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Copper-Catalyzed Intramolecular Tandem Reaction of (2-Halogenphenyl)(3-phenyloxiran-2-yl)methanones: Synthesis of (*Z*)-Aurones

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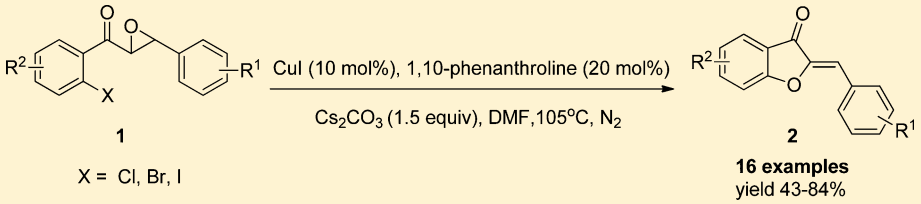
Supporting Information



ABSTRACT: A convenient and efficient method for the copper-catalyzed synthesis of (*Z*)-aurones via intramolecular tandem reaction of (2-halogenphenyl)(3-phenyloxiran-2-yl)methanones is reported. Moreover, a plausible mechanism for the formation of (*Z*)-aurones is proposed. This is the first report on the synthesis of (*Z*)-aurones through copper-catalyzed Ullmann coupling reaction employing epoxides as substrates.

Aurones [2-benzylidenebenzofuran-3(2*H*)-ones] are isomers of flavones, a subclass of the flavonoid family,[1] widely present in fruits and the bright golden yellow color of flowers.[2] Aurones exhibit a wide range of biological activities,[1] such as antioxidant,[3] insect antifeedant,[4] anticancer,[5] inhibition of tyrosinase,[6] antiparasitic,[7] antimicrobial,[8] etc. Therefore, the synthesis of aurones is still in great demand due to their wide range of biological activities.

Common synthetic routes for the preparation of aurones involve condensation of benzaldehydes with benzofuran-3(2*H*)-ones catalyzed by alumina,[9] acid,[5] or base,[6] but this aldol-like coupling reaction always requires the multistep synthesis of benzofuran-3(2*H*)-ones from available starting materials. Other methods such as oxidative cyclization of 2′-hydroxychalcones catalyzed by Thallium(III) nitrate (3 equiv)[10] or $Hg(OAc)_2$ (1 equiv),[11] ring-closing reaction of 2-(1-hydroxy-3-arylprop-2-ynyl)phenols catalyzed by AuCl[12] or silver nanoparticles,[13] and alkynylation−cyclization of terminal alkynes catalyzed by Cy_3P−silver complex with salicylaldehydes have also been reported.[14] However, many of these methods are limited in their use by not easily available starting materials, harsh reaction conditions, low selectivity, expensive metal catalysts, etc. Thus, a general and practical method to prepare aurones is still required.

In the past two decades, Cu-mediated C-X (X = N, O, S, etc.) bond formation reactions have come into a renaissance.[15] Among them copper-catalyzed O-arylation has attracted much attention, and many five- and six-membered oxygen heterocycles have been constructed with copper-catalyzed O-arylation.[16] However, most of the reactions are hydroxyl or carbonyl coupling arylations. There are no reports of copper-catalyzed intramolecular arylations of epoxides. We realized that (2-halogenphenyl)(3-phenyloxiran-2-yl)methanones could act as active substrates for further aryl C−O coupling. Herein, we would like to describe a copper-catalyzed intramolecular cascade ring-opening/coupling reaction to prepare aurones from (2-halogenphenyl)(3-phenyloxiran-2-yl)methanones (Scheme 1).

Scheme 1. Copper-Catalzyed Intramolecular Tandem Process for Synthesis of Aurone

In initial experiments, (2-bromophenyl)(3-phenyloxiran-2-yl)methanone **1a**[17] was chosen to screen the optimal reaction conditions (Table 1).[18] Fortunately, the corresponding product **2a** was obtained in 59% yield when the reaction was conducted in the presence of catalyst CuI (10 mol %), ligand 2,2-bipyridyl (20 mol %), and base Cs_2CO_3 (2 equiv) in DMF at 100 °C for 8 h (Table 1, entry 1). The product configuration was confirmed with the ^{1}H NMR spectra of **2a**, in which the vinylic proton was consistent with reported (*Z*)-aurones.[12] Only the *Z*-isomer was observed through ^{1}H NMR spectroscopy of the crude product.

In order to obtain more satisfactory results, a series of experiments were carried out using different temperatures,

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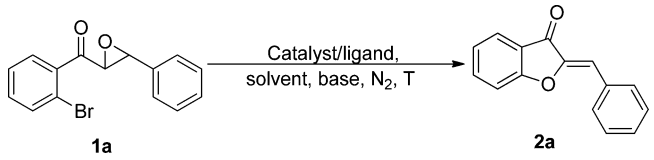
Table 1. Optimization of Reaction Conditions[a]



