Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron Letters 47 (2006) 5681–5685
Tetrahedron Letters

Regioselective construction of polysubstituted phenols from Baylis–Hillman adducts via formal [4+2] annulation strategy

Seung Chan Kim,[a] Hyun Seung Lee,[a] Young Ju Lee[b] and Jae Nyoung Kim[a,*]

[a]*Department of Chemistry and Institute of Basic Science, Chonnam National University, Gwangju 500-757, Republic of Korea*
[b]*Korea Basic Science Institute, Gwangju branch, Gwangju 500-757, Republic of Korea*

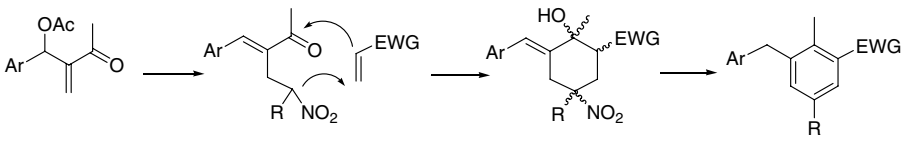
Received 28 April 2006; revised 1 June 2006; accepted 2 June 2006
Available online 27 June 2006

Abstract—Polysubstituted phenol derivatives were synthesized regioselectively starting from the Baylis–Hillman adducts via the formal [4+2] annulation protocol as the key step.

Recently, we reported the synthesis of polysubstituted benzenes starting from the Baylis–Hillman adducts.[1] These valuable compounds were prepared from the Baylis–Hillman acetates of alkyl vinyl ketone by the sequential S_N2' reaction with primary nitroalkane, Michael addition, aldol condensation, elimination of HNO_2, and the final aromatization process (Scheme 1).[1] In the reaction, the modified Baylis–Hillman derivative with nitroalkane served as a four-carbon component and the Michael acceptor as a two-carbon unit. During the projects we reasoned that we could synthesize polysubstituted phenol derivatives by using a similar protocol when we used the Baylis–Hillman adducts of methyl acrylate.[2]

Due to the importance of phenol derivatives in pharmacologically important molecules[3,5] and their usefulness as synthetic intermediates, much attention has been focused on their synthesis.[3–5] A variety of methods have been examined including palladium-catalyzed enyne–diyne cross-benzannulation,[3b] cycloaddition of Fisher carbenes with alkynes,[3c] stepwise construction method of benzene ring of phenol by condensation reaction as the key reaction.[3a,d,4]

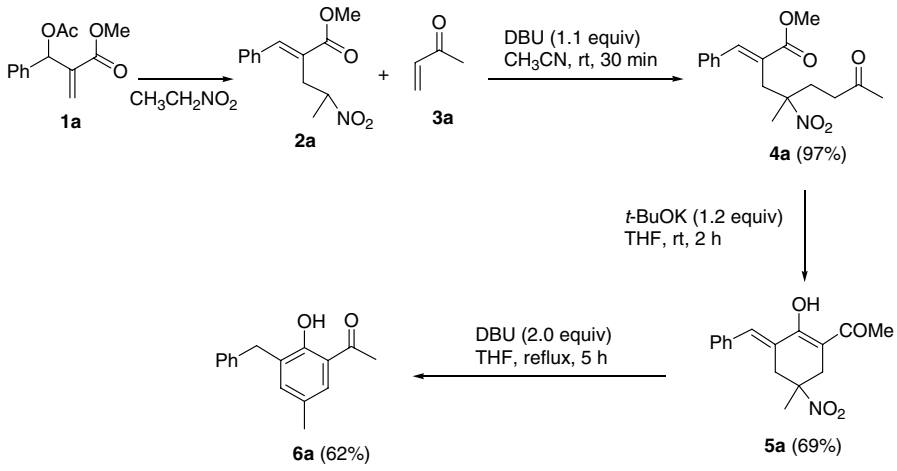
In order to examine the feasibility for the construction of polysubstituted phenol derivatives, we made **2a** from Baylis–Hillman acetate of methyl acrylate **1a** and nitroethane by following the previous method[1,6] and examined the reaction with methyl vinyl ketone (**3a**) as shown in Scheme 2. We used DBU as the base for the Michael addition and obtained the desired product **4a** in excellent yield (97%).[7] However, the following aldol-type cyclization did not occur under the influence of DBU. Thus we used potassium *tert*-butoxide in THF conditions and obtained **5a** in 69% yield.[7] This compound **5a** must be formed via the successive aldol-type cyclization of **4a**, followed by enolization. During the conversion of **4a** into **5a** we observed the formation of trace amount of phenol derivative **6a** (4%); however, the amount of **6a** was not increased by elevating the reaction temperature for long time. The final step, elimination of HNO_2 and concomitant formal 1,3-hydrogen shift, was conducted with DBU again to produce **6a** in 62% yield.[7]



