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# Regioselective Syntheses of 5- and 6-Aminoanthracene-2,3-dimethanol

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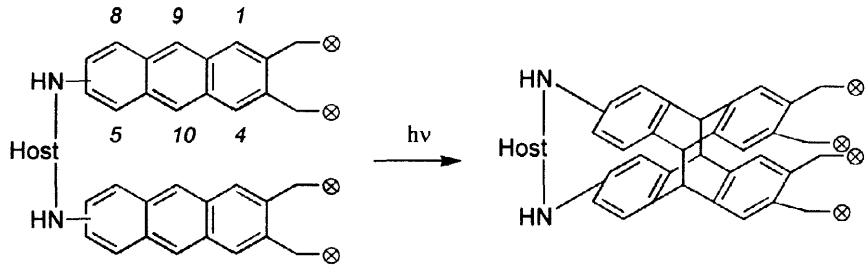
***Abstract:*** We report the regioselective synthesis of 6-amino-2,3-anthracenedimethanol (**2**) beginning from commercially available 2,3-dimethylanthraquinone. The more reactive 9- and 10-positions of the anthracene core are masked from electrophilic attack by "protection" of the molecule through formation of its corresponding ethano anthracene ("barrelane") adduct. Also reported is the synthesis of the corresponding 5-amino isomer (**1**) from readily available anthraquinone-2,3-dicarboxylic acid. 

## INTRODUCTION

We are developing a research program that utilizes the photochemical [4+4] dimerization of anthracene in host-guest systems. Towards this goal, we required anthracene derivatives that contained (i) points (such as the amine nitrogens shown below) for covalent attachment to larger molecular frameworks, and (ii) moieties (indicated as ⊗ below) that lend hydrophilicity to the otherwise hydrophobic molecule. Introduction of substituents *via* electrophilic aromatic substitution at the central 9- and 10- positions, while being the most straightforward approach, was undesirable, since the presence of substituents in these positions is known to hinder photodimerization.[1] In addition, differential functionality on the peripheral rings was required to suit our two purposes stated above, and we chose to target 5- and 6-amino substituted anthracene-2,3-dimethanols **1** and **2**.

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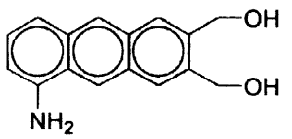
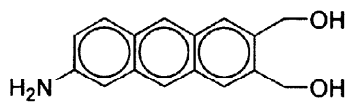
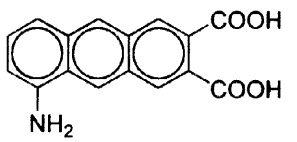
Anthracene has seen extensive application in the fields of molecular recognition and sensing. Anthracene derivatives have been employed in host-guest systems by Lehn,[2] Rebek,[3] Dougherty,[4] Stoddart,[5] Whitlock,[6] and Zimmerman.[7] Several groups have taken advantage of the fluorescence properties of anthracenes for the design of molecular sensors.[8] Anthracene has been explored for use in conducting polymers.[9] Finally, the anthracene / dianthracene photoequilibrium has been coupled to metal binding to afford metal ion responsive sensors.[10]



