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Gallium(III) chloride-catalyzed three-component coupling of naphthol, alkyne and aldehyde: a novel synthesis of 1,3-disubstituted-3*H*-benzo[*f*]chromenes

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ABSTRACT

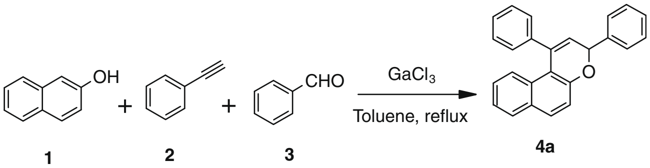
Three-component coupling of naphthol, alkyne and aldehyde has been achieved in the presence of 10 mol % gallium(III) chloride in toluene under reflux conditions to afford the corresponding 1,3-disubstituted-3*H*-benzo[*f*]chromenes in good yields. This is the first example on the preparation of chromenes from naphthol, alkyne and aldehyde.

There has been considerable interest in chromenes and their benzo-derivatives, not least because of their value for a variety of industrial, biological and chemical synthetic uses.[1] In particular, benzo[*f*]chromenes (naphthopyrans) are of special interest as photochromic compounds, which have a wide variety of applications such as ophthalmic glasses, electronic display systems, optical switches and temporary or permanent memories.[2] Consequently, there have been some reports on the preparation of benzo[*f*]chromenes.[3] Recently; there has been considerable interest in gallium-mediated transformations.[4] Owing to their unique catalytic properties, gallium halides have been widely used for a variety of organic transformations. In particular, gallium(III) compounds are considered as effective Lewis acids to activate alkynes under extremely mild conditions.[5] However, there have been no reports on the use of gallium(III) chloride for the synthesis of 1,3-disubstituted-3*H*-benzo[*f*]chromenes.

In this Letter, we report a novel protocol for the one-pot synthesis of 1,3-diaryl-3*H*-benzo[*f*]chromenes by means of coupling of naphthol, alkyne and aldehyde using a catalytic amount of $GaCl_3$.[6] Accordingly, we first attempted a three-component coupling (3CC) of 2-naphthol (**1**) with phenyl acetylene (**2**) and benzaldehyde (**3**) using 10 mol % $GaCl_3$ in toluene. The reaction proceeded at 110 °C in toluene and the desired product, 1,3-phenyl-3*H*-benzo[*f*]chromene **4a**, was obtained in 75% yield (Scheme 1).

This result provided incentive to extend this process for various substrates. Interestingly, a wide variety of aldehydes such as cyclohexanecarboxaldehyde, 1-octanal, 4-methoxy-benzaldehyde, 2-bromobenzaldehyde, cinnamaldehyde and citral underwent smooth coupling with 2-naphthol and phenyl acetylene under identical conditions (Table 1, entries **c**–**h**). Other alkynes such as 1-ethynyl-4-methylbenzene and 1-octyne also underwent coupling with naphthol and benzaldehyde to give the corresponding chromene derivatives in good yields (Table 1, entries **b**, **l** and **i**). Besides β-naphthol, α-naphthol and *p*-cresol also participated in the 3CC reaction (Table 1, entries **j**–**m**). The products were fully characterized by NMR, IR and mass spectroscopy. Both aromatic and aliphatic aldehydes were found to be equally effective for this conversion (Table 1).

In the absence of catalyst, no reaction was observed even after long reaction time (12 h) under reflux conditions. The effects of various metal halides such as $FeCl_3$, $BiCl_3$, $InCl_3$, $ZnCl_2$ and $CeCl_3{\cdot}7H_2O$ and metal triflates such as $In(OTf)_3$, $Bi(OTf)_3$, $Sc(OTf)_3$ and $Yb(OTf)_3$ were screened for this conversion. Surprisingly, none



Scheme 1.

