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Synthesis of 3-arylcoumarins through *N*-heterocyclic carbene catalyzed condensation and annulation of 2-chloro-2-arylacetaldehydes with salicylaldehydes

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ABSTRACT

The condensation reaction of 2-chloro-2-arylacetaldehyde with salicylaldehyde catalyzed by *N*-heterocyclic carbene (NHC) leading to 3-arylcoumarin was studied. A number of 3-arylcoumarin derivatives were obtained in good to excellent yields via this umpolung reaction. This reaction is facile and experimentally simple and mild.

1. Introduction

3-Arylcoumarins as fundamental structures of drugs, natural products, and organic materials have attracted great attention during the past few decades because of their biological activities[1] and photochemistry properties.[2] Several reactions have been employed to prepare 3-arylcoumarins. Pechmann condensation[3] of phenols with β-ketoesters affords 3-arylcoumarins (Eq. 1), which requires strong acid catalyst, such as sulfuric acid, aluminum chloride, or trifluoromethanesulfonic acid. Perkin reaction is one of the most direct and widely used methods to prepare 3-arylcoumarins from salicylaldehydes and arylacetic acids or anhydrides, but it suffers from the need of harsh conditions, tedious work-up, and unsatisfactory yields (Eq. 2).[1c,4] Pd-catalyzed three-component annulation of internal alkynes, 2-iodophenols, and carbon monoxide is quite efficient giving 3-arylcoumarins in good yields (Eq. 3).[5] The reaction is not suitable for unsymmetric alkynes since mixtures of regioisomers are formed. Functionalization via transition-metal-catalyzed coupling reactions has also been reported (Eq. 4),[6] however, preformed coumarin nuclei are necessary. There are other synthetic strategies leading to 3-arylcoumarins including microwave-assisted Pechmann condensation,[7] the coupling reaction between coumarin and potentially explosive benzenediazonium salt[8] as well as three-component reaction using in situ generated benzyne as key intermediate.[9]

Synthesis of coumarins via umpolung reactions catalyzed by *N*-heterocyclic carbene has been developed in recent years.[10] Bräse's group[11] and our group[12] have recently reported that 3-benzyl-coumarin could be prepared from salicylaldehyde and cinnamaldehyde employing NHCs as catalyst (Eq. 5),[12] however, the synthetic method is not appropriate for 3-arylcoumarins. We envisioned that cinnamaldehyde could proceed an intramolecular redox reaction mediated by NHC in which the aldehyde group was oxidized to an ester group and simultaneously the α,β carbon–carbon double bond was reduced to a single bond. Thus 3-arylcoumarin could be obtained when cinnamaldehyde was replaced by 2-arylacetaldehyde bearing an oxidative group at α position. As a matter of fact, many functional groups that have the higher oxidation state could act as oxidants in the NHC catalyzed intramolecular redox reactions, such as carbon–halogen bond,[13] carbon–oxygen bond,[10a,14] carbon–nitrogen bond[14a] as well as carbon–carbon single bond.[15]

We found that 2-chloro-2-phenylacetaldehyde could undergo such a redox reaction that the C–Cl bond was reduced and the aldehyde group was oxidized to ester group in the presence of

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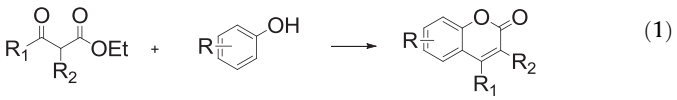
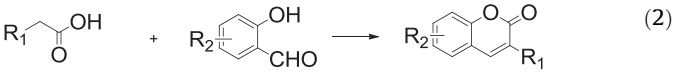
a suitable NHC catalyst. In this paper, we report an efficient condensation reaction catalyzed by NHC between 2-chloro-2-arylacetaldehydes and salicylaldehydes to yield 3-arylcoumarins (Eq. 6).

Pechmann reaction:



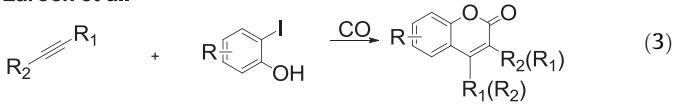
(1)

Perkin reaction:



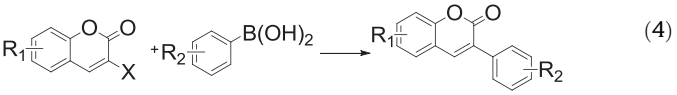
(2)

Larock et al.



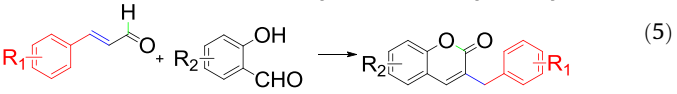
(3)

Transition-metal-catalyzed coupling reactions:



(4)

Condensation of cinnamaldehydes with salicylaldehydes:



(5)

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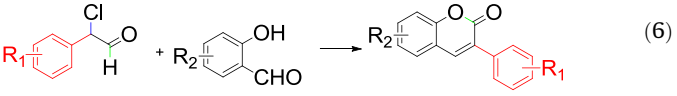
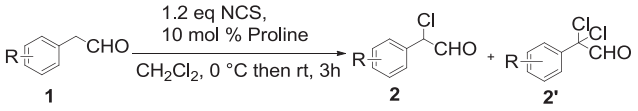


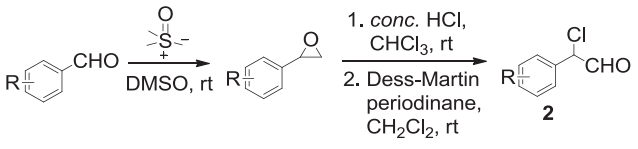
(6)

2. Result and discussion

Monochlorinated aldehydes containing strong electron-donating groups could be obtained in good yields through Jørgensen's direct chlorination[16] (Scheme 1). Unfortunately, chlorination of aldehydes without strong electron-donating groups generated mixtures of mono- and di-chlorinated products (**2** and **2′**, see Table S1 in Supplementary data). The monochlorinated aldehydes without strong electron-donating group could be obtained through the reactions shown in Scheme 2. Benzaldehyde



Scheme 1. Synthesis of 2-chloro-2-arylacetaldehydes using Jørgensen's method. Results: R=H, **2a** and **2a′** (3:1), 80%; 4-CH_3O, **2b**, 89%; 2-CH_3O, **2c**, 84%; 4-BocNH, **2d**, 87%; 3-CH_3O, **2e**, 73%.

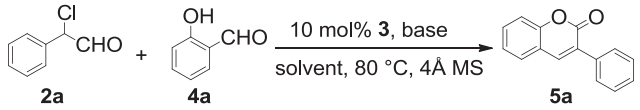


Scheme 2. Synthesis of 2-chloro-2-arylacetaldehydes **2a** and **2f**–**k**.[17] Results: R=H, **2a**, 76%; 4-Me, **2f**, 80%; 4-Cl, **2g**, 53%; 4-Br, **2h**, 65%; 4-F, **2i**, 45%; [3,4]-benzo, **2j**, 73%; [2,3]-benzo, **2k**, 69%.

derivatives were first converted to 2-aryloxiranes by using *in situ* generated Corey–Chaykovsky Reagent. Treatment of the resulting 2-aryloxiranes with concentrated hydrochloric acid afforded 2-chloro-2-arylethanols after ring cleavage. Further oxidation of 2-chloro-2-arylethanols with Dess–Martin periodinane gave the corresponding 2-chloro-2-arylacetaldehydes in up to 80% yield.

