Iodine-catalysed synthesis of thiopyrano[3,4-*c*]quinoline derivatives via imino-Diels–Alder reaction

Wei Wang[a,b], Ming-Yue Yin[a,b], Mei-Mei Zhang[a,b] and Xiang-Shan Wang[a,b]*

[a]*School of Chemistry and Chemical Engineering, Jiangsu Key Laboratory of Green Synthetic Chemistry for Functional Materials, Jiangsu Normal University, Xuzhou Jiangsu 221116, P. R. China*

[b]*The Key Laboratory of Biotechnology on Medical Plant of Jiangsu Province, Jiangsu Normal University, Xuzhou Jiangsu 221116, P. R. China*

A mild and efficient method for the synthesis of thiopyrano[3,4-*c*]quinoline derivatives via an imino-Diels–Alder reaction of an aromatic aldehyde, 5-amino-1*H*-indazole or 2-aminoanthracene and tetrahydrothiopyran-4-one catalysed by iodine is described. This new procedure has the advantages of mild reaction conditions, high yields and metal-free catalysis. This is useful since quinoline and its derivatives have extensive biological activities.

Keywords: quinoline, 5-amino-1*H*-indazole, 2-aminoanthracene, iodine, synthesis

Quinoline and its derivatives occur in a large number of biologically active natural products,[1–4] so the synthesis of quinolines has been extensively researched over the years.[5–7] Povarov and coworkers[8] have explored an important methodology that provides access to quinoline derivatives from an imino Diels–Alder reaction, using a Schiff base and an electron-rich dienophile as reactants. This approach, also known as the Povarov reaction, is usually catalysed by various Lewis acids and is described elsewhere.[9]

This methodology has been improved greatly by using iodine catalysis and an aliphatic aldehyde starting material,[10] in which the catalysis promotes formation of the enol tautomer which acts as a dienophile. In our previous work, the range of dienophiles was expanded to various types of ketones, such as aliphatic, aromatic, and cyclicketone, all gave the satisfactory results. In connection with our continued research on this iodine-catalysed Povarov reaction,[11–13] we now report an efficient synthesis of thiopyrano[3,4-*c*]pyrazolo[4,3-*f*] quinoline and thiopyrano[3,4-*c*]naphtho[2,3-*f*] quinoline derivatives catalysed by iodine. This novel pentacyclic ring skeleton containing naphthalene or pyrazole, thiopyran and quinoline rings may possess potential bioactivity for screening.

Results and discussion

Treatment of aromatic aldehyde **1**, 5-amino-1*H*-indazole **2** and tetrahydrothiopyran-4-one **3** in THF in the presence of iodine (5 mol%) under reflux conditions gave the corresponding 7-aryl-3,8,10,11-tetrahydrothiopyrano[3,4-*c*] pyrazolo[4,3-*f*] quinoline derivatives **4** in high yields (Scheme 1).

In our initial study, the optimum amount of catalyst was identified initially. Therefore, the model reactions were conducted using 4-chlorobenzaldehyde (**1a**), 5-amino-1*H*-indazole and tetrahydrothiopyran-4-one in THF at reflux in the presence of various catalytic amounts of iodine. The screening results from these reactions are summarised in Table 1. 1, 5 and 10 mol% iodine were used to mediate the reaction, it was found that 5 mol% I_2 at reflux in THF is sufficient to initiate the reaction (Table 1, entries 4–6). To find the optimum reaction temperature, the reaction was carried out with 5 mol% of I_2 at room temperature, 50 °C and reflux temperature, resulting in the isolation of **4a** in trace amount, 74% and 89% yields (Table 1, entries 2, 3 and 5), respectively. Thus, 5 mol% of I_2 and a reaction temperature at reflux were optimal conditions. In addition, CH_3CN, benzene, DMF and $CHCl_3$ (Table 1, entries 7–10) were also tested as the solvents. In these cases, product **4a** was formed in slightly lower yields.

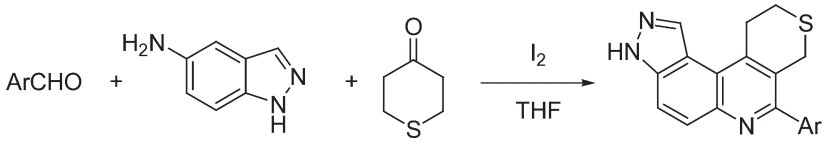
Table 1 Yield optimisation for **4a** under different conditions[a]

Entry	Temp. /°C	Catalyst/mol %	Solvent	Yields/%[b]
1	Reflux	0	THF	0
2	r.t.	5	THF	Trace
3	50	5	THF	74
4	Reflux	1	THF	80
5	Reflux	5	THF	89
6	Reflux	10	THF	89
7	Reflux	5	CH_3CN	82
8	Reflux	5	Benzene	78
9	80	5	DMF	84
10	Reflux	5	$CHCl_3$	80

[a]Reagents and conditions: 4-chlorobenzaldehyde **1a** (0.281 g, 2.0 mmol), **2** (0.266 g, 2.0 mmol), **3** (0.232 g, 2.0 mmol), solvent (10 mL).
[b]Isolated yields.

