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## FACILE PREPARATION OF 3,4-BENZOCOUMARINS FROM 2-ARYLBENZOIC ACIDS WITH NCS AND NaI

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**Abstract** – Treatment of 2-arylbenzoic acids with *N*-chlorosuccinimide (NCS) and NaI at 70 °C under fluorescent lighting condition gave the corresponding 3,4-benzocoumarins in good yields under transition-metal-free condition. It was found that the reactivity of NCS with NaI for the formation of 3,4-benzocoumarins from 2-arylbenzoic acids was as high as that with NIS. Thus, the formation of carboxyl radicals and their cyclization onto an aromatic ring from 2-arylbenzoic acids with much less expensive NCS and NaI, than NIS could be successfully carried out to form 3,4-benzocoumarins.

### INTRODUCTION

3,4-Benzocoumarins are one of the most important aromatic lactones because they are metabolites derived from fungi, bacteria, plants, and animals feces, and some of them show biological activities, such as antioxidant, anti-allergic, and antimicrobial activities.<sup>1</sup> As typical examples, urolithins A and B possess antioxidant activity<sup>1a</sup> and anti-proliferative effect against human cancer cells,<sup>1b</sup> and atenuisol exhibits potent antibacterial activity, as shown in Figure 1.<sup>1</sup>

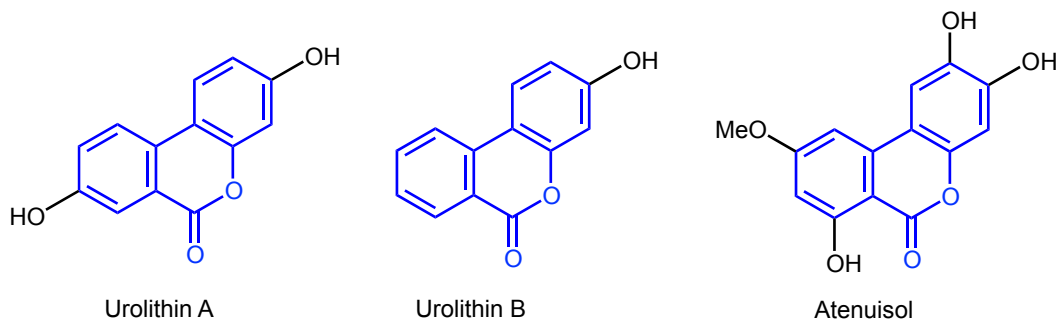


Figure 1. Biologically Active 3,4-Benzocoumarins

Extensive synthetic studies of the 3,4-benzocoumarin core have been carried out. One of the most efficient methods for the preparation of 3,4-benzocoumarins is the cyclization of 2-arylbenzoic acids with oxidants, such as toxic chromic acid<sup>2a</sup> and Pb(OAc)<sub>4</sub>.<sup>2b</sup> Recent reports of the preparation of

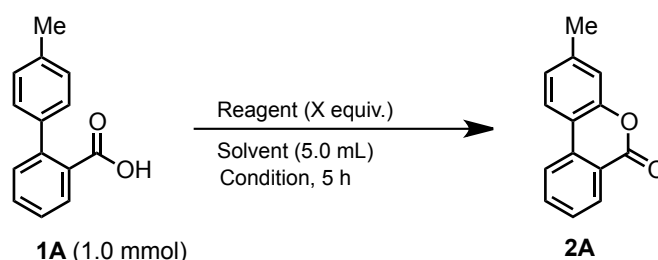
3,4-benzocoumarins from 2-arylbenzoic acids are as follows:<sup>3</sup> the preparation with  $\text{PhCO}_3\text{Bu}^t$  in the presence of  $\text{Cu}(\text{OAc})_2$  in  $\text{ClCH}_2\text{CH}_2\text{Cl}$  (DCE) and with  $\text{K}_2\text{S}_2\text{O}_8$  in the presence of  $\text{AgNO}_3$  in  $\text{MeCN}/\text{H}_2\text{O}$ ;<sup>3a</sup> the preparation in the presence of  $[\text{Acr-Mes}]\text{ClO}_4$  and  $\text{Co}(\text{dmgH})_2\text{Cl}_2$  in  $\text{MeCN}$  under blue LED irradiation;<sup>3b</sup> the preparation using Kolbe anodic oxidation with Pt electrode in  $\text{MeOH}/\text{H}_2\text{O}$ <sup>3c</sup> and in  $\text{MeCN}$ ;<sup>3d</sup> the preparation in the presence of (-)-riboflavin in  $\text{MeOH}$  under UV irradiation;<sup>3e</sup> the preparation with  $\text{K}_2\text{S}_2\text{O}_8$  in the presence of  $\text{AgNO}_3$  in  $\text{MeCN}/\text{H}_2\text{O}$ ;<sup>3f</sup> the preparation in the presence of  $\text{CeCl}_3$  in  $\text{CHCl}_3$  under blue LED irradiation;<sup>3g</sup> the preparation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) and  $t\text{BuONO}$  in DCE under blue LED irradiation;<sup>3h</sup> and the preparation with  $\text{NaBrO}_3$  in the presence of  $\text{Fe}(\text{NO}_3)_3$  under irradiation with 40 W LED.<sup>3i</sup> The preparation of 3,4-benzocoumarins with *N*-methoxy-2-arylbenzamides and  $t\text{BuONO}$  was also reported.<sup>4</sup> Examples of condensation reactions to generate the 3,4-benzocoumarin core include the reaction of salicylaldehydes, malononitrile, and ethyl acetoacetate with  $\text{MgO}$ ;<sup>5a</sup> the reaction of *O*-aryl acrylates bearing an  $\alpha,\beta$ -alkenoyl group at *o*-position with DBU in DMSO;<sup>5b</sup> the reaction of 3-acetylcoumarins and malononitrile with piperidine in  $\text{EtOH}$ ;<sup>5c</sup> and the reaction of 3-acetylcoumarin and  $\alpha,\beta$ -unsaturated aldehydes with DBU in  $\text{CHCl}_3$ .<sup>5d</sup> The preparation of 3,4-benzocoumarins through the carbonylation of 10-hydroxy-10,9-boroxarophenanthrenes with CO in the presence of  $\text{Pd}(\text{OAc})_2$  in  $\text{DMSO}/\text{MeOH}$ ;<sup>6a</sup> through the carbonylation of 2-arylphenols with CO in the presence of  $[\text{RuCl}_2(p\text{-cymene})]_2$  in mesitylene;<sup>6b</sup> through the [3+3] annulation of *N*-methoxyarylamides and *p*-quinols in the presence of  $[\text{Cp}^*\text{RhCl}_2]_2$  in  $\alpha,\alpha,\alpha$ -trifluorotoluene/acetone;<sup>6c</sup> and through the oxidative lactonization of 2-methylbiaryls in the presence of  $[\text{Acr-Mes}]\text{ClO}_4$  with  $\text{O}_2$  in  $\text{MeCN}/\text{H}_2\text{O}$  under blue LED irradiation<sup>6d</sup> is known as well.

Among those methods, the preparation of the 3,4-benzocoumarin core from *o*-arylbenzoic acids with less toxic oxidants is very attractive because the cyclization of 2-arylbenzoic acids to 3,4-benzocoumarins is a simple, efficient, and atom-economic approach, and 2-arylbenzoic acids can be easily obtained by the reaction of ethyl 2-iodobenzoate and arylboronic acids in the presence of Pd catalyst. Previously, we reported the preparation of 3,4-benzocoumarin from the reaction of 2-phenylbenzoic acid with  $\text{PhI}(\text{O}_2\text{CCF}_3)_2$  (BTIB) and iodine,<sup>7a</sup> and with 1,3-diiodo-5,5-dimethylhydantoin (DIH)<sup>7b</sup> under irradiation with a tungsten lamp. Wei *et al.* reported a practical and useful method for the preparation of 3,4-benzocoumarins from 2-arylbenzoic acids with *N*-iodosuccinimide (NIS).<sup>8</sup> We reported the transformation of aliphatic carboxylic acids into the corresponding decarboxylated alkyl iodides and *N*-alkylsuccinimides by the reaction with NIS, and NCS with  $\text{NaI}$ .<sup>9</sup> In that work, the transformation of aromatic carboxylic acids into aryl iodides and *N*-arylsuccinimides with NIS did not occur at all because the rate constant for the decarboxylation of aromatic carboxyl radicals ( $k = \sim 10^6 \text{ s}^{-1}$ , 25 °C) is rather low as compared with that of aliphatic carboxyl radicals ( $k = \sim 10^{10} \text{ s}^{-1}$ , 25 °C).<sup>10</sup> Therefore, the formation of

arenecarboxyl radicals and their cyclization onto an aromatic ring with arenecarboxylic acids and NIS are very efficient. However, NIS is rather expensive and not so stable on the bench. On the other hand, *N*-chlorosuccinimide (NCS) is affordable and much more stable than NIS. Here, we would like to report the preparation of 3,4-benzocoumarins from 2-arylbenzoic acids with NCS in the presence of NaI, and the comparison of NCS/NaI reactivity with NIS reactivity.

## RESULTS AND DISCUSSION

First, 2-(4'-methylphenyl)benzoic acid (**1A**, 1.0 mmol) was treated with NIS (1.5, 2.0, and 2.5 equiv.) in DCE (5.0 mL) under irradiation with a 300 W tungsten lamp to form 3,4-benzo-7-methylcoumarin **2A** in 77%, 96%, and >99% yields, respectively, as shown in Table 1 (entries 1~3), and NIS (2.5 equiv.) showed the best result (entry 3). When the reaction of acid **1A** was carried out under irradiation with a 40 W tungsten lamp and a white LED (13.6 W) instead of a 300 W tungsten lamp under the same conditions, compound **2A** was obtained in 99% and 95% yields, respectively (entries 4, 5). Under warming at 70 °C and fluorescent lighting conditions (room light), as shown in the reported method,<sup>8</sup> compound **2A** was obtained in 97% yield (entry 6). When DCE was changed to acetonitrile and methanol under the same conditions, compound **2A** was obtained in 89% yield in the former solvent. Methanol in contrast, reduced the yield of compound **2A** dramatically, probably due to  $\alpha$ -hydrogen-atom abstraction of methanol by the formed carboxyl radical (entries 7, 8). The same reaction with 1,3-diiodo-5,5-dimethylhydantoin (1.5 equiv.), which has two N-I bonds, instead of NIS (2.5 equiv.), also gave compound **2A** in >99% yield (entry 9). In contrast, the same treatment of acid **1A** with I<sub>2</sub> (2.5 equiv.) and K<sub>2</sub>CO<sub>3</sub> (1.5 equiv.) instead of NIS gave compound **2A** in only 4% yield (entry 10). When the reaction shown in entry 3 was carried out in the presence of 2,6-di-*tert*-butyl-*p*-cresol (BHT, 1.5 equiv.), which is a hydrogen-atom donor, and in the presence of 2,2,6,6-tetramethylpiperidine 1-oxyl radical (TEMPO, 1.5 equiv.), which is a radical trapping agent, compound **2A** was not formed at all for both (entries 11, 12) and acid **1A** was recovered in high yields. Thus, the present reaction proceeds through radical-mediated pathways. On the other hand, when 2-phenylbenzoic acid **1C** was treated with *N*-bromosuccinimide (NBS) and *N*-chlorosuccinimide (NCS) instead of NIS under the same conditions as those for entry 3, 3,4-benzocoumarin **2C** was not formed at all for both and acid **1C** was recovered in high yields (entries 13, 14). Thus, the iodine of NIS and DIH plays an important role in the formation of compound **2A**. A gram-scale experiment with acid **1A** (5.0 mmol) under the same conditions gave 3,4-benzo-7-methylcoumarin **2A** in 99% yield, as shown in Table 2.

