Molecular Iodine-Catalyzed Imino-Diels–Alder Reactions: Efficient One-Pot Synthesis of Pyrano[3,2-*c*]quinolines

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Received 15 July 2005

Abstract: The successful use of molecular iodine as a catalyst in the intermolecular imino-Diels–Alder reaction is described. A one-pot synthesis of pyrano[3,2-*c*]quinolines was achieved by three-component coupling of aldehydes and anilines with 2,3-dihydropyran catalyzed by iodine. The reactions could be carried out smoothly at room temperature within three to six hours to offer the target products in good yields. We also investigated solvent effect, substituent effect, and the amount of iodine required.

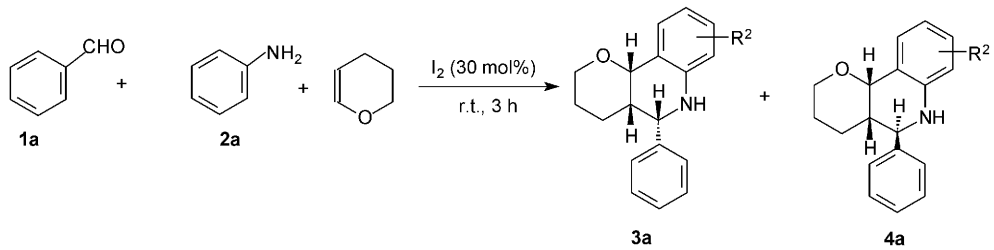
Key words: Iodine, imino-Diels–Alder, one-pot, three-component, tetrahydroquinolines

Tetrahydroquinoline derivatives are a significant class of natural products and exhibit biological activities in various fields,[1] such as psychotropic,[2] antiallergenic,[3] anti-inflammatory[4] and estrogenic activity,[5] besides, pyranoquinoline derivatives are also used as potent pharmaceuticals.[6] It has been established that imino-Diels–Alder reactions of *N*-arylimines (the heterodienes) with electron-rich alkenes are one of the most powerful routes to build the 1,2,3,4-tetrahydroquinoline scaffold.[7] Many Lewis acids such as $InCl_3$[8], $Yb(OTf)_3$,[9] $Sc(OTf)_3$,[10] $BF_3{\cdot}OEt_2$,[11] $GdCl_3$,[12] $LiClO_4$,[13] $LiBF_4$,[14] TFA[15] etc were found to catalyze this reaction. Montmorillonite[16] and fluorinated alcohols[17] were also reported to be efficient for the formation of tetrahydroquinolines. However, all these methods required a lengthy procedure to prepare the starting materials. Moreover, most imines are hygroscopic, unstable at high temperature, and difficult to purify by distillation or column chromatography. Therefore, it is necessary to develop a simple and effective approach to tetrahydroquinolines under mild conditions.

The use of a convergent three-component reaction from aldehydes, anilines, and alkenes in which the heterocycles are assembled in a one-pot operation is an efficient method with particularly valuable application in the combinatorial synthesis of tetrahydroquinolines. Unfortunately, for many Lewis acids in a one-pot procedure, the presence of amines and water from the formation of imines can decompose or deactivate them. Even if the desired reactions proceed, more than stoichiometric amounts of the catalysts are needed, since they are trapped by nitrogen.[18] Although the one-pot operation using lanthanide triflate[19] as the catalyst was reported, its strong acidity and high cost prohibited its use as a versatile reagent in the synthesis of tetrahydroquinolines.

Recently, molecular iodine has received considerable attention as an inexpensive and readily available catalyst for various organic transformations.[20] Due to its moderate Lewis acidity reactions catalyzed by iodine effectively take place in neutral media under very mild conditions. Moreover, its water-tolerance and weak ability to accept electrons make it an excellent candidate for reactions like the one-pot synthesis of tetrahydroquinolines. To the best of our knowledge, there is no report on the use of iodine as a catalyst for this type of reaction. Herein, we describe our first example of the preparation for pyrano[3,2-*c*]quinolines by an iodine-catalyzed three-component reaction of aldehydes, anilines, and 2,3-dihydropyran in a one-pot operation.

A remarkable solvent effect was found to exist in our iodine-catalyzed one-pot protocol. The selected model reaction was carried out with benzaldehyde, aniline, and 2,3-dihydropyran in several organic solvents (Scheme 1) and the results are collected in Table 1.



