  Bull. Chem. Soc. Jpn., 62, 808—815 (1989)

Stereoselective Synthesis of [1]Benzopyrano[4,3-*b*]pyrrol-4(3*H*)-ones through Cycloadditions of Azomethine Ylides with α,β-Unsaturated Esters

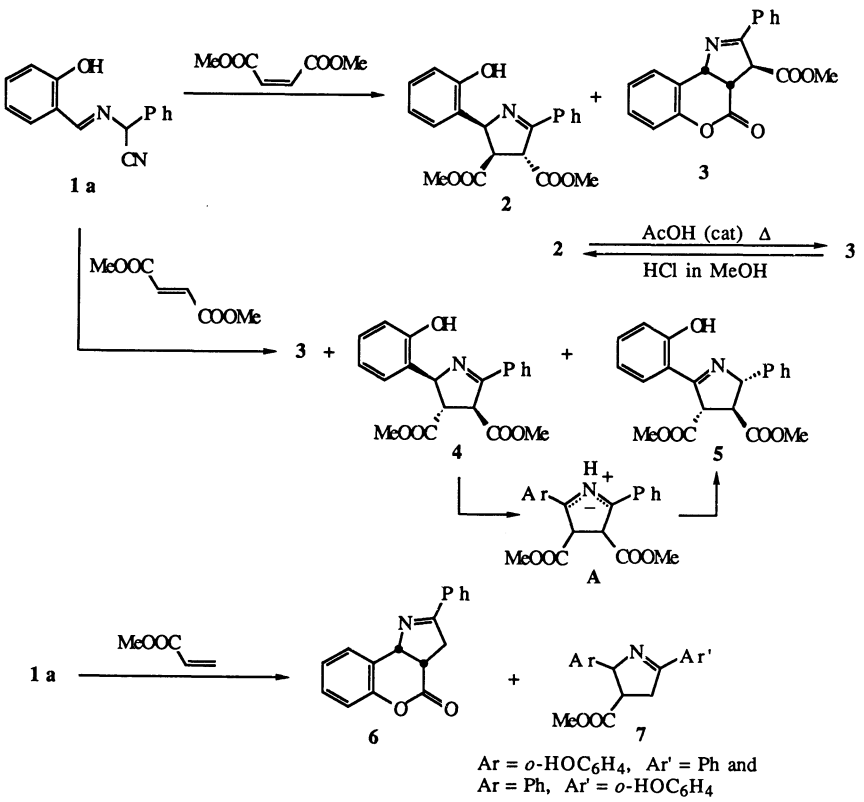
Kazunori UENO, Shuji KANEMASA,* and Otohiko TSUGE*
Institute of Advanced Material Study, and Department of Molecular Science and Technology,
Interdisciplinary Graduate School of Engineering Sciences,
Kyushu University, Kasugakoen, Kasuga 816
(Received August 3, 1988)

Cycloadditions of azomethine ylides generated from α-benzylideneamino nitriles bearing a hydroxyl or its *O*-protected moiety with α,β-unsaturated esters such as dimethyl maleate, fumarate, methyl acrylate, crotonate, methacrylate, and cinnamate lead stereoselectively to 3,3a-*trans*-3a,9b-*cis*-3a,9b-dihydro[1]benzopyrano[4,3-*b*]pyrrole-4(3*H*)-ones after subsequent lactonization.

The imines, bearing an electron-withdrawing substituent at the sp^3 carbon adjacent to the imine nitrogen, undergo a thermal imine–azomethine ylide tautomerism.[1] Since this tautomerism is catalyzed by a weak acid,[2] an intramolecular hydrogen bond to the nitrogen would accelerate such ylide generation. The replacement of the benzylidene moiety of α-benzylideneamino nitriles with a 2-hydroxybenzylideneamino group offers model compounds with which catalysis by an intramolecular hydrogen bond could be conveniently tested.

N-Unsubstituted azomethine ylides generated by the thermal tautomerism of *C*-aryl imines undergo stereo- and regioselective cycloadditions with α,β-unsaturated esters to produce cycloadducts, pyrrolidines or pyrrolines, in which the aryl and the ester groups are cis to each other. Therefore, the use of α-(2-hydroxybenzylideneamino) nitriles would lead to [1]benzopyrano[4,3-*b*]pyrrol-4(3*H*)-ones, which could be useful compounds for the synthesis of the hetero analogs of cannabinoids.[3]

The present article describes the generation of azomethine ylides from α-(arylmethyleneamino) nitriles bearing a hydroxy moiety or their *O*-protected derivatives. The ylides were utilized in stereoselective cycloadditions with α,β-unsaturated esters, followed by lactonization to give pyrrole ring-fused [1]benzopyrans.



Scheme 1.

Results and Discussion

Among the *N*-unsubstituted azomethine ylides generated by a thermal tautomerism of α-benzylideneamino nitriles, the compounds bearing an aryl group on C_2 of the nitrile is one of the most reactive ylides toward α,β-unsaturated esters.[4] 2-(2-Hydroxybenzylidenamino)-2-phenylacetonitrile (**1a**) underwent a smooth and stereoselective cycloaddition with dimethyl maleate under reflux in toluene to give 4,5-*cis*-1-pyrroline **2** and its lactonized product **3** in a combined yield of 96% (Scheme 1).

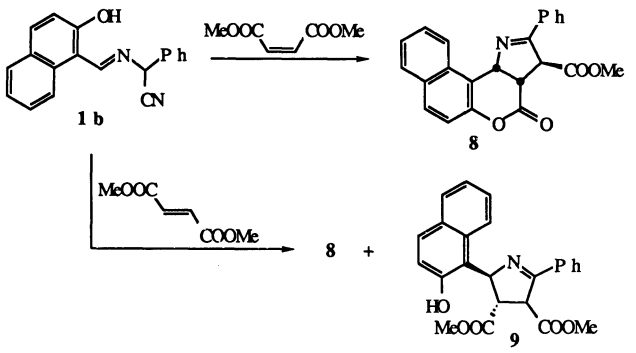
The 3,4-trans geometry of **2** is due to epimerization through an imine–enamine tautomerism.[4] The 4,5-cis configuration of **2** was assigned on the basis of the strong shielding of the ester methyl protons on C_4 by the adjacent phenyl ring. The structures of **2** and **3** were confirmed by the facts that **2** could be quantitatively converted into **3** on heating with a catalytic amount of acetic acid, and that **3** underwent methanolysis giving **2** in 85% yield.

With dimethyl fumarate under similar conditions, the lactone **3** (31%) and an inseparable mixture of two isomeric 1-pyrrolines **4** and **5** (2:1, 62%) were obtained. The latter 1-pyrroline **5** must have been derived from **4**, presumably through a double-bond migration via an *N*-protonated azomethine ylide intermediate **A**. On the other hand the 4,5-cis stereoisomer **2** did not isomerize at all under comparable conditions.

The exclusive cis-selectivity achieved in the cycloaddition of **1a** with dimethyl maleate and the poor trans/cis ratio (2/1) observed in that with dimethyl fumarate correspond to the results previously observed in reactions of 2-(benzylideneamino)-2-phenylacetonitrile with both esters.[4]

In a reaction of **1a** with methyl acrylate, the expected lactone **8** was produced in 67% yield, together with an inseparable mixture (26%, 2:1) of two regioisomeric 1-pyrrolines **9**.

Similar stereoselectivities were observed in the reactions of 2-[(2-hydroxy-1-naphthyl)methylenamino]-2-phenylacetonitrile (**1b**) with dimethyl maleate and fumarate. Thus, lactone **6** was the sole product (91%) from the maleate, whereas a mixture of **6** (50%) and 1-pyrroline **7** (41%) was obtained from the fumarate (Scheme 2).



Scheme 2.