**Table 1.** Optimization of Reaction Conditions

Entry	Reagent (equiv.)	Solvent	Conditions	Yield (%)
1	NIS (1.5)	DCE	300 W W-hv	77
2	NIS (2.0)	DCE	300 W W-hv	96
<b>3</b>	<b>NIS (2.5)</b>	<b>DCE</b>	<b>300 W W-hv</b>	<b>&gt;99</b>
<b>4</b>	NIS (2.5)	<b>DCE</b>	40 W W-hv	99
5	NIS (2.5)	DCE	13.6 W LED	95
6	NIS (2.5)	DCE	70 °C, fluorescent lighting (32 W)	97
7	NIS (2.5)	MeCN	300 W W-hv	89
8	NIS (2.5)	MeOH	300 W W-hv	6
9	DIH (1.5)	DCE	300 W W-hv	>99
10 <sup>a</sup>	I <sub>2</sub> , K <sub>2</sub> CO <sub>3</sub>	DCE	300 W W-hv	4
11 <sup>b</sup>	NIS (2.5)	DCE	300 W W-hv	0 (96) <sup>c</sup>
12 <sup>d</sup>	NIS (2.5)	DCE	300 W W-hv	0 (95) <sup>c</sup>
13 <sup>e</sup>	NBS (2.5)	DCE	300 W W-hv	0 (97) <sup>c</sup>
14 <sup>e</sup>	NCS (2.5)	DCE	300 W W-hv	0 (98) <sup>c</sup>

<sup>a</sup> I<sub>2</sub> (2.5 equiv.) and K<sub>2</sub>CO<sub>3</sub> (1.5 equiv.) instead of NIS were used.

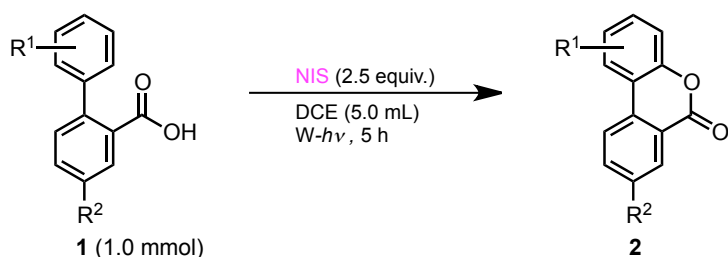
<sup>b</sup> BHT (1.5 equiv.) was added.

<sup>c</sup> Recovery of **1A**.

<sup>d</sup> TEMPO (1.5 equiv.) was added.

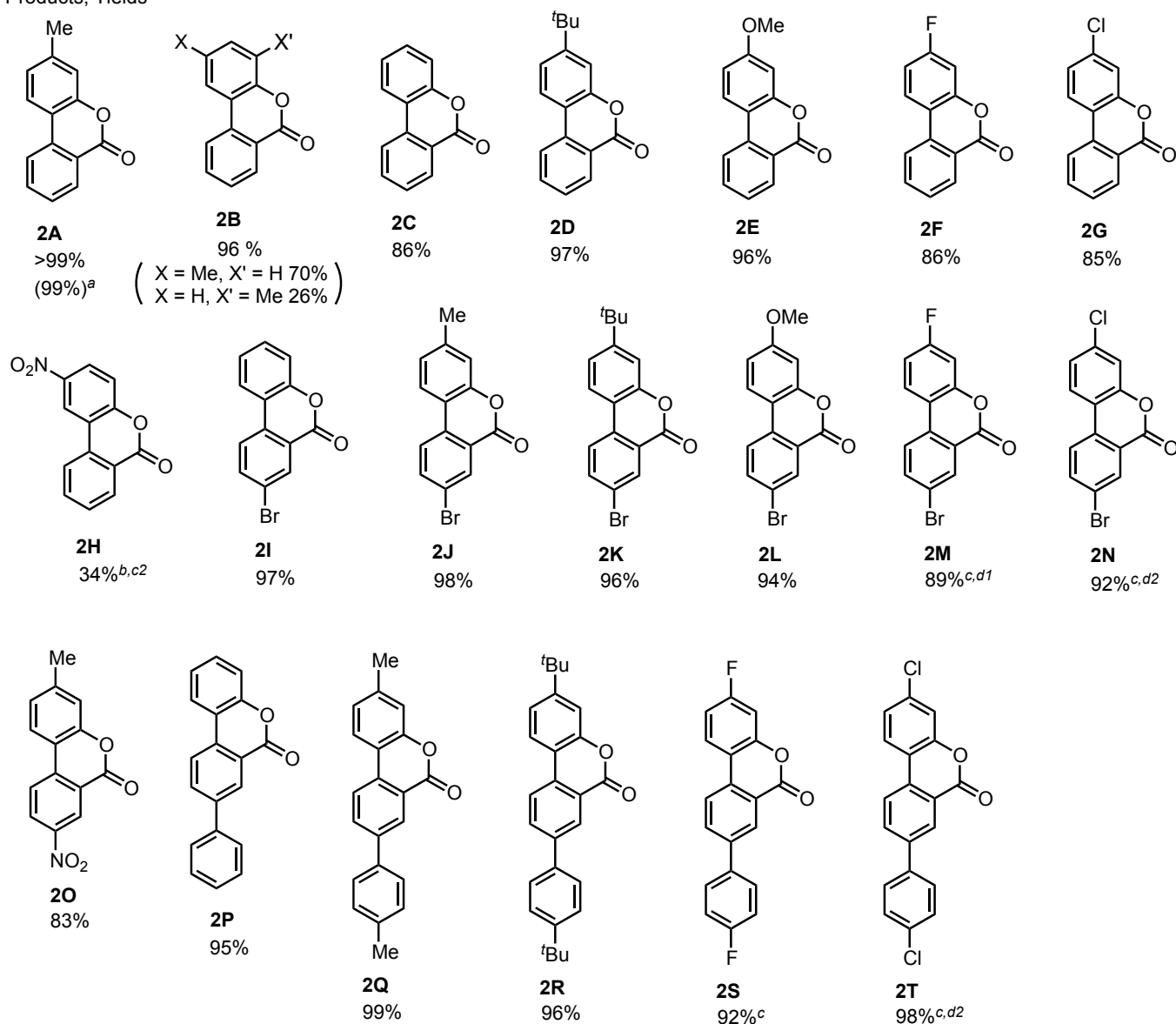
<sup>e</sup> 2-Phenylbenzoic acid **1C** was used instead of **1A**.

Based on those results, 2-arylbenzoic acids **1B~1H** (1.0 mmol) and 2-aryl-5-bromobenzoic acids **1I~1N** bearing 3-methylphenyl, phenyl, 4-*tert*-butylphenyl, 4-methoxyphenyl, 4-fluorophenyl, 4-chlorophenyl, and 3-nitrophenyl groups were treated with NIS (2.5 equiv.) in DCE (5.0 mL) in the temperature range of 38 °C~40 °C under irradiation with a 300 W tungsten lamp for 5 h to give 3,4-benzocoumarins **2B~2H** and 3,4-(2'-bromo)benzocoumarins **2I~2N** in good yields except compound **2H**, as shown in Table 2. The reason for the low yield of **2H** may be that the formed electrophilic carboxyl radical has to react with the electron-deficient 3-nitrophenyl group. On the other hand, the same treatment of 5-nitro-2-(4'-methylphenyl)benzoic acid **1O** gave 3,4-(2'-nitro)benzo-7-methylcoumarin **2O** in 83% yield. Further treatment of 2,5-diarylbenzoic acids **1P~1T** under the same conditions gave also 3,4-benzocoumarins **2P~2T** in good yields.

**Table 2.** Transformation of *o*-Arylbenzoic Acids **1** to 3,4-Benzocoumarins **2** with NIS

**A:** R<sup>1</sup> = 4-Me, R<sup>2</sup> = H; **B:** R<sup>1</sup> = 3-Me, R<sup>2</sup> = H; **C:** R<sup>1</sup> = R<sup>2</sup> = H; **D:** R<sup>1</sup> = 4-<sup>t</sup>Bu, R<sup>2</sup> = H; **E:** R<sup>1</sup> = 4-OMe, R<sup>2</sup> = H; **F:** R<sup>1</sup> = 4-F, R<sup>2</sup> = H; **G:** R<sup>1</sup> = 4-Cl, R<sup>2</sup> = H; **H:** R<sup>2</sup> = 3-NO<sub>2</sub>, R<sup>1</sup> = H; **I:** R<sup>1</sup> = H, R<sup>2</sup> = Br; **J:** R<sup>1</sup> = 4-Me, R<sup>2</sup> = Br; **K:** R<sup>1</sup> = 4-<sup>t</sup>Bu, R<sup>2</sup> = Br; **L:** R<sup>1</sup> = 4-OMe, R<sup>2</sup> = Br; **M:** R<sup>1</sup> = 4-F, R<sup>2</sup> = Br; **N:** R<sup>1</sup> = 4-Cl, R<sup>2</sup> = Br; **O:** R<sup>1</sup> = 4-Me, R<sup>2</sup> = NO<sub>2</sub>; **P:** R<sup>1</sup> = H, R<sup>2</sup> = Ph; **Q:** R<sup>1</sup> = 4-Me, R<sup>2</sup> = 4-MeC<sub>6</sub>H<sub>4</sub>; **R:** R<sup>1</sup> = 4-<sup>t</sup>Bu, R<sup>2</sup> = 4-<sup>t</sup>BuC<sub>6</sub>H<sub>4</sub>; **S:** R<sup>1</sup> = 4-F, R<sup>2</sup> = 4-FC<sub>6</sub>H<sub>4</sub>; **T:** R<sup>1</sup> = 4-Cl, R<sup>2</sup> = 4-ClC<sub>6</sub>H<sub>4</sub>

Products, Yields

<sup>a</sup> Reaction was carried out with **1A** (5.0 mmol).<sup>b</sup> NIS (3.5 equiv.) was used.<sup>c</sup> NIS (3.5 equiv.) in DCE (10 mL) was used.<sup>d</sup> Reaction was carried out for <sup>1</sup>7 h or <sup>2</sup>8 h.

Then, a combination system of NCS and NaI was studied although NCS alone did not react at all (Table 1, entry 14). A mixture of NCS (2.5 equiv.) and NaI (2.5 equiv.) in DCE (5.0 mL) was stirred at room temperature for 2 h (1st step). Then, 2-(4'-methylphenyl)benzoic acid (**1A**, 1.0 mmol) was added to the mixture, and irradiation of the obtained mixture in the temperature range of 38~40 °C with a 300 W tungsten lamp for 7 h (2nd step) gave 3,4-benzo-7-methylcoumarin **2A** in 89% yield, as shown in Table 3 (entry 1). Moreover, after stirring mixtures of NCS (2.5 equiv.) and NaI (1.0, 1.5, and 2.5 equiv.) in DCE at room temperature for 2 h (1st step), treatment of acid **1A** with those solutions at 70 °C for 7 h under fluorescent lighting (32 W) condition (2nd step) gave compound **2A** in 61%, 81%, and 99% yields, respectively (entries 2~4). Entry 4 showed the best result to form compound **2A** in good yield. When KI (2.5 equiv.) was used instead of NaI under the same procedure and conditions, the yield of compound **2A** was slightly decreased to 90% (entry 5). On the other hand, when Et<sub>4</sub>NI (2.5 equiv.), which is more soluble than NaI, was used, the yield of compound **2A** was trace and instead, β-chloroethyl 2-(4'-methylphenyl)benzoate was obtained in 87% yield (entry 6). When the reaction in entry 4 was carried out in the dark (2nd step), the yield of compound **2A** was decreased to 38% (entry 7). Thus, a combination of NCS (2.5 equiv) and NaI (2.5 equiv.) instead of NIS (2.5 equiv.) can be used effectively

**Table 3.** Optimization of Reaction Conditions

1) NCS (2.5 equiv.)  
NaI (2.5 equiv.)  
DCE (5.0 mL), rt, 2 h  
(1st step)

2) 70 °C, 7 h  
fluorescent lighting (32 W)  
(2nd step)

**1A** (1.0 mmol) → **2A**

Entry	Reagent (equiv.)	Additive (equiv.)	Solvent	Conditions	Yield (%)
1	NCS (2.5)	NaI (2.5)	DCE	300 W- <i>hν</i> , 38 °C~40 °C <sup>a</sup>	89
2	NCS (2.5)	NaI (1.0)	DCE	70 °C	61
3	NCS (2.5)	NaI (1.5)	DCE	70 °C	81
<b>4</b>	<b>NCS (2.5)</b>	<b>NaI (2.5)</b>	<b>DCE</b>	70 °C	<b>99</b>
5	NCS (2.5)	KI (2.5)	DCE	70 °C	90
6	NCS (2.5)	Et <sub>4</sub> NI (2.5)	DCE	70 °C	<1 (87%) <sup>b</sup>
7 <sup>c</sup>	NCS (2.5)	NaI (2.5)	DCE	70 °C	38
8	NCS (2.5)	NaI (2.5)	MeCN	70 °C	60
9	NCS (2.5)	NaI (2.5)	MeOH	70 °C	4

<sup>a</sup> Reaction was carried out under irradiation with a 300 W tungsten lamp instead of a fluorescent lamp.

