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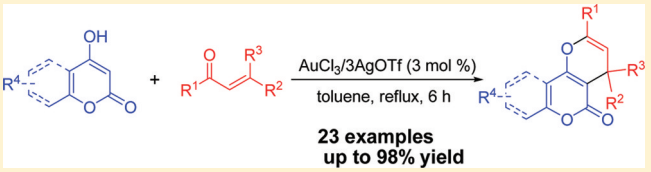
Gold(III)-Catalyzed Tandem Conjugate Addition/Annulation of 4-Hydroxycoumarins with α,β-Unsaturated Ketones

Yunkui Liu,* Jie Zhu, Jianqiang Qian, Bo Jiang, and Zhenyuan Xu

State Key Laboratory Breeding Base of Green Chemistry-Synthesis Technology, Zhejiang University of Technology, Hangzhou 310014, People's Republic of China

Supporting Information

ABSTRACT: An efficient and selective approach for the synthesis of functionalized pyranocoumarins has been developed via a gold(III)-catalyzed tandem conjugate addition/annulation reaction of 4-hydroxycoumarins with α,β-unsaturated ketones.



Pyranocoumarins are an important class of heterocycles of wide occurrence in natural products as well as synthetic molecules, exhibiting a broad spectrum of biological activities such as antifungal, insecticidal, anticancer, anti-HIV, anti-inflammatory, and antibacterial activities.[1] The pyranocoumarins have several scaffold patterns according to different structural arrays between the pyran[2] and the coumarin[3] rings (Figure 1), among which the pyrano[3,2-*c*]coumarins are the most synthetically feasible.[4]

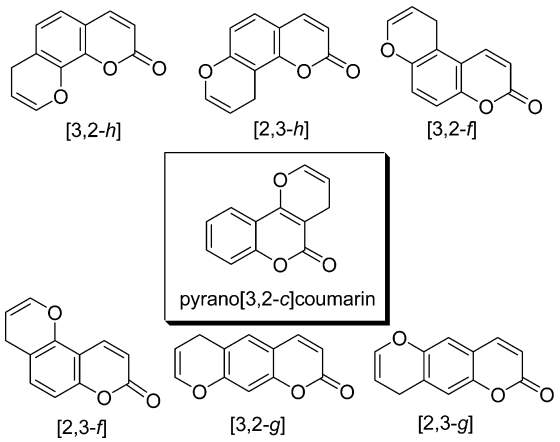


Figure 1. Different scaffold patterns of pyranocoumarins.

The general approaches to pyrano[3,2-*c*]coumarins involve cyclization of commercially available 4-hydroxycoumarins with the proper electrophiles.[4a−j] For example, pyrano[3,2-*c*]-coumarins could be synthesized via a one-pot reaction of 4-hydroxycoumarins with propargylic alcohols catalyzed by either an I_2/H_2SO_4 system[4a] or a ruthenium complex.[4b] Unsatisfyingly, this protocol suffered from the use of H_2SO_4 as a catalyst[4a] or a regioselectivity problem.[4b] He et al. reported a mild synthesis of pyrano[3,2-*c*]coumarins involving DDQ-mediated oxidative cross-coupling of 4-hydroxycoumarins with 1,3-diarylallylic compounds.[4c] However, the reaction required a stoichiometric amount of DDQ and resulted in poor regioselectivity. The reaction of 4-hydroxycoumarins with α,β-unsaturated aldehydes[4d] or ketones[4e] could also give functionalized pyrano[3,2-*c*]coumarins, but the former suffered from a regioselectivity issue, while the latter used the toxic reagent $POCl_3$. Renaud[4f] and co-workers have reported a highly regioselective synthesis of pyrano[3,2-*c*]coumarins from 4-hydroxycoumarins and α,β-unsaturated aldehydes, but the requirement of a commercially unavailable acid catalyst was a drawback. Thiol-mediated cyclization of coumarin-4-yl prop-2-ynyl ethers provided an alternative approach to the pyrano[3,2-*c*]coumarin derivatives,[4k] but the scope of the substrates was limited. As such, it is still desirable to develop efficient and selective protocols with broad substrate scope for the synthesis of pyranocoumarins.

On the other hand, tandem reactions[5] usually provide processes more efficient and environmentally benign than conventional procedures by omitting the steps of separation and purification of the reaction intermediates, thus enabling the construction of molecular diversity and structural complexity from simple substrates in a single synthetic step. Owing to the extraordinary reactivity and high selectivity of gold catalysts,[6] gold-catalyzed tandem reactions have recently received great attention and have become powerful tools for the construction of C−C and C−X bonds.[6] In this regard, we are particularly interested in the construction of heterocyclic systems involving gold-catalyzed tandem reactions with high selectivity.[7,8] For example, in our previous work, we have successfully developed efficient and selective methods for the construction of benzofuran,[8a] benzopyran,[8b] and 3,4-dihydrocoumarin[8c] frameworks via the strategy of gold-catalyzed tandem reactions. Herein, we describe an efficient and selective approach to access functionalized pyrano[3,2-*c*]coumarins involving a

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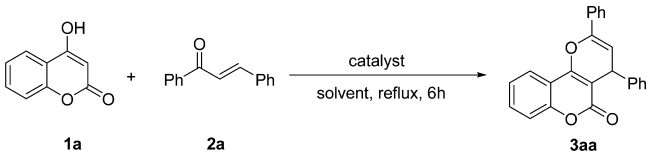
gold(III)-catalyzed tandem conjugate addition/annulation reaction of 4-hydroxycoumarins with α,β-unsaturated ketones.

