Baylis-Hillman Reaction of Isatin Derivatives: Isatins as a New Entry for the Baylis-Hillman Reaction

Yun Mi Chung, Yang Jin Im, and Jae Nyoung Kim*

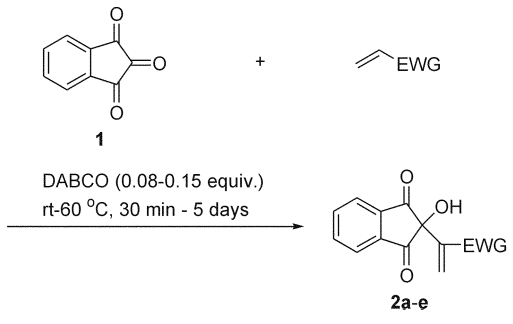
Department of Chemistry and Institute of Basic Science, Chonnam National University, Gwangju 500-757, Korea
Received July 18, 2002

Key Words : Baylis-Hillman reaction, Ninhydrin, Isatins, *N*-Acylisatins

The Baylis-Hillman reaction is well known as a coupling reaction of activated vinyl compounds and aldehydes or *N*-sulfonylimines.[1] Besides aldehydes and *N*-sulfonylimines, substituted ketones with electron withdrawing substituents can be used specially in the Baylis-Hillman reaction.[1b,2] Simple ketones such as acetone showed sluggish reactivity in the normal Baylis-Hillman reaction conditions.[1b] High pressure or special techniques must be needed. However, activated ketones such as halogenated ketones, α-diketones, α-keto esters and α-keto lactones can generate the corresponding Baylis-Hillman adducts under normal reaction conditions.[2]

Activated ketones with another carbonyl group such as ninhydrin (1,2,3-indanetrione) or isatin have never been studied systematically.[3] Only one report dealing with the Baylis-Hillman reaction of ninhydrin and methyl acrylate was studied.[3a] During the course of our studies on the Baylis-Hillman reaction[4] we intended to study on the Baylis-Hillman reaction of activated ketones such as ninhydrin, isatin, alloxan and parabanic acid.[3b] We thought that the reaction would proceed without difficulty. The adducts derived from these compounds have interesting backbone for further transformation in order to prepare biologically important compounds.[4,5]

Initially, the reaction of ninhydrin (**1**) with acrylates was carried out without additional solvent by using DABCO as a catalyst. Ethyl- or methyl acrylate was used as a solvent and we could obtain the adducts **2a** and **2b** in reasonable yields (Scheme 1, Table 1). For alkyl vinyl ketones, methylene chloride must be used for reasonable yields of products. Otherwise, severe contamination with dimer or polymers of the used alkyl vinyl ketones was observed. When we used acrylonitrile as the activated alkene, complex mixtures were observed in various reaction conditions. Among the conditions, the best result was observed when we used DMF as solvent (entry 5).



Scheme 1

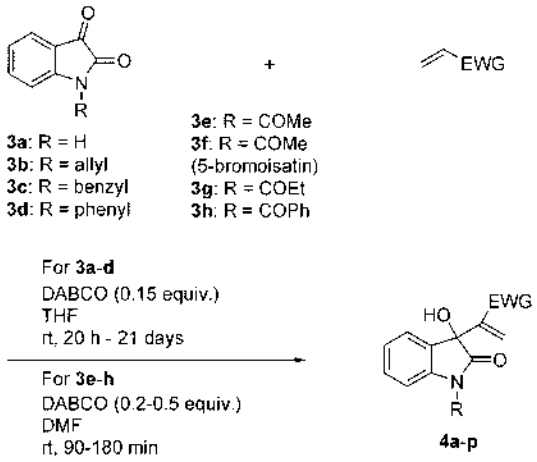
We examined the Baylis-Hillman reaction of isatin and its derivatives also. Various solvents were examined for the solubility problem of starting materials. Reasonable results were observed for isatin (**3a**), *N*-alkyl isatins (**3b** and **3c**) or *N*-phenylisatin (**3d**) in THF. When the substrates have good solubility in methyl acrylate such as **3b-d**, additional solvent was not necessary (see, Table 2).