Scheme 1.

Keywords: Phenols; Baylis–Hillman adducts; [4+2] Annulation; Regioselective.
* Corresponding author. Tel.: +82 62 530 3381; fax: +82 62 530 3389; e-mail: kimjn@chonnam.ac.kr

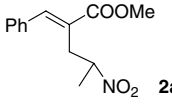
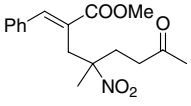
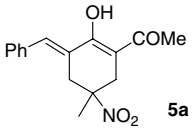
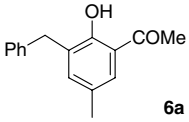
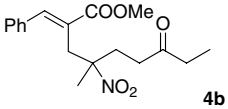
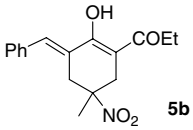
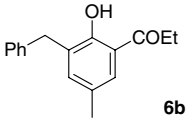
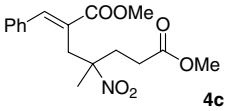
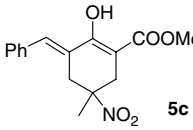
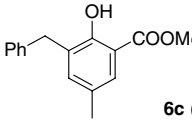
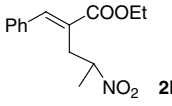
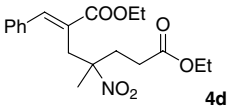
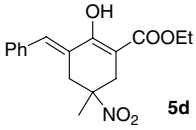
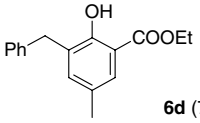
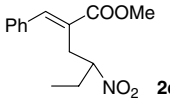
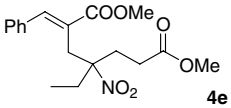
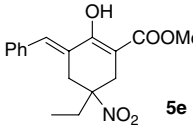
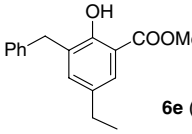
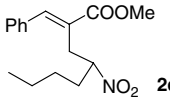
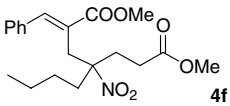
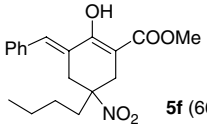
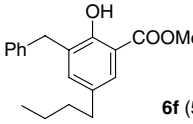
0040-4039/$ - see front matter
doi:10.1016/j.tetlet.2006.06.031



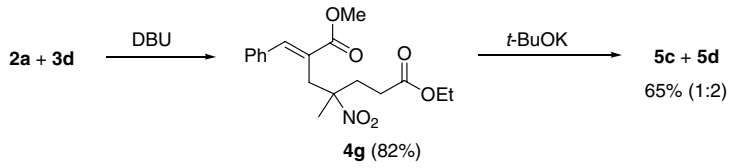
Scheme 2.

With the optimized reaction conditions, we carried out the synthesis of polysubstituted phenols **6b–f** and the results are summarized in Table 1. We used Baylis–Hillman derivatives **2a–d** as the four-carbon unit and Michael acceptors **3a–d** as the two-carbon component. As shown, the whole reactions proceeded similarly irrespective of the differences of substrates. In all cases the Michael addition reaction showed high yields of products **4a–f** (72–97%). The next aldol-type (entries 1 and 2) or Dieckmann (entries 3–6) condensation occurred

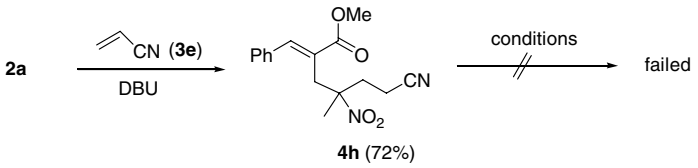
Table 1. Synthesis of polysubstituted phenols

