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Xanthone Natural Products via *N*-Heterocyclic Carbene Catalysis: Total Synthesis of Atroviridin

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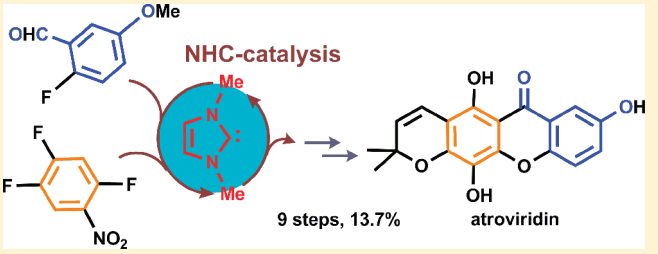
Supporting Information

ABSTRACT: The total synthesis of atroviridin has been accomplished by a linear route involving the *N*-heterocyclic carbene (NHC)-catalyzed aroylation of the fluorobenzene derivative, Claisen cyclization of the *O*-propargylated benzophenones, and intramolecular 1,4-addition of the quinone intermediates. The result provides a viable route to xanthone natural products.



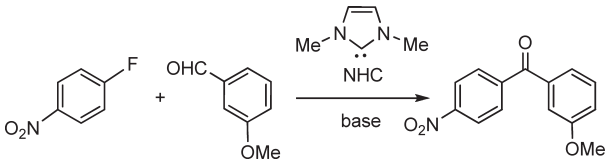
INTRODUCTION

N-Heterocyclic carbenes (NHCs) are widely employed both as ligands for transition-metal systems[1,2] and as small-molecule organic catalysts for chemical synthesis.[1,3] We have focused our research interests on the use of NHCs as organocatalysts[4] and developed a method to catalyze the nucleophilic aroylation of fluorobenzenes by NHC (Scheme 1).[5] In this reaction, the fluoro substituents are replaced by aroyl groups originating from aldehydes to afford benzophenones. It is thought that the "Breslow intermediate," which is also produced during benzoin condensation, is a part of the reaction pathway (Scheme 2). In the course of developing a synthetic route to heterocyclic compounds through NHC catalysis,[6] we envisioned the potential use of this catalysis in the total synthesis of atroviridin (**1**), which is a xanthone natural product (Figure 1).

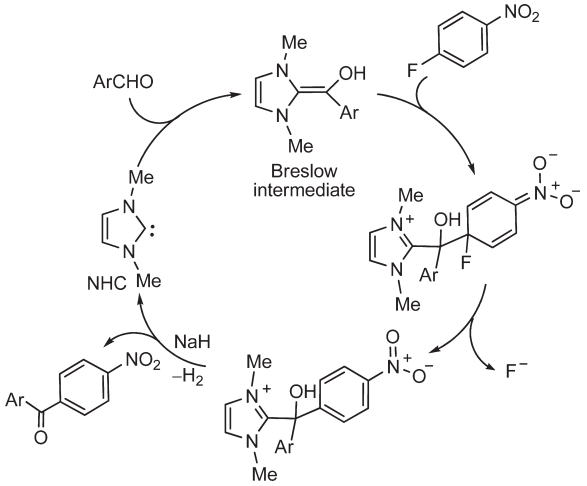
Atroviridin (**1**) is a polyphenolic xanthone isolated from the stem bark of *Garcinia atroviridis* (Guttiferae), a lofty tree indigenous to Thailand.[7] A decoction of the leaves and root of this tree is used as a folk medicine for earache. A number of xanthone and xanthonoid natural products isolated from tropical trees of the genus *Garcinia* have been reported to possess bioactivities.[8] The first total synthesis of **1** was reported by the Theodorakis' group.[9]

With the aim of developing an alternative synthetic route to xanthone natural products, we set out to investigate a total synthesis of **1** (Scheme 3). We sought to construct a xanthone nucleus at the last stage of synthesis through intramolecular conjugate addition of the quinone intermediate **2**, a procedure that mirrors a presumed biosynthetic pathway.[9] We believed the quinone **2** to be accessible from benzophenone/chromene **3** by oxidation. We expected **3** to be formed from the benzophenone **4** via substitution of the fluoro and nitro groups by *O*-nucleophiles, propargylation of the hydroxyl group, and subsequent Claisen cyclization. We planned to prepare **4** from 2,4,5-trifluoronitrobenzene (**5**) and 2-fluoro-6-methoxybenzaldehyde (**6**) by NHC catalysis.

Scheme 1. Nucleophilic Aroylation Catalyzed by NHC



Scheme 2. Plausible Mechanism for Aroylation



RESULTS AND DISCUSSION

The synthesis of benzophenone/chromene **15** via benzophenone **4** is summarized in Scheme 4. The reaction of **5** with **6** in

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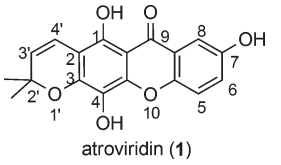
DMF at room temperature for 2 h, in the presence of NHC derived from 1,3-dimethylimidazolium iodide (**7**) (10 mol %), produced **4** in 76% yield. After removal of the methyl group, the fluorine group at the 4 position (atroviridin numbering) of **8** was regioselectively substituted by a methoxy group, and the 7-hydroxy group was protected with the benzyl group in the reaction with K_2CO_3 and benzyl bromide in methanol at room temperature to afford the intermediate **9**. Conversion of the nitro group to the hydroxyl group[10] took place by the reaction of **9** with the anion of benzaldoxime in DMSO at room temperature. The resulting compound **10** was *O*-propargylated with 3-chloro-3-methylbutyne[11] using DBU and catalytic $CuCl_2$ in CH_2Cl_2, followed by Claisen cyclization[12] in toluene heated at reflux to produce the chromene **12** in good yield. The remaining fluoro groups of **12** were replaced by methoxy groups in the reaction with sodium methoxide in DMF at 80 °C to afford the intermediate **13**. The deprotection of benzyl ether was accomplished quantitatively by Pd/C-catalyzed hydrogenation in the presence of 1,4-cyclohexadiene,[13] leaving the C(3′)−C(4′) double bond intact. The acetylation of **14** using Ac_2O in pyridine provided **15**.

The attempted oxidation of **15** using CAN failed to give the quinone **16** (Scheme 5). The tosylate **18** was then prepared from **14** using NaH and *p*-TsCl in THF, and the removal of methyl groups of **15** and **18** was examined prior to the oxidation to quinone. However, all attempts including treatment with BBr_3, $MgBr_2$, or $AlBr_3$ were unsuccessful. These results, which are shown in Scheme 5, prompted us to abandon the use of methyl ethers for protecting 1-, 4-, and 10a-hydroxy groups.

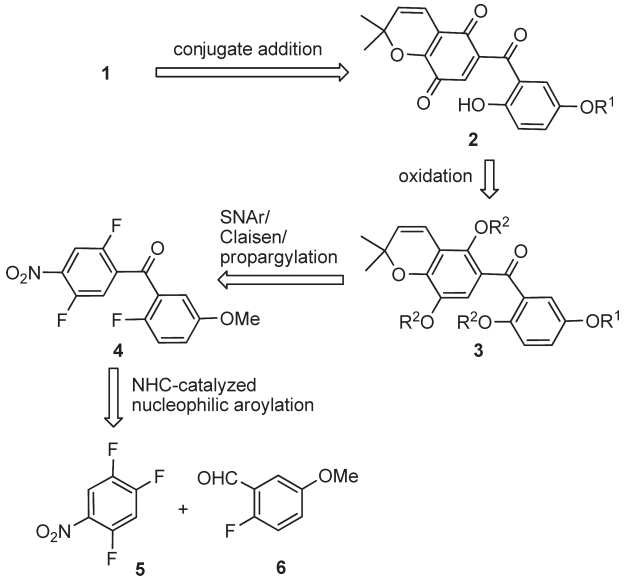
Atroviridin (**1**) was synthesized as summarized in Scheme 6. The fluorine group at the 4 position of **4** was regioselectively substituted by an allyloxy group in the reaction with K_2CO_3/allyl alcohol at room temperature to afford the intermediate **20** in 81% yield. Conversion of the nitro group to the hydroxyl group took place by the reaction of **20** with the anion of benzaldoxime in DMSO at room temperature for 3 h (73% yield). The resulting compound **21** was *O*-propargylated with 3-chloro-3-methylbutyne using DBU and catalytic $CuCl_2$ in CH_2Cl_2 (**22**, 70% yield, 100% conversion) followed by Claisen cyclization in toluene heated at reflux to produce the chromene **23** quantitatively. The remaining fluoro groups of **23** were replaced by allyloxy groups in the reaction with the alkoxide of allyl alcohol in DMF at 60 °C for 3.5 h to afford the intermediate **24** in 87% yield. The removal of allyl groups using dimedone and $Pd(PPh_3)_4$ in THF quantitatively afforded the trihydroxy intermediate **25**. Our aim was to obtain the quinone **26**; therefore, we subjected **25** to oxidation using MnO_2 in CH_2Cl_2 at room temperature for 2 h to afford tetracyclic the triketone **27** (86% yield), which was produced by the spontaneous intramolecular conjugate addition of **26**. We had expected the annulation of **26** to produce an aromatized



