J = 14), 2.61 (1 H, dd, J = 4.8, 12), 2.30 (3 H, s), 2.29 (3 H, s), 2.26 (3 H, s), 2.24 (3 H, s), 2.13 (3 H, s), 2.04 (1 H, d, J = 12), 1.68 (3 H, s), 1.22 (3 H, s), 1.12 (3 H, s), 1.10 (3 H, s), 1.06 (3 H, s).

7: ^{1}H NMR (360 MHz, C_6D_6) δ 7.03 (1 H, bs), 6.8 (1 H, bs), 6.71 (1 H, bs), 6.67 (1 H, bs), 5.29 (1 H, bs), 3.44 (2 H, bs), 2.93 (2 H, d, J = 16), 2.89 (2 H, d, J = 7), 2.71 (1 H, bs), 2.47 (1 H, bd, J = 12), 2.15 (1 H, d, J = 12), 1.95 (3 H, s), 1.89 (3 H, s), 1.80 (3 H, s), 1.73 (3 H, s), 1.69 (3 H, s), 1.62 (3 H, s), 1.47 (3 H, s), 1.16 (3 H, s), 1.11 (3 H, s), 0.98 (3 H, s).

High-resolution mass spectra for 7: $M^+ - 2$ AcOH = m/z 488.2535 (calcd for $C_{31}H_{36}O_5$ 488.256), 488.2535 (1.3), 446.2419 ($C_{29}H_{34}O_4$, 1.5), 428.2350 ($C_{29}H_{32}O_3$, 1.0), 404.2345 ($C_{27}H_{32}O_3$, 2.4), 386.2029 ($C_{27}H_{30}O_2$, 2.8), 368.2120 ($C_{27}H_{28}O$, 1.2), 263.0847 ($C_{14}H_{15}O_5$, 70.1), 261.1079 ($C_{15}H_{17}O_4$, 55), 233.1427 ($C_{14}H_{17}O_3$, 19.2), 221.0811 ($C_{12}H_{13}O_4$, 100), 219.0871 ($C_{13}H_{15}O_3$, 86.7), 193.0845 ($C_{11}H_{13}O_3$, 15.7), 179.0709 ($C_{11}H_{15}O_2$, 89.0), 177.0819 ($C_{11}H_{13}O_2$, 51.6), 137.0612 ($C_8H_9O_2$, 18.4), 95.0853 (C_6H_7O, 57.0).

Silver Oxide Oxidation of 2 and 5. Ag_2O (100 mg) and Na_2SO_4 (80 mg) were added to the mixture of **2** and **5** (40 mg) in Et_2O (5 mL), and the suspension was stirred for 1 h. After filtration, the solution was evaporated to give 33 mg of a material that was purified by HPLC (10% AcOEt in isooctane): 7 and 4 mg were obtained.

Data for the first quinone (7 mg): IR (film) 3400, 1700, 1655, 1625, 1615 cm^{-1}; UV (MeOH) 252 nm (ϵ 10 000) 237 (8900); ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.55 (1 H, d, J = 2.5), 6.47 (1 H, d, J = 2.5), 5.91 (1 H, d, J = 1.8), 5.88 (1 H, d, J = 1.8), 5.24 (1 H, t, J = 7), 3.13 (2 H, bd, J = 7), 3.07 (2 H, s), 3.05 (1 H, d, J = 4), 2.69 (1 H, d, J = 15), 2.40 (1 H, dd, J = 3.9, 12), 2.06 (3 H, s), 1.98 (1 H, d, J = 12), 1.64 (3 H, s), 1.25 (3 H, s), 1.21 (3 H, s), 1.10 (3 H, s), 1.06 (3 H, s).

Data for the second quinone (4 mg): IR (film) 3400, 1705, 1650, 1625, 1615 cm^{-1}; UV (MeOH) λ_{max} 252 nm (ϵ 12 000) 237 (10 500); ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.54 (1 H, d, J = 2.5), 6.48 (1 H, d, J = 2.5), 5.98 (1 H, d, J = 1.8), 5.91 (1 H, d, J = 1.8), 5.22 (1 H, t, J = 6.5), 3.11 (2 H, bd, J = 7), 3.07 (2 H, s), 3.04 (1 H, d, J = 4.5), 2.7 (1 H, d, J = 15), 2.56 (1 H, dd, J = 4, 12.5), 2.05 (3 H, s), 1.93 (1 H, d, J = 12.5), 1.63 (3 H, s), 1.21 (3 H, s), 1.10 (6 H, bs), 1.06 (3 H, s).

Reduction of 3 with $LiAlH_4$. A cold solution of **3** (10 mg) in dry ether (1 mL) containing $LiAlH_4$ (15 mg) was stirred at 0 °C for 1.30 h. Excess reagent was destroyed by slow addition of EtOAc. Addition of a saturated $MgSO_4$ solution and extraction with ether yielded 8 mg of an oil that was chromatographed on HPLC (10% AcOEt in isooctane) to give 3 mg of the corresponding reduction product: IR (film) 3450, 1615, 1595 cm^{-1}; selected values, ^{1}H NMR (360 MHz, $CDCl_3$) δ 4.1 (1 H, m), 2.3 (2 H, d, J = 7), 2.04 (1 H, dd, J = 16, 6), 1.82 (1 H, dd, J = 16, 8.5), 1.27 (3 H, s), 1.17 (3 H, s), 1.08 (3 H, s), 1.03 (3 H, s).