Entry	Substrate	Michael acceptor	Intermediate **4** (%)[a]	Cyclohexene **5** (%)[b]	Phenol **6** (%)[c]
1	 **2a**	MVK (**3a**)	 **4a** (97)	 **5a** (69)	 **6a** (62)
2	**2a**	EVK (**3b**)	 **4b** (95)	 **5b** (68)	 **6b** (44)
3	**2a**	Methyl acrylate (**3c**)	 **4c** (83)	 **5c** (67)	 **6c** (76)
4	 **2b**	Ethyl acrylate (**3d**)	 **4d** (72)	 **5d** (63)	 **6d** (71)
5	 **2c**	**3c**	 **4e** (82)	 **5e** (71)	 **6e** (47)
6	 **2d**	**3c**	 **4f** (74)	 **5f** (66)	 **6f** (56)

[a] Conditions: **2** (1.0 equiv), **3** (1.1 equiv), DBU (1.1 equiv), CH_3CN, rt, 30–180 min.
[b] Conditions: **4** (1.0 equiv), *t*-BuOK (1.2 equiv), THF, rt, 1–5 h.
[c] Conditions: **5** (1.0 equiv), DBU (2.0 equiv), CH_3CN (or THF), reflux, 5–29 h.



Scheme 3.



Scheme 4.

in similar yields (63–71%). But, the yields of final elimination of nitrous acid and aromatization stage were much different. The yields of **6b**, **6e**, and **6f** were relatively low.

The reaction of the Michael addition product **4g** was also examined (Scheme 3). This compound **4g** was prepared by the reaction of **2a** and **3d** in 82% yield. When **4g** was treated with *t*-BuOK, we found the formation of **5c** and **5d** (1:2) in 65% yield. Compound **5c** must be produced via the transesterification process by the methoxide ion, which was generated during the Dieckmann cyclization of **4g**. The reaction of **2a** and acrylonitrile (**3e**) gave **4h** in 72% yield. However, the cyclization of **4h** under various reaction conditions failed, unfortunately (Scheme 4).

In summary, we disclosed the facile and regioselective synthesis of polysubstituted phenol derivatives starting from the Baylis–Hillman adducts via the formal [4+2] annulation protocol as the key step.

Acknowledgments

This work was supported by the Korea Research Foundation Grant funded by the Korean Government (MOEHRD, KRF-2005-041-C00248). Spectroscopic data was obtained from the Korea Basic Science Institute, Gwangju branch.

