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Triple Benzannulation of Naphthalene via a 1,3,6-Naphthotriyne Synthetic Equivalent. Synthesis of Dibenz[*a*,*c*]anthracene

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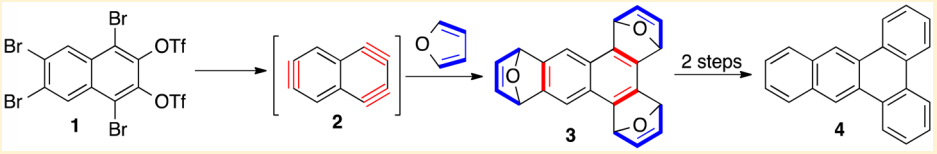
Supporting Information



ABSTRACT: A new synthesis of dibenzo[*a*,*c*]anthracene (**4**) is described that features the generation, from tetrabromo-bis-triflate **1** and phenyllithium, of a 1,3,6-naphthotriyne (**2**) synthetic equivalent that is trapped with 3 equiv of furan to form Diels–Alder tris-adduct **3**. A subsequent two-step deoxygenation of **3** represents the first synthesis of dibenz[*a*,*c*]anthracene (**4**) that involves a tandem aryne Diels–Alder cycloaddition–deoxygenation strategy.

In continuation of our previous work on the syntheses of polycyclic aromatic hydrocarbons (PAHs) via Diels–Alder reactions of naphthalynes and naphthodiynes (as generated by organolithium metalation or Grignard formation) with furans, pyrroles, and isoindoles, followed by extrusion of the bridging atoms,[1−4] we now describe the generation of the 1,3,6-naphthotriyne synthetic equivalent **2** from 1,4,6,7-tetrabromo-2,3-bis-triflate (**1**) and trapping with furan to afford, after deoxygenation, dibenz[*a*,*c*]anthracene (**4**). This PAH, also known as benzo[*b*]triphenylene, is unlike other structurally similar PAHs, which are carcinogenic,[5−7] in that the carcinogenicity of **4** is a subject of debate but is clearly weaker than, for example, that of dibenz[*a*,*h*]anthracene.[8,9] Interestingly, PAH **4** has found use in optoelectronics.[10]

As mentioned above, we have previously generated and trapped synthetic equivalents of naphthodiynes **5**–**7** to afford the corresponding PAHs **8**–**10**, respectively, after deoxygenation (Figure 1).[4] However, the difficulty of generating tris-arynes is well-documented,[11−13] and a search of the literature returned no examples in which 1,3,5-benztriyne or a naphthotriyne had been generated from halogenated arenes or synthetic analogues and trapped in a Diels–Alder reaction.

Our study commenced with the regioselective bromination of the commercially available 2,3-dihydroxynaphthalene (**11**) using 4 equiv of bromine in refluxing glacial acetic acid to give the known 1,4,6,7-tetrabromonaphthalene (**12**) in 90% yield (Scheme 1).[14] Triflation (Tf_2O/2,6-lutidine) of **12** furnished 1,4,6,7-tetrabromonaphthalene-2,3-diyl bis(trifluoromethanesulfonate) (**1**) in 79% yield, which was purified by recrystallization from hexanes and characterized by spectral and elemental analysis.

Using our earlier conditions, when we treated **1** with either phenyllithium, methyllithium, or *n*-butyllithium at 0 °C (Scheme 2) and allowed the reaction mixture to warm to room temperature, there was afforded after workup and isolation a mixture of *syn* and *anti* isomers of bis-adduct triflate **13** (cf. Supporting Information), and a trace of what we subsequently determined was the desired tris-adduct **3**. Attempts to convert **13** to benz[*a*]anthracene (**10**) as shown in Scheme 2 instead gave the unstable 5-hydroxybenz[*a*]-anthracene[15] that was converted to its known acetate **14**.[15] The trace amount of **3** collected by preparative TLC was hydrogenated (Pd/C/hydrogen) and dehydrated (concentrated HCl at 90 °C) to yield a small amount of dibenz[*a*,*c*]anthracene (**4**).

