# Synthesis of 9-Oxo-9,13b-dihydro-7*H*-benzo[3,4]azepino[2,1-*a*]isoindole-6-carboxylic Acid Derivatives from Baylis-Hillman Adducts

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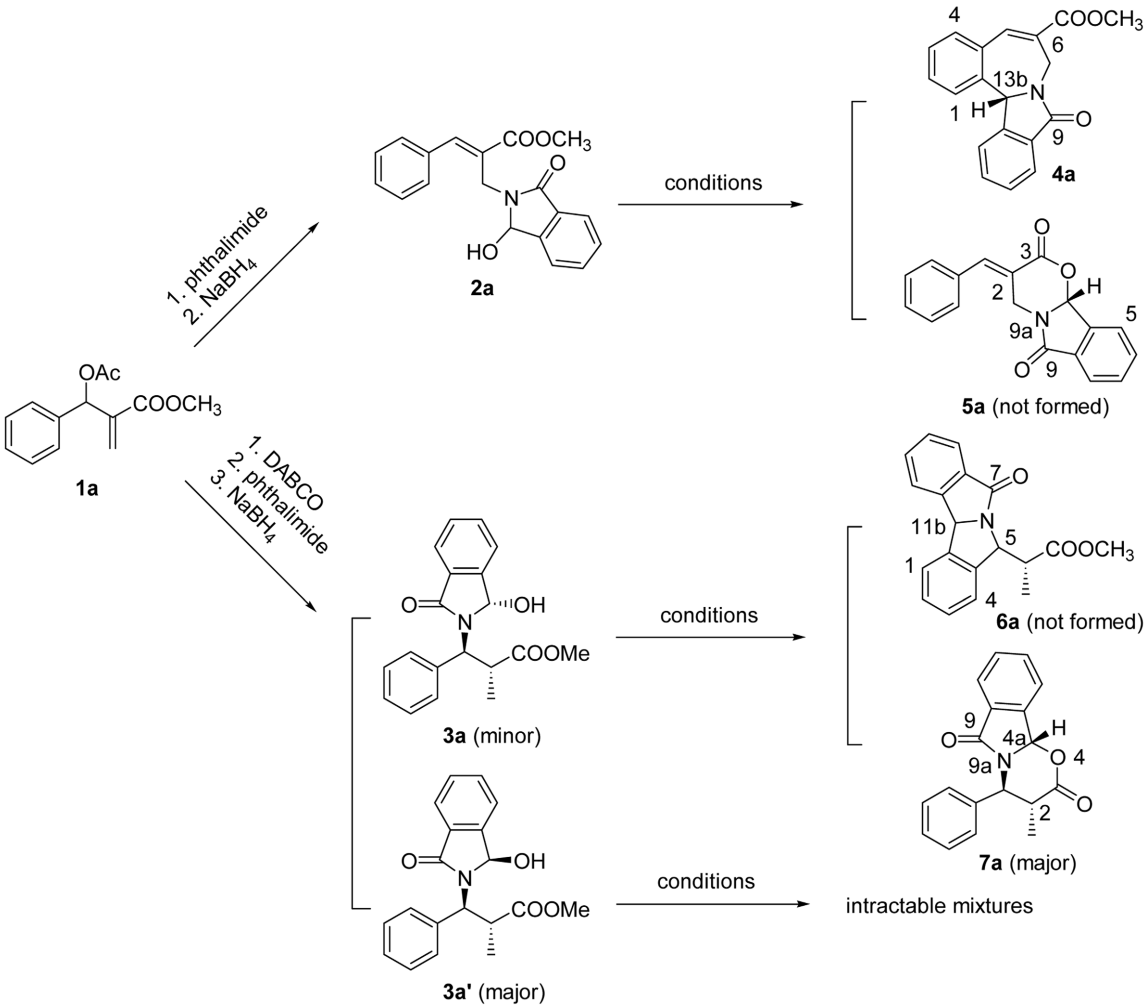
Recently we have reported the synthesis of various kinds of heterocyclic compounds starting from the Baylis-Hillman adducts.[1] As a continuing effort we intended to examine the synthesis of 9-oxo-9,13b-dihydro-7*H*-benzo[3,4]azepino-[2,1-*a*]isoindole-6-carboxylic acid derivatives **4**[2-4] and 2-(7-oxo-7,11b-dihydro-5*H*-isoindolo[1,2-*a*]isoindol-5-yl)propionic acid derivatives **6**[5] as shown in Scheme 1.