According to the optimised conditions, various aromatic aldehydes **1** were then subjected to reaction with **2** and **3** to generate a library of thiopyrano[3,4-*c*]pyrazolo[4,3-*f*] quinoline derivatives **4a–k** (Table 2). For aldehydes **1**, the yields of **4** were not sensitive to the electronic properties of the aromatic ring in the presence of electron-withdrawing groups (such as halide) or electron-donating groups (such as alkyl or alkoxy group, Table 2).

The optimised conditions were also suitable for 2-aminoanthracene **5**, which was reacted with a variety of aromatic aldehydes **1** and tetrahydrothiopyran-4-one **3** (Scheme 2). The reactions proceeded smoothly and gave thiopyrano[3,4-*c*] naphtho[2,3-*f*]quinoline derivatives **6a–l** in high yields (Table 3). The structures of the products **4** and **6** were characterised by ^{1}H NMR, IR and HRMS, they are all in good agreement with their structures.



Scheme 1

* Correspondent. E-mail: xswang1974@yahoo.com

Table 2 Synthetic results of **4a–k** catalysed by iodine in THF[a]

Ar	Products	Time/h	Yields/%[b]
4-ClC_6H_4	**4a**	12	89
4-FC_6H_4	**4b**	12	84
4-MeC_6H_4	**4c**	14	86
3-ClC_6H_4	**4d**	12	90
2-ClC_6H_4	**4e**	10	90
Piperonyl	**4f**	14	82
3-$MeOC_6H_4$	**4g**	12	92
2-FC_6H_4	**4h**	10	87
3,4-$Cl_2C_6H_3$	**4i**	10	82
2,3-$Cl_2C_6H_3$	**4j**	8	87
4-$MeOC_6H_4$	**4k**	15	90

[a]Reagents and conditions: **1** (2.0 mmol), **2** (0.266 g, 2.0 mmol), **3** (0.232 g, 2.0 mmol), I_2 (0.1 mmol, 0.026 g), THF (10 mL).
[b]Isolated yields.

Table 3 Synthetic results of **6a–l** catalysed by iodine in THF[a]

Ar	Products	Time/h	Yields/%[b]
4-BrC_6H_4	**6a**	12	90
4-MeC_6H_4	**6b**	16	86
4-ClC_6H_4	**6c**	10	89
3-ClC_6H_4	**6d**	10	92
2-ClC_6H_4	**6e**	10	93
3,4-$Cl_2C_6H_3$	**6f**	10	82
3,4-$(MeO)_2C_6H_3$	**6g**	16	84
3-$MeOC_6H_4$	**6h**	14	88
4-FC_6H_4	**6i**	10	83
2-BrC_6H_4	**6j**	10	90
3-BrC_6H_4	**6k**	10	90
2,3-$Cl_2C_6H_3$	**6l**	10	92

[a]Reagents and conditions: **1** (1.0 mmol), **5** (0.193 g, 1.0 mmol), **3** (0.116 g, 1.0 mmol), I_2 (0.05 mmol, 0.013 g), THF (10 mL).

Experimental

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a Tensor 27 spectrometer in KBr pellet. ^{1}H NMR spectra were obtained from a solution in DMSO-d_6 or $CDCl_3$ with Me_4Si as internal standard using a Bruker-400 spectrometer. HRMS analyses were carried out using a Bruker-micro- TOF-Q-MS analyser.

Syntheses of thiopyrano[3,4-c]pyrazolo[4,3-f] quinoline derivatives **4a–k***; general procedure*

A dry 50 mL flask was charged with aromatic aldehyde (2.0 mmol), 5-amino-1*H*-indazole (0.266 g, 2.0 mmol), tetrahydrothiopyran-4-one (0.232 g, 2.0 mmol), I_2 (0.026 g, 0.1 mmol) and THF (10 mL). The reaction mixture was stirred at reflux for 8–15 h. After completion of the reaction as indicated by TLC, part of the products dissolved out in the boiling THF as a yellow solid; consequently a little DMF was added to the hot mixture until it was dissolved entirely. The powder generated was collected by filtration to give **4** when the mixture was cooled to room temperature.

7-(4-Chlorophenyl)-3,8,10,11-tetrahydrothiopyrano[3,4-c]pyrazolo[4,3-f]quinoline (**4a**): M.p. 265–267 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 3.18 (t, J = 6.0 Hz, 2H, CH_2), 3.65 (t, J = 6.0 Hz, 2H, CH_2), 3.90 (s, 2H, CH_2), 7.58 (d, J = 8.4 Hz, 2H, ArH), 7.64 (d, J = 8.4 Hz, 2H, ArH), 7.87 (d, J = 9.2 Hz, 1H, ArH), 7.93 (d, J = 8.8 Hz, 1H, ArH), 8.65 (s, 1H, ArH), 13.74 (s, 1H, NH). IR (KBr, cm^{-1}): ν 3201, 3038, 2932, 2889, 1660, 1595, 1556, 1529, 1491, 1435, 1421, 1396, 1373, 1354, 1267, 1172, 1085, 1014, 962, 938, 837, 811, 797, 758. HRMS (ESI, *m/z*): Calcd for $C_{19}H_{15}{}^{35}ClN_3S$ [M+H]$^+$ 352.0675, found 352.0670.

