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$Al(OTf)_3$-Catalyzed Preparation of 4-Hydroxy-3-propargylic Coumarins and Subsequent Regioselective Cyclization towards Furo- or Pyrano[3,2-*c*]coumarins

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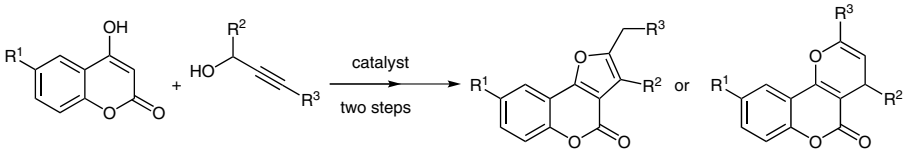

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Abstract An efficient and economical approach to functionalized furo[3,2-*c*]coumarin and pyrano[3,2-*c*]coumarin derivatives has been developed from 4-hydroxy-3-(prop-2-ynyl)coumarin derivatives through organocatalysis or metallo-organocatalysis. Selective '5-*exo*-dig' or '6-*endo*-dig' cyclization of the 4-hydroxy-3-(prop-2-ynyl)coumarin substrates could be achieved under organocatalytic {1,8-diazabicyclo[5.4.0]undec-7-ene} or metallo-organocatalytic (*N*-methylmorpholine/CuBr) conditions, respectively, to yield potentially bioactive heterocycles in excellent yields.

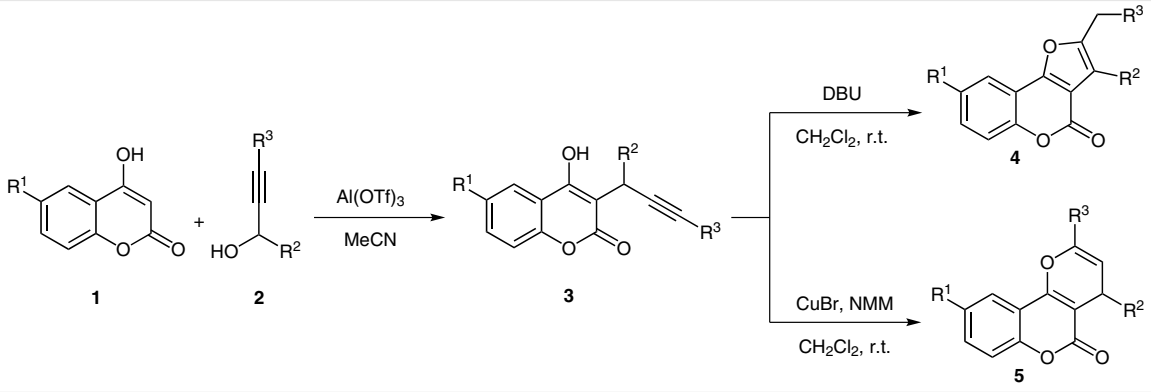
Key words furo[3,2-*c*]coumarin, pyrano[3,2-*c*]coumarin, $Al(OTf)_3$, DBU, NMM, propargylic alcohol

Carbon–carbon and carbon–heteroatom bond-forming reactions play a vital role in the efficacy of chemical transformations in synthetic organic chemistry. Due to selectivity, environmental friendliness, and mild reaction conditions, organocatalytic processes have achieved considerable attention as one of the main branches of enantioselective synthesis next to metal and biocatalysis. Small organic molecules can act as powerful organocatalysts to introduce multiple carbon–carbon or carbon–heteroatom bonds in a single operation.[1–8] More recently metallo-organocatalysts have been demonstrated to act as synthetic entities for dual activation of both the electrophilic and nucleophilic centers in reactions.[9–13] Dual activation is usually the combination of two separate catalysts in one system, that is, the combination of a metal catalyst and either a stoichiometric or catalytic amount of an organocatalyst. These two-component activation systems have been successfully employed in various reactions.[14–17]