Suitably substituted isoindolobenzazepines and related compounds have been prepared and studied deeply due to their interesting biological activities[2] and due to the abundance of the skeleton in natural products.[3] Most of the reported synthetic methods used *N*-acyliminium ion




**4a**; 9-Oxo-9,13b-dihydro-7*H*-benzo[3,4]azepino[2,1-*a*]isoindole-6-carboxylic acid methyl ester
**5a**: 2-Benzylidene-1,2-dihydro-4a*H*-4-oxa-9a-azafluorene-3,9-dione
**6a**: 2-(7-Oxo-7,11b-dihydro-5*H*-isoindolo[1,2-*a*]isoindol-5-yl)propionic acid methyl ester
**7a**: 2-Methyl-1-phenyl-1,2-dihydro-4a*H*-4-oxa-9a-azafluorene-3,9-dione

**Scheme 1**

chemistry.[6-8] As mentioned above we expected that we could prepare both isoindolobenzazepines **4** and isoindoloisoindole **6** easily starting from the acetates of the Baylis-Hillman adducts **1** (Scheme 1) by using the cyclization of *N*-acyliminium ion intermediates as the key step.

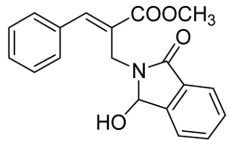
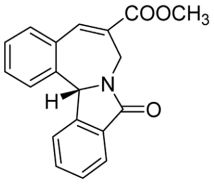
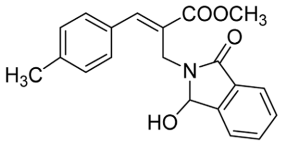
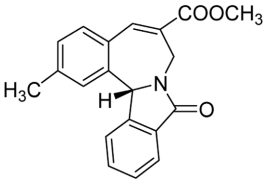
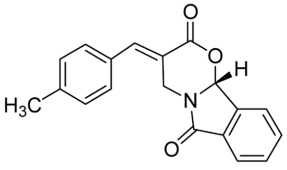
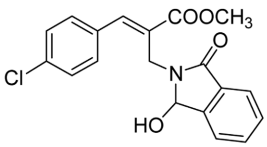
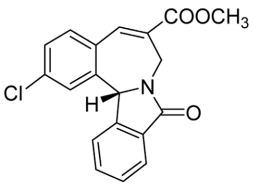
The introduction of the requisite phthalimide moiety at the primary position of the Baylis-Hillman adduct can be carried out easily from **1a** by following the published procedure by us.[9] Reduction of the phthalimide moiety with $NaBH_4$ (1.5 equiv, MeOH) was carried out to give the corresponding hydroxylactam **2a** in good yield (overall 71%). With **2a** in our hands, we examined the cyclization of **2a** under acidic conditions including $H_2SO_4$, TsOH, $CF_3COOH$, TfOH, $CH_3SO_3H$. Among the conditions the use of $CH_3SO_3H$ (3 equiv) in 1,2-dichloroethane at refluxing temperature gave the best result (78%) for the formation of **4a** (entry 1 in Table 1).

Synthesis of **2b** and **2c** was carried out similarly in 60 and 68%, respectively. The synthesis of **4b** was conducted under the same conditions in 83% yield. During the synthesis of **4b** we found that the reaction of **2b** in the presence of $CF_3COOH$ (relatively weaker acid than $CH_3SO_3H$) afforded 2-benzylidene-1,2-dihydro-4a*H*-4-oxa-9a-azafluorene-3,9-dione derivative **5b** as the major product (52%, vide infra, entry 3 in Table 1) presumably by direct intramolecular esterification. However, for the reaction of less reactive (due to *p*-Cl substituent) **2c**, the use of $CH_3SO_3H$ under refluxing conditions gave low yield of **4c** and many intractable side products. Fortunately, when we increased the acidity of the reaction medium by addition of 1 equiv of TfOH (entry 4 in Table 1) we could obtain **4c** at room temperature in reasonable yield.

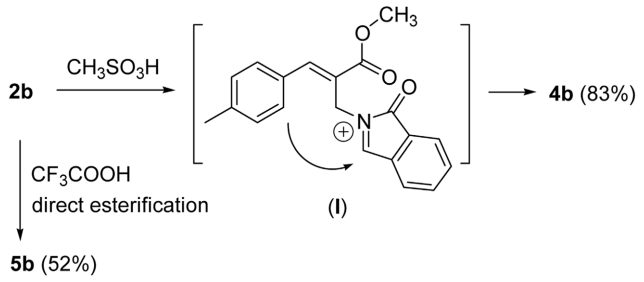
The plausible reaction mechanism for the formation of **4b** and **5b** was depicted in Scheme 2 as the representative example. Corresponding *N*-acyliminium ion (**I**) was formed from **2b** under strongly acidic conditions and the following cyclization with the arene moiety gave the benzo[3,4]-azepino[2,1-*a*]isoindole derivative **4b**. Direct intramolecular esterification reaction of **2b** afforded the corresponding 4-oxa-9a-azafluorene derivative **5b** under relatively weak acidic conditions. But, for the formation of **5b**, we could not exclude completely the possibility for the formation of **5b** by the attack of ester moiety to the *N*-acyliminium ion (**I**) at this stage.[8]

