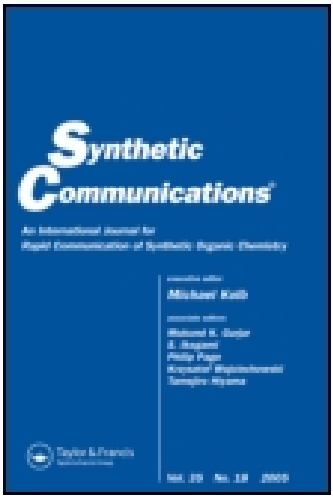

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Iodine-Catalyzed Synthesis of 3-Arylbenzoquinoline Derivatives by Three-Component Reactions

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Abstract: A mild, efficient, and general method for the synthesis of benzo[*f*]quinoline derivatives via three-component reaction of arylaldehyde, naphthalen-2-amine, and acetone or acetophenone is described using iodine as catalyst. The features of this procedure are mild reaction conditions, high yields, and operational simplicity.

Keywords: Acetone, acetophenone, benzo[*f*]quinoline, iodine, synthesis

INTRODUCTION

In recent years, the use of molecular iodine in organic synthesis has received considerable attention as an inexpensive, nontoxic, readily available mild Lewis acid catalyst for organic transformations such as dehydration of tertiaryalcohols to alkenes,[1] synthesis of benzyl alkyl ethers,[2] synthesis of mixed ethers under hydrogen pressure,[3] synthesis of benzothiophenes[4] and bis-indoles,[5] deprotection of acetals,[6] esterification,[7] transesterification,[8] Michael addition,[9] and many other reactions.[10]

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Multicomponent reactions (MCRs), often with three or more reactants combined in a one-pot procedure to generate a complex organic molecule, have become increasingly popular during the past decade.[11] They provide a powerful tool toward one-pot synthesis of diverse and complex compounds as well as small and drug-like heterocycles. Benzo[*f*]quinoline and its derivatives are very useful compounds in various fields of chemistry including biological and pharmacological areas. Some of these exhibit antibacterial activity,[12] uridine diphosphate-glucuronosyl transferase (UGT) activity,[13] inhibitory activity,[14] antimicrobial activity,[15] antimalarial activity,[16] antipsychotic activity,[17] and antagonist activity.[18]

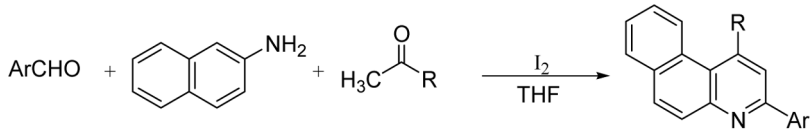
In view of the importance of benzoquinoline and its derivatives, several methods for the synthesis of benzo[*f*]quinoline and its derivatives were developed by Kozlov et al.[19] and other groups.[20] However, many of these reported methods suffer from drawbacks such as harsh reaction conditions, unsatisfactory yields, prolonged reaction time, and cumbersome product isolation procedure. Kozlov et al.[21] recently reported three-component reactions from arylaldehyde, naphthalen-2-amine, and acetone catalyzed by $SnCl_2$ but with low to moderate yields (6–74%). Thus the development of an efficient and mild process for the preparation of biologically active 3-arylbenzoquinoline derivatives appeared interesting.

Wang et al.[22] recently reported a Schiff base with aliphatic aldehyde catalyzed by iodine to give 2-aryl-3-substitutedquinolines, demonstrating that iodine was an efficient catalyst for this reaction; however, no ketones were explored in this iodine-catalyzed reaction. In connection with our previous research on MCRs,[23] the procedure reported herein was successfully realized via a three-component reaction of arylaldehyde, naphthalen-2-amine, and acetone or acetophenone catalyzed by iodine without isolating and purifying the intermediates to afford 3-aryl-1-substituedbenzo[*f*]quinolines in high yields.

RESULTS AND DISCUSSION

The treatment of arylaldehyde **1**, naphthalen-2-amine **2**, and acetone or acetophenone **3** in THF in the presence of 5 mol% iodine at refluxing temperature afforded the corresponding 3-aryl-1-substituedbenzo[*f*] quinoline derivatives **4** in high yields (Scheme 1).

Initially, the reaction of 4-chlorobenzaldehyde **1a**, naphthalen-2-amine **2**, and acetone **3** was used as a model reaction to optimize the conditions. The reaction was first carried out in THF in the absence of I_2. No product was obtained at room temperature and reflux (Table 1, entries 1 and 2). We also evaluated the amount of catalyst required for



1 2 3 4

Scheme 1. The reaction of arylaldehyde, naphthalen-2-amine, and ketone.

this transformation. It was found that that 5 mol% I_2 at reflux in THF was sufficient to push the reaction forward. More amounts of the catalyst did not improve yields. To find the optimum reaction temperature, the reaction was carried out with 5 mol% of I_2 at room temperature, 50 °C, and reflux, resulting in the isolation of **4a** in trace amount, 82% and 94% yields (Table 1, entries 3, 4, and 6) respectively. Thus, 5 mol% of I_2 and a reaction temperature at reflux were optimal conditions. In addition, we also looked into the solvent effect for this reaction. As showed in Table 1, tetrahydrofuran (THF) gave the most satisfactory result in comparison with other solvents (Table 1, entries 8–11).

Similarly, several benzaldehydes reacted with naphthalen-2-amine and acetone to give 3-arylbenzo[*f*]quinoline derivatives in high yield in a few hours. The results are summarized in Table 2. It can be observed that the process tolerates both electron-donating and electron-withdrawing substituents in the benzaldehyde. In all cases, the reactions proceeded efficiently at reflux under mild conditions to afford the corresponding benzo[*f*]quinolines in high yields. Interestingly, the reactions also

Table 1. Synthesis of **4a** under different reaction conditions[a]

Entry	Temp. (°C)	Amount (mol%)	Solvent	Yields[b] (%)
1	Rt	0	THF	0
2	Reflux	0	THF	0
3	Rt	5	THF	trace
4	50 °C	5	THF	82
5	Reflux	5	THF	94
6	Reflux	10	THF	94
7	Reflux	20	THF	92
8	Reflux	5	CH_3CN	86
9	Reflux	5	Benzene	87
10	80 °C	5	DMF	82
11	Reflux	5	$ClCH_2CH_2Cl$	86

[a]Reagents and conditions: **1** (2 mmol), **2** (2 mmol), **3** (2 mmol), solvent (10 mL).
[b]Isolated yields.