With these 2-chloro-2-arylacetaldehydes in hand, we tested their condensation reactions with salicylaldehydes, and the results were summarized in Table 1. Initially we used the reaction condition, which was proven suitable for the condensation of cinnamaldehydes with salicylaldehydes employing **3c** as NHC precursor and DBU as base in THF (entry 1).[12] Although we could obtain the target product **5a**, the yield was poor. When **3c** and DBU were replaced by **3a** and Et_3N, the yield of **5a** was sharply increased to 68% from 19% (entry 2). This improvement strongly suggested that the catalytic process was significantly affected by the NHC precursors and bases. The reactivity of NHCs is dominated by their steric and electronic properties. Thus, we examined the influence of the carbene precursors listed in Fig. 1. When electron-deficient triazolium salt **3b** was used, the reaction gave **5a** in a poor yield (entry 3). The NHC (IMes) generated from **3c** are considered to be one of the most electron-rich NHCs, however, **5a** was only obtained in 48% yield in the presence of **3c** and Et_3N (entry 4). When the bulkier and electron-richer NHC (IPr) generated from **3d** was used, the annulation reaction proceeded with a poor yield (entry 5). The NHCs derived from thiazolium salts **3e** and **3f** are considered to have much less steric hindrance among the NHCs tested, however, they were less active than **3a** (entries 6 and 7). A brief survey of solvent indicated that ethyl acetate was the most suitable solvent. The use of THF, toluene, and 1,4-dioxane resulted in slightly lower yields (entries 2, 9, and 11). **5a** was obtained in 45% yield in CH_2Cl_2 even the reaction time was prolonged to 24 h maybe due to the

Table 1
Optimization of reaction conditions[a]



2a **4a** **5a**

Entry	3	Base	Solvent	Yield(%)
1	**3c**	DBU[b]	THF	19
2	**3a**	Et_3N	THF	68
3	**3b**	Et_3N	THF	23
4	**3c**	Et_3N	THF	48
5	**3d**	Et_3N	THF	32
6	**3e**	Et_3N	THF	24
7	**3f**	Et_3N	THF	15
8	**3a**	Et_3N	EtOAc	80
9	**3a**	Et_3N	Toluene	69
10	**3a**	Et_3N	CH_2Cl_2	45[c]
11	**3a**	Et_3N	1,4-Dioxane	66
12	**3a**	DBU	EtOAc	24
13	**3a**	DIPEA[d]	EtOAc	65
14	**3a**	DMAP[e]	EtOAc	77
15	**3a**	DABCO[f]	EtOAc	63
16	**3a**	K_2CO_3	EtOAc	37
17	**3a**	Et_3N	EtOAc	73[g]
18	**3a**	Et_3N	EtOAc	30[h]
19	—	Et_3N	EtOAc	—

[a] Reaction conditions: **2a**, 1 mmol; **4a**, 0.5 mmol; **3**, 0.05 mmol; base, 2 mmol; 4 Å MS, 0.5 g; solvent, 1 mL; 80 °C, 4 h.
[b] DBU (1,8-diazabicyclo[5.4.0]undec-7-ene).
[c] 30 °C, 24 h.
[d] DIPEA=*N*,*N*-diisopropylethylamine.
[e] DMAP=4-dimethylaminopryidine.
[f] DABCO=1,4-diazabicyclo[2.2.2]octane triethylenediamine.
[g] Et_3N, 1 mmol.
[h] 2-Bromo-2-phenylacetaldehyde was used instead of **2a**.

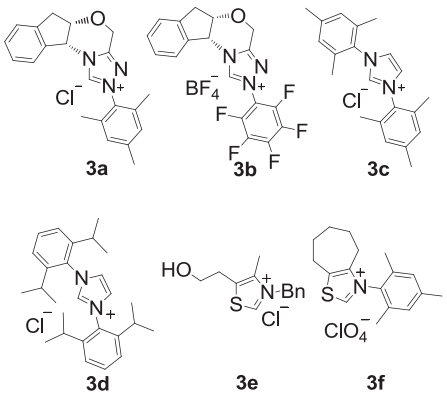


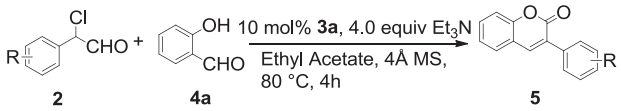
Fig. 1. The *N*-heterocyclic carbene precursors.

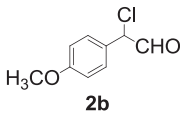
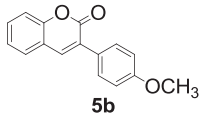
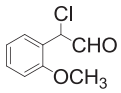
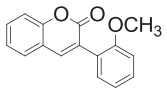
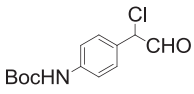
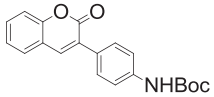
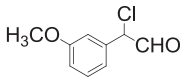
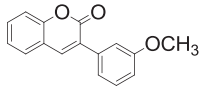
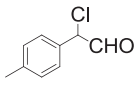
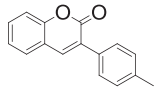
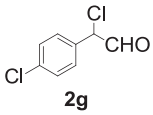
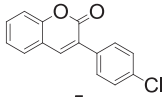
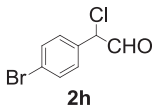
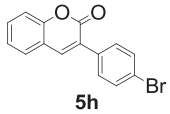
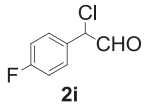
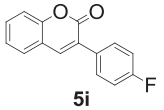
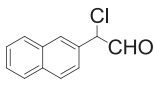
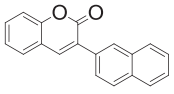
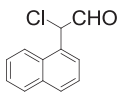
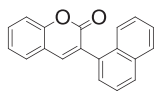
lower reaction temperature (entry 10). Among the bases tested, Et_3N was more suitable than other bases. Although DBU is often used for the deprotonation of imidazolium salts, it led to a low yield of 24% in the condensation of 2-chloro-2-phenylacetaldehyde with salicylaldehyde (entry 12). DMAP was also a good base similar to Et_3N (entry 14). When the loading of base was reduced, the reaction gave **5a** in a lower yield. Maybe higher concentration of base would be beneficial to the elimination of hydrochloride (73%, entry 17). Thus, we were able to obtain **5a** in the yield of 80% at 80 °C in the presence of 10 mol % of **3a** and Et_3N in ethyl acetate. Under the optimized reaction conditions, the condensation of 2-bromo-2-phenyl-acetaldehyde with **4a** gave the same product **5a**, however, with a low yield of 30% (entry 18). The result of control experiment shows that without NHC catalyst, the desired product could not be obtained (entry 19).

We further examined the reactions of a number of 2-chloro-2-arylacetaldehydes (**2**) with salicylaldehyde (**4a**), and the results were listed in Table 2. The reactions of 2-chloro-2-arylacetaldehydes bearing methoxy and methyl group at their *para*- and *ortho*-positions gave **5b**, **5c**, and **5f** in up to 85% yield (entries 1, 2, and 5). However **2d** was considered to be one of the electron-rich substrates containing a protected amino group at the *para*-position, **5d** was obtained in a lower yield of 65% (entry 3). Generally, 2-chloro-2-arylacetaldehyedes with electron-withdrawing groups furnished corresponding products in lower yields, such as **2e** bearing a *m*-CH_3O, **2g** bearing a *p*-Cl and **2h** bearing a *p*-Br (entries 4, 6, and 7). For *p*-F substituted aldehyde **2i**, the yield of corresponding product **5i** could be increased to 45% when 20 mol % of **3a** was employed (entry 8). Aldehyde **2j** furnished the corresponding product **5j** in an excellent yield of 90%, while a slightly lower yield of 83% was obtained for **5k** (entries 9 and 10).

The reaction scope of variable salicylaldehydes (**4**) was investigated, and the corresponding products were obtained in up to 90% yield (Table 3). Salicylaldehydes having methoxy and methyl groups at their 3- and 5-positions gave higher yields of corresponding products due to the higher nucleophilic ability of the hydroxy group (entries 1, 3, 10, and 11). The electron-withdrawing groups, such as *m*-CH_3O, Cl, and Br significantly lowered the yields (entries 2, 6, 7, 8, and 9). The yield of **6e** was quite low, however, the yield of its isomer **6f** was dramatically high (entries 4 and 5). **4m** with two bulky *tert*-butyl groups generated **6m** in moderate yield due to the steric hindrance (entry 12). **4n** with a protected amino group furnished **6n** in an excellent yield, which could generate an active amino group for further functionalization after deprotection (entry 13). The substrates containing an ester group or even an extra hydroxy group provided the desired coumarin products **6o** and **6p**, albeit in slightly reduced yields of 55% and 52%, respectively (entries 14 and 15).

Table 2
The reactions between 2-chloro-2-arylacetaldehydes and salicylaldehyde[a]

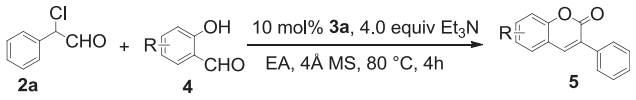


Entry	Substrate	Product	Yield (%)
1	 **2b**	 **5b**	85
2	 **2c**	 **5c**	82
3	 **2d**	 **5d**	65
4	 **2e**	 **5e**	57
5	 **2f**	 **5f**	84
6	 **2g**	 **5g**	58
7	 **2h**	 **5h**	62
8	 **2i**	 **5i**	32 (45[b])
9	 **2j**	 **5j**	90
10	 **2k**	 **5k**	83

[a] Reaction condition: **2**, 1.0 mmol; **4a**, 0.5 mmol; **3a**, 0.05 mmol; Et_3N, 2.0 mmol; 4 Å MS, 0.5 g; ethyl acetate, 1 mL.
[b] **3a**, 0.1 mmol.