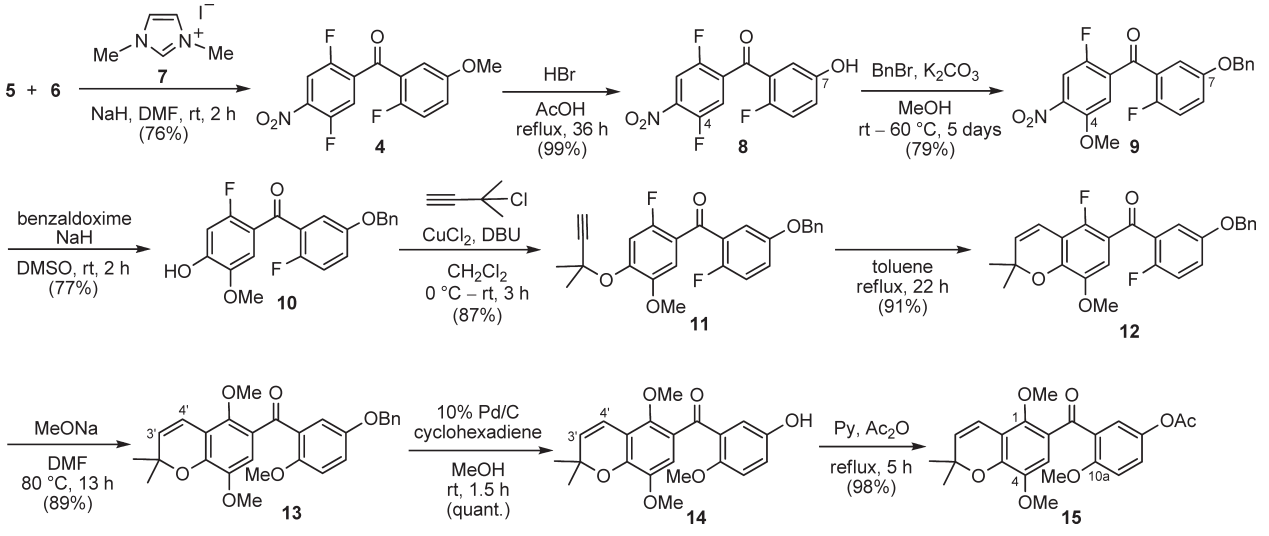
atroviridin (**1**)

Figure 1. Structure for atroviridin.

Scheme 3. Retrosynthetic Analysis of Atroviridin (1)



Scheme 4. Synthesis of Benzophenone/Chromene Intermediate 15



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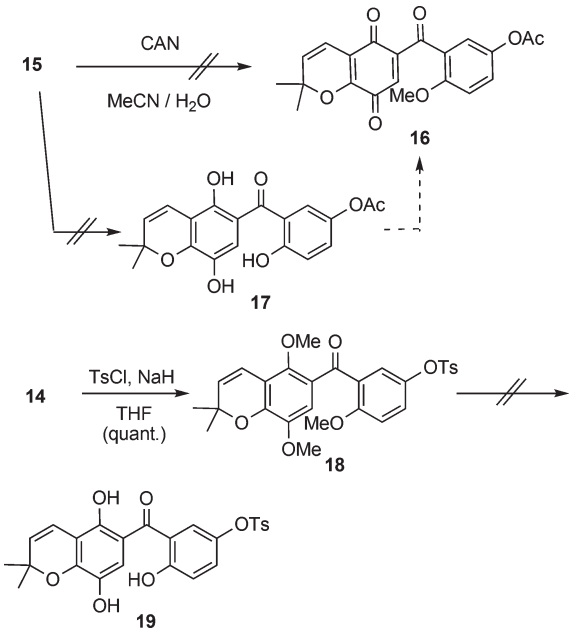
dihydroxy product **28** (enol tautomer of **27**), owing to its stability. However, we found that the keto tautomer is kinetically stable[14] enough to be isolated in pure form by recrystallization. Removal of the methyl group from **27** using BBr_3 in CH_2Cl_2 between −78 °C and −60 °C for 2 h afforded **1** in 58% yield.

Given that the last step of the synthesis in Scheme 6—the removal of the methyl group—showed low reproducibility because of difficulties both in preventing undesired products and in purifying **1**, we planned to use an alternative protecting group for the 7-hydroxy group. Thus, the benzyl ether **29** was prepared from **8** and then subjected to the conversion of the nitro group to the hydroxyl group, followed by *O*-propargylation and Claisen cyclization to produce the benzophenone/chromene **30** (Scheme 7). The substitutions of the remaining fluoro groups to allyloxy groups needed to be performed carefully at 30 °C to avoid the co-occurring Claisen rearrangement of the 10a-allyloxy group of **31**. After removal of the allyl groups, oxidation with MnO_2 afforded the trihydroxy intermediate **32** in good yield. Deprotection of the benzyl ether using BBr_3 and the aromatization to xanthone promoted by *n*-Bu_4NI in toluene heated to reflux provided **1**.

In summary, we have completed the total synthesis of atroviridin (**1**) in 9 and 11 steps. In comparison with Theodorakis' synthesis (14 steps), the numbers of synthetic steps were reduced. The key features of this synthesis are the use of NHC-catalyzed aroylation to prepare a benzophenone intermediate, regio- and chemoselective nucleophilic aromatic substitutions by *O*-nucleophiles, Claisen cyclization, and intramolecular 1,4-addition. This result provides a viable route to xanthone natural products. Further synthetic studies on this class of xanthonoids are underway.

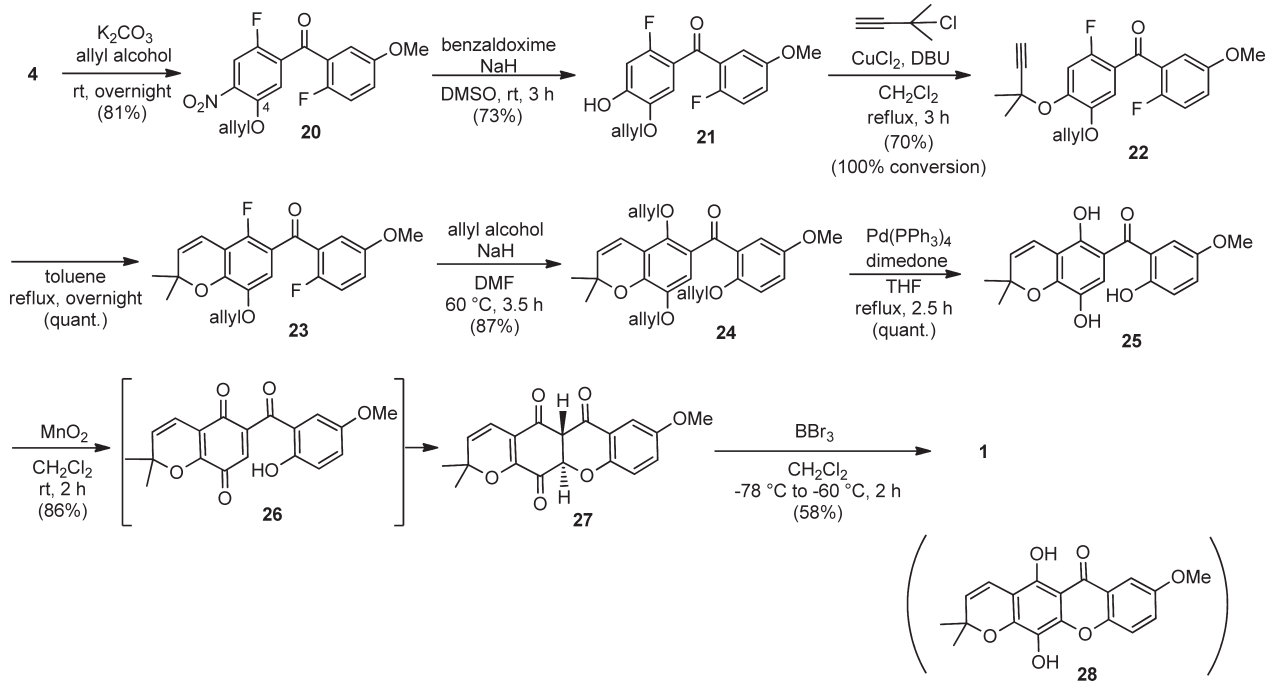
Scheme 5. Attempted Syntheses of Quinone Intermediates 16 and 19



