HETEROCYCLES, Vol. 100, No. 9, 2020, pp. -. © 2020 The Japan Institute of Heterocyclic Chemistry
Received, 27th May, 2020, Accepted, 1st July, 2020, Published online, 6th July, 2020
DOI: 10.3987/COM-20-14292

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

Momoko Nakamura and Hideo Togo*

Graduate School of Science, Chiba University, Yayoi-cho 1-33, Inage-ku, Chiba 263-8522, Japan; E-mail: togo@faculty.chiba-u.jp

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.[1] As typical examples, urolithins A and B possess antioxidant activity[1a] and anti-proliferative effect against human cancer cells,[1b] and atenuisol exhibits potent antibacterial activity, as shown in Figure 1.[1]

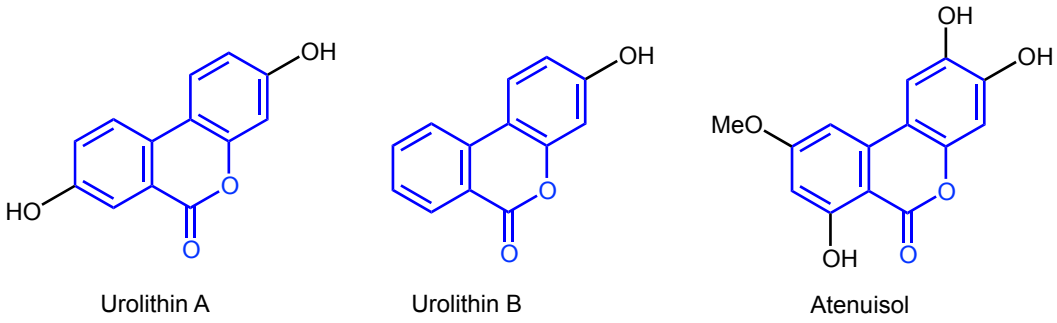


Figure 1. Biologically Active 3,4-Benzocoumarins

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[2a] and $Pb(OAc)_4$.[2b] Recent reports of the preparation of

3,4-benzocoumarins from 2-arylbenzoic acids are as follows:[3] the preparation with $PhCO_3Bu^t$ in the presence of $Cu(OAc)_2$ in $ClCH_2CH_2Cl$ (DCE) and with $K_2S_2O_8$ in the presence of $AgNO_3$ in $MeCN/H_2O$;[3a] the preparation in the presence of $[Acr\text{-}Mes]ClO_4$ and $Co(dmgH)_2Cl_2$ in MeCN under blue LED irradiation;[3b] the preparation using Kolbe anodic oxidation with Pt electrode in $MeOH/H_2O$[3c] and in MeCN;[3d] the preparation in the presence of (-)-riboflavin in MeOH under UV irradiation;[3e] the preparation with $K_2S_2O_8$ in the presence of $AgNO_3$ in $MeCN/H_2O$;[3f] the preparation in the presence of $CeCl_3$ in $CHCl_3$ under blue LED irradiation;[3g] the preparation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) and ^{t}BuONO in DCE under blue LED irradiation;[3h] and the preparation with $NaBrO_3$ in the presence of $Fe(NO_3)_3$ under irradiation with 40 W LED.[3i] The preparation of 3,4-benzocoumarins with *N*-methoxy-2-arylbenzamides and ^{t}BuONO was also reported.[4] Examples of condensation reactions to generate the 3,4-benzocoumarin core include the reaction of salicylaldehydes, malononitrile, and ethyl acetoacetate with MgO;[5a] the reaction of *O*-aryl acrylates bearing an α,β-alkenoyl group at *o*-position with DBU in DMSO;[5b] the reaction of 3-acetylcoumarins and malononitrile with piperidine in EtOH;[5c] and the reaction of 3-acetylcoumarin and α,β-unsaturated aldehydes with DBU in $CHCl_3$.[5d] The preparation of 3,4-benzocoumarins through the carbonylation of 10-hydroxy-10,9-boroxarophenanthrenes with CO in the presence of $Pd(OAc)_2$ in DMSO/MeOH;[6a] through the carbonylation of 2-arylphenols with CO in the presence of $[RuCl_2(p\text{-cymene})]_2$ in mesitylene;[6b] through the [3+3] annulation of *N*-methoxyarylamides and *p*-quinols in the presence of $[Cp^*RhCl_2]_2$ in α,α,α-trifluorotoluene/acetone;[6c] and through the oxidative lactonization of 2-methylbiaryls in the presence of $[Acr\text{-}Mes]ClO_4$ with O_2 in $MeCN/H_2O$ under blue LED irradiation[6d] is known as well.

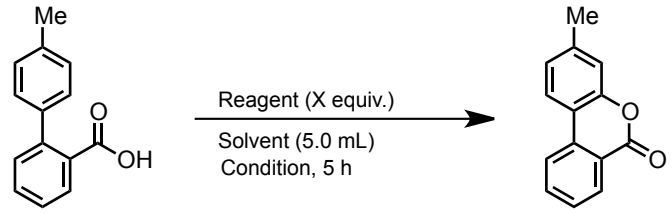
Among those methods, the preparation of the 3,4-benzocoumarin core from *o*-arylbenzoic acids with less toxic oxidants is very attractive because the cyclization of 2-arylbenzoic acids to 3,4-benzocoumarins is a simple, efficient, and atom-economic approach, and 2-arylbenzoic acids can be easily obtained 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 $PhI(O_2CCF_3)_2$ (BTIB) and iodine,[7a] and with 1,3-diiodo-5,5-dimethylhydantoin (DIH)[7b] 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).[8] 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 NaI.[9] 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 ($k = \sim 10^6$ s^{-1}, 25 °C) is rather low as compared with that of aliphatic carboxyl radicals ($k = \sim 10^{10}$ s^{-1}, 25 °C).[10] 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,[8] 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 α-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_2 (2.5 equiv.) and K_2CO_3 (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