Reduction of 6 with $LiAlH_4$. Reduction of the ketone of **6** (5 mg) was performed as described for **3**, and 1 mg of the reductive product was obtained after HPLC: IR (film) 3450, 1620, 1595 cm^{-1}; selected values, ^{1}H NMR (360 MHz, $CDCl_3$) δ 4.05 (1 H, m), 2.35 (2 H, d, J = 7), 2.0 (1 H, dd, J = 16, 9), 1.85 (1 H, dd, J = 16, 5), 1.23 (3 H, s), 1.12 (3 H, s), 1.09 (3 H, s), 1.04 (3 H, s).

Oxidative Cleavage of 3. To a solution of **3** (20 mg) in *tert*-butyl alcohol and hydrogen peroxide was added a catalytic amount of OsO_4 in *tert*-butyl alcohol (2.5 wt %) and the resultant mixture stirred at room temperature overnight. The reaction mixture was extracted with EtOAc. After removal of the solvent in vacuo, the resulting oil was treated with $PbO(Ac)_4$ in EtOAc during 2 h and after filtration, purified by rapid open-column chromatography. The main fraction (60% EtOAc/isooctane) was further purified by HPLC (30% EtOAc/isooctane), and the main product was submitted to CH_2N_2 in order to obtain the corresponding methyl ester **11**: 6 mg; IR (film) 1735 cm^{-1}; HRMS, M^+ m/z 314.726 (calcd for $C_{16}H_{16}O_6$ 314.1731); ^{1}H NMR (360 MHz, $CDCl_3$) δ 3.72 (3 H, s), 3.65 (3 H, s), 3.61 (3 H, s), 3.37 (1 H, dd, J = 12.5, 6.5), 2.75 (1 H, d, J = 15.7), 2.32 (1 H, bt, J = 12), 2.27 (1 H, d, J = 15.7), 2.23 (1 H, dd, J = 11.5, 6.5), 1.49 (3 H, s), 1.12 (3 H, s), 1.09 (3 H, s), 1.06 (3 H, s).

Oxidative Cleavage of 6. Oxidative cleavage of **6** (15 mg) with OsO_4 was performed as described above: IR (film) 1735 cm^{-1}; HRMS, M^+ m/z 314.722 (calcd for $C_{16}H_{16}O_6$ 314.1731); ^{1}H NMR (360 MHz, $CDCl_3$) δ 3.72 (3 H, s), 3.65 (3 H, s), 3.61 (3 H, s), 3.37 (1 H, dd, J = 12.5, 6.5), 2.75 (1 H, d, J = 15.7), 2.55 (1 H, bt, J = 12), 2.27 (1 H, d, J = 15.7), 2.24 (1 H, dd, J = 11.5, 6.5), 1.49 (3 H, s), 1.17 (3 H, s), 1.10 (3 H, s), 1.07 (3 H, s).

Mediterraneol C (8/9). The oily substance **9** was obtained from the main fraction after methylation of **8** by HPLC purification: 100 mg, 0.11% from dry weight alga; HRMS M^+ 482.3032 (calcd for $C_{30}H_{42}O_5$ 482.3029); IR (film) and UV (MeOH), similar to those obtained for **3**.

NMR ^{1}H–^{13}C shift correlation: the applied pulse sequence was (π/2, ^{1}H) – ($t_{1/2}$) – (π, ^{13}C) – ($t_{1/2}$) – τ_1 – (π/2, ^{1}H; π/2, ^{13}C) – τ_2 – (BB, ^{1}H; FID, t_2) with τ_1 = 3.3 ms and τ_2 = 1.67 ms. Spectral width in F_1 was W_1 = ±500 Hz, and in F_2, W_2 = 6024 Hz.

NMR ^{1}H–^{13}C long-range shift correlation: Pulse sequence identical with ^{1}H–^{13}C shift correlation above except τ_1 = τ_2 = 41.7 ms. The pulse sequence was optimized to give maximum polarization for J = 12 Hz and at the same time suppress ^1J = 144 Hz interactions.

Mediterraneol D (10/11). Repeated HPLC (8% EtOAc/isooctane) gave the pure oily substance: 125 mg, 0.14% from dry weight alga; HRMS, M^+ m/z 482.3033 (calcd for $C_{30}H_{42}O_5$ 482.3029); IR (film) and UV (MeOH), similar to those obtained for **6**.

^{1}H–^{13}C shift correlation: See above.

Acknowledgment. We thank Prof. L. Codomier for identifying *C. mediterranea*. B.B. is indebted to the "Fondation pour la Recherche Médicale" for financial support.

