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Synthesis of Hexadehydrotribenzo[*a,e,i*][12]annulenes by Acetylene Insertion into an Open-Chain Precursor

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S *Supporting Information*

ABSTRACT: A simple synthesis of a hexadehydrotribenzo[*a,e,i*][12]annulene by insertion of acetylene into an open-chain diiodo precursor under Sonogashira coupling conditions has been developed and used to prepare a rigid three-armed star connector for testing as a building block for a two-dimensional hexagonal hydrogen-bonding array.

■ INTRODUCTION

Hexadehydrotribenzo[*a,e,i*][12]annulene derivatives and their multiply fused analogues[1,2] have attracted considerable interest, mainly because they combine a delocalized cyclic π-electron system with a well-defined rigid triangular geometry.[3−5] They have been recently investigated as optoelectronic materials[6−14] and as building blocks in supramolecular chemistry[15−24] and crystal engineering.[16,19,25] However, in spite of the availability of several coupling methods,[27−29] such as those by Sonogashira, Suzuki, Castro-Stevens, and Negishi, the reported syntheses of these macrocycles generally suffer from low yields and difficult product isolation.

The drawbacks of the most commonly used procedure, the trimerization of *o*-iodoethynylbenzenes, are the usually relatively poor accessibility of starting materials and the generally quite low yields (5−64%).[9,18,19,21,23,26,30−35] Alkyne metathesis is a promising approach that affords good yields in some cases (54−86%) but often requires strictly anaerobic conditions.[36−39] There is only one communication that describes what would appear to be the simplest synthetic approach, a direct connection of an *o*-diiodobenzene with acetylene under Sonogashira coupling conditions, in yields varying between 11 and 39%.[40] An inspiring approach has been provided by the Sonogashira coupling of a rod-shaped diiodo derivative with a bis-ethynyl derivative, which gave the desired trigonal macrocycles in yields of 25−30%.[15,24]

We are interested in the use of hexadehydrotribenzo[*a,e,i*][12]annulenes as 3-fold connectors in the construction of two-dimensional hydrogen-bonded networks and describe an alternative approach to this ring system, the insertion of acetylene into an open chain diiodide. Acetylene has been used in Sonogashira coupling since the early days,[41] and considerable precedent for the reactions used in our approach exists.[42−45] The new ring closure still has an only moderate yield of 57%, but it uses easily accessible starting materials and permits facile product isolations.

■ RESULTS

Our initial efforts to prepare the hexadehydrotribenzo[*a,e,i*][12]annulene hexaester **1**, a key intermediate for the desired star connector **2** (Chart 1), followed the most common literature procedures. These are the trimerization of an *o*-iodoethynylbenzene or its phthalimide analogue and the cyclization of *o*-diiodobenzene or the corresponding phthalimide derivative with acetylene under Sonogashira or Castro-Stevens coupling conditions. These attempts all yielded complex mixtures, and neither the desired product nor the starting materials were isolated in significant yield.

Only the trimerization of *o*-iodoethynylbenzene **3** under Sonogashira coupling and high dilution conditions led to the formation of any trigonal derivative **1**, and it was mixed with the square **4**. Most of the reaction products did not pass through a silica gel column and were presumably of oligomeric or polymeric nature, and only a 10% yield of **1** and 5% yield of **4** were isolated.

Following this initial discouragement, two synthetic pathways were developed for the sextuple methyl ester derivative of **1**. The first one was inspired by a published procedure in which a doubly terminally iodinated rod is coupled with a bis-ethynyl derivative.[15,24] In the second and superior one, **1** was formed by acetylene insertion into the diiodo derivative **5**. An attempt to replace acetylene with calcium carbide[46] failed.

A Classical Route (Scheme 1). Our first successful synthesis of hexadehydrotribenzo[*a,e,i*][12]annulenes followed the classical approach.[15,24] It started from *o*-xylene (**6**), which was converted to 1,2-diiodo-4,5-dimethylbenzene (**7**) by oxidative iodination[47] in 65% yield. Oxidation of **7** by potassium permanganate in water in the presence of pyridine led to the corresponding dicarboxylic acid **8** (72%).[48] The

