Improved Synthesis of 1,8-Diiodoanthracene and Its Application to the Synthesis of Multiple Phenylethynyl-Substituted Anthracenes

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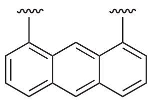
Abstract: 1,8-Diiodoanthracene was synthesized from 1,8-dichloroanthraquinone in three steps by improved procedures in 41% overall yield. Some anthracene derivatives carrying multiple phenylethynyl groups were synthesized from 1,8-diiodoanthracene and 4,5-diiodo-9-anthrone.

Key words: halogenation, reduction, cross-coupling, ethynylation, anthracenes

A 1,8-anthrylene unit **1** has been utilized as a spacer connecting two functional groups at an appropriate interval of ca. 5.0 Å (Figure 1).[1,2] In some cases, the fluorescent property of anthracene chromophores is intelligently applied for the design of molecular sensors.[3] One of the most practical precursors of these compounds is 1,8-dichloroanthracene, which can be coupled with organometallic reagents or amines by metal-catalyzed reactions to give the corresponding alkyl, alkynyl, aryl, and amino derivatives.[1,4] Occasionally, 1,8-dibromoanthracene is also used in the Sonogashira and other related coupling reactions.[5] Although these precursors are sufficient for a range of reactions, the more reactive derivative, 1,8-diiodoanthracene (**2**), is expected to widen the scope of applications of this spacer. The literature survey revealed that compound **2** has been unknown until Lovell and Joule reported the first synthesis in 1997.[6] Although **2** and its 10-OCH_3 analogue were used for reactants of the Suzuki and Sonogashira couplings since then, further applications of these precursors were rather limited because of the synthetic inaccessibility. Recently, we reported the synthesis and properties of 1,8-anthrylene-ethynylene oligomers, where 1,8-diiodoanthracene was a key building unit.[7] Therefore, we needed to facilitate the supply of the starting material to promote the series of studies. We herein report an improved synthesis of **2** and its anthrone analogue **5** as well as their applications to the synthesis of anthracene derivatives with multiple phenylethynyl groups as novel fluorophors.[8]



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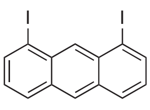

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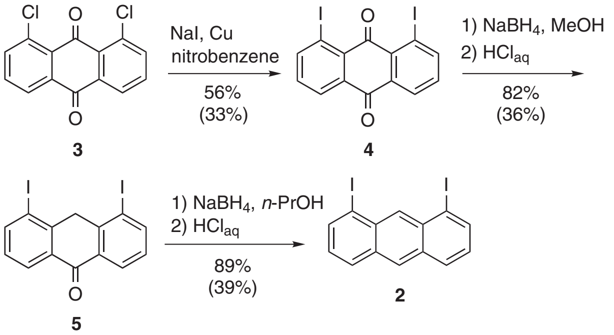
Figure 1 1,8-Anthrylene unit **1** as spacer and 1,8-diiodoanthracene (**2**)

Compound **2** was prepared from 1,8-dichloroanthraquinone in three steps as shown in Scheme 1, in which the improved yields are indicated together with those reported in the literature.[6]



Scheme 1 Synthesis of 1,8-diiodoanthracene (**2**). The yields from the original procedure[6] are indicated in parentheses.

In the first step of iodination, the reaction time was extended from 16 to 43 hours to give the diiodide **4** in 56% yield. It is important to purify this product sufficiently by recrystallization from chlorobenzene for the next reaction. The anthraquinone **4** was reduced with $NaBH_4$ in methanol followed by acid-catalyzed dehydration to give the anthrone **5**. After several attempts, we found that the use of finely powdered **4** and the slow addition of $NaBH_4$ afforded a satisfactory result. When $NaBH_4$ was added in small portions to a suspension of **4** in methanol over three hours (cf. 15 min in the original procedure), **5** was obtained in 82% yield after chromatographic purification together with small amounts of **2** and its 10-OCH_3 derivative. No 1,8-diiodo-9-anthrone was found in the reaction mixture. Compound **4** was poorly soluble in methanol, but the solid dissolved in the solvent as the reaction proceeded. When $NaBH_4$ was added rapidly, not only the formation of the by-products but also the recovery of the insoluble starting material became significant. We consider that the above condition meets the balance between the solubility of the substrate and the concentration of $NaBH_4$ for the smooth conversion into the anthrone. In the next reduction step, the poor solubility of **5** in methanol was a problem in the original procedure. When the reaction was carried out in propan-1-ol instead of methanol, the reduction occurred

