Sulfamic Acid-Catalyzed Synthesis of 13-Aryl-indeno[1,2-*b*]-naphtha[1,2-e]pyran-12(13*H*)-ones under Solvent-Free Conditions

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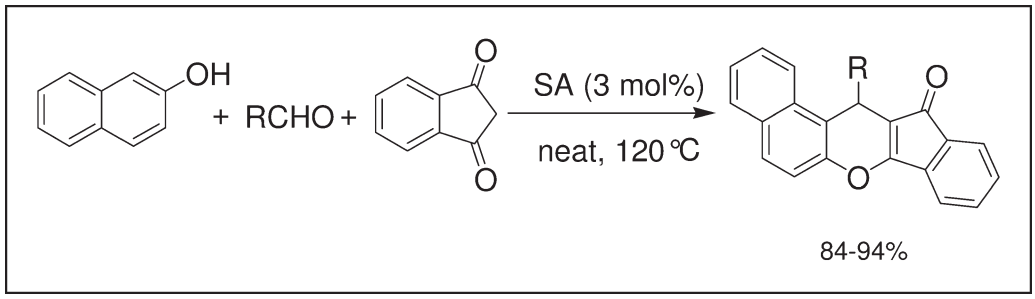

The reaction of β-naphthol with arylaldehydes and 2H-indene-1,3-dione in the presence of sulfamic acid (3 mol %) under solvent-free conditions led to 13-aryl-indeno[1,2-*b*]naphtho[1,2-*e*]pyran-12(13*H*)-ones in good yields.

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INTRODUCTION

Multicomponent reactions have attracted considerable attention as they are performed without need to isolate any intermediate during their processes; this reduces time and saves both energy and raw materials [1]. They have merits over two-component reactions in several aspects including the simplicity of a one-pot procedure, possible structural variations and building up complex molecules.

Natural compounds possessing naphthopyran moiety have been attracted by their antimicrobial [2], antitumor [3], antifungal [4], cytotoxic [5], antioxidative, and 5-lipoxygenase inhibitory activity [6]. A variety of naphthopyran derivatives have been isolated and identified as natural phytochemicals [7]. A plethora of biological activities have also been associated with a large number of synthetic naphthopyran analogs [8]. Indenopyrans are a ''privileged medicinal scaffolds,'' which are used for the development of pharmaceutical agents of various applications. Compounds with the motif show a wide range of pharmacological activities, such as antiulcer [9], antiallergenic [10], and antidepressant activities [11].

Molecule frame works for the development of 12-aryl-8,9,10,12-tetrahydrobenzo[*a*] xanthen-11-ones have also been described [12]. However, there is no report about the synthesis of 13-aryl-indeno[1,2-*b*]naphtho[1,2-*e*]pyran-12(13*H*)-ones, which may show potential pharmaceutical activities.

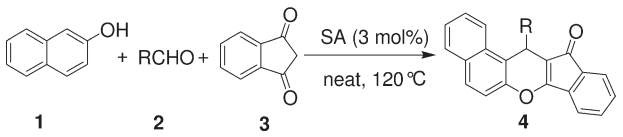
In recent years, the use of solid acidic catalysts has offered important advantages in organic synthesis, for example, operational simplicity, environmental compatibility, nontoxic, low cost, and ease of isolation. A tremendous upsurge of interest in various chemical transformations processes by catalysts under heterogeneous conditions has occurred. One of those heterogeneous catalysts is sulfamic acid (SA). It makes reaction processes convenient, more economic, and environmentally benign. Owing to the numerous advantages associated with this cheap and nonhazardous catalyst, SA has been explored as a powerful catalyst for various organic transformations [13]. We now report a highly efficient procedure for the preparation of 13-aryl-indeno[1,2-*b*]naphtho[1,2-*e*]pyran-12(13*H*)-ones using SA as an efficient and versatile catalyst under solvent-free conditions (Scheme 1).