entry	catalyst	ligand	base	solvent	temp (°C)	yield (%)[b]
1	CuI	2,2′-dipyridyl	Cs_2CO_3	DMF	100	59
2	CuI	2,2′-dipyridyl	Cs_2CO_3	DMF	105	70
3	CuI	2,2′-dipyridyl	Cs_2CO_3	DMF	115	63
4	CuI	2,2′-dipyridyl	Cs_2CO_3	toluene	105	trace
5	CuI	2,2′-dipyridyl	Cs_2CO_3	1,4-dioxane	105	38
6	CuI	2,2′-dipyridyl	Cs_2CO_3	DMSO	105	41
7	CuI	2,2′-dipyridyl	K_2CO_3	DMF	105	trace
8	CuI	2,2′-dipyridyl	DABCO	DMF	105	54
9	CuI	2,2′-dipyridyl	pyridine	DMF	105	trace
10	CuI	2,2′-dipyridyl	K_3PO_4	DMF	105	43
11	CuI		Cs_2CO_3	DMF	105	43
12	CuI	DMAP	Cs_2CO_3	DMF	105	57
13	CuI	8-hydroxyquinoline	Cs_2CO_3	DMF	105	38
14	CuI	L-proline	Cs_2CO_3	DMF	105	13
15	CuI	1,10-phenanthroline hydrate	Cs_2CO_3	DMF	105	79
16	CuI	1,10-phenanthroline	Cs_2CO_3	DMF	105	82
17	CuBr	1,10-phenanthroline	Cs_2CO_3	DMF	105	69
18	CuCl	1,10-phenanthroline	Cs_2CO_3	DMF	105	64

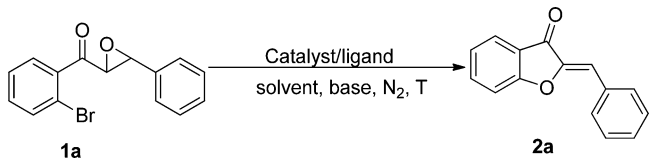
[a]All reactions were run using **1a** (1.0 mmol) as substrate under N_2 protection, and the reaction time was determined by TLC. [b]Yield based on **1a**.

solvents, bases, ligands, and copper catalysts (Table 1). Raising the reaction temperature to 105 °C had a good effect on the outcome (Table 1, entry 2, 70% yield). Solvent screening showed that using 1,4-dioxane, DMSO, and toluene made the yields sharply decline (Table 1, entries 4−6). Among the bases tested (Cs_2CO_3, K_2CO_3, DABCO, pyridine, K_3PO_4), Cs_2CO_3 was found to be the optimal base. Many ligands such as 2,2′-dipyridyl, DMAP, 8-hydroxy quinolone, L-proline, 1,10-phenanthroline, and 1,10-phenanthroline hydrate were screened, and 1,10-phenanthroline was proved to be the most efficient ligand (Table 1, entry 16). When the copper source was switched to CuBr and CuCl (Table 1, entries 17 and 18), the yields slightly decreased. Finally, the optimal reaction conditions were identified as described in Table 1, entry 16.

With the encouraging initial results in hand, a more detailed screening of conditions was carried out by changing the amount of CuI, 1,10-phenanthroline, and Cs_2CO_3 (Table 2). Interestingly, the yield increased slightly by decreasing the base loading to 1.5 mmol (Table 2, entry 7, 84% yield). The optimal reaction was established with 1.5 equiv of Cs_2CO_3 in DMF catalyzed by CuI (10 mol %)/1,10-phenanthroline (20 mol %) at 105 °C.

With the optimized reaction conditions in hand, various substituted (2-halogenphenyl)(3-phenyloxiran-2-yl)-methanones were used to test the generality of the reaction (Table 3). Both aryl R^1 groups bearing substituents with electron-donating (Table 3, entries 2−5) or electron-withdrawing groups (Table 3, entries 6−8) were well tolerated. Substituents R^1 in the *ortho* and *meta* position or R^1 = H usually afforded the higher yields, while R^1 in the *para* position gave moderate yields. The reactions of compounds **1j**, **1k**, and **1l**, all with substituent R^2 possessing a *m*-methoxy group, worked well to give products **2j**, **2k**, and **2l**, respectively (Table 3, entries 10−12). The successful synthesis of substituted aurones from

Table 2. Investigation of the Amount of the Reagents[a]



entry	catalyst (mol %)	ligand (mol %)	base (mmol)	yield (%)[b]
1	5	10	2.0	60
2	10	20	2.0	82
3	20	40	2.0	63
4	10	10	2.0	66
5	10	20	1.0	52
6	10	20	1.2	75
7	10	20	1.5	84
8	10	20	1.7	77

[a]All the reactions were run using **1a** (1 mmol) as substrate in DMF at 105 °C, catalyst: CuI, ligand: 1,10-Phenanthroline, base: Cs_2CO_3 under N_2 protect and the reaction time determined by TLC. [b]Yield based on **1a**.

bromo precursors encouraged us to investigate the reactivity of the corresponding iodo and chloro substituents. It is worth mentioning that (2-chlorophenyl)(3-phenyloxiran-2-yl)-methanones under the standard reaction conditions could afford the corresponding products (Table 3, entries 13 and 14) in moderate yields. We also attempted to synthesize 2-alkylidenecoumaranone in order to test the generality of the reaction but failed to get the desired products.[19]

Many articles have reported that the product aurones may exist as *E*- and *Z*-isomers, and the *Z*-isomer is generally regarded as the thermodynamically stable form.[20] The relative configuration of aurones can be determined by using ^{1}H NMR and ^{13}C NMR spectroscopy.[21] The regio- and stereochemistry

