Synthesis of Extended Linear Aromatics Using Tandem Diels–Alder Aromatization Reactions

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Introduction

Extended aromatic structures such as the naphthyl and anthryl nucleus have interesting physical and chemical characteristics. Anthracenes generally fluoresce between 400 and 680 nm.[1] Molecules with variously substituted anthracene nuclei react as Diels–Alder dienes.[2] Anthracene also undergoes photochemical 4 + 4 cycloaddition reactions across the 9,10 positions to form a thermoreversible dimer. This reaction of anthracene has been known for more than a century.[3] This note describes an efficient synthesis of extended aromatics such as 2,3-disubstituted naphthalenes and 2,3,6,7-tetrasubstituted anthracenes, which were previously difficult and expensive to synthesize. These compounds may now be readily exploited as a result of this simple methodology. To illustrate the potential of the tandem Diels–Alder aromatization reaction, we synthesized benz[*f*]indanone, 2,3:6,7-dibenzofluorenone, and 2,3,6,7-tetrakis(methoxycarbonyl)anthracene.

Benz[*f*]indanone was synthesized by a five-step process.[4,5] Friedel–Crafts reaction of indan with succinic acid gave an indan keto acid derivative that underwent a Clemmensen reduction and acid-catalyzed cyclization. The semicarbazone was formed from the resulting ketone which was decomposed to benz[*f*]indane. Benz[*f*]indane was then brominated in the 1 position by NBS and oxidized with chromic acid to benz[*f*]indan–1–one in an overall yield of less than 1%. A potential modern improvement to this synthesis is that of Carpino and Lin[6] who synthesized 10-bromobenz[*f*]indan-1-one in six steps. Their initial bromination of both the 1 and the benzylic positions of 2-methylnaphthalene was followed by displacement of the benzylic bromide with sodium diethyl malonate. Hydrolysis, decarboxylation, and a Friedel–Crafts ring closure yielded the 10-bromobenz[*f*]indanone in a 23% yield overall. Obtaining benz[*f*]indan-1-one, however, requires dehalogenation of 10-bromobenz[*f*]-indan-1-one. This operation would reduce the overall yield, but such a method should yield products in greater than 1% overall.

2,3:6,7-Dibenzofluorenone was synthesized by Martin[7] from methyl 3-bromo-2-naphthoate. Copper/bronze coupling was employed to assemble the tetraphenyl ring sequence. Basic ester hydrolysis then yielded the disodium salt. The formation of an intramolecular lead dicarboxylate aligned the rings for subsequent pyrolysis of the lead salt. Pyrolysis introduced the bridging ketone to finish the synthesis. The overall yield was 8%.

We were able to locate only three methods for the synthesis of 2,3,6,7-tetrasubstituted anthracenes. The first synthesis of 2,3,6,7-tetrasubstituted anthracene was by Morgan and Coulson,[8] who reacted 2,3-disubstituted butadienes with *p*-benzoquinone. The resulting quinone was reduced with zinc and ammonia and aromatized with sulfur to give the corresponding anthracene.

The second published synthesis was by Marschalk,[9] who synthesized 2,3,6,7-anthracenetetracarboxylic acid in five steps from 2,3,6,7-tetramethylanthracene. Oxiation of the methyl substituents was accompanied by anthraquinone formation. The synthesis entailed reduction to 9,10-dihydro-2,3,6,7-anthracenetetracarboxylic acid. Aromatization required conversion of the tetraacid to the bis-anhydride followed by dehydrogenation of the 9,10 positions with sulfur. Hydrolysis of the resultant anhydride gave 2,3,6,7-anthracenetetracarboxylic acid. This synthesis is difficult to conduct on a large scale because the 2,3,6,7-tetramethylanthracene is not readily available.

The third method based upon a benzo[1,2-*c*:4,5-*c*']-difuran intermediate was developed by Luo and Hart.[10] Reaction of anthracenediene dioxide with tetraphenylcyclone produced an adduct which liberated benzo-[1,2-*c*:4,5-*c*']difuran upon heating in decalin. If the thermolysis is conducted in the presence of dienophiles such as dimethyl fumarate, 2,3,6,7-tetrakis((alkyloxy)-carbonyl)anthracenes are formed along with carbon monoxide and tetraphenylbenzene. This is a very elegant synthesis, but rather expensive reagents are required.

