inorganics

MDPI

Article

Synthesis of Anthraquinones by Iridium-Catalyzed [2 + 2 + 2] Cycloaddition of a 1,2-Bis(propiolyl)benzene Derivative with Alkynes

Takahiro Sawano, Yuko Toyoshima and Ryo Takeuchi *

Department of Chemistry and Biological Science, Aoyama Gakuin University, 5-10-1 Fuchinobe, Chuo-ku, Sagamihara, Kanagawa 252-5258, Japan; tsawano@chem.aoyama.ac.jp (T.S.)

* Correspondence: takeuchi@chem.aoyama.ac.jp; Tel.: +81-42-759-6231

Received: 4 October 2019; Accepted: 11 November 2019; Published: 18 November 2019

Abstract: [2 + 2 + 2] cycloaddition of a 1,2-bis(propiolyl)benzene derivative with terminal and internal alkynes takes place in the presence of $[Ir(cod)Cl]_2$ (cod = 1,5-cyclooctadiene) combined with bis(diphenylphosphino)ethane (DPPE) to give anthraquinones in 42% to 93% yields with a simple experimental procedure. A fluorenone derivative can also be synthesized by iridium-catalyzed [2 + 2 + 2] cycloaddition of a benzene-linked ketodiyne with an internal alkyne to give a 94% yield.

Keywords: catalysis; cycloaddition; anthraquinones; fluorenones; diynes; iridium

1. Introduction

Anthraquinones and their derivatives are important structures found in natural products and bioactive compounds and show a broad range of bioactivities including anti-tumor [1,2], cytotoxic [3], anti-cancer [4–6], anti-bacterial [7,8], laxative [9], anti-arthritic [10], anti-fungal [11], anti-platelet [12,13], and neuroprotective effects [14]. Moreover, anthraquinones have been widely used as catalysts for producing hydrogen peroxide [15], dyes for fibers [16,17] and cells [18], a digestion catalyst for wood [19], and chemical sensors [20]. Thus, the development of synthetic methods for the formation of multi-substituted anthraquinones is an important research topic, and several synthtic methods including the oxidation of anthracene [21,22], the Friedel-Crafts reaction of phthalic anhydride [23], and the Diels-Alder reaction of naphthoquinones followed by aromatization [24] have been developed.

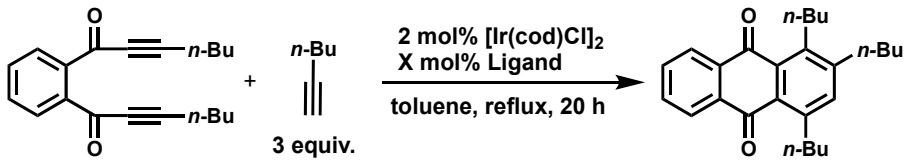
Transition metal-catalyzed [2 + 2 + 2] cycloaddition represents a powerful and atom-economical method to access a variety of complex aromatic carbocycles and heterocycles in short steps [25–30]. From 1,2-bis(propiolyl)benzene derivatives and alkynes, [2 + 2 + 2] cyclization has realized the synthesis of anthraquinones. After the success of stoichiometric reactions with a large amount of highly toxic $Ni(CO)_4$ [31] and isolated naphthoquinone-fused rhodacyclopentadiene [32], catalytic reactions were realized by the use of $Ni(PPh_3)_2(CO)_2$ [33], $CpCo(CO)_2$ [34], and $RhCl(PPh_3)_3$ [35]. However, the reaction systems require high reaction temperatures, and the yields of the desired anthraquinones are moderate. Yamamoto and co-workers elegantly demonstrated that Cp*RuCl(cod) (cod = 1,5-cyclooctadiene) can catalyze the [2 + 2 + 2] cycloaddition of 1,2-bis(propiolyl)benzene derivatives with terminal alkynes and methyl-substituted internal alkynes under mild reaction conditions in high yields [36–40]. On the other hand, the rhodium-catalyzed reaction reported by Tanaka realized [2 + 2 + 2] cycloaddition with aryl-substituted diynes to give anthraquinones in high yields [41]. Despite this progress with methods for the synthesis of anthraquinones, few highly atom-economical methods are available, and, thus, novel methods to efficiently obtain anthraquinones are still desired. Our laboratory has developed an iridium-catalyzed [2 + 2 + 2] cycloaddition of diynes with alkynes, nitriles, and isocyanate to provide a variety of aromatic carbocycles and

heterocycles [42–50]. In the course of our ongoing investigation into iridium-catalyzed [2 + 2 + 2] cycloaddition, we found that an iridium/bisphosphine catalytic system catalyzed the [2 + 2 + 2] cycloaddition of 1,2-bis(propiolyl)benzene derivatives to provide anthraquinones bearing a variety of substituents in an atom-economical manner.

2. Results and Discussion

The reaction of 1,2-bis(propiolyl)benzene derivative **1** with three equivalents of 1-hexyne (**2a**) in the presence of 2 mol % of $[Ir(cod)Cl]_2$ in toluene under reflux for 20 h gave the anthraquinone **3a** in 20% yield (entry 1, Table 1). The phosphine ligand was found to improve the yield of anthraquinone **3a**. With a monophosphine ligand, PPh_3, the cyclized product was obtained in a moderate yield (Yield 64%, entry 2). Sufficient yield was achieved with the use of 1,2-bis(diphenylphosphino)ethane (DPPE) as a ligand to give 83% yield of anthraquinone **3a** (entry 3), while other representative bidentate phosphine ligands such as 1,3-bis(diphenylphosphino)propane (DPPP), 1,4-bis(diphenylphosphino)butane (DPPB), and 1,1′-bis(diphenylphosphino)ferrocene (DPPF) were ineffective at achieving a high yield (Yield 22% to 45%, entries 4 to 6).

Table 1. Ligand effects [a].



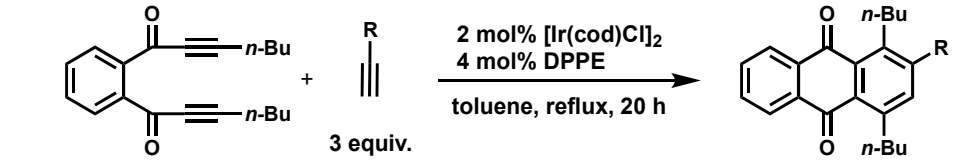
1 **2a** **3a**

Entry	Ligand (mol %)	Yield of 3a (%) [b]
1	none	20
2	PPh_3 (8)	64
3	DPPE (4)	83
4	DPPP (4)	40
5	DPPB (4)	45
6	DPPF (4)	22

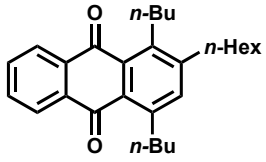
[a] Reaction conditions: **1** (0.5 mmol), **2a** (1.5 mmol), $[Ir(cod)Cl]_2$ (0.1 mmol), ligand, toluene (2.5 mL), under reflux for 20 h. [b] Isolated yield.

The Ir/dppe complex demonstrates high activity for [2 + 2 + 2] cycloaddition with various kinds of terminal alkynes to provide anthraquinone derivatives **3b–i** in good to high yields (Table 2). Cyclized products were obtained in high yields with 1-octyne and 1-decyne, respectively (Yields 92 and 93%, **3b** and **3c**). A chloride group can be tolerated under the reaction conditions (Yield 73%, **3d**). As well as aliphatic alkynes, the aromatic alkyne can also be used in the reaction (Yield 77%, **3e**). The present iridium-catalyzed [2 + 2 + 2] cyclization can introduce a sterically hindered functional group such as a trimethylsilyl group to give the corresponding cyclized product in a moderate yield (Yield 42%, **3f**). Terminal alkynes with primary, secondary, and tertiary alcohols are also good substrates for this [2 + 2 + 2] cyclization (Yields 75–85%, **3g**–**3i**).

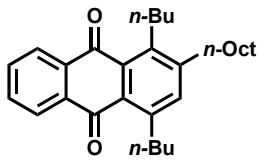
Table 2. Synthesis of anthraquinones with terminal alkynes [a].



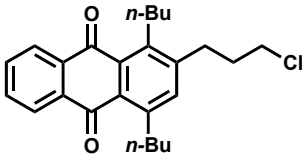
1 2b-i 3



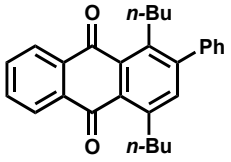
3b Yield 92%



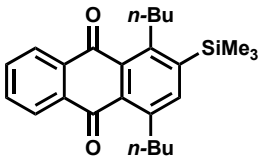
3c Yield 93%



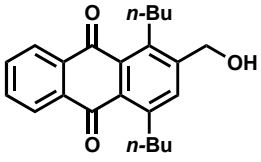
3d Yield 73%



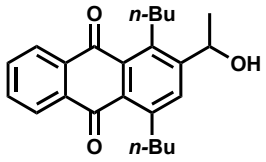
3e Yield 77%



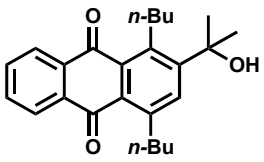
3f Yield 42%



3g Yield 76%



3h Yield 85%

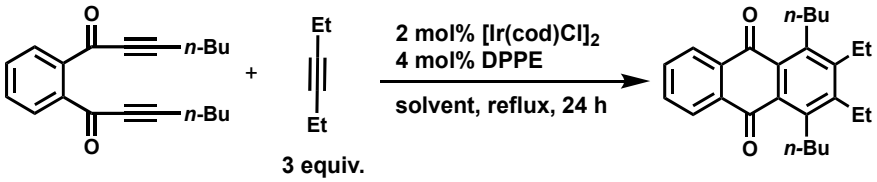


3i Yield 75%

[a] Reaction conditions: **1** (0.5 mmol), **2** (1.5 mmol), $[Ir(cod)Cl]_2$ (0.1 mmol), DPPE (0.2 mmol), toluene (2.5 mL) under reflux for 20 h. Yields are isolated yields.