The deprotonation of triazolium salt yields the nucleophilic NHC (Scheme 3). The nucleophilic addition of NHC to **2a** is supposed to form intermediate **I**. The enolate analogue **II** might result from **I** by E_1cb elimination. Nucleophilic addition of the 1,2-dipole equivalent **II** to the carbonyl group of salicylaldehyde affords **III**. **IV** would be generated through the following annulation of **III**. Protonization and subsequent dehydration occur giving the final product **5a**.

Table 3
Influence of substituents on salicylaldehydes[a]



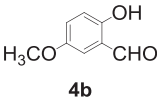
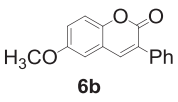
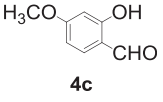
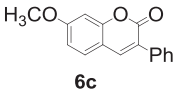
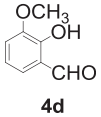
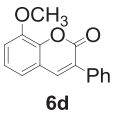
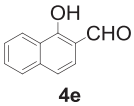
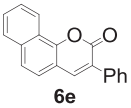
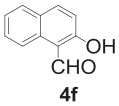
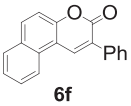
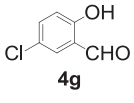
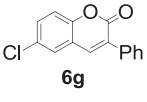
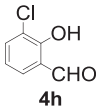
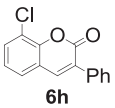
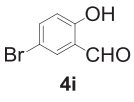
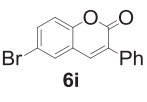
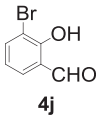
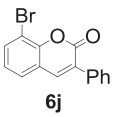
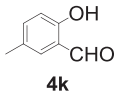
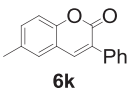
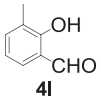
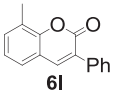
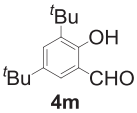
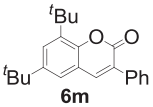
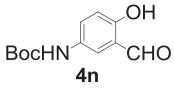
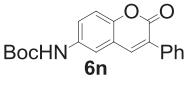
Entry	Substrate	Product	Yield (%)
1	 4b	 6b	85
2	 4c	 6c	57
3	 4d	 6d	80
4	 4e	 6e	29
5	 4f	 6f	89
6	 4g	 6g	35
7	 4h	 6h	35
8	 4i	 6i	39
9	 4j	 6j	47
10	 4k	 6k	86
11	 4l	 6l	83
12	 4m	 6m	56
13	 4n	 6n	90

Table 3 (*continued*)

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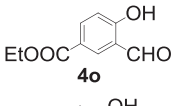
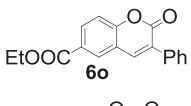
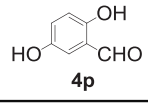
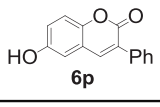
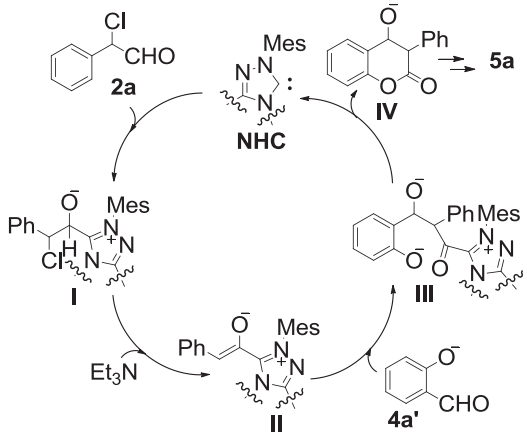
14	 4o	 6o	55
15	 4p	 6p	52[b]

[a] Reaction condition: **2a**, 1.0 mmol; **4**, 0.5 mmol; **3a**, 0.05 mmol; Et_3N, 2.0 m mol; 4 Å MS, 0.5 g; ethyl acetate, 1 mL.
[b] Et_3N, 2.5 mmol.



Scheme 3. Proposed reaction pathways.

3. Conclusions

In summary, we have developed an *N*-heterocyclic carbene (NHC) catalyzed condensation reaction using easily prepared 2-chloro-2-arylacetaldehydes as substrates affording 3-arylcoumarins in moderate to good yields. The intermediate enolate analogue **II** existed in alkaline environment was assumed to result from the E_1cb elimination of tetrahedral intermediate **I** and act as a 1,2-dipole equivalent. This condensation reaction is compatible with a wide range of substituents, such as methyl, methoxy, fluorine, chlorine, bromine, ester group, and hydroxyl group.

4. Experiment section

4.1. General information

All reactions were carried out under dry nitrogen atmosphere. THF, 1,4-dioxane, and toluene were dried and freshly distilled from sodium using benzophenone as an indicator. *t*-BuOH, dichloromethane (DCM), ethyl acetate (EA), and DMSO were dried by distillation from calcium hydride. Flash chromatography was carried out with silica gel (silica gel, 300–400 mesh). Before the measurement of melting point, the solid products were recrystallized from petroleum ether and ethyl acetate. ^1H and ^{13}C NMR spectra were recorded on Bruker AV-400 spectrometers with deuterated chloroform, methyl sulfoxide, or acetone solutions of the compounds at a temperature of 300 K. Chemical shifts (δ) are expressed in parts per million downfield to TMS at δ=0 ppm and coupling constants (J) are expressed in Hertz. IR spectra were recorded on a Bruker Vector-22 spectrophotometer and reported in cm^{-1}. HRMS were recorded on GC-TOF.

4.2. Representative procedure for 2-chloro-2-phenylacetaldehyde (2a)[17]

Under the atmosphere of nitrogen, a mixture of trimethylsulfoxonium iodide (440 mg, 2.0 mmol) and NaH (60%, 96 mg, 2.4 mmol) in dry DMSO (2.0 mL) was stirred at 0 °C for 1 h. A solution of benzaldehyde (191 mg, 1.8 mmol) in DMSO (1.8 mL) was added and the resulting mixture was stirred for 3 h at room temperature. The solution was separated by chloroform (20 mL) and brine (100 mL). The organic layer was washed with brine (30 mL×3) and then stirred with concentrated hydrochloric acid (30 mL) for 3 h at room temperature. The heterogeneous mixture was separated and the aqueous layer was extracted with chloroform (10 mL×3). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography to afford 2-chloro-2-phenylethanol (petroleum ether/EA=4:1, R_f=0.3). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.42–7.31 (m, 5H), 4.99 (q, J=1.5 Hz, 1H), 3.95–3.92 (m, 2H), 2.13 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 138.0, 129.0, 129.0, 127.6, 68.0, 65.0; IR (neat): 3410, 2930, 1257, 1043, 752 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for C_8H_9ClO, m/z 156.0342, found 156.0345.

Under the atmosphere of nitrogen, Dess–Martin periodinane (920 mg, 2.16 mmol) was added into a solution of 2-chloro-2-phenylethanol (282 mg, 1.8 mmol) in dichloromethane (10.0 mL). After stirred for 1 h at room temperature, the heterogeneous mixture was purified by flash chromatography (petroleum ether/EA=8:1, R_f=0.4). **2a** was obtained (211.4 mg, 76% over three steps) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.52 (d, J=2.8 Hz, 1H), 7.43–7.42 (m, 5H), 5.21 (d, J=2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.5, 133.1, 129.7, 129.4, 128.5, 65.2; IR (neat): 2925, 1688, 1255, 1047, 752 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for C_8H_7ClO, m/z 154.0185, found 154.0182.

2f–**k** were prepared according to the procedure for **2a**.

*4.2.1. 2-Chloro-2-(4-tolyl)acetaldehyde (**2f**).* Yield: 242.6 mg, 80%. Yellow oil. R_f (petroleum ether/EA=8:1) 0.4. Intermediate [2-chloro-2-(*p*-tolyl)ethanol]: R_f (petroleum ether/EA=4:1) 0.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.30 (d, J=8.0 Hz, 2H), 7.19 (d, J=7.6 Hz, 2H), 4.98–4.95 (m, 1H), 3.96–3.87 (m, 2H), 2.44 (br, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 139.0, 135.0, 129.6, 127.5, 68.0, 65.0, 21.3; IR (neat): 3400, 2930, 1285, 1180, 1121, 1047, 820, 754 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_9H_{11}ClO$, m/z 170.0498, found 170.0495. **2f**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.51 (d, J=3.2 Hz, 1H), 7.29 (d, J=8.4 Hz, 2H), 7.23 (d, J=8.0 Hz, 2H), 5.18 (d, J=3.2 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.5, 140.0, 130.1, 130.1, 128.4, 65.2, 21.4; IR (neat): 2923, 1683, 1610, 1283, 1178, 1121, 1045, 817, 754 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for C_9H_9ClO, m/z 168.0342, found 168.0345.