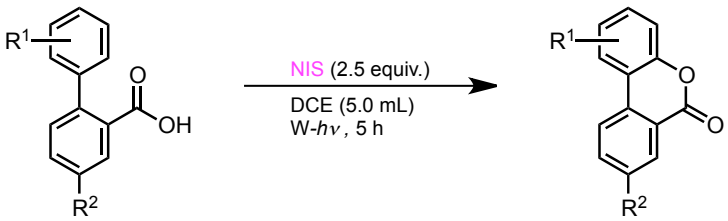
1A (1.0 mmol) **2A**

Entry	Reagent (equiv.)	Solvent	Conditions	Yield (%)
1	NIS (1.5)	DCE	300 W W-*hν*	77
2	NIS (2.0)	DCE	300 W W-*hν*	96
3	**NIS (2.5)**	**DCE**	**300 W W-*hν***	**>99**
4	NIS (2.5)	**DCE**	40 W W-*hν*	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-*hν*	89
8	NIS (2.5)	MeOH	300 W W-*hν*	6
9	DIH (1.5)	DCE	300 W W-*hν*	>99
10[a]	I_2, K_2CO_3	DCE	300 W W-*hν*	4
11[b]	NIS (2.5)	DCE	300 W W-*hν*	0 (96)[c]
12[d]	NIS (2.5)	DCE	300 W W-*hν*	0 (95)[c]
13[e]	NBS (2.5)	DCE	300 W W-*hν*	0 (97)[c]
14[e]	NCS (2.5)	DCE	300 W W-*hν*	0 (98)[c]

[a] I_2 (2.5 equiv.) and K_2CO_3 (1.5 equiv.) instead of NIS were used.
[b] BHT (1.5 equiv.) was added.
[c] Recovery of **1A**.
[d] TEMPO (1.5 equiv.) was added.
[e] 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.

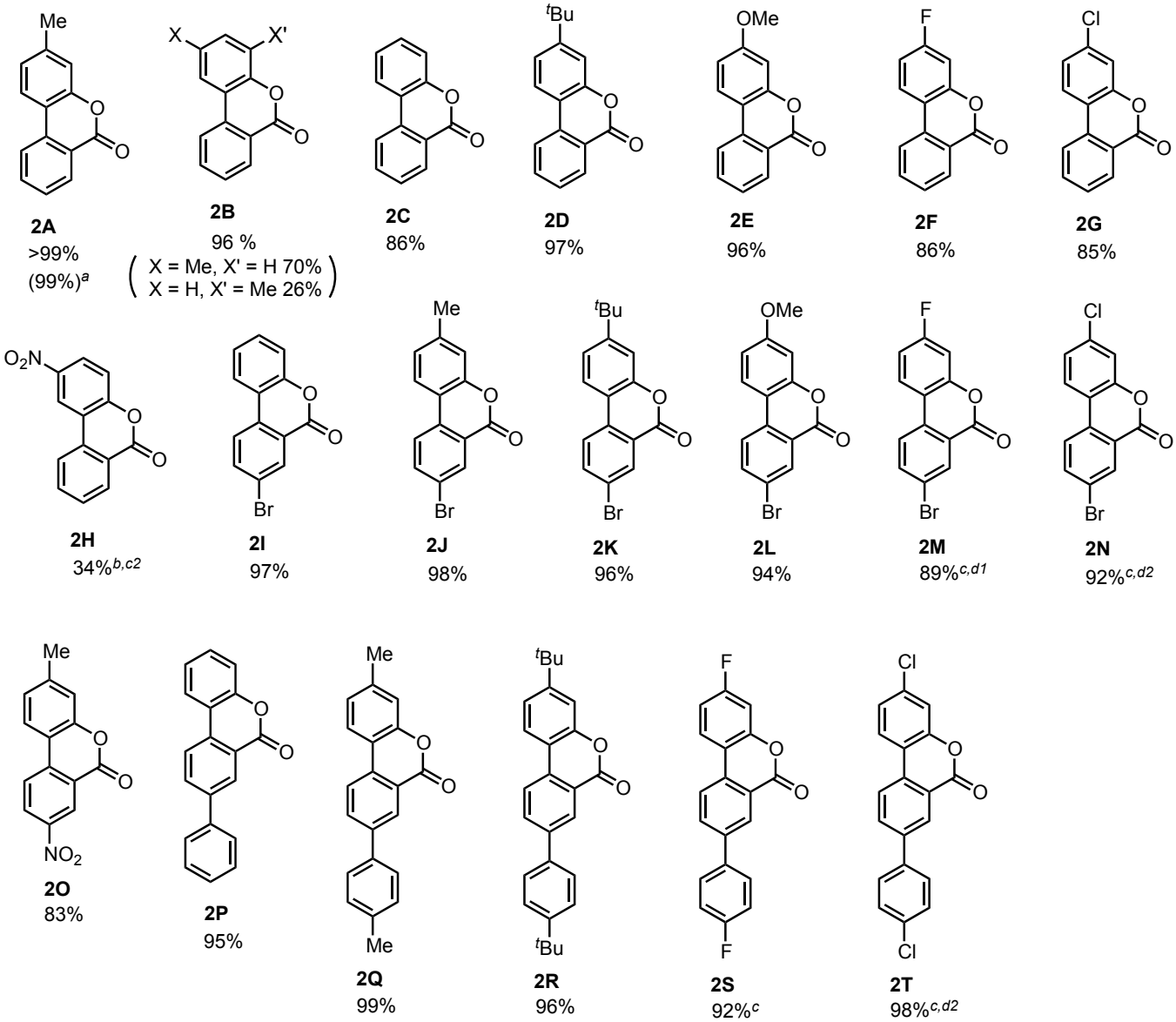
Table 2. Transformation of *o*-Arylbenzoic Acids **1** to 3,4-Benzocoumarins **2** with NIS