<sup>b</sup> β-Chloroethyl 2-(4'-methylphenyl)benzoate was obtained.

<sup>c</sup> Reaction was carried out under dark conditions.

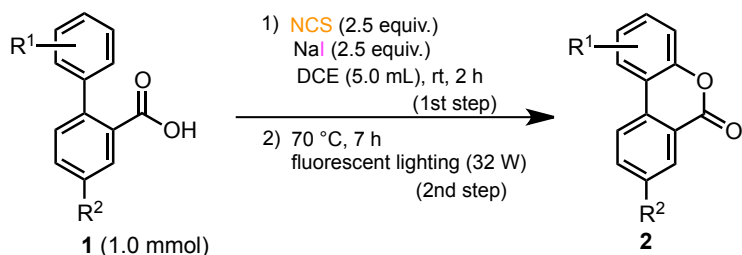
for the transformation of 2-(4'-methylphenyl)benzoic acid **1A** into 3,4-benzo-7-methylcoumarin **2A**, and warming at 70 °C for 7 h under fluorescent lighting condition was the best to form compound **2A** in good yield (entry 4).

When DCE was changed to acetonitrile and methanol under the same procedure and conditions, compound **2A** was obtained in 60% and 4% yields, respectively (entries 8, 9). A gram-scale experiment with acid **1A** (5.0 mmol) with NCS and NaI under the same procedure and conditions gave 3,4-benzo-7-methylcoumarin **2A** in 99% yield, as shown in Table 4.

Based on those results, we performed the following procedure: after stirring a mixture of NCS (2.5 equiv.) and NaI (2.5 equiv.) in DCE (5.0 mL) at room temperature for 2 h, 2-arylbenzoic acids **1B~1H** and 2-aryl-5-bromobenzoic acids **1I~1N** (1.0 mmol) bearing 3-methylphenyl, phenyl, 4-*tert*-butylphenyl, 4-methoxyphenyl, 4-fluorophenyl, 4-chlorophenyl, and 3-nitrophenyl groups were treated at 70 °C for 7 h under fluorescent lighting (32 W) condition to provide 3,4-benzocoumarins **2B~2H** and 3,4-(2'-bromo)benzocoumarins **2I~2N** in good yields except compound **2H**, as shown in Table 4.

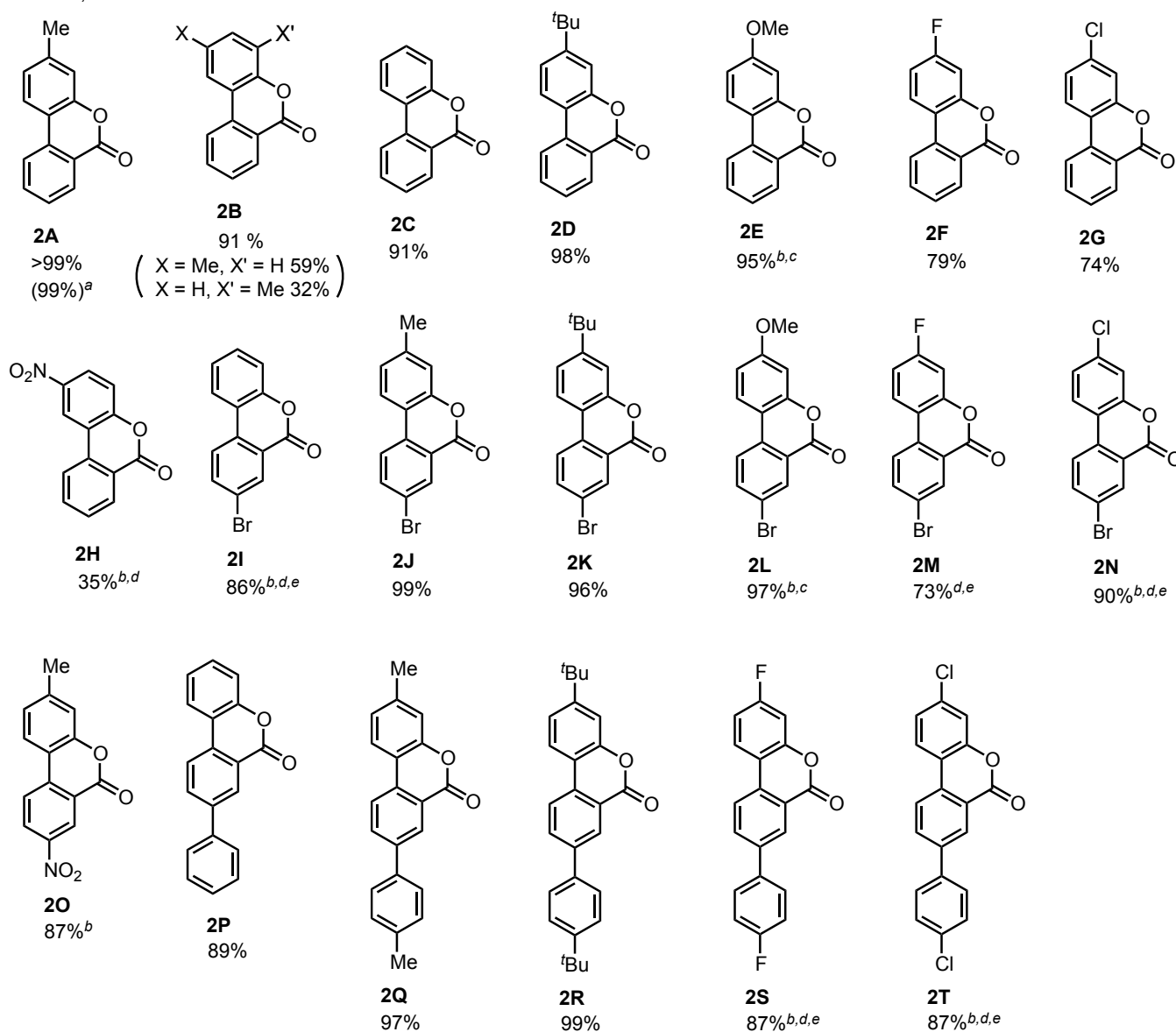
Overall, the reactivities of the NIS system and the NCS/NaI system are rather similar. Therefore, the same treatment of 5-nitro-2-(4'-methylphenyl)benzoic acid **1O** gave 3,4-(2'-nitro)benzo-7-methylcoumarin **2O** in 87% yield. Further treatment of 2,5-diarylbenzoic acids **1P~1T** under the same procedure and conditions gave the corresponding 3,4-(2'-aryl)benzocoumarins **2P~2T** in good yields, respectively.

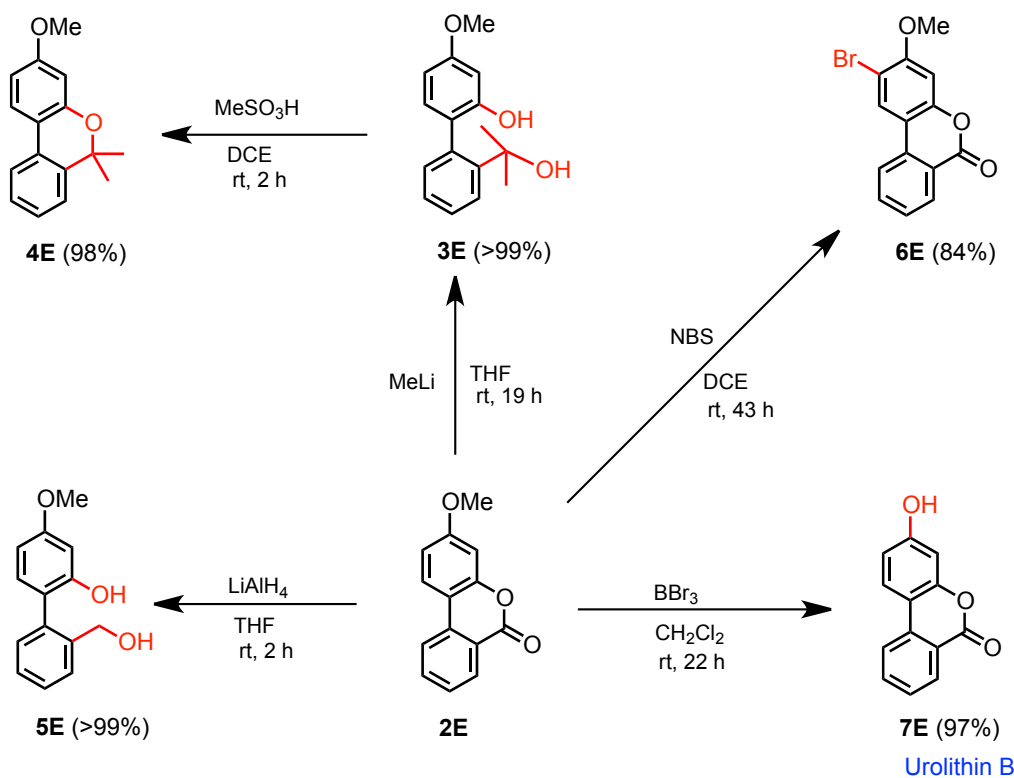
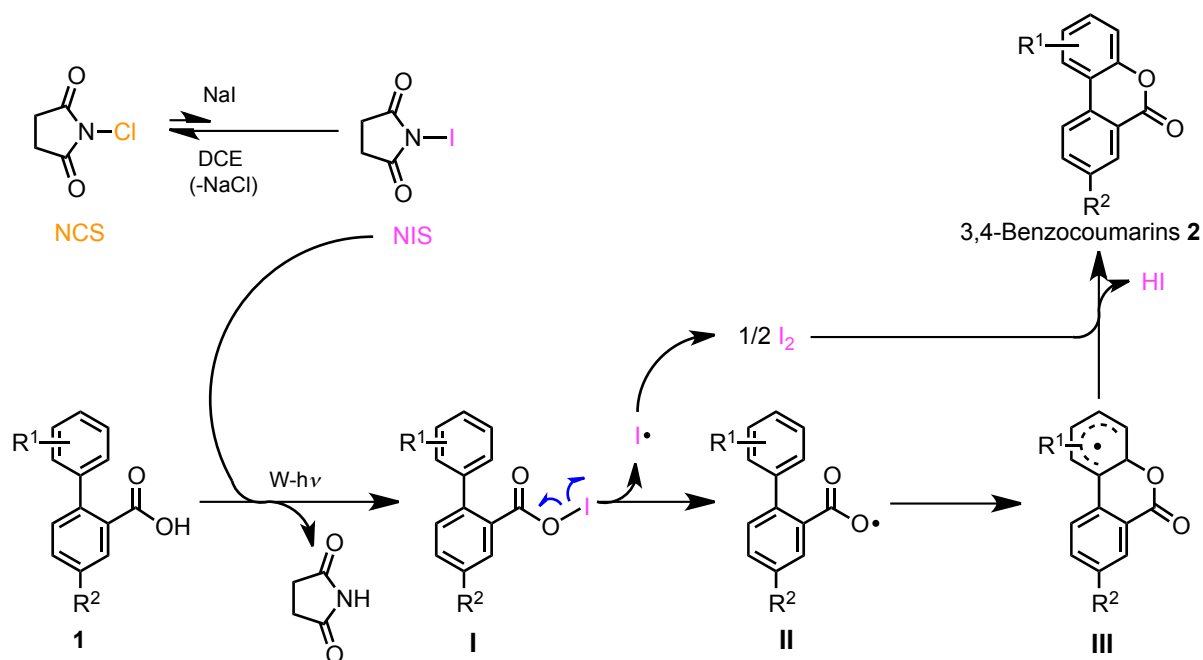
Once the 3,4-benzocoumarins were obtained, they could be transformed into a variety of 3,4-benzocoumarin derivatives. Treatment of 3,4-benzo-7-methoxycoumarin **2E** with methyllithium (4.5 equiv.) gave diol **3E** in >99% yield, and **3E** was further reacted with methanesulfonic acid (2.0 equiv.) to form dehydrated 3,4,5,6-dibenzo-2,2-dimethylpyran **4E** in 98% yield, as shown in Scheme 1. Reduction of compound **2E** with LiAlH<sub>4</sub> (1.5 equiv.) gave diol **5E** in >99% yield. Reaction of compound **2E** with NBS (1.4 equiv.) gave 3,4-benzo-6-bromo-7-methoxycoumarin **6E** in 84% yield. Furthermore, treatment of compound **2E** with BBr<sub>3</sub> (5.0 equiv.) generated urolithin B (**7E**) in 97% yield.