RESULTS AND DISCUSSION

Initially, to optimize the reaction temperatures, the reaction of β-naphthol (1 mmol) with benzaldehyde (1 mmol) and 2H-indene-1,3-dione was studied under solvent-free conditions in the presence of 3 mol % SA at different temperatures. The results are summarized in Table 1. As shown in Table 1, the reaction at 120°C proceeded in highest yield.

To optimize the catalyst loading, 0, 1, 2, 3, 4, and 5 mol % of was tested, respectively. The results are

Scheme 1



summarized in Table 2. A 3 mol % loading of SA was sufficient to push the reaction forward and 2 mol % of SA was not enough. Higher amounts of SA did not lead to significant change in the reaction yields.

Based on the optimized reaction conditions, a range of 13-aryl-indeno[1,2-*b*]naphtho[1,2-*e*]pyran-12(13*H*)-ones (**4**) was synthesized by the reaction of β-naphthol (**1**, 1 mmol) with arylaldehydes (**2**, 1 mmol) and 2H-indene-1,3-dione (**3**, 1 mmol). The reaction proceeded at 120°C within 4 h in excellent yields after the addition of the catalyst SA (Table 3). All of the products **4** exhibited a singlet in their ^{1}H spectra at δ = 5.58–6.01 ppm for H-13 and also a distinguishing peak at δ = 28.8–35.7 ppm for C-13 in their ^{13}C NMR spectra. The resonance of carbonyl group in their ^{13}C NMR spectrum of **4** appeared at δ = 191.7–192.4 ppm. When this reaction was carried out with aliphatic aldehyde, such as butanal or pentanal, TLC and ^{1}H NMR spectra of the reaction mixture showed a mixture of starting materials and numerous products, the yield of the expected product was very poor. In 2-naphthol, the electron density at the benzylic C-1 position (which is in conjugation with the aromatic ring) is higher than that at the C-3 position. Thus, the regioselective formation of the *ortho*-quinone methide from this compound involving the C-1 and C-2 positions is favored. In simple phenolic compounds and 1-naphthol (which are weaker nucleophiles compared with 2-naphthol), the electron density at the *ortho* position of the hydroxyl group is not sufficient for the reaction of these compounds with the aldehydes leading to the formation of the corresponding *ortho*-quinone methides. When the reaction of 1-naphthol (1 mmol) with benzaldehyde (1 mmol) and 2H-indene-1,3-dione was carried out under solvent-free conditions in the presence of 3 mol % SA at 120°C, the yield of the expected product was 0%.

In conclusion, we have demonstrated a rapid and very efficient SA-catalyzed one-pot synthesis of 13-aryl-indeno[1,2-*b*]naphtho[1,2-*e*]pyran-12(13*H*)-ones under solvent-free conditions. The current methodology has the advantages of operational simplicity, neutral and mild reaction conditions, high to excellent yields of products, lack of toxicity, and low costs.

Table 1

Temperature optimization for the synthesis of 13-phenyl-indeno [1,2-b]naphtha [1,2-e]pyran-12(13H)-ones.[a]

Entry	Temp. (°C)	Yield (%)[b]
1	80	56
2	90	62
3	100	76
4	110	82
5	120	89
6	130	87
7	140	88

[a] Reaction conditions: β-naphthol (1 mmol); benzaldehyde (1 mmol); 2H-indene-1,3-dione (1 mmol); SA (0.03 mmol); solvent-free; 3 h.
[b] Isolated yield after chromatographic purification.

Table 2

The amounts of catalyst optimization for the synthesis of 13-phenyl-indeno[1,2-b]naphtho[1,2-e]pyran-12(13H)-ones.[a]

Entry	SA (mol %)	Yield (%)[b]
1	0	0
2	1	58
3	2	79
4	3	89
5	4	88
6	5	87

[a] Reaction conditions: β-naphthol (1 mmol); benzaldehyde (1 mmol); 2H-indene-1,3-dione (1 mmol); solvent-free;120°C; 3 h.
[b] Isolated yield after chromatographic purification.

