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Two-Photon Photochemical Generation of Reactive Enediyne

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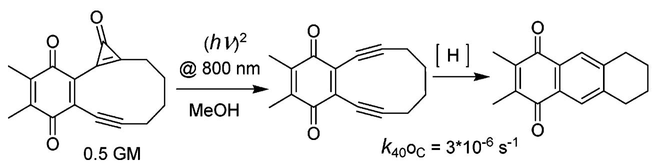

p-Quinoid cyclopropenone-containing enediyne precursor (**1**) has been synthesized by monocyclopropanation of one of the triple bonds in *p*-dimethoxy-substituted 3,4-benzocyclodeca-1,5-diyne followed by oxidative demethylation. Cyclopropenone **1** is stable up to 90 °C but readily produces reactive enediyne **2** upon single-photon ($\Phi_{300nm} = 0.46$) or two-photon ($\sigma_{800nm} = 0.5$ GM) photolysis. The photoproduct **2** undergoes Bergman cyclization at 40 °C with the lifetime of 88 h.

Introduction

The cytotoxicity of enediyne antitumor antibiotics is attributed to the ability of the (*Z*)-3-ene-1,5-diyne fragment to undergo Bergman[1] cyclization. The *p*-benzyne diradical produced in this reaction is believed to abstract hydrogen atoms from both strands of DNA, ultimately causing double-strand DNA scission.[2] These natural products are highly potent antineoplastic agents, but their clinical use is hampered by inadequate antitumor selectivity.[2] The cycloaromatization of enediynes is also employed in the development of novel potent nucleases[3] and *p*-phenylene polymers for microelectronic fabrication.[4] The photochemical triggering of enediyne cycloaromatization is a very attractive idea as it allows for the spatial and temporal control of the Bergman cyclization. The direct irradiation of acyclic[5,6] and cyclic[7] enediynes, as well as of natural antibiotic Dynemicin A,[8] is known to cause light-induced cycloaromatization. However, quantum and chemical yields of this process are usually low. The efficiency of the photochemical Bergman cyclization can be substantially improved by adjusting the electronic properties of substituents[9] and/or by using different modes of excitation energy transfer, for example, MLCT.[6] In addition, several caged enediynes have been prepared, which undergo conventional chemical activation after the photochemical uncaging step.[10]

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Our group explores the alternative strategy: the in situ photochemical generation of reactive enediynes from thermally stable precursors. The photogenerated enediyne then undergoes facile thermal Bergman reaction. Thus, replacement of one of the triple bonds in an enediyne structure with a cyclopropenone group produces thermally stable precursors.[11] UV photolysis of these compounds results in the decarbonylation of cyclopropenone moiety[12] and the formation of reactive enediynes. UV irradiation, however, is not compatible with many biomedical applications, which require the use of light in a so-called "phototherapeutic window", a region of relative tissue transparency between 650 and 950 nm. The energy of red or NIR photons, on the other hand, is not sufficient to trigger most photochemical reactions. One of the approaches allowing for the alleviation of this problem is to employ nonresonant two-photon excitation (2PE). At high light fluxes chromophores might simultaneously absorb two red/NIR photons producing excited states the same as or similar to ones accessible by excitation with UV light of twice the frequency.[13] In addition, 2PE also allows for the 3-D spatial control of photoinduced processes.[14] While many efficient two-photon fluorophores have been reported,[15] the field of two-photon photochemistry remains relatively unexplored.[16] Even fewer examples of two-photon induced activation or release of bilogicaly relevant structures are known.[17]

This report describes the first two-photon induced generation of reactive enediyne, as well as the Bergman cyclization of the photoproduct (Scheme 1). We also report direct determination of the two-photon absorption cross-section of the precursor **1**.