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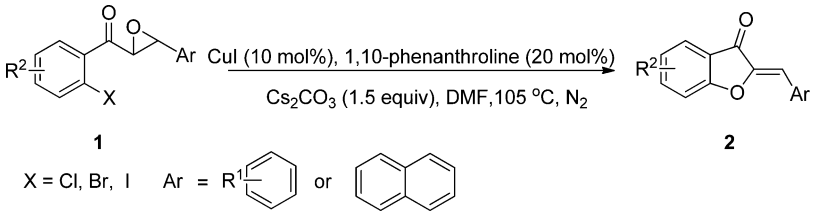
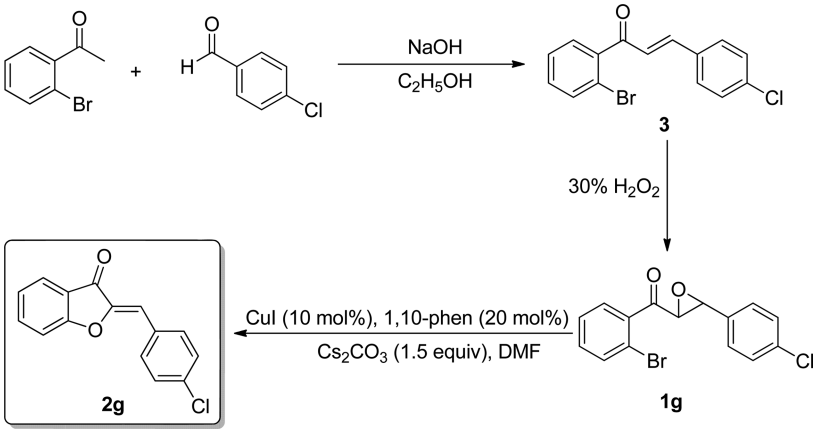
Table 3. Scope of the Copper-Catalyzed Aurones Synthesis[a]



entry	R^2	Ar	X	time (h)[b]	product	yield (%)
1		Ph	Br	4.0	**2a**	84
2		3-Me-C_6H_4	Br	4.5	**2b**	79
3		4-Me-C_6H_4	Br	4.5	**2c**	67
4		2-OMe-C_6H_4	Br	4.5	**2d**	81
5		3-OMe-C_6H_4	Br	4.5	**2e**	74
6		2-Cl-C_6H_4	Br	5.0	**2f**	80
7		4-Cl-C_6H_4	Br	5.0	**2g**	62
8		4-Br-C_6H_4	Br	5.0	**2h**	57
9		1-naphthyl	Br	5.5	**2i**	81
10	5-OMe	Ph	Br	5.0	**2j**	66
11	5-OMe	3-Me-C_6H_4	Br	5.0	**2k**	75
12	5-OMe	4-Cl-C_6H_4	Br	6.0	**2l**	43
13		Ph	Cl	6.0	**2a**	49
14		3-Me-C_6H_4	Cl	6.5	**2b**	59
15		3-Me-C_6H_4	I	4.5	**2b**	52
16		1-naphthyl	I	4.5	**2i**	59

[a]Reaction conditions: (2-halogenphenyl)(3-phenyloxiran-2-yl)methanones (1 mmol), CuI (10 mol %), 1,10-phenanthroline (20 mol %), Cs_2CO_3 (1.5 mmol), in DMF (6 mL), N_2 protect at 105 °C. [b]The time of the reaction monitored by TLC.

Scheme 2. Applications in the Synthesis of the Natural Product 2g



of the aurones **2a**, **2d**, and **2g** could be determined by comparing both ^1H and ^{13}C chemical shifts with the reported (*Z*)-aurones.[12]

The product (*Z*)-2-(4-chlorobenzylidene)benzofuran-3(2*H*)-one **2g** is a natural product that can be isolated from the marine brown alga*Spatoglossum variabile*.[20] It could also be systhesized by this method (Table 3, entry 7, 62%). We took the reaction to gram scale. The Claisen condensation reaction of 1-(2-bromophenyl)ethanone and 4-chlorobenzaldehyde produced (2-bromophenyl)(3-(4-chlorophenyl)oxiran-2-yl)methanone **3** (Scheme 2). Subsequently, (2-bromophenyl)(3-(4-chlorophenyl)oxiran-2-yl)methanone **3** was oxidized to the (2-bromophenyl)(3-(4-chlorophenyl) oxiran-2-yl)methanone **1g**. To our delight, **1g** could easily precipitate from the reaction system, and the yield of the two steps was 85%. Then the intermediate (2-bromophenyl)(3-(4-chlorophenyl)oxiran-2-yl)methanone (**1g**, 2.026g, 6 mmol) generated product (*Z*)-2-(4-chlorobenzylidene)benzofuran-3(2*H*)-one (**2g**, 1.008g) in 65% yield through an intramolecular tandem ring-opening/coupling cyclization process. The overall yield was 55%.

The possible mechanism of the reaction is proposed in Scheme 3. Cu^IL oxidative addition of the aryl halide generated **A**, followed by a coordination to the oxygen of epoxy to give **B**. Subsequently, the halide ion attacks on the benzyl position of **B** to give copper(III) intermediates **C**[18d] with regeneration of X-Cu^IL.[22,23] Then, a reductive elimination to release intermediates **D** occurred. At last, the intermediates **D** underwent an E1-like β-elimination of HX affording the thermodynamically more stable *Z*-products.

In summary, we have developed an original and convenient one-pot protocol to synthesize (*Z*)-aurone through Cu-catalyzed intramolecular tandem cyclization reaction. The