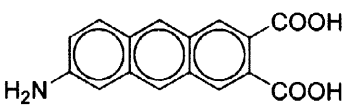

**1**




**2**




**3**

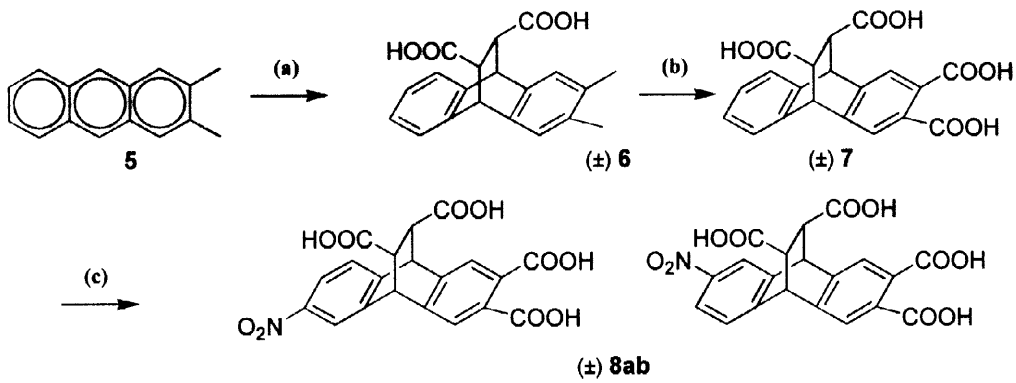



**4**

A search of the literature revealed, aside from an impractical synthesis of 2-amino-6-methylanthracene,[11] a single useful reference for nitrogenated anthracenes with the desired regiochemistry and functionality: Gundermann *et al.*[12] have published syntheses of both 5- and 6-aminoanthracenedicarboxylic acid **3** and **4**. We have made modifications to their synthesis of **3** and have extended it to provide the desired amino diol **1**. In contrast, the reported synthesis of **4** was unsatisfactory for preparative scale work: The first step in the literature scheme is the the Friedel-Crafts acylation of *o*-xylene with 4-nitrophthalic anhydride, which yields the desired quinone in only 10% yield. Since we anticipated further transformations beyond this step, it was necessary to improve the synthesis of **1**. Here we describe the synthesis of diols **1** and **2**.

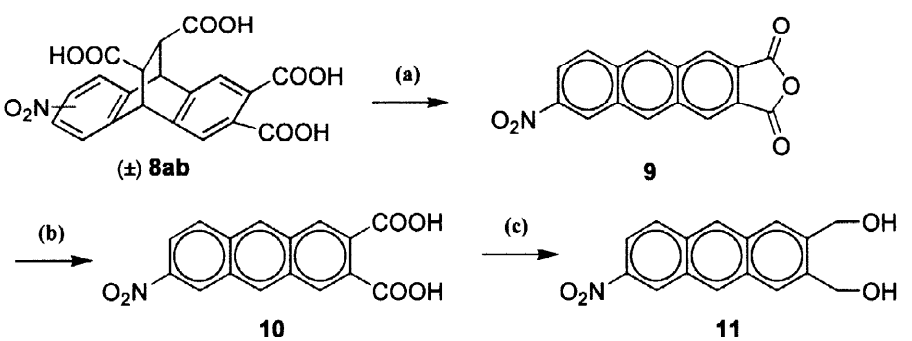
## RESULTS

*Synthesis of* **2**. Our approach towards construction of an efficient synthesis of **2** was prompted by a communication from McCormick and Marquardt[13] on the selective oxidation of alkyl anthracenes to anthracenecarboxylic acids *via* 9,10-ethano anthracenes (also termed "dibenzobarrelanes.") The Diels-Alder reaction between anthracenes and dienophiles can be smoothly performed in either direction, depending on conditions.[14] Formation of the Diels-Alder adduct precludes electrophilic reactivity at the 9- and 10- positions and thus oxidation to anthraquinone is prevented. Furthermore, Baldwin *et al.*[15] have nitrated ethano anthracenes and performed further electrophilic transformations on the amines thus obtained. Pyrolytic retro Diels-Alder extrusion of ethylene then affords anthracenes with functionality on the peripheral rings — in contrast to the regiochemistry of direct nitration or halogenation of anthracene.[12] We reasoned that electrophilic substitution on tetracarboxylate **7** would occur on the ring with the most electron density, *i.e.*, the unsubstituted ring lacking the electron-withdrawing carboxylates.




