

2,3-Dichloro-5,6-dicyanobenzoquinone (DDQ) mediated oxidation-dehydrogenation of 2-aryl-3,4-dihydro-2H-benzopyrans : synthesis of 2-arylbenzopyran-4-ones

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Abstract

DDQ mediated an oxidation-dehydrogenation of 2-aryl-3,4-dihydro-2H-benzopyran prepared from salicylaldehyde to yield 2-arylbenzopyran-4-one. Stoichiometric amount of DDQ, acetic acid and water in refluxing dioxane are the optimal condition for this oxidation-dehydrogenation reaction. A rationally proposed mechanism for this oxidation-dehydrogenation process is based on the isolation of a reaction intermediate viz., 2-benzoyl-8-methoxy-3,4-dihydrobenzopyran-4-one and the identification of the ¹⁸O-labeled carbonyl group of benzopyran-4-one demonstrating incorporation of labeled H₂¹⁸O.

Keywords: 2-Aryl-3,4-dihydro-2H-benzopyrans; 2-arylbenzopyran-4-ones, DDQ, oxidation-dehydrogenation

Introduction

DDQ (2,3-dichloro-5,6-dicyanobenzoquinone) is a chemical reagent widely used in organic synthesis. The major functions of DDQ include the deprotection of thioacetals, acetals and ketals and conversion to aldehydes and ketones,¹ and the deprotection of benzyl, MPM (4-methoxybenzyl) and DMPM (3,4-dimethoxybenzyl) groups into hydroxy groups,² the mediated carbon-carbon bond formation for the synthesis of quinolines from imines and alkynes or alkenes,³ the catalyzed benzylic acetoxylation of arylalkanes,⁴ the synthesis of methoxylated (*E*)-arylalkenes and arylalkanones,⁵ the mediation of direct cross-dehydrogenative-coupling (CDC) between ethers and active methylene compounds,^{6a} or simple ketones,^{6b} the oxidative cyclization of phenolic Schiff base for the synthesis of 2-arylbenzoxazoles,⁷ the facile synthesis of vicinal

diamines via oxidation of the *N*-phenyltetrahydroisoquinolines,⁸ the oxidation of *beta*-asarone to phenylpropanoids,⁹ and the oxidation of arylpropanes to (*E*)-cinnamaldehydes,¹⁰ as well as others.¹¹ On the other hand, 1-benzopyran-4-one (1-chromen-4-one) is a core structure of isoflavones and flavones which are notable for their biological activities.¹² However, the synthesis of 2-arylbenzopyran-4-ones has received little attention. The methods reported include oxidation of benzylchromones with SeO₂,^{13a} and the reaction of chromonecarbonyl chlorides with benzene catalyzed by aluminum chloride to yield the biologically active 2-arylchromen-4-ones.^{13b,13c} The tedious reaction condition, and absence of straightforward protocols are shortcoming of the reported methods. We recently reported on our use of DDQ to oxidize; chromene to chromen-2-one (coumarin),¹⁴ 4-hydroxychroman to chromen-4-one,¹⁵ and 5,6-dimethoxy-3-methyl-2-arylchroman to 5,6-dimethoxy-3-methyl-2-arylchromen-4-one.¹⁶ Despite a number of examples that have been reported on the oxidation-dehydrogenation mediation by DDQ, a detailed study on the optimal reaction conditions and mechanism are still outstanding. Herein, we report on an extension of our preliminary results,¹⁷ on the efficient oxidation of chroman to chromen-4-one by DDQ and provide a rational mechanism deduced by the isolation of a key reaction intermediate as well as the final product which incorporated the ¹⁸O when acetic acid and H₂¹⁸O were used in the reaction.

Results and Discussion

A model reaction was designed for determining the optimal condition for this DDQ oxidation. From careful investigations (Table 1), we found that DDQ (3.5 equiv.) in the refluxing dioxane and with HOAc-H₂O as an additive (entry 4) are the optimized conditions. Omission of HOAc-H₂O as additive (entry 3), increases the reaction time and lowers the yield. Using one or two equivalents DDQ (entries 1 and 2) in this oxidation reaction results in no product being observed. This result indicates that the stoichiometric amounts of DDQ are necessary in this oxidation reaction. In DMF as solvent and HOAc (few drops) as additive, the reaction takes place but purification is tedious (entry 5). Moreover, with EtOAc as solvent and HOAc as additive, the reaction occurs but a longer reaction time is required (entry 6). This result points to the fact that this type of oxidation requires higher boiling point solvents than that of EtOAc. If only HOAc is used as solvent without H₂O as an additive, the reaction time is a little longer (entry 7). In the case of using H₂O as solvent, without HOAc as additive, the yield of product is lower with most of starting material being recovered (entry 8). This result implies that HOAc is a requisite for the enhanced rate of this oxidation. When DMSO was used as solvent under refluxing conditions, the product mixture is difficult to purify resulting in a lower yield (entry 9). Employing the optimized conditions, DDQ (3.5 equiv.) in the refluxing dioxane and HOAc-H₂O as an additive, a series of 2-aryl-3,4-dihydro-2*H*-benzopyrans prepared from salicylaldehyde were oxidized with DDQ to yield the title compounds in moderate to good yield.

Table 1. The results of the oxidation of **1b** (2 mmol) with DDQ under various conditions in refluxing solvent (4 mL) to yield **2b**



Entry	DDQ/Solvent	Additive	T. ^a	Y. ^b	Entry	DDQ/Solvent	Additive	T. ^a	Y. ^b
1	1 equiv/dioxane	-	12	N D ^c	6	3.5 equiv/EA	HOAc ^b	6	82
2	2 equiv/dioxane	-	12	- ^d	7	3.5 equiv/HOAc	-	6	81
3	3.5 equiv/dioxane	-	12	75	8	3.5 equiv/H ₂ O	-	12	32
4	3.5 equiv/dioxane	HOAc ^e H ₂ O	4	86	9	3.5 equiv/DMSO	- ^g	2	25
5	3.5 equiv/DMF	HOAc ^f	2	80					

^aT= Reaction time in hours; ^bY = % Yield; ^cND = non-detective; ^dincomplete oxidation; ^eHOAc(0.2 mL), H₂O (1-2 drops) in 2 mmol reaction scale, see experimental section; ^fReaction time is shorter but purification is difficulty; ^gProduct together with the messy by-products were observed.