Table 2. I_2-catalyzed reactions of benzaldehyde, naphthalen-2-amine, and acetone or acetophenone in THF[a]

Entry	Ar	R	Products	Time (h)	Yields (%)[b]
1	4-ClC_6H_4	Me	**4a**	5	94
2	3-$NO_2C_6H_4$	Me	**4b**	6	92
3	3-ClC_6H_4	Me	**4c**	8	90
4	2,4-$Cl_2C_6H_3$	Me	**4d**	6	92
5	3-BrC_6H_4	Me	**4e**	6	88
6	2-Thiophenyl	Me	**4f**	8	89
7	4-FC_6H_4	Me	**4g**	6	96
8	3,4-$Cl_2C_6H_3$	Me	**4h**	6	92
9	4-$NO_2C_6H_4$	Me	**4i**	5	88
10	4-BrC_6H_4	Me	**4j**	6	90
11	2-$NO_2C_6H_4$	Me	**4k**	5	91
12	4-$CH_3OC_6H_4$	Me	**4l**	8	88
13	3,4-$(CH_3)_2C_6H_3$	Me	**4m**	7	86
14	2,3-$(CH_3O)_2C_6H_3$	Me	**4n**	8	90
15	3-BrC_6H_4	C_6H_5	**4o**	12	83
16	4-ClC_6H_4	4-$CH_3C_6H_4$	**4p**	14	86
17	4-ClC_6H_4	4-$NO_2C_6H_4$	**4q**	10	88
18	3-$NO_2C_6H_4$	4-$NO_2C_6H_4$	**4r**	10	90
19	3-ClC_6H_4	4-BrC_6H_4	**4s**	14	82
20	2,4-$Cl_2C_6H_3$	4-BrC_6H_4	**4t**	12	85
21	3-$NO_2C_6H_4$	4-BrC_6H_4	**4u**	12	84
22	4-FC_6H_4	4-BrC_6H_4	**4v**	12	83
23	3-BrC_6H_4	4-FC_6H_4	**4w**	14	84
24	2,3-$Cl_2C_6H_3$	4-ClC_6H_4	**4x**	12	87

[a]Reagents and conditions: **1** (2 mmol), **2** (2 mmol), **3** (2 mmol), I_2 (10 mol%), and THF (10 mL).
[b]Isolated yields.

proceeded efficiently with acetophenone to generate 1,3-diarylbenzo[*f*] quinoline in high yields (Table 2, entries 15–24). However, we failed to get the expected products when aliphatic aldehydes were used. All the products were characterized by ^{1}H NMR, IR, melting points, and elemental analyses.

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a Tensor 27 spectrometer in KBr pellets. ^{1}H NMR spectra were obtained from solution in DMSO-d_6 or $CDCl_3$,

with Me_4Si as internal standard, using an Inova-400 spectrometer. Elemental analyses were carried out using a Perkin-Elmer 240 II analyzer.

General Procedure for the Syntheses of 3-Aryl-1-substitutedbenzo[*f*]quinoline Derivatives 4

A dry 50-mL flask was charged with arylaldehyde (2.0 mmol), naphthalen-2-amine (2.0 mmol, 0.286 g), acetone (3.0 mmol, 0.174 g) or acetophenone (2.0 mmol), I_2 (0.2 mmol, 0.051 g), and THF (10 mL). The reaction mixture was stirred at reflux for 5–14 h. After completion of the reaction, as indicated by thin-layer chromatography (TLC), a little DMF was added to the mixture until the all yellow solid was dissolved. The generated crystals were collected by filtration to give **4** when the mixture was cooled to room temperature.

Data

3-(4-Chlorophenyl)-1-methylbenzo[*f*]quinoline **4a**

Mp 179–181 °C (lit.[21]: 182 °C). ^{1}H NMR (DMSO-d_6, δ, ppm): 3.20 (s, 3H, CH_3), 7.63 (d, $J = 7.6$ Hz, 2H, ArH), 7.73 ~ 7.77 (m, 2H, ArH), 7.96–7.99 (m, 1H, ArH), 8.10–8.19 (m, 3H, ArH), 8.36 (d, $J = 7.6$ Hz, 2H, ArH), 8.90 (d, $J = 8.0$ Hz, 1H, ArH). IR (KBr, ν, cm^{-1}): 3055, 1619, 1579, 1546, 1480, 1456, 1405, 1377, 1350, 1264, 1091, 1011, 889, 872, 840, 756, 713, 677.

1-Methyl-3-(3-nitrophenyl)benzo[*f*]quinoline **4b**

Mp 183–185 °C (lit.[21]: 186 °C). ^{1}H NMR (DMSO-d_6, δ, ppm): 3.23 (s, 3H, CH_3), 7.75–7.86 (m, 2H, ArH), 7.87–7.90 (m, 1H, ArH), 8.01–8.05 (m, 1H, ArH), 8.11–8.17 (m, 2H, ArH), 8.34–8.36 (m, 2H, ArH), 8.77 (d, $J = 7.2$ Hz, 1H, ArH), 8.93 (d, $J = 8.0$ Hz, 1H, ArH), 9.14 (d, $J = 2.0$ Hz, 1H, ArH). IR (KBr, ν, cm^{-1}): 3049, 2966, 1587, 1537, 1481, 1451, 1395, 1377, 1338, 1254, 1134, 1106, 1074, 930, 916, 809, 825, 802, 791, 741, 714.