**Scheme 1. Synthesis of nitro tetracarboxylate 8ab. (a) fumaric acid, dioxane, Δ (91%) (b) $KMnO_4$, $H_2O$, 60 °C (90%) (c) $HNO_3$, HOAc, $H_2SO_4$ (86%).**

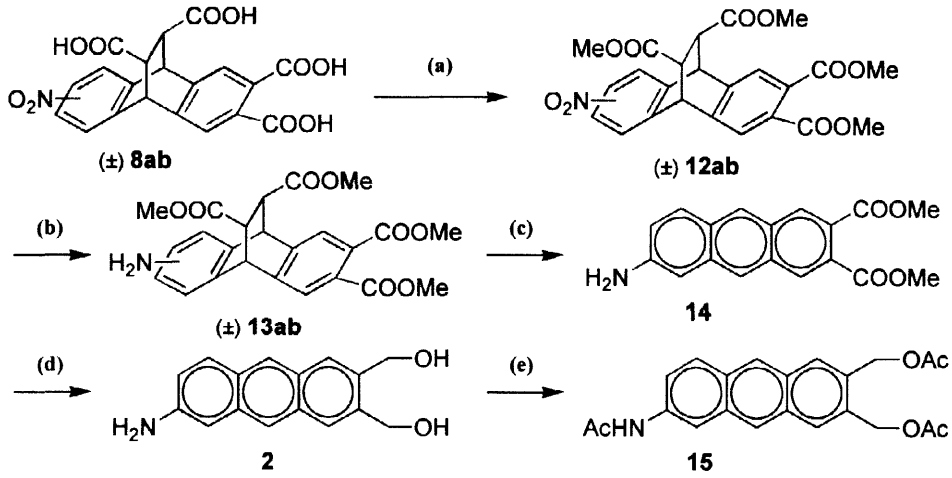
Synthesis begins with 2,3-dimethylanthracene **5**[16,17] (obtained from the corresponding quinone.[18]) Reaction of the acene with fumaric acid in dioxane at reflux gives adduct (±) **6** (Scheme 1), in accordance with the literature reports for this[13] and related[14] compounds. Oxidation of the benzylic methyl groups[13] followed by electrophilic nitration gave tetraacid **8** as an inseparable mixture of diastereomers. The literature procedure[19] ($Ac_2O$, $HNO_3$, $CH_2Cl_2$, -45 °C) for nitration of a related barrelene failed to nitrate **7**, due perhaps to low solubility or electron deficiency of the substrate. After considerable experimentation we found conditions (HOAc, $H_2SO_4$, $HNO_3$) that successfully nitrated tetraacid **7** in high yield. The NMR signals of the product were present in two sets, presumably belonging to the two diastereomers **8a** and **8b** (Scheme 1). No effort was made to assign the isomers, which were present in an ~1:1 mixture. The existence of isomers is inconsequential for this scheme, since both isomers are converted to the same nitro anthracene in the following step.




**Scheme 2. Synthesis of nitro-diol 11. (a) $Ph_2O$, Δ (94%) (b) $Na_2CO_3$, $H_2O$, Δ (86%) (c) $BH_3$•THF, THF (49%).**

Retro-Diels-Alder reaction was induced by heating **8ab** in diphenyl ether at reflux. This reaction proceded with concomitant dehydration, to afford anhydride **9** (Scheme 2). Extrusion of the fumarate moiety simplified substantially the NMR: presence of four downfield singlets indicated that the 1,4,9, and 10-positions were, as expected, unaffected by nitration. The coupling pattern of the remaining 3 protons was consistent with a 1,2,4- trisubstituted benzene ring, *i.e.*, nitration occured in the 6-position. The pattern was also unambi-

guously different from the 5-isomer prepared by an alternate route (*vide infra*). Treatment of **9** with dilute base readily provides diacid **10** which is then reduced with borane-THF to nitro diol **11**. Attempts to reduce the nitro group of either **10** or **11** were complicated by solubility problems and the formation of unidentified impurities. In an attempt to provide more tractable intermediates, we therefore rearranged steps in the synthetic scheme:

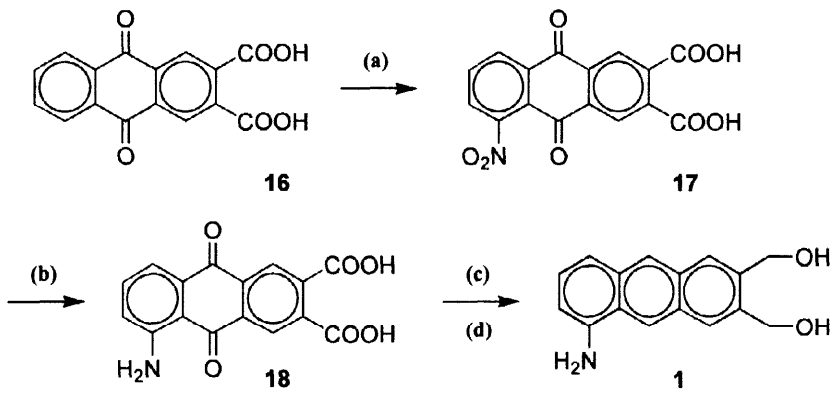



**Scheme 3. Synthesis of amino diol 2. (a) MeOH, $H^+$ (96%) (b) $Fe^0$, HCl, EtOH (99%) (c) $Ph_2O$, Δ (85%) (d) Red-Al®, THF, 0 °C (50%) (e) $Ac_2O$, pyr (80%).**

Synthesis began with esterification of tetraacid **8ab** (Scheme 3), in order to improve organic solubility. The resulting nitro ester **12ab** was reduced with metallic iron to give amine **13ab**. As with **8**, both **12** and **13** existed as a mixture of diastereomers. Retro Diels-Alder fragmentation of tetraester **13ab** turned out to be more convenient than for tetraacid **7**: (1) Instead of fumaric acid, dimethyl fumarate (bp 192 °C) is produced, which co-distills with diphenyl ether (bp 259 °C) upon vacuum, and (2) Since there are no free carboxylic acid groups, anhydride formation is obviated. Also, despite our concerns, there was no evidence for intermolecular amide formation between the esters and the amine. Reduction of ester **14** to diol **2** was achieved by treatment with Red-Al®, a reagent that we have found to be convenient for reduction of this and other anthracenecarboxylates. We have found that alternative reducing agents such as $LiAlH_4$[20] can give as significant side products both 9,10-dihydroanthracenes and methyl anthracenes.[21] The diol-amine proved to be somewhat unstable: chromatography afforded fractions that were bright yellow on elution but which on standing discolored to give a brownish tint. We attribute this behavior to autoxidation, which has been reported in other anthraceneamines.[22] The compound was therefore characterized as its triacetate **15**. The stability of the triacetate was much higher than that of amine/diol **2**.

*Synthesis of* **1**. The synthesis of the alternate isomer, 5-aminoanthracene-2,3-dicarboxylic acid **3** was achieved by modification of a known procedure (Scheme 4). Nitration of readily available[23] diacid **16** under

literature conditions[12] (fuming $HNO_3$, $H_2SO_4$, 0 °C) was plagued by poor solubility of the substrate. In contrast, nitration was accomplished smoothly at 55 °C (Scheme 4) to afford nitro diacid **17**. Reduction was achieved in a three step sequence: (i) treatment with $Na_2S$ (in place of Sn(II)[12]) which reduced the nitro compound **17** to amine **18**; (ii) zinc / $NH_4OH$ reduction to give the amino diacid **3**; and (iii) $BH_3$•THF reduction of the diacid to give the target bis(hydroxymethyl) molecule **1**. Our new sequence proceeds in comparable yields to the previously reported procedure and has the advantage of avoiding the use of heavy metal salts. Although amine/diol **1** will decompose on prolonged standing, it had sufficient stability that we were able to characterize fully this compound.




