Electroorganic Chemistry. 60. Electroorganic Synthesis of Enamides and Enecarbamates and Their Utilization in Organic Synthesis[1]

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Abstract: A variety of enecarbamates and enamides were synthesized from α-methoxy carbamates and α-methoxy amides prepared by anodic methoxylation of amine derivatives. Some new carbon–carbon bond-forming reactions and hydroxylation at the β position of amines have been accomplished by using these enecarbamates and enamides as key intermediates. Also, new synthetic routes of nicotinaldehyde and pyrrole derivatives have been exploited by utilizing anodic dimethoxylation of carbamates of piperidine and pyrrolidine, respectively.

In our continuing study on the electroorganic reactions of amine derivatives,[2,3] anodic methoxylation of amides and carbamates at the position α to nitrogen and subsequent nucleophilic substitution at the α position with a variety of nucleophiles have been shown to be highly valuable tools in the synthesis of compounds closely related with useful natural products such as alkaloids,[3] vitamins,[4] amino acids,[5] or weedicides[6] as exemplified by the synthesis of tropane skeleton (**1**)[3] starting from pyrrolidine (Scheme I).

The amine derivatives having a functional group at the β position are, however, also very important in the synthesis of the useful compounds mentioned above. In the present study, we found that carbamates and amides possessing a substituent at the β position could be synthesized by using enecarbamates (**5**) and enamides (**6**), prepared from α-methoxylated carbamates (**3**) and amides (**4**), as key intermediates.

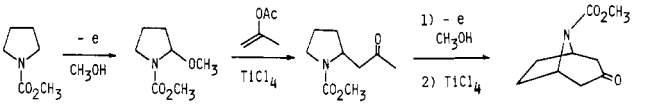
In the first place, the preparation of enecarbamates and enamides was studied in detail, because only a few methods[7] had been reported for their synthesis, although we had already described the facile formation of enecarbamates from α-methoxycarbamates under acidic and thermolytic conditions.[2,8]

In the second place, some new reactions of enecarbamates and enamides with a variety of electrophiles (E^+) at the β position were investigated,[10] as shown in Scheme II.

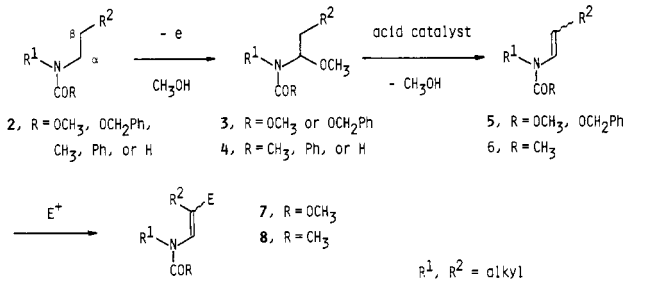
Results and Discussion

The synthetic method of enamides hitherto known is the acylation of imines[7a] with acid chlorides or anhydrides. Catalytic isomerization[7b] of allylamine derivatives to enamides and enecarbamates has also recently been reported. These methods are, however, rather limited in the variety of synthesizable enamides and enecarbamates.

Scheme I



Scheme II



The synthesis of enecarbamates and enamides was achieved by eliminating methanol from α-methoxy carbamates and α-methoxy amides synthesized by anodic methoxylation of the corresponding amine derivatives. Heating α-methoxy carbamates in the presence of ammonium chloride as an acid catalyst gave enecarbamates whereas under the similar reaction conditions α-methoxy amides did not give enamides but formed tar. Enamides could be obtained from α-methoxy amides by simple distillation or by heating in the presence of silica gel as an acid catalyst. These results suggest that α-methoxy amides are less stable than α-methoxy carbamates.

The results for enecarbamate and enamide synthesis are shown in Table I.

One of the advantages in the electrochemical method is the high regioselectivity. Thus, enecarbamates having less substituted double bonds (**5f,g**) were selectively obtained from α-substituted carbamates (runs 6 and 7, Table I), since anodic α-methoxylation took place selectively at the less substituted carbon atom. However, since alkyl substituents on the β position show only a minor effect on the regioselectivity of the anodic oxidation as shown in run 8 (Table I), a mixture of enecarbamates **5h** and **5i** (64:36) was formed by elimination of methanol from the methoxylated compounds.

The enecarbamates having two different groups on the nitrogen were obtainable by alkylation of primary α-methoxy carbamates with alkyl halides followed by elimination of methanol. For example, α-methoxy carbamate **9** was alkylated by benzyl bromide ($RX = PhCH_2Br$) to give a mixture of N-benzylated compound

(1) A part of this study has been preliminarily reported: *Tetrahedron Lett.* **1982**, *23*, 1201.
(2) Shono, T.; Hamaguchi, H.; Matsumura, Y. *J. Am. Chem. Soc.* **1975**, *97*, 4264.
(3) Shono, T.; Matsumura, Y.; Tsubata, K. *J. Am. Chem. Soc.* **1981**, *103*, 1172.
(4) Shono, T.; Matsumura, Y.; Tsubata, K.; Takata, J. *Chem. Lett.* **1981**, 1121.
(5) Shono, T.; Matsumura, Y.; Tsubata, K. *Tetrahedron Lett.* **1981**, *22*, 2411.
(6) Shono, T.; Matsumura, Y.; Tsubata, K. *Tetrahedron Lett.* **1981**, *22*, 3249.
(7) (a) Lenz, G. R. *Synthesis* **1978**, 489 and references cited therein. (b) Stille, J. K.; Becker, Y. *J. Org. Chem.* **1980**, *45*, 2139.
(8) Preparation of five enformamides of cyclic amides from α-methoxylated formamides was reported in 1976.[9]
(9) Nyberg, K. *Synthesis* **1976**, 545.
(10) Some studies related to the reaction of enamides and encarbamates have been reported: (a) Becker, Y.; Eisenstadt, A.; Stille, J. K. *J. Org. Chem.* **1980**, *45*, 2145. (b) Overman, L. E.; Clizbe, L. A.; Freerks, R. L.; Marlowe, C. K. *J. Am. Chem. Soc.* **1981**, *103*, 2807. Overman, L. E.; Freerks, R. L.; Petty, C. B.; Clizbe, L. A.; Ono, R. K.; Taylor, G. F.; Jessup, P. J. *Ibid.* **1981**, *103*, 2816 and references cited therein.

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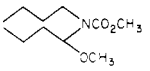
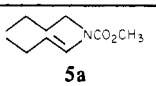
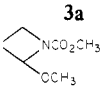
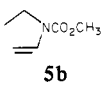
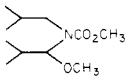
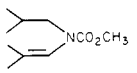
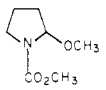
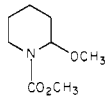
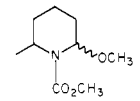
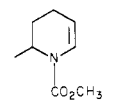
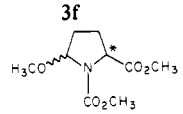
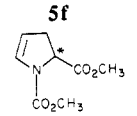
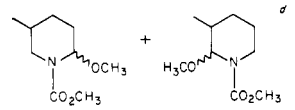
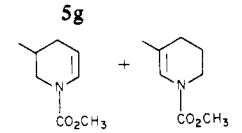
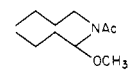
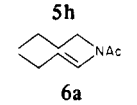
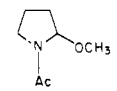
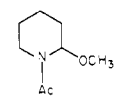
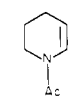
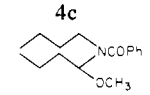
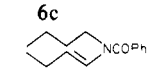
Table I. Synthesis of Enecarbamates and Enamides

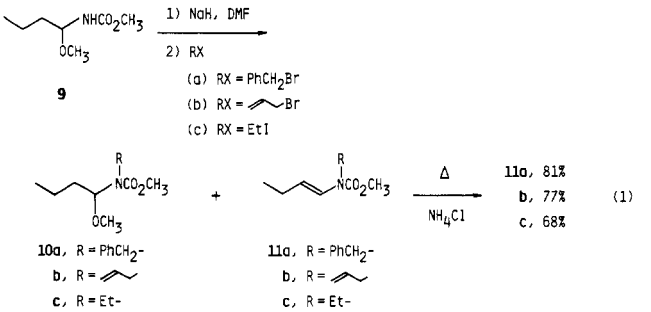
run	3 or 4	reaction condition: catalyst	reaction condition: bath temp, °C	reaction condition: time, h	5 or 6	yield[a] of 5 or 6, %
1	 **3a**	NH_4Cl	110–120	3	 **5a**	94
2	 **3b**	NH_4Cl	120–130	4.5	 **5b**	51[b]
3	 **3c**	NH_4Cl	140–150	2	 **5c**	92
4	 **3d**	NH_4Cl	100–120	3	 **5d**	91
5	 **3e**	NH_4Cl	100–120	2	**5e**	96
6	 **3f**	NH_4Cl			 **5f**	68
7	 **3g**	NH_4Cl	150	1	 **5g**	70
8	 **3h** **3i**[d]	NH_4Cl	100–110	5	 **5h** **5i**	96[e]
9	 **4a**	SiO_2	140–150	2	 **6a**	85
10	 **4b**	SiO_2	150–160	2	 **6b**	38
11	 **4c**	[c]			 **6c**	83
12	 **4d**	SiO_2	140–160	22	 **6d**	77

[a] Isolated yields. [b] Determined by GLC. [c] Distillation of **3** or **4** gave **5** or **6** directly, respectively. [d] The ratio of **3h** and **3i** was not clear. [e] **5h**:**5i** = 64:36.

