http://dx.doi.org/10.5012/bkcs.2012.33.4.1337

Facile Synthesis of 5-Alkylidene-1,5-dihydropyrrol-2-ones from Morita-Baylis-Hillman Adducts

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Received December 5, 2011, Accepted December 27, 2011

Key Words : 5-Alkylidene-1,5-dihydropyrrol-2-ones, 5-Hydroxypyrrol-2(5*H*)-ones, Morita-Baylis-Hillman adducts, γ-Alkylidenebutenolides

5-Alkylidene-1,5-dihydropyrrol-2-ones have received a special attention due to their abundance in biologically important substances including pukeleimide,[1a] ampullicin,[1b,c] isoampullicin,[1b,c] pulchellalactam,[1d-f] pandamarine,[1b] and holomycin,[1a] as shown in Figure 1. Thus numerous methods for the synthesis of 5-alkylidene-1,5-dihydropyrrol-2-ones have been reported;[1,2] however, a facile synthetic pathway to this class of compounds is highly required until now. In addition, various 5-hydroxypyrrol-2(5*H*)-one derivatives, the precursors of 5-alkylidene-1,5-dihydropyrrol-2-ones in this paper, have been known to possess interesting biological activites.[3]

Recently various cyclic compounds have been synthesized from Morita-Baylis-Hillman (MBH) adducts.[4] Among the cyclic compounds, syntheses of various lactam derivatives have received much attention by us[5] and other groups.[6] Very recently, we reported a facile synthesis of γ-alkylidene-butenolides (such as **1a**) from MBH bromides, as shown in Scheme 1.[7] As a continuous work, we decided to examine the synthesis of 5-alkylidene-1,5-dihydropyrrol-2-ones (such as **3a**) from the readily available γ-alkylidenebutenolides.[7]

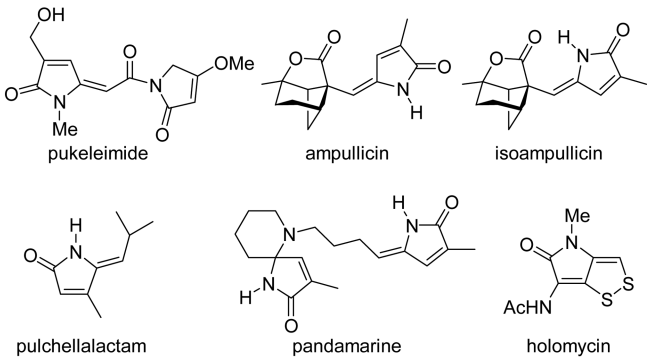
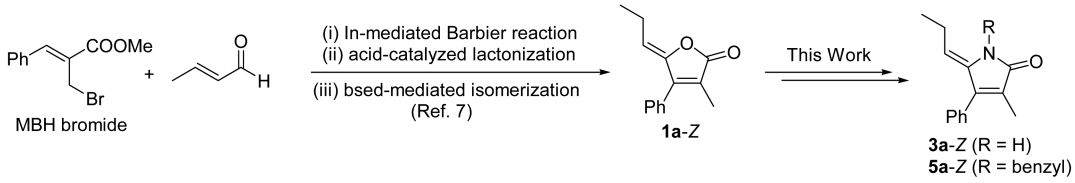