EXPERIMENTAL

NMR spectra were determined on Bruker AV-400 spectrometer in $CDCl_3$ and were expressed in δ values relative to tetramethylsilane, coupling constants (*J*) were measured in Hz; IR spectra were determined on FTS-40 infrared spectrometer; Mass spectra were recorded on a Finnigan LCQ Advantage mass spectrometer; Elemental analysis were recorded on a Vario ELIII elemental analyzer; Melting points were determined on a Mel-Temp capillary tube apparatus and were uncorrected; Commercially available reagents were used throughout without further purification unless otherwise stated.

Table 3

Synthesis of 13-aryl-indeno[1,2-b]naphtho [1,2-e]pyran-12(13H)-ones using SA as catalyst.[a]

Entry	R	Time (h)	Product	Yield (%)[b]
1	C_6H_5	3	**4a**	89
2	4-Cl-C_6H_4	2	**4b**	92
3	3-NO_2-C_6H_4	3	**4c**	89
4	2-F-5-CF_3-C_6H_3	4	**4d**	86
5	4-Me-C_6H_4	4	**4e**	86
6	2,4-Cl_2-C_6H_3	3	**4f**	93
7	2-Cl-C_6H_4	2	**4g**	94
8	4-MeO-C_6H_4	4	**4h**	84
9	4-F-C_6H_4	2	**4i**	92
10	3,4-Cl_2-C_6H_3	3	**4j**	91

[a] Reaction conditions: β-naphthol (1 mmol); arylaldehyde (1 mmol); 2H-indene-1,3-dione (1 mmol); SA (0.03 mmol); solvent-free;120°C.
[b] Isolated yield after chromatographic purification.

General procedure for the preparation of 4. To a mixture of β-naphthol (1 mmol), aldehyde (1 mmol) and 2H-indene-1,3-dione (1 mmol), SA (0.03 mmol) was added. The mixture was stirred (use a high power electric mixer) at 120°C for an appropriate time (Table 3). After completion of the reaction (TLC), the reaction mixture was treated with water (10 mL) and extracted with CH_2Cl_2 (2 × 10 mL), filtered and the solvent evaporated *in vacuo*. Products were puried by silica gel column chromatography using petroleum ether:chloroform (2:3) as eluent.

13-Phenyl-indeno[1,2-b]naphtho[1,2-e]pyran-12(13H)-one (4a). Yellow solid, mp 202–203°C. IR (KBr) ν: 3080, 1660, 1236, 1006 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.89–7.82 (m, 3H), 7.51 (d, J = 8.8 Hz, 1H), 7.43–7.29 (m, 8H), 7.23 (t, J = 8.0 Hz, 2H), 7.12 (t, J = 7.6 Hz, 1H), 5.64 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 192.3, 167.3, 149.0, 143.7, 136.9, 132.4, 132.2, 131.9, 131.8, 130.1, 129.6, 128.5, 128.4, 128.1, 127.1, 126.6, 125.2, 124.4, 121.6, 118.3, 117.1, 116.6, 111.0, 35.7 ppm. MS (ESI): m/z 361 $[M + H]^+$. *Anal*. calcd for $C_{26}H_{16}O_2$: C, 86.65; H, 4.47. found: C, 86.73; H, 4.38.

13-(4-Chlorophenyl)-indeno[1,2-b]naphtho[1,2-e]pyran-12(13H)-one (4b). Yellow solid, mp 225–226°C. IR (KBr) ν: 3042, 1667, 1235, 1015 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.88–7.84 (m, 2H), 7.75 (t, J = 9.2 Hz, 1H), 7.51 (d, J = 8.8 Hz, 1H), 7.45–7.25 (m, 8H), 7.18 (d, J = 8.4 Hz, 2H), 5.63 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 192.3, 167.3, 149.0, 142.1, 136.7, 132.3, 132.2, 131.9, 131.6, 130.2, 129.9, 129.5, 128.7, 128.6, 127.3, 125.4, 124.2, 121.7, 118.4, 117.7, 116.0, 110.4, 35.1 ppm. MS (ESI): m/z 395 $[M + H]^+$. *Anal*. calcd for $C_{26}H_{15}ClO_2$: C, 79.09; H, 3.83. found: C, 79.29; H, 3.75.