For the initial study, 4-hydroxycoumarin **1a** and chalcone **2a** were selected as the model substrates to optimize the reaction conditions (Table 1). When **1a** and **2a** were treated with AuCl/AgOTf (3 mol % based on **1a**) in toluene at reflux for 6 h, the desired product **3aa** was isolated in 65% yield (entry 1, Table 1). When the PPh_3AuCl/AgOTf catalytic system was used, the yield of **3aa** was reduced to 23% (entry 2, Table 1). Satisfyingly, the yield of **3aa** was increased to 78% in the presence of the $AuCl_3$/3AgOTf catalytic system (entry 5, Table 1). Solvent screening showed that toluene was much more suitable than other solvents, such as DCE, CH_3CN, dioxane, and THF (entry 5, Table 1). Control experiments showed that no desired product was detected without a catalyst (entry 27, Table 1) or in the presence of AuCl (entry 10, Table 1) or Ph_3PAuCl (entry 11, Table 1) alone. The reaction also gave none of the desired product when the square-planar complex dichloro(pyridine-2-carboxylato)gold(III) (**4**)[9] was employed as a catalyst in the presence or absence of AgOTf (entries 7–9, Table 1). When $AuCl_3$ or AgOTf was used alone as a catalyst, the yield of **3aa** only reached 37% and 41%, respectively, a sharp contrast to the high catalytic efficiency of the combined $AuCl_3$/3AgOTf system (entries 5, 6, and 12, Table 1). The role of AgOTf in the combined $AuCl_3$/3AgOTf system is believed to help the generation of the cationic gold(III) species with OTf as the counteranion, which thus can efficiently catalyze the reaction.[10,11] Further studies revealed that the catalyst systems $AuCl_3$/AgOTf, $AuCl_3$/2AgOTf, $AuCl_3$/3AgSbF$_6$, $AuCl_3$/3AgBF$_4$, and $AuCl_3$/3AgNTf$_2$ gave poor results for the reaction (entries 3, 4, and 13–15, Table 1). Moreover, when conventional Lewis or Brønsted acids such as $ZnCl_2$, $BiCl_3$, $FeCl_3$, $FeBr_3$/3AgOTf,[10] $AlCl_3$, HCl, and HOTf were surveyed as catalysts for the reaction, the results showed far less effectiveness even at a catalyst loading of 30 mol % (entries 16–26, Table 1), indicating that cationic gold(III) species generated from the $AuCl_3$/3AgOTf catalytic system played a unique role in achieving high reactivity and selectivity for the tandem reaction.[11]

Table 1. Optimization of Reaction Conditions[a]



1a **2a** **3aa**

entry	catalyst (3 mol %)	solvent	yield of **3aa** (%)[b]
1	AuCl/AgOTf	toluene	65
2	PPh_3AuCl/AgOTf	toluene	23
3	$AuCl_3$/AgOTf	toluene	38
4	$AuCl_3$/2AgOTf	toluene	45
5	**$AuCl_3$/3AgOTf**	**toluene**	**78**
		DCE	60
		THF	5
		MeCN	57
		dioxane	62
6	$AuCl_3$	toluene	37
7	**4**[c]	toluene	0
8	**4**/AgOTf	toluene	0
9	**4**/2AgOTf	toluene	0
10	AuCl	toluene	0
11	PPh_3AuCl	toluene	0
12	AgOTf[d]	toluene	41
13	$AuCl_3$/3AgSbF$_6$	toluene	27
14	$AuCl_3$/3AgBF$_4$	toluene	21
15	$AuCl_3$/3AgNTf$_2$	toluene	45
16	$ZnCl_2$[e]	toluene	16
17	$BiCl_3$[e]	toluene	15
18	$FeCl_3$[e]	toluene	0
19	$FeCl_3$[e]/AgOTf	toluene	5
20	$FeCl_3$[e]/2AgOTf	toluene	10
21	$FeCl_3$[e]/3AgOTf	toluene	25
22	$FeBr_3$[e]	toluene	0
23	$FeBr_3$[e]/3AgOTf	toluene	10
24	$AlCl_3$[e]	toluene	0
25	HCl[e,f]	toluene	0
26	HOTf[e]	toluene	0
27	none	toluene	0[g]

[a]Carried out with 1 mmol of **1a** and 1 mmol of **2a** in the presence of catalyst in solvent (3 mL) at reflux for 6 h. [b]Isolated yields. [c]**4**: dichloro(pyridine-2-carboxylato)gold(III). [d]The amount of catalyst is 0.09 mmol. [e]The amount of catalyst is 0.3 mmol. [f]Aqueous HCl (37 wt %) was used. [g]**1a** and **2a** were recovered quantitatively.

With optimized conditions in hand, we then turned our attention to the scope of the reaction, and the results are shown in Table 2. First, a variety of α,β-unsaturated ketones **2** reacted with 4-hydroxycoumarin (**1a**) under the optimized reaction conditions. In most cases, **2** reacted with **1a** smoothly to give the corresponding products **3** in moderate to excellent yields (45–91%, entries 1–10, Table 2). It seemed that substrates bearing electron-deficient aromatic rings at the 4-position of **2** (entries 4, 7, and 8, Table 2) gave higher yields of **3** than did those bearing electron-rich aromatic rings (entries 1, 2, 5, and 6, Table 2). It was found that **2** with electron-deficient aromatic rings in the 2-position gave better yields of **3** than those with electron-rich ones (entry 6 vs 5 and 7 vs 8, Table 2). The more sterically hindered ketone **2i** also reacted with **1a** smoothly to furnish the target product in 78% yield (entry 9, Table 2). When the α,β-unsaturated aldehyde **2k** was treated with **1a** under the same conditions, the reaction resulted in a complex mixture which could not be separated by column chromatography (entry 11, Table 2).