References and notes

1. (a) Lee, M. J.; Lee, K. Y.; Park, D. Y.; Kim, J. N. *Tetrahedron* **2006**, *62*, 3128; (b) Lee, M. J.; Lee, K. Y.; Gowrisankar, S.; Kim, J. N. *Tetrahedron Lett.* **2006**, *47*, 1355.
2. For our recent publications on the chemical transformations of Baylis–Hillman adducts, see: (a) Lee, K. Y.; Gowrisankar, S.; Kim, J. N. *Bull. Korean Chem. Soc.* **2005**, *26*, 1481; (b) Park, D. Y.; Lee, M. J.; Kim, T. H.; Kim, J. N. *Tetrahedron Lett.* **2005**, *46*, 8799; (c) Lee, M. J.; Park, D. Y.; Lee, K. Y.; Kim, J. N. *Tetrahedron Lett.* **2006**, *47*, 1833; (d) Lee, K. Y.; Kim, S. C.; Kim, J. N. *Tetrahedron Lett.* **2006**, *47*, 977; (e) Kim, J. N.; Lee, K. Y. *Curr. Org. Chem.* **2002**, *6*, 627.
3. For the synthesis of polysubstituted phenol derivatives, see: (a) Nakaike, Y.; Kamijo, Y.; Mori, S.; Tamura, M.; Nishiwaki, N.; Ariga, M. *J. Org. Chem.* **2005**, *70*, 10169; (b) Gevorgyan, V.; Quan, L. G.; Yamamoto, Y. *J. Org. Chem.* **1998**, *63*, 1244; (c) Barluenga, J.; Aznar, F.; Gutierrez, I.; Martin, A.; Garcia-Granda, S.; Llorca-Baragano, M. A. *J. Am. Chem. Soc.* **2000**, *122*, 1314; (d) Poly, W.; Schomburg, D.; Hoffmann, H. M. R. *J. Org. Chem.* **1988**, *53*, 3701; (e) Fukuhara, K.; Takayama, Y.; Sato, F. *J. Am. Chem. Soc.* **2003**, *125*, 6884; (f) Padwa, A.; Dimitroff, M.; Waterson, A. G.; Wu, T. *J. Org. Chem.* **1997**, *62*, 4088; (g) Kobayashi, S.; Moriwaki, M.; Hachiya, I. *Tetrahedron Lett.* **1996**, *37*, 2053; (h) Cimarelli, C.; Palmieri, G. *Tetrahedron* **1998**, *54*, 15711.
4. Kim, J. N.; Im, Y. J.; Kim, J. M. *Tetrahedron Lett.* **2002**, *43*, 6597.
5. For the usefulness of phenol derivatives as synthetic intermediates, see: (a) Simaan, S.; Siegel, J. S.; Biali, S. E. *J. Org. Chem.* **2003**, *68*, 3699; (b) Crisp, G. T.; Turner, P. D. *Tetrahedron* **2000**, *56*, 407; (c) Caruso, A. J.; Lee, J. L. *J. Org. Chem.* **1997**, *62*, 1058; (d) Brigati, G.; Lucarini, M.; Mugnaini, V.; Pedulli, G. F. *J. Org. Chem.* **2002**, *67*, 4828; (e) Gobbi, S.; Rampa, A.; Bisi, A.; Belluti, F.; Piazzi, L.; Valenti, P.; Caputo, A.; Zampiron, A.; Carrara, M. *J. Med. Chem.* **2003**, *46*, 3662; (f) Leahy, J. J. J.; Golding, B. T.; Griffin, R. J.; Hardcastle, I. R.; Richardson, C.; Rigoreau, L.; Smith, G. C. M. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 6083; (g) Fougerousse, A.; Gonzalez, E.; Brouillard, R. *J. Org. Chem.* **2000**, *65*, 583; (h) Klymchenko, A. S.; Ozturk, T.; Pivovarenko, V. G.; Demchenko, A. P. *Tetrahedron Lett.* **2001**, *42*, 7967; (i) Horino, Y.; Naito, M.; Kimura, M.; Tanaka, S.; Tamaru, Y. *Tetrahedron Lett.* **2001**, *42*, 3113; (j) Rao, M. L. N.; Houjou, H.; Hiratani, K. *Tetrahedron Lett.* **2001**, *42*, 8351; (k) Perez-Serrano, L.; Blanco-Urgoiti, J.; Casarrubios, L.; Dominguez, G.; Perez-Castells, J. *J. Org. Chem.* **2000**, *65*, 3513; (l) Ruchirawat, S.; Mutarapat, T. *Tetrahedron Lett.* **2001**, *42*, 1205.
6. Synthesis of starting materials, see: Kim, J. M.; Im, Y. J.; Kim, T. H.; Kim, J. N. *Bull. Korean Chem. Soc.* **2002**, *23*, 657.
7. *Synthesis of* **4a** (*Typical procedure*): To a stirred mixture of **2a**[6] (498 mg, 2.0 mmol) and methyl vinyl ketone (**3a**, 154 mg, 2.2 mmol) in CH_3CN (5 mL) was added DBU (335 mg, 2.2 mmol) and stirred for further 30 min at room temperature. After the usual aqueous extractive workup with ether and column chromatographic purification process (hexanes/EtOAc, 5:1), we obtained **4a** as a colorless oil, 619 mg (97%). The other compounds were synthesized analogously and the spectroscopic data are as follows.