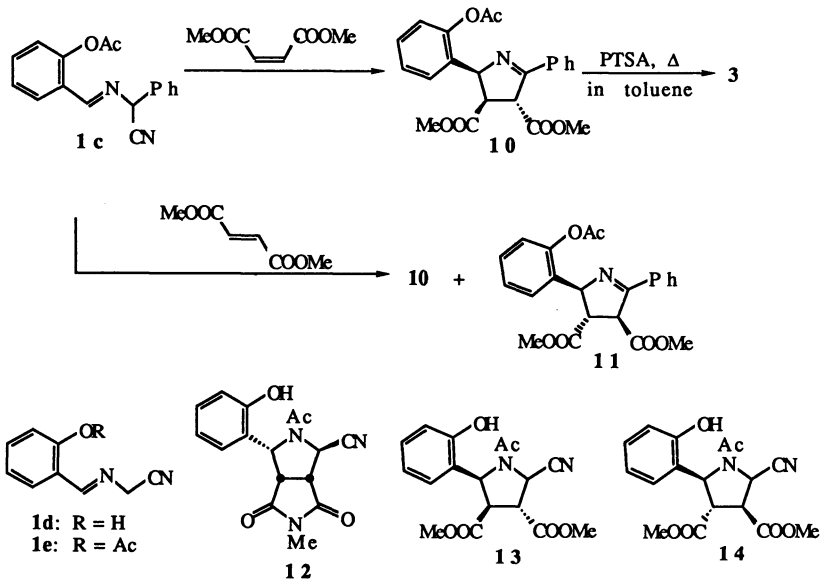
Thus, imines **1a** and **1b** can thermally generate, without *O*-protection, the corresponding *N*-unsubstituted azomethine ylides. These ylides undergo cycloadditions to several α,β-unsaturated esters producing 4,5-cis cycloadducts as exclusive or major isomers, which give lactones after spontaneous or acid-catalyzed lactonization. However, catalysis for ylide generation by an intramolecular hydrogen bond was unexpectedly insufficient, no remarkable rate acceleration of the ylide generation being observed. Accordingly, *O*-protected imines were employed in the following reactions.

O-Acetylation of **1a** gave imine **1c**. 4,5-*cis*-1-Pyrroline **10** (91%) or a mixture of **10** and 4,5-*trans*-1-pyrroline **11** (70% and 26%) was yielded from **1c** and dimethyl maleate or fumarate, respectively. The isomer ratio agrees with that obtained from 2-(benzylideneamino)-2-phenylacetonitrile and the fumarate.[4] The cis isomer **10** was converted into lactone **3** upon heating in toluene in the presence of a catalytic amount of *p*-toluenesulfonic acid (PTSA) in a moderate yield (60%).

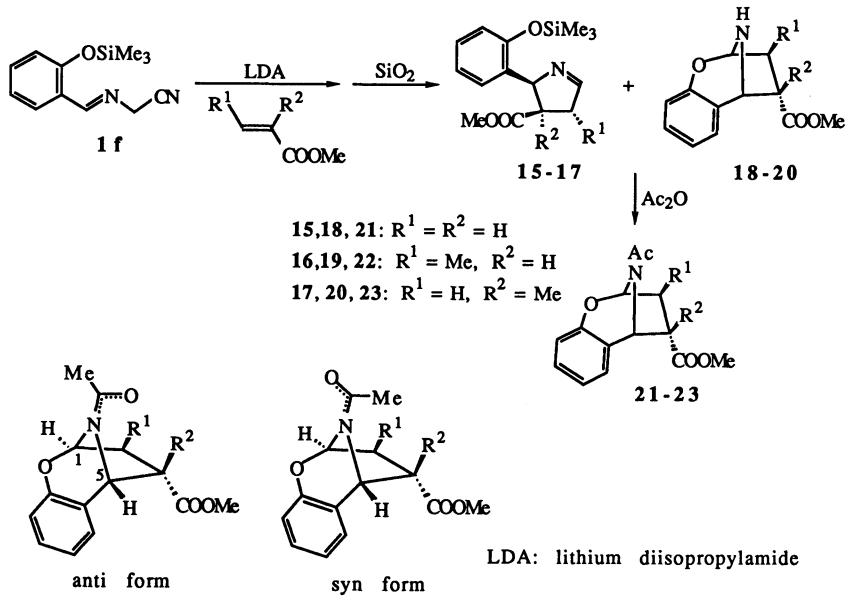
(2-Hydroxybenzylideneamino)acetonitrile (**1d**) was found to be much less reactive than expected. Thus, the reactions of **1e** with *N*-methylmaleimide and dimethyl fumarate, under reflux in toluene for 14 h, gave unsatisfactory yields of the *N*-acetylated 6,6a-cis cycloadduct **12** (35%) and a mixture of two stereoisomeric cycloadducts, **13** (34%) and **14** (9%). The acetyl group migration from the phenolic oxygen atom to the pyrrolidine nitrogen atom occurred presumably through intramolecular aminolysis, since it is already known that the formation of 1-pyrrolines by the elimination of HCN is extremely slow in these systems.[4,5]

As *N*-unsubstituted (or *N*-protonated) azomethine ylides show only a limited reactivity toward the unsaturated esters, a higher degree of activation of ylides is needed. *N*-Lithiated azomethine ylides are our choice. A highly enhanced reactivity as well as an exclusive cis-selectivity in their cycloadditions was recently reported.[6,7]

The *O*-silyl derivative **1f**, readily prepared by the silylation of **1d** with chlorotrimethylsilane and triethylamine, generated the *N*-lithiated azomethine ylide upon a treatment with LDA in THF at −78 °C. The ylide smoothly underwent stereoselective cycloadditions to methyl acrylate, crotonate, and methacrylate at −78 °C. Though the unpurified reaction mixtures were shown to consist mostly of the *O*-silylated 4,5-*cis*-1-pyrrolines **15**—**17** by ^{1}H NMR, their purification by silica-gel chromatography brought about desilylation to give bicyclic *N,O*-acetals **18**—**20** as single stereo-



Scheme 3.



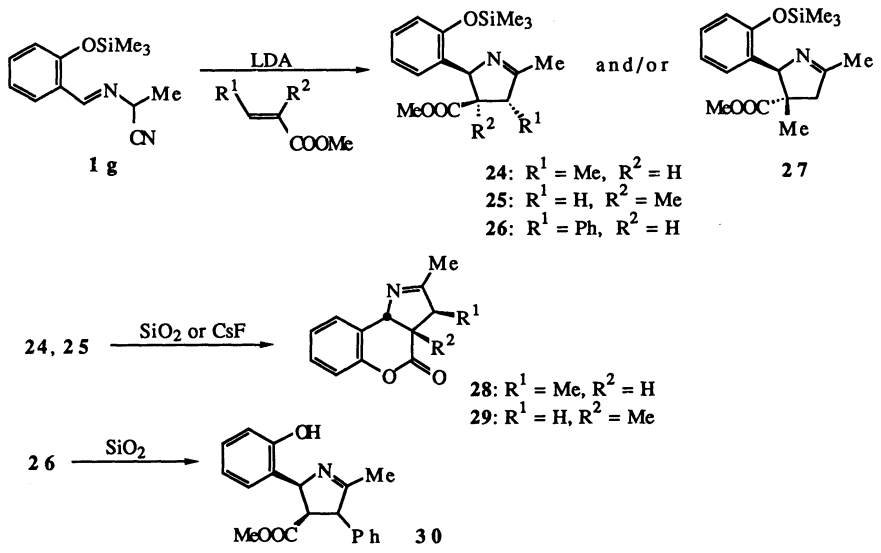
Scheme 4.

isomers in all cases (Scheme 4). Since they were too unstable to be further purified, their acetylation was carried out, leading to **21—23**.

Interestingly, these *N*-acetylated bicyclic *N,O*-acetals **21—23** exist as two isomeric forms in deuteriochloroform in 2:3 to 1:2 ratios. The major isomers, which show lower acetyl methyl protons, lower 5-Hs, and higher 1-Hs in their ^{1}H NMR spectra, were assigned as anti forms and, hence, the minor ones as syn forms. Ready formation of the bicyclic *N,O*-acetals **18—20** occurred probably because of the absence of substituents at C_2 of 1-pyrrolines **15—17**. Accordingly, methyl-substituted imine **1g** was employed in similar cycloadditions (Scheme 5).