1 (1.0 mmol) **2**

A: R^1 = 4-Me, R^2 = H; **B**: R^1 = 3-Me, R^2 = H; **C**: R^1 = R^2 = H; **D**: R^1 = 4-^{t}Bu, R^2 = H; **E**: R^1 = 4-OMe, R^2 = H; **F**: R^1 = 4-F, R^2 = H; **G**: R^1 = 4-Cl, R^2 = H; **H**: R^2 = 3-NO_2, R_2 = H; **I**: R^1 = H, R^2 = Br; **J**: R^1 = 4-Me, R^2 = Br; **K**: R^1 = 4-^{t}Bu, R^2 = Br; **L**: R^1 = 4-OMe, R^2 = Br; **M**: R^1 = 4-F, R^2 = Br; **N**: R^1 = 4-Cl, R^2 = Br; **O**: R^1 = 4-Me, R^2 = NO_2; **P**: R^2 = H, R^2 = Ph; **Q**: R^1 = 4-Me, R^2 = 4-MeC_6H_4; **R**: R^1 = 4-^{t}Bu, R^2 = 4-^{t}BuC_6H_4; **S**: R^1 = 4-F, R^2 = 4-FC_6H_4; **T**: R^1 = 4-Cl, R^2 = 4-ClC_6H_4

Products, Yields



2A >99% (99%)[a]

2B 96 % (X = Me, X' = H 70% / X = H, X' = Me 26%)

2C 86%

2D 97%

2E 96%

2F 86%

2G 85%

2H 34%[b,c2]

2I 97%

2J 98%

2K 96%

2L 94%

2M 89%[c,d1]

2N 92%[c,d2]

2O 83%

2P 95%

2Q 99%

2R 96%

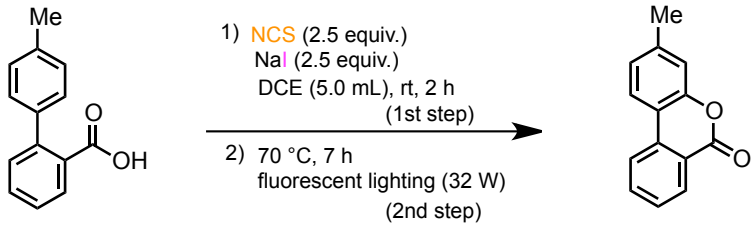
2S 92%[c]

2T 98%[c,d2]

[a] Reaction was carried out with **1A** (5.0 mmol).
[b] NIS (3.5 equiv.) was used.
[c] NIS (3.5 equiv.) in DCE (10 mL) was used.
[d] Reaction was carried out for [1] 7 h or [2] 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_4NI (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



1A (1.0 mmol) **2A**

Entry	Reagent (equiv.)	Additive (equiv.)	Solvent	Conditions	Yield (%)
1	NCS (2.5)	NaI (2.5)	DCE	300 W-*hν*, 38 °C~40 °C[a]	89
2	NCS (2.5)	NaI (1.0)	DCE	70 °C	61
3	NCS (2.5)	NaI (1.5)	DCE	70 °C	81
4	**NCS (2.5)**	**NaI (2.5)**	**DCE**	70 °C	**99**
5	NCS (2.5)	KI (2.5)	DCE	70 °C	90
6	NCS (2.5)	Et_4NI (2.5)	DCE	70 °C	<1 (87%)[b]
7[c]	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

[a] Reaction was carried out under irradiation with a 300 W tungsten lamp instead of a fluorecent lamp.
[b] β-Chloroethyl 2-(4'-methylphenyl)benzoate was obtained.
[c] 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).

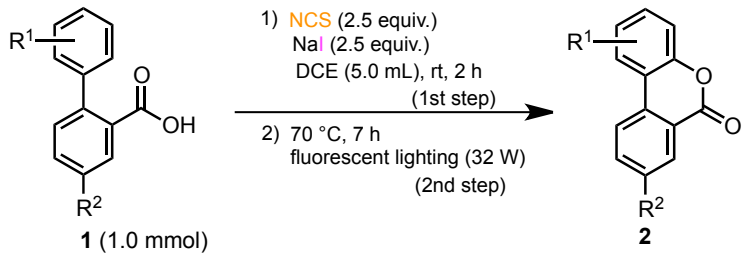
When DCE was changed to acetonitrile and methanol under the same procedure and conditions, compound **2A** was obtained in 60% and 4% yields, respectively (entries 8, 9). A gram-scale experiment with acid **1A** (5.0 mmol) with NCS and NaI under the same procedure and conditions gave 3,4-benzo-7-methylcoumarin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