**Scheme 4. Synthesis of amino diol 1. (a) $HNO_3$, $H_2SO_4$, 55 °C (80%) (b) $Na_2S$, EtOH / $H_2O$, Δ (74%) (c) Zn, $NH_4OH$, Δ (77%) (d) $BH_3$•THF, THF, 0 °C (33%).**

## DISCUSSION

This synthetic scheme was aimed at obtaining differentially functionalized, trisubstituted anthracenes — with well-defined regiochemistry — for purposes described above. Towards this goal, we chose to place both carbon and nitrogen substituents on the ring, in order to maximize the "orthogonality" of these groups. Our plan involved electrophilic nitration as the means of introduction of nitrogen. Anthracene will react with electrophiles at the 9- and 10- carbons, due to the large HOMO coefficient at these sites, which was precisely where substitution was undesired. These sites were blocked in two ways: (1) Diels-Alder addition across C-9 and C-10, which converted hybridization to $sp^3$ and shut down their reactivity towards electrophiles, and (2) utilization of the corresponding quinones, reversing the electronic demand C-9 and C-10. In addition, these strategies provided complementary regiocontrol towards nitration. Although the target amine diols **1** and **2** are susceptible to decomposition, they should be valuable as synthetic intermediates under the proper conditions. (Conversely, the electron-poor members of these synthetic scheme were much more robust and showed very little tendency to decompose).

## CONCLUSION

We expect that this methodology will be advantageous for the synthesis of substituted anthracenes that are of current interest in organic and materials chemistry. Both the hydroxyl and amino functionalities allow for several synthetic manipulations. In addition, the Diels-Alder strategy should be of use to functionalize both larger acenes and heterocyclic compounds. Furthermore, the amine barrelanes might be converted to amine anthranilates using Baldwin's procedure.[15] These anthranilates could then be used in a benzyne cycloaddition scheme to homologate the acene.[24] Because of the favorable solubility properties of the ethano anthracenes, compared to their acene relatives, these molecules could be easily incorporated into polymers, followed by thermolytic fumarate extrusion to give poly(acene)s.[25]

Several advantages of this synthesis are apparent: regioselectivity, robustness of intermediates towards oxidative damage, and favorable solubility properties. In addition, the only metals employed in this synthesis are benign (Fe, Mn, Zn), in contrast to those used in several other acene syntheses. Further studies to explore the photochemistry of these molecules and host-guest systems derived from them will be reported in due course.

## ACKNOWLEDGMENTS

Acknowledgment is made to the Donors of the Petroleum Research Fund, administered by the American Chemical Society, and Vanderbilt University, for support of this research.

## EXPERIMENTAL

All melting points are uncorrected. $^1$H and $^{13}$C NMR were recorded on a Bruker AM-300 NMR. FTIR were recorded on a Nicolet Magna-IR 550 spectrometer. FAB-MS were performed at the University of Illinois mass spectrometry facility. Elemental analyses were performed by Atlantic Microlab, Inc. (Norcross, GA). All samples for elemental analysis were dried *in vacuo* at 80 °C for at least 24 hr before submission. Proton assignments are given for all protons for which assignment is unambiguous.

**(±)2,3-Dimethyl-9,10-ethanoanthracene-*trans*-11,12-dicarboxylic acid (6)** A mixture of 2,3-dimethyl-anthracene **5**[17] (4.64 g, 22.5 mmol) and fumaric acid (4.64 g, 40.0 mmol) in dioxane (100 mL) was refluxed for 3 d. After cooling to room temp, the solvent was removed *in vacuo*. The residue was stirred in 200 mL of 5% $NaHCO_3$ solution for 3 h. The solution was filtered and the filtrate was slowly added with stirring to 150 mL of warm 10% HCl solution, whereupon a yellow solid formed. The solution was filtered while warm (to keep unreacted fumaric acid in solution). The ppt was dried to yield 6.60 g (20.5 mmol, 91%) of the Diels-Alder adduct **6** as a off-white solid, $R_f$ 0.45 ($CH_3CN$). A sample was recrystallized from EtOH, mp 266-268 °C. $^1$H NMR (DMSO-$d_6$) δ 2.11 (s, 3 H) 2.12 (s, 3 H), 3.06-3.11 (m, 2H), 4.59-4.61 (m, 2H), 7.01 (s, 1H), 7.04-7.08 (m, 2H), 7.14 (s, 1H), 7.19-7.22 (m, 1H), 7.33-7.36 (m, 1H). $^{13}$C NMR (DMSO-$d_6$) δ 173.5, 173.4, 143.1,