Regiospecific annulation of *o*-quinodimethane derivatives is the best approach to the synthesis of 2,3-disubstituted naphthalenes and 2,3,6,7-tetrasubstituted anthracenes. The concept was defined by Cava, Deana, and Muth,[11] who published a synthesis of 2,3-disubstituted naphthalenes via a tandem Diels–Alder aromatization reaction. In their synthesis, α,α,α′,α′-tetrabromo-*o*-xylene is reacted with a dienophile in the presence of NaI in DMF, such as *N*-phenylmaleimide or maleic anhydride, to give the corresponding naphthalene derivative.

The Diels–Alder aromatization reaction, based on *o*-quinodimethane intermediates, provides remarkable flexibility. Not only can 2,3-disubstituted naphthalenes by synthesized with remarkable regiospecificity but a bis-annulation with 2 mol of an *o*-quinodimethane intermediate yields molecules containing two 2,3-disubstituted naphthalene subunits. In a similar manner, bis-annulation with a difunctional *o*-quinodimethane intermediate yields 2,3,6,7-tetrasubstituted anthracenes.

Experimental Section

All reagents were purchased from the Aldrich Chemical Co. and used without further purification. *N*,*N*-dimethylformamide (DMF) and *N*,*N*-dimethylacetamide (DMAc) were purchased as anhydrous grade. Melting points were taken on a Fischer-Johns melting point apparatus and are uncorrected. NMR spectra were recorded with an IBM/Bruker AR-100 MHz or AC-200 MHz

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instrument as specified. IR spectra were recorded with a Perkin-Elmer 1760X instrument. Mass spectra were recorded with a Finnigan TSQ 70 instrument using the fast atom bombardment mode.

Benz[*f*]indan-1-one (2). α,α,α′,α′-Tetrabromo-*o*-xylene (30.0 g, 0.0710 mol) and 2-cyclopenten-1-one (5.83 g, 0.0710 mol) were dissolved in 270 mL of DMF. Sodium iodide (69.7 g, 0.465 mol) was added and the mixture heated to 80 °C and stirred overnight. The resulting dark red solution was poured into an ice/water mixture and decolorized by addition of sodium bisulfite, and a yellow precipitate formed. The solid was collected and recrystallized form 95% ethanol to give benz[*f*]indan-1-one (**1**) in a 57% yield (7.36 g, 0.0404 mol): mp 144–145 °C; lit.[5] mp 140–141 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.77–2.83 (t, 2H), 3.29–3.35 (t, 2H), 7.45–8.32 (m, 6H).

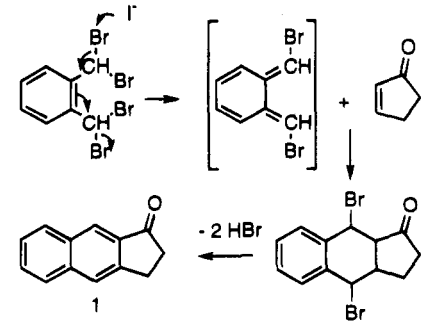
2,3:6,7-Dibenzofluorenone (3). Benz[*f*]indan-1-one (**1**) (2.02 g, 0.0111 mol), NBS (2.17 g, 0.0149 mol), and benzoyl peroxide (20 mg) were refluxed in 20 mL of dry CCl_4 for 2 h. The solution was cooled, the succinimide was removed by filtration, and the crude product was used directly in the next step. The crude brominated product in CCl_4 was cooled in an ice bath, and 1.93 mL (1.41 g, 0.0140 mol) of triethylamine was slowly added. The mixture was allowed to warm to room temperature and stir overnight. The solid precipitate was removed and dried in vacuo. Yellow crystals of benz[*f*]inden-1-one (**2**) were obtained by sublimation. This material was used without further purification: ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.11–6.14 (d, 2H), 7.30–7.95 (m, 6H); GC/MS *m/z* 180. α,α,α′,α′-Tetrabromo-*o*-xylene (0.468 g, 1.11 mmol) and benz[*f*]inden-1-one (**2**) (0.200 g, 1.11 mmol) were dissolved in 10 mL of DMF. Sodium iodide (1.09 g, 7.27 mmol) was added and the mixture stirred at 80 °C overnight. The reaction was quenched in 25 mL of an ice/water mixture and decolorized with sodium bisulfite. The resulting yellow precipitate was filtered and recrystallized first from glacial acetic acid, then from xylene, and sublimed to yield bright yellow needles of 2,3:6,7-dibenzofluorenone (0.0871 g, 0.311 mmol) in a 28% overall yield: mp 275-276 °C, lit.[7] mp 269–270 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.48–7.57 (m, 4H), 7.86–7.90 (t, 4H), 8.10 (s, 2H), 8.28 (s, 2H); IR 1706.2 cm^{-1}; GC/MS *m/z* 280.