Several substituted 4-hydroxycoumarins **1b–e** reacted with α,β-unsaturated ketones **2** (Table 3). It was found that **1** bearing electron-donating substituents at the 6-position generally reacted with **2** more smoothly and gave higher yields of **3** than those bearing electron-withdrawing groups (entries 1–6 vs 7, Table 3). 4-Hydroxy-6-methyl-2-pyrone (**5**), an analogue of 4-hydroxycoumarin, also exhibited a good adaptability with a variety of chalcones with different substituent patterns and furnished the corresponding products in moderate to excellent yields (65–91%, entries 8–12, Table 3). In all cases, **3** (or **6**) arising from the 1,4-conjugate addition/annulation process was obtained as the sole product, suggesting that the reaction is highly regioselective.

On the basis of a previous report,[8b,12,13] a possible mechanism concerning the gold(III)-catalyzed tandem reaction of **1** (or **5**) with **2** is proposed (Scheme 1). First, the activation of the carbonyl group of the enone **2** by gold(III) species was followed by the conjugate addition of **1** (or **5**) to **2** to form the intermediate **8**.[8b,12,13] Protodeauration of **8** furnished the intermediate **9** and regenerated the gold catalyst.[8b,b,12] The intramolecular annulation of **9** with the aid of the gold catalyst eventually furnished **3** (or **6**).[14]

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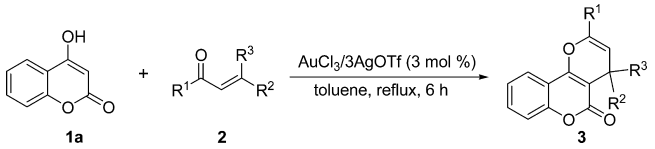
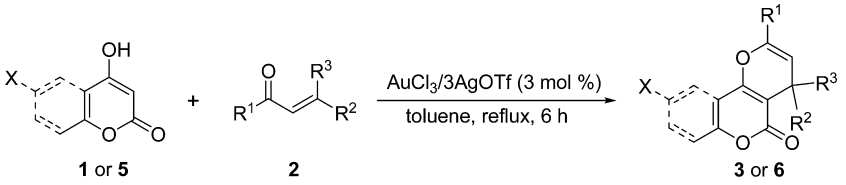
Table 2. Gold(III)-Catalyzed Reaction of 4-Hydroxycoumarin 1a with α,β-Unsaturated Ketones 2[a]



entry	R^1	R^2	R^3	2	product (3)	yield (%)[b]
1	Ph	Ph	H	**2a**	**3aa**	78
2	Ph	4-MeC_6H_4	H	**2b**	**3ab**	74
3	Ph	3,4-$OCH_2OC_6H_3$	H	**2c**	**3ac**	90
4	Ph	4-$NO_2C_6H_4$	H	**2d**	**3ad**	88
5	4-MeC_6H_4	Ph	H	**2e**	**3ae**	45
6	4-BrC_6H_4	Ph	H	**2f**	**3af**	61[c]
7	4-ClC_6H_4	4-ClC_6H_4	H	**2g**	**3ag**	91
8	4-MeC_6H_4	4-ClC_6H_4	H	**2h**	**3ah**	86
9	Ph	Ph	Me	**2i**	**3ai**	78
10	Me	Ph	H	**2j**	**3aj**	86
11	H	Ph	H	**2k**	**3ak**	complex mixture

[a]Reaction conditions: **1a** (1 mmol), **2** (1 mmol), $AuCl_3$/3AgOTf (0.03 mmol), toluene (3 mL), reflux, 6 h. [b]Isolated yields. [c]The reaction time was 8 h.

Table 3. Gold(III)-Catalyzed Reaction of Substituted 4-Hydroxycoumarins (1) or 4-Hydroxy-6-methyl-2-pyrone (5) with α,β-Unsaturated Ketones (2) [a]



entry	1 or 5	R^1	R^2	R^3	2	yield (%)[b] (3 or 6)
1	X = Me (**1b**)	Ph	Ph	H	**2a**	98 (**3ba**)
2	**1b**	Ph	4-MeC_6H_4	H	**2b**	94 (**3bb**)
3	**1b**	Ph	4-$MeOC_6H_4$	H	**2l**	97 (**3bl**)
4	**1b**	Ph	Ph	Me	**2i**	87 (**3bi**)
5	X = MeO (**1c**)				**2a**	85 (**3ca**)
6	X = *t*-Bu (**1d**)				**2a**	82 (**3da**)
7	X = Cl (**1e**)				**2a**	58 (**3ea**)
8	**5**				**2a**	65 (**6aa**)
9	**5**				**2b**	70 (**6ab**)
10	**5**				**2l**	91 (**6al**)
11	**5**	4-MeC_6H_4	4-ClC_6H_4	H	**2h**	66 (**6ah**)
12	**5**				**2i**	72 (**6ai**)

[a]Reaction conditions: **1** (or **5**) (1 mmol), **2** (1 mmol), $AuCl_3$/3AgOTf (0.03 mmol), toluene (3 mL), reflux, 6 h. [b]Isolated yields.