With methyl crotonate and cinnamate, 4,5-*cis*-1-pyrrolines **24** and **26** were exclusively formed, however, the reaction with methyl methacrylate was rather nonstereoselective; a 3.5:1 mixture of 4,5-*cis*- **25** and 4,5-*trans*-1-pyrroline **27** was obtained.

Desilylation of **24** occurred easily on its chromatography over silica gel to give lactone **28** in 84% yield based on **1g**. The more stable **25** was only partly desilylated by a similar treatment, but was cleanly converted into **29** (78%) when **25** (as a mixture with **27**) was treated with cesium fluoride in THF. The desilylated derivative of the minor cycloadduct **27** was



Scheme 5.

also separated.

A chromatographic treatment of the cinnamate adduct **26** resulted in a rather slow desilylation, giving a mixture of **26** and the desilylated product, 4,5-*cis*-1-pyrroline **30**. Smooth lactonization of **30** was not observed under various conditions since it was decomposed in all cases.

Experimental

General. Melting points were determined on a Yanagimoto melting-point apparatus and are uncorrected. IR spectra were taken with a JASCO IRA-1 or a JASCO A-702 spectrometer. ^{1}H NMR spectra were recorded on a Hitachi R-40 (90 MHz), a JEOL FX-100 (100 MHz), or a JEOL GSX-270 (270 MHz) instruments, and ^{13}C NMR on a JEOL FX-100 (25.05 MHz) or a JEOL GSX-270 spectrometer (67.94 MHz). Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. Mass spectra were measured with a JEOL-01SG-2 spectrometer at 70 eV of ionization energy. High-resolution mass spectra (HRMS) were obtained on the same instrument. Elemental analyses were performed on a Hitachi 026 CHN analyzer. Thin-layer chromatography (TLC) was accomplished on 0.2 mm precoated plates of silica gel 60 F-254 (Merck). Visualization was made with ultraviolet light (254 and 365 nm), iodine, molybdophosphoric acid (5% in ethanol), or *p*-anisaldehyde (5% in ethanol containing 5% of sulfuric acid). For preparative column chromatography, Wakogel C-200, C-300 (Wako), and Silicagel 60 (Merck) were employed. Flash chromatography was carried out on an Eyela EF-10 apparatus using a column (20×180 mm) packed with Silicagel 60 (Merck, size: 0.04—0.063 mm). Gas liquid chromatography (GLC) was accomplished on a Yanaco G-2800 gas chromatograph (Yanagimoto) with an ionization flame detector using a glass column (SE-30, 3×2000 mm) or a glass capillary column (Silicone GE, SE-30, 0.25×50000 mm). Micro vacuum distillation was carried out on a Sibata GTO-250R Kugelrohr distilling apparatus. Solvents were evaporated with a Tokyo Rikakikai rotary evaporator type-V at about 50 °C unless otherwise stated.

Materials and Solvents. 2-(2-Hydroxybenzylideneamino)-2-phenylacetonitrile (**1a**), 2-[(2-hydroxy-1-naphthyl)methyleneamino]-2-phenylacetonitrile (**1b**), 2-(2-acetoxybenzylideneamino)-2-phenylacetonitrile (**1c**), (2-hydroxybenzylideneamino)acetonitrile (**1d**), and (2-acetoxybenzylideneamino)-acetonitrile (**1e**) were prepared by condensations of the corresponding aldehydes with amino nitriles by an application of the reported methods.[4] **1a:** Colorless prisms (diethyl ether–hexane); mp 59—60 °C; IR (KBr) 3200—2400, 2240, and 1630 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=5.53 (1H, d, J=1.0 Hz, CH), 6.7—7.4 (9H, m, Ar), 8.47 (1H, d, J=1.0 Hz, CH=N), and 11.86 (1H, br s, OH); MS *m/z* (rel intensity, %) 236 (M^+, 2), 116 (base peak), and 89 (58). Found: C, 76.20; H, 5.12; N, 11.71%. Calcd for $C_{15}H_{12}N_2O$: C, 76.25; H, 5.12; N, 11.86%. **1b:** Colorless prisms (diethyl ether–hexane); mp 116—117 °C; IR (KBr) 3350, 2230, and 1630 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=4.84 (1H, s, CH), 7.0—8.3 (12H, m, Ar and CH=N), and 10.65 (1H, s, OH). Found: C, 79.66; H, 5.06; N, 9.58%. Calcd for $C_{19}H_{14}N_2O$: C, 79.70; H, 4.93; N, 9.78%. **1c:** Colorless liquid; IR (KBr) 2240, 1740, and 1630 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.20 (3H, s, Ac), 5.66 (1H, d, J=1.0 Hz, CH), 7.0—7.5 (8H, m, Ar), 7.82 (1H, m, Ar), and 8.55 (1H, d, J=1.0 Hz, CH=N). **1e:** Colorless liquid; IR (neat) 2250, 1765, and 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.30 (3H, s, Ac), 4.52 (2H, t, J=1.5 Hz, CH_2), 6.7—7.8 (4H, Ar), and 8.43 (1H, t, J=1.5 Hz, CH=N). 2-[2-(Trimethylsilyloxy)benzylideneamino]-acetonitrile (**1f**) was prepared as follows: A solution of chlorotrimethylsilane (0.48 g, 4.1 mmol) in dry benzene (3 ml) was slowly added to a mixture of **1a** (0.56 g, 4 mmol) and triethylamine (0.45 g, 4.5 mmol) in benzene (10 ml). After stirring at room temperature for 1 h, the precipitate was removed off by filtration and the filtrate was subjected to vacuum distillation to give **1f** (0.66 g, 71%): Yellow liquid; bp 150 °C/133 Pa (bulb-to-bulb), IR (neat) 2220, 1640, 920, 840, and 760 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.30 (9H, s, $SiMe_3$), 4.63 (2H, d, J=2.0 Hz, CH_2) 6.8—7.9 (4H, m, Ar), and 8.90 (1H, t, J=2.0 Hz, CH=N); MS *m/z* (rel intensity, %) 232 (M^+, 8), 218

(17), 217 (base peak), 135 (38), 120 (25), 91 (23), and 77 (15). HRMS Found: *m/z* 232.1055. Calcd for $C_{12}H_{16}N_2OSi$: M, 232.1057. 2-[2-(Trimethylsilyloxy)benzylideneamino]propanenitrile (**1g**) was synthesized according to the following procedure: To a solution of freshly prepared LDA (10 mmol in THF (15 ml)) was added dropwise a solution of **1f** (1.6 g, 6.9 mmol) in THF (10 ml) at −78 °C. After 5 min, methyl iodide (1.56 g, 7.6 mmol) in THF (5 ml) was added. Stirring was continued at −78 °C for 3 h. The mixture was poured into saturated ammonium chloride and extracted with diethyl ether (20 ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was assigned as 2-(2-hydroxybenzylideneamino)-propanenitrile: Pale yellow liquid; IR (neat) 3200—2400, 2250, and 1630 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.75 (3H, d, J=7.0 Hz, Me), 4.73 (1H, dq, J=7.0 and 2.0 Hz, CH), 6.9—7.5 (4H, m, Ar), 8.60 (1H, d, J=2.0 Hz, CH=N), and 12.20 (1H, br s, OH); MS *m/z* (rel intensity, %) 174 (M^+, 78), 173 (13), 160 (11), 159 (16), 120 (base peak), 106 (13), 102 (16), 91 (13), and 77 (23). HRMS Found: *m/z* 174.0790. Calcd for $C_{10}H_{10}N_2O$: M, 174.0790. To a mixture of this imine (2.25 g, 12.9 mmol) and chlorotrimethylsilane (1.72 g, 15.8 mmol) in dry benzene (35 ml) was added triethylamine (1.6 g, 15.8 mmol) in benzene (5 ml). After stirring at room temperature for 1 h, the precipitate was filtered off and the filtrate was distilled under reduced pressure to give **1g** (2.7 g, 85%): Yellow liquid; bp 180 °C/133 Pa (bulb-to-bulb); IR (neat) 2215, 1640, 920, 850, and 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.30 (9H, s, $SiMe_3$), 1.67 (3H, d, J=7.0 Hz, Me), 4.66 (1H, dq, J=7.0 and 1.5 Hz, CH), 6.8—7.9 (4H, m, Ar), and 8.90 (1H, d, J=1.5 Hz, CH=N).