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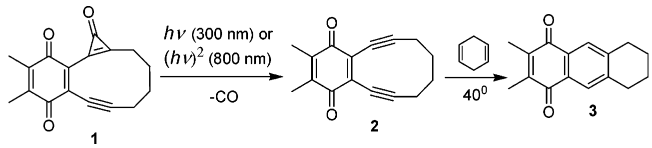
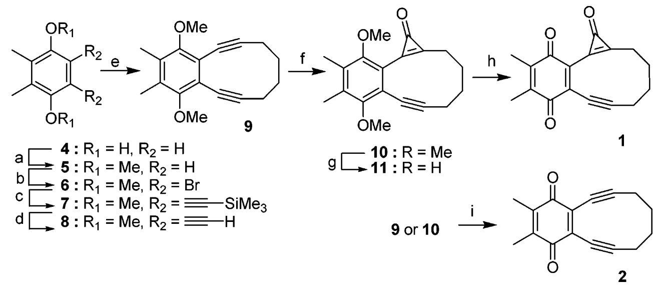
SCHEME 1



SCHEME 2 [a]



[a] Reagents and conditions: (a) Me_2SO_4, K_2CO_3, acetone; (b) Br_2, $CHCl_3$, 77% (two steps); (c) HC≡$CSiMe_3$, $Pd(PPh_3)_2Cl_2$, CuI, PPh_3, piperidine; (d) K_2CO_3, MeOH, 71% (two steps); (e) *n*-BuLi, $I(CH_2)_4I$, THF, HMPA, −78 °C → rt, 42%; (f) $CHCl_3$, *n*-BuLi, THF, −78 °C, 86%; (g) BBr_3, CH_2Cl_2, −78 °C → rt; (h) $FeCl_3$, THF, 23% (two steps); (i) CAN in aq acetonitrile, 81% (**10**) or 89% (**9**).

Results and Discussion

Synthesis of Cyclopropenone 1. Cyclopropenone **1** was prepared in eight steps starting from 2,3-dimethyl-1,4-hydroquinone (**4**). The methylation of hydroquinone **4** followed by the bromination of the product **5** provided 1,2-dibromo-3,6-dimethoxy-4,5-dimethylbenzene (**6**) in a good yield. The Pd(0)/Cu(I) mediated coupling of dibromide **6** with trimethylsilyl acetylene in piperidine and the subsequent cleavage of trimethylsilyl protection in methanol under basic conditions afforded diacetylene **8** in 71% yield. The benzannulated enediyne **9** has been prepared by the reaction of the dianion of **8** with 1,4-diiodobutane in THF−HMPA solvent. The crucial monocyclopropanation step was achieved by the addition of dichlorocarbene, generated in situ from chloroform and *n*-BuLi, followed by the hydrolysis in concentrated hydrochloric acid at −78 °C to form cyclopropenone **10** in excellent yield (Scheme 2).

The oxidative demethylation of the hydroqiunone moiety of **10** proved to be challenging. Complex mixtures of ring-open products were formed under various conditions (e.g., AgO/HNO_3[18] or H_2SO_4/HNO_3[19]). Treatment of **10** with CAN in aqueous acetonitrile[20] resulted in clean formation of enediyne **2**. Recognizing that the cyclopropenone group might be extremely sensitive to strong oxidants we turned our attention to stepwise demethylation and oxidation protocols. Reaction of cyclopropenone **10** with boron tribromide gave rise to hydroquinone **11**, which in turn was oxidized by $FeCl_3$ to produce the cyclopropenone-containing enediyne precursor **1** in 23% yield. Enediyne **2** was prepared by CAN oxidation of **9** (Scheme 2).

Single-Photon Photochemistry of 1. The UV spectrum of the cyclopropenone (**1**) in methanol shows a strong absorption

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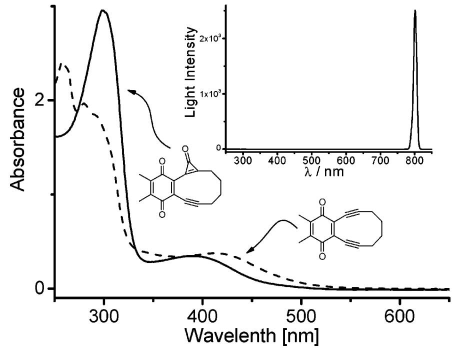

FIGURE 1. UV spectra of ca. 3 × 10^{-4} M methanol solutions of cyclopropenone **1** (solid line) and enediyne **2** (dotted line). The insert shows the spectral width of the Ti:sapphire laser pulse.