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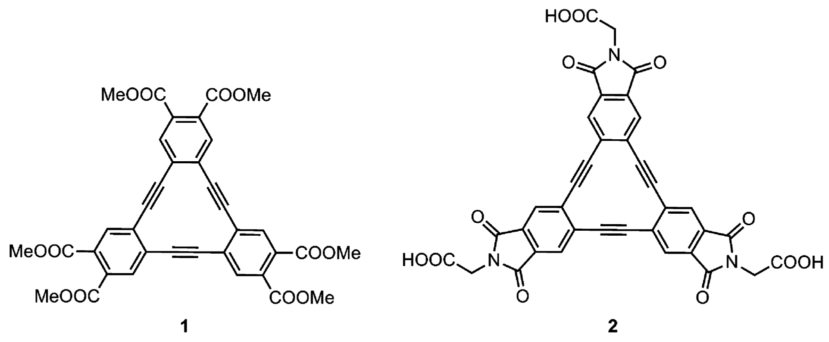
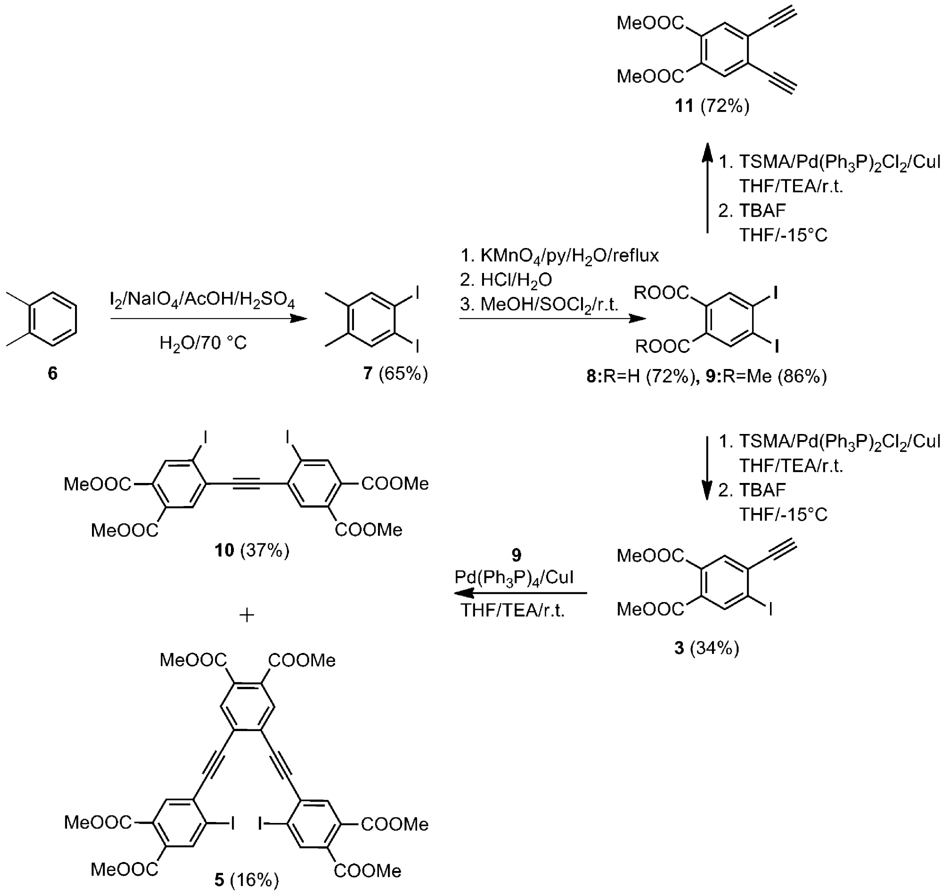
Chart 1



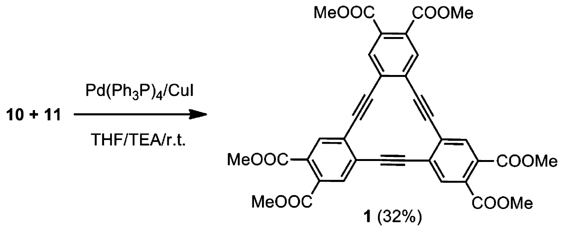
Scheme 1



addition of pyridine greatly improved the yield since it allowed the portion of **7** that sublimed into the condenser to be flushed back into the reaction vessel. The diacid **8** was esterified with methanol in the presence of thionyl chloride in 86% yield, and Sonogashira coupling of the diester **9**[49] with ethynyltrimethylsilane (1.05 equiv) followed by deprotection with tetrabutylammonium fluoride afforded the monoiodomonoethynyl compound **3** in a statistical mixture, from which it was isolated in a 34% yield.

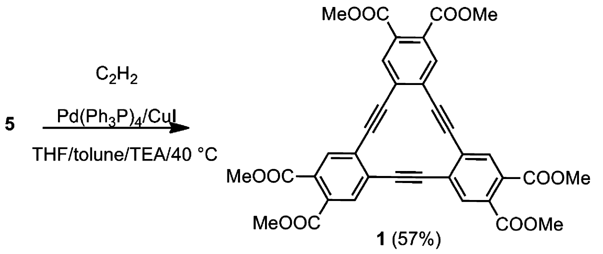
The last step in the synthesis of the doubly iodinated rod **10** was the coupling of **3** with excess **9**, which proceeded in a yield of 37%, limited by the formation of the byproduct **5**, which was isolated in a 16% yield. The bis-ethynyl derivative **11** was prepared in 72% yield by the reaction of **9** with an excess of ethynyltrimethylsilane followed by deprotection (Scheme 2). Under high dilution conditions, the Sonogashira coupling of **10** with **11** afforded the desired macrocycle **1** in 32% yield.

Scheme 2



A New Route (Scheme 3). The open-chain side product **5** is nearly identical with the full desired annulene, except for only one missing acetylene link, and its formation therefore