7-(4-Fluorophenyl)-3,8,10,11-tetrahydrothiopyrano[3,4-c]pyrazolo[4,3-f]quinoline (**4b**): M.p. 268–269 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 3.18 (s, 2H, CH_2), 3.65 (s, 2H, CH_2), 3.89 (s, 2H, CH_2), 7.35 (t, J = 8.4 Hz, 2H, ArH), 7.64–7.67 (m, 2H, ArH), 7.88 (d, J = 8.8 Hz, 1H, ArH), 7.93 (d, J = 8.8 Hz, 1H, ArH), 8.65 (s, 1H, ArH), 13.74 (s, 1H, NH). IR (KBr, cm^{-1}): ν 3204, 3150, 3056, 2959, 2924, 2885, 1661, 1604, 1509, 1420, 1364, 1326, 1268, 1224, 1157, 1094, 947, 845, 815, 740. HRMS (ESI, *m/z*): Calcd for $C_{19}H_{15}FN_3S$ [M+H]$^+$ 336.0971, found 336.1023.

7-(p-Tolyl)-3,8,10,11-tetrahydrothiopyrano[3,4-c]pyrazolo[4,3-f]quinoline (**4c**): M.p. 270–272 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 2.41 (s, 3H, CH_3), 3.18 (t, J = 6.0 Hz, 2H, CH_2), 3.64 (t, J = 5.6 Hz, 2H, CH_2), 3.89 (s, 2H, CH_2), 7.33 (d, J = 8.0 Hz, 2H, ArH), 7.49 (d, J = 8.0 Hz, 2H, ArH), 7.86 (d, J = 9.2 Hz, 1H, ArH), 7.92 (d, J = 8.8 Hz, 1H, ArH), 8.64 (s, 1H, ArH), 13.73 (s, 1H, NH). IR (KBr, cm^{-1}): ν 3190, 3132, 3042, 2922, 2881, 1667, 1589, 1557, 1511, 1447, 1424, 1367, 1327, 1269, 1179, 1157, 1105, 935, 834, 819, 787, 738. HRMS (ESI, *m/z*): Calcd for $C_{20}H_{18}N_3S$ [M+H]$^+$ 332.1221, found 332.1255.

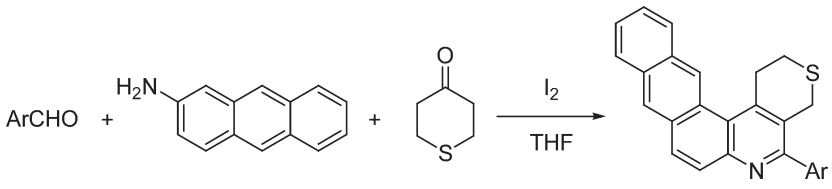
7-(3-Chlorophenyl)-3,8,10,11-tetrahydrothiopyrano[3,4-c]pyrazolo[4,3-f]quinoline (**4d**): M.p. 238–240 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 3.18 (t, J = 6.0 Hz, 2H, CH_2), 3.64 (s, 2H, CH_2), 3.91 (s, 2H, CH_2), 7.56 (s, 3H, ArH), 7.66 (s, 1H, ArH), 7.89 (d, J = 8.8 Hz, 1H, ArH), 7.94 (d, J = 8.8 Hz, 1H, ArH), 8.66 (s, 1H, ArH), 13.78 (s, 1H, NH). IR (KBr, cm^{-1}): ν 3191, 3150, 3049, 2963, 2923, 2871, 1665, 1592, 1567, 1516, 1473, 1424, 1377, 1352, 1344, 1269, 1256, 1208, 1159, 1094, 934, 897, 885, 837, 807, 783, 733, 719. HRMS (ESI, *m/z*): Calcd for $C_{19}H_{15}{}^{35}ClN_3S$ [M+H]$^+$ 352.0675, found 352.0686.

7-(2-Chlorophenyl)-3,8,10,11-tetrahydrothiopyrano[3,4-c]pyrazolo[4,3-f]quinoline (**4e**): M.p. 283–285 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 3.16 (d, J = 6.0 Hz, 2H, CH_2), 3.62 (s, 2H, CH_2), 3.66 (s, 2H, CH_2), 7.47–7.66 (m, 3H, ArH), 7.63 (d, J = 7.2 Hz, 1H, ArH), 7.86 (d, J = 8.8 Hz, 1H, ArH), 7.95 (d, J = 8.8 Hz, 1H, ArH), 8.66 (s, 1H, ArH), 13.77 (s, 1H, NH). IR (KBr, cm^{-1}): ν 2962, 2934, 2865, 2840, 1695, 1604, 1557, 1514, 1467, 1411, 1383, 1363, 1253, 1226, 1170, 1137, 1107, 1022, 961, 893, 813, 755, 661. HRMS (ESI, *m/z*): Calcd for $C_{19}H_{15}{}^{35}ClN_3S$ [M+H]$^+$ 352.0675, found 352.0689.

