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An expedient synthesis of indolo[1,2-*a*]quinolines via $Mn(OAc)_3$-mediated oxidative free radical cyclization and NaI/O_2-assisted dealkoxycarbonylation/aerobic oxidation cascade

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ABSTRACT

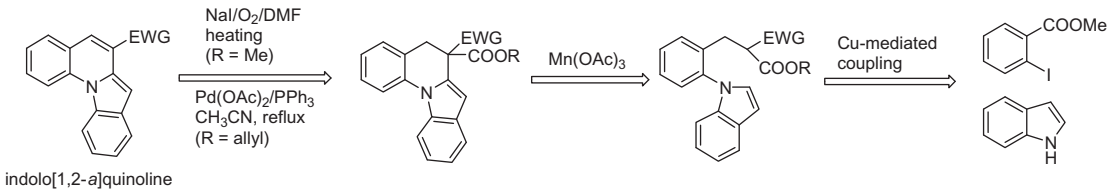
An expedient synthetic procedure of indolo[1,2-*a*]quinolines was developed using a sequential Cu-mediated N-arylation of indole, $Mn(OAc)_3$-mediated oxidative free radical cyclization, and NaI/O_2-assisted concomitant dealkoxycarbonylation/aerobic oxidation. The last step was replaced by a palladium-catalyzed decarboxylation/elimination protocol for the allyl ester derivatives.

Indole moiety-containing poly-fused heterocyclic compounds have been found in many biologically important natural products.[1,2] For example, numerous indole alkaloids have tetra- to hepta-fused heterocyclic structures, as in mersicarpine, tronocarpine, strychnine, vincamine, and dippinine.[1] N-Fused tetracyclic indolo[1,2-*a*]quinoline derivatives have also been synthesized in a variety of methods.[2]

Very recently, we reported an efficient synthesis of poly-fused tetracyclic compounds having an indole moiety via the Pd-catalyzed cyclization from the Baylis–Hillman adducts.[3] Due to the potential biological activities of poly-fused indole moiety-containing compounds including hepatitis C virus (HCV) NS5B polymerase inhibitory activity,[3] we were interested in the synthesis of indolo[1,2-*a*]quinoline scaffold. However, the reported synthetic approaches of indolo[1,2-*a*]quinoline were somewhat restricted to a special case and did not provide a general way.[2] Thus we wish to report herein an efficient and practical procedure for the synthesis of indolo[1,2-*a*]quinoline derivatives.

We reasoned out that indolo[1,2-*a*]quinoline could be synthesized from indole and methyl 2-iodobenzoate using a sequential Cu-mediated N-arylation of indole, $Mn(OAc)_3$-mediated oxidative free radical cyclization,[4,5] and NaI/O_2-assisted concomitant dealkoxycarbonylation/aerobic oxidation,[4a,6] as shown in Scheme 1. The final step could be replaced with a Pd-catalyzed decarboxylation/elimination protocol for the allyl ester.[7]

The required starting materials **7a–g** were prepared from methyl 2-iodobenzoate (**1**) in four steps, as shown in Scheme 2. The first Cu-catalyzed N-arylation of indoles **2a–c** (CuI, K_2CO_3, DMF, 120 °C, 2 h) afforded **3a–c** in reasonable yields (60–70%).[8] Reduction of **3a–c** with $LiAlH_4$ (THF, rt, 5 min) to the corresponding



Scheme 1.