3-(3-Chlorophenyl)-1-methylbenzo[*f*]quinoline **4c**

Mp 127–128 °C. ^{1}H NMR (DMSO-d_6, δ, ppm): 3.20 (s, 3H, CH_3), 7.56–7.62 (m, 2H, ArH), 7.72–7.78 (m, 2H, ArH), 7.99 (d, $J = 8.8$ Hz,

1H, ArH), 8.10–8.14 (m, 2H, ArH), 8.24 (s, 1H, ArH), 8.30 (d, $J = 7.2$ Hz, 1H, ArH), 8.39 (s, 1H, ArH), 8.90 (d, $J = 8.0$ Hz, 1H, ArH). IR (KBr, ν, cm^{-1}): 3054, 2984, 1594, 1578, 1549, 1481, 1452, 1422, 1376, 1335, 1293, 1276, 1252, 1211, 1142, 1096, 1077, 1033, 967, 914, 865, 832, 799, 785, 770, 749, 729, 692. Anal. Calcd. for $C_{20}H_{14}ClN$: C, 79.07; H, 4.65; N, 4.61. Found: C, 78.90; H, 4.66; N, 4.78.

3-(2,4-Dichlorophenyl)-1-methylbenzo[*f*]quinoline **4d**

Mp 175–177 °C. ^{1}H NMR (DMSO-d_6, δ, ppm): 3.19 (s, 3H, CH_3), 7.63 (dd, $J = 8.4$ Hz, $J' = 2.0$ Hz, 1H, ArH), 7.76–7.80 (m, 3H, ArH), 7.82–7.84 (m, 2H, ArH), 7.96 (d, $J = 8.4$ Hz, 1H, ArH), 8.13–8.17 (m, 2H, ArH), 8.94 (m, 1H, ArH). IR (KBr, ν, cm^{-1}): 3050, 2982, 1588, 1556, 1475, 1453, 1383, 1344, 1245, 1101, 1046, 1031, 896, 875, 859, 829, 813, 794, 747, 706. Anal. calcd. for $C_{20}H_{13}Cl_2N$: C, 71.02; H, 3.87; N, 4.14. Found: C, 70.92; H, 3.94; N, 4.12.

3-(3-Bromophenyl)-1-methylbenzo[*f*]quinoline **4e**

Mp 157–158 °C. ^{1}H NMR (DMSO-d_6, δ, ppm): 3.20 (s, 3H, CH_3), 7.52–7.56 (m, 1H, ArH), 7.69–7.78 (m, 3H, ArH), 8.00 (d, $J = 8.8$ Hz, 1H, ArH), 8.10–8.14 (m, 2H, ArH), 8.24 (s, 1H, ArH), 8.34 (d, $J = 7.6$ Hz, 1H, ArH), 8.54 (s, 1H, ArH), 8.91 (d, $J = 8.0$ Hz, 1H, ArH). IR (KBr, ν, cm^{-1}): 3050, 1580, 1548, 1477, 1450, 1419, 1378, 1337, 1255, 1093, 1071, 907, 865, 833, 797, 782, 742, 710, 688. Anal. calcd. for $C_{20}H_{14}BrN$: C, 68.98; H, 4.05; N, 4.02. Found: C, 68.72; H, 4.20; N, 4.16.

1-Methyl-3-(2-thiophenyl)benzo[*f*]quinoline **4f**

Mp 128–129 °C. ^{1}H NMR (DMSO-d_6, δ, ppm): 3.15 (s, 3H, CH_3), 7.24 (dd, $J = 4.8$ Hz, $J' = 4.0$ Hz, 1H, ArH), 7.67–7.76 (m, 3H, ArH), 7.88 (d, $J = 9.2$ Hz, 1H, ArH), 7.98–8.00 (m, 1H, ArH), 8.07–8.10 (m, 3H, ArH), 8.86 (d, $J = 8.0$ Hz, 1H, ArH). IR (KBr, ν, cm^{-1}): 3064, 2969, 1581, 1549, 1484, 1455, 1421, 1379, 1355, 1256, 1230, 1123, 1072, 1037, 977, 866, 530, 750, 729, 700, 665. Anal. calcd. for $C_{18}H_{13}NS$: C, 78.51; H, 4.76; N, 5.09. Found: C, 78.40; H, 4.57; N, 5.19.

3-(4-Fluorophenyl)-1-methylbenzo[*f*]quinoline **4g**

Mp 129–130 °C (lit.[21]: 130 °C). ^{1}H NMR (DMSO-d_6, δ, ppm): 3.20 (s, 3H, CH_3), 7.40 (t, $J = 8.8$ Hz, 2H, ArH), 7.71–7.78 (m, 2H, ArH),

7.98 (d, $J = 8.8$ Hz, 1H, ArH), 8.10–8.13 (m, 2H, ArH), 8.18 (s, 1H, ArH), 8.38–8.41 (m, 2H, ArH), 8.90 (d, $J = 8.0$ Hz, 1H, ArH). IR (KBr, ν, cm^{-1}): 3059, 1596, 1581, 1548, 1496, 1480, 1455, 1389, 1350, 1294, 1263, 1222, 1153, 1098, 1029, 890, 808, 758.

3-(3,4-Dichlorophenyl)-1-methylbenzo[*f*]quinoline **4h**

Mp 172–174 °C. ^{1}H NMR (DMSO-d_6, δ, ppm): 3.17 (s, 3H, CH_3), 7.72–7.81 (m, 3H, ArH), 7.97 (d, $J = 8.8$ Hz, 1H, ArH), 8.08–8.13 (d, 2H, ArH), 8.22 (s, 1H, ArH), 8.30 (dd, $J = 8.4$ Hz, $J' = 2.0$ Hz, 1H, ArH), 8.54 (d, $J = 2.0$ Hz, 1H, ArH), 8.88 (d, $J = 8.0$ Hz, 1H, ArH). IR (KBr, ν, cm^{-1}): 3048, 2967, 1606, 1585, 1545, 1471, 1452, 1402, 1370, 1345, 1273, 1251, 1145, 1126, 1093, 1025, 917, 874, 827, 791, 744, 699, 676, 660. Anal. calcd. for $C_{20}H_{13}Cl_2N$: C, 71.02; H, 3.87; N, 4.14. Found: C, 71.30; H, 3.70; N, 4.05.