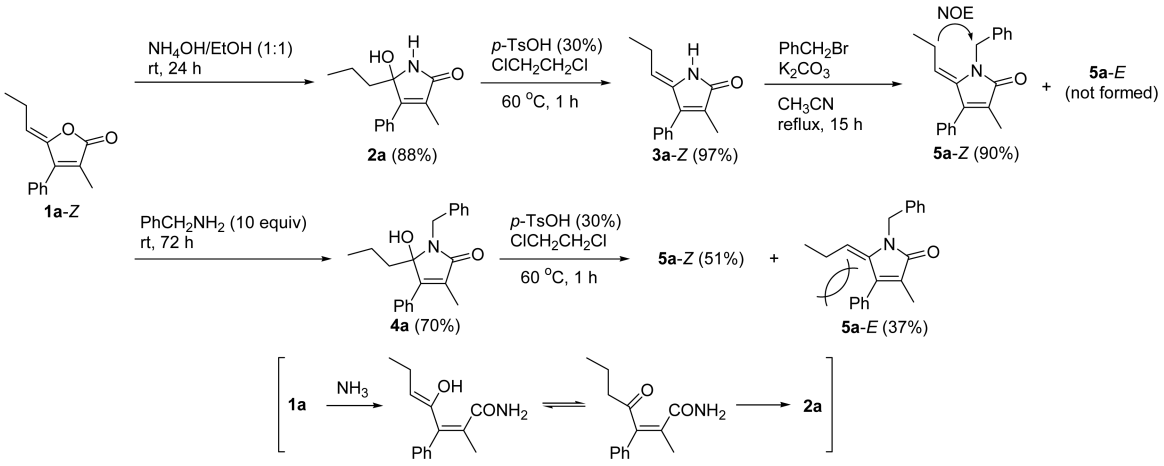
Figure 1

At the outset of our study, we examined the reaction of γ-propylidenebutenolide **1a**[7] with ammonia in ethanol at room temperature,[8] as shown in Scheme 2. As expected, 5-hydroxypyrrol-2(5*H*)-one **2a** was obtained in good yield (88%) by following the mechanism shown below in Scheme 2.[8,9b] Subsequent acid-catalyzed dehydration of **2a** produced 5-propylidene-1,5-dihydropyrrol-2-one (**3a**) in good yield (97%) in a highly stereoselective manner. As observed in a similar case[8,9b] and in our previous paper,[7] the *Z*-isomer was formed exclusively due to the unfavorable steric hindrance between the ethyl group of a propylidene moiety and the phenyl group at the 4-position. However, the reaction of **1a** and benzylamine afforded **4a** in moderate yield (70%) although excess amounts (10 equiv) of benzylamine were used. Moreover, an acid-catalyzed dehydration[9] of **4a** produced a mixture of *E*/*Z* isomers of *N*-benzyl-5-propylidene-1,5-dihydropyrrol-2-one (**5a**). The *Z*-isomer was formed as a major product (51%) along with appreciable amounts of *E*-isomer (37%). The stereochemistry of **5a**-*Z* was confirmed by NOE experiments. The ratio of *E*/*Z* stated that the unfavorable steric hindrance between the ethyl group of a propylidene moiety and the phenyl group at the 4-position is larger than that of the *N*-benzyl moiety. The *Z*-form of this compound could be synthesized more easily from **3a** and benzyl bromide in good yield (90%) in the presence of K_2CO_3. In the reaction we did not observe the formation of **5a**-*E* in any trace amount.

Encouraged by the successful results, we carried out the synthesis of 5-hydroxypyrrol-2(5*H*)-ones **2b-d** from γ-alkylidenebutenolides **1b-d**,[7] and the results are summarized in Table 1. The yields of **2b-d** were moderate to good (62-80%). For the synthesis of compound **2d**, we used THF as a co-solvent due to the limited solubility of **1d** in EtOH. These compounds were converted to 5-alkylidene-1,5-dihydro-

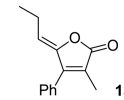
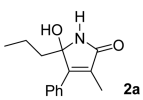
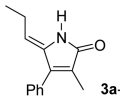
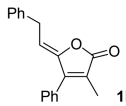
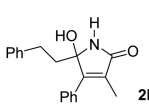
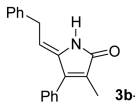
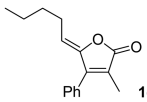
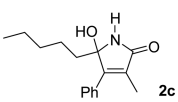
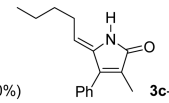
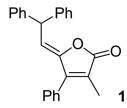
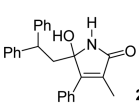
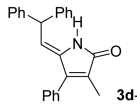


Scheme 1



Scheme 2

Table 1. Conversion of γ-alkylidenebutenolides to 5-alkylidene-1,5-dihydropyrrol-2-ones **3a-d**