Reaction of 1a with Dimethyl Maleate Leading to 2 and 3. A mixture of **1a** (0.146 g, 0.6 mmol) and dimethyl maleate (0.09 g, 0.6 mmol) in dry toluene (3 ml) was heated under reflux for 20 h. The toluene was evaporated in vacuo and the residue was chromatographed over silica gel by using chloroform as an eluent to give **3** (0.1 g, 50%) and then **2** (0.1 g, 46%). **2**: Colorless liquid; IR (neat) 3500—3050, 1740, and 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.12 (3H, s, COOMe), 3.63 (3H, s, Me), 3.95 (1H, dd, J_{4-5}=7.0 and J_{4-3}=2.0 Hz, 4-H), 4.64 (1H, t, J_{3-4}=J_{3-5}=2.0 Hz, 3-H), 5.97 (1H, dd, J_{5-4}=7.0 and J_{5-3}=2.0 Hz, 5-H), 6.6—7.5 (7H, m, Ar), 7.85 (2H, m, Ar), and 8.40 (1H, br, OH); ^{13}C NMR ($CDCl_3$) δ=30.83 (d, 4-C), 53.00, 53.30 (each q, COOMe), 56.83 (d, 3-C), 75.12 (d, 5-C), 116.60, 119.71, 123.07, 128.25, 128.72, 128.91 (each d, Ar), 132.01 (s, Ar), 155.40 (s, Ar), 170.19 (s, 2-C), 170.30, and 171.78 (each s, COOMe); MS *m/z* (rel intensity, %) 353 (M^+, 40), 295 (15), 294 (78), 263 (20), 262 (base peak), 235 (35), 234 (11), 209 (31), 208 (15), 206 (13), 148 (24), 131 (21), 115 (24), 106 (11), 105 (21), 104 (15), 103 (18), 102 (9), 91 (10), 78 (30), and 77 (44). Found: C, 68.23; H, 5.32; N, 4.20%. Calcd for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96%. **3**: Colorless liquid; IR (neat) 1750, 1735, 1610, 1490, and 1460 cm^{-1}; ^1H NMR ($CDCl_3$) δ=3.64 (3H, s, COOMe), 3.85 (1H, dd, J_{3a-9b}=7.0 and J_{3a-3}=2.0 Hz, 3a-H), 5.00 (1H, t, J_{3-3a}=J_{3-9b}=2.0 Hz, 3-H), 5.49 (1H, dd, J_{9b-3a}=7.0 and J_{9b-3}=2.0 Hz, 9b-H), and 6.9—7.9 (9H, m, Ar); ^{13}C NMR ($CDCl_3$) δ=46.47 (d, 3a-C), 53.00 (q, COOMe), 58.71 (d, 3-C), 70.12 (d, 9b-C), 117.23, 125.42, 128.83, 129.13, 130.25, 130.72 (each d, Ar), 131.83, 132.13 (each s, Ar), 150.72 (s, Ar), 167.54 (s, 2-C), 168.78, and 169.66 (each s, COO and COOMe); MS *m/z* (rel intensity, %) 321 (M^+, 21), 320 (base peak), 262 (13), 260 (36), 209 (39), and 105 (21). Found: C, 71.05; H, 4.74; N, 4.38%. Calcd for $C_{19}H_{15}NO_4$: C, 71.02; H, 4.71; N, 4.36%.

Acid-Catalyzed Cyclization of 2 Leading to 3 and Acid-Catalyzed Methanolysis of 3 into 2. Cyclization: A solution of **2** (0.1 g, 0.28 mmol) in toluene (3 ml) containing a catalytic amount of acetic acid was heated under reflux for 24 h. The mixture was evaporated to dryness in vacuo to give **3** (0.88 g, 98%). Methanolysis: A solution of **3** (0.084 g, 0.2 mmol) in methanol (10 ml) containing a catalytic amount of hydrochloric acid was heated under reflux for 1 h. The mixture was poured into ice water and extracted with chloroform (20 ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo to afford almost pure **2** (0.06 g, 85%).

Reaction of 1a with Dimethyl Fumarate Leading to 3—5. A mixture of **1a** (0.236 g, 1 mmol) and dimethyl fumarate (0.144 g, 1 mmol) in dry toluene (3 ml) was heated under reflux for 3.5 h. The solvent was evaporated in vacuo and the residue was chromatographed over silica gel by using chloroform to give **3** (0.1 g, 31%) and, then, an inseparable mixture of **4** and **5** (0.237 g, 62%). **4** and **5** (a 2:1 mixture (^1H NMR)): Colorless liquid; IR (neat) 3400—3100, 1740, 1640, 1495, and 1455 cm^{-1}; ^1H NMR ($CDCl_3$) one isomer: δ=3.53, 3.70 (each 3H, s, COOMe), 3.70 (1H, t, J_{4-3}=J_{4-5}=7.0 Hz, 4-H), 4.65 (1H, dd, J_{3-4}=7.0 and J_{3-5}=2.0 Hz, 3-H), 5.68 (1H, dd, J_{5-4}=7.0 and J_{5-3}=2.0 Hz, 5-H), 6.7—7.4 (7H, m, Ar), 7.70 (2H, m, Ar), and 9.00 (1H, br, OH); the other isomer: δ=3.58, 3.68 (each 3H, s, COOMe), 3.65 (1H, dd, J_{4-3}=7.5 and J_{4-5}=7.0 Hz, 4-H), 4.60 (1H, dd, J_{3-4}=7.5 and J_{3-5}=2.0 Hz, 3-H), 5.87 (1H, dd, J_{5-4}=7.0 and J_{5-3}=2.0 Hz, 5-H), 6.7—7.4 (7H, m, Ar), 7.70 (2H, m, Ar), and 8.20 (1H, m, OH); MS *m/z* (rel intensity, %) 353 (M^+, 50), 295 (15), 294 (71), 263 (20), 262 (base peak), 261 (13), 235 (41), 234 (13), 209 (30), 206 (18), 131 (31), 115 (28), 106 (13), 105 (20), 104 (20), 103 (20), 78 (32), and 77 (43). Found: C, 67.87; H, 5.46; N, 3.84%. Calcd for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96%.

Reaction of 1a with Methyl Acrylate Leading to 6 and 7. A mixture of **1a** (0.4 g, 1.69 mmol) and methyl acrylate (0.36 g, 4.29 mmol) was heated under reflux in toluene (10 ml) for 28 h. The residue obtained by the evaporation of all the volatile materials in vacuo, was triturated with diethyl ether–hexane to give **6** (0.32 , 67%) as a colorless solid. The filtrate was evaporated and the residue chromatographed over silica gel with chloroform to afford **7** (0.14 g, 26%) as a 2:1 mixture of two isomers (^1H NMR). **6**: Colorless needles (benzene–hexane); mp 183—184 °C; IR (KBr) 1755, 1610, 1490, 1455, 1220, and 1195 cm^{-1}; ^1H NMR ($CDCl_3$) δ= 3.3—3.9 (3H, m, 3- and 3a-H), 5.36 (1H, dt, J_{9b-3a}=5.0 and J_{9b-3}= 3.0 Hz, 9b-H), and 7.0—7.9 (9H, m, Ar); ^{13}C NMR ($CDCl_3$) δ=40.94 (t and d, 3- and 3a-C), 70.12 (d, 9b-C), 117.24, 120.13, 125.24, 128.07, 128.77, 129.83, 130.25 (each d, Ar), 131.48, 133.24, 150.54 (each s, Ar), 169.12 (s, 2-C), and 172.60 (s, 4-C); MS *m/z* (rel intensity, %) 263 (M^+, 24), 209 (17), 208 (base peak), 160 (14), 132 (18), 131 (30), 115 (25), 105 (26), 104 (16), 103 (22), 102 (11), 89 (13), 77 (75), and 76 (19). Found: C, 77.48; H, 4.98; N, 5.43%. Calcd for $C_{17}H_{13}NO_2$: C, 77.55; H, 4.98; N, 5.32%. **7** (an inseparable 2:1 mixture of two regioisomers (^1H NMR)): Colorless liquid; IR (neat) 3400—2800, 1740, 1615, 1580, 1495, 1450, 1340, and 1250 cm^{-1}; ^1H NMR ($CDCl_3$) major isomer: δ=2.2—2.6 (1H, m, one of 4-H), 2.8—3.1 (1H, m, the other of 4-H), 3.63 (3H, s, COOMe), 4.27 (1H, dt, J_{3-4}=10.0 and J_{3-5}=2.0 Hz, 3-H), 5.60 (1H, dt, J_{5-4}=8.0 Hz and J_{5-3}=2.0 Hz, 5-H), 6.8—7.9 (9H, m, Ar), and 8.5—9.5 (1H, br, OH); minor isomer: δ=2.2—2.6