Structural assignment of 2-benzoyl-8-methoxybenzopyran-4-one **2b** is based on the following spectral data. A three-proton singlet at δ 3.98 in the ¹H-NMR spectrum is assigned to the 8-methoxy group while the NOESY spectrum illustrates the following; a one proton double doublet signal at δ 7.25 (dd, J = 8.0, 1.2 Hz) cross linked to the methoxy group can be assigned to H-7; cross linking between H-6 and H-7 and H-5 with H-6 allows the signals for H-6 at δ 7.39 (t, J = 8.4 HZ) and H-5 at δ 7.78 (dd, J = 8.2, 1.2 Hz) to be assigned. Based on the HSQC technique, C-3 at δ 114.6 is shown linked to H-3 at δ 6.92; C-7 at δ 115.1 is shown linked to H-7 at δ 7.25; C-5 at δ 116.4 is shown linked with H-5 at δ 7.78 and C-6 at δ 125.7 is shown linked to H-6 at δ 7.37. Based on the HMBC technique, the (C-4) carbonyl carbon at δ 146.3 shows cross links with H-3 and H-5 while the benzoyl carbon at δ 149.3 shows cross links with H-3, H-2', and H-6'. The DEPT ¹³C-NMR spectra for **2b** illustrates the following; in a broad band-decouple spectrum, which shows signals for 15 carbons; in DEPT-90 spectrum, which shows signals for seven CH carbons and one CH₃ carbon; and in DEPT-135 spectrum, which shows seven CH positive signals and shows no negative signals of CH₂. All DEPT ¹³C-NMR spectra

which are obtained further support the correctness of structure **2b**. Additionally EI-MS and EA data are consistent with the structure.

In order to clarify and establish the detailed reaction mechanism, an optimized reaction was quenched after 3h. The resultant intermediate which was analyzed by spectral analysis ^1H -NMR, ^{13}C -NMR, and EI-MS, proved to be 2-benzoyl-8-methoxychroman-4-one **2b-1** and was shown to be further oxidized to yield **2b** under the same reaction conditions. This result implies that the chroman ring is firstly oxidized to chroman-4-one and then followed by dehydrogenation to yield chromen-4-one. Moreover, in order to clarify the origin of the oxygen of chroman-4-one as well as the involvement of H_2O in the oxidation reaction, H_2O^{18} was used at the beginning of reaction using the optimized condition to determine if it was incorporated. The products we isolated proved to be a mixture of the labeled 2-benzoyl-8-methoxybenzopyran-4-one (^{18}O) (**2b**- ^{18}O) and the unlabeled one **2b**. The labeled benzopyran-4-one (^{18}O) can be easily verified and distinguished by comparing the MS spectra with the unlabeled one. Chart 1 illustrates the EI-MS spectrum of unlabeled benzopyran-4-one **2b** (HRMS, calcd for $\text{C}_{17}\text{H}_{12}\text{O}_4$, 280.0736. Found: 280.0738), and Chart 2 illustrates labeled (HRMS, calcd for $\text{C}_{17}\text{H}_{12}\text{O}_3^{18}\text{O}$, 282.0778. Found: 282.0776). The inference of this is that the oxygen atom at C4 of chroman-4-one may arise from either water or acetate. Water may be present in undried solvent or from environmental moisture. In a previous study of Harvey, R. G. et al., they proposed that benzylic oxidation by DDQ occurred through the addition of an acetate anion to the benzylic cation to form the acetic ester, which was subsequently oxidized to a carbonyl intermediate,¹⁸ but failed to provide a detailed reaction mechanism.

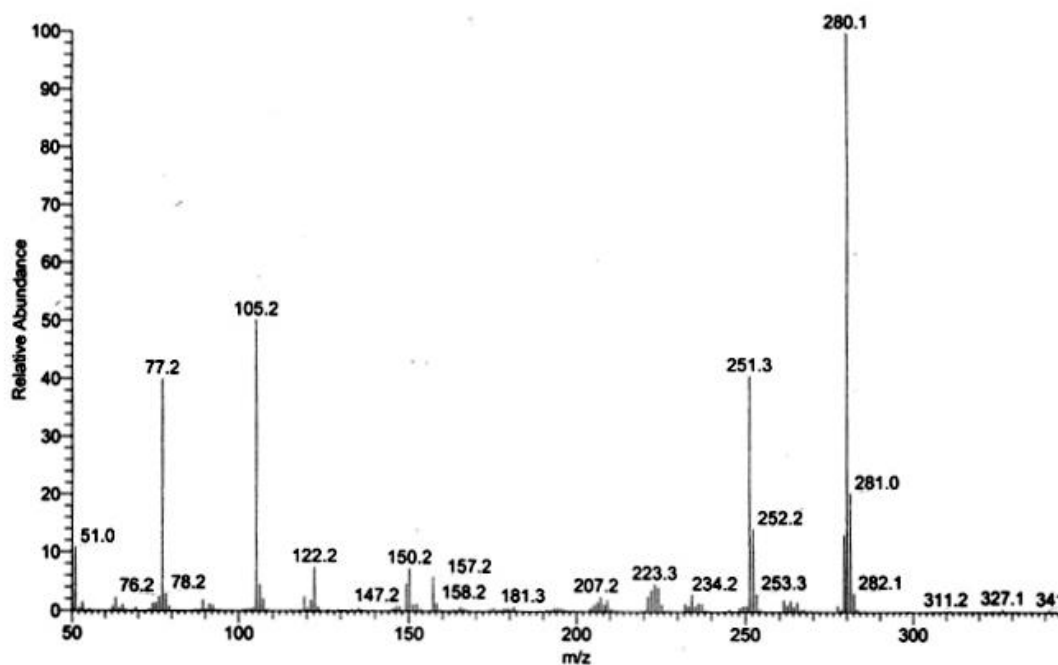


Chart 1. The mass spectrum of pure **2b**.

