A Facile One-Pot Operations of Reduction and Allylation of Nitrobenzaldehydes Mediated by Indium and Their Applications†

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Received April 2, 2002

Various nitrobenzaldehydes were simultaneously allylated and reduced using indium in the presence of HCl in aqueous media to give compounds having both functionality of homoallylic alcohol and aromatic amine. Sequential protection of the amino group and oxidation of the anilinyl homoallylic alcohol provided useful precursors of heterocyclic compounds such as dihydroindolones and dihydroquinolones, which could be efficiently synthesized through intramolecular cyclization reaction.

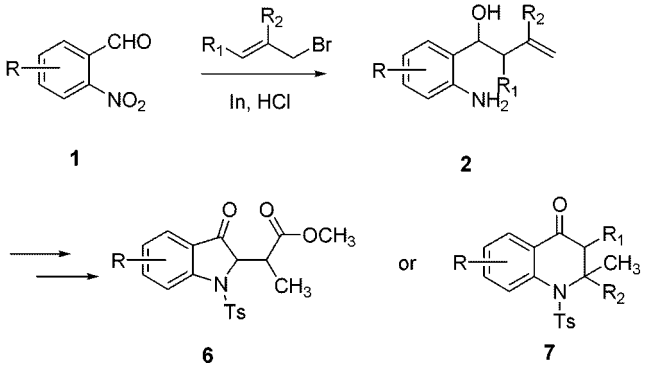
Key Words : Simultaneous reduction-allylation, Indium, Aqueous media

Introduction

Heterocycles such as quinolone, dihydroquinolone, indole, and dihydroindolone have been found in a variety of the biologically active compounds. Development of efficient synthetic protocol for these compounds is very important in organic and medicinal chemistry. Both metal-mediated allylation reactions[1] and reduction reactions of nitro group[2,3] are important processes frequently met in organic synthesis. Recently, we found that indium can mediate the reduction of nitro group to amine in the presence of HCl in aqueous THF.[4] Combining these two actions of indium, we have performed one-pot reduction and allylation reaction of nitro and aldehyde groups. Herein we report simultaneous reduction-allylation reactions of nitro and aldehyde groups of various nitrobenzaldehydes **1** in aqueous media to give anilinyl homoallylic alcohols **2** under a mild reaction condition (Scheme 1). The anilinyl homoallylic alcohols **2** could successfully transform into dihydroindolones **6** and dihydroquinolones **7** by using base without protection for the intramolecular cyclization.

Results and Discussion

The results of the reactions of various *o*-nitrobenzaldehydes were summarized in Table 1. The first three nitrobenzaldehydes were converted to the corresponding anilinyl homoallylic alcohol **2** in moderate yields (Entry 1-12). The 6-nitropiperonal in entry 13-16 gave low yields suggesting an unfavorable effect of electron-releasing substituents and labile moiety in acidic condition. In case of 3-methoxy-2-nitrobenzaldehyde (Entry 17-20), only the allylation products **3a-3d** were obtained in 88-94% yields, probably due

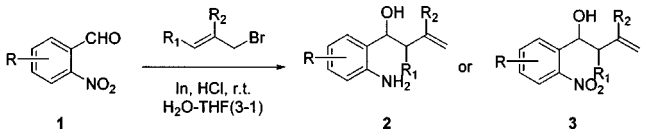


1 **2** **6** **7**

Scheme 1

†This paper is dedicated to the late Professor Sang Chul Shim.

Table 1. Allylation-Reduction Reactions of *o*-Nitrobenzaldehyde

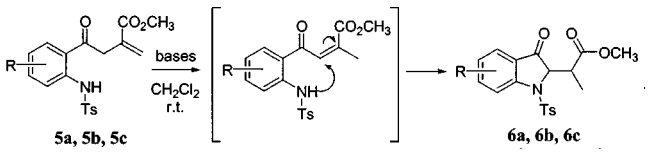


1 **2** **3**

Entry	R	Allyl bromides R_1	Allyl bromides R_2	Time (min)	Products (Yield %)[e]
1	H	H	H	15	**2a**(39)
2		CH_3	H	25	**2b**(78)
3		H	CO_2CH_3	30	**2c**(72)
4		H	CH_3	20	**2d**(60)
5	2-Cl[a]	H	H	15	**2e**(90)
6		CH_3	H	15	**2f**(76)
7		H	CO_2CH_3	15	**2g**(74)
8		H	CH_3	15	**2h**(79)
9	3-Cl[b]	H	H	30	**2i**(59)
10		CH_3	H	25	**2j**(66)
11		H	CO_2CH_3	30	**2k**(64)
12		H	CH_3	30	**2l**(54)
13	3,4-(OCH_2O)[c]	H	H	15	**2m**(22)
14		CH_3	H	15	**2n**(47)
15		H	CO_2CH_3	30	**2o**(27)
16		H	CH_3	30	**2p**(20)
17	3-OMe[d]	H	H	5	**3a**(88)
18		CH_3	H	15	**3b**(88)
19		H	CO_2CH_3	10	**3c**(91)
20		H	CH_3	15	**3d**(94)

[a]2-Chloro-6-nitrobenzaldehyde; [b]3-Chloro-2-nitrobenzaldehyde; [c]6-Nitropiperonal; [d]3-Methoxy-2-nitrobenzaldehyde; [e]Isolated yield.