Unfortunately, the optimized reaction conditions in Table 2 resulted in a diminished yield for the cyclization with internal alkyne **2j**, likely due to the formation of the dimer or oligomer of **1** as byproducts (Yield 36%, entry 1, Table 3). Our examination of the reaction conditions found that halogenated solvent was more suitable for the reaction than toluene. With dichloroethane (DCE) as a solvent, 62% of the cyclized product **3j** was obtained (entry 2). The yield was slightly improved in dichloromethane (DCM) under reflux to give **3j** in a 72% yield (entry 3).

Table 3. The [2 + 2 + 2] cycloaddition of 1 with internal alkyne **2j** [a].



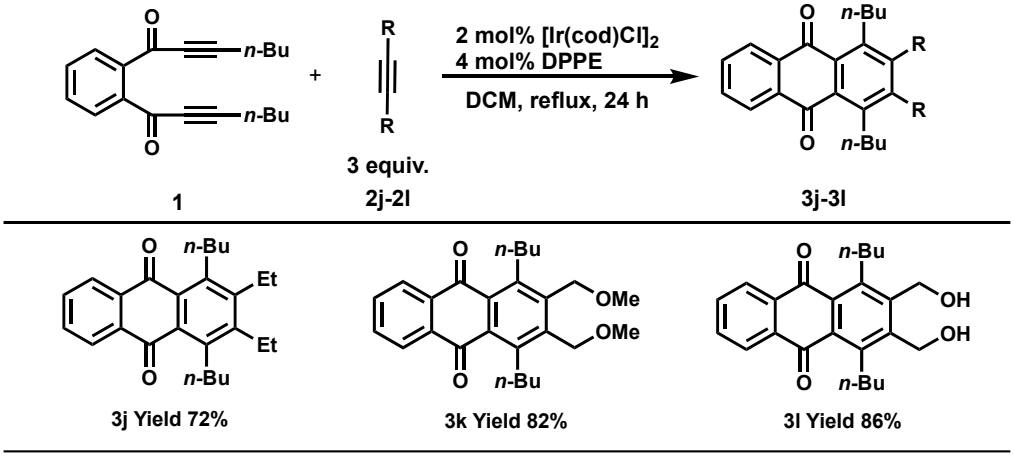
1 2j 3j

Entry	Reaction Conditions	Yield of 3j (%) [b]
1	Toluene, reflux	36
2	DCE, reflux	62
3	DCM, reflux	72

[a] Reaction conditions: **1** (0.5 mmol), **2j** (1.5 mmol), $[Ir(cod)Cl]_2$ (0.1 mmol), DPPE (0.2 mmol), solvent (2.5 mL) under reflux for 24 h. [b] Isolated yield.

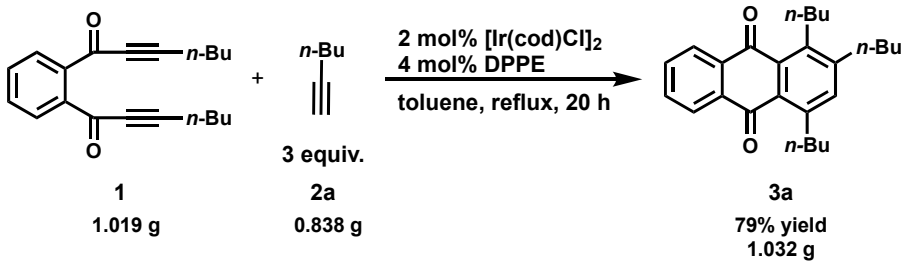
The results obtained for the iridium-catalyzed [2 + 2 + 2] cycloaddition of 1,2-bis(propiolyl)benzene derivative with internal alkynes are summarized in Table 4. In refluxing DCM, [2 + 2 + 2] cycloaddition with several internal alkynes proceeded to form tetra-substituted anthraquinones in good yields (Yield 72–86%, **3j**–**3l**).

Table 4. Synthesis of tetra-substituted anthraquinones [a].



[a] **1** (0.5 mmol), **2** (1.5 mmol), $[Ir(cod)Cl]_2$ (0.1 mmol), DPPE (0.2 mmol), DCM (2.5 mL) under reflux for 24 h. Yields are isolated yields.

As shown in Scheme 1, a gram-scale reaction of **1** with **2a** also proceeded smoothly. The yield was comparable as in the 0.5 mmol scale.

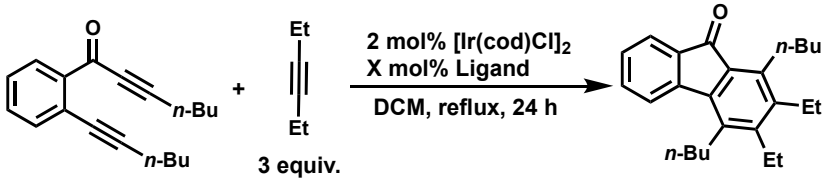


Scheme 1. Gram-scale synthesis of anthraquinone 3a.

Based on our previous results [45,46,48,49], we envision that the catalytic reaction is initiated by the coordination of diyne **1** to the iridium(I) complex. Oxidative addition of diyne **1** to an iridium(I) complex forms iridacyclopentadiene [51–54]. Reaction of alkyne **2** with the iridacyclopentadiene gives anthraquinone **3** and regenerates the iridium(I) complex.

Fluorenones, which have structures similar to those of anthraquinones, are also a fascinating class of compounds due to their wide range of bioactivities [55–58], and photochemical [59–62] and electronic natures [63–65]. Fortunately, the [2 + 2 + 2] cyclization of benzene-linked ketodyne **4** with alkyne **2j** in the presence of $[Ir(cod)Cl]_2$ (2 mol %), DPPE (4 mol %) in DCM under reflux for 24 h afforded the fluorenone **5j** in a 43% yield (entry 1, Table 5). The proper choice of the ligand was found to be essential for the formation of fluorenone **5j** in a good yield. While PPh_3, 2,2′-bis(diphenylphosphino)biphenyl (BIPHEP), and DPPF were ineffective at catalyzing the formation of fluorenone **5j** (Yield 28% to 63%, entries 2 to 4), excellent yield was realized with the use of 1,2-bis[bis(pentafluorophenyl)phosphino]ethane (F-DPPE) (Yield 94%, entry 5).

Table 5. Synthesis of fluorenone from diyne **4** and alkyne **2j** [a].



4 **2j** **5j**

Entry	Ligand (mol %)	Yield of 5j (%) [b]
1	DPPE (4)	43
2	PPh_3 (8)	45
3	BIPHEP (4)	63
4	DPPF (4)	28
5	F-DPPE (4)	94

[a] Reaction conditions: **4** (0.5 mmol), **2j** (1.5 mmol), $[Ir(cod)Cl]_2$ (0.1 mmol), ligand, DCM (2.5 mL) under reflux for 24 h. [b] Isolated yield.

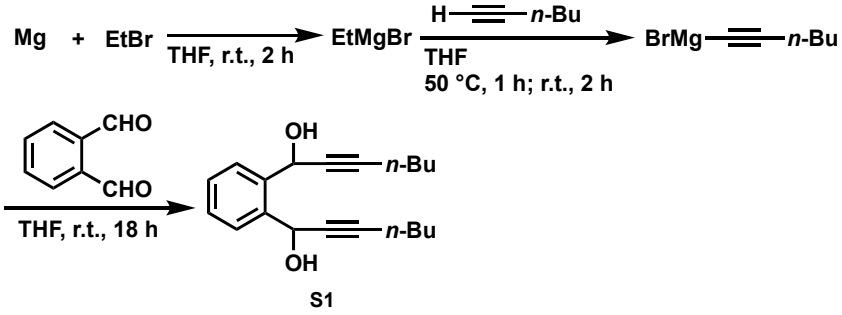
3. Materials and Methods

3.1. General Methods and Materials

All anaerobic and moisture-sensitive manipulations were carried out with standard Schlenk techniques under pre-dried argon. ^1H and ^{13}C NMR spectra were measured on JEOL ECX 500II spectrometers (500 MHz for ^1H, 125 MHz for ^{13}C) (JEOL Ltd., Tokyo, Japan). Chemical shifts are reported in δ (ppm) referenced to the tetramethylsilane (δ 0.00) for ^1H NMR and the residual peaks of $CDCl_3$ (δ 77.00) for ^{13}C NMR. The following abbreviations are used: s: singlet, d: doublet, t: triplet, q: quartet, sext: sextet, m: multiplet, br: broad. High-resolution mass spectra were obtained with a JEOL Mstation JMS-700 (JEOL Ltd., Tokyo, Japan). IR spectra were measured on a JASCO FTIR-4100A spectrometer (JASCO Corporation, Tokyo, Japan). The products were purified by column chromatography on 63–210 mesh silica gel (Silica Gel 60N) (Kanto Chemical Co., Inc., Tokyo, Japan). All solvents were dried and distilled before use by the usual procedures. $[Ir(cod)Cl]_2$ was prepared as described in the literature [66]. Alkynes **2a** (FUJIFILM Wako Pure Chemical Corporation, Osaka, Japan), **2b** (FUJIFILM Wako Pure Chemical Corporation, Osaka, Japan), **2c** (Tokyo Chemical Industry Co., Ltd., Tokyo, Japan), **2d** (Sigma-Aldrich Co. LLC., St. Louis, USA), **2e** (Tokyo Chemical Industry Co., Ltd., Tokyo, Japan), **2f** (Tokyo Chemical Industry Co., Ltd., Tokyo, Japan), **2g** (Tokyo Chemical Industry Co., Ltd., Tokyo, Japan), **2h** (Sigma-Aldrich Co. LLC., St. Louis, USA), **2i** (Tokyo Chemical Industry Co., Ltd., Tokyo, Japan), **2j** (FUJIFILM Wako Pure Chemical Corporation, Osaka, Japan), **2l** (Tokyo Chemical Industry Co., Ltd., Tokyo, Japan), 1,2-bis(diphenylphosphino)ethane (DPPE) (Kanto Chemical Co., Inc., Tokyo, Japan), and 1,2-bis[bis(pentafluorophenyl)phosphino]ethane (F-DPPE) (Tokyo Chemical Industry Co., Ltd., Tokyo, Japan) were purchased and used as received. 2-(1-Hexyn-1-yl)benzaldehyde and 1,4-dimethoxybut-2-yne (**2k**) were prepared by analogy to the reported procedure [67,68].