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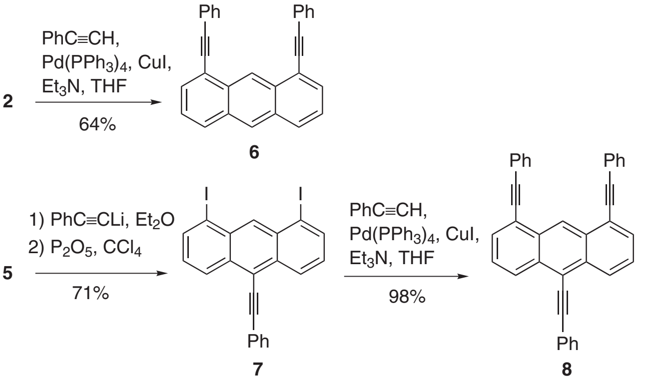
smoothly at room temperature. The reduced product was treated with concentrated HCl to give the anthracene **2** in 89% yield. So far, the overall yield of the three-step conversion was considerably improved from 4.6% to 41% by the optimization of the reaction conditions.

We applied compounds **2** and **5** to the synthesis of phenylethynyl substituted anthracene derivatives, which were attractive as highly fluorescent compounds (Scheme 2). The Sonogashira reaction of **2** with phenylacetylene worked smoothly at room temperature to form the 1,8-disubstituted derivative **6** in moderate yield. The treatment of anthrone **5** with lithium phenylacetylide, which was prepared from phenylacetylene and butyllithium, followed by P_2O_5 afforded the 10-substituted derivative **7**. The coupling of this compound with phenylacetylene afforded the 1,8,10-trisubstituted derivative **8**. Compounds **6** and **8** showed strong emission bands at 423 and 464 nm, respectively, upon excitation at 393 nm in cyclohexane. The fluorescence quantum yields were 0.80 and 0.67 for **6** and **8**, respectively, these values being a little smaller than that of 9,10-bis(phenylethynyl)anthracene (Φ_f 0.96).[8]



Scheme 2 Synthesis of anthracene derivatives with multiple phenylethynyl groups.

These examples reveal that **2** and **5** are versatile precursors toward multiply substituted anthracenes. Iodo groups in these compounds can be converted to various functional groups by metal-catalyzed coupling reactions more readily than the corresponding bromides and chlorides.

Melting points are uncorrected. Elemental analyses were performed by a Perkin-Elmer 2400 series analyzer. ^{1}H and ^{13}C NMR spectra were measured on a JEOL GSX 400 (^{1}H: 400 MHz and ^{13}C: 100 MHz) or a Varian Gemini-300 (^{1}H: 300 MHz and ^{13}C: 75 MHz) spectrometer with TMS as an internal reference. High-resolution FAB mass spectra were measured on a JEOL MStation-700 spectrometer. UV and fluorescence spectra were measured on a Hitachi U-3000 spectrometer and a JASCO FP-6500 spectrofluorometer, respectively, with a 10 mm cell in spectroscopic grade solvents. Column chromatography and TLC were carried out with Merck Silica Gel 60 and Silica Gel 60 F_{254}, respectively. Product yields are values after chromatographic separation except for **4**.

1,8-Diiodoanthraquinone (4)

A mixture of 1,8-dichloroanthraquinone (**3**; 25.0 g, 90.2 mmol), Cu powder (2.01 g, 31.5 mmol), and NaI (50.0 g, 334 mmol) in $PhNO_2$ (110 mL) was heated under reflux for 43 h. The solvent was removed by steam distillation, and H_2O was removed by decantation followed by evaporation. The solid was dissolved in a minimum amount of boiling chlorobenzene (ca. 1.0 L), and the insoluble materials were removed by filtration while hot. The filtrate was allowed to stand for 3 d, and the formed brown crystals were collected by filtration. The filtrate was concentrated by evaporation to give an extra amount of pure **1**. The total yield was 23.5 g (56%); mp 269–270 °C (Lit.[6,9] mp 278–280 °C).

^{1}H NMR ($CDCl_3$): δ = 7.35 (t, *J* = 7.7 Hz, 2 H), 8.28 (dd, *J* = 1.4, 7.7 Hz, 2 H), 8.40 (dd, *J* = 1.4, 7.7 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 93.19, 127.51, 133.39, 134.60, 134.69, 148.23, 180.82.