Scheme 1

SYNLETT 2005, No. 15, pp 2357–2361
Advanced online publication: 07.09.2005
DOI: 10.1055/s-2005-872676; Art ID: U22705ST

Table 1 Solvent Effect on Iodine-Catalyzed One-Pot Synthesis of Pyrano[3,2-*c*]quinolines

Entry	Solvent	Yield (%)[a]	**3a**/**4a** Ratio[b]
1	EtOH	trace	–
2	CH_2Cl_2	81	23:77
3	CH_3CN	84	23:77
4	Et_2O	37	25:75
5	EtOAc	21	29:71
6	$CHCl_3$	–	–
7	THF	–	–
8	Benzene	trace	–
9	DMF	–	–
10	CH_3COCH_3	trace	–

[a] Refers to isolated yields by chromatography.
[b] Determined by ^{1}H NMR spectroscopy.

It was found that both CH_3CN and CH_2Cl_2 were the best solvents for our reaction while Et_2O and EtOAc resulted in poor yields of the required compounds. Other solvents afforded either trace or no products. In our later experiments, CH_3CN was chosen as the organic solvent to carry out the iodine-catalyzed reactions. Interestingly, there appeared to be no link between the ratio of the two isomers formed and the solvent; the *trans* isomer was always the major product.

Apart from solvents, a range of catalytic amounts of iodine were also considered. The parallel reactions of benzaldehyde, aniline, and 2,3-dihydropyran in CH_3CN were carried out in the presence of varying amounts of iodine and the results are included in Table 2.

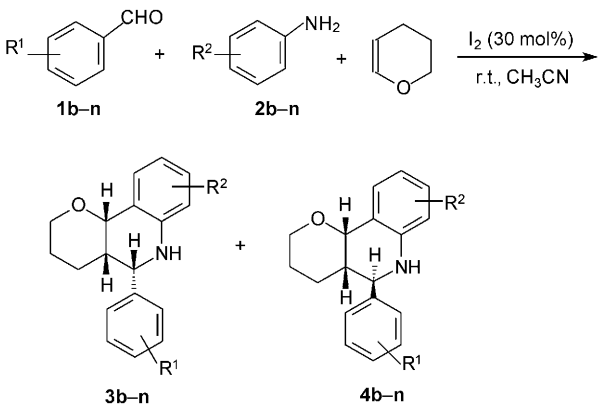
Table 2 Influence of Iodine on the One-Pot Reaction

Entry	Amount (mol%)	Yield (%)[a]
1	5	56
2	10	68
3	20	76
4	30	84
5	50	88

[a] Isolated yield (chromatography).

It was observed that the yields improved from 56% to 84% as the catalytic amounts of iodine were increased from 5 mol% to 30 mol%, respectively. However, when the amount of iodine was enhanced from 30 mol% to 50 mol%, the yields increased only slightly from 84% to 88%. It was decided that 30 mol% amount of iodine was sufficient to drive the reaction forward.

According to the above facts, the reactions were extended to other aldehydes and anilines (Scheme 2) and the results are shown in Table 3.



Scheme 2

It was found that each reaction could be carried out smoothly by iodine catalysis at room temperature, the products were obtained as *cis*/*trans* isomers without any other isomer detected. There was no substituent effect by the aldehydes observed, since aldehydes both with electron-donating groups and electron-withdrawing groups could be effectively utilized to generate the required compounds in good yields. Moreover, the reaction time for every aldehyde was approximately the same. However, an

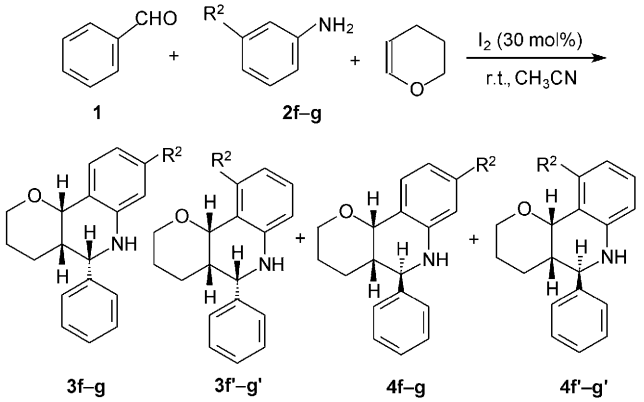
Table 3 One-Pot Synthesis of Pyrano[3,2-*c*]quinolines Catalyzed by Iodine from Aldehydes and Anilines in CH_3CN.[22]

