(C_1); mass spectrum, m/e (relative intensity) 126 (M^+, 17), 96 (45), 68 (100); calcd for $C_7H_{10}O_2$ m/e 126.0681, found m/e 126.0687. ***trans*-17**: yield 65% (from *threo*-**7c**), 49% (from **11c**); bp 103 °C (12 mmHg); IR (neat film) 3000 (m), 1780 (s), 1645 (w), 1010 (s), 920 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 1.24 (d, J = 7.6 Hz, 3 H), 2.36 (dq, J = 12.0, 7.6 Hz, 1 H), 2.62–2.90 (m, 1 H), 3.93 (dd, J = 9.0, 9.0 Hz, 1 H), 4.40 (dd, J = 9.0, 8.0 Hz, 1 H), 5.12–5.36 (m, 2 H), 5.66 (ddd, J = 18.0, 9.0, 8.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 12.8 (C_2-*Me*), 40.0 (C_3), 48.7 (C_2), 69.8 (C_4), 118.6 (CH_2=), 134.7 (CH=), 178.1 (C_1); mass spectrum, m/e (relative intensity) 126 (M^+, 4), 96 (9), 68 (100); calcd for $C_7H_{10}O_2$ m/e 126.0681, found m/e 126.0687.

Acknowledgment. We acknowledge support for this work provided by the Ministry of Education of the Japanese Government (Grant in Aid for Special Project Research No. 57118006 and for Scientific Research C No. 56550588).

Registry No. **6a**, 5309-94-4; **6b**, 78904-41-3; **6c**, 67797-33-5; **6d**, 17709-95-4; **6e**, 10441-57-3; **6f**, 13070-07-0; *erythro*-**7a**, 76454-96-1; *threo*-**7a**, 76454-95-0; *erythro*-**7b**, 85892-04-2; *threo*-**7b**, 85892-05-3; *erythro*-**7c**, 86943-07-9; *threo*-**7c**, 86943-08-0; *erythro*-**7d**, 86943-09-1; *threo*-**7d**, 86943-10-4; *erythro*-**7e**, 85892-08-6; *threo*-**7e**, 85892-09-7; *erythro*-**7f**, 85892-15-5; *threo*-**7f**, 85892-14-4; *erythro*-**7g**, 86943-11-5; *threo*-**7g**, 86943-12-6; *erythro*-**7h**, 86943-13-7; *threo*-**7h**, 86943-14-8; *erythro*-**7i**, 86943-15-9; *threo*-**7i**, 86943-16-0; *erythro*-**7j**, 85892-17-7; *threo*-**7j**, 85892-18-8; **10a**, 2955-69-3; **10b**, 6636-01-7; *erythro*-**11a**, 82080-82-8; *threo*-**11a**, 82080-83-9; *erythro*-**11b**, 86943-17-1; *threo*-**11b**, 86943-18-2; *erythro*-**11c**, 86943-19-3; *threo*-**11c**, 86943-20-6; *erythro*-**11d**, 86943-21-7; *threo*-**11d**, 86943-22-8; *erythro*-**11e**, 86943-23-9; *threo*-**11e**, 86943-24-0; *erythro*-**15**, 86943-25-1; *threo*-**15**, 86943-26-2; *cis*-**16**, 86943-27-3; *trans*-**16**, 86943-28-4; *cis*-**17**, 86943-29-5; *trans*-**17**, 78657-18-8; *trans*-crotyl alcohol, 504-61-0; *cis*-crotyl alcohol, 4088-60-2; *trans*-4-[(trimethylsilyl)oxy]-2-butenyl chloride, 86943-30-8; *cis*-4-[(trimethylsilyl)oxy]-2-butenyl chloride, 86943-31-9; *trans*-crotyl bromide, 29576-14-5; α-methallyl bromide, 22037-73-6; *trans*-cinnamyl bromide, 26146-77-0; *trans*-cinnamyl alcohol, 4407-36-7; *N*-methyl-3-(*trans*-cinnamyl)pyrolidine-2-thione, 86943-32-0.

[1 + 4] Cycloaddition of Isocyanides with 1-Aryl-2-nitro-1-propenes, Methyl 2-Nitro-3-arylpropenoates, and Methyl 2-Nitro-2,4-pentadienoates. Synthesis of 1-Hydroxyindoles and 1-Hydroxypyrroles

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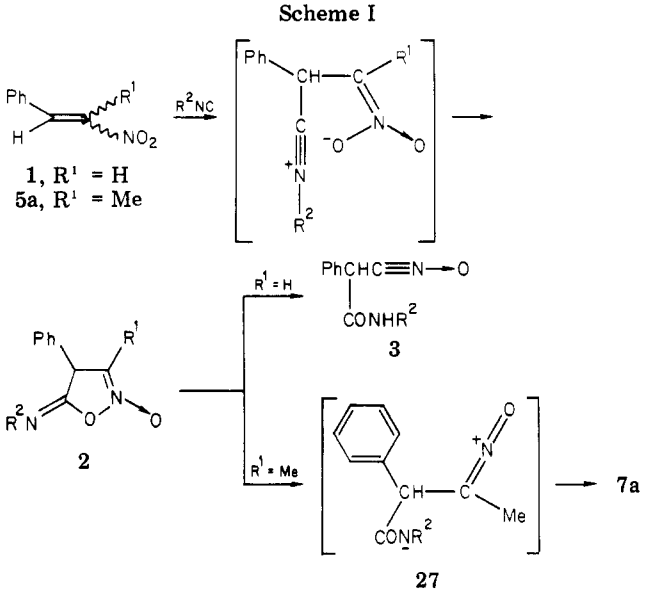
The [1 + 4] cycloadditions of isocyanides with various aryl nitroalkenes have been investigated. When the aryl groups were XC_6H_4, naphthyl, and 2-pyridinyl, the reactions gave the 1-hydroxyindoles, 1-hydroxybenzoindoles, and 1-hydroxy-7-azaindole. When the aryl group was thienyl or furyl, fused 1-hydroxypyrroles were obtained. The reaction of isocyanide with methyl 2-nitro-2,4-pentadienoates gave 1-hydroxypyrroles. A mechanism involving the formation of an unstable oxazoline *N*-oxide which decomposes to the reaction products has been suggested.

The [1 + 4] cycloaddition reactions of isocyanides with electrophilic heterodienes are of interest for the synthesis of heterocyclic compounds. cycloaddition of isocyanides with *N*-acyl imines,[1] aza dienes,[2] diaza dienes,[3,4] α,β-unsaturated esters,[5] and α,β-unsaturated ketones,[6-8] particularly with diethylaluminium chloride as a catalyst,[9] were described. Saegusa et al.[10] suggested that the cycloaddition reaction of isocyanides with nitroalkenes **1** gave an initial cycloadduct, **2**. The ring opening of the unstable isoxazoline *N*-oxide **2**, with a hydrogen shift, gave the nitrile oxide **3** that was reduced by excess of isocyanide into 2-cyanoacetamide (Scheme I).[11] The replacement of a hydrogen atom by an alkyl or ester group in the 3-position

Scheme I



of **2** should change the process of evolution of the corresponding oxazoline *N*-oxide.[12] In this paper, we describe the results of the reaction of isocyanides **4** with various