(1H, m, one of 4-H), 2.8—3.1 (3H, m, the other of 4-H), 3.53 (3H, s, COOMe), 4.16 (1H, m, 3-H), 5.36 (1H, dt, J_{5-4}=10.0 and J_{5-3}=2.0 Hz, 5-H), 6.8—7.9 (9H, m, Ar), and 8.5—9.5 (1H, br, OH); ^{13}C NMR ($CDCl_3$) major isomer: δ=35.71 (t, 3-C), 53.47 (q and d, COOMe and 4-C), 73.12 (d, 5-C), 169.42 (s, 2-C), 171.54 (s, COOMe); minor isomer: δ=36.12 (t, 3-C), 52.65 (q, COOMe), 53.47 (d, 4-C), 72.36 (d, 5-C), 169.95 (s, 2-C), 172.36 (s, COOMe); the other signals: δ=117.07, 119.71, 126.48, 127.89, 128.59, 128.89, 131.53, 131.54, 136.12, 156.25.

Reaction of 1b with Dimethyl Maleate Leading to 8. A solution of **1b** (0.278 g, 1 mmol) and dimethyl maleate (0.144 g, 1 mmol) in dry toluene (3 ml) was heated under reflux for 14 h. The mixture was evaporated in vacuo and the residue was chromatographed over silica gel by using chloroform to give **8** (0.36 g, 91%): Colorless needles (benzene-hexane); mp 203—204 °C; IR (KBr) 1755, 1730, 1625, 1510, 1430, 1305, 1270, 1220, and 1160 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.67 (3H, s, COOMe), 3.90 (1H, dd, J_{3a-11c}=8.0 and J_{3a-3}=1.5 Hz, 3a-H), 5.10 (1H, dd, J_{3-11a}=2.0 and J_{3-3a}=1.5 Hz, 3-H), 6.00 (1H, dd, J_{11c-3a}=8.0 and J_{11c-3}= 2.0 Hz, 11c-H), 7.0—8.0 (10H, m, Ar), and 8.25 (1H, m, Ar); ^{13}C NMR ($CDCl_3$) δ=46.03 (d, 3a-C), 52.89 (q, Me), 58.12 (d, 3-C), 67.34 (d, 11c-C), 112.19, 117.00, 124.05, 125.46, 127.58, 128.19, 128.40, 128.63, 130.92 (each d), 131.04, 131.51, 131.92, 148.19 (each d, Ar), 167.26 (s, 2-C), 168.62, and 169.43 (each s, COOMe and 4-C); MS *m/z* (rel intensity, %) 371 (M^+, 38), 312 (34), 284 (13), 258 (86), and 152 (base peak). Found: C, 74.45; H, 4.83; N, 3.77%. Calcd for $C_{23}H_{17}NO_4$: C, 74.38; H, 4.61; N, 3.77%.

Reaction of 1b with Dimethyl Fumarate Leading to 8 and 9. By a similar procedure, using **1b** (0.43 g, 1.5 mmol) and dimethyl fumarate (0.216 g, 1.5 mmol) in toluene (6 ml), after heating under reflux for 20 h and chromatography over silica gel with chloroform-ethyl acetate (49:1 v/v), **8** (0.28 g, 50%) and then **9** (0.28 g, 41%) were obtained, **9**: Colorless prisms (benzene-hexane); mp 188—189 °C; IR (KBr) 3500—2900, 1740, 1620, 1575, 1515, 1440, 1270, and 1210 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=3.60 (3H, s, COOMe), 3.80 (1H, dd, J_{4-5}=5.0 and J_{4-3}=2.0 Hz, 4-H), 4.70 (1H, dd, J_{3-4}=J_{3-5}= 2.0 Hz, 3-H), 6.32 (1H, dd, J_{5-4}=5.0 and J_{5-3}=2.0 Hz, 5-H), 7.0—8.0 (11H, m, Ar), and 10.00 (1H, br s, OH); MS *m/z* (rel intensity, %) 403 (M^+, 23), 344 (15), 313 (23), 312 (base peak), 285 (25), 284 (15), 259 (37), 258 (19), 256 (16), 228 (15), 181 (17), 153 (21), 128 (45), 127 (30), 115 (38), 105 (10), 104 (15), and 77 (27). Found: C, 71.71; H, 5.18; N, 3.72%. Calcd for $C_{24}H_{21}NO_5$: C, 71.45; H, 5.25; N, 3.47%.

Reaction of 1c with Dimethyl Maleate Leading to 10. A mixture of **1c** (0.278 g, 1 mmol) and dimethyl maleate (0.144 g, 1 mmol) was heated under reflux in toluene (1 ml) for 14 h. The mixture was evaporated in vacuo and the residue was chromatographed over silica gel by using chloroform-ethyl acetate (9:1 v/v) to give **10** (0.36 g, 91%): Colorless prisms (benzene-hexane); mp 96—97 °C; IR (KBr) 1765, 1730, 1620, 1570, 1430, 1200, and 1160 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.24 (3H, s, OAc), 3.06 (3H, s, 4-COOMe), 3.58 (3H, s, 3-COOMe), 3.86 (1H, dd, J_{4-5}=9.0 and J_{4-3}=3.0 Hz, 4-H), 4.80 (1H, dd, J_{3-4}=3.0 and J_{3-5}=1.5 Hz, 3-H), 5.95 (1H, dd, J_{5-4}=9.0 and J_{5-3}=1.5 Hz, 5-H), 7.0—7.4 (7H, m, ArH), and 7.90 (2H, m, Ar); MS *m/z* (rel intensity, %) 395 (M^+, 18), 294 (26), 262 (30), 261 (10), 208 (19), 131 (14), 115 (16), 105 (14), 77 (12), 76 (30), 51 (14), and 42 (base peak). Found: C, 67.11; H, 5.34; N, 3.75%. Calcd for $C_{22}H_{21}NO_6$: C, 66.87; H, 5.35; N, 3.54%.

refluxing for 8.5 h and the subsequent column chromatography over silica gel by using chloroform-ethyl acetate (9:1

This compound **10** (0.395 g, 1 mmol) and a catalytic amount of *p*-toluenesulfonic acid were heated under reflux in toluene (5 ml) for 13 h. The mixture was poured into water and extracted with dichloromethane (20 ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel with chloroform to give **3** (0.193 g, 60%).

Reaction of 1c with Dimethyl Fumarate Leading to 10 and 11. By a similar procedure, using **1c** (0.278 g, 1 mmol) and dimethyl fumarate (0.144 g, 1 mmol) in toluene (1 ml), after v/v), a mixture of **10** and **11** (1:1 (^{1}H NMR), 0.208 g) and then **10** (0.17 g, 43%) were obtained. The yield of **10** was 69% and that of **11** was 26%. The latter product **11** could not be isolated in its pure form. **11**: ^{1}H NMR ($CDCl_3$): δ=2.20 (3H, s, OAc), 3.43 (1H, t, J_{4-3}=6.0 Hz, 4-H), 3.53 (3H, s, 3-COOMe), 3.65 (3H, s, 4-COOMe), 4.50 (1H, dd, J_{3-4}=6.0 and J_{3-5}=1.5 Hz, 3-H), 5.67 (1H, dd, J_{5-4}=6.0 and J_{5-3}=1.5 Hz, 5-H).