10a and enecarbamate **11a**. Heating the mixture in the presence of ammonium chloride yielded **11a** as a single product (eq 1). This N-alkylation was successfully performed with active alkyl halides such as alkyl iodide, benzyl bromide, or allyl bromide (**11c,a,b**).

Reaction of Enecarbamates and Enamides. Although **5** and **6** are less reactive than enamines, several electrophiles can react with them to give the products possessing functional groups at the β position of **5** or **6**. The following types of electrophilic reactions with **5** and **6** were studied: (a) the Friedel–Crafts reaction; (b) the Vilsmeier reaction; (c) hydroboration.

(a) Friedel–Crafts Reaction. The reaction of enecarbamates

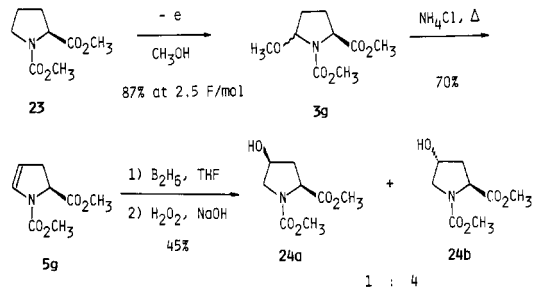


(1)

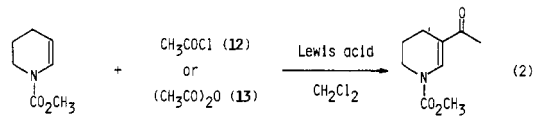
Table II. Reaction of **5e** with **12** or **13**

run	electrophile (equiv)	Lewis acid (equiv)	reacn temp, °C	reacn time, h	yield of **14a**, %
1	**12** (2)	$SnCl_4$ (1)	−60 → room temp	5	37
2	**12** (2)	$SnCl_4$ (2)	−70 → room temp	20	30
3	**12** (2)	$TiCl_4$ (2)	−70 → room temp	30	21
4	**12** (2)	$AlCl_3$ (1.5)	−70 → room temp	15	25
5	**12** (5)	$SnCl_4$ (2)	−70 → room temp	16	45
6	**12** (10)	$SnCl_4$ (10)	−70 → room temp	20	58
7	**13** (2)	$SnCl_4$ (2)	−70	5	34

Scheme III



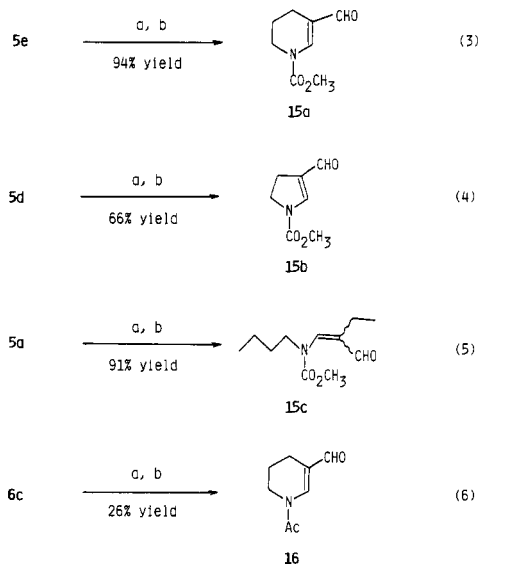
with acid chlorides or acid anhydrides in the presence of a Lewis acid catalyst yielded acylated enecarbamates (**14**). For example, reaction of enecarbamate **5e** with acetyl chloride (**12**) or acetic anhydride (**13**) gave **14a** (eq 2).



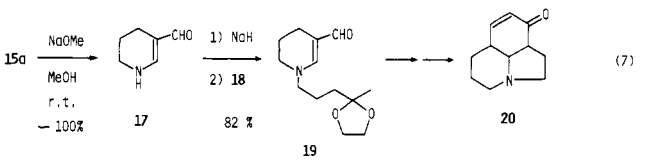
This reaction was studied to determine the optimum reaction conditions. The results in Table II indicate that satisfactory results could be obtained by using a large excess of electrophiles and Lewis acids.

Other Friedel–Crafts reactions carried out under similar conditions to run 6 in Table II are summarized in Table III.

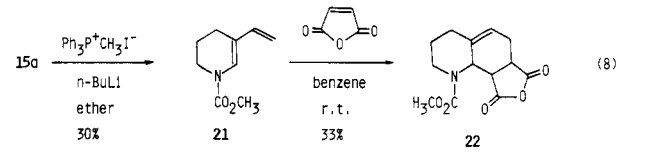
(b) Vilsmeier Reaction. The Vilsmeier reaction with enecarbamates gave β-formylenecarbamates (eq 3–5) in satisfactory yields, whereas the Vilsmeier reaction with an enamide resulted in a poor yield (eq 6). β-Formylenecarbamates (**15**) obtained



by this method are important synthetic intermediates, as exemplified in eq 7 and 8. Treatment of **15a** with a catalytic amount of sodium methoxide in methanol gave **17**[11] quantitatively; **17** was alkylated with 5-iodo-2-pentanone ethylene ketal (**18**) to give **19** in an 82% yield. The cyclization of **19** to the hydrololidine derivative **20** is achievable by acetalization of **19** and subsequent treatment with acid as described in ref[13] (eq 7). Also, a Wittig

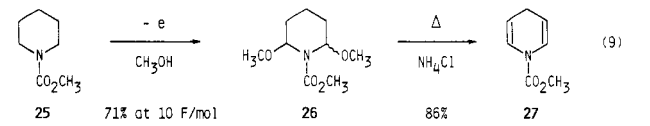


reaction with **15a** followed by a Diels–Alder reaction with maleic anhydride afforded a product (**22**) useful in the synthesis of quinoline derivatives (eq 8).

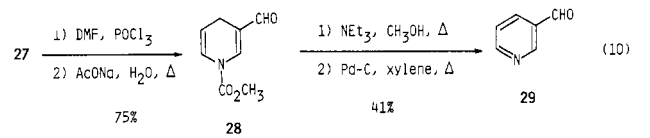


(c) Hydroboration of Enecarbamates. The reaction of enecarbamates with diborane[14] made it possible to introduce a hydroxyl group into the β position of enecarbamates.[15] The anodic methoxylation of *N*-carbomethoxy-L-proline methyl ester (**23**), prepared from L-proline in a 70% yield, followed by heating the product (**3g**) in the presence of ammonium chloride gave enecarbamate **5g**, which was then subjected to hydroboration to get a mixture of **24a** and **24b** in a ratio of 1:4 (Scheme III). The IR and ^1H NMR spectra of the major isomer **24b** coincided with those of *N*-carbomethoxy-*trans*-4-hydroxy-L-proline prepared independently from the natural amino acid 4-hydroxy-L-proline. The results of hydroboration of enecarbamates are summarized in Table IV.

Preparation and Reaction of Dienecarbamates and N-Substituted Pyrroles. Anodic dimethoxylation of carbamate **25** to yield α,α′-dimethoxy carbamate (**26**) is possible, if a sufficient amount of electricity is used. When a large excess of electricity (10 F/mol) was passed, **26** was obtained in a 71% yield from **25**. Heating **26** in the presence of ammonium chloride afforded dienecarbamate **27**[16] in an 86% yield (eq 9).