EXPERIMENTAL SECTION

5′-Methoxy-4-nitro-2, 2′,5-trifluorobenzophenone (4)[4]. Under an atmosphere of argon, 60% sodium hydride in oil (812 mg, 20.3 mmol) was added to a mixture of 1,3-dimethylimidazolium iodide 7 (302 mg, 1.35 mmol), 2,4,5-trifluoronitrobenzene (**5**) (1.54 mL, 13.5 mmol), and 2-fluoro-5-methoxybenzaldehyde (**6**) (1.60 mL, 20.3 mmol) in dehydrated DMF (30 mL). The mixture was stirred at 0 °C for 10 min and then at room temperature for 1 h. After the reaction, the mixture was poured into ice−water and then neutralized with dilute hydrochloric acid. The product was extracted with ethyl acetate and then washed with water and brine. After the product was dried over Na_2SO_4, the organic layer was concentrated, and the residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **4** (3.19 g,

Scheme 6. Synthesis of 1



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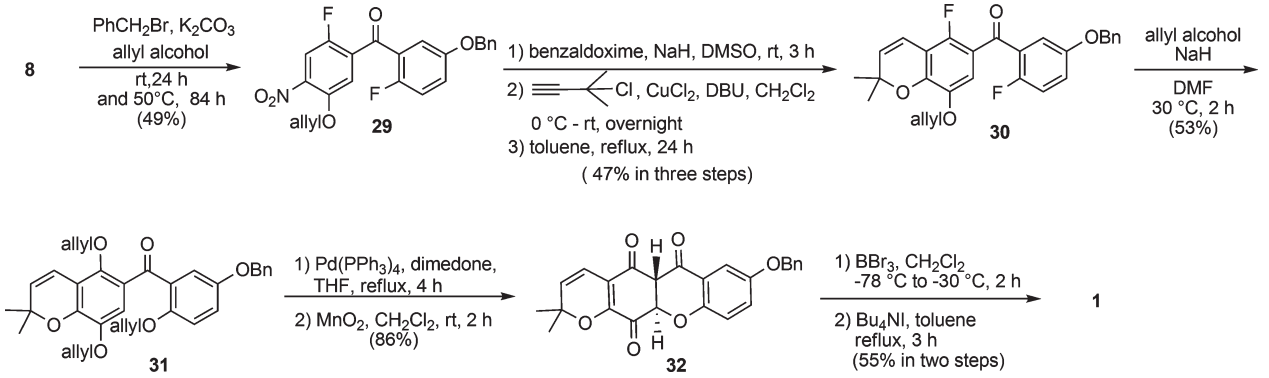
Scheme 7. Alternative Synthesis of 1



76%) as yellow prisms (recrystallized from hexane−dichloromethane): mp 98−99 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.86 (3H, s), 7.06 (2H, t, J = 9.5 Hz), 7.15−7.18 (1H, m), 7.29 (1H, dd, J = 5.5, 3.0 Hz), 7.58 (1H, dd, J = 9.5, 5.5 Hz), 7.86 (1H, dd, J = 9.0, 5.5 Hz); ^{13}C NMR ($CDCl_3$) δ 56.0, 113.4, 114.1 (dd, J_{FC} = 29.4, 3.0 Hz), 117.5 (d, J_{FC} = 24.0 Hz), 119.9 (dd, J_{FC} = 25.2, 2.4 Hz), 122.7 (d, J_{FC} = 8.4 Hz), 125.2 (d, J_{FC} = 13.1 Hz), 134.2 (dd, J_{FC} = 16.8, 8.4 Hz), 138.7 (dd, J_{FC} = 16.2, 8.4 Hz), 151.5 (dd, J_{FC} = 263.9, 3.6 Hz), 154.9 (dd, J_{FC} = 258.0, 2.4 Hz), 156.0, 156.2 (d, J_{FC} = 249.5 Hz), 186.2; IR ($CHCl_3$) 1537 (NO_2), 1668 (C═O) cm^{-1}; HRMS (FAB) m/z calcd for $C_{14}H_9F_3NO_4$ $(M + 1)^+$ 312.0484, found 312.0504.

5′-Hydroxy-4-nitro-2, 2′, 5-trifluorobenzophenone (8). Hydrobromic acid (9 mL) and a few drops of benzalkonium chloride were added to a solution of **4** (3.2 g, 10.3 mmol) in acetic acid (20 mL). The mixture was stirred at reflux for 36 h and then neutralized with 10% NaOH. The product was extracted with ethyl acetate and then washed with water and brine. After the product was dried over $MgSO_4$, the organic layer was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **23** (3.02 g, 99%) as a yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.03(1H, s), 7.03 (1H, t, J = 9.5 Hz), 7.14−7.11 (1H, m), 7.27 (1H, dd, J = 5.5, 3.5 Hz), 7.57 (1H, dd J = 10.0, 5.5 Hz), 7.86 (1H, dd, J = 8.5, 5.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 114.3 (dd, J_{FC} = 32.0, 2.4 Hz), 116.0, 117.7 (d, J_{FC} = 25.2 Hz), 119.9 (dd, J_{FC} = 24.0, 2.4 Hz), 123.4 (d, J_{FC} = 8.5 Hz), 125.2 (d, J_{FC} = 13.2 Hz), 133.9 (dd, J_{FC} = 16.0, 7.8 Hz), 138.7 (dd, J_{FC} = 18.0, 8.4 Hz), 151.6 (dd, J_{FC} = 264.1, 3.6 Hz), 152.5 (d, J_{FC} = 2.4 Hz), 154.9 (d, J_{FC} = 235.5 Hz), 156.0 (d, J_{FC} = 247.1 Hz), 186.6; IR ($CHCl_3$) 1533 (NO_2), 1664 (CO), 3442 (OH) cm^{-1}; HRMS (FAB) m/z calcd for $C_{13}H_7F_3NO_4$ $(M + 1)^+$ 298.0327, found 298.0297.

5′-Benzyloxy-2,2′-difluoro-5-methoxy-4-nitrobenzophenone (9). Under an atmosphere of argon, benzyl bromide (3.3 g, 19.3 mmol) and potassium carbonate (3.55 g, 25.7 mmol) were added to a solution of **4** (3.82 g, 12.9 mmol) in methanol (70 mL). The mixture was stirred at room temperature for 2 days and then at 60 °C for 3 days. After the reaction was complete, methanol was evaporated off, and the residue was extracted with ethyl acetate and then washed with water and brine. After being dried over $MgSO_4$, the organic layer was concentrated, and the residue was recrystallized from dichloromethane and hexane to afford **9**. The filtrate was concentrated and purified by silica gel column chromatography (hexane−ethyl acetate) to give **9** as yellow prisms (recrystallized from hexane−dichloromethane): yield 4.06 g (79%); mp 80−80.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.99 (3H, s), 5.10 (2H, s), 7.06 (1H, t, J = 9.5 Hz), 7.20−7.19 (1H, m), 7.40−7.36 (7H, m),7.61 (1H, d, J = 9.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 57.2, 70.9, 113.8 (d, J_{FC} = 28.8 Hz), 115.0 (d, J_{FC} = 10.8 Hz), 117.5 (d, J_{FC} = 24.0 Hz), 122.7 (d, J_{FC} = 8.4 Hz), 126.2 (d, J_{FC} = 12.0 Hz), 127.7, 128.4, 128.8, 132.2 (d, J_{FC} = 15.6 Hz), 136.3, 141.1 (d, J_{FC} = 8.4 Hz), 149.3 (d, J_{FC} = 2.4 Hz), 153.0 (d, J_{FC} = 250.7 Hz), 155.1, 156.1 (d, J_{FC} = 249.5 Hz), 186.6; IR ($CHCl_3$) 1527 (NO_2), 1666 (CO) cm^{-1}; HRMS (FAB) m/z calcd for $C_{21}H_{16}F_2NO_5$ $(M + 1)^+$ 400.0997, found 400.1011.