Compound **4a**: (30 min, 97%); colorless oil; IR (CH_2Cl_2) 1716, 1632, 1539, 1436 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.33 (s, 3H), 1.81–1.92 (m, 1H), 2.04 (s, 3H), 2.13–2.25 (m, 3H), 3.26 (d, $J = 14.4$ Hz, 1H), 3.38 (d, $J = 14.4$ Hz, 1H), 3.78 (s, 3H), 7.27–7.29 (m, 2H), 7.32–7.44 (m, 3H), 7.91 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.79, 29.80, 32.62, 35.11, 37.84, 52.17, 90.12, 127.74, 128.42, 128.62, 128.78, 135.02, 143.76, 168.06, 206.15; ESIMS *m/z* 320 (M^++H).

Compound **4b**: (30 min, 95%); colorless oil; IR (CH_2Cl_2) 1716, 1631, 1539, 1442 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.00 (t, $J = 7.2$ Hz, 3H), 1.32 (s, 3H), 1.84–1.94 (m, 1H), 2.15–2.23 (m, 3H), 2.31 (q, $J = 7.2$ Hz, 2H), 3.26 (d, $J = 14.7$ Hz, 1H), 3.38 (d, $J = 14.7$ Hz, 1H), 3.78 (s, 3H), 7.27–7.43 (m, 5H), 7.91 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 7.65, 21.73, 32.72, 35.23, 35.81, 36.49, 52.15, 90.20, 127.76, 128.43, 128.60, 128.75, 135.02, 143.72, 168.06, 208.93.

Compound **4c**: (30 min, 83%); colorless oil; IR (CH_2Cl_2) 1732, 1716, 1631, 1543, 1439 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.35 (s, 3H), 1.84–1.94 (m, 1H), 2.03–2.22 (m, 2H), 2.27–2.37 (m, 1H), 3.25 (d, $J = 14.7$ Hz, 1H), 3.38 (d, $J = 14.7$ Hz, 1H), 3.63 (s, 3H), 3.79 (s, 3H), 7.26–7.29 (m, 2H), 7.31–7.44 (m, 3H), 7.92 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.43, 28.63, 33.95, 35.47, 51.78, 52.19, 89.96, 127.60, 128.41, 128.67, 128.77, 134.98, 143.92, 168.04, 172.41.

Compound **4d**: (30 min, 72%); colorless oil; IR (CH_2Cl_2) 1733, 1715, 1632, 1541, 1446 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.21 (t, $J = 7.2$ Hz, 3H), 1.33 (t, $J = 7.2$ Hz, 3H), 1.35 (s, 3H), 1.84–1.93 (m, 1H), 2.01–2.22 (m, 2H), 2.28–2.37 (m, 1H), 3.26 (d, $J = 14.7$ Hz, 1H), 3.38 (d, $J = 14.7$ Hz, 1H), 4.08 (q, $J = 7.2$ Hz, 2H), 4.24 (q, $J = 7.2$ Hz, 2H), 7.27–7.43 (m, 5H), 7.92 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.90, 13.97, 21.31, 28.78, 33.88, 35.36, 60.50, 61.26, 89.89, 127.87, 128.31, 128.47, 128.64, 134.99, 143.44, 167.44, 171.81.

Compound **4e**: (60 min, 82%); white solid, mp 78–80 °C; IR (CH_2Cl_2) 1738, 1712, 1539, 1492, 1446 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.62 (t, $J = 7.5$ Hz, 3H), 1.65–1.77 (m, 1H), 1.81–1.94 (m, 1H), 1.97–2.23 (m, 4H), 3.26 (s, 2H), 3.64 (s, 3H), 3.78 (s, 3H), 7.26–7.29 (m, 2H), 7.31–7.43 (m, 3H), 7.88 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 7.88, 28.20, 28.43, 29.19, 32.20, 51.74, 52.16, 93.25, 127.89, 128.40, 128.57, 128.74, 135.02, 143.52, 168.11, 172.44.

Compound **4f**: (180 min, 74%); colorless oil; IR (CH_2Cl_2) 1739, 1720, 1635, 1539, 1439 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.75 (t, $J = 7.2$ Hz, 3H), 0.81–0.94 (m, 2H), 1.12 (quintet, $J = 7.2$ Hz, 2H), 1.57–1.67 (m, 1H), 1.73–1.84 (m, 1H), 1.96–2.25 (m, 4H), 3.27 (s, 2H), 3.64 (s, 3H), 3.77 (s, 3H), 7.27–7.43 (m, 5H), 7.87 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.60, 22.64, 25.60, 28.50, 29.84, 32.59, 34.92, 51.75, 52.16, 92.85, 127.92, 128.39, 128.58, 128.75, 135.05, 143.38, 168.11, 172.45.