Scheme 3



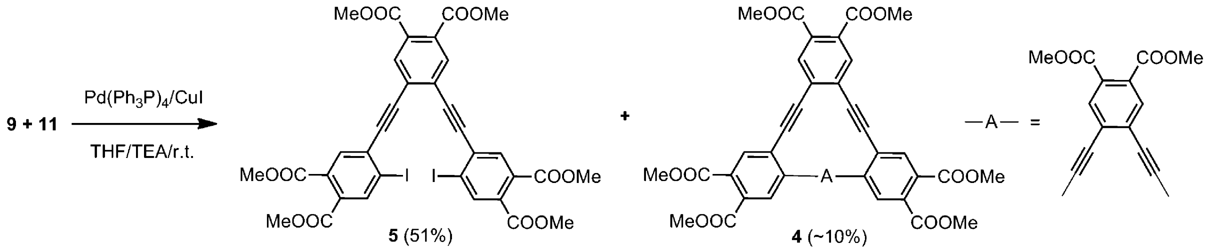
suggested an alternative path to **1**. Indeed, introduction of anhydrous gaseous acetylene into a solution of **5** in the presence of tetrakis(triphenylphosphine)palladium(0) and copper(I) iodide produced **1** in 57% yield. The exact dimensions of the annulene **1** were determined by single-crystal X-ray diffraction (Figure S1, Supporting Information). Interestingly, we were only able to grow suitable crystals from THF in the presence of metal triflates such as silver triflate, even though the salt was not incorporated in the crystal. The molecules are packed in columns similarly as in certain other compounds of this type[26] (Figure S1, Supporting Information).

The straightforward procedure of Scheme 3 suffers from the low yield in which the precursor **5** is formed to start with. A search for the best conditions for its preparation by Sonogashira coupling of **11** with a large excess of **9** (Scheme 4) produced a yield of 51%. This value is affected by the formation of the square derivative **4**, which was isolated in a ~10% yield and less than 90% purity, and whose structure was confirmed only by high resolution mass spectrometry and ^{1}H and ^{13}C NMR spectroscopy.

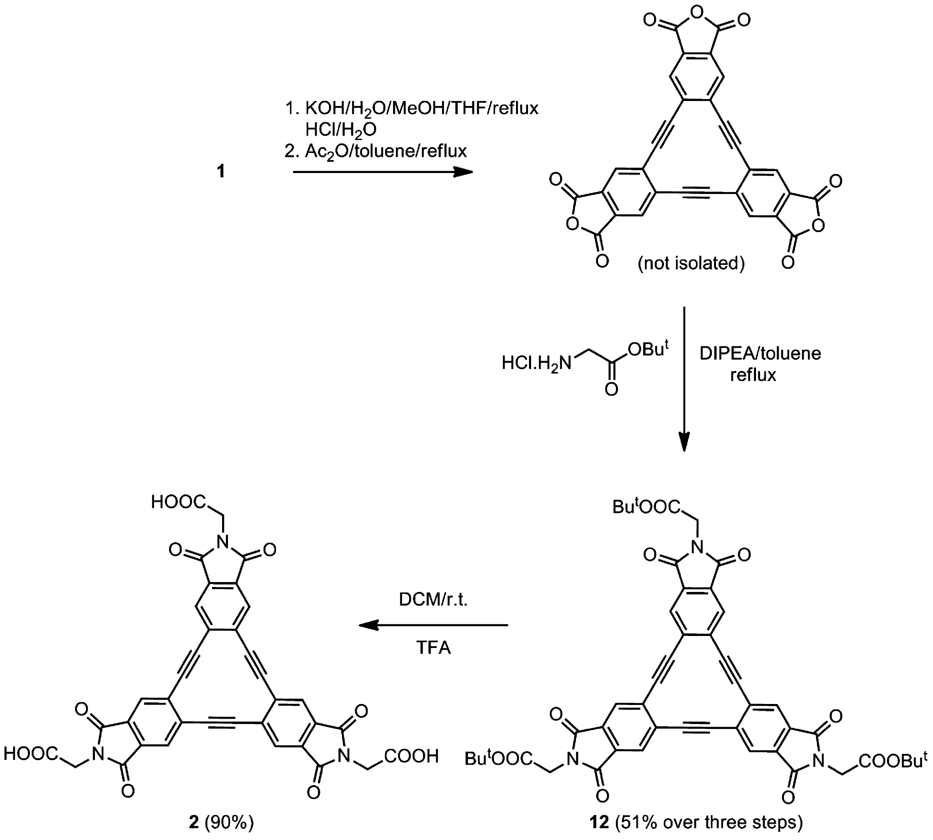
The transformation of **1** into the desired rigid star connector **2** was performed in four steps (Scheme 5). Methyl ester hydrolysis, anhydride formation, and subsequent glycine *tert*-butyl ester insertion afforded the tri-*tert*-butyl derivative **12** in a 51% overall yield. After the removal of *tert*-butyl groups with trifluoroacetic acid the final product **2** was isolated in 90% yield.

The use of the cheaper glycine methyl ester instead of *tert*-butyl ester is unsatisfactory due to difficulties with selectivity in the final hydrolysis step. Several methods that we expected to

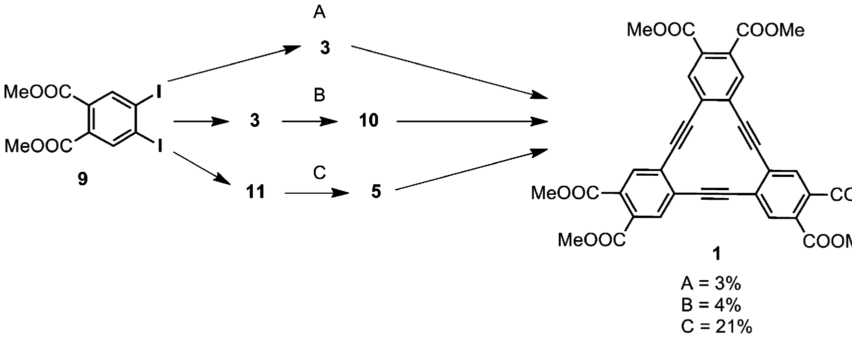
Scheme 4



Scheme 5



Scheme 6



preferentially remove the methyl ester group in the presence of a phthalimide moiety (NaOH/H_2O at 20 or 60 °C, LiI[50] in EtOAc or THF, $AlCl_3$,[51] and HCl[52]) were tested on a model, methyl 2-(5,6-diiodo-1,3-dioxo-2,3-dihydro-1*H*-isoindol-2-yl)-acetate, and yielded either the starting methyl ester or a mixture of the desired material with products in which the phthalimide rings were partially hydrolyzed.