Reaction of 1e with *N*-Methylmaleimide Leading to 12. A solution of **1e** (0.404 g, 2 mmol) and *N*-methylmaleimide (0.222 g, 2 mmol) in dry toluene (15 ml) was heated under reflux for 14 h. The solvent was evaporated in vacuo and the residue was triturated with diethyl ether to give a colorless solid of **12** (0.057 g). The ether filtrate was evaporated and the residue was chromatographed over silica gel with chloroform-ethyl acetate (3:2 v/v) to afford another portion of **12** (0.16 g, total yield: 35%): **12**: Colorless prisms (acetonitrile); mp 239—240 °C; IR (KBr) 3100, 2225, 1790, 1710, and 1620 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.70 (3H, s, OAc), 2.65 (3H, s, NMe), 4.00 (1H, dd, J_{3a-6a}=10.0 and J_{3a-4}=2.0 Hz, 3a-H), 4.24 (1H, t, J_{6a-3a}=J_{6a-6}=10.0 Hz, 6a-H), 5.14 (1H, d, J_{4-3a}=2.0 Hz, 4-H), 5.38 (1H, d, J_{6-6a}=10.0 Hz, 6-H), 6.6—7.2 (4H, m, Ar), and 9.78 (1H, br s, OH); ^{13}C NMR ($CDCl_3$) δ=22.35 (q, NAc), 24.59 (NMe), 48.77 (d, 3a-C), 50.24 (d, 6a-C), 57.00 (d, 4-C), 63.24 (d, 6-C), 116.13 (d, Ar), 118.18 (s, CN), 119.42, 122.60 (each d, Ar), 130.18 (s, Ar), 131.60 (d, Ar), 154.19 (s, Ar), 169.48 (s, NAc), 173.54, and 175.60 (each s, CON); MS *m/z* (rel intensity, %) 313 (M^+, 19), 286 (8), 270 (38), and 160 (base peak). Found: C, 61.23; H, 4.90; N, 13.39%. Calcd for $C_{16}H_{15}N_3O_4$: C, 61.33, H, 4.83; N, 13.41%.

Reaction of 1e with Dimethyl Fumarate Leading to 13 and 14. A solution of **1e** (0.404 g, 2 mmol) and dimethyl fumarate (0.288 g, 2 mmol) in dry toluene (10 ml) was heated under reflux. When the mixture was cooled down to room temperature, a colorless solid of **13** (0.252 g, 34%) was precipitated. The filtrate was evaporated in vacuo and the residue was chromatographed over silica gel by using chloroform-ethyl acetate (3:1 v/v) to give **14** (0.06 g, 9%). **13**: Colorless prisms (acetonitrile); mp 222—223 °C; IR (KBr) 3600—3000, 2250, 1740, and 1620 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.64 (3H, s, NAc), 3.36 (3H, s, 4-COOMe), 3.70 (3H, s, 3-COOMe), 3.93 (2H, m, 3- and 4-H), 5.46 (1H, d, J_{2-3}=7.6 Hz, 2-H), 5.75 (1H, d, J_{5-4}=7.6 Hz, 5-H), 6.6—7.1 (4H, m, Ar), and 9.76 (1H, br s, OH); ^{13}C NMR ($CDCl_3$) δ=21.47 (q, NAc), 45.42 (d, 3-C), 47.83 (d, 4-C), 49.36 (d, 2-C), 51.77, 52.83 (each q, COOMe), 57.47 (d, 5-C), 115.42 (d, Ar), 116.48 (s, CN), 119.24 (d, Ar), 123.48 (s, Ar), 128.42, 129.54 (each d, Ar), 154.66 (s, Ar), 168.54, 168.83, and 169.19 (each s, COOMe and NAc); MS *m/z* (rel intensity, %) 346 (M^+, 51), 303 (42), 271 (28), 160 (73), and 42 (base peak); Found: C, 58.88; H, 5.29; N, 8.15%. Calcd for $C_{17}H_{18}N_2O_6$: C, 58.95; H,

5.24; N, 8.09%. **14**: Colorless prisms (acetonitrile); mp 194—195 °C; IR (KBr) 3270, 1750, 1730, 1635, and 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.27 (3H, s, NAc), 3.46 (1H, dd, J_{3-4}=12.0 and J_{3-2}=9.0 Hz, 3-H), 3.62, 3.68 (each 3H, s, COOMe), 3.88 (1H, dd, J_{4-3}=12.0 and J_{4-5}=9.0 Hz, 4-H), 5.30 (1H, d, J_{2-3}=9.0 Hz, 2-H), 5.40 (1H, d, J_{5-4}=9.0 Hz, 5-H), 6.8—7.3 (4H, m, Ar), and 9.63 (1H, br s, OH); ^{13}C NMR ($CDCl_3$) δ=21.94 (q, NAc), 48.47 (d, 3-C), 50.12 (d, 4-C), 53.42 (d, 2-C), 53.71, 54.89 (each q, COOMe), 61.24 (d, 5-C), 116.83 (d, Ar), 117.89 (s, CN), 122.24 (d, Ar), 127.18 (s, Ar), 128.01, 130.83 (each d, Ar), 155.31 (s, Ar), 169.36, 170.00, and 171.66 (each s, COOMe and NAc); MS *m/z* (rel intensity, %) 346 (M^+, 26), 303 (11), 271 (12), 245 (10), 218 (12), 193 (31), 186 (21), 185 (17), 176 (27), 161 (18), 160 (30), 159 (13), 133 (17), 132 (13), 131 (22), 77 (18), and 43 (base peak). Found: C, 58.74; H, 5.20; N, 7.91%. Calcd for $C_{17}H_{18}N_2O_6$: C, 58.95; H, 5.24; N, 8.09%.

General Procedure for the Reaction of 1f with Olefins in the Presence of LDA Leading to 15—17 and 18—20. To a freshly prepared solution of LDA (1.6 mmol) in dry THF (5 ml) was slowly added a solution of **1f** (1.5 mmol) in THF (5 ml) at −78 °C. After 5 min, an olefin (1.5 mmol) in THF (5 ml) was added. The mixture was stirred at −78 °C for 5 h, poured into saturated aqueous ammonium chloride, and extracted with diethyl ether (20 ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel by using chloroform to give an inseparable mixture of **15** and **18** or **17** and **20**. However **16** and **19** could be separated from each other.

15 and **18** (a 3:2 mixture (^1H NMR)): Yield 94%; ^1H NMR ($CDCl_3$) **15**: δ=0.30 (9H, s, $SiMe_3$), 2.3—2.6 (2H, m, 3-H), 3.15 (1H, m, 3-H), 5.75 (1H, d, J_{5-4}=9.0 Hz, 5-H), 6.6—7.2 (4H, m, Ar), and 7.80 (1H, br s, 2-H); **18**: δ=2.3—2.6 (3H, m, CH_2 and CH), 3.50 (3H, s, COOMe), 4.40 (1H, d, J=6.0 Hz, NCH), 5.50 (1H, d, J=4.0 Hz, OCHN), and 6.6—7.2 (4H, m, Ar).