Table 2. Intramolecular Cyclization of **5a**-**5c** in the Presence of Bases



1	H (**5a**)	DBU (2)	20	**6a**(45)
2	H (**5a**)	DIPEA (2)	4h	**6a**(88)
3	2-Cl (**5b**)	DBU (2)	20	**6b**(–)[b]
4	2-Cl (**5b**)	DIPEA (2)	10	**6d**(84)
5	3-Cl[a](**5c**)	DIPEA(2)	40	**6c**(67)

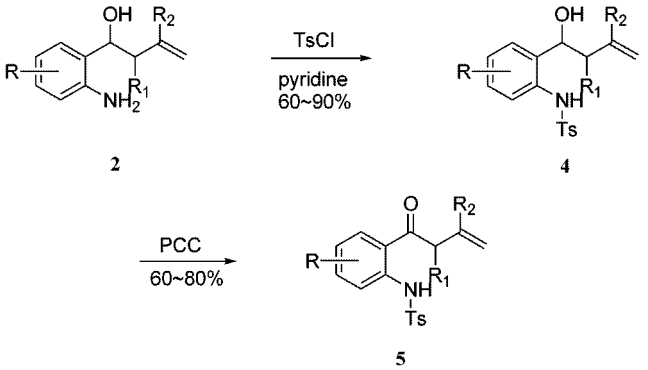
[a]Isolated yield; [b]No product was obtained

to the electron donating effect of the methoxy group at the 3-position.

Simultaneous reactions of allylation and reduction could be accomplished in the presence of HCl by indium. Without HCl, only the allylation of aldehyde group only proceeded indicating that HCl made a crucial role for the reduction. For example, the reaction between 3-chloro-2-nitrobenzaldehyde and allyl bromide by indium without HCl gave the only allylated product at room temperature for 12 h, along with 40% of the recovered starting material.

Various anilinyl homoallylic alcohols **2** generated were protected by tosylation with TsCl at 0 °C in pyridine for 4 h-12 h to afford the sulfonamides **4** in 62% to 97% yields. Sulfonamides **4** were oxidized with using PCC at rt for 4 h-12 h to give **5a-5i** in 44% to 91% yields (Scheme 2).

We carried out the intramolecular cyclization of **5a**, which has electron-defficient methoxycarbonyl moiety with 2 eq. of DBU as shown in entry 1 of Table 2. The 1,4-addition to α,β-unsaturated ester after migration of double bond by DBU occurred to give the five-membered dihydroindolone **6a** in moderate yield (45%). In case of **5b**, no product was

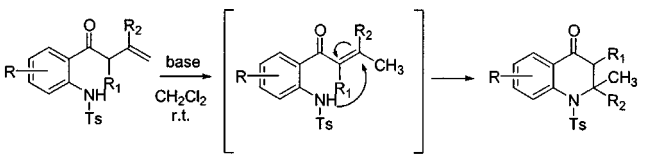


4a(78%):R=H,R_1=H, R_2=CO_2CH_3;
4b(76%):R=2-Cl,R_1=H, R_2=CO_2CH_3;
4c(62%):R=3-Cl,R_1=H, R_2=CO_2CH_3;
4d(80%):R=H, R_1=R_2=H;
4e(97%):R=3-Cl,R_1=R_2=H;
4f(87%):R=H, R_1=CH_3, R_2=H;
4g(92%):R=3-Cl, R_1=CH_3, R_2=H;
4h(89%):R=H, R_1=H, R_2=CH_3;
4i(94%):R=3-Cl, R_1=H, R_2=CH_3.

5a(84%):R=H,R_1=H, R_2=CO_2CH_3;
5b(65%):R=2-Cl,R_1=H, R_2=CO_2CH_3;
5c(85%):R=3-Cl,R_1=H, R_2=CO_2CH_3;
5d(73%):R=H, R_1=R_2=H;
5e(86%):R=3-Cl,R_1=R_2=H;
5f(44%):R=H, R_1=CH_3, R_2=H;
5g(70%):R=3-Cl, R_1=CH_3, R_2=H;
5h(71%):R=H, R_1=H, R_2=CH_3;
5i(77%):R=3-Cl, R_1=H, R_2=CH_3.

Scheme 2

Table 3. Intramolecular Cyclization of **5d**-**5i** in the Presence of DBU (2 eq.)



Entry	R	R_1	R_2	Time (min)	Products (Yield %)[a]
1	H	H	H	30	**7d**(77)
2	3-Cl	H	H	30	**7e**(78)
3	H	CH_3	H	90	**7f**(91)
4	3-Cl	CH_3	H	10	**7g**(86)
5	H	H	CH_3	50h[b]	**7h**(70)
6	3-Cl	H	CH_3	48h[b]	**7i**(76)

[a]Isolated yield; [b]Reaction mixture was refluxed at 40 °C in sealed tube.

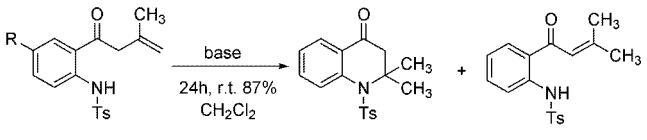
obtained (entry 3) that might be due to the strong basicity of DBU.