Enrty	γ-Alkylidene-butenolide[a]	5-Hydroxypyrrol-2(5*H*)-one[b]	γ-Alkylidene lactam[c]
1	 **1a**-*Z*	 **2a** (88%)	 **3a**-*Z* (97%)
2	 **1b**-*Z*	 **2b** (62%)	 **3b**-*Z* (91%)
3	 **1c**-*Z*	 **2c** (80%)	 **3c**-*Z* (96%)
4	 **1d**-*Z*	 **2d** (75%)[d]	 **3d**-*Z* (93%)

[a]Prepared according to Ref. 7. [b]Conditions: substrate **1** (1.0 mmol), NH_4OH/EtOH (1:1, 4.0 mL), rt, 24 h. [c]Conditions: substrate **2** (0.5 mmol), *p*-TsOH (0.3 equiv), 1,2-dichloroethane, 60 °C, 1 h. [d]THF was added as a co-solvent.

pyrrol-2-ones **3b-d** in excellent yields (91-96%) in the presence of *p*-TsOH.[9] In all entries, the corresponding *Z*-isomers were formed exclusively, as in the case of **3a** (vide supra).

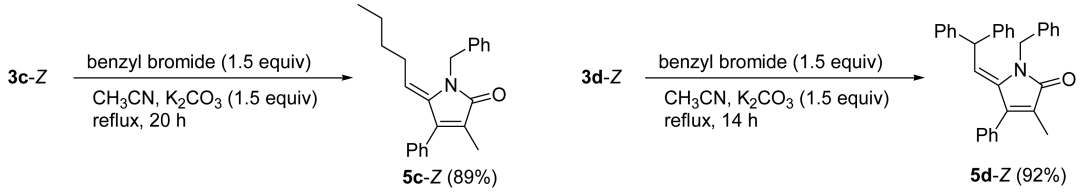
As for the synthesis of **5a**-*Z* (vide supra, Scheme 2), *N*-benzylation reactions of **3c**-*Z* and **3d**-*Z* were carried out similarly, and compounds **5c**-*Z* and **5d**-*Z* were synthesized in good yields (89-92%), as shown in Scheme 3. The formation of the corresponding *E*-form was not observed in any trace amount due to a similar steric reason.

In summary, an expedient synthetic procedure of 5-alkylidene-1,5-dihydropyrrol-2-ones was disclosed from the corresponding γ-alkylidenebutenolides which were prepared from the Morita-Baylis-Hillman bromides. The reaction of γ-alkylidenebutenolides and ammonia and subsequent dehydration produced 5-alkylidene-1,5-dihydropyrrol-2-ones stereoselectively, and the stereochemistry was not changed during the benzylation to furnish a stereoselective synthetic protocol of *N*-benzyl-5-alkylidene-1,5-dihydropyrrol-2-ones.

Experimental Section

Typical Procedure for the Synthesis of 2a. To a stirred solution of γ-alkylidenebutenolide **1a**[7] (214 mg, 1.0 mmol) in EtOH (2.0 mL) was added NH_4OH (28%, 2.0 mL), and the reaction mixture was stirred at room temperature for 24 h. After the aqueous extractive workup and column chromatographic purification process (hexanes/EtOAc/CH_2Cl_2, 3:2:1), compound **2a** was obtained as a white solid, 203 mg (88%). Other compounds were synthesized similarly, and the spectroscopic data of **2a-d** are as follows.

Compound 2a: 88%; white solid, mp 164-166 °C; IR (KBr) 3375, 3214, 1708, 1666 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.79 (t, *J* = 7.5 Hz, 3H), 1.05-1.17 (m, 1H), 1.25-1.41 (m, 1H), 1.59-1.71 (m, 1H), 1.79-1.89 (m, 1H), 1.81 (s, 3H), 4.66 (br s, OH), 7.34-7.44 (m, 3H), 7.61-7.65 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.47, 14.00, 16.63, 38.95, 90.29, 128.39, 128.54, 128.63, 128.78, 132.44, 154.19, 173.65; ESIMS *m/z* 232 (M^++H). Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.89; H,



Scheme 3

7.53; N, 5.97.