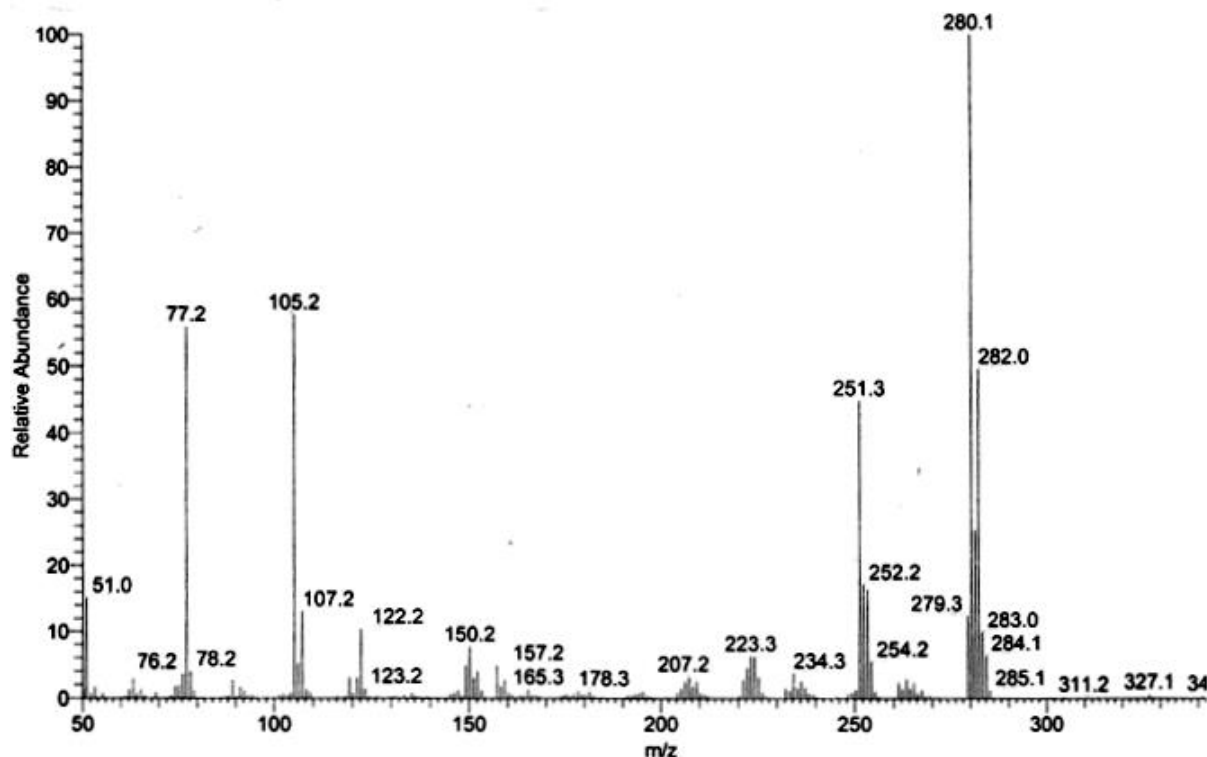
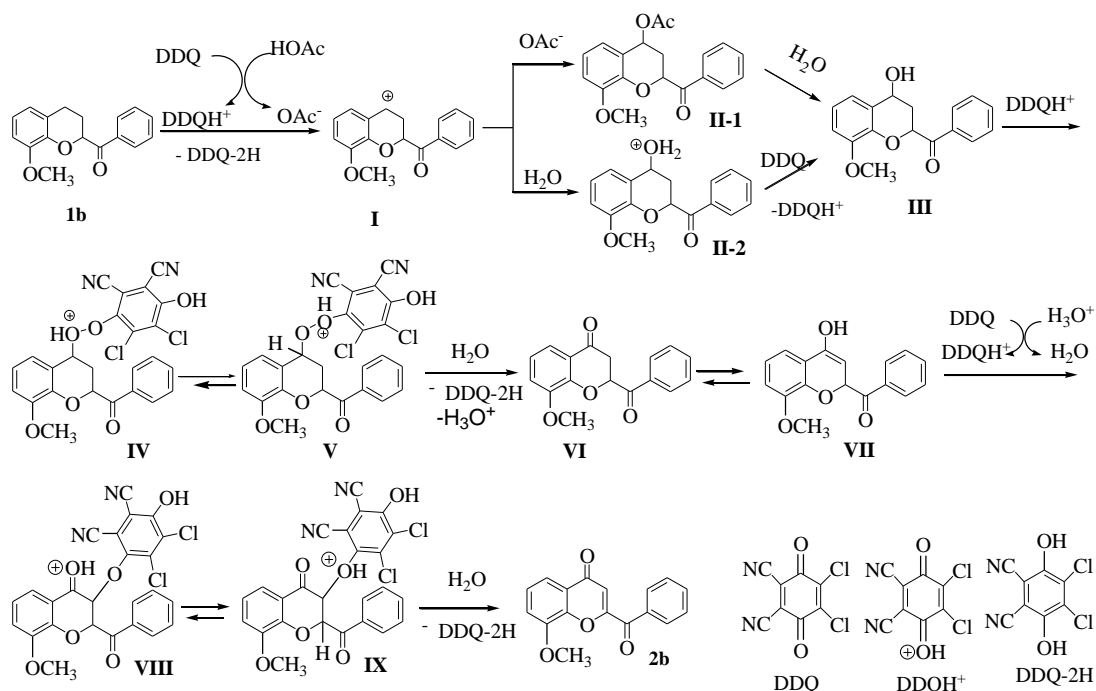


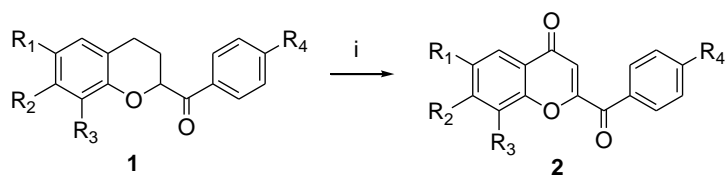
Chart 2. The mass spectrum of the mixture of **2b** and **2b**-¹⁸O.