1,2,4,5-Tetrakis(dibromomethyl)benzene (4). The general procedure of Soyer, Kerfanto, and Raphalen[12] was used. 1,2,4,5-Tetramethylbenzene (87.5 g, 0.653 mol) was dissolved in 3.5 L of carbon tetrachloride in a 4 L quartz vessel. The solution was heated to reflux and irradiated by 3000 Å UV light in a Rayonette chemical reactor. Bromine (280 mL, 874 g, 5.46 mol) was added over a period of 6 h. After 2 days, the product was filtered and washed with boiling chloroform. Average yields were 78% (390 g, 0.510 mol). The crude product was used without further purification. An analytical sample was prepared by recrystallization from *p*-dioxane, mp 305 °C dec; lit. mp 305 °C dec.

***N,N′*-Diphenyl-2,3:6,7-anthracenedicarboximide (5).** *Tetrakis*-1,2,4,5-(dibromomethyl)benzene (20 g, 0.0261 mol), *N*-phenylmaleimide (9.00 g, 0.0520 mol), NaI (45 g, 0.300 mol), and 300 mL of DMAc were charged into a capped Erlenmeyer and maintained at 80 °C while stirring. After 10 h, a yellow precipitate formed. The precipitate was filtered, triturated once with boiling water and three times with boiling *p*-dioxane, and dried. The resulting bright yellow solid, 5.35 g (47%, 0.0123 mol), is insoluble in organic solvents and is resistant to methanesulfonic and polyphosphoric acids. The diimide **5** gradually darkens on heating in air to 300 °C: IR (KBr cm^{-1}) 1773.2, 1724.2, 1504, 1373.4, 1128.7; FAB mass spec [M$^{\bullet+}$] = 468.4.

2,3,6,7-Anthracenetetracarboxylic Acid (6). Diimide **5** (2.00 g, 4.27 mmol) and 50 mL of 20% NaOH were charged into a round bottomed flask and refluxed under nitrogen for 12 h. The resulting solution was decolorized with charcoal and extracted with 2 × 50 mL portions of ether. The aqueous solution was acidified and the resulting yellow precipitate was isolated by centrifugation, washed with distilled water, recentrifuged, and dried in vacuo. Tetraacid **6** is a pale yellow amorphous solid which dissolves in 5% potassium carbonate solution with evolution of carbon dioxide: mp dec >300 °C in air; IR (KBr cm^{-1}) 3044.1, 2663.3, 1707.4, 1483.3, 1408.7, 1304.1, 1251.8, 1139.6, 1035.3, 938.2; FAB mass spec [M+H$^+$] = 355.4; ^{1}H NMR (200 MHz, D_2O) (as potassium salt) δ 8.65 (s, 2H) and 8.20 (s, 4H); ^{13}C NMR δ 180.0, 138.9, 134.0, 130.2, 129.8.

Scheme 1. Mechanism of Diels–Alder Aromatization Reaction



2,3,6,7-Tetrakis(methoxycarbonyl)anthracene. Tetraacid **6** (1.00 g, 2.82 mmol) was converted to the tetrasodium salt with excess potassium carbonate (3.15 g, 0.0214 mol) in 45 mL of water. The resulting brown salt solution was filtered into a round bottomed flask. The water was removed and the residue dried in vacuo. To this were added 50 mL of dry acetone and a 1.5 molar excess (12.14 g, 0.0169 mol) of dimethyl sulfate. The solution was allowed to reflux overnight. The resulting suspension was filtered and the acetone evaporated. The residual oil was diluted with about 3 mL of acetonitrile and refrigerated. Crystals of the of the tetraester were isolated by filtration, sublimed in vacuo, and recrystallized from acetonitrile to yield 0.360 g (0.877 mmol) of crystals suitable for X-ray analysis (31% from the tetraacid): mp 226–228 °C; ^{1}H NMR (200 MHz, DMSO-d_6) δ 9.01 (s, 2H), 8.59 (s, 4 H) 3.91 (s, 12H); ^{13}C NMR δ 52.7, 128.4, 129.9, 131.0, 131.4, 167.0; GC/MS single peak *m/z* 410.

Results and Discussion

Our synthesis of benz[*f*]indan-1-one utilizes the tandem Diels–Alder aromatization reaction, which proceeds through an *o*-quinodimethane intermediate brought about by the action of sodium iodide on α,α,α′α′-tetrabromo-*o*-xylene in DMF (Scheme 1).[13] The resulting diene then reacts with 2-cyclopentenone and spontaneously dehydrohalogenates to benz[*f*]indan-1-one.