■ DISCUSSION

After the common methods for the formation of hexadehydrotribenzo[*a*,*e*,*i*][12]annulene failed, we looked for alternatives. We first turned to the published path[15,24] in which a rodlike diiodide is connected with a bis-ethynyl derivative under Sonogashira coupling conditions, and this indeed led to the goal (Scheme 2). However, the low-yield access to the intermediates **3** and **10**, due to competing reactions and difficult isolations, makes this route less than ideal.

When we noticed the facile formation of the byproduct **3** in the coupling of **7** with **8**, we decided to attempt a ring closure of **5** to **1** by direct coupling with acetylene, which promised to simplify the reaction sequence and improve the yield. This attempt was successful and afforded **1** in a 57% yield, thus opening a new route to hexadehydrotribenzo[*a*,*e*,*i*][12]-annulenes.

A comparison with the overall yields of other methods used for the preparation of **1** unequivocally showed the benefit of the new insertion procedure. While the overall yields of trimerization of **3** and of the alternative route via **10** are only 3% and 4%, respectively, the use of the new insertion procedure affords **1** from **9** in an overall yield of 21% (Scheme 6).

Since model reactions with *tert*-butyl and methyl phthalimidoacetates showed that the *tert*-butyl group but not the methyl group can be easily removed selectively without disturbing the imide, the next task was the preparation of the *tert*-butyl triester **12**, which was straightforward. The triester was finally hydrolyzed to the triacid **2**, which is extremely insoluble. We attribute this to the formation of an extensive hydrogen bond network and take it to be a promising indication for our future attempts to form a monolayer hydrogen bonded network on a surface.

■ CONCLUSION

In developing a synthetic method for the key intermediate **1** needed for the preparation of the rigid trigonal star connector **2**, we found that the coupling of **10** and **11** under high dilution conditions, analogous to published syntheses, is successful. In the course of this work, we discovered that the insertion of acetylene into **5** represents a shorter and superior approach to the hexadehydrotribenzo[12]annulene ring system. Although **5** is presently accessible in an only modest yield, its preparation and the isolation of all intermediates and of the final products require no difficult separations. We conclude that this method may well represent a superior general approach to the preparation of hexadehydrotribenzo[*a*,*e*,*i*][12]annulenes.

■ EXPERIMENTAL SECTION

All chemicals were of standard commercial quality. Solvents were dried, distilled, and degassed before use. NMR spectra were recorded at 400 and 500 MHz at 25 °C in DMSO-d_6 and $CDCl_3$. ^1H NMR spectra were referenced to TMS. ^{13}C NMR with total decoupling of protons was referenced against the solvent (DMSO, → 31.5 ppm and $CDCl_3$, → 77.0 ppm). IR spectra were measured in KBr matrix.

X-ray Diffraction of 1. Initial attempts at crystallization of **1** gave powders, but a suitable single crystal grew upon slow evaporation of a solution of **1** (5 mg, 0.0077 mmol) and silver trifluoromethanesulfonate (2 mg, 0.0077 mmol) in tetrahydrofuran-d_8 (0.5 mL) in an NMR tube. Monoclinic, $P2_1/c$ (No. 14), a = 26.5365(6) Å, b = 32.7390(8) Å, c = 17.4054(4)Å, β = 98.3440(10)°, V = 14961.4(6) Å^3, Z = 16, D_x = 1.152 Mg m^{-3}. A yellow crystal of dimensions 0.43 × 0.19 × 0.19 mm was mounted into a Lindemann capillary and measured at a diffractometer by monochromatized Mo Kα radiation (λ = 0.71073 Å) at 150(2) K. A multiscan absorption correction was applied during data reduction (μ = 0.09 mm^{-1}). A total of 121763 measured reflections was obtained (θ_{max}= 26°), of which 29370 were unique (R_{int} = 0.037) and 13952 met the $I > 2\sigma(I)$ criterion. The structure was solved by direct methods (SHELXS[53]) and refined by full matrix least-squares based on F^2 (SHELXL97[53]). Hydrogen atoms were fixed into idealized positions (riding model) and assigned temperature factors of either $H_{iso}(H) = 1.2U_{eq}$ (pivot atom) or $H_{iso}(H) = 1.5U_{eq}$ (pivot atom) for the methyl moiety. The refinement converged (Δ/σ_{max} = 0.002) to R = 0.054 for the observed reflections and w$R(F^2)$ = 0. 167, GOF = 0.89 for 1753 parameters,and all 29370 reflections. The final difference map displayed no peaks of chemical significance ($\Delta\rho_{max}$ = 0.45, $\Delta\rho_{min}$ = −0.22 e.Å^{-3}). The contributions of disordered tetrahydrofuran molecules were removed from the diffraction data with the PLATON/SQUEEZE (PLATON[54]) procedure to improve the precision of the main part of the structure.[53,54]