	R^1	R^2	Time (h)	Yield (%)[a]	**3**/**4** Ratio[b]
a	H	H	3	84	23:77
b	H	4-Cl	3	81	43:57
c	H	4-CH_3O	3	95	8: 92
d	H	4-CH_3	3	91	16:84
e	H	2-CH_3	4	82	24:76
f	H	3-Cl	5	77	–
g	H	3-CF_3	6	58	–
h	4-CH_3	H	3	88	17:83
i	4-Br	H	4	81	17:83
j	2-Cl	H	3.5	83	24:76
k	3-NO_2	H	4	79	26:74
l	4-CH_3O	H	3	84	9: 91
m	4-Cl	4-Cl	3.5	84	25:75
n	4-CH_3O	4-CH_3O	3	96	3: 97

[a] Isolated yield (chromatography).
[b] Determined by ^{1}H NMR spectroscopy.

apparent substituent effect took place on the anilines. Compared to those with electron-donating groups, anilines with electron-withdrawing groups resulted in low yields and a long reaction time was required.

The reaction of benzaldehyde, 3-chloroaniline, and 2,3-dihydropyran in our case generated a mixture of four isomers **3f**, **3f′**, **4f**, and **4f′**, in a ratio of 17:14:55:14, respectively, which was determined by ^{1}H NMR spectroscopy; the four isomers were formed in a combined yield of 77%. Unfortunately, the four isomers could not be separated as pure compounds by column chromatography. In addition, the reaction of 3-trifluoromethylaniline with benzaldehyde and 2,3-dihydropyran also produced a mixture of three isomers **3g**, **4g**, and **4g′** in a ratio of 13:40:47, respectively, in a combined yield of 58%; only **4g′** could be isolated as a pure compound (Scheme3).



Scheme 3

In conclusion, molecular iodine was an effective catalyst in the one-pot three-component reaction of aldehydes and anilines with 2,3-dihydropyran, providing pyrano[3,2-*c*]quinolines in good yields. In comparison with those reported methods, our approach was superior in terms of cost, operation, temperature, yields, and reaction time. Further application of this protocol is now in progress.

Acknowledgment

We are grateful for the financial support from the NSFC (project 20402013).

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(22) Pyrano[3,2-*c*]quinolines **3** and **4**; General Procedure. To a mixture of aldehyde **1** (2 mmol), aniline **2** (2 mmol), and 2,3-dihydropyran (4 mmol) in CH_3CN (10 mL) was added iodine (0.15 g, 30 mol%) and the solution was stirred at r.t. for the appropriate time (Table 3). To the reaction mixture was added 10% aq NaS_2O_3 soln (20 mL) and the product was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were washed with brine, dried (Na_2SO_4), filtered, and the solvent was evaporated. The

residue was purified by silica gel column chromatography with petroleum ether (60–90 °C)–EtOAc (95:5) as the eluent to afford the pure compounds.

3a: white solid; mp 131–133 °C (Lit.[12] 130–132 °C).
IR (KBr): 3373, 3055, 3027, 2938, 2856, 1610, 1492, 1365, 1306, 1265, 1071, 913, 749, 702 cm^{-1}.
^1H NMR (400MHz, $CDCl_3$): δ = 1.27–1.53 (4 H, m), 2.18 (1 H, m), 3.61–3.88 (3 H, m), 4.66 (1 H, d, *J* = 2.6 Hz), 5.33 (1 H, d, *J* = 5.6 Hz), 6.58 (1 H, d, *J* = 7.8 Hz), 6.78 (1 H, t, *J* = 7.6 Hz), 7.03 (1 H, t, *J* = 7.6 Hz), 7.28–7.47 (6 H, m).
MS: *m*/*z* (%) = 265 (M^+, 77), 206 (100).