Synthesis of Substituted 1,2-Dihydroisoquinolines by the Intramolecular 1,3-Dipolar Alkyl Azide–Olefin Cycloaddition

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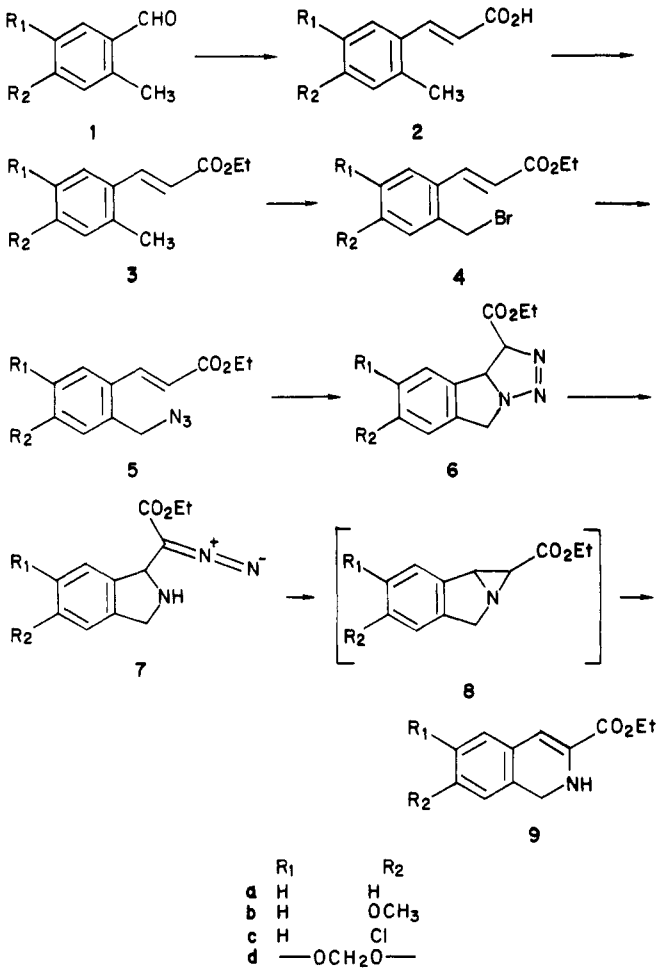
Received August 1, 1985

A general synthesis of substituted 1,2-dihydroisoquinolines based on intramolecular 1,3-dipolar cycloaddition of alkyl azides and olefins is described. Reaction of bromide **4** with sodium azide afforded azide **5**, which underwent 1,3-dipolar cycloaddition intramolecularly to give triazoline **6**. Rearrangement of triazoline **6** on silica gel gave diazo compound **7**. Treatment of **7** with rhodium acetate afforded substituted 1,2-dihydroisoquinoline **9** in good overall yield.

1,2-Dihydroisoquinolines are important heterocyclic systems.[1-3] Their use as the building blocks in the synthesis of alkaloids and medicinal compounds are indispensable to many preparations.[4] However, 1,2-dihydro-

0022-3263/86/1951-1120$01.50/0

Scheme I



isoquinolines have often been considered to be unstable species. Many of the substituted 1,2-dihydroisoquinolines are rather difficult to prepare and to purify. Common methods for the synthesis of 1,2-dihydroisoquinolines can be classified into two approaches: (1) reduction of isoquinolines or isoquinolinium salts[2] and (2) cyclization of (benzylamino)acetaldehyde dialkyl acetals.[1,3] In practice, the former method relies on an efficient preparation of the isoquinolines.[5] The latter method requires an electron-rich aromatic ring or a strong Lewis acid catalyst to facilitate the cyclization.[1,6]

Recently we reported a new 1,2-dihydroisoquinoline synthesis based on an intramolecular 1,3-dipolar cycloaddition of alkyl azides and olefins.[7] Herein, we report the extension and details of the method to the synthesis of substituted 1,2-dihydroisoquinolines.

As shown in Scheme I, Knoevenagel condensation of *o*-methylbenzaldehyde **1**[8] with malonic acid followed by decarboxylation gave cinnamic acid **2**. Esterification of **2** gave cinnamate ester **3**. Bromination of **3** with *N*-bromosuccinimide gave bromide **4**. Treatment of **4** with sodium azide in dimethylformamide afforded azide **5** at room temperature. Azide **5a** was isolated, however, contaminated with a small amount of **6a**, due to the partial cyclization of **5a** to **6a** at room temperature. On the other hand, intramolecular 1,3-dipolar cycloaddition of **5b**, **5c**, and **5d** occurred at 50–60 °C to give **6b**, **6c**, and **6d**. During the process of isolating **6**, most of compound **6** was isomerized to **7** on silica gel,[9] which accounted for the low isolated yield of **6**. Alternatively, heating **5** (except **5d**) in tetrahydrofuran solution followed by silica gel column chromatography afforded **7** (except **7d**) directly in 85% yield. Compound **5d**, which was not stable to heat, was stored at 5 °C for 10 days to give **6d** in 20% yield. The crude **6d** was passed through silica gel to give crude **7d**. Silica gel chromatography gave **7d** in 30% from **5d**. Treatment of **7** with rhodium acetate[10] in dry benzene at room temperature afforded the desired 1,2-dihydroisoquinolines **9**. Compund **9** was purified by silica gel chromatography and was found to be unstable in air. Compound **9a** could be further purified by sublimation for elemental analysis, but we have not been able to obtain satisfactory elemental analyses for **9b**, **9c**, and **9d**. High-resolution mass spectra of **9b**, **9c**, and **9d** all gave correct exact masses.

In summary, our method based on an intramolecular 1,3-dipolar cycloaddition reaction served as a new entry into 1,2-dihydroisoquinolines. It is compatible with various substituents on the benzene ring and therefore complementary to the other known methods. Starting from the readily available bromide **4**, the reaction only involved simple and mild reaction conditions, and generally gave good overall yields.