140.9, 140.2, 137.9, 133.4, 133.2, 125.9, 125.9, 125.7, 124.8, 124.5, 123.3, 47.5, 47.5, 45.6, 45.6, 19.2, 19.2. FAB-MS calcd for $C_{20}H_{19}O_4$ ($M+H^+$) 323.1283; found 323.1282. Anal. calcd for $C_{20}H_{18}O_4 \cdot \frac{1}{4} H_2O$ C: 73.49 H: 5.71; found C: 72.99 H: 5.71.

**(±)9,10-Ethanoanthracene-2,3,*trans*-11,12-tetracarboxylic acid (7)** Diels-Alder adduct **6** (6.00 g, 18.6 mmol) was dissolved in 185 mL of 0.5 N aq NaOH, and the solution was warmed to 60 °C. $KMnO_4$ (14.7 g, 93.0 mmol) was added in portions, while keeping the temperature below 80 °C to avoid overoxidation. After the addition was completed, the reaction was maintained at 65-75 °C overnight. The mixture was cooled and filtered. The $MnO_2$ residue that had formed was removed by filtration and rinsed with hot water. The combined solution was made acidic with conc HCl. The solution was extracted with 3x20 mL $Et_2O$. The organic extracts were combined, washed with brine, and dried over anhydrous $Na_2SO_4$. Evaporation of the solvent gave tetraacid **7** as a white solid (6.40 g, 16.7 mmol, 90%) mp 160-164 °C (with softening at 140 °C). IR (KBr pellet) 2500-3500 $cm^{-1}$, $^1H$ NMR (DMSO-$d_6$) δ 3.13-3.15 (m, 2H), 4.87-4.89 (m, 2H), 7.10-7.14 (m, 2H), 7.27-7.30 (m, 1H), 7.41-7.44 (m, 1H), 7.56 (s, 1H), 7.70 (s, 1H). $^{13}C$ NMR (DMSO-$d_6$) δ 173.2, 173.0, 168.7, 168.4, 145.6, 143.4, 141.8, 139.7, 131.3, 130.4, 126.4, 126.2, 125.0, 124.7, 123.8, 123.6, 47.0, 46.9, 45.6, 45.5. FAB-MS calcd for $C_{20}H_{15}O_8$ ($M+H^+$) 383.0767; found 383.0763. Anal. calcd for $C_{20}H_{14}O_8 \cdot \frac{1}{4} H_2O$ C: 62.1 H: 3.79; found C: 62.1 H: 4.66.

**(±)6-Nitro-9,10-ethanoanthracene-2,3,*trans*-11,12-tetracarboxylic acid (8ab)** To 4 mL glacial HOAc was added 2.00 g (5.23 mmol) of tetraacid **7**, and then 4 mL of conc $H_2SO_4$ was added carefully. The reaction mixture was then cooled to 0 °C, and 4 mL of a 1:1 mixture of conc $H_2SO_4$ and conc $HNO_3$ was added dropwise while keeping the temperature below 10 °C. After all the acid was added, the mixture was allowed to stir at room temp for 2 h. The mixture was poured onto ice, and extracted with 3x20 mL $Et_2O$. The extracts were combined, washed with brine, and dried over anhydrous $Na_2SO_4$. Evaporation of the solvent gave the desired nitro compound as a white solid (1.93 g; 4.52 mmol, 86%) as an approximately 1:1 mixture of diastereomers arbitrarily labeled **8a** and **8b** (*vide supra*). IR (KBr pellet) 1524, 1348 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$) δ 3.18-3.21 (m, 2H), 5.11-5.16 (m, 2H), 7.56-7.76 (m, 3H), 8.03-8.10 (m, 1H), 8.15 (d, $J$=2.3 Hz, 0.5 H, $H_5$ of isomer **8a**), 8.33 (d, $J$=2.3 Hz, 0.5 H, $H_5$ of isomer **8b**). $^{13}C$ NMR (DMSO-$d_6$) δ 172.9, 172.8, 172.8, 172.7, 168.6, 168.6, 168.3, 168.3, 149.4, 147.7, 146.0, 145.9, 144.5, 144.0, 143.6, 142.5, 142.0, 141.9, 131.7, 131.6, 130.9, 130.8, 126.3, 125.3, 125.2, 125.1, 124.2, 124.0, 122.2, 122.0, 119.8, 119.1, 46.6, 46.5, 46.4, 46.4, 45.3, 45.3, 45.1, 45.1.