3.2. Preparation of Anthraquinone **1**

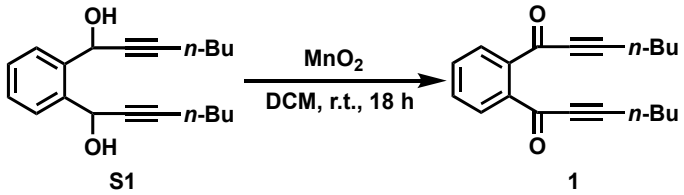
To a solution of magnesium (1.632 g, 67.15 mmol) in tetrahydrofuran (THF) (120 mL) was added bromoethane (8.17 g, 75.0 mmol) dropwise at room temperature, and the mixture was stirred for 2 h. At the same temperature, 1-hexyne (5.400 g, 65.74 mmol) was added. After being stirred at 50 °C for 1 h, the reaction mixture was stirred at room temperature for 2 h. In addition, *o*-phthalaldehyde (4.039 g, 30.11 mmol) was added to the reaction mixture. After the mixture was stirred for 18 h, sat. NH_4Cl was added, and the mixture was extracted with EtOAc. The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated on a rotary evaporator. The residue was subjected to column chromatography (silica gel, hexane/ethyl acetate = 8/2) to give compound **S1** (8.647 g, 28.98 mmol, 96% yield, Scheme 2).



Scheme 2. Synthesis of **S1**.

S1: Yellow oil, Yield 96%, 8.647 g, ^{1}H NMR (500 MHz, $CDCl_3$, a mixture of two diastereomers) δ 0.91 (t, *J* = 7.3 Hz, 6H), 0.92 (t, *J* = 7.5 Hz, 6H), 1.37–1.49 (m, 8H), 1.49–1.62 (m, 8H), 2.25–2.35 (m, 8H), 3.33 (d, *J* = 4.5 Hz, 2H), 3.70 (d, *J* = 5.5 Hz, 2H), 5.80–5.86 (m, 2H), 5.96–6.02 (m, 2H), 7.31–7.35 (m, 2H), 7.35–7.40 (m, 2H), 7.59–7.65 (m, 2H), 7.79–7.86 (m, 2H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.5, 18.5, 22.0, 30.52, 30.55, 62.0, 63.4, 78.7, 79.1, 88.1, 88.6, 127.8, 128.7, 128.9, 138.3, 138.7, IR (neat, cm^{-1}) 3338, 2958, 2931, 2870, 2280, 2232, 1604, 1456, 1433, 1328, 1280, 1253, 1203, 1133, 1050, 998, 807, 758, High Resolution Mass Spectrometer (HRMS) (EI^+) *m*/*z* $[M]^+$ calculated (calcd) for $C_{20}H_{26}O_2$ 298.1933, found 298.1933.

To a solution of MnO_2 (28.79 g, 331.1 mmol) in DCM (120 mL), S1 (4.945 g, 16.57 mmol) was added at room temperature. After being stirred for 18 h, the reaction mixture was filtered through a pad of Celite and subjected to column chromatography (silica gel, hexane/ethyl acetate = 8/2) to give 1,1′-(1,2-phenylene)bis(hept-2-yn-1-one) (**1**) (4.553 g, 15.48 mmol, 93% yield, Scheme 3).

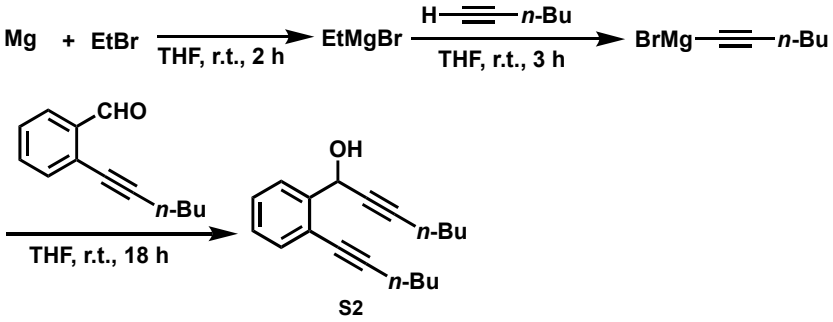


Scheme 3. Synthesis of **1**.

1: Yellow oil, Yield 93%, 4.553 g, ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.93 (t, *J* = 7.3 Hz, 6H), 1.45 (sext, *J* = 7.5 Hz, 4H), 1.55–1.64 (m, 4H), 2.43 (t, *J* = 7.3 Hz, 4H), 7.56–7.62 (m, 2H), 7.76–7.81 (m, 2H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.4, 18.9, 22.0, 29.6, 80.7, 97.9, 129.4, 131.6, 139.2, 179.4, IR (neat, cm^{-1}) 3275, 3065, 2959, 2872, 2206, 1647, 1572, 1465, 1324, 1264, 915, 778, 724, HRMS (EI^+) *m*/*z* $[M]^+$ calcd for $C_{20}H_{22}O_2$ 294.1620, found 294.1619.

3.3. Preparation of Fluorenone **4**

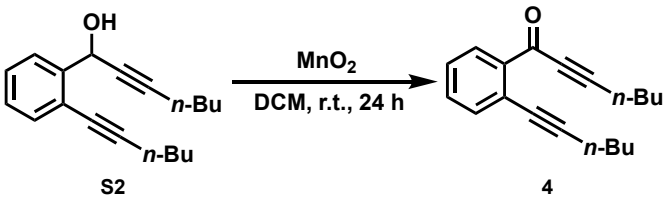
To a solution of magnesium (390.5 mg, 16.07 mmol) in THF (35 mL) bromoethane (2.059 g, 18.89 mmol) was added dropwise at room temperature, and the mixture was stirred for 2 h. At the same temperature, 1-hexyne (1.409 g, 17.16 mmol) was added. After the mixture was stirred for 3 h, 2-(1-hexyn-1-yl)benzaldehyde (1.853 g, 9.947 mmol) was added, and the reaction mixture was stirred for 18 h. The mixture was quenched by saturated NH_4Cl and extracted with EtOAc. The combined organic extracts were dried ($MgSO_4$), filtered, and concentrated on a rotary evaporator. The residue was subjected to column chromatography (silica gel, hexane/ethyl acetate = 95/5) to give compound **S2** (2.489 g, 9.273 mmol, 93% yield, Scheme 4).



Scheme 4. Synthesis of **S2**.

S2: Yellow oil, Yield 93%, 2.489 g, ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.91 (t, *J* = 7.5 Hz, 3H), 0.96 (t, *J* = 7.5 Hz, 3H), 1.37–1.47 (m, 2H), 1.47–1.57 (m, 4H), 1.57–1.66 (m, 2H), 2.27 (td, *J* = 7.3, 1.8 Hz, 2H), 2.46 (t, *J* = 7.3 Hz, 2H), 2.66 (d, *J* = 5.0 Hz, 1H), 5.83 (dt, *J* = 5.5, 2.0 Hz, 1H), 7.23 (td, *J* = 7.5, 1.3 Hz, 1H), 7.31 (td, *J* = 7.5, 1.0 Hz, 1H), 7.40 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.64–7.69 (m, 1H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.57, 13.60, 18.5, 19.3, 21.9, 22.0, 30.6, 30.7, 63.5, 77.9, 79.2, 87.4, 96.1, 122.1, 126.5, 127.9, 128.0, 132.4, 142.7, IR (neat, cm^{-1}) 3421, 2958, 2934, 2871, 2226, 1708, 1465, 1379, 1328, 1134, 1005, 758, 630, HRMS (EI^+) *m*/*z* $[M]^+$ calcd for $C_{19}H_{24}O$ 268.1827, found 268.1827.

To a solution of MnO_2 (7.960 g, 91.56 mmol) in DCM (26 mL) **S2** (1.233 g, 4.595 mmol) was added at room temperature. After being stirred for 24 h, the reaction mixture was filtered through a pad of Celite and subjected to column chromatography (silica gel, hexane/ethyl acetate = 7/3) to give **4** (1.177 g, 4.418 mmol, 96% yield, Scheme 5).



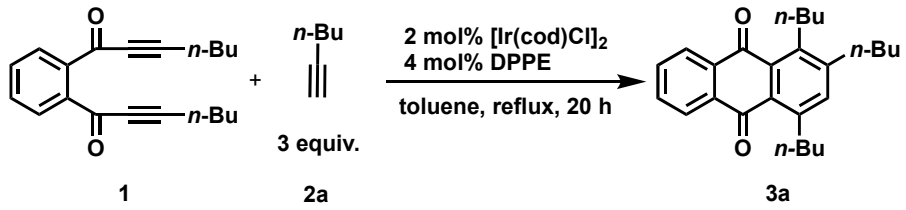
Scheme 5. Synthesis of **4**.