5′-Benzyloxy-2,2′-difluoro-4-hydroxy-5-methoxybenzophenone (10). Under an atmosphere of argon, benzaldoxime (533 mg, 4.4 mmol) and 60% sodium hydride in oil (220 mg, 5.5 mmol) were added to a solution of **9** (880 mg, 2.2 mmol) in dehydrated DMSO (22 mL). The mixture was stirred at room temperature for 2 h and acidified with 10% hydrochloric acid with ice-cooling. The product was extracted with ethyl acetate, washed with water and brine, and then dried over $MgSO_4$. The organic layer was concentrated, and the residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **10** (627 mg, 77%) as yellow prisms (recrystallized from hexane−dichloromethane): mp 119−122 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.95 (3H, s), 5.06 (2H, s), 6.18 (1H, s), 6.65 (1H, d, J = 11.0 Hz), 7.02 (1H, t, J = 9.0 Hz), 7.09−7.07 (1H, m), 7.19 (1H, dd, J = 5.5, 3.0 Hz), 7.30 (1H, d, J = 6.0 Hz), 7.43−7.34 (5H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 56.4, 70.7, 102.9 (d, J_{FC} = 27.6 Hz), 111.2 (d, J_{FC} = 3.6 Hz), 115.0, 116.7 (d, J_{FC} = 25.2 Hz), 118.0 (d, J_{FC} = 12.0 Hz), 120.1 (d, J_{FC} = 8.4 Hz), 127.6, 128.1, 128.6, 136.3, 148.2, 151.5 (d, J_{FC} = 13.2 Hz), 154.7, 154.9 (d, J_{FC} = 245.9 Hz), 157.7 (d, J_{FC} = 250.7 Hz), 188.3; IR ($CHCl_3$) 1647 (CO), 3369 (OH) cm^{-1}; HRMS (FAB) m/z calcd for $C_{21}H_{17}F_2O_4$ $(M + 1)^+$ 371.1095, found 371.1097.

5-Benzyloxy-2,2′-difluoro-4-(1,1-dimethylpropargyloxy)-5′-methoxybenzophenone (11). Under an atmosphere of argon, copper(II) chloride (0.10 mg, 0.0007 mmol) and 3-chloro-3-methyl-1-butyne (120 μL, 1.04 mmol) were added to a solution of **10** (964 mg, 2.6 mmol) in distilled dichloromethane (25 mL). The mixture was cooled to 0 °C, and DBU (504 μL, 3.4 mmol) was added. The mixture was stirred at room temperature for 3 h, and the solvent was evaporated. The product was extracted with ethyl acetate, washed with water and brine, and then dried over $MgSO_4$. The organic layer was concentrated, and the residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **11** (983 mg, 87%) as a slightly yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.75 (6H, s), 2.66 (1H, s), 3.86 (3H, s), 5.07 (2H, s), 7.03 (1H, t, J = 9.5 Hz), 7.10−7.09 (1H, m), 7.44−7.21 (8H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 14.1, 22.6, 29.3, 56.4, 70.7, 74.0, 75.3, 84.6, 107.6 (d, J_{FC} = 27.6 Hz), 112.1 (d, J_{FC} = 3.6 Hz), 115.0, 116.8 (d, J_{FC} = 24.0 Hz), 119.6 (d, J_{FC} = 13.2 Hz), 120.2 (d, J_{FC} = 8.4 Hz), 127.6, 128.1, 128.6, 128.8, 136.3, 148.0, 150.3 (d, J_{FC} = 10.8 Hz), 155.0 (d, J_{FC} = 248.3 Hz), 156.0 (d, J_{FC} = 250.0 Hz), 188.5; IR ($CHCl_3$) 1654 (CO), 3264 (alkyne) cm^{-1}; HRMS (FAB) m/z calcd for $C_{26}H_{23}F_2O_4$ $(M + 1)^+$ 437.1564, found 437.1566.

6-(5-Benzyloxy-2-fluorobenzoyl)-2,2-dimethyl-5-fluoro-8-methoxychromene (12). Under an atmosphere of argon, a solution of **11** (265 mg, 0.6 mmol) in dehydrated toluene (15 mL) was refluxed for 22 h. After the solution was cooled, the solvent was

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evaporated. The residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **12** (242 mg, 91%) as a colorless amorphous powder: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.53 (6H, s), 3.89 (3H, s), 5.07 (2H, s), 5.69 (1H, d, J = 10.0), 6.48 (1H, d, J = 10.0), 7.04 (1H, t, J = 9.0 Hz), 7.08−7.07 (1H, m), 7.21−7.18 (2H, m), 7.44−7.34 (5H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 28.1, 30.9, 56.5, 70.7, 78.2, 110.2 (d, J_{FC} = 20.4 Hz), 112.1 (d, J_{FC} = 2.4 Hz), 114.7 (d, J_{FC} = 6.0 Hz) 115.0, 116.7 (d, J_{FC} = 24.0 Hz), 117.7 (d, J_{FC} = 13.2 Hz), 119.9 (d, J_{FC} = 7.2 Hz), 127.6, 128.2, 128.6, 130.7, 136.3, 144.8, 147.6 (d, J_{FC} = 7.2 Hz), 151.8 (d, J_{FC} = 253.1 Hz), 154.7, 154.8 (d, J_{FC} = 245.9 Hz), 188.3, 207.1; IR ($CHCl_3$) 1637 (CO) cm^{-1}; HRMS (FAB) m/z calcd for $C_{26}H_{23}F_2O_4$ $(M + 1)^+$ 437.1564, found 437.1549.

6-(5-Benzyloxy-2-methoxybenzoyl)-5,8-dimethoxy-2,2-dimethylchromene (13). Under an atmosphere of argon, 1 M sodium methoxide in methanol (2.58 mL, 2.58 mmol) was added to a solution of **12** (225 mg, 0.516 mmol) in dehydrated DMF (12 mL). The mixture was stirred at 80 °C for 25 h, poured into ice−water, and then neutralized with hydrochloric acid. The product was extracted with ethyl acetate, washed with water and brine, and then dried over $MgSO_4$. The organic layer was concentrated, and the residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **13** (212 mg, 89%) as colorless prisms (recrystallized from hexane−acetone): mp 124−126 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.52 (6H, s), 3.42 (3H, s), 3.66 (3H, s), 3.83 (3H, s), 5.04 (2H, s), 5.66 (1H, d, J = 10.0), 6.54 (1H, d, J = 10.0), 6.87 (1H, d, J = 8.5 Hz), 7.09−7.03 (3H, m), 7.42−7.30 (5H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 28.0, 56.6, 63.3, 70.8, 77.2, 113.0, 113.3, 115.5, 115.8, 117.1, 118.7, 124.6, 127.7, 128.1, 128.6, 130.4, 131.5, 137.0, 144.7, 146.8, 150.9, 152.3, 152.5, 194.1, 207.2; IR ($CHCl_3$) 1635 (CO) cm^{-1}; HRMS (FAB) m/z calcd for $C_{28}H_{28}O_6$ $(M + 1)^+$ 461.1964, found 461.1953.

6-(5-Hydroxy-2-methoxybenzoyl)-5,8-dimethoxy-2,2-dimethylchromene (14). Under an atmosphere of argon, 1,4-cyclohexadiene (85 μL, 0.9 mmol) and Pd/C (41 mg) were added to a solution of **13** (41 mg, 0.09 mmol) in methanol (2 mL). The mixture was stirred for 1.5 h and then filtered through Celite. The filtrate was concentrated, and the residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **14** (35.2 mg, quant) as colorless prisms (recrystallized from hexane−acetone): mp 131−133 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.50 (6H, s, CH_3), 3.49 (3H, s, OCH_3), 3.66 (3H, s, OCH_3), 3.83 (3H, s, OCH_3), 4.85 (1H, s), 5.66 (1H, d, J = 10.0 Hz), 6.55 (1H, d, J = 10.0 Hz), 6.83 (1H, d, J = 9.0 Hz), 6.93−6.92 (2H, m), 7.07 (1H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 27.8, 56.2, 56.3, 63.2, 77.4, 113.0, 113.4, 115.3, 116.3, 116.7, 119.0, 124.1 130.3 130.7, 144.3, 146.7, 149.7, 150.7, 151.6, 194.8; IR ($CHCl_3$) 1637 (CO), 3437 (OH) cm^{-1}; HRMS (FAB) m/z calcd for $C_{21}H_{23}O_6$ $(M + 1)^+$ 371.1495, found 371.1489.