**Table 4.** Transformation of *o*-Arylbenzoic Acids **1** to 3,4-Benzocoumarins **2** with NCS and NaI

**A:** R<sup>1</sup> = 4-Me, R<sup>2</sup> = H; **B:** R<sup>1</sup> = 3-Me, R<sup>2</sup> = H; **C:** R<sup>1</sup> = R<sup>2</sup> = H; **D:** R<sup>1</sup> = 4-<sup>t</sup>Bu, R<sup>2</sup> = H; **E:** R<sup>1</sup> = 4-OMe, R<sup>2</sup> = H; **F:** R<sup>1</sup> = 4-F, R<sup>2</sup> = H; **G:** R<sup>1</sup> = 4-Cl, R<sup>2</sup> = H; **H:** R<sup>2</sup> = 3-NO<sub>2</sub>, R<sub>2</sub> = H; **I:** R<sup>1</sup> = H, R<sup>2</sup> = Br; **J:** R<sup>1</sup> = 4-Me, R<sup>2</sup> = Br; **K:** R<sup>1</sup> = 4-<sup>t</sup>Bu, R<sup>2</sup> = Br; **L:** R<sup>1</sup> = 4-OMe, R<sup>2</sup> = Br; **M:** R<sup>1</sup> = 4-F, R<sup>2</sup> = Br; **N:** R<sup>1</sup> = 4-Cl, R<sup>2</sup> = Br; **O:** R<sup>1</sup> = 4-Me, R<sup>2</sup> = NO<sub>2</sub>; **P:** R<sup>2</sup> = H, R<sup>2</sup> = Ph; **Q:** R<sup>1</sup> = 4-Me, R<sup>2</sup> = 4-MeC<sub>6</sub>H<sub>4</sub>; **R:** R<sup>1</sup> = 4-<sup>t</sup>Bu, R<sup>2</sup> = 4-<sup>t</sup>BuC<sub>6</sub>H<sub>4</sub>; **S:** R<sup>1</sup> = 4-F, R<sup>2</sup> = 4-FC<sub>6</sub>H<sub>4</sub>; **T:** R<sup>1</sup> = 4-Cl, R<sup>2</sup> = 4-ClC<sub>6</sub>H<sub>4</sub>

Products, Yields

<sup>a</sup> Reaction was carried out with **1A** (5.0 mmol).<sup>b</sup> 2nd step reaction was carried out for 21 h.<sup>c</sup> NaI (3.0 equiv.) was used.<sup>d</sup> NCS (3.5 equiv.) and NaI (3.5 equiv.) were used.<sup>e</sup> DCE (10.0 mL) was used.

Scheme 1. Derivatization of **2E**

Scheme 2. Possible Reaction Mechanism

A possible reaction mechanism is shown in Scheme 2. NIS would be formed in situ by the reaction of NCS and NaI. Practically, the formation of NIS (3.04 ppm by  $^1\text{H-NMR}$  in  $\text{CDCl}_3$ ) was observed by the reaction of NCS (2.93 ppm by  $^1\text{H-NMR}$  in  $\text{CDCl}_3$ ) and NaI in DCE at room temperature. Once NIS is formed, it would react with 2-arylbzoic acid **1** to form carboxyl radical **II** through the homolytic O-I

bond cleavage of *O*-aroyl hypoiodite **I**. Carboxyl radical **II** would cyclize onto an aromatic ring to generate 3,4-benzocoumarin **2** via the oxidation of cyclized intermediate **III**.

## CONCLUSION

A NCS with NaI system instead of NIS could be used for the transformation of 2-arylbenzoic acids into 3,4-benzocoumarins in good yields. We believe that the present NCS with NaI system would be quite useful and practical because NCS and NaI are much less expensive and more stable than NIS.

## EXPERIMENTAL

<sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were obtained with JEOL-JNM-ECX400 and JEOL-JNM-ECS400 spectrometers. Chemical shifts were recorded as follows: chemical shift in ppm from internal tetramethylsilane (TMS) on the  $\delta$  scale, multiplicity (s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet; b = broad), coupling constant (Hz) and integration. High-resolution mass spectra (HRMS) were recorded by a Thermo Fisher Scientific Exactive Orbitrap mass spectrometer. IR spectra were measured with a JASCO FT/IR-4100 spectrometer. Melting points were determined with a Yamato Melting Point Apparatus Model MP-21. Silica gel 60F<sub>254</sub> (Merck) was used for TLC and Silica gel 60N (63~210 mesh, Kanto Kagaku Co.) was used for short column chromatography.

**Starting Materials.** 2-(4'-Methylphenyl)benzoic acid (**1A**) and 2-phenylbenzoic acid (**1C**) are commercially available. Other 2-arylbenzoic acids were prepared, as shown below.

**Typical Procedure for Preparation of 2-Arylbenzoic Acids 1.** To a solution of ethyl 2-iodobenzoate (10.0 mmol, 2.76 g) in DMF (100.0 mL) were added 4-methoxyphenylboronic acid (12.5 mmol, 1.89 g) and bis(triphenylphosphine)palladium(II) dichloride (0.5 mmol, 0.35 g) at room temperature under argon atmosphere. After being stirred at room temperature for 30 min, K<sub>2</sub>CO<sub>3</sub> (20.0 mmol, 2.76 g) in H<sub>2</sub>O (20.0 mL) was added to the mixture, and the obtained mixture was stirred at 60 °C for 6 h. Then, the mixture was filtered through celite and washed with Et<sub>2</sub>O. The product was extracted from the filtrates with Et<sub>2</sub>O (45.0 mL  $\times$  3). The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>. After filtration and removal of the solvent, the residue was purified by silica-gel column chromatography (eluent: *n*-hexane:EtOAc = 20:1) to give ethyl 2-(4'-methoxyphenyl)benzoate. To a solution of ethyl 2-(4'-methoxyphenyl)benzoate in EtOH (10.0 mL) was added KOH (50.0 mmol, 1.89 g) in H<sub>2</sub>O (5.0 mL). The mixture was stirred at 80 °C for 8 h. HCl aq. solution (15.0 mL) was added to the reaction mixture at 0 °C, and the product was extracted with CHCl<sub>3</sub> (20.0 mL  $\times$  3). The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>. After filtration and removal of the solvent, 2-(4'-methoxyphenyl)benzoic acid **1E** was obtained in 87% yield (1.99 g). Other 2-arylbenzoic acids were obtained in 62%~88% yield by the same procedure.

**2-(3'-Methylphenyl)benzoic Acid (1B):** orange solid; mp 90-91 °C; IR (neat): 3310-2501 (broad), 1678,

1050  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 2.38 (s, 3H), 7.13 (d, 1H,  $J$  = 8.2 Hz), 7.16-7.18 (m, 2H), 7.27 (t, 1H,  $J$  = 7.9 Hz), 7.37 (dd, 1H,  $J$  = 7.7, 0.9 Hz), 7.41 (td, 1H,  $J$  = 7.7, 1.4 Hz), 7.55 (td, 1H,  $J$  = 7.6, 1.4 Hz), 7.93 (dd, 1H,  $J$  = 7.6, 1.4 Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 21.4, 125.6, 127.1, 127.9, 128.1, 129.1, 129.3, 130.6, 131.2, 132.0, 137.6, 140.8, 143.4, 173.9; HRMS (ESI): Calcd for  $\text{C}_{14}\text{H}_{11}\text{O}_2$   $[\text{M-H}]^-$  = 211.0765, Found = 211.0763.

**2-(4'-*tert*-Butylphenyl)benzoic Acid (1D):** white solid; mp 131-132 °C; IR (neat): 3261-2529 (broad), 1678, 932  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.35 (s, 9H), 7.28 (d, 2H,  $J$  = 8.6 Hz), 7.36-7.43 (m, 4H), 7.55 (td, 1H,  $J$  = 7.7, 1.4 Hz), 7.93 (dd, 1H,  $J$  = 7.7, 1.4 Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 31.4 (3C), 34.5, 125.1 (2C), 126.9, 128.1 (2C), 129.3, 130.7, 131.3, 132.0, 137.8, 143.2, 150.2, 173.7; HRMS (ESI): Calcd for  $\text{C}_{17}\text{H}_{19}\text{O}_2$   $[\text{M+H}]^+$  = 255.1380, Found = 255.1383.

**2-(4'-Methoxyphenyl)benzoic Acid (1E):** white solid; mp 143-144 °C; IR (neat): 3281-2435 (broad), 1697, 1240, 943  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 3.85 (s, 3H), 6.94 (d, 2H,  $J$  = 8.6 Hz), 7.28 (d, 2H,  $J$  = 8.6 Hz), 7.36 (d, 1H,  $J$  = 7.7 Hz), 7.40 (td, 1H,  $J$  = 7.7, 1.4 Hz), 7.55 (td, 1H,  $J$  = 7.5, 1.4 Hz), 7.93 (dd, 1H,  $J$  = 7.7, 1.4 Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 55.2, 113.6 (2C), 126.8, 129.2, 129.6 (2C), 130.7, 131.2, 132.0, 133.3, 142.9, 159.1, 173.3; HRMS (APCI): Calcd for  $\text{C}_{14}\text{H}_{13}\text{O}_3$   $[\text{M+H}]^+$  = 229.0859, Found = 229.0856.

**2-(4'-Fluorophenyl)benzoic Acid (1F):** white solid; mp 130-131 °C; IR (neat): 3358-2498 (broad), 1687, 906  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.07 (t, 2H,  $J$  = 8.8 Hz), 7.27-7.31 (m, 2H), 7.33 (dd, 1H,  $J$  = 7.6, 1.1 Hz), 7.43 (td, 1H,  $J$  = 7.6, 1.4 Hz), 7.57 (td, 1H,  $J$  = 7.6, 1.4 Hz), 7.96 (dd, 1H,  $J$  = 7.9, 1.4 Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 115.0 (d,  $J_{\text{C-F}}$  = 21.6 Hz), 127.4, 129.1, 130.0 (d,  $J_{\text{C-F}}$  = 7.5 Hz), 130.9, 131.2, 132.3, 137.0 (d,  $J_{\text{C-F}}$  = 2.8 Hz), 142.5, 162.3 (d,  $J_{\text{C-F}}$  = 246.2 Hz), 173.8; HRMS (APCI): Calcd for  $\text{C}_{13}\text{H}_{10}\text{O}_2\text{F}$   $[\text{M+H}]^+$  = 217.0659, Found = 217.0659.

**2-(4'-Chlorophenyl)benzoic Acid (1G):** white solid; mp 166-167 °C; IR (neat): 3334-2473 (broad), 1698, 904  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.26 (d, 2H,  $J$  = 8.6 Hz), 7.33 (dd, 1H,  $J$  = 7.7, 0.9 Hz), 7.36 (d, 2H,  $J$  = 8.4 Hz), 7.45 (td, 1H,  $J$  = 7.5, 1.4 Hz), 7.58 (td, 1H,  $J$  = 7.5, 1.4 Hz), 7.98 (dd, 1H,  $J$  = 7.7, 1.4 Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 127.7, 128.3, 129.0, 129.9, 131.1, 131.2, 132.4, 133.6, 139.6, 142.4, 173.0; HRMS (APCI): Calcd for  $\text{C}_{13}\text{H}_{10}\text{O}_2^{35}\text{Cl}$   $[\text{M+H}]^+$  = 233.0364, Found = 233.0365.

**2-(3'-Nitrophenyl)benzoic Acid (1H):** white solid; mp 152-154 °C; IR (neat): 3299-2449 (broad), 1692, 1283, 1256, 913  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.36 (dd, 1H,  $J$  = 7.6, 0.9 Hz), 7.52 (dt, 1H,  $J$  = 7.6, 1.4 Hz), 7.55 (t, 1H,  $J$  = 7.6 Hz), 7.62-7.66 (m, 2H), 8.08 (dd, 1H,  $J$  = 7.9, 0.9 Hz), 8.20 (s, 1H), 8.22-8.25 (m, 1H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 122.2, 123.4, 128.4 (2C), 128.8, 131.2, 131.4, 132.9, 134.7, 141.4, 142.8, 147.8, 172.7; HRMS (ESI): Calcd for  $\text{C}_{13}\text{H}_8\text{O}_4\text{N}$   $[\text{M-H}]^-$  = 242.0459, Found = 242.0462.