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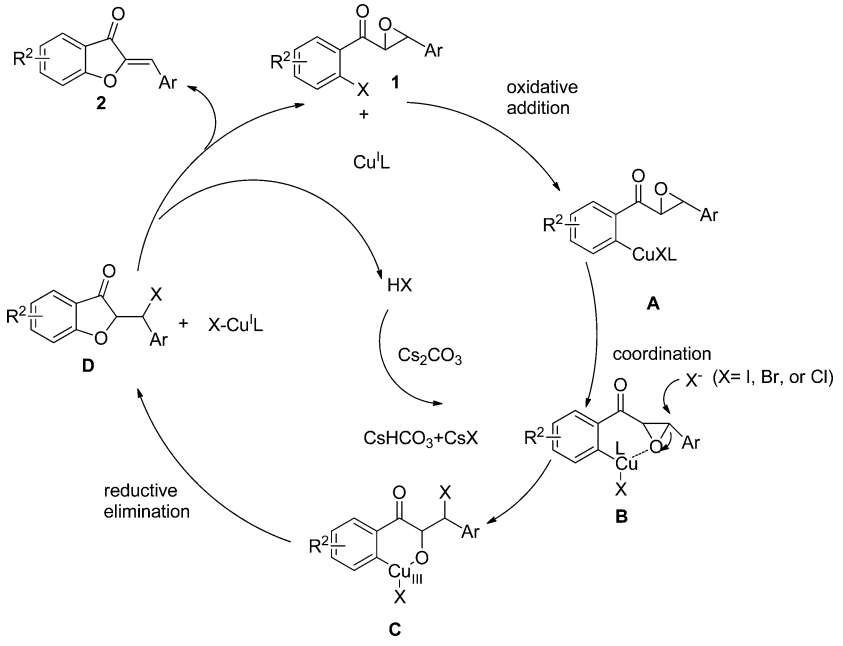
Scheme 3. Possible Mechanism of the Reaction



reaction is applicable to a variety of (2-halogenphenyl)(3-phenyloxiran-2-yl)methanones, and moderate to good yields are attained. The proton NMR spectroscopic data reported for the product match those reported for the known (*Z*)-aurones. We proposed a possible mechanism to explain the results.

EXPERIMENTAL SECTION

General Methods. All reagents were obtained from commercial suppliers and used without further purification, unless otherwise indicated. Reactions were performed in oven-dried round-bottom flasks. TLC analysis was performed using precoated glass plates. NMR spectra were recorded with 400 MHz spectrometer for ^{1}H and 100 MHz for ^{13}C, and TMS was used as internal standard. All reactions were monitored by TLC.

Typical Procedure for Synthesis of (2-Bromophenyl)(3-phenyloxiran-2-yl)methanone (1a).[17] An aqueous solution of NaOH (10.0 mL, 1 mol/L) was slowly added to a solution of 1-(2-bromophenyl)ethanone (2.00 g, 10 mmol) and benzaldehyde (1.06 g, 10 mmol) in ethanol (20 mL) at 0 °C. The solution was stirred at room temperature until disappearance of starting material (3−10 h) as monitored by TLC. Then the reaction mixture was cooled to 0 °C, and water was added (20 mL), resulting in a light yellow viscous liquid that was isolated from the solution and used directly in the next step without purification. The obtained product was dissolved in methanol (15 mL), and 10% aqueous NaOH (0.5 mL, 0.1 mmol) was added. Then, 3.0 mL of 30% hydrogen peroxide was added slowly to the resulting mixture at 0 °C. The solution was stirred at room temperature and monitored by TLC. Then the reaction mixture was cooled to 0 °C, and water was added (20 mL), resulting in a light yellow viscous liquid that was separated from the solution. The crude product was purified by column chromatography on silica gel using petroleum ether/EtOAc (20:1) to give the desired product **1a** (2.27 g, 75%) as a pale yellow viscous liquid.: ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.59 (dd, J = 8.0, 1.2 Hz, 1H), 7.52 (dd, J = 7.6, 1.6 Hz, 1H), 7.43−7.29 (m, 7H), 4.11 (d, J = 2.0 Hz, 1H), 4.09 (d, J = 2.0 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 196.9, 138.6, 135.0, 133.4, 132.6, 129.7, 128.9, 128.5, 127.4, 125.7, 119.7, 62.5, 60.5; MS (ESI) 324.8 (90), 326.7 (100) ([M + Na]$^+$); HRMS (ESI) m/z [M + NH_4]$^+$ calcd for $C_{15}H_{15}BrNO_2$ 320.0281, found 320.0294.

(2-Bromophenyl)(3-(*m*-tolyl)oxiran-2-yl)methanone (1b). Yellow viscous liquid (2.31 g, 73% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.58 (dd, J = 8.0, 1.2 Hz, 1H), 7.51 (dd, J = 7.2, 2.0 Hz, 1H), 7.41−7.30 (m, 2H), 7.27−7.20 (m, 1H), 7.15−7.12 (m, 3H), 4.10 (d, J = 1.6 Hz, 1H), 4.05 (d, J = 1.6 Hz, 1H), 2.34 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 197.0, 138.5, 138.3, 134.9, 133.3, 132.5, 129.6, 128.4, 127.4, 126.1, 122.9, 119.7, 62.4, 60.5, 21.4; MS (ESI) 338.8 (98), 340.8 (100) ([M + Na]$^+$); HRMS (ESI) m/z [M + NH_4]$^+$ calcd for $C_{16}H_{17}BrNO_2$ 334.0437, found 334.0436.

(2-Bromophenyl)(3-(*p*-tolyl)oxiran-2-yl)methanone (1c). White solid (2.38 g, 75% yield); mp 76.0−77.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.62 (d, J = 1.2 Hz, 1H), 7.46 (d, J = 1.2 Hz, 2H), 7.22−7.16 (m, 5H), 4.05 (d, J = 1.6 Hz, 1H), 4.04 (d, J = 1.6 Hz, 1H), 2.36 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 197.0, 138.8, 138.6, 133.4, 132.5, 132.0, 129.7, 129.2, 127.4, 125.7, 119.7, 62.5, 60.6, 21.4; MS (ESI) 338.7 (100), 340.8 (95) ([M + Na]$^+$); HRMS (ESI) m/z [M + NH_4]$^+$ calcd for $C_{16}H_{17}BrNO_2$ 334.0437, found 334.0451.