In summary, we have developed an efficient and highly regioselective tandem conjugate addition/annulation of 4-hydroxycoumarins with α,β-unsaturated ketones catalyzed by $AuCl_3$/3AgOTf, which furnished various functionalized pyrano-[3,2-*c*]coumarins in moderate to excellent yields with water as the sole byproduct.

EXPERIMENTAL SECTION

General Considerations. Unless otherwise stated, all reagents were purchased from commercial suppliers and used without purifications. All experiments were carried out under a nitrogen atmosphere. All solvents for the reactions were dried and distilled prior to use according to standard methods. Melting points were determined on Buchi B-545 melting point apparatus and were uncorrected. The ^1H NMR and ^{13}C NMR spectra were recorded at 25 °C in $CDCl_3$ at 500 and 125 MHz, respectively, with TMS as the internal standard. Chemical shifts (δ) are expressed in ppm, and coupling constants *J* are given in Hz. The IR spectra were recorded on an FT-IR spectrometer. GC-MS experiments were obtained on an instrument with an EI source. Elemental analyses were performed on an EA-1110 instrument.

General Procedure for the Gold(III)-Catalyzed Tandem Conjugate Addition/Annulation of 4-Hydroxycoumarins (1) or 4-Hydroxy-6-methyl-2-pyrone (5) with α,β-Unsaturated

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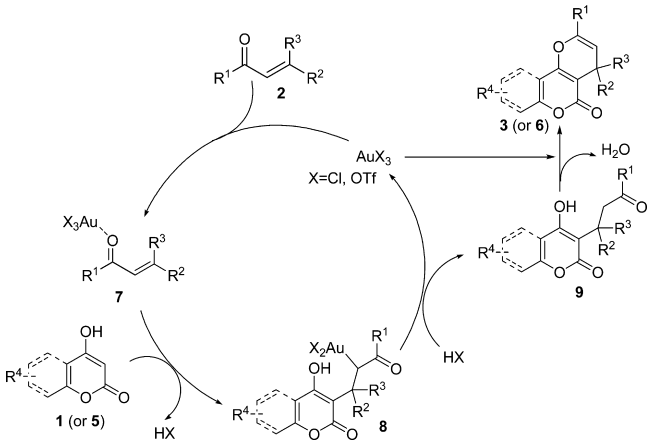
Scheme 1. Proposed Mechanism



Ketones (2). In a 10 mL flask, $AuCl_3$ (9.1 mg, 0.03 mmol), AgOTf (23.1 mg, 0.09 mmol), and toluene (1 mL) were added. The mixture was stirred at room temperature for 5 min before a toluene solution (2 mL) of **1** (or **5**) (1.0 mmol) and **2** (1.0 mmol) was added. Then the mixture was stirred under reflux for 6 h. Upon completion, the resulting mixture was diluted with CH_2Cl_2 (10 mL) and filtered through Celite. After evaporation of the solvent under vacuum, the residue was purified by column chromatography on silica gel (100–200 mesh) using petroleum ether/EtOAc (3/1–10/1, v/v) as eluent to give pure **3** (or **6**).

2,4-Diphenylpyrano[3,2-c]chromen-5(4H)-one[4a] ***(3aa):*** white solid; R_f = 0.38 (cyclohexane/EtOAc, 6/1); IR (KBr) ν 1720 (C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.02 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H), 7.74–7.72 (m, 2H), 7.58–7.54 (m, 1H), 7.46–7.21 (m, 10H), 5.84 (d, J = 5.0 Hz, 1H), 4.71 (d, J = 4.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.4, 155.8, 152.8, 147.0, 143.6, 132.7, 132.0, 129.3, 128.7 (2C), 128.6 (2C), 128.5 (2C), 127.2, 124.7 (2C), 124.2, 122.7, 116.8, 114.6, 103.8, 103.7, 36.7; MS (EI, 70 eV) m/z (%) 352 (33) $[M^+]$, 275 (100); mp 170–171 °C (lit.[4a] mp 173–175 °C).

2-Phenyl-4-p-tolylpyrano[3,2-c]chromen-5(4H)-one ***(3ab):*** white solid; R_f = 0.20 (cyclohexane/EtOAc, 6/1); IR (KBr) ν 1726 (C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.01 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H), 7.73–7.72 (m, 2H), 7.54 (dd, J_1 = 2.0 Hz, J_2 = 8.0 Hz, 1H), 7.46–7.25 (m, 7H), 7.12 (d, J = 8.0 Hz, 2H), 5.83 (d, J = 5.0 Hz, 1H), 4.67 (d, J = 5.0 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.5, 155.6, 152.8, 146.8, 140.7, 136.9, 132.7, 131.9, 129.3 (2C), 129.2, 128.7 (2C), 128.4 (2C), 124.7 (2C), 124.1, 122.7, 116.8, 114.6, 103.91, 103.85, 36.2, 21.1; MS (EI, 70 eV) m/z (%) 366 (79) $[M^+]$, 351 (16), 275 (100); mp 188–189 °C. Anal. Calcd for $C_{25}H_{18}O_3$: C, 81.95; H, 4.95. Found: C, 81.71; H, 4.91.