However, when the reaction mixture was refluxed following the addition of phenyllithium (PhLi), the amount of **3** increased dramatically. Thus, we believe that upon addition of PhLi to a solution of **1** and furan in Et_2O at 0 °C, halogen–lithium exchange occurs rapidly to form a transient trimetalated species **15**, which collapses to **16** (Scheme 3). The metalated species **16** has a longer lifetime at room temperature and is trapped by furan (pathway A) to form **13** after aqueous workup. The plausible existence of **16** was not all that surprising because a literature search revealed similar aryllithium species with extended lifetimes at low temperatures.[12,16] At elevated temperatures, aryllithium species **15** undergoes elimination of LiBr and double elimination of LiOTf to generate naphthotriyne **2**, or its equivalent, which is then trapped by furan (pathway B) to form tris-adduct **3** as the major product in 41% yield. Bis-adduct **13** (~7%) was also obtained from this reaction. No other cycloadduct was isolated from the reaction mixture. The structure of **3** was assigned on the basis of its ^{1}H NMR and HRMS analysis and its subsequent conversion to **4**. In particular, ^{1}H NMR spectra of **3** (Figure 2) had a set (shoulders from other diastereomers) of singlet protons at 7.47–7.49 ppm corresponding to the C-14 aromatic ring protons [dibenz[*a*,*c*]anthracene ring numbering (Figure 2)]. The spectrum also displays the characteristic nonequivalent

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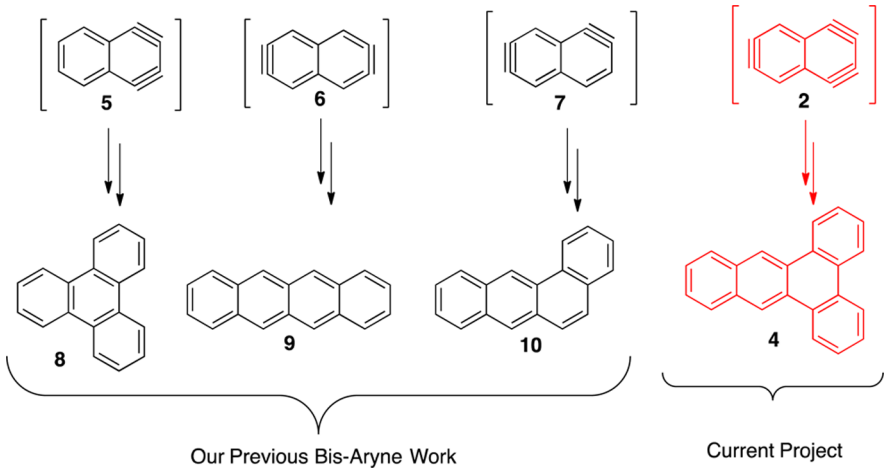
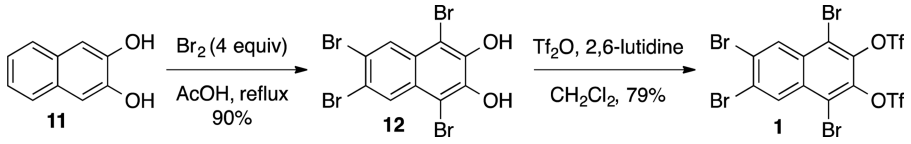
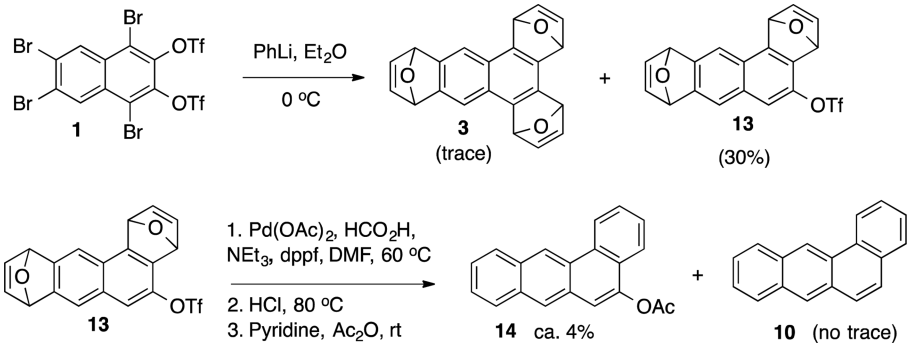


Figure 1. Previous and present work.