4,5-Diiodophthalic Acid (8). A mixture of 1,2-diiodo-4,5-dimethylbenzene (**7**)[47] (10 g, 27.9 mmol), potassium permanganate (53 g, 335 mmol), pyridine (80 mL), and water (120 mL) was refluxed for 48 h. The hot mixture was filtered through a paper filter. The solid residue was washed with a hot aqueous potassium hydroxide solution (1 M, 200 mL), and the filtrate was acidified with concentrated hydrochloric acid to pH 1−2. The suspension was filtered off and washed with concentrated hydrochloric acid (2 × 30 mL), water (2 × 30 mL), and toluene (2 × 30 mL). The resulting solid was dried for 5 h at 0.2 Torr and 80 °C. The product was obtained as a white powder (8.9 g). Yield: 72%. Mp: >300 °C (ethanol). ^1H NMR (400 MHz, DMSO-d_6): δ 8.17 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 166.6, 138.2, 133.1, 112.3. IR (KBr) 3422, 3084, 2937, 2909, 2633, 2603, 2533, 2496, 2478, 2442, 2366, 2343, 2073, 2034, 2003, 1906, 1722, 1699, 1667, 1648, 1587, 1540, 1489, 1460, 1386, 1311, 1258, 1223, 1146, 1101, 1078, 909, 886, 849, 821, 791, 778, 755, 700, 680, 655, 613, 570, 480, 447 cm^{-1}. UV−vis (methanol): λ_{max} (ε) 241 (3.9×10^4) nm (M^{-1} cm^{-1}). HRMS (EI$^+$) for ($C_8H_4I_2O_4-H_2O$): calcd 399.8093, found 399.8098. Anal. Calcd for $C_8H_4I_2O_4$: C, 22.93; H, 0.96; I, 60.73. Found C, 23.02; H, 1.06; I, 60.53.

4,5-Diiodophthalic Acid Dimethyl Ester (9). To a solution of 4,5-diiodophthalic acid (**8**) (9.7 g, 22.3 mmol) in methanol (100 mL) was added thionyl chloride (13.6 mL, 0.185 mol) dropwise. The mixture was stirred at rt overnight. The suspension was neutralized by an aqueous potassium carbonate solution (5%, 300 mL) and extracted with dichloromethane (2 × 200 mL). The combined organic phases were dried over magnesium sulfate. The product was obtained as a white solid (8.9 g). Yield: 86%. Mp = 123−124 °C (methanol). ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.17 (s, 2H), 3.90 (s, 6H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 165.3, 139.2, 132.2, 111.6, 52.9. IR (KBr) 3073, 3052, 1732, 1571, 1528, 1483, 1430, 1336, 1282, 1223, 1212, 1198, 1187, 1131, 1078, 973, 905, 897, 854, 817, 776, 738, 692, 666, 592, 572, 488, 431 cm^{-1}. UV−vis (dichloromethane): λ_{max} (ε) 242 (2.2×10^4) nm (M^{-1} cm^{-1}). HRMS (EI$^+$) for ($C_{10}H_8I_2O_4$): calcd 445.8512, found 445.8505. Anal. Calcd. for $C_{10}H_8I_2O_4$: C, 26.93; H, 1.81; I, 56.91. Found: C, 26.92; H, 1.82; I, 57.01.

4-Ethynyl-5-iodophthalic Acid Dimethyl Ester (3). A two-necked flask was charged with 4,5-diiodophthalic acid dimethyl ester (**9**) (2 g, 4.48 mmol), bis(triphenylphosphine)palladium(II) dichloride (0.158 g, 0.22 mmol), copper(I) iodide (0.086 g, 0.45 mmol), and triphenylphosphine (0.118 g, 0.45 mmol) under an inert atmosphere. After three successive vacuum/argon cycles, tetrahydrofuran (20 mL, anhydrous, freeze−pump−thaw degassed) and triethylamine (15 mL, anhydrous, degassed) were added. After 15 min of stirring at rt, ethynyltrimethylsilane (0.665 mL, 4.71 mmol, degassed) was added, and the reaction mixture was stirred for 48 h at rt. The volatiles were evaporated under reduced pressure, and the residue was dissolved in tetrahydrofuran (20 mL). Tetrabutylammonium fluoride was added as a 1 M tetrahydrofuran solution (4.6 mL, 4.6 mmol) at −15 °C, and the mixture was stirred for 30 min at −15 °C. The reaction mixture was quenched with water (30 mL), extracted with dichloromethane (2 × 30 mL), and dried over magnesium sulfate. The crude mixture was purified by column chromatography (silica gel, acetone−petroleum ether 1:9). The product was obtained as a white solid (513 mg). Yield: 34% over two steps. Mp: 99−101 °C (ethanol). ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.18 (s, 1H), 7.81 (s, 1H), 3.91 (s, 3H), 3.90 (s, 3H) 3.55 (s, 1H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 166.6, 165.9, 139.1, 133.2, 132.4, 131.9, 131.5, 103.5, 84.1, 83.7, 53.0, 52.9. IR (KBr) 3441, 3267, 3084, 3060, 3005, 2955, 2901, 2845, 2720, 2547, 2261, 2114, 1792, 1732, 1636, 1589, 1534, 1507, 1498, 1434, 1389, 1361, 1292, 1254, 1229, 1202, 1133, 1083, 993, 970, 918, 893, 821, 789, 764, 700, 681, 658, 608, 589, 526, 462, 424 cm^{-1}. UV−vis (dichloromethane): λ_{max} (ε) 241 (3.0×10^4) 268 (1.3×10^4) nm (M^{-1} cm^{-1}). HRMS (ESI) for ($C_{12}H_9IO_4Na$): calcd 366.94377, found 366.94375. Anal. Calcd for $C_{12}H_9IO_4$: C, 41.89; H, 2.64; I, 36.88. Found: C, 41.78; H, 2.75; I, 36.59.