1-Methyl-3-(4-nitrophenyl)benzo[*f*]quinoline **4i**

Mp 192–194 °C; (lit.[21]: 193–194 °C). ^{1}H NMR (DMSO-d_6, δ, ppm): 3.15 (s, 3H, CH_3), 7.72–7.75 (m, 2H, ArH), 7.96 (d, $J = 8.8$ Hz, 1H, ArH), 8.07–8.12 (m, 2H, ArH), 8.21 (s, 1H, ArH), 8.33 (d, $J = 8.0$ Hz, 2H, ArH), 8.51 (d, $J = 8.0$ Hz, 2H, ArH), 8.85 (d, $J = 8.0$ Hz, 1H, ArH). IR (KBr, ν, cm^{-1}): 3050, 1596, 1580, 1550, 1514, 1484, 1452, 1430, 1372, 1337, 1268, 1166, 1108, 1012, 981, 849, 836, 753, 693, 675.

3-(4-Bromophenyl)-1-methylbenzo[*f*]quinoline **4j**

Mp 174–176 °C (lit.[21]: 177–178 °C). ^{1}H NMR (DMSO-d_6, δ, ppm): 3.20 (s, 3H, CH_3), 7.71–7.78 (m, 4H, ArH), 7.98 (d, $J = 8.8$ Hz, 1H, ArH), 8.10–8.14 (m, 2H, ArH), 8.20 (s, 1H, ArH), 8.30 (d, $J = 8.4$ Hz, 2H, ArH), 8.91 (d, $J = 8.4$ Hz, 1H, ArH). IR (KBr, ν, cm^{-1}): 3054, 2983, 2932, 1604, 1578, 1545, 1479, 1450, 1402, 1377, 1348, 1263, 1176, 1103, 1088, 1067, 1034, 1007, 980, 945, 886, 871, 828, 799, 753, 707.

1-Methyl-3-(2-nitrophenyl)benzo[*f*]quinoline **4k**

Mp 184–186 °C; (lit.[21]: 188 °C). ^{1}H NMR (DMSO-d_6, δ, ppm): 3.19 (s, 3H, CH_3), 7.72–7.81 (m, 4H, ArH), 7.84–7.88 (m, 1H, ArH), 7.91 (s, 1H, ArH), 7.94–7.96 (m, 1H, ArH), 8.06 (dd, $J = 8.8$ Hz, $J' = 0.8$ Hz, 1H, ArH), 8.08–8.14 (m, 2H, ArH), 8.92 (d, $J = 8.4$ Hz, 1H, ArH). IR (KBr, ν, cm^{-1}): 3050,

2998, 2891, 1603, 1581, 1536, 1479, 1455, 1392, 1368, 1296, 1255, 1168, 1106, 982, 880, 863, 852, 836, 803, 777, 764, 747, 730, 715, 697.

3-(4-Methoxyphenyl)-1-methylbenzo[*f*]quinoline **4l**

Mp 121–122 °C; (lit.[21]: 124–125 °C). ^{1}H NMR ($CDCl_3$, δ, ppm): 3.16 (s, 3H, CH_3), 3.88 (s, 3H, CH_3O), 7.04 ($J = 8.8$ Hz, $J' = 2.0$ Hz, 2H, ArH), 7.61–7.66 (m, 2H, ArH), 7.76 (s, 1H, ArH), 7.94–7.97 (m, 2H, ArH), 8.05 (d, $J = 9.2$ Hz, 1H, ArH), 8.18 (dd, $J = 8.8$ Hz, $J' = 2.0$ Hz, 2H, ArH), 8.80 (d, $J = 8.0$ Hz, 1H, ArH). IR (KBr, ν, cm^{-1}): 3050, 2990, 2934, 2838, 1602, 1582, 1546, 1509, 1480, 1454, 1356, 1303, 1290, 1245, 1173, 1115, 1036, 983, 947, 873, 835, 818, 791, 716.

3-(3,4-Dimethylphenyl)-1-methylbenzo[*f*]quinoline **4m**

Mp 141–142 °C. ^{1}H NMR ($CDCl_3$, δ, ppm): 2.35 (s, 3H, CH_3), 2.40 (s, 3H, CH_3), 3.19 (s, 3H, CH_3), 7.29 (d, $J = 8.0$ Hz, 1H, ArH), 7.62–7.67 (m, 2H, ArH), 7.81 (s, 1H, ArH), 7.91 (dd, $J = 8.0$ Hz, $J' = 1.6$ Hz, 1H, ArH), 7.96 (d, $J = 9.2$ Hz, 2H, ArH), 8.02 (s, 1H, ArH), 8.08 (d, $J = 8.8$ Hz, 1H, ArH), 8.83 (d, $J = 8.4$ Hz, 1H, ArH). IR (KBr, ν, cm^{-1}): 3059, 3016, 2970, 2911, 1583, 1548, 1504, 1486, 1451, 1392, 1373, 1338, 1264, 1169, 1139, 1119, 1023, 997, 980, 911, 861, 829, 822, 744, 711. Anal. calcd. for $C_{22}H_{19}N$: C, 88.85; H, 6.44; N, 4.71. Found: C, 88.73; H, 6.52; N, 4.72.

3-(2,3-Dimethoxyphenyl)-1-methylbenzo[*f*]quinoline **4n**

Mp > 300 °C, (lit.[21]: 305 °C). ^{1}H NMR ($CDCl_3$, δ, ppm): 3.18 (s, 3H, CH_3), 3.72 (s, 3H, CH_3O), 3.94 (s, 3H, CH_3O), 7.02 (dd, $J = 8.0$ Hz, $J' = 1.6$ Hz, 1H, ArH), 7.20–7.25 (m, 1H, ArH), 7.52 (dd, $J = 8.0$ Hz, $J' = 1.6$ Hz, 1H, ArH), 7.62–7.70 (m, 2H, ArH), 7.94–7.98 (m, 3H, ArH), 8.08 (d, $J = 9.2$ Hz, 1H, ArH), 8.87 (d, $J = 8.4$ Hz, 1H, ArH). IR (KBr, ν, cm^{-1}): 3059, 2998, 2965, 2932, 2838, 1579, 1544, 1468, 1421, 1355, 1304, 1257, 1169, 1083, 1062, 997, 976, 940, 862, 833, 798, 756. Anal. calcd. for $C_{22}H_{19}NO_2$: C, 80.22; H, 5.81; N, 4.25. Found: C, 80.37; H, 5.93; N, 4.10.