4a: yellowish viscous liquid.
IR (neat film): 3378, 3061, 2945, 2857, 1612, 1499, 1366, 1271, 1072, 913, 756, 708 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.27 (1 H, m), 1.58 (1 H, m), 1.69 (1 H, m), 1.85 (1 H, m), 2.15 (1 H, m), 3.76 (1 H, dt, *J* = 2.5, 11.6 Hz), 4.11 (2 H, m), 4.43 (1 H, d, *J* = 2.7 Hz), 4.76 (1 H, d, *J* = 10.8 Hz), 6.59 (1 H, d, *J* = 7.4 Hz), 6.73 (1 H, t, *J* = 7.2 Hz), 7.11 (1 H, t, *J* = 7.2 Hz), 7.27 (1 H, d, *J* = 7.4 Hz), 7.39–7.46 (5 H, m).
MS: *m*/*z* (%) = 265 (M^+, 100), 207 (69).

3b: white solid; mp 171–172 °C (Lit.[12]170–172 °C).
IR (KBr): 3389, 3078, 3027, 2920, 2855, 1605, 1512, 1321, 1277, 818 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.26–1.31 (1 H, m), 1.42–1.51 (3 H, m), 2.03–2.13 (1 H, m), 3.37–3.42 (1 H, m), 3.58–3.61 (1 H, m), 3.81–3.93 (1 H, br), 4.64 (1 H, d, *J* = 2.4 Hz), 5.25 (1 H, d, *J* = 5.6 Hz), 6.51 (1 H, d, *J* = 8 Hz), 7.02 (1 H, dd, *J* = 8.0, 2.4 Hz), 7.28–7.38 (6 H, m).
MS: *m*/*z* (%) = 299 (M^+, 100), 241 (48).

4b: pale solid; mp 129–131 °C (Lit.[12] 125–126 °C).
IR (KBr): 3383, 3066, 3027, 2921, 2867, 1607, 151, 1366, 1265, 1079, 824 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.33–1.37 (1 H, m), 1.45–1.49 (1 H, m), 1.60–1.68 (1 H, m), 1.81–1.84 (1 H, m), 2.04–2.08 (1 H, m), 3.71 (1 H, dt, *J* = 2.6, 7.6 Hz), 4.06–4.10 (1 H, m), 4.34 (1 H, d, *J* = 2.8 Hz), 4.67 (1 H, d, *J* = 10.8 Hz), 6.46 (1 H, d, *J* = 8.4 Hz), 7.03 (1 H, dt, *J* = 8.4, 2.4 Hz), 7.21 (1 H, d, *J* = 2.4 Hz), 7.32–7.41 (5 H, m).
MS: *m*/*z* (%) = 299 (M^+, 67), 241 (100).

3c: white solid; mp 146–147 °C (Lit.[12] 144–146 °C).
IR (KBr): 3340, 3051, 2970, 2860, 1610, 1520, 1365, 1270, 1065, 837, 776 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.25–1.33 (1 H, m), 1.45–1.55 (3 H, m), 2.12–2.18 (1 H, m), 3.41–3.46 (1 H, m), 3.58 (1 H, m), 3.77 (3 H, s), 4.62 (1 H, d, *J* = 2.4 Hz), 5.30 (1 H, d, *J* = 5.6 Hz), 6.57 (1 H, d, *J* = 9.2 Hz), 6.71 (1 H, dd, *J* = 6.4, 1.8 Hz), 7.03 (1 H, dd, *J* = 2.9, 0.8 Hz), 7.29–7.43 (5 H, m).
MS: *m*/*z* (%) = 295 (M^+, 100), 237 (33).

4c: pale solid; mp 97–99 °C (Lit.[12] 98–100 °C).
IR (KBr):3340, 3021, 2975, 2845, 160, 1495, 1260, 1080, 845 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.31–1.35 (1 H, m), 1.45–1.48 (1 H, m), 1.62–1.67 (1 H, m), 1.78–1.85 (1 H, m), 2.06–2.11 (1 H, m), 3.46–3.55 (1 H, br), 3.70 (1 H, dt, *J* = 2.6, 7.0 Hz), 3.75 (3 H, s), 4.10 (1 H, dt, *J* = 11.2, 2.2 Hz), 4.36 (1 H, d, *J* = 2.8 Hz), 4.65 (1 H, d, *J* = 10.4 Hz), 6.49 (1 H, d, *J* = 8.8 Hz), 6.74 (1 H, dd, *J* = 8.8, 2.9 Hz), 6.81 (1 H, d, *J* = 2.8 Hz), 7.30–7.43 (5 H, m).
MS: *m*/*z* (%) = 295 (M^+, 58), 237 (100).