4,5-Diiodo-9-anthrone (5)

To a stirred suspension of **4** (2.76 g, 6.00 mmol), which was ground to a fine powder with a motor prior to use, in MeOH (120 mL) was added $NaBH_4$ (1.13 g, 30.0 mmol) in small portions over 3 h (ca. 0.3 g every 1 h). The mixture was further stirred for 1 h at r.t. to give a clear brown solution. After addition of conc. HCl (15 mL), the mixture was refluxed for 1 h. The formed solid was collected by filtration, washed with H_2O (300 mL), and air-dried. The solid was separated by chromatography on silica gel (hexane–CH_2Cl_2, 10:1 to 1:1). The desired compound was separated as the most polar fraction (2.19 g, 82%, R_f 0.32, hexane–CH_2Cl_2, 1:1) from two by-products, 1,8-diiodoanthracene (26 mg, 1%, R_f 0.35, hexane) and 1,8-diiodo-10-methoxyanthracene (243 mg, 9%, R_f 0.11, hexane). Recrystallization from toluene afforded **5** as yellow crystals; mp 211–212 °C (Lit.[6] mp 210–212 °C).

^{1}H NMR (CD_2Cl_2): δ = 4.06 (s, 2 H), 7.26 (t, *J* = 7.8 Hz, 2 H), 8.20 (d, *J* = 7.8 Hz, 2 H), 8.33 (d, *J* = 7.8 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 46.87, 101.23, 128.05, 129.16, 132.87, 142.65, 144.10, 183.25.

1,8-Diiodoanthracene (2)

To a stirred suspension of **5** (2.00 g, 4.48 mmol) in *n*-PrOH (90 mL) was added $NaBH_4$ (0.847 g, 22.4 mmol) with small portions over 30 min (ca. 0.1 g every 5 min). The mixture was further stirred for 1 h at r.t. to give a clear orange solution. After addition of conc. HCl (12 mL), the mixture was refluxed for 1 h. The formed solid was collected by filtration, washed with H_2O (100 mL), and air-dried. The solid was separated by chromatography on silica gel (hexane–CH_2Cl_2, 5:1) to give the desired compound as a yellow solid (1.72 g, 89%, R_f 0.35, hexane) with the recovery of the starting material (123 mg, 6%). Recrystallization from EtOH afforded **2** as yellow crystals; mp 190–191 °C (Lit.[6,9] mp 201–202 °C).

^{1}H NMR ($CDCl_3$): δ = 7.21 (dd, *J* = 6.9, 8.2 Hz, 2 H), 8.02 (d, *J* = 8.5 Hz, 2 H), 8.16 (d, *J* = 6.9 Hz, 2 H), 8.33 (s, 1 H), 8.96 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 99.94, 126.75, 128.12, 128.81, 132.12, 133.24, 136.80, 137.70.

1,8-Bis(phenylethynyl)anthracene (6)

A solution of 1,8-diiodoanthracene (**2**; 172 mg, 400 μmol) in a mixture of THF (10 mL) and Et_3N (10 mL) was degassed by bubbling argon for 20 min. To the solution were added phenylacetylene (176 μL, 1.60 mmol), $Pd(PPh_3)_4$ (69 mg, 60 μmol), and CuI (11 mg, 60 μmol). The mixture was refluxed for 24 h under argon. The solvent was removed by evaporation. The crude product was purified by chromatography on silica gel (hexane–$CHCl_3$, 8:1) to give the desired product as a yellow solid (96 mg, 64%). Recrystallization from hexane afforded **6** as yellow crystals; mp 152–153 °C (Lit.[10] mp 153–154 °C).

^{1}H NMR ($CDCl_3$): δ = 7.22 (m, 4 H), 7.33 (m, 2 H), 7.48 (dd, *J* = 6.8, 8.8 Hz, 2 H), 7.59 (m, 4 H), 7.81 (dd, *J* = 1.0, 6.8 Hz, 2 H), 8.02 (d, *J* = 8.8 Hz, 2 H), 8.47 (s, 1 H), 9.64 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 87.67, 94.96, 121.56, 123.35, 124.15, 125.16, 127.47, 128.25, 128.38, 128.91, 130.52, 131.48, 131.56, 131.80.