4: Orange oil, Yield 96%, 1.177 g, ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.945 (t, *J* = 7.5 Hz, 3H), 0.953 (t, *J* = 7.5 Hz, 3H), 1.42–1.56 (m, 4H), 1.58–1.67 (m, 4H), 2.46 (t, *J* = 6.5 Hz, 2H), 2.48 (t, *J* = 6.8 Hz, 2H), 7.35 (td, *J* = 7.8, 1.3 Hz, 1H), 7.44 (td, *J* = 7.5, 1.2 Hz, 1H), 7.50 (dd, *J* = 7.5, 1.3 Hz, 1H), 8.04 (dd, *J* = 8.0, 1.3 Hz, 1H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.5, 13.6, 19.0, 19.6, 22.0, 29.8, 30.6, 79.2, 80.7, 96.5, 96.8, 123.6, 127.0, 131.5, 132.0, 134.5, 138.4, 177.9, IR (neat, cm^{-1}) 3062, 2959, 2871, 2207, 1651, 1593, 1561, 1478, 1466, 1272, 1242, 909, 756, HRMS (EI^+) *m*/*z* $[M]^+$ calcd for $C_{19}H_{22}O$ 266.1671, found 266.1670.

3.4. General Procedure for the Reaction of 1,2-Bis(propiolyl)benzene Derivative **1** *with Alkyne* **2**

Representative Procedure for the Reaction of 1,2-Bis(propiolyl)benzene Derivative **1** with Alkyne **2a** (Tables 1 and 2).

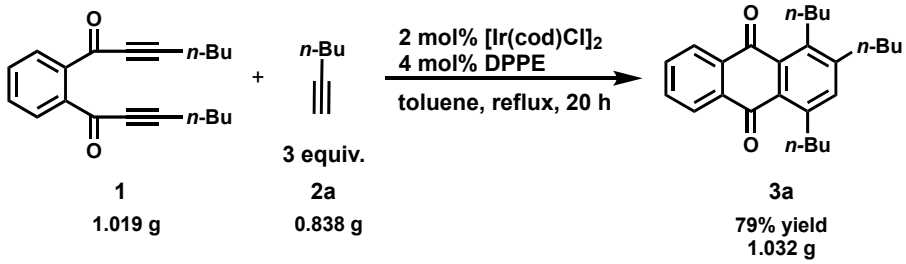
To a solution of $[Ir(cod)Cl]_2$ (6.7 mg, 0.010 mmol) and DPPE (8.0 mg, 0.020 mmol) in toluene (1.0 mL), 1-hexyne (125.7 mg, 1.530 mmol) and a solution of **1** (148.1 mg, 0.5031 mmol) in toluene (1.5 mL) were added. The mixture was stirred under reflux for 20 h. After removal of the solvent on a rotary evaporator, the residue was subjected to column chromatography (silica gel, hexane/EtOAc = 99/1) to give compound 1,2,4-tributylanthracene-9,10-dione (**3a**) (157.8 mg, 0.4191 mmol, 83% yield, Scheme 6).



Scheme 6. Synthetic procedure for **3a**.

A procedure for the Gram-Scale Synthesis of Anthraquinone **3a** from 1,2-Bis(propiolyl)benzene Derivative **1** and Alkyne **2a**.

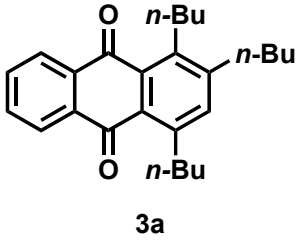
To a solution of $[Ir(cod)Cl]_2$ (45.6 mg, 0.068 mmol) and DPPE (53.8 mg, 0.135 mmol) in toluene (6.8 mL), 1-hexyne (0.838 g, 10.2 mmol) and a solution of **1** (1.019 g, 3.46 mmol) in toluene (10.1 mL) were added, and the mixture was stirred under reflux for 20 h. After removal of the solvent on a rotary evaporator, the residue was subjected to column chromatography (silica gel, hexane/EtOAc = 99/1) to give compound 1,2,4-tributylanthracene-9,10-dione (**3a**) (1.032 g, 2.740 mmol, 79% yield, Scheme 7).



Scheme 7. Gram-scale synthesis of **3a**.

3.5. Characterization of **3a**–**3l**

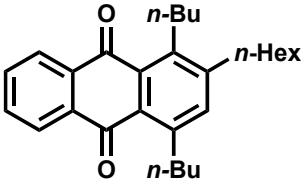
1,2,4-Tributylanthracene-9,10-dione (**3a**, Scheme 8). Brown solid, mp 42.0–43.0 °C, Yield 83%, 157.8 mg, ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.99 (t, *J* = 7.5 Hz, 6H), 1.02 (t, *J* = 6.8 Hz, 3H), 1.40–1.53 (m, 4H), 1.52–1.70 (m, 8H), 2.68–2.72 (m, 2H), 3.02–3.18 (m, 4H), 7.32 (s, 1H), 7.65–7.73 (m, 2H), 8.07–8.15 (m, 2H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9, 14.0, 14.1, 22.9, 23.1, 23.5, 29.9, 33.0, 33.1, 33.4, 33.5, 35.7, 126.1, 126.3, 131.1, 133.0, 133.1, 133.9, 134.3, 135.0, 138.2, 142.5, 144.0, 148.4, 185.9, 187.1, IR (KBr, cm^{-1}) 2956, 2927, 2869, 1665, 1590, 1536, 1456, 1320, 1288, 1262, 1102, 1020, 898, 802, 726, HRMS (EI^+) *m*/*z* $[M]^+$ calcd for $C_{26}H_{32}O_2$ 376.2402, found 376.2401.



Scheme 8. Characterization of **3a**.

1,4-Dibutyl-2-hexylanthracene-9,10-dione (**3b**, Scheme 9). Yellow solid, mp 41.0–41.5 °C, 188.0 mg, Yield 92%, ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.91 (t, *J* = 6.8 Hz, 3H), 0.98 (t, *J* = 7.0 Hz, 3H), 1.02 (t, *J* = 7.0 Hz, 3H), 1.29–1.38 (m, 4H), 1.38–1.45 (m, 2H), 1.45–1.68 (m, 2H), 1.53–1.68 (m, 8H), 2.67–2.76 (m, 2H), 3.03–3.17 (m, 4H), 7.32 (s, 1H), 7.68 (t, *J* = 3.8 Hz, 1H), 7.70 (t, *J* = 4.0 Hz, 1H), 8.07–8.15 (m, 2H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 14.1, 22.6, 23.1, 23.5, 29.5, 29.9, 31.3, 31.6, 33.1, 33.3, 33.4, 35.7, 126.1, 126.3, 131.1, 133.0, 133.1, 133.9, 134.4, 135.0, 138.3, 142.5, 144.0, 148.4, 185.9, 187.1, IR (KBr, cm^{-1}) 2959,

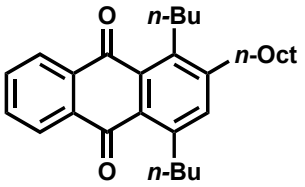
2927, 2854, 1668, 1595, 1539, 1462, 1320, 1288, 1265, 727; HRMS (EI$^+$) *m*/*z* [M]$^+$ calcd for $C_{28}H_{36}O_2$ 404.2715, found 404.2722.



3b

Scheme 9. Characterization of **3b**.

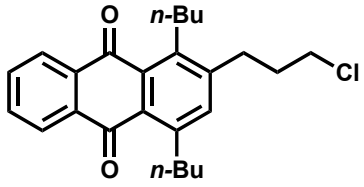
1,4-Dibutyl-2-octylanthracene-9,10-dione (**3c**, Scheme 10). Brown solid, mp 39.5–39.8 °C, 200.0 mg, Yield 93%, ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.89 (t, *J* = 7.0 Hz, 3H), 0.98 (t, *J* = 7.5 Hz, 3H), 1.02 (t, *J* = 7.0 Hz, 3H), 1.21–1.38 (m, 8H), 1.38–1.45 (m, 2H), 1.45–1.53 (m, 2H), 1.53–1.69 (m, 8H), 2.68–2.75 (m, 2H), 3.01–3.17 (m, 4H), 7.32 (s, 1H), 7.68 (t, *J* = 3.8 Hz, 1H), 7.70 (t, *J* = 3.8 Hz, 1H), 8.08–8.14 (m, 2H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 14.1, 22.7, 23.1, 23.5, 29.2, 29.4, 29.8, 29.9, 31.3, 31.8, 33.1, 33.3, 33.4, 35.7, 126.1, 126.3, 131.1, 133.0, 133.1, 133.9, 134.4, 135.0, 138.3, 142.5, 144.0, 148.4, 185.9, 187.1, IR (KBr, cm^{-1}) 3460, 2964, 2925, 2856, 1668, 1595, 1540, 1461, 1324, 1288, 1262, 996, 904, 728, HRMS (EI$^+$) *m*/*z* [M]$^+$ calcd for $C_{30}H_{40}O_2$ 432.3028, found 432.3024.



3c

Scheme 10. Characterization of **3c**.