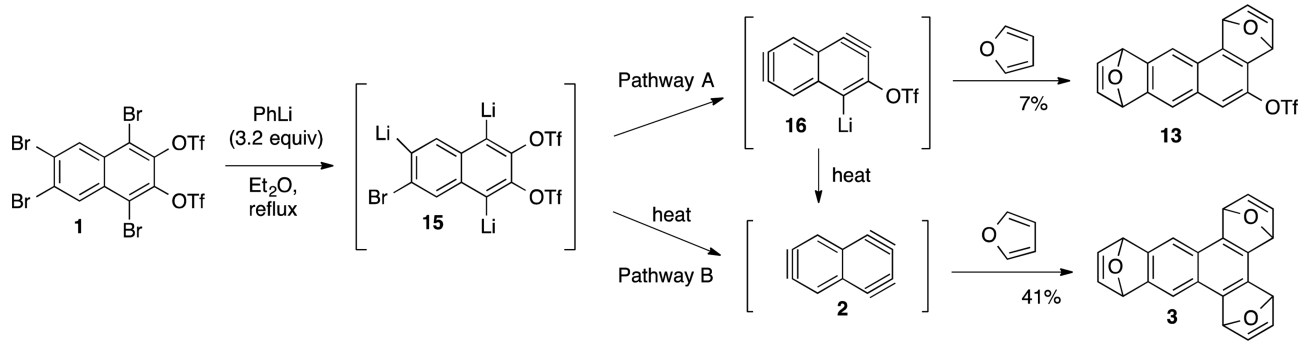
Scheme 1. Synthesis of 1,3,6-Naphthotriyne Precursor 1



Scheme 2. Synthesis and Conversion of Bis-adduct 13 to 5-Acetoxybenz[*a*]anthracene



Scheme 3. Generation and Diels–Alder Cycloaddition of 1,3,6-Naphthotriyne (2)



alkenic and bridgehead protons at 6.89–7.13 and 5.73–6.13 ppm, respectively. Further support for the formation of tris-adduct **3** comes from a comparison of the ^{1}H NMR spectrum of the product resulting from its hydrogenation to **17**. Thus, the disappearance of protons around 6.89–7.13 ppm and appearance of multiplets, which integrated to six protons, in the aliphatic region of the spectrum revealed that the protons at 6.89–7.13 ppm were olefinic. Attempts to generate **2** using magnesium[17] returned mainly starting material and a trace of other unidentified side products.

Without trying to separate the presumed *syn* and *anti* isomers of **3**, we obtained dibenz[*a*,*c*]anthracene (**4**) in two steps by hydrogenation (Pd/C/hydrogen, 99%) of **3** followed by dehydration in refluxing concentrated HCl (Scheme 4, 86%). The spectral data (NMR, UV,[18] and HRMS) were completely identical to those reported in the literature for this PAH.[4,8,9]