6-(5-Acetoxy-2-methoxybenzoyl)-5,8-dimethoxy-2,2-dimethylchromene (15). Under an atmosphere of argon, pyridine (2 μL) was added to a solution of **14** (38.7 mg, 0.104 mmol) in acetic anhydride (3 mL). The mixture was stirred at reflux for 5 h, poured into 2% hydrochloric acid, and then extracted with diethyl ether. The organic layer was washed with 2% sodium hydroxide and brine. After being dried over Na_2SO_4, the organic layer was concentrated, and the residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **15** (42 mg, 98%) as a colorless powder (recrystallized from hexane−acetone): mp 121−123 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.50 (6H, s), 2.27 (3H, s), 3.44 (3H, s), 3.72 (3H, s), 3.85 (3H, s), 5.66 (1H, d, J = 10.0), 6.54 (1H, d, J = 10.0), 6.92 (1H, dd, J = 7.0, 2.5 Hz), 7.11 (1H, s), 7.16−7.15 (2H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 21.1, 26.8, 28.0, 56.3, 56.5, 63.4, 112.1, 113.2, 115.5, 117.0, 122.6, 124.1, 124.7, 130.4, 131.6, 143.7, 144.8, 147.0, 151.1, 155.6, 193.0; IR ($CHCl_3$) 1647 (CO), 1761 (CO) cm^{-1}; HRMS (FAB) m/z calcd for $C_{23}H_{25}O_7$ $(M + 1)^+$ 413.1600, found 413.1600.

5,8-Dimethoxy-2,2-dimethyl-6-(2-methoxy-5-tosyloxybenzoyl)chromene (18). Under an atmosphere of argon, TsCl (95 mg, 0.50 mmol) was added to a solution of **14** (169 mg, 0.46 mmol) in dehydrated THF (7 mL). The mixture was stirred at room temperature for 20 min, and then 60% NaH in oil (22 mg, 0.55 mmol) was added. After being stirred for another 30 min, the mixture was poured into water, and the product was extracted with ethyl acetate. The organic layer was washed with water, dried over $MgSO_4$, and concentrated. The residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **18** (242 mg, 100%) as colorless prisms (recrystallized from hexane−dichloromethane): mp 146−147 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.51 (6H, s), 2.43 (3H, s), 3.32 (3H, s), 3.69 (3H, s), 3.86 (3H, s), 5.68 (1H, d, J = 10.0 Hz), 6.50 (1H, d, J = 10.0 Hz), 6.83 (1H, d, J = 9.0 Hz), 6.98 (1H, d, J = 3.0 Hz), 7.09 (1H, s), 7.11 (1H, dd, J = 9.0, 3.0 Hz), 7.30 (2H, d, J = 8.0 Hz), 7.71 (2H, d, J = 8.0 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 21.7, 27.9, 56.1, 56.4, 63.1, 76.9, 111.9, 113.0, 115.3, 116.7, 122.9, 123.6, 125.4, 128.5, 129.8, 130.4, 131.9, 132.1, 142.4, 144.8, 145.5, 147.3, 151.1, 156.3, 192.2; IR ($CHCl_3$) 1636 (C═O) cm^{-1}; HRMS (FAB) m/z calcd for $C_{28}H_{29}O_8S(M + 1)^+$ 525.1583, found 525.1569.

5-Allyloxy-2,2′-difluoro-5′-methoxy-4-nitrobenzophenone (20). Under an atmosphere of argon, potassium carbonate (553 mg, 4 mmol) was added to a solution of **4** (622 mg, 2 mmol) in allyl alcohol (15 mL). The mixture was stirred at room temperature overnight. After the reaction, the allyl alcohol was evaporated off, and the residue was extracted with ethyl acetate, washed with water and brine, and dried over $MgSO_4$. The organic layer was concentrated, and the residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **20** (568 g, 81%) as yellow prisms (recrystallized from hexane-dichloromethane): mp 80−80.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.86 (3H, s), 4.72 (2H, dt, J = 5.0, 1.5 Hz), 5.36 (1H, dd, J = 11.0, 1.0 Hz), 5.49 (1H, dd, J = 17.5, 1.5 Hz), 5.99−6.07 (1H, m), 7.05 (1H, t, J = 9.5 Hz), 7.12−7.15 (1H, m), 7.25 (1H, dd, J = 5.5, 3.5 Hz), 7.34 (1H, d, J = 5.5 Hz), 7.62 (1H, d, J = 8.5 Hz); ^{13}C NMR ($CDCl_3$) δ 56.0, 70.8, 113.5 (d, J_{FC} = 2.4 Hz), 113.6 (d, J_{FC} = 24.0 Hz), 116.3 (d, J_{FC} = 2.4 Hz), 117.3 (d, J_{FC} = 24.0 Hz), 119.0, 121.9 (d, J_{FC} = 8.4 Hz), 126.1 (d, J_{FC} = 13.2 Hz), 131.1, 132.1 (dd, J_{FC} = 14.4, 2.4 Hz), 141.4 (d, J_{FC} = 7.2 Hz), 148.1 (d, J_{FC} = 3.6 Hz), 153.1 (dd, J_{FC} = 252.5, 2.4 Hz), 155.9, 155.9 (dd, J_{FC} = 251.5, 2.4 Hz), 187.5; IR ($CHCl_3$) 1528 (NO_2), 1668 (C═O) cm^{-1}; HRMS (FAB) m/z calcd for $C_{17}H_{14}F_2NO_5$ $(M + 1)^+$ 350.0840, found 350.0839.

5-Allyloxy-2,2′-difluoro-4-hydroxy-5′-methoxybenzophenone (21). Under an atmosphere of argon, benzaldoxime (250 μL, 3.3 mmol) and 60% sodium hydride in oil (164 mg, 4.1 mmol) were added to a solution of **20** (572 mg, 1.6 mmol) in dehydrated DMSO (15 mL). The mixture was stirred at room temperature for 3 h and acidified with 10% hydrochloric acid with ice-cooling. The product was extracted with ethyl acetate, washed with water and brine, and dried over $MgSO_4$. The organic layer was concentrated, and the residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **21** (381 mg, 73%) as yellow prisms (recrystallized from hexane−dichloromethane): mp 66−67 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.83 (3H, s), 4.66 (2H, d, J = 5.5 Hz), 5.36 (1H, dd, J = 10.5, 1.0 Hz), 5.43 (1H, dd, J = 17.0, 1.0 Hz), 6.02−6.10 (1H, m), 6.32 (1H, s), 6.67 (1H, d, J = 11.5 Hz), 7.02 (2H, dd, J = 6.5, 1.5 Hz), 7.09 (1H, d, J = 5.5 Hz), 7.31 (1H, d, J = 7.0 Hz); ^{13}C NMR ($CDCl_3$) δ: 55.9, 70.3, 102.5 (dd, J_{FC} = 28.8, 2.4 Hz), 113.8 (d, J_{FC} = 2.4 Hz), 116.9 (d, J_{FC} = 24.0 Hz), 117.3 (dd, J_{FC} = 21.6, 3.6 Hz), 119.2, 120.0 (d, J_{FC} = 8.4 Hz), 127.9 (d, J_{FC} = 15.6 Hz), 131.3, 147.5 (d, J_{FC} = 2.4 Hz), 149.5 (d, J_{FC} = 2.4 Hz), 151.5 (d, J_{FC} = 10.8 Hz), 155.0 (dd, J_{FC} = 245.9, 2.4 Hz), 155.7, 158.2 (dd, J_{FC} = 254.9, 2.4 Hz), 187.5; IR ($CHCl_3$): 1647 (C═O), 3370 (OH) cm^{-1}; HRMS (FAB) m/z calcd for $C_{17}H_{15}F_2O_4$ $(M + 1)^+$ 321.0938, found 321.0936.