1,4-Dibutyl-2-(3-chloropropyl) anthracene-9,10-dione (**3d**, Scheme 11). Yellow oil, 144.4 mg, Yield 73%, ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.99 (t, *J* = 7.5 Hz, 3H), 1.02 (t, *J* = 7.0 Hz, 3H), 1.49 (sext, *J* = 6.8 Hz, 2H), 1.53–1.70 (m, 6H), 2.05–2.14 (m, 2H), 2.92 (t, *J* = 7.3 Hz, 2H), 3.05–3.17 (m, 4H), 3.63 (t, *J* = 6.3 Hz, 2H), 7.35 (s, 1H), 7.69 (t, *J* = 3.8 Hz, 1H), 7.71 (t, *J* = 4.0 Hz, 1H), 8.08–8.16 (m, 2H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 14.1, 23.1, 23.4, 29.9, 30.3, 33.2, 33.4, 33.7, 35.6, 44.4, 126.1, 126.3, 131.5, 133.1, 133.2, 134.1, 134.3, 134.9, 138.3, 142.6, 144.2, 146.2, 185.9, 186.9, IR (neat, cm^{-1}) 2956, 2934, 2860, 1669, 1595, 1541, 1456, 1392, 1331, 1287, 1251, 997, 904, 798, 727, 653, HRMS (EI$^+$) *m*/*z* [M]$^+$ calcd for $C_{25}H_{29}O_2{}^{35}Cl$ 396.1856, found 396.1863.

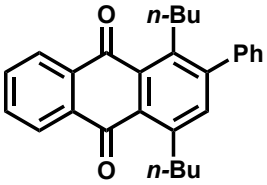


3d

Scheme 11. Characterization of **3d**.

1,4-Dibutyl-2-phenylanthracene-9,10-dione (**3e**, Scheme 12). Yellow oil, 152.6 mg, Yield 77%, ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.75 (t, *J* = 7.5 Hz, 3H), 0.97 (t, *J* = 7.5 Hz, 3H), 1.24 (sext, *J* = 7.1 Hz, 2H), 1.39–1.54 (m, 4H), 1.62–1.72 (m, 2H), 3.01–3.09 (m, 2H), 3.12–3.20 (m, 2H), 7.29 (d, *J* = 7.0 Hz, 2H), 7.36 (s, 1H), 7.38–7.48 (m, 3H), 7.71 (t, *J* = 3.8 Hz, 1H), 7.73 (t, *J* = 3.8 Hz, 1H), 8.11–8.19 (m, 2H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.7, 14.0, 23.0, 23.1, 30.8, 33.2, 33.4, 35.6, 126.2, 126.4, 127.5, 128.1, 128.8, 132.4, 133.2, 133.3,

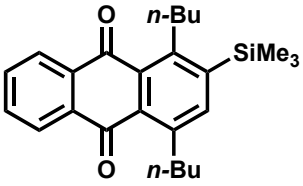
133.8, 134.3, 135.0, 138.6, 141.0, 142.6, 143.7, 149.1, 186.0, 186.7, IR (neat, cm^{-1}) 3059, 3022, 2958, 2931, 2862, 1672, 1595, 1535, 1458, 1324, 1256, 1018, 886, 723, 703, HRMS (EI^+) *m*/*z* $[M]^+$ calcd for $C_{28}H_{28}O_2$ 396.2089, found 396.2087.



3e

Scheme 12. Characterization of **3e**.

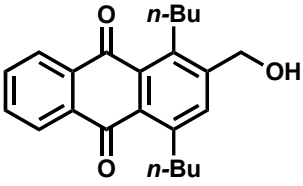
1,4-Dibutyl-2-(trimethylsilyl) anthracene-9,10-dione (**3f**, Scheme 13). Brown oil, 83.0 mg, Yield 42%, ^1H NMR (500 MHz, $CDCl_3$) δ 0.41 (s, 9H), 1.00 (t, *J* = 7.3 Hz, 6H), 1.44–1.60 (m, 6H), 1.61–1.70 (m, 2H), 3.10–3.17 (m, 2H), 3.32 (br, 2H), 7.64 (s, 1H), 7.68–7.75 (m, 2H), 8.10–8.17 (m, 2H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 0.7, 14.0, 14.1, 23.1, 23.5, 33.5, 34.5, 35.7, 35.8, 126.1, 126.4, 132.2, 133.1, 133.3, 133.7, 134.2, 135.0, 142.7, 143.8, 148.1, 150.8, 186.5, 186.9, IR (neat, cm^{-1}) 2960, 2934, 2866, 1669, 1595, 1457, 1312, 1287, 1255, 1103, 959, 887, 883, 841, 800, 727, 659, HRMS (EI^+) *m*/*z* $[M]^+$ $C_{25}H_{32}O_2Si$ calcd for 392.2172, found 392.2172.



3f

Scheme 13. Characterization of **3f**.

1,4-Dibutyl-2-(hydroxymethyl) anthracene-9,10-dione (**3g**, Scheme 14). Yellow solid, mp 123.5–124.0 °C, 134.3 mg, Yield 76%, ^1H NMR (500 MHz, $CDCl_3$) δ 0.98 (t, *J* = 7.5 Hz, 3H), 1.01 (t, *J* = 6.5 Hz, 3H), 1.43–1.53 (m, 2H), 1.53–1.70 (m, 6H), 1.94 (t, *J* = 5.3 Hz, 1H), 3.00–3.12 (m, 2H), 3.12–3.21 (m, 2H), 4.89 (d, *J* = 5.5 Hz, 2H), 7.66–7.74 (m, 3H), 8.08–8.15 (m, 2H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.96, 14.05, 23.1, 23.4, 29.5, 32.7, 33.4, 35.8, 62.3, 126.2, 126.4, 132.1, 133.2, 133.3, 133.5, 134.3, 134.9, 135.5, 141.9, 144.6, 145.1, 185.9, 186.7, IR (KBr, cm^{-1}) 3371, 3320, 2956, 2927, 2859, 1666, 1591, 1469, 1319, 1287, 1259, 1046, 981, 907, 730, HRMS (EI^+) *m*/*z* $[M]^+$ calcd for $C_{23}H_{26}O_3$ 350.1882, found 350.1882.

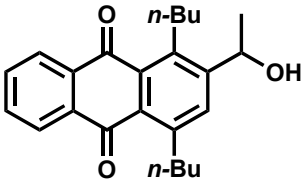


3g

Scheme 14. Characterization of **3g**.

1,4-Dibutyl-2-(1-hydroxyethyl) anthracene-9,10-dione (**3h**, Scheme 15). Brown oil, 156.4 mg, Yield 85%, ^1H NMR (500 MHz, $CDCl_3$) δ 0.98 (t, *J* = 7.0 Hz, 3H), 1.01 (t, *J* = 7.3 Hz, 3H), 1.42–1.60 (m, 8H), 1.60–1.71 (m, 3H), 2.00 (s, 1H), 2.78–2.92 (m, 1H), 3.16 (t, *J* = 8.0 Hz, 2H), 3.20–3.31 (m, 1H), 5.35 (q, *J* = 5.8 Hz, 1H), 7.69 (t, *J* = 3.5 Hz, 1H), 7.70 (t, *J* = 3.8 Hz, 1H), 7.80 (s, 1H), 8.06–8.13 (m, 2H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.96, 14.05, 23.1, 23.4, 25.3, 29.2, 33.4, 33.5, 35.9, 65.7, 126.1, 126.3, 132.1, 133.17, 133.24,

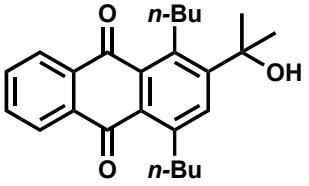
133.8, 134.0, 134.2, 135.0, 140.4, 144.8, 150.6, 185.9, 186.9, IR (neat, cm^{-1}) 3453, 3073, 2957, 2862, 1672, 1594, 1542, 1462, 1291, 1123, 1062, 908, 759, 727, HRMS (EI^+) *m*/*z* $[M]^+$ calcd for $C_{24}H_{28}O_3$ 364.2038, found 364.2044.



3h

Scheme 15. Characterization of **3h**.

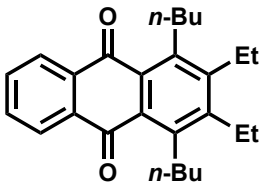
1,4-Dibutyl-2-(2-hydroxypropan-2-yl) anthracene-9,10-dione (**3i**, Scheme 16). Brown solid, mp 77.5–78.2 °C, 140.3 mg, Yield 75%, ^1H NMR (500 MHz, $CDCl_3$) δ 0.96 (t, *J* = 7.3 Hz, 3H), 0.98 (t, *J* = 7.5 Hz, 3H), 1.39–1.59 (m, 6H), 1.59–1.68 (m, 2H), 1.75 (s, 6H), 1.94 (s, 1H), 3.08–3.16 (m, 2H), 3.54 (br, 2H), 7.66–7.73 (m, 2H), 7.75 (s, 1H), 8.05–8.12 (m, 2H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.9, 14.0, 23.1, 23.6, 30.3, 31.9, 33.6, 35.4, 36.0, 74.0, 125.9, 126.3, 132.4, 133.0, 133.3, 134.1, 134.2, 135.5, 135.6, 143.6, 143.7, 151.8, 186.0, 187.8, IR (KBr, cm^{-1}) 3372, 2956, 2931, 2872, 1666, 1592, 1462, 1316, 1291, 1142, 728, HRMS (EI^+) *m*/*z* $[M]^+$ calcd for $C_{25}H_{30}O_3$ 378.2195, found 378.2196.



3i

Scheme 16. Characterization of **3i**.