*4.2.2. 2-Chloro-2-(4-chlorophenyl)acetaldehyde (**2g**).*[18] Yield: 179.3 mg, 53%. Yellow oil. R_f (petroleum ether/EA=8:1) 0.4. Intermediate [2-chloro-2-(4-chlorophenyl)-ethanol]: R_f (petroleum ether/EA=4:1) 0.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35 (s, 4H), 4.95 (t, J=6.4 Hz, 1H), 3.90 (m, 2H), 2.34 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 136.6, 134.9, 129.1, 129.0, 67.8, 64.0; IR (neat): 3390, 2925, 1491, 1407, 1089, 1069, 1014, 825, 794, 756 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_8H_8Cl_2O$, m/z 189.9952, found 189.9951. **2g**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.51 (d, J=2.8 Hz, 1H), 7.41 (d, J=8.8 Hz, 2H), 7.34 (d, J=8.4 Hz, 2H), 5.18 (d, J=2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.1, 135.9, 131.6, 129.8, 129.6, 64.4; IR (neat): 2925, 1688, 1490, 1146, 1085, 821, 747 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_8H_6Cl_2O$, m/z 187.9796, found 187.9798.

*4.2.3. 2-Chloro-2-(4-bromophenyl)acetaldehyde (**2h**).* Yield: 272.1 mg, 65%. Brown oil. R_f (petroleum ether/EA=8:1) 0.4. Intermediate [2-(4-bromophenyl)-2-chloroethanol]: R_f (petroleum ether/EA=4:1) 0.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.50 (d, J=8.4 Hz, 2H), 7.28 (d, J=8.4 Hz, 2H), 4.93 (t, J=6.4 Hz, 1H), 3.90 (m, 2H), 2.30 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 137.1, 132.1, 129.3, 123.0, 67.8, 64.0; IR (neat): 3388, 1488, 1404, 1069, 1034, 1010, 821 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for C_8H_8BrClO, m/z 233.9447, found 233.9448. **2h**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.49 (d, J=2.4 Hz, 1H), 7.55 (d, J=8.8 Hz, 2H), 7.26 (d, J=8.4 Hz, 2H), 5.17 (d, J=2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.1, 132.5, 132.0, 130.0, 124.0, 64.4; IR (neat): 2923, 1730, 1691, 1588, 1488, 1400, 1131, 1071, 1009, 821, 741 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for C_8H_6BrClO, m/z 231.9291, found 231.9293.

*4.2.4. 2-Chloro-2-(4-fluorophenyl)acetaldehyde (**2i**).* Yield: 139.7 mg, 45%. Yellow oil. R_f (petroleum ether/EA=8:1) 0.4. Intermediate [2-chloro-2-(4-fluorophenyl)ethanol]: R_f (petroleum ether/EA=4:1) 0.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41–7.37 (m, 2H), 7.09–7.04 (m, 2H), 4.97 (t, J=6.6 Hz, 1H), 3.92–3.90 (m, 2H), 2.19 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.0 (d, J=246.8 Hz), 134.0 (d, J=3.0 Hz), 129.5 (d, J=8.5 Hz), 115.9 (d, J=21.8), 68.0, 64.2; IR (neat): 3395, 2925, 1511, 1428, 1297, 1236, 1155, 823 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for C_8H_8ClFO, m/z 174.0248, found 174.0246. **2i**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.52 (d, J=2.8 Hz, 1H), 7.41–7.37 (m, 2H), 7.15–7.10 (m, 2H), 5.20 (d, J=2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.3, 163.5 (d, J=248.6 Hz), 130.4 (d, J=9.3 Hz), 129.0 (d, J=2.8 Hz), 116.5 (d, J=21.2 Hz), 64.4; IR (neat): 2925, 1680, 1603, 1511, 1428, 1294, 1232, 1158, 1050, 839, 768, 738 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for C_8H_6ClFO, m/z 172.0091, found 172.0091.

*4.2.5. 2-Chloro-2-(naphthalen-2-yl)acetaldehyde (**2j**).* Yield: 168.7 mg, 73%. Yellow oil. R_f (petroleum ether/EA=6:1) 0.5. Intermediate [2-chloro-2-(naphthalen-2-yl)ethanol]: R_f (petroleum ether/EA=3:1) 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.89–7.83 (m, 4H), 7.53–7.45 (m, 3H), 5.17–5.14 (m, 1H), 4.08–3.98 (m, 2H), 2.27 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 135.2, 133.5, 133.1, 129.0, 128.2, 127.9, 127.1, 126.9, 126.8, 124.8, 67.9, 65.1; IR (neat): 3441, 3054, 2923, 1122, 1039, 858, 817, 747 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{12}H_{11}ClO$, m/z 206.0498, found 206.0498. **2j**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.62 (d, J=2.4 Hz, 1H), 7.91–7.85 (m, 4H), 7.57–7.53 (m, 2H), 7.47 (dd, J=8.8, 1.6 Hz, 1H), 5.39 (d, J=2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.5, 133.7, 133.3, 130.3, 129.5, 128.4, 128.3, 128.0, 127.4, 127.1, 125.1, 65.6; IR (neat): 2922, 1689, 1124, 1048, 817, 782, 748 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{12}H_9ClO$, m/z 204.0342, found 204.0343.

*4.2.6. 2-Chloro-2-(naphthalen-1-yl)acetaldehyde (**2k**).* Yield: 254.0 mg, 69%. Yellow oil. R_f (petroleum ether/EA=6:1) 0.5. Intermediate [2-chloro-2-(naphthalen-1-yl)ethanol]: R_f (petroleum ether/EA=3:1) 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.13 (d, J=8.4 Hz, 1H), 7.90 (d, J=8.4 Hz, 1H), 7.86 (d, J=8.4 Hz, 1H), 7.73 (d, J=7.2 Hz, 1H), 7.59 (dt, J=7.4, 1.3 Hz, 1H), 7.55–7.48 (m, 2H), 5.86 (t, J=6.2 Hz, 1H), 4.17 (d, J=6.0 Hz, 2H), 2.38 (br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 133.9, 133.3, 130.7, 129.7, 129.2, 126.9, 126.1, 125.4, 125.4, 122.7, 67.3, 61.4; IR (neat): 3420, 3050, 2924, 1166, 1050, 797, 775 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{12}H_{11}ClO$, m/z 206.0498, found 206.0497. **2k**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.69 (d, J=1.6 Hz, 1H), 8.02 (d, J=8.4 Hz, 1H), 7.92 (d, J=8.0 Hz, 2H), 7.65–7.50 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 192.0, 134.2, 130.8, 130.7, 129.3, 129.0, 128.0, 127.4, 126.6, 125.5, 123.2, 63.7; IR (neat): 2970, 1733, 1685, 1511, 1408, 1050, 774 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{12}H_9ClO$, m/z 204.0342, found 204.0343.

4.3. Representative procedure for 2-chloro-2-(4-methoxyphenyl) acetaldehyde (2b)[18]

At 0 °C, to a solution of 2-(4-methoxyphenyl)acetaldehyde (300 mg, 2.0 mmol) and L-proline (23 mg, 0.2 mmol) in DCM

(4.0 mL), *N*-chlorosuccinimide (0.32 g, 2.4 mmol) was added. The mixture was stirred for 3 h at room temperature. **2b** was obtained (328.6 mg, 89%) as yellow oil by flash chromatography (petroleum ether/EA=6:1, R_f=0.5). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.50 (d, J=2.4 Hz, 1H), 7.32 (d, J=8.4 Hz, 2H), 6.94 (d, J=8.4 Hz, 2H), 5.18 (d, J=2.4 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.4, 160.7, 129.9, 125.0, 114.8, 65.1, 55.5; IR (neat): 2934, 1686, 1601, 1511, 1249, 1172, 1028, 832, 735 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_9H_9ClO_2$, *m*/*z* 184.0291, found 184.0291.

2c, **2d**, and **2e** were prepared according to the procedure for **2b**.

*4.3.1. 2-Chloro-2-(2-methoxyphenyl)acetaldehyde (**2c**).*[18] Yield: 309.9 mg, 84%. Yellow oil. R_f (petroleum ether/EA=6:1) 0.6. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.62 (d, J=1.6 Hz, 1H), 7.40–7.34 (m, 2H), 7.01 (t, J=7.3 Hz, 1H), 6.93 (d, J=8.0 Hz, 1H), 5.55 (s, 1H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 192.9, 156.9, 131.2, 130.5, 122.9, 121.3, 111.4, 61.4, 55.8; IR (neat): 2923, 1734, 1491, 1463, 1248, 1023, 753 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_9H_9ClO_2$, *m*/*z* 184.0291, found 184.0292.