Compound 2b: 62%; white solid, mp 140-142 °C; IR (KBr) 3335, 3263, 1702 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.83 (s, 3H), 1.93-2.04 (m, 1H), 2.15-2.25 (m, 1H), 2.45-2.55 (m, 1H), 2.67-2.77 (m, 1H), 4.71 (br s, OH), 6.99-7.02 (m, 2H), 7.09-7.21 (m, 3H), 7.34-7.43 (m, 3H), 7.62-7.65 (m, 2H), 7.79 (br s, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.54, 29.75, 38.62, 90.08, 125.87, 128.30, 128.32, 128.48, 128.55, 128.80, 128.94, 132.22, 141.15, 154.21, 173.79; ESIMS *m/z* 294 (M^++H). Anal. Calcd for $C_{19}H_{19}NO_2$: C, 77.79; H, 6.53; N, 4.77. Found: C, 77.71; H, 6.42; N, 4.56.

Compound 2c: 80%; white solid, mp 114-116 °C; IR (KBr) 3401, 3293, 2953, 1700, 1649 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.77 (t, *J* = 6.6 Hz, 3H), 1.05-1.20 (m, 5H), 1.25-1.34 (m, 1H), 1.62-1.72 (m, 1H), 1.80-1.90 (m, 1H), 1.82 (s, 3H), 4.80 (br s, OH), 7.33-7.44 (m, 3H), 7.58-7.64 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.46, 13.82, 22.31, 22.81, 31.53, 36.65, 90.35, 128.36, 128.54, 128.64, 128.75, 132.44, 154.15, 173.68; ESIMS *m/z* 260 (M^++H). Anal. Calcd for $C_{16}H_{21}NO_2$: C, 74.10; H, 8.16; N, 5.40. Found: C, 74.44; H, 8.37; N, 5.19.

Compound 2d: 75%; white solid, mp 106-108 °C; IR (KBr) 3313, 3301, 1699, 1493 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.76 (s, 3H), 2.50 (dd, *J* = 14.4 and 8.7 Hz, 1H), 2.62 (dd, *J* = 14.4 and 5.7 Hz, 1H), 4.04 (br s, OH), 4.15 (dd, *J* = 8.7 and 5.7 Hz, 1H), 5.90 (br s, NH), 7.04-7.24 (m, 10H), 7.32-7.38 (m, 3H), 7.45-7.51 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.60, 42.23, 46.27, 89.31, 126.28, 126.57, 127.41, 127.93, 128.35, 128.56, 128.58, 128.65, 128.76, 128.92, 132.10, 143.90, 144.64, 153.74, 172.36; ESIMS *m/z* 370 (M^++H). Anal. Calcd for $C_{25}H_{23}NO_2$: C, 81.27; H, 6.27; N, 3.79. Found: C, 81.06; H, 6.44; N, 3.68.

Typical Procedure for the Synthesis of 3a-*Z*. A stirred solution of compound **2a** (116 mg, 0.5 mmol) and *p*-TsOH (27 mg, 0.15 mmol) in 1,2-dichloroethane (1.0 mL) was heated to 60 °C for 1 h. After the aqueous extractive workup and column chromatographic purification process (CH_2Cl_2/Et_2O, 20:1), compound **3a**-*Z* was obtained as a white solid, 103 mg (97%). Other compounds were synthesized similarly, and the spectroscopic data of **3a-d** are as follows.

Compound 3a-*Z*: 97%; white solid, mp 102-104 °C; IR (KBr) 3183, 1686 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.09 (t, *J* = 7.5 Hz, 3H), 1.95 (s, 3H), 2.29-2.39 (m, 2H), 5.12 (t, *J* = 7.8 Hz, 1H), 7.26-7.31 (m, 2H), 7.37-7.48 (m, 3H), 8.91 (br s, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.10, 13.94, 21.13, 116.62, 128.29, 128.33, 128.73, 129.44, 132.10, 137.12, 144.45, 172.20; ESIMS *m/z* 214 (M^++H). Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.79; H, 7.35; N, 6.41.