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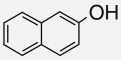
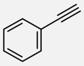
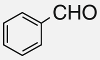
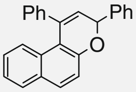
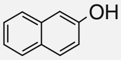
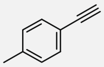
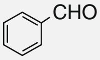
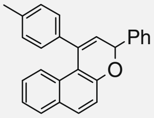
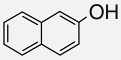
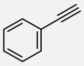
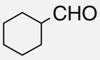
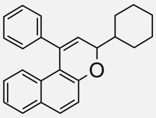
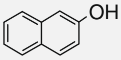
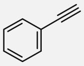
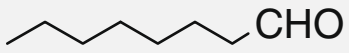
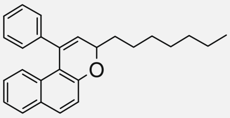
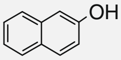
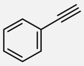
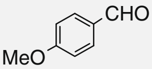
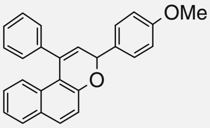
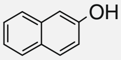
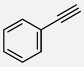
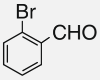
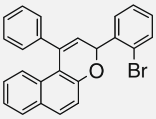
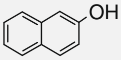
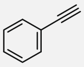
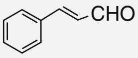
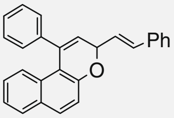
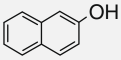
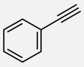
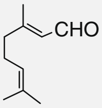
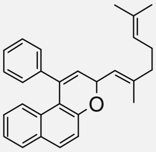
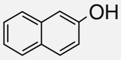
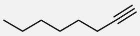
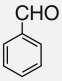
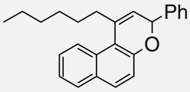
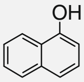
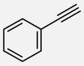
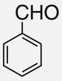
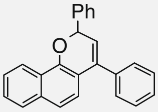
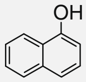
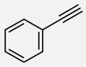
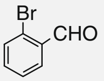
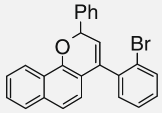
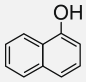
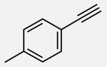
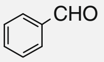
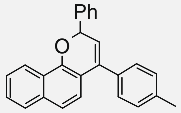
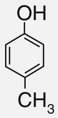
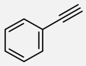
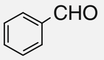
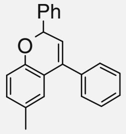
Table 1
Gallium(III) chloride-catalyzed three-component coupling of naphthol, alkyne and aldehyde

Entry	Naphthol/phenol	Alkyne	Aldehyde	Product[a]	Time (h)	Yield[b] (%)
a					2.0	75
b					2.0	72
c					2.5	75
d					2.5	70
e					2.5	69
f					3.0	76
g					2.0	68
h					2.0	70
i					3.0	68
j					2.0	72

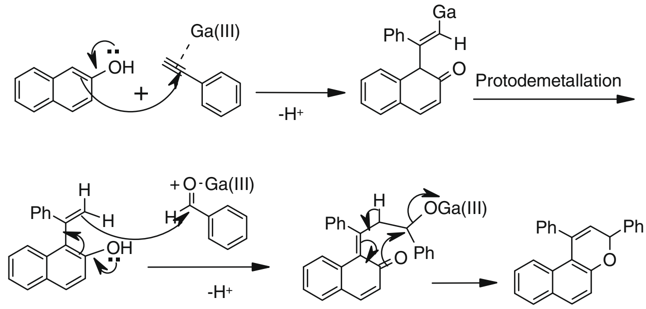
(*continued on next page*)

Table 1 (*continued*)

Entry	Naphthol/phenol	Alkyne	Aldehyde	Product[a]	Time (h)	Yield[b] (%)
k					2.0	72
l					2.0	70
m					4.0	65

[a] Products were characterized by NMR, IR and mass spectroscopy.

[b] Yield refers to pure products after column chromatography.



Scheme 2.

of these catalysts gave the desired product under the reaction conditions. The reaction was successful only with $GaCl_3$. Furthermore, Brønsted acids such as montmorillonite K10, heteropoly acid and ion-exchange resins also failed to produce the desired product. In the absence of aldehyde, only 1-(1-phenylvinyl)naphthalen-2-ol was obtained exclusively.[7] In the absence of 2-naphthol, α,β-unsaturated ketone was obtained from the reaction of alkyne with aldehyde under similar reaction conditions.[8] The reaction probably proceeds via arylation of alkyne to afford vinyl naphthalen-2-ol. This intermediate may subsequently undergo cyclization with aldehyde to give the desired chromene (Scheme 2).

Alternatively, in situ formed propargyl alcohol, from aldehyde and alkyne in presence of gallium(III) chloride may react with 2-naphthol to give the propargyl ether which may undergo Claisen rearrangement and a subsequent cyclization of the resulting quinonemethide would give the desired naphthopyran.[3a] Further studies addressing these issues are currently underway in our laboratory. The scope of this method is illustrated with respect to various aldehydes and alkynes and the results are presented in Table 1.[9] The effects of various solvents were examined in the three-component coupling of 2-naphthol, phenylacetylene and benzaldehyde and the results are presented in Table 2. As seen from Table 2, the reaction did not proceed in dichloromethane even at reflux temperature. Although, the reaction was successful in acetonitrile and 1,2-dichloroethane under reflux conditions, the desired product was obtained in low yields. Among these solvents, toluene gave the best conversions (Table 2).

Table 2
Effects of various solvents in the coupling of naphthol, phenylacetylene and benzaldehyde

Entry	Solvent	Time (h)	Catalyst (mol %)	Yield[a] (%)	Conversion[b] (%)
i	Toluene	9	5	75	80
			10	90	98
			20	90	98
ii	Benzene	9	5	72	80
			10	80	85
			20	80	85
iii	CH_3CN	19	5	40	50
			10	50	60
			20	55	60
iv	CH_2ClCH_2Cl	11	5	35	45
			10	45	50
			20	45	50
v	CH_2Cl_2	24	5	0	0
			10		
			20		

[a] Yield refers to pure product after column chromatography.