The introduction of phthalimide at the secondary position of **1a** was carried out by using the DABCO salt concept (Scheme 1) as reported.[9] The following reduction with $NaBH_4$ (3.0 equiv, MeOH) afforded the compounds **3a** and **3a'** in 22% and 39%, respectively. We could isolate only **3a** and **3a'** in pure states although there were many spots on TLC of the reaction mixture. It is interesting to note that besides the reduction of the amide carbonyl group, the

**Table 1**. Synthesis of benzo[3,4]azepino[2,1-*a*]isoindole derivatives **4a-c**

| Entry | Substrates[a] | Conditions | Products (%) |
|---|---|---|---|
| 1 |  **2a** (71) | $CH_3SO_3H$ (3 equiv)<br>$ClCH_2CH_2Cl$<br>80 °C, 2 h |  **4a** (78) |
| 2 |  **2b** (60) | $CH_3SO_3H$ (3 equiv)<br>$ClCH_2CH_2Cl$<br>80 °C, 2 h |  **4b** (83) |
| 3 | **2b** | $CF_3COOH$ (10 equiv)<br>$ClCH_2CH_2Cl$<br>60 °C, 12 h |  **5b** (52) |
| 4 |  **2c** (68) | $CH_3SO_3H$ (3 equiv)<br>$CF_3SO_3H$ (1 equiv)<br>$ClCH_2CH_2Cl$<br>rt, 2 h |  **4c** (80)[b] |

[a]Yields in parenthesis for the substrates **2a-c**. [b]Corresponding **5c** was formed in low yield when we used $CH_3SO_3H$ alone.



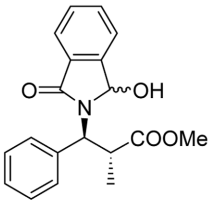
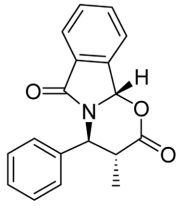
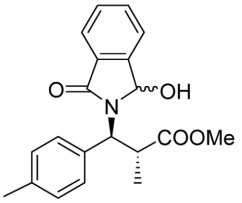
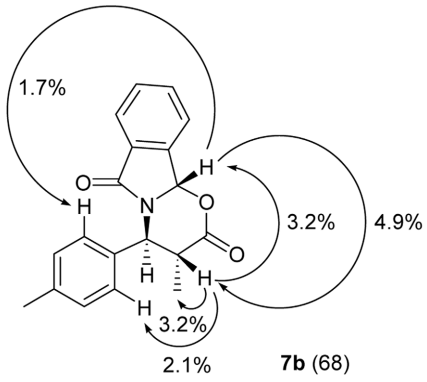
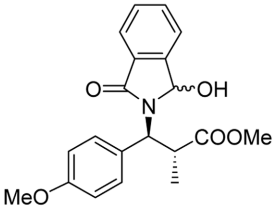
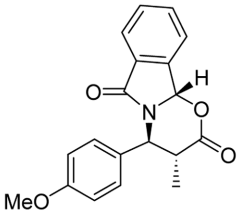

**Scheme 2**

methylene double bond was also reduced simultaneously under the reaction conditions.[10] Based on the $^1$H NMR spectra,[11] both of the two isomers **3a** and **3a'** have *anti* relationships between the methyl group (at C-2 position) and the phthalimide substituent (at C-3 position) as depicted in Scheme 1 and in Table 2. The coupling constants between the protons at C-2 and C-3 was 12.3 Hz (for **3a**) and 11.7 Hz (for **3a'**), which is the characteristic value of *anti* isomers in a similar systems.[10,11] Thus, we could conclude tentatively that the two isomers as the diastereoisomers having different configurations at the carbon bearing the OH group (vide infra).