Experimental Section

General. IR spectra were recorded on Perkin-Elmer 710B or 580 infrared spectrometer. ^{1}H NMR spectra were recorded at 90 MHz on a Varian EM-390 NMR spectrometer or at 100 MHz on a JEOL FX-100 FT-NMR spectrometer. Data are reported in the following manner: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broadened, and m = unsolved multiplet), integration, coupling constant. ^{13}C NMR spectra were recorded on a JEOL FX-100 FT-NMR spectrometer at 25.02 MHz. Data was reported as follows: {^{1}H}^{13}C, chemical shift and multiplicity as obtained from the coupled spectra (s = singlet, t = triplet, q = quartet). Mass spectra were recorded on a JEOL TMS D-100 mass spectrometer. Mass spectra refer to the electron impact mass spectra. High-resolution mass spectra were recorded on a JEOL JMS DX-303 mass spectrometer. Melting points are determined with a Fisher-Johns melting point block and are uncorrected. Chromatography was performed as follows: silica gel, Merck #7736 Kieselgel 60H, was placed in a sintered-glass funnel packed dry. Solvent was flushed through the silica gel under water aspirator vacuum. The compound was deposited with a minimal amount of solvent and then eluted with solvent by using the water aspirator as the vacuum source. Ether and tetrahydrofuran (THF) were distilled from potassium/sodium metal under a nitrogen atmosphere with benzophenone ketyl as

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the indicator. Dimethylformamide (DMF) was distilled at reduced pressure from calcium hydride prior to use. All reactions were conducted under nitrogen atmosphere. Elemental analyses were carried out by analytical chemistry laboratory operated by the Chun-Shan Institute of Science and Technology, Lungtan, Taiwan, Republic of China.

Preparation of (*E*)-3-(2-Methylphenyl)-2-propenoic Acid (2). To a mixture of the appropriate aldehyde **1** (16 mmol) and malonic acid (35.4 mmol) in dry pyridine (60 mL) was added piperidine (0.5 mL). The mixture was refluxed for 18 h, then was cooled to room temperature, and poured into a 200-mL beaker containing concentrated hydrochloric acid (40 mL) and crushed ice (40 g). The solid was filtered, washed with 5% hydrochloric acid and water (2 × 30 mL), and recrystallized from 95% ethanol to give **2** as white needle crystals.

(*E*)-3-(2-Methylphenyl)-2-propenoic acid (2a): 61%; mp 175–176 °C; IR ($CHCl_3$) 1685, 1625 cm^{-1}; ^1H NMR ($CDCl_3$ + Me_2SO-d_6) δ 2.41 (s, 3 H), 6.22 and 6.39 (d, 1 H, J = 16 Hz), 7.10–7.30 (m, 2 H), 7.40–7.60 (m, 2 H), 7.82 and 7.98 (d, 1 H, J = 16 Hz); MS, m/e (relative intensity) 162 (100, M^+), 147 (37), 144 (41), 116 (49).

(*E*)-3-(4-Methoxy-2-methylphenyl)-2-propenoic acid (2b): 76%; IR (Nujol) 1690, 1600 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 2.36 (s, 3 H), 3.76 (s, 3 H), 6.19 and 6.36 (d, 1 H, J = 16 Hz), 6.64–6.84 (m, 2 H), 7.52–7.72 (m, 1 H), 7.64 and 7.80 (d, 1 H, J = 16 Hz); MS, m/e (relative intensity) 192 (100, M^+), 175 (11).

(*E*)-3-(4-Chloro-2-methylphenyl)-2-propenoic acid (2c): 76%; IR (Nujol) 1685, 1630 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 2.36 (s, 3 H), 6.32 and 6.48 (d, 1 H, J = 16 Hz), 7.16–7.72 (m, 3 H), 7.62 and 7.77 (d, 1 H, J = 16 Hz); MS, m/e (relative intensity) 196 (100, M^+), 198 (31, M^+ + 2), 181 (23), 178 (23), 150 (31).

(*E*)-3-[4,5-(Methylenedioxy)-2-methylphenyl]-2-propenoic acid (2d): 84%; IR (Nujol) 1685, 1605 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 2.33 (s, 3 H), 6.03 (s, 2 H), 6.23 and 6.33 (d, 1 H, J = 15.6 Hz), 6.85 (s, 1 H), 7.32 (s, 1 H), 7.67 and 7.83 (d, 1 H, J = 15.6 Hz); MS, m/e (relative intensity) 206 (100, M^+), 189 (9), 160 (9), 103 (36).

Preparation of Ethyl (*E*)-3-(2-Methylphenyl)-2-propenoate (3). Anhydrous ethanol (80 mL) saturated with hydrochloric acid gas was added to the appropriate compound **2** (5.2 mmol). The mixture was heated to reflux for 6 h, and then ca. 60 mL of solvent was removed on a rotary evaporator. The residue was extracted with ether (2 × 30 mL). The combined organic layers were washed with water (20 mL) and brine (20 mL) and dried ($MgSO_4$). Concentration gave an oil, which was purified by silica gel chromatography (4:1 hexane–ethyl acetate) to give **3**.