3d: white solid; mp 143–144 °C (Lit.[21] 142–143 °C).
IR (KBr): 3366, 3023, 2933, 2859, 1617, 1499, 1454, 1352, 1307, 1258, 1082, 808, 698 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.27–1.32 (1 H, m), 1.42–1.55 (3 H, m), 2.15 (1 H, m), 2.27 (3 H, s), 3.44 (1 H, dt, *J* = 2.4, 7.0 Hz), 3.60 (1 H, m), 4.64 (1 H, d, *J* = 2.2 Hz), 5.30 (1 H, d, *J* = 5.6 Hz), 6.52 (1 H, d, *J* = 8.0 Hz), 6.91 (1 H, d, *J* = 8.0 Hz), 7.24 (1 H, s), 7.29–7.42 (5 H, m).
MS: *m*/*z* (%) = 279 (M^+, 100), 220 (30).

4d: white solid; mp 89–91 °C.
IR (KBr): 3378, 3045, 2967, 2855, 1613, 1505, 1334, 1267, 1078, 826 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.24–1.27 (1 H, m), 1.30–1.34 (1 H, m), 1.43–1.50 (1 H, m), 1.61–1.69 (1 H, m), 2.06–2.09 (1 H, m), 2.23 (3 H, s), 3.69–3.74 (1 H, m), 4.08–4.11 (1 H, m), 4.36 (1 H, d, *J* = 2.7 Hz), 4.68 (1 H, d, *J* = 10.8 Hz), 6.45 (1 H, d, *J* = 8.0 Hz), 6.90 (1 H, dd, *J* = 8.0, 1.7 Hz), 7.04 (1 H, d, *J* = 1.0 Hz), 7.31–7.43 (5 H, m).
MS: *m*/*z* (%) = 279 (M^+, 100), 221 (82).

3e: white solid; mp 147–148 °C (Lit.[12] 143–144 °C).
IR (KBr): 3338, 3023, 2933, 2864, 1601, 1474, 1348, 1303, 1270, 1086, 1037, 759, 702 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.24–1.33 (1 H, m), 1.40–1.55 (3 H, m), 2.14–2.17 (4 H, m), 3.42 (1 H, m), 3.55–3.59 (1 H, m), 3.69 (1 H, br), 4.70 (1 H, d, *J* = 2.4 Hz), 5.36 (1 H, d, *J* = 5.6 Hz), 6.74 (1 H, t, *J* = 7.2 Hz), 7.00 (1 H, d, *J* = 7.2 Hz), 7.32–7.47 (6 H, m).
MS: *m*/*z* (%) = 279 (M^+, 100), 220 (52).

4e: white solid; mp 128–129 °C (Lit.[12] 130–132 °C).
IR (KBr): 3387, 3060, 3027, 2933, 2876, 2827, 1601, 1474, 1364, 1254, 1053, 747, 706 cm^{-1}.
^1H NMR (400MHz, $CDCl_3$): δ = 1.30–1.36 (1 H, m), 1.44–1.50 (1 H, m), 1.62–1.69 (1 H, m), 1.82–1.90 (1 H, m), 2.05 (3 H, s), 2.07–2.11 (1 H, m), 3.72 (1 H, dt, *J* = 2.4, 11.6 Hz), 4.11 (1 H, dt, *J* = 11.2, 2.2 Hz), 4.39 (1 H, d, *J* = 2.6 Hz), 4.75 (1 H, d, *J* = 11.2 Hz), 6.65 (1 H, t, *J* = 7.2 Hz), 7.00 (1 H, d, *J* = 7.2 Hz), 7.12 (1 H, d, *J* = 7.6 Hz), 7.33–7.46 (5 H, m).
MS: *m*/*z* (%) = 279 (M^+, 100), 221 (80).

4g′: white solid; mp 155–156 °C.
IR (KBr): 3411, 3035, 2937, 2847, 1597, 1499, 1474, 1433, 1307, 1123, 1053, 918, 796, 735, 702 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.33 (1 H, d, *J* = 13.2 Hz), 1.49 (1 H, dd, *J* = 13.8, 2 Hz), 1.66–1.73 (1 H, m), 1.89–1.95 (1 H, m), 2.02 (1 H, d, *J* = 11.5 Hz), 3.73 (1 H, dt, *J* = 2.4, 12 Hz), 4.13 (1 H, dd, *J* = 11.6, 4.8 Hz), 4.69 (1 H, s), 4.86 (1 H, d, *J* = 11.6 Hz), 6.65 (1 H, d, *J* = 8.0 Hz), 6.98 (1 H, d, *J* = 7.6 Hz), 7.13 (1 H, t, *J* = 8.0 Hz), 7.32–7.43 (5 H, m).
MS: *m*/*z* (%) = 333 (M^+, 38), 275 (100).