7-Piperonyl-3,8,10,11-tetrahydrothiopyrano[3,4-c]pyrazolo[4,3-f]quinoline (**4f**): M.p. 255–257 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 3.17 (t, J = 6.0 Hz, 2H, CH_2), 3.62 (s, 2H, CH_2), 3.92 (s, 2H, CH_2), 6.11 (s, 2H, CH_2), 7.03–7.08 (m, 2H, ArH), 7.17 (s, 1H, ArH), 7.86 (d, J = 9.2 Hz, 1H, ArH), 7.92 (d, J = 9.2 Hz, 1H, ArH), 8.64 (s, 1H, ArH), 13.75 (s, 1H, NH). IR (KBr, cm^{-1}): ν 3202, 3146, 3048, 2885, 1659, 1604, 1562, 1493, 1371, 1330, 1231, 1160, 1151, 1112, 1037, 939, 901, 848, 814, 785. HRMS (ESI, *m/z*): Calcd for $C_{20}H_{16}N_3O_2S$ [M+H]$^+$ 362.0963, found 362.0933.

7-(3-Methoxyphenyl)-3,8,10,11-tetrahydrothiopyrano[3,4-c]pyrazolo[4,3-f]quinoline (**4g**): M.p. 252–254 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 3.18 (s, 2H, CH_2), 3.62 (s, 2H, CH_2), 3.83 (s, 3H, CH_3O), 3.88 (s, 2H, CH_2), 7.05 (d, J = 7.6 Hz, 1H, ArH), 7.13 (d, J = 8.8 Hz, 2H, ArH), 7.43 (t, J = 7.6 Hz, 1H, ArH), 7.86 (d, J = 8.8 Hz, 1H, ArH), 7.93 (d, J = 8.8 Hz, 1H, ArH), 8.67 (s, 1H, ArH), 13.78 (s, 1H, NH). IR (KBr, cm^{-1}): ν 3182, 3129, 3043, 2925, 1668, 1608, 1578, 1517, 1486, 1450, 1426, 1365, 1327, 1286, 1223, 1175, 1156, 1115, 1095, 1045, 972, 932, 887, 853, 788, 733, 709. HRMS (ESI, *m/z*): Calcd for $C_{20}H_{18}N_3OS$ [M+H]$^+$ 348.1171, found 348.1183.

7-(2-Fluorophenyl)-3,8,10,11-tetrahydrothiopyrano[3,4-c]pyrazolo[4,3-f]quinoline (**4h**): M.p. 280–282 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 3.18 (s, 2H, CH_2), 3.65 (s, 2H, CH_2), 3.72 (s, 2H, CH_2), 7.36–7.40 (m, 2H, ArH), 7.50–7.57 (m, 2H, ArH), 7.88 (d, J = 8.4 Hz, 1H, ArH), 7.94 (d, J = 8.4 Hz, 1H, ArH), 8.66 (s, 1H, ArH), 13.78 (s, 1H, NH). IR (KBr, cm^{-1}): ν 3193, 3130, 3036, 2915, 2878, 1615, 1573, 1561, 1520, 1490, 1446, 1373, 1332, 1280, 1253, 1206, 1158, 1091, 941, 845, 821, 786, 755. HRMS (ESI, *m/z*): Calcd for $C_{19}H_{15}FN_3S$ [M+H]$^+$ 336.0971, found 336.0962.



Scheme 2

7-(3,4-Dichlorophenyl)-3,8,10,11-tetrahydrothiopyrano[3,4-c]pyrazolo[4,3-f]quinoline **(4i)**: M.p. 296–298 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 3.18 (s, 2H, CH_2), 3.63 (s, 2H, CH_2), 3.93 (s, 2H, CH_2), 7.61 (d, J = 8.4 Hz, 1H, ArH), 7.77 (d, J = 8.0 Hz, 1H, ArH), 7.88 (s, 2H, ArH), 7.93 (d, J = 8.4 Hz, 1H, ArH), 8.66 (s, 1H, ArH), 13.76 (s, 1H, NH). IR (KBr, cm^{-1}): ν 3180, 3144, 2927, 1667, 1582, 1550, 1517, 1469, 1430, 1382, 1355, 1323, 1271, 1249, 1174, 1134, 1106, 1030, 973, 946, 884, 848, 826, 786, 755. HRMS (ESI, *m/z*): Calcd for $C_{19}H_{14}{}^{35}Cl_2N_3S$ [M+H]$^+$ 386.0285, found 386.0288.

7-(2,3-Dichlorophenyl)-3,8,10,11-tetrahydrothiopyrano[3,4-c]pyrazolo[4,3-f]quinoline (**4j**): M.p. 295–298 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 3.17 (s, 2H, CH_2), 3.59–3.68 (m, 4H, $2CH_2$), 7.46 (d, J = 7.2 Hz, 1H, ArH), 7.51–7.55 (m, 1H, ArH), 7.79 (d, J = 8.0 Hz, 1H, ArH), 7.86 (d, J = 8.8 Hz, 1H, ArH), 7.94 (d, J = 8.8 Hz, 1H, ArH), 8.66 (s, 1H, ArH), 13.78 (s, 1H, NH). IR (KBr, cm^{-1}): ν 3188, 3141, 3047, 2979, 2932, 1671, 1605, 1586, 1557, 1517, 1453, 1407, 1365, 1327, 1277, 1190, 1152, 1089, 1048, 940, 883, 843, 813, 783, 745, 720, 700. HRMS (ESI, *m/z*): Calcd for $C_{19}H_{14}{}^{35}Cl_2N_3S$ [M+H]$^+$ 386.0285, found 386.0290.

