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Rh(III)-CATALYZED CASCADE C-H ACTIVATION/ANNULATION OF CYCLIC 2-DIAZO-1,3-DIKETONES WITH BENZOYLACETONITRILES TO POLYCYCLIC BENZO[*de*]CHROMENES

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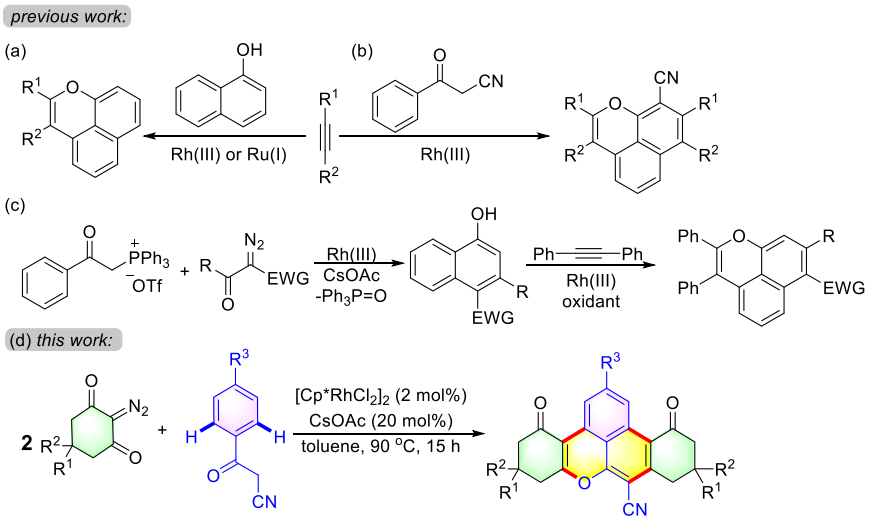
Abstract – The Rh(III)-catalyzed cascade C-H activation/benzannulation reactions of cyclic 2-diazo-1,3-diketones with benzoylacetonitriles leading to a simple and efficient strategy for the synthesis of polycyclic benzo[*de*]chromenes in good-to-high yields has been described. Four new bonds and two rings are generated through sequential C-H activation, carbenoid insertion, migratory insertion, and intramolecular annulation process in a single procedure. This protocol is features with readily available starting materials, favorable functional group compatibility, and high efficiency, atom- and step-economy.

INTRODUCTION

Benzo[*de*]chromene is one of the most important skeletons among oxygen-containing heterocycles and has been found in natural products and bioactive compounds.[1-5] Its derivatives have aroused increasing attention because of their unusually fused tricyclic structures and interesting biological properties,[6-8] such as anti-HIV, antibacterial, antitumor activities, and antiarrhythmic properties as a result of their *β*-blocking activity.[9] As an important class of fused heteroaromatic molecules, considerable efforts have been devoted to the development of efficient methods for the construction of benzo[*de*]chromene derivatives.[10-12] However, most of them require multiple steps, elaborate-to-access starting materials, or harsh reaction

conditions. Therefore, it is of current interest to establish more general, atom- and step-economical approaches to rapidly assemble diversely functionalized benzo[*de*]chromene derivatives from easily available starting materials.

Transition-metal-catalyzed direct C-H bond functionalization has focused increasing attention in recent years as a powerful and step-economical way to construct carbon–carbon and carbon–heteroatom bonds without prior functionalization.[13-18] In particular, Rh-, Ru-, or Ir-catalyzed C-H activation and subsequent intramolecular cyclization of aromatic compounds with alkynes, or diazo compounds have provided a number of efficient methods for the synthesis of fused (hetero)cyclic compounds.[19-21] In this aspect, Miura's group[22] and Ackermann's group[23] respectively described an alternative synthesis of benzo[*de*]chromene derivatives through Rh- or Ru-catalyzed C-H activation/annulation of 1-naphthols with alkynes (Scheme 1a). Subsequently, Wang and co-workers successfully developed rhodium-catalyzed sequential C-H functionalization of benzoylacetonitriles and tandem intramolecular annulation with alkynes to produce substituted benzo[*de*]chromanes (Scheme 1b).[24] Li and co-workers have recently reported Rh(III)-catalyzed C-H activation of phosphonium ylides with diazo compounds to access substituted 1-naphthols, which underwent another oxidative annulation with an alkyne to afford the benzo[*de*]chromanes, however, a two-step operation was necessary in this conversion (Scheme 1c).[25] Diazo compounds, a class of environmentally friendly and highly reactive coupling reagents, have been widely used for synthesis of diversified substituted benzo[*de*]chromenes by Liu's,[26] Fan's,[27] and Wang's group,[28] respectively. Inspired by these elegant pioneering studies and as a continuation of our own interest in the synthesis of fused heterocycles *via* Rh(III)-catalyzed cascade reaction of diazo compounds,[29-33] we herein report a simple and efficient preparation of polycyclic benzo[*de*]chromanes *via* Rh(III)-catalyzed cascade C-H activation/benzannulation reactions of cyclic 2-diazo-1,3-diketones with benzoylacetonitriles (Scheme 1d).