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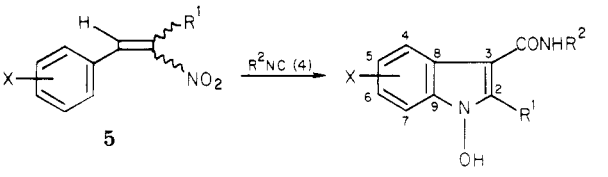
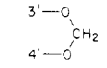
Table I. Preparation of 1-Hydroxyindoles



5 7-13

olefin precursor			isocyanide 4	reaction time, h	hydroxyindole[a]		yield,[b] %	mp, °C
no.	X	R^1			no.	X		
5a	H	Me	4a	6	7a	H	53	246-247
5b	4-MeO	Me	4a	1	7b	6-MeO	15	257
5c	4-NO_2	Me	4a	1	7c	6-NO_2	21	295
5d	4-NO_2	CO_2Me	4a	1	7d	6-NO_2	56	275-276
5d	4-NO_2	CO_2Me	4b	1	8	6-NO_2	57	253
5d	4-NO_2	CO_2Me	4c	1	9	6-NO_2	50	250-252
5d	4-NO_2	CO_2Me	4d	1	10	6-NO_2	87	241-243
5d	4-NO_2	CO_2Me	4e	0.5	11	6-NO_2	35	260
5e	3-NO_2	Me	4a	5	12e	5-NO_2	25	280
5f	3-NO_2	CO_2Me	4a	22	12f	5-NO_2	41	268-270
5g	3-Cl	Me	4a	18	12g 13g	5-Cl 7-Cl	26	272-274[c]
5h	3-Me	Me	4a	18	12h 13h	5-Me 7-Me	38	240-241[c]
5i	3-MeO	Me	4a	24	12i 13i	5-MeO 7-MeO	17	198-200[c]
5j		CO_2Me	4a	6	7j		38	270

[a] Satisfactory elemental analyses were obtained for all compounds: C, ±0.4; H, ±0.3; N, ±0.4. [b] Isolated product yield. [c] Mixture of isomers 12 and 13.

1-aryl-2-nitroalkenes **5**, **6**, and methyl 5-phenyl-2-nitro-2,4-pentadieneoates **19**.

Results and Discussion

The 1-aryl-2-nitro-1-alkenes (one isomer, *E*?) or the mixture of the (*E*)- and (*Z*)-methyl 3-aryl-2-nitropropenoates, with a free ortho position on the aryl ring, when allowed to react with a small excess of isocyanide **4** (Chart I), afforded the formation of compounds with the 1-hydroxypyrrole ring. The reaction of **5** with isocyanides, in benzene or acetonitrile, gave the corresponding 1-hydroxyindoles **7** (Table I).[12] Sometimes the yield of the adduct was poor, due to loss of isocyanide by polymerization catalysed by the acidic 1-hydroxyindole formed. Moreover, the product was extracted with difficulty from the mixture of hydroxyindole and polymers. The isomers **5d** (*E*) and **5d** (*Z*) gave the 1-hydroxyindole without a detectable difference in the yields. The reaction of nitroalkenes bearing a dissymetrically substituted phenyl group (**5g–i**) with **4a** gave a mixture of two isomeric hydroxyindoles: **5g** gave a 50:50 ratio of **12g/13g**, **5h** gave a 66:34 ratio of **12h/13h**, and **5i** gave a 60:40 ratio of **12i/13i**. However, when **5e** and **5f** were heated with *t*-BuNC, only hydroxyindoles **12e** and **12f** were obtained. The reactions with nitro olefins **5j** and **6a–d** gave a regioselective cyclization in the corresponding heterocycles **7j**, **15a,b** **16b**, and **18**. The intermediate 1-hydroxythieno[2,3-*b*]pyrrole **16a**, obtained from **6d**, was not isolated. It was reduced, probably by the excess of *t*-BuNC, to **16b**.[13] The methyl 5-phenyl-2-nitro-2,4-pentadienoates **19a–c**, heated with *t*-BuNC, gave the 1-hydroxypyrroles **20a–c**.

The indoles **21** and **23** were easily produced by reduction of the corresponding 1-hydroxyindoles **7a** and **7j** with trimethyl phosphite. The hydrolysis of **16b** and **17b** by aqueous NaOH gave the acids **16c** and **17c**, respectively. The 1-methoxyindoles **22** and **24–26** were obtained by alkylation at the oxygen of the hydroxyindole anion by using methyl iodide as the alkylating agent. Under these conditions, the 1-hydroxyindoles **7d** and **8** were not alkylated.

Structural assignments of cyclization products were made on the basis of spectroscopic data. The IR spectra (Nujol) showed bands near 3350 (ν_{NH}) and 2600 cm^{-1} (vbr, ν_{OH}) except for **16b**, which showed two sharp bands at 3390 and 3455 cm^{-1} (ν_{NH}). The formation of the fused pyrrole ring was confirmed by using ^{13}C NMR analysis, which identified the quaternary carbons. The structures of **18** and **16b** were proved by the assignments of the ring carbons based on the premise that the largest values of the coupling constant $^1J_{C-H}$ are found for the carbon directly bonded to the heteroatom.[14,15] The structures of **12** and **13** were differentiated by the ^1H NMR analysis of the aromatic protons.

The H_4 atom of **12** was coupled only with the H_6 atom, with a small coupling constant of about 2 Hz. The H_4 atom of **13** was coupled with H_5 and H_6. Moreover, the more shielded carbon of the benzene ring of **12** (C_7) is a doublet with coupling constant $^1J_{C-H}$ but without coupling constant $^3J_{C-H}$. The low solubility of compound **7j** made it impossible to obtain its NMR spectrum. The ^1H NMR data of its reduced derivative **23** showed two uncoupled aromatic protons, which supported the structure of this compound, along with H_4 and H_7 protons. The presence of the nitrone tautomer[16,17] of the 1-hydroxyindoles in solution

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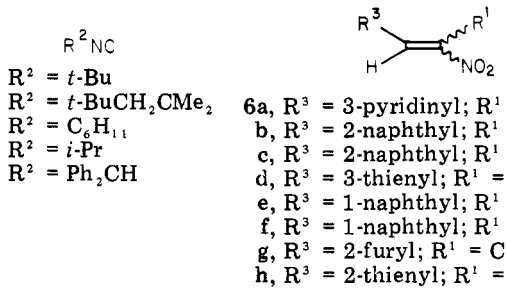
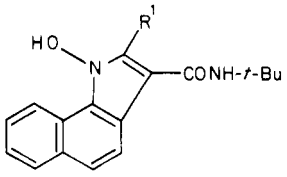
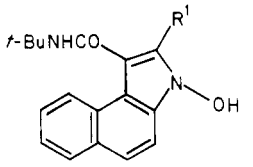
Chart I

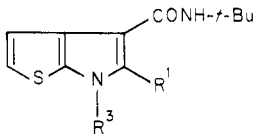




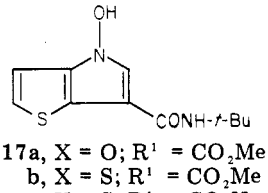
14a, R¹ = Me
b, R¹ = CO_2Me



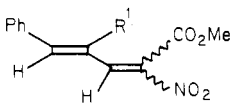
15a, R¹ = Me
b, R¹ = CO_2Me



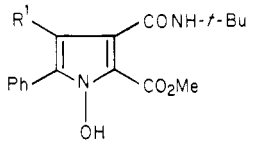
16a, R³ = OH; R¹ = CO_2Me
b, R³ = H; R¹ = CO_2Me
c, R³ = H; R¹ = CO_2H



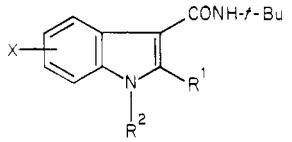
17a, X = O; R¹ = CO_2Me
b, X = S; R¹ = CO_2Me
c, X = S; R¹ = CO_2H



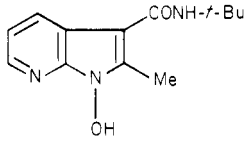
19a, R¹ = H
b, R¹ = Me
c, R¹ = Cl



20a, R¹ = H
b, R¹ = Cl
c, R¹ = Me



21, X = H; R¹ = Me; R³ = H
22, X = H; R¹ = Me; R³ = MeO
23, X = 5,6-(O-CH_2-O); R¹ = CO_2Me; R³ = H
24, X = 6-MeO; R¹ = Me; R³ = MeO
25, X = 7-Cl; R¹ = Me; R³ = MeO
26, X = 5-Cl; R¹ = Me; R³ = MeO



18

in $CDCl_3$ or CD_3SOCD_3 was not observed.