The intramolecular cyclizations were improved by using DIPEA (*i*-Pr_2NEt). Three substrates **5a**-**5c** smoothly proceeded to give the corresponding dihydroindolone rings **6a**-**6c** in 67-88% yields by using DIPEA (Table 2) through the migration of the double bond under the mild basic condition.

The intramolecular cyclizations of sulfonamides **5d-5i** generated from the other allyl bromides such as allyl bromide, 3-bromo-2-methylpropene, and crotyl bromide were also studied. As shown in Table 3, the dihydroquinolone rings could be obtained by Michael addition reaction of α,β-unsaturated ketones *in situ* generated by using DBU. Intramolecular cyclizations of **5d-5g** smoothly proceeded to give **7d-7g** at room temperature.

In case of **5h** and **5i**, which compounds have methylpropenyl moiety (entry 5, 6 Table 3), treatment with DBU at room temperature for 24 h gave both the cyclized product **7h** and **7i** and the migrated intermediate **8h** and **8i** in a ratio of 1 : 1.2 as shown in Scheme 3. These cyclizations could be completed to the corresponding product **7h** and **7**i at 40 °C in sealed tube for 48 h-50 h, respectively.

In conclusion, various substituted nitrobenzaldehydes underwent a simultaneous allylation and reduction reaction mediated by indum in the presence of HCl in aqueous media. Sequential protection and oxidation reactions of various anilinyl homoallylic alcohols provided useful precursors for the 5- and 6-membered heterocyclic compounds such as dihydroindolone or dihydroquinolone rings which could be efficiently obtained by intramolecular cyclization using DIEA or DBU.



Scheme 3

Experimental Section

All the commercially available reagents were obtained from Aldrich, Fluka, and generally used without further purification. Anhydrous procedures were performed with purified solvents. Reaction was performed under nitrogen atmosphere.

^{1}H NMR and ^{13}C NMR spectra were obtained on a Varian Gemini 300 and Bruker Advance 300 spectrometers. Nuclear magnetic resonance spectra were acquired at 300 (or 200) MHz for ^{1}H, and 75 MHz for ^{13}C. Infrared spectra were obtained on a Perkin Elmer 16FPC FT-IR spectrometer using KBr pellet, $CHCl_3$ or neat. GC/MSD were obtained on a Hewlett Packard 5890. HRMS spectra were obtained on a JMS-700 mass spectrometer (Jeol). Analytical thin layer chromatographies (TLC) were carried out on precoated silica gel plates (Merck Kieselgel 60F254, layer thickness 0.25 mm). Flash column chromatographies were conducted with silica gel grade 230-400 mesh (Merck Kiesegel 60 Art 9385).

Representative procedure for a simultaneous allylation and reduction reactions.

Synthesis of 1-(2-aminophenyl)but-3-en-1-ol (2a): 2-Nitrobenzaldehyde (40.5 mg, 0.27 mmol), indium (184 mg, 1.60 mmol) and allyl bromide (34.6 μL, 0.4 mmol) were dissolved in aqueous solution (H_2O-THF, v/v, 3 : 1, 3 mL) and concentrated HCl (37%, 180 mL) was added dropwise to the reaction mixture. After stirring for 5 min at room temperature, the reaction mixture was extracted with ethyl-acetate (10 mL × 2) and sequentially washed with saturated $NaHCO_3$, water, and brine. The combined organic layers were dried ($MgSO_4$), concentrated *in vacuo*, and purified by column chromatography to give product (17.6 mg, 39%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.56-2.75 (2H, m), 3.90 (2H, brs), 4.68 (1H, dd, J = 5.43 Hz, J = 8.49 Hz), 5.14 (1H, d, J = 5.58 Hz), 5.19 (1H, d, 13.9 Hz), 5.86 (1H, m), 6.65 (1H, d, J = 7.83 Hz), 6.73 (1H, t, J = 6.6 Hz), 7.04 (2H, overlap m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 41.3, 74.3, 118.1, 119.5, 127.7, 128.8, 129.9, 135.2; IR (neat, cm^{-1}) 3714, 3415, 3046, 2917; MS(EI) Anal. Calcd. for $C_{10}H_{13}NO$: 163.09. Found: 163.00.

1-(2-Aminophenyl)-2-methylbut-3-en-1-ol (2b): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.16 (3H, d, J = 6.66 Hz), 2.28 (1H, m), 3.7 (2H, brs), 4.45 (1H, d, J = 7.47 Hz), 4.96 (1H, d, J = 12.0 Hz), 5.02 (1H, d, J = 17.7 Hz), 5.72 (1H, m), 6.71 (2H, overlap m), 7.11 (2H, overlap m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 38.7, 41.6, 71.7, 116.4, 119.0, 124.2, 127.5, 131.2, 134.6, 145.1; IR (neat, cm^{-1}) 3704, 3418, 3045, 2950; MS(EI) Anal. Calcd. for $C_{11}H_{15}NO$: 177.11. Found: 177.00.

