Synthesis of Indeno[1,2-*b*]quinolin-10-ones via Pd/C-Assisted Dehydrogenation of 4b,5,10a,11-Tetrahydroindeno[1,2-*b*]quinolin-10-ones

Chang Gon Lee, Ka Young Lee, Seung Chan Kim, and Jae Nyoung Kim*

Department of Chemistry and Institute of Basic Science, Chonnam National University, Gwangju 500-757, Korea
**E-mail: kimjn@chonnam.ac.kr*
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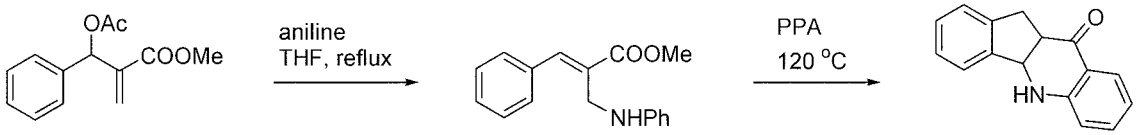
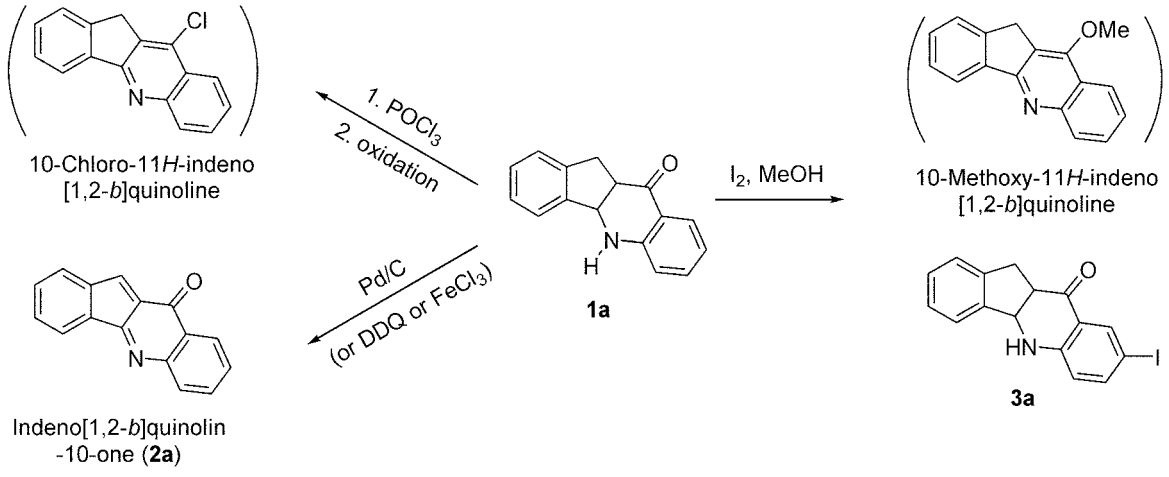
Recently, we have reported the synthesis of 4b,5,10a,11-tetrahydroindeno[1,2-*b*]quinolin-10-ones starting from the acetates of Baylis-Hillman adducts as in Scheme 1.[1] Indenoquinoline derivatives[2,3] showed a wide range of biological activities such as 5-HT-receptor binding activity,[2h] anti-inflammatory activity,[2c] and also act as antitumor agents,[2e] inhibitor for steroid reductase,[2i] acetylcholinesterase inhibitors,[2f] and antimalarials.[2d] These compounds could be synthesized *via* the aza-Bergman cyclization[3j] or *via* the radical cyclization of isonitrile derivatives.[3f] In these contexts, development of a facile synthetic method of indeno[1,2-*b*]quinoline derivatives would be very important.[3]

Thus, we examined the possibility for the synthesis of a variety of indenoquinolines from 4b,5,10a,11-tetrahydroindeno[1,2-*b*]quinolin-10-one (**1a**) as shown in Scheme 2. Oxidation of **1a** with iodine in methanol would produce 10-methoxy-11*H*-indeno[1,2-*b*]quinoline. Treatment of **1a** with $POCl_3$ followed by dehydrogenation would generate 10-chloro-11*H*-indeno[1,2-*b*]quinoline. Dehydrogenation of **1a** with Pd/C or with related oxidant might produce indeno[1,2-*b*]quinolin-10-one (Scheme 2).