(2-Bromophenyl)(3-(2-methoxyphenyl)oxiran-2-yl)-methanone (1d). White solid (2.36 g, 71% yield); mp 80.1−82.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.61 (dd, J = 8.0, 1.2 Hz, 1H), 7.55 (dd, J = 7.6, 2.0 Hz, 1H), 7.41−7.26 (m, 3H), 7.20 (dd, J = 7.6, 1.6 Hz, 1H), 6.94 (t, J = 7.6 Hz, 1H), 6.87 (d, J = 8.4 Hz, 1H), 4.42 (d, J = 2.0 Hz, 1H), 4.00 (d, J = 2.0 Hz, 1H), 3.84 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 197.2, 158.0, 138.4, 133.3, 132.2, 129.5, 129.4, 127.1, 125.0, 123.5, 120.5, 119.6, 110.2, 61.8, 56.4, 55.4; MS (ESI) 332.7 (97), 334.8 (100) ([M + H]$^+$); HRMS (ESI) m/z [M + NH_4]$^+$ calcd for $C_{16}H_{17}BrNO_3$ 350.0386, found 350.0376.

(2-Bromophenyl)(3-(3-methoxyphenyl)oxiran-2-yl)-methanone (1e). Pale yellow viscous liquid (2.43 g, 73% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.62−7.57 (dd, J = 8.0, 1.2 Hz, 1H), 7.51 (dd, J = 7.6, 2.0 Hz, 1H), 7.39−7.34 (m, 2H), 7.26 (t, J = 8.0 Hz, 1H), 6.95−6.91 (m, 1H), 6.91−6.83 (m, 2H), 4.09 (d, J = 2.0 Hz, 1H), 4.07 (d, J = 2.0 Hz, 1H), 3.79 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 196.8, 159.7, 138.5, 136.6, 133.4, 132.6, 129.7, 129.6, 127.4, 119.7, 118.2, 114.6, 110.8, 62.4, 60.4, 55.3; MS (ESI) 355.8 (98), 357.8 (100) ([M + Na]$^+$); HRMS (ESI) m/z [M + NH_4]$^+$ calcd for $C_{16}H_{17}BrNO_3$ 350.0386, found 350.0392.

(2-Bromophenyl)(3-(2-chlorophenyl)oxiran-2-yl)methanone (1f). White solid (2.87 g, 85% yield); mp 55.5−57.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.62 (dd, J = 8.0, 1.2 Hz, 1H), 7.54 (dd, J = 7.6, 1.6 Hz, 1H), 7.44−7.33 (m, 3H), 7.32−7.25 (m, 3H), 4.45 (d, J = 2.0 Hz, 1H), 3.97 (d, J = 2.0 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$, ppm) δ 196.5,138.3, 133.4, 133.3, 133.1, 132.5, 129.6, 129.5, 129.2, 127.3, 127.0, 125.6, 119.7, 61.8, 57.6; MS (ESI) 358.7 (72),

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360.7 (100) ([M + Na]$^+$); HRMS (ESI) m/z [M + NH_4]$^+$ calcd for $C_{15}H_{14}BrClNO_2$ 353.9891, found 353.9892.

(2-Bromophenyl)(3-(4-chlorophenyl)oxiran-2-yl)methanone (1g). White solid (2.87 g, 85% yield); mp 80.0−80.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.60 (dd, J = 7.6, 0.8 Hz, 1H), 7.54−7.47 (m, 3H), 7.44−7.33 (m, 2H), 7.22−7.20 (m, 2H), 4.06−4.08 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 196.5, 138.4, 134.8, 133.6, 133.4, 132.7, 129.8, 128.8, 127.5, 127.0, 119.7, 62.4, 59.9; MS (ESI) 358.7 (72), 360.7 (100) ([M + Na]$^+$); HRMS (ESI) m/z [M + NH_4]$^+$ calcd for $C_{15}H_{14}BrClNO_2$ 353.9891, found 353.9876.

(2-Bromophenyl)(3-(4-bromophenyl)oxiran-2-yl)methanone (1h). White solid (3.13 g, 82% yield); mp 74.5−76.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.63 (dd, J = 8.0, 1.2 Hz, 1H), 7.57−7.54 (m, 2H), 7.45−7.27 (m, 4H), 7.24−7.18 (m, 1H), 4.39 (d, J = 2.0 Hz, 1H), 3.96 (d, J = 2.0 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 196.4,138.4, 134.1, 133.4, 132.7, 131.7, 129.8, 127.5, 127.3, 122.9, 119.7, 62.3, 59.9; MS (ESI) 404.7 (100), 406.7 (43) ([M + Na]$^+$); HRMS (ESI) m/z [M + NH_4]$^+$ calcd for $C_{15}H_{14}Br_2NO_2$ 397.9386, found 397.9384.

(2-Bromophenyl)(3-(naphthalen-1-yl)oxiran-2-yl)-methanone (1i). Pale yellow solid (2.68 g, 76% yield); mp 105.0−107.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.11−8.04 (m, 1H), 7.91−7.81 (m, 2H), 7.65−7.33 (m, 8H), 4.75 (d, J = 1.6 Hz, 1H), 4.11 (d, J = 1.6 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 197.3, 138.4, 133.4, 133.1, 132.5, 131.0, 129.5, 128.8, 128.6, 127.3, 126.5, 125.9, 125.2, 122.5, 122.3, 119.7, 61.9, 58.3; MS (ESI) 374.8 (100), 376.8 (94) ([M + Na]$^+$); HRMS (ESI) m/z [M + NH_4]$^+$ calcd for $C_{19}H_{17}BrNO_2$ 370.0437, found 370.0448.