However, for *N*-acetylisatin (**3e**) we could not obtain good results without solvent. As an example, we could obtain the desired product **4j** in 11% isolated yield after 42 days when the reaction was performed without solvent. Unfortunately, however, the use of THF, methylene chloride or ethanol gave complex mixtures of products. After scrutinizing the obtained side products in the reaction and literature survey, we concluded that *N*-acetylisatin is unstable toward nucleophilic solvent. Especially, nucleophilic solvents such as methanol, ethanol or water cannot be used for *N*-acetylisatin. The labile

Table 1. Synthesis of the Baylis-Hillman adducts of ninhydrin **1**

Entry	Alkenes[a]	Conditions	Product	Yield (%)
1	COOMe	DABCO (0.1 equiv.) 50-60 °C, 60 min	**2a**	86
2	COOEt	DABCO (0.1 equiv.) 50-60 °C, 60 min	**2b**	82
3	COMe	DABCO (0.15 equiv.) CH_2Cl_2, rt, 90 min	**2c**	71
4	COEt	DABCO (0.15 equiv.) CH_2Cl_2, rt, 30 min	**2d**	64
5	CN	DABCO (0.08 equiv.) DMF, rt, 5 days	**2e**	25

[a]Methyl- or ethyl acrylate was used as solvent. In other cases 1.5 equiv. of alkenes were used.



Scheme 2

Table 2. Synthesis of Baylis-Hillman adducts of isatin (**3a**) and their alkyl or aryl derivatives **3b-d**

Conditions[a]	Product	Conditions[a]	Product
methyl acrylate DABCO (0.15 equiv.) THF, rt, 5 days	**4a** (63%)	methyl acrylate DABCO (0.15 equiv.) rt, 5 days	**4f** (50%)
ethyl acrylate DABCO (0.15 equiv.) THF, rt, 8 days	**4b** (71%)	acrylonitrile DABCO (0.15 equiv.) THF, rt, 20 h	**4g** (94%)
acrylonitrile DABCO (0.15 equiv.) THF, rt, 4 days	**4c** (69%)	methyl acrylate DABCO (0.15 equiv.) rt, 9 days	**4h** (87%)
methyl acrylate DABCO (0.15 equiv.) rt, 21 days	**4d** (64%)	acrylonitrile DABCO (0.15 equiv.) THF, rt, 25 h	**4i** (79%)
acrylonitrile DABCO (0.15 equiv.) THF, rt, 8 days	**4e** (81%)		

[a]For the synthesis of **4d**, **4f** and **4h** methyl acrylate was used as solvent. In other cases the alkene substrate was used in 1.5 equiv.

property of *N*-acetyl- or *N*-tosylisatin toward nucleophiles such as ammonia, amines, alcohols and hydroxylamine has been reported.[6] Ring opening reaction by the nucleophile at the N_1-C_2 bond of these compounds can occur easily.[6] After many trials we eventually found the best conditions for the Baylis-Hillman reaction of *N*-acylisatin derivatives **3e-h**: *(1) The use of N,N-dimethylformamide as a solvent, (2) the use of somewhat larger amounts of DABCO catalyst (0.2-0.5 equiv.), and (3) short reaction time*. The results are shown in Table 3. Quite recently, Garden and Skakle have reported on the Baylis-Hillman reaction of isatin derivatives.[3c] They used ethanol or ethanol/THF system as solvents and examined on the reaction of isatin, *N*-methylisatin and *N*-benzylisatin. They did not examine the reaction with *N*-acetylisatin or