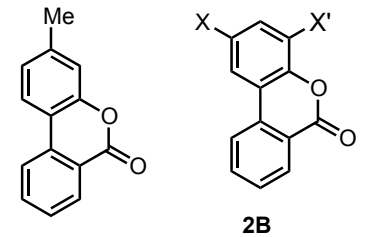
Once the 3,4-benzocoumarins were obtained, they could be transformed into a variety of 3,4-benzocoumarin derivatives. Treatment of 3,4-benzo-7-methoxycoumarin **2E** with methyllithium (4.5 equiv.) gave diol **3E** in >99% yield, and **3E** was further reacted with methanesulfonic acid (2.0 equiv.) to form dehydrated 3,4,5,6-dibenzo-2,2-dimethylpyran **4E** in 98% yield, as shown in Scheme 1. Reduction of compound **2E** with $LiAlH_4$ (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_3 (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



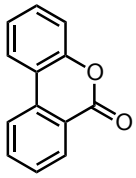
A: R^1 = 4-Me, R^2 = H; **B**: R^1 = 3-Me, R^2 = H; **C**: R^1 = R^2 = H; **D**: R^1 = 4-^{t}Bu, R^2 = H; **E**: R^1 = 4-OMe, R^2 = H; **F**: R^1 = 4-F, R^2 = H; **G**: R^1 = 4-Cl, R^2 = H; **H**: R^2 = 3-NO_2, R_2 = H; **I**: R^1 = H, R^2 = Br; **J**: R^1 = 4-Me, R^2 = Br; **K**: R^1 = 4-^{t}Bu, R^2 = Br; **L**: R^1 = 4-OMe, R^2 = Br; **M**: R^1 = 4-F, R^2 = Br; **N**: R^1 = 4-Cl, R^2 = Br; **O**: R^1 = 4-Me, R^2 = NO_2; **P**: R^2 = H, R^2 = Ph; **Q**: R^1 = 4-Me, R^2 = 4-MeC_6H_4; **R**: R^1 = 4-^{t}Bu, R^2 = 4-^{t}BuC_6H_4; **S**: R^1 = 4-F, R^2 = 4-FC_6H_4; **T**: R^1 = 4-Cl, R^2 = 4-ClC_6H_4

Products, Yields

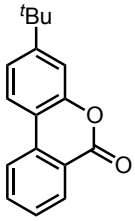


2A
>99%
(99%)[a]

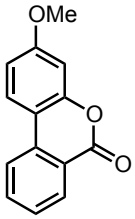
2B
91 %
(X = Me, X' = H 59%
X = H, X' = Me 32%)



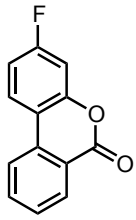
2C
91%



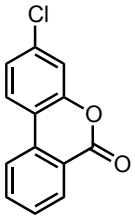
2D
98%



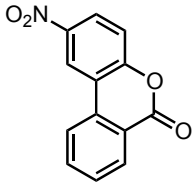
2E
95%[b,c]



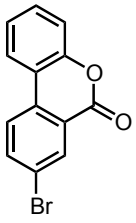
2F
79%



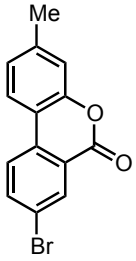
2G
74%



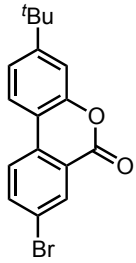
2H
35%[b,d]



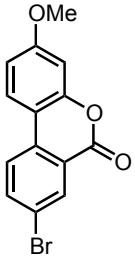
2I
86%[b,d,e]



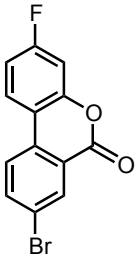
2J
99%



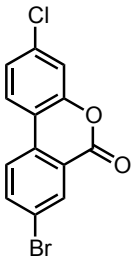
2K
96%



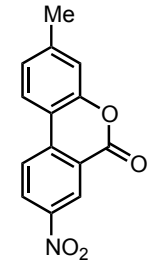
2L
97%[b,c]



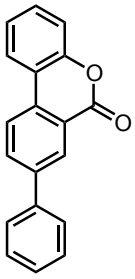
2M
73%[d,e]



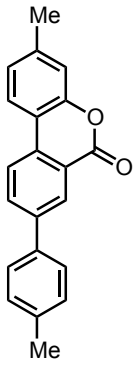
2N
90%[b,d,e]



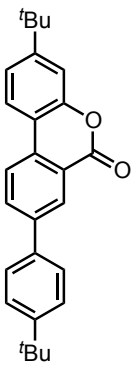
2O
87%[b]