(2-Bromo-5-methoxyphenyl)(3-phenyloxiran-2-yl)-methanone (1j). White solid (2.43 g, 73% yield); mp 84.0−85.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.46 (d, J = 8.8 Hz, 1H), 7.40−7.30 (m, 5H), 7.04 (d, J = 3.2 Hz, 1H), 6.90 (dd, J = 8.8, 3.2 Hz, 1H), 4.10 (d, J = 1.6 Hz, 1H), 4.12 (d, J = 1.6 Hz, 1H), 3.81 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 196.8, 158.7, 139.2,135.0, 134.2, 128.8, 128.5, 125.7, 119.1, 114.7, 109.9, 62.4, 60.6, 55.7; MS (ESI) 354.8 (100), 356.8 (98) ([M + Na]$^+$); HRMS (ESI) m/z [M + NH_4]$^+$ calcd for $C_{16}H_{17}BrNO_3$ 350.0386, found 350.0388.

(2-Bromo-5-methoxyphenyl)(3-(*m*-tolyl)oxiran-2-yl)-methanone (1k). White solid (2.64 g, 76% yield); mp 108.9−110.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.45 (d, J = 8.8 Hz, 1H), 7.24−7.22 (m, 1H), 7.15−7.12 (m, 3H), 7.03 (d, J = 3.2 Hz, 1H), 6.89 (dd, J = 8.8, 3.2 Hz, 1H), 4.11 (d, J = 1.6 Hz, 1H), 4.06 (d, J = 1.6 Hz, 1H), 3.80 (s, 3H), 2.35 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 196.9, 158.7, 139.3, 138.3, 134.9, 134.2, 129.7, 128.4, 126.2, 122.9, 119.0, 114.7, 110.0, 62.4, 60.7, 55.7, 21.4; MS (ESI) 368.7 (94), 370.8 (100) ([M + Na]$^+$); HRMS (ESI) m/z [M + NH_4]$^+$ calcd for $C_{17}H_{19}BrNO_3$ 364.0543, found 364.0549.

(2-Bromo-5-methoxyphenyl)(3-(4-chlorophenyl)oxiran-2-yl)methanone (1l). Pale yellow solid (2.98 g, 81% yield); mp 77.0−78.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.46 (d, J = 8.8 Hz, 1H), 7.18−7.10 (m, 4H), 7.03 (d, J = 3.2 Hz, 1H), 6.90 (dd, J = 8.8, 3.2 Hz, 1H), 4.10−4.06 (m, 2H), 3.81 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 196.4, 158.8, 139.2, 134.8, 134.3, 133.7, 128.8, 127.1, 119.3, 114.9, 110.0, 62.4, 60.0, 55.8; MS (ESI) 388.6 (55), 390.7 (100) ([M + Na]$^+$); HRMS (ESI) m/z [M + NH_4]$^+$ calcd for $C_{16}H_{16}BrClNO_3$ 383.9997, found 383.9979.

(2-Chlorophenyl)(3-phenyloxiran-2-yl)methanone (1m). White viscous liquid (1.89 g, 73% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.58 (dd, J = 7.6, 1.6 Hz, 1H), 7.44−7.28 (m, 8H), 4.13 (d, J = 2.0 Hz, 1H), 4.07 (d, J = 2.0 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 195.8, 136.2, 135.0, 132.7, 131.8, 130.2, 129.8, 128.7, 128.4, 126.9, 125.6, 62.7, 60.2; MS (ESI) 280.8 (100), 282.8 (36) ([M + Na]$^+$); HRMS (ESI) m/z [M + NH_4]$^+$ calcd for $C_{15}H_{15}ClNO_2$ 276.0786, found 276.0795.

(2-Chlorophenyl)(3-(*m*-tolyl)oxiran-2-yl)methanone (1n). White viscous liquid (2.10 g, 77% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.59 (m, 1H), 7.46−7.37 (m, 2H), 7.36−7.31 (m, 1H), 7.26−7.22 (m, 1H), 7.17−7.09 (m, 3H), 4.14 (d, J = 1.6 Hz, 1H), 4.05 (d, J = 1.6 Hz, 1H), 2.34 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 196.0, 138.2, 136.3, 134.9, 132.7, 131.9, 130.2, 129.8, 129.6, 128.4, 126.9, 126.1, 122.9, 62.8, 60.4, 21.4; MS (ESI) 294.8 (100), 296.9 (40) ([M + Na]$^+$); HRMS (ESI) m/z [M + NH_4]$^+$ calcd for $C_{16}H_{17}ClNO_2$ 290.0942, found 290.0945.

(2-Iodophenyl)(3-(*m*-tolyl)oxiran-2-yl)methanone (1o). White yellow viscous liquid (2.80 g, 77% yield); ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.88 (dd, J = 7.6, 0.8 Hz, 1H), 7.47−7.37 (m, 2H), 7.27−7.20 (m, 1H), 7.19−7.08 (m, 4H), 4.05−4.03 (m, 2H), 2.34 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 197.8, 141.6, 140.1, 138.3, 134.7, 132.3, 129.7, 129.0, 128.4, 127.9, 126.2, 122.9, 91.6, 61.8, 60.4, 21.4; MS (ESI) 386.7 (100), 387.8 (21) ([M + Na]$^+$); HRMS (ESI) m/z [M + NH_4]$^+$ calcd for $C_{16}H_{17}INO_2$ 382.0298, found 382.0312.