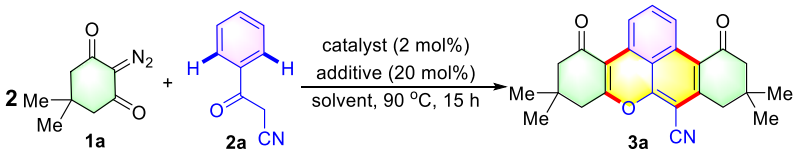


Scheme 1. Synthesis of polycyclic benzo[*de*]chromenes via transition metal-catalyzed cascade C-H activation/annulation reactions

RESULTS AND DISCUSSION

At the outset of our study, we treated 2-diazo-5,5-dimethylcyclohexane-1,3-dione **1a** with benzoylacetonitrile **2a** by employing $[Cp^*RhCl_2]_2$ as the catalyst and CsOAc as the additive in toluene at 90 °C for 15 h and achieved a polycyclic product **3a** in 56% yield (Table1, entry 1). Replacing $[Cp^*RhCl_2]_2$ to other rhodium catalysts, no desired product was detected (Table 1, entries 2-4). Increasing the catalyst loading showed that 2 mol% of catalyst could give the highest yield (73%, Table 1, entries 5,6). Subsequently, different solvents including DMF, DCE, THF, MeCN, EtOH, MeOH, and 1,4-dioxane were investigated (Table 1, entries 7-13), and the results revealed that the use of toluene and DCE as the solvent in the reaction gave the desired product in 73% and 65% yields, respectively. Next, the replacement of CsOAc with another base, including Ag_2CO_3, Na_2CO_3, $Cu(OAc)_2$, CsOPiv, DBU, and Et_3N, did not enhance the product formation (Table 1, entries 14-19). Moreover, both decreasing and increasing the additive loading could not improve the yield (Table 1, entries 21, 22). Further studies showed that decreasing either the reaction temperature or the reaction time was detrimental to the yield (Table 1, entries 23-26). After extensive experimentation, we selected the conditions used in entry 5 as the optimal ones for the further investigations.

Table 1. Optimization of the reaction conditions[a]