3h: white solid; mp 126–128 °C.
IR (KBr): 3366, 3019, 2941, 2859, 1609, 1477, 1352, 1315, 1213, 1090, 1029, 927, 816, 751 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.29–1.34 (1 H, m), 1.42–1.55 (3 H, m), 2.13 (1 H, m), 2.36 (3 H, s), 3.43 (1 H, m), 3.56–3.60 (1 H, m), 4.65 (1 H, d, *J* = 2.4 Hz), 5.31 (1 H, d, *J* = 5.6 Hz), 6.58 (1 H, d, *J* = 8.0 Hz), 6.78 (1 H, t, *J* = 7.6 Hz), 7.08 (1 H, dt, *J* = 0.6, 8.0 Hz), 7.18 (2 H, d, *J* = 8.0 Hz), 7.29 (2 H, d, *J* = 8.0 Hz), 7.41 (1 H, d, *J* = 7.6 Hz).
MS: *m*/*z* (%) = 279 (M^+, 100), 221 (73).

4h: white solid; mp 123–125 °C.
IR (KBr): 3370, 3019, 2937, 2855, 1609, 1491, 1372, 1307, 1262, 1078, 812, 743 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.33 (1 H, m), 1.50 (1 H, m), 1.63 (1 H, m), 1.88 (1 H, m), 2.08 (1 H, m), 2.36 (3 H, s), 3.70 (1 H, dt, *J* = 2.5, 11.6 Hz), 4.09 (1 H, dt, *J* = 10.8, 2.6 Hz), 4.37 (1 H, d, *J* = 2.7 Hz), 4.67 (1 H, d, *J* = 10.8 Hz), 6.50 (1 H, d, *J* = 8.0 Hz), 6.69 (1 H, dt, *J* = 1.0, 7.2 Hz), 7.06 (1 H, dt, *J* = 1.6, 8.0 Hz), 7.16–7.23 (3 H, m), 7.30 (2 H, d, *J* = 8.0 Hz).
MS: *m*/*z* (%) = 279 (M^+, 100), 221 (35).

3i: white solid; mp 168–170 °C.
IR (KBr): 3346, 3051, 2941, 2859, 1605, 1482, 1315, 1262, 1060, 755, 620, 489 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.26–1.33 (1 H, m), 1.44–1.54 (3 H, m), 2.15 (1 H, m), 3.42 (1 H, m), 3.57–3.61 (1 H,

m), 4.64 (1 H, d, *J* = 2.4 Hz), 5.30 (1 H, d, *J* = 5.5 Hz), 6.60 (1 H, d, *J* = 7.4 Hz), 6.80 (1 H, dt, *J* = 0.8, 7.4 Hz), 7.08 (1 H, t, *J* = 7.4 Hz), 7.29 (2 H, d, *J* = 8.4 Hz), 7.42 (1 H, d, *J* = 8.0 Hz), 7.50 (2 H, dd, *J* = 6.8, 1.8 Hz).
MS: *m*/*z* (%) = 235 (M + 1, 25), 286 (100).

4i: white solid; mp 131–133 °C.
IR (KBr): 3358, 3015, 2937, 2847, 1609, 1495, 1364, 1266, 1078, 1033, 1008, 841, 816, 747, 465 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.32–1.36 (1 H, m), 1.41–1.47 (1 H, m), 1.62–1.68 (1 H, m), 1.74–1.83 (1 H, m), 2.01–2.05 (1 H, m), 3.71 (1 H, dt, *J* = 2.4, 11.6 Hz), 4.09 (1 H, dt, *J* = 11.2, 2.1 Hz), 4.37 (1 H, d, *J* = 2.7 Hz), 4.67 (1 H, d, *J* = 10.8 Hz), 6.52 (1 H, d, *J* = 8.0 Hz), 6.71 (1 H, dt, *J* = 1.0, 7.6 Hz), 7.09 (1 H, t, *J* = 7.2 Hz), 7.21 (1 H, dd, *J* = 1.3, 7.6 Hz), 7.29 (2 H, dd, *J* = 1.6, 8.4 Hz), 7.48 (2 H, dd, *J* = 1.7, 8.4 Hz).
MS: *m*/*z* (%) = 235 (M + 1, 29), 286 (100).