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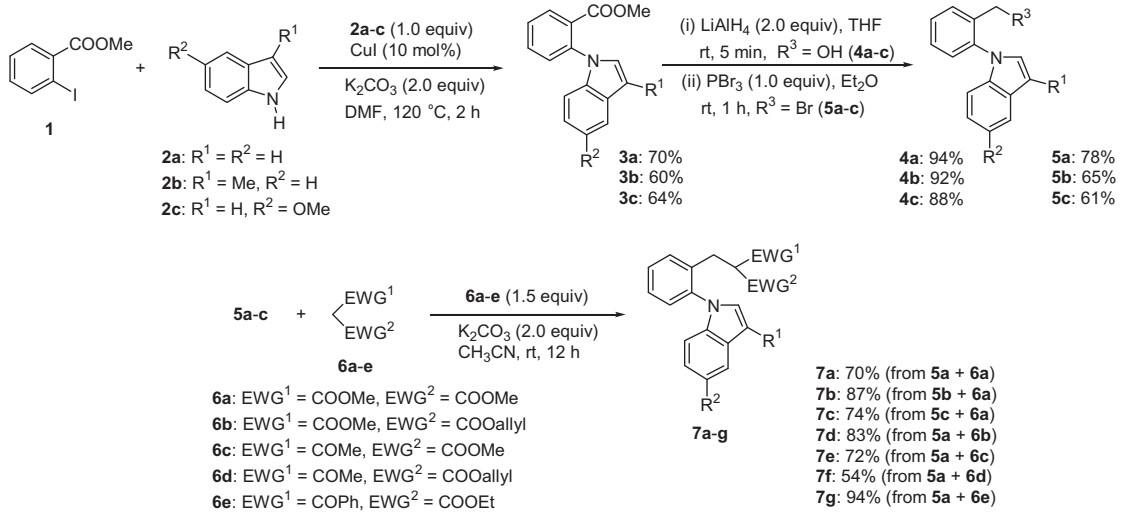
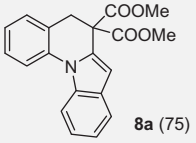
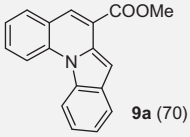
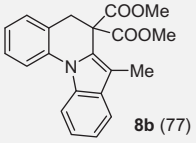
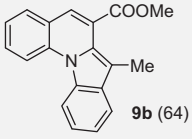
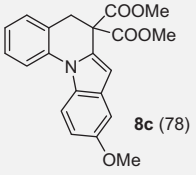
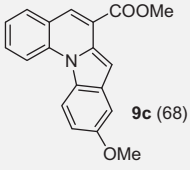
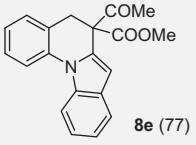
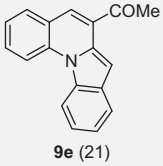
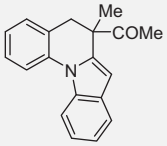
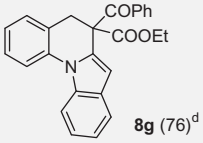
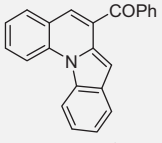
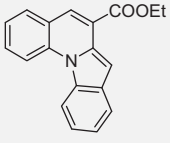


Scheme 2.

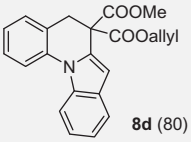
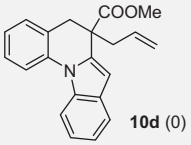
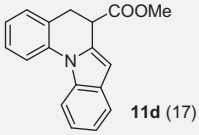
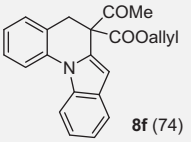
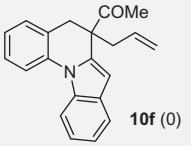
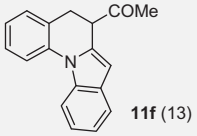
alcohols **4a–c** (88–94%) and the following bromination with PBr_3 (Et_2O, rt, 1 h) gave the bromides **5a–c** (61–78%). The reactions of **5a–c** and active methylene compounds **6a–e** (K_2CO_3, CH_3CN, rt, 12 h) produced the starting materials **7a–g** in moderate-to-good yields (54–94%).[9] Dimethyl malonate (**6a**), allyl methyl malonate (**6b**), methyl acetoacetate (**6c**), allyl acetoacetate (**6d**), and ethyl benzoylacetate (**6e**) were used as the representative active methylene compounds. During the synthesis of **7**, a bis-alkylation prod-

Table 1
Synthesis of indolo[1,2-*a*]quinolines **9a–c**, **9e**, and **9g**

Entry	Substrate **7**	Product **8**[a] (%)	Product **9**[b] (%)	
1	**7a**	 **8a** (75)	 **9a** (70)	
2	**7b**	 **8b** (77)	 **9b** (64)	
3	**7c**	 **8c** (78)	 **9c** (68)	
4	**7e**	 **8e** (77)	 **9e** (21)	 **10e** (52)
5	**7e**	**8e**	**9e**[c] (46)	**9a**[c] (14)
6	**7g**	 **8g** (76)[d]	 **9g** (45)[c]	 **9g'** (17)[c]