Compound 3b-*Z*: 91%; white solid, mp 160-162 °C; IR (KBr) 3190, 1682 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.94 (s, 3H), 3.72 (d, *J* = 8.1 Hz, 2H), 5.33 (t, *J* = 8.1 Hz, 1H), 7.16-7.31 (m, 7H), 7.33-7.45 (m, 3H), 9.79 (br s, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.12, 33.91, 113.25, 126.34, 128.32, 128.35, 128.55, 128.61, 129.22, 129.42, 131.92, 138.18, 139.46, 144.55, 172.76; ESIMS *m/z* 276 (M^++H). Anal. Calcd for $C_{19}H_{17}NO$: C, 82.88; H, 6.22; N, 5.09. Found: C, 82.57; H, 6.03; N, 4.97.

Compound 3c-*Z*: 96%; white solid, mp 125-127 °C; IR (KBr) 3183, 2957, 1690, 1361 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.91 (t, *J* = 7.2 Hz, 3H), 1.31-1.50 (m, 4H), 1.95 (s, 3H), 2.33 (dt, *J* = 7.8 and 7.2 Hz, 2H), 5.14 (t, *J* = 7.8 Hz, 1H), 7.26-7.31 (m, 2H), 7.36-7.48 (m, 3H), 9.17 (br s, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.06, 13.84, 22.37, 27.47, 31.50, 115.35, 128.24, 128.31, 128.68, 129.44, 132.16, 137.69, 144.30, 172.29; ESIMS *m/z* 242 (M^++H). Anal. Calcd for $C_{16}H_{19}NO$: C, 79.63; H, 7.94; N, 5.80. Found: C, 79.91; H, 8.08; N, 5.83.

Compound 3d-*Z*: 93%; white solid, mp 207-209 °C; IR (KBr) 3175, 3028, 1680 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.95 (s, 3H), 5.24 (d, *J* = 9.9 Hz, 1H), 5.62 (d, *J* = 9.9 Hz, 1H), 7.16-7.33 (m, 12H), 7.39-7.48 (m, 3H), 9.22 (br s, NH); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.15, 49.13, 115.95, 126.69, 128.25, 128.42, 128.46, 128.68, 129.38, 129.42, 131.86, 137.82, 143.15, 144.72, 172.39; ESIMS *m/z* 352 (M^++H). Anal. Calcd for $C_{25}H_{21}NO$: C, 85.44; H, 6.02; N, 3.99. Found: C, 85.78; H, 6.32; N, 3.85.

Typical Procedure for the Synthesis of 5a-*Z*. A stirred solution of compound **3a** (85 mg, 0.4 mmol), benzyl bromide (103 mg, 0.6 mmol), and K_2CO_3 (83 mg, 0.6 mmol) in CH_3CN (1.0 mL) was heated to reflux for 15 h. After the aqueous extractive workup and column chromatographic purification process (hexanes/EtOAc/CH_2Cl_2, 6:1:1), compound **5a**-*Z* was obtained as colorless oil, 109 mg (90%). Other compounds **5c**-*Z* and **5d**-*Z* were synthesized similarly, and the spectroscopic data including **4a** are as follows.

Compound 5a-*Z*: 90%; colorless oil; IR (film) 2964, 1691, 1439 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.78 (t, *J* = 7.5 Hz, 3H), 1.96 (s, 3H), 2.15-2.25 (m, 2H), 4.96 (t, *J* = 8.1 Hz, 1H), 5.13 (s, 2H), 7.13-7.17 (m, 2H), 7.20-7.35 (m, 5H), 7.36-7.48 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.53, 14,47, 20.40, 44.74, 118.18, 125.82, 126.81, 126.88, 128.22, 128.24, 128.59, 129.72, 132.41, 137.78, 138.31, 145.62, 171.43; ESIMS *m/z* 304 (M^++H). Anal. Calcd for $C_{21}H_{21}NO$: C, 83.13; H, 6.98; N, 4.62. Found: C, 83.23; H, 7.12; N, 4.46.