Ethyl (*E*)-3-(2-methylphenyl)-2-propenoate (3a): 99%; IR (neat) 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (t, 3 H, J = 7.0 Hz), 2.42 (s, 3 H, J = 7.0 Hz), 4.26 (q, 2 H, J = 7.0 Hz), 6.25 and 6.40 (d, 1 H, J = 16 Hz), 7.00–7.60 (m, 4 H), 7.86 and 8.01 (d, 1 H, J = 16 Hz); MS, m/e (relative intensity) 190 (55, M^+), 175 (20), 145 (100), 116 (50).

Ethyl (*E*)-3-(4-methoxy-2-methylphenyl)-2-propenoate (3b): 94%; IR (neat) 1713, 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (t, 3 H, J = 7.2 Hz), 2.44 (s, 3 H), 3.81 (s, 3 H), 4.20 (q, 2 H, J = 7.2 Hz), 6.16 and 6.32 (d, 1 H, J = 16 Hz), 6.60–6.80 (m, 2 H), 7.4–7.56 (m, 1 H), 7.80 and 7.96 (d, 1 H, J = 16 Hz); MS, m/e (relative intensity) 220 (100, M^+), 175 (55).

Ethyl (*E*)-3-(4-chloro-2-methylphenyl)-2-propenoate (3c): 86%; IR (KBr) 1720, 1635 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (t, 3 H, J = 7.0 Hz), 2.39 (s, 3 H), 4.24 (q, 2 H, J = 7.0 Hz), 6.20 and 6.36 (d, 1 H, J = 16 Hz), 7.04–7.48 (m, 3 H), 7.74 and 7.90 (d, 1 H, J = 16 Hz); MS, m/e (relative intensity) 224 (100, M^+), 226 (31, M^+ + 2), 181 (30), 179 (98).

Ethyl (*E*)-3-[4,5-(methylenedioxy)-2-methylphenyl]-2-propenoate (3d): 90%; IR (neat) 1710, 1630, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (t, 3 H, J = 7.2 Hz), 2.38 (s, 3 H), 4.24 (q, 2 H, J = 7.2 Hz), 5.93 (s, 2 H), 6.10 and 6.26 (d, 1 H, J = 16 Hz), 6.64 (s, 1 H), 7.00 (s, 1 H), 7.80 and 7.94 (d, 1 H, J = 16 Hz); MS, m/e (relative intensity) 234 (100, M^+), 220 (15), 189 (23). Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.66, H, 6.02. Found: C, 66.80; H, 5.96.

Preparation of Ethyl (*E*)-3-[2-(Bromomethyl)phenyl]-2-propenoate (4). To a mixture of the appropriate compound **3** (6 mmol) and *N*-bromosuccinimide (7.2 mmol) in carbon tetrachloride (40 mL) was added dibenzoyl peroxide (15 mg). The reaction mixture was heated to reflux for 6 h, then was diluted with dichloromethane (20 mL), and washed with water (2 × 15 mL) and brine (20 mL). The aqueous layer was extracted with dichloromethane (20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated. Silica gel chromatography (12:1 hexane–ethyl acetate) gave **4**.

Ethyl (*E*)-3-[2-(bromomethyl)phenyl]-2-propenoate (4a): 67.5%; IR ($CHCl_3$) 1705, 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (t, 3 H, J = 7.0 Hz), 4.25 (q, 2 H, J = 7.0 Hz), 4.55 (s, 2 H), 6.30 and 6.47 (d, 1 H, J = 16 Hz), 7.10–7.61 (m, 4 H), 7.92 and 8.08 (d, 1 H, J = 16 Hz); MS, m/e (relative intensity) 268 (6, M^+), 270 (6, M^+ + 2), 189 (100), 145 (17), 117 (36).

Ethyl (*E*)-3-[4-methoxy-2-(bromomethyl)phenyl]-2-propenoate (4b): 72%; IR ($CHCl_3$) 1705, 1635 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (t, 3 H, J = 7 Hz), 3.80 (s, 3 H), 4.26 (q, 2 H, J = 7 Hz), 4.53 (s, 2 H), 6.22 and 6.40 (d, 1 H, J = 16.2 Hz), 6.76–6.93 (m, 2 H), 7.48–7.60 (m, 1 H), 7.88 and 8.07 (d, 1 H, J = 16.2 Hz); MS, m/e (relative intensity) 298 (54, M^+), 300 (54, M^+ + 2), 219 (100). Anal. Calcd for $C_{13}H_{15}O_3Br$: C, 52.19; H, 5.05; Br, 26.71. Found: C, 52.98; H, 4.90; Br, 26.43.

Ethyl (*E*)-3-[4-chloro-2-(bromomethyl)phenyl]-2-propenoate (4c): 52%; IR (KBr) 1720, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.33 (t, 3 H, J = 7.0 Hz), 4.28 (q, 2 H, J = 7.0 Hz), 4.51 (s, 2 H), 6.30 and 6.48 (d, 1 H, J = 16.5 Hz), 7.30–7.57 (m, 3 H), 7.87 and 8.06 (d, 1 H, J = 16.5 Hz); MS, m/e (relative intensity) 302 (17, M^+), 304 (22, M + 2), 306 (6, M + 4), 225 (33).

