Silica Chloride Catalysed One-pot 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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A simple and facile synthesis of 13-aryl-indeno[1,2-*b*]naphtha[1,2-*e*]pyran-12(13*H*)-ones has been accomplished by the one-pot condensation of β-naphthol, aldehydes, and 2*H*-indene-1,3-dione under solvent-free conditions in the presence of the heterogeneous catalyst silica chloride.

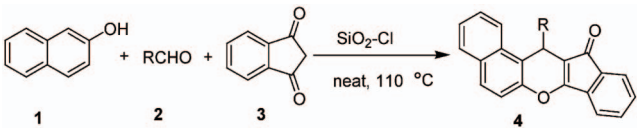
Keywords: Indeno[1,2-*b*]naphtho[1,2-*e*]pyran-12(13*H*)-one; Silica chloride; β-Naphthol; 2*H*-Indene-1,3-dione; Solvent-free.

INTRODUCTION

Natural compounds possessing naphthopyran moiety have been attracted by their antimicrobial,[1] antitumor,[2] antifungal,[3] cytotoxic,[4] antioxidative and 5-lipoxygenase inhibitory activity.[5] A variety of naphthopyran derivatives have been isolated and identified as natural phytochemicals.[6] A plethora of biological activities have also been associated with a large number of synthetic naphthofuran analogs.[7] 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,[8] antiallergenic,[9] antidepressant activities.[10]

Silica chloride (SiO_2-Cl), which was easily prepared from silica gel and thionyl chloride, is a good solid acid in terms of convenience, cheapness, easy production, and insolubility in all organic solvents. Due to its insolubility in organic solvents, excellent *in situ* proton generation, and accepting different nucleophiles, it can be used for different purposes in organic chemistry, like SiO_2-Cl catalyzed protection of carbonyl compounds,[11a] acetylation of alcohols,[11b] synthesis of 2-aminothiazoles,[11c] SiO_2-Cl as a starting material for the preparation of other silica bonded reagents.[11d] In this paper, we report a simple and efficient synthesis of 13-aryl-indeno[1,2-*b*]naphtho[1,2-*e*]pyran-12(13*H*)-ones, which may show potential pharmaceutical activities, under solvent-free conditions in the presence of SiO_2-Cl (see Scheme I).

Scheme I



RESULTS AND DISCUSSION

First, to optimize the amount of catalyst and the reaction temperature, the reaction of β-naphthol (1 mmol), benzaldehyde (1 mmol) and 2*H*-indene-1,3-dione (1 mmol) under thermal solvent-free conditions was selected as a model. The best result was obtained by carrying out the reaction using 150 mg/mmol SiO_2-Cl at 110 °C under solvent-free conditions.

Based on the optimized reaction conditions, a range of 13-aryl-indeno[1,2-*b*]naphtha[1,2-*e*]pyran-12(13*H*)-ones (**4**) was synthesized by the reaction of β-naphthol (**1**, 1 mmol), aldehyde (**2**, 1 mmol) and 2*H*-indene-1,3-dione (**3**, 1 mmol). The reaction proceeded at 110 °C within 2 hour in excellent yields after the addition of 150 mg/mol SiO_2-Cl (Table 2). The structures of the products were established from their spectral properties (^{1}H NMR, ^{13}C NMR and elemental analysis). All of the products **4** exhibited a singlet in ^{1}H spectra at δ = 5.58-6.05 ppm for H-13 and also a distinguishing peak at δ = 28.8-35.7 ppm for C-13 in the ^{13}C NMR spectra. The resonances of carbonyl groups in the ^{13}C NMR spectrum of **4** appeared at δ = 191.6-192.5 ppm. In

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Table 1. Optimization one-pot synthesis of 13-aryl-indeno[1,2-*b*]naphtha[1,2-*e*]pyran-12(13*H*)-ones[a]

Entry	SiO_2-Cl (mg/mmol)	Temp. (°C)	Time (h)	Yield (%)[b]
1	0	110	5	0
2	50	110	3	38
3	100	100	3	62
4	100	110	2	79
5	100	120	1.5	84
6	150	90	2	72
7	150	100	1.5	80
8	150	110	1.5	89
9	150	120	1.5	88
10	150	130	1.5	88
11	200	110	1.5	86
12	250	110	1	89

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

Table 2. Synthesis of 13-aryl-indeno[1,2-*b*]naphtha [1,2-*e*]pyran-12(13*H*)-ones using SiO_2-Cl as catalyst[a]

Entry	R	Time (h)	Product	Yield (%)[b]
1	C_6H_5	1.5	**4a**	89 (81, 75, 71)[c]
2	4-Cl-C_6H_4	1	**4b**	90
3	3-NO_2-C_6H_4	2	**4c**	80
4	2-F-5-CF_3-C_6H_3	2	**4d**	85
5	4-Me-C_6H_4	2	**4e**	87
6	2,4-Cl_2-C_6H_3	1	**4f**	89
7	2-Cl-C_6H_4	2	**4g**	84
8	4-MeO-C_6H_4	1.5	**4h**	92
9	4-F-C_6H_4	1	**4i**	91
10	3,4-Cl_2-C_6H_3	1	**4j**	91