Compound **4g**: (30 min, 82%); colorless oil; IR (CH_2Cl_2) 1720, 1631, 1543, 1442 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.22 (t, $J = 7.2$ Hz, 3H), 1.35 (s, 3H), 1.84–1.94 (m, 1H), 2.02–2.21 (m, 2H), 2.27–2.37 (m, 1H), 3.25 (d, $J = 14.7$ Hz, 1H), 3.38 (d, $J = 14.7$ Hz, 1H), 3.79 (s, 3H), 4.08 (q, $J = 7.2$ Hz, 2H), 7.27–7.30 (m, 2H), 7.31–7.43 (m, 3H), 7.92 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.08, 21.39, 28.88, 33.96, 35.52, 52.17, 60.66, 89.99, 127.61, 128.41, 128.65, 128.76, 134.97, 143.87, 168.03, 171.95.

Compound **4h**: (30 min, 72%); colorless oil; IR (CH_2Cl_2) 2251, 1714, 1632, 1541, 1494, 1445 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.41 (s, 3H), 1.86–1.96 (m, 1H), 2.13–2.19 (m, 2H), 2.31–2.41 (m, 1H), 3.27 (d, $J = 14.4$ Hz, 1H), 3.37 (d, $J = 14.4$ Hz, 1H), 3.81 (s, 3H), 7.27–7.29 (m, 2H), 7.35–7.46 (m, 3H), 7.97 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 12.44, 21.84, 34.08, 34.96, 52.37, 89.47, 118.24, 126.89, 128.29, 128.95, 128.99, 134.73, 144.55, 167.81.

Synthesis of **5a** (*Typical procedure*): To a stirred mixture of **4a** (319 mg, 1.0 mmol) in THF (3 mL) was added *t*-BuOK (135 mg, 1.2 mmol) and the reaction mixture was stirred at room temperature for 2 h. After the usual aqueous extractive workup with ether and column chromatographic purification process (hexanes/EtOAc, 7:1), we obtained **5a** as a white solid, 199 mg (69%). The other compounds were synthesized analogously and the spectroscopic data are as follows.

Compound **5a**: (2 h, 69%); white solid, mp 173–174 °C; IR (KBr) 2900, 1621, 1534, 1446, 1418 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.65 (s, 3H), 2.28 (s, 3H), 2.81 (d, $J = 15.9$ Hz, 1H), 2.96 (d, $J = 15.9$ Hz, 1H), 3.38 (d, $J = 15.9$ Hz, 1H), 3.56 (d, $J = 15.9$ Hz, 1H), 7.33–7.45 (m, 5H), 7.76 (s, 1H), 15.85 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 26.03, 26.19, 34.76, 35.81, 85.90, 103.79, 126.65, 128.56, 128.65, 129.63, 135.30, 136.19, 169.52, 200.91; ESIMS *m/z* 288 (M^++H). Anal. Calcd for $C_{16}H_{17}NO_4$: C, 66.89; H, 5.96; N, 4.88. Found: C, 66.95; H, 6.05; N, 4.75.

Compound **5b**: (1 h, 68%); white solid, mp 135–137 °C; IR (KBr) 2980, 2903, 1624, 1577, 1535, 1446, 1414, 1342 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.18 (t, $J = 7.2$ Hz, 3H), 1.64 (s, 3H), 2.48–2.70 (m, 2H), 2.80 (d, $J = 15.9$ Hz, 1H), 2.95 (d, $J = 15.9$ Hz, 1H), 3.38 (d, $J = 15.9$ Hz, 1H), 3.55 (d, $J = 15.9$ Hz, 1H), 7.32–7.45 (m, 5H), 7.74 (s, 1H), 15.81 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 8.03, 26.06, 31.65, 34.14, 35.79, 85.91, 103.36, 126.69, 128.55 (2C), 129.60, 135.39, 135.79, 168.51, 204.23. Anal. Calcd for $C_{17}H_{19}NO_4$: C, 67.76; H, 6.36; N, 4.65. Found: C, 67.65; H, 6.25; N, 4.63.