Coumarins are important oxygen-containing fused heterocycles that display interesting biological activities.[18,19] In addition to their vital effects in plant biochemistry and physiology, these compounds can be used as drugs,[20] dyes, antioxidants, enzyme inhibitors,[21,22] and as precursors to lethal substances.[18,19] Coumarin derivatives also possess anti-inflammatory, antioxidant, antiallergic, hepatoprotective, antithrombotic, antiviral, and anticarcinogenic activities.[18,19] Furthermore they have found relevance as plant growth hormones, growth regulators, in control of respiration, photosynthesis, defense against infection, as well as additives to food and cosmetics and optical brightening agents.[18,19,23] The furan ring is a common structural motif in several important natural products, including furanoflavonoids, furanolactones, furanocoumarins, and many natural terpenoids. Furthermore, the chromane skeleton is found in numerous medicinally important compounds that have extensive biological activities.[24–30] Dihydropyranones, for example, occur widely as the key structural subunit in numerous natural products such as obolactone,[31,32] cyclocurcumin,[33,34] and have also been reported as a synthetic precursor for hypocholesteromic compounds.[35,36] Although there are several procedures available for the synthesis of coumarin-fused furan or pyran derivatives, the search for new methodologies proceeding via more efficient routes and involving readily available starting materials still remains an active area of research.

In 2006, Cardierno et al.[37] reported a catalytic system involving a 16-electron allyl-ruthenium(II) complex [Ru(η³-2-C_3H_4Me)(CO)(dppf)][SbF_6] [dppf = 1,1′-bis(diphenylphosphino)ferrocene] and trifluoroacetic acid (TFA) to promote coupling between activated secondary propargylic alcohols and cyclic 1,3-diketones for the synthesis of either pyran or furan structures. This one-pot protocol, however, involved the use of an expensive metal complex and corrosive acid. Furthermore, the ring size of the resulting products was found to be dependent on the nature of the dicarbonyl compound. Herein we report on the preparation 4-hydroxy-3-(prop-2-ynyl)coumarin derivatives **3** (Scheme 1) and the organocatalytic or metallo-organocatalytic cyclization of these compounds to either furo[3,2-*c*]coumarin or pyrano[3,2-*c*]coumarin derivatives **4** and **5**, respectively, as a result of '5-*exo*-dig' or '6-*endo*-dig' cyclization.

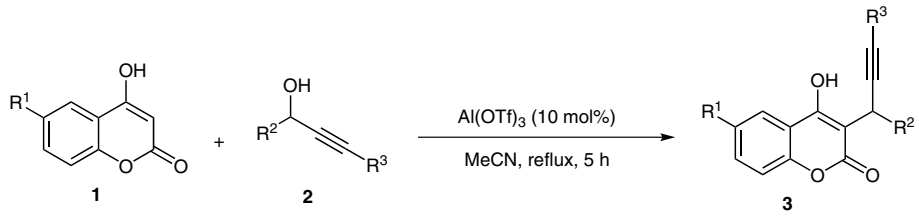
Recently, our group has reported the $Al(OTf)_3$-catalyzed alkylation of indoles using secondary/tertiary propargylic alcohols to produce 3-propargylated indoles in excellent yields and high selectivity.[38] The current investigation is a



Scheme 1 Synthesis of 4-hydroxy-3-(prop-2-ynyl)coumarin, furo[3,2-*c*]coumarin, and pyrano[3,2-*c*]coumarin derivatives **3**–**5**

continuation of this work, and the aforementioned protocol was extended to the preparation of 4-hydroxy-3-(prop-2-ynyl)coumarin derivatives **3** from propargylic alcohols **2** and 4-hydroxycoumarins **1**. Preliminary studies with 4-hydroxycoumarin **1a** and 1,3-diphenylprop-2-yn-1-ol (**2a**) established the optimized reaction conditions as refluxing MeCN for five hours in the presence of 10 mol% $Al(OTf)_3$. This protocol[43] was then applied to the preparation of a variety of 4-hydroxy-3-(prop-2-ynyl)coumarins (**3**, Table 1) producing comparable yields with both electron-donating (**1b**, Table 1, entry 13 vs. entry 2) and electron-withdrawing (**1c**, Table 1, entry 14 vs. entry 3) substituents in the 6-position of the coumarin moiety. Similarly, the reaction conditions were found tolerant towards electron-donating and electron-withdrawing phenyl substituents on the propargylic alcohol **2b**–**f** producing the substituted coumarins **3** in