**5-Bromo-2-phenylbenzoic Acid (1I):** white solid; mp 162-164 °C; IR (neat): 3261-2390 (broad), 1683,

942  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.23\text{-}7.32$  (m, 3H), 7.34-7.41 (m, 3H), 7.68 (dd, 1H,  $J = 8.3$ , 2.2 Hz), 8.08 (d, 1H,  $J = 2.0$  Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 121.1$ , 127.7, 128.2 (2C), 128.3 (2C), 130.7, 132.7, 133.4, 135.1, 139.7, 142.3, 172.4; HRMS (ESI): Calcd for  $\text{C}_{13}\text{H}_8\text{O}_2^{79}\text{Br}$   $[\text{M-H}]^- = 274.9713$ , Found = 274.9720,  $\text{C}_{13}\text{H}_8\text{O}_2^{81}\text{Br}$   $[\text{M-H}]^- = 276.9692$ , Found = 276.9696.

**5-Bromo-2-(4'-methylphenyl)benzoic Acid (1J):** white solid; mp 147-149 °C; IR (neat): 3316-2390 (broad), 1687, 880  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 2.39$  (s, 3H), 7.19-7.22 (m, 4H), 7.24 (d, 1H,  $J = 8.2$  Hz), 7.67 (dd, 1H,  $J = 8.3$ , 2.0 Hz), 8.06 (bs, 1H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 21.2$ , 120.8, 128.1 (2C), 129.0 (2C), 130.7, 132.7, 133.4, 135.0, 136.7, 137.5, 142.2, 172.8; HRMS (ESI): Calcd for  $\text{C}_{14}\text{H}_{10}\text{O}_2^{79}\text{Br}$   $[\text{M-H}]^- = 288.9870$ , Found = 288.9876,  $\text{C}_{14}\text{H}_{10}\text{O}_2^{81}\text{Br}$   $[\text{M-H}]^- = 290.9849$ , Found = 290.9856.

**5-Bromo-2-(4'-tert-butylphenyl)benzoic Acid (1K):** white solid; mp 144-146 °C; IR (neat): 3303-2459 (broad), 1707, 821  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.35$  (s, 9H), 7.22-7.26 (m, 3H), 7.40 (d, 2H,  $J = 8.5$  Hz), 7.66 (dd, 1H,  $J = 8.3$ , 2.2 Hz), 8.06 (d, 1H,  $J = 2.0$  Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 31.3$  (3C), 34.6, 120.8, 125.2 (2C), 128.0 (2C), 130.8, 132.9, 133.4, 135.0, 136.6, 142.1, 150.7, 172.4; HRMS (ESI): Calcd for  $\text{C}_{17}\text{H}_{16}\text{O}_2^{79}\text{Br}$   $[\text{M-H}]^- = 331.0339$ , Found = 331.0346,  $\text{C}_{17}\text{H}_{16}\text{O}_2^{81}\text{Br}$   $[\text{M-H}]^- = 333.0318$ , Found = 333.0326.

**5-Bromo-2-(4'-methoxyphenyl)benzoic Acid (1L):** white solid; mp 145-146 °C; IR (neat): 3362-2438 (broad), 1685, 1247, 823  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 3.85$  (s, 3H), 6.93 (d, 2H,  $J = 8.8$  Hz), 7.21-7.25 (m, 3H), 7.66 (dd, 1H,  $J = 8.3$ , 2.0 Hz), 8.05 (d, 1H,  $J = 2.0$  Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 55.2$ , 113.7 (2C), 120.6, 129.5 (2C), 130.7, 132.0, 132.7, 133.4, 135.0, 141.8, 159.3, 172.5; HRMS (ESI): Calcd for  $\text{C}_{14}\text{H}_{10}\text{O}_3^{79}\text{Br}$   $[\text{M-H}]^- = 304.9819$ , Found = 304.9819, 304.9819,  $\text{C}_{14}\text{H}_{10}\text{O}_3^{81}\text{Br}$   $[\text{M-H}]^- = 306.9798$ , Found = 306.9803.

**5-Bromo-2-(4'-fluorophenyl)benzoic Acid (1M):** yellow solid; mp 165-167 °C; IR (neat): 3316-2390 (broad), 1691, 819  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.08$  (t, 2H,  $J = 8.6$  Hz), 7.21 (d, 1H,  $J = 8.2$  Hz), 7.24-7.27 (m, 2H), 7.69 (dd, 1H,  $J = 8.2$ , 2.0 Hz), 8.10 (d, 1H,  $J = 2.3$  Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{DMSO-}d_6$ ):  $\delta = 115.1$  (d,  $J_{\text{C-F}} = 21.6$  Hz, 2C), 120.6, 130.3 (d,  $J_{\text{C-F}} = 8.5$  Hz, 2C), 131.8, 132.7, 133.8, 131.4, 136.1 (d,  $J_{\text{C-F}} = 2.8$  Hz), 139.3, 161.9 (d,  $J_{\text{C-F}} = 244.3$  Hz), 168.1; HRMS (ESI): Calcd for  $\text{C}_{13}\text{H}_7\text{O}_2^{79}\text{BrF}$   $[\text{M-H}]^- = 292.9619$ , Found = 292.9626,  $\text{C}_{13}\text{H}_7\text{O}_2^{81}\text{BrF}$   $[\text{M-H}]^- = 294.9598$ , Found = 294.9603.

**5-Bromo-2-(4'-chlorophenyl)benzoic Acid (1N):** white solid; mp 199-200 °C; IR (neat): 3338-2285 (broad), 1695, 903  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.20\text{-}7.25$  (m, 3H), 7.37 (d, 2H,  $J = 8.6$  Hz), 7.70 (dd, 1H,  $J = 8.2$ , 2.2 Hz), 8.11 (d, 1H,  $J = 2.3$  Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{DMSO-}d_6$ ):  $\delta = 120.8$ , 128.2 (2C), 130.1 (2C), 131.8, 132.5, 132.6, 133.8, 133.9, 138.6, 139.0, 167.8; HRMS (ESI): Calcd for  $\text{C}_{13}\text{H}_7\text{O}_2^{79}\text{Br}^{35}\text{Cl}$   $[\text{M-H}]^- = 308.9323$ , Found = 308.9330,  $\text{C}_{13}\text{H}_7\text{O}_2^{81}\text{Br}^{35}\text{Cl}$   $[\text{M-H}]^- = 310.9302$ , Found =

310.9307.

**2-(4'-Methylphenyl)-5-nitrobenzoic Acid (1O):** yellow solid; mp 209-210 °C; IR (neat): 3303-2390 (broad), 1704, 1289, 1263, 920  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 2.42 (s, 3H), 7.24-7.26 (m, 4H), 7.57 (d, 1H,  $J$  = 8.6 Hz), 8.39 (dd, 1H,  $J$  = 8.6, 2.5 Hz), 8.79 (d, 1H,  $J$  = 2.3 Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  = 20.8, 124.0, 125.2, 128.3 (2C), 129.1 (2C), 132.1, 133.6, 136.0, 138.0, 146.1, 147.2, 168.0; HRMS (ESI): Calcd for  $\text{C}_{14}\text{H}_{10}\text{O}_4\text{N}$   $[\text{M-H}]^-$  = 256.0615, Found = 256.0617.

**2,5-Diphenylbenzoic Acid (1P):** white solid; mp 174-176 °C; IR (neat): 3348-2480 (broad), 1684, 904  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.35-7.50 (m, 9H), 7.66 (d, 2H,  $J$  = 7.0 Hz), 7.80 (dd, 1H,  $J$  = 8.0, 2.0 Hz), 8.19 (d, 1H,  $J$  = 2.0 Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 127.1 (2C), 127.4, 127.9, 128.1 (2C), 128.5 (2C), 128.9 (2C), 129.3, 129.6, 130.6, 131.8, 139.5, 140.2, 140.6, 142.1, 173.5; HRMS (ESI): Calcd for  $\text{C}_{19}\text{H}_{13}\text{O}_2$   $[\text{M-H}]^-$  = 273.0921, Found = 273.0927.

**2,5-Di(4'-methylphenyl)benzoic Acid (1Q):** white solid; mp 207-209 °C; IR (neat): 3313-2455 (broad), 1682, 905  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 2.40 (s, 3H), 2.41 (s, 3H), 7.22 (d, 2H,  $J$  = 7.7 Hz), 7.27-7.30 (m, 4H), 7.43 (d, 1H,  $J$  = 7.9 Hz), 7.55 (d, 2H,  $J$  = 8.2 Hz), 7.76 (dd, 1H,  $J$  = 8.2, 2.0 Hz), 8.15 (d, 1H,  $J$  = 2.0 Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 21.1, 21.2, 126.8 (2C), 128.4 (2C), 128.9 (2C), 129.0, 129.6 (2C), 130.3, 131.7, 136.6, 137.2, 137.6, 137.7, 139.9, 141.7, 173.7, 173.8; HRMS (ESI): Calcd for  $\text{C}_{21}\text{H}_{19}\text{O}_2$   $[\text{M+H}]^+$  = 303.1380, Found = 303.1378.

**2,5-Di(4'-tert-butylphenyl)benzoic Acid (1R):** white solid; mp 218-219 °C; IR (neat): 3299-2505 (broad), 1693, 911  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.36 (s, 9H), 1.38 (s, 9H), 7.33 (d, 2H,  $J$  = 8.5 Hz), 7.41-7.45 (m, 3H), 7.50 (d, 2H,  $J$  = 8.5 Hz), 7.60 (d, 2H,  $J$  = 8.8 Hz), 7.77 (dd, 1H,  $J$  = 8.1, 2.0 Hz), 8.17 (d, 1H,  $J$  = 1.8 Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 31.3 (3C), 31.4 (3C), 34.5, 34.6, 125.1 (2C), 125.9 (2C), 126.7 (2C), 128.2 (2C), 129.1, 129.6, 130.3, 131.8, 136.6, 137.5, 139.8, 141.6, 150.3, 150.9, 173.2; HRMS (ESI): Calcd for  $\text{C}_{27}\text{H}_{31}\text{O}_2$   $[\text{M+H}]^+$  = 387.2319, Found = 387.2315.

**2,5-Di(4'-fluorophenyl)benzoic Acid (1S):** white solid; mp 173-175 °C; IR (neat): 3344-2477 (broad), 1693, 860  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.10 (t, 2H,  $J$  = 8.6 Hz), 7.17 (t, 2H,  $J$  = 8.6 Hz), 7.30-7.35 (m, 2H), 7.41 (d, 1H,  $J$  = 7.9 Hz), 7.58-7.63 (m, 2H), 7.74 (dd, 1H,  $J$  = 7.9, 2.0 Hz), 8.15 (d, 1H,  $J$  = 2.0 Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 115.1 (d,  $J_{\text{C-F}}$  = 21.6 Hz, 2C), 115.9 (d,  $J_{\text{C-F}}$  = 21.6 Hz, 2C), 128.7 (d,  $J_{\text{C-F}}$  = 7.5 Hz, 2C), 129.3, 129.5, 130.1 (d,  $J_{\text{C-F}}$  = 8.5 Hz, 2C), 130.6, 131.9, 135.5 (d,  $J_{\text{C-F}}$  = 2.8 Hz), 136.5 (d,  $J_{\text{C-F}}$  = 2.8 Hz), 139.4, 141.3, 162.4 (d,  $J_{\text{C-F}}$  = 246.2 Hz), 162.8 (d,  $J_{\text{C-F}}$  = 247.1 Hz), 173.5; HRMS (ESI): Calcd for  $\text{C}_{19}\text{H}_{11}\text{O}_2\text{F}_2$   $[\text{M-H}]^-$  = 309.0733, Found = 309.0737.