13-(3-Nitrophenyl)-indeno[1,2-b]naphtho[1,2-e]pyran-12(13H)-one (4c). Yellow solid, mp 240–241°C. IR (KBr) ν: 3075, 1665, 1232, 1005 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 8.07 (s, 1H), 7.99 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.8 Hz, 1H), 7.89–7.87 (m, 1H), 7.79 (d, J = 7.6 Hz, 1H), 7.68 (d, J = 8.8 Hz, 1H), 7.55 (d, J = 9.2 Hz, 1H), 7.47–7.41 (m, 6H), 7.35–7.31 (m, 1H), 5.77 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 192.1, 167.7, 149.2, 148.5, 145.7, 136.5, 134.4, 132.5, 132.1, 132.0, 131.3, 130.5, 130.4, 129.4, 128.8, 127.5, 125.5, 125.5, 123.9, 123.0, 121.9, 118.7, 117.9, 115.0, 109.5, 35.6 ppm. MS (ESI): m/z 406 $[M + H]^+$. *Anal*. calcd for $C_{26}H_{15}NO_4$: C, 77.03; H, 3.73; N, 3.46. found: C, 76.85; H, 3.70; N, 3.58.

13-(2-Fluoro-5-(trifluoromethyl)phenyl)-indeno[1,2-b]naphtho[1,2-e]pyran-12(13H)-one (4d). Yellow solid, mp 216–217°C. IR (KBr) ν: 3042, 1659, 1230, 1007 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.91–7.81 (m, 3H), 7.54–7.32 (m, 9H), 7.17 (t, J = 8.8 Hz, 1H), 5.92 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.7, 168.1, 149.0, 136.6, 132.4, 132.1, 131.9, 131.8, 131.4, 130.5, 130.2, 128.7, 127.6, 127.3, 126.1, 125.5, 124.8, 123.1, 122.1, 121.8, 118.7, 117.8, 116.5, 116.2, 115.2, 109.1, 28.8 ppm. MS (ESI): m/z 447 $[M + H]^+$. *Anal*. calcd for $C_{27}H_{14}F_4O_2$: C, 72.65; H, 3.16. found: C, 72.48; H, 3.12.

13-(4-Methylphenyl)-indeno[1,2-b]naphtho[1,2-e]pyran-12(13H)-one (4e). Yellow solid, mp 192–193°C. IR (KBr) ν: 2980, 1675, 1237, 1010 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.88–7.82 (m, 3H), 7.50 (d, J = 9.2 Hz, 1H), 7.43–7.28 (m, 6H), 7.21 (d, J = 8.0 Hz, 2H), 7.02 (d, J = 8.0 Hz, 2H), 5.61 (s, 1H), 2.24 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 192.4, 167.2, 149.0, 140.8, 136.9, 136.1, 132.4, 132.2, 131.9, 130.0, 129.5, 129.2, 128.4, 128.0, 127.1, 125.2, 124.4, 121.6, 118.2, 117.7, 116.8, 111.2, 35.3, 21.0 ppm. MS (ESI): m/z 375 $[M + H]^+$. *Anal*. calcd for $C_{27}H_{18}O_2$: C, 86.61; H, 4.85. found: C, 86.49; H, 4.92.

13-(2,4-Dichlorophenyl)-indeno[1,2-b]naphtho[1,2-e]pyran-12(13H)-one (4f). Yellow solid, mp 252–253°C. IR (KBr) ν: 3052, 1677, 1232, 1025 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.89–7.81 (m, 3H), 7.51–7.41 (m, 7H), 7.35–7.31 (m, 1H), 7.02–6.97 (m, 2H), 6.01 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.6, 167.5, 148.8, 140.1, 136.7, 133.5, 132.9, 132.3, 132.2, 131.9, 131.7, 131.6, 130.4, 130.0,129.4, 128.6, 127.8, 127.5, 125.5, 123.8, 121.7, 118.5, 117.7, 116.5, 110.0, 32.4 ppm. MS (ESI): m/z 429 $[M + H]^+$. *Anal*. calcd for $C_{26}H_{14}Cl_2O_2$: C, 72.74; H, 3.29. found: C, 72.85; H,3.18.