Nicotinaldehyde **29** was synthesized from **27**. Formylation of **27** by the Vilsmeier reaction gave **28** in a 75% yield. Subsequent hydrolytic elimination of the *N*-carbomethoxy group followed by dehydrogenation with palladium catalyst afforded **29** in a 41% overall yield from **28** (eq 10).



(11) 1,4,5,6-Tetrahydronicotinaldehyde (**17**) was also prepared by hydrogenation of nicotinaldehyde.[12]

(12) Wenkert, E.; Dave, K. G.; Haglid, F.; Lewis, R. G.; Oishi, T.; Stevens, R. V.; Terashima, M. *J. Org. Chem.* **1968**, *33*, 747.

(13) Wenkert, E.; Dave, K. G.; Stevens, R. V. *J. Am. Chem. Soc.* **1968**, *90*, 6177.

(14) Zweifel, G.; Brown, H. C. *Org. React.* **1963**, *13*, 1.

(15) Hydroboration of enamines has already been known: Borowitz, I. J.; Williams, G. J. *J. Org. Chem.* **1967**, *32*, 4157.

(16) Fowler, F. W. *J. Org. Chem.* **1972**, *37*, 1321.

Table III. Reaction of 5 with Acid Chlorides

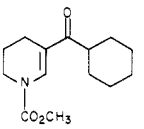
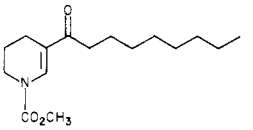
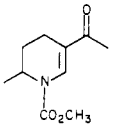
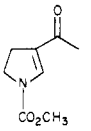
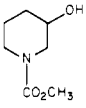
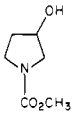
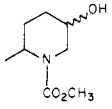
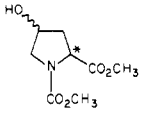
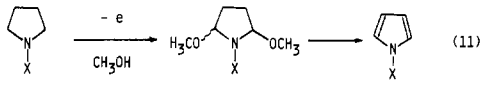
run	5	R in RCOCl	reacn temp, °C	reacn time, h	product, (% yield)	
1	5e	cyclohexyl	−60 → room temp	14.5	 14b	(85)
2	5e	*n*-octyl	−70 → room temp	9	 14c	(69)
3	5f	methyl	−70 → room temp	5	 14d	(70)
4	5d	methyl	−70	3	 14e	(32)

Table IV. Hydroboration of Enecarbamates

enecarbamate	reacn temp, °C	product	% yield
5e	room temp	 24c	60
5d	room temp −20	 24d	37 62
5f	room temp	 24e,f	60
5g	room temp −20	 24a,b	24 45

N-Acylated pyrroles were also synthesized by a similar method (eq 11), which is useful for the synthesis of pyrrole derivatives.[17]



(11)

30a, X = CO_2CH_3 31a, 77% 32a, 62 %
b, X = Ac b, 56% b, 63 %
c, X = CO_2CH_2Ph c, 72% c, 42 %

(17) *N*-Carbomethoxypyrrole: (a) Acheson, M.; Vernon, J. M. *J. Chem. Soc.* **1961**, 457. (b) Gabel, N. W. *J. Org. Chem.* **1962**, *27*, 301. (c) Hodge, P.; Richards, R. W. *J. Chem. Soc.* **1963**, 2543. *N*-Acetylpyrrole: (d) Reddy, G. S. *Chem. Ind. (London)* **1965**, 1426. (e) Gross, H.; Beier, U. *Chem. Ber.* **1962**, *95*, 2270. Substituted *N*-acetylpyrrole: (f) Horikawa, H.; Iwasaki, T.; Matsumoto, K.; Miyoshi, M. *J. Org. Chem.* **1978**, *43*, 335.

Experimental Section[18]

Anodic Oxidation of Carbamates and Amides to α-Methoxy Carbamates and α-Methoxy Amides. Anodic oxidation of carbamates and amides was carried out according to the reported procedure.[2,3] The general procedure is exemplified by the preparation of **3c**.

***N*-Carbomethoxy-α-methoxydiisobutylamine (3c).** A solution of *N*-(carbomethoxy)diisobutylamine (23 g, 0.123 mol) in methanol (250 mL) containing tetraethylammonium *p*-toluenesulfonate (5 g, 0.017 mol) as a supporting electrolyte was placed into an electrolysis cell equipped with carbon electrodes (30 cm^2). A constant current (4 A) was passed through the solution, which was externally cooled with ice water. After 4.3 F/mol of electricity was passed, the solvent was evaporated under reduced pressure at room temperature. Water (50 mL) was added to the residue and the product was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layer was dried over anhydrous magnesium sulfate. After the drying agent was removed by filtration, the solvent was evaporated and the residue was distilled to afford **3c** (22.28 g, 0.103 mol, 83% yield): bp 53–54 °C (0.5 mm); IR (neat) 2950, 2875, 2827, 1700, 1673, 1445, 1330, 1265, 1138, 1075, 982, 833, 772 cm^{-1}; NMR (CCl_4) δ 0.87 (m, 12 H), 1.5–2.1 (m, 2 H), 2.65–3.20 (m, 2 H), 3.20 (s, 3 H), 3.64 (s, 3 H), 4.27–4.91 (m, 1 H). Anal. Calcd for $C_{11}H_{23}NO_3$: C, 60.80; H, 10.65; N, 6.45. Found: C, 60.57; H, 10.89; N, 6.46.

The data of the other new compounds are as follows.[19]

***N*-Carbomethoxy-α-methoxydiethylamine (3b)**: 58% yield at 4.0 F/mol; bp 78–80 °C (25 mm); IR (neat) 2975, 2935, 2820, 1678, 1435, 1402, 1365, 1335, 1312, 1280, 1245, 1218, 1188, 1152, 1120, 1078, 1050, 1018, 920, 848, 767 cm^{-1}; NMR (CCl_4) δ 1.10 (t, *J* = 7 Hz, 3 H), 1.23 (d, *J* = 6 Hz, 3 H), 3.15 (s, 3 H), 3.15 (q, *J* = 7 Hz, 2 H), 3.65 (s, 3 H), 5.28 (q, *J* = 6 Hz, 1 H). Anal. Calcd for $C_7H_{15}NO_3$: C, 52.16; H, 9.38; N, 8.69. Found: C, 51.96; H, 9.37; N, 8.83.

1-Carbomethoxy-5-methoxy-L-proline methyl ester (3g): 87% yield at 2.5 F/mol; bp 110–113 °C (1 mm); IR (neat) 2830, 1740, 1700, 1200, 1090 cm^{-1}; NMR (CCl_4) δ 1.48–2.51 (m, 4 H), 3.30 (s, 3 H), 3.65 (s, 3 H), 3.71 (s, 3 H), 4.20 (m, 1 H), 5.20 (m, 1 H). Anal. Calcd for $C_9H_{15}NO_5$: C, 49.96; H, 6.96; N, 6.48. Found: C, 50.04; H, 7.18; N, 6.22.

1-Carbomethoxy-2-methoxy-5-methylpiperidine (3h) and 1-Carbomethoxy-2-methoxy-3-methylpiperidine (3i). Distillation of the anodic products gave a mixture of **3h** and **3i**, the ratio of which was not clear

(18) Boiling and melting points are uncorrected. ^1H NMR spectra were recorded on a Varian EM-360 or EM-390 spectrometer. IR spectra were obtained with a Hitachi 215 infrared spectrophotometer. GLC analyses were carried out on a Yanaco GCG 550T gas chromatograph. Solvents (CH_2Cl_2, THF, benzene, and ethylene dichloride) were dried and distilled under an atmosphere of nitrogen. DMF was dried over calcium hydride.

(19) The data not listed here were described in the previous papers.[2,3]

at this stage, whereas it may be suggested from the ratio of enecarbamates **5h** and **5i**: 82% yield at 2.7 F/mol; bp 71–72 °C (0.65 mm); IR (neat) 2930, 2870, 2825, 1683, 1437, 1403, 1338, 1308, 1265, 1240, 1188, 1160, 1100, 1082, 1067, 975, 935, 887, 767 cm^{-1}; NMR (CCl_4) δ 0.93 (m, 3 H), 1.25–1.80 (m, 5 H), 3.13 (s, 3 H), 3.60 (s, 3 H), 3.5–4.0 (m, 2 H), 4.75–5.36 (m, 1 H). Anal. Calcd for $C_9H_{17}NO_3$: C, 57.73; H, 9.15; N, 7.48. Found: C, 57.59; H, 9.37; N, 7.37.