The mass spectra of the 1-hydroxyindoles (supplementary material) showed the molecular ion and the peaks arising from the loss of an oxygen atom and of the isobutene (when the hydroxyindoles were obtained from the *tert*-butyl isocyanide).

The foregoing data are consistent with the mechanism shown in Scheme I. The nucleophilic attack of isocyanide on the (*E*)- or (*Z*)-nitroalkene is followed by the formation of an isoxazoline *N*-oxide (**2**)[10] that rearranges, via rupture of the N–O bond, to the intermediate **27**. The conversion of **27** into **7a** involves an intramolecular electrophilic substitution reaction. In agreement with this mechanism, the reactions of isocyanides with the electrophilic alkene **6d** was fast, and the two isomeric alkenes *Z* and *E* gave the same reaction. When two unequivalent positions for the ring closure are available, the reaction involves preferentially the position of highest reactivity for the electrophilic substitution reaction. This mechanism accounts for the exclusive obtention of the compounds **7j**, **14**, and **16b**.

The procedure described here may be an acceptable method for the preparation of 1-hydroxyindoles and 1-hydroxypyrroles which are difficult to prepare.[18-20]

Experimental Section

Melting points (uncorrected) were determined on a Reichert apparatus. Mass spectra were obtained on a Varian MAT 311 mass spectrometer at an ionization potential of 70 eV. ^1H NMR (internal standard Me_4Si) spectra were taken on a Bruker WP-80 spectrometer. ^{13}C NMR spectra were recorded on an FT Bruker WP-80 spectrometer at 20.115 MHz. Infrared spectra were determined on a Perkin-Elmer 225 spectrometer. Elemental analyses were performed by the analytical laboratory, Centre National de la Recherche Scientifique. Isocyanides were obtained by following the known procedure.[21,22]

Methyl 2-nitro-3-(nitrophenyl)propenoate (**5d**) was prepared by the nitration of methyl *p*-nitrocinnamate, according to the established method;[23] 2-nitro-1-phenyl-1-propene (**5a**),[25] 1-(*p*-methoxyphenyl)-2-nitro-1-propene (**5**),[24] 1-(*p*-nitrophenyl)-2-nitro-1-propene (**5c**),[26] 1-(*m*-methoxyphenyl)-2-nitro-1-propene (**5i**),[26] and 1-(*m*-nitrophenyl)-2-nitro-1-propene (**5e**)[27] were prepared as described. The other 2-nitro-1-propenes were prepared by the procedure of Knoevenagel:[24] 50 mmol of aldehyde, 50 mmol of nitroethane, and 0.25 mL of *n*-butylamine in 30 mL of benzene was refluxed for 8 days. The solvent was removed, and one isomer (*E*?) of the alkene was obtained.

1-(*m*-Chlorophenyl)-2-nitro-1-propene (5g): mp 40 °C (petroleum ether); yield 90%; ^1H NMR ($CDCl_3$) δ 2.43 (s, 3 H), 7.39–7.41 (m, 4 H), 8.01 (s, 1 H). Anal. Calcd for $C_9H_8NO_2Cl$: C 54.70; H, 4.05; N, 7.09. Found: C, 54.63; H, 4.17; N, 6.87.

1-(*m*-Methylphenyl)-2-nitro-1-propene (5h): oil; yield 85%; ^1H NMR ($CDCl_3$) δ 2.40 (s, 3 H), 2.43 (d, J_{HH} = 1 Hz, 3 H), 7.20 (m, 4 H), 8.00 (s, 1 H).

2-Nitro-1-(3-pyridinyl)-1-propene (6a): mp 68–69 °C (ether); yield 55%; ^1H NMR ($CDCl_3$) δ 2.77 (s, 3 H), 7.26–7.94 (m, 3 H), 7.89 (s, 1 H), 8.79 (m, 1 H). Anal. Calcd for $C_8H_8N_2O_2$: C, 58.54; H, 4.88; N, 17.67. Found: C, 58.60; H, 4.86; N, 17.95.

1-(β-Naphthyl)-2-nitro-1-propene (6b): mp 96 °C (ether); yield 86%; ^1H NMR ($CDCl_3$) δ 2.49 (s, 3 H), 7.50–8.28 (m, 8 H). Anal. Calcd for $C_{13}H_{11}NO_2$: C, 73.24; H, 5.16; N, 6.57. Found: C, 73.02; H, 5.20; N, 6.72.

1-(α-Naphthyl)-2-nitro-1-propene (6e): mp 68 °C (ether); yield 80%; ^1H NMR ($CDCl_3$) δ 2.35 (d, J_{HH} = 1 Hz, 3 H), 7.44–8.10 (m, 7 H), 8.68 (s, 1 H). Anal. Calcd for $C_{13}H_{11}NO_2$: C, 73.24; H, 5.16; N, 6.57. Found: C, 73.16; H, 5.29; N, 6.74.

General Procedure for the Synthesis of Methyl 3-Aryl-2-nitropropenoates and Methyl 5-Phenyl-2,4-pentadienoates.

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These compounds were prepared by the procedure of Lehnert.[28] The reaction gave a mixture of *Z* and *E* isomers. The structure of the isomers (designated by A and B) was not attributed.

Methyl 3-(*m*-nitrophenyl)-2-nitropropenoate (5f): yellow crystals; 60% yield; mp 106–108 °C (ether); ^{1}H NMR ($CDCl_3$) δ 3.97 (s, 3 H), 7.62–7.77 (m, 3 H), 8.28–8.30 (m, 2 H). Anal. Calcd for $C_{10}H_8N_2O_6$: C, 47.62; H, 3.17; N, 11.10. Found: C, 47.94; H, 3.06; N, 10.95.

Methyl 3-[3′,4′-(methylenedioxy)phenyl]-2-nitropropenoate (5j): 4:6 mixture of A and B isomers; 94% yield; mp 108–110 °C (benzene); ^{1}H NMR ($CDCl_3$) for **5j** (isomer A) δ 4.01 (s, 3 H), 6.08 (s, 2 H), 6.8–7.1 (m, 3 H), 8.04 (s, 1 H); ^{1}H NMR ($CDCl_3$) for **5j** (isomer B) δ 3.93 (s, 3 H), 6.06 (s, 2 H), 6.8–7.1 (m, 3 H), 7.47 (s, 1 H). Anal. Calcd for $C_{11}H_9NO_6$: C, 52.59; H, 3.58; N, 5.58. Found: C, 52.71; H, 3.35; N, 5.60.