Table 1 Synthesis of 4-Hydroxy-3-(prop-2-ynyl)coumarin Derivatives **3**[a]



Entry	Substrates	Substituents	Product	Yield (%)[b]
1	**1a**, **2a**	R^1 = H; R^2 = R^3 = Ph	**3a**	91
2	**1a**, **2b**	R^1 = H; R^2 = 4-MeC_6H_4; R^3 = Ph	**3b**	85
3	**1a**, **2c**	R^1 = H; R^2 = 4-$MeOC_6H_4$; R^3 = Ph	**3c**	91
4	**1a**, **2d**	R^1 = H; R^2 = 2-MeC_6H_4; R^3 = Ph	**3d**	90
5	**1a**, **2e**	R^1 = H; R^2 = 4-ClC_6H_4; R^3 = Ph	**3e**	87
6	**1a**, **2f**	R^1 = H; R^2 = 4-BrC_6H_4; R^3 = Ph	**3f**	88
7	**1a**, **2g**	R^1 = H; R^2 = Me; R^3 = Ph	**3g**	81
8	**1a**, **2h**	R^1 = R^2 = R^3 = H	**3h**	72
9	**1a**, **2i**	R^1 = H; R^2 = 2-SC_4H_4; R^3 = Ph	**3i**	75
10	**1a**, **2j**	R^1 = H; R^2 = 4-$MeOC_6H_4$; R^3 = *t*-Bu	**3j**	93
11	**1a**, **2k**	R^1 = H; R^2 = 4-ClC_6H_4; R^3 = *i*-Pr	**3k**	94
12	**1a**, **2l**	R^1 = H; R^2 = 4-MeC_6H_4; R^3 = C_5H_{11}	**3l**	96
13	**1b**, **2b**	R^1 = Me; R^2 = 4-MeC_6H_4; R^3 = Ph	**3m**	92
14	**1c**, **2c**	R^1 = Cl; R^2 = 4-$MeOC_6H_4$; R^3 = Ph	**3n**	89

[a] Reaction conditions: **1** (1 mmol), **2** (1.2 mmol), $Al(OTf)_3$ (0.1 mmol), MeCN (3 mL), reflux, 5 h.
[b] Isolated yield.

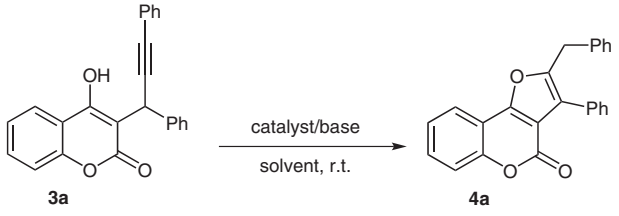
high to excellent yields (Table 1, entries 2–6). Aliphatic (**2g**) and heterocyclic (**2i**) 1-substituted propargylic alcohols could be coupled in high yields under the optimized conditions (Table 1, entries 7 and 9). Good to excellent yields were also obtained for propargylic alcohols **2h** ($R^2 = R^3 = H$; Table 1, entry 8) and **2j–l** (R^2 = aromatic, R^3 = aliphatic; Table 1, entries 10–12) demonstrating the wide scope of this protocol.

With the propargyl-substituted coumarin substrates **3** in hand, attention was turned towards producing the desired cyclic analogues. Reaction of substituted coumarin **3a** with a stoichiometric amount of *N*-methylmorpholine (NMM) in CH_2Cl_2 resulted in the exclusive formation of the '5-*exo*-dig' product, furo[3,2-*c*]coumarin **4a**, albeit in moderate yield (Table 2, entry 1). Reducing the NMM to catalytic quantities (10 mol%), however, led to a severe drop in yield to only 20% (Table 2, entry 2). When the NMM and CH_2Cl_2 were replaced with DBU (10 mol%), a base with profound importance in various organic transformations,[39–42] and acetonitrile as solvent, the furo[3,2-*c*]coumarin **4a** was obtained in 55% yield (Table 2, entry 3). The presence of DBU proved to be crucial in this result as reactions in the absence of the catalyst revealed no product formation at all (Table 2, entry 12).