Based on the evidences at hand, we wish to propose a reaction mechanism for this oxidation-dehydrogenation process. Using **1b** as an example and depicted as follows (Scheme 1). Initially, one of the benzylic hydrogen of **1b** was abstracted by DDQH⁺ which was generated by DDQ and HOAc, to form the benzylic cation **I**. DDQH⁺ having a positive charge acts as a stronger electrophile than that of neutral DDQ, and thus enhances the deprotonation process of chroman at C-4 position. Following on from this addition of an acetate anion (from acetic acid) or H₂O (from additive / surrounding / solvent) **II-1** and **II-2** could be generated, respectively. In this step, **II-1** has a higher priority than **II-2** since the nucleophilicity of acetate > H₂O. Consequently, **II-1** could be transferred into **III** by hydrolysis with H₂O and **II-2** could be converted to **III** by deprotonation by DDQ. Reaction between DDQH⁺ and **III** would then form 2-aroyle-3,4-dihydrobenzopyran-4-one **VI** as an intermediate by going through transition states **IV** and **V**. Subsequently tautomerism of **VI** to the enolic form **VII** and attack by DDQH⁺ generated between DDQ and H₃O⁺ would yield **VIII**. After a deprotonation-protonation process, intermediate **IX** is attacked by water to eliminate a neutral DDQ-2H and finally yield 2-aroyle-benzopyran-4-one **2b**. In the overall reaction, three equivalents of DDQ are consumed with three equivalent of DDQ-2H being generated.



Scheme 1. The proposed mechanism of oxidation-dehydrogenation of chroman to chromen-4-one by DDQ.

The proposed mechanism strongly supports the finding that stoichiometric amounts of DDQ are required in this oxidation-dehydrogenation reaction. Using the optimal conditions found in this study, 2-aryl-3,4-dihydro-2*H*-benzopyrans **1a-j** were oxidized to the corresponding 2-arylchromen-4-ones **2a-j** using DDQ (3.5 equiv) as oxidant, and HOAc-H₂O as additives in refluxing dioxane (Scheme 2). The physical data and selected spectra data of **2a-j** are summarized in Table 2.



- a. R₁ = R₂ = R₃ = R₄ = H; b. R₁ = R₂ = R₄ = H, R₃ = OMe;
 c. R₁ = Br, R₂ = R₃ = R₄ = H; d. R₁ = Cl, R₂ = R₃ = R₄ = H;
 e. R₁ = R₂ = H, R₃ = R₄ = OMe; f. R₁ = R₃ = H, R₂ = R₄ = OMe;
 g. R₁ = R₃ = Cl, R₂ = R₄ = H; h. R₁ = R₄ = Cl, R₂ = R₃ = H;
 i. R₁ = Cl, R₂ = R₃ = H, R₄ = OMe; j. R₁ = R₂ = R₃ = H, R₄ = OMe

Reagents and Conditions: i. DDQ (3.5 equiv), dioxane, HOAc-H₂O reflux; 34-86%

Scheme 2. The oxidation of 2-aryl-3,4-dihydro-2*H*-benzopyrans **1a-j** with DDQ to yield 2-arylbenzopyran-4-ones **2a-j**.

Table 2. The physical and selected spectral data of **2a-j**

Compd	MP (°C)	% Yield	Reaction time (hr)	IR (cm ⁻¹)	H-3 (δ)	C-2 ^b	C-3 ^b	C=O (C-4) ^b	ArC=O ^b
2a	87-88	76	4	1655, 1615	6.85	157.8	114.8	178.1	187.8
2b	182-183	86	4	1677, 1647	6.92	157.8	114.5	178.2	187.2
2c	159-160	68	8	1654, 1597	6.89	158.0	115.0	176.9	187.6
2d	150-152	70	8	1657, 1598	6.89	157.9	114.8	177.0	187.5
2e	166-167	82	4	1646, 1599	6.92	158.6	115.0	178.3	185.3
2f	181-182	85	4	1648, 1600	6.78	158.1	114.8	177.4	186.2
2g	132-134	34 ^a	12	1661, 1595	7.02	158.3	114.4	176.4	186.5
2h	168-170	48 ^a	8	1651, 1607	6.89	157.7	114.7	176.9	186.3
2i	151-152	65	8	1655, 1598	6.84	158.8	114.2	177.0	185.7
2j	82-83	73	4	652, 1597	6.85	158.7	114.3	178.2	186.0

^aEven prolong reaction time, the % yield cannot be improved, but recovery starting material.

^bThe chemical shift of C-2, C-3, and two C=O group are determined by HSQC or HMBC technique.

Considering Table 2 and based simply on the % yields, the effect of substituents on the reaction outcome demonstrate the following trend, OCH₃ > H > Br > Cl. For example, the % yields of **2b**, **2e**, and **2f** which have a methoxy group on the benzene and chroman ring are 86, 82, and 85% yield, respectively. The % yield of **2a** which has no substituents on either the benzene or chroman ring is 76% while **2d** and **2i** which both have a Cl at R₁ are formed in 70 and 65% yield respectfully. However **2g** (R₁= R₃ = Cl) and **2h** (R₁ = R₄ = Cl), both having two Cl atoms were only formed in 35 and 49 % yield respectively. These findings support our proposed reaction mechanism since the formation of a benzylic cation in the first step is stabilized by electron-donating groups in the aromatic ring although not directly conjugated except for **2f**.