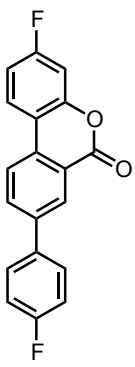
2P
89%



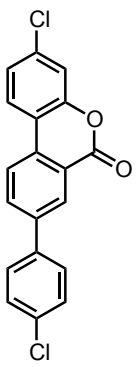
2Q
97%



2R
99%

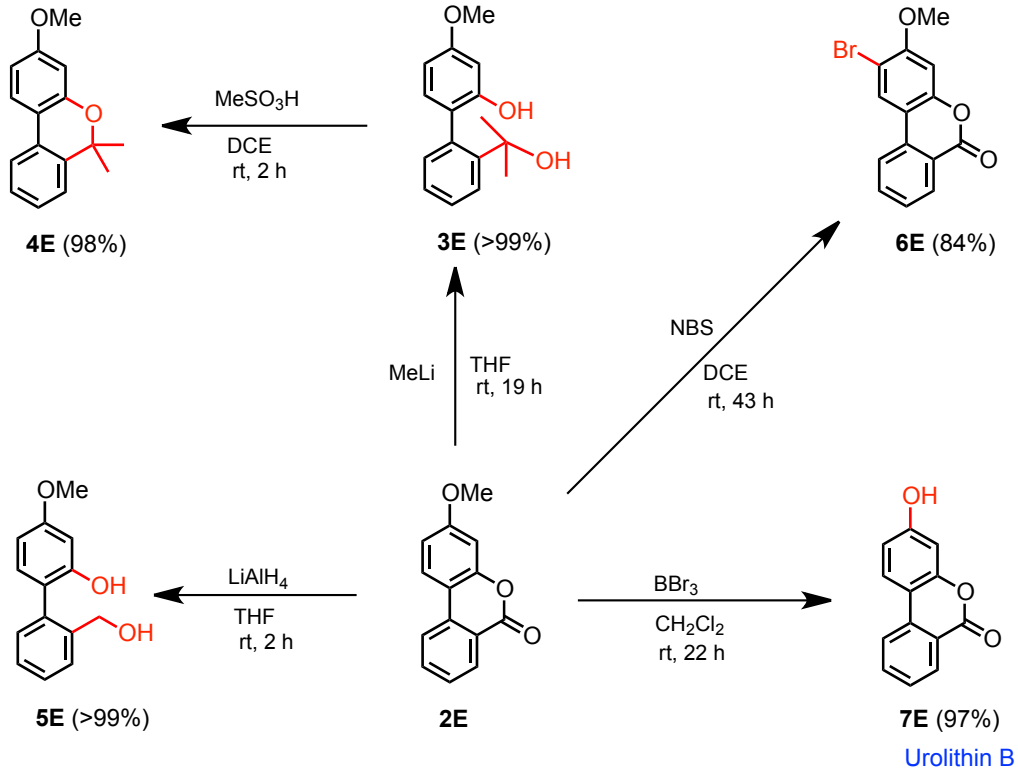


2S
87%[b,d,e]

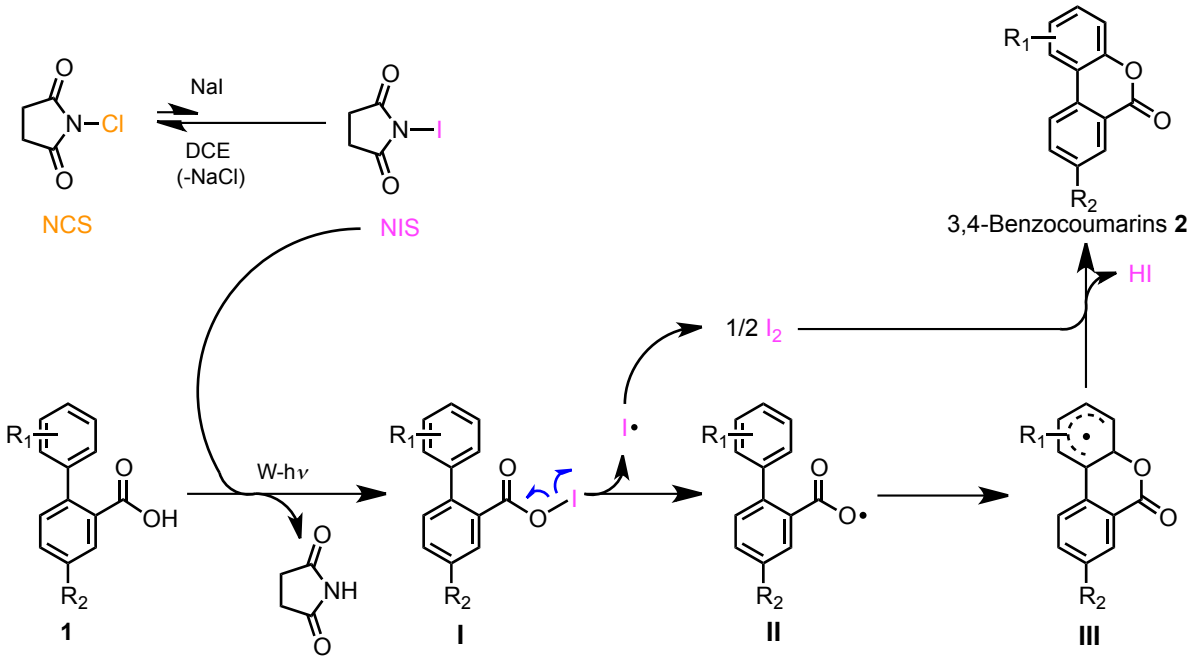


2T
87%[b,d,e]

[a] Reaction was carried out with **1A** (5.0 mmol).
[b] 2nd step reaction was carried out for 21 h.
[c] NaI (3.0 equiv.) was used.
[d] NCS (3.5 equiv.) and NaI (3.5 equiv.) were used·
[e] 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}H-NMR in $CDCl_3$) was observed by the reaction of NCS (2.93 ppm by ^{1}H-NMR in $CDCl_3$) and NaI in DCE at room temperature. Once NIS is formed, it would react with 2-arylbenzoic 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

^{1}H NMR and ^{13}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 δ 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 $60F_{254}$ (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_2CO_3 (20.0 mmol, 2.76 g) in H_2O (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_2O. The product was extracted from the filtrates with Et_2O (45.0 mL × 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 = 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_2O (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 $CHCl_3$ (20.0 mL × 3). The organic layer was dried over Na_2SO_4. 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{14}H_{11}O_2$ $[M-H]^-$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{17}H_{19}O_2$ $[M+H]^+$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{14}H_{13}O_3$ $[M+H]^+$ = 229.0859, Found = 229.0856.