Optimization of the reaction conditions revealed CH_2Cl_2 to be the solvent of choice (Table 2, entry 5) for the reaction with DBU as well and led to the yield being increased to 96%. While a decrease in DBU concentration from 10 mol% to 5 mol% resulted in diminished product yield (Table 2, entry 9), higher loadings (20 mol%) gave comparable results (Table 2, entry 8). Although a decrease in reaction time from four to three hours had a detrimental effect on product yield (Table 2, entry 10), an increase in reaction time exhibited no improvement (Table 2, entry 11). Optimized conditions for the cyclization reaction were thus established as 10 mol% DBU in CH_2Cl_2 for four hours at room temperature (Table 2, entry 5).[43]

The optimum conditions were subsequently applied to the cyclization of the remaining propargyl-substituted coumarin substrates (Table 3). The substrates containing diaryl substituted propargylic units, (**3a**–**e**,**m**,**n**) including thiophene **3i**, all gave excellent yields of their respective furo[*2,3-c*]coumarin derivatives. The substrate with a 2-methylphenyl unit in the 1-position of the propargyl moiety (**3d**, Table 3, entry 4), however, did not lead to any observable product, probably due to steric interference by the 2-methyl group as the 4-methyl analogue (**3b**, Table 3, entry 2) gave the product **4b** in excellent yield (96%). The reac-

Table 2 Optimization of DBU-Catalyzed Cyclization Reaction Conditions[a]

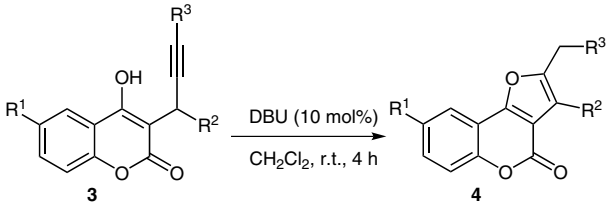


3a **4a**

Entry	Catalyst/base (mol%)	Solvent	Time (h)	Yield (%)[b]
1	NMM (100)	CH_2Cl_2	4	72
2	NMM (10)	CH_2Cl_2	4	20
3	DBU (10)	MeCN	4	55
4	DBU (20)	MeCN	4	55
5	DBU (10)	CH_2Cl_2	4	96
6	DBU (10)	THF	4	41
7	DBU (10)	MeOH	4	55
8	DBU (20)	CH_2Cl_2	4	96
9	DBU (5)	CH_2Cl_2	4	82
10	DBU (10)	CH_2Cl_2	3	78
11	DBU (10)	CH_2Cl_2	6	96
12	–	MeCN	10	0

[a] Reaction conditions: **3a** (1 mmol), catalyst/base, solvent (2 mL), r.t.
[b] Isolated yield.

Table 3 Synthesis of Furo[3,2-*c*]coumarin Derivatives **4**[a]