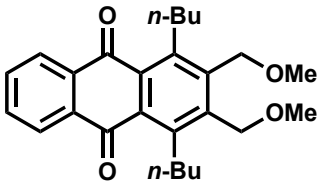
1,4-Dibutyl-2,3-diethylanthracene-9,10-dione (**3j**, Scheme 17). Yellow oil, 134.6 mg, Yield 72%, ^1H NMR (500 MHz, $CDCl_3$) δ 1.02 (t, *J* = 7.3 Hz, 6H), 1.22 (t, *J* = 7.3 Hz, 6H), 1.50–1.69 (m, 8H), 2.82 (q, *J* = 7.5 Hz, 4H), 3.11 (br, 4H), 7.63–7.69 (m, 2H), 8.02–8.09 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 15.3, 22.5, 23.5, 30.1, 33.6, 125.9, 132.2, 132.8, 135.1, 142.4, 147.9, 187.3, IR (neat, cm^{-1}) 3316, 3065, 2961, 2934, 2870, 1669, 1595, 1536, 1458, 1401, 1377, 1328, 1287, 1265, 1102, 1055, 907, 797, 730, HRMS (EI^+) *m*/*z* $[M]^+$ calcd for $C_{26}H_{32}O_2$ 376.2402, found 376.2401.



3j

Scheme 17. Characterization of **3j**.

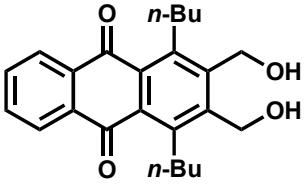
1,4-Dibutyl-2,3-bis(methoxymethyl)anthracene-9,10-dione (**3k**, Scheme 18). Yellow solid, mp 86.2–86.5 °C, 167.5 mg, Yield 82%, ^1H NMR (500 MHz, $CDCl_3$) δ 1.03 (t, *J* = 7.3 Hz, 6H), 1.53–1.70 (m, 8H), 3.18 (br, 4H), 3.52 (s, 6H), 4.58 (s, 4H), 7.65–7.72 (m, 2H), 8.03–8.10 (m, 2H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 23.5, 30.1, 33.7, 59.0, 67.8, 126.1, 133.1, 134.1, 134.9, 142.6, 144.1, 186.8, IR (KBr, cm^{-1}) 2953, 2927, 2870, 2807, 1670, 1593, 1462, 1320, 1288, 1191, 1097, 947, HRMS (EI^+) *m*/*z* $[M]^+$ calcd for $C_{26}H_{32}O_4$ 408.2301, found 408.2300.



3k

Scheme 18. Characterization of **3k**.

1,4-Dibutyl-2,3-bis(hydroxymethyl)anthracene-9,10-dione (**3l**, Scheme 19). Yellow solid, mp 153.2–154.0 °C, 162.8 mg, Yield 86%, ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.02 (t, *J* = 7.0 Hz, 6H), 1.52–1.72 (m, 8H), 2.96 (s, 2H), 3.15 (br, 4H), 4.95 (s, 4H), 7.66–7.73 (m, 2H), 8.02–8.08 (m, 2H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 23.3, 30.4, 34.1, 58.9, 126.1, 133.2, 134.2, 134.9, 143.2, 145.0, 186.8, IR (neat, cm^{-1}) 3233, 2952, 2923, 2869, 1670, 1593, 1468, 1318, 1290, 1260, 1007, 907, 729, HRMS (EI^+) *m*/*z* $[M]^+$ calcd for $C_{24}H_{28}O_4$ 380.1988, found 380.1988.

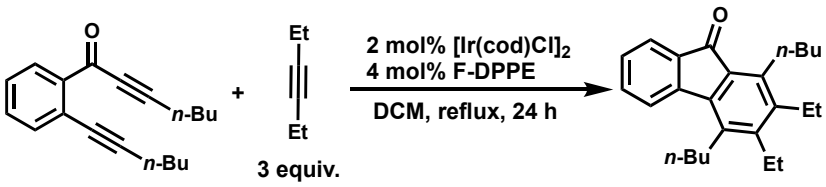


3l

Scheme 19. Characterization of **3l**.

3.6. Procedure for the Reaction of Diyne 4 with Alkyne **2j**

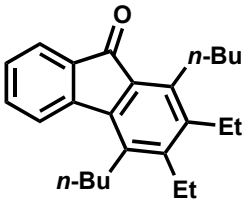
To a solution of $[Ir(cod)Cl]_2$ (6.7 mg, 0.010 mmol) and F-DPPE (15.2 mg, 0.0200 mmol) in DCM (1.0 mL), 3-hexyne (125.9 mg, 1.530 mmol) and a solution of diyne (133.5 mg, 0.5012 mmol) in DCM (1.5 mL) were added. The mixture was stirred under reflux for 24 h. After removal of the solvent on a rotary evaporator, the residue was subjected to column chromatography (silica gel, hexane/EtOAc = 99.5/0.5) to give compound 1,4-dibutyl-2,3-diethyl-9*H*-fluoren-9-one (**5j**) (164.1 mg, 0.4708 mmol, 94% yield, Scheme 20).



4 **2j** **5j**

Scheme 20. Synthetic procedure for **5j**.

1,4-Dibutyl-2,3-diethyl-9H-fluoren-9-one (**5j**, Scheme 21). Yellow oil, 164.1 mg, Yield 94%, ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.99 (t, *J* = 7.0 Hz, 3H), 1.03 (t, *J* = 7.3 Hz, 3H), 1.18 (t, *J* = 7.8 Hz, 3H), 1.21 (t, *J* = 7.5 Hz, 3H), 1.45–1.66 (m, 8H), 2.67 (q, *J* = 7.5 Hz, 2H), 2.71 (q, *J* = 7.5 Hz, 2H), 2.84–2.92 (m, 2H), 3.00–3.14 (m, 2H), 7.22 (t, *J* = 7.0 Hz, 1H), 7.43 (td, *J* = 7.5, 1.0 Hz, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 7.0 Hz, 1H), ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.0, 15.5, 15.6, 21.4, 22.3, 23.3, 23.5, 27.3, 29.1, 32.2, 33.3, 122.8, 123.5, 127.7, 129.3, 134.1, 135.4, 135.5, 140.7, 141.5, 142.2, 144.3, 147.8, 195.1, IR (neat, cm^{-1}) 2963, 2876, 1704, 1606, 1564, 1464, 1261, 1098, 1058, 1026, 800, HRMS (EI^+) *m*/*z* $[M]^+$ calcd for $C_{25}H_{32}O$ 348.2453, found 348.2453.



5j

Scheme 21. Characterization of **5j**.

4. Conclusions

In summary, we have developed an efficient and convenient method for the synthesis of anthraquinones ranging from a 42% yield to a 93% yield through an iridium/dppe complex-catalyzed [2 + 2 + 2] cycloaddition of a 1,2-bis(propiolyl)benzene derivative with a broad range of terminal and internal alkynes. The use of dichloromethane as a solvent is important for the success of [2 + 2 + 2] cyclization with internal alkynes to lead to the desired anthraquinones in 72–86% yields. Furthermore, the synthesis of the fluorenone was also achieved by [2 + 2 + 2] cyclization with the iridium/F-dppe catalytic system to give a 94% yield.

Author Contributions: Conceptualization, R.T. Methodology, Y.T. Investigation, Y.T. and T.S. Writing-Original Draft Preparation, T.S. Writing-Review & Editing, T.S. and R.T. Visualization, T.S. Supervision, R.T. Project Administration, R.T. Funding Acquisition, R.T.

Funding: Grant-in-Aid for Scientific Research (KAKENHI) (No. 17K05867) from JSPS supported this work.

Acknowledgments: This work was partly supported by Grant-in-Aid for Scientific Research (KAKENHI) (No. 19K23636) from JSPS.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Cichewicz, R.H.; Zhang, Y.; Seeram, N.P.; Nair, M.G. Inhibition of Human Tumor Cell Proliferation by Novel Anthraquinones from Daylilies. *Life Sci.* **2004**, *74*, 1791–1799. [CrossRef] [PubMed]
2. Tietze, L.F.; Gericke, K.M.; Schuberth, I. Synthesis of Highly Functionalized Anthraquinones and Evaluation of Their Antitumor Activity. *Eur. J. Org. Chem.* **2007**, 4563–4577. [CrossRef]
3. Isaka, M.; Chinthanom, P.; Rachtawee, P.; Srichomthong, K.; Srikitikulchai, P.; Kongsaeree, P.; Prabpai, S. Cytotoxic Hydroanthraquinones from the Mangrove-Derived Fungus Paradictyoarthrinium Diffractum BCC 8704. *J. Antibiot.* **2015**, *68*, 334–338. [CrossRef] [PubMed]
4. Teiten, M.-H.; Mack, F.; Debbab, A.; Aly, A.H.; Dicato, M.; Proksch, P.; Diederich, M. Anticancer Effect of Altersolanol A, a Metabolite Produced by the Endophytic Fungus *Stemphylium Globuliferum*, Mediated by Its Pro-Apoptotic and Anti-Invasive Potential via the Inhibition of NF-κB Activity. *Bioorg. Med. Chem.* **2013**, *21*, 3850–3858. [CrossRef]
5. Shrestha, J.P.; Fosso, M.Y.; Bearss, J.; Chang, C.-W.T. Synthesis and Anticancer Structure Activity Relationship Investigation of Cationic Anthraquinone Analogs. *Eur. J. Med. Chem.* **2014**, *77*, 96–102. [CrossRef]
6. Shrestha, J.P.; Subedi, Y.P.; Chen, L.; Chang, C.-W.T. A Mode of Action Study of Cationic Anthraquinone Analogs: A New Class of Highly Potent Anticancer Agents. *Med. Chem. Commun.* **2015**, *6*, 2012–2022. [CrossRef]
7. Fosso, M.Y.; Chan, K.Y.; Gregory, R.; Chang, C.-W.T. Library Synthesis and Antibacterial Investigation of Cationic Anthraquinone Analogs. *ACS Comb. Sci.* **2012**, *14*, 231–235. [CrossRef]
8. Ondeyka, J.; Buevich, A.V.; Williamson, R.T.; Zink, D.L.; Polishook, J.D.; Occi, J.; Vicente, F.; Basilio, A.; Bills, G.F.; Donald, R.G.K.; et al. Isolation, Structure Elucidation, and Biological Activity of Altersolanol P Using *Staphylococcus Aureus* Fitness Test Based Genome-Wide Screening. *J. Nat. Prod.* **2014**, *77*, 497–502. [CrossRef]
9. van Gorkom, B.A.P.; de Vries, E.G.E.; Karrenbeld, A.; Kleibeuker, J.H. Review Article: Anthranoid Laxatives and Their Potential Carcinogenic Effects. *Aliment. Pharmacol. Ther.* **1999**, *13*, 443–452. [CrossRef]