In order to prepare the isoindoloisoindole compound **6a** from **3** via the *N*-acyliminium ion intermediate, we tried the reaction of both isomers **3a** and **3a'** under the influence of $CH_3SO_3H$ and $CF_3SO_3H$ in 1,2-dichloroethane. Unfortunately, we could not obtain any major compounds from the reaction of major components **3a'**. Intractable mixtures were formed in the reaction. Fortunately, from the reaction of the minor isomer **3a**, we obtained 4a*H*-4-oxa-9a-azafluorene-3,9-dione derivative **7a** in 60% yield. This compound might be formed via direct intramolecular esterification reaction of **3a** as in the case of **5b** (vide supra). Synthesis of **3b-c** and **3b'-c'** was carried out similarly and we obtained similar results as shown in Table 2. The reaction of **3b** and **3c** toward **7b** and **7c** was carried out in the same manner to afford the desired products in 68 and 52%, respectively.

The structure of **7a** was confirmed by various spectroscopic methods. Especially, in the $^1$H NMR spectrum of **7a**, we confirmed again the *anti* relationships of the two vicinal protons ($J$ = 11.1 Hz) at $C_1$ and $C_2$. Moreover from the NOE difference spectra of **7b** (shown in entry 2 of Table 2) we found that the proton at the 4a-position is positioning in the same direction with the proton at the $C_2$ position. Based on

**Table 2**. Synthesis of 4-oxa-9a-azafluorene derivatives **7a-c**

| Entry | Substrates[a] | Conditions | Products (%) |
|---|---|---|---|
| 1 |  **3a**-OH down (22)<br>**3a'**-OH up (39) | $CH_3SO_3H$ (3 equiv)<br>$CF_3SO_3H$ (1 equiv)<br>$ClCH_2CH_2Cl$<br>rt, 30 min |  **7a** (60) |
| 2 |  **3b**-OH down (29)<br>**3b'**-OH up (49) | $CH_3SO_3H$ (3 equiv)<br>$CF_3SO_3H$ (1 equiv)<br>$ClCH_2CH_2Cl$<br>rt, 60 min |  **7b** (68) |
| 3 |  **3c**-OH down (30)<br>**3c'**-OH up (42) | $CH_3SO_3H$ (3 equiv)<br>$CF_3SO_3H$ (1 equiv)<br>$CH_2Cl_2$<br>rt, 20 min |  **7c** (52) |

[a]Yields in parenthesis for the substrates **3a-c** and **3a'-c'**. We used **3a-c** for the synthesis of **7a-c**.

the structure of **7**, we could assign the stereochemistry of the OH group of **3a-c** (minor isomers) as downwards (vide supra).

In summary, we prepared some benzo[3,4]azepino[2,1-*a*]isoindole derivatives **4a-c** and 4-oxa-9a-azafluorene derivatives **7a-c** starting from the acetates of the Baylis-Hillman adducts.

## Experimental Section

**Typical procedure for the synthesis of 2a:** To a stirred solution of phthalimide-attached Baylis-Hillman adduct (160 mg, 0.5 mmol) in methanol (5 mL) was added $NaBH_4$ (55 mg, 1.5 mmol) at 0 °C and stirred for 30 min at room temperature. After the normal aqueous workup and column chromatographic purification process (hexanes/EtOAc, 7 : 3) we obtained the hydroxylactam derivative **2a**, 115 mg (71%). Synthesis of **2b** and **2c** was performed similarly. For the synthesis of **3a-c** and **3a'-c'** we used 3 equiv of $NaBH_4$ under the same reaction conditions.

**Typical procedure for the synthesis of 4a:** To a stirred solution of hydroxylactam derivative **2a** (70 mg, 0.22 mmol) in 1,2-dichloroethane (3 mL) was added $CH_3SO_3H$ (62 mg, 0.65 mmol) and heated to reflux for 2 h under nitrogen atmosphere. After the normal aqueous workup and column chromatographic purification process (hexanes/EtOAc, 7 : 3) we obtained the desired product **4a**, 52 mg (78%). Synthesis of other compounds was carried out similarly.

Spectroscopic data of prepared compounds **2a-c**, **3a-c**, **3a'-c'**, **4a-c**, **5b**, and **7a-c** are as follows.

Compound **2a**: 71%; $^1$H NMR ($CDCl_3$) $\delta$ 3.88 (s, 3H), 4.39 (d, $J$ = 15.0 Hz, 1H), 4.58 (d, $J$ = 6.9 Hz, 1H), 4.97 (d, $J$ = 15. 0 Hz, 1H), 5.85 (d, $J$ = 6.9 Hz, 1H), 7.37-7.80 (m, 9H), 7.98 (s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 36.61, 52.99, 81.68, 123.55, 123.66, 126.60, 129.00, 129.91, 129.92, 130.31, 131.91, 132.40, 134.17, 143.64, 145.41, 167.34, 170.19.