16 (50%) and **19** (20%): **16**: Pale yellow liquid; IR (neat) 1730, 1635, 1595, 1450, 910, 840, 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ=0.30 (9H, s, $SiMe_3$), 1.25 (3H, d, J_{Me-3}=7.5 Hz, 3-Me), 2.16 (3H, d, J=6.5 Hz, Me), 3.13 (3H, s, COOMe), 3.6—3.8 (2H, m, 3- and 4-H), 5.75 (1H, dd, J_{5-4}=8.0 Hz, J_{5-3}=2.0 Hz, 5-H), and 6.6—7.2 (4H, m, Ar); MS *m/z* (rel intensity, %) 319 (M^+, 23), 304 (19), 260 (33), 219 (31), 186 (29), 146 (19), 128 (50), 86 (13), 77 (10), 73 (30), and 44 (20). HRMS Found: *m/z* 319.1619. Calcd for $C_{17}H_{25}NO_3$: M, 319.1617. **19**: Colorless liquid; IR (neat) 3350, 2980, 1730, 1610, 1585, 1490, 1460, 1025, 910, and 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.16 (3H, d, J=7.0 Hz, Me), 2.1—2.7 (1H, br NH), 2.8—3.3 (2H, m, CH), 3.56 (3H, s, COOMe), 4.41 (1H, d, J=6.0 Hz, NCH), 5.10 (1H, s, OCHN), and 6.6—7.4 (4H, m, Ar); ^{13}C NMR ($CDCl_3$) δ=19.38 (Me), 42.08 (CHMe), 51.72 (COOMe), 58.64 (CHCOOMe), 60.44 (NCH), 93.90 (OCHN), 116.38, 119.36, 125.19, 126.45, 129.25, 151.41 (each Ar), and 171.37 (COOMe); MS *m/z* (rel intensity, %) 233 (M^+, 38), 175 (25), 174 (21), 85 (61), 83 (base peak), and 47 (29). HRMS Found: *m/z* 233.1049. Calcd for $C_{13}H_{15}NO_3$: M, 233.1047.

17 and **20** (**17**: 62%; **20**: 16% (^1H NMR)). Only **20** was isolated in a pure form): **17**: ^1H NMR ($CDCl_3$) δ=0.30 (9H, s, $SiMe_3$), 3.14 (3H, s, COOMe), and 7.70 (1H, d, J=2.0 Hz, 2-H). Other signals were overlapped with those of **20**. **20**: Colorless liquid; IR (neat) 3320, 2950, 1720, 1590, 1450, 1250, and 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.52 (3H, s, Me), 1.90 (1H, dd, J_{gem}=15.0 and J=4.0 Hz, one of CH_2), 2.95 (1H, d, J_{gem}=15.0 Hz, the other of CH_2), 3.0—3.3 (1H, br, NH), 3.46 (3H, s, COOMe), 3.95 (1H, s, NCH), 5.47 (1H, d, J=4.0 Hz, OCHN), and 6.6—7.3 (4H, m, Ar); ^{13}C NMR ($CDCl_3$) δ=25.80 (q, Me), 42.48 (t, CH_2), 51.79 (q, COOMe), 58.10 (s, *q*-C), 63.51 (d, NCH), 88.52 (OCHN), 116.35, 119.13, 125.45, 126.83, 129.08 (each d, Ar), 151.51 (s, Ar), and 174.77 (s, COOMe); MS *m/z* (rel intensity, %) 233 (M^+, 35), 175 (15), 174 (base peak), 172 (10), 133 (29), 132 (17), 131 (13), 112 (21), 105 (22), 104 (14), 91 (29), 84 (18), 82 (29), and 77 (21). HRMS Found: *m/z* 233.1049. Calcd for $C_{13}H_{15}NO_3$: M, 233.1049.

Acetylation of 18 Leading to 21. A mixture of **15** and **18** (2:1, 0.23 g) in acetic acid (1 ml) containing acetic anhydride (1 ml) was stirred at room temperature for 1 h. After the reaction was complete, ethanol (30 ml) was added. The mixture was evaporated in vacuo and the residue was triturated with diethyl ether to give a colorless solid of **21** (0.16 g, 71%): Colorless prisms (benzene-hexane); mp 129—130 °C; IR (KBr) 1725, 1640, 1475, 1400, 1200, 1170, 1020, 930, 890, and 745 cm^{-1}; ^1H NMR ($CDCl_3$) δ=2.13 (1/3×3H, s, Ac (syn)), 2.23 (2/3×3H s, Ac (anti)), 2.3—3.0 (2H, m, CH_2), 3.2—3.6 (1H, m, CH), 3.56 (3H, s, COOMe), 4.98 (1/3H, d, J=7.0 Hz, NCH (syn)), 5.49 (2/3H, d, J=6.5 Hz, NCH (anti)), 5.91 (2/3H, d, J=5.5 Hz, OCHN (anti)), 6.35 (1/3H, d, J=5.5 Hz, OCHN (syn)), and 6.6—7.3 (3H, m, Ar); MS *m/z* (rel intensity, %) 261 (M^+, 26), 202 (20), 160 (base peak), 132 (16), 131 (11), and 76 (13). Found: C, 64.64; H, 5.90; N, 5.31%. Calcd for $C_{14}H_{15}NO_4$:C, 64.36; H, 5.79; N, 5.36%.

Acetylation of 19 Leading to 22. A similar procedure using a mixture of **16** and **19** (3:1, 0.3 g) gave **22** (0.21 g, 73%): Colorless needles (benzene-hexane); IR (KBr) 1735, 1650, 1420, 1360, 1310, 1250, 1200, and 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.22 (3H, d, J=7.6 Hz, Me), 2.09 (2/5×3H, s, Ac (syn)), 2.20 (3/5×3H, s, Ac (anti)), 2.8—3.3 (2H, m, CH), 4.96 (2/5H, d, J=6.0 Hz, NCH (syn)), 5.44 (3/5H, br s, OCHN (anti)), 5.49 (3/5H, d, J=6.0 Hz, NCH (anti)), 5.94 (2/5H, br s, OCHN (syn)), and 6.7—7.2 (4H, m, Ar); MS *m/z* (rel intensity, %) 275 (M^+, 33), 216 (26), 175 (14), 174 (base peak), 132 (16), and 77 (15). Found: C, 65.44; H, 6.26; N, 4.90%. Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09%.

Acetylation of 20 Leading to 23. A similar procedure using a mixture of **17** and **20** (4:1, 0.24 g) gave **23** (0.165 g, 73%): Colorless prisms (benzene-hexane); mp 137—138 °C; IR (KBr) 1725, 1650, 1410, 1290, 1200, 1160, 1120, and 750 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.44 (2/3×3H, s, Me (anti)), 1.50 (1/3×3H, s, Me (syn)), 2.10 (1/3×3H, s, Ac (syn)), 2.23 (2/3×3H, s, Ac (anti)), 2.8—3.3 (2H, m, CH_2), 3.50 (3H, s, COOMe), 4.50 (1/3H, s, NCH (syn)), 5.06 (2/3H, s, NCH (anti)), 5.92 (2/3H, d, J=6.0 Hz, OCHN (anti)), 6.35 (1/3H, d, J=6.0 Hz, OCHN (syn)), and 6.6—7.2 (4H, m, Ar); MS *m/z* (rel intensity, %) 275 (M^+, 20), 216 (30), 175 (10), 174 (66), 172 (16), 133 (17), 132 (25), 131 (14), 78 (13), and 77 (26). Found: C, 65.56; H, 6.47; N, 5.09%. Calcd for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09%.