3-(3-Bromophenyl)-1-phenylbenzo[*f*]quinoline **4o**

Mp 208–210 °C. ^{1}H NMR (DMSO-d_6, δ, ppm): 7.19–7.23 (m, 1H, ArH), 7.50–7.62 (m, 8H, ArH), 7.70–7.72 (m, 1H, ArH), 8.03–8.09 (m, 3H, ArH), 8.18 (d, $J = 8.8$ Hz, 1H, ArH), 8.37 (d, $J = 7.6$ Hz, 1H, ArH),

8.58–8.59 (m, 1H, ArH). IR (KBr, ν, cm^{-1}): 3054, 1601, 1576, 1543, 1477, 1419, 1389, 1345, 1328, 1275, 1252, 1231, 1150, 1083, 1069, 996, 943, 870, 838, 781, 756, 702, 689 cm^{-1}. Anal. calcd. for $C_{25}H_{16}BrN$: C, 73.18; H, 3.93; N, 3.41. Found: C, 73.22; H, 3.79; N, 3.59.

3-(4-Chlorophenyl)-1-(4-methylphenyl)benzo[*f*]quinoline **4p**

Mp 158–160 °C. ^{1}H NMR (DMSO-d_6, δ, ppm): 2.47 (s, 3H, CH_3), 7.22–7.26 (m, 1H, ArH), 7.41 (s, 4H, ArH), 7.53–7.57 (m, 1H, ArH), 7.61 (d, $J = 8.8$ Hz, 2H, ArH), 7.67 (d, $J = 8.8$ Hz, 1H, ArH), 7.97 (s, 1H, ArH), 8.02–8.06 (m, 2H, ArH), 8.17 (d, $J = 9.2$ Hz, 1H, ArH), 8.39 (d, $J = 8.4$ Hz, 2H, ArH). IR (KBr, ν, cm^{-1}): 3056, 3027, 2917, 1592, 1578, 1543, 1523, 1509, 1475, 1449, 1387, 1354, 1328, 1254, 1107, 1092, 1012, 875, 867, 832, 815, 759, 717 cm^{-1}. Anal. calcd. for $C_{26}H_{18}ClN$: C, 82.20; H, 4.78; N, 3.69. Found: C, 82.09; H, 4.91; N, 3.67.

3-(4-Chlorophenyl)-1-(4-nitrophenyl)benzo[*f*]quinoline **4q**

Mp 286–288 °C. ^{1}H NMR (DMSO-d_6, δ, ppm): 7.28–7.32 (m, 1H, ArH), 7.48–7.50 (m, 1H, ArH), 7.57–7.64 (m, 3H, ArH), 7.85 (d, $J = 8.4$ Hz, 2H, ArH), 8.08 (d, $J = 8.4$ Hz, 2H, ArH), 8.09 (s, 1H, ArH), 8.21–8.23 (m, 1H, ArH), 8.41–8.47 (m, 4H, ArH). IR (KBr, ν, cm^{-1}): 3101, 3074, 3048, 1596, 1580, 1544, 1514, 1493, 1476, 1449, 1408, 1388, 1344, 1305, 1282, 1177, 1152, 1107, 1091, 1010, 851, 832, 797, 758, 744, 717, 704, 692 cm^{-1}. Anal. calcd. for $C_{25}H_{15}ClN_2O_2$: C, 73.08; H, 3.68; N, 6.82. Found: C, 72.91; H, 3.70; N, 6.97.

3-(3-Nitrophenyl)-1-(4-nitrophenyl)benzo[*f*]quinoline **4r**

Mp 208–210 °C. ^{1}H NMR ($CDCl_3$, δ, ppm): 7.22–7.26 (m, 1H, ArH), 7.54–7.58 (m, 2H, ArH), 7.70–7.75 (m, 3H, ArH), 7.82 (s, 1H, ArH), 7.95 (d, $J = 7.6$ Hz, 1H, ArH), 8.09 (d, $J = 8.8$ Hz, 1H, ArH), 8.15–8.17 (m, 1H, ArH), 8.34 (d, $J = 8.0$ Hz, 1H, ArH), 8.45 (d, $J = 8.4$ Hz, 2H, ArH), 8.61–8.63 (m, 1H, ArH), 9.10 (s, 1H, ArH). IR (KBr, ν, cm^{-1}): 3094, 1597, 1579, 1511, 1450, 1343, 1257, 1170, 1154, 1106, 1071, 1014, 894, 886, 852, 835, 805, 756, 714, 704, 684 cm^{-1}. Anal. calcd. for $C_{25}H_{15}N_3O_4$: C, 71.25; H, 3.59; N, 9.97. Found: C, 71.38; H, 3.71; N, 9.82.

1-(4-Bromophenyl)-3-(3-chlorophenyl)benzo[*f*]quinoline **4s**

Mp 194–195 °C. ^{1}H NMR (DMSO-d_6, δ, ppm): 7.30–7.34 (m, 1H, ArH), 7.52 (d, $J = 7.6$ Hz, 2H, ArH), 7.57–7.65 (m, 4H, ArH), 7.81 (d, $J = 7.6$ Hz, 2H, ArH), 8.05–8.09 (m, 3H, ArH), 8.19 (d, $J = 8.8$ Hz, 1H, ArH), 8.34 (d, $J = 6.4$ Hz, 1H, ArH), 8.44 (s, 1H, ArH). IR (KBr, ν, cm^{-1}): 3051, 1589, 1572, 1524, 1477, 1449, 1423, 1391, 1351, 1331, 1255, 1238, 1102, 1070, 1010, 949, 889, 871, 845, 822, 801, 754, 730, 704 cm^{-1}. Anal. calcd. for $C_{25}H_{15}BrClN$: C, 67.51; H, 3.40; N, 3.15. Found: C, 67.55; H, 3.32; N, 3.18.