Conclusions

We have, by isolating the intermediate 2-aroylechroman-4-one during the DDQ mediated oxidation process, verified that the C-4 of the chroman ring of 2-aroyle-3,4-dihydro-2*H*-benzopyrans is initially oxidized to the carbonyl group followed by dehydrogenation to form chromen-4-one. By identifying labeled 2-aroylechromen-4-one (^{18}O) by EI-MS, the possible role H_2O plays in this DDQ oxidation is also evident. Furthermore, HOAc as an additive facilitated the DDQ oxidation. Thus, we have optimized conditions for conversion of 2-aroylechromans to 2-aroylechromen-4-ones by DDQ in refluxing dioxane with HOAc- H_2O as additives.

Experimental Section

General. All melting points were determined on a Yanaco micro melting-point apparatus. ^1H NMR and ^{13}C NMR spectra were obtained on a Varian Unity plus 400 Spectrometer. Chemical shifts are indicated in parts per million with respect to TMS. IR spectra were measured on a Perkin Elmer system 2000 FT-IR spectrometer. Elemental analyses were recorded on a Heraeus CHN-O Rapid analyzer. Mass spectra were recorded on a Chem/hp/middle spectrometer connected to a Hewlett Packard series II model gas- liquid chromatography. HRMS spectra were performed on a JEOL JMS SX/SX 102A instrument. Silica gel (230-400 mesh) for column chromatography and precoated silica gel plates (60 F-254) for TLC was purchased from E. Merck Co. UV light (254 nm) was used to detect spots on TLC plates after development.

Compounds (1a-j) were prepared according to the procedure of our previous report.¹⁷

General procedure for the preparation of 2-Aroyle-1-benzopyran-4-one (2a-j)

Compound **1a-j** (2 mmol) dissolved in 1,4-dioxane (4 mL) was stirred and added DDQ (1.60 g, 7 mmol), HOAc (0.2 mL) and H_2O (1-2 drops). The reaction mixture was heated to the reflux for 4-8 h. The resultant mixture was quenched with saturated brine (20 mL) and was extracted with CH_2Cl_2 (10 mL \times 3). The organic layers were combined, washed with brine, and dried with anhydrous MgSO_4 , in sequence. After filtration, the filtrate was concentrated *in vacuo*. The resultant residue was purified by silica gel column chromatography (ethyl acetate/*n*-hexane = 1:10) to give pure **2a-j**.

2-Benzoyl-1-benzopyran-4-one (2a). It (0.38 g, 76%) was obtained as colorless crystals, mp 91 $^\circ\text{C}$ (lit.^{13c} 94 $^\circ\text{C}$); R_f 0.31 (ethyl acetate/*n*-hexane=1:4); IR (neat) ν_{max} 3066 (w), 1655 (vs), 1615 (m), 1464 (s), 1379 (s), 1302 (m), 1263 (s), 1240 (s), 1104 (m), 983 (s), 869 (s) cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 6.85 (s, 1H, H-3), 7.44 (td, $J=8.0$, 0.8 Hz, 1H, ArH), 7.50-7.56 (m, 3H, ArH), 7.66, (tt, $J=7.6$, 1.2 Hz, 1H, ArH), 7.73 (ddd, $J=8.4$, 7.2, 1.6 Hz, 1H, ArH), 7.93-7.96 (m, 2H, ArH), 8.20 (dd, $J=8.0$, 2.0 Hz, 1H, ArH); ^{13}C NMR (CDCl_3 , 100 MHz) δ 114.8 (d), 118.6 (d), 124.4 (s), 125.7 (d), 125.9 (d), 128.7 (d), 130.0 (d), 134.1 (d), 134.6 (d), 134.7 (s), 155.7 (s), 157.8 (s), 178.1 (s), 187.8 (s); EI-MS (70 eV) m/z (rel.

intensity, %) 250 (M^+ , 11), 249 (14), 223 (16), 222 (100), 221 (17), 105 (68), 77 (42); Anal. calcd for $C_{16}H_{10}O_3$: C, 76.79; H, 4.03. Found: C, 76.77; H, 4.06.

2-Benzoyl-8-methoxy-1-benzopyran-4-one (2b). It (0.48 g, 86%) was obtained as a colorless crystals, mp 183-184 °C; R_f 0.18 (ethyl acetate/*n*-hexane=1:4); IR (neat) ν_{max} 1677 (s), 1647 (vs), 1577 (s), 1488 (s), 1451 (s), 1381 (s), 1277 (vs), 1180 (s), 1054 (s), 735 (s) cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) δ 3.99 (s, 3H, OCH_3), 6.94 (s, 1H, H-3), 7.25 (dd, $J=8.0, 1.2$ Hz, 1H, H-7), 7.39 (t, $J=8.0$ Hz, 1H, H-6), 7.55 (t, $J=8.0$, 2H, H-5' and H-3'), 7.69 (t, $J=8.0$ Hz, 1H, H-4'), 7.78 (dd, $J=8.0, 1.4$ Hz, 1H, H-5), 8.09 (dd, $J=8.0, 1.2$ Hz, 2H, H-2' and H-6'); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 56.4 (q) (OCH_3), 114.6 (d) (C-3), 115.1 (d) (C-7), 116.4 (d) (C-5), 125.5 (s), 125.7 (d) (C-6), 128.7 (d) (C-3', C-5), 130.3 (d) (C-2', 5'), 134.2 (d) (C-4'), 134.7 (s), 146.3 (s), 149.3 (s), 157.8 (s) (C-2), 178.2 (s) (C-4), 187.2 (s) ($Ar'C=O$); EI-MS (70 eV) m/z (rel intensity, %) 280 (M^+ , 82), 279 (10), 252 (12), 251 (37), 150 (11), 122 (12), 105 (100), 77 (52); Anal. calcd for $C_{17}H_{12}O_4$: C, 72.85; H, 4.32. Found: C, 72.88; H, 4.37.