3 **4**

Entry	Substrate	Substituents	Product	Yield (%)[b]
1	**3a**	$R^1 = H$; $R^2 = R^3 = Ph$	**4a**	96
2	**3b**	$R^1 = H$; $R^2 = 4\text{-}MeC_6H_4$; $R^3 = Ph$	**4b**	96
3	**3c**	$R^1 = H$; $R^2 = 4\text{-}MeOC_6H_4$; $R^3 = Ph$	**4c**	95
4	**3d**	$R^1 = H$; $R^2 = 2\text{-}MeC_6H_4$; $R^3 = Ph$	**4d**	0
5	**3e**	$R^1 = H$; $R^2 = 4\text{-}ClC_6H_4$; $R^3 = Ph$	**4e**	94
6	**3f**	$R^1 = H$; $R^2 = 4\text{-}BrC_6H_4$; $R^3 = Ph$	**4f**	98
7	**3g**	$R^1 = H$; $R^2 = Me$; $R^3 = Ph$	**4g**	0
8	**3h**	$R^1 = H$; $R^2 = R^3 = H$	**4h**	0
9	**3i**	$R^1 = H$; $R^2 = 2\text{-}SC_4H_4$; $R^3 = Ph$	**4i**	97
10	**3j**	$R^1 = H$; $R^2 = 4\text{-}MeOC_6H_4$; $R^3 = t\text{-}Bu$	**4j**	0
11	**3k**	$R^1 = H$; $R^2 = 4\text{-}ClC_6H_4$; $R^3 = i\text{-}Pr$	**4k**	0
12	**3l**	$R^1 = H$; $R^2 = 4\text{-}MeC_6H_4$; $R^3 = C_5H_{11}$	**4l**	0
13	**3m**	$R^1 = Me$; $R^2 = 4\text{-}MeC_6H_4$; $R^3 = Ph$	**4m**	94
14	**3n**	$R^1 = Cl$; $R^2 = 4\text{-}MeOC_6H_4$; $R^3 = Ph$	**4n**	91

[a] Reaction conditions: **3** (1 mmol), DBU (0.1 mmol), CH_2Cl_2 (2 mL), r.t., 4 h.
[b] Isolated yield.

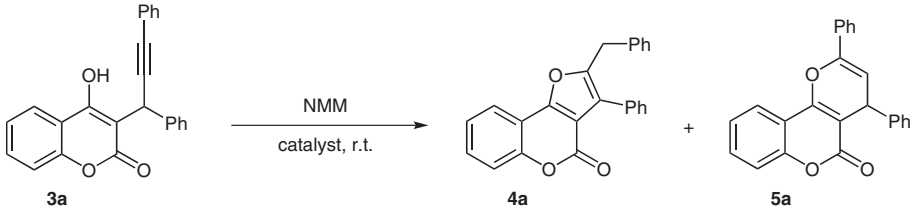
tion was also unsuccessful for substrates containing only hydrogen (**3h**, Table 3, entry 8) or alkyl substituents (**3g**,**3j**–**l**) attached to the propargyl unit (R^2 and/or R^3 = H or alkyl, Table 3, entries 7, 10–12).

In an effort to shift the cyclization mode to '6-*endo*-dig' and pyrano[3,2-*c*]coumarin formation, the cyclization of the substituted coumarin **3a** was repeated with NMM in the presence of CuBr and the desired product (**5a**) obtained in 91% yield (Table 4, entry 1).[43] Consequently, CuI (Table 4, entry 2) and $Cu(OTf)_2$ (Table 4, entry 3) were also evaluated with **3a** as model substrate but CuBr produced the highest conversion and selectivity toward **5a**. The reaction time was then shortened to three hours (Table 4, entry 4) which yielded results similar to those of the four-hour reaction. A further shortening of the reaction time to two hours (Table 4, entry 5) had a detrimental effect on product yield (71%) as conversion was significantly lower. Different CuBr loadings were next investigated, of which 20 mol% (Table 4, entry 6) exhibited no improvement over 10 mol% (Table 4, entry 4). A significant loss in regioselectivity was, however, observed upon lowering of the CuBr loading to 5 mol% (Table 4, entry 7). Other polar solvents, that is, MeCN and MeOH, were also tested, but gave inferior results with respect to conversion (Table 4, entries 8 and 9).

The scope of this protocol was investigated by subjecting the previously prepared propargyl-substituted coumarins **3** to the optimized conditions (Table 5). Similarly to the DBU system, excellent yields were obtained when both R^2 and R^3 were aromatic groups (Table 5, entries 1–6) and R^2 being heterocyclic (Table 5, entry 9). In contrast to the DBU system, a 4-methyl substituent on R^3 did not prevent cyclization (Table 5, entry 5). Furthermore, all of the aliphatic-substituted propargylic derivatives (Table 5, entry 7, entries 10–12) were readily converted into their respective pyrano[3,2-*c*]coumarins **5g**,**j**–**l**. Similarly to the DBU system, no product formation could be observed in the absence of any R^2 and R^3 substituents (**3h**, Table 5, entry 8). The presence of either an electron-donating (**3m**) or electron-withdrawing group (**3n**) in the 9-position of the coumarin skeleton did not reflect any significant influence on the outcome of the reaction (Table 5, entries 13 and 14).