13-(2-Chlorophenyl)-indeno[1,2-b]naphtho[1,2-e]pyran-12(13H)-one (4g). Yellow solid, mp 240–241°C. IR (KBr) ν: 3048, 1671, 1230, 1018 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.91–7.81 (m, 3H), 7.51–7.30 (m, 8H), 7.06–7.02 (m, 3H), 6.05 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.7, 167.4, 148.8, 136.8, 132.8, 132.3, 132.2, 131.9, 131.8, 130.8, 130.2, 129.8, 129.7, 128.5, 127.9, 127.4, 127.3, 125.3, 124.1, 121.6, 118.3, 117.7, 117.1, 32.7 ppm. MS (ESI): m/z 395 $[M + H]^+$. *Anal*. calcd for $C_{26}H_{15}ClO_2$: C, 79.09; H, 3.83. found: C, 79.25; H, 3.92.

13-(4-Methoxylphenyl)-indeno[1,2-b]naphtho[1,2-e]pyran-12(13H)-one (4h). Yellow solid, mp 225–226°C. IR (KBr) ν: 2945, 1676, 1232, 1004 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.87–7.82 (m, 3H), 7.49 (d, J = 9.2 Hz, 1H), 7.43–7.27 (m, 6H), 7.23 (d, J = 8.8 Hz, 2H), 6.75 (d, J = 8.8 Hz, 2H), 5.58 (s, 1H), 3.71(s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 192.5, 167.0, 158.1, 148.9, 136.9, 136.1, 132.4, 132.2, 131.9, 131.8, 130.0, 129.5, 129.1, 128.4, 127.1, 125.2, 124.4, 121.6, 118.2, 117.7, 116.8, 113.9, 111.2, 55.1, 34.8 ppm. MS (ESI): m/z 391 $[M + H]^+$. *Anal*. calcd for $C_{27}H_{18}O_3$: C, 83.06; H, 4.65. found: C, 82.96; H, 4.75.

13-(4-Fluorophenyl)-indeno[1,2-b]naphtho[1,2-e]pyran-12(13H)-one (4i). Yellow solid, mp 208–209°C. IR (KBr) ν: 3052, 1668, 1230, 1016 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.90–7.76 (m, 3H), 7.50 (d, J = 8.8 Hz, 1H), 7.43–7.28 (m, 8H), 6.91 (t, J = 8.4 Hz, 2H), 5.63 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 192.3, 167.2, 149.0, 139.4, 136.8, 132.3, 131.9, 131.7, 130.2, 129.8, 129.7, 129.6, 128.5, 127.2, 125.3, 124.3, 121.7, 118.3, 117.7, 116.3, 115.5, 115.3, 35.0 ppm. MS (ESI): m/z 379 $[M + H]^+$. *Anal*. calcd for $C_{26}H_{15}FO_2$: C, 82.53; H, 4.00. found: C, 82.44; H, 4.17.

13-(3,4-Dichlorophenyl)-indeno[1,2-b]naphtho[1,2-e]pyran-12(13H)-ones (4j). Yellow solid, mp 245–246°C. IR (KBr) ν: 3050, 16728, 1238, 1023 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.93–7.86 (m, 2H), 7.73–7.71 (m, 1H), 7.52 (d, J = 9.2 Hz, 1H), 7.48–7.22 (m, 9H), 5.61 (s, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ: 192.1, 167.5, 149.1, 143.8, 136.6, 132.6, 132.4, 132.2, 131.9, 131.5, 130.7, 130.4, 130.2, 130.0, 128.7, 127.6, 127.5, 125.5, 124.0, 121.8, 118.5, 117.8, 115.3, 35.0 ppm. MS (ESI): m/z 429 $[M + H]^+$. *Anal*. calcd for $C_{26}H_{14}Cl_2O_2$: C, 72.74; H, 3.29. found: C, 72.60; H,3.40.

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