-9; **51c**, 86953-96-0; **51d**, 86953-97-1; **51e**, 86953-98-2; **52c**, 86953-99-3; **52d**, 86954-00-9; **52e**, 40163-21-1; **53c**, 86954-01-0; **53e**, 86954-02-1; **54c**, 86954-03-2; **54e**, 86954-04-3; **55**, 1148-11-4; **56**, 86954-05-4; **57**, 86954-06-5; **58**, 86954-07-6; benzylamine, 100-46-9; methyl vinyl ketone, 78-94-4; benzyloxycarbonyl chloride, 501-53-1; diethyl malonate, 105-53-3; 2,3-dibromopropene, 513-31-5; *N*-benzyl-4-bromo-4-pentenamide, 86754-08-7; acetylacetone, 123-54-6; 1-pyrrolidyl-1-cyclohexene, 1125-99-1; 3-bromopropyl 2-tetrahydropyranyl ether, 33821-94-2; 3-bromopropanol, 627-18-9; dihydropyran, 110-87-2; 3-aminopropanol, 156-87-6; 3-aminopropyl 2-tetrahydropyranyl ether, 75744-51-3; benzyl bromide, 100-39-0; 3-(benzylamino)propyl 2-tetrahydropyranyl ether, 86954-09-8.

Supplementary Material Available: Detailed experimental procedure of electrochemical oxidation of *N*-acyl cyclic amine **44** and condensation reaction of **45** with active methylene compound **46**, iodo-oxidation of hydrazone, and palladium-catalyzed carbonylation of vinyl halide (10 pages). Ordering information is given on any current masthead page.

Photolytic Generation of Anti-Bredt Imines from 1-Azidobicyclo[2.2.2]octane, 1-Azidobicyclo[3.3.1]nonane, and 3-Azidonoradamantane[1]

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Photolysis of 1-azidobicyclo[2.2.2]octane (**18**), 1-azidobicyclo[3.3.1]nonane (**24**), and 3-azidonoradamantane (**37**) generated the corresponding bridgehead imines **12a**, **13**, **14**, **15**, and **16**, respectively. These bridgehead imines were trapped spontaneously with solvent methanol except for unreactive **14**, which was reduced with $NaBH_4$ to afford the corresponding azabicycle **28**. Hydrocyanation succeeded with imines **12a** and **13** to afford amino nitriles **21** and **30**, respectively, which were converted to novel iminohydantoins **22** and **32**. In the formation of methoxyamines **20**, **26**, **39**, and **40**, the intermediacy of bridgehead imines **12a**, **13**, **15**, and **16** was proved by photolysis of the azides at 77 K in a hydrocarbon matrix, followed by treatment with MeOH at 195 K to afford the methoxyamines. The reactivity of the bridgehead imines is discussed on the basis of Wiseman's stability criterion for bridgehead olefins. The selective ring expansion of unsymmetrical bridgehead azides **24** and **37** on photolysis is also discussed.

The synthesis and chemistry of anti-Bredt olefins have received considerable attention.[2] Adamantene, an extremely distorted bridgehead olefin, has been investigated extensively.[3] However, there are few studies on bridge-

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