10. Davis, R.H.; Agnew, P.S.; Shapiro, E. Antiarthritic Activity of Anthraquinones Found in Aloe for Podiatric Medicine. *J. Am. Podiatr. Med. Assoc.* **1986**, *76*, 61–66. [CrossRef]
11. Wuthi-udomlert, M.; Kupittayanant, P.; Gritsanapan, W. In Vitro Evaluation of Antifungal Activity of Anthraquinone Derivatives of *Senna Alata*. *J. Health Res.* **2010**, *24*, 117–122.
12. Seo, E.J.; Ngoc, T.M.; Lee, S.-M.; Kim, Y.S.; Jung, Y.-S. Chrysophanol-8-*O*-glucoside, an Anthraquinone Derivative in Rhubarb, Has Antiplatelet and Anticoagulant Activities. *J. Pharmacol. Sci.* **2012**, *118*, 245–254. [CrossRef] [PubMed]
13. Gan, K.-H.; Teng, C.-H.; Lin, H.-C.; Chen, K.-T.; Chen, Y.-C.; Hsu, M.-F.; Wang, J.-P.; Teng, C.-M.; Lin, C.-N. Antiplatelet Effect and Selective Binding to Cyclooxygenase by Molecular Docking Analysis of 3-Alkylaminopropoxy-9,10-anthraquinone Derivatives. *Biol. Pharm. Bull.* **2008**, *31*, 1547–1551. [CrossRef] [PubMed]
14. Jackson, T.C.; Verrier, J.D.; Kochanek, P.M. Anthraquinone-2-sulfonic Acid (AQ2S) is a Novel Neurotherapeutic Agent. *Cell Death Dis.* **2013**, *4*, 451. [CrossRef]
15. Campos-Martin, J.M.; Blanco-Brieva, G.; Fierro, J.L.G. Hydrogen Peroxide Synthesis: An Outlook Beyond the Anthraquinone Process. *Angew. Chem. Int. Ed.* **2006**, *45*, 6962–6984. [CrossRef]
16. Hattori, M.; Seidel, A. *Kirk-Othmer Encyclopedia of Chemical Technology*, 5th ed.; Wiley: Hoboken, NJ, USA, 2005; Volume 9, pp. 300–349.
17. Malik, E.M.; Baqi, Y.; Müller, C.E. Syntheses of 2-Substituted 1-Amino-4-bromoanthraquinones (Bromaminic Acid Analogues)–Precursors for Dyes and Drugs. *Beilstein J. Org. Chem.* **2015**, *11*, 2326–2333. [CrossRef]
18. Edward, R. Use of DNA-Specific Anthraquinone Dye to Directly Reveal Cytoplasmic and Nuclear Boundaries in Live and Fixes Cells. *Mol. Cells* **2009**, *27*, 391–396. [CrossRef]
19. Hart, P.W.; Rudie, A.W. Anthraquinone a Review of the Rise and Fall of a Pulping Catalyst. *TAPPI J.* **2014**, *13*, 23–31. [CrossRef]
20. Kampmann, B.; Lian, Y.; Klinkel, K.L.; Vecchi, P.A.; Quiring, H.L.; Soh, C.C.; Sykes, A.G. Luminescence and Structural Comparisons of Strong-Acid Sensor Molecules. 2. *J. Org. Chem.* **2002**, *67*, 3878–3883. [CrossRef]
21. Tandon, P.K.; Gayatri; Sahgal, S.; Srivastava, M.; Singh, S.B. Catalysis by Ir (III), Rh (III) and Pd (II) Metal Ions in the Oxidation of Organic Compounds with H_2O_2. *Appl. Organomet. Chem.* **2007**, *21*, 135–138. [CrossRef]
22. Charleton, K.D.M.; Prokopchuk, E.M. Coordination Complexes as Catalysts: The Oxidation of Anthracene by Hydrogen Peroxide in the Presence of $VO(acac)_2$. *J. Chem. Educ.* **2011**, *88*, 1155–1157. [CrossRef]
23. Thomson, R. *The Chemistry of the Quinoid Compounds, Part I and II*; Patai, S., Ed.; Wiley: New York, NY, USA, 1974.
24. Tietze, L.F.; Güntner, C.; Gericke, K.M.; Schuberth, I.; Bunkoczi, G. Diels–Alder Reaction for the Total Synthesis of the Novel Antibiotic Antitumor Agent Mensacarcin. *Eur. J. Org. Chem.* **2005**, 2459–2467. [CrossRef]
25. Amatore, M.; Aubert, C. Recent Advances in Stereoselective [2+2+2] Cycloadditions. *Eur. J. Org. Chem.* **2015**, 265–286. [CrossRef]
26. Tanaka, K. (Ed.) *Transition-Metal-Mediated Aromatic Ring Construction*; Wiley: New York, NY, USA, 2013.
27. Broere, D.L.J.; Ruijter, E. Recent Advances in Transition-Metal-Catalyzed [2+2+2] Cyclo(co)trimerization Reactions. *Synthesis* **2012**, *44*, 2639–2672. [CrossRef]
28. Shibata, Y.; Tanaka, K. Rhodium-Catalyzed [2+2+2] Cycloaddition of Alkynes for the Synthesis of Substituted Benzenes: Catalysts, Reaction Scope, and Synthetic Applications. *Synthesis* **2012**, *44*, 323–350. [CrossRef]
29. Dominguez, G.; Pérez-Castells, J. Recent Advances in [2+2+2] Cycloaddition Reactions. *Chem. Soc. Rev.* **2011**, *40*, 3430–3444. [CrossRef]
30. Agenet, N.; Buisine, O.; Slowinski, F.; Gandon, V.; Aubert, C.; Malacria, M. Cotrimerizations of Acetylenic Compounds. *Org. React.* **2007**, *68*, 1–302. [CrossRef]
31. Wagner, F.; Meier, H. Thermische und Photochemische Umsetzungen von Acetylenen mit Metallcarbonylen–IV: Cycloadditionen von Bis[α-oxo-alkinen] in Gegenwart von Nickeltetracarbonyl. *Tetrahedron* **1974**, *30*, 773–780. [CrossRef]
32. Müller, E. The Diyne Reaction of 1,4-, 1,5-, 1,6-, and 1,7-Diynes via Transition Metal Complexes to New Compounds. *Synlett* **1974**, 761–774. [CrossRef]
33. Müeller, E.; Scheller, A.; Winter, W.; Wagner, F.; Meier, H. Diyne Reactions. XXXVII. Thermal and Photochemical Reactions of Acetylenes with Metal Carbonyls. V. Quinone Synthesis from o-Bis(α-oxoalkynes) with Dicarbonylbis(triphenylphosphine) Nickel (0). *Chem.-Ztg.* **1975**, *99*, 155–157.