Compound **2b**: 60%; $^1$H NMR ($CDCl_3$) $\delta$ 2.36 (s, 3H), 3.87 (s, 3H), 4.36 (d, $J$ = 14.7 Hz, 1H), 4.84 (d, $J$ = 6.9 Hz, 1H), 4.97 (d, $J$ = 14.7 Hz, 1H), 5.83 (d, $J$ = 6.9 Hz, 1H), 7.22-7.78 (m, 8H), 7.94 (s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 21.62, 36.55, 52.93, 81.54, 123.54, 123.61, 125.34, 129.75, 129.82, 130.52, 131.25, 131.90, 132.34, 140.44, 143.62, 145.58, 167.36, 170.42.

Compound **2c**: 68%; $^1$H NMR ($CDCl_3$) $\delta$ 3.88 (s, 3H), 4.35 (d, $J$ = 14.7 Hz, 1H), 4.61 (d, $J$ = 7.2 Hz, 1H), 4.90 (d, $J$ = 14.7 Hz, 1H), 5.85 (d, $J$ = 7.2 Hz, 1H), 7.39-7.79 (m, 8H), 7.90 (s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 36.55, 53.06, 81.76, 123.58, 123.67, 127.10, 129.28, 129.97, 131.69, 131.75, 132.51, 132.54, 136.07, 143.61, 143.92, 167.46, 169.95.

Compound **3a**:[11] 22%; $^1$H NMR ($CDCl_3$) $\delta$ 1.12 (d, $J$ = 6.9 Hz, 3H), 3.67 (s, 3H), 3.82 (d, $J$ = 11.7 Hz, 1H, $D_2O$ exchangeable), 3.82-3.93 (m, 1H), 5.52 (d, $J$ = 11.7 Hz, 1H, changed into singlet with $D_2O$), 5.58 (d, $J$ = 12.3 Hz, 1H), 7.31-7.75 (m, 9H); $^{13}$C NMR ($CDCl_3$) $\delta$ 14.62, 43.25, 52.47, 58.48, 81.44, 123.10, 123.47, 128.43, 128.85, 129.07, 129.60, 130.66, 132.35, 136.27, 144.35, 166.35, 176.27.

Compound **3a'**:[11] 39%; $^1$H NMR ($CDCl_3$) $\delta$ 1.37 (d, $J$ = 6.9 Hz, 3H), 2.56 (d, $J$ = 11.1 Hz, 1H, $D_2O$ exchangeable), 3.50 (s, 3H), 3.86-3.93 (m, 1H), 5.54 (d, $J$ = 11.1 Hz, 1H, changed into singlet with $D_2O$), 5.61 (d, $J$ = 11.7 Hz, 1H), 7.23-7.80 (m, 9H); $^{13}$C NMR ($CDCl_3$) $\delta$ 16.03, 42.35, 51.68, 58.11, 81.89, 122.94, 123.70, 128.14, 128.45, 128.75, 130.03, 131.23, 132.49, 138.09, 143.48, 167.29, 175.08.

Compound **3b**: 29%; $^1$H NMR ($CDCl_3$) $\delta$ 1.11 (d, $J$ = 6.9 Hz, 3H), 2.34 (s, 3H), 3.66 (s, 3H), 3.78-3.89 (m, 1H), 3.86 (d, $J$ = 12.3 Hz, 1H), 5.48 (d, $J$ = 11.7 Hz, 1H), 5.58 (d, $J$ = 12.3 Hz, 1H), 7.18-7.74 (m, 8H); $^{13}$C NMR ($CDCl_3$) $\delta$ 14.85, 21.33, 43.53, 52.67, 58.38, 81.60, 123.29, 123.65, 128.95, 129.78, 129.93, 130.93, 132.52, 133.47, 138.44, 144.60, 166.55, 176.57.

Compound **3b'**: 49%; $^1$H NMR ($CDCl_3$) $\delta$ 1.35 (d, $J$ = 6.9 Hz, 3H), 2.30 (s, 3H), 2.66 (d, $J$ = 10.8 Hz, 1H), 3.51 (s, 3H), 3.80-3.89 (m, 1H), 5.53 (d, $J$ = 10.8 Hz, 1H), 5.59 (d, $J$ = 11.7 Hz, 1H), 7.11-7.79 (m, 8H); $^{13}$C NMR ($CDCl_3$) $\delta$ 16.26, 21.32, 42.65, 51.91, 57.95, 81.99, 123.15, 123.88, 128.53, 129.64, 130.19, 131.51, 132.65, 135.28, 138.06, 143.76, 167.53, 175.39.