2-[2-(2-Aminophenyl)-2-hydroxyethyl]acrylic acid methyl ester (2c): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.67 (1H, dd, J = 9.09 Hz, 13.9 Hz), 2.81 (1H, dd, J = 3.6 Hz, 13.9 Hz), 3.74 (2H, brs), 3.78 (3H, s), 4.85 (1H, dd, J = 3.63 Hz, 9.12 Hz), 5.69 (1H, d, J = 1 Hz), 6.25 (1H, d, J = 1 Hz), 6.65 (1H, d, J = 7.92 Hz), 6.73 (1H, t, J = 7.47 Hz), 7.08 (1H, t, J = 7.74 Hz), 7.16 (1H, d, J = 6.09 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 39.3, 51.9, 71.0, 116.2, 117.9, 126.2, 127.4, 128.1, 128.3, 136.8, 143.9, 168.0; IR (KBr, cm^{-1}) 3405, 3335, 3246, 2957, 1715 (-C=O); MS (EI) Anal. Calcd. for $C_{12}H_{15}NO_3$: 221.10. Found: 221.00.

1-(2-Aminophenyl)-3-methylbut-3-en-1-ol (2d): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.82 (3H, s), 2.47 (1H, dd, J = 4.05 Hz, 10.5 Hz), 2.73 (1H, dd, J = 4.5 Hz, 9.87 Hz), 3.60 (2H, brs), 4.82 (1H, dd, J = 4.14 Hz, 11.0 Hz), 4.89 (1H, s), 4.95 (1H, s), 6.66 (1H, d, J = 7.86 Hz), 6.73 (1H, t, J = 6.33 Hz), 7.09 (2H, overlap m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.8, 44.4, 71.7, 116.9, 118.2, 127.3, 128.1, 128.5, 129.3, 143.0, 145.6; IR (KBr, cm^{-1}) 3365, 3286, 2937, 2997; MS(EI) Anal. Calcd. for $C_{11}H_{15}NO$: 177.11. Found: 177.10.

1-(2-Amino-6-chlorophenyl)but-3-en-1-ol (2e): ^{1}H NMR (300 MHz, $CDCl_3$) δ ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.52 (1H, m), 2.73 (1H, m), 4.72 (2H, brs), 5.14 (1H, d, J = 10.3 Hz), 5.19 (1H, d, J = 14.0 Hz), 5.88 (1H, m), 6.5 (1H, d, J = 8.04 Hz), 6.70 (1H, d, J = 7.89 Hz), 6.94 (1H, t, J = 7.98 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 38.9, 71.8, 116.8, 118.8, 124.2, 128.8, 129.0, 134.9, 143.0, 148.0; IR (neat, cm^{-1}) 3475, 3375, 3036, 2947; MS (EI) Anal. Calcd. for $C_{10}H_{12}NO$: 197.06. Found: 196.95.

1-(2-Amino-6-chlorophenyl)-2-methylbut-3-en-1-ol (2f): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.20 (3H, d, J = 6.78 Hz), 3.02 (1H, m), 3.38 (2H, brs), 4.90 (1H, d, J = 16.7 Hz), 4.95 (1H, d, J = 14.0 Hz), 5.87 (1H, m), 6.53 (1H, t, J = 7.41 Hz), 6.72 (1H, d, J = 7.98 Hz), 6.96 (1H, d, J = 8.73 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.6, 41.4, 75.3, 114.6, 116.5, 119.0, 120.2, 128.6, 134.0, 140.1, 147.2; IR (KBr, cm^{-1}) 3245, 3335, 3066, 2976, 2877; MS (EI) Anal. Calcd. for $C_{11}H_{14}ClNO$: 211.07. Found: 211.00.

2-[2-(2-Amino-6-chlorophenyl)-2-hydroxyethyl]acrylic acid methyl ester (2g): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.75 (1H, dd, J = 5.43 Hz, 13.8 Hz), 3.02 (1H, dd, J = 8.52 Hz, 13.7 Hz), 3.71 (3H, s), 4.22 (2H, brs), 5.55 (1H, overlap), 5.56 (1H, d, J = 1.4 Hz), 6.19 (1H, d, J = 1.35 Hz), 6.49 (1H, d, J = 8.01 Hz), 6.66 (1H, d, J = 7.98 Hz), 6.92 (1H, t, J = 7.95 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 37.5, 53.3, 71.5, 116.1, 116.7, 119.2, 124.0, 128.9, 134.1, 137.7, 148.2, 169.0; IR (KBr, cm^{-1}) 3405, 3296, 3146, 2957, 2847,1561; MS (EI) Anal. Calcd. for $C_{11}H_{14}ClNO$: 255.06. Found: 255.00.

1-(2-Amino-6-chlorophenyl)-3-methylbut-3-en-1-ol (2h): ^{1}H NMR (300 MHz, CD_3OD) δ ^{1}H NMR (300 MHz, CD_3OD) δ 1.79 (3H, s), 2.42 (1H, m), 2.65 (1H, m), 4.71 (1H, s), 4.77 (1H, s), 5.52 (1H, m), 6.61 (1H, t, J = 8.01 Hz), 6.79 (1H, d, J = 7.8 Hz), 7.10 (1H, d, J = 7.98 Hz); ^{13}C NMR (75 MHz, CD_3OD) δ 22.9, 42.7, 70.1, 116.0, 124.8, 129.0, 133.0, 142.9, 143.2, 148.2, 151.4; IR (KBr, cm^{-1}) 3395, 3325, 3266, 2777; MS (EI) Anal. Calcd. for $C_{11}H_{14}ClNO$: 211.07. Found: 211.00.