34. Hillard, R.L., III; Vollhardt, K.P.C. Substituted Benzocyclobutenes, Indans, and Tetralins via Cobalt-Catalyzed Cooligomerization of α, ω-Diynes with Substituted Acetylenes. Formation and Synthetic Utility of Trimethylsilylated Benzocycloalkenes. *J. Am. Chem. Soc.* **1977**, *99*, 4058–4069. [CrossRef]
35. McDonald, F.E.; Zhu, H.Y.H.; Holmquist, C.R. Rhodium-Catalyzed Alkyne Cyclotrimerization Strategies for *C*-Arylglycoside Synthesis. *J. Am. Chem. Soc.* **1995**, *117*, 6605–6606. [CrossRef]
36. Yamamoto, Y.; Hata, K.; Arakawa, T.; Itoh, K. Ru(II)-Catalyzed [2+2+2] Cycloaddition of 1,2-Bis(propiolyl)benzenes with Monoalkynes Leading to Substituted Anthraquinones. *Chem. Commun.* **2003**, 1290–1291. [CrossRef]
37. Yamamoto, Y.; Saigoku, T.; Ohgai, T.; Nishiyama, H.; Itoh, K. Synthesis of *C*-Arylglycosides via Ru(II)-Catalyzed [2+2+2] Cycloaddition. *Chem. Commun.* **2004**, 2702–2703. [CrossRef]
38. Yamamoto, Y.; Arakawa, T.; Itoh, K. Synthesis of Naphthoquinone-Fused Cyclobutadiene Ruthenium Complexes. *Organometallics* **2004**, *23*, 3610–3614. [CrossRef]
39. Yamamoto, Y.; Saigoku, T.; Nishiyama, H.; Ohgai, T.; Itoh, K. Selective Synthesis of *C*-Arylglycosides *via* Cp*RuCl-Catalyzed Partially Intramolecular Cyclotrimerizations of *C*-alkynylglycosides. *Org. Biomol. Chem.* **2005**, *3*, 1768–1775. [CrossRef]
40. Yamamoto, Y.; Hattori, K.; Ishii, J.; Nishiyama, H. Synthesis of Arylboronates via Cp*RuCl-Catalyzed Cycloaddition of Alkynylboronates. *Tetrahedron* **2006**, *62*, 4294–4305. [CrossRef]
41. Tanaka, K.; Suda, T.; Noguchi, K.; Hirano, M. Catalytic [2+2+2] and Thermal [4+2] Cycloaddition of 1,2-Bis(arylpropiolyl)benzenes. *J. Org. Chem.* **2007**, *72*, 2243–2246. [CrossRef]
42. Kezuka, S.; Okado, T.; Niou, E.; Takeuchi, R. Iridium Complex-Catalyzed Reaction of 1,6-Enynes: Cycloaddition and Cycloisomerization. *Org. Lett.* **2005**, *7*, 1711–1714. [CrossRef]
43. Kezuka, S.; Tanaka, S.; Ohe, T.; Nakaya, Y.; Takeuchi, R. Iridium Complex-Catalyzed [2+2+2] Cycloaddition of α, ω-Diynes with Monoynes and Monoenes. *J. Org. Chem.* **2006**, *71*, 543–552. [CrossRef]
44. Onodera, G.; Matsuzawa, M.; Aizawa, T.; Kitahara, T.; Shimizu, Y.; Kezuka, S.; Takeuchi, R. $[Ir(cod)Cl]_2$ /FDPPE-Catalyzed Chemo- and Regioselective Cyclotrimerization of Two Different Terminal Alkynes to Give 1,3,5-Trisubstituted Benzenes. *Synlett* **2008**, 755–758. [CrossRef]
45. Onodera, G.; Shimizu, Y.; Kimura, J.; Kobayashi, J.; Ebihara, Y.; Kondo, K.; Sakata, K.; Takeuchi, R. Iridium-Catalyzed [2+2+2] Cycloaddition of α, ω -Diynes with Nitriles. *J. Am. Chem. Soc.* **2012**, *134*, 10515–10531. [CrossRef]
46. Onodera, G.; Suto, M.; Takeuchi, R. Iridium-Catalyzed [2+2+2] Cycloaddition of α,ω-Diynes with Isocyanates. *J. Org. Chem.* **2012**, *77*, 908–920. [CrossRef]
47. Hashimoto, T.; Okabe, A.; Mizuno, T.; Izawa, M.; Takeuchi, R. Iridium-Catalyzed [2+2+2] Cycloaddition of α, ω-Diynes with Alkynyl Ketones and Alkynyl Esters. *Tetrahedron* **2014**, *70*, 8681–8689. [CrossRef]
48. Hashimoto, T.; Ishii, S.; Yano, R.; Miura, H.; Sakata, K.; Takeuchi, R. Iridium-Catalyzed [2+2+2] Cycloaddition of α, ω-Diynes with Cyanamides. *Adv. Synth. Catal.* **2015**, *357*, 3901–3916. [CrossRef]
49. Hashimoto, T.; Kato, K.; Yano, R.; Natori, T.; Miura, H.; Takeuchi, R. Iridium-Catalyzed Synthesis of Acylpyridines by [2+2+2] Cycloaddition of Diynes with Acyl Cyanides. *J. Org. Chem.* **2016**, *81*, 5393–5400. [CrossRef]
50. Takeuchi, R.; Fujisawa, S.; Yoshida, Y.; Sagano, J.; Hashimoto, T.; Matsunami, A. Synthesis of Multisubstituted Azatriphenylenes by Iridium-Catalyzed [2+2+2] Cycloaddition of Biaryl-Linked Diynes with Nitriles. *J. Org. Chem.* **2018**, *83*, 1852–1860. [CrossRef]
51. Paneque, M.; Poveda, M.L.; Rendón, N.; Mereiter, K. Isolation of a Stable 1-Iridabicyclo[3.2.0]hepta-1,3,6-triene and Its Reversible Transformation into an Iridacycloheptatriene. *J. Am. Chem. Soc.* **2004**, *126*, 1610–1611. [CrossRef]
52. O'Connor, J.M.; Closson, A.; Hiibner, K.; Merwin, R.; Gantzel, P.; Roddick, D.M. Iridacyclopentadiene Reactions with Terminal Alkynes: Tandem Cycloaromatization and Orthometalation. *Organometallics* **2001**, *20*, 3710–3717. [CrossRef]
53. Bianchini, C.; Caulton, K.G.; Johnson, T.J.; Meli, A.; Peruzzini, M.; Vizza, F. Mechanistic Study of Ir $(H)_2$-Assisted Transformations of Ethyne: Cyclotrimerization, Cooligomerization with Ethene, and Reductive Coupling. *Organometallics* **1995**, *14*, 933–943. [CrossRef]
54. Collman, J.P.; Kang, J.W.; Little, W.F.; Sullivan, M.F. Metalocyclopentadiene Complexes of Iridium and Rhodium and Their Role in the Catalytic Cyclotrimerization of Disubstituted Acetylenes. *Inorg. Chem.* **1968**, *7*, 1298–1303. [CrossRef]

55. Perry, P.J.; Read, M.A.; Davies, R.T.; Gowan, S.M.; Reszka, A.P.; Wood, A.A.; Kelland, L.R.; Neidle, S. 2,7-Disubstituted Amidofluorenone Derivatives as Inhibitors of Human Telomerase. *J. Med. Chem.* **1999**, *42*, 2679–2684. [CrossRef]
56. Hu, Q.-F.; Zhou, B.; Huang, J.-M.; Gao, X.-M.; Shu, L.-D.; Yang, G.-Y.; Che, C.-T. Antiviral Phenolic Compounds from *Arundina Gramnifolia*. *J. Nat. Prod.* **2013**, *76*, 292–296. [CrossRef]
57. Niu, D.-Y.; Han, J.-M.; Kong, W.-S.; Cui, Z.-W.; Hu, Q.-F.; Gao, X.-M. Antiviral Fluorenone Derivatives from Arundina Gramnifolia. *Asian J. Chem.* **2013**, *25*, 9514–9516. [CrossRef]
58. Shi, Y.; Gao, S. Recent Advances of Synthesis of Fluorenone and Fluorene Containing Natural Products. *Tetrahedron* **2016**, *72*, 1717–1735. [CrossRef]
59. Itami, K.; Tonogaki, K.; Nokami, T.; Ohashi, Y.; Yoshida, J. Palladium-Catalyzed Convergent Synthesis and Properties of Conjugated Dendrimers Based on Triarylethene Branching. *Angew. Chem. Int. Ed.* **2006**, *45*, 2404–2409. [CrossRef]
60. Estrada, L.A.; Yarnell, J.E.; Neckers, D.C. Revisiting Fluorenone Photophysics via Dipolar Fluorenone Derivatives. *J. Phys. Chem. A* **2011**, *115*, 6366–6375. [CrossRef]
61. Xia, J.-B.; Zhu, C.; Chen, C. Visible Light-Promoted Metal-Free C-H Activation: Diarylketone-Catalyzed Selective Benzylic Mono- and Difluorination. *J. Am. Chem. Soc.* **2013**, *135*, 17494–17500. [CrossRef]
62. Capodilupo, A.L.; Vergaro, V.; Fabiano, E.; De Giorgi, M.; Baldassarre, F.; Cardone, A.; Maggiore, A.; Maiorano, V.; Sanvitto, D.; Gigli, G.; et al. Design and Synthesis of Fluorenone-Based Dyes: Two-Photon Excited Fluorescent Probes for Imaging of Lysosomes and Mitochondria in Living Cells. *J. Mater. Chem. B* **2015**, *3*, 3315–3323. [CrossRef]
63. Usta, H.; Facchetti, A.; Marks, T.J. Synthesis and Characterization of Electron-Deficient and Highly Soluble (Bis)Indenofluorene Building Blocks for n-Type Semiconducting Polymers. *Org. Lett.* **2008**, *10*, 1385–1388. [CrossRef]
64. Ye, F.; Haddad, M.; Michelet, V.; Ratovelomanana-Vidal, V. Access toward Fluorenone Derivatives through Solvent-Free Ruthenium Trichloride Mediated [2+2+2] Cycloadditions. *Org. Lett.* **2016**, *18*, 5612–5615. [CrossRef]
65. Kaiser, R.P.; Hessler, F.; Mosinger, J.; Císařová, I.; Kotora, M. A [2+2+2]-Cyclotrimerization Approach to Selectively Substituted Fluorenes and Fluorenols, and Their Conversion to 9,9′-Spirobifluorenes. *Chem. Eur. J.* **2015**, *21*, 13577–13582. [CrossRef]
66. Crabtree, R.H.; Quirk, J.M.; Felkin, H.; Fillebeen-Khan, T. An Efficient Synthesis of [Ir(cod)Cl]2 and Its Reaction with PMe2Ph to Give FAC-[IrH(PMe2C6H4) (PMe2Ph)3]. *Synth. React. Inorg. Met. -Org. Chem.* **1982**, *12*, 407–413. [CrossRef]
67. Martins, G.M.; Zeni, G.; Back, D.F.; Kaufman, T.S.; Silveira, C.C. Expedient Iodocyclization Approach Toward Polysubstituted 3H-Benzo[e]indoles. *Adv. Synth. Catal.* **2015**, *357*, 3255–3261. [CrossRef]
68. Řezníčková, E.; Tenora, L.; Pospísilová, P.; Galeta, J.; Jorda, R.; Berka, K.; Majer, P.; Potáček, M.; Kryštof, V. ALK5 Kinase Inhibitory Activity and Synthesis of 2,3,4-Substituted 5,5-Dimethyl-5,6-Dihydro-4H-pyrrolo[1,2-b]pyrazoles. *Eur. J. Med. Chem.* **2017**, *127*, 632–642. [CrossRef]