3j: white solid; mp 165–167 °C.
IR (KBr): 3387, 3072, 3011, 2937, 2847, 1605, 1474, 1315, 1258, 1086, 1029, 743, 702 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.20–1.25 (1 H, m), 1.44–1.49 (1 H, m), 1.52–1.58 (2 H, m), 2.39–2.42 (1 H, m), 3.42 (1 H, dt, *J* = 2.3, 11.6 Hz), 3.56–3.61 (1 H, m), 5.06 (1 H, d, *J* = 2.1 Hz), 5.33 (1 H, d, *J* = 5.6 Hz), 6.61 (1 H, d, *J* = 7.6 Hz), 6.80 (1 H, t, *J* = 7.6 Hz), 7.09 (1 H, t, *J* = 7.6 Hz), 7.23–7.29 (2 H, m), 7.38–7.45 (2 H, m), 7.65 (1 H, dd, *J* = 1.5, 7.6 Hz).
MS: *m*/*z* (%) = 299 (M^+, 70), 241 (100).

4j: colorless viscous liquid.
IR (neat film): 3358, 3056, 3019, 2941, 2855, 1613, 1491, 1364, 1319, 1260, 1082, 755 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.40–1.49 (2 H, m), 1.67–1.74 (1 H, m), 1.86–1.94 (1 H, m), 2.18–2.22 (1 H, m), 3.6 (1 H, dt, *J* = 2.8, 11.6 Hz), 3.96–4.00 (1 H, m), 4.43 (1 H, d, *J* = 3.1 Hz), 5.17 (1 H, d, *J* = 9.3 Hz), 6.52 (1 H, d, *J* = 8.0 Hz), 6.73 (1 H, t, *J* = 7.4 Hz), 7.20 (1 H, t, *J* = 8.0 Hz), 7.20–7.25 (3 H, m), 7.36 (1 H, dd, *J* = 1.2, 7.6 Hz), 7.48 (1 H, d, *J* = 7.6 Hz).
MS: *m*/*z* (%) = 299 (M^+, 40), 241 (100).

3k: yellow solid; mp 181–183 °C.
IR (KBr): 3407, 3076, 3011, 2987, 2856, 1601, 1530, 1477, 1266, 1078, 886, 784, 698 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.20 (1 H, m), 1.44–1.60 (3 H, m), 2.19–2.22 (1 H, m), 3.44 (1 H, dt, *J* = 2.5, 11.2 Hz), 3.60 (1 H, dt, *J* = 11.6, 2.0 Hz), 3.83 (1 H, br), 4.80 (1 H, d, *J* = 2.3 Hz), 5.34 (1 H, d, *J* = 5.6 Hz), 6.66 (1 H, d, *J* = 8.0 Hz), 6.85 (1 H, t, *J* = 8.0 Hz), 7.13 (1 H, t, *J* = 7.6 Hz), 7.44 (1 H, d, *J* = 8.0 Hz), 7.56 (1 H, t, *J* = 8.0 Hz), 7.76 (1 H, d, *J* = 8.0 Hz), 8.17 (1 H, dd, *J* = 1.5, 8.0 Hz), 8.33 (1 H, s).
MS: *m*/*z* (%) = 310 (M^+, 53), 251 (100).

4k: yellow solid; mp 159–161 °C.
IR (KBr): 3417, 3056, 2966, 2887, 1604, 1534, 1491, 1345, 1277, 1080, 874, 778, 702 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.40 (2 H, m), 1.67–1.74 (1 H, m), 1.79–1.86 (1 H, m), 2.12 (1 H, m), 3.74 (1 H, t, *J* = 11.2 Hz), 4.11 (1 H, d, *J* = 9.2 Hz), 4.40 (1 H, d, *J* = 2.5 Hz), 4.83 (1 H, d, *J* = 10.8 Hz), 6.57 (1 H, d, *J* = 8.0 Hz), 6.75 (1 H, t, *J* = 7.6 Hz), 7.12 (1 H, t, *J* = 7.6 Hz), 7.24 (1 H, d, *J* = 7.6 Hz), 7.55 (1 H, t, *J* = 8.0 Hz), 7.76 (1 H, d, *J* = 7.3 Hz), 8.18 (1 H, dd, *J* = 1.9, 8.0 Hz), 8.31 (1 H, s)
MS: *m*/*z* (%) = 310 (M^+, 52), 251 (100).