1-(2-Amino-5-chlorophenyl)but-3-en-1-ol (2i): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.59 (2H, m), 3.65 (2H, brs), 4.63 (1H, dd, J = 5.28 Hz, 8.31 Hz), 5.16 (1H, d, J = 10.1 Hz), 5.19 (1H, d, J = 17.0 Hz), 5.82 (1H, m), 6.57 (1H, d, J = 3.21 Hz), 7.02 (2H, overlap); ^{13}C NMR (75 MHz, $CDCl_3$) δ 39.6, 72.4, 117.8, 118.6, 122.6, 127.1, 128.1, 134.3, 143.4; IR (KBr, cm^{-1}) 3345, 3226, 2917; MS(EI) Anal. Calcd. for $C_{10}H_{12}ClNO$: 197.06. Found: 197.05.

1-(2-Amino-5-chlorophenyl)-2-methylbut-3-en-1-ol (2j): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.19 (3H, d, J = 6.6 Hz), 3.64 (2H, br s), 4.41 (1H, d, J = 6.4 Hz), 4.99 (1H, d, J = 12 Hz), 5.03 (1H, d, J = 17 Hz), 5.72 (1H, m), 6.57 (1H, d, J = 3.21 Hz), 7.02 (2H, overlap); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.9, 41.6, 76.9, 115.2, 122.5, 126.5, 128.1, 128.9, 140.1, 142.8; IR (KBr, cm^{-1}) 3415, 3276, 2947, 2847; MS (EI) Anal. Calcd. for $C_{11}H_{14}ClNO$: 211.07. Found: 211.00.

2-[2-(2-Amino-5-chlorophenyl)-2-hydroxyethyl]acrylic acid methyl ester (2k): ^{1}H NMR (300 MHz, CD_3COCD_3) δ 2.53 (1H, dd, J = 9.06 Hz, 13.9 Hz), 2.74 (1H, dd, J = 3.57 Hz, 14 Hz), 3.09 (2H, brs), 3.71 (3H, s), 4.73 (1H, dd, J = 3.42 Hz, 9 Hz), 5.67 (1H, s), 6.21 (1H, s), 6.55 (1H, d, J = 8.43 Hz), 6.96 (1H, d, J = 8.43 Hz), 7.12 (1H, s); ^{13}C NMR (75 MHz, CD_3COCD_3) δ 37.1, 51.1, 68.4, 116.6, 121.1, 124, 126.3, 127.0, 137.1, 140.9, 167.2; IR (KBr, cm^{-1}) 3365, 3216, 2986, 2827, 1696 ; MS(EI) Anal. Calcd. for $C_{12}H_{14}ClNO_3$: 255.06. Found: 255.01.

1-(2-Amino-5-chlorophenyl)-2-methylbut-3-en-1-ol (2l): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.81 (3H, s), 2.43 (1H, dd, J = 3.57 Hz, 13.8 Hz), 2.66 (1H, dd, J = 10.1 Hz, 13.9 Hz), 3.6 (2H, brs), 4.75 (1H, dd, J = 3.84 Hz, 9.96 Hz), 4.88 (1H, s), 4.96 (1H, s), 6.57 (1H, d, J = 8.7 Hz), 7.18 (1H, d, J = 2.4 Hz), 7.04 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.0, 44.1, 71.5, 118.1, 119.0, 127.3, 129.1, 129.3, 142.8, 144.3; IR (KBr, cm^{-1}) 3455, 3355, 3036, 2927; MS (EI) Anal. Calcd. for $C_{11}H_{14}ClNO$: 211.07. Found: 211.00.

1-(6-Aminobenzo[1,3]dioxol-5-yl)but-3-en-1-ol (2m): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.61 (1H, m), 4.67 (1H, dd, J = 5.49 Hz, 8.25 Hz), 5.14 (1H, d, J = 7.4 Hz), 5.19 (1H, d, J = 11.0 Hz), 5.79 (1H, m), 5.83 (2H, s), 6.28 (1H, s), 6.62 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 40.1, 72.0, 98.8, 100.6, 107.2, 118.3, 134.7, 139.7, 144.3, 147.8, 149.2; IR (neat, cm^{-1}) 3330, 3250, 2978; MS (EI) Anal. Calcd. for $C_{11}H_{13}NO_3$: 207.08. Found: 207.06.

1-(6-Aminobenzo[1,3]dioxol-5-yl)-2-methylbut-3-en-1-ol (2n): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.14 (3H, d, J = 6.66 Hz), 2.81 (1H, m), 3.30 (2H, brs), 4.40 (1H, d, J = 7.44 Hz), 4.97 (1H, d, J = 9.9 Hz), 5.11 (1H, d, J = 17.1 Hz), 5.80 (1H, m), 5.84 (2H, s), 6.23 (1H, s), 6.58 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.1, 42.7, 77.6, 100.5, 108.9, 114.8, 119.6, 139.7, 140.1, 140.5, 146.9; IR (neat, cm^{-1}) 3350, 3255, 2976; MS (EI) Anal. Calcd. for $C_{12}H_{15}NO_3$: 221.10. Found: 221.00.