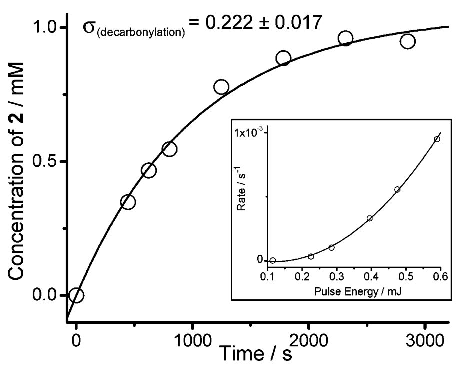

FIGURE 2. Formation of enediyne **2** in the two-photon induced decarbonylation of 1 mM methanol solutions of cyclopropenone **1**. The line shown was drawn with parameters obtained by the least-squares fitting of the experimental data to eq 1. The insert illustrates the dependence of the rate of the photochemical reaction on the pulse energy. The line shows the fit of the data to a second-order polynomial equation.

at 298 nm (log $\epsilon = 3.99$) and a somewhat weaker band at 393 nm (log $\epsilon = 3.06$, Figure 1). The irradiation of **1** in methanol with 300 nm broad-band lamps, as well as monochromatic 355 nm light from the frequency tripled Nd:YAG laser, results in the rapid decarbonylation of the substrate and the formation of enediyne **2**. The quantum yield of this reaction at room temperature is $\Phi = 0.46 \pm 0.04$ at 300 nm in methanol. Incomplete photolysis (up to 40% conversion) of the precursor **1** produces only the target enediyne **2**. However, further irradiation results in the formation of substantial amounts of byproducts and reduces the isolated yield of **2** to 76%. The UV spectrum of the product overlaps substantially with the starting material (Figure 1), which makes us believe that the lower yield of the complete conversion photolysis is due to a secondary photochemical reaction.

Two-Photon Induced Generation of Enediyne 2. The irradiation of **1** in methanol with 800 nm pulses from a Ti: sapphire laser results in the same process as the UV photolysis, i.e., decarbonylation of the cyclopropenone group and the formation of enediyne **2**. The progress of this reaction was monitored by HPLC following the disappearance of starting material **1**, as well as the formation of **2** (Figure 2, Table S1[21]). It is interesting to note that the two-photon induced decarbonylation of cyclopropenone **1** is much cleaner than the single-

(21) See the Supporting information.

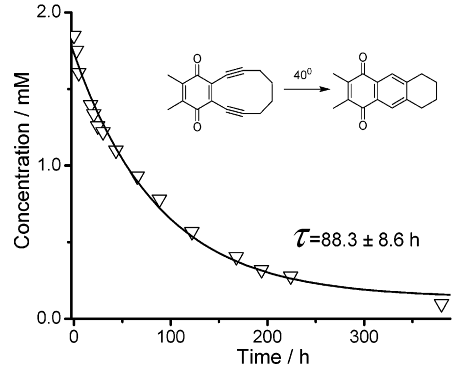

FIGURE 3. Decay of enediyne **2** in 2-propanol at 40 °C. The curve represents the calculated fit to a single-exponential equation.

photon photolysis. The HPLC analysis of reaction mixtures was unable to detect any byproducts in the former case.