Compound **3c**: 30%; $^1$H NMR ($CDCl_3$) $\delta$ 1.11 (d, $J$ = 6.9 Hz, 3H), 3.66 (s, 3H), 3.81 (s, 3H), 3.75-3.86 (m, 2H), 5.47 (d, $J$ = 11.7 Hz, 1H), 5.58 (d, $J$ = 12.3 Hz, 1H), 6.90-7.75 (m, 8H); $^{13}$C NMR ($CDCl_3$) $\delta$ 14.84, 43.79, 52.68, 55.51, 58.11, 81.60, 114.57, 123.31, 123.67, 128.60, 129.81, 130.24, 130.96, 132.54, 144.58, 159.73, 166.51, 176.57.

Compound **3c'**: 42%; $^1$H NMR ($CDCl_3$) $\delta$ 1.35 (d, $J$ = 6.9 Hz, 3H), 2.84 (d, $J$ = 11.4 Hz, 1H), 3.51 (s, 3H), 3.76 (s, 3H), 3.72-3.87 (m, 1H), 5.54 (d, $J$ = 11.7 Hz, 2H), 6.81-7.78 (m, 8H); $^{13}$C NMR ($CDCl_3$) $\delta$ 16.26, 42.90, 51.92, 55.42, 57.79, 82.08, 114.25, 123.15, 123.89, 129.90, 130.25, 130.44, 131.56, 132.68, 143.71, 159.45, 167.46, 175.36.

Compound **4a**: 78%; IR (neat) 3298, 1712 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 3.69 (ddd, $J$ = 15.0, 2.1, and 1.2 Hz, 1H), 3.89 (s, 3H), 5.15 (d, $J$ = 15.0 Hz, 1H), 5.58 (s, 1H), 7.17-7.96 (m, 8H), 8.12 (s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 38.96, 52.80, 61.58, 124.40, 124.56, 126.70, 128.68, 129.00, 130.05, 130.21, 130.36, 131.40, 134.14, 135.78, 135.91, 141.97, 143.42, 166.61, 166.90; ESIMS $m/z$ 306 ($M^+$+H).

Compound **4b**: 83%; IR (neat) 3275, 1712 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 2.31 (s, 3H), 3.70 (ddd, $J$ = 15.0, 1.8, and 1.2 Hz, 1H), 3.87 (s, 3H), 5.12 (d, $J$ = 15.0 Hz, 1H), 5.55 (s, 1H), 6.99 (s, 1H), 7.21-7.95 (m, 6H), 8.08 (s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 21.71, 38.94, 52.65, 61.60, 124.28, 124.51, 127.30, 128.89, 129.30, 129.35, 130.43, 131.35, 133.03, 134.05, 135.72, 140.48, 142.03, 143.51, 166.66, 166.81; ESIMS $m/z$ 320 ($M^+$+H).

Compound **4c**: 80%; IR (neat) 2951, 1712 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 3.71 (ddd, $J$ = 14.7, 1.8, and 1.2 Hz, 1H), 3.88 (s, 3H), 5.14 (d, $J$ = 14.7 Hz, 1H), 5.53 (s, 1H), 7.16 (s, 1H), 7.37-7.96 (m, 6H), 8.05 (s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 39.16, 52.87, 61.12, 124.43, 124.56, 126.97, 128.91, 129.32, 130.67, 131.68, 131.77, 133.98, 134.29, 136.02, 137.62, 141.26, 142.08, 166.37, 166.87; ESIMS $m/z$ 340 ($M^+$+H).

Compound **5b**: 52%; $^1$H NMR ($CDCl_3$) $\delta$ 2.43 (s, 3H), 4.57 (dd, $J$ = 17.4 and 2.4 Hz, 1H), 5.31 (dd, $J$ = 17.4 and 2.4 Hz, 1H), 6.38 (s, 1H), 7.30 (d, $J$ = 8.1 Hz, 2H), 7.38 (d, $J$ =

8.1 Hz, 2H), 7.60-7.90 (m, 4H), 7.98 (s, 1H); $^{13}$C NMR ($CDCl_3$) $\delta$ 21.75, 39.78, 83.60, 119.13, 124.25, 124.36, 130.00, 131.04, 131.07, 131.15, 131.74, 133.06, 139.78, 141.38, 144.22, 164.98, 166.50.

Compound **7a**: 60%; mp 213-215 °C; IR (neat) 3433, 1701 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.26 (d, $J$ = 6.6 Hz, 3H), 3.09-3.19 (m, 1H), 4.82 (d, $J$ = 11.1 Hz, 1H), 6.77 (s, 1H), 7.31-7.83 (m, 9H); $^{13}$C NMR ($CDCl_3$) $\delta$ 12.77, 41.10, 58.13, 84.03, 124.22, 124.33, 127.15, 128.78, 129.05, 129.23, 131.25, 133.01, 139.44, 139.63, 167.29, 171.38; ESIMS *m/z* 294 ($M^+$+H).