Methyl 3-(β-naphthyl)-2-nitropropenoate (6c): 2:3 mixture of A and B isomers; 60% yield; mp 107–108 °C (benzene); ^{1}H NMR (CD_3SOCD_3) for **6c** (A) δ 4.05 (s, 3 H), 7.40–8.20 (m, 8 H), 8.64 (s, 1 H); ^{1}H NMR (CD_3SOCD_3) for **6c** (B) δ 3.96 (s, 3 H), 7.40–8.20 (m, 7 H), 8.26 (s, 1 H). Anal. Calcd for $C_{14}H_{11}NO_4$: C, 65.37; H, 4.28; N, 5.44. Found: C, 65.26; H, 4.29; N, 5.45.

Methyl 2-nitro-3-(3-thienyl)propenoate (6d): 5:2 mixture of A and B isomers; 70% yield; mp 54–56 °C (ether); ^{1}H NMR ($CDCl_3$) for **6d** (B) δ 3.99 (s, 3 H), 7.10–7.90 (m, 3 H), 8.10 (s, 1 H); ^{1}H NMR ($CDCl_3$) for **6d** (A) δ 3.90 (s, 3 H), 7.10–7.90 (m, 3 H), 7.56 (s, 1 H). Anal. Calcd for $C_8H_7NSO_4$: C, 45.07; H, 3.29; N, 6.57. Found: C, 45.12; H, 3.02; N, 6.72.

Methyl 3-(α-naphthyl)-2-nitropropenoate (6f): 5:2 mixture of A and B isomers; 80% yield; mp 128–130 °C (benzene); ^{1}H NMR for **6f** (B) δ 3.79 (s, 3 H), 7.32–8.01 (m, 7 H), 8.82 (s, 1 H); ^{1}H NMR for **6f** (A) δ 4.05 (s, 3 H), 7.32–8.01 (m, 7 H), 8.29 (s, 1 H). Anal. Calcd for $C_{14}H_{11}NO_4$: C, 65.37; H, 4.28; N, 5.45. Found: C, 65.33; H, 4.02; N, 5.59.

Methyl 3-(2-furyl)-2-nitropropenoate (6g): 32:28 mixture of A and B isomers; 66% yield; mp 65–66 °C (ether); ^{1}H NMR for **6g** (B) δ 3.99 (s, 3 H), 6.60 (m, 1 H), 7.06 (m, 1 H), 7.71 (m, 1 H), 7.95 (s, 1 H); ^{1}H NMR for **6g** (A) δ 3.90 (s, 3 H), 6.60 (m, 1 H), 7.06 (m, 1 H), 7.39 (s, 1 H), 7.71 (m, 1 H). Anal. Calcd for $C_8H_7NO_5$: C, 48.73; H, 3.55; N, 7.10. Found: C, 48.86; H, 3.53; N, 7.25.

Methyl 2-nitro-3-(2-thienyl)propenoate (6h): 70:30 mixture of A and B isomers; 65% yield; oil; ^{1}H NMR for **6h** (B) δ 4.02 (s, 3 H), 7.20–7.80 (m, 3 H), 8.30 (s, 1 H); ^{1}H NMR for **6h** (A) δ 3.90 (s, 3 H), 7.20–7.80 (m, 3 H), 7.75 (s, 1 H).

Methyl 2-nitro-5-phenyl-2,4-pentadienoate (19a): 28:35 mixture of A and B isomers; 74% yield; isomer A, mp 107 °C (ether); ^{1}H NMR ($CDCl_3$) for **19a** (A) δ 3.84 (s, 3 H), 6.95–7.60 (m, 8 H); ^{1}H NMR ($CDCl_3$) for **19a** (B) δ 3.93 (s, 3 H), 6.95–7.80 (m, 8 H). Anal. Calcd for $C_{12}H_{11}NO_4$: C, 61.80; H, 4.72; N, 6.00. Found: C, 61.91; H, 4.82; N, 6.00.

Methyl 4-methyl-2-nitro-5-phenyl-2,4-pentadienoate (19b): 50:50 mixture of A and B isomers; 68% yield. For **19b** (A): yellow needles; mp 64–66 °C (ether) ^{1}H NMR δ 2.07 (s, 3 H), 3.99 (s, 3 H), 7.15 (s, 1 H), 7.4 (m, 5 H), 7.86 (s, 1 H). For **19b** (B): mp 63 °C (petroleum ether); ^{1}H NMR δ 1.98 (s, 3 H), 3.87 (s, 3 H), 6.99 (s, 1 H), 7.23 (s, 1 H), 7.35 (m, 5 H). Anal. Calcd for $C_{13}H_{13}NO_4$: C, 63.16; H, 5.26; N, 5.67. Found: C, 62.98; H, 5.07; N, 5.72.

Methyl 4-chloro-2-nitro-5-phenyl-2,4-pentadienoate (19c): oil; 65% yield; ^{1}H NMR δ 3.90 (s, 3 H), 7.20–7.90 (m, 7 H).

General Procedure for the Reaction of Isocyanides with Nitroalkenes. To a magnetically stirred solution of 10 mmol of nitroalkene in 10 mL of benzene (or acetonitrile) was added 12 mmol of isocyanide. The mixture was refluxed for 0.5–20 h. Then, the solution was evaporated, and the brown solid (or oily) residue was treated with ether. The resulting crystals were filtered and recrystallized from methanol.

***N*-*tert*-Butyl-1-hydroxy-2-methyl-3-indolecarboxamide (7a)**: ^{1}H NMR (CD_3SOCD_3) δ 1.44 (s, 9 H), 2.58 (s, 3 H), 6.72 (s, 1 H, NH), 7.02–7.77 (m, 4 H); ^{13}C NMR (CD_3SOCD_3) δ 10.1 (2-CH_3), 28.9 ((CH_3)$_3$C), 50.3 ((CH_3)$_3C$), 104.5 (C_3), 108.2 (C_7) 119.3, 120.1, 121.1 (C_4, C_5, C_6), 121.5 (C_8), 132.6 (C_9), 136.6 (C_2), 164.8 (CO).

***N*-*tert*-Butyl-1-hydroxy-2-methyl-6-methoxy-3-indolecarboxamide (7b)**: ^{1}H NMR (CD_3SOCD_3) δ 1.42 (s, 9 H), 2.52 (s, 3 H), 3.79 (s, 3 H), 6.65 (s, 1 H), 7.2 (m, 3 H), 14.02 (s, 1 H).

***N*-*tert*-Butyl-1-hydroxy-2-methyl-6-nitro-3-indolecarboxamide (7c)**: ^{1}H NMR (CD_3SOCD_3) δ 1.40 (s, 9 H), 2.56 (s, 3 H), 7.10 (s, 1 H), 7.63–8.28 (m, 3 H).

***N*-*tert*-Butyl-1-hydroxy-2-(methoxycarbonyl)-6-nitro-3-indolecarboxamide (7d)**: ^{1}H NMR (CD_3SOCD_3) δ 1.40 (s, 9 H), 3.89 (s, 3 H), 8.0 (m, 2 H), 8.32 (m, 1 H); ^{13}C NMR (CD_3SOCD_3) δ 28.5 ((CH_3)$_3$C), 50.8 ((CH_3)$_3C$), 52.5 (OCH_3), 106.4 (C_7), 114.0 (C_3), 115.8 (C_5), 122.6 (C_4), 124.4 (C_8), 129.6 (C_2), 132.5 (C_9), 144.8 (C_6), 159.7 (CO), 161.9 (CONH).