At the same reaction condition for preparing **2b** but it was quenched after the reflux for 3 h. Worked up and purified by silica gel column chromatography (ethyl acetate/*n*-hexane=1:10) to give 2-benzoyl-8-methoxychroman-4-one **2b-1**. It (0.34 g, 61%) was obtained as colorless crystals, mp 121-122°C, R_f 0.41 (EA/*n*-hexane = 1:3), IR (KBr) cm^{-1} : 1693 (vs), 1583 (m), 1488 (s), 1297 (m), 1264 (s), 1211 (m), 1182 (m); 1H -NMR ($CDCl_3$, 400 MHz) δ 3.08 (dd, $J=17.0, 4.4$ Hz, 1H, H-3a), 3.18 (dd, $J=17.0, 9.2$ Hz, 1H, H-3b), 3.84 (s, 3H, OCH_3), 5.89 (dd, $J=9.2$ Hz, 4.4 Hz, 1H, H-2), 6.98 (t, $J=8.0$ Hz, 1H), 7.06 (dd, $J=8.0$ Hz, 1.6 Hz, 1H), 7.48-7.52 (m, 3H, ArH), 7.62 (tt, $J=7.6$ Hz, 1.2 Hz, 1H, ArH), 8.07 (dd, $J=8.4$ Hz, 1.2 Hz, 1H), ^{13}C -NMR ($CDCl_3$, 100 MHz) δ 39.1 (t), 56.3 (q), 78.5 (d), 117.5 (d), 118.0 (d), 121.6 (d), 121.8 (s), 128.7 (d), 129.3 (d), 133.9 (s), 134.0 (d), 148.9 (s), 150.2 (s), 190.2 (s), 194.1 (s); EIMS (70 eV) m/z (rel. intensity, %) 282 ($[M]^+$, 75), 177 (69), 162 (29), 161 (85), 160 (85), 149 (17), 121 (30), 105 (100), 77 (61), 51(15); Anal. calcd for $C_{17}H_{14}O_4$: C, 72.33; H, 5.00. Found: C, 72.31; H, 4.98.

2-Benzoyl-6-bromo-1-benzopyran-4-one (2c). It (0.45 g, 69%) was obtained as colorless crystals, mp 161-162 °C (lit.^{13c} 161 °C); R_f 0.46 (ethyl acetate/*n*-hexane = 1: 4); IR (neat) ν_{max} 1654 (vs), 1597 (m), 1462 (s), 1433 (s), 1358 (m), 1271 (s), 1236 (m), 984 (m), 726 (m) cm^{-1} ; 1H NMR ($CDCl_3$, 400 MHz) δ 6.89 (s, 1H, H-3), 7.49 (d, $J=8.8$ Hz, 1H, H-8), 7.54-7.58 (m, 2H, H-3' and H-5'), 7.71 (tt, $J=7.6, 1.2$ Hz, 1H, H-4'), 7.84 (dd, $J=8.8, 2.4$ Hz, 1H, H-7), 7.94-7.97 (m, 2H, H-2' and H-6'), 8.36 (d, $J=2.4$ Hz, 1H, H-5); ^{13}C NMR ($CDCl_3$, 100 MHz) δ ^{13}C NMR ($CDCl_3$, 100 MHz) δ 115.0 (d) (C-3), 119.6 (s), 120.6 (d), 125.7 (s), 128.5 (d), 128.8 (d), 130.0 (d), 134.3 (d), 134.5 (s), 137.8 (d), 154.6 (s), 158.0 (s) (C-2), 176.9 (s) (C-4), 187.6 (s) ($Ar'C=O$); EI-MS (70 eV) m/z (rel. intensity, %) 330 ($[M+2]^+$, 15), 328 (M^+ , 16), 302 (50), 301 (16), 300 (50), 221 (12), 105 (100), 77 (62); Anal. calcd for $C_{16}H_9BrO_3$: C, 58.38; H, 2.76. Found: C, 58.32; H, 3.05.

2-Benzoyl-6-chloro-1-benzopyran-4-one (2d). It (0.40 g, 70%) was obtained as colorless crystals, mp 150-152 °C (lit.^{13b} 150 °C); R_f 0.45 (ethyl acetate/ *n*-hexane=1:4); IR (neat) ν_{max} 3065 (w), 2924 (w), 1657 (vs), 1598 (sh), 1465 (s), 1437 (s), 1359 (m), 1271 (s), 1236 (m), 1113 (w), 984 (m), 857 (m), 726 (m), 683 (m) cm^{-1} ; 1H NMR($CDCl_3$, 400 MHz) δ 6.89 (s, 1H, H-3),

7.55 (d, $J=8.8$ Hz, 1H, H-8), 7.54-7.58 (m, 2H, H-3' and H-5'), 7.70 (dd, $J=8.8$, 2.6 Hz, 1H, H-7), 7.71 (tt, $J=8.4$, 1.2 Hz, 1H, H-4'), 7.95-7.97 (m, 2H, H-2' and H-6'), 8.20 (d, $J=2.6$ Hz, 1H, H-5); ^{13}C NMR(CDCl_3 , 100 MHz) δ 114.8 (d) (C-3), 120.4 (d), 125.2 (s), 125.3 (d), 128.8 (s), 130.0 (d), 132.1 (d), 134.3 (d), 134.5 (s), 135.0 (d), 154.1 (s), 157.9 (s) (C-2), 177.0 (s) (C-4), 187.5 (s) ($\text{Ar}'\text{C}=\text{O}$); EI-MS (70 eV) m/z (rel. intensity, %) 286 ($[\text{M}+2]^+$, 7), 284 (M^+ , 22), 283 (12), 258 (29), 257 (19), 256 (91), 255 (15), 221 (10), 105 (100), 77 (59); Anal. calcd for $\text{C}_{16}\text{H}_9\text{ClO}_3$: C, 67.50; H, 3.19. Found: C, 67.23; H, 3.38.