[a] Conditions: compound **7**, $Mn(OAc)_3$ (3.0 equiv), MeOH, reflux, 3 h (for **8a–c**) and 1 h (for **8e** and **8g**).
[b] Conditions: compound **8**, NaI (3.0 equiv), O_2 balloon, DMF, 120 °C, 2 h.
[c] Conditions: compound **9**, NaI (3.0 equiv), O_2 balloon, DMF, H_2O (3.0 equiv), 120 °C, 4 h.
[d] EtOH was used as a solvent.

Table 2
Pd-catalyzed synthesis of indolo[1,2-*a*]quinolines **9a** and **9e**

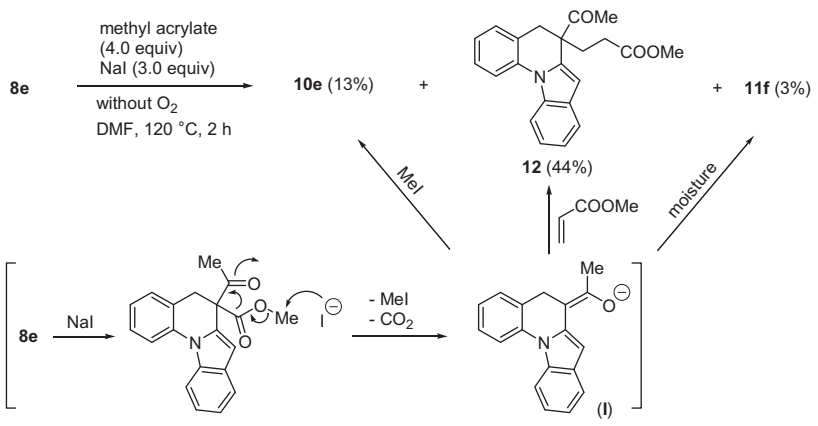
Entry	Substrate **7**	Product **8**[a] (%)	Conditions	Products (%)		
1	**7d**	 **8d** (80)	$Pd(OAc)_2$ (10 mol %) PPh_3 (4 mol %) CH_3CN, reflux, 15 min	**9a** (73)	 **10d** (0)	 **11d** (17)
2	**8d**		$Pd(OAc)_2$ (5 mol %) PPh_3 (40 mol %) toluene, reflux, 20 min	**9a** (0)	**10d** (85)	**11d** (5)
3	**8d**		$Pd(OAc)_2$ (5 mol %) PPh_3 (10 mol %) Et_3N (2.0 equiv) HCOOH (1.7 equiv) CH_3CN, reflux, 10 min	**9a** (0)	**10d** (0)	**11d** (85)
4	**7f**	 **8f** (74)	$Pd(OAc)_2$ (10 mol %) PPh_3 (4 mol %) CH_3CN, reflux, 15 min	**9e** (78)	 **10f** (0)	 **11f** (13)
5	**8f**		$Pd(OAc)_2$ (5 mol %) PPh_3 (40 mol %) toluene, reflux, 20 min	**9e** (0)	**10f** (83)	**11d** (8)
6	**8f**		$Pd(OAc)_2$ (5 mol %) PPh_3 (10 mol %) Et_3N (2.0 equiv) HCOOH (1.7 equiv) CH_3CN, reflux, 10 min	**9e** (0)	**10f** (0)	**11d** (84)

[a] Conditions: compound **7**, $Mn(OAc)_3$ (3.0 equiv), MeOH, reflux, 3 h (for **8d**) and 1 h (for **8f**).