1-(4-Bromophenyl)-3-(2,4-dichlorophenyl)benzo[*f*]quinoline **4t**

Mp 172–173 °C. ^{1}H NMR (DMSO-d_6, δ, ppm): 7.31–7.35 (m, 1H, ArH), 7.48 (d, $J = 8.4$ Hz, 2H, ArH), 7.59–7.67 (m, 3H, ArH), 7.71 (s, 1H, ArH), 7.78–7.87 (m, 4H, ArH), 8.03 (d, $J = 9.2$ Hz, 1H, ArH), 8.08 (d, $J = 7.6$ Hz, 1H, ArH), 8.21 (d, $J = 8.8$ Hz, 1H, ArH). IR (KBr, ν, cm^{-1}): 3082, 3046, 1586, 1562, 1551, 1524, 1473, 1448, 1389, 1378, 1347, 1332, 1248, 1139, 1100, 1069, 1047, 1037, 1009, 952, 871, 862, 834, 820, 801, 790, 750 cm^{-1}. Anal. calcd. for $C_{25}H_{14}BrCl_2N$: C, 62.66; H, 2.94; N, 2.92. Found: C, 62.70; H, 2.78; N, 3.01.

1-(4-Bromophenyl)-3-(3-nitrophenyl)benzo[*f*]quinoline **4u**

Mp 194–195 °C. ^{1}H NMR (DMSO-d_6, δ, ppm): 7.30–7.34 (m, 1H, ArH), 7.52 (d, $J = 8.4$ Hz, 2H, ArH), 7.58–7.65 (m, 2H, ArH), 7.81–7.87 (m, 3H, ArH), 8.07 (d, $J = 7.6$ Hz, 1H, ArH), 8.11 (d, $J = 8.8$ Hz, 1H, ArH), 8.18 (s, 1H, ArH), 8.21 (d, $J = 8.8$ Hz, 1H, ArH), 8.34–8.37 (m, 1H, ArH), 8.80 (d, $J = 8.0$ Hz, 1H, ArH), 9.16–9.17 (m, 1H, ArH). IR (KBr, ν, cm^{-1}): 3051, 1578, 1531, 1478, 1449, 1392, 1343, 1314, 1256, 1152, 1103, 1069, 1013, 917, 894, 878, 833, 805, 755, 747, 712, 686 cm^{-1}. Anal. calcd. for $C_{25}H_{15}BrN_2O_2$: C, 65.95; H, 3.32; N, 6.15. Found: C, 65.83; H, 3.44; N, 6.10.

1-(4-Bromophenyl)-3-(4-fluorophenyl)benzo[*f*]quinoline **4v**

Mp 124–125 °C. ^{1}H NMR (DMSO-d_6, δ, ppm): 7.27–7.31 (m, 1H, ArH), 7.36–7.40 (m, 2H, ArH), 7.48 (d, $J = 8.4$ Hz, 2H, ArH), 7.54–7.61 (m, 2H, ArH), 7.79 (d, $J = 8.4$ Hz, 2H, ArH), 7.98 (s, 1H, ArH), 8.04 (d, $J = 9.2$ Hz, 2H, ArH), 8.16 (d, $J = 9.2$ Hz, 1H, ArH), 8.39–8.42 (m, 2H, ArH). IR (KBr, ν, cm^{-1}): 3049, 1596, 1578, 1544, 1528, 1508, 1450,

1387, 1357, 1301, 1227, 1155, 1100, 1067, 1011, 946, 868, 835, 801, 744, 717 cm^{-1}. Anal. calcd. for $C_{25x}H_{15}BrFN$: C, 70.11; H, 3.53; N, 3.27. Found: C, 70.25; H, 3.47; N, 3.40.

3-(3-Bromophenyl)-1-(4-fluorophenyl)benzo[*f*]quinoline **4w**

Mp 216–218 °C. ^1H NMR (DMSO-d_6, δ, ppm): 7.27–7.31 (m, 1H, ArH), 7.43–7.47 (m, 2H, ArH), 7.51–7.61 (m, 5H, ArH), 7.71–7.73 (m, 1H, ArH), 8.05–8.09 (m, 3H, ArH), 8.19 (d, $J = 8.8$ Hz, 1H, ArH), 8.38 (d, $J = 8.0$ Hz, 1H, ArH), 8.58–8.59 (m, 1H, ArH). IR (KBr, ν, cm^{-1}): 3049, 1603, 1575, 1543, 1507, 1477, 1446, 1387, 1345, 1328, 1295, 1252, 1231, 1156, 1092, 1083, 1069, 1040, 995, 945, 874, 836, 795, 782, 757, 710, 690 cm^{-1}. Anal. calcd. for $C_{25}H_{15}BrFN$: C, 70.11; H, 3.53; N, 3.27. Found: C, 70.05; H, 3.49; N, 3.38.

1-(4-Chlorophenyl)-3-(2,3-dichlorophenyl)benzo[*f*]quinoline **4x**

Mp 145–146 °C. ^1H NMR (DMSO-d_6, δ, ppm): 7.29–7.33 (m, 1H, ArH), 7.51–7.67 (m, 8H, ArH), 7.73 (dd, $J = 8.0$ Hz, $J' = 1.6$ Hz, 1H, ArH), 7.78 (dd, $J = 8.0$ Hz, $J' = 1.2$ Hz, 1H, ArH), 8.01 (d, $J = 9.2$ Hz, 1H, ArH), 8.06 (d, $J = 8.8$ Hz, 1H, ArH), 8.19 (d, $J = 8.8$ Hz, 1H, ArH). IR (KBr, ν, cm^{-1}): 3048, 1573, 1557, 1540, 1521, 1493, 1474, 1446, 1416, 1348, 1329, 1251, 1192, 1125, 1093, 1048, 1016, 953, 840, 829, 788, 767, 756, 740, 721, 710 cm^{-1}. Anal. calcd. for $C_{25}H_{14}Cl_3N$: C, 69.07; H, 3.25; N, 3.22. Found: C, 68.87; H, 3.41; N, 3.19.