**2,5-Di(4'-chlorophenyl)benzoic Acid (1T):** white solid; mp 207-209 °C; IR (neat): 3334-2481 (broad), 1692, 813  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.30 (d, 2H,  $J$  = 8.6 Hz), 7.39 (d, 2H,  $J$  = 7.39 Hz), 7.42 (d, 1H,  $J$  = 7.9 Hz), 7.45 (d, 2H,  $J$  = 8.8 Hz), 7.58 (d, 2H,  $J$  = 8.6 Hz), 7.76 (dd, 1H,  $J$  = 7.9, 2.0 Hz), 8.18 (d, 1H,  $J$  = 1.8 Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 127.4, 128.2 (2C), 128.6 (2C), 129.1 (3C),

130.2 (2C), 131.3, 132.3, 132.7, 133.0, 137.5, 138.1, 139.2, 139.3, 169.2; HRMS (ESI): Calcd for  $C_{19}H_{11}O_2^{35}Cl_2 [M-H]^- = 341.0142$ , Found = 341.0148.

**Typical Procedure for Preparation of 3,4-Benzocoumarins 2 from 2-Arylbenzoic Acids 1 with NIS.**

To a solution of 2-(4'-methylphenyl)benzoic Acid **1A** (1.0 mmol, 212.3 mg) in 1,2-dichloroethane (DCE, 5.0 mL) was added NIS (2.5 mmol, 562.5 mg) at room temperature under argon atmosphere. The mixture was stirred in the temperature range of 38 °C~40 °C for 5 h under irradiation with a 300 W tungsten lamp. Sat.  $Na_2SO_3$  aq. solution (15.0 mL) was added to the reaction mixture and the product was extracted with  $CHCl_3$  (15.0 mL  $\times$  3). The organic layer was dried over  $Na_2SO_4$ . After filtration and removal of the solvent, the residue was purified by silica-gel column chromatography (eluent: *n*-hexane:EtOAc = 4:1) to give 3,4-benzo-7-methylcoumarin **2A** in >99% yield (209.3 mg).

**Typical Procedure for Preparation of 3,4-Benzocoumarins 2 from 2-Arylbenzoic Acids 1 with NCS and NaI.**

To a solution of NCS (2.5 mmol, 333.8 mg) in DCE (5.0 mL) was added NaI (2.5 mmol, 374.7 mg) at room temperature under argon atmosphere. After being stirred at room temperature for 2 h, 2-(4'-methylphenyl)benzoic acid **1A** (1.0 mmol, 212.3 mg) was added to the mixture. The obtained mixture was stirred at 70 °C for 7 h under fluorescent lighting (32 W) condition. Sat.  $Na_2SO_3$  aq. solution (15.0 mL) was added to the reaction mixture and the product was extracted with  $CHCl_3$  (15.0 mL  $\times$  3). The organic layer was dried over  $Na_2SO_4$ . After filtration and removal of the solvent, the residue was purified by silica-gel column chromatography (eluent: *n*-hexane:EtOAc = 4:1) to give 3,4-benzo-7-methylcoumarin **2A** in >99% yield (209.6 mg).

**3,4-Benzo-7-methylcoumarin (2A):** Yield: 209.6 mg (99%); white solid; mp 128-130 °C; IR (neat): 3063, 1720, 1605, 1251  $cm^{-1}$ ;  $^1H$ -NMR (400 MHz,  $CDCl_3$ ):  $\delta$  = 2.46 (s, 3H), 7.17 (d, 1H,  $J$  = 8.6 Hz), 7.19 (s, 1H), 7.56 (t, 1H,  $J$  = 8.2 Hz), 7.8 (t, 1H,  $J$  = 8.2 Hz) 7.95 (d, 1H,  $J$  = 7.9 Hz), 8.01 (d, 1H,  $J$  = 8.2 Hz), 8.40 (d, 1H,  $J$  = 8.0 Hz);  $^{13}C$ -NMR (100 MHz,  $CDCl_3$ ):  $\delta$  = 21.4, 115.4, 117.8, 120.8, 121.4, 122.5, 125.6, 128.3, 130.5, 134.7, 135.0, 141.3, 151.2, 161.4; HRMS (APCI): Calcd for  $C_{14}H_{11}O_2 [M+H]^+ = 211.0754$ , Found = 211.0750.

**3,4-Benzo-6-methylcoumarin and 3,4-Benzo-8-methylcoumarin (2B):** Yield: 192.0 mg (91%, a mixture of two regioisomers 59:32); white solid; mp 101-103 °C; IR (neat): 2919, 1716, 1181  $cm^{-1}$ ;  $^1H$ -NMR (400 MHz,  $CDCl_3$ ):  $\delta$  = 2.47 (s, 3H), 2.51 (s, 3H), 7.23-7.31 (m, 3H), 7.35 (d, 1H,  $J$  = 7.3 Hz), 7.58 (t, 2H,  $J$  = 8.2 Hz), 7.83 (t, 2H,  $J$  = 8.0 Hz), 7.86 (s, 1H), 7.93 (d, 1H,  $J$  = 6.8 Hz), 8.13 (d, 1H,  $J$  = 8.2 Hz), 8.14 (d, 1H,  $J$  = 7.9 Hz), 8.41 (d, 1H,  $J$  = 7.9 Hz), 8.42 (d, 1H,  $J$  = 7.9 Hz); HRMS (ESI): Calcd for  $C_{14}H_{11}O_2 [M+H]^+ = 211.0754$ , Found = 211.0751.

**3,4-Benzocoumarin (2C):** Yield: 178.9 mg (91%); white solid; mp 93-94 °C; IR (neat): 3067, 1725, 1077  $cm^{-1}$ ;  $^1H$ -NMR (400 MHz,  $CDCl_3$ ):  $\delta$  = 7.36 (td, 1H,  $J$  = 7.8, 1.1 Hz), 7.39 (dd, 1H,  $J$  = 8.5, 1.4 Hz), 7.50 (td, 1H,  $J$  = 7.7, 1.4 Hz), 7.60 (td, 1H,  $J$  = 7.6, 1.1 Hz), 7.84 (td, 1H,  $J$  = 7.5, 1.4 Hz), 8.09 (dd, 1H,  $J$

= 7.9, 1.6 Hz), 8.15 (d, 1H,  $J = 8.2$  Hz), 8.42 (dd, 1H,  $J = 7.9, 0.9$  Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 117.7, 117.9, 121.1, 121.6, 122.7, 124.5, 128.8, 130.4, 130.5, 134.6, 134.8, 151.2, 161.1$ ; HRMS (APCI): Calcd for  $\text{C}_{13}\text{H}_9\text{O}_2$   $[\text{M}+\text{H}]^+ = 197.0597$ , Found = 197.0593.

**3,4-Benzo-7-(tert-butyl)coumarin (2D)**: Yield: 249.1 mg (99%); white solid; mp 157-158 °C; IR (neat): 2951, 1732, 1263, 1095  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.38$  (s, 9H), 7.38 (dd, 1H,  $J = 6.3, 1.8$  Hz), 7.39 (bs, 1H), 7.57 (t, 1H,  $J = 7.9$  Hz), 7.81 (t, 1H,  $J = 7.9$  Hz), 7.99 (d, 1H,  $J = 9.1$  Hz), 8.10 (d, 1H,  $J = 8.2$  Hz), 8.40 (d, 1H,  $J = 7.9$  Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 31.0$  (3C), 35.0, 114.5, 115.3, 120.9, 121.4, 121.9, 122.3, 128.4, 130.8, 134.7, 134.8, 151.1, 154.6, 161.5; HRMS (APCI): Calcd for  $\text{C}_{17}\text{H}_{17}\text{O}_2$   $[\text{M}+\text{H}]^+ = 235.1223$ , Found = 235.1218.

**3,4-Benzo-7-methoxycoumarin (2E)**: Yield: 215.4 mg (95%); white solid; mp 139-141 °C; IR (neat): 3003, 1730, 1029  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 3.89$  (s, 3H), 6.88 (d, 1H,  $J = 2.5$  Hz), 6.93 (dd, 1H,  $J = 8.7, 2.5$  Hz), 7.51 (t, 1H,  $J = 7.9$  Hz), 7.80 (t, 1H,  $J = 7.7$  Hz), 7.96 (d, 1H,  $J = 8.8$  Hz), 8.02 (d, 1H,  $J = 7.9$  Hz), 8.37 (d, 1H,  $J = 7.5$  Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 55.7, 101.6, 111.1, 112.4, 119.9, 121.0, 123.7, 127.7, 130.5, 134.8, 135.1, 152.6, 161.5$  (2C); HRMS (APCI): Calcd for  $\text{C}_{14}\text{H}_{11}\text{O}_3$   $[\text{M}+\text{H}]^+ = 227.0703$ , Found = 227.0698.

**3,4-Benzo-7-fluorocoumarin (2F)**: Yield: 170.1 mg (79%); white solid; mp 156-158 °C; IR (neat): 3074, 1744, 1152  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.07$ -7.13 (m, 2H), 7.59 (t, 1H,  $J = 7.5$  Hz), 7.85 (t, 1H,  $J = 7.7$  Hz), 8.03-8.07 (m, 2H), 8.40 (dd, 1H,  $J = 7.9, 1.4$  Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 105.1$  (d,  $J_{\text{C-F}} = 25.4$  Hz), 112.4 (d,  $J_{\text{C-F}} = 21.6$  Hz), 114.6, 120.4, 121.5, 124.3 (d,  $J_{\text{C-F}} = 9.4$  Hz), 128.7, 130.7, 134.2, 135.1, 152.1 (d,  $J_{\text{C-F}} = 12.2$  Hz), 160.8, 163.4 (d,  $J_{\text{C-F}} = 251.8$  Hz); HRMS (APCI): Calcd for  $\text{C}_{13}\text{H}_8\text{O}_2\text{F}$   $[\text{M}+\text{H}]^+ = 215.0503$ , Found = 215.0498.

**3,4-Benzo-7-chlorocoumarin (2G)**: Yield: 170.7 mg (74%); white solid; mp 153-154 °C; IR (neat): 3066, 1740, 1069  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.33$  (dd, 1H,  $J = 8.5, 2.0$  Hz), 7.40 (d, 1H,  $J = 2.0$  Hz), 7.62 (t, 1H,  $J = 7.1$  Hz), 7.85 (t, 1H,  $J = 7.5$  Hz), 8.00 (d, 1H,  $J = 8.4$  Hz), 8.09 (d, 1H,  $J = 8.2$  Hz), 8.41 (dd, 1H,  $J = 7.9, 0.9$  Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 116.6, 117.8, 120.8, 121.6, 123.7, 125.0, 129.1, 130.6, 133.9, 135.0, 135.9, 151.4, 160.5$ ; HRMS (APCI): Calcd for  $\text{C}_{13}\text{H}_8\text{O}_2^{35}\text{Cl}$   $[\text{M}+\text{H}]^+ = 231.0207$ , Found = 231.0205.

**3,4-Benzo-6-nitrocoumarin (2H)**: Yield: 85.2 mg (35%); yellow solid; mp 249-251 °C; IR (neat): 2922, 1734, 1132  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{DMF-}d_7$ ):  $\delta = 7.72$  (d, 1H,  $J = 9.1$  Hz), 7.86 (t, 1H,  $J = 7.6$  Hz), 8.10 (t, 1H,  $J = 7.6$  Hz), 8.38 (dd, 1H,  $J = 7.9, 1.1$  Hz), 8.47 (dd, 1H,  $J = 9.1, 2.7$  Hz), 8.78 (d, 1H,  $J = 7.9$  Hz), 9.28 (d, 1H,  $J = 2.7$  Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{DMF-}d_7$ ):  $\delta = 119.3, 119.5, 120.1, 121.5, 123.9, 125.8, 130.3, 130.9, 133.6, 136.1, 144.9, 155.5, 159.9$ ; HRMS (APCI): Calcd for  $\text{C}_{13}\text{H}_8\text{O}_4\text{N}$   $[\text{M}+\text{H}]^+ = 242.0448$ , Found = 242.0452.

**3,4-(2'-Bromo)benzocoumarin (2I)**: Yield: 237.7 mg (86%); white solid; mp 170-172 °C; IR (neat):

3070, 1725, 1197  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.34\text{-}7.40$  (m, 2H), 7.52 (t, 1H,  $J = 7.6$  Hz), 7.94 (dd, 1H,  $J = 8.6, 2.3$  Hz), 8.02 (d, 1H,  $J = 8.6$  Hz), 8.04 (dd, 1H,  $J = 7.9, 1.6$  Hz), 8.56 (d, 1H,  $J = 2.3$  Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 117.2, 117.8, 122.5, 122.6, 122.7, 123.4, 124.8, 130.8, 133.0, 133.5, 137.8, 151.0, 159.8$ ; HRMS (APCI): Calcd for  $\text{C}_{13}\text{H}_8\text{O}_2^{79}\text{Br}$   $[\text{M}+\text{H}]^+ = 274.9702$ , Found = 274.9701,  $\text{C}_{13}\text{H}_8\text{O}_2^{81}\text{Br}$   $[\text{M}+\text{H}]^+ = 276.9681$ , Found = 276.9678.