Compound **7b**: 68%; mp 239-241 °C; IR (neat) 1763, 1701 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.26 (d, $J$ = 6.6 Hz, 3H), 2.35 (s, 3H), 3.07-3.16 (m, 1H), 4.79 (d, $J$ = 11.1 Hz, 1H), 6.75 (s, 1H), 7.18-7.82 (m, 8H); $^{13}$C NMR ($CDCl_3$) $\delta$ 12.84, 21.35, 41.15, 57.88, 84.00, 124.22, 124.33, 127.06, 129.92, 131.25, 132.17, 132.96, 136.46, 138.64, 139.63, 167.22, 171.50; ESIMS *m/z* 308 ($M^+$+H).

Compound **7c**: 52%; mp 225-228 °C; IR (neat) 2920, 1763, 1701 cm$^{-1}$; $^1$H NMR ($CDCl_3$) $\delta$ 1.26 (d, $J$ = 6.6 Hz, 3H), 3.07-3.17 (m, 1H), 3.81 (s, 3H), 4.79 (d, $J$ = 10.8 Hz, 1H), 6.73 (s, 1H), 6.91-7.82 (m, 8H); $^{13}$C NMR ($CDCl_3$) $\delta$ 12.62, 40.96, 55.33, 57.39, 83.70, 114.41, 124.00, 124.11, 128.14, 131.04, 131.20, 131.96, 132.75, 139.39, 159.68, 167.06, 171.29; ESIMS *m/z* 324 ($M^+$+H).