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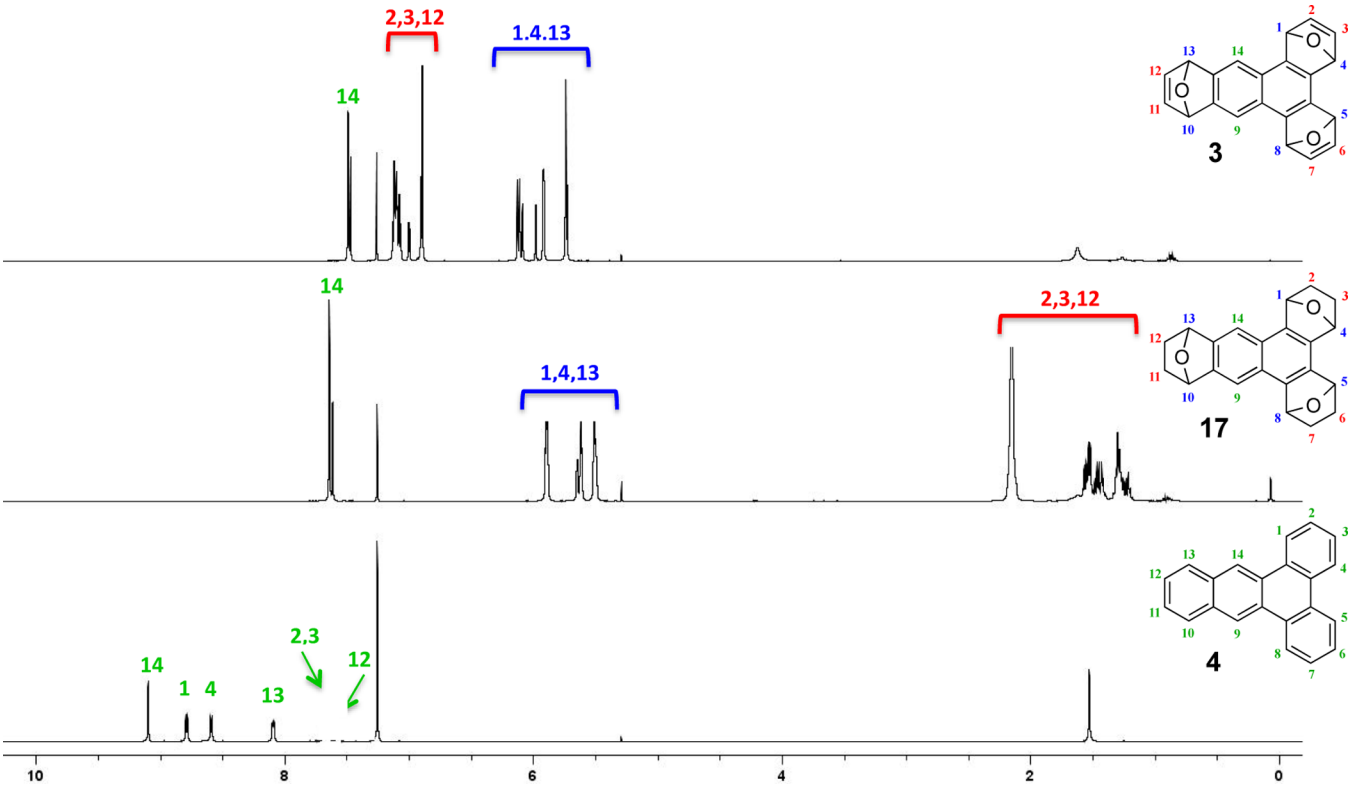
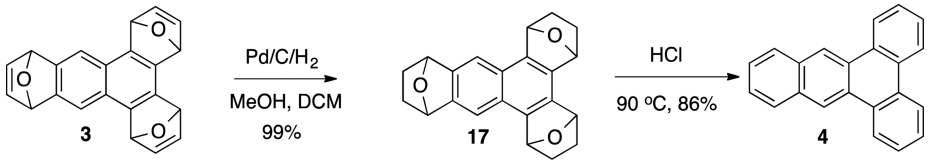


Figure 2. ^{1}H NMR spectrum of tris-adduct **3** and its comparison to that of the product of subsequent hydrogenation (**17**) and that of dibenz[*a*,*c*]anthracene (**4**).

Scheme 4. Synthesis of Dibenz[*a*,*c*]anthracene 4



In conclusion, the generation and trapping of 1,3,6-naphthotriyne (**2**) (or its equivalent) were achieved from the conveniently synthesized 1,4,6,7-tetrabromo-2,3-bis-triflate (**1**).

EXPERIMENTAL SECTION

The general supplemental methods are provided in the Supporting Information.

1,4,6,7-Tetrabromonaphthalene-2,3-diol (12). To a magnetically stirred solution of 2,3-dihydroxynaphthalene (**11**) (3.0 g, 18.7 mmol) in acetic acid (30 mL) was slowly added bromine (3.85 mL, 74.8 mmol). The solution was stirred and heated at reflux for 45 min. After cooling to rt, the reaction mixture was poured onto ice/water (60 mL), and the resulting precipitate was suction filtered. The solid residue was taken up in diethyl ether and washed with 5% $Na_2S_2O_3$, saturated $NaHCO_3$, and brine, dried over $MgSO_4$, and concentrated *in vacuo* to give the product as a yellowish/brown powder (7.97 g, 90%): R_f = 0.51 (1:1 hexanes/ethyl acetate); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.37 (s, 2H), which was in agreement with the literature.[19]