8-Methoxy-2-(4-methoxybenzoyl)-1-benzopyran-4-one (2e). It (0.51 g, 82%) was obtained as colorless crystals, mp 166-167 °C; R_f 0.31 (ethyl acetate/*n*-hexane=1:2); IR (neat) ν_{max} 3072 (w), 2927 (w), 1646 (vs), 1599 (vs), 1575 (s), 1491 (m), 1384 (m), 1257 (s), 1178 (s), 1152 (m), 1056 (m), 1025 (m), 908 (m), 850 (m), 744 (m) cm^{-1} ; ^1H NMR(CDCl_3 , 400 MHz) δ 3.93 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 6.92 (s, 1H, H-3), 7.02 (d, $J=9.2$ Hz, 2H, H-3' and H-5'), 7.24 (dd, $J=8.0$, 1.4 Hz, 1H, H-7), 7.39 (t, $J=8.0$ Hz, 1H, H-6), 7.79 (dd, $J=8.0$, 1.4 Hz, 1H, H-5), 8.14 (d, $J=9.2$ Hz, 2H, H-2' and H-6'); ^{13}C NMR(CDCl_3 , 100 MHz) δ 55.6 (q), 56.4 (q), 113.9 (d), 114.0 (d), 115.0 (d) (C-3), 116.4 (d), 125.5 (s), 125.6 (d), 127.4 (s), 133.0 (d), 146.3 (s), 149.3 (s), 158.6 (s) (C-2), 164.6 (s), 178.3 (s) (C-4), 185.3 (s) ($\text{ArC}=\text{O}$); EI-MS (70 eV) m/z (rel. intensity, %) 310 (M^+ , 27), 281 (8), 136 (9), 135 (100), 107 (9), 77 (15); Anal. Calcd for $\text{C}_{18}\text{H}_{14}\text{O}_5$: C, 69.67; H, 4.55. Found: C, 69.27; H, 4.59.

7-Methoxy-2-(4-methoxybenzoyl)-1-benzopyran-4-one (2f). It (0.53 g, 85%) was obtained as a colorless crystals, mp 178 °C; R_f 0.38 (ethyl acetate/*n*-hexane=1:2); IR (neat) ν_{max} 2925 (w), 1648 (s), 1600 (s), 1507 (w), 1437 (m), 1382 (w), 1257 (vs), 1169 (m), 1023 (w), 842 (w), 767 (w) cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 3.92 (s, 6H, 2 x OCH_3), 6.78 (s, 1H, H-3), 6.96 (d, $J=2.4$ Hz, 1H, H-8), 7.02 (d, $J=9.0$ Hz, 2H, H-3' and H-5'), 7.03 (dd, $J=8.8$, 2.4 Hz, 1H, H-6), 7.99 (d, $J=9.0$ Hz, 2H, H-2' and H-6'), 8.14 (d, $J=8.8$ Hz, 1H, H-5); ^{13}C NMR(CDCl_3 , 100 MHz) δ 55.6 (q), 55.9 (q), 100.5 (d), 114.1 (d), 114.8 (d) (C-3), 115.5 (s), 118.4 (s), 127.1 (d), 127.5 (d), 132.7 (d), 157.8 (s), 158.1 (s) (C-2), 164.6 (s), 164.8 (s), 177.4 (s) (C-4), 186.2 (s) ($\text{Ar}'\text{C}=\text{O}$); EI-MS (70 eV) m/z (rel. intensity, %) 310 (M^+ , 46), 282 (34), 281 (39), 135 (100), 107 (11), 77 (26); Anal. calcd for $\text{C}_{18}\text{H}_{14}\text{O}_5$: C, 69.67; H, 4.55. Found: C, 69.56; H, 4.59.

2-Benzoyl-6,8-dichloro-1-benzopyran-4-one (2g). It (0.22 g, 35%) was obtained as a colorless crystals, mp 132-133 °C; R_f 0.58 (ethyl acetate/*n*-hexane = 1:4); IR (neat) ν_{max} 3073 (w), 1661 (vs), 1595 (m), 1562 (w), 1446 (s), 1355 (m), 1319 (w), 1265 (s), 1194 (w), 1131 (w), 1106 (w), 987 (m), 863 (s), 723 (s) cm^{-1} ; ^1H NMR(CDCl_3 , 400 MHz) δ 7.02 (s, 1H, H-3), 7.55-7.59 (m, 2H, H-3' and H-5'), 7.71 (tt, $J=7.6$, 1.2 Hz, 1H, H-4'), 7.81 (d, $J=2.6$ Hz, 1H, H-7), 8.06-8.09 (m, 2H, H-2' and H-6'), 8.12 (d, $J=2.6$ Hz, 1H, H-5); ^{13}C NMR(CDCl_3 , 100 MHz) δ 114.4 (d) (C-3), 124.0 (d), 125.1 (s), 126.3 (d), 128.8 (s), 130.3 (s), 131.9 (s), 134.3 (d), 134.5 (d), 134.8 (d), 150.3 (s), 158.3 (s) (C-2), 176.4 (s) (C-4), 186.5 (s) ($\text{Ar}'\text{C}=\text{O}$); EI-MS (70 eV) m/z (rel. intensity, %) 320 ($[\text{M}+2]^+$, 20), 318 (M^+ , 29), 292 (46), 291 (17), 290 (71), 105 (100), 77 (78); Anal. calcd for $\text{C}_{16}\text{H}_8\text{Cl}_2\text{O}_3$: C, 60.22; H, 2.53. Found: C, 60.25; H, 2.63.