7-(4-Methoxyphenyl)-3,8,10,11-tetrahydrothiopyrano[3,4-c]pyrazolo[4,3-f]quinoline (**4k**): M.p. 254–257 °C; ^{1}H NMR (DMSO-d_6, 400 MHz): δ_H 3.18 (s, 2H, CH_2), 3.63 (s, 2H, CH_2), 3.84 (s, 3H, CH_3O), 3.91 (s, 2H, CH_2), 7.07 (d, J = 7.6 Hz, 2H, ArH), 7.55 (d, J = 7.6 Hz, 2H, ArH), 7.87 (d, J = 8.4 Hz, 1H, ArH), 7.91 (d, J = 8.8 Hz, 1H, ArH), 8.64 (s, 1H, ArH), 13.72 (s, 1H, NH). IR (KBr, cm^{-1}): ν 3178, 3123, 3080, 3035, 3007, 2920, 1610, 1560, 1510, 1458, 1425, 1367, 1326, 1297, 1257, 1175, 1106, 1028, 930, 836, 820, 790, 742. HRMS (ESI, *m/z*): Calcd for $C_{20}H_{18}N_3OS$ [M+H]$^+$ 348.1171, found 348.1174.

Syntheses of 5-aryl-2,4-dihydro-1H-thiopyrano[3,4-c]naphtho[2,3-f]quinoline derivatives **6a-l**; *general procedure*

A dry 50 mL flask was charged with aromatic aldehyde (1.0 mmol), 2-aminoanthracene (0.193 g, 1.0 mmol), tetrahydrothiopyran-4-one (0.116 g, 1.0 mmol), I_2 (0.013 g, 0.05 mmol) and THF (10 mL). The reaction mixture was stirred at reflux for 10–16 h. After completion of the reaction as indicated by TLC, part of the products dissolved out in the boiling THF as yellow solid; consequently a little DMF was added to the hot mixture until it was dissolved entirely. The generated powder was collected by filtration to give **6** when the mixture was cooled to room temperature.

5-(4-Bromophenyl)-2,4-dihydro-1H-thiopyrano[3,4-c]naphtho[2,3-f]quinoline **(6a)**: M.p. 239–241°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.90 (t, J = 6.4 Hz, 2H, CH_2), 3.95 (s, 2H, CH_2), 4.05 (t, J = 6.4 Hz, 2H, CH_2), 7.54–7.69 (m, 6H, ArH), 7.81 (d, J = 8.8 Hz, 1H, ArH), 7.97 (d, J = 9.2 Hz, 1H, ArH), 8.10 (dd, J = 9.2 Hz, J' = 4.4 Hz, 2H, ArH), 8.43 (s, 1H, ArH), 8.93 (s, 1H, ArH). IR (KBr, cm^{-1}): ν 3047, 2924, 1588, 1547, 1474, 1439, 1421, 1386, 1264, 1176, 1113, 1100, 1070, 1010, 954, 892, 836, 825, 811, 746. HRMS (ESI, *m/z*): Calcd for $C_{26}H_{19}{}^{79}BrNS$ [M+H]$^+$ 456.0422, found 456.0422.

5-(p-Tolyl)-2,4-dihydro-1H-thiopyrano[3,4-c]naphtho[2,3-f]quinoline **(6b)**: M.p. 233–236°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.45 (s, 3H, CH_3), 2.89 (t, J = 6.0 Hz, 2H, CH_2), 4.00 (s, 2H, CH_2), 4.03 (t, J = 6.0 Hz, 2H, CH_2), 7.34 (d, J = 7.6 Hz, 2H, ArH), 7.55–7.62 (m, 4H, ArH), 7.82 (d, J = 9.2 Hz, 1H, ArH), 7.95 (d, J = 9.2 Hz, 1H, ArH), 8.09 (dd, J = 9.2 Hz, J' = 6.0 Hz, 2H, ArH), 8.41 (s, 1H, ArH), 8.93 (s, 1H, ArH). IR (KBr, cm^{-1}): ν 3060, 3031, 2939, 2917, 2849, 1611, 1543, 1477, 1436, 1387, 1369, 1286, 1265, 1225, 1213, 1180, 1140, 1112, 1016, 949, 892, 827, 743. HRMS (ESI, *m/z*): Calcd for $C_{27}H_{22}NS$ [M+H]$^+$ 392.1473, found 392.1483.

5-(4-Chlorophenyl)-2,4-dihydro-1H-thiopyrano[3,4-c]naphtho[2,3-f]quinoline **(6c)**: M.p. 243–246°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.89 (t, J = 6.4 Hz, 2H, CH_2), 3.95 (s, 2H, CH_2), 4.04 (t, J = 6.4 Hz, 2H, CH_2), 7.51 (d, J = 8.4 Hz, 2H, ArH), 7.61–7.63 (m, 4H, ArH), 7.79 (d, J = 8.8 Hz, 1H, ArH), 7.97 (d, J = 9.2 Hz, 1H, ArH), 8.09 (dd, J = 9.2 Hz, J' = 4.4 Hz, 2H, ArH), 8.42 (s, 1H, ArH), 8.93 (s, 1H, ArH). IR (KBr, cm^{-1}): ν 3048, 2932, 2869, 1596, 1547, 1476, 1440, 1422, 1388, 1285, 1263, 1215, 1174, 1171, 1087, 1012, 954, 934, 891, 838, 746. HRMS (ESI, *m/z*): Calcd for $C_{26}H_{19}{}^{35}ClNS$ [M+H]$^+$ 412.0927, found 412.0954.