2-(4'-Fluorophenyl)benzoic Acid (1F): white solid; mp 130-131 °C; IR (neat): 3358-2498 (broad), 1687, 906 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 115.0 (d, J_{C-F} = 21.6 Hz), 127.4, 129.1, 130.0 (d, J_{C-F} = 7.5 Hz), 130.9, 131.2, 132.3, 137.0 (d, J_{C-F} = 2.8 Hz), 142.5, 162.3 (d, J_{C-F} = 246.2 Hz), 173.8; HRMS (APCI): Calcd for $C_{13}H_{10}O_2F$ $[M+H]^+$ = 217.0659, Found = 217.0659.

2-(4'-Chlorophenyl)benzoic Acid (1G): white solid; mp 166-167 °C; IR (neat): 3334-2473 (broad), 1698, 904 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{13}H_{10}O_2{}^{35}Cl$ $[M+H]^+$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{13}H_8O_4N$ $[M-H]^-$ = 242.0459, Found = 242.0462.

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

942 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.23-7.32 (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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{13}H_8O_2{}^{79}Br$ $[M-H]^-$ = 274.9713, Found = 274.9720, $C_{13}H_8O_2{}^{81}Br$ $[M-H]^-$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{14}H_{10}O_2{}^{79}Br$ $[M-H]^-$ = 288.9870, Found = 288.9876, $C_{14}H_{10}O_2{}^{81}Br$ $[M-H]^-$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{17}H_{16}O_2{}^{79}Br$ $[M-H]^-$ = 331.0339, Found = 331.0346, $C_{17}H_{16}O_2{}^{81}Br$ $[M-H]^-$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 3.85 (s, 3H), 6.93 (d, 2H, *J* = 8.8Hz), 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{14}H_{10}O_3{}^{79}Br$ $[M-H]^-$ = 304.9819, Found = 304.9819, 304.9819, $C_{14}H_{10}O_3{}^{81}Br$ $[M-H]^-$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, DMSO-*d*$_6$): δ = 115.1 (d, J_{C-F} = 21.6 Hz, 2C), 120.6, 130.3 (d, J_{C-F} = 8.5 Hz, 2C), 131.8, 132.7, 133.8, 131.4, 136.1 (d, J_{C-F} = 2.8 Hz), 139.3, 161.9 (d, J_{C-F} = 244.3 Hz), 168.1; HRMS (ESI): Calcd for $C_{13}H_7O_2{}^{79}BrF$ $[M-H]^-$ = 292.9619, Found = 292.9626, $C_{13}H_7O_2{}^{81}BrF$ $[M-H]^-$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.20-7.25 (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}C-NMR (100 MHz, DMSO-*d*$_6$): δ = 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 $C_{13}H_7O_2{}^{79}Br{}^{35}Cl$ $[M-H]^-$ = 308.9323, Found = 308.9330, $C_{13}H_7O_2{}^{81}Br{}^{35}Cl$ $[M-H]^-$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, DMSO-d_6): δ = 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 $C_{14}H_{10}O_4N$ $[M-H]^-$ = 256.0615, Found = 256.0617.

2,5-Diphenylbenzoic Acid (1P): white solid; mp 174-176 °C; IR (neat): 3348-2480 (broad), 1684, 904 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{19}H_{13}O_2$ $[M-H]^-$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{21}H_{19}O_2$ $[M+H]^+$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{27}H_{31}O_2$ $[M+H]^+$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 115.1 (d, J_{C-F} = 21.6 Hz, 2C), 115.9 (d, J_{C-F} = 21.6 Hz, 2C) 128.7 (d, J_{C-F} = 7.5 Hz, 2C), 129.3, 129.5, 130.1 (d, J_{C-F} = 8.5 Hz, 2C), 130.6, 131.9, 135.5 (d, J_{C-F} = 2.8 Hz), 136.5 (d, J_{C-F} = 2.8 Hz), 139.4, 141.3, 162.4 (d, J_{C-F} = 246.2 Hz), 162.8 (d, J_{C-F} = 247.1 Hz), 173.5; HRMS (ESI): Calcd for $C_{19}H_{11}O_2F_2$ $[M-H]^-$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 × 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 × 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}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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, $CDCl_3$): δ =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}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ =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 $C_{13}H_9O_2$ $[M+H]^+$ =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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ =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 $C_{17}H_{17}O_2$ $[M+H]^+$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{14}H_{11}O_3$ $[M+H]^+$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 105.1 (d, $J_{C\text{-}F}$ = 25.4 Hz), 112.4 (d, $J_{C\text{-}F}$ = 21.6 Hz), 114.6, 120.4, 121.5, 124.3 (d, $J_{C\text{-}F}$ = 9.4 Hz), 128.7, 130.7, 134.2, 135.1, 152.1 (d, $J_{C\text{-}F}$ = 12.2 Hz), 160.8, 163.4 (d, $J_{C\text{-}F}$ = 251.8 Hz); HRMS (APCI): Calcd for $C_{13}H_8O_2F$ $[M+H]^+$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{13}H_8O_2{}^{35}Cl$ $[M+H]^+$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, DMF-d_7): δ = 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}C-NMR (100 MHz, DMF-d_7): δ =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 $C_{13}H_8O_4N$ $[M+H]^+$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.34-7.40 (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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{13}H_8O_2{}^{79}Br$ $[M+H]^+$ = 274.9702, Found = 274.9701, $C_{13}H_8O_2{}^{81}Br$ $[M+H]^+$ = 276.9681, Found = 276.9678.