The formation of the furo[3,2-*c*]coumarin and pyrano[3,2-*c*]coumarin derivatives **4** and **5** is probably explicable in terms of two mechanistic routes (Scheme 2). In the presence of DBU, compound **3** undergoes '5-*exo*-dig' mode of cyclization to give the intermediate **A** that undergoes isomerization of the olefinic double bond to introduce the aromatic system in the furan moiety of **4**. In the presence of the Lewis acidic copper salt, the alkyne may be activated by π-complex formation (intermediate **B**) that then undergoes '6-*endo*-dig' cyclization to produce **5**. This hypothesis was confirmed by introducing 1 mol% CuBr along with 10 mol% DBU which produced both the furo[3,2-*c*]coumarin and pyrano[3,2-*c*]coumarin derivatives **4** and **5**. Upon removal of the DBU, in presence of only CuBr, the reaction was found to be slow requiring extended reaction times to reach completion. In the presence of NMM, however, the reaction times were reduced to only three hours.

Table 4 Optimization of Metallo-Organocatalyst-Mediated Cyclization Reaction Conditions[a]

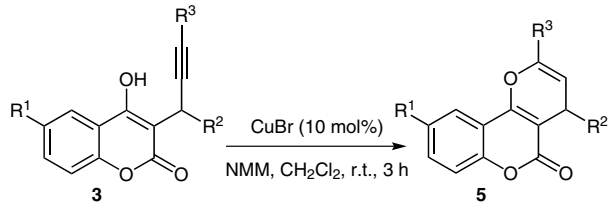


3a **4a** **5a**

Entry	Catalyst (mol%)	Solvent	Time (h)	Yield of **4a**/**5a** (%)[b]
1	CuBr (10)	CH_2Cl_2	4	5:91
2	CuI (10)	CH_2Cl_2	4	5:86
3	$Cu(OTf)_2$ (10)	CH_2Cl_2	4	7:84
4	CuBr (10)	CH_2Cl_2	3	5:91
5	CuBr (10)	CH_2Cl_2	2	3:71
6	CuBr (20)	CH_2Cl_2	3	5:91
7	CuBr (5)	CH_2Cl_2	3	19:63
8	CuBr (10)	MeCN	3	3:56
9	CuBr (10)	MeOH	3	2:52

[a] Reaction conditions: **3a** (1 mmol), NMM (1 mmol), catalyst, solvent (2 mL), r.t.
[b] Isolated yield.

Table 5 Synthesis of Pyrano[3,2-*c*]coumarin Derivatives **5**[a]



Entry	Substrate	Substituents	Product	Yield (%)[b]
1	**3a**	R^1 = H; R^2 = R^3 = Ph	**5a**	91
2	**3b**	R^1 = H; R^2 = 4-MeC_6H_4; R^3 = Ph	**5b**	92
3	**3c**	R^1 = H; R^2 = 4-MeOC_6H_4; R^3 = Ph	**5c**	90
4	**3d**	R^1 = H; R^2 = 2-MeC_6H_4; R^3 = Ph	**5d**	88
5	**3e**	R^1 = H; R^2 = 4-ClC_6H_4; R^3 = Ph	**5e**	89
6	**3f**	R^1 = H; R^2 = 4-BrC_6H_4; R^3 = Ph	**5f**	81
7	**3g**	R^1 = H; R^2 = Me; R^3 = Ph	**5g**	76
8	**3h**	R^1 = H; R^2 = R^3 = H	**5h**	0
9	**3i**	R^1 = H; R^2 = 2-SC_4H_4; R^3 = Ph	**5i**	90
10	**3j**	R^1 = H; R^2 = 4-MeOC_6H_4; R^3 = *t*-Bu	**5j**	94
11	**3k**	R^1 = H; R^2 = 4-ClC_6H_4; R^3 = *i*-Pr	**5k**	94
12	**3l**	R^1 = H; R^2 = 4-MeC_6H_4; R^3 = C_5H_{11}	**5l**	92
13	**3m**	R^1 = Me; R^2 = 4-MeC_6H_4; R^3 = Ph	**5m**	93
14	**3n**	R^1 = Cl; R^2 = 4-MeOC_6H_4; R^3 = Ph	**5n**	88