***N*-Acetyl-α-methoxydibutylamine (4a)** was not isolated in a pure form because distillation of crude **4a** gave a mixture that contained a small amount of enamide **6a**. Thus, the distillation mixture was used directly in the following step.

***N*-Benzoyl-α-methoxydibutylamine (4d)** was isolated by column chromatography on silica gel (*n*-hexane–AcOEt, 2:1): 89% yield at 3.5 F/mol; IR (neat) 3058, 2953, 2870, 2823, 1638, 1443, 1408, 1355, 1340, 1190, 1132, 1100, 1072, 940, 785, 728, 700 cm^{-1}; NMR (CCl_4) δ 0.70–1.10 (m, 6 H), 1.10–1.90 (m, 8 H), 3.10 (s, 3 H), 3.25 (m, 2 H), 4.70 (br, 1 H), 7.30 (s, 5 H). Anal. Calcd for $C_{16}H_{25}NO_2$: C, 72.97; H, 9.57; N, 5.32. Found: C, 72.71; H, 9.74; N, 5.29.

Synthesis of Enecarbamates. General Procedure. A mixture of α-methoxy carbamates **3** (30 mmol) containing ammonium chloride (5 mmol) was heated under reduced pressure (20–100 mm) in a flask equipped with a reflux condenser. The reaction was carried out under an atmosphere of nitrogen at the bath temperature shown in Table I. After the reaction was completed,[20] products except **5g** were isolated by distillation directly from the reaction flask. Isolation of **5g** was carried out by column chromatography on silica gel (*n*-hexane–AcOEt, 2:1).

Methyl *N*-(1-Butenyl)-*N*-butylcarbamate (5a):[21] bp 115–118 °C (23 mm); IR (neat) 2950, 2925, 2865, 1695, 1655, 1437, 1392, 1325, 1282, 1247, 1212, 1153, 1085, 1025, 945, 765 cm^{-1}; NMR (CCl_4) δ 1.00 (m, 6 H), 1.2–1.6 (m, 4 H), 2.05 (d q, J = 6.5, 8 Hz, 2 H), 3.1–3.6 (m, 2 H), 3.70 (s, 3 H), 4.72 (d t, J = 14, 6.5 Hz, 1 H), 6.65 (d, J = 14 Hz, 1 H). Anal. Calcd for $C_{10}H_{19}NO_2$: C, 64.83; H, 10.34; N, 7.56. Found: C, 64.96; H, 10.41; N, 7.39.

Methyl *N*-Ethyl-*N*-vinylcarbamate (5b): bp 72–74 °C (33 mm); IR (neat) 3090, 2950, 1700, 1685, 1615, 1435, 1365, 1345, 1308, 1275, 1255, 1240, 1190, 1150, 1077, 1030, 977, 958, 833, 785, 767 cm^{-1}; NMR (CCl_4) δ 1.33 (t, J = 7 Hz, 3 H), 3.55 (q, J = 7 Hz, 2 H), 3.70 (s, 3 H), 4.11 (d, J = 9.5 Hz, 1 H), 4.18 (d, J = 16 Hz, 1 H), 6.90 (d d, J = 9.5, 16 Hz, 1 H). Anal. Calcd for $C_6H_{11}NO_2$: C, 55.80; H, 8.58; N, 10.84. Found: C, 55.24; H, 8.62; N, 10.85.

Methyl *N*-Isobutyl-*N*-(2-methyl-1-propenyl)carbamate (5c): bp 100–102 °C (20 mm); IR (neat) 2950, 2872, 1685, 1445, 1383, 1333, 1275, 1212, 1193, 1153, 985, 820, 767 cm^{-1}; NMR (CCl_4) δ 0.90 (d, J = 6.5 Hz, 3 H), 1.56 (d, J = 1 Hz, 1 H), 1.70 (d, J = 1.5 Hz, 3 H), 1.85 (m, 1 H), 3.07 (d, J = 7 Hz, 2 H), 3.56 (s, 3 H), 5.55 (m, 1 H). Anal. Calcd for $C_{10}H_{19}NO_2$: C, 64.38; H, 10.34; N, 7.56. Found: C, 64.38; H, 10.44; N, 7.54.

***N*-Carbomethoxy-2-pyrroline (5d)**: bp 88 °C (22 mm); IR (neat) 2950, 2920, 2860, 1680, 1615, 1445, 1397, 1362, 1345, 1220, 1190, 1132, 1095, 973, 947, 918, 850, 755, 700 cm^{-1}; NMR (CCl_4) δ 2.60 (m, 2 H), 3.60 (s, 3 H), 3.66 (m, 2 H), 4.88 (m, 1 H), 6.41 (br m, 1 H). Anal. Calcd for $C_6H_9NO_2$: C, 56.68; H, 7.14; N, 11.02. Found: C, 56.49; H, 7.22; N, 11.02.

***N*-Carbomethoxy-1,2,3,4-tetrahydropyridine (5e)**: bp 102 °C (23 mm); IR (neat) 2940, 2850, 1690, 1645, 1438, 1400, 1355, 1320, 1295, 1257, 1230, 1188, 1115, 1053, 995, 960, 922, 763, 712 cm^{-1}; NMR (CCl_4) δ 1.55–2.10 (m, 4 H), 3.40–3.70 (m, 2 H), 3.63 (s, 3 H), 4.75 (br m, 1 H), 6.64 (br d, J = 7 Hz, 1 H). Anal. Calcd for $C_9H_{11}NO_2$: C, 59.56; H, 7.85; N, 9.92. Found: C, 59.46; H, 8.03; N, 10.01.

***N*-Carbomethoxy-1,2,3,4-tetrahydro-2-picoline (5f)**: bp 52 °C (0.35 mm); IR (neat) 2930, 2848, 1685, 1650, 1435, 1405, 1335, 1283, 1235, 1187, 1140, 1103, 1082, 1040, 1012, 967, 882, 830, 762, 712 cm^{-1}; NMR (CCl_4) δ 1.10 (d, J = 7 Hz, 3 H), 1.45–2.15 (m, 4 H), 3.67 (s, 3 H), 4.30 (m, 1 H), 4.75 (m, 1 H), 6.62 (br d, J = 8 Hz, 1 H). Anal. Calcd for $C_8H_{13}NO_2$: C, 61.91; H, 8.44; N, 9.03. Found: C, 61.30; H, 8.59; N, 9.03.

***N*-Carbomethoxy-4,5-dehydroproline methyl ester (5g)**: IR (neat) 1755, 1700, 1620, 1400, 1205 cm^{-1}; NMR (CCl_4) δ 2.30–3.50 (m, 2 H), 3.70 (s, 6 H), 4.55 (d d, J = 5.3, 2.6 Hz, 1 H), 4.85 (m, 1 H), 6.50 (br s, 1 H). Anal. Calcd for $C_8H_{11}NO_4$: C, 51.88; H, 6.00; N, 7.56. Found: C, 51.92; H, 6.19; N, 7.42.

***N*-Carbomethoxy-1,2,3,4-tetrahydro-3-picoline (5h).** Separation of **5h** and **5i** from their mixture was accomplished by GLC after distillation: bp of the mixture, 106–107 °C (18 mm); IR (neat) 2945, 2915, 2860, 1683, 1648, 1435, 1400, 1340, 1247, 1190, 1117, 992, 948, 880, 850, 825, 760, 713 cm^{-1}; NMR (CCl_4) δ 1.00 (d, J = 6 Hz, 3 H), 1.25–2.10 (m, 3 H), 3.60 (s, 3 H), 3.60–4.10 (m, 2 H), 4.73 (m, 1 H), 6.65 (m, 1 H). Anal. Calcd for $C_8H_{13}NO_2$: C, 61.91; H, 8.44; N, 9.03. Found: C, 61.98; H, 8.56; N, 9.02.

***N*-Carbomethoxy-1,4,5,6-tetrahydro-3-picoline (5i)**: IR (neat) 2915, 2870, 2830, 1683, 1662, 1435, 1387, 1350, 1307, 1255, 1177, 1107, 1078, 1020, 978, 843, 820, 760 cm^{-1}; NMR (CCl_4) δ 1.65 (s, 3 H), 1.73–2.00 (m, 4 H), 3.35–3.70 (m, 2 H), 3.67 (s, 3 H), 6.45 (br s, 1 H). Anal. Calcd for $C_8H_{13}NO_2$: C, 61.91; H, 8.44; N, 9.03. Found: C, 61.95; H, 8.57; N, 8.91.