1,4,6,7-Tetrabromonaphthalene-2,3-diyl Bis(trifluoromethanesulfonate) (1). To a stirred solution of 1,4,6,7-tetrabromonaphthalene-2,3-diol (**12**) (2.00 g, 4.25 mmol) and 2,6-lutidine (1.47 mL, 12.7 mmol) in methylene chloride (40 mL) at 0 °C was added triflic anhydride (1.79 mL, 10.6 mmol) over 30 min (5 portions). The reaction mixture was warmed to rt and stirred for 3 h. TLC analysis indicated that the reaction was incomplete. Additional 2,6-lutidine (0.50 mL, 4.32 mmol) and triflic anhydride (0.100 mL, 0.592 mmol) were added. The reaction was quenched when the mixture was washed with saturated NH_4Cl, 5% HCl, saturated $NaHCO_3$, and finally brine. The organic layer was dried over $MgSO_4$ and then loaded onto silica (2.5 g) and the solvent removed *in vacuo*. Purification by dry-pack column chromatography (SiO_2, 100% hexanes) gave **1** as a white solid (2.47 g, 79%). Recrystallization from hexanes afforded **1** as white crystals: R_f = 0.66 (10:1 hexanes/ethyl acetate); mp 132−134 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.68 (s, 2H); ^{13}C NMR (600 MHz, $CDCl_3$) δ 115.2, 117.4, 118.1, 119.4, 128.8, 130.9, 133.1, 138.1; UV (EtOH) λ_{max} 203, 242, 254, 297, 308, 322 nm; HRMS (EI) calcd for $C_{12}H_2O_6S_2F_6{}^{81}Br_2{}^{79}Br_2$ $[M]^+$ 739.5890, found 739.5901. Anal. Calcd for $C_{12}H_2O_6S_2F_6Br_4$ (739.59): C, 19.49; H, 0.27; S, 8.67; F, 15.41; Br, 43.22. Found: C, 19.56; H, 0.18; S, 8.83; F, 15.23; Br, 43.41.

1,4,5,8,10,13-Hexahydro-1,4:5,8:10,13-triepoxybenzo[*f*]tetraphene (3) and 1,4,8,11-Tetrahydro-1,4:8,11-diepoxytetraphen-5-yl Trifluoromethanesulfonate (13). To a solution of **1** (1.138 g, 1.55 mmol) and furan (7.9 mL, 109 mmol) in diethyl ether (20 mL) at reflux was slowly added PhLi (1.7 M in di-*n*-butyl ether, 2.9 mL, 4.96 mmol) in diethyl ether (2.9 mL). The resulting yellow suspension was refluxed for 1 h. After cooling to rt, the reaction mixture was taken up on silica (2 g), concentrated *in vacuo*, and purified by dry-pack column chromatography (SiO_2, 5:1 hexanes/EtOAc) to afford both tris-adduct **3** as a pale yellow solid (206 mg, 41%) and bis-adduct **13** as a yellow/orange solid (45 mg, 7%). *1,4,5,8,10,13-Hexahydro-1,4:5,8:10,13-triepoxybenzo[f]tetraphene* (**3**). From the reaction described above, **3** was isolated as a mixture of *syn* and *anti* isomers: R_f = 0.43 (1:1 hexanes/ethyl acetate); ^{1}H NMR

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(500 MHz, $CDCl_3$) δ 5.73−5.74 (m, 2H), 5.91−5.98 (m, 2H), 6.08−6.13 (m, 2H), 6.89−6.90 (m, 2H), 6.99−7.13 (m, 4H), 7.47−7.49 (m, 2H); HRMS (EI) calcd for $C_{22}H_{14}O_3$ $[M]^+$ 326.0943, found 326.0943. *1,4,8,11-Tetrahydro-1,4:8,11-diepoxytetraphen-5-yl trifluoromethanesulfonate (13)*. Also from the above reaction described above, **13** was isolated as a mixture of *syn* and *anti* isomers: R_f = 0.50 (1:1 hexanes/ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.79−5.80 (m, 2H), 5.90 (br s, 1H), 6.12−6.16 (m, 2H), 6.94 (d, J = 10.6 Hz, 2H), 7.12−7.21 (m, 2H), 7.49 (s, 1H), 7.79 (d, J = 5.8 Hz, 1H); ^{19}F NMR (565 MHz, $CDCl_3$) δ −78.9; HRMS (ES) calcd for $C_{19}H_{10}O_5F_3S$ $[M - H]^-$ 407.0201, found 407.0196.