2-[2-(6-Aminobenzo[1,3]dioxol-5-yl)-2-hydroxyethyl]-acrylic acid methyl ester (2o): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.62 (1H, dd, J = 9.06 Hz, 13.9 Hz), 2.78 (1H, dd, J = 3.54 Hz, 17.4 Hz), 3.70 (3H, brs), 4.80 (1H, dd, J = 3.57 Hz, 9.06 Hz), 5.71 (1H, s), 5.82 (2H, s), 6.24 (1H, s), 6.25 (1H, s), 6.72 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 39.9, 52.0, 70.3, 98.4, 100.5, 106.3, 120.0, 128.3, 136.8, 138.6, 140.0, 147.1, 168.0; IR (neat, cm^{-1}) 3385, 3256, 2976, 1688, 1646; MS (EI) Anal. Calcd. for $C_{13}H_{15}NO_5$: 265.09. Found: 265.00.

1-(6-Aminobenzo[1,3]dioxol-5-yl)-3-methylbut-3-en-1-ol (2p): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.75 (3H, s), 2.43 (1H, dd, J = 4.14 Hz, J = 13.6 Hz), 2.66 (1H, dd, J = 9.96 Hz, J = 10.7 Hz), 3.5 (2H, brs), 4.75 (1H, dd, J = 3.96 Hz, 9.66 Hz), 4.87 (1H, s), 4.93 (1H, s), 5.81 (2H, s), 6.25 (1H, s), 6.62 (1H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.3, 44.0, 70.1, 98.8, 100.6, 107.1, 113.9, 119.2, 139.9, 142.4, 146.9, 147.1; IR (neat, cm^{-1}) 3455, 3345, 2996, 2847; MS (EI) Anal. Calcd. for $C_{12}H_{15}NO_3$: 221.10. Found: 221.00.

1-(3-Methoxy-2-nitrophenyl)but-3-en-1-ol (3a): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.56 (2H, m), 3.67 (3H, s), 4.72 (1H, dd, J = 5.37 Hz, 8.46 Hz), 5.12 (1H, d, J = 9.2 Hz), 5.16 (1H, d, J = 17.0 Hz), 5.79 (1H, m), 6.70-6.74 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 39.7, 55.5, 72.6, 109.3, 117.2, 118.5, 119.3, 131.0, 133.5, 134.9, 147.5; IR (neat, cm^{-1}) 3365 (-OH), 2907(aromatic C-H), 1541, 1399 (-N=O).

1-(3-Methoxy-2-nitrophenyl)-2-methylbut-3-en-1-ol (3b): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.15 (3H, d, J = 6.7 Hz), 2.79 (1H, m), 3.81 (3H, s), 4.49 (1H, d, J = 7.2 Hz), 4.95 (1H, d, J = 8.9 Hz), 5.03 (1H, d, J = 17.1 Hz), 5.71 (1H, m), 6.65-6.72 (3H, m); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.0, 41.7, 55.4, 78.2, 108.9, 114.6, 116.6, 120.4, 134.0, 140.5, 147.5, 154.2; IR (neat, cm^{-1}) 3435, 3395, 3076, 2937,1501, 1277.

2-[2-Hydroxy-2-(3-methoxy-2-nitrophenyl)ethyl]acrylic acid methyl ester (3c): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.67 (1H, dd, J = 9.09 Hz, J = 14.0 Hz), 2.81 (1H, dd, J = 3.63 Hz, J = 14.0 Hz), 3.7 (3H, s), 3.83 (3H, s), 4.86 (1H, dd, J = 3.57 Hz, J = 9.06 Hz), 5.68 (1H, s), 6.23 (1H, s), 6.70-6.80 (2H, overlap H), 6.81 (1H, d, J = 7.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.2, 43.5, 55.5, 70.9, 109.3, 113.6, 117.1, 119.2, 126.9, 134.6, 142.5, 147.5; IR (KBr, cm^{-1}) 3490, 3390, 2744, 1496, 1297, 1222.

1-(3-Methoxy-2-nitrophenyl)-3-methylbut-3-en-1-ol (3d): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.81 (3H, s), 2.46 (1H, dd, J = 3.84 Hz, J = 14.0 Hz), 2.73 (1H, dd, J = 10.0 Hz, 13.9 Hz), 3.84 (3H, s), 3.84 (1H, dd, J = 4.11 Hz, 9.87 Hz), 4.88 (1H, s), 4.93 (1H, s), 6.68-6.76 (3H, overlap); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.2, 43.5, 55.5, 70.9, 109.3, 113.6, 117.1, 119.2, 126.9, 134.6, 142.5, 147.5, 154.2; IR (neat, cm^{-1}) 3176, 2907, 1501 (-N=O), 1247 (-N=O).

Representative intramolecular cyclization procedure: Synthesis of 6a.

2-{2-Hydroxy-2-[2-(*p*-toluenesulfonylamino phenyl]ethyl}-acrylic acid methyl ester (4a): To a stirred solution of **2c** (51.4 mg, 0.23 mmol) in 3 mL of pyridine was added TsCl (88.6 mg, 0.46 mmol) under N_2 atmosphere. The reaction mixture was stirred at room temperature for about 12 h. The mixture was poured into the cooled water, and extracted with methylene chloride. The combined organic layer was dried ($MgSO_4$), concentrated and purified over silica gel to give 87.4 mg (78%) of tosylate. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.33 (3H, s), 2.47 (2H, d, J = 6.48 Hz), 3.35 (1H, d, J = 3.18 Hz), 3.76 (3H, s), 4.78 (1H, m), 5.44 (1H, s), 6.15 (1H, d, J = 1.2 Hz), 6.98-7.17 (3H, overlap H), 7.18 (2H, d, J = 8.01 Hz), 7.42 (1H, d, J = 7.95 Hz), 7.67 (2H, d, J = 8.25 Hz), 8.58 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.9, 41.2, 52.7, 60.8, 122.2, 124.9, 127.5, 127.6, 128.7, 129.4, 130.0, 133.3, 135.5, 136.6, 137.4, 144.1; IR (neat, cm^{-1}) 3482, 3238, 1718, 1710, 1340, 1158, 928.