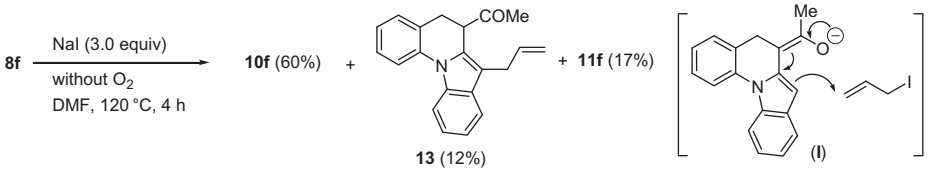
uct was formed in small amounts (ca. 5%), and the yield of **7** was low in some cases even though **6** was used in excess amounts (1.5 equiv).

$Mn(OAc)_3$-assisted cyclizations of **7a–g** were carried out in MeOH,[4,5] and the dihydroindolo[1,2-*a*]quinoline derivatives **8a–g** were prepared in good yields (74–80%), as shown in Table 1 (see also Table 2).[10] With these compounds **8a–g** in our hands, we examined the synthesis of indolo[1,2-*a*]quinolines **9a–g**. Conversions of **8a–c** to **9a–c** were carried out under the conditions of NaI/O_2 (balloon) in DMF at 120 °C for 2 h (entries 1–3 in Table 1) in good yields (64–70%) according to the reported method.[4a,11] The reaction of **8e**, however, provided low yield of **9e** (21%, entry 4) along with a methylation product **10e** in 52% yield. Compound **10e** must be formed by the reaction of iodomethane and an enolate (**I**), which was liberated during NaI-mediated decarboxylation stage (vide infra, Scheme 3). Thus we modified the reaction conditions in order to increase the yield of **9e**. We thought that a rapid quenching of the in situ-generated enolate with water could increase the yield of **9e** by suppressing the formation of **10e**. As shown in entry 5, the yield of **9e** was increased to 46% in the presence of 3.0 equiv of water.[12] The formation of a methylated product **10e** was controlled completely as expected; however, deacetylation[13]/oxidation product **9a** was produced in 14% yield (entry 5). The reaction of benzoyl derivative **8g** produced **9g** (45%) similarly in the presence of water (entry 6) along with debenzoylation/oxidation compound **9g′** (17%).[12]

A Pd(0)-catalyzed decarboxylation/elimination protocol was used for the allyl esters **8d** and **8f**, and the results are summarized in Table 2. The decarboxylation/elimination reaction was carried out in CH_3CN with low loading of PPh_3 ($Pd/PPh_3 = 5:2$) as reported.[7] Indolo[1,2-*a*]quinolines **9a** and **9e** were prepared in good yields (73–78%) along with low yields (13–17%) of protonation products **11d** and **11f** (entries 1 and 4).[14] Besides the Pd(0)-catalyzed decarboxylation/elimination, decarboxylative allylation[15]



Scheme 3.



Scheme 4.

and decarboxylative protonation[15] were also carried out with **8d** and **8f**. Decarboxylative allylation was performed with high loading of PPh_3 (Pd/PPh_3 = 1:8) in toluene (entries 2 and 5), and allyl derivatives **10d** and **10f** were obtained in good yields (83–85%) along with small amounts of protonation products (5–8%). Decarboxylative protonation was carried out in the presence of Et_3N/HCOOH in CH_3CN (entries 3 and 6). The reaction was very fast and compounds **11d** and **11f** were obtained in good yields (84–85%).

As noted above, a methyl derivative **10e** was formed as the major product (52%) in the reaction of **8e** under the typical NaI/O_2 conditions in DMF (entry 4 in Table 1). Based on the results, we examined the feasibility of Michael reaction with methyl acrylate, as shown in Scheme 3. The reaction of **8e** and methyl acrylate (4.0 equiv) under N_2 atmosphere in the presence of NaI in DMF afforded **12** in a reasonable yield (44%). Compound **12** was formed, most likely, by the Michael addition of the in situ-generated enolate (**I**) to methyl acrylate.[2b] Small amounts of a methyl derivative **10e** and a protonation product **11f** were also formed.

Similarly the synthesis of allyl derivative **10f** was examined in the absence of oxygen, as shown in Scheme 4. Compound **10f** was obtained in moderate yield (60%) along with a protonation product **11f** (17%). Interestingly, allyl derivative **13** was isolated in 12% yield via the allylation of enolate (**I**) at the C-3 position of the indole moiety and the following 1,3-H shift.