***N*-*tert*-Octyl-1-hydroxy-2-(methoxycarbonyl)-6-nitro-3-indolecarboxamide (8)**: ^{1}H NMR (CD_3SOCD_3) δ 0.96 (s, 9 H), 1.41 (s, 6 H), 1.86 (s, 2 H), 3.87 (s, 3 H), 7.86–7.95 (m, 2 H), 8.22 (s, 1 H).

***N*-Cyclohexyl-1-hydroxy-2-(methoxycarbonyl)-6-nitro-3-indolecarboxamide (9)**: ^{1}H NMR (CD_3SOCD_3) δ 1.27–1.89 (m, 10 H), 3.88 (m, 1 H), 3.90 (s, 3 H), 8.04–8.37 (m, 3 H).

***N*-Isopropyl-1-hydroxy-2-(methoxycarbonyl)-6-nitro-3-indolecarboxamide (10)**: ^{1}H NMR (CD_3SOCD_3) δ 1.15 (d, 6 H), 3.93 (s, 3 H), 4.04 (m, 1 H), 8.00–8.34 (m, 3 H).

***N*-(Diphenylmethyl)-1-hydroxy-2-(methoxycarbonyl)-6-nitro-3-indolecarboxamide (11)**: ^{1}H NMR (CD_3SOCD_3) δ 2.67 (s, 3 H), 6.41 (d, J_{HH} = 11 Hz, 1 H), 7.35–8.35 (m, 13 H), 9.33 (d, J = 11 Hz, 1 H).

***N*-*tert*-Butyl-1-hydroxy-2-methyl-5-nitro-3-indolecarboxamide (12e)**: ^{1}H NMR (CD_3SOCD_3) δ 1.45 (s, 9 H), 2.00 (s, 3 H), 7.31 (s, 1 H, NH), 7.52 (d, J = 9.4 Hz, 1 H, H_7), 8.05 (dd, J = 9.4, 2 Hz, 1 H, H_6), 8.65 (d, J = 2 Hz, 1 H, H_4); ^{13}C NMR (CD_3SOCD_3) δ 10.4 (2-CH_3), 28.8 ((CH_3)$_3$C), 50.7 ((CH_3)$_3C$), 107.5 (C_3), 108.6 (d, J = 169 Hz, C_7), 116.8 (C_4), 119.3 (C_6), 120.8 (C_8), 135.0 (C_5), 139.8 (C_2), 141.5 (C_9), 163.7 (CO).

***N*-*tert*-Butyl-1-hydroxy-2-(methoxycarbonyl)-5-nitro-3-indolecarboxamide (12f)**: ^{1}H NMR (CD_3SOCD_3) δ 1.45 (s, 9 H), 3.98 (s, 3 H), 7.66 (d, J = 8.8 Hz, 1 H, H_7), 8.12 (s, 1 H, NH), 8.20 (d, J = 8.8 Hz, 1 H, H_6), 8.75 (s, 1 H, H_4); ^{13}C NMR (CD_3SOCD_3) δ 28.5 ((CH_3)$_3$C), 50.9 ((CH_3)$_3C$), 52.5 (OCH_3), 110.6 (d, J = 171 Hz, C_7), 119.5 (C_8), 119.9 (C_4), 127.5 (C_2), 115.8 (C_3), 118.9 (C_6), 136.1 (C_5), 142.4 (C_9), 159.8 (COO), 161.7 (CONH).

***N*-*tert*-Butyl-1-hydroxy-2-methyl-5-chloro-3-indolecarboxamide (12g) and *N*-*tert*-butyl-1-hydroxy-2-methyl-7-chloro-3-indolecarboxamide (13g)**: **12g** and **13g** were separated after O-methylation; ^{1}H NMR (CD_3SOCD_3) δ 1.41 (s, 9 H), 2.49, 2,52 (s, s, 3 H), 7.08–7.71 (m, 4 H), 11.35 (s, 1 H, OH).

***N*-*tert*-Butyl-1-hydroxy-2,5-dimethyl-3-indolecarboxamide (12h) and *N*-*tert*-butyl-1-hydroxy-2,7-dimethyl-3-indolecarboxamide (13h)**: ^{1}H NMR (CD_3SOCD_3) δ 1.42 (s, 9 H), 2.39, 2.65 (s, s, 3 H), 2.52 (s, 3 H), 6.85 (m, 2 H), 7.50 (m, 1 H), 11.13 (s, 1 H); ^{13}C NMR (CD_3SOCD_3) for **12h** δ 10.2 (2-CH_3), 21.3 (5-CH_3), 28.9 ((CH_3)$_3$C), 50.4 (C(CH_3)$_3$), 104.0 (C_3), 108.0 (d, J_{CH} = 162 Hz, C_7), 119.1 (C_4), 119.8 (C_5), 122.6 (C_6), 121.7 (C_8), 128.8 (C_9), 136.4 (C_2), 164.9 (CO). ^{13}C NMR (CD_3SOCD_3) for **13h** δ 10.2 (2-CH_3), 17.9 (7-CH_3), 28.9 ((CH_3)$_3$C), 50.4 ((CH_3)$_3C$), 104.8 (C_3), 117.1 (C_4), 120.1 (C_5), 121.8 (C_7), 123.3 (C_6), 131.1 (C_9), 136.8 (C_2), 164.9 (CO).

***N*-*tert*-Butyl-1-hydroxy-2-methyl-5-methoxy-3-indolecarboxamide (12i) and *N*-*tert*-butyl-1-hydroxy-2-methyl-7-methoxy-3-indolecarboxamide (13i)**: ^{1}H NMR (CD_3SOCD_3) δ 1.42 (s, 9 H), 2.50 (s, 3 H), 3.80, 3.87 (s, s, 3 H), 6.65 (m, 2 H), 7.25 (m, 1 H), 14.02 (s, 1 H); ^{13}C NMR (CD_3SOCD_3) for **12i** δ 10.2 (2-CH_3), 28.9 ((CH_3)$_3$C), 50.2 (C(CH_3)$_3$), 55.2 (OCH_3), 104.1 (C_3), 109.0 (d, J = 164 Hz, C_7), 122.1, 123.5, 128.0, 154.4, 165.0. ^{13}C NMR (CD_3SOCD_3) for **13i** δ 10.1 (2-CH_3), 28.9 ((CH_3)$_3$C), 50.4 (C(CH_3)$_3$), 55.6 (OCH_3), 105.1 (C_3), 120.6, 122.4, 136.7, 145.9, 164.8.

***N*-*tert*-Butyl-1-hydroxy-2-methyl-6,7-benzo-3-indolecarboxamide (14a)**: reflux 30 h; 0.89 g (30%); mp 270–272 °C (MeOH); ^{1}H NMR (CD_3SOCD_3) δ 1.44 (s, 9 H), 2.61 (s, 3 H), 7.14 (s, 1 H, br), 7.54 (m, 3 H), 7.95 (m, 2 H), 8.91 (d, 1 H), 11.73 (s, 1 H); ^{13}C NMR (CD_3SOCD_3) δ 10.1 (2-CH_3), 28.9, 50.5 ((CH_3)$_3C$), 106.7 (C_3), 117.7 (C_8), 119.6 (d, J = 163 Hz, C_4), 120.6 (C_5), 134.1 (C_2), 120.9, 121.5, 123.6, 125.0, 125.6, 128.2, 130.1, 164.8 (CO).