Note: The purification should be carried out under inert atmosphere to avoid decomposition of **3**.

Tetramethyl 4,4′-Ethyne-1,2-diylbis(5-iodobenzene-1,2-dicarboxylate) (10). A two-necked flask was charged with 4,5-diiodophthalic acid dimethyl ester (**9**) (3.85 g, 8.6 mmol), 4-ethynyl-5-iodophthalic acid dimethyl ester (**3**) (0.655 g; 1.9 mmol), tetrakis(triphenylphosphine)palladium(0) (0.22 g, 0.19 mmol), and copper(I) iodide (0.73 g, 0.38 mmol) under inert atmosphere. After three successive vacuum/argon cycles, tetrahydrofuran (40 mL, anhydrous, degassed) and triethylamine (20 mL, anhydrous, degassed) were added under inert atmosphere, and the mixture was stirred overnight at rt and 2 h at 40 °C. Aqueous ammonium chloride (10%, 40 mL) was added to the reaction mixture, which was then extracted with dichloromethane (2 × 20 mL). Combined organic phases were dried over magnesium sulfate. The crude mixture was purified by column chromatography (silica gel, acetone−petroleum ether 1:4). The principal product **10** (461 mg, 37% yield) and the byproduct **5** (277 mg, 16% yield) were isolated as white solids. Mp: 203−204 °C (ethanol). ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.23 (s, 2H), 7.89 (s, 2H), 3.92 (s, 12H). ^{13}CNMR (100 MHz, CDCl$_3$): δ 166.6, 165.8, 139.32, 133.0, 132.5, 132.0, 131.7, 103.4, 95.7, 53.0). IR (KBr): 3425, 3011, 2957, 2926, 2852, 1728, 1589, 1538, 1437, 1384, 1313, 1278, 1280, 1240, 1193, 1133, 1084, 1051, 999, 962, 929, 902, 889, 829, 806, 786, 774, 741, 724, 703, 694, 645, 631, 566, 543, 514, 456 cm^{-1}. UV−vis (dichloromethane): λ_{max} (ε) 256 (3.1×10^4), 317 (2.2×10^4) nm (M^{-1} cm^{-1}). HRMS (EI$^+$) calcd for ($C_{22}H_{16}I_2O_8$): 661.8935, found 661.8945. Anal. Calcd for $C_{22}H_{16}I_2O_8$: C, 39.90; H, 2.44; I, 38.33. Found: C, 40.19; H, 2.58; I, 38.13.

4,5-Diethynylphthalic Acid Dimethyl Ester (11). A two-necked flask was charged with 4,5-diiodophthalic acid dimethyl ester (**9**) (3 g, 6.72 mmol), bis(triphenylphosphine)palladium(II) dichloride (0.472 g, 0.67 mmol), copper(I) iodide (0.128 g, 0.67 mmol), and triphenylphosphine (176 mg, 0.67 mmol) under inert atmosphere. After three successive vacuum/argon cycles, tetrahydrofuran (40 mL, anhydrous, degassed) and triethylamine (40 mL, anhydrous, degassed) were added. After 15 min of stirring at rt, ethynyltrimethylsilane (2.1 mL, 14.8 mmol, degassed) was added, and the mixture was stirred for 24 h at rt. The volatiles were evaporated under reduced pressure, and the residue was dissolved in tetrahydrofuran (50 mL). Tetrabutylammonium fluoride was added as a 1 M tetrahydrofuran solution (16.3 mL, 16.3 mmol) at −15 °C. The mixture was stirred for 30 min at −15 °C, quenched with water (30 mL), extracted with dichloromethane (2 × 20 mL), and dried over magnesium sulfate. The crude product was purified by column chromatography (silica gel, acetone−petroleum ether 1:4) to yield a white solid (1.2 g). Yield: 72% over two steps. Mp: 99−100 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.84 (s, 2H), 3.90 (s, 6H), 3.48 (s, 2H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 166.5,133.2,131.59,127.86,84.23,80.22,52.8. IR (KBr): 3268, 3244, 2104, 1730, 1715, 1604, 1540, 1489, 1436, 1380, 1298, 1269, 1255, 1242, 1214, 1193, 1148, 1131, 1030, 967, 929, 907, 895, 833, 790, 771, 737, 726, 686, 660, 544, 507, 451, 422 cm^{-1}. UV−vis (dichloromethane): λ_{max} (ε) 239 (6.4×10^4), 279 (2.0×10^4) nm (M^{-1} cm^{-1}). HRMS (EI$^+$), calcd for ($C_{14}H_{10}O_4$): 242.0579, found 242.0584. Anal. Calcd for $C_{14}H_{10}O_4$: C, 69.42; H, 4.16. Found: C, 69.42; H, 4.28.