CONCLUSION

In conclusion, we found an efficient method for the synthesis of 3-aryl-1-substitutedbenzo[*f*]quinoline derivatives via three-component reaction of arylaldehyde, naphthalen-2-amine, and acetone or acetophenone using 5 mol% iodine as catalyst. The features of this procedure are mild reaction conditions, high yield, and operational simplicity.

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REFERENCES

1. Whitmore, F. C.; Rothrock, H. S. Studies on the rearrangement of tertiarybutylmethylcarbinol (pinacolyl alcohol), I. *J. Am. Chem. Soc.* **1933**, *55*, 1106–1109.
2. Rutherford, K. G.; Mamer, O. A.; Prokipcak, J. M.; Jobin, R. A. A novel synthesis of some mixed arylmethyl-alkyl ethers. *Can. J. Chem.* **1966**, *44*, 2337–2339.
3. Jenner, G. Iodine mediated synthesis of alkyl tert-alkyl ethers. *Tetrahedron Lett.* **1988**, *29*, 2445–2448.
4. Hessian, K. O.; Flynn, B. L. Iodine-induced reaction cascades for the rapid construction of variously substituted benzothiophenes. *Org. Lett.* **2003**, *5*, 4377–4380.
5. Bandgar, B. P.; Shaikh, K. A. Molecular iodine–catalyzed efficient and highly rapid synthesis of bis(indolyl)methanes under mild conditions. *Tetrahedron Lett.* **2003**, *44*, 1959–1961.
6. Sun, J.; Dong, Y.; Cao, L.; Wang, X.; Wang, S.; Hu, Y. Highly efficient chemoselective deprotection of *O*,*O*-acetals and *O*,*O*-ketals catalyzed by molecular iodine in acetone. *J. Org. Chem.* **2004**, *69*, 8932–8934.
7. Ramalinga, K.; Vijayalakshimi, P.; Kaimal, T. N. B. A mild and efficient method for esterification and transesterification catalyzed by iodine. *Tetrahedron Lett.* **2002**, *43*, 879–882.
8. Chavan, S. P.; Kale, R. R.; Shivasankar, K.; Chandake, S. I.; Benjamin, S. B. A simple and efficient method for transesterification of β-keto esters catalyzed by iodine. *Synthesis* **2003**, 2695–2698.
9. (a) Yadav, J. S.; Reddy, B. V. S.; Sadasiv, K.; Satheesh, G. 1,4-Conjugate addition of allyltrimethylsilane to α,β-unsaturated ketones. *Tetrahedron Lett.* **2002**, *43*, 9695–9697; (b) Wang, S. Y.; Ji, S. J.; Loh, T. P. The Michael addition of indole to α,β-unsaturated ketones catalyzed by iodine at room temperature. *Synlett* **2003**, 2377–2379.
10. (a) Lee, B. S.; Mahajan, S.; Janda, K. D. Molecular iodine–catalyzed imine activation for three-component nucleophilic addition reactions. *Synlett* **2005**, 1325–1327; (b) Bandgar, B. P.; Bettigeri, S. V.; Joshi, N. S. Molecular iodine–catalyzed highly rapid synthesis of 1,5-benzodiazepine derivatives under mild conditions. *Synth. Commun.* **2004**, *34*, 1447–1453; (c) Phukan, P. Mukaiyama aldol reactions of silylenolates catalyzed by iodine. *Synth Commun.* **2004**, *34*, 1065–1070; (d) Deka, N.; Kalita, D. J.; Borah, R. Sarma, J. C. Iodine as acetylation catalyst in the preparation of 1,1-diacetates from aldehydes. *J. Org. Chem.* **1997**, *62*, 1563–1564.
11. (a) Vijjay, N. C.; Rajesh, A. U.; Vinod, S.; Bindu, A. R.; Sreekanth, J. S.; Lakshmi, B. Strategies for heterocyclic construction via novel multicomponent reactions based on isocyanides and nucleophilic carbenes. *Acc. Chem. Res.* **2003**, *36*, 899–907; (b) Shin-Ichi, I. Nickel-catalyzed intermolecular domino reactions. *Acc Chem Res.* **2000**, *33*, 511–519; (c) Tietze, L. F. Domino reactions in organic synthesis. *Chem. Rev.* **1996**, *96*, 115–136; (d) Bunce, R. A. Recent advances in the use of tandem reactions for organic synthesis. *Tetrahedron* **1995**, *51*, 13103–13159; (e) Nicolaou, K. C.; Edmonds,