Synthesis of Enamides. General Procedure. Enamides were prepared in a similar procedure to that of enecarbamates from α-methoxy amide (35 mmol) using silica gel (0.4 g) as an acid catalyst. Enamide **6c** was obtained by distillation without a catalyst. The identification of **6b** and **6c** was carried out by comparison of the spectroscopic data described in the literature.[7b]

***N*-(1-Butenyl)-*N*-butylacetamide (6a)**:[21] bp 91 °C (2 mm); IR (neat) 2955, 2930, 2870, 1637, 1402, 1320, 1273, 1247, 1213, 1150, 1048, 935 cm^{-1}; NMR (CCl_4) δ 0.70–1.20 (m, 6 H), 1.10–1.70 (m, 4 H), 1.85–2.25 (m, 2 H), 2.05 (s, 3 H), 3.25–3.70 (m, 2 H), 4.88 (d t, J = 14, 7 Hz, 1 H), 6.37 (d, J = 14 Hz, 1 H). Anal. Calcd for $C_{10}H_{19}NO$: C, 70.96; H, 11.31; N, 8.28. Found: C, 70.73; H, 11.58; N, 8.18.

***N*-(1-Butenyl)-*N*-butylbenzamide (6d)**:[21] bp 124 °C (1 mm); IR (neat) 2955, 2930, 2870, 1635, 1630, 1578, 1492, 1445, 1400, 1325, 1215, 1100, 950, 787, 717, 698 cm^{-1}; NMR (CCl_4) δ 0.90 (t, J = 7 Hz, 6 H), 1.15–2.27 (m, 6 H), 3.66 (br t, J = 7 Hz, 2 H), 4.95 (d t, J = 14, 6.5 Hz, 1 H), 6.45 (d, J = 14 Hz, 1 H), 7.33 (s, 5 H). Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.87; H, 9.27; N, 6.04.

Synthesis of Unsymmetrical Enecarbamates. General Procedure. To a stirred suspension of sodium hydride (30 mmol) in dry DMF (30 mL) was added dropwise **9** (20 mmol) at 0 °C under an atmosphere of nitrogen. After the solution was stirred at 0 °C for 1 h, alkyl halide (30 mmol) was added to the reaction mixture, which was then stirred at 0 °C for 2 h and at room temperature overnight. The mixture was poured into brine and extracted with ether (5 × 30 mL). The combined ethereal solution was dried over anhydrous magnesium sulfate. After the drying agent was removed by filtration, the solvent was evaporated to give the mixture of **10** and **11**. The mixture was heated under reduced pressure (20–100 mm) with ammonium chloride for 4 h at the bath temperature of 100–120 °C and then cooled. Isolation of **11** was achieved by column chromatography on silica gel (*n*-hexane–AcOEt, 20:1).

Methyl *N*-Benzyl-*N*-(1-butenyl)carbamate (11a):[21] IR (neat) 3015, 2950, 2860, 1695, 1653, 1437, 1387, 1320, 1275, 1240, 1210, 942, 763, 730, 692 cm^{-1}; NMR (CCl_4) δ 0.90 (t, J = 7 Hz, 3 H), 2.00 (d q, J = 6.5, 7 Hz, 2 H), 3.80 (s, 3 H), 4.65 (s, 2 H), 4.70 (d t, J = 14.5, 6.5 Hz, 1 H), 6.85 (d, J = 14.5 Hz, 1 H), 7.20 (s, 5 H). Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.20; H, 7.82; N, 6.39. Found: C, 71.01; H, 7.90; N, 6.26.

Methyl *N*-Allyl-*N*-(1-butenyl)carbamate (11b):[21] IR (neat) 2950, 2930, 2870, 2850, 1690, 1652, 1438, 1388, 1320, 1275, 1243, 1220, 1150, 940, 840, 765 cm^{-1}; NMR (CCl_4) δ 1.00 (t, J = 7 Hz, 3 H), 2.05 (d q, J = 8, 8 Hz, 2 H), 3.75 (s, 3 H), 4.10 (d, J = 4 Hz, 2 H), 4.80 (d t, J = 14, 7 Hz, 1 H), 5.05 (d, J = 16 Hz, 1 H), 5.10 (d, J = 8 Hz, 1 H), 5.75 (d d t, J = 16, 8, 4 Hz, 1 H), 6.77 (d, J = 14 Hz, 1 H). Anal. Calcd for $C_9H_{15}NO_2$: C, 63.88; H, 8.93; N, 8.28. Found: C, 63.63; H, 9.10; N, 8.26.

Methyl *N*-(1-Butenyl)-*N*-ethylcarbamate (11c):[21] IR (neat) 2952, 2870, 1695, 1653, 1437, 1392, 1320, 1262, 1245, 1190, 1155, 1075, 1025, 995, 985, 945, 800, 767 cm^{-1}; NMR (CCl_4) δ 1.00 (t, J = 7 Hz, 3 H), 1.10 (t, J = 7 Hz, 3 H), 2.05 (d q, J = 7, 7 Hz, 2 H), 3.55 (q, J = 7 Hz, 2 H), 3.70 (s, 3 H), 4.80 (d t, J = 14, 7 Hz, 1 H), 6.63 (d, J = 14 Hz, 1 H). Anal. Calcd for $C_8H_{15}NO_2$: C, 61.12; H, 9.62; N, 8.91. Found: C, 60.96; H, 9.78; N 8.90.

Friedel–Crafts Reaction. The general procedure was exemplified by the reaction of **5e** with **12**. To a stirred solution of **12** (50 mmol) in CH_2Cl_2 (15 mL) was added dropwise stannic chloride (50 mmol) over a period of 5 min at −70 °C under an atmosphere of nitrogen, and the reaction mixture was stirred for 15 min. To the mixture was added dropwise a solution of **5e** (5 mmol) in CH_2Cl_2 (5 mL) in a period of 30 min. After the reaction mixture was stirred for 4 h at −70 °C, it was gradually warmed to room temperature and was stirred for 16 h. The mixture was poured into cold water (100 mL) and products were extracted with CH_2Cl_2 (4 × 50 mL). The combined organic layer was washed with aqueous sodium bicarbonate (2 × 30 mL) and was dried over anhydrous magnesium sulfate. After the drying agent was removed by filtration, the solvent was evaporated and the residue was purified by column chromatography on silica gel (*n*-hexane–AcOEt, 2:1) to afford **14a**.

***N*-Carbomethoxy-3-acetyl-1,4,5,6-tetrahydropyridine (14a)**: mp 52.8–53.3 °C (from ether); IR (KBr) 3100, 3008, 2955, 2885, 1703,

(20) The progress of the reaction was checked by GLC and/or TLC.
(21) The coupling constants between two olefinic protons imply that the configuration is trans.

1620, 1440, 1380, 1343, 1315, 1283, 1240, 1198, 1185, 1175, 1117, 1077, 1065, 1018, 985, 965, 902, 760 cm^{-1}; NMR (CCl_4) δ 1.84 (m, 2 H), 2.20 (m, 2 H), 2.23 (s, 3 H), 3.57 (br t, J = 5.5 Hz, 2 H), 3.80 (s, 3 H), 7.90 (s, 1 H). Anal. Calcd for $C_9H_{13}NO_3$: C, 59.00; H, 7.15; N, 7.65. Found: C, 59.16; H, 7.38; N, 7.80.

N-Carbomethoxy-3-(cyclohexylcarbonyl)-1,4,5,6-tetrahydropyridine (14b): IR (neat) 2925, 2850, 1700, 1608, 1437, 1380, 1300, 1243, 1215, 1180, 1135, 973, 887, 763 cm^{-1}; NMR (CCl_4) δ 1.05–2.05 (m, 12 H), 2.25 (br t, J = 6 Hz, 2 H), 2.80 (m, 1 H), 3.60 (t, J = 5.6 Hz, 2 H), 3.80 (s, 3 H), 7.87 (s, 1 H). Anal. Calcd for $C_{14}H_{21}NO_3$: C, 66.91; H, 8.42; N, 5.57. Found: C, 66.72; H, 8.64; N, 5.59.