**6-Nitro-anthracene-2,3-dicarboxylic anhydride (9)** Barrelane **8ab** (1.72 g, 4.03 mmol) was suspended in $Ph_2O$ (20 mL) under $N_2$. The mixture was refluxed for 4 h (during this period, the starting material dissolved and fumaric acid deposited on the walls of the flask and the condenser). The mixture was cooled slightly, and then the solution was decanted from the solid. The solution was cooled to room temp, whereupon a brown ppt formed. The mixture was filtered, and the ppt was washed with $CCl_4$ and dried to give 1.10 g

(3.75 mmol, 94%) of crude anhydride **9** as a yellow solid, which was typically carried on without purification. IR (KBr pellet) 1839, 1776 $cm^{-1}$, $^1H$ NMR (DMSO-$d_6$) δ 8.29 (dd, $J_{7,8}$=9.3 Hz, $J_{7,5}$=2.1 Hz, 1H, $H_7$), 8.41 (d, $J_{8,7}$=9.3 Hz, 1H, $H_8$), 8.96 (s, 1H), 8.97 (s, 1H), 9.11 (s, 1H), 9.22 (d, $J_{5,7}$=2.1 Hz, 1H, $H_5$), 9.32 (s, 1H).

**6-Nitro-anthracene-2,3-dicarboxylic acid (10)** A mixture of anhydride **9** (1.48 g, 5.05 mmol), $Na_2CO_3$ (1.2 g, 11 mmol), and $H_2O$ (13 mL) was refluxed for 2 h. The solution was cooled to room temp, and washed with $Et_2O$. The ether washes were back extracted with $H_2O$, and the combined aqueous layers were acidified by the slow addition of 10% $H_2SO_4$, whereupon a brown ppt formed. The mixture was filtered, and the ppt was dried to give 1.35 g (4.34 mmol, 86%) of diacid **10** as a yellow solid, $R_f$ 0.20 ($CH_3CN$), mp >310 °C. IR (KBr pellet) 2500-3500 $cm^{-1}$. $^1H$ NMR (DMSO-$d_6$) δ 8.22 (dd, $J_{7,8}$=9.3 Hz, $J_{7,5}$=2.1 Hz, 1H, $H_7$), 8.33 (d, $J_{8,7}$=9.3 Hz, 1H, $H_8$), 8.66 (s, 2H), 8.93 (s, 1H), 9.16 (s, 1H), 9.20 (d, $J_{5,7}$=2.1 Hz, 1H, $H_5$). $^{13}C$ NMR (DMSO-$d_6$) δ 168.2, 168.1, 145.2, 133.1, 132.3, 131.7, 131.7, 131.4, 131.1, 131.0, 130.7, 130.6, 130.1, 128.2, 126.0, 119.0. FAB-MS calcd for $C_{16}H_{10}NO_6$ (M+1) 312.0508; found 312.0509. Anal. calcd for $C_{16}H_9NO_6 \cdot H_2O$ C: 58.36, H: 3.37, N: 4.26; found C: 58.27, H: 3.32, N: 3.88.