5-(3-Chlorophenyl)-2,4-dihydro-1H-thiopyrano[3,4-c]naphtho[2,3-f]quinoline (**6d**): M.p. 209–210°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.89 (t, J = 6.0 Hz, 2H, CH_2), 3.96 (s, 2H, CH_2), 4.04 (t, J = 6.0 Hz, 2H, CH_2), 7.45–7.47 (m, 2H, ArH), 7.52–7.55 (m, 1H, ArH), 7.61–7.63 (m, 2H, ArH), 7.69 (s, 1H, ArH), 7.80 (d, J = 9.2 Hz, 1H, ArH), 7.97 (d, J = 9.2 Hz, 1H, ArH), 8.09 (dd, J = 9.2 Hz, J' = 5.6 Hz, 2H, ArH), 8.42 (s, 1H, ArH), 8.93 (s, 1H, ArH) .. IR (KBr, cm^{-1}): ν 3047, 2909, 1594, 1546, 1531, 1470, 1410, 1384, 1361, 1285, 1258, 1141, 1077, 955, 890, 814, 791, 743, 704. HRMS (ESI, *m/z*): Calcd for $C_{26}H_{19}{}^{35}ClNS$ [M+H]$^+$ 412.0927, found 412.0942.

5-(2-Chlorophenyl)-2,4-dihydro-1H-thiopyrano[3,4-c]naphtho[2,3-f]quinoline **(6e)**: M.p. 219–220°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.70–2.76 (m, 1H, CH_2), 3.04–3.09 (m, 1H, CH_2), 3.67 (d, J = 14.8 Hz, 1H, CH_2), 3.83–3.94 (m, 2H, CH_2), 4.26–4.32 (m, 1H, CH_2), 7.42–7.64 (m, 6H, ArH), 7.82 (d, J = 8.8 Hz, 1H, ArH), 7.98 (d, J = 9.2 Hz, 1H, ArH), 8.10 (dd, J = 9.6 Hz, J' = 7.2 Hz, 2H, ArH), 8.43 (s, 1H, ArH), 9.01 (s, 1H, ArH). IR (KBr, cm^{-1}): ν 3051, 2917, 2853, 1548, 1529, 1468, 1429, 1381, 1361, 1285, 1275, 1119, 1046, 952, 887, 819, 747, 708. HRMS (ESI, *m/z*): Calcd for $C_{26}H_{19}{}^{35}ClNS$ [M+H]$^+$ 412.0927, found 412.0957.

5-(3,4-Dichlorophenyl)-2,4-dihydro-1H-thiopyrano[3,4-c]naphtho[2,3-f]quinoline (**6f**): M.p. 226–229°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.89 (t, J = 2.8 Hz, 2H, CH_2), 3.95 (s, 2H, CH_2), 4.05 (t, J = 6.0 Hz, 2H, CH_2), 7.50 (dd, J = 8.4 Hz, J' = 2.0 Hz, 1H, ArH), 7.60–7.64 (m, 3H, ArH), 7.77–7.81 (m, 2H, ArH), 7.98 (d, J = 9.2 Hz, 1H, ArH), 8.10 (dd, J = 8.8 Hz, J' = 4.4 Hz, 2H, ArH), 8.43 (s, 1H, ArH), 8.93 (s, 1H, ArH). IR (KBr, cm^{-1}): ν 3053, 2914, 2854, 1546, 1533, 1469, 1383, 1361, 1267, 1246, 1181, 1115, 1067, 1028, 956, 895, 837, 749, 709. HRMS (ESI, *m/z*): Calcd for $C_{26}H_{18}{}^{35}Cl_2NS$ [M+H]$^+$ 446.0537, found 446.0556.

5-(3,4-Dimethoxyphenyl)-2,4-dihydro-1H-thiopyrano[3,4-c]naphtho[2,3-f]quinoline (**6g**): M.p. 227–229°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.90 (t, J = 6.0 Hz, 2H, CH_2), 3.97 (d, J = 5.2 Hz, 6H, $2CH_3O$), 4.03 (s, 2H, CH_2), 4.05 (d, J = 6.0 Hz, 2H, CH_2), 7.02 (d, J = 8.0 Hz, 1H, ArH), 7.35 (dd, J = 8.0 Hz, J' = 1.6 Hz, 1H, ArH), 7.27 (s, 1H, ArH), 7.61 (dd, J = 6.4 Hz, J' = 3.2 Hz, 2H, ArH), 7.83 (d, J = 9.2 Hz, 1H, ArH), 7.96 (d, J = 9.2 Hz, 1H, ArH), 8.09 (dd, J = 8.8 Hz, J' = 5.6 Hz, 2H, ArH), 8.42 (s, 1H, ArH), 8.93 (s, 1H, ArH). IR (KBr, cm^{-1}): ν 3055, 2927, 2835, 1602, 1583, 1536, 1514, 1461, 1448, 1425, 1372, 1326, 1256, 1229, 1166, 1136, 1026, 900, 880, 803, 746. HRMS (ESI, *m/z*): Calcd for $C_{28}H_{22}NO_2S$ [M-H]$^+$ 436.1370, found 436.1363.