5-Allyloxy-2,2′-difluoro-4-(1,1-dimethylpropargyloxy)-5′-methoxybenzophenone (22). Under an atmosphere of argon, copper(II) chloride (0.10 mg, 0.0007 mmol) and 3-chloro-3-methyl-1-butyne (120 μL, 1.04 mmol) were added to a solution of **21** (303 mg, 0.95 mmol) in distilled dichloromethane (10 mL). The mixture was cooled to 0 °C, and DBU (184 μL, 1.23 mmol) was added. The mixture was refluxed overnight and evaporated. The product was extracted with ethyl acetate, washed with water and brine, and dried over $MgSO_4$. The organic layer was concentrated, and the residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **22** (226 mg, 70%) as a yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.74 (6H, s), 2.65 (1H, s), 3.83 (3H, s), 4.56 (2H, dt, *J* = 5.5, 1.5 Hz), 5.28 (1H, dq, *J* = 10.0, 1.5 Hz), 5.42 (1H, dq, *J* = 17.5, 1.5 Hz), 6.01−6.08 (1H, m), 7.01−7.03 (2H, m), 7.10−7.12 (1H, m), 7.28 (1H, d, *J* = 3.5 Hz), 7.30 (1H, d, *J* = 2.5 Hz); ^{13}C NMR ($CDCl_3$) δ 29.3, 55.9, 70.4, 74.2, 75.1, 84.7, 108.2 (d, J_{FC} = 27.6 Hz), 113.8 (d, J_{FC} = 2.4 Hz), 115.0 (d, J_{FC} = 3.6 Hz), 116.7 (d, J_{FC} = 24.0 Hz), 117.7, 119.5 (d, J_{FC} = 8.4 Hz), 119.9 (d, J_{FC} = 13.2 Hz), 128.5 (d, J_{FC} = 16.8 Hz), 132.9, 147.1 (d, J_{FC} = 2.4 Hz), 151.0 (d, J_{FC} = 10.8 Hz), 155.0 (d, J_{FC} = 244.7 Hz), 155.6, 156.3 (d, J_{FC} = 253.0 Hz), 188.6; IR ($CHCl_3$) 1653 (C═O) cm^{-1}; HRMS (FAB) *m*/*z* calcd for $C_{22}H_{21}F_2O_4$ $(M + 1)^+$ 387.1408, found 387.1433.

8-Allyloxy-5-fluoro-6-(2-fluoro-5-methoxybenzoyl)-2,2-dimethylchromene (23). Under an atmosphere of argon, a solution of **22** (187 mg, 0.48 mmol) in dehydrated toluene (35 mL) was refluxed overnight. After cooling, the solvent was evaporated. The residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **23** (187 mg, quant) as a yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.52 (6H, s), 3.82 (3H, s), 4.61 (2H, dt, *J* = 5.5, 1.5 Hz), 5.28 (1H, dq, *J* = 11.0, 1.5 Hz), 5.39 (1H, dq, *J* = 17.5, 1.5 Hz), 5.69 (1H, d, *J* = 10.0 Hz), 6.01−6.09 (1H, m), 6.49 (1H, d, *J* = 10.0 Hz), 7.01−7.02 (2H, m), 7.07−7.09 (1H, m), 7.21 (1H, d, *J* = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 28.2, 55.9, 70.8, 78.1, 110.4 (d, J_{FC} = 19.2 Hz), 113.8 (d, J_{FC} = 2.4 Hz), 114.8 (d, J_{FC} = 6.0 Hz), 115.6 (d, J_{FC} = 2.4 Hz), 116.7 (d, J_{FC} = 24.0 Hz), 117.8 (dd, J_{FC} = 9.7, 4.8 Hz), 118.0, 119.2 (d, J_{FC} = 8.4 Hz), 128.9 (d, J_{FC} = 15.6 Hz), 130.8 (d, J_{FC} = 2.4 Hz), 143.5 (d, J_{FC} = 2.4 Hz), 148.5 (d, J_{FC} = 7.2 Hz), 153.0 (d, J_{FC} = 255.6 Hz), 154.7 (d, J_{FC} = 244.6, 2.4 Hz), 155.5, 188.4; IR ($CHCl_3$) 1647 (C═O) cm^{-1}; HRMS (FAB) *m*/*z* calcd for $C_{22}H_{21}F_2O_4$ $(M + 1)^+$ 387.1408, found 387.1427.

6-(2-Allyloxy-5-methoxybenzoyl)-5,8-diallyloxy-2,2-dimethylchromene (24). Under an atmosphere of argon, 60% sodium hydride in oil (25 mg, 0.63 mmol) was added to a solution of **23** (45.8 mg, 0.12 mmol) and allyl alcohol (44 μL, 0.63 mmol) in dehydrated DMF (2 mL). The mixture was stirred at 60 °C for 3.5 h, poured into ice−water, and then neutralized with hydrochloric acid. The product was extracted with ethyl acetate, washed with water and brine, and dried over $MgSO_4$. The organic layer was concentrated, and the residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **24** (48.0 mg, 87%) as a yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.46 (6H, s), 3.79 (3H, s), 4.12 (2H, dt, *J* = 5.5, 1.5 Hz), 4.36 (2H, dt, *J* = 5.5, 1.5 Hz), 4.57 (2H, dt, *J* = 5.5, 1.5 Hz), 5.00−5.10 (4H, m), 5.23 (1H, dq, *J* = 10.5, 1.5 Hz), 5.34 (1H, dq, *J* = 17.5, 1.5 Hz), 5.65 (1H, d, *J* = 10.0 Hz), 5.60−5.73 (2H, m), 5.99−6.07 (1H, m), 6.54 (1H, d, *J* = 10.0 Hz), 6.84 (1H, d, *J* = 9.0 Hz), 6.96 (1H, dd, *J* = 9.0, 3.5 Hz), 7.06 (1H, d, *J* = 3.5 Hz), 7.10 (1H, s); ^{13}C NMR ($CDCl_3$) δ 27.8, 55.8, 70.0, 70.7, 76.8, 114.3, 114.4, 115.9, 116.5, 116.9, 117.2, 117.4, 117.6, 118.0, 125.1, 130.3, 131.3, 132.8, 133.1, 133.5, 143.4, 147.3, 149.4, 151.5, 153.5, 193.8; IR ($CHCl_3$) 1647 (C═O) cm^{-1}; HRMS (FAB) *m*/*z* calcd for $C_{28}H_{30}O_6$ M^+ 462.2042, found 462.2042.

5,8-Dihydroxy-6-(2-hydroxy-5-methoxybenzoyl)-2,2-dimethylchromene (25). Under an atmosphere of argon, dimedone (387 mg, 2.76 mmol) was added to a solution of **24** (213 mg, 0.46 mmol) and tetrakis(triphenylphosphine)palladium (266 mg, 0.23 mmol) in distilled THF (15 mL). The mixture was refluxed for 2.5 h. After the reaction, the solvent was evaporated. The product was extracted with ethyl acetate, washed with water and brine, and dried over $MgSO_4$. The organic layer was concentrated, and the residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **25** (163 mg, quant) as yellow prisms (recrystallized from hexane−dichloromethane): mp 202−204 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.53 (6H, s), 3.78 (3H, s), 5.12 (1H, s), 5.65 (1H, d, *J* = 9.5 Hz), 6.77 (1H, d, *J* = 9.5 Hz), 7.00 (1H, d, *J* = 9.5 Hz), 7.07−7.10 (2H, m), 7.16 (1H, s), 9.65 (1H, s), 11.54 (1H, s); ^{13}C NMR ($CDCl_3$) δ 28.5, 56.0, 79.3, 109.8, 111.9, 115.7, 116.1, 117.2, 119.1, 120.3, 122.1, 128.4, 136.9, 147.0, 151.6, 154.0, 154.5, 201.2; IR ($CHCl_3$) 1643 (C═O), 3420 (OH) cm^{-1}; HRMS (FAB) *m*/*z* calcd for $C_{19}H_{19}O_6$ $(M + 1)^+$ 343.1182, found 343.1193.

2,2-Dimethyl-8-methoxypyrano[2,3-*b*]xanthene-5,6,12-(2*H*,5a*H*,12a*H*)-trione (27). Manganese dioxide (967 mg, 11.2 mmol) was added to a solution of **25** (385 mg, 1.12 mmol) in distilled dichloromethane (25 mL). The mixture was stirred at room temperature for 3.5 h and filtrated through Celite. The filtrate was concentrated, and the residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **27** (330 mg, 86%) as yellow prisms (recrystallized from hexane−dichloromethane): mp 172−174 °C; H NMR (500 MHz, $CDCl_3$) δ 1.56 (3H, s), 1.61 (3H, s), 3.07 (1H, d, *J* = 16.5 Hz), 3.28 (1H, d, *J* = 16.5 Hz), 3.78 (3H, s), 5.71 (1H, d, *J* = 10.0 Hz), 6.45 (1H, d, *J* = 10.0 Hz), 6.98 (1H, d, *J* = 3.0 Hz), 7.20 (1H, d, *J* = 9.0 Hz), 7.33 (1H, dd, *J* = 9.0, 3.0 Hz); ^{13}C NMR ($CDCl_3$) δ 27.5, 28.1, 43.3, 55.9, 81.1, 92.4, 104.5, 114.4, 115.2, 117.7, 119.3, 129.2, 131.3, 155.6, 156.6, 167.6, 183.5, 186.5, 194.8; IR ($CHCl_3$) 1711, 1674, 1632 (C═O) cm^{-1}; HRMS (FAB) *m*/*z* calcd for $C_{19}H_{17}O_6$ $(M + 1)^+$ 341.1025, found 341.1032.