D. J.; Bulger, P. G. Cascade reactions in total synthesis. *Angew. Chem. Int. Ed.* **2006**, *45*, 7134–7186.

12. (a) Selvi, G.; Rajendran, S. P. Synthesis of some new 2-[3-(2-chloroquinolinyl)]-3-aryl-4-thiazolidinones as potent antibacterial agents. *Asian J. Chem.* **2004**, *16*, 1017–1022; (b) Bahuguna, R. P.; Joshi, B. C. Synthesis and antibacterial activity of some novel substituted arylsulfonylbenzo[*f*]quinolines. *Indian J. Heterocycl. Chem.* **1994**, *3*, 265–268.
13. (a) Carr, B. A.; Franklin, M. R. Drug-metabolizing enzyme induction by 2,2′-dipyridyl, 1,7-phenanthroline, 7,8-benzoquinoline, and oltipraz in mouse. *Xenobiotica* **1998**, *28*, 949–956; (b) Le, H. T.; Lamb, J. G.; Franklin, M. R. Drug metabolizing enzyme induction by benzoquinolines, acridine, and quinacrine: Tricyclic aromatic molecules containing a single heterocyclic nitrogen. *J. Biochem. Toxic.* **1996**, *11*, 297–303.
14. Abell, A. D.; Erhard, K. F.; Yen, H. K.; Yamashita, D. S.; Brandt, M.; Mohammed, H.; Levy, M. A.; Holt, D. A. Preparative chiral HPLC separation of all possible stereoisomers of LY191704 and LY266111 and their in vitro inhibition of human types 1 and 2 steroid 5a-reductases. *Bioorg. Med. Chem. Lett.* **1994**, *4*, 1365–1368.
15. Bahuguna, R. P.; Joshi, B. C.; Mangal, H. N. Studies on benzoquinoline derivatives: Preparation and antimicrobial activity of azo-derivatives of arylthiobenzo[*f*]quinoline. *J. Indian Chem. Soc.* **1992**, *69*, 401–402.
16. Mikhailitsyn, F. S.; Kozyreva, N. P.; Rabinovich, S. A.; Maksakovskaya, Y. V.; Kulikovskaya, I. M.; Dadasheva, N. R.; Lebedeva, M. N.; Bekhli, A. F.; Lychko, N. D.; Uvarova, N. A. Search for new antiparasitic agents, 10: Synthesis, toxicity, and antimalarial effect of some nitrogen-containing heterocycles with 4-(4-alkylpiperazin-1-yl)phenylamino substituents. *Med. Parazitol. Parazit. Bolezni.* **1992**, 50–53.
17. Szmuszkovicz, J.; Darlington, W. H.; Von Voigtlander, P. F. Preparation and formulation of antipsychotic aminopolyhydrobenz(iso)quinolines and intermediates. WO 8804292 A1, 1988. *Chem. Abstr.* **1988**, *110*, 75335.
18. Cannon, J. G.; Walker, K. A.; Montanari, A.; Long, J. P.; Flynn, J. R. Monomethyl ether derivatives of 7,8-dihydroxy- and 8,9-dihydroxy-4-propyl-1,2,3,4,4a,5,6,10b-octahydrobenzo [*f*]quinolines as possible products of metabolism by catechol-*O*-methyltransferase. *J. Med. Chem.* **1990**, *33*, 2000–2006.
19. (a) Kozlov, N. S.; Mikhalevskaya, S. V.; Serzhanina, V. A. Reaction of 3-[(*N*-2-naphthyl)formimidoyl]pyridine with substituted acetophenones. *Khim. Geterotsikl. Soedin.* **1989**, 351–354 (Russian); (b) Kozlov, N. S.; Shmanai, G. S.; Dang, N. T. Synthesis and spectral characteristics of acenaphthene derivatives of benzo[*f*]quinoline. *Khim. Geterotsikl. Soedin.* **1986**, 1102–1106 (Russian); (c) Kozlov, N. S.; Zhikhareva, O. D.; Stremok, I. P. Synthesis and spectra of 1-ethyl- and 1,2-dimethyl-3-(p-nitrophenyl) benzo[*f*]quinolines, their salts and dyes. *Dokl. Akad. Nauk BSSR* **1977**, *21*, 425–428; (d) Kozlov, N. S.; Gladchenko, L. F.; Sauts, R. D.; Serzhanina, V. A. Synthesis and spectral characteristics of 1-(3-pyridyl)-3-aryl-8-nitro(amino)benzo[*f*] quinolines. *Khim. Geterotsikl. Soedin.* **1978**, 1646–1649.

20. (a) Beller, N. R.; Neckers, D. C.; Papadopoulos, E. P. Photochemical synthesis of benzo[*f*]quinolines. *J. Org. Chem.* **1977**, *42*, 3514–3518; (b) Kozlov, N. G.; Sauts, R. D.; Gusak, K. N. Synthesis of benzo[*f*]quinoline derivatives by condensation of arylmethylene-2-naphthylamines with ethyl acetoacetate. *Russ. J. Org. Chem.* **2000**, *36*, 531–538; (c) Ripa, L.; Hallberg, A. Aryl radical endo cyclization of enamidines: Selective preparation of trans and cis fused octahydrobenzo[*f*]quinolines. *J. Org. Chem.* **1998**, *63*, 84–91; (d) Stetsenko, A. V.; Fursii, F. A. Synthesis of tetrahydrobenzo[*f*]quinoline. *Ukr. Khim. Zh.* **1986**, *52*, 755–759; (e) Bahuguna, R. P.; Joshi, B. C. Synthesis of substituted thioaryl and aryl sulfonyl benzo[*f*]quinolines. *Egypt. J. Chem.* **1988**, *31*, 89–96; (f) Tagmatarchis, N.; Katerinopoulos, H. E. Synthetic studies of the octahydrobenzo[*f*]quinoline system. *J. Heterocycl. Chem.* **1996**, *33*, 983–985; (g) Bahuguna, R. P.; Joshi, B. C. Synthesis and antibacterial activity of some novel substituted arylsulfonylbenzo[*f*]quinolines. *Indian J. Heterocycl. Chem.* **1994**, *3*, 265–268.
21. Kozlov, N. G.; Basalaeva, L. I. Synthesis of new 3-aryl-1-methylbenzo[*f*] quinolines. *Russ. J. Org. Chem.* **2003**, *39*, 718–722.
22. Lin, X. F.; Cui, S. L.; Wang, Y. G. Molecular iodine-catalyzed one-pot synthesis of substituted quinolines from imines and aldehydes. *Tetrahedron Lett.* **2006**, *47*, 3127–3130.
23. (a) Wang, X. S.; Zhang, M. M.; Jiang, H.; Shi, D. Q.; Tu, S. J.; Wei, X. Y.; Zong, Z. M. An improved and benign synthesis of 9,10-diarylacridine-1,8-dione and indenoquinoline derivatives from 3-anilino-5,5-dimethylcyclohex-2-enones, benzaldehydes, and 1,3-dicarbonyl compounds in an ionic liquid medium. *Synthesis* **2006**, 4187–4199; (b) Wang, X. S.; Zhang, M. M.; Jiang, H.; Yao, C. S.; Tu, S. J. Three-component green synthesis of *N*-arylquinoline derivatives in ionic liquid [Bmim][BF_4]: Reactions of arylaldehyde, 3-arylamino-5,5-dimethylcyclohex-2-enone, and active methylene compounds. *Tetrahedron* **2007**, *63*, 4439–4449.