5-Acetoxybenz[*a*]anthracene (14). To a solution of **13** (35 mg, 0.086 mmol), formic acid (0.052 mL, 1.86 mmol), and triethylamine (0.286 mL, 2.04 mmol) in DMF (2 mL) were added $Pd(OAc)_2$ (1.0 mg, 0.0043 mmol) and 1,1′-bis(diphenylphosphino)ferrocene (2.4 mg, 0.0043 mmol). The reaction mixture was stirred overnight at 60 °C. After cooling to room temperature, the reaction mixture was diluted with methylene chloride, washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The resulting residue was subsequently heated in concentrated HCl (3 mL) at 80 °C for 2 h. After cooling to rt, the reaction mixture was diluted in methylene chloride and then washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to afford a yellow residue. The yellow residue was then dissolved in methylene chloride (2 mL) and treated with pyridine (0.250 mL, 3.1 mmol) and acetic anhydride (0.250 mL, 2.6 mmol). After being stirred overnight, the reaction mixture was purified with preparative thin layer chromatography (10:1 hexanes/ethyl acetate) to afford **14** as a yellow waxy solid (1.0 mg, 4%, for three steps): ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.51 (s, 3H), 7.54−7.56 (m, 2H), 7.59 (s, 1H), 7.65−7.68 (m, 1H), 7.72−7.76 (m, 1H), 7.90−7.92 (m, 1H), 8.01−8.03 (m, 1H), 8.10−8.13 (m, 1H), 8.32 (s, 1H), 8.86 (d, J = 8.2 Hz, 1H), 9.14 (s, 1H);[15] HRMS (ES) calcd for $C_{20}H_{14}O_2$ $[M]^+$ 286.0994, found 286.0989.

1,2,3,4,5,6,7,8,10,11,12,13-Dodecahydro-1,4:5,8:10,13-triepoxybenzo[*f*]tetraphene (17). A suspension of **3** (192 mg, 0.589 mmol) and 10% Pd-C (15 mg) in a methylene chloride/methanol mixture (1:1, 16 mL) was placed under H_2 and stirred overnight. The reaction mixture was subsequently filtered through Celite and concentrated *in vacuo*, to furnish **17** as a light yellow solid (195 mg, 99%). Compound **17** was isolated as a mixture of *syn* and *anti* isomers: R_f = 0.57 (1:1 hexanes/ethyl acetate); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.27−1.58 (m, 6H), 2.15 (m, 6H), 5.49 (m, 2H), 5.61−5.64 (m, 2H), 5.88−5.90 (m, 2H), 7.61−7.64 (m, 2H); HRMS (EI) calcd for $C_{22}H_{20}O_3$ $[M]^+$ 332.1413, found 332.1406.

Dibenz[*a*,*c*]anthracene (4). A solution of **17** (188 mg, 0.566 mmol) in concentrated HCl (10 mL) was heated at 90 °C overnight. After cooling to rt, the reaction mixture was diluted in methylene chloride and washed with brine, dried over $MgSO_4$, and concentrated *in vacuo* to afford a brown solid (135 mg, 86%), which was determined to be homogeneous by TLC. Passage through silica gel (50:1 hexanes/ethyl acetate) afforded 104 mg (66%) of colorless material. The sample was recrystallized from EtOH to give colorless silky needles: mp 203−204 °C (lit.[8] mp 205−206 °C); R_f = 0.46 (10:1 hexanes/ethyl acetate); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.56−7.59 (m, 2H), 7.64−7.69 (m, 4H), 8.08−8.12 (m, 2H), 8.59−8.61 (m, 2H), 8.78−8.80 (m, 2H), 9.10 (s, 2H), which are in agreement with those reported previously;[4] ^{13}C NMR (125 MHz, $CDCl_3$) δ 122.1, 123.5, 123.7, 126.1, 127.5, 127.7, 128.1, 128.4, 130.1, 130.2, 132.3, which are in agreement with those reported previously;[11] UV (EtOH) λ_{max} 208, 219, 242, 251, 267, 276, 286, 323 nm, which are in agreement with those reported previously;[18] HRMS (EI) calcd for $C_{22}H_{14}$ $[M]^+$ 278.1096, found 278.1096.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01972.

^{1}H and ^{13}C NMR spectra for new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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