2-{2-Oxo-2-[2-(*p*-toluenesulfonylamino)phenyl]ethyl} acrylicacid methyl ester (5a): To a stirred solution of **4a**

(33.6 mg, 0.0895 mmol) in 10 mL of CH_2Cl_2. was added 20 mg of silica gel and PCC (38.6 mg, 0.179 mmol). After stirring for 16 h at room temperature, the reaction mixture was filtered through celite pad. The solvent was removed *in vacuo*. The residue was purified by flash chromatography over silica gel to yield 28 mg (84%) of product. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.19 (3H, s), 3.87 (3H, s), 3.98 (2H, s), 5.63 (1H, s), 6.4 (1H, s), 7.0-7.88 (8H, overlap H), 11.25 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.6, 43.1, 52.6, 119.3, 123.0, 124.9, 127.6, 129.3, 130.0, 131.6, 133.2, 134.4, 136.6, 140.6, 140.3, 167.1; IR (neat, cm^{-1}) 3124, 1726, 1650, 1334, 1160.

2-[3-Oxo-1-(*p*-toluenesulfonyl)-2,3-dihydro-*1H*-indol-2-yl]propionic acid methyl ester (6a): To a stirred solution of **5a** (63.6 mg, 0.14 mmol) in 3 mL of methylene chloride was added 60 mL (0.34 mmol) of DIPEA. After stirring for 4 hour at rt, the reaction mixture was quenched by 1 mL of water and extracted with CH_2Cl_2. The organic layer was dried, concentrated, and purified over silica gel to give 47 mg (88%) of dihydroindolone product **6a**. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.26 (3H, d, J = 9.03 Hz), 2.35 (3H, s), 3.67 (1H, m), 3.73 (3H, s), 4.22 (1H, d, J = 2.46 Hz), 7.20-8.1 (8H, overlap H of another isomer); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.6, 21.9, 43.4, 52.6, 68.1, 117.6, 124.6, 125.2, 125.7, 127.8, 130.4, 130.5, 137.5, 145.6, 153.7, 173.7, 197.3.; IR (neat, cm^{-1}) 1724, 1602, 1364, 1174.; HRMS (EI) Anal. Calcd. for $C_{19}H_{19}NO_5S$: 373.0984. Found: 373.0991.

2-[4-Chloro-3-oxo-1-(*p*-toluenesulfonyl)-2,3-dihydro-1*H*-indol-2-yl]propionic acid methyl ester (6b): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.32 (3H, d, J = 7.26 Hz), 2.37 (3H, s), 3.50 (1H, m), 3.72 (3H, s), 4.22 (1H, d, J = 2.49 Hz), 7.13 (1H, d, J = 8.19 Hz), 7.23 (3H, overlap of proton), 7.52-7.62 (4H, overlap of protons); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.4, 21.5, 43.3, 52.2, 67.8, 115.2, 126.1, 127.4, 130.1, 132.1, 132.4, 136.9, 145.5, 154.6, 173.1, 194.0; IR (neat, cm^{-1}) 1730, 1590, 1366, 1174.; HRMS (EI) Anal. Calcd for $C_{19}H_{18}ClNO_5S$: 409.0565. Found: 409.0560.

2-[5-Chloro-3-oxo-1-(*p*-toluenesulfonyl)-2,3-dihydro-1*H*-indol-2-yl]propionic acid methyl ester (6c): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.30 (3H, d, J = 6.48 Hz), 2.37 (3H, s), 3.52 (1H, m), 3.71 (3H, s), 4.15 (1H, d, J = 2.64 Hz), 7.23-8.06 (7H, overlap with isomer respectively); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.1, 21.9, 43.8, 52.7, 68.5, 118.9, 124.1, 127.8, 130.5, 131.2, 132.8, 137.6, 145.9, 151.9, 173.6, 196.1; IR (neat, cm^{-1}) 1728, 1602, 1366, 1174, 1130; HRMS (EI) Anal. Calcd. for $C_{19}H_{18}ClNO_5S$: 407.0594. Found: 407.0591.

2-Methyl-1-(*p*-toluenesulfonyl)-2,3-dihydro-1*H*-quinolin-4-one (7d): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.26 (3H, d, J = 6.45 Hz), 2.23 (1H, d, J = 19.4 Hz), 2.29 (1H, overlap), 2.38 (3H, s), 4.89 (1H, m), 7.21 (2H, d, J = 6.3 Hz), 7.29 (2H, overlap m), 7.55 (2H, d, J = 12.9 Hz), 7.60 (1H, t, J = 8.55 Hz), 7.91 (1H, t, J = 8.28 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.5, 21.5, 41.9, 51.8, 125.3, 125.6, 126.3, 126.8, 127.0, 130.0, 134.9, 136.5, 139.6, 144.4, 192.4.; IR (neat, cm^{-1}) 1688, 1350**,** 1168; HRMS (EI) Anal. Calcd. for $C_{17}H_{17}NO_3S$: 315.0929. Found: 315.0929.