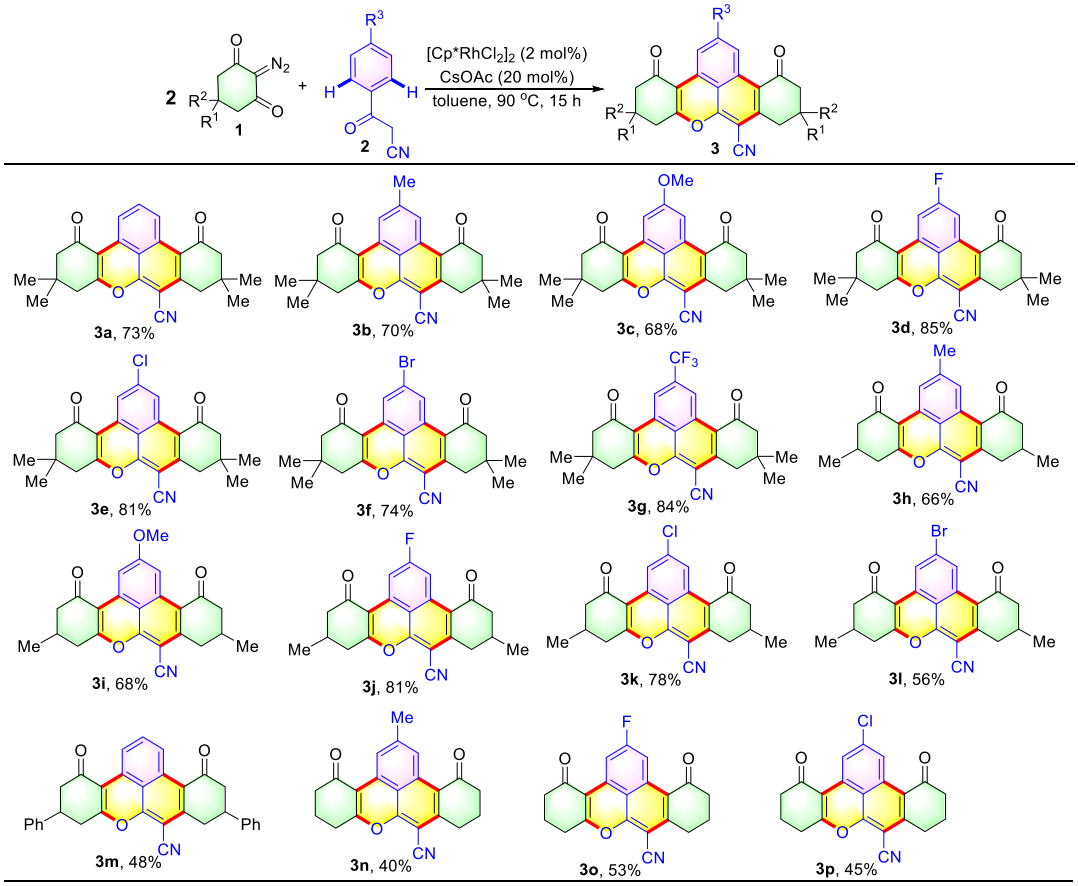


entry	catalyst	additve	solvent	yield(%[b])
1[c]	$[Cp^*RhCl_2]_2$	CsOAc	toluene	56
2	$Rh_2(OAc)_4$	CsOAc	toluene	nd
3	$Rh_2(oct)_4$	CsOAc	toluene	nd
4	$RhClPPh_3$	CsOAc	toluene	nd
5	$[Cp^*RhCl_2]_2$	CsOAc	toluene	73
6[d]	$[Cp^*RhCl_2]_2$	CsOAc	toluene	73
7	$[Cp^*RhCl_2]_2$	CsOAc	DMF	43
8	$[Cp^*RhCl_2]_2$	CsOAc	DCE	65
9	$[Cp^*RhCl_2]_2$	CsOAc	THF	21
10	$[Cp^*RhCl_2]_2$	CsOAc	MeCN	56
11	$[Cp^*RhCl_2]_2$	CsOAc	EtOH	30
12	$[Cp^*RhCl_2]_2$	CsOAc	MeOH	23

13	$[Cp^*RhCl_2]_2$	CsOAc	1,4-dioxane	48
14	$[Cp^*RhCl_2]_2$	Ag_2CO_3	toluene	40
15	$[Cp^*RhCl_2]_2$	Na_2CO_3	toluene	36
16	$[Cp^*RhCl_2]_2$	$Cu(OAc)_2$	toluene	22
17	$[Cp^*RhCl_2]_2$	CsOPiv	toluene	63
18	$[Cp^*RhCl_2]_2$	DBU	toluene	16
19	$[Cp^*RhCl_2]_2$	Et_3N	toluene	20
20	$[Cp^*RhCl_2]_2$	-	toluene	32
21[e]	$[Cp^*RhCl_2]_2$	CsOAc	toluene	62
22[f]	$[Cp^*RhCl_2]_2$	CsOAc	toluene	73
23[g]	$[Cp^*RhCl_2]_2$	CsOAc	toluene	42
24[h]	$[Cp^*RhCl_2]_2$	CsOAc	toluene	73
25[i]	$[Cp^*RhCl_2]_2$	CsOAc	toluene	60
26[j]	$[Cp^*RhCl_2]_2$	CsOAc	toluene	73

[a]Reaction conditions: 2-diazo-5,5-dimethylcyclohexane-1,3-dione **1a** (0.6 mmol), benzoylacetonitrile **2a** (0.3 mmol), catalyst (2 mol%), and additive (20 mol%) in solvent (2 mL), at 90 °C for 15 h. [b] Isolated yields. [c] The catalyst loading was 1.5 mol%. [d] The catalyst loading was 2.5 mol%. [e] The additive loading was 15 mol%. [f] The additive loading was 25 mol%. [g] At 70 °C. [h] At 100 °C. [i]For 14 h. [j] For 16 h. nd = not detected.

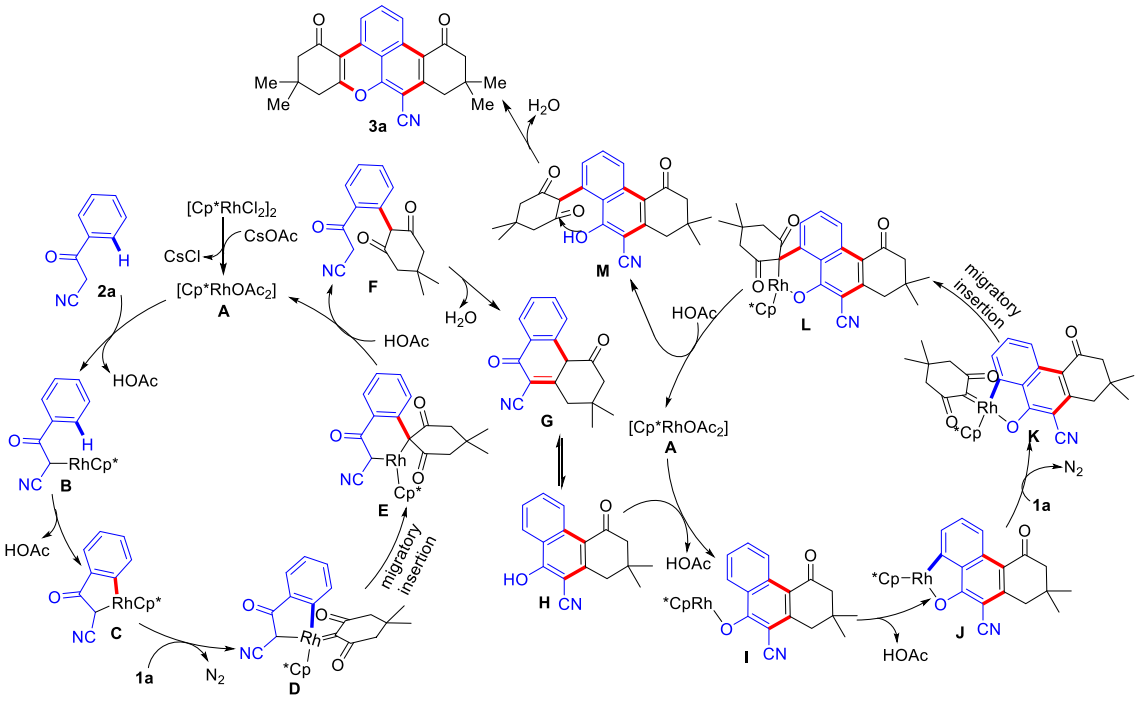
The substrate scope was investigated under the optimized reaction conditions obtained above. As shown in Scheme 2, the scope of benzoylacetonitriles was first investigated in this cascade C-H functionalization/benzannulation process by performing the reactions with 2-diazo-5,5-dimethylcyclohexane-1,3-dione **1a**. Generally, benzoylacetonitriles bearing either various electron-donating groups (-Me, -OMe) or electron-withdrawing groups (-F, -Cl, -Br, $-CF_3$) reacted smoothly with **1a** and provided the corresponding products **3b**−**3g** in good yields (68-85%). Moreover, we found that the benzoylacetonitriles with the *para*-position substituted by various electron-donating groups (e.g. −Me, −OMe) proceeded smoothly, and the desired products **3b** and **3c** were obtained in 70% and 68% yields, respectively. Meanwhile, introduction of the electron-withdrawing groups (e.g., −F, −Cl, −Br, $-CF_3$) was also subjected to the standard conditions, and the reaction efficiencies were maintained at a higher level (**3d-3g**, 74-85% yields). Thereafter, other cyclic 2-diazo-1,3-diketones were also investigated under the standard conditions. The substrate bearing with both alkyl (Me) and aryl (phenyl) of R^1 groups resulted in satisfactory yields.