N-Carbomethoxy-3-nonanoyl-1,4,5,6-tetrahydropyridine (14c): IR (neat) 2960, 2930, 2860, 1725, 1657, 1625, 1442, 1390, 1315, 1255, 1230, 1185, 1125, 980, 770 cm^{-1}; NMR (CCl_4) δ 0.88 (t, J = 5 Hz, 3 H), 1.08–1.67 (m, 12 H), 1.82 (m, 2 H), 2.00–2.70 (m, 4 H), 3.62 (m, 2 H), 3.82 (s, 3 H), 7.91 (s, 1 H); mass spectrum, m/e 281 (M^+), 167 ($M^+ - C_8H_{17}$).

N-Carbomethoxy-5-acetyl-1,2,3,4-tetrahydro-2-picoline (14d): IR (neat) 2950, 2855, 1705, 1610, 1440, 1390, 1347, 1313, 1285, 1250, 1200, 1118, 1090, 1053, 995, 950, 898, 767 cm^{-1}; NMR (CCl_4) δ 1.13 (d, J = 6.5 Hz, 3 H), 1.60–2.50 (m, 4 H), 2.20 (s, 3 H), 3.80 (s, 3 H), 4.35 (m, 1 H), 7.83 (s, 3 H). Anal. Calcd for $C_{10}H_{15}NO_3$: C, 60.90; H, 7.67; N, 7.10. Found: C, 60.66; H, 7.83; N, 7.23.

N-Carbomethoxy-3-acetyl-2-pyrroline (14e): mp 107.5–109 °C (from n-hexane–AcOEt, 2:1); IR (KBr) 3090, 2970, 2955, 1713, 1635, 1600, 1457, 1442, 1418, 1375, 1308, 1260, 1250, 1230, 1192, 1122, 993, 937, 897, 880, 867, 758 cm^{-1}; NMR ($CDCl_3$) δ 2.28 (s, 3 H), 2.86 (br t, J = 9.6 Hz, 2 H), 3.83 (s, 3 H), 3.90 (m, 2 H), 7.47 (s, 1 H); mass spectrum, m/e 169 (M^+), 154 ($M^+ - CH_3$).

Vilsmeier Reaction. General Procedure. Phosphorus oxychloride (8.5 mmol) was added dropwise to DMF (8.5 mmol) at 10–20 °C in a period of 3 min and the mixture was stirred for 20 min. After the mixture was cooled under 5 °C, ethylene dichloride (10 mL) was added, and then a solution of **5** (7.08 mmol) in ethylene dichloride (5 mL) was added over a period of 30 min. The solution was stirred at 0–5 °C for 1 h and was refluxed for 15 min. To a cooled mixture was added a solution of sodium acetate trihydrate (5.3 g, 39 mmol) in water (30 mL). After the reaction mixture was refluxed for 15 min, the mixture was cooled to room temperature. The organic layer was separated and the aqueous phase was extracted with CH_2Cl_2 (6 × 15 mL). The combined organic portion was dried over anhydrous magnesium sulfate. After the drying agent was filtered off, the residue was purified by column chromatography on silica gel (n-hexane–AcOEt) to give **15**.

N-Carbomethoxy-1,4,5,6-tetrahydronicotinaldehyde (15a): mp 182–183 °C (from ether); IR (KBr) 3070, 2950, 2850, 1700, 1615, 1440, 1405, 1375, 1340, 1312, 1292, 1265, 1223, 1175, 975, 763, 725 cm^{-1}; NMR (CCl_4) δ 1.90 (m, 2 H), 2.25 (br t, J = 6 Hz, 2 H), 3.67 (br t, J = 5.5 Hz, 2 H), 3.80 (s, 3 H), 7.63 (s, 1 H), 9.20 (s, 1 H); mass spectrum, m/e 169 (M^+).

N-Carbomethoxy-3-formyl-2-pyrroline (15b): mp 102–103 °C (from n-hexane–AcOEt, 3:8); IR (KBr) 3090, 2952, 2830, 1713, 1642, 1610, 1440, 1410, 1297, 1215, 972, 902, 765 cm^{-1}; NMR (CCl_4) δ 2.84 (br t, J = 9.8 Hz, 2 H), 3.80 (s, 3 H), 3.95 (br t, J = 9.8 Hz, 2 H), 7.42 (s, 1 H), 9.60 (s, 1 H); mass spectrum, m/e 155 (M^+).

Methyl N-Butyl-N-(2-formyl-1-butenyl)carbamate (15c): IR (neat) 2955, 2870, 1718, 1675, 1620, 1438, 1357, 1265, 1212, 1188, 1150, 1090, 1055, 770 cm^{-1}; NMR (CCl_4) δ 0.85–1.20 (m, 6 H), 1.15–1.85 (m, 4 H), 2.35 (q, 2 H), 3.70 (m, 2 H), 3.86 (s, 3 H), 7.42 (s, 1 H), 9.25 (s, 1 H); mass spectrum, m/e 213 (M^+).

N-Acetyl-1,4,5,6-tetrahydronicotinaldehyde (16): mp 85–87 °C (from n-hexane–AcOEt, 1:3); IR (KBr) 2920, 1597, 1415, 1397, 1378, 1303, 1250, 1220, 1168, 1082, 1070, 1022, 975, 915 cm^{-1}; NMR (CCl_4) δ 1.50–2.20 (m, 4 H), 2.25 (s, 3 H), 3.68 (br t, J = 6 Hz, 2 H), 7.57 (br, 1 H), 9.25 (s, 1 H). Anal. Calcd for $C_8H_{11}NO_2$: C, 62.72; H, 7.24; N, 9.14. Found: C, 62.44; H, 7.30; N, 8.87.

Synthesis of N-(4-Oxopentyl)-1,4,5,6-tetrahydronicotinaldehyde Ethylene Ketal (19). To a solution of **15a** (10 mmol) in methanol (10 mL) was added a catalytic amount of sodium (50 mg, 2.2 mmol), and the reaction mixture was stirred at room temperature for 4 h. After the solvent was evaporated, the residue was purified by column chromatography on alumina (AcOEt) to afford **17** (~10 mmol).

The alkylation of **17** with 5-iodo-2-pentanone ethylene ketal (**18**), which was prepared by ketalization[22] of 5-iodo-2-pentanone[23] in an 82% yield, was carried out in a procedure similar to that described in the synthesis of unsymmetrical enecarbamates. Thus, the reaction of **17** (4.5 mmol) with sodium hydride (6.8 mmol) in DMF (15 mL) at 0 °C for 1 h was followed by the addition of **18** (6.8 mmol), and the reaction mixture was stirred at 0 °C for 2.5 h and at room temperature overnight. The mixture was poured into brine (30 mL) and unreacted **18** was recovered by extraction with ether (2 × 5 mL). The product was extracted with CH_2Cl_2 (5 × 15 mL). After the extract was dried over anhydrous magnesium sulfate, the solvent was filtered and evaporated under reduced pressure. The residue was purified by column chromatography on alumina (AcOEt) to afford **19** (3.7 mmol, 82% yield).

The identification of **17**[12] and **19**[13] was carried out by comparison of spectroscopic data described in the literature.

Synthesis of N-Carbomethoxy-3-vinyl-1,4,5,6-tetrahydropyridine (21). To a stirred solution of n-butyllithium (2.12 mmol) in ether (10 mL) was added triphenylmethylphosphonium iodide (2.12 mmol), and the resulting mixture was stirred at room temperature for 5 h. Into the mixture was added dropwise a solution of **15a** (1.77 mmol) in ether (3 mL). After additional ether (5 mL) was introduced, the reaction mixture was refluxed for 14 h. The solid was filtered off and the solvent was evaporated in vacuo. The residue was purified by column chromatography on silica gel (n-hexane–AcOEt, 5:1) to give **21** (0.54 mmol, 30% yield): IR (neat) 3090, 3000, 2950, 2870, 1705, 1635, 1440, 1375, 1315, 1260, 1188, 1115, 980, 873, 762 cm^{-1}; NMR (CCl_4) δ 1.65–2.30 (m, 4 H), 3.55 (m, 2 H), 3.70 (s, 3 H), 4.75 (d, J = 10 Hz, 1 H), 4.85 (d, J = 18 Hz, 1 H), 6.22 (d d, J = 18, 10 Hz, 1 H), 6.80 (br s, 1 H); mass spectrum, m/e 167 (M^+), 152 ($M^+ - CH_3$), 108 ($M^+ - CO_2CH_3$).