Treatment of **1a** with $POCl_3$ showed the formation of intractable mixtures, unfortunately.[2a,2b,3c] Oxidation of **1a** with $FeCl_3$ in methanol (reflux, 3 days)[4] produced low yield of indeno[1,2-*b*]quinolin-10-one (**2a**, 21%). The use of 2.5 equivalents of DDQ (benzene, reflux, 10 h) for the oxidation of **1a** showed moderate yield of **2a** (52%). After many trials, we found that dehydrogenation conditions using Pd/C in refluxing decaline generate **2a** in good yield (83%).[5] As shown in Table 1, we prepared some indeno[1,2-*b*]quinolines **2b-e** similarly by using Pd/C. It is noteworthy that dechlorination occurred simultaneously for the chlorine-substituted compounds **1c** and **1e** at refluxing temperature to give **2a** as the major product instead of the desired **2c** and **2e**.[6] But, fortunately, we could obtain the desired products **2c** and **2e** without dechlorination in good yields (75 and 68%, respectively) when we carried out the reaction at lower temperature (140 °C). We tried next the oxidation of **1a** with iodine in methanol,[7] which resulted in the formation of iodinated compound **3a** (49%)[8] instead of the expected 10-

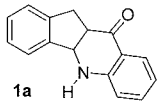
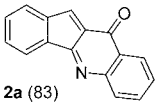
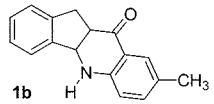
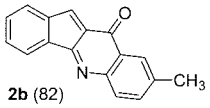
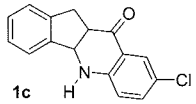
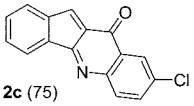
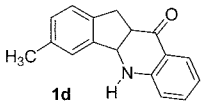
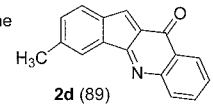
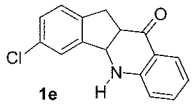
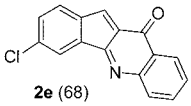


Scheme 1



Scheme 2

Table 1. Synthesis of indeno[1,2-*b*]quinolin-10-ones

Entry	Substrates	Conditions	Products (% yield)
1	 **1a**	Pd/C, decaline reflux, 24 h	 **2a** (83)
2	 **1b**	Pd/C, decaline reflux, 24 h	 **2b** (82)
3	 **1c**	Pd/C, decaline 140 °C, 30 h[a]	 **2c** (75)
4	 **1d**	Pd/C, decaline reflux, 26 h	 **2d** (89)
5	 **1e**	Pd/C, decaline 140 °C, 28 h[b]	 **2e** (68)

[a]Compound **1c** was converted into **2a** in 84% yield (reflux decaline, 24 h). [b]Compound **1e** was converted into **2a** in 79% yield (reflux, decaline, 24 h).

methoxy-11*H*-indeno[1,2-*b*]quinoline.

In summary, we synthesized indeno[1,2-*b*]quinolin-10-one derivatives via dehydrogenation with Pd/C from the corresponding 4b,5,10a,11-tetrahydroindeno[1,2-*b*]quinolin-10-ones. We also found that dehydrogenation was very facile for the nitrogen atom containing heterocyclic compounds.

Experimental Section

Typical procedure for the synthesis of 2a: To a stirred solution of **1a** (235 mg, 1.0 mmol) in decaline (5 mL) was added 10% Pd/C (15 mg) and heated to reflux for 24 h. After removal of the solvent and column chromatographic separation (hexanes/ether, 3 : 2), we obtained **2a** as a yellow solid, 192 mg (83%). The other compounds were synthesized similarly and the spectroscopic data of products are as follows.

2a: 83%, yellow solid, mp 213-214 °C; IR (KBr) 1712, 1566 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.49 (td, J = 7.5 and 0.9 Hz, 1H), 7.62 (td, J = 7.8 and 1.5 Hz, 1H), 7.66-7.72 (m, 1H), 7.75-7.79 (m, 1H), 7.82-7.88 (m, 1H), 8.12 (d, J = 7.8 Hz, 1H), 8.18 (d, J = 8.4 Hz, 1H), 8.48 (d, J = 8.7 Hz, 1H), 9.16 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 123.65, 124.54, 124.84, 124.90, 125.02, 128.23, 131.12, 131.14, 132.15, 134.01, 134.70, 142.54, 144.86, 151.15, 152.63, 193.02; Mass (70 eV) *m/z* (rel. intensity) 75 (16), 87 (55), 101 (25), 150 (13), 176 (23), 203 (75), 231 (M^+, 100).