Ethyl (*E*)-3-[4,5-(methylenedioxy)-2-(bromomethyl)-phenyl]-2-propenoate (4d): 75%; IR ($CHCl_3$) 1710, 1635, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (t, 3 H, J = 7.0 Hz), 4.24 (q, 2 H, J = 7.0 Hz), 4.52 (s, 2 H), 5.96 (s, 2 H), 6.19 and 6.34 (d, 1 H, J = 14.8 Hz), 6.80 (s, 1 H), 7.00 (s, 1 H), 7.84 and 8.00 (d, 1 H, J = 14.8 Hz); MS m/e (relative intensity) 312 (21, M^+), 314 (20, M + 2), 233 (60), 165 (100). Anal. Calcd for $C_{13}H_{13}O_4Br$: C, 49.86; H, 4.18; Br, 25.52. Found: C, 49.69; H, 4.42; Br, 25.33.

Preparation of Ethyl (*E*)-3-[2-(Azidomethyl)phenyl]-2-propenoate (5). A mixture of the appropriate compound **4** (1.68 mmol) and sodium azide (5.04 mmol) in dry dimethylformamide (10 mL) was stirred in dark for 1 h. After the removal of dimethylformamide, water (5 mL) was added, and the resulting mixture was extracted with ether (2 × 20 mL). The combined ether layers were dried ($MgSO_4$) and concentrated to give **5**.

Ethyl (*E*)-3-[2-(azidomethyl)phenyl]-2-propenoate (5a): 94%; ^1H NMR ($CDCl_3$) δ 1.32 (t, 3 H, J = 7 Hz), 4.24 (q, 2 H, J = 7 Hz), 4.44 (s, 2 H), 6.32 and 6.44 (d, 1 H, J = 16 Hz), 7.04–7.65 (m, 4 H), 7.80 and 7.96 (d, 1 H, J = 16 Hz).

Ethyl (*E*)-3-[4-methoxy-2-(azidomethyl)phenyl]-2-propenoate (5b): 96%; IR (KBr) 2090, 1710 cm^{-1}; ^1H NMR (C_6D_6) δ 1.07 (t, 3 H, J = 7.2 Hz), 3.23 (s, 3 H), 3.76 (s, 2 H), 4.13 (q, 2 H, J = 7.2 Hz), 6.25 and 6.43 (d, 1 H, J = 15.5 Hz), 6.53–6.67 (m, 2 H), 7.27–7.70 (m, 1 H), 7.93 and 8.10 (d, 1 H, J = 15.5 Hz); MS, m/e (relative intensity) 261 (1, M^+), 233 (17), 160 (100).

Ethyl (*E*)-3-[4-chloro-2-(azidomethyl)phenyl]-2-propenoate (5c): 90%; IR ($CHCl_3$) 2090, 1710 cm^{-1}; ^1H NMR (C_6D_6) δ 0.75 (t, 3 H, J = 7.0 Hz), 3.30 (s, 2 H), 3.80 (q, 2 H, J = 7.0 Hz), 5.87 and 6.00 (d, 1 H, J = 15 Hz), 6.47–6.93 (m, 3 H), 7.42 and 7.60 (d, 1 H, J = 15 Hz); MS, m/e (relative intensity) 265 (1, M^+), 237 (12), 164 (100), 153 (38).

Ethyl (*E*)-3-[4,5-(methylenedioxy)-2-(azidomethyl)-phenyl]-2-propenoate (5d): 90%; IR (KBr) 2100, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.36 (t, 3 H, M = 7.2 Hz), 4.28 (q, 2 H, J = 7.2 Hz), 4.45 (s, 2 H), 6.04 (s, 2 H), 6.20 and 6.36 (d, 1 H, J = 16 Hz), 6.82 (s, 1 H), 7.10 (s, 1 H), 7.76 and 7.92 (d, 1 H, J = 16 Hz); MS, m/e (relative intensity) 275 (6, M^+), 247 (38), 174 (88), 161 (100), 114 (53).

Preparation of 3-(Ethoxycarbonyl)-3,3a-dihydro-8*H*-[1,2,3]triazolo[5,1-*a*]isoindole (6). A solution of the appropriate compound **5** (except **5d**) (0.96 mmol) in dry tetrahydrofuran (10 mL) was stirred for 2 h at 60 °C. The solvent was then removed on a rotary evaporator. Silica gel chromatography (6:1 hexane–ethyl acetate) gave triazoline **6**, but most of triazoline **6** isomerized to diazo compound **7** on silica gel.

3-(Ethoxycarbonyl)-3,3a-dihydro-8*H*-[1,2,3]triazolo[5,1-*a*]isoindole (6a): 12%; IR ($CHCl_3$) 1740 cm^{-1}; ^1H NMR (CCl_4) δ 1.33 (t, 3 H, J = 7.0 Hz), 4.27 (q, 2 H, J = 7.0 Hz), 4.52, 4.70, 5.00, and 5.18 (AB q, 2 H), 5.18, 5.23, 5.27, and 5.32 (AB q, 2 H), 7.21 (s, 4 H); MS, m/e (relative intensity) 231 (8, M^+), 202 (20),

201 (20), 174 (40), 158 (30), 130 (40), 117 (100).