In summary, an expedient synthetic pathway of indolo[1,2-*a*]quinolines was developed using a sequential Cu-mediated N-arylation of indole, $Mn(OAc)_3$-mediated oxidative cyclization, and NaI/O_2-assisted concomitant dealkoxycarbonylation/aerobic oxidation process.

Acknowledgments

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9. *Typical procedure for the preparation of* **7a**: preparation of compound **3a** was carried out according to the reported method,[8a,b] and its reduction to **4a** ($LiAlH_4$, THF, 0 °C to rt, 5 min) and the following bromination (PBr_3, Et_2O, rt, 1 h) to **5a** were performed according to the general method. A mixture of **5a** (572 mg, 2.0 mmol), dimethyl malonate (**6a**, 490 mg, 3.0 mmol), and K_2CO_3 (555 mg, 4.0 mmol) in CH_3CN (5 mL) was stirred at room temperature for 12 h. After the usual aqueous workup and column chromatographic purification process (hexanes/CH_2Cl_2/Et_2O, 20:20:1) compound **7a** was obtained as a colorless oil, 472 mg (70%). Other compounds were prepared similarly and the selected spectroscopic data of **7a** and **7d** are as follows.
Compound **7a**: 70%; colorless oil; IR (film) 1737, 1497, 1461 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.00–3.18 (m, 2H), 3.23–3.28 (m, 1H), 3.47 (s, 3H), 3.53 (s, 3H), 6.68 (d, J = 3.0 Hz, 1H), 6.99–7.38 (m, 8H), 7.65–7.69 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 30.57, 51.62, 52.29, 103.06, 110.19, 119.99, 120.82, 122.23, 128.07, 128.24, 128.46, 128.61, 128.85, 130.65, 135.41, 137.15, 138.22, 168.65; ESIMS m/z 360 (M^++Na). Anal. Calcd for $C_{20}H_{19}NO_4$: C, 71.20; H, 5.68; N, 4.15. Found: C, 71.57; H, 5.44; N, 4.07.
Compound **7d**: 83%; colorless oil; IR (film) 1736, 1497, 1461, 1235 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, 60 °C) δ 3.10 (br s, 2H), 3.27 (t, J = 7.8 Hz, 1H), 3.53 (s, 3H), 4.42 (d, J = 4.8 Hz, 2H), 5.09–5.17 (m, 2H), 5.64–5.77 (m, 1H), 6.67 (d, J = 3.3 Hz, 1H), 6.68–7.01 (m, 1H), 7.09–7.17 (m, 3H), 7.26–7.39 (m, 4H), 7.63–7.68 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 30.76, 51.78, 52.41, 65.86, 103.18, 110.32, 118.38, 120.09, 120.92, 122.34, 128.18, 128.36, 128.55, 128.71, 128.97, 130.88, 131.32, 135.51, 137.24, 138.37, 168.04, 168.75; ESIMS m/z 364 (M^++1). Anal. Calcd for $C_{22}H_{21}NO_4$: C, 72.71; H, 5.82; N, 3.85. Found: C, 72.67; H, 5.58; N, 3.97. The ^1H NMR spectrum of **7d** showed somewhat complex and broad peaks presumably due to slow rotation around the single bond between benzene and indole. Thus the ^1H NMR spectrum was taken at 60 °C, and appreciable coalescence of peaks were observed. The ^{13}C NMR spectrum of **7d** was taken at room temperature. For the line broadening and complex nature of peaks of similar compounds, see: Hwang, S. J.; Cho, S. H.; Chang, S. *J. Am. Chem. Soc.* **2008**, *130*, 16158–16159.
10. *Typical procedure for the synthesis of* **8a**: A mixture of **7a** (337 mg, 1.0 mmol) and $Mn(OAc)_3$ (696 mg, 3.0 mmol) in MeOH (4 mL) was heated to reflux for 3 h. After cooling to rt, the reaction mixture was filtered through a Celite pad. After dilution with CH_2Cl_2 and the usual aqueous workup, the product **8a** was obtained by column chromatographic separation process (hexanes/EtOAc, 4:1) as a colorless oil, 251 mg (75%). Other compounds were synthesized similarly and the selected spectroscopic data of **8a** and **8d** are as follows.
Compound **8a**: 75%; white solid, mp 123–125 °C; IR (KBr) 1740, 1495, 1456 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.52 (s, 2H), 3.74 (s, 6H), 6.62 (s, 1H), 7.12 (t, J = 7.5 Hz, 1H), 7.20 (t, J = 7.5 Hz, 1H), 7.27–7.43 (m, 3H), 7.65 (d, J = 7.5 Hz, 1H), 7.87 (d, J = 8.1 Hz, 1H), 7.96 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 34.95, 53.31, 56.53, 102.43, 111.59, 117.14, 121.18, 121.41, 123.14,