***N*-*tert*-Butyl-1-hydroxy-2-(methoxycarbonyl)-6,7-benzo-3-indolecarboxamide (14b)**: reflux 1 h; 0.88 g (26%); mp 248 °C (MeOH); ^{1}H NMR (CD_3SOCD_3) δ 1.39 (s, 9 H), 3.82 (s, 3 H), 7.30–8.05 (m, 5 H), 8.90 (m, 1 H); ^{13}C NMR (CD_3SOCD_3) δ 28.6,

(28) Lehnert, W. *Tetrahedron* **1972**, *28*, 663.

50.7 ($(CH_3)_3C$), 51.7 (OCH_3), 116.2 (C_3), 117.3 (C_8), 120.0 (d, ^1J = 165 Hz, C_4), 121.3, 122.4, 122.5, 122.7, 125.7, 125.9, 128.0, 132.1, 160.4, 163.1. Anal. Calcd for $C_{19}H_{20}N_2O_4$: C, 67.06; H, 5.88; N, 8.23. Found: C, 66.94; H, 5.97; N, 7.95.

***N*-*tert*-Butyl-1-hydroxy-2-methyl-4,5-benzo-3-indolecarboxamide (15a)**: reflux 24 h; 1.12 g (38%); mp 289–291 °C (MeOH); ^1H NMR (CD_3SOCD_3) δ 1.44 (s, 9 H), 2.46 (s, 3 H), 7.42 (m, 2 H), 7.62 (s, 1 H), 7.89 (m, 2 H), 8.61 (m, 1 H); ^{13}C NMR (CD_3SOCD_3) δ 9.8 (2-Me), 28.7, 50.4 ($(CH_3)_3C$), 108.9 (C_3), 110.1 (d, J_{C-H} = 164 Hz, C_7), 114.3 (C_8), 122.1, 122.8, 124.0, 125.2, 127.2, 128.6, 129.3, 130.9, 166.9 (CO). Anal. Calcd for $C_{18}H_{20}N_2O_2$: C, 72.97; H, 6.76; N, 9.46. Found: C, 72.97; H, 6.59; N, 9.46.

***N*-*tert*-Butyl-1-hydroxy-2-(methoxycarbonyl)-4,5-benzo-3-indolecarboxamide (15b)**: reflux 2 h; 1.46 g (43%); mp 277–280 °C (MeOH); ^1H NMR (CD_3SOCD_3) δ 1.44 (s, 9 H), 3.81 (s, 3 H), 8.43–7.33 (m, 7 H); ^{13}C NMR (CD_3SOCD_3) δ 28.3, 50.7 ($(CH_3)_3C$), 51.3 (OCH_3), 110.7 (d, ^1J = 167 Hz, C_7), 112.9 (C_8), 120.1 (C_2), 123.1, 124.1, 126.7, 127.0, 127.6, 129.0, 129.7, 131.8, 159.6 (COO), 165.2 (CONH). Anal. Calcd for $C_{19}H_{20}N_2O_4$: C, 67.06; H, 5.88; N, 8.23. Found: C, 66.78; H, 6.00; N, 7.98.

Methyl 4-[(*tert*-Butylamino)carbonyl]thieno[2,3-*b*]pyrrole-5-carboxylate (16b). To a stirred solution of 2 g (10 mmol) of nitroalkene **6d** in 11 mL of benzene was added 1.2 g (14.5 mmol) of **4a**. The mixture was refluxed for 2 h, the solution was evaporated, and the residue was extracted with 1 M NaOH (10 mmol). The aqueous solution, acidified with 3 M HCl, gave a brown oil. This oil was dissolved in CH_2Cl_2 (10 mL) and extracted with 1 M $NaCO_3H$ (2 × 10 mL). The residue, treated with ether, gave **16b**: 0.1 g (5%); yellow crystals; mp 232–233 °C (50:50 ether/acetone); ^1H NMR (CD_3SOCD_3) δ 1.41 (s, 9 H), 3.96 (s, 3 H), 7.30 (d, J = 5.2 Hz, 1 H), 7.53 (d, J = 5.2 Hz, 1 H), 9.42 (s, 1 H), 11.70 (s, 1 H); ^{13}C NMR (CD_3SOCD_3) δ 28.5, 50.2 ($(CH_3)_3C$), 52.4 (OCH_3), 118.9 (C_4), 119.5 ($^1J_{C-H}$ = 175 Hz, C_3), 122.7 (C_5), 123.3 ($^1J_{C-H}$ = 186 Hz, C_2), 133.6 (C_8), 137.1 (C_7), 161.6 (CONH), 162.4 (COO). The aqueous solution was acidified and gave the acid **16c**: 0.45 g (18%); colorless crystal; mp 222 °C; ^1H NMR (CD_3SOCD_3) δ 1.46 (s, 9 H), 7.24 (d, J = 4.5 Hz, 1 H), 7.31 (d, J = 4.5 Hz, 1 H), 8.88 (s, 1 H), 12.63 (s, 1 H). Anal. Calcd for $C_{12}H_{14}N_2O_3S$: C, 54.13; H, 5.26; N, 10.52; S, 12.03. Found: C, 54.13; H, 5.19; N, 10.22; S, 12.02.

Methyl 4-hydroxy-6-[(*tert*-butylamino)carbonyl]furo[3,2-*b*]pyrrole-5-carboxylate (17a): reflux 1 h; 1.12 g (40%); mp 209 °C (chloroforme/ether, 1:1); ^1H NMR (CD_3SOCD_3) δ 1.40 (s, 9 H), 3.87 (s, 3 H), 6.76 (d, J_{HH} = 2.25 Hz, 1 H), 7.87 (d, J_{HH} = 2.25 Hz, 1 H), 8.43 (s, 1 H); ^{13}C NMR (CD_3SOCD_3) δ 28.5, 50.4 ($(CH_3)_3C$), 51.7 (OCH_3), 98.2 ($^1J_{CH}$ = 182 Hz, C_3), 106.8 (C_6), 118.9 (C_5), 127.3 (C_8), 141.8 (C_7), 150.0 ($^1J_{CH}$ = 207 Hz, C_2), 160.6 (CONH), 161.3 (COO). Anal. Calcd for $C_{13}H_{16}N_2O_5$: C, 55.71; H, 5.71; N, 10.00. Found: C, 54.99; H, 5.66; N, 9.82.

Methyl 4-hydroxy-6-[(*tert*-butylamino)carbonyl]thieno[3,2-*b*]pyrrole-5-carboxylate (17b): reflux 1 h; 8% yield; mp 226 °C (ether/acetone, 1:1); ^1H NMR (CD_3SOCD_3) δ 1.42 (s, 9 H), 3.96 (s, 3 H), 7.08 (d, J_{HH} = 5.1 Hz, 1 H), 7.68 (d, J_{HH} = 5.1 Hz, 1 H), 9.33 (s, 1 H).

6-[(*tert*-Butylamino)carbonyl]-4-hydroxythieno[3,2-*b*]pyrrole-5-carboxylic Acid (17c). To a stirred solution of 6.39 g (30 mmol) of nitroalkene **6h** in 12 mL of benzene was added 2.49 g (30 mmol) of **4a**. The mixture was refluxed for 1 h, the solution was evaporated, and the residue was extracted with 1 M NaOH (3 × 10 mL). The aqueous solution acidified with 3 M HCl gave the acid **17c**: 0.19 g (22%); mp 213–214 °C (tetrahydrofuran); ^1H NMR (CD_3SOCD_3) δ 1.46 (s, 9 H), 7.17 (d, J_{HH} = 5 Hz, 1H), 7.76 (d, J_{HH} = 5 Hz, 1 H), 9.93 (s, 1 H), 10.59 (br s, 1 H). Anal. Calcd for $C_{12}H_{14}N_2O_4S$: C, 51.06; H, 4.96; N, 9.93; S, 11.35. Found: C, 50.88; H, 4.97; N, 9.73; S, 11.31.