3,4-(2'-Bromo)benzo-7-methylcoumarin (2J): Yield: 288.6 mg (99%); white solid; mp 201-202 °C; IR (neat): 2925, 1723, 1127 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{14}H_{10}O_2{}^{79}Br$ $[M+H]^+$ = 288.9859, Found = 288.9859, Calcd for $C_{14}H_{10}O_2{}^{81}Br$ $[M+H]^+$ = 290.9838, Found = 290.9835.

3,4-(2'-Bromo)benzo-7-(*tert*-butyl)coumarin (2K): Yield: 317.1 mg (96%); white solid; mp 170-172 °C; IR (neat): 2960, 1727, 1134 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{17}H_{16}O_2{}^{79}Br$ $[M+H]^+$ = 331.0328, Found = 331.0327, $C_{17}H_{16}O_2{}^{81}Br$ $[M+H]^+$ = 333.0307, Found = 333.0304.

3,4-(2'-Bromo)benzo-7-methoxycoumarin (2L): Yield: 296.9 mg (97%); white solid; mp 169-170 °C; IR (neat): 3083, 1721, 1167 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{14}H_{10}O_3{}^{79}Br$ $[M+H]^+$ = 304.9808, Found = 304.9807, $C_{14}H_{10}O_3{}^{81}Br$ $[M+H]^+$ = 306.9787, Found = 306.9785.

3,4-(2'-Bromo)benzo-7-fluorocoumarin (2M): Yield: 213.5 mg (73%); white solid; mp 183-185 °C; IR (neat): 3096, 1728, 1148 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 7.08-7.13 (m, 2H), 7.93-7.94 (m, 2H), 7.99-8.04 (m, 1H), 8.53 (s, 1H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ = 105.2 (d, $J_{C\text{-}F}$ = 25.4 Hz), 112.8 (d, $J_{C\text{-}F}$ = 22.6 Hz), 113.8 (d, $J_{C\text{-}F}$ = 3.8 Hz), 121.8, 122.5, 123.3, 124.3 (d, $J_{C\text{-}F}$ = 9.4 Hz), 133.0, 133.1, 138.1, 152.0 (d, $J_{C\text{-}F}$ = 12.2 Hz), 159.4, 163.6 (d, $J_{C\text{-}F}$ = 251.8 Hz); HRMS (APCI): Calcd for $C_{13}H_7O_2{}^{79}BrF$ $[M+H]^+$ = 292.9608, Found = 292.9610, $C_{13}H_7O_2{}^{81}BrF$ $[M+H]^+$ = 294.9587, Found = 294.9589.

3,4-(2'-Bromo)benzo-7-chlorocoumarin (2N): Yield: 279.8 mg (90%); white solid; mp 200-202 °C; IR (neat): 3094, 1730, 1233 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{13}H_7O_2{}^{79}Br{}^{35}Cl$ $[M+H]^+$ = 308.9312, Found = 308.9315, $C_{13}H_7O_2{}^{81}Br{}^{35}Cl$ $[M+H]^+$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{14}H_{10}O_4N$ $[M+H]^+$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{19}H_{13}O_2$ $[M+H]^+$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{21}H_{17}O_2$ $[M+H]^+$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{27}H_{29}O_2$ $[M+H]^+$ = 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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 105.1 (d, J_{C-F} = 25.4 Hz), 112.6 (d, J_{C-F} = 22.6 Hz), 114.4 (d, J_{C-F} = 3.8 Hz), 116.1 (d, J_{C-F} = 21.6 Hz, 2C), 120.8, 122.2, 124.3 (d, J_{C-F} = 10.3 Hz), 128.4, 128.7 (d, J_{C-F} = 8.5 Hz, 2C), 132.9, 133.4 , 134.9 (d, J_{C-F} = 2.8 Hz), 140.6, 151.9 (d, J_{C-F} = 12.2 Hz), 160.8, 163.0 (d, J_{C-F} = 248.1 Hz), 163.4 (d, J_{C-F} = 251.8 Hz); HRMS (APCI): Calcd for $C_{19}H_{11}O_2F_2$ $[M+H]^+$ = 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): cm^{-1}; 3082, 1732, 1228 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ =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 $C_{19}H_{11}O_2{}^{35}Cl_2$ $[M+H]^+$ = 341.0131, Found = 341.0129.

Transformation of 3,4-Benzo-7-methoxycoumarin (2E) into 2'-(α,α-Dimethyl-α-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 Et_2O, 4.5 mmol, 3.22 mL) at -60 °C under argon atmosphere, and the mixture was stirred at room temperature for 19 h. 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 × 3). The organic layer was dried over Na_2SO_4. After filtration and removal of the solvent, 2'-(α,α-dimethyl-α-hydroxy)methyl-2-hydroxy-4-methoxybiphenyl (**3E**) was obtained in >99% yield (256.1 mg).