3-(Ethoxycarbonyl)-6-methoxy-3,3a-dihydro-8*H*-[1,2,3]-triazolo[5,1-*a*]isoindole (6b): 8%; IR ($CHCl_3$) 1730 cm^{-1}; ^1H NMR (C_6D_6) δ 0.94 (t, 3 H, J = 7.0 Hz), 3.26 (s, 3 H), 3.96 (q, 2 H, J = 7.0 Hz), 4.12 and 4.27 (d, 1 H, J = 15.6 Hz), 4.93 and 5.08 (d, 1 H, J = 15.6 Hz), 4.98 and 5.01 (d, 1 H, J = 2.9 Hz), 5.33 and 5.36 (d, 1 H, J = 2.9 Hz), 6.30–6.57 (m, 3 H); MS, m/e (relative intensity) 233 (67, M^+ – 28), 160 (92), 147 (100).

3-(Ethoxycarbonyl)-6-chloro-3,3a-dihydro-8*H*-[1,2,3]triazolo[5,1-*a*]isoindole (6c): 16%; IR ($CHCl_3$) 1730 cm^{-1}; ^1H NMR (C_6D_6) δ 0.9 (t, 3 H, J = 7.0 Hz), 3.80–4.10 (m, 3 H), 4.72–4.90 (m, 2 H), 5.17 and 5.26 (d, 1 H, J = 3 Hz), 6.17–6.93 (m, 3 H); MS, m/e (relative intensity) 237 (31, M^+ – 28), 164 (100), 151 (94).

Preparation of 3-(Ethoxycarbonyl)-5,6-(methylenedioxy)-3,3a-dihydro-8*H*-[1,2,3]triazolo[5,1-*a*]isoindole (6d). A solution of **5d** (50 mg, 0.18 mmol) in chloroform (10 mL) was stored in a refrigerator for 10 days at 5 °C. The solvent was then removed on a rotary evaporator. The residue was purified by the silica gel chromatography (4:1 hexane–ethyl acetate) to give **6d** (10 mg, 20%): IR (neat) 1737 cm^{-1}; ^1H NMR (C_6D_6) δ 0.90 (t, 3 H, J = 7 Hz), 3.94 (m, 3 H), 4.74–4.92 (m, 2 H), 5.16–5.32 (m, 3 H), 5.99 (s, 1 H), 6.07 (s, 1 H); MS, m/e (relative intensity) 275 (9, M^+), 247 (4), 174 (84), 164 (100), 161 (69).

Preparation of Ethyl 1,2-Dihydro-3*H*-isoindole-3-α-diazoacetate (7). A solution of the appropriate compound **5** (except **5d**) (1.61 mmol) in dry tetrahydrofuran (10 mL) was stirred for 2 h at 60 °C. The solvent was then removed on a rotary evaporator. The residue was passed through a silica gel column by a mixed solvent system (300 mL, 20:1 hexane–ethyl acetate). During this process, **5** was isomerized to **7**, the crude product was then purified by silica gel chromatography (2:1 hexane–ethyl acetate) to give pure **7** (except **7d**).

Ethyl 1,2-dihydro-3*H*-isoindole-3-α-diazoacetate (7a): 86%; IR (neat) 3375, 2980, 2075, 1670 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (t, 3 H, J = 7.0 Hz), 2.49 (br s, 1 H), 4.12–4.36 (m, 4 H), 5.55 (br s, 1 H), 7.20 (s, 4 H); ^{13}C NMR ($CDCl_3$) δ 14.5 (q), 51.2 (t), 55.4 (s), 59.0 (d), 60.6 (t), 122.5 (d), 122.8 (d), 127.0 (d), 127.7 (d), 138.9 (s), 140.5 (s), 166.2 (s); MS, m/e (relative intensity) 203 (21, M^+ – 28), 175 (17), 131 (25), 130 (24), 127 (100).

Ethyl 5-methoxy-1,2-dihydro-3*H*-isoindole-3-α-diazoacetate (7b): 84%; IR (KBr) 2090, 1680 cm^{-1}; ^1H NMR (C_6D_6) δ 1.0 (t, 3 H, J = 7 Hz), 2.32 (br, 1 H), 3.28 (s, 3 H), 3.64, 3.76, 3.88, and 4.03 (AB q, 2 H, J = 13 Hz), 4.10 (q, 2 H, J = 7 Hz), 5.48 (br s, 1 H), 6.44–7.12 (m, 3 H); MS, m/e (relative intensity) 233 (32, M – 28), 205 (22), 189 (16), 161 (22), 148 (100).

Ethyl 5-chloro-1,2-dihydro-3*H*-isoindole-3-α-diazoacetate (7c): 86%; IR ($CHCl_3$) 2090, 1690 cm^{-1}; ^1H NMR (C_6D_6) δ 0.97 (t, 3 H, J = 7.2 Hz), 2.13 (br, 1 H), 3.36, 3.53, 3.63, and 3.80 (AB q, 2 H, J = 15 Hz), 4.07 (q, 2 H, J = 7.2 Hz), 5.30 (br s, 1 H), 6.90 and 7.73 (m, 3 H); MS, m/e (relative intensity) 237 (13, M^+ – 28), 239 (4, M^+ + 2 – 28), 209 (15), 193 (14), 152 (100).