Table 3. Synthesis of Baylis-Hillman adducts of *N*-acylisatins **3e-h**

Entry	Isatins	Conditions[a]	Product	Yield (%)
1	**3e**	DABCO (0.2 equiv.) methyl acrylate DMF, rt, 120 min	**4j**	58[b]
2	**3e**	DABCO (0.2 equiv.) acrylonitrile DMF, rt, 120 min	**4k**	70[c]
3	**3f**	DABCO (0.2 equiv.) methyl acrylate DMF, rt, 100 min	**4l**	59
4	**3f**	DABCO (0.2 equiv.) acrylonitrile DMF, rt, 90 min	**4m**	50
5	**3g**	DABCO (0.5 equiv.) methyl acrylate DMF, rt, 180 min	**4n**	55
6	**3g**	DABCO (0.5 equiv.) acrylonitrile DMF, rt, 100 min	**4o**	84[d]
7	**3h**	DABCO (0.5 equiv.) acrylonitrile DMF, rt, 90 min	**4p**	52

[a]Methyl acrylate and acrylonitrile was used in 3.0 equiv. [b]Product **4j** was isolated in 11% after 42 days when methyl acrylate was used as solvent. [c]Product **4k** was isolated in 31% after 11 days when acrylonitrile was used as solvent. [d]When we used 0.15 equiv. of DABCO in the same reaction **4o** was isolated in 38% after 9 days.

related derivatives. Unfortunately, alloxan and parabanic acid did not undergo the reaction under the examined conditions.

In conclusion, we described optimized reaction conditions for the preparation of the Baylis-Hillman adducts of ninhydrin and isatin derivatives. For *N*-acylisatins the use of DMF as a solvent in the presence of somewhat larger amounts of DABCO is crucial for high yields of products. Thus, ninhydrin and isatin derivatives can be added as new entries for the Baylis-Hillman reaction.

Experimental Section

Solvents and other chemicals were used as purchased. Starting materials were purchased (ninhydrin, isatin, *N*-phenylisatin, 5-bromoisatin) or prepared from isatin in good yields: *N*-allylisatin (allyl bromide, K_2CO_3, DMF, rt, 5 h, 43%), *N*-benzylisatin (benzyl bromide, K_2CO_3, DMF, rt, 4 h, 63%), *N*-acetylisatin (Ac_2O, 80-90 °C, 6 h, 79%), 5-bromo-

N-acetylisatin (Ac_2O, 80-90 °C, 3 h, 84%), *N*-propionylisatin (propionyl chloride, pyridine, CH_2Cl_2, rt, 2 h, 94%). *N*-benzoylisatin (benzoic anhydride, Et_3N, CH_2Cl_2, rt, 3 h, 80%).

Typical procedure for the synthesis of Baylis-Hillman adduct 2a: To a stirred solution of ninhydrin (178 mg, 1.0 mmol) and methyl acrylate (2.0 mL) was added DABCO (11 mg, 0.1 mmol) and stirred 50-60 °C for 60 min. After removal of methyl acrylate and flash column chromatography (hexane/ethyl acetate, 1 : 1), we could obtain the desired compound **2a** in 86% isolated yield as a white solid, 212 mg: mp 137-138 °C; IR (KBr) 3422, 1755, 1715, 1693 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.27 (br s, 1H), 3.60 (s, 3H), 6.52 (s, 1H), 6.72 (s, 1H), 7.88-8.07 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 52.31, 76.35, 124.35, 130.33, 136.21, 136.74, 140.98, 165.52, 197.00; Mass (70 eV) *m z* (rel. intensity) 76 (23), 104 (35), 130 (19), 186 (34), 214 (100), 246 (M^+, 2). The following compounds were synthesized analogously. **2b**: 82%; yellow solid; mp 77-78 °C; ^1H NMR ($CDCl_3$) δ 1.05 (t, J = 7.2 Hz, 3H), 3.26 (br s, 1H), 4.01 (q, J = 7.2 Hz, 2H), 6.49 (s, 1H), 6.74 (s, 1H) 7.89-7.93 (m, 2H), 8.03-8.07 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 13.53, 61.42, 76.27, 124.28, 130.19, 136.12, 136.81, 140.94, 164.71, 196.97. **2c**: 71%; white solid; mp 202-203 °C; ^1H NMR ($CDCl_3$) δ 2.30 (s, 3H), 2.46 (s, 1H), 6.60 (s, 1H), 6.79 (s, 1H), 7.85-7.88 (m, 2H), 7.99-8.02 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 25.39, 76.44, 124.31, 130.70, 136.02, 140.85, 146.25, 196.80, 198.63. **2d**: 64%; oil; ^1H NMR ($CDCl_3$) δ 0.94 (t, J = 7.2 Hz, 3H), 2.72 (q, J = 7.2 Hz, 2H), 3.93 (s, 1H), 6.58 (s, 1H), 6.67 (s, 1H), 7.85-7.88 (m, 2H), 7.98-8.01 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 7.37, 30.39, 76.47, 124.20, 129.59, 135.89, 140.68, 145.42, 197.33, 201.34. **2e**: 25%; ^1H NMR ($CDCl_3$) δ 4.10 (br s, 1H), 6.30 (s, 1H), 6.44 (s, 1H), 7.98-8.01 (m, 2H), 8.06-8.09 (m, 2H).