5-Allyloxy-5′-benzyloxy-2,2′-difluoro-4-nitrobenzophenone (29). Under an atmosphere of argon, benzyl bromide (2.08 mL, 17.5 mmol) and potassium carbonate (3.22 g, 23.3 mmol) were added to a solution of **8** (3.29 g, 11.6 mmol) in allyl alcohol (50 mL). The mixture was stirred at room temperature for 24 h and then at 50 °C for 84 h. After the reaction, allyl alcohol was evaporated off, and the residue was extracted with ethyl acetate, washed with water and brine, and then dried over $MgSO_4$. The organic layer was concentrated, and the residue was concentrated and purified by silica gel column chromatography (hexane−ethyl acetate) to give **29** (2.42 g, 49%) as yellow needles (recrystallized from hexane−acetone): mp 133.5−137 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.71 (2H, d, *J* = 5.0 Hz), 5.09 (2H, s), 5.36 (1H, d, *J* = 11.5 Hz), 5.49 (1H, d, *J* = 17.0 Hz), 5.99−5.99 (1H, m), 7.06 (1H, t, *J* = 9.5 Hz), 7.17−7.18 (1H, m), 7.31−7.31 (7H, m), 7.61 (1H, d, *J* = 8.5 Hz); ^{13}C NMR (126 MHz, $CDCl_3$) δ 70.84, 113.66 (d, J_{FC} = 28.8 Hz), 114.93, 116.36 (d, J_{FC} = 2.4 Hz), 117.41 (d, J_{FC} = 24.0 Hz), 118.98, 122.66 (d, J_{FC} = 8.4 Hz), 126.12 (d, J_{FC} = 13.2 Hz), 127.54, 128.30, 128.70, 131.14, 132.00 (d, J_{FC} = 14.4 Hz), 136.08 141.46 (d, J_{FC} = 8.4 Hz), 148.12 (d, J_{FC} = 2.4 Hz), 153.11 (d, J_{FC} = 249.5 Hz), 155.03, 156.02 (d, J_{FC} = 248.3 Hz), 187.51; IR (ATR) 1526 (NO_2), 1654 (CO) cm^{-1}; HRMS (FAB) *m*/*z* calcd for $C_{23}H_{18}F_2NO_5$ $(M + 1)^+$ 426.1153, found 426.1185.

5-Allyloxy-5′-benzyloxy-2,2′-difluoro-4-hydroxybenzophenone (33). Under an atmosphere of argon, benzaldoxime (254 mg, 2.1 mmol) and 60% sodium hydride in oil (84 mg, 2.1 mmol) were added to a solution of **29** (425 mg, 1.0 mmol) in dehydrated DMSO (10 mL). The mixture was stirred at 20 °C for 7 h and then acidified with 10% hydrochloric acid with ice-cooling. The product was extracted with ethyl acetate, washed with water and brine, and then dried over $MgSO_4$. The organic layer was concentrated, and the residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **33** (281 mg, 71%) as a yellow oil: H NMR (500 MHz, $CDCl_3$) δ 4.65 (2H, d, *J* = 5.7 Hz), 5.06 (2H, s), 5.36 (1H, d, *J* = 10.2 Hz), 5.43 (1H, d, *J* = 17.0 Hz), 6.03−6.08 (1H, m), 6.27 (1H, s), 6.66 (1H, d, *J* = 10.8 Hz), 7.02 (1H, t, *J* = 9.4 Hz), 7.07−7.10 (1H, m), 7.18−7.19 (1H, m), 7.29−7.43 (6H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 70.45, 70.74,

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103.11 (d, J_{FC} = 27.6 Hz), 112.95 (d, J_{FC} = 3.6 Hz), 115.05 (d, J_{FC} = 2.4 Hz), 116.76 (d, J_{FC} = 24.0 Hz), 118.06 (d, J_{FC} = 12.0 Hz), 119.20, 120.15 (d, J_{FC} = 8.4 Hz), 127.58, 128.17, 128.63, 128.85 (d, J_{FC} = 15.6 Hz), 132.07, 136.38, 142.16 (d, J_{FC} = 2.4 Hz), 151.87 (d, J_{FC} = 13.2 Hz), 154.73, 154.96 (d, J_{FC} = 248.3 Hz), 157.76 (d, J_{FC} = 251.9 Hz); IR (ATR) 1649 (CO), 3360 (OH) cm^{-1}; HRMS (FAB) m/z calcd for $C_{23}H_{19}F_2O_4$ $(M + 1)^+$ 397.1251, found 397.1242.

5-Allyloxy-5′-benzyloxy-2,2′-difluoro-4-(1,1-dimethylpropargyloxy)benzophenone (34). Under an atmosphere of argon, copper(II) chloride (0.20 mg, 0.0015 mmol) and 3-chloro-3-methyl-1-butyne (279 μL, 2.43 mmol) were added to a solution of **33** (876 mg, 2.21 mmol) in distilled dichloromethane (25 mL). The mixture was cooled to 0 °C, and DBU (430 μL, 2.87 mmol) was added. The mixture was stirred at room temperature overnight, and the solvent was evaporated. The product was extracted with ethyl acetate, washed with water and brine, and then dried over $MgSO_4$. The organic layer was concentrated, and the residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **34** (678 mg, 66%) as a yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.74 (6H, s), 2.65 (1H, s), 4.55 (2H, d, J = 5.0 Hz), 5.06 (2H, s), 5.28 (1H, dd, J = 11.0, 1.0 Hz), 5.42 (1H, dd, J = 17.5, 1.0 Hz), 6.02−6.07 (1H, m), 7.02 (1H, t, J = 9.0 Hz), 7.07−7.11 (1H, m), 7.20−7.21 (1H, m), 7.28−7.29 (2H, m), 7.34−7.41 (7H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 29.34, 70.40, 70.75, 74.17, 75.09, 84.74, 108.24 (d, J_{FC} = 27.6 Hz), 115.03 (d, J_{FC} = 3.6 Hz), 115.09 (d, J_{FC} = 2.4 Hz), 116.82 (d, J_{FC} = 24.0 Hz), 117.69, 119.91 (d, J_{FC} = 12.0 Hz), 120.29 (d, J_{FC} = 8.4 Hz), 127.59, 128.17, 128.59 (d, J_{FC} = 12.0 Hz), 128.64, 132.93, 136.36, 147.15, 151.00 (d, J_{FC} = 10.8 Hz), 154.73 (d, J_{FC} = 2.4 Hz), 155.07 (d, J_{FC} = 247.1 Hz), 156.24 (d, J_{FC} = 252.3 Hz), 188.49; IR (ATR) 1654 (CO), 3292 (alkyne) cm^{-1}; HRMS (FAB) m/z calcd for $C_{28}H_{25}F_2O_4$ $(M + 1)^+$ 463.1721, found 463.1738.

6-(5-Benzyloxy-2-fluorobenzoyl)-2,2-dimethyl-5-fluoro-8-allyloxychromene (30). Under an atmosphere of argon, a solution of **34** (678 mg, 1.47 mmol) in dehydreated toluene (15 mL) was refluxed for 24 h. After the solution was cooled, the solvent was evaporated. The residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **30** (678 mg, 100%) as a yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.52 (6H, s), 4.60 (2H, d, J = 5.1 Hz), 5.06 (2H, s), 5.28 (1H, d, J = 11.5 Hz), 5.39 (1H, dd, J = 17.0, 1.0 Hz), 5.69 (1H, d, J = 10.0 Hz), 6.00−6.10 (1H, m), 6.49 (1H, d, J = 10.0 Hz), 7.02 (1H, t, J = 9.0 Hz), 7.06−7.10 (1H, m), 7.16−7.22 (2H, m), 7.32−7.43 (5H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 28.15, 70.74, 70.76, 78.12, 110.43 (d, J_{FC} = 20.4 Hz), 114.75, 114.79, 115.03 (d, J_{FC} = 2.4 Hz), 115.62 (d, J_{FC} = 3.6 Hz), 116.76 (d, J_{FC} = 24.0 Hz), 117.78 (d, J_{FC} = 12.0 Hz), 118.01, 119.95 (d, J_{FC} = 8.4 Hz), 127.58, 128.17, 128.63, 128.94 (d, J_{FC} = 15.6 Hz), 130.78 (d, J_{FC} = 2.4 Hz), 133.12, 136.37, 143.51, 148.53 (d, J_{FC} = 7.2 Hz), 152.97 (d, J_{FC} = 255.5 Hz), 154.71 (d, J_{FC} = 247.1 Hz), 188.26; IR (ATR) 1639 (CO) cm^{-1}; HRMS (FAB) m/z calcd for $C_{28}H_{25}F_2O_4$ $(M + 1)^+$ 463.1721, found 463.1739.