Compound 5c-*Z*: 89%; colorless oil; IR (film) 2957, 2925, 1694, 1441 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.71 (t, *J* = 7.2 Hz, 3H), 1.04-1.14 (m, 4H), 1.96 (s, 3H), 2.17 (dt, *J* = 7.8 and 7.2 Hz, 2H), 4.98 (t, *J* = 7.8 Hz, 1H), 5.14 (s, 2H), 7.12-7.17 (m, 2H), 7.19-7.37 (m, 5H), 7.38-7.47 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.47, 13.61, 22.16, 26.71, 32.14, 44.71, 116.89, 125.76, 126.62, 126.82, 128.16, 128.18, 128.53, 129.65, 132.39, 138.03, 138.26, 145.56, 171.39; ESIMS *m/z* 332 (M^++H). Anal. Calcd for $C_{23}H_{25}NO$: C, 83.34; H, 7.60; N, 4.23. Found: C, 83.39; H, 7.85; N, 4.32.

Compound 5d-*Z*: 92%; yellow solid, mp 96-98 °C; IR (KBr) 3027, 1695, 1444 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.99 (s, 3H), 5.03 (s, 2H), 5.05 (d, *J* = 10.8 Hz, 1H), 5.44 (d, *J* = 10.8 Hz, 1H), 6.75-6.79 (m, 4H), 7.08-7.24 (m, 9H), 7.26-7.46 (m, 7H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.64, 44.64, 47.60, 117.12, 125.58, 126.50, 127.23, 127.68, 127.76, 128.37, 128.39, 128.59, 129.02, 129.65, 132.06,

138.18, 138.41, 143.85, 145.78, 171.50; ESIMS *m/z* 442 (M^++H). Anal. Calcd for $C_{32}H_{27}NO$: C, 87.04; H, 6.16; N, 3.17. Found: C, 86.89; H, 6.47; N, 3.04.

Compound 4a: 70%; white solid, mp 144-146 °C; IR (KBr) 3324, 2959, 1675, 1436 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.25 (t, *J* = 7.2 Hz, 3H), 0.37-0.49 (m, 1H), 0.55-0.66 (m, 1H), 1.53-1.70 (m, 2H), 1.90 (s, 3H), 3.55 (br s, OH), 4.42 (d, *J* = 15.0 Hz, 1H), 4.76 (d, *J* = 15.0 Hz, 1H), 7.20-7.46 (m, 8H), 7.57-7.62 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.91, 13.10, 16.03, 36.51, 42.05, 93.46, 127.33, 128.39, 128.41, 128.55, 128.73, 128.75, 129.71, 132.29, 138.35, 151.52, 171.36; ESIMS *m/z* 322 (M^++H). Anal. Calcd for $C_{21}H_{23}NO_2$: C, 78.47; H, 7.21; N, 4.36. Found: C, 78.75; H, 7.39; N, 4.18.

Typical Procedure for the Synthesis of 5a-*E*. A stirred solution of compound **4a** (96 mg, 0.3 mmol) and *p*-TsOH (16 mg, 30 mol %) in 1,2-dichloroethane (1.0 mL) was heated to 60 °C for 1 h. After the aqueous extractive workup and column chromatographic purification process (CH_2Cl_2), compound **5a**-*E* was obtained as colorless oil, 34 mg (37%), along with **5a**-*Z* (46 mg, 51%). The spectroscopic data of **5a**-*E* are as follows.

Compound 5a-*E*: 37%; colorless oil; IR (film) 2964, 1688, 1411 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.71 (t, *J* = 7.5 Hz, 3H), 1.63-1.73 (m, 2H), 1.85 (s, 3H), 4.90 (s, 2H), 5.27 (t, *J* = 8.4 Hz, 1H), 7.21-7.27 (m, 5H), 7.29-7.35 (m, 2H), 7.36-7.44 (m, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 9.14, 14.66, 20.37, 42.74, 118.12, 126.95, 127.05, 128.10, 128.38, 128.53, 128.61, 131.45, 134.67, 137.05, 137.79, 142.70, 169.40; ESIMS *m/z* 304 (M^++H). Anal. Calcd for $C_{21}H_{21}NO$: C, 83.13; H, 6.98; N, 4.62. Found: C, 83.01; H, 7.17; N, 4.45.