Typical procedure for the synthesis of Baylis-Hillman adduct 4a: To a stirred solution of isatin (441 mg, 3.0 mmol) and methyl acrylate (387 mg, 4.5 mmol) in THF (5 mL) was added DABCO (50 mg, 0.45 mmol) and stirred at rt for 5 days. After the usual aqueous workup process and flash column chromatography (hexane/ethyl acetate, 2 : 1), we could obtain the desired compound **4a** in 63% isolated yield as a white solid, 440 mg: mp 192-194 °C; IR (KBr) 3423, 1708, 1621 cm^{-1}; ^1H NMR ($CDCl_3$ + DMSO-d_6) δ 3.59 (s, 3H), 4.80 (br s, 1H), 6.55 (s, 1H), 6.57 (s, 1H), 6.86-7.23 (m, 4H), 9.63 (br s, 1H); ^{13}C NMR ($CDCl_3$ + DMSO-d_6) δ 51.34, 75.66, 109.79, 121.60, 123.37, 127.28, 129.24, 130.72, 139.02, 142.35, 164.75, 177.81; Mass (70 eV) *m z* (rel. intensity) 146 (79), 172 (70), 174 (100), 201 (43), 233 (M^+, 34). The following compounds were synthesized analogously. **4b**: 71 %; ^1H NMR ($CDCl_3$) δ 1.47 (t, J = 7.2 Hz, 3H), 4.01-4.13 (m, 2H), 6.41 (s, 1H), 6.59 (s, 1H), 6.86 7.28 (m, 4H), 8.36 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.77, 61.19, 76.61, 110.49, 122.97, 124.22, 127.88, 130.02, 130.21, 138.96, 141.62, 164.77, 178.37. **4c**: 69%; brown solid; mp 182-184 °C; ^1H NMR ($CDCl_3$ + DMSO-d_6) δ 5.15 (br s, 1H), 6.15 (s, 1H), 6.37 (s, 1H), 6.91-7.38 (m, 4H), 9.98 (br s, 1H); ^{13}C NMR ($CDCl_3$ + DMSO-d_6) δ 76.64, 110.80, 116.20, 122.88, 123.55, 124.75, 128.75, 130.49, 131.28, 141.75, 176.08. **4d**: 64%; yellow solid; mp 170-171 °C; ^1H NMR ($CDCl_3$) δ 3.63 (s, 3H), 3.69 (br s, 1H), 4.31-4.43 (m, 2H), 5.24-5.41 (m, 2H), 5.83-5.93 (m, 1H), 6.44 (s, 1H), 6.58 (s, 1H), 6.85-7.33 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 42.63, 52.09, 76.13, 109.62, 117.91, 122.95, 123.88, 127.88, 129.21, 130.16, 131.10, 139.06, 143.73, 165.04, 176.00. **4e**: 81%; brown oil; ^1H NMR ($CDCl_3$) δ 4.19-4.26 (m, 1H), 4.80 (br s, 1H), 4.41-4.48 (m, 1H), 5.22-5.30 (m, 2H), 5.76-5.87 (m, 1H), 6.17 (s, 1H), 6.39 (s, 1H), 6.89 (d, J = 7.8 Hz, 1H), 7.11-7.41 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 42.78, 76.67, 110.19, 115.64, 118.16, 122.98, 124.06, 124.66, 127.29, 130.24, 130.94, 131.54, 142.46, 174.34. **4f**: 50%; white solid; mp 193-194 °C; ^1H NMR ($CDCl_3$) δ 3.57 (s, 3H), 4.15 (br s, 1H), 4.92 (dd, J = 30.0 and 15.8 Hz, 2H), 6.47 (s, 1H), 6.58 (s, 1H), 6.71 (d, J = 7.8 Hz, 1H), 6.95-7.40 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 44.11, 52.02, 76.21, 109.74, 123.02, 123.82, 127.40, 127.61, 128.11, 128.76, 129.44, 130.08, 135.50, 139.01, 143.64, 165.06, 176.53. **4g**: 94%; brown solid; mp 122-123 °C; ^1H NMR ($CDCl_3$) δ 4.70 (br s, 1H), 4.79 (d, J = 16.0 Hz, 1H), 5.03 (d, J = 16.0 Hz, 1H), 6.17 (s, 1H), 6.40 (s, 1H), 6.75 (d, J = 7.8 Hz, 1H), 7.10-7.39 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 44.29, 76.62, 110.32, 115.65, 122.94, 124.08, 124.66, 127.08, 127.16, 127.90, 128.90, 130.95, 131.60, 134.47, 142.42, 174.66. **4h**: 87%; white solid; mp 187-188 °C; ^1H NMR ($CDCl_3$) δ 3.65 (s, 3H), 3.86 (br s, 1H), 6.52 (s, 1H), 6.60 (s, 1H), 6.79-7.55 (m, 9H); ^{13}C NMR ($CDCl_3$) δ 52.06, 76.15, 109.82, 123.29, 124.09, 126.48, 127.78, 128.15, 128.88, 129.57 130.04, 134.17, 139.41, 144.63, 164.92, 175.81. **4i**: 79 %; brown solid; mp 137-138 °C; ^1H NMR ($CDCl_3$) δ 4.34 (br s, 3H), 6.20 (s, 1H), 6.44 (s, 1H), 6.81-7.54 (m, 9H); ^{13}C NMR ($CDCl_3$) δ 75.81, 109.49, 114.55, 122.07, 123.47, 123.85, 125.49, 125.67, 127.85, 128.85, 130.00, 130.33, 132.25, 142.53, 172.90.