4-(Benzo[d][1,3]dioxol-5-yl)-2-phenylpyrano[3,2-c]chromen-5(4H)-one ***(3ac):*** white solid; R_f = 0.45 (cyclohexane/EtOAc, 4/1); IR (KBr) ν 1718 (C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.01 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H), 7.74–7.71 (m, 2H), 7.59–7.55 (m, 1H), 7.47–7.33 (m, 5H), 6.90–6.89 (m, 2H), 6.75 (d, J = 8.0 Hz, 1H), 5.90 (d, J = 1.5 Hz, 2H), 5.82 (d, J = 5.0 Hz, 1H), 4.63 (d, J = 5.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.5, 155.6, 152.7, 147.9, 146.8, 146.7, 137.7, 132.6, 132.0, 129.2, 128.7 (2C), 124.7 (2C), 124.2, 122.7, 121.7, 116.8, 114.5, 108.9, 108.3, 103.8, 103.7, 101.0, 36.2; MS (EI, 70 eV) m/z (%) 396 (100) $[M^+]$, 275 (76), 189 (19); mp 177–178 °C. Anal. Calcd for $C_{25}H_{16}O_5$: C, 75.75; H, 4.07. Found: C, 75.92; H, 4.03.

4-(4-Nitrophenyl)-2-phenylpyrano[3,2-c]chromen-5(4H)-one ***(3ad):*** pale yellow solid; R_f = 0.38 (cyclohexane/EtOAc, 4/1); IR (KBr): ν 1723 (C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.18 (dd, J_1 = 1.5 Hz, J_2 = 7.0 Hz, 2H), 8.04 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H), 7.74 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 2H), 7.63–7.59 (m, 3H), 7.49–7.35 (m, 5H), 5.80 (d, J = 5.0 Hz, 1H), 4.85 (d, J = 5.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.3, 156.3, 152.8, 150.6, 147.8, 147.1, 132.5, 132.1, 129.7, 129.4 (2C), 128.8 (2C), 124.8 (2C), 124.4, 123.9 (2C), 122.8, 117.0, 114.2, 102.4, 102.1, 36.7; MS (EI, 70 eV) m/z (%) 397 (62) $[M^+]$, 350 (15), 275 (100); mp 230–231 °C. Anal. Calcd for $C_{24}H_{15}NO_5$: C, 72.54; H, 3.80. Found: C, 72.76; H, 3.82.

4-Phenyl-2-p-tolylpyrano[3,2-c]chromen-5(4H)-one ***(3ae):*** pale yellow solid; R_f = 0.68 (cyclohexane/EtOAc, 6/1); IR (KBr) ν 1719 (C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.0 (dd, J_1 = 1.5 Hz, J_2 = 7.5 Hz, 1H), 7.66 (dd, J_1 = 2.0 Hz, J_2 = 7.0, Hz, 2H), 7.58–7.54 (m, 1H), 7.42–7.22 (m, 7H), 6.96 (dd, J_1 = 2.0 Hz, J_2 = 6.5, Hz, 2H), 5.71 (d, J = 5.0 Hz, 1H), 4.69 (d, J = 5.0 Hz, 1H), 3.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.5, 160.4, 155.7, 152.7, 146.8, 143.8, 131.9, 128.6 (2C), 128.4 (2C), 127.1, 126.1, 125.3 (2C), 124.1, 122.6, 116.8, 114.6, 114.0 (2C), 103.8, 102.0, 55.4, 36.6; MS (EI, 70 eV) m/z (%) 366 (39) $[M^+]$, 351 (100), 289 (93); mp 156–158 °C.. Anal. Calcd for $C_{25}H_{18}O_3$: C, 81.95; H, 4.95. Found: C, 81.76; H, 4.91

2-(4-Bromophenyl)-4-phenylpyrano[3,2-c]chromen-5(4H)-one[4e] ***(3af):*** white solid; R_f = 0.40 (cyclohexane/EtOAc, 6/1); IR (KBr) ν 1720 (C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.98 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H), 7.60–7.56 (m, 5H), 7.41–7.22 (m, 7H), 5.84 (d, J = 5.0 Hz, 1H), 4.70 (d, J = 4.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.3, 155.6, 152.8, 146.0, 143.2, 132.1, 131.8 (2C), 131.6, 128.7 (2C), 128.4 (2C), 127.3, 126.2 (2C), 124.2, 123.4, 122.5, 116.9, 114.4, 104.4, 103.6, 36.6; MS (EI, 70 eV) m/z (%) 432 (16) $[M^+]$, 353 (100); mp 202–203 °C.

2,4-Bis(4-chlorophenyl)pyrano[3,2-c]chromen-5(4H)-one ***(3ag):*** white solid; R_f = 0.38 (cyclohexane/EtOAc, 6/1); IR (KBr) ν 1720 (C=O) cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$) δ 7.98 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H), 7.67–7.57 (m, 3H), 7.44–7.26 (m, 8H), 5.78 (d, J = 5.0 Hz, 1H), 4.68 (d, J = 5.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.3, 155.8, 152.8, 146.4, 141.9, 135.4, 133.2, 132.3, 131.0, 129.9 (2C), 129.0 (2C), 128.9 (2C), 126.1 (2C), 124.4, 122.7, 117.0, 114.3, 103.8, 103.3, 36.2; MS (EI, 70 eV) m/z (%) 420 (51) $[M^+]$, 385 (21), 309 (100); mp 239–241 °C. Anal. Calcd for $C_{24}H_{14}Cl_2O_3$: C, 68.43; H, 3.35. Found: C, 68.60; H, 3.38.