[b] Conversion refers to crude product determined by GC analysis.

In conclusion, we have developed a novel one-pot procedure for the preparation of 1,3-disubstituted-3*H*-benzo[*f*]chromenes from naphthol, alkyne and aldehyde using a catalytic amount of $GaCl_3$. It is entirely a new approach for the preparation of benzo[*f*]chromenes in a single-step operation. The products are potentially very useful precursors for the preparation of photochromic materials.

Acknowledgement

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References and notes

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9. *General procedure*: A mixture of β-napthol (1 mmol), phenyl acetylene (1.2 mmol), aldehyde (1 mmol) and $GaCl_3$ (0.1 mmol) was refluxed in toluene for the appropriate time (Table 1). After complete conversion as indicated by TLC, the reaction mixture was quenched with water (10 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting product was purified by column chromatography on silica gel (Merck, 100–200 mesh, ethyl acetate–hexane) to afford the pure product. Spectral data for selected products. *1,3-Diphenyl-3H-benzo[f]chromene* (**4a**): Liquid, IR (KBr): ν_{max} 3059, 3028, 2922, 2853, 1953, 1736, 1686, 1600, 1492, 1449, 1336, 1265, 1246, 1211, 1177, 1083, 1064, 1023, 805, 752, 698, 566, 487 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.99 (d, 1H, J = 8.3 Hz), 7.90 (d, 1H, J = 8.3 Hz), 7.63–7.35 (m, 8H), 7.31 (d, 2H, J = 9.8 Hz) 7.26–7.17 (m, 3H), 7.08 (d, 1H, J = 8.3 Hz) 6.04 (d, 1H, J = 1.5 Hz), 5.34 (d, 1H, J = 1.5 Hz) ppm; ^{13}C NMR (100 MHz, Proton decoupled $CDCl_3$): δ 154.1, 140.7, 138.9, 138.1, 135.1, 133.8, 132.9, 130.7, 129.8, 129.3, 128.5, 128.3, 127.8, 127.5, 127.0, 126.6, 125.3, 124.1, 123.4, 117.8, 75.6 ppm; ESIMS: *m/z* 335 $[M+H]^+$, 323, 391; HRMS calcd for $C_{25}H_{18}O$: 334.4173, found: 334.4171. *3-Cyclohexyl-1-phenyl-3H-benzo[f]-chromene* (**4c**): Liquid, IR (KBr): ν_{max} 2926, 2855, 1734, 1622, 1461, 1380, 1234, 1163, 1110, 813, 758, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.82 (d, 1H, J = 8.0 Hz), 7.70 (dd, 1H, J = 8.0, 1.4 Hz), 7.51–7.20 (m, 8H), 7.00 (d, 1H, J = 3.6 Hz), 5.62 (d, 1H, J = 5.8 Hz), 4.12 (dd, 1H, J = 2.9, 5.8 Hz), 1.81 (m, 1H), 1.58–1.18 (m, 10H) ppm; ^{13}CNMR (100 MHz, Proton decoupled $CDCl_3$): δ 152.5, 136.8, 134.4, 134.0, 132.7, 132.4, 131.7, 129.9, 127.8, 127.5, 127.0, 126.7, 126.7, 126.4, 126.2, 125.2, 122.2, 67.5, 38.9, 30.5, 30.2, 27.7 ppm; ESIMS: *m/z* 341 $[M+H]^+$, 342, 376; HRMS calcd for $C_{25}H_{24}O$: 340.4649; found: 340.4651. *3-(2-Bromophenyl)-1-phenyl-3H-benzo[f]chromene* (**4f**): Liquid, IR (KBr): ν_{max} 3056, 2854, 1696, 1623, 1589, 1511, 1463, 1438, 1334, 1225, 1090, 1025, 998, 861, 817, 751, 699, 629 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.90 (d, 1H, J = 3.6 Hz), 7.87 (d, 1H, J = 3.6 Hz), 7.75–7.53 (m, 5H), 7.47–7.31 (m, 4H), 7.29–7.20 (m, 2H), 7.11 (d, 1H, J = 10.2 Hz), 7.04 (t, 1H, J = 8.0 Hz), 5.96 (d, 1H, J = 3.6 Hz), 5.80 (d, 1H, J = 3.6 Hz) ppm; ^{13}C NMR (100 MHz, Proton decoupled $CDCl_3$): δ 154.2, 140.8, 139.0, 138.1, 135.2, 133.7, 132.9, 130.8, 130.4, 129.9, 129.4, 128.3, 127.8, 127.5, 127.4, 127.0, 126.6, 125.3, 124.1, 123.4, 122.1, 117.3, 75.4 ppm; ESIMS: *m/z* 435$[M+Na]^+$, 437, 452, 238; HRMS calcd for $C_{25}H_{17}BrNaO$: 435.3031; found: 436.3036.