UV (cyclohexane): λ_{max} (ε) = 264 (126000), 283 (41600), 354 (7400), 373 (12300), 393 (19500), 416 nm (18400).

FL (cyclohexane): λ_{max} = 423 nm (λ_{ex} = 393 nm).

1,8-Diiodo-10-(phenylethynyl)anthracene (7)

To a solution of phenylacetylene (330 μL, 3.00 mmol) in anhyd Et_2O (10 mL) was added a 1.56 mol/L hexane solution of BuLi (1.47 mL, 2.70 mmol) with a syringe over 5 min at –78 °C under argon. The mixture was allowed to warm up to r.t., and stirred for 1.5 h. After addition of **5** (233 mg, 0.500 mmol), the mixture was stirred for 48 h at r.t. and then quenched with aq NH_4Cl (5 mL). The organic layer was separated, and the aqueous layer was extracted with Et_2O (10 mL). The combined organic layers were dried ($MgSO_4$), and evaporated. The residue was dissolved in CCl_4 (5 mL), and the solution was heated with P_2O_5 (500 mg) under reflux for 20 min. The solid was washed with $CHCl_3$ (3 × 50 mL), and the combined solution was evaporated. The crude product was purified by chromatography on silica gel (hexane–CH_2Cl_2, 5:1) to give the desired compound as a yellow solid (188 mg, 71%, R_f 0.60, hexane–CH_2Cl_2, 2:1). Recrystallization from hexane afforded **7** as yellow crystals; mp 239–241 °C.

^{1}H NMR ($CDCl_3$): δ = 7.31 (dd, *J* = 7.3, 8.8 Hz, 2 H), 7.42–7.49 (m, 3 H), 7.75–7.77 (m, 2 H), 8.20 (d, *J* = 6.8 Hz, 2 H), 8.67 (d, *J* = 8.3 Hz, 2 H), 9.01 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 85.38, 100.56, 101.70, 119.54, 123.07, 127.69, 127.73, 128.54, 128.84, 131.64, 132.63, 133.06, 137.93, 138.09.

UV (cyclohexane): λ_{max} (ε) = 267 (97000), 304 (14400), 409 (19000), 432 nm (18400).

Anal. Calcd for $C_{22}H_{12}I_2$: C, 49.84; H, 2.28. Found: C, 50.05; H, 2.30.

1,8,10-Tris(phenylethynyl)anthracene (8)

A solution of **7** (106 mg, 200 μmol) in a mixture of THF (10 mL) and Et_3N (10 mL) was degassed by bubbling argon for 20 min. To the solution were added phenylacetylene (88 μL, 0.80 mmol), $Pd(PPh_3)_4$ (35 mg, 30 μmol), and CuI (5.7 mg, 30 μmol). The mixture was refluxed for 14 h under argon. The solvent was removed by evaporation. The crude product was purified by chromatography on silica gel (hexane–CH_2Cl_2, 3:1) to give the desired product as a yellow solid (94 mg, 98%). Recrystallization from hexane–$CHCl_3$ afforded **8** as yellow crystals; mp 207–208 °C. The elemental analysis of this compound was difficult because of the incomplete combustion, and the compound was characterized by HRMS and its purity was confirmed by ^{1}H and ^{13}C NMR spectra.

^{1}H NMR ($CDCl_3$): δ = 7.20 (t, *J* = 7.3 Hz, 4 H), 7.33 (t, *J* = 7.3 Hz, 2 H), 7.43–7.48 (m, 3 H), 7.57–7.61 (m, 6 H), 7.77 (d, *J* = 6.8 Hz, 2 H), 7.84 (d, *J* = 6.8 Hz, 2 H), 8.66 (d, *J* = 8.8 Hz, 2 H), 9.65 (s, 1 H).

^{13}C NMR ($CDCl_3$): δ = 86.03, 87.49, 101.49, 104.42, 118.67, 122.03, 123.15, 123.34, 125.23, 126.29, 127.54, 128.34, 128.39, 128.54, 128.68, 130.86, 130.98, 131.65, 131.79, 132.41.

HRMS: *m/z* calcd for $C_{38}H_{22}$ [M^+]: 478.1722; found: 478.1687.

UV (C_6H_{12}): λ_{max} (ε) = 270 (138400), 309 (12400), 330 (6800), 426 (30300), 452 nm (31600).

FL (C_6H_{12}): λ_{max} = 464 nm (λ_{ex} = 393 nm).

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