5-(3-Methoxyphenyl)-2,4-dihydro-1H-thiopyrano[3,4-c]naphtho[2,3-f]quinoline (**6h**): M.p. 209–211°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.89 (t, J = 6.0 Hz, 2H, CH_2), 3.90 (s, 3H, CH_3O), 3.99 (s, 2H, CH_2), 4.05 (t, J = 6.0 Hz, 2H, CH_2), 7.01–7.03 (m, 1H, ArH), 7.21 (d, J = 7.2 Hz, 2H, ArH), 7.42–7.46 (m, 1H, ArH), 7.61 (dd, J = 6.0 Hz, J' = 3.6 Hz, 2H, ArH), 7.83 (d, J = 9.2 Hz, 1H, ArH), 7.97 (d, J = 8.8 Hz, 1H, ArH), 8.09 (dd, J = 9.2 Hz, J' = 6.0 Hz, 2H, ArH), 8.42 (s, 1H, ArH), 8.94 (s, 1H, ArH). IR (KBr, cm^{-1}): ν 3043, 2994, 2946, 2927, 2839, 1605, 1575, 1544, 1474, 1449, 1433, 1373, 1327, 1314, 1282, 1270, 1245, 1222, 1163, 1109, 1039, 952, 894, 872, 825, 787, 754, 702. HRMS (ESI, *m/z*): Calcd for $C_{27}H_{21}NO_2S$ [M+H]$^+$ 408.1422, found 408.1420.

5-(4-Fluorophenyl)-2,4-dihydro-1H-thiopyrano[3,4-c]naphtho[2,3-f]quinoline **(6i)**: M.p. 254–256°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.90 (t, J = 6.0 Hz, 2H, CH_2), 3.96 (s, 2H, CH_2), 4.05 (t, J = 6.0 Hz, 2H, CH_2), 7.22 (d, J = 8.8 Hz, 2H, ArH), 7.61–7.68 (m, 4H, ArH), 7.82 (d, J = 9.2 Hz, 1H, ArH), 7.98 (d, J = 8.8 Hz, 1H, ArH), 8.10 (dd, J = 8.4 Hz, J' = 4.4 Hz, 2H, ArH), 8.43 (s, 1H, ArH), 8.93 (s, 1H, ArH). IR (KBr, cm^{-1}): ν 3040, 2947, 2924, 2851, 1601, 1550, 1537, 1506, 1478, 1437, 1421, 1390, 1371, 1286, 1261, 1217, 1180, 1156, 1139, 1118, 1093, 956, 894, 842, 812, 747. HRMS (ESI, *m/z*): Calcd for $C_{26}H_{19}FNS$ [M+H]$^+$ 396.1222, found 396.1218.

5-(2-Bromophenyl)-2,4-dihydro-1H-thiopyrano[3,4-c]naphtho[2,3-f]quinoline **(6j)**: M.p. 225–227 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.70–2.76 (m, 1H, CH_2), 3.04–3.08 (m, 1H, CH_2), 3.66 (d, J = 14.8 Hz, 1H, CH_2), 3.84–3.92 (m, 2H, CH_2), 4.26–4.32 (m, 1H, CH_2), 7.32–7.36 (m, 1H, ArH), 7.48–7.55 (m, 2H, ArH), 7.61–7.63 (m, 2H, ArH), 7.71 (d, J = 8.0 Hz, 1H, ArH), 7.82 (d, J = 9.2 Hz, 1H, ArH), 7.98 (d, J = 9.2 Hz, 1H, ArH), 8.08–8.12 (m, 2H, ArH), 8.43 (s, 1H, ArH), 9.02 (s, 1H, ArH). IR (KBr, cm^{-1}): ν 3050, 2927, 2910, 1547, 1530, 1468, 1426, 1382, 1360, 1286, 1274, 1257, 1116, 1025, 953, 889, 821, 815, 745. HRMS (ESI, *m/z*): Calcd for $C_{26}H_{19}{}^{79}BrNS$ [M+H]$^+$ 456.0422, found 456.0420.

5-(3-Bromophenyl)-2,4-dihydro-1H-thiopyrano[3,4-c]naphtho[2,3-f]quinoline **(6k)**: M.p. 214–215°C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ_H 2.90 (t, J = 6.0 Hz, 2H, CH_2), 3.96 (s, 2H, CH_2), 4.05 (t, J = 6.0 Hz, 2H, CH_2), 7.38–7.42 (m, 1H, ArH), 7.57–7.63 (m, 4H, ArH), 7.80 (d, J = 8.8 Hz, 1H, ArH), 7.85 (s, 1H, ArH), 7.98 (d, J = 9.2 Hz, 1H, ArH), 8.10 (dd, J = 9.2 Hz, J' = 5.2 Hz, 2H, ArH), 8.43 (s, 1H, ArH), 8.94 (s, 1H, ArH). IR (KBr, cm^{-1}): ν 3061, 2930, 2861, 1591, 1543, 1467, 1444, 1426, 1382, 1370, 1264, 1224, 1181, 1142, 1064, 996,

964, 890, 824, 805, 787, 770, 751, 701. HRMS (ESI, *m/z*): Calcd for $C_{26}H_{19}{}^{79}BrNS$ $[M+H]^+$ 456.0422, found 456.0420.