Scheme 2. Substrate scope[a,b]; [a] Reaction conditions: cyclic 2-diazo-1,3-diketones **1** (0.6 mmol), benzoylacetonitriles **2** (0.3 mmol), $[Cp^*RhCl_2]_2$ (2 mol%), and CsOAc (20 mol%) in toluene (2 mL) at 90 °C for 15 h. [b]Isolated yields.

Based on the above mentioned experimental results and previous studies,[26-28] a plausible mechanism for this sequential cascade C-H activation/annulation reaction for the formation of **3a** was proposed in Scheme 3. Initially, an active catalyst $Cp^*Rh(OAc)_2$ was generated through anion exchange, and then activated the C(sp^3)-H bond yielding the intermediate **B**, owing to the strong acidity of the C(sp^3)-H bond of substrate **2a**. Subsequently, a five-membered rhodacycle **C** was formed by the C(sp^2)-H bond activation process. Next, intermediate **C** was trapped by the diazo compound **2a** to form the rhodium-carbene intermediate **D** through dediazotization. Migratory insertion of the carbene unit into the rhodium-carbon bond in intermediate **D** generated the six-membered rhodacycle **E**, followed by protonation to afford the intermediate **F** with regeneration of the Rh(III) complex to start a new catalytic cycle. Then, intermediate **F** underwent an intramolecular aldol condensation to afford intermediate **G**, followed by a double bond shift and aromatization to form intermediate **H**. In the second stage of this cascade process, intermediate **I** then entered into another new cycle. The catalytic cycle may also underwent a cascade process of O-H functionalization, C(sp^2)–H activation, formation of Rh(III)–carbene species, migratory insertion, protonolysis to release rhodium complex $Cp^*Rh(OAc)_2$ for the next catalytic cycle, and produced

intermediate **L**. Finally, the desired product **3a** was obtained through an intramolecular nucleophilic addition of the hydroxyl group to carbonyl in intermediate **L**, followed by elimination of water.



Scheme 3. Proposed mechanism for the formation of compound **3a**

In summary, we have developed a simple and efficient synthesis of polycyclic benzo[*de*]chromenes *via* Rh(III)-catalyzed cascade sequential C-H activation/benzannulation of cyclic 2-diazo-1,3-diketones with benzoylacetonitriles. In this cascade process, both four new bonds (three C-C bonds and one C-O bond) and two new rings (a benzene ring and a pyran scaffold) were efficiently constructed in one-pot *via* double C-H bond carenoid insertion and subsequent annulation of simple substrates. Furthermore, this transformation tolerated common functional groups well with a broad substrate scope, and is highly atom-, step-economy and environmentally benign with only N_2 and H_2O as byproducts.

EXPERIMENTAL

Unless otherwise specified, all reagents were purchased from commercial sources and used as received without purification. The ^{1}H and ^{13}C NMR data were recorded on 300 MHz and 125 MHz NMR spectrometers, unless otherwise specified. HRMS analysis with a quadrupole time-of-flight mass spectrometer yielded ion mass/charge (*m/z*) ratios in atomic mass units. IR spectra were measured as dry films (KBr), and the peaks are reported in terms of wave number (cm^{-1}). The melting points were measured using SGWX-4 melting point apparatus.

General procedure for the synthesis of benzoylacetonitriles 3. A mixture of cyclic 2-diazo-1,3-diketones **1** (0.5 mmol), benzoylacetonitriles **2** (0.3 mmol), $[Cp^*RhCl_2]_2$ (0.006 mmol), and CsOAc (0.06 mmol) in

toluene (2 mL) was heated to 90 °C in an oil bath for 15 h. After the reaction completed (as determined using TLC), the reaction mixture was cooled to room temperature, extracted with CH_2Cl_2 (3 × 10 mL), and washed with brine. The organic layers were combined, dried over Na_2SO_4, filtered, and then evaporated under vacuum. The residue was purified using flash column chromatography with a silica gel (200-300 mesh), using EtOAc and petroleum ether (1:4, v/v) as the elution solvent to give the desired product **3**.