*4.3.2. 2-Chloro-2-[4-(Boc-amino)phenyl]acetaldehyde (**2d**).* Prepared from 2-[4-(Boc-amino)phenyl]acetaldehyde.[19] Yield: 468.9 mg, 87%. Viscous oil. R_f (petroleum ether/EA=5:1) 0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.49 (d, J=2.8 Hz, 1H), 7.43 (d, J=8.4 Hz, 2H), 7.32 (d, J=8.4 Hz, 2H), 6.56 (br, 1H), 5.16 (d, J=2.8 Hz, 1H), 1.52 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.3, 139.9, 129.3, 127.1, 119.1, 81.2, 65.0, 28.4; IR (neat): 2972, 2904, 1701, 1400, 1232, 1053, 895 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{13}H_{16}ClNO_3$, *m*/*z* 269.0819, found 269.0818.

*4.3.3. 2-Chloro-2-(3-methoxyphenyl)acetaldehyde (**2e**).* Yield: 269.4 mg, 73%. Yellow oil. R_f (petroleum ether/EA=6:1) 0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.49 (d, J=2.4 Hz, 1H), 7.35–7.30 (m, 1H), 6.98 (t, J=7.6 Hz, 1H), 6.94–6.93 (m, 2H), 5.18 (d, J=2.4 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.3, 160.2, 134.3, 130.5, 120.6, 115.3, 113.8, 65.2, 55.5; IR (neat): 2925, 1705, 1495, 1249, 1030, 755 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_9H_9ClO_2$, *m*/*z* 184.0291, found 184.0291.

4.4. General procedure for 3-arylcoumarins (5 and 6)

*Representative experimental procedure for 3-phenylcoumarin (**5a**).*[20] Under an atmosphere of nitrogen, a mixture of **3a** (18.4 mg, 0.05 mmol), 4 Å MS (0.5 g), Et_3N (202.0 mg, 2.0 mmol), 2-chloro-2-phenylacetaldehyde (1.0 mmol), and salicylaldehyde (0.5 mmol) in ethyl acetate (1.0 mL) was heated at 80 °C for 4 h. The mixture was filtered and the residue was washed with 5 mL ethyl acetate. The filtrate was concentrated and the crude product was purified by flash chromatography (petroleum ether/EA=4:1, R_f=0.5). **5a** was obtained as a white solid (88.5 mg, 80%). Mp: 139–141 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.82 (s, 1H), 7.71 (d, J=7.6 Hz, 2H), 7.55 (d, J=8.0 Hz, 1H), 7.53 (d, J=8.8 Hz, 1H), 7.47–7.41 (m, 3H), 7.37 (d, J=8.4 Hz, 1H), 7.30 (t, J=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.7, 153.7, 140.0, 134.9, 131.5, 129.0, 128.7, 128.6, 128.5, 128.1, 124.7, 119.8, 116.6; IR (neat): 2979, 1710, 1610, 1400, 1250, 1055, 755 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{15}H_{10}O_2$, *m*/*z* 222.0681, found 222.0681.

*4.4.1. 3-(4-Methoxyphenyl)coumarin (**5b**).*[20] Yield: 107.2 mg, 85%. White solid. Mp: 141–142 °C. R_f (petroleum ether/EA=6:1) 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.77 (s, 1H), 7.68 (d, J=8.4 Hz, 2H), 7.53 (d, J=7.6 Hz, 1H), 7.50 (d, J=7.6 Hz, 1H), 7.36 (d, J=8.4 Hz, 1H), 7.29 (t, J=8.0 Hz, 1H), 6.98 (d, J=8.8 Hz, 2H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.9, 160.3, 153.4, 138.6, 131.1, 130.0, 128. 0, 127.9, 127.2, 124.6, 120.0, 116.5, 114.1, 55.5; IR (neat): 2970, 1721, 1605, 1505, 1238, 753 cm^{-1}. HRMS (TOFMS EI$^+$) calcd for $C_{16}H_{12}O_3$, *m*/*z* 252.0786, found 252.0787.

*4.4.2. 3-(2-Methoxyphenyl)coumarin (**5c**).*[8] Yield: 103.2 mg, 82%. White solid. Mp: 140–141 °C. R_f (petroleum ether/EA=4:1) 0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.74 (s, 1H), 7.53–7.49 (m, 2H), 7.41–7.36 (m, 3H), 7.28 (t, J=7.2 Hz, 1H) 7.05–6.99 (m, 2H), 3.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.5, 157.4, 153.9, 141.9, 131.3, 130.9, 130.4, 128.0, 126.8, 124.4, 124.2, 120.8, 119.7, 116.7, 111.5, 55.9; IR (neat): 2962, 1723, 1605, 1491, 1458, 1244, 1124, 1099, 1049, 1024, 751 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{16}H_{12}O_3$, *m*/*z* 252.0786, found 252.0786.

*4.4.3. 3-[4-(Boc-amino)phenyl]coumarin (**5d**).* Yield: 109.6 mg, 65%. Yellow solid. Mp: 177–178 °C. R_f (petroleum ether/EA=4:1) 0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.77 (s, 1H), 7.66 (d, J=8.8 Hz, 2H), 7.54–7.48 (m, 2H), 7.44 (d, J=8.4 Hz, 2H), 7.34 (d, J=8.0 Hz, 1H), 7.28 (t, J=6.8 Hz, 1H), 6.73 (br, 1H), 1.53 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.7, 153.5, 152.8, 139.2, 139.0, 131.3, 129.4, 129.3, 128.0, 127.8, 124.6, 119.9, 118.3, 116.5, 80.9, 28.5; IR (neat): 2977, 1716, 1610, 1522, 1230, 1154, 1052, 735 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{20}H_{19}NO_4$, *m*/*z* 337.1314, found 337.1315. Anal. Calcd for $C_{20}H_{19}NO_4$: C, 71.20; H, 5.68; N, 4.15. Found: C, 71.31; H, 5.71; N, 4.03.

*4.4.4. 3-(3-Methoxyphenyl)coumarin (**5e**).*[6b] Yield: 72.0 mg, 57%. White solid. Mp: 78–79 °C. R_f (petroleum ether/EA=6:1) 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81 (s, 1H), 7.54–7.50 (m, 2H), 7.37–7.33 (m, 2H), 7.31–7.26 (m, 3H), 6.95 (dd, J=8.2, 1.4 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.6, 159.7, 153.6, 140.2, 136.1, 131.6, 129.6, 128.2, 128.1, 124.6, 121.0, 119.7, 116.6, 114.6, 114.3, 55.5; IR (neat): 2970, 2904, 1720, 1603, 1456, 1260, 1105, 1046, 787, 755, 692 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{16}H_{12}O_3$, *m*/*z* 252.0786, found 252.0788.

*4.4.5. 3-(4-Tolyl)coumarin (**5f**).*[21] Yield: 98.9 mg, 84%. White solid. Mp: 157–158 °C. R_f (petroleum ether/EA=6:1) 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.80 (s, 1H), 7.61 (d, J=8.4 Hz, 2H), 7.55–7.51 (m, 2H), 7.37 (d, J=8.0 Hz, 1H), 7.32–7.26 (m, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.9, 153.5, 139.4, 139.1, 131.9, 131.3, 129.3, 128.5, 128.4, 127.9, 124.6, 119.9, 116.5, 21.4; IR (neat): 2968, 1718, 1610, 1272, 1102, 1060, 753 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{16}H_{12}O_2$, *m*/*z* 236.0837, found 236.0837.

*4.4.6. 3-(4-Chlorophenyl)coumarin (**5g**).*[22] Yield: 74.3 mg, 58%. Yellow solid. Mp: 184–185 °C. R_f (petroleum ether/EA=6:1) 0.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.83 (s, 1H), 7.67 (d, J=8.4 Hz, 2H), 7.57–7.54 (m, 2H), 7.43 (d, J=8.4 Hz, 2H), 7.38 (d, J=8.8 Hz, 1H), 7.32 (t, J=8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.5, 153.7, 140.1, 133.2, 131.9, 130.2, 130.0, 128.9, 128.2, 127.3, 124.8, 119.6, 116.7; IR (neat): 2973, 2903, 1713, 1608, 1512, 1221,1072, 835, 755 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{15}H_9ClO_2$, *m*/*z* 256.0291, found 256.0293.

*4.4.7. 3-(4-Bromophenyl)coumarin (**5h**).*[23] Yield: 93.3 mg, 62%. White solid. Mp: 193–194 °C. R_f (petroleum ether/EA=6:1) 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.83 (s, 1H), 7.62–7.54 (m, 6H), 7.38 (d, J=8.4 Hz, 1H), 7.32 (t, J=7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.4, 153.6, 140.1, 133.7, 131.9, 131.8, 130.2, 128.2, 127.2, 124.8, 123.3, 119.6, 116.6; IR (neat): 2972, 2903, 1715, 1608, 1510, 1218, 1056, 833, 752 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{15}H_9BrO_2$, *m*/*z* 299.9786, found 299.9784.