124.03, 124.95, 128.29, 129.05, 129.35, 133.42, 134.32, 136.28, 168.94; ESIMS m/z 358 (M^++Na). Anal. Calcd for $C_{20}H_{17}NO_4$: C, 71.63; H, 5.11; N, 4.18. Found: C, 71.83; H, 5.45; N, 4.01.

Compound **8d**: 80%; colorless oil; IR (film) 1741, 1495, 1456, 1227 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.52 (s, 2H), 3.73 (s, 3H), 4.54–4.68 (m, 2H), 5.13–5.21 (m, 2H), 5.67–5.80 (m, 1H), 6.64 (s, 1H), 7.10 (t, J = 7.8 Hz, 1H), 7.18 (t, J = 7.8 Hz, 1H), 7.26–7.40 (m, 3H), 7.64 (d, J = 7.8 Hz, 1H), 7.86 (d, J = 7.8 Hz, 1H), 7.95 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 34.94, 53.20, 56.57, 66.60, 102.43, 111.54, 117.11, 118.74, 121.11, 121.38, 123.08, 123.95, 124.91, 128.24, 129.04, 129.34, 131.00, 133.38, 134.29, 136.32, 168.08, 168.81; ESIMS m/z 362 (M^++1). Anal. Calcd for $C_{22}H_{19}NO_4$: C, 73.12; H, 5.30; N, 3.88. Found: C, 73.17; H, 5.48; N, 3.63.

11. *Typical procedure for the synthesis of* **9a** (NaI/O_2 method: entry 1 in Table 1): A mixture of **8a** (168 mg, 0.5 mmol) and NaI (225 mg, 1.5 mmol) in DMF (2 mL) was heated to 120 °C for 2 h under O_2 atmosphere (O_2 balloon). After the usual aqueous workup and column chromatographic purification process (hexanes/EtOAc, 4:1) compound **9a** was obtained as a reddish solid, 96 mg (70%). Other compounds were synthesized similarly and the selected spectroscopic data of **9a**, **9c**, **10e**, **12**, and **13** are as follows.

Compound **9a**: 70%; reddish solid, mp 120–122 °C; IR (KBr) 1719, 1446, 1231, 1213 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 4.03 (s, 3H), 7.31–7.48 (m, 3H), 7.62 (s, 1H), 7.67–7.76 (m, 2H), 7.90–7.94 (m, 1H), 8.04 (s, 1H), 8.45 (d, J = 8.1 Hz, 1H), 8.58 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 52.59, 99.77, 114.45, 115.67, 121.14, 122.05, 122.50, 122.57, 122.75, 123.31, 130.80, 130.86, 131.04, 131.62, 133.01, 133.04, 138.34, 165.82; ESIMS m/z 276 (M^++1). Anal. Calcd for $C_{18}H_{13}NO_2$: C, 78.53; H, 4.76; N, 5.09. Found: C, 78.84; H, 4.95; N, 4.92.

Compound **9c**: 68%; reddish solid, mp 101–103 °C; IR (KBr) 1720, 1452, 1214 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 3.94 (s, 3H), 4.03 (s, 3H), 7.08 (dd, J = 9.0 and 2.4 Hz, 1H), 7.30–7.36 (m, 2H), 7.55 (s, 1H), 7.66–7.77 (m, 2H), 8.04 (s, 1H), 8.34 (d, J = 9.0 Hz, 1H), 8.52 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 52.25, 55.61, 99.11, 102.18, 112.71, 114.99, 115.06, 120.56, 122.24, 122.79, 127.92, 130.26, 130.77, 131.33, 131.63, 133.42, 137.83, 155.45, 165.57; ESIMS m/z 306 (M^++1). Anal. Calcd for $C_{19}H_{15}NO_3$: C, 74.74; H, 4.95; N, 4.59. Found: C, 74.59; H, 5.01; N, 4.38.