Acknowledgments. This work was supported by the National Research Foundation of Korea Grant funded by the Korean Government (2011-0002570). Spectroscopic data were obtained from the Korea Basic Science Institute, Gwangju branch.

References and Notes

1. For the biologically interesting 5-alkylidene-1,5-dihydropyrrol-2-ones, see: (a) Anders, J. T.; Gorls, H.; Langer, P. *Eur. J. Org. Chem*. **2004**, 1897-1910 and further references cited therein. (b) Rico, R.; Bermejo, F. *Tetrahedron Lett*. **1996**, *37*, 5809-5812. (c) Bermejo, F. A.; Rico-Ferreira, R. *J. Org. Chem*. **2001**, *66*, 8287-8292. (d) Felluga, F.; Ghelfi, F.; Pagnoni, U. M.; Parsons, A. F.; Pattarozzi, M.; Roncaglia, F.; Valentin, E. *Synthesis* **2007**, 1882-1886. (e) Bessho, J.-I.; Shimotsu, Y.; Mizumoto, S.; Mase, N.; Yoda, H.; Takabe, K. *Heterocycles* **2004**, *63*, 1013-1016. (f) Li, W.-R.; Lin, S. T.; Hsu, N.-M.; Chern, M.-S. *J. Org. Chem*. **2002**, *67*, 4702-4706.
2. For the synthesis and synthetic applications of 5-alkylidene-1,5-dihydropyrrol-2-ones, see: (a) Coperet, C.; Sugihara, T.; Wu, G.; Shimoyama, I.; Negishi, E.-I. *J. Am. Chem. Soc*. **1995**, *117*, 3422-3431. (b) Haase, C.; Langer, P. *Tetrahedron* **2009**, *65*, 4530-4539. (c) Mykhaylychenko, S.; Harakat, D.; Dupas, G.; Shermolovich, Y. G.; Bouillon, J.-P. *J. Fluorine Chem*. **2009**, *130*, 418-427. (d) Ngwe, H.; Kinoshita, H.; Inomata, K. *Bull. Chem. Soc. Jpn*. **1994**, *67*, 3320-3326. (e) Kinoshita, H.; Ngwe, H.; Kobori, K.; Inomata, K. *Chem. Lett*. **1993**, 1441-1442.
3. For the synthesis and biological activity of 5-hydroxypyrrol-2(5*H*)-ones, see: (a) Ma, S.; Xie, H. *Org. Lett*. **2000**, *2*, 3801-3803. (b) Boukouvalas, J; Loach, R. P.; Ouellet, E. *Tetrahedron Lett*. **2011**, *52*, 5047-5050 and further references cited therein. (c) Watson, A. F.; Liu, J.; Bennaceur, K.; Drummond, C. J.; Endicott, J. A.; Golding, B. T.; Griffin, R. J.; Haggerty, K.; Lu, X.; McDonnell, J. M.; Newell, D. R.; Noble, M. E. M.; Revill, C. H.; Riedinger, C.; Xu, Q.; Zhao, Y.; Lunec, J.; Hardcastle, I. R. *Bioorg. Med. Chem. Lett*. **2011**, *21*, 5916-5919.
4. For the general review on Baylis-Hillman reaction, see: (a) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev.* **2003**, *103*, 811-891. (b) Basavaiah, D.; Reddy, B. S.; Badsara, S. S. *Chem. Rev.* **2010**, *110*, 5447-5674. (c) Singh, V.; Batra, S. *Tetrahedron* **2008**, *64*, 4511-4574. (d) Declerck, V.; Martinez, J.; Lamaty, F. *Chem. Rev.* **2009**, *109*, 1-48. (e) Ciganek, E. In *Organic Reactions*; Paquette, L. A., Ed.; John Wiley & Sons: New York, 1997; Vol. 51, pp 201-350. (f) Kim, J. N.; Lee, K. Y. *Curr. Org. Chem*. **2002**, *6*, 627-645. (g) Lee, K. Y.; Gowrisankar, S.; Kim, J. N. *Bull. Korean Chem. Soc*. **2005**, *26*, 1481-1490. (h) Radha Krishna, P.; Sachwani, R.; Reddy, P. S. *Synlett* **2008**, 2897-2912. (i) Gowrisankar, S.; Lee, H. S.; Kim, S. H.; Lee, K. Y.; Kim, J. N. *Tetrahedron* **2009**, 65, 8769-8780.