*4.4.8. 3-(4-Fluorophenyl)coumarin (**5i**).* Yield: 54.0 mg, 45%. White solid. Mp: 152–154 °C. R_f (petroleum ether/EA=6:1) 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.80 (s, 1H), 7.72–7.68 (m, 2H), 7.56–7.52 (m, 2H), 7.37 (d, J=8.8 Hz, 1H), 7.31 (t, J=7.4 Hz, 1H), 7.16–7.11 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.3 (d, J=247.9 Hz), 160.7, 153.7,

139.9, 131.7, 130.9 (d, J=3.5 Hz), 130.6 (d, J=8.8 Hz), 128.1, 127.5, 124.8, 119.7, 116.7, 115.7 (d, J=21.6 Hz); IR (neat): 2972, 2904, 1721, 1605, 1510, 1227, 1072, 836, 757 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{15}H_9FO_2$, m/z 240.0587, found 240.0585. Anal. Calcd for $C_{15}H_9FO_2$: C, 75.00; H, 3.78. Found: C, 75.13; H, 3.82.

*4.4.9. 3-(Naphthalen-2-yl)coumarin (**5j**).*[8] Yield: 122.4 mg, 90%. Yellow solid. Mp: 178 °C. R_f (petroleum ether/EA=6:1) 0.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.25 (s, 1H), 7.95 (s, 1H), 7.93–7.86 (m, 3H), 7.81 (d, J=8.8 Hz, 1H), 7.60–7.51 (m, 4H), 7.41 (d, J=8.0 Hz, 1H), 7.33 (t, J=7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.8, 153.6, 140.3, 133.4, 133.2, 132.2, 131.6, 128.6, 128.2, 128.1, 127.7, 126.9, 126.5, 126.0, 124.7, 119.8, 116.6; IR (neat): 2972, 1715, 1608, 1505, 1411, 1257, 1071, 760 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{19}H_{12}O_2$, m/z 272.0837, found 272.0838.

*4.4.10. 3-(Naphthalen-1-yl)coumarin (**5k**).*[8] Yield: 112.8 mg, 83%. Yellow solid. Mp: 154–156 °C. R_f (petroleum ether/EA=6:1) 0.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.92 (t, J=7.6 Hz, 2H), 7.84 (s, 1H), 7.79 (d, J=8.4 Hz, 1H), 7.62–7.45 (m, 7H), 7.35 (t, J=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.0, 154.1, 143.0, 133.8, 132.8, 131.8, 131.7, 129.5, 128.7, 128.4, 128.1, 127.8, 126.6, 126.2, 125.4, 125.3, 124.7, 119.4, 116.8; IR (neat): 2972, 1718, 1685, 1511, 1085, 755 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{19}H_{12}O_2$, m/z 272.0837, found 272.0838.

*4.4.11. 6-Methoxy-3-phenylcoumarin (**6b**).*[24] Yield: 107.3 mg, 85%. Pale yellow solid. Mp: 155–157 °C. R_f (petroleum ether/EA=6:1) 0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.78 (s, 1H), 7.70 (d, J=7.2 Hz, 2H), 7.47–7.41 (m, 3H), 7.31 (d, J=9.2 Hz, 1H), 7.14 (dd, J=9.2, 2.4 Hz, 1H), 6.98 (d, J=2.4 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.9, 156.3, 148.1, 139.8, 134.9, 129.0, 128.8, 128.7, 128.6, 120.2, 119.3, 117.6, 110.1, 56.0; IR (neat): 2969, 1722, 1611, 1511, 1255, 1051, 752 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{16}H_{12}O_3$, m/z 252.0786, found 252.0789.

*4.4.12. 7-Methoxy-3-phenylcoumarin (**6c**).*[6c] Yield: 71.8 mg, 57%. White solid. Mp: 122–124 °C. R_f (petroleum ether/EA=6:1) 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.76 (s, 1H), 7.69 (d, J=7.6 Hz, 2H), 7.45–7.36 (m, 4H), 6.87 (d, J=7.6 Hz, 1H), 6.86 (s, 1H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.7, 161.6, 155.4, 140.2, 135.1, 129.0, 128.6, 128.5, 124.9, 113.5, 112.9, 100.5, 55.9; IR (neat): 2973, 1717, 1238, 1607, 1506, 1238, 1055, 753 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{16}H_{12}O_3$, m/z 252.0786, found 252.0788.

*4.4.13. 8-Methoxy-3-phenylcoumarin (**6d**).*[25] Yield: 100.7 mg, 80%. White solid. Mp: 154–156 °C. R_f (petroleum ether/EA=6:1) 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.80 (s, 1H), 7.72 (d, J=7.2 Hz, 2H), 7.47–7.40 (m, 3H), 7.22 (d, J=8.0 Hz, 1H), 7.12 (d, J=8.0 Hz, 1H), 7.08 (d, J=8.0 Hz, 1H), 3.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.1, 147.1, 143.2, 140.1, 134.8, 129.0, 128.6, 124.5, 120.4, 119.4, 113.3, 56.3; IR (neat): 2977, 1713, 1608, 1508, 1277, 1100, 752 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{16}H_{12}O_3$, m/z 252.0786, found 252.0788.

*4.4.14. 3-Phenyl-benzo[h]coumarin (**6e**).*[26] Yield: 39.5 mg, 29%. Yellow solid. Mp: 213–215 °C. R_f (petroleum ether/EA=5:1) 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.61–8.59 (m, 1H), 7.95 (s, 1H), 7.90–7.88 (m, 1H), 7.79 (d, J=6.8 Hz, 2H), 7.70 (d, J=8.8 Hz, 1H), 7.67–7.64 (m, 2H), 7.53–7.41 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.9, 150.8, 140.8, 135.0, 134.8, 129.0, 128.8, 128.7, 128.6, 128.0, 127.8, 127.4, 124.7, 123.9, 123.1, 122.6, 115.3; IR (neat): 2976, 1729, 1605, 1403, 1265, 1124, 1053, 752, 692 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{19}H_{12}O_2$, m/z 272.0837, found 272.0838.

*4.4.15. 2-Phenyl-benzo[f]coumarin (**6f**).*[27] Yield: 120.9 mg, 89%. Yellow solid. Mp: 181–182 °C. R_f (petroleum ether/EA=6:1) 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.61 (s, 1H), 8.32 (d, J=8.4 Hz, 1H), 8.00 (d, J=9.2 Hz, 1H), 7.94 (d, J=8.0 Hz, 1H), 8.12 (d, J=6.8 Hz, 2H), 7.71 (t, J=7.8 Hz, 1H), 7.59 (t, J=7.6 Hz, 1H), 7.53–7.43 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.8, 153.2, 135.9, 135.2, 132.9, 130.4, 129.2, 129.0, 128.7, 128.3, 127.3, 126.2, 121.5, 116.8, 113.9; IR (neat): 2970, 1731, 1605, 1403, 1258, 1055, 758, 696 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{19}H_{12}O_2$, m/z 272.0837, found 272.0839.

*4.4.16. 6-Chloro-3-phenylcoumarin (**6g**).*[28] Yield: 44.9 mg, 35%. White solid. Mp: 200 °C. R_f (petroleum ether/EA=6:1) 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.74 (s, 1H), 7.69 (d, J=7.2 Hz, 2H), 7.53 (s, 1H), 7.49–7.41 (m, 4H), 7.32 (d, J=8.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.2, 152.0, 138.6, 134.4, 131.5, 129.9, 129.7, 129.4, 128.7, 127.2, 120.9, 118.1; IR (neat): 2972, 2903, 1709, 1603, 1225, 1070, 780, 696 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{15}H_9ClO_2$, m/z 256.0291, found 256.0293.

*4.4.17. 8-Chloro-3-phenylcoumarin (**6h**).*[29] Yield: 44.8 mg, 35%. White solid. Mp: 167–169 °C. R_f (petroleum ether/EA=6:1) 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.79 (s, 1H), 7.70 (d, J=7.2 Hz, 2H), 7.57 (d, J=8.0 Hz, 1H), 7.47–7.40 (m, 4H), 7.23 (t, J=7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.6, 149.4, 139.5, 134.3, 131.8, 129.3, 129.2, 128.7, 126.5, 124.8, 121.4, 121.1; IR (neat): 2972, 2904, 1711, 1600, 1450, 1225, 1109, 1072, 778, 692 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{15}H_9ClO_2$, m/z 256.0291, found 256.0292.