Reaction of Diene 21 with Maleic Anhydride. Preparation of Diels–Alder Adduct 22. A solution of diene **21** (1.1 mmol) and maleic anhydride (1.2 mmol) in benzene (5 mL) was stirred at room temperature for 8 h. After the solvent was evaporated, the residue was purified by preparative TLC (n-hexane–AcOEt, 2:1) to afford crystalline **22** (0.358 mmol, 33% yield): mp 144–147 °C (from n-hexane–AcOEt, 2:1); IR (KBr) 2960, 1845, 1775, 1687, 1465, 1410, 1375, 1275, 1260, 1200, 1130, 1055, 1000, 963, 922, 898, 775 cm^{-1}; NMR ($CDCl_3$) δ 1.25–2.10 (m, 2 H), 2.10–2.50 (m, 4 H), 2.75 (m, 1 H), 3.40–3.75 (m, 3 H), 3.77 (s, 3 H), 4.66 (br, 1 H), 5.68 (m, 1 H). Anal. Calcd for $C_{13}H_{15}NO_5$: C, 58.86; H, 5.70; N, 5.28. Found: C, 59.12; H, 5.68; N, 5.19.

Hydroboration of Enecarbamates. General Procedure. To a stirred suspension of **5** (5 mmol) and sodium borohydride (3.1 mmol) in THF (3.5 mL) was added dropwise boron trifluoride etherate (4.2 mmol), and the solution was stirred at the temperature shown in Table IV for 7–8 h. Water (0.5 mL), 3 N aqueous sodium hydroxide (1.2 mL), and 30% hydrogen peroxide (1.5 mL) were successively added to the reaction mixture. After the solution was stirred overnight, the product was extracted with CH_2Cl_2 (5 × 5 mL). The combined organic layer was dried over anhydrous magnesium sulfate and the drying agent was removed by filtration. Concentration of the residue and its purification by column chromatography on silica gel (n-hexane–AcOEt, 2:1) afforded β-hydroxy carbamates **24**.

N-Carbomethoxy-*cis*-4-hydroxy-L-proline methyl ester (24a): IR (neat) 3400 (br), 1743, 1680, 1460, 1390, 1200, 1128, 1050, 775 cm^{-1}; NMR ($CDCl_3$) δ 1.50–2.20 (m, 2 H), 3.10–4.70 (m, 5 H), 3.70 (s, 6 H); mass spectrum, m/e 203 (M^+), 144 ($M^+ - CO_2CH_3$).

N-Carbomethoxy-*trans*-4-hydroxy-L-proline methyl ester (24b): IR (neat) 3450 (br), 2960, 2892, 1745, 1705, 1690, 1460, 1393, 1280, 1208, 1175, 1132, 1088, 1020, 967, 880, 775 cm^{-1}; NMR ($CDCl_3$) δ 1.70–2.60 (m, 2 H), 3.12 (s, 1 H), 3.65 (m, 1 H), 3.70 (s, 3 H), 3.75 (s, 3 H), 4.20–4.70 (m, 3 H). Anal. Calcd for $C_8H_{13}NO_5$: C, 47.28; H, 6.46; N, 6.89. Found: C, 47.05; H, 6.49; N, 6.73.

The ratio of **24a** and **24b** was 1:4. The identification of the stereochemistry of **24b** was achieved by comparison with an authentic sample that was synthesized from 4-hydroxy-L-proline as follows.

Synthesis of 24b from 4-Hydroxy-L-proline. 4-Hydroxy-L-proline was esterified in methanol saturated with dry hydrogen chloride. Methanol and hydrogen chloride were removed under reduced pressure, and the residue was transformed to carbamate in a usual manner with methyl chlorocarbonate and excess (3 equiv) potassium carbonate in methylene chloride. Purification of the product by column chromatography on silica gel gave a compound that was identical with **24b** spectroscopically.

N-Carbomethoxy-3-hydroxypiperidine (24c): bp 128–131 °C (6.5 mm); IR (neat) 3420 (br), 2940, 2860, 1670, 1443, 1408, 1260, 1240, 1193, 1147, 1070, 1000, 960, 860, 767 cm^{-1}; NMR (CCl_4) δ 1.10–2.10 (m, 4 H), 2.70–4.07 (m, 6 H), 3.65 (s, 3 H). Anal. Calcd for $C_7H_{13}NO_3$: C, 52.82; H, 8.23; N, 8.80. Found: C, 52.66; H, 8.41; N, 8.78.

N-Carbomethoxy-3-hydroxypyrrolidine (24d): IR (neat) 3410 (br), 2955, 2895, 1687, 1678, 1465, 1455, 1395, 1345, 1203, 1122, 1103, 998, 985, 965, 910, 872, 823, 775 cm^{-1}; NMR (CCl_4) δ 1.67–2.14 (m, 2 H), 3.22–3.63 (m, 4 H), 3.66 (s, 3 H), 3.73–4.10 (br, 1 H), 4.35 (m, 1 H). Anal. Calcd for $C_6H_{11}NO_3$: C, 49.64; H, 7.64; N, 9.65. Found: C, 49.79; H, 7.78; N, 9.58.

(22) Doyle, P.; Maclean, I. R.; Murray, R. D. H.; Parker, W.; Raphael, R. A. *J. Chem. Soc.* **1965**, 1344.

(23) Findlay, J. A.; MacKay, W. D.; Bowers, W. S. *J. Chem. Soc. C* **1970**, 2631.

N-Carbomethoxy-5-hydroxy-2-pipecoline (24e,f). Though the isomers **24e** and **24f** were separable, their stereochemistry was not determined.

24e: R_f 0.20 (silica, *n*-hexane–AcOEt, 1:1); IR (neat) 3420, 2950, 2872, 1675, 1445, 1410, 1345, 1255, 1242, 1195, 1168, 1150, 1070, 1028, 1002, 773 cm^{-1}; NMR ($CDCl_3$) δ 1.15 (d, J = 7 Hz, 3 H), 1.40–2.00 (m, 4 H), 2.28–2.97 (br, 1 H), 2.65 (d d, J = 10, 12 Hz, 1 H), 3.25–4.60 (m, 3 H), 3.67 (s, 3 H).

24f: R_f 0.10 (silica, *n*-hexane–AcOEt, 1:1); IR (neat) 3425 (br), 2950, 1687, 1677, 1462, 1455, 1412, 1370, 1340, 1265, 1195, 1160, 1140, 1097, 1068, 1028, 770 cm^{-1}; NMR ($CDCl_3$) δ 1.15 (d, J = 7 Hz, 3 H), 1.25–2.25 (m, 4 H), 2.37 (br s, 1 H), 3.06 (d d, J = 12.5, 2.5 Hz, 1 H), 3.70 (s, 3 H), 3.78–4.72 (m, 3 H). Anal. Calcd for $C_8H_{15}NO_3$: C, 55.46; H, 8.75; N, 8.09. Found: C, 55.45; H, 8.72; N, 7.82.

Synthesis of N-Carbomethoxy-1,4-dihydropyridine (27). *N*-Carbomethoxypiperidine (15 g, 0.105 mol) was anodically oxidized in methanol (180 mL) containing tetraethylammonium *p*-toluenesulfonate (1 g, 3.3 mmol) as described previously. After 10 F/mol of electricity was passed, usual workup was followed by purification through column chromatography on silica gel (*n*-hexane–AcOEt, 5:1) to give *N*-carbomethoxy-2,6-dimethoxypiperidine (**26**) (15.2 g, 0.075 mol, 71% yield): IR (neat) 2950, 2827, 1703, 1440, 1410, 1367, 1315, 1267, 1198, 1088, 1000, 958, 945, 925, 900, 863, 787, 775, 742 cm^{-1}; NMR (CCl_4) δ 1.10–2.10 (m, 6 H), 3.27 (s, 6 H), 3.70 (s, 3 H), 4.97–5.50 (m, 2 H); mass spectrum, m/e 203 (M^+).

Heating of **26** (12 g, 59 mmol) (bath temperature, 110–120 °C) under reduced pressure (50 mm) in the presence of ammonium chloride (0.53 g, 10 mmol) for 5 h under an atmosphere of nitrogen gave **27** (7.075 g, 50.8 mmol, 86% yield): bp 107–108 °C (18 mm); IR (neat) 3000, 2953, 2830, 1705, 1637, 1440, 1413, 1372, 1340, 1318, 1210, 1195, 1120, 985, 960, 887, 810, 760, 718 cm^{-1}; NMR (CCl_4) δ 2.82 (m, 2 H), 3.73 (s, 3 H), 4.77 (m, 2 H), 6.60 (br d, J = 7 Hz, 2 H); mass spectrum, m/e 139 (M^+), 80 ($M^+ - CO_2CH_3$).