[a] Reaction conditions: **3** (1 mmol), CuBr (0.1 mmol), NMM (1 mmol), CH_2Cl_2 (2 mL), r.t., 3 h.
[b] Isolated yield.

In conclusion, practical strategies have been developed to access potentially bioactive furo[3,2-*c*]coumarin or pyrano[3,2-*c*]coumarin derivatives **4** and **5** in high yield via organocatalytic (DBU) or metallo-organocatalytic (CuBr/NMM) cyclization of 4-hydroxy-3-(prop-2-ynyl)coumarins **3**. The latter is readily accessible through $Al(OTf)_3$-catalyzed substitution of propargylic alcohols **2** with 4-hydroxycoumarins **1**. The protocols reported herein are quick and simple to perform and utilize readily available, cost-effective materials that are converted into the desired products in high to excellent yields. As a result of affordability and operational simplicity these methods can thus be applied toward the synthesis of a large number of naturally occurring and pharmaceutically important compounds.

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0034-1379971.

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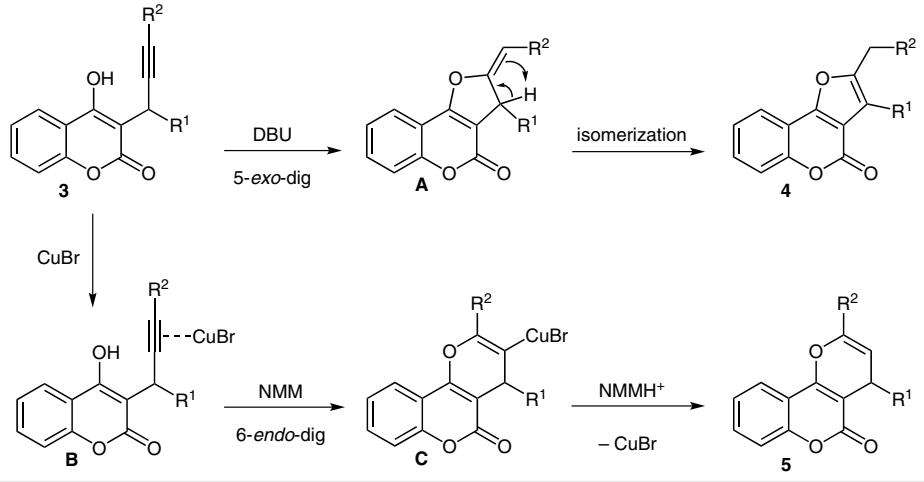

Scheme 2 Proposed pathway for the cyclization of 4-hydroxy-3-(prop-2-ynyl)coumarin to furo[3,2-*c*]coumarin and pyrano[3,2-*c*]coumarin derivatives **3** to **4** and **5**

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(43) **Typical Procedures**

4-Hydroxy-3-(prop-2-ynyl)coumarins 3a–n

Substituted 4-hydroxycoumarin derivatives (1 mmol) were dissolved in MeCN (3 mL), and the solution was stirred at r.t. for 5 min before the substituted propargyl alcohol (1.2 mmol) was added and stirring continued for an additional 5 min. After subsequent addition of $Al(OTf)_3$ (0.1 mmol) the mixture was heated to reflux for 5 h. Upon completion of the reaction (TLC) the solvent was removed in vacuo, H_2O was added (25 mL), and the crude product was extracted into CH_2Cl_2 (3 × 25 mL). The organic phases were combined, washed with brine (4 × 25 mL), and dried over anhydrous Na_2SO_4. After filtration and removal of the solvent, the pure products **3** were obtained by column chromatography (hexane–EtOAc, 4:1).