There are many advantages of this synthesis over previous methods. The greatest advantage from a practical viewpoint is that it uses inexpensive, readily available starting materials. The simplicity of the methodology is also important as the reagents are easily mixed together and allowed to stir at 80 °C overnight. Finally, this synthesis generates the product in one step with typical isolated yields of 57%. Benz[*f*]indan-1-one is readily transformed to the benz[*f*]indene.[13]

The tandem Diels–Alder aromatization reaction may be used to synthesize 2,3:6,7-dibenzofluorenone by a simple extension of the previous chemistry. The reaction is almost identical to that for the synthesis of benz[*f*]-indan-1-one except that the dienophile is itself a modified product of the tandem Diels–Alder aromatization reaction. NBS bromination at the benzylic position in benz-[*f*]indan-1-one followed by dehydrohalogenation with triethylamine yields benz[*f*]inden-1-one, which reacts with α,α,α′,α′-tetrabromo-*o*-xylene as before to yield 2,3,6,7-dibenzofluorenone in a 28% yield overall (Scheme 2).

Octabromodurene undergoes a bis tandem Diels–Alder aromatization reaction with *N*-phenylmaleimide in the

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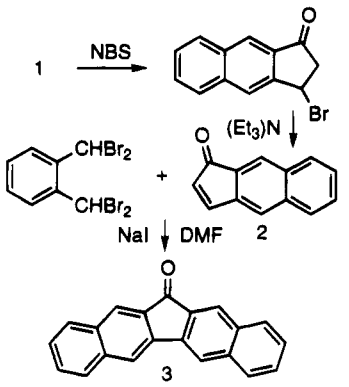
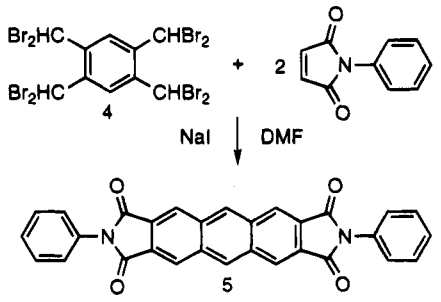
Scheme 2. Synthesis of 2,3:6,7-dibenzofluorenone



Scheme 3. Synthesis of *N,N'*-Diphenyl-2,3:6,7-anthracenedicarboximide



presence of NaI in DMAc to give the *N,N'*-diphenyl-2,3:6,7-anthracenedicarboxyimide (Scheme 3). This diimide is highly insoluble, which limits the methods with which it can be characterized. The IR spectrum and FAB mass spectroscopy analyses were consistent with the proposed structure but were not definitive. In order to better characterize the 2,3,6,7-anthracenetetracarboxyl nucleus, we synthesized a soluble derivative from the diimide.[14] Basic hydrolysis of the diimide yields a water soluble 2,3,6,7-anthracenetetracarboxylate salt which could then be analyzed by ^{13}C and ^{1}H NMR. The tetraacid, precipitated by HCl, can be redissolved in organic solvents containing an organic base such as triethylamine. Since the diimide and the tetraacid were not crystallizable, we could not obtain X-ray data to confirm that our product was a 2,3,6,7-tetrasubstituted anthracene.

To break up the presumed solubility limiting microcrystallinity characteristic of flat polynuclear aromatic compounds and dimerization of organic acids, we formed the tetramethyl ester. A modified procedure of Grundy, Jones, and Pattenden[15] was used successfully. 2,3,6,7-Tetrakis(methoxycarbonyl)anthracene is a pale yellow, soluble, crystalline compound. X-ray crystallography verified the structure.[16]

We have demonstrated that the tandem Diels-Alder aromatization reaction is a flexible synthetic method not only for the synthesis of 2,3-disubstituted naphthalenes but also for 2,3,6,7-tetrasubstituted anthracenes. This method is simpler, uses less expensive reagents, and gives improved yields over previous methods. Building on this method, we are now engaged in developing reactive monomers and polymers based on 2,3,6,7-tetrasubstituted anthracenes. A full account of this research is to be reported elsewhere.

Acknowledgment. M.L.M. and C.L.B. thank the NSF (CHE-9122842) for partial support of this research.

(14) We attempted the synthesis of the corresponding dianhydride and tetramethyl and tetraethyl esters by substituting maleic anhydride and dimethyl fumarate and diethyl maleate for *N*-phenylmaleimide. While indications were that these reactions were at least partly successful, the products were very difficult to isolate from byproducts.

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(16) The authors have deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.