Note: The purification should be carried out under inert atmosphere to avoid decomposition of **11**.

Tetramethyl 5,5′-(4,5-Bis(methoxycarbonyl)-1,2-phenylene)bis(ethyne-2,1-diyl)bis (4-iodophthalate) (5). A two-necked flask was charged with 4,5-diiodophthalic acid dimethyl ester (**9**) (10 g, 22.3 mmol), 4,5-diethynylphthalic acid dimethyl ester (**11**, 0.6 g, 2.48 mmol), tetrakis(triphenylphosphine)palladium(0) (0.29 g, 0.248 mmol), and copper(I) iodide (0.047 g, 0.248 mmol) under inert atmosphere. After three successive vacuum/argon cycles, tetrahydrofuran (40 mL, anhydrous, degassed) and triethylamine (40 mL, anhydrous, degassed) were added. The mixture was stirred for 72 h at rt under inert atmosphere, quenched with an aqueous ammonium chloride (10%; 50 mL), extracted with dichloromethane (2 × 50 mL), and dried over magnesium sulfate. The crude product was purified by column chromatography (silica gel, acetone−petroleum ether 1:4 and 1:2), affording the principal product **5** as a white solid (1.1 g, 51%) and the byproduct **4** (0.053 g; ∼10%), which was only ∼90% pure judging by ^{1}H NMR (400 MHz, CDCl$_3$), δ 7.90 (s, 8H), 3.91 (s, 24H), and ^{13}C NMR (150 MHz, CDCl$_3$), δ 166.7, 132.9, 131.9, 127.8, 92.4, 53.1, and whose identity was secured by HRMS (ESI$^+$), calcd for ($C_{48}H_{32}O_{16}Na$): 887.15826, found 887.15755. **5**. Mp: 194−195 °C (methanol). ^{1}H NMR (400 MHz, CDCl$_3$): δ 8.20 (s, 2H), 8.00 (s, 2H), 7.90 (s, 2H), 3.95 (s, 6H), 3.92(s, 6H), 3.87 (s, 6H). ^{13}C NMR (150 MHz, CDCl$_3$): δ 166.5, 166.3, 166.0, 139.1, 133.18, 133.0, 132.7, 132.0, 131.9, 131.3, 127.3, 103.9, 96.5, 92.4, 53.1, 53.0. IR (KBr): 3441, 2952, 2217, 1729, 1629, 1600, 1586, 1539, 1499, 1435, 1403, 1376, 1353, 1320, 1288, 1254, 1193, 1130, 1081, 1040, 993, 965, 939, 906, 894, 838, 826, 804, 788, 773, 755, 727, 706, 684, 676, 592, 542, 531, 460 cm^{-1}. UV−vis (dichloromethane)(λ_{max} (ε) 262 (6.0×10^4), 302 (4.9×10^4) nm (M^{-1} cm^{-1}). HRMS (EI$^+$): calcd for ($C_{34}H_{24}I_2O_{12}$) 877.9357, found 877.9388. Anal. Calcd for $C_{34}H_{24}I_2O_{12}$: C, 46.49; H, 2.75; I, 28.9. Found: C, 46.31; H, 2.72; I, 28.67.

Hexamethyl 5,6,11,12,17,18-Hexadehydrotribenzo[*a*,*e*,*i*]-[12]annulene-2,3,8,9,14,15-hexacarboxylate (1). *Method A.* A two-necked flask was charged with **11** (0.376 g, 1.55 mmol), **10** (1.03 g, 1.55 mmol), tetrakis(triphenylphosphine)palladium(0) (0.18 g, 0.155 mmol), and copper(I) iodide (0.03 g, 0.155 mmol) under inert atmosphere. After three successive vacuum/argon cycles, tetrahydrofuran (150 mL, anhydrous, degassed) and triethylamine (150 mL, anhydrous, degassed) were added. The reaction mixture was stirred for 48 h at rt under an inert atmosphere, quenched with an aqueous ammonium chloride solution (10%; 100 mL), and extracted with dichloromethane (2 × 100 mL). The combined organic phases were dried over magnesium sulfate. The crude product was purified by column chromatography (silica gel, dichloromethane−acetone 30:1) and obtained as a light yellow solid (0.32 g, yield 32%).

Method B. A two-necked flask was charged with **5** (0.63 g; 0.717 mmol), tetrakis(triphenylphosphine)palladium (0) (0.083 g, 0.0717 mmol), and copper(I) iodide (0.014 g, 0.0717 mmol). After three successive vacuum/argon cycles, tetrahydrofuran (130 mL, anhydrous, degassed), toluene (130 mL, anhydrous, degassed), and triethylamine (130 mL, anhydrous, degassed) were added. Dried acetylene gas was bubbled into the solution for 3 min. The reaction mixture was stirred at 40 °C for 18 h under an inert atmosphere, quenched with aqueous ammonium chloride (10%; 100 mL), extracted with dichloromethane (2 × 50 mL), and dried over magnesium sulfate. The crude product was purified by column chromatography (silica gel, dichloromethane−acetone 40:1 and 30:1) to afford a yellow solid (0.265 g). Yield: 57%. Mp: 275−276 °C (dichloromethane−diethyl ether). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (s, 6H), 3.92 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.3, 132.7, 132.3, 128.3, 93.9, 52.9. IR (KBr): 3438, 3073, 3027, 3004, 2954, 2853, 2361, 2213, 2065, 1730, 1635, 1600, 1558, 1538, 1499, 1435, 1387, 1325, 1286, 1258, 1194, 1129, 1057, 1021, 969, 912, 846, 803, 787, 779, 743, 728, 667, 565, 479. UV−vis (dichloromethane): λ_{max} (ε) 249 (1.8×10^4), 311 (1.72×10^5), 346 (1.0×10^4), 361 (1.4×10^4) nm (M^{-1} cm^{-1}). HRMS (EI$^+$), calcd for ($C_{36}H_{24}O_{12}$): 648.1278, found 648.1278. Anal. Calcd for $C_{36}H_{24}O_{12}$: C, 66.67; H, 3.73. Found: C, 66.29; H, 3.75.