Furo[3,2-*c*]coumarins 4a–n

To a stirring solution of compound **3** (1 mmol) in CH_2Cl_2 (2 mL) was added DBU (0.1 mmol), and the mixture was stirred for 4 h. Upon completion of the reaction (TLC) H_2O (25 mL) was added, and the product was extracted into CH_2Cl_2 (3 × 25 mL). The combined organic phases were washed with brine (4 × 25 mL), and dried over anhydrous Na_2SO_4. After filtration, the solvent was removed by distillation and the crude product purified by column chromatography (hexane–EtOAc, 6:1).

Pyrano-[3,2-*c*]coumarins 5a–n

To a stirred solution of 4-hydroxy-3-(prop-2-ynyl)coumarin **3** (1 mmol) in CH_2Cl_2 (2 mL) at r.t. were added NMM (1 mmol) and CuBr (0.1 mmol), and stirring was continued for 4 h. Upon completion of the reaction (TLC) the mixture was filtered to remove excess solid CuBr, H_2O (25 mL) was added, and the product was extracted into CH_2Cl_2 (3 × 25 mL). The combined organic phases were washed with brine (4 × 25 mL), and dried over anhydrous Na_2SO_4. Filtration of the extract and removal of the solvent by distillation followed by column chromatography (hexane–EtOAc, 5:1) gave the desired product **5**.

Representative Analytical Data

4-Hydroxy-3-(prop-2-ynyl)-coumarin (3m)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.25 (s, 3 H), 2.31 (s, 3 H), 5.67 (s, 1 H), 7.10 (m, 3 H), 7.24–7.29 (m, 4 H), 7.41–7.44 (m, 4 H), 7.56 (br d, 1 H, *J* = 2.3 Hz), 8.25 (s, 1 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.9, 21.1, 33.0, 86.8, 87.6, 105.0, 115.6, 116.3, 121.5, 123.1, 127.0, 128.5, 129.1, 129.7, 131.8, 133.4, 133.8, 135.6, 137.5, 150.8, 161.1, 162.8. ESI-HRMS: *m/z* calcd for $C_{26}H_{20}O_3$ [M + Na]$^+$: 403.1310; found: 403.1320.

Furo[3,2-*c*]coumarin (4m)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.32 (s, 3 H), 2.35 (s, 3 H), 4.08 (s, 2 H), 7.15–7.25 (m, 9 H), 7.34 (d, 2 H, *J* = 9.0 Hz), 7.55 (m, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.9, 21.4, 32.5, 109.5, 112.5, 116.9, 120.6, 121.8, 126.8, 127.6, 128.4, 128.8, 129.1, 129.7, 131.5, 134.1, 137.4, 137.9, 150.7, 152.7, 157.0, 158.0. ESI-HRMS: *m/z* calcd for $C_{26}H_{20}O_3$ [M + Na]$^+$: 403.1310; found: 403.1324.

Pyrano[3,2-*c*]coumarin (5m)

Mp 172–174 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.25 (s, 3 H), 2.43 (s, 3 H), 5.19 (s, 1 H), 5.62 (s, 1 H), 7.09 (d, 2 H, *J* = 6.0 Hz), 7.13–7.22 (m, 3 H), 7.22 (d, 1 H, *J* = 6.0 Hz), 7.28–7.38 (m, 3 H), 7.52–7.58 (m, 3 H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.0, 21.2, 49.8, 106.5, 107.6, 111.3, 117.0, 122.3, 127.1, 127.8, 128.5, 128.6, 129.7, 134.0, 134.1, 134.2, 136.8, 137.5, 153.5, 158.0, 158.8, 164.2. ESI-HRMS: *m/z* calcd for $C_{26}H_{20}O_3$ [M + Na]$^+$: 403.1310; found: 403.1319.