4-(4-Chlorophenyl)-2-p-tolylpyrano[3,2-c]chromen-5(4H)-one ***(3ah):*** Pale yellow solid; R_f = 0.50 (cyclohexane/EtOAc, 6/1); IR (KBr) ν 1720 (C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.01 (dd, J_1 = 1.5 Hz, J_2 = 7.5 Hz, 1H), 7.62–7.56 (m, 3H), 7.39–7.25 (m, 8H), 5.74 (d, J = 5.0 Hz, 1H), 4.67 (d, J = 5.0 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.4, 155.8, 152.8, 147.3, 142.2, 139.5, 133.0, 132.1, 129.8 (2C), 129.6, 129.4 (2C), 128.7 (2C), 124.6 (2C), 124.2, 122.7, 116.8, 114.5, 103.3, 102.3, 36.1, 21.3; MS (EI, 70 eV) m/z (%) 400 (48) $[M^+]$, 365 (14), 289 (100); mp 225–227 °C. Anal. Calcd for $C_{25}H_{17}ClO_3$: C, 74.91; H, 4.27. Found: C, 74.73; H, 4.30.

4-Methyl-2,4-diphenylpyrano[3,2-c]chromen-5(4H)-one ***(3ai):*** white solid; R_f = 0.375 (cyclohexane/EtOAc, 6/1); IR (KBr) ν 1722 (O–C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.05 (dd, J_1 = 1.0 Hz, J_2 = 9.0 Hz, 1H), 7.72 (dd, J_1 = 1.5 Hz, J_2 = 7.0 Hz, 2H), 7.56–7.21 (m, 11H), 5.52 (s, 1H), 2.05 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.3, 155.0, 152.8, 147.2, 143.8, 132.6, 131.9, 129.1, 128.7 (2C), 128.2 (2C), 127.5 (2C), 126.5, 124.6 (2C), 124.0, 123.1, 116.6, 114.5, 110.0, 107.3, 38.2, 26.2; MS (EI, 70 eV) m/z (%) 366 (40) $[M^+]$, 351 (100), 289 (96); mp 183–184 °C. Anal. Calcd for $C_{25}H_{18}O_3$: C, 81.95; H, 4.95. Found: C, 81.74; H, 4.91.

2-Methyl-4-phenylpyrano[3,2-c]chromen-5(4H)-one[4b] ***(3aj):*** pale yellow solid; R_f = 0.70 (cyclohexane/EtOAc, 6/1); IR (KBr) ν 1724 (C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.86 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 1H), 7.54–7.50 (m, 1H), 7.35–7.19 (m, 7H), 5.06 (dd, J_1 = 1.0 Hz, J_2 = 4.5 Hz, 1H), 4.50 (d, J = 4.5 Hz, 1H), 2.07 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.5, 155.9, 152.8, 146.0, 144.2, 131.8, 128.5 (2C), 128.2 (2C), 127.0, 124.0, 122.7, 116.7, 114.5, 104.0, 103.5, 36.5, 18.6; MS (EI, 70 eV) m/z (%) 290 (38) $[M^+]$, 275 (7), 213 (100); mp 136–137 °C.

9-Methyl-2,4-diphenylpyrano[3,2-c]chromen-5(4H)-one[4c] ***(3ba):*** white solid; R_f = 0.5 (cyclohexane/EtOAc, 6/1); IR (KBr) ν 1715 (C=O) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.77–7.72 (m, 3H), 7.47–7.21 (m, 10H), 5.83 (d, J = 5.0 Hz, 1H), 4.70 (d, J = 5.0 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.6, 155.7, 150.9, 146.9, 143.6, 133.9, 133.0, 132.8, 129.2, 128.64 (2C), 128.58 (2C), 128.4 (2C), 127.1, 124.7 (2C), 122.3, 116.6, 114.2, 103.8, 103.6,

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36.6, 21.0; MS (EI, 70 eV) *m/z* (%) 366 (52) [M$^+$], 289 (100); mp 216−218 °C.

9-Methyl-2-phenyl-4-p-tolylpyrano[3,2-c]chromen-5(4H)-one (**3bb**): white solid; R_f = 0.50 (cyclohexane/EtOAc, 8/1); IR (KBr) ν 1721 (C═O) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76−7.72 (m, 3H), 7.47−7.11 (m, 9H), 5.82 (d, J = 5.0 Hz, 1H), 4.66 (d, J = 5.0 Hz, 1H), 2.49 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.6, 155.6, 150.9, 146.8, 140.8, 136.8, 133.8, 132.9, 132.8, 129.3 (2C), 129.1, 128.6 (2C), 128.3 (2C), 124.7 (2C), 122.2, 116.6, 114.3, 104.0, 103.7, 36.2, 21.0 (2C); MS (EI, 70 eV) *m/z* (%) 380(80) [M$^+$], 365 (15), 303 (7), 289 (100); mp 210−211 °C. Anal. Calcd for $C_{26}H_{20}O_3$: C, 82.08; H, 5.30. Found: C, 82.25; H, 5.26.