Synthesis of N-Carbomethoxy-3-formyl-1,4-dihydropyridine (28) and Nicotinaldehyde (29). Phosphorus oxychloride (0.75 mL, 8 mmol) was added dropwise into DMF (0.7 mL, 9 mmol) at 10–20 °C. To the mixture was added ethylene dichloride (15 mL) and a solution of **27** (0.50 g, 3.6 mmol) in ethylene dichloride (5 mL), successively, at 0–5 °C in a period of 40 min. The reaction mixture was stirred at that temperature for 2.5 h and at room temperature overnight. A solution of sodium acetate (5 g) in water (20 mL) was added to the mixture, which was then refluxed for 15 min. After the usual workup, column chromatography on silica gel (*n*-hexane–AcOEt, 5:1 and 2:1) afforded **28** (0.450 g, 2.69 mmol, 75% yield): mp 76–78.5 °C (from *n*-hexane–AcOEt, 3:2); IR (KBr) 3080, 2960, 2845, 1730, 1662, 1623, 1452, 1415, 1360, 1215, 990, 760, 713 cm^{-1}; NMR (CCl_4) δ 2.95 (m, 2 H), 3.88 (s, 3 H), 5.10 (d t, J = 9, 4 Hz, 1 H), 6.73 (d, J = 9 Hz, 1 H), 7.56 (s, 1 H), 9.42 (s, 1 H). Anal. Calcd for $C_8H_9NO_3$: C, 57.48; H, 5.43; N, 8.38. Found: C, 57.20; H, 5.34; N, 8.10.

A solution of **28** (0.20 g, 1.2 mmol) in methanol (5 mL) containing triethylamine (0.08 g, 0.8 mmol) was refluxed for 4 h. After the mixture was concentrated, xylene (5 mL) and 5% palladium-on-carbon (0.03 g) were added and the solution was refluxed for 3 h. The yield of **29** was determined by GLC, and identification was carried out by comparison of IR spectrum described in the literature:[24] IR (neat) 3390 (br), 3040, 2840, 2740, 1700, 1660, 1585, 1573, 1470, 1425, 1390, 1327, 1242, 1218, 1192, 1115, 1087, 1025, 830, 800, 700 cm^{-1}.

(24) Pouchert, C. J. "The Aldrich Library of Infrared Spectra"; Aldrich Chemical Co., Inc., 979H.

Synthesis of N-Carbomethoxy-2,5-dimethoxypyrrolidine (31a), N-Acetyl-2,5-dimethoxypyrrolidine (31b), and N-Carbobenzoxy-2,5-dimethoxypyrrolidine (31c). *N*-Carbomethoxy-2,5-dimethoxypyrrolidine (**31a**), *N*-acetyl-2,5-dimethoxypyrrolidine (**31b**), and *N*-carbobenzoxy-2,5-dimethoxypyrrolidine (**31c**) were prepared by anodic oxidation in methanol from *N*-carbomethoxypyrrolidine (**30a**), *N*-acetylpyrrolidine (**30b**), and *N*-carbobenzoxypyrrolidine (**30c**), respectively. The procedure was similar to that in the preparation of **26**. The electricities passed were 7.4 F/mol for **30a**, 6.3 F/mol for **30b**, and 7.8 F/mol for **30c**. The isolation of **31a** and **31b** was carried out by distillation, and **31c** was isolated by column chromatography on silica gel (*n*-hexane–AcOEt, 2:1).

31a: bp 64–65 °C (1 mm); IR (neat) 2980, 2950, 2930, 1710, 1442, 1368, 1330, 1200, 1080, 960, 920, 847, 775 cm^{-1}; NMR (CCl_4) δ 1.92 (m, 4 H), 3.26 (s, 6 H), 3.66 (s, 3 H), 4.70–5.27 (m, 2 H); mass spectrum, m/e 189 (M^+), 158 ($M^+ - OCH_3$). Anal. Calcd for $C_8H_{15}NO_4$: C, 50.78; H, 7.99; N, 7.40. Found: C, 50.51; H, 8.15; N, 7.24.

31b: bp 73–75 °C (0.9 mm); IR (neat) 2940, 2830, 1660, 1390, 1328, 1202, 1068, 1000, 958, 920, 845 cm^{-1}; NMR (CCl_4) δ 1.50–2.30 (m, 4 H), 2.03 (s, 3 H), 3.22 (s, 3 H), 3.27 (s, 3 H), 4.77 and 5.21 (m, 2 H); mass spectrum, m/e 173 (M^+), 158 ($M^+ - CH_3$), 142 ($M^+ - OCH_3$), 111 ($M^+ - 2(OCH_3)$). Anal. Calcd for $C_8H_{15}NO_3$: C, 55.47; H, 8.73; N, 8.09. Found: C, 55.26; H, 8.95; N, 7.88.

31c: IR (neat) 2980, 2950, 2830, 1708, 1500, 1440, 1410, 1355, 1205, 1075, 958, 923, 695 cm^{-1}; NMR (CCl_4) δ 1.96 (m, 4 H), 3.29 (s, 6 H), 4.83–5.34 (m, 2 H), 5.12 (s, 2 H), 7.33 (m, 5 H). Anal. Calcd for $C_{14}H_{19}NO_4$: C, 63.38; H, 7.22; N, 5.28. Found: C, 63.17; H, 7.41; N, 5.33.

Synthesis of N-Carbomethoxypyrrole (32a). A mixture of **31a** (74.5 g, 0.39 mol) and *p*-toluenesulfonic acid (0.5 g) in benzene (60 mL) was refluxed for 4 h. The cooled solution was poured into aqueous sodium bicarbonate (150 mL), and the product was extracted with ether (3 × 100 mL). After the ethereal solution was dried over anhydrous magnesium sulfate, the drying agent was removed by filtration and the solvent was evaporated. The residue was distilled to yield **32a** (30.1 g, 0.24 mol, 62% yield): bp 65–66 °C (14 mm) [lit.[17b] bp 71–73 °C (21 mm)]; IR (neat) 3150, 2960, 1735, 1473, 1440, 1402, 1340, 1313, 1202, 1168, 1072, 1035, 980, 925, 800, 768, 732 cm^{-1}; NMR (CCl_4) δ 3.91 (s, 3 H), 6.12 (m, 2 H), 7.18 (m, 2 H).

Synthesis of N-Acetylpyrrole (32b). A mixture of **31b** (20 g, 0.116 mol) and ammonium bromide (2 g) in dimethyl phthalate (20 mL) was heated at the bath temperature of 140–150 °C for 1.5 h. After ammonium bromide was filtered, the filtrate was distilled to afford **32b** (7.9 g, 0.073 mol, 63% yield): bp 72–75 °C (14 mm) [lit.[17e] bp 70–71 °C (12 mm)]; IR (neat) 3045, 1702, 1465, 1400, 1368, 1320, 1300, 1138, 1062, 920, 735 cm^{-1}; NMR (CCl_4) δ 2.44 (s, 3 H), 6.16 (m, 2 H), 7.20 (m, 2 H).

Synthesis of N-Carbobenzoxypyrrole (32c). A mixture of **31c** (12.833 g, 0.0484 mol) and ammonium chloride (3 g) was heated at the bath temperature of 160–170 °C for 3.3 h. After ammonium chloride was removed by filtration, the product was isolated by column chromatography on silica gel (*n*-hexane–AcOEt, 10:1) to give **32c** (4.045 g, 0.020 mol, 42% yield), which was further purified by distillation: bp 101–101.5 °C (0.9 mm); IR (neat) 3145, 2950, 1740, 1698, 1470, 1402, 1378, 1332, 1303, 1168, 1070, 1030, 958, 732, 690 cm^{-1}; NMR (CCl_4) δ 5.30 (s, 2 H), 6.14 (m, 2 H), 7.20 (m, 2 H), 7.37 (m, 5 H). Anal. Calcd for $C_{12}H_{11}NO_2$: C, 71.62; H, 5.51; N, 6.96. Found: C, 71.36; H, 5.44; N, 7.00.