6,6,11,11-Tetramethyl-4,13-dioxo-4,5,6,7,10,11,12,13-octahydrodibenzo[*b,mn*]xanthene-9-carbonitrile (**3a**)**.** This compound was purified by column chromatography (EtOAc/petroleum ether = 1: 4, R_f = 0.5) to afford a yellow solid; mp 242-243 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.30 (d, J = 7.8 Hz, 1H), 8.81 (d, J = 6.0 Hz, 1H), 7.79 (t, J = 7.2 Hz, 1H), 3.11 (s, 2H), 2.82 (s, 2H), 2.61 (s, 2H), 2.53 (s, 2H), 1.20 (s, 6H), 1.15 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.3, 196.8, 166.8, 158.2, 147.0, 134.8, 134.2, 125.3, 124.8, 121.9, 121.0, 120.6, 114.7, 112.6, 93.7, 54.3, 53.2, 43.8, 42.4, 33.5, 32.4, 28.6, 28.4; IR (KBr) ν 2947, 2216, 1666, 1631, 1483, 1355, 1255, 1022, 819, 526 cm^{-1}; HRMS (APCI-TOF), *m/z* calcd for $[C_{25}H_{23}NO_3+H]^+$ 386.1751, found 386.1750.

2,6,6,11,11-Pentamethyl-4,13-dioxo-4,5,6,7,10,11,12,13-octahydrodibenzo[*b,mn*]xanthene-9-carbonitrile (**3b**)**.** This compound was purified by column chromatography (EtOAc/petroleum ether = 1: 4, R_f = 0.5) to afford a yellow solid; mp 260-261 °C;^{1}H NMR (300 MHz, $CDCl_3$) δ 9.13 (s, 1H), 8.67 (s, 1H), 3.09 (s, 2H), 2.81 (s, 2H), 2.60 (s, 2H), 2.56 (s, 3H), 2.53 (s, 2H), 1.20 (s, 6H), 1.14 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.3, 196.9, 167.0, 158.0, 147.3, 146.2, 134.5, 125.1, 124.4, 122.2, 121.3, 119.2, 114.8, 112.4, 92.7, 54.4, 53.2, 43.8, 42.4, 33.5, 32.3, 28.5, 28.4, 23.8.ppm; IR (KBr) ν 3086, 2960, 2216, 1670, 1633, 1589, 1359, 1269, 1062, 893cm^{-1}; HRMS (APCI-TOF), *m/z* calcd for $[C_{26}H_{25}NO_3+H]^+$ 400.1907, found 400.1908.

2-Methoxy-6,6,11,11-tetramethyl-4,13-dioxo-4,5,6,7,10,11,12,13-octahydrodibenzo[*b,mn*]xanthene-9-carbonitrile (**3c**)**.** This compound was purified by column chromatography (EtOAc/petroleum ether = 1: 4, R_f = 0.5) to afford a yellow solid; mp 233-234 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.48 (s, 1H), 3.97 (s, 3H), 3.09 (s, 2H), 2.84 (s, 2H), 2.58 (s, 2H), 2.53 (s, 2H), 1.20 (s, 6H), 1.14 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.5, 196.8, 167.5, 165.4, 157.5, 148.5, 136.7, 126.9, 120.3, 116.3, 112.1, 111.6, 91.4, 56.1, 54.4, 53.1, 43.9, 42.4, 33.4, 32.3, 28.6, 28.4; IR (KBr) ν 3458, 2919, 2347, 1676, 1558, 1375, 1232, 1020, 869, 572 cm^{-1}; HRMS (APCI-TOF), *m/z* calcd for $[C_{26}H_{26}NO_4+H]^+$ 416.1856, found 416.1853.

2-Fluoro-6,6,11,11-tetramethyl-4,13-dioxo-4,5,6,7,10,11,12,13-octahydrodibenzo[*b,mn*]xanthene-9-carbonitrile (**3d**)**.** This compound was purified by column chromatography (EtOAc/petroleum ether = 1: 4, R_f = 0.5) to afford a yellow solid; mp 246-247 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.09 (d, J = 12.5 Hz, 1H), 8.65 (d, J = 9.9 Hz, 1H), 3.12 (s, 2H), 2.85 (s, 2H), 2.58 (d, J = 18.6 Hz, 4H), 1.21 (s, 6H), 1.15 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.9, 196.4, 167.8, 167.2 (d, $J_{C\text{-}F}$ = 250 Hz), 157.7, 148.4, 136.3 (d, $J_{C\text{-}F}$ = 17.5 Hz), 128.3, 121.3 (d, $J_{C\text{-}F}$ = 6.25 Hz), 118.3, 114.4 (d, $J_{C\text{-}F}$ = 3.75 Hz), 112.0, 110.5 (d, $J_{C\text{-}F}$ =

30 Hz), 110.1 (d, J_{C-F} = 27.5 Hz), 93.3, 54.1, 53.0, 43.9, 42.4, 33.4, 32.4, 28.5, 28.4; IR (KBr) *v* 3458, 2922, 2366, 1676, 1637, 1438, 1369, 1238, 1022, 869 cm^{-1}; HRMS (APCI-TOF), *m/z* calcd for $[C_{25}H_{22}FNO_3+H]^+$ 404.1656, found 404.1655.