The conversion of the starting material (in terms of molar concentration, *C*) by the two-photon induced photoreaction can be described by eq 1,

$$C = C_0 \exp(-\sigma_R \int_{-100\ \mathrm{fs}}^{100\ \mathrm{fs}} I_0^{\,2}\, \mathrm{d}t\ \nu t) \qquad (1)$$

which has been derived from the differential form of Beer's law for the two-photon absorption.[22] In eq 1 I^2 is a squared light flux (photons^2 cm^{-4} s^{-2}), which is integrated for the duration of the laser pulse, ν represents the repetition rate, and σ_R is a two-photon cross-section for the induction of photodecarbonylation reaction. The latter term can be further defined as $\sigma_R = \Phi_{2PE}{*}\sigma$, where Φ_{2PE} is a fraction of two-photon excited molecules that undergo chemical transformation, and σ is the 2PE cross-section of the substrate.

Least-squares fitting of the experimental data to the equation (eq 1) gave us $\sigma_R = 0.222 \pm 0.017$ GM.[23] To convert the experimentally determined two-photon cross-section for the induction of the photodecarbonylation reaction, σ_R, into the two-photon absorption cross-sections of enediyne precursor **1**, we need to know the fraction of two-photon excited molecules that undergo decarbonylation, Φ_{2PE}. The excited state initially populated upon two-photon excitation might be different from that initially populated upon single-photon excitation. However, according to Kasha's rule, photochemical reactions generally occur from the lowest singlet or triplet excited states regardless of the excitation method and the initial exited state.[24] Thus, we can assume that the quantum yield of the two-photon initiated process is equal to its single-photon counterpart, $\Phi_{2PE} = \Phi_{SPE}$. The two-photon absorption cross-section of cyclopropenone **1** is, therefore, equal to $\sigma_{2PE(800)} = \sigma_{R(800)}/\Phi_{SPE} = 0.483 \pm 0.058$ GM.

Bergman Cyclization of 2,3(Octa-1,7-diyne-1,8-diyl)-5,6-dimethylhydroqiunone 1,4-Dimethyl Ether (2). The enediyne **2** undergoes efficient Bergman cyclization upon heating in the degassed benzene at 75 °C in the presence of 1,4-cyclohexadiene. The starting material is completely consumed within 4 h producing 2,3-dimethyl-5,6,7,8-tetrahydroanthracene-1,4-dione (**3**) in 87% yield (Scheme 1). The rate of Bergman cyclization

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of **2** was measured in a 2-propanol solution at 40 °C. The progress of the reaction was followed by HPLC (Figure 3).

The observed rate of Bergman cyclization of **2**, $k_{40°C} = (3.14 \pm 0.31) \times 10^{-6}$ s^{-1}, is much faster than that of the parent 3,4-benzocyclodeca-1,5-diyne. The latter is stable below 50 °C and cyclized at 84 °C with $k = 8 \times 10^{-6}$ s^{-1}.[25] Direct comparison of these rates, however, should be done with caution because the rate of enediyne cyclization is known to depend on the solvent, as well as on the concentration and nature of hydrogen donor.[25]

It is important to note that the starting cyclopropenone **1** is perfectly stable at 40 °C and shows no signs of decomposition up to 90 °C.

Conclusions. We have shown the feasibility of the in situ two-photon induced generation of reactive enediynes using light within the "phototherapeutic window". The cyclopropenone-containing enediyne precursor **1** is stable in the dark even at elevated temperatures but undergoes efficient photodecarbonylation producing reactive enediyne **2**. The latter undergoes Bergman cyclization at biologically relevant temperatures. The two-photon induced photochemical reaction of **1** is much cleaner because it is not accompanied by the secondary photochemistry.

Experimental Section

Single-Photon Photochemistry. The preparative and analytical photolyses of **1** were conducted in methanol solutions with a Rayonet photoreactor. Preparative 300 nm irradiation of **1** in methanol allowed us to isolate 2,3-(octa-1,7-diyne-1,8-diyl)-5,6-dimethyl-1,4-benzoquinone (**2**), which was found to be identical with the sample prepared independently. The quantum yield of the photodecarbonylation reaction of **1** was measured in methanol solutions by using ferrioxalate actinometry.[26]