2b: 82%, yellow solid, mp 209-210 °C; IR (CH_2Cl_2) 1709, 1566 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.58 (s, 3H), 7.44 (td, J = 7.8 and 0.9 Hz, 1H), 7.53-7.61 (m, 2H), 7.66-7.70 (m, 1H), 7.95-7.98 (m, 2H), 8.04 (s, 1H), 8.99 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.17, 123.73 (two carbon is overlapped), 124.51, 124.90, 125.13, 130.81, 131.05, 134.12, 134.61, 134.74, 138.55, 142.74, 143.99, 150.20, 151.37, 193.22; Mass (70 eV) *m/z* (rel. intensity) 50 (22), 62 (21), 94 (75), 122 (20), 189 (27), 216 (74), 230 (20), 245 (M^+, 100).

2c: 75%, yellow solid, mp 232-233 °C; IR (KBr) 1716, 1612, 1562 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.49 (t, J = 7.8 Hz, 1H), 7.62 (td, J = 7.8 and 1.5 Hz, 1H), 7.71-7.76 (m, 2H), 8.00 (d, J = 7.8 Hz, 1H), 8.08 (d, J = 9.0 Hz, 1H), 8.33 (d, J = 2.1 Hz, 1H), 9.08 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 123.83, 124.21, 124.76, 124.91, 125.64, 131.59, 132.75, 133.05, 133.85, 134.49, 135.09, 142.10, 145.10, 150.31, 151.07, 192.69.

2d: 89%, yellow solid, mp 206-207 °C; IR (CH_2Cl_2) 1709, 1562 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.60 (s, 3H), 7.44 (td, J = 7.5 and 0.9 Hz, 1H), 7.55-7.63 (m, 2H), 7.69-7.72 (m, 1H), 7.98-8.03 (m, 2H), 8.09 (s, 1H), 9.01 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.96, 123.53, 123.56, 124.32, 124.71, 124.95, 130.61, 130.85, 133.94, 134.41, 134.54, 138.35, 142.56, 143.80, 150.04, 151.19, 193.04; Mass (70 eV) *m/z* (rel. intensity) 94 (75), 189 (33), 202 (22), 216 (54), 230 (17), 245 (M^+, 100).

2e: 68%, yellow solid, mp 229-230 °C; IR (CH_2Cl_2) 1712, 1566, 1431 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.59 (dd, J = 8.1 and 2.1 Hz, 1H), 7.68-7.74 (m, 2H), 7.84-7.90 (m, 1H), 8.05 (d, J = 8.1 Hz, 1H), 8.19 (d, J = 8.5 Hz, 1H), 8.41 (d, J = 8.5 Hz, 1H), 9.15 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 122.40, 123.77, 123.89, 124.01, 124.69, 127.48, 130.28, 131.46, 133.08, 134.67, 136.50, 139.59, 143.87, 149.50, 151.74, 190.61; Mass (70 eV) *m/z* (rel. intensity) 74 (37), 87 (100), 101 (47), 175 (29), 202 (50), 237 (26), 265 (M^+, 46), 267 (M^++2, 15).

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8. The reaction of **1a** (235 mg, 1.0 mmol) and iodine (508 mg, 2.0 mmol) in methanol (5 mL) under refluxing condition gave the iodinated compound **3a** in 49% yield (175 mg) as a white solid, mp 169-170 ^{o}C; IR (KBr) 3340, 1712, 1589 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.16-3.22 (m, 1H), 3.29 (dd, J = 11.1 and 4.8 Hz, 1H), 3.74 (dd, J = 11.1 and 2.7 Hz, 1H), 3.70 (br s, 1H), 4.58 (d, J = 4.8 Hz, 1H), 6.31 (d, J = 8.4 Hz, 1H), 7.24-7.28 (m, 1H), 7.32-7.41 (m, 1H), 7.56-7.63 (m, 2H), 7.73 (d, J = 8.4 Hz, 1H), 7.80 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 40.02, 44.16, 50.16, 80.72, 118.20, 123.65, 126.42, 127.24, 128.28, 135.73, 135.84, 136.09, 137.79, 146.43, 155.93, 207.30; Mass (70 eV) *m/z* (rel. intensity) 102 (70), 129 (18), 204 924), 233 (21), 361 (M^{+}, 100).