(2-Iodophenyl)(3-(naphthalen-1-yl)oxiran-2-yl)methanone (1p). White solid (3.16 g, 79% yield); mp 104.0−106.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.12−8.03 (m, 1H), 7.92 (dd, J = 8.0, 0.8 Hz, 1H), 7.89−7.79 (m, 2H), 7.59−7.39 (m, 6H), 7.19−7.15 (m, 1H), 4.72 (d, J = 2.0 Hz, 1H), 4.05 (d, J = 2.0 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 198.2, 141.4, 140.2, 133.1, 132.4, 131.0,131.0, 129.0, 128.9, 128.7, 127.9, 126.6, 126.0, 125.3, 122.6, 122.4, 91.8, 61.4, 58.2; MS (ESI) 422.8 (100), 423.8 (21) ([M + Na]$^+$); HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{19}H_{14}IO_2$ 401.0033, found 401.0031.

Typical Procedure for Synthesis of (*Z*)-2-Benzylidenebenzofuran-3(2*H*)-one (2a). A mixture of (2-bromophenyl)(3-phenyloxiran-2-yl)methanone **1a** (303 mg, 1 mmol), Cs_2CO_3 (487 mg, 1.5 mmol), CuI (10 mol %), 1,10-phenanthroline (20 mol %) and DMF (6 mL) was heated in a Schlenk tube at 105 °C under nitrogen. The reaction was monitored by TLC until disappearance of starting material (4 h). Then the cooled reaction mixture was dissolved in H_2O and extracted with EtOAc. The combined organic layer was dried (Mg_2SO_4). The product was further purified by column chromatography (silica gel, petroleum ether/EtOAc (20:1)) to afford the pure product **2a** (187 mg, 84%) as a pale yellow solid: mp 102.0−104.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.91−7.89 (m, 2H), 7.78 (d, J = 7.6 Hz, 1H), 7.63 (t, J = 8.4 Hz, 1H), 7.47−7.35 (m, 3H), 7.30 (d, J = 8.4 Hz, 1H), 7.19 (t, J = 7.6 Hz, 1H), 6.87 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 184.5, 165.9, 146.6, 136.7, 132.1, 131.4, 129.7, 128.7, 124.5, 123.3, 121.5, 113.0, 112.9; MS (ESI) 223.2 (100) ([M + H]$^+$). The data were consistent with that reported in the literature.[12]

(*Z*)-2-(3-Methylbenzylidene)benzofuran-3(2*H*)-one (2b). Yellow solid (187 mg, 79% yield); mp 72.2−74.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.79 (dd, J = 7.6, 0.8 Hz, 1H), 7.74 (d, J = 7.6 Hz, 1H), 7.68 (s, 1H), 7.64−7.63 (m, 1H), 7.33 (dd, J = 7.6, 7.2 Hz, 2H), 7.22−7.20 (m, 2H), 6.85 (s, 1H), 2.41 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 184.4, 165.9, 146.6, 138.3, 136.6, 132.0, 130.6, 129.7, 128.6, 128.5, 124.5, 123.3, 121.5, 113.2, 112.8, 21.5; MS (ESI) 237.1 (100) ([M + H]$^+$). The data were consistent with that reported in the literature.[24]

(*Z*)-2-(4-Methylbenzylidene)benzofuran-3(2*H*)-one (2c). Yellow solid (161 mg, 68% yield); Mp. 91.4−94.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.82−7.78 (m, 3H), 7.64−7.62 (m, 1H), 7.32 (d, J = 8.4 Hz, 1H), 7.26−7.24 (m, 2H), 7.20 (t, J = 7.6 Hz, 1H), 6.88 (s, 1H), 2.41 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, ppm) δ 183.2, 165.1, 145.7, 140.1, 137.4, 131.3, 129.5, 128.9, 124.1, 123.8, 120.8, 113.1, 112.4, 21.3; MS (ESI) 495.1 (100) ([2M + Na]$^+$). The data were consistent with that reported in the literature.[3]

(*Z*)-2-(2-Methoxybenzylidene)benzofuran-3(2*H*)-one (2d). Yellow solid (204 mg, 81% yield); mp 170.8−172.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.29 (d, J = 7.6 Hz, 1H), 7.80 (d, J = 7.6 Hz, 1H), 7.62 (t, J = 8.0 Hz, 1H), 7.46 (s, 1H), 7.41−7.28 (m, 2H), 7.19 (t, J = 7.6 Hz, 1H), 7.05 (t, J = 7.6 Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H), 3.90 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 184.3, 165.7, 158.7, 146.8, 136.4, 131.9, 131.3, 124.5, 123.1, 121.8, 121.3, 120.7, 112.8, 110.7, 107.2, 55.7; MS (ESI) 253.1 (100) ([M + H]$^+$). The data were consistent with that reported in the literature.[12]

(*Z*)-2-(3-Methoxybenzylidene)benzofuran-3(2*H*)-one (2e). Yellow solid (187 mg, 74% yield); mp 115.7−117.3 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.82−7.78 (m, 1H), 7.65 (ddd, J = 8.4, 7.2, 1.6 Hz, 1H), 7.50−7.48 (m, 2H), 7.39−7.30 (m, 2H), 7.21 (t, J = 7.6 Hz, 1H), 6.98−6.94 (m, 1H), 6.86 (s, 1H), 3.88 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 184.5, 165.9, 159.6, 146.8, 136.8,

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133.4, 129.7, 124.6, 124.2, 123.4, 121.5, 116.4, 115.6, 112.8, 55.4; MS (ESI) 253.1 (100) ($[M + H]^+$). The data were consistent with that reported in the literature.[24]