Two-Photon Induced Enediyne Generation. TPE experiments were conducted with 800 nm pulses generated by an amplified Ti: sapphire laser operating at 1 kHz. The laser beam was attenuated by a diaphragm with a 6.15 mm opening. The power output of the laser after the diaphragm was 0.61 W, which was reduced to 0.55 W after passing through the sample. At the concentration of the substrate used in these experiments the loss of energy after the sample is mostly due to the losses on the phase boundaries, which allows us to evaluate the laser power within the sample as 0.58 W or 580 μJ per pulse^{-1}. The shape of the laser pulse was determined to be close to Gaussian with the half-height width of 94 fs. Using these parameters we have calculated the distribution of light intensity and squared light intensity within the pulse assuming ideal Gaussian shape of the pulse. For the integration of the squared light intensity we have selected the integration limits of ±100 fs from the center of the pulse, as the value of I^2 at these extremes drops to less than 0.2% of the maximum.

1,2-Dibromo-3,6-dimethoxy-4,5-dimethylbenzene (6).[27] A suspension of 2,3-dimethyl-1,4-hydroquinone (**4**) (5 g, 36.23 mmol), Me_2SO_4 (10.4 g, 72.46 mmol), and K_2CO_3 (25 g) in acetone (300 mL) was refluxed for 24 h under argon. The reaction mixture was cooled to room temperature, filtered, and concentrated in a vacuum. The oily residue was dissolved in ethyl acetate−hexanes (1:12) mixture, passed through a short silica gel column, and concentrated under vacuum to give 5.2 g of crude 2,3-dimethyl-1,4-dimethylbenzene (**5**).

A solution of bromine (11 g, 68.3 mmol) in 50 mL of chloroform was added dropwise to a solution of crude **5** in chloroform (100 mL), and the resulting mixture was protected from light and stirred for 60 min at room temperature. The reaction mixture was washed with an aqueous solution of $Na_2S_2O_5$ and water, dried over anhydrous $MgSO_4$, and concentrated. The residue was purified by chromatography on silica gel (ethyl acetate−hexanes 1:20) to give 9 g (27.8 mmol, 77%) of 1,2-dibroro-3,6-dimethoxy-4,5-dimethylbenzane (**6**). R_f 0.55 (ethyl acetate−hexanes 1:5); mp 117−118 °C (lit.[27] mp 117−119 °C).

1,2-Diethynyl-3,6-dimethoxy-4,5-dimethylbenzene (8).[28] Pd-$(PPh_3)_2Cl_2$ (1 g, 1.43 mmol), CuI (0.36 g, 1.88 mmol), and trimethylsilylacetylene (17.0 g, 173 mmol) were added to a degassed solution of dibromide **6** (8 g, 24.70 mmol) in piperidine (ca. 120 mL) at room temperature. The reaction vessel was sealed and the mixture was stirred for 24 h at 85 °C. After being cooled to room temperature, the reaction mixture was filtered and concentrated in a vacuum. The residue was dissolved in a ethyl acetate−hexanes (1:30) mixture, passed through a short silica gel column, and concentrated in a vacuum to give crude 1,4-dimethoxy-2,3-dimethyl-5,6-bis(trimethylsilanylethynyl)benzene (**7**). R_f 0.36 (ethyl acetate−hexanes 1:20); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.82 (s, 6 H), 2.16 (s, 6 H), 0.27 (s, 18 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.9, 132.5, 117.8, 102.3, 99.6, 60.5, 12.8, 0.0; MS calcd for $C_{20}H_{30}O_2Si_2$ (M^+) 358, found 358.

A methanol solution of crude diacetylene **7** was added to a stirred suspension of K_2CO_3 (14 g, 100 mmol) in methanol (120 mL), and the resulting mixture was stirred for 1 h at room temperature. The reaction was quenched by saturated aqueous NH_4Cl, and most of the solvent was removed in a vacuum. Ethyl acetate was added to the mixture, then the organic layer was separated, washed with water and brine, dried over anhydrous $MgSO_4$, and concentrated in a vacuum. The residue was purified by chromatography on silica gel (ethyl acetate−hexanes 1:25) to give 3.76 g of **8** (17.57 mmol, 71% over two steps) as a white powder. R_f 0.38 (ethyl acetate−hexanes 1:5); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.81 (s, 6 H), 3.49 (s, 2 H), 2.17 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.2, 133.1, 117.2, 84.5, 78.3, 60.8, 12.9; MS calcd for $C_{14}H_{14}O_2$ (M^+) 214, found 214.