**3,4-(2'-Bromo)benzo-7-methylcoumarin (2J)**: Yield: 288.6 mg (99%); white solid; mp 201-202  $^\circ\text{C}$ ; IR (neat): 2925, 1723, 1127  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 2.46$  (s, 3H), 7.17 (d, 1H,  $J = 7.4$  Hz), 7.18 (s, 1H), 7.89 (d, 1H,  $J = 8.8$  Hz), 7.90 (d, 1H,  $J = 8.8$  Hz), 7.96 (d, 1H,  $J = 8.8$  Hz), 8.52 (d, 1H,  $J = 2.0$  Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 21.5, 114.6, 118.0, 122.1, 122.2, 122.4, 123.2, 125.9, 133.0, 133.8, 137.8, 141.9, 151.1, 160.1$ ; HRMS (APCI): Calcd for  $\text{C}_{14}\text{H}_{10}\text{O}_2^{79}\text{Br}$   $[\text{M}+\text{H}]^+ = 288.9859$ , Found = 288.9859, Calcd for  $\text{C}_{14}\text{H}_{10}\text{O}_2^{81}\text{Br}$   $[\text{M}+\text{H}]^+ = 290.9838$ , Found = 290.9835.

**3,4-(2'-Bromo)benzo-7-tert-butylcoumarin (2K)**: Yield: 317.1 mg (96%); white solid; mp 170-172  $^\circ\text{C}$ ; IR (neat): 2960, 1727, 1134  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 1.37$  (s, 9H), 7.38 (s, 1H), 7.39 (dd, 1H,  $J = 7.9, 2.0$  Hz), 7.90 (dd, 1H,  $J = 8.6, 2.0$  Hz), 7.94 (d, 1H,  $J = 9.4$  Hz), 7.97 (d, 1H,  $J = 8.8$  Hz), 8.52 (d, 1H,  $J = 2.0$  Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 31.0$  (3C), 35.0, 114.4 (2C), 122.0, 122.2, 123.2, 132.8 (2C), 133.5 (2C), 137.7, 150.9, 155.1, 160.0; HRMS (APCI): Calcd for  $\text{C}_{17}\text{H}_{16}\text{O}_2^{79}\text{Br}$   $[\text{M}+\text{H}]^+ = 331.0328$ , Found = 331.0327,  $\text{C}_{17}\text{H}_{16}\text{O}_2^{81}\text{Br}$   $[\text{M}+\text{H}]^+ = 333.0307$ , Found = 333.0304.

**3,4-(2'-Bromo)benzo-7-methoxycoumarin (2L)**: Yield: 296.9 mg (97%); white solid; mp 169-170  $^\circ\text{C}$ ; IR (neat): 3083, 1721, 1167  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 3.89$  (s, 3H), 6.87 (d, 1H,  $J = 2.5$  Hz), 6.93 (dd, 1H,  $J = 8.8, 2.5$  Hz), 7.87-7.88 (m, 2H), 7.91 (d, 1H,  $J = 8.8$  Hz), 8.49 (s, 1H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 55.7, 101.7, 110.4, 112.7, 121.3, 121.4, 122.9, 123.7, 133.0, 134.0, 137.9, 152.5, 160.2, 161.8$ ; HRMS (APCI): Calcd for  $\text{C}_{14}\text{H}_{10}\text{O}_3^{79}\text{Br}$   $[\text{M}+\text{H}]^+ = 304.9808$ , Found = 304.9807,  $\text{C}_{14}\text{H}_{10}\text{O}_3^{81}\text{Br}$   $[\text{M}+\text{H}]^+ = 306.9787$ , Found = 306.9785.

**3,4-(2'-Bromo)benzo-7-fluorocoumarin (2M)**: Yield: 213.5 mg (73%); white solid; mp 183-185  $^\circ\text{C}$ ; IR (neat): 3096, 1728, 1148  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.08\text{-}7.13$  (m, 2H), 7.93-7.94 (m, 2H), 7.99-8.04 (m, 1H), 8.53 (s, 1H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 105.2$  (d,  $J_{\text{C-F}} = 25.4$  Hz), 112.8 (d,  $J_{\text{C-F}} = 22.6$  Hz), 113.8 (d,  $J_{\text{C-F}} = 3.8$  Hz), 121.8, 122.5, 123.3, 124.3 (d,  $J_{\text{C-F}} = 9.4$  Hz), 133.0, 133.1, 138.1, 152.0 (d,  $J_{\text{C-F}} = 12.2$  Hz), 159.4, 163.6 (d,  $J_{\text{C-F}} = 251.8$  Hz); HRMS (APCI): Calcd for  $\text{C}_{13}\text{H}_7\text{O}_2^{79}\text{BrF}$   $[\text{M}+\text{H}]^+ = 292.9608$ , Found = 292.9610,  $\text{C}_{13}\text{H}_7\text{O}_2^{81}\text{BrF}$   $[\text{M}+\text{H}]^+ = 294.9587$ , Found = 294.9589.

**3,4-(2'-Bromo)benzo-7-chlorocoumarin (2N)**: Yield: 279.8 mg (90%); white solid; mp 200-202  $^\circ\text{C}$ ; IR (neat): 3094, 1730, 1233  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta = 7.34$  (dd, 1H,  $J = 8.5, 2.0$  Hz), 7.39 (d, 1H,  $J = 2.0$  Hz), 7.94-7.96 (m, 3H), 8.53 (s, 1H);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 115.9, 118.1, 122.3, 123.1, 123.4, 123.7, 125.3, 132.8, 133.2, 136.4, 138.1, 151.3, 159.2$ ; HRMS (ESI): Calcd for  $\text{C}_{13}\text{H}_7\text{O}_2^{79}\text{Br}^{35}\text{Cl}$   $[\text{M}+\text{H}]^+ = 308.9312$ , Found = 308.9315,  $\text{C}_{13}\text{H}_7\text{O}_2^{81}\text{Br}^{35}\text{Cl}$   $[\text{M}+\text{H}]^+ = 310.9291$ , Found =

310.9291.

**3,4-(2'-Nitro)benzo-7-methylcoumarin (2O):** Yield: 220.9 mg (87%); yellow solid; mp 205-206 °C; IR (neat): 3091, 1738, 1107  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 2.50 (s, 3H), 7.24-7.25 (m, 2H), 7.99 (d, 1H,  $J$  = 8.5 Hz), 8.25 (d, 1H,  $J$  = 9.0 Hz), 8.61 (dd, 1H,  $J$  = 9.0, 2.5 Hz), 9.23 (d, 1H,  $J$  = 2.5 Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 21.7, 113.8, 118.2, 121.5, 123.0, 123.6, 126.4, 126.5, 128.8, 140.1, 144.3, 147.1, 152.0, 159.5; HRMS (APCI): Calcd for  $\text{C}_{14}\text{H}_{10}\text{O}_4\text{N}$   $[\text{M}+\text{H}]^+$  = 256.0604, Found = 256.0608.

**3,4-(2'-Phenyl)benzocoumarin (2P):** Yield: 241.6 mg (89%); white solid; mp 175-177 °C; IR (neat): 3070, 1725, 1197  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.36-7.45 (m, 3H), 7.49-7.53 (m, 3H), 7.72 (d, 2H,  $J$  = 7.3 Hz), 8.10 (t, 2H,  $J$  = 8.5 Hz), 8.22 (d, 1H,  $J$  = 8.4 Hz), 8.67 (d, 1H,  $J$  = 2.0 Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 117.7, 117.8, 121.5, 122.3, 122.7, 124.6, 126.9 (2C), 128.2, 128.4, 129.0 (2C), 130.3, 133.3, 133.4, 138.8, 141.6, 151.1, 161.2; HRMS (ESI): Calcd for  $\text{C}_{19}\text{H}_{13}\text{O}_2$   $[\text{M}+\text{H}]^+$  = 273.0910, Found = 273.0906.

**3,4-[2'-(4"-Methylphenyl)benzo]-7-methylcoumarin (2Q):** Yield: 290.2 mg (97%); white solid; mp 215-217 °C; IR (neat): 3033, 1717, 1131  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 2.42 (s, 3H), 2.46 (s, 3H), 7.17 (d, 1H,  $J$  = 8.2 Hz), 7.19 (s, 1H), 7.30 (d, 2H,  $J$  = 7.9 Hz), 7.60 (d, 2H,  $J$  = 8.2 Hz), 7.95 (d, 1H,  $J$  = 7.9 Hz), 8.03 (dd, 1H,  $J$  = 8.4, 2.0 Hz), 8.13 (d, 1H,  $J$  = 8.4 Hz), 8.61 (d, 1H,  $J$  = 1.8 Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 21.1, 21.4, 115.3, 117.8, 121.2, 122.0, 122.4, 125.7, 126.8 (2C), 128.1, 129.8 (2C), 133.2, 133.4, 136.1, 138.1, 141.1 (2C), 151.1, 161.6; HRMS (ESI): Calcd for  $\text{C}_{21}\text{H}_{17}\text{O}_2$   $[\text{M}+\text{H}]^+$  = 301.1223, Found = 301.1219.

**3,4-[2'-(4"-tert-Butylphenyl)benzo]-7-tert-butylcoumarin (2R):** Yield: 383.0 mg (99%); white solid; mp 166-167 °C; IR (neat): 2961, 1738, 1134  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.38 (s, 9H), 1.39 (s, 9H), 7.40 (dd, 1H,  $J$  = 7.0, 1.8 Hz), 7.41 (bs, 1H), 7.52 (d, 2H,  $J$  = 8.8 Hz), 7.67 (d, 2H,  $J$  = 8.8 Hz), 8.01 (d, 1H,  $J$  = 9.2 Hz), 8.06 (dd, 1H,  $J$  = 8.3, 2.0 Hz), 8.16 (d, 1H,  $J$  = 8.3 Hz), 8.64 (d, 1H,  $J$  = 1.8 Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 31.1(3C), 31.3 (3C), 34.6, 35.0, 114.5, 115.3, 121.3, 122.0, 122.1, 122.3, 126.0 (2C), 126.6 (2C), 128.2, 133.2, 133.4, 136.1, 141.1, 151.1, 151.4, 154.5, 161.6; HRMS (ESI): Calcd for  $\text{C}_{27}\text{H}_{29}\text{O}_2$   $[\text{M}+\text{H}]^+$  = 385.2162, Found = 385.2162.

**3,4-[2'-(4"-Fluorophenyl)benzo]-7-fluorocoumarin (2S):** Yield: 269.3 mg (87%); white solid; mp 213-215 °C; IR (neat): 3093, 1738, 1268  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.09-7.15 (m, 2H), 7.20 (t, 2H,  $J$  = 8.5 Hz), 7.65-7.69 (m, 2H), 8.03 (dd, 1H,  $J$  = 8.4, 2.2 Hz), 8.06-8.09 (m, 1H), 8.13 (d, 1H,  $J$  = 8.5 Hz), 8.58 (d, 1H,  $J$  = 2.0 Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 105.1 (d,  $J_{\text{C-F}}$  = 25.4 Hz), 112.6 (d,  $J_{\text{C-F}}$  = 22.6 Hz), 114.4 (d,  $J_{\text{C-F}}$  = 3.8 Hz), 116.1 (d,  $J_{\text{C-F}}$  = 21.6 Hz, 2C), 120.8, 122.2, 124.3 (d,  $J_{\text{C-F}}$  = 10.3 Hz), 128.4, 128.7 (d,  $J_{\text{C-F}}$  = 8.5 Hz, 2C), 132.9, 133.4, 134.9 (d,  $J_{\text{C-F}}$  = 2.8 Hz), 140.6, 151.9 (d,  $J_{\text{C-F}}$  = 12.2 Hz), 160.8, 163.0 (d,  $J_{\text{C-F}}$  = 248.1 Hz), 163.4 (d,  $J_{\text{C-F}}$  = 251.8 Hz); HRMS (APCI): Calcd for  $\text{C}_{19}\text{H}_{11}\text{O}_2\text{F}_2$   $[\text{M}+\text{H}]^+$  = 309.0722, Found = 309.0718.