*4.4.18. 6-Bromo-3-phenylcoumarin (**6i**).*[4d] Yield: 58.7 mg, 39%. White solid. Mp: 170–171 °C. R_f (petroleum ether/EA=6:1) 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.73 (s, 1H), 7.70–7.68 (m, 3H), 7.62 (dd, J=8.8, 2.0 Hz, 1H), 7.48–7.43 (m, 3H), 7.26 (t, J=4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.1, 152.4, 138.5, 134.3, 134.2, 130.3, 129.6, 129.4, 128.7, 121.3, 118.3, 117.2; IR (neat): 2971, 1710, 1607, 1218, 1054, 835, 756 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{15}H_9BrO_2$, m/z 299.9786, found 299.9784.

*4.4.19. 8-Bromo-3-phenylcoumarin (**6j**).*[29] Yield: 70.7 mg, 47%. White solid. Mp: 185–186 °C. R_f (petroleum ether/EA=8:1) 0.3. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.78 (s, 1H), 7.75 (dd, J=7.8, 1.4 Hz, 1H), 7.70 (dd, J=8.0, 1.6 Hz, 2H), 7.51–7.41 (m, 4H), 7.18 (t, J=7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.7, 150.3, 139.5, 134.9, 134.2, 129.3, 129.1, 128.7, 128.6, 127.3, 125.3, 121.0, 110.0; IR (neat): 2976, 2906, 1713, 1598, 1400, 1221, 1068, 782, 697 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{15}H_9BrO_2$, m/z 299.9786, found 299.9785.

*4.4.20. 6-Methyl-3-phenylcoumarin (**6k**).*[1c] Yield: 101.5 mg, 86%. White solid. Mp: 144–145 °C. R_f (petroleum ether/EA=6:1) 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.73 (s, 1H), 7.68 (dd, J=8.2, 1.4 Hz, 2H), 7.45–7.38 (m, 3H), 7.31 (d, J=7.6 Hz, 1H), 7.30 (s, 1H), 7.23 (d, J=9.2 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.9, 151.7, 140.0, 134.9, 134.3, 132.6, 128.9, 128.6, 128.5, 128.2, 127.8, 119.5, 116.2, 20.9; IR (neat): 2971, 2905, 1718, 1618, 1294, 1104, 1073, 958, 787, 694 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{16}H_{12}O_2$, m/z 236.0837, found 236.0836.

*4.4.21. 8-Methyl-3-phenylcoumarin (**6l**).*[25] Yield: 98.0 mg, 83%. White solid. Mp: 112–114 °C. R_f (petroleum ether/EA=5:1) 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.79 (s, 1H), 7.71 (dd, J=8.2, 1.4 Hz, 2H), 7.19 (t, J=7.4 Hz, 1H), 7.48–7.40 (m, 3H), 7.37 (d, J=7.6 Hz, 2H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.8, 152.0, 140.4, 135.0, 132.8, 128.9, 128.6, 128.0, 126.0, 125.8, 124.2, 119.5, 15.6; IR (neat): 2971, 2905, 1712, 1602, 1227, 1109, 1062, 777, 736, 696 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{16}H_{12}O_2$, m/z 236.0837, found 236.0837.

*4.4.22. 6,8-Di-tert-butyl-3-phenylcoumarin (**6m**).* Yield: 93.6 mg, 56%. White solid. Mp: 140–141 °C. R_f (petroleum ether/EA=6:1) 0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.84 (s, 1H), 7.77–7.75 (m, 2H), 7.61 (d, J=2.4 Hz, 1H), 7.47–7.38 (m, 4H), 1.58 (s, 9H), 1.40 (s, 9H); ^{13}C

NMR (100 MHz, $CDCl_3$) δ: 160.5, 150.4, 146.8, 141.4, 137.1, 135.1, 128.7, 128.6, 128.5, 127.1, 126.8, 122.7, 119.7, 35.2, 34.8, 31.5, 30.1; IR (neat): 2968, 2904, 1715, 1452, 1397, 1229, 1110, 1072, 950, 899, 696 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{23}H_{26}O_2$, m/z 334.1933, found 334.1934. Anal. Calcd for $C_{23}H_{26}O_2$: C, 82.60; H, 7.84. Found: C, 82.69; H, 7.91.

*4.4.23. 6-(Boc-amino)-3-phenylcoumarin (**6n**).* Prepared from **2a** (154.5 mg, 1.0 mmol) and **4n**[30] (118.6 mg, 0.5 mmol). Yield: 151.7 mg, 90%. Yellow solid. Mp: 133–135 °C. R_f (petroleum ether/EA=4:1) 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.85 (s, 1H), 7.78 (s, 1H), 7.68 (d, J=6.8 Hz, 2H), 7.47–7.41 (m, 3H), 7.28 (s, 2H), 6.62 (br, 1H), 1.53 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.9, 153.0, 149.3, 140.0, 135.2, 134.8, 129.0, 128.7, 128.6, 122.3, 120.0, 116.8, 116.7, 81.1, 28.4; IR (neat): 2979, 1706, 1619, 1579, 1539, 1229, 1158, 1111, 1055 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{20}H_{19}NO_4$, m/z 337.1314, found 337.1317. Anal. Calcd for $C_{20}H_{19}NO_4$: C, 71.20; H, 5.68; N, 4.15. Found: C, 71.33; H, 5.75; N, 4.06.

*4.4.24. 6-Ethoxy-carbonyl-3-phenylcoumarin (**6o**).* Prepared from **2a** (154.5 mg, 1.0 mmol) and **4o**[31] (97.1 mg, 0.5 mmol). Yield: 80.9 mg, 55%. White solid. Mp: 180–181 °C. R_f (petroleum ether/EA=3:1) 0.4. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.28 (d, J=2.0 Hz, 1H), 8.20 (dd, J=9.0, 1.8 Hz, 1H),7.87 (s, 1H), 7.72–7.70 (m, 2H), 7.49–7.40 (m, 4H), 4.42 (d, J=7.2 Hz, 2H), 1.43 (t, J=7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 165.4, 160.0, 156.3, 139.4, 134.3, 132.4, 130.0, 129.3, 129.2, 128.7, 128.6, 127.1, 119.5, 116.7, 61.6, 14.4; IR (neat): 2975, 2905, 1720, 1690, 1613, 1505, 1398, 1225, 1147, 1060, 853, 754 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{18}H_{14}O_4$, m/z 294.0892, found 294.0893. Anal. Calcd for $C_{18}H_{14}O_4$: C, 73.46; H, 4.79. Found: C, 73.53; H, 4.86.

*4.4.25. 6-Hydroxy-3-phenylcoumarin (**6p**).*[4c] Prepared from **2a** (154.5 mg, 1.0 mmol) and **4p**[32] (69.1 mg, 0.5 mmol) in the presence of Et_3N (252.5 mg, 2.5 mmol). Yield: 61.9 mg, 52%. White solid. Mp: 201–203 °C. R_f (petroleum ether/EA=2:1) 0.3. ^{1}H NMR (400 MHz, Acetone-d_6) δ: 7.72 (s, 1H), 7.69 (dd, J=7.6, 1.2 Hz, 2H), 7.47–7.41 (m, 3H), 7.25 (d, J=8.8 Hz, 1H), 7.04 (dd, J=8.8, 3.2 Hz, 1H), 6.97 (d, J=2.4 Hz, 1H), 5.50 (br, 1H); ^{13}C NMR (100 MHz, Acetone-d_6) δ: 159.9, 153.9, 147.3, 140.0, 135.3, 128.6, 128.5, 128.1, 127.9, 120.4, 119.5, 116.8, 112.6; IR (neat): 3220, 2977, 1710, 1620, 1510, 1215, 763 cm^{-1}; HRMS (TOFMS EI$^+$) calcd for $C_{15}H_{10}O_3$, m/z 238.0630, found 238.0630.

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Supplementary data

Copies of ^{1}H NMR and ^{13}C NMR for **2**, **5**, and **6**. This material is available free of charge via the Internet. Supplementary data related to this article can be found online at http://dx.doi.org/10.1016/j.tet.2013.03.025.