2,3-(Octa-1,7-diyne-1,8-diyl)-5,6-dimethyl-1,4-hydroquinone Dimethyl Ether (9). *n*-BuLi (2.5 M solution in hexanes, 7.85 mL, 19.6 mmol) was added to a stirred solution of 1,2-diethynyl-3,6-dimethoxy-4,5-dimethylbenzene (**8**) (2.0 g, 9.35 mmol) in THF (400 mL) and HMPA (20 mL) at −78 °C under argon. After 2 h at this temperature, 1,4-diiobutane (2.91 g, 9.40 mmol) was added dropwise, then the reaction mixture was allowed to reach room temperature and stirred for 24 h. The reaction was quenched by addition of phosphate buffer, partially concentrated, diluted with hexanes passed through a short silica gel column, and concentrated in a vacuum. The residue was purified by chromatography on silica gel (ethyl acetate−hexanes 1:30 → 1:25) to give 1.05 g (3.91 mmol, 42%) of 2,3-(octa-1,7-diyne-1,8-diyl)-5,6-dimethylhydroquinone 1,4-dimethyl ether (**9**) as colorless crystals, which decompose upon heating. R_f 0.40 (ethyl acetate−hexanes 1:5); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.85 (s, 6 H), 2.49 (m, 4 H), 2.16 (s, 6 H), 1.96 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.3, 130.8, 120.8, 102.4, 79.0, 60.8, 28.6, 21.9, 12.7; HRMS calcd for $C_{18}H_{20}O_2$ (M^+) 268.1463, found 268.1462.

Cyclopropenone 10. A solution of *n*-BuLi (2.5 M solution in hexanes, 2.34 mL, 5.87 mmol) was added dropwise over ca. 1.5 h to a stirred solution of enediyne **9** and $CHCl_3$ (0.8 g 6.67 mmol) in THF at −78 °C. The resulting solution was stirred for 30 min, quenched by 3 mL of concentrated HCl, and slowly warmed to room temperature. Most THF was removed in a vacuum. The reaction mixture was diluted with ether, washed with a saturated solution of $NaHCO_3$, water, and brine, dried over anhydrous $MgSO_4$, and concentrated. The residue was purified by chromatography on silica gel (CH_2Cl_2−hexanes 1:5 → CH_2Cl_2 → ethyl

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acetate) to give 0.353 g (1.19 mmol, 86% calculated on recovered enediyne) of cyclopropenone **10** as dark orange oil, and 0.347 g (1.29 mmol) of enediyne **9**. R_f 0.42 (ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.91, 3.89 (s, 6 H), 3.04 (t, J = 6.6 Hz, 2 H), 2.52 (t, J = 5.4 Hz, 2 H), 2.26 (s, 6 H), 2.09−2.05 (m, 2 H), 1.8−1.72 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.7, 156.6, 155.2, 154.3, 153.2, 136.4, 132.3, 120.8, 114.9, 102.0, 96.1, 78.9, 62.5, 61.0, 26.39, 26.41, 26.0, 18.8, 13.2, 12.8; IR (CCl_4) 2934 (m), 2858 (w), 1840 (s), 1627 (s), 1461 (m), 1397 (m); HRMS calcd for $C_{19}H_{20}O_3$ (M^+) 296.1412, found 296.1414.