Typical procedure for the synthesis of Baylis-Hillman adduct 4j: To a stirred solution of *N*-acetylisatin (189 mg, 1.0 mmol) and methyl acrylate (258 mg, 3 mmol) in DMF (1 mL) was added DABCO (23 mg, 0.2 mmol) and stirred at rt for 120 min. After the usual aqueous workup process and flash column chromatography (hexane/ethyl acetate, 3 : 1), we could obtain the desired compound **4j** in 58% isolated yield as a pale yellow solid, 160 mg: mp 130-131 °C; IR (KBr) 3448, 1774, 1711 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.63 (s, 3H), 3.60 (br s, 1H), 3.64 (s, 3H), 6.50 (s, 1H), 6.67 (s, 1H), 7.19-7.43 (m, 3H), 8.24 (d, J = 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 26.33, 52.25, 76.04, 117.03, 123.65, 125.47, 128.00, 128.12, 130.74, 139.07, 140.97, 164.99, 170.89, 176.87; Mass (70 eV) *m z* (rel. intensity) 43 (34), 90 (21), 146 (100), 156 (28), 174 (31), 201 (18), 232 (47), 275 (M^+, 16). The following compounds were synthesized analogously. **4k**: 70 %; yellow solid; mp 139-140 °C; ^1H NMR ($CDCl_3$) δ 2.67 (s, 3H), 3.65 (br s, 1H), 6.25 (s, 1H), 6.28 (s, 1H), 7.26-7.51 (m, 3H), 8.27 (d, J = 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 26.46, 76.36, 115.08, 117.34, 122.78, 124.52, 125.73, 126.40, 131.76, 132.34, 140.16, 170.28, 174.92. **4l**: 59%; brown solid; mp 176-177 °C; ^1H NMR ($CDCl_3$) δ 2.62 (s, 3H), 3.66 (s, 3H), 3.79 (br s, 1H), 6.53 (s, 1H), 6.64 (s, 1H), 7.30-7.52 (m, 2H), 8.12 (d, J = 8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 26.33, 52.43, 75.66, 118.38, 118.69, 126.89, 128.54, 130.20,