Tri-*tert*-butyl 2,2′,2″-(1,3,8,10,15,17-Hexaoxo-5,6,12,13,19,20-hexadehydro-8,10,15,17-tetrahydro-1*H*-cyclododeca[1,12-*f*:4,5-*f*′:8,9-*f*″]triisoindole-2,9,16(3*H*)-triyl)triacetate (12). Potassium hydroxide (377 mg, 6.7 mmol) and **1** (162 mg, 0.25 mmol) were refluxed for 48 h in a mixture of tetrahydrofuran (15 mL), methyl alcohol (15 mL), and water (15 mL). The reaction mixture was extracted with dichloromethane (2 × 10 mL), and the organic phase was washed with aqueous potassium hydroxide (20 mL, 20%). The combined aqueous phases were acidified with concentrated hydrochloric acid to pH 1−2 and evaporated under reduced pressure. The residue was dried for 5 h by azeotropic distillation with toluene (2 × 20 mL) under reduced pressure (0.2 Torr) at 80 °C, suspended into toluene (70 mL, anhydrous), and acetanhydride (50 mL; freshly distilled) was added. The apparatus was equipped with a Dean−Stark trap, and the mixture was refluxed for 48 h. Toluene and acetanhydride were removed under reduced pressure and the residue was dried at 0.2 Torr at 80 °C for 5 h. Glycine *tert*-butyl ester hydrochloride (139 mg, 0.82 mmol), *N*,*N*-diisopropylethylamine (0.31 mL, 1.75 mmol), and toluene (100 mL, anhydrous) were added. The apparatus was equipped with a Dean−Stark trap, and the mixture was refluxed for 48 h. Toluene was removed under reduced pressure and the crude product was purified by column chromatography (silica gel, dichloromethane−acetone 80:1; 60:1; 40:1), affording a yellow solid (0.108 g). Yield: 51% over three steps. Mp: > 300 °C dec. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (s, 6H), 4.34 (s, 6H); 1.48 (s, 27H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.8, 165.7, 132.1, 131.7, 127.3, 95.4, 83.2, 40.0, 28.0. IR (KBr): 3441, 2980, 2938, 1783, 1743, 1722, 1477, 1455, 1421, 1393, 1371, 1307, 1235, 1159, 1118, 1035, 1010, 933, 908, 848, 815, 769, 752, 737, 628, 616, 574, 551, 522, 481, 458, 437 cm^{-1}.UV−vis λ_{max} (ε): 216 (3.1×10^4), 296 (1.08×10^5), 345 (5.9×10^4), 350 (5.5×10^4) nm (M^{-1} cm^{-1}). HRMS (APCI), calcd for ($C_{48}H_{39}O_{12}N_3$): 849.25392, found 849.25360. Anal. Calcd for $C_{48}H_{39}O_{12}N_3$: C, 67.84; H, 4.63; N, 4.94. Found: C, 67.46; H, 4.73; N, 4.58.

2,2′,2″-(1,3,8,10,15,17-Hexaoxo-5,6,12,13,19,20-hexadehydro-8,10,15,17-tetrahydro-1*H*-cyclododeca[1,12-*f*:4,5-*f*′:8,9-*f*″]-triisoindole-2,9,16(3*H*)-triyl)triacetic Acid (2). A mixture of **12** (70 mg, 0.082 mmol) and trifluoroacetic acid (7 mL; freshly distilled) in dry tetrahydrofuran (20 mL) was stirred at rt for 48 h in an inert atmosphere. The volatiles were removed under reduced pressure, and the residue was triturated with methyl alcohol. The product was dried at 0.2 Torr at 80 °C for 5 h and obtained as a yellow solid (51 mg). Yield: 90%. ^{1}H NMR (400 MHz, DMSO-d_6): δ 7.99 (s, 6H), 4.32 (s, 6H). IR (KBr): 3474, 3068, 2993, 2945, 2539, 2360, 2216, 1783, 1719, 1614, 1477, 1424, 1391, 1311, 1200, 1179, 1149, 1122, 1037, 1011, 935, 816, 754, 737, 677, 617, 559, 526, 481, 457, 418 cm^{-1}. HRMS (ESI$^+$), calcd for ($C_{36}H_{15}O_{12}N_3Na$): 704.05448, found 704.05479.

Note: Additional analytical characterization was prevented by the extremely low solubility of **2**.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H, ^{13}C NMR spectra of all new compounds and a packing view of a crystal of **1**. This material is available free of charge via the Internet at http://pubs.acs.org.

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