**3,4-[2'-(4"-Chlorophenyl)benzo]-7-chlorocoumarin (2T):** Yield: 298.1 mg (87%); white solid; mp 238-240 °C; IR (neat):  $\text{cm}^{-1}$ : 3082, 1732, 1228  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 7.35 (dd, 1H,  $J$  = 8.5, 2.0 Hz), 7.41 (d, 1H,  $J$  = 2.2 Hz), 7.48 (d, 2H,  $J$  = 8.5 Hz), 7.63 (d, 2H,  $J$  = 8.5 Hz), 8.00-8.06 (m, 2H), 8.15 (d, 1H,  $J$  = 8.5 Hz), 8.59 (d, 1H,  $J$  = 2.0 Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 116.5, 118.0, 121.4, 122.5, 123.8, 125.2, 128.3, 128.5, 129.3, 133.0, 133.4, 134.7, 136.0, 137.2, 140.8, 151.4, 160.6; HRMS (APCI): Calcd for  $\text{C}_{19}\text{H}_{11}\text{O}_2^{35}\text{Cl}_2$   $[\text{M}+\text{H}]^+$  = 341.0131, Found = 341.0129.

**Transformation of 3,4-Benzo-7-methoxycoumarin (2E) into 2'-( $\alpha,\alpha$ -Dimethyl- $\alpha$ -hydroxy)methyl-2-hydroxy-4-methoxybiphenyl (3E).** To a solution of 3,4-benzo-7-methoxycoumarin **2E** (1.0 mmol, 226.2 mg) in THF (5.0 mL) was added MeLi (1.16M in  $\text{Et}_2\text{O}$ , 4.5 mmol, 3.22 mL) at -60 °C under argon atmosphere, and the mixture was stirred at room temperature for 19 h. Sat.  $\text{NH}_4\text{Cl}$  aq. solution (15.0 mL) was added to the reaction mixture and the product was extracted with  $\text{CHCl}_3$  (15.0 mL  $\times$  3). The organic layer was dried over  $\text{Na}_2\text{SO}_4$ . After filtration and removal of the solvent, 2'-( $\alpha,\alpha$ -dimethyl- $\alpha$ -hydroxy)methyl-2-hydroxy-4-methoxybiphenyl (**3E**) was obtained in >99% yield (256.1 mg).

**2'-( $\alpha,\alpha$ -Dimethyl- $\alpha$ -hydroxy)methyl-2-hydroxy-4-methoxybiphenyl (3E):** Yield: 256.1 mg (>99%); yellow solid; mp 153-155 °C; IR (neat): 3422, 2984, 1590, 1518, 1197  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.44 (s, 3H), 1.60 (s, 3H), 2.01 (bs, 1H), 3.83 (s, 3H), 5.46 (bs, 1H), 6.54-6.57 (m, 2H), 8.53 (d, 1H,  $J$  = 8.5 Hz), 7.10 (dd, 1H,  $J$  = 7.4, 1.6 Hz), 7.31 (td, 1H,  $J$  = 7.4, 1.4 Hz), 7.39 (td, 1H,  $J$  = 7.4, 1.6 Hz), 7.64 (dd, 1H,  $J$  = 7.9, 1.4 Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 31.3, 31.7, 55.3, 73.9, 101.8, 106.4, 123.0, 126.1, 127.4, 128.4, 131.2, 133.7, 134.2, 147.3, 153.9, 160.5; HRMS (APCI): Calcd for  $\text{C}_{16}\text{H}_{17}\text{O}_3$   $[\text{M}-\text{H}]^-$  = 257.1172, Found = 257.1167.

**Transformation of 3,4-Benzo-7-methoxycoumarin (2E) into 3,4-Benzo-5,6-(3'-methoxy)benzo-2,2-dimethylpyran (4E).** To a solution of 2'-( $\alpha,\alpha$ -dimethyl- $\alpha$ -hydroxy)methyl-2-hydroxy-4-methoxybiphenyl **3E** (1.0 mmol, 258.3 mg) in DCE (6.0 mL) was added  $\text{MeSO}_3\text{H}$  (2.0 mmol, 129.9  $\mu\text{L}$ ) in DCE (1.0 mL) at room temperature under argon atmosphere. The mixture was stirred for 2 h at room temperature. Sat.  $\text{NaHCO}_3$  aq. solution (15.0 mL) was added to the reaction mixture and the product was extracted with  $\text{CHCl}_3$  (15.0 mL  $\times$  3). The organic layer was dried over  $\text{Na}_2\text{SO}_4$ . After filtration and removal of the solvent, the residue was purified by silica-gel column chromatography (eluent: *n*-hexane:EtOAc = 4:1) to give 3,4-benzo-5,6-(3'-methoxy)benzo-2,2-dimethylpyran (**4E**) in 98% yield (235.7 mg).

**3,4-Benzo-5,6-(3'-methoxy)benzo-2,2-dimethylpyran (4E):** Yield: 235.7 mg (98%); clear oil; IR (neat): 2977, 2935, 1227  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 1.64 (s, 6H), 3.82 (s, 3H), 6.51 (s, 1H), 6.60 (dd, 1H,  $J$  = 8.6, 2.5 Hz), 7.21-7.24 (m, 2H), 7.32 (t, 1H,  $J$  = 7.4 Hz), 7.62 (d, 1H,  $J$  = 8.6 Hz), 7.63 (d, 1H,  $J$  = 7.6 Hz);  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  = 27.5 (2C), 55.2, 77.8, 102.7, 108.2, 115.3, 121.4, 123.0, 123.7,

126.9, 127.6, 128.6, 138.2, 153.9, 160.9; HRMS (APCI): Calcd for  $C_{16}H_{17}O_2$   $[M+H]^+$  = 241.1223, Found = 241.12219.

**Transformation of 3,4-Benzo-7-methoxycoumarin (2E) into 2-Hydroxy-2'-hydroxymethyl-4-methoxybiphenyl (5E).** To a solution of 3,4-benzo-7-methoxycoumarin **2E** (1.0 mmol, 226.2 mg) in THF (4.0 mL) was added  $LiAlH_4$  (1.5 mmol, 56.9 mg) at 0 °C under argon atmosphere. The mixture was stirred at room temperature for 2 h. Ice and sat.  $NH_4Cl$  aq. solution (15.0 mL) was added to the reaction mixture, and the product was extracted with  $CHCl_3$  (15.0 mL  $\times$  3). The organic layer was dried over  $Na_2SO_4$ . After filtration and removal of the solvent, the residue was purified by silica-gel column chromatography (eluent: *n*-hexane:EtOAc = 1:1) to give 2-hydroxy-2'-hydroxymethyl-4-methoxybiphenyl (**5E**) in >99% yield (228.9 mg).

**2-Hydroxy-2'-hydroxymethyl-4-methoxybiphenyl (5E):** Yield: 228.9 mg (>99%); clear oil; IR (neat): 3379, 3093, 2938, 1234  $cm^{-1}$ ;  $^1H$ -NMR (400 MHz,  $CDCl_3$ ):  $\delta$  = 1.96 (bs, 1H), 3.83 (s, 3H), 4.53 (d, 2H,  $J$  = 4.7 Hz), 5.70 (bs, 1H), 6.56-6.59 (m, 2H), 7.03 (d, 1H,  $J$  = 9.2 Hz), 7.25-7.27, (m, 1H), 7.39-7.45 (m, 2H), 7.54 (d, 1H,  $J$  = 7.9 Hz);  $^{13}C$ -NMR (100 MHz,  $CDCl_3$ ):  $\delta$  = 55.2, 63.6, 101.9, 106.5, 120.4, 128.1, 128.3, 129.1, 131.0, 131.4, 136.7, 138.7, 153.8, 160.3; HRMS (ESI): Calcd for  $C_{14}H_{13}O_3$   $[M-H]^-$  = 229.0859, Found = 229.0859.

**Transformation of 3,4-Benzo-7-methoxycoumarin (2E) into 3,4-Benzo-6-bromo-7-methoxycoumarin (6E).** To a solution of 3,4-benzo-7-methoxycoumarin **2E** (1.0 mmol, 226.2 mg) in DCE (3.0 mL) was added NBS (1.1 mmol, 195.8 mg) at 0 °C under argon atmosphere. The mixture was stirred at 0 °C for 1 h, and then, the mixture was stirred at room temperature for 4 h. NBS (0.3 mmol, 53.4 mg) was added again to the mixture, and the mixture was further stirred at room temperature for 39 h. Sat.  $Na_2SO_3$  aq. solution (15.0 mL) was added to the reaction mixture and the product was extracted with  $CHCl_3$  (15.0 mL  $\times$  3). The organic layer was dried over  $Na_2SO_4$ . After filtration and removal of the solvent, the residue was purified by silica-gel column chromatography (eluent: *n*-hexane:EtOAc = 4:1) to give 3,4-benzo-6-bromo-7-methoxycoumarin (**6E**) in 84% yield (257.1 mg).

**3,4-Benzo-6-bromo-7-methoxycoumarin (6E):** Yield: 257.1 mg (84%); white solid; mp 214-216 °C; IR (neat): 2920, 1713, 1264, 1046  $cm^{-1}$ ;  $^1H$ -NMR (400 MHz,  $CDCl_3$ ):  $\delta$  = 3.98 (s, 3H), 6.90 (s, 1H), 7.56 (t, 1H,  $J$  = 7.3 Hz), 7.82 (t, 1H,  $J$  = 8.2 Hz), 7.98 (d, 1H,  $J$  = 7.7 Hz), 8.21 (s, 1H), 8.38 (dd, 1H,  $J$  = 7.9, 1.4 Hz);  $^{13}C$ -NMR (100 MHz,  $CDCl_3$ ):  $\delta$  = 56.6, 100.9, 107.7, 112.1, 119.9, 121.1, 126.9, 128.3, 130.6, 133.9, 135.0, 151.6, 157.3, 160.8; HRMS (ESI): Calcd for  $C_{14}H_{10}O_3$   $^{79}Br$   $[M+H]^+$  = 304.9808, Found = 304.9809,  $C_{14}H_{10}O_3$   $^{81}Br$   $[M+H]^+$  = 306.9788, Found = 306.9787,

**Transformation of 3,4-Benzo-7-methoxycoumarin (2E) into Urolithin B (7E).** To a solution of 3,4-benzo-7-methoxycoumarin **2E** (1.0 mmol, 226.2 mg) in  $CH_2Cl_2$  (2.0 mL) was added  $BBr_3$  ( $CH_2Cl_2$  1.0 M, 3.0 mmol, 3.0 mL) at 0 °C under argon atmosphere. The mixture was stirred at 0 °C for 30 min.

BBr<sub>3</sub> (2.0 mmol, 2.0 mL) was added again to the mixture, and the mixture was stirred at room temperature for 22 h. Ice and sat. NaHCO<sub>3</sub> aq. solution (15.0 mL) was added to the reaction mixture and the product was extracted with EtOAc (15.0 mL × 3). The organic layer was dried over Na<sub>2</sub>SO<sub>4</sub>. After filtration and removal of the solvent, Urolithin B (**7E**) was obtained in 97% yield (207.0 mg).

**Urolithin B (7E):** Yield: 207.0 mg (97%); white solid; mp 229-230 °C; IR (neat): 3235, 2987, 1688, 1103 cm<sup>-1</sup>; <sup>1</sup>H-NMR (400 MHz, DMSO-*d*<sub>6</sub>): δ = 6.73 (bs, 1H), 6.82 (dd, 1H, *J* = 8.8, 2.5 Hz), 7.53 (t, 1H, *J* = 7.6 Hz), 7.85 (t, 1H, *J* = 7.4 Hz), 8.14 (d, 1H, *J* = 8.8 Hz), 8.15 (dd, 1H, *J* = 8.0, 1.1 Hz), 8.22 (d, 1H, *J* = 8.1 Hz), 10.4 (bs, 1H); <sup>13</sup>C-NMR (100 MHz, DMSO-*d*<sub>6</sub>): δ = 102.9, 109.4, 113.1, 118.9, 121.5, 124.7, 127.6, 129.6, 130.1, 135.2, 152.1, 159.9, 160.6; HRMS (APCI): Calcd for C<sub>13</sub>H<sub>9</sub>O<sub>3</sub> [M+H]<sup>+</sup> = 213.0546, Found = 213.0544.

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