Compound **10e**: 52%; white solid, mp 83–85 °C; IR (KBr) 1711, 1494, 1458, 1352 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.63 (s, 3H), 1.90 (s, 3H), 2.75 (d, J = 14.7 Hz, 1H), 3.35 (d, J = 14.7 Hz, 1H), 6.62 (s, 1H), 7.09 (t, J = 8.1 Hz, 1H), 7.17–7.38 (m, 4H), 7.66 (d, J = 8.1 Hz, 1H), 7.85 (d, J = 8.1 Hz, 1H), 7.97 (d, J = 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.09, 27.09, 37.40, 49.70, 100.62, 111.52, 117.12, 120.95, 121.04, 122.72, 124.01, 127.69, 127.70, 129.50, 129.54, 134.41, 136.10, 140.84, 209.30; ESIMS m/z 276 (M^++1). Anal. Calcd for $C_{19}H_{17}NO$: C, 82.88; H, 6.22; N, 5.09. Found: C, 82.72; H, 6.47; N, 5.02.

Compound **12**: 44%; colorless oil; IR (film) 1736, 1710, 1495, 1458 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.97 (s, 3H), 2.29–2.61 (m, 4H), 2.72 (d, J = 14.4 Hz, 1H), 3.37 (d, J = 14.4 Hz, 1H), 3.66 (s, 3H), 6.64 (s, 1H), 7.11 (t, J = 7.5 Hz, 1H), 7.19–7.38 (m, 4H), 7.67 (d, J = 7.5 Hz, 1H), 7.85 (d, J = 8.1 Hz, 1H), 7.98 (d, J = 8.1 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.11, 29.02, 29.65, 33.86, 51.79, 53.01, 101.41, 111.68, 117.02, 121.09, 121.18, 122.91, 124.13, 127.05, 127.78, 129.47, 129.78, 134.38, 135.80, 138.54, 173.31, 207.97; ESIMS m/z 370 (M^++Na). Anal. Calcd for $C_{22}H_{21}NO_3$: C, 76.06; H, 6.09; N, 4.03. Found: C, 76.41; H, 6.37; N, 3.87.

Compound **13**: 12%; colorless oil; IR (film) 1715, 1494, 1458 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.90 (s, 3H), 3.07 (dd, J = 15.0 and 5.7 Hz, 1H), 3.36 (dd, J = 15.0 and 2.4 Hz, 1H), 3.48–3.66 (m, 2H), 4.10 (dd, J = 5.7 and 2.4 Hz, 1H), 5.05–5.17 (m, 2H), 5.95–6.08 (m, 1H), 7.09 (t, J = 7.5 Hz, 1H), 7.18–7.39 (m, 4H), 7.65 (d, J = 7.5 Hz, 1H), 7.85 (d, J = 7.5 Hz, 1H), 7.97 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.64, 29.07, 30.09, 45.86, 111.39, 111.49, 115.62, 117.20, 119.41, 120.71, 122.84, 123.78, 126.79, 127.85, 129.55, 129.62, 131.87, 134.07, 135.95, 136.60, 206.96; ESIMS m/z 302 (M^++1). Anal. Calcd for $C_{21}H_{19}NO$: C, 83.69; H, 6.35; N, 4.65. Found: C, 83.53; H, 6.67; N, 4.46.