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## References and Notes

1. For our recent publications on the synthesis of heterocyclic compounds by using the Baylis-Hillman adducts, see (a) Lee, C. G.; Lee, K. Y.; Kim, S. C.; Kim, J. N. *Bull Korean Chem. Soc.* **2005**, *26*, 485. (b) Lee, C. G.; Gowrisankar, S.; Kim, J. N. *Bull. Korean Chem. Soc.* **2005**, *26*, 481. (c) Lee, M. J.; Lee, K. Y.; Kim, J. N. *Bull. Korean Chem. Soc.* **2005**, *26*, 477. (d) Gowrisankar, S.; Na, J. E.; Lee, M. J.; Kim, J. N. *Bull. Korean Chem. Soc.* **2005**, *26*, 319. (e) Lee, C. G.; Lee, K. Y.; Lee, S.; Kim, J. N. *Tetrahedron* **2005**, *61*, 1493. (f) Lee, K. Y.; Kim, T. H.; Kim, J. N. *Bull. Korean Chem. Soc.* **2004**, *25*, 1966. (g) Gowrisankar, S.; Lee, C. G.; Kim, J. N. *Tetrahedron Lett.* **2004**, *45*, 6949. (h) Gowrisankar, S.; Lee, K. Y.; Lee, C. G.; Kim, J. N. *Tetrahedron Lett.* **2004**, *45*, 6141. (i) Lee, K. Y.; Gowrisankar, S.; Kim, J. N. *Tetrahedron Lett.* **2004**, *45*, 5485. (j) Kim, J. M.; Lee, K. Y.; Lee, S.-k.; Kim, J. N. *Tetrahedron Lett.* **2004**, *45*, 2805. (k) Lee, K. Y.; Kim, J. M.; Kim, J. N. *Tetrahedron Lett.* **2003**, *44*, 6737. (l) Kim, J. N.; Kim, J. M.; Lee, K. Y. *Synlett* **2003**, 821.
2. For the biological activities of benzazepine derivatives, see (a) Hall, I.; Murthy, A. R. K.; Wyrick, S. D. *J. Pharm. Sci.* **1986**, *75*, 622. (b) Steiner, G.; Franke, A.; Haedicke, E.; Lenke, D.; Teschendorf, H.; Hofmann, H.; Kreiskott, H.; Worstmann, W. *J. Med. Chem.* **1986**, *29*, 1877. (c) Wunderlich, H.; Strak, A.; Carstens, E.; Lohmann, D.; Gritsenko, A. N.; Skoldinov, A. P. *Pharmazie* **1985**, *40*, 827.
3. For the representative examples of natural products containing benzazepine moiety, see (a) Mazzocchi, P. H.; Kimg, C. R.; Ammon, H. L. *Tetrahedron Lett.* **1987**, *28*, 2473. (b) Ishibashi, H.; Kawanami, H.; Iriyama, H.; Lkeda, M. *Tetrahedron Lett.* **1995**, *36*, 6733. (c) Weinreb, S. M.; Auerbach, J. *J. Am. Chem. Soc.* **1975**, *97*, 2503.
4. For the synthesis of isoindolobenzazepines and related compounds, see (a) Koseki, Y.; Kusano, S.; Sakata, H.; Nagasaka, T. *Tetrahedron Lett.* **1999**, *40*, 2169. (b) Cid, M. M.; Dominguez, D.; Castedo, L.; Vazquez-Lopez, E. M. *Tetrahedron* **1999**, *55*, 5599. (c) Pigeon, P.; Decroix, B. *Tetrahedron Lett.* **1997**, *38*, 1041. (d) Mamouni, A.; Pigeon, P.; Daich, A.; Decroix, B. *J. Heterocyclic Chem.* **1997**, *34*, 1495. (e) Pigeon, P.; Othman, M.; Netchitailo, P.; Decroix, B. *Tetrahedron* **1998**, *54*, 1497.
5. For the synthesis of isoindoloisoindolinone derivatives, see (a) Chihab-Eddine, A.; Daich, A.; Jilale, A.; Decroix, B. *Heterocycles* **2002**, *58*, 449. (b) Bahajaj, A. A.; Vernon, J. M.; Wilson, G. D. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1446.
6. Synthetic applications of *N*-acyliminium cyclization, see (a) Lee, Y. S.; Min, B. J.; Park, Y. K.; Lee, J. Y.; Lee, S. J.; Park, H. *Tetrahedron Lett.* **1999**, *40*, 5569. (b) Katritzky, A. R.; He, H.-Y.; Jiang, R. *Tetrahedron Lett.* **2002**, *43*, 2831. (c) Zhang, X.; Jiang, W.; Schmitt, A. C. *Tetrahedron Lett.* **2001**, *42*, 4943. (d) Boto, A.; Hernandez, R.; Suarez, E. *Tetrahedron Lett.* **1999**, *40*, 5945. (e) Othman, M.; Pigeon, P.; Decroix, B. *Tetrahedron* **1998**, *54*, 8737. (f) Maryanoff, B. E.; Zhang, H.-C.; Cohen, J. H.; Turchi, I. J.; Maryanoff, C. A. *Chem. Rev.* **2004**, *104*, 1431 and further references cited therein.
7. For the synthesis of phorbol derivatives by the combination of Baylis-Hillman chemistry and *N*-acyliminium ion chemistry, see (a) Marson, C. M.; Pink, J. H.; Smith, C. *Tetrahedron Lett.* **1995**, *36*, 8107. (b) Marson, C. M.; Pink, J. H.; Hall, D.; Hursthouse, M. B.; Malik, A.; Smith, C. *J. Org. Chem.* **2003**, *68*, 792.
8. For the examples of ring-cyclization via *N*-acyliminium ion with ethereal oxygen atom, with acid, or with ester moiety, see (a) Sikoraiova, J.; Marchalin, S.; Daich, A.; Decroix, B. *Tetrahedron Lett.* **2002**, *43*, 4747. (b) Pinho e Melo, T. M. V. D.; Santos, C. I. A.; Rocha Gonsalves, A. M. d'A.; Paixao, J. A.; Beja, A. M. *Tetrahedron* **2004**, *60*, 3949.
9. Gong, J. H.; Kim, H. R.; Ryu, E. K.; Kim, J. N. *Bull. Korean Chem. Soc.* **2002**, *23*, 789.
10. For the diastereoselective reduction of Baylis-Hillman adducts, see (a) Mateus, C. R.; Almeida, W. P.; Coelho, F. *Tetrahedron Lett.* **2000**, *41*, 2533. (b) Mateus, C. R.; Feltrin, M. P.; Costa, A. M.; Coelho, F.; Almeida, W. P. *Tetrahedron* **2001**, *57*, 6901. (c) Bouzide, A. *Org. Lett.* **2002**, *4*, 1347. (d) Almeida, W. P.; Coelho, F. *Tetrahedron Lett.* **2003**, *44*, 937. (e) Das, B.; Banerjee, J.; Majhi, A.; Mahender, G. *Tetrahedron Lett.* **2004**, *45*, 9225. (f) Patra, A.; Batra, S.; Bhaduri, A. P. *Synlett* **2003**, 1611. (g) Basavaiah, D.; Krishnamacharyulu, M.; Hyma, R. S.; Sarma, P. K. S.; Kumaragurubaran, N. *J. Org. Chem.* **1999**, *64*, 1197.
11. As shown in the experimental section, we assigned the peaks of **3a** and **3a'** definitively by $D_2O$ treatment. When we added two drops of $D_2O$ to the sample, OH peak disappeared and the proton of the phthalimide moiety was converted as a singlet.