5. For the synthesis of various lactams from MBH adducts in our group, see: (a) Lee, K. Y.; Lee, Y. J.; Kim, J. N. *Bull. Korean Chem. Soc*. **2007**, *28*, 143-146. (b) Kim, S. C.; Gowrisankar, S.; Kim, J. N. *Tetrahedron Lett*. **2006**, *47*, 3463-3466. (c) Kim, S. C.; Lee, K. Y.; Gowrisankar, S.; Kim, J. N. *Bull. Korean Chem. Soc*. **2006**, *27*, 1133-1139. (d) Lee, H. S.; Kim, S. J.; Kim, J. N. *Bull. Korean Chem. Soc*. **2006**, *27*, 1063-1066. (e) Lee, M. J.; Lee, K. Y.; Park, D. Y.; Kim, J. N. *Bull. Korean Chem. Soc*. **2005**, *26*, 1281-1285.
6. For the synthesis of various lactams from MBH adducts in other groups, see: (a) Amri, H.; El Gaied, M. M.; Ben Ayed, T.; Villieras, J. *Tetrahedron Lett*. **1992**, *33*, 6159-6160. (b) Buchholz, R.; Hoffmann, H. M. R. *Helv. Chim. Acta* **1991**, *74*, 1213-1220. (c) Singh, V.; Saxena, R.; Batra, S. *J. Org. Chem*. **2005**, *70*, 353-356. (d) Singh, V.; Yadav, G. P.; Maulik, P. R.; Batra, S. *Tetrahedron* **2008**, *64*, 2979-2991. (e) Singh, V.; Yadav, G. P.; Maulik, P. R.; Batra, S. *Tetrahedron* **2006**, *62*, 8731-8739. (f) Coelho, F.; Diaz, G.; Abella, C. A. M.; Almeida, W. P. *Synlett* **2006**, 435-439. (g) Basavaiah, D.; Rao, J. S. *Tetrahedron Lett*. **2004**, *45*, 1621-1625. (h) Ramachandran, P. V.; Madhi, S.; Bland-Berry, L.; Reddy, M. V. R.; O'Donnell, M. J. *J. Am. Chem. Soc*. **2005**, *127*, 13450-13451. (i) Kawahara, S.; Nakano, A.; Esumi, T.; Iwabuchi, Y.; Hatakeyama, S. *Org. Lett*. **2003**, *5*, 3103-3105. (j) Song, Y. S.; Lee, C. H.; Lee, K.-J. *J. Heterocyclic Chem*. **2003**, *40*, 939-941.
7. Park, B. R.; Kim, K. H.; Lim, J. W.; Kim, J. N. *Tetrahedron Lett*. **2012**, *53*, 36-40.
8. (a) Abell, A. D.; Oldham, M. D.; Taylor, J. M. *J. Org. Chem*. **1995**, *60*, 1214-1220. (b) Beck, J. J.; Stermitz, F. R. *J. Nat. Prod*. **1995**, *58*, 1047-1055. (c) Tripathi, R. P.; Dwivedi, N.; Singh, N.; Misra, M. *Med. Chem. Res*. **2008**, *17*, 53-61.
9. For the acid-catalyzed dehydration of similar compounds, see: (a) Goh, W. K.; Black, D. StC.; Kumar, N. *Tetrahedron Lett*. **2007**, *48*, 9008-9011. (b) Goh, W. K.; Iskander, G.; Black, D. StC.; Kumar, N. *Tetrahedron Lett*. **2007**, *48*, 2287-2290.