6-(2-Allyloxy-5-benzyloxybenzoyl)-5,8-diallyloxy-2,2-dimethylchromene (31). Under an atmosphere of argon, 60% NaH in oil (200 mg, 5.0 mmol) was added to a solution of **30** (462 mg, 1.0 mmol) and allyl alcohol (340 μL, 5.0 mmol) in dehydrated DMF (20 mL). The mixture was stirred at 30 °C for 2 h, poured into ice−water, and then neutralized with hydrochloric acid. The product was extracted with ethyl acetate, washed with water and brine, and then dried over $MgSO_4$. The organic layer was concentrated, and the residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **31** (281 mg, 53%) as a slightly yellow oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.48 (6H, s), 4.07 (2H, d, J = 5.5 Hz), 4.36 (2H, d, J = 4.5 Hz), 4.57 (2H, d, J = 5.0 Hz), 5.01−5.08 (6H, m), 5.23 (1H, dd, J = 11.0, 1.0 Hz), 5.34 (1H, dd, J = 17.0, 1.0 Hz), 5.57−5.73 (3H, m), 6.00−6.05 (1H, m), 6.53 (1H, d, J = 10.0 Hz), 6.83 (1H, d, J = 9.0 Hz), 7.02 (1H, dd, J = 9.0, 3.0 Hz), 7.10 (1H, s), 7.14 (1H, d, J = 3.0 Hz), 7.22−7.50 (5H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 27.8, 70.0, 70.7, 70.8, 114.3, 115.8, 115.9, 116.6, 117.0, 117.3, 117.4, 117.6, 119.0, 125.2, 127.5, 127.9, 128.5, 130.3, 131.5, 132.9, 133.2, 133.6, 137.0, 143.5, 147.4, 149.5, 151.8, 152.7, 193.7; IR (ATR) 1645 (CO), 1633 cm^{-1}; HRMS (FAB) m/z calcd for $C_{34}H_{34}O_6$ $(M + 1)^+$ 538.2355, found 538.2332.

6-(5-Benzyloxy-2-hydroxybenzoyl)-5,8-dihydroxy-2,2-dimethylchromene (35). Under an atmosphere of argon, dimedone (480 mg, 3.42 mmol) was added to a solution of **31** (307 mg, 0.57 mmol) and tetrakis(triphenylphosphine)palladium (330 mg, 0.29 mmol) in dehydrated THF (15 mL). The mixture was refluxed for 4 h. After the reaction, the solvent was evaporated. The product was extracted with ethyl acetate, washed with water and brine, and then dried over $MgSO_4$. The organic layer was concentrated, and the residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **35** (204 mg, 86%) as a yellow solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.53 (6H, s), 5.02 (2H, s), 5.06 (1H, s), 5.64 (1H, d, J = 10.0 Hz), 6.77 (1H, d, J = 10.0 Hz), 6.99 (1H, d, J = 9.0 Hz), 7.11 (1H, s), 7.13−7.17 (2H, m), 7.32 (1H, t, J = 7.0 Hz), 7.37−7.43 (4H, m), 9.70 (1H, s), 11.52 (1H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 28.4, 71.0, 79.2, 109.8, 111.9, 116.1, 117.1, 117.1, 119.1, 120.4, 123.2, 127.6, 128.1, 128.4, 128.6, 136.7, 136.9, 147.1, 150.7, 154.0, 154.8, 200.1; IR (ATR) 1639 (CO), 3458 (OH) cm^{-1}; HRMS (FAB) m/z calcd for $C_{25}H_{23}O_6$ $(M + 1)^+$ 419.1495, found 419.1507.

8-Benzyloxy-2,2-dimethylpyrano[2,3-*b*]xanthene-5,6,12-(2*H*,5a*H*,12a*H*)-trione (32). Manganese dioxide (382 mg, 4.4 mmol) was added to a solution of **35** (184 mg, 0.44 mmol) in dehydrated dichloromethane (15 mL). The mixture was stirred at room temperature for 12 h and filtrated through Celite. The filtrate was concentrated, and the residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **32** (183 mg, quant) as an orange amorphous solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.54 (6H, s), 3.06 (1H, d, J = 16.5 Hz), 3.27 (1H, d, J = 16.5 Hz), 5.02 (2H, s), 5.70 (1H, d, J = 10.0 Hz), 6.45 (1H, d, J = 10.0 Hz), 7.04 (1H, d, J = 2.5 Hz), 7.21 (1H, d, J = 9.0 Hz), 7.33−7.41 (6H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 27.7, 28.4, 43.5, 70.8, 81.4, 92.5, 106.3, 114.7, 115.4, 117.9, 119.6, 127.5, 128.3, 128.7, 129.9, 131.5, 136.0, 154.9, 156.8, 167.9, 183.7, 186.6, 194.9; IR (ATR) 1716 (CO), 1705 (CO), 1676 (CO) cm^{-1}; HRMS (FAB) m/z calcd for $C_{25}H_{21}O_6$ $(M + 1)^+$ 417.1338, found 417.1333.

Atroviridin (1) from 27. Under an atmosphere of argon, tribromoborate (24 μL, 0.25 mmol) was added to a solution of **27** (17.0 mg, 0.05 mmol) in dehydrated dichloromethane (3 mL) at −78 °C. The mixture was stirred at −78 °C for 10 min and then at −60 °C for 2 h. The reaction was stopped by addition of methanol. The product was extracted with ethyl acetate, washed with water and brine, and dried over $MgSO_4$. The organic layer was concentrated, and the residue was purified by silica gel column chromatography (hexane−ethyl acetate) to give **1** (9.4 mg, 58%) as a yellow solid: ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.46 (6H, s), 5.78 (1H, d, J = 10.3 Hz), 6.63 (1H, d, J = 10.3 Hz), 7.31 (1H, dd, J = 9.2, 2.9 Hz), 7.41 (1H, d, J = 2.9 Hz), 7.52 (1H, d, J = 9.2 Hz), 8.77 (1H, br s), 10.03 (1H, br s), 12.71 (1H, s); ^{1}H NMR (acetone-d_6) δ 1.49 (6H, s), 5.77 (2H, d, J = 9.7 Hz), 6.72 (2H, d, J = 9.7 Hz), 7.38 (2H, dd, J = 9.2, 2.9 Hz), 7.50 (2H, d, J = 9.2 Hz), 7.58 (2H, d, J = 2.9 Hz), 7.90 (1H, s), 8.98 (1H, s), 12.80 (1H, s); ^{13}C NMR (126 MHz, DMSO-d_6) δ 28.3, 78.5, 102.8, 104.1, 108.5, 115.5, 119.7, 120.7, 125.3, 126.0, 129.2, 145.7, 149.0, 149.3, 149.7, 154.6, 181.0; ^{13}C NMR (126 MHz, acetone-d_6) δ 27.7, 78.6, 102.8, 104.0, 108.8, 115.5, 119.0, 120.8, 124.9, 128.4, 144.8, 148.0, 149.7, 149.9, 154.3, 181.3; HRMS (FAB) m/z calcd for $C_{18}H_{15}O_6$ $(M + 1)^+$ 327.0869, found 327.0862.

Atroviridin (1) from 32. Under an atmosphere of argon, 1 M tribromoborate in dichloromethane (0.5 mL) was added to a solution of **32** (30 mg, 0.072 mmol) in dehydrated dichloromethane (30 mL) at −78 °C. The mixture was stirred at −78 °C for 10 min, and then the temperature was allowed to rise to −17 °C in 3.5 h. The reaction was stopped by adding methanol at −78 °C. The product was extracted with chloroform, washed with water and brine, and then dried over $MgSO_4$.

The organic layer was concentrated, and the residue was purified by silica gel column chromatography (hexane/ethyl acetate/dichloromethane) to give the crude debenzylated product. A mixture of the product and tetrabutylammonium iodide (30 mg) in toluene was refluxed for 3 h and concentrated. The residue was purified by silica gel column chromatography (hexane/ethyl acetate/dichloromethane) to give **1** (13 mg, 55%) as a yellow solid.

■ ASSOCIATED CONTENT

Supporting Information. Experimental procedures and compound characterization data for the synthesis of **8**−**15**, **17**, **18**, and **29**−**35** and copies of ^{1}H and ^{13}C NMR spectra of **1**, **4**, **8**, **20**−**25**, **27**, and **29**−**35**. This material is available free of charge via the Internet at http://pubs.acs.org.

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