4-(4-Methoxyphenyl)-9-methyl-2-phenylpyrano[3,2-c]chromen-5(4H)-one (**3bl**): brown solid; R_f = 0.20 (cyclohexane/EtOAc, 6/1); IR (KBr) ν 1717 (C═O) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76−7.72 (m, 3H), 7.48−7.20 (m, 7H), 6.84 (dd, J_1 = 2.0 Hz, J_2 = 7.0 Hz, 2H), 5.81 (d, J = 5.0 Hz, 1H), 4.64 (d, J = 5.0 Hz, 1H), 3.76 (s, 3H), 2.48 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.7, 158.7, 155.5, 150.9, 146.8, 135.9, 133.9, 132.9, 132.8, 129.5 (2C), 129.1, 128.6 (2C), 124.7 (2C), 122.2, 116.5, 114.2, 114.0 (2C), 103.9, 103.8, 55.2, 35.7, 21.0; MS (EI, 70 eV) *m/z* (%) 396 (100) [M$^+$], 365 (18), 319 (12), 289 (78); mp 218−219 °C. Anal. Calcd for $C_{26}H_{20}O_4$: C, 78.77; H, 5.09. Found: C, 78.99; H, 5.12.

4,9-Dimethyl-2,4-diphenylpyrano[3,2-c]chromen-5(4H)-one (**3bi**): pale yellow solid; R_f = 0.50 (cyclohexane/EtOAc, 6/1); IR (KBr) ν 1720 (C═O) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, J = 1.0 Hz, 1H), 7.72 (dd, J_1 = 1.5 Hz, J_2 = 3.5 Hz, 2H), 7.50−7.18 (m, 10H), 5.50 (s, 1H), 2.49 (s, 3H), 2.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.4, 155.0, 151.0, 147.3, 143.8, 133.7, 132.9, 132.7, 129.1, 128.6 (2C), 128.1 (2C), 127.4 (2C), 126.4, 124.6 (2C), 122.6, 116.3, 114.1, 110.1, 107.1, 38.2, 26.2, 21.1; MS (EI, 70 eV) *m/z* (%) 380 (40) [M$^+$], 365 (100), 303 (95); mp 245−247 °C. Anal. Calcd for $C_{26}H_{20}O_3$: C, 82.08; H, 5.30. Found: C, 82.27; H, 5.27.

9-Methoxy-2,4-diphenylpyrano[3,2-c]chromen-5(4H)-one (**3ca**): white solid; R_f = 0.6 (cyclohexane/EtOAc, 6/1); IR (KBr) ν 1714 (C═O) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (dd, J_1 = 1.5 Hz, J_2 = 8.5 Hz, 2H), 7.46−7.40 (m, 6H), 7.33−7.13 (m, 5H), 5.83 (d, J = 5.0 Hz, 1H), 4.71 (d, J = 5.0 Hz, 1H), 3.92 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.6, 156.0, 155.5, 147.2, 147.0, 143.6, 132.7, 129.3, 128.7 (2C), 128.6 (2C), 128.5 (2C), 127.2, 124.7 (2C), 119.3, 117.9, 115.0, 105.5, 104.0, 103.9, 56.0, 36.7; MS (EI, 70 eV) *m/z* (%) 382 (59) [M$^+$], 305 (100); mp 206−207 °C. Anal. Calcd for $C_{25}H_{18}O_4$: C, 78.52; H, 4.74. Found: C, 78.69; H, 4.70.

9-tert-Butyl-2,4-diphenylpyrano[3,2-c]chromen-5(4H)-one (**3da**): white solid; R_f = 0.6 (cyclohexane/EtOAc, 6/1); IR (KBr) ν 1722 (C═O) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99 (d, J = 2.0 Hz, 1H), 7.73 (dd, J_1 = 1.5 Hz, J_2 = 8.5 Hz, 2H), 7.61 (dd, J_1 = 2.0 Hz, J_2 = 8.5 Hz, 1H), 7.48−7.45 (m, 5H), 7.43−7.40 (m, 4H), 5.84 (d, J = 5.0 Hz, 1H), 4.71 (d, J = 5.0 Hz, 1H), 1.42 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.8, 156.1, 150.9, 147.4, 147.0, 143.8, 132.9, 129.7, 129.3, 128.8 (2C), 128.7 (2C), 128.5 (2C), 127.2, 124.7 (2C), 118.6, 116.5, 113.9, 104.0, 103.5, 36.7, 34.8, 31.5; MS (EI, 70 eV) *m/z* (%) 408 (3) [M$^+$]; mp 181−182 °C. Anal. Calcd for $C_{28}H_{24}O_3$: C, 82.33; H, 5.92. Found: C, 82.55; H, 5.88.

9-Chloro-2,4-diphenylpyrano[3,2-c]chromen-5(4H)-one[4c] (**3ea**): pale yellow solid; R_f = 0.40 (cyclohexane/EtOAc, 10/1); IR (KBr) ν 1721 (C═O) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (d, J = 2.5 Hz, 1H), 7.71 (dd, J_1 = 1.0 Hz, J_2 = 8.5 Hz, 2H), 7.52−7.22 (m, 10H), 5.83 (d, J = 5.0 Hz, 1H), 4.70 (d, J = 5.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.8, 154.7, 151.1, 147.1, 143.2, 132.4, 132.0, 129.8, 129.4, 128.8 (2C), 128.7 (2C), 128.5 (2C), 127.4, 124.7 (2C), 122.2, 118.3, 115.7, 104.6, 103.8, 36.7; MS (EI, 70 eV) *m/z* (%) 386 (56) [M$^+$], 309 (100); mp 231−232 °C.