5-(2,3-Dichlorophenyl)-2,4-dihydro-1H-thiopyrano[3,4-c]naphtho[2,3-f]quinoline (**6l**): M.p. 241–244°C; ^1H NMR ($CDCl_3$, 400 MHz): δ_H 2.71–2.77 (m, 1H, CH_2), 3.03–3.09 (m, 1H, CH_2), 3.65 (d, J = 14.8 Hz, 1H, CH_2), 3.84–3.91 (m, 2H, CH_2), 4.25–4.32 (m, 1H, CH_2), 7.37–7.41 (m, 1H, ArH), 7.46 (dd, J = 7.6 Hz, J' = 1.6 Hz, 1H, ArH), 7.58–7.65 (m, 3H, ArH), 7.79 (d, J = 9.2 Hz, 1H, ArH), 7.99 (d, J = 9.2 Hz, 1H, ArH), 8.10 (dd, J = 9.6 Hz, J' = 6.8 Hz, 2H, ArH), 8.43 (s, 1H, ArH), 9.01 (s, 1H, ArH). IR (KBr, cm^{-1}): ν 3054, 2969, 2921, 2852, 1548, 1480, 1437, 1422, 1408, 1389, 1375, 1270, 1178, 1154, 1135, 1045, 948, 891, 805, 788, 745, 716. HRMS (ESI, *m/z*): Calcd for $C_{26}H_{18}{}^{35}Cl_2NS$ $[M+H]^+$ 446.0537, found 446.0523.

Conclusion

In conclusion, we have found a mild and efficient method for the synthesis of thiopyrano[3,4-*c*]pyrazolo[4,3-*f*]quinoline and thiopyrano[3,4-*c*]naphtho[2,3-*f*] quinoline derivatives via three-component reactions of aromatic aldehyde, 5-amino-1*H*-indazole or 2-aminoanthracene and tetrahydrothiopyran-4-one catalysed by iodine. The features of this procedure are mild reaction conditions, high yields, operational simplicity and metal-free catalysis.

We are grateful to a Project Funded by the Priority Academic Program Development of Jiangsu Higher Education Institutions, the Graduate Foundation of Jiangsu Normal University and Qing Lan Project (08QLT001, 10QLD008) of Jiangsu Education Committee for financial support.

Received 27 October 2011; accepted 20 March 2012
Paper 1100956 doi: 10.3184/174751912X13352797144052
Published online: 4 June 2012

References

1 S. Eswaran, A.V. Adhikari, N.S. Shetty, *Eur. J. Med. Chem*., 2009, **44**, 4637.
2 C.L. Yang, C.H. Tseng, Y.L. Chen, C.M. Lu, C.L. Kao, M.H. Wu, C.C. Tzeng, *Eur. J. Med. Chem.*, 2010, **45**, 602.
3 P.W. Smith, P.A. Wyman, P. Lovell, C. Goodacre, H.T. Serafinowska, A. Vong, F. Harrington, S. Flynn, D.M. Bradley, R. Porter, S. Coggon, G. Murkitt, K. Searle, D.R. Thomas, J.M. Watson, W. Martin, Z.N. Wu, L.A. Dawson, *Bioorg. Med. Chem. Lett.*, 2009, **19**, 837.
4 I.J. Kang, L.W. Wang, S.J. Hsu, C.C. Lee, Y.C. Lee, Y.S. Wu, T.A. Hsu, A. Yueh, Y.S. Chao, J.H. Chern, *Bioorg. Med. Chem. Lett*., 2009, **19**, 4134.
5 B.W. Michel, L.D. Steffens, and M.S. Sigman, *J. Am. Chem. Soc.*, 2011, **133**, 8317.
6 M. Li, Y.L. Hou, L.R. Wen, and F.M. Gong, *J. Org. Chem.*, 2010, **75**, 8522.
7 Y. Luo, X.L. Pan, and J. Wu, *Org. Lett.*, 2011, **13**, 1150.
8 L.S. Povarov, *Russ. Chem. Rev*., 1967, **36**, 656.
9 V.V. Kouznetsov, *Tetrahedron*, 2009, **65**, 2721.
10 X.F. Lin, S.L. Cui and Y.G. Wang, Tetrahedron Lett., 2006, **47**, 3127.
11 X.S. Wang, Q. Li, J.R. Wu and S.J. Tu, *J. Comb. Chem*., 2009, **11**, 433.
12 X.S. Wang, Q. Li, C.S. Yao and S.J. Tu, *Eur. J. Org. Chem*., 2008, 3513.
13 M.Y. Yin, W. Wang, M.M. Zhang, and X.S. Wang, *J. Chem. Res.*, 2011, **35**, 513.

Copyright of Journal of Chemical Research is the property of Science Reviews 2000 Ltd. and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.