(*Z*)-2-(2-Chlorobenzylidene)benzofuran-3(2*H*)-one (2f). Pale yellow solid (205 mg, 80% yield); mp 136.5−137.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 8.32 (dd, J = 8.0, 1.6 Hz, 1H), 7.79 (d, J = 7.6 Hz, 1H), 7.70−7.60 (m, 1H), 7.43 (dd, J = 8.0, 1.2 Hz, 1H), 7.40−7.26 (m, 4H), 7.21 (t, J = 7.6 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 184.2, 165.9, 147.4, 136.9, 135.8, 132.1, 130.4, 130.2, 129.8, 126.9, 124.7, 123.5, 121.4, 112.8, 107.8; MS (ESI) 257.0 (100), 259.0 (35) ($[M + H]^+$) ($[M + H]^+$). The data were consistent with that reported in the literature.[25]

(*Z*)-2-(4-Chlorobenzylidene)benzofuran-3(2*H*)-one (2g). Orange solid (159 mg, 62% yield); mp 160.8−162.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.84 (d, J = 8.4 Hz, 2H), 7.79 (d, J = 7.6 Hz, 1H), 7.67−7.63 (m, 1H), 7.41 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.4 Hz, 1H), 7.21 (d, J = 7.6 Hz, 1H), 6.82 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 184.3, 165.8, 146.7, 136.8, 135.6, 132.4, 130.6, 129.0, 124.6, 123.5, 121.3, 112.8, 111.4; MS (ESI) 257.1 (100), 259.1 (30) ($[M + H]^+$); The data were consistent with that reported in the literature.[12]

(*Z*)-2-(4-Bromobenzylidene)benzofuran-3(2*H*)-one (2h). Yellow solid (172 mg, 57% yield); mp 163.1−164.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.84−7.74 (m, 3H), 7.66 (ddd, J = 8.4, 7.2, 1.6 Hz, 1H), 7.61−7.54 (m, 2H), 7.32 (d, J = 8.4 Hz, 1H), 7.21 (d, J = 8.0 Hz, 1H), 6.80 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 184.3, 165.8, 146.9, 136.9, 132.6, 132.0, 131.1, 124.6, 124.2, 123.5, 121.4, 112.8, 111.4; MS (ESI) 301.0 (98), 303.0 (100) ($[M + H]^+$). The data were consistent with that reported in the literature.[26]

(*Z*)-2-(Naphthalen-1-ylmethylene)benzofuran-3(2*H*)-one (2i). Yellow solid (221 mg, 81% yield); mp 139.1−140.8 °C; ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 8.40−8.29 (m, 2H), 8.03 (dd, J = 14.8, 8.0 Hz, 2H), 7.82 (dd, J = 17.6, 8.0 Hz, 2H), 7.73−7.52 (m, 5H), 7.33 (t, J = 7.2 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 184.3, 166.0, 147.5, 136.7, 133.5, 132.1, 130.4, 130.1, 128.8, 128.1, 126.9, 126.0, 125.4, 124.6, 123.4, 123.2, 121.6, 112.9, 108.4; MS (ESI) 273.0 (100) ($[M + H]^+$); HRMS (ESI) $C_{19}H_{12}NaO_2$ ($[M + Na]^+$): calcd.: 295.0730, Found: 295.0728.

(*Z*)-2-Benzylidene-5-methoxybenzofuran-3(2*H*)-one (2j). Yellow solid (166 mg, 66% yield); mp 122.1−124.3 °C; ^{1}H NMR (400 MHz, DMSO-d_6, ppm) δ 7.94 (d, J = 7.2 Hz, 2H), 7.51−7.41 (m, 4H), 7.34 (dd, J = 8.8, 2.8 Hz, 1H), 7.20 (d, J = 2.8 Hz, 1H), 6.88 (s, 1H), 3.78 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6, ppm) δ 183.4, 160.2, 155.6, 146.8, 131.7, 131.1, 129.8, 128.8, 125.9, 120.9, 114.0, 112.00, 105.4, 55.8; MS (ESI) 253.0 (100) ($[M + H]^+$); HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{16}H_{12}NaO_3$ 275.0679, found 275.0683.

(*Z*)-5-Methoxy-2-(3-methylbenzylidene) benzofuran-3(2*H*)-one (2k). Yellow solid (199 mg, 75% yield); mp 125.4−127.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.71 (d, J = 7.6 Hz, 1H), 7.66 (s, 1H), 7.32 (t, J = 7.6 Hz, 1H), 7.22 (d, J = 1.2 Hz, 2H), 7.19−7.17 (m, 2H), 6.82 (s, 1H), 3.81 (s, 3H), 2.40 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 184.6, 160.9, 155.8, 147.4, 138.3, 132.0, 131.9, 130.6, 128.6, 125.9, 121.6, 115.2, 113.6, 113.2, 105.1, 55.9, 21.5; MS (ESI) 267.1 (100) ($[M + H]^+$); HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{17}H_{14}NaO_3$ 289.0835, found 289.0834.

(*Z*)-2-(4-Chlorobenzylidene)-5-methoxybenzofuran-3(2*H*)-one (2l). Yellow solid (123 mg, 43% yield); mp 151.6−153.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$, ppm) δ 7.78 (d, J = 8.0 Hz, 2H), 7.37 (d, J = 8.4 Hz, 2H), 7.15−7.21 (m, 3H), 6.76 (s, 1H), 3.81 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$, ppm) δ 184.4, 160.9, 155.9, 147.5, 135.6, 132.4, 130.7, 129.0, 126.1, 121.4, 113.6, 111.4, 105.2, 55.9; MS (ESI) 287.1 (100), 289.1 (35) ($[M + H]^+$); HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{16}H_{11}ClNaO_3$ 309.0289, found 309.0284.

■ ASSOCIATED CONTENT

Supporting Information

Investigation of the amount of the reagents, copies of ^{1}H and ^{13}C NMR spectra for **1a−p** and **2a−l**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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