***N*-*tert*-Butyl-7-aza-1-hydroxy-2-methyl-3-indolecarboxamide (18)**: reflux 6 h; 0.64 g (26%); mp 230 °C (MeOH); ^1H NMR (CD_3SOCD_3) δ 1.47 (s, 9 H), 2.64 (s, 3 H), 6.90 (br s, 1 H, NH), 7.06 (q, J = 4.5, 7.5 Hz, H_5), 7.97 (q, J = 7.5, 1.5 Hz, H_4), 8.09 (q, J = 4.5, 1.5 Hz, H_6), 11.76 (s, 1 H); ^{13}C NMR (CD_3SOCD_3) δ 10.2 (2-CH_3), 28.8, 50.5 ($(CH_3)_3C$), 102.9 (C_3), 114.6 (C_8), 116.7 (d, J = 164 Hz, C_5), 127.7 (d, J = 166 Hz, C_4), 138.0 (C_2), 142.3 (J = 176.8 Hz, C_6), 143.3 (C_9), 164.2 (CO). Anal. Calcd for $C_{13}H_{17}N_3O_2$: C, 63.16; H, 6.88; N, 17.00. Found: C, 63.05; H, 7.07; N, 17.09.

Methyl 3-[(*tert*-butylamino)carbonyl]-1-hydroxy-5-phenylpyrrole-2-carboxylate (20a): reflux 2 h; 0.63 g (20%); mp 218–219 °C (MeOH); ^1H NMR (CD_3SOCD_3) δ 1.35 (s, 9 H), 3.84 (s, 3 H), 6.69 (s, 1 H), 7.40–7.85 (m, 5 H), 8.30 (s, 1 H), 11.78 (s, 1 H); ^{13}C NMR (CD_3SOCD_3) δ 28.5, 50.3 ($(CH_3)_3C$), 118.6 (C_3), 122.8 (C_2), 127.7, 128.0, 128.5, 129.7, 133.1, 161.1 (COO), 162.3 (CONH). Anal. Calcd for $C_{17}H_{20}N_2O_4$: C, 64.56; H, 6.33; N, 8.86. Found: C, 64.77; H, 6.44; N, 8.85.

Methyl 3-[(*tert*-butylamino)carbonyl]-4-chloro-1-hydroxy-5-phenylpyrrole-2-carboxylate (20b): reflux 5 h; 0.8 g (23%); mp 231 °C; ^1H NMR (CD_3SOCD_3/CF_3CO_2H) δ 1.80 (s, 9 H) 4.26 (s, 3 H), 7.71 (m, 5 H). Anal. Calcd for $C_{17}H_{19}N_2O_4Cl$: C, 58.20; H, 5.42; N, 7.99; Cl, 10.13. Found: C, 58.13; H, 5.59; N, 8.08; Cl, 10.34.

Methyl 3-[(*tert*-butylamino)carbonyl]-1-hydroxy-4-methyl-5-phenylpyrrole-2-carboxylate (20c): reflux 1 h; 0.76 g (23%); mp 234 °C (MeOH); ^1H NMR (CD_3SOCD_3/CF_3CO_2H) δ 1.38 (s, 9 H), 2.04 (s, 3 H), 3.81 (s, 3 H), 7.56 (m, 5 H), 8.22 (br, 1 H). Anal. Calcd for $C_{18}H_{22}N_2O_4$: C, 65.45; H, 6.67; N, 8.48. Found: C, 65.37; H, 6.71; N, 8.56.

***N*-*tert*-Butyl-5,6-(methylenedioxy)-2-(methoxycarbonyl)-3-indolecarboxamide (23).** A mixture of 0.5 g (1.5 mmol) of **7j** and 5 mL of trimethyl phosphite was heated at 100 °C for 4 h. The trimethyl phosphite was removed under reduced pressure, and the solid residue was washed with ether. Recrystallization from methanol gave yellow crystals of **23**: 0.44 g (93%); mp 196–197 °C; ^1H NMR (CD_3SOCD_3) δ 1.44 (s, 9 H), 3.96 (s, 3 H), 6.06 (s, 2 H), 6.94 (s, 1 H), 7.68 (s, 1 H), 9.15 (s, 1 H), 12.15 (s, 1 H). Anal. Calcd for $C_{16}H_{18}N_2O_5$: C, 60.38; H, 5.66; N, 8.80. Found: C, 60.01; H, 5.82; N, 8.55.

***N*-*tert*-Butyl-2-methyl-3-indolecarboxamide (21).** The preparation was carried out as described for **23**: yield 57%; mp 230–240 °C; ^1H NMR (CD_3SOCD_3) δ 1.44 (s, 9 H), 2.55 (s, 3 H), 6.72 (s, 1 H), 7.05 (m, 2 H), 7.32 (m, 1 H), 7.68 (m, 1 H); mass spectrum, exact mass calcd for $C_{14}H_{18}N_2O$ m/e 230.1419, found m/e 230.1421.

O-Methylation of 1-Hydroxyindoles 12g and 13g. A solution of 2 g (7.1 mmol) of a mixture of 1-hydroxyindoles **12g** and **13g** in 40 mL of THF was added to 0.48 g (20 mmol) of sodium hydride under dry N_2. The resulting mixture was stirred at room temperature for 1 h. Then, 2.43 g (17 mmol) of methyl iodide was added. The solution was refluxed for 1 h and concentrated under reduced pressure. The residue was poured into 1 M HCl (10 mL) and extracted with $CHCl_3$ (2 × 10 mL). The combined extracts were washed with water, dried (Na_2SO_4), and concentrated to give 1.8 g (86%) of a crystalline material which was a mixture of **25** and **26**. This mixture was extracted with 5 mL of ether. The solid residue was recrystallized from ether to give **25** as colorless needles, mp 164 °C. The fraction extracted with ether was recrystallized from CCl_4 to give **26**, mp 126 °C. The spectral data for **25** follow: ^1H NMR ($CDCl_3$) δ 1.53 (s, 9 H), 2.71 (s, 3 H), 4.08 (s, 3 H), 5.76 (s, 1 H), 7.14 (d, J = 7.6 Hz, 1 H), 7.18 (d, J = 1.9 Hz, 1 H), 7.65 (dd, J = 1.9, 7.6 Hz, 1 H). Anal. Calcd for $C_{15}H_{19}N_2O_2Cl$: C, 61.12; H, 6.45; N, 9.51; Cl, 12.05. Found: C, 60.94; H, 6.63; N, 9.47; Cl, 11.79. The spectral data for **26** follow: ^1H NMR ($CDCl_3$) δ 1.50 (s, 9 H), 2.65 (s, 3 H), 3.98 (s, 3 H), 5.67 (s, 1 H), 7.11 (dd, J = 7.5, 1.7 Hz, 1 H), 7.28 (d, J = 7.5 Hz, 1 H), 7.65 (d, J = 1.7 Hz, 1 H). Anal. Calcd for $C_{15}H_{19}N_2O_2Cl$: C, 61.12; H, 6.45; N, 9.51. Found: C, 61.23; H, 6.31; N, 9.41.