6-Chloro-2-methyl-1-(*p*-toluenesulfonyl)-2,3-dihydro-1*H*-quinolin-4-one (7e): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.27 (3H, d, J = 6.9 Hz), 2.25 (1H, d, J = 1.83 Hz), 2.29 (1H, d, J = 5.52 Hz), 2.36 (3H, s), 4.87 (1H, m), 7.23 (2H, d, J = 8.19 Hz), 7.51 (2H, d, J = 6.15 Hz), 7.54 (1H, d, J = 9.15 Hz), 7.87 (1H, d, J = 8.01 Hz), 7.88 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.4, 21.5, 41.5, 51.8, 77.1, 126.1, 126.6, 126.8, 127.8, 130.1, 131.6, 134.6, 136.2, 138.0, 144.6, 191.2; IR (neat, cm^{-1}) 1694, 1470, 1354, 1166.; HRMS (EI) Anal. Calcd. for $C_{17}H_{16}ClNO_3S$: 349.0539. Found: 349.0539.

2,3-Dimethyl-1-(*p*-toluenesulfonyl)-2,3-dihydro-1*H*-quinolin-4-one (7f): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.05 (3H, d, J = 6.84 Hz), 1.16 (3H, d, J = 6.9 Hz), 2.38 (3H, s), 2.54 (1H, m), 4.79 (1H, m), 7.19 (4H, overlap), 7.57 (1H, t, J = 9.15 Hz), 7.59 (2H, d, J = 8.25 Hz), 7.90 (1H, t, J = 8.37 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.2, 13.8, 21.5, 44.2, 57.3, 124.8, 124.9, 124.99, 126.7, 127.2, 129.9, 134.6, 137.1, 139.7, 144.3, 195.2; IR (KBr, cm^{-1}) 1684, 1596, 1356, 1166; HRMS (EI) Anal. Calcd. for $C_{18}H_{19}NO_3S$: 329.1086. Found: 329.1074.

6-Chloro-2,3-dimethyl-1-(*p*-toluenesulfonyl)-2,3-dihydro-1*H*-quinolin-4-one (7g): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.04 (3H, d, J = 6.9 Hz), 1.12 (3H, d, J = 6.24 Hz), 2.39 (3H, s), 2.48 (1H, m), 4.76 (1H, m), 7.25 (2H, d, J = 8.07 Hz), 7.49 (1H, d, J = 2.52 Hz), 7.59 (2H, d, J = 8.25 Hz), 7.87 (3H, overlap); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 11.5, 14.2, 22.0, 44.6, 57.8, 126.1, 126.9, 127.1, 127.2, 130.5, 131.5, 134.8, 137.2, 138.6, 145.0, 194.6; IR (KBr, cm^{-1}) 1694, 1594, 1354, 1164.; HRMS (EI) Anal. Calcd. for $C_{18}H_{18}ClNO_3S$: 363.0696. Found: 363.0691.

2,2-Dimethyl-1-(*p*-toluenesulfonyl)-2,3-dihydro-1*H*-quinolin-4-one (7h): To a stirred solution of **5h** (20.8 mg, 0.06 mmol) in 3 mL of methylene chloride was added 18 mL (0.12mmol) of DBU. After stirring for 50 h at reflux, the reaction mixture was quenched by 1 mL of water and extracted with CH_2Cl_2. The organic layer was dried, concentrated, and purified over silica gel to give 48 mg (70%) of the cyclized product **7h**. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.46 (6H, s), 2.29 (2H, s), 2.42 (3H, s), 7.26 (2H, d, J = 7.6 Hz), 7.44 (2H, d, J = 7.54 Hz), 7.56 (1H, d, J = 7.7 Hz), 7.70 (1H, d, J = 8.6 Hz), 7.94 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.4, 21.5, 27.9, 48.9, 60.4, 121.7, 122.7, 126.9, 129.5, 130.7, 134.1, 142.7, 144.1, 194.1; IR (neat, cm^{-1}) 1690, 1598, 1354, 1162.; HRMS (EI) Anal. Calcd. for $C_{18}H_{19}NO_3S$: 329.1086. Found: 329.1091.

6-Chloro-2,2-dimethyl-1-(*p*-toluenesulfonyl)-2,3-dihydro-1*H*-quinolin-4-one (7i): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.44 (6H, s), 2.25 (2H, s), 2.41 (3H, s), 7.24 (2H, d, J = 7.56 Hz), 7.43 (2H, d, J = 7.68 Hz), 7.57 (1H, d, J = 7.71 Hz), 7.70 (1H, d, J = 8.79 Hz), 7.90 (1H, s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.0, 29.7, 30.0, 49.0, 60.9, 126.6, 127.6, 129.9, 130.0, 130.5, 132.3, 133.5, 134.4, 138.4, 141.6, 144.8, 193.3.; IR (neat, cm^{-1}) 1692, 1466, 1356, 1164; HRMS (EI) Anal. Calcd. for $C_{18}H_{18}ClNO_3S$: 363.0696. Found: 363.0691.

Acknowledgment. This work was supported by grants from "Critical Technology 21" of the Korea Ministry of Science and Technology

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