Compound **5c**: (4 h, 67%); white solid, mp 144–146 °C; IR (KBr) 3024, 2958, 2897, 1655, 1616, 1589, 1539, 1442, 1346 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.61 (s, 3H), 2.74 (d, $J = 16.5$ Hz, 1H), 2.93 (d, $J = 15.6$ Hz, 1H), 3.35 (d, $J = 16.5$ Hz, 1H), 3.52 (d, $J = 15.6$ Hz, 1H), 3.84 (s, 3H), 7.30–7.44 (m, 5H), 7.60 (s, 1H), 12.35 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 25.87, 33.11, 35.94, 52.07, 85.75, 95.56, 126.19, 128.28, 128.50,129.46, 133.89, 135.51, 163.88, 172.36; ESIMS *m/z* 304 (M^++H). Anal. Calcd for $C_{16}H_{17}NO_5$: C, 63.36; H, 5.65; N, 4.62. Found: C, 63.51; H, 5.81; N, 4.46.

Compound **5d**: (4 h, 63%); white solid, mp 123–125 °C; IR (KBr) 2984, 2909, 1643, 1616, 1585, 1537, 1445 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.36 (t, $J = 7.2$ Hz, 3H), 1.61 (s, 3H), 2.75 (d, $J = 16.8$ Hz, 1H), 2.94 (d, $J = 15.6$ Hz, 1H), 3.34 (d, $J = 16.8$ Hz, 1H), 3.51 (d, $J = 15.6$ Hz, 1H), 4.29 (q, $J = 7.2$ Hz, 2H), 7.31–7.44 (m, 5H), 7.59 (s, 1H), 12.45 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.23, 25.82, 33.16, 35.96, 61.16, 85.81, 95.75, 126.32, 128.23, 128.50, 129.46, 133.70, 135.57, 163.79, 172.07.

Compound **5e**: (5 h, 71%); white solid, mp 80–82 °C; IR (KBr) 2949, 1644, 1589, 1544, 1445, 1345 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.84 (t, $J = 7.5$ Hz, 3H), 1.94 (q, $J = 7.5$ Hz, 2H), 2.71 (d, $J = 16.8$ Hz, 1H), 2.89 (d, $J = 15.6$ Hz, 1H), 3.34 (d, $J = 16.8$ Hz, 1H), 3.54 (d, $J = 15.6$ Hz, 1H), 3.84 (s, 3H), 7.31–7.44 (m, 5H), 7.57 (s, 1H), 12.33 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 7.92, 30.99, 32.10, 34.03, 52.06, 89.39, 95.59, 126.11, 128.21, 128.50, 129.39, 133.77, 135.57, 164.07, 172.40.

Compound **5f**: (4 h, 66%); white solid, mp 94–96 °C; IR (KBr) 2954, 2869, 1651, 1621, 1593, 1542, 1438 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.84 (t, $J = 7.2$ Hz, 3H), 1.10–1.30 (m, 4H), 1.85–1.91 (m, 2H), 2.71 (d, $J = 16.8$ Hz, 1H), 2.89 (d, $J = 15.6$ Hz, 1H), 3.35 (d, $J = 16.8$ Hz, 1H), 3.54 (d, $J = 15.6$ Hz, 1H), 3.84 (s, 3H), 7.30–7.45 (m, 5H), 7.57 (s, 1H), 12.33 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.68,

22.35, 25.45, 31.35, 34.46, 38.80, 52.06, 89.10, 95.63, 126.16, 128.21, 128.50, 129.38, 133.76, 135.59, 164.05, 172.41.

Synthesis of **6a** (*Typical procedure*): To a stirred mixture of **5a** (144 mg, 0.5 mmol) in THF (2 mL) was added DBU (152 mg, 1.0 mmol) and the reaction mixture was heated to reflux for 5 h. After the usual aqueous extractive workup with ether and column chromatographic purification process (hexanes/ether, 10:1), we obtained **6a** as a white solid, 75 mg (62%). The other compounds were synthesized analogously and the spectroscopic data are as follows.