References and notes

1. (a) Aggarwal, B. B.; Bhardwaj, A.; Aggarwal, R. S.; Seeram, N. P.; Shishodia, S.; Takada, Y. *Anticancer Res.* **2004**, *24*, 2783–2840; (b) Zhao, H. P.; Yan, B.; Peterson, L. B.; Blagg, B. S. J. *ACS Med. Chem. Lett.* **2012**, *3*, 327–331; (c) Matos, M. J.; Terán, C.; Pérez-Castillo, Y.; Uriarte, E.; Santana, L.; Viña, D. *J. Med. Chem.* **2011**, *54*, 7127–7137.
2. Rajendran, M.; Inbaraj, J. J.; Gandhidasan, R.; Murugesan, R. *J. Photochem. Photobiol., A* **2006**, *182*, 67–74.
3. (a) Sethna, S. M.; Shah, N. M. *Chem. Rev.* **1945**, *36*, 1–62; (b) Reddy, Y. T.; Sonar, V. N.; Crooks, P. A.; Dasari, P. K.; Reddy, P. N.; Rajitha, B. *Synth. Commun.* **2008**, *38*, 2082–2088; (c) Kim, S.; Kang, D.; Lee, C.-H.; Lee, P. H. *J. Org. Chem.* **2012**, *77*, 6530–6537; (d) Vilar, S.; Quezada, E.; Santana, L.; Uriarte, E.; Yanez, M.; Fraiz, N.; Alcaide, C.; Cano, E.; Orallo, F. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 257–261.
4. (a) Sashidhara, K. V.; Palnati, G. R.; Avula, S. R.; Kumar, A. *Synlett* **2012**, 611–621; (b) Roussaki, M.; Kontogiorgis, C. A.; Hadjipavlou-Litina, D.; Hamilakis, S.; Detsi, A. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 3889–3892; (c) Kabeya, L. M.; de Marchi, A. A.; Kanashiro, A.; Lopes, N. P.; da Silva, C. H. T. P.; Pupo, M. T.; Lucisano-Valima, Y. M. *Bioorg. Med. Chem.* **2007**, *15*, 1516–1524; (d) Mashraqui, S. H.; Vashi, D.; Mistry, H. D. *Synth. Commun.* **2004**, *34*, 3129–3134.
5. (a) Kadnikov, D. V.; Larock, R. C. *Org. Lett.* **2000**, *2*, 3643–3646; (b) Kadnikov, D. V.; Larock, R. C. *J. Org. Chem.* **2003**, *68*, 9423–9432; (c) Park, K. H.; Jung, I. G.; Chung, Y. K. *Synlett* **2004**, 2541–2544.
6. (a) Schiedel, M. S.; Briehn, C. A.; Bauerle, P. *Angew. Chem., Int. Ed.* **2001**, *40*, 4677–4680; (b) Matos, M. J.; Vazquez-Rodriguez, S.; Borges, F.; Santana, L.; Uriarte, E. *Tetrahedron Lett.* **2011**, *52*, 1225–1227; (c) Messaoudi, S.; Brion, J. D.; Alami, M. *Org. Lett.* **2012**, *14*, 1496–1499.
7. Manhas, M. S.; Ganguly, S. N.; Mukherjee, S.; Jain, A. K.; Bose, A. K. *Tetrahedron Lett.* **2006**, *47*, 2423–2425.
8. Buchynskyy, A.; Kempin, U.; Vogel, S.; Hennig, L.; Findeisen, M.; Müller, D.; Giesa, S.; Knoll, H.; Welzel, P. *Eur. J. Org. Chem.* **2002**, 1149–1162.
9. Yoshida, H.; Ito, Y.; Ohshita, J. *Chem. Commun.* **2011**, 8512–8514.
10. (a) Phillips, E. M.; Wadamoto, M.; Roth, H. S.; Ott, A. W.; Scheidt, K. A. *Org. Lett.* **2009**, *11*, 105–108; (b) Zeitler, K.; Rose, C. A. *J. Org. Chem.* **2009**, *74*, 1759–1762; (c) Nair, V.; Sinu, C. R.; Rejithamol, R.; Lakshmi, K. C. S.; Suresh, E. *Org. Biomol. Chem.* **2011**, *9*, 5511–5514.
11. (a) Toräng, J.; Vanderheiden, S.; Nieger, M.; Bräse, S. *Eur. J. Org. Chem.* **2007**, 943–952; (b) Behrenswerth, A.; Volz, N.; Torang, J.; Hinz, S.; Bräse, S.; Muller, C. E. *Bioorg. Med. Chem.* **2009**, *17*, 2842–2851; (c) Gross, U.; Gross, P. J.; Shi, M.; Bräse, S. *Synlett* **2011**, 635–638.
12. Jiang, Y.; Chen, W.; Lu, W. *RSC Adv.* **2012**, *2*, 1540–1546.
13. (a) Reynolds, N. T.; de Alaniz, J. R.; Rovis, T. *J. Am. Chem. Soc.* **2004**, *126*, 9518–9519; (b) Reynolds, N. T.; Rovis, T. *J. Am. Chem. Soc.* **2005**, *127*, 16406–16407; (c) He, M.; Uc, G. J.; Bode, J. W. *J. Am. Chem. Soc.* **2006**, *128*, 15088–15089; (d) Vora, H. U.; Rovis, T. *J. Am. Chem. Soc.* **2007**, *129*, 13796–13797; (e) He, M.; Beahm, B. J.; Bode, J. W. *Org. Lett.* **2008**, *10*, 3817–3820; (f) Padmanaban, M.; Biju, A. T.; Glorius, F. *Org. Lett.* **2011**, *13*, 98–101.
14. (a) Chow, K. Y. K.; Bode, J. W. *J. Am. Chem. Soc.* **2004**, *126*, 8126–8127; (b) Vora, H. U.; Moncecchi, J. R.; Epstein, O.; Rovis, T. *J. Org. Chem.* **2008**, *73*, 9727–9731; (c) Kawanaka, Y.; Phillips, E. M.; Scheidt, K. A. *J. Am. Chem. Soc.* **2009**, *131*, 18028–18029.
15. (a) Sohn, S. S.; Bode, J. W. *Angew. Chem., Int. Ed.* **2006**, *45*, 6021–6024; (b) Bode, J. W.; Sohn, S. S. *J. Am. Chem. Soc.* **2007**, *129*, 13798–13799.
16. Halland, N.; Braunton, A.; Bachmann, S.; Marigo, M.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2004**, *126*, 4790–4791.
17. Boni, M.; Ghelfi, F.; Pagnoni, U. M.; Pinetti, A. *Synth. Commun.* **1993**, *23*, 1915–1921.
18. Villieras, J.; Bacquet, C.; Normant, J. F. *J. Organomet. Chem.* **1975**, *97*, 325–354.
19. Joossens, J.; Ali, O. M.; El-Sayed, I.; Surpateanu, G.; Van der Veken, P.; Lambeir, A.-M.; Setyono-Han, B.; Foekens, J. A.; Schneider, A.; Schmalix, W.; Haemers, A.; Augustyns, K. *J. Med. Chem.* **2007**, *50*, 6638–6646.
20. Taksande, K.; Borse, D. S.; Lokhande, P. *Synth. Commun.* **2010**, *40*, 2284–2290.
21. Zhao, Y.; Zhang, Y.; Lv, X.; Liu, Y. L.; Chen, M. L.; Wang, P.; Liu, J.; Guo, W. *J. Mater. Chem.* **2011**, *21*, 13168–13171.
22. Mosrin, M.; Monzon, G.; Bresser, T.; Knochel, P. *Chem. Commun.* **2009**, 5615–5617.
23. Martins, S.; Branco, P. S.; de la Torre, M. C.; Sierra, M. A.; Pereira, A. *Synlett* **2010**, 2918–2922.
24. Eicher, T.; Schneider, V. *Synthesis* **1989**, 372–378.
25. Viña, D.; Matos, M. J.; Ferino, G.; Cadoni, E.; Laguna, R.; Borges, F.; Uriarte, E.; Santana, L. *ChemMedChem* **2012**, *7*, 464–470.
26. Suresh, S.; Periasamy, M. *J. Chem. Res., Synop.* **2006**, 688–690.
27. Kamat, S. P.; D'Souza, A. M.; Paknikar, S. K.; Beauchamp, P. S. *J. Chem. Res., Synop.* **2002**, 242–246.
28. Mhiri, C.; Ladhar, F.; El Gharbi, R.; Le Bigot, Y. *Synth. Commun.* **1999**, *29*, 1451–1461.
29. Liang, X. R.; Zhao, B.; Zhou, Z. H. *Acta Phys. Sin.* **2006**, *55*, 723–728.
30. Di Bella, S.; Consiglio, G.; Leonardi, N.; Failla, S.; Finocchiaro, P.; Fragala, I. *Eur. J. Inorg. Chem.* **2004**, 2701–2705.
31. Hada, K.; Suda, A.; Asoh, K.; Tsukuda, T.; Hasegawa, M.; Sato, Y.; Ogawa, K.; Kuramoto, S.; Aoki, Y.; Shimma, N.; Ishikawa, T.; Koyano, H. *Bioorg. Med. Chem.* **2012**, *20*, 1442–1460.
32. Passiniemi, M.; Myllymaki, M. J.; Vuokko, J.; Koskinen, A. M. P. *Lett. Org. Chem.* **2011**, *8*, 48–52.