Preparation of Ethyl 5,6-(Methylenedioxy)-1,2-dihydro-3*H*-isoindole-3-α-diazoacetate (7d). A solution of **5d** (0.50 g, 1.8 mmol) in chloroform (10 mL) was stored in a refrigerator for 15 days at 5 °C; the solvent was then removed on a rotary evaporator. The residue was passed through a silica gel column by a mixed solvent system (300 mL, 20:1 hexane–ethyl acetate). During this process, compound **7d** was formed. Silica gel chromatography (2:1 hexane–ethyl acetate) gave pure **7d** (0.15 g, 30%): IR ($CHCl_3$) 2092, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (t, 3 H, J = 7.0 Hz), 2.64 (br, 1 H), 4.08–4.36 (m, 4 H), 5.44 (br s, 1 H), 5.92 (s, 2 H), 6.64 (s, 1 H), 6.68 (s, 1 H); MS, m/e (relative intensity) 275 (9, M^+), 247 (100), 175 (38), 174 (46), 173 (54), 162 (23), 161 (12).

Preparation of 3-(Ethoxycarbonyl)-1,2-dihydroisoquinoline (9). To a solution of the appropriate compound **7** (1.34 mmol) in dry benzene (15 mL) was added rhodium acetate (45 mg). The mixture was stirred in dark at room temperature for 10 h. The solvent was removed on a rotary evaporator. Silica gel chromatography (6:1 hexane–ethyl acetate) gave **9**.

3-(Ethoxycarbonyl)-1,2-dihydroisoquinoline (9a): 66%; IR ($CHCl_3$) 3450, 3040, 1660, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (t, 3 H, J = 7.0 Hz), 4.17 (q, 2 H, J = 7.0 Hz), 4.60 (s, 2 H), 5.15 (s, 1 H), 7.16–7.60 (m, 4 H), 8.16 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.6 (q), 51.0 (t), 58.4 (t), 74.8 (d), 121.2 (d), 122.3 (d), 127.2 (d), 129.8 (d), 134.9 (s), 141.0 (s), 160.5 (s), 170.6 (s); MS, m/e (relative intensity) 203 (100, M^+), 204 (18), 158 (15), 131 (94), 130 (14). Anal. Calcd for $C_{12}H_{13}O_2N$: C, 70.92; H, 6.45; N; 6.89. Found: C, 70.68; H, 6.72; N, 6.81.

3-(Ethoxycarbonyl)-7-methoxy-1,2-dihydroisoquinoline (9b): 62%; IR ($CHCl_3$) 3400, 1655, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.33 (t, 3 H, J = 7.2 Hz), 3.9 (s, 3 H), 4.23 (q, 2 H, J = 7.2 Hz), 4.7 (br s, 2 H), 5.16 (s, 1 H), 6.9–7.67 (m, 3 H), 8.27 (br, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.8 (q), 51.2 (t), 55.6 (q), 58.6 (t), 74.2 (d), 107.3 (d), 114.4 (d), 122.6 (d), 128.0 (s), 143.4 (s), 160.9 (s), 161.7 (s), 170.9 (s); MS, m/e (relative intensity) 233 (100, M^+), 188 (21), 161 (93); high-resolution mass spectrum, exact mass calcd for $C_{13}H_{15}NO_3$ (M^+), 233.1052, found 233.1036.

3-(Ethoxycarbonyl)-7-chloro-1,2-dihydroisoquinoline (9c): 56%; IR ($CHCl_3$) 3400, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.25 (t, 3 H, J = 7.0 Hz), 4.15 (q, 2 H, J = 7.0 Hz), 4.63 (br s, 2 H), 5.13 (s, 1 H), 7.33–7.6 (m, 3 H), 8.12 (br, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.7 (q), 51.0 (t), 58.8 (t), 75.8 (d), 122.5 (d), 123.0 (d), 128.0 (d), 133.9 (s), 136.2 (s), 142.8 (s), 159.5 (s), 170.6 (s); MS, m/e (relative intensity) 237 (100, M^+), 239 (34, M^+ + 2), 192 (16), 167 (27), 165 (71); high-resolution mass spectrum, exact mass calcd for $C_{12}H_{12}O_2N^{35}Cl$ (M^+) 237.0558, found 237.0540, calcd for $C_{12}H_{12}O_2N^{37}Cl$ (M^+), 239.0528, found 239.0518.

3-(Ethoxycarbonyl)-6,7-(methylenedioxy)-1,2-dihydroisoquinoline (9d): 37%; IR ($CHCl_3$) 3405, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.30 (t, 3 H, J = 7.2 Hz), 4.16 (q, 2 H, J = 7.2 Hz), 4.56 (s, 2 H), 5.00 (s, 1 H), 6.04 (s, 2 H), 6.84 (s, 1 H), 6.96 (s, 1 H), 8.14 (br, 1 H); ^{13}C NMR ($CDCl_3$) δ 14.8 (q), 51.2 (t), 58.6 (t), 74.3 (d), 101.4 (d), 101.7 (t), 102.8 (d), 128.9 (s), 136.4 (s), 147.8 (s), 150.2 (s), 161.0 (s), 170.8 (s); MS, m/e (relative intensity) 247 (100, M^+), 200 (14), 175 (25), 161 (14); high-resolution mass spectrum, exact mass calcd for $C_{13}H_{13}O_4N$ (M^+) 247.0845, found 247.0838.

Acknowledgment. We are grateful to the National Science Council of the Republic of China for the financial support. We thank Dr. Y. Itagaki and Mr. K. Nojima of JEOL LTD. for obtaining the high-resolution mass spectra.