Compound **6a**: (THF, 5 h, 62%); white solid, mp 80–82 °C; IR (KBr) 2858, 1631 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.25 (s, 3H), 2.60 (s, 3H), 3.98 (s, 2H), 7.11 (s, 1H), 7.18–7.30 (m, 5H), 7.39 (s, 1H), 12.46 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.57, 26.77, 35.07, 119.03, 126.01, 127.39, 128.37, 128.63, 128.90, 130.20, 138.05, 140.37, 158.35, 204.60; ESIMS *m/z* 241 (M^++H). Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 79.91; H, 6.59.

Compound **6b**: (THF, 11 h, 44%); white solid, mp 81–83 °C; IR (KBr) 2916, 1636, 1610, 1456 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.22 (t, $J = 7.2$ Hz, 3H), 2.25 (s, 3H), 3.01 (q, $J = 7.2$ Hz, 2H), 3.98 (s, 2H), 7.09 (s, 1H), 7.16–7.30 (m, 5H), 7.42 (s, 1H), 12.55 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 8.35, 20.62, 31.61, 35.11, 118.54, 125.99, 127.28, 127.74, 128.36, 128.91, 130.26, 137.72, 140.43, 158.34, 207.20. Anal. Calcd for $C_{17}H_{18}O_2$: C, 80.28; H, 7.13. Found: C, 80.42; H, 7.11.

Compound **6c**: (THF, 29 h, 76%); yellow solid, mp 51–53 °C; IR (KBr) 3155, 2951, 1662, 1612, 1442 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.21 (s, 3H), 3.91 (s, 3H), 3.98 (s, 2H), 7.08 (d, $J = 2.1$ Hz, 1H), 7.15–7.30 (m, 5H), 7.51 (d, $J = 2.1$ Hz, 1H), 10.87 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.41, 35.32, 52.16, 111.62, 125.97, 127.73 (2C), 128.34, 128.86, 129.33, 137.31, 140.46, 157.51, 170.91; ESIMS *m/z* 257 (M^++H). Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 75.12; H, 6.43.

Compound **6d**: (CH_3CN, 6 h, 71%); pale yellow solid, mp 52–53 °C; IR (KBr) 2928, 1666, 1614 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.40 (t, $J = 7.2$ Hz, 3H), 2.23 (s, 3H), 3.98 (s, 2H), 4.38 (q, $J = 7.2$ Hz, 2H), 7.07 (s, 1H), 7.16–7.30 (m, 5H), 7.52 (s, 1H), 10.96 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 14.21, 20.43, 35.33, 61.27, 111.88, 125.96, 127.64, 127.71, 128.34, 128.87, 129.30, 137.20, 140.52, 157.59, 170.54.

Compound **6e**: (CH_3CN, 5 h, 47%); pale yellow solid, mp 31–33 °C; IR (KBr) 2952, 1667, 1613 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.17 (t, $J = 7.5$ Hz, 3H), 2.52 (q, $J = 7.5$ Hz, 2H), 3.92 (s, 3H), 4.00 (s, 2H), 7.12 (d, $J = 1.8$ Hz, 1H), 7.18–7.30 (m, 5H), 7.54 (d, $J = 1.8$ Hz, 1H), 10.89 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 15.68, 27.89, 35.45, 52.17, 111.69, 125.96, 126.52, 128.34, 128.85, 129.35, 134.29, 136.34, 140.48, 157.74, 170.96; ESIMS *m/z* 271 (M^++H).

Compound **6f**: (CH_3CN, 4 h, 56%); yellow oil; IR (CH_2Cl_2) 2954, 1674, 1612, 1442 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.90 (t, $J = 7.2$ Hz, 3H), 1.25–1.35 (m, 2H), 1.47–1.57 (m, 2H), 2.48 (t, $J = 7.8$ Hz, 2H), 3.91 (s, 3H), 3.99 (s, 2H), 7.10 (d, $J = 2.1$ Hz, 1H), 7.15–7.30 (m, 5H), 7.52 (d, $J = 2.1$ Hz, 1H), 10.88 (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.89, 22.22, 33.69, 34.65, 35.45, 52.15, 111.64, 125.94, 127.12, 128.32, 128.83, 129.24, 132.95, 136.79, 140.49, 157.71, 170.95.