O-Methylation of 1-Hydroxyindoles 7a and 7b. The methylation was carried out as described for **12g**. For **22**: yield 60%; mp 106 °C; ^1H NMR ($CDCl_3$) δ 1.52 (s, 9 H), 2.64 (s, 3 H), 3.97 (s, 3 H), 5.74 (br s, 1 H), 7.3–8.0 (m, 4 H). Anal. Calcd for $C_{15}H_{20}N_2O_2$: C, 69.29; H, 7.69; N, 10.77. Found: C, 69.18; H, 7.78; N, 10.59. For **24**: yield 60%; mp 88 °C (ether); ^1H NMR ($CDCl_3$) δ 1.46 (s, 9 H), 2.65 (s, 3 H), 2.84 (s, 3 H), 3.00 (s, 3 H), 5.72 (br s, 1 H), 6.77–6.86 (m, 2 H), 7.56 (d, 1 H). Anal. Calcd for $C_{16}H_{22}N_2O_3$: C, 66.20; H, 7.59; N, 9.63. Found: C, 65.95; H, 7.63; N, 9.63.

Registry No. **4a**, 7188-38-7; **4b**, 14542-93-9; **4c**, 931-53-3; **4d**, 598-45-8; **4e**, 3128-85-6; **5a**, 705-60-2; **5b**, 17354-63-1; **5c**, 4231-16-7; (*E*)-**5d**, 81928-74-7; (*Z*)-**5d**, 78727-98-7; **5e**, 31253-16-4; (*E*)-**5f**, 86969-36-0; (*Z*)-**5f**, 86969-74-6; **5g**, 19394-34-4; **5h**, 86969-37-1; **5i**, 18738-95-9; (*E*)-**5j**, 49571-79-1; (*Z*)-**5j**, 49571-78-0; **6a**, 3156-53-4; **6b**, 59832-12-1; (*E*)-**6c**, 86969-48-4; (*Z*)-**6c**, 86969-52-0; (*E*)-**6d**,

86969-49-5; (*Z*)-**6d**, 86969-53-1; **6e**, 23854-03-7; (*E*)-**6f**, 86969-50-8; (*Z*)-**6f**, 86969-54-2; (*E*)-**6g**, 61973-99-7; (*Z*)-**6g**, 61973-98-6; (*E*)-**6h**, 86969-51-9; (*Z*)-**6h**, 86969-55-3; **7a**, 74458-30-3; **7b**, 74458-31-4; **7c**, 74458-33-6; **7d**, 74458-36-9; **7j**, 86969-47-3; **8**, 74458-38-1; **9**, 74458-39-2; **10**, 74458-37-0; **11**, 86969-38-2; **12e**, 86969-39-3; **12f**, 86969-40-6; **12g**, 86969-41-7; **12h**, 86969-43-9; **12i**, 86969-45-1; **13g**, 86969-42-8; **13h**, 86969-44-0; **13i**, 86969-46-2; **14a**, 86969-61-1; **14b**, 86969-62-2; **15a**, 86969-63-3; **15b**, 86969-64-4; **16b**, 86969-65-5; **16c**, 86969-75-7; **17a**, 86993-46-6; **17b**, 86969-66-6; **17c**, 86969-67-7; **18**, 86969-68-8; (*E,E*)-**19a**, 86969-57-5; (*Z,E*)-**19a**, 86969-56-4; (*E,E*)-**19b**, 86969-58-6; (*Z,E*)-**19b**, 86969-59-7; (*Z,E*)-**19c**, 86969-60-0; (*Z,Z*)-**19c**, 86969-76-8; **20a**, 86969-69-9; **20b**, 86993-47-7; **20c**, 86969-70-2; **21**, 74458-42-7; **22**, 74458-40-5; **23**, 86969-71-3; **24**, 74458-41-6; **25**, 86969-72-4; **26**, 86969-73-5.

Supplementary Material Available: Mass spectral data for compounds **7**, **9**, and **14–20** (1 page). Ordering information is given on any current masthead page.

Novel Synthesis of the Pyrrolizidine Skeleton by Sulfenocycloamination. Total Synthesis of (±)-Retronecine and (±)-Turneforcidine†

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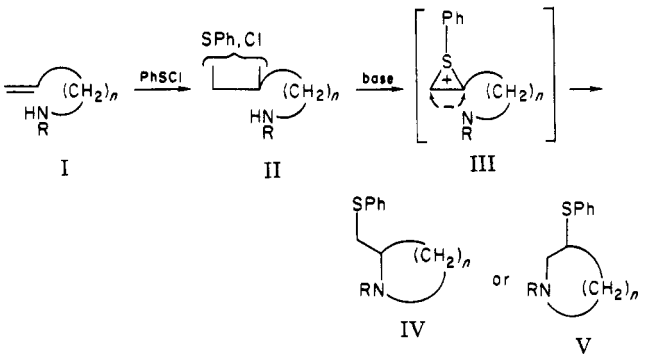
The ω-unsaturated amines **1**, **6**, and **7** were converted into pyrrolidines **4** and **8** and piperidine **9**, respectively, by treatment of their hydrochlorides with benzenesulfenyl chloride followed by base-induced ring closure. This novel sulfenocycloamination ring closure was applied to the synthesis of the pyrrolizidine ring (e.g., **20**) and to the total synthesis of (±)-retronecine (**32**) and (±)-turneforcidine (**34**).

In the past decade several new methods for forming C–N bonds have been devised. For example, ring closures of suitably substituted amines to nitrogen heterocycles have been effected by palladium chloride,[1] benzeneselenyl chloride,[2] mercuric acetate,[3,4] and sodium hydride–cuprous halides.[5] In our investigation of C–N bond-forming reactions we have focused on the use of benzenesulfenyl halides because of their strong electrophilicity for double bonds[6–8] and their ready availability. We now report on the cyclization of some ω-unsaturated alkenylamines (I), as shown in Scheme I. The ring closure, which can be called "sulfenocycloamination", probably proceeds via an *epi*-sulfonium ion III. We also report the application of this ring closure to a facile and efficient synthesis of the pyrrolizidine ring system,[9] culminating in the total synthesis of (±)-retronecine and (±)-turneforcidine.[10]

Sulfenocycloamination. As shown in Scheme I, there are two possibilities for ring formation: endo and exo cyclization. We examined these possibilities by running the sulfenocycloamination on amines with different chain lengths between the nitrogen and the olefinic group. In the reaction of benzenesulfenyl chloride with 3-butenylaniline (**1**),[11] (all reactions of benzenesulfenyl chloride were carried out on the amine hydrochlorides to avoid reaction with the basic amino nitrogen), a mixture of adducts **2a** and **2b** (Scheme II) was formed. Treatment of this mixture with potassium carbonate and sodium iodide gave the single product **4** in 90% overall yield. The reaction proceeds entirely by endo ring closure; there was no evidence for a four-membered ring product that would have resulted from exo closure. The fact that both **2a** and **2b** were converted into **4** is evidence for the common *epi*-sulfonium ion intermediate **3**. Although sodium iodide was not essential in the ring closure, the reaction was sluggish in its absence. Potassium hydroxide in benzene–water with tetrabutylammonium bromide as a phase-transfer catalyst[8] was examined in the ring closure, but the reaction did not give a clean result. The five-membered-ring structure of

Scheme I



† All compounds reported in this paper are racemic. For convenience, only one enantiomer is shown.

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