Reaction of 1g with Methyl Crotonate Leading to 24 and 28. To a solution of freshly prepared LDA (1.6 mmol) in THF (5 ml) was added at −78 °C a solution of **1g** (0.369 g, 1.5 mmol) in THF (5 ml). After the addition of methyl crotonate (0.16 g, 1.6 mmol in THF (5 ml)), the mixture was stirred at −78 °C for 1.5 h, poured into saturated aqueous ammonium chloride, and then extracted with diethyl ether (20 ml×2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was assigned as

24 on the basis of the following ^{1}H NMR spectrum ($CDCl_3$): δ=0.30 (9H, s, $SiMe_3$), 2.15 (3H, d, J_{Me-3}=6.5 Hz, 3-Me), 3.13 (3H, s, COOMe), 3.1—3.4 (1H, m, 3-H), 3.6—3.7 (1H, m, 4-H), 5.75 (1H, d, J_{5-4}=9.0 Hz, 5-H), and 6.7—7.2 (4H, m, Ar). It was chromatographed over silica gel by using chloroform as an eluent to give **28** (0.271 g, 84%): Colorless liquid; IR (neat) 2960, 1750, 1730, 1630, 1580, 1490, 1450, 1375, and 760 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.38 (3H, d, J_{Me-3}=7.0 Hz, 3-Me), 2.05 (3H, d, J=1.0 Hz, 2-Me), 3.08 (1H, dq, J_{3-Me}=7.0 and J_{3-Me}=1.0 Hz, 3-H), 3.73 (1H, d, J_{3a-9b}=8.0 Hz, 3a-H), 5.30 (1H, br d, J_{9b-3a}=8.0 Hz, 9b-H), and 6.7—7.7 (4H, m, Ar); ^{13}C NMR ($CDCl_3$) δ=15.98 (3-Me), 17.55 (2-Me), 48.64 (3a-C), 51.86 (3-C), 67.10 (9b-C), 116.93, 117.48, 125.09, 129.40, 129.56, 149.46, 168.59, and 178.28 (COO); MS *m/z* (rel intensity, %) 215 (M^+, 28), 174 (19), 146 (base peak), 131 (16), and 43 (21). HRMS Found: *m/z* 215.0933. Calcd for $C_{13}H_{13}NO_2$: M, 215.0933.

Reaction of 1g with Methyl Methacrylate Leading to 25, 27, and 29. A similar procedure using LDA (1.6 mmol) in THF (5 ml), **1g** (0.369 g, 1.5 mmol) in THF (5 ml), and methyl methacrylate (0.16 g, 1.6 mmol) in THF (5 ml), after column chromatography over silica gel with chloroform, gave **29** (0.16 g, 50%), and then an inseparable mixture of **25** and **27** (1:1 (^{1}H NMR), 0.17 g, 36%). The mixture of **25** and **27** (1:1, 0.17 g, 0.53 mmol) was stirred at room temperature for 1 h in the presence of cesium fluoride (10 mg) in THF (2 ml). After the reaction was completed, the mixture was poured into ice water and extracted with diethyl ether (20 ml). The extract was dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel by using chloroform to give **29** (0.045 g, 79%) and **27** (0.06 g, 91%). **27**: Colorless prisms (benzene–hexane); mp 143—144 °C; IR (KBr) 3200—2800, 1730, 1640, 1590, 1450, 1370, 1110, and 750 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.43 (3H, s, 4-Me), 2.05 (3H, d, J_{Me-5}=2.0 Hz, 2-Me), 2.5—2.7 (2H, m, 3-H), 3.71 (3H, s, COOMe), 5.22 (1H, q, J=2.0 Hz, 5-H), and 6.8—7.2 (4H, m, Ar). Found: C, 69.39; H, 6.62; N, 5.32%. Calcd for $C_{14}H_{17}NO_3$: C, 69.48; H, 6.61; N, 5.40%. **29**: Colorless liquid; IR (neat) 1760, 1630, 1495, 1460, 1430, 1380, 1250, 1220, 1190, 1140, 1090, and 760 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.50 (3H, s, 3a-Me), 2.06 (3H, d, J_{Me-9b}=1.0 Hz, 2-Me), 2.70 (1H, d, J_{gem}=16.0 Hz, one of 3-H), 3.45 (1H, d, J_{gem}=16.0 Hz, the other of 3-H), 4.76 (1H, br s, 9b-H), and 6.7—7.7 (4H, m, Ar); ^{13}C NMR ($CDCl_3$) δ=20.23 (3a-Me), 22.54 (3-C), 48.94 (4-C), 51.84 (COOMe), 76.44 (9b-C), 117.11, 120.03, 129.94, 130.50, 150.42 (each Ar), and 175.73 (2C, COOMe and 4-C); MS *m/z* (rel intensity, %) 215 (M^+, 2), 213 (11), 146 (10), 100 (12), 94 (89), 85 (11), 83 (14), and 75 (base peak). HRMS Found: *m/z* 215.0934. Calcd for $C_{13}H_{13}NO_2$: M, 215.0933.

Reaction of 1g with Methyl Cinnamate Leading to 26 and 30. A similar procedure using LDA (1 mmol) in THF (3 ml), **1g** (0.246 g, 1 mmol) in THF (3 ml), and methyl cinnamate (0.162 g, 1 mmol) in THF (3 ml) gave **26** as a single product (by ^{1}H NMR). This crude product was chromatographed over silica gel with chloroform to give **26** (35%) and **30** (32%): **26**: Pale yellow liquid; IR (neat) 1735, 1650, 920, and 850 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=0.30 (9H, s, $SiMe_3$), 2.05 (3H, d, J_{Me-5}=2.0 Hz, 2-Me), 3.12 (3H, s, COOMe), 3.53 (1H, dd, J_{4-5}=9.0 and J_{4-3}=5.0 Hz, 4-H), 4.50 (1H, d, J_{3-4}=5.0 Hz, 3-H), 6.00 (1H, dd, J_{5-4}=9.0 and J_{5-Me}=2.0 Hz, 5-H), and 6.7—7.4 (9H, m, Ar); MS *m/z* (rel intensity, %) 381 (M^+, 10), 366 (3), 219 (15), 121 (13), and 86 (69). HRMS Found: *m/z* 381.1765. Calcd for $C_{22}H_{27}NO_3Si$: M, 381.1760. **30**: Pale yellow liquid; IR (neat) 3400—2800, 1730, and 1650 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.10 (3H, s, Me), 3.23 (3H, s, COOMe), 3.60 (1H, dd, J_{4-5}=9.0 and J_{4-3}= 4.0 Hz, 4-H), 4.40 (1H, br s, 3-H), 5.90 (1H, br d, J_{5-4}=9.0 Hz, 5-H), and 6.7—7.5 (9H, m, Ar); MS *m/z* (rel intensity, %) 309 (M^+, 42), 251 (23), 250 (base peak), 236 (25), 147 (24), 84 (55), and 47 (18). HRMS Found: *m/z* 309.1347. Calcd for $C_{19}H_{19}NO_3$: M, 309.1363.

This work was financially supported by a Grant-in-Aid for Scientific Research (No. 63550652) from the Ministry of Education, Science and Culture.

References

1) As reviews: R. Grigg, *Chem. Soc. Rev.*, **16**, 89 (1987); R. Grigg, *Bull. Chim. Soc. Belg.*, **93**, 593 (1984).

2) R. Grigg and H. Q. N. Gunaratne, *J. Chem. Soc., Chem. Commun.*, **1982**, 384; R. Grigg, H. Q. N. Gunaratne, and V. Sridharan, *Tetrahedron*, **43**, 5887 (1987).

3) H. G. Pars, F. E. Granchelli, R. K. Razdan, and J. K. Keller, *J. Med. Chem.*, **19**, 445 (1976); R. K. Razdan, B. Z. Terris, G. R. Handrick, H. C. Dalzel, J. F. Howes, N. Plotnikoff, and P. Dodge, *ibid.*, **19**, 549 (1976); R. K. Razdan, "The Total Synthesis of Cannabinoids," in "The Total Synthesis of Natural Products," ed by J. ApSimon, A. Wiley-Interscience Publication, New York, Chichester, Brisbane, Toronto (1981), Vol. 4, Chap. 2, pp. 245—252.

4) O. Tsuge, K. Ueno, S. Kanemasa, and K. Yorozu, *Bull. Chem. Soc. Jpn.*, **59**, 1809 (1986).

5) O. Tsuge, S. Kanemasa, K. Yorozu, and K. Ueno, *Chem. Lett.*, **1985**, 1601.

6) O. Tsuge, S. Kanemasa, K. Yorozu, and K. Ueno, *Bull. Chem. Soc. Jpn.*, **60**, 3359 (1987).

7) O. Tsuge, S. Kanemasa, and M. Yoshioka, *J. Org. Chem.*, **53**, 1384 (1988); D. A. Barr, R. Grigg, H. Q. N. Gunaratne, J. Kemp, P. McMeekin, and V. Sridharan, *Tetrahedron*, **44**, 557 (1988).