2-Chloro-6,6,11,11-tetramethyl-4,13-dioxo-4,5,6,7,10,11,12,13-octahydrodibenzo[*b,mn*]xanthene-9-carbonitrile (**3e**)**.** This compound was purified by column chromatography (EtOAc/petroleum ether = 1: 4, R_f = 0.5) to afford a yellow solid; mp 268-269 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.38 (s, 1H), 8.83 (s, 1H), 3.11 (s, 2H), 2.83 (s, 2H), 2.61 (s, 2H), 2.54 (s, 2H), 1.21 (s, 6H), 1.15 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.9, 196.4, 167.7, 157.7, 148.2, 142.4, 134.8, 126.8, 124.1, 121.3, 121.1, 119.3, 114.3, 111.7, 94.1, 54.2, 53.0, 43.7, 42.4, 33.5, 32.4, 28.5, 28.4.ppm; IR (KBr) *v* 3425, 2960, 2216, 1683, 1627, 1556, 1421, 1355, 1257, 875 cm^{-1}; HRMS (APCI-TOF), *m/z* calcd for $[C_{25}H_{22}ClNO_3+H]^+$ 420.1361, found 420.1365.

2-Bromo-6,6,11,11-tetramethyl-4,13-dioxo-4,5,6,7,10,11,12,13-octahydrodibenzo[*b,mn*]xanthene-9-carbonitrile (**3f**)**.** This compound was purified by column chromatography (EtOAc/petroleum ether = 1: 4, R_f = 0.5) to afford a yellow solid; mp 230-231 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.54 (s, 1H), 8.97 (s, 1H), 3.11 (s, 2H), 2.83 (s, 2H), 2.60 (s, 2H), 2.54 (s, 2H), 1.20 (s, 6H), 1.14 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.5, 196.0, 167.4, 157.4, 147.7, 134.4, 131.1, 126.9, 126.2, 123.5, 120.5, 119.1, 114.0, 111.2, 93.8, 53.8, 52.6, 43.5, 42.1, 33.1, 32.0, 28.2, 28.0; IR (KBr) *v* 3205, 2958, 2216, 1675, 1629, 1576, 1401, 1335, 1237, 885 cm^{-1}; HRMS (APCI-TOF), *m/z* calcd for $[C_{25}H_{22}BrNO_3+H]^+$ 464.0856, found 464.0852.

6,6,11,11-Tetramethyl-4,13-dioxo-2-(trifluoromethyl)-4,5,6,7,10,11,12,13-octahydrodibenzo[*b,mn*]xanthene-9-carbonitrile (**3g**)**.** This compound was purified by column chromatography (EtOAc/petroleum ether = 1: 4, R_f = 0.5) to afford a yellow solid; mp 213-214 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.68 (s, 1H), 9.09 (s, 1H), 3.16 (s, 2H), 2.86 (s, 2H), 2.64 (s, 2H), 2.56 (s, 2H), 1.22 (s, 6H), 1.17 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.1, 195.8, 167.2, 157.2, 147.5, 133.2, 126.3, 122.1, 121.9 (d, J_{C-F} = 3.8 Hz), 121.8 (d, J_{C-F} = 10 Hz), 116.2 (d, J_{C-F} = 3.8 Hz), 116.3 (d, J_{C-F} = 8.8 Hz), 113.6, 111.5, 95.5, 53.6, 52.8, 43.4, 42.1, 33.6, 32.0, 28.4; IR (KBr) *v* 3425, 2954, 2229, 1674, 1641, 1589, 1290, 1238, 1172, 1128, 906, 673 cm^{-1}; HRMS (APCI-TOF), *m/z* calcd for $[C_{26}H_{22}FNO_3+H]^+$ 454.1625, found 454.1626.

2,6,11-Trimethyl-4,13-dioxo-4,5,6,7,10,11,12,13-octahydrodibenzo[*b,mn*]xanthene-9-carbonitrile (**3h**)**.** This compound was purified by column chromatography (EtOAc/petroleum ether = 1: 4, R_f = 0.5) to afford a yellow solid; mp 282-283 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.10 (s, 1H), 8.66 (s, 1H), 3.34-3.32 (m, 1H), 2.95-2.91 (m, 1H), 2.82-2.67 (m, 4H), 2.56 (s, 3H), 2.46-2.35 (m, 4H), 1.21 (d, *J* = 5.3 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.8, 196.5, 167.5, 157.2, 148.1, 145.8, 134.2, 124.8, 124.1, 121.9, 121.4, 118.9, 114.4, 112.6, 91.9, 48.5, 47.1, 37.8, 36.4, 29.4, 27.6, 23.4, 21.2, 20.8; IR (KBr) *v* 3425, 2914, 2347,

2216, 1674, 1637, 1533, 1379, 1022, 873 cm^{-1}; HRMS (APCI-TOF), *m/z* calcd for $[C_{24}H_{21}NO_3+H]^+$ 372.1594, found 372.1596.