6-Chloro-2-(4-chlorobenzoyl)-1-benzopyran-4-one (2h). It (0.31 g, 49%) was obtained as a colorless crystals, mp 175-176 °C; R_f 0.58 (ethyl acetate/*n*-hexane=1:4); IR (neat) ν_{max} 3063 (w),

1651 (vs), 1607 (m), 1463 (m), 1437 (m), 1360 (w), 1278 (m), 1091 (m), 984 (m), 833 (m) 762 (m) cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 6.89 (s, 1H, H-3), 7.54 (d, $J=8.8$ Hz, 1H, H-8), 7.54 (d, $J=8.8$ Hz, 2H, H-3' and H-5'), 7.71 (dd, $J=8.8$, 2.4 Hz, 1H, H-7), 7.93 (d, $J=8.8$ Hz, 2H, H-2' and H-6'), 8.21 (d, $J=2.4$ Hz, 1H, H-5); ^{13}C NMR (CDCl_3 , 100 MHz) δ 114.7 (d) (C-3), 120.4 (d), 125.3 (s), 129.2 (d), 129.3 (s), 131.4 (d), 132.3 (d), 132.8 (s), 135.1 (d), 141.1 (s), 154.1 (s), 157.7 (s) (C-2), 176.9 (s) (C-4), 186.3 (s) ($\text{Ar}'\text{C}=\text{O}$); EI-MS (70 eV) m/z (rel. intensity, %) 320 ($[\text{M}+2]^+$, 10), 318 (M^+ , 15), 292 (17), 290 (26), 141 (32), 139 (100), 111 (30), 75 (14); Anal. calcd for $\text{C}_{16}\text{H}_8\text{Cl}_2\text{O}_3$: C, 60.22; H, 2.53. Found: C, 59.94; H, 2.69.

6-Chloro-2-(4-methoxybenzoyl)-1-benzopyran-4-one (2i). It (0.41 g, 65%) was obtained as a colorless crystals, mp 116-117 $^\circ\text{C}$ (lit.^{13b} 114 $^\circ\text{C}$); R_f 0.35 (ethyl acetate/*n*-hexane = 1:4); IR (neat) ν_{max} 1655 (vs), 1598 (vs), 1464 (s), 1437 (s), 1359 (m), 1262 (vs), 1174 (s), 1026 (m), 983 (m), 860 (m), 772 (m) cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 3.93 (s, 3H, OCH_3), 6.84 (s, 1H, H-3), 7.02 (d, $J=8.8$ Hz, 2H, H-3' and H-5'), 7.55 (d, $J=8.8$ Hz, 1H, H-8), 7.70 (dd, $J=8.8$, 2.6 Hz, 1H, H-7), 7.99 (d, $J=8.8$ Hz, 2H, H-2' and H-6'), 8.21 (d, $J=2.6$ Hz, 1H, H-5); ^{13}C NMR (CDCl_3 , 100 MHz) δ 55.7 (q), 114.21 (d), 114.23 (d) (C-3), 120.4 (d), 125.3 (d), 125.4 (s), 127.2 (s), 132.0 (d), 132.7 (d), 134.9 (s), 154.2 (s), 158.8 (s) (C-2), 164.8 (s), 177.0 (s) (C-4), 185.7 (s) ($\text{ArC}=\text{O}$); EI-MS (70 eV) m/z (rel. intensity, %) 316 ($[\text{M}+2]^+$, 5), 314 (M^+ , 15), 286 (8), 285 (8), 136 (9), 135 (100), 107 (8), 77 (14); Anal. calcd for $\text{C}_{17}\text{H}_{11}\text{ClO}_4$: C, 64.88; H, 3.52. Found: C, 64.86; H, 3.55.

2-(4-Methoxybenzoyl)-1-benzopyran-4-one (2j). It (0.41 g, 73%) was obtained as a colorless crystal, mp 73-74 $^\circ\text{C}$ (lit.^{13b} 72 $^\circ\text{C}$); R_f 0.20 (ethyl acetate/*n*-hexane = 1:5); IR (neat) ν_{max} 2929 (w), 1652 (vs), 1597 (vs), 1463 (s), 1379 (m), 1312 (m), 1259 (vs), 1174 (s), 1135 (w), 1024 (m), 873 (m), 767 (m) cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 3.93 (s, 3H, OCH_3), 6.85 (s, 1H, H-3), 7.02 (d, $J=8.8$ Hz, 2H, H-3' and H-5'), 7.48 (ddd, $J=8.0$, 7.2, 0.8 Hz, 1H, H-6), 7.58 (dd, $J=8.8$, 0.8 Hz, 1H, H-8), 7.76 (ddd, $J=8.8$, 7.2, 1.0 Hz, 1H, H-7), 8.01 (d, $J=8.8$ Hz, 2H, H-2' and H-6'), 8.25 (d, $J=8.0$, 1.0 Hz, 1H, H-5); ^{13}C NMR (CDCl_3 , 100 MHz) δ 55.7 (q), 114.1 (d), 114.3 (d) (C-3), 118.6 (d), 124.5 (s), 125.8 (d), 125.9 (d), 127.3 (d), 132.7 (d), 134.6 (s), 155.8 (s), 158.7 (s) (C-2), 164.6 (s), 178.2 (s) (C-4), 186.0 (s) ($\text{Ar}'\text{C}=\text{O}$); EI-MS (70 eV) m/z (rel. intensity, %) 280 (M^+ , 46), 252 (27), 251 (23), 135 (100), 107 (10), 77 (27); Anal. calcd for $\text{C}_{17}\text{H}_{12}\text{O}_4$: C, 72.85; H, 4.32. Found: C, 72.57; H, 4.28.

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