7-Methyl-2,4-diphenylpyrano[4,3-b]pyran-5(4H)-one[4c] (**6aa**): brown solid; R_f = 0.25 (cyclohexane/EtOAc, 6/1); IR (KBr) ν 1721 (C═O) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (dd, J_1 = 2.0 Hz, J_2 = 8.5 Hz, 2H), 7.39−7.21 (m, 8H), 6.02 (s, 1H), 5.73 (d, J = 5.0 Hz, 1H), 4.56 (d, J = 5.0 Hz, 1H), 2.24 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.3, 161.4, 160.4, 146.8, 143.8, 132.6, 129.1, 128.52 (2C), 128.51 (2C), 128.4 (2C), 127.0, 124.6 (2C), 103.8, 100.8, 99.1, 36.0, 19.9; MS (EI, 70 eV) *m/z* (%) 316 (52) [M$^+$], 239 (100); mp 170−171 °C.

7-Methyl-2-phenyl-4-p-tolylpyrano[4,3-b]pyran-5(4H)-one (**6ab**): pale yellow solid; R_f = 0.40 (cyclohexane/EtOAc, 6/1); IR (KBr) ν 1720 (C═O) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (dd, J_1 = 1.5 Hz, J_2 = 8.0 Hz, 2H), 7.40−7.38 (m, 3H), 7.37−7.35(m, 2H), 7.12 (d, J = 8.0 Hz, 2H), 6.00 (s, 1H), 5.72 (d, J = 5.0 Hz, 1H), 4.52 (d, J = 5.0 Hz, 1H), 2.30 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.3, 161.3, 160.3, 146.7, 140.9, 136.6, 132.6, 129.2 (2C), 129.0, 128.5 (2C), 128.2 (2C), 124.5 (2C), 103.9, 100.9, 99.1, 35.6, 21.0, 19.9; MS (EI, 70 eV) *m/z* (%) 330 (75) [M$^+$], 315 (12), 253 (11), 239 (100); mp 195−196 °C. Anal. Calcd for $C_{22}H_{18}O_3$: C, 79.98; H, 5.49. Found: C, 80.21; H, 5.53.

4-(4-Methoxyphenyl)-7-methyl-2-phenylpyrano[4,3-b]pyran-5(4H)-one (**6al**): pale yellow solid; R_f = 0.45 (cyclohexane/EtOAc, 3:1); IR (KBr) ν 1721 (C═O) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (d, J = 7.0 Hz, 2H), 7.40−7.25 (m, 5H), 6.84 (d, J = 8.5 Hz, 2H), 6.00 (s, 1H), 5.71 (d, J = 4.5 Hz, 1H), 4.50 (d, J = 5.0 Hz, 1H), 3.76 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.3, 161.2, 160.1, 158.6, 146.7, 136.1, 132.6, 129.4 (2C), 129.0, 128.5 (2C), 124.5 (2C), 113.9 (2C), 103.8, 101.0, 99.1, 55.2, 35.1, 19.8; MS (EI, 70 eV) *m/z* (%) 346(100) [M$^+$], 331 (2), 239 (76); mp 132−134 °C. Anal. Calcd for $C_{22}H_{18}O_4$: C, 76.29; H, 5.24. Found: C, 76.01; H, 5.28.

4-(4-Chlorophenyl)-7-methyl-2-p-tolylpyrano[4,3-b]pyran-5(4H)-one (**6ah**): brown solid; R_f = 0.25 (cyclohexane/EtOAc, 6/1); IR (KBr) ν 1721 (C═O) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (d, J = 8.0 Hz, 2H), 7.31−7.25 (m, 4H), 7.19 (d, J = 8.0 Hz, 2H), 6.01 (s, 1H), 5.63 (d, J = 5.0 Hz, 1H), 4.52 (d, J = 5.0 Hz, 1H), 2.37 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.2, 161.6, 160.5, 147.2, 142.4, 139.3, 132.8, 129.8 (2C), 129.6, 129.2 (2C), 128.6 (2C), 124.5 (2C), 102.3, 100.5, 99.1, 35.5, 21.3, 19.9; MS (EI, 70 eV) *m/z* (%) 364 (49) [M$^+$], 253 (100); mp 180−181 °C. Anal. Calcd for $C_{22}H_{17}ClO_3$: C, 72.43; H, 4.70. Found: C, 72.73; H, 4.75.

4,7-Dimethyl-2,4-diphenylpyrano[4,3-b]pyran-5(4H)-one (**6ai**): brown solid; R_f = 0.3 (cyclohexane/EtOAc, 6/1); IR (KBr) ν 1722 (C═O) cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60−7.58 (m, 2H), 7.46−7.45 (m, 2H), 7.40−7.30 (m, 5H), 7.20 (m, 1H), 6.01 (d, J = 0.5 Hz, 1H), 5.44 (s, 1H), 2.22 (s, 3H), 1.96 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.2, 161.4, 159.6, 147.2, 143.8, 132.5, 128.9, 128.4 (2C), 128.0 (2C), 127.4 (2C), 126.3, 124.4 (2C), 110.0, 104.3, 99.0, 37.4, 25.9, 19.8; MS (EI, 70 eV) *m/z* (%) 330 (36) [M$^+$], 315 (100), 253 (98), 226 (4); mp 137−139 °C. Anal. Calcd for $C_{22}H_{18}O_3$: C, 79.98; H, 5.49. Found: C, 79.65; H, 5.45.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Figures giving ^{1}H and ^{13}C NMR spectra of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: ykuiliu@zjut.edu.cn.

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