12. During the evaluation process one of the reviewers suggested to insert the plausible mechanisms for the formation of **9e** and **9g′**. The mechanism for the formation of **9e** from **8e** could be thought as follows: NaI-assisted formation of (**I**) as proposed in Scheme 3, protonation of (**I**) to form the dihydro analog of **9e** (**11f** in Table 2), and the following aerobic oxidation to **9e**. Actually, the dihydro derivative of **9e** (**11f**) was observed during the reaction progress; however, the dihydro analog of **9e** was air-oxidized to **9e** completely after 4 h, as summarized in entry 5 (Table 1). The mechanism for the formation of **9g′** could be proposed as follows: water-mediated debenzoylation[13] of **8g** to the corresponding dihydro analog of **9g′** and the following aerobic oxidation to **9g′**.
13. (a) Chamakh, A.; Amri, H. *Tetrahedron Lett.* **1998**, *39*, 375–378; (b) Im, Y. J.; Lee, C. G.; Kim, H. R.; Kim, J. N. *Tetrahedron Lett.* **2003**, *44*, 2987–2990. and further examples were mentioned in Ref. 1b.
14. *Typical procedure for the synthesis of* **9a** (Pd method: entry 1 in Table 2): A mixture of **8d** (181 mg, 0.5 mmol), $Pd(OAc)_2$ (11 mg, 10 mol %), and PPh_3 (5 mg, 4 mol %) in CH_3CN (1.5 mL) was heated to reflux for 15 min. After the usual aqueous workup and column chromatographic purification process (hexanes/EtOAc, 4:1) compound **9a** was obtained as a colorless oil, 100 mg (73%) along with **11d** (24 mg, 17%). Other entries in Table 2 were performed similarly, and the selected spectroscopic data of **9e** and **10d** are as follows.

Compound **9e**: 78%; reddish solid, mp 145–147 °C; IR (KBr) 1673, 1445, 1217 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.65 (s, 3H), 7.25 (t, J = 7.5 Hz, 1H), 7.34–7.43 (m, 2H), 7.58–7.71 (m, 4H), 7.85–7.90 (m, 1H), 8.31–8.35 (m, 1H), 8.43 (d, J = 9.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 27.29, 100.41, 114.05, 115.25, 121.82, 122.11, 122.14, 122.31, 122.82, 127.59, 130.59, 130.63, 130.84, 131.48, 131.88, 132.28, 137.89, 196.39; ESIMS m/z 260 (M^++1). Anal. Calcd for $C_{18}H_{13}NO$: C, 83.37; H, 5.05; N, 5.40. Found: C, 83.52; H, 5.09; N, 5.17.

Compound **10d**: 85%; white solid, mp 96–98 °C; IR (KBr) 1734, 1495, 1458 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 2.59 (dd, J = 14.1 and 7.2 Hz, 1H), 2.89 (dd, J = 14.1 and 7.2 Hz, 1H), 2.93 (d, J = 15.0 Hz, 1H), 3.30 (d, J = 15.0 Hz, 1H), 3.60 (s, 3H), 5.06–5.16 (m, 2H), 5.75–5.88 (m, 1H), 6.63 (s, 1H), 7.07–7.38 (m, 5H), 7.63 (d, J = 7.2 Hz, 1H), 7.85 (d, J = 8.1 Hz, 1H), 7.95 (d, J = 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 34.61, 40.63, 48.07, 52.38, 100.92, 111.58, 116.96, 119.31, 120.94, 121.05, 122.59, 123.80, 126.85, 127.64, 129.42, 129.52, 132.71, 134.19, 136.18, 138.35, 172.89; ESIMS m/z 340 (M^++Na). Anal. Calcd for $C_{21}H_{19}NO_2$: C, 79.47; H, 6.03; N, 4.41. Found: C, 79.70; H, 6.13; N, 4.37.
15. For the Pd-catalyzed decarboxylative allylation and protonation, see: (a) Kim, S. H.; Kim, E. S.; Kim, T. H.; Kim, J. N. *Tetrahedron Lett.* **2009**, *50*, 6256–6260; (b) Gowrisankar, S.; Kim, K. H.; Kim, S. H.; Kim, J. N. *Tetrahedron Lett.* **2008**, *49*, 6241–6244; (c) Kim, J. M.; Kim, S. H.; Lee, H. S.; Kim, J. N. *Tetrahedron Lett.* **2009**, *50*, 1734–1737; (d) Gowrisankar, S.; Kim, E. S.; Kim, J. N. *Bull. Korean Chem. Soc.* **2009**, *30*, 33–34; (e) Kim, S. H.; Lee, H. S.; Kim, S. H.; Kim, J. N. *Tetrahedron Lett.* **2009**, *50*, 3038–3041.