4l: white solid; mp 134–135 °C.
IR (KBr): 3387, 3039, 2941, 2892, 2835, 1609, 1495, 1368, 1241, 1057, 767 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.30–1.33 (1 H, m), 1.47–1.52 (1 H, m), 1.61–1.67 (1 H, m), 1.78–1.85 (1 H, m), 2.06 (1 H, m), 3.71 (1 H, dt, *J* = 2.4, 11.6 Hz), 4.10 (1 H, dt, *J* = 11.2, 2.2 Hz), 4.38 (1 H, d, *J* = 2.6 Hz), 4.68 (1 H, d, *J* = 10.8 Hz), 6.51 (1 H, d, *J* = 8.0 Hz), 6.70 (1 H, t, *J* = 7.2 Hz), 6.90 (2 H, d, *J* = 8.4 Hz), 7.08 (1 H, dt, *J* = 1.4, 8.0 Hz), 7.21 (1, dd, *J* = 1.1, 7.6 Hz), 7.34 (2 H, d, *J* = 8.4 Hz)
MS: *m*/*z* (%) = 295 (M^+, 100), 236 (182).

3m: white solid; mp 187–189 °C.
IR (KBr): 3382, 3068, 2941, 2868, 1601, 1486, 1274, 1082, 841, 808 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.25–1.28 (1 H, m), 1.44–1.50 (3 H, m), 2.10 (1 H, m), 3.40–3.46 (1 H, m), 3.59–3.63 (1 H, m), 4.63 (1 H, d, *J* = 2.4 Hz), 5.24 (1 H, d, *J* = 5.6 Hz), 6.53 (1 H, d, *J* = 8.6 Hz), 7.03 (1 H, dd, *J* = 2.2, 8.4 Hz), 7.31–7.36 (4 H, m), 7.38 (1 H, d, *J* = 1.4 Hz).
MS: *m*/*z* (%) = 333 (M^+, 53), 274 (100).

4m: white solid; mp 154–156 °C.
IR (KBr): 3346, 2933, 2847, 1613, 1491, 1268, 1033, 882, 812 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.32–1.38 (1 H, m), 1.43–1.47 (1 H, m), 1.63–1.69 (1 H, m), 1.75–1.82 (1 H, m), 2.04 (1 H, m), 3.70 (1 H, dt, *J* = 2.4, 11.6 Hz), 4.07 (1 H, d, *J* = 11.6 Hz), 4.34 (1 H, d, *J* = 2.7 Hz), 4.67 (1 H, d, *J* = 10.8 Hz), 6.46 (1 H, d, *J* = 8.4 Hz), 7.04 (1 H, dd, *J* = 2.4, 8.8 Hz), 7.21 (1 H, d, *J* = 2.3 Hz), 7.35 (4 H, m).
MS: *m*/*z* (%) = 333 (M^+, 55), 274 (100).

4n: white solid; mp 151–153 °C.
IR (KBr): 3346, 3035, 3002, 2970, 2941, 2884, 2839, 1609, 1511, 1462, 1298, 1241, 1172, 1045, 890, 824 cm^{-1}.
^1H NMR (400 MHz, $CDCl_3$): δ = 1.33–1.38 (1 H, m), 1.45–1.52 (1 H, m), 1.63 (1 H, m), 1.78–1.84 (1 H, m), 2.05–2.11 (1 H, m), 3.71 (1 H, dt, *J* = 2.4, 11.2 Hz), 3.75 (3 H, s), 3.83 (3 H, s), 4.36 (1 H, d, *J* = 2.7 Hz), 4.62 (1 H, d, *J* = 10.8 Hz), 6.48 (1 H, d, *J* = 8.8 Hz), 6.72 (1 H, dd, *J* = 2.8, 8.8 Hz), 6.81 (1 H, d, *J* = 2.8 Hz), 6.90 (2 H, d, *J* = 8.4 Hz), 7.34 (2 H, d, *J* = 8.4 Hz).
MS: *m*/*z* (%) = 325 (M^+, 100), 266 (30).