Cyclopropenone 1. A solution of BBr_3 (1 M in CH_2Cl_2, 7 mL, 7 mmol) was added dropwise to a solution of dimethyl ether **10** (0.45 g, 1.52 mmol) in 80 mL of CH_2Cl_2 at −78 °C. The resulting mixture was stirred for 4 h at −78 °C, slowly warmed to room temperature, and stirred for another 4 h. Reaction was quenched by water (50 mL), the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were dried over anhydrous sodium sulfate and concentrated in a vacuum to give 0.2 g of crude hydroquinone **11**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.91 (t, J = 6.6 Hz, 2 H), 2.52 (t, J = 6.0 Hz, 2 H), 2.24, 2.23 (s, 6 H), 2.05−1.95 (m, 2 H), 1.83−1.75 (m, 2 H); MS calcd for $C_{17}H_{16}O_3$ (M^+) 268, found 268.

Anhydrous $FeCl_3$ was added to the solution of crude hydroquinone **11** in 30 mL of THF at room temperature. The reaction mixture was stirred for 30 min, then quenched with water and ethyl acetate. The organic layer was separated, washed with water and brine, dried over anhydrous sodium sulfate, and concentrated in a vacuum. The residue was purified by chromatography on silica gel (ethyl acetate−hexanes 5:1) to give 92 mg (0.346 mmol, 23% over two steps) of quinoid cyclopropenone **1** as a deep orange oil, which crystallizes upon standing in the refridgerator. R_f =0.29 (ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.96 (t, J = 6.6 Hz, 2 H), 2.55 (t, J = 5.4 Hz, 2 H), 2.058, 2.045 (s, 6 H), 1.73−1.64 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.9, 182.2, 163.1, 157.2, 152.0, 141.9, 141.3, 133.7, 130.3, 117.2, 79.1, 27.1, 26.3, 26.05, 19.6, 12.62, 12.58; HRMS calcd for $C_{17}H_{14}O_3$ (M^+) 266.0943, found 266.0931.

2,3-(Octa-1,7-diyne-1,8-diyl)-5,6-dimethylquinone (2). A solution of **9** (0.1 g, 0.373 mmol) in 5 mL of acetonitrile was added to a stirred solution of CAN (1.63 g, 2.98 mmol) in 10 mL of a acetonitrile−water mixture (1:1). The reaction mixture was stirred for 45 min, then diluted with water and CH_2Cl_2. The organic layer was separated, and the aqueous layer was extracted with 2 × 5 mL of CH_2Cl_2. Combined organic layers were washed with water and dried over anhydrous sodium sulfate. The solvent was removed in a vacuum to give 79 mg (0.332 mmol, 89%) of quinone **2** as yellow crystalline material. Mp 118−120 °C dec. R_f 0.25 (EtOAc: Hex 1:5); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.51 (s, b, 4 H), 2.00 (s, 6 H), 1.96−1.90 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.6, 140.8, 137.3, 114.9, 79.6, 28.2, 22.4, 12.5; HRMS calcd for $C_{16}H_{14}O_2$ (M^+) 238.0994, found 238.0997.

2,3-Dimethyl-5,6,7,8-tetrahydroanthracene-1,4-dione (3). A solution of **2** (0.087 g, 0.37 mmol) in benzene:1,4-cyclohaxadiene (4:1, 15 mL) was degassed, the reaction vessel was sealed, and the mixture was stirred for ∼5 h at 75 °C. After cooling and removing the solvent, the residue was chromatographed on silica gel (ethyl acetate−hexanes 1:1) to give 78 mg (0.33 mmol, 87%) of **3** as yellow crystals. Mp 159−161 °C. R_f 0.25 (EtOAc:hexanes 1:5); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (s, 2 H), 2.87 (m, 4 H), 2.15 (s, 6 H), 1.83 (m. 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 185.1, 143.5, 143.2, 129.7, 127.0, 29.7, 22.6, 12.8; HRMS calcd for $C_{16}H_{16}O_2$ (M^+) 240.1150, found 240.1143.

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Supporting Information Available: Experimental details of two-photon photolyses, complete ref 16b, and NMR spectra of compounds **1**−**3** and **7**−**10**. This material is available free of charge via the Internet at http://pubs.acs.org.

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