2-Methoxy-6,11-dimethyl-4,13-dioxo-4,5,6,7,10,11,12,13-octahydrodibenzo[*b,mn*]xanthene-9-carbonitrile (**3i**)**.** This compound was purified by column chromatography (EtOAc/petroleum ether = 1: 4, R_f = 0.5) to afford a yellow solid; mp 267-268 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.47 (s, 1H), 3.96 (s, 3H), 3.30-3.35 (m, 1H), 2.94-3.00 (m, 1H), 2.65-2.83 (m, 4H), 2.45-2.35 (m, 4H), 1.22 (d, *J* = 5.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.3, 196.7, 168.3, 165.3, 157.1, 149.6, 136.8, 127.0, 121.0, 116.3, 114.9, 112.6, 111.7, 105.4, 91.0, 56.0, 49.0, 47.4, 38.3, 36.7, 29.7, 29.7, 28.0, 28.0, 21.4, 21.2; IR (KBr) *v* 3425, 2922, 1668, 1637, 1571, 1433, 1375, 1269, 1047, 873 cm^{-1}; HRMS (APCI-TOF), *m/z* calcd for $[C_{25}H_{21}NO_4+H]^+$ 388.1543, found 388.1543.

2-Fluoro-6,11-dimethyl-4,13-dioxo-4,5,6,7,10,11,12,13-octahydrodibenzo[*b,mn*]xanthene-9-carbonitrile (**3j**)**.** This compound was purified by column chromatography (EtOAc/petroleum ether = 1: 4, R_f = 0.5) to afford a yellow solid; mp 254-255 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.06 (d, *J* = 12.3 Hz, 1H), 8.65 (d, *J* = 11.7 Hz, 1H), 3.33-3.39 (m, 1H), 2.99-3.04 (m, 1H), 2.64-2.83 (m, 4H), 2.55-2.17 (m, 4H), 1.22 (d, *J* = 3.6 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.6, 196.1, 168.4, 167.8 (d, *J* = 255 Hz), 156.9, 149.2, 135.9 (d, *J* = 13.8 Hz), 117.82, 113.95, 110.2 (d, *J* = 28.8 Hz),109.8 (d, *J* = 27.5 Hz), 48.3, 46.9, 37.9, 36.3, 29.3, 27.58, 21.1, 20. 8; IR (KBr) *v* 3450, 2922, 2229, 1672, 1637, 1577, 1367, 1301, 1043, 883 cm^{-1}; HRMS (APCI-TOF), *m/z* calcd for $[C_{23}H_{18}FNO_3+H]^+$ 376.1343, found 376.1350.

2-Chloro-6,11-dimethyl-4,13-dioxo-4,5,6,7,10,11,12,13-octahydrodibenzo[*b,mn*]xanthene-9-carbonitrile (**3k**)**.** This compound was purified by column chromatography (EtOAc/petroleum ether = 1: 4, R_f = 0.5) to afford a yellow solid; mp 261-262 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.33 (s, 1H), 8.81 (s, 1H), 3.33-3.38 (m, 1H), 2.70-2.83 (m, 1H), 2.63-2.77 (m, 4H), 2.28-2.77 (m, 4H), 1.22 (d, *J* = 5.0 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.8, 196.4, 168.7, 157.2, 149.3, 142.3, 134.8, 126.7, 124.1, 121.5, 121.3, 119.2, 114.2, 112.2, 93.7, 48.7, 47.3, 38.3, 36.6, 29.6, 28.1, 21.4, 21.2; IR (KBr) *v* 3431, 2927, 2366, 2216, 1676, 1631, 1581, 1566, 1026, 883 cm^{-1}; HRMS (APCI-TOF), *m/z* calcd for $[C_{23}H_{18}ClNO_3+H]^+$ 392.1048, found 392.1047.

2-Bromo-6,11-dimethyl-4,13-dioxo-4,5,6,7,10,11,12,13-octahydrodibenzo[*b,mn*]xanthene-9-carbonitrile (**3l**)**.** This compound was purified by column chromatography (EtOAc/petroleum ether = 1: 4, R_f = 0.5) to afford a yellow solid; mp 287-288 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.48 (s, 1H), 8.94 (s, 1H), 3.33-3.39 (m, 1H), 2.96-3.02 (m, 1H), 2.735-2.87 (m, 4H), 2.37-2.46 (m, 4H), 1.22 (d, *J* = 5.5 Hz, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.4, 196.0, 168.5, 168.3, 156.8, 148.9, 134.4, 131.0, 126.8, 126.3, 123.5, 121.0, 119.0, 113.8, 111.7, 93.4, 48.3, 46.9, 37.8, 36.3, 29.3, 27.5, 21.0, 20.8; IR (KBr) *v* 3444, 2954, 2229, 1676, 1639, 1581, 1381, 1269, 1043, 879 cm^{-1}; HRMS (APCI-TOF), *m/z* calcd for $[C_{23}H_{18}BrNO_3+H]^+$ 437.0621, found 437.0624.