133.61, 138.68, 139.91, 164.84, 170.83, 176.27. **4m**: 50%; oil: ^{1}H NMR ($CDCl_3$) δ 2.68 (s, 3H), 3.78 (br s, 1H), 6.28 (s, 1H), 6.33 (s, 1H), 7.52-7.62 (m, 2H), 8.17 (d, J = 8.7 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 26.41, 76.17, 114.79, 118.95, 119.36, 122.19, 127.69, 132.65, 134.67, 139.09, 170.05, 174.26 (one carbon is overlapped). **4n**: 55%; pale pink solid: mp 159-160 °C; ^{1}H NMR ($CDCl_3$) δ 1.88 (t, J = 7.2 Hz, 3H), 2.97-3.06 (m, 2H), 3.63 (s, 3H), 3.71 (s, 1H), 6.51 (s, 1H), 6.61 (s, 1H), 7.16-7.42 (m, 3H), 8.25 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 8.24, 31.69, 52.28, 76.04, 117.02, 123.67, 125.37, 128.08, 128.25, 130.76, 139.04, 141.17, 165.01, 175.02, 176.82. **4o**: 84%; yellow solid: mp 114-115 °C; ^{1}H NMR ($CDCl_3$) δ 1.23 (t, J = 7.2 Hz, 3H), 3.02 (q, J = 7.2 Hz, 2H), 5.28 (br s, 1H), 6.22 (s, 1H), 6.32 (s, 1H), 7.27-8.25 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 8.09, 31.76, 76.28, 115.05, 117.13, 122.51, 124.46, 125.97, 126.19, 131.60, 132.40, 140.16, 174.59, 174.71. **4p**: 52%; oil; ^{1}H NMR ($CDCl_3$) δ 3.32 (s, 1H), 6.28 (s, 1H), 6.43 (s, 1H), 7.26-7.87 (m, 9H); ^{13}C NMR ($CDCl_3$) δ 76.86, 115.37, 115.79, 122.60, 124.72, 126.11, 128.57, 129.45, 131.66, 131.94, 133.14, 133.63, 140.29, 168.51, 174.22 (one carbon is overlapped).

Acknowledgment. This work was supported by the grant (R05-2000-000-00074-0) from the Basic Research Program of the Korea Science & Engineering Foundation. The support of the Korea Basic Science Institute (Kwangju branch) is also acknowledged.