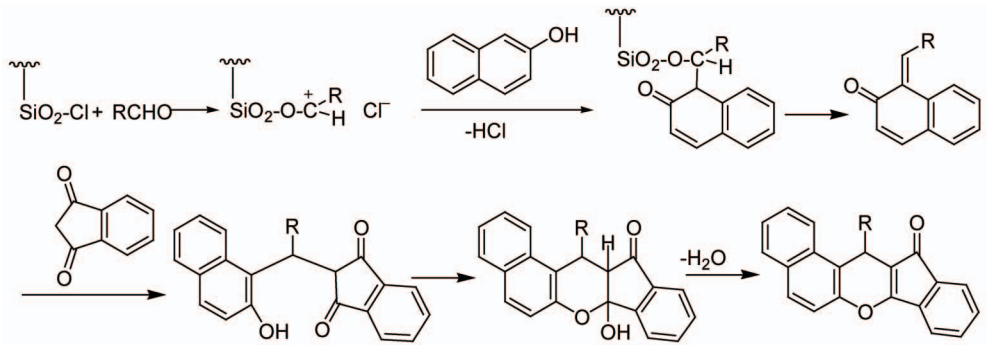
[a] Reaction conditions: β-naphthol (1 mmol); arylaldehydes (1 mmol); 2*H*-indene-1,3-dione (1 mmol); SiO_2-Cl (150 mg); solvent-free; 110 °C.
[b] Isolated yield after chromatographic purification.
[c] Yields after three times of catalyst recovery.

these experiments the catalyst was isolated by filtration and could be run up to three recycles without significant loss of activity (entry 1). 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 combination of starting materials and numerous products, the yield of the expected product was very poor.

This synthetic strategy enhanced the utilization efficiency of the modified silica chloride, decreases the production of chemical waste without using highly toxic reagent for the synthesis of 13-aryl-indeno[1,2-*b*]naphtha-[1,2-*e*]pyran-12(13*H*)-ones. The Si-Cl bond is labile and can give rise to Lewis acid centers on silica (see Scheme II). The Cl is easily displaced selectively by the oxygen atom of an aldehydes by a nucleophilic substitution reaction generating a cationic centre on the carbonyl carbon which is easily attacked by the nucleophilic 2-napthol to form an *ortho*-quinone methide intermediate. Subsequent Michael addition to the *ortho*-quinone methide with nucleophile and followed by addition of the phenolic hydroxyl moiety to the carbonyl of ketone provides cyclic hemiketal which on dehydration afforded **4**. 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 favoured. In simple phenolic compounds and 1-naphthol (which are weaker nucleophiles compared to 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.

In summary, an efficient methodoly for the synthesis of 13-aryl-indeno[1,2-*b*]naphtha[1,2-*e*]pyran-12(13*H*)-

Scheme II



ones has been developed. To our best knowledge, this is the first report for the synthesis of these compounds by multi-component condensation of β-naphthol, arylaldehydes, and 2*H*-indene-1,3-dione in the presence of SiO_2-Cl as a catalyst under solvent-free conditions. The simple experimental procedure, solvent-free reaction conditions, utilization of an inexpensive and readily available catalyst, short period of conversion and excellent yields are the advantages of the present method.

EXPERIMENTAL

NMR spectra were determined on Bruker AV-400 instrument at room temperature using TMS as internal standard, coupling constants (*J*) were measured in Hz; Elemental analysis were performed by a Vario-III elemental analyzer; Melting points were determined on a XT-4 binocular microscope and were uncorrected. Commercially available reagents were used throughout without further purification unless otherwise stated.

Preparation of SiO_2-Cl

To an oven-dried (120 °C, vacuum) sample of silica gel (10 g) in a round bottomed flask (250 mL) equipped with a condenser and a drying tube, was added thionyl chloride (40 mL) and the mixture was refluxed for 48 h. The unreacted thionyl chloride was distilled off. The resulting white-grayish powder was flame-dried and stored in a tightly capped bottle.

Typical Procedure: Preparation of 13-aryl-indeno[1,2-*b*]naphtha[1,2-*e*]pyran-12(13*H*)-one

To a mixture of β-naphthol (1 mmol), aldehyde (1 mmol), 2*H*-indene-1,3-dione, and SiO_2-Cl (150 mg) was added. The mixture was stirred at 110 °C for an appropriate time (see Table 1). After completion of the reaction (TLC), CH_2Cl_2 (20 mL) was added, and the solid catalyst was removed by filtration. The solvent was evaporated and the crude product were puried by silica gel column chromatography using CH_2Cl_2 as eluent.

13-Phenyl-indeno[1,2-*b*]naphtho[1,2-*e*]pyran-12(13*H*)-one (4a)

Yellow solid, mp 202-203 °C. ^{1}H 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* = 7.6 Hz, 2H), 7.12 (t, *J* = 7.4 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. 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(13*H*)-one (4b)

Yellow solid, mp 225-226 °C. ^{1}H 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. 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(13*H*)-one (4c)

Yellow solid, mp 240-241 °C. ^{1}H 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. 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(13*H*)-one (4d)

Yellow solid, mp 216-217 °C. ^{1}H 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. 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(13*H*)-one (4e)

Yellow solid, mp 192-193 °C. ^{1}H 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. Anal. calcd for $C_{27}H_{18}O_2$: C, 86.61; H,

4.85. found: C, 86.49; H, 7.92.

13-(2,4-Dichlorophenyl)-indeno[1,2-*b*]naphtho[1,2-*e*]-pyran-12(13*H*)-one (4f)

Yellow solid, mp 252-253 °C. ^{1}H 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. 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*]py-ran-12(13*H*)-ones (4g)

Yellow solid, mp 240-241 °C. ^{1}H 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. 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*]py-ran-12(13*H*)-one (4h)

Yellow solid, mp 225-226 °C. ^{1}H 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. 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(13*H*)-one (4i)

Yellow solid, mp 208-209 °C. ^{1}H 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 = 8.6 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. 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(13*H*)-one (4j)

Yellow solid, mp 245-246 °C. ^{1}H 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. 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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