4,13-Dioxo-6,11-diphenyl-4,5,6,7,10,11,12,13-octahydrodibenzo[*b,mn*]xanthene-9-carbonitrile (**3m**)**.** This compound was purified by column chromatography (EtOAc/petroleum ether = 1: 4, R_f = 0.5) to afford a yellow solid; mp 302-304 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.34 (d, J = 8.6 Hz, 1H), 8.88 (d, J = 6.7 Hz, 1H), 7.87-7.80 (t, J = 8.1 Hz, 1H), 7.50-7.27 (m, 10H), 3.62-3.56 (m, 4H), 3.56-3.30 (m, 1H), 3.26-3.21 (m, 1H), 3.07-2.91 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.1, 195.7, 167.2, 157.4, 147.6, 134.6, 134.0, 129.1, 129.0, 127.6, 127.4, 126.7, 126.6, 124.9, 124.7, 122.1, 120.6, 114.0, 113.0, 93.0, 47.1, 45.8, 39.8, 37.8, 37.3, 35.9; IR (KBr) ν 3445, 2945, 2301, 1672, 1485, 1344, 1249, 1132, 1024, 825, 696 cm^{-1}; HRMS (APCI-TOF), *m/z* calcd for $[C_{34}H_{25}NO_3+H]^+$ 480.1751, found 480.1753.

2-Methyl-4,13-dioxo-4,5,6,7,10,11,12,13-octahydrodibenzo[b,mn]xanthene-9-carbonitrile (**3n**)**.** This compound was purified by column chromatography (EtOAc/petroleum ether = 1: 4, R_f = 0.5) to afford a yellow solid; mp 251-252 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.05 (s, 1H), 8.63 (s, 1H), 3.19 (t, J = 5.7 Hz, 2H), 2.93 (t, J = 6.0 Hz, 2H), 2.74 (t, J = 6.3 Hz, 2H), 2.66 (t, J = 6.6 Hz, 2H), 2.54 (s, 3H), 2.17-2.22 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.6, 196.5, 168.1, 157.0, 148.7, 145.8, 134.3, 126.5, 124.8, 124.2, 122.1, 121.9, 118.8, 114.3, 113.1, 91.9, 40.5, 38.9, 29.8, 28.5, 23.3, 22.0, 19.9; IR (KBr) ν 3429, 2956, 2235, 1660, 1641, 1448, 1359, 1309, 1182, 819 cm^{-1}; HRMS (APCI-TOF), *m/z* calcd for $[C_{22}H_{17}NO_3+H]^+$ 344.1281, found 344.1272.

2-Fluoro-4,13-dioxo-4,5,6,7,10,11,12,13-octahydrodibenzo[*b,mn*]xanthene-9-carbonitrile (**3o**)**.** This compound was purified by column chromatography (EtOAc/petroleum ether = 1: 4, R_f = 0.5) to afford a yellow solid; mp 305-306 °C;^{1}H NMR (300 MHz, $CDCl_3$) δ 9.02 (d, J = 14.9 Hz, 1H), 8.63 (d, J = 10.4 Hz, 1H), 3.20-3.25 (m, 2H), 2.94-3.00 (m, 2H), 2.66-2.78 (m, 4H), 2.19-2.2 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.3, 196.1, 168.8, 166.7 (d, J_{C-F} = 255 Hz), 156.7, 149.8, 136.0 (d, J_{C-F} = 12.5 Hz), 128.0 (d, J_{C-F} = 12.5 Hz), 121.8, 117.8, 113.9, 112.5, 110.4 (d, J_{C-F} = 30 Hz), 109.9 (d, J_{C-F} = 27.5 Hz), 92.6, 40.4, 38.7, 29.9, 28.5, 21.9, 19.8; IR (KBr) ν 3458, 3105, 2222, 1666, 1627, 1581, 1438, 1172, 1001, 866, 685 cm^{-1}; HRMS (APCI-TOF), *m/z* calcd for $[C_{21}H_{14}FNO_3+H]^+$ 348.1030, found 348.1029.

2-Chloro-4,13-dioxo-4,5,6,7,10,11,12,13-octahydrodibenzo[*b,mn*]xanthene-9-carbonitrile (**3p**)**.** This compound was purified by column chromatography (EtOAc/petroleum ether = 1: 4, R_f = 0.5) to afford a yellow solid; mp 289-290 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.26 (s, 1H), 8.76 (s, 1H), 3.22 (t, J = 6.0 Hz, 2H), 2.96 (t, J = 6.3 Hz, 2H), 2.75 (t, J = 6.6 Hz, 2H), 2.68 (t, J = 6.6 Hz, 2H), 2.25-2.19 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 197.3, 196.1, 169.0, 156.5, 149.6, 141.7, 134.3, 126.4, 123.6, 121.4, 120.8, 118.6, 113.7, 112.0, 93.3, 40.2, 38.7, 29.8, 28.4, 21.8, 19.7; IR (KBr) ν 3373, 2914, 2366, 1670, 1631, 1577, 1421, 1379, 1247, 1029, 879, 682 cm^{-1}; HRMS (APCI-TOF), *m/z* calcd for $[C_{21}H_{14}ClNO_3+H]^+$ 364.0735, found 364.0737.

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