References and Notes

1. (a) Basavaiah, D.; Rao, P. D.; Hyma, R. S. *Tetrahedron* **1996**, *52*, 8001. (b) Ciganek, E. *Organic Reactions*; John Wiley & Sons: New York, 1997; Vol. 51, pp 201-350. (c) Drewes, S. E.; Roos, G. H. P. *Tetrahedron* **1988**, *44*, 4653. (d) Langer, P. *Angew. Chem., Int. Ed.* **2000**, *39*, 3049. (e) Kim, J. N.; Lee, K. Y. *Curr. Org. Chem.* **2002**, *6*, 627.
2. (a) Hill, J. S.; Isaacs, N. S. *Tetrahedron Lett.* **1986**, *27*, 5007. (b) Hill, J. S.; Isaacs, N. S. *J. Chem. Res. (M)* **1988**, *1*, 2641. (c) Hill, J. S.; Isaacs, N. S. *J. Chem. Res. (S)* **1988**, 330. (d) Alcaide, B.; Almendros, P.; Aragoncillo, C. *Chem. Commun.* **2000**, 757. (e) Alcaide, B.; Almendros, P.; Aragoncillo, C. *Tetrahedron Lett.* **1999**, *40*, 7537. (f) Basavaiah, D.; Bharathi, T. K.; Gowriswari, V. V. L. *Tetrahedron Lett.* **1987**, *28*, 4351. (g) Strunz, G. M.; Bethell, R.; Sampson, G.; White, P. *Can. J. Chem.* **1995**, *73*, 1666. (h) Basavaiah, D.; Muthukumaran, K.; Sreenivasulu, B. *Synlett* **1999**, 1249.
3. (a) Vojkovsky, T. *Abstr. 211th Meeting of the American Chemical Society, New Orleans*, **1996**, ORGN 288. (b) The preliminary results of ours have been reported earlier in the 88th Annual Meeting of the Korean Chemical Society, S23P80 (October 19, 2001). (c) During the preparation of this manuscript the Baylis-Hillman reaction of isatin derivatives was reported: Garden, S. J.; Skakle, J. M. S. *Tetrahedron Lett.* **2002**, *43*, 1969.
4. For our recent papers, see: (a) Kim, J. N.; Lee, H. J.; Lee, K. Y.; Gong, J. H. *Synlett* **2002**, 173. (b) Gong, J. H.; Im, Y. J.; Lee, K. Y.; Kim, J. N. *Tetrahedron Lett.* **2002**, *43*, 1247. (c) Chung, Y. M.; Gong, J. H.; Kim, T. H.; Kim, J. N. *Tetrahedron Lett.* **2001**, *42*, 9023. (d) Kim, J. N.; Kim, H. S.; Gong, J. H.; Chung, Y. M. *Tetrahedron Lett.* **2001**, *42*, 8341. (e) Kim, J. N.; Im, Y. J.; Gong, J. H.; Lee, K. Y. *Tetrahedron Lett.* **2001**, *42*, 4195. (f) Kim, J. N.; Lee, H. J.; Lee, K. Y.; Kim, H. S. *Tetrahedron Lett.* **2001**, *42*, 3737. (g) Kim, H. S.; Kim, T. Y.; Lee, K. Y.; Chung, Y. M.; Lee, H. J.; Kim, J. N. *Tetrahedron Lett.* **2000**, *41*, 2613. (h) Kim, J. N.; Lee, K. Y.; Kim, H. S.; Kim, T. Y. *Org. Lett.* **2000**, *2*, 343.
5. (a) Garden, S. J.; Torres, J. C.; Ferreira, A. A.; Silva, R. B.; Pinto, A. C. *Tetrahedron Lett.* **1997**, *38*, 1501. (b) Kawasaki, T.; Ohtsuka, H.; Chien, C.-S.; Omata, M.; Sakamoto, M. *Chem. Pharm. Bull.* **1987**, *35*, 1339. (c) Desarbre, E.; Savelon, L.; Cornec, O.; Merour, J. Y. *Tetrahedron* **1996**, *52*, 2983.
6. (a) Angell, E. C.; Black, D. St C.; Kumar, N. *Magn. Reson. Chem.* **1992**, *30*, 1. (b) Meyer, F. J. *Chem. Ber.* **1966**, *99*, 3060. (c) Popp, F. D.; Piccirilli, R. M. *J. Heterocyclic Chem.* **1971**, *8*, 473. (c) de Mayo, P.; Ryan, J. J. *Can. J. Chem.* **1967**, *45*, 2117. (d) Bergman, J.; Carlsson, R.; Lindstrom, J.-O. *Tetrahedron Lett.* **1976**, 3611.