2'-(α,α-Dimethyl-α-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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ = 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 $C_{16}H_{17}O_3$ $[M-H]^-$ = 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'-(α,α-dimethyl-α-hydroxy)methyl-2-hydroxy-4-methoxybiphenyl **3E** (1.0 mmol, 258.3 mg) in DCE (6.0 mL) was added $MeSO_3H$ (2.0 mmol, 129.9 μL) in DCE (1.0 mL) at room temperature under argon atmosphere. The mixture was stirred for 2 h at room temperature. Sat. $NaHCO_3$ aq. solution (15.0 mL) was added to the reaction mixture and the product was extracted with $CHCl_3$ (15.0 mL × 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-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 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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}C-NMR (100 MHz, $CDCl_3$): δ =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 × 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}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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, $CDCl_3$): δ =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-methoxy-coumarin (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 × 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}; ^{1}H-NMR (400 MHz, $CDCl_3$): δ = 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, $CDCl_3$): δ = 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_3 (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. $NaHCO_3$ 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_2SO_4. 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^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6): 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); ^{13}C-NMR (100 MHz, DMSO-d_6): 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 $C_{13}H_9O_3$ $[M+H]^+$ = 213.0546, Found = 213.0544.

ACKNOWLEDGEMENT

This work was supported by JSPS KAKENHI Grant number JP18K05118.

REFERENCES

1. Recent reviews: (a) Z. Mao, W. Sun, L. Fu, H. Luo, D. Lai, and L. Zhou, *Molecules*, 2014, **19**, 5088; (b) Y. L. Garazd and M. M. Garazd, *Chemistry of Natural Compounds*, 2016, **52**, 1; (c). A. Solhaug, G. S. Eriksen, and J. A. Holme, *Basic Clinical Pharmacology Toxicology*, 2016, **119**, 533; (d) T. F. Schäberle, *Beilstein J. Org. Chem*., 2016, **12**, 571; (e) J. C. Espin, M. Larrosa, M. T. Garcia-Conesa, and F. Tomás-Barberán, *Evidence-Based Complementary and Alternative Medicine*, 2013, ID 270418, 1.
2. (a) G. W. Kenner, M. A. Murray, and C. M. B. Tylor, *Tetrahedron*, 1957, **1**, 259; (b) D. Davies and C. Warning, *Chem. Commun*., 1965, 263.
3. (a) Y. Wang, A. V. Gulevich, and V. Gevorgyan, *Chem. Eur. J*., 2013, **19**, 15836; (b) A. Shao, J. Zhan, N. Li, C. Chiang, and A. Lei, *J. Org. Chem*., 2018, **83**, 3582; c) L. Zhang, Z. Zhang, J. Hong, J. Yu, J. Zhang, and F. Mo, *J. Org. Chem*., 2018, **83**, 3200; (d) X. Tao, J. Dai, J. Zhou, J. Xu, and H. Xu, *Chem. Eur. J*., 2018, **24**, 6932; (e) T. Morack, J. B. Metternich, and R. Gilmour, *Org. Lett*., 2018, **20**, 1316; (f) J. Boonsombat, S. Thongnest, and S. Ruchirawat, *Eur. J. Org. Chem*., 2019, 2971; (g) K. Wadekar, S. Aswale, and V. R. Yatham, *Org. Biomol. Chem*., 2020, **18**, 983; (h) Y. Wang, S. Wang, B. Chen, M. Li, X. Hu, B. Hu, L. Jin, N. Sun, and Z. Shen, *Synlett*, 2020, **31**, 261; (i) S. Xia, K. Hu, C. Lei, and J. Jin, *Org. Lett*., 2020, **22**, 1385.
4. S. L. Yedage and B. M. Bhanage, *J. Org. Chem*., 2017, **82**, 5769.
5. (a) H. Valizadeh and A. Fakhari, *Mol. Divers.*, 2011, **15**, 233; (b) S. C. Schlitzer, D. Arunprasath, K. G. Stevens, and I. Sharma, *Org. Chem. Front.*, 2020, **7**, 913; (c) M. Khoobi, A. Ramazani, A.

Foroumadi, A. Souldozi, K. Slepokura, T. Lis, A. Mahyari, A. Shafiee, and S. W. Joo, *Helv. Chim. Acta*, 2013, **96**, 906; (d) C. Mou, T. Zhu, P. Zheng, S. Yang, B. Song, and Y. R. Chi, *Adv. Synth. Catal*., 2016, **358**, 707.

6. (a) Q. J. Zhou, K. Worm, and R. E. Dolle, *J. Org. Chem*., 2004, **69**, 5147; (b) K. Inamoto, J. Kadokawa, and Y. Kondo, *Org. Lett*., 2013, **15**, 3962; (c) L. Pan, J. Dong, D. Xie, Y. Li, and Q. Liu, *Adv. Synth. Catal*., 2018, **360**, 958; (d) Z. Luo, Z. Gao, Z. Song, Y. Han, and S. Ye, *Org. Biomol. Chem*., 2019, **17**, 4212.
7. (a) H. Togo, T. Muraki, and M. Yokoyama, *Tetrahedron Lett*., 1995, **36**, 7089; (b) S. Furuyama and H. Togo, *Synlett*, 2010, 2325.
8. P. Gao and W. Wei, *Synthesis*, 2014, **46**, 343.
9. Y. Nakai, K. Moriyama, and H. Togo, *Eur. J. Org. Chem*., 2016, 768.
10. (a) J. Fossey, D. Lefort, and J. Sorba, "Free Radicals in Organic Chemistry", Chap. 26, p 295, John Willy & Sons 1995; (b) H. Togo, "Advanced Free Radical Reactions for Organic Synthesis", Chap. 1, p 34, Elsevier, 2004.