**6-Nitro-2,3-bis(hydroxymethyl)anthracene (11)** In a 25-mL flask, flushed with $N_2$, were placed diacid **10** (360 mg, 1.16 mmol), THF (2 mL), and a magnetic stir bar. Next 3.5 mL $BH_3$•THF (1 M in THF, 3.5 mM) was added dropwise (*ca.* 1 h) to the stirred mixture kept at 0 °C. The mixture was then kept at 0 °C for 1 h. The mixture was allowed to warm to room temp, and stirred for 12 h. To the mixture was carefully added 50% (v/v) aqueous THF (6 mL) to quench unreacted borane. The solution was saturated with anhydrous $K_2CO_3$. The layers were separated, and the water layer was extracted with THF three times. The organic layers were combined, and dried over anhydrous $MgSO_4$. The solvent was evaporated, and the residue was chromatographed ($SiO_2$ / EtOAc). The fractions were evaporated to give 162 mg (0.572 mmol, 49%) of diol **11** as an orange solid, $R_f$ 0.35 (EtOAc), mp 212-214 °C. $^1H$ NMR (DMSO-$d_6$) δ 4.75 (d, *J*=5.3 Hz, 4 H), 5.39 (t, *J*=5.3 Hz, 1H), 5.40 (t, *J*=5.3 Hz, 1H), 8.11-8.15 (m, 3 H), 8.29 (d, $J_{8,7}$=9.3 Hz, 1H, $H_8$), 8.73 (s, 1H), 8.97 (s, 1H), 9.19 (d, $J_{5,7}$=2.1 Hz, 1H, $H_5$). $^{13}C$ NMR (DMSO-$d_6$) δ 144.3, 140.7, 139.6, 132.8, 131.9, 131.3, 130.2, 129.6, 128.7, 126.0, 126.0, 124.6, 124.4, 117.6, 60.5, 60.4. FAB-MS calcd for $C_{16}H_{13}NO_4$: 283.0845; found: 283.0844. Anal. calcd for $C_{16}H_{13}NO_4$ C: 67.84, H: 4.63, N: 4.94; found C: 67.92, H: 4.53, N: 4.98.

**(±)Tetramethyl 6-nitro-9,10-ethanoanthracene-2,3,*trans*-11,12-tetracarboxylate (12ab)** A mixture of 2.32 g (5.43 mmol) of the nitro tetraacid **8ab,** 125 mL of absolute MeOH, and 2 mL of conc $H_2SO_4$ were refluxed for 2 d. The mixture was cooled to room temp, and the solvent was removed. To the residue was added 30 mL of cold $H_2O$. The resulting solid was filtered and dried to give 2.51 g (5.19 mmol, 96%) of tetraester **12ab** as bright yellow crystals, $R_f$ 0.65 (EtOAc). $^1H$ NMR ($CDCl_3$) δ 3.43-3.48 (m, 2H), 3.65-3.68 (4 lines, 6H, -COOC$\underline{H}_3$), 3.88-3.91 (4 lines, 6H, -COOC$\underline{H}_3$), 4.92-4.96 (m, 2H), 7.42 (d, *J*=8.1 Hz, 0.5H), 7.50 (d, *J*=8.1 Hz, 0.5H), 7.68-7.72 (m, 2H), 8.05 (d, *J*=2.3 Hz, 0.5H, $H_5$ of isomer **12a**), 8.07-8.12 (m, 1H), 8.21 (d, *J*=2.3 Hz, 0.5H, $H_5$ of isomer **12b**). $^{13}C$ NMR ($CDCl_3$) δ 171.7, 171.4, 167.8, 167.7, 167.5, 167.4, 148.0, 146.8,

146.5, 144.2, 143.7, 142.6, 142.4, 142.2, 140.9, 131.2, 131.1, 130.7, 125.8, 125.7, 124.9, 124.7, 124.6, 122.8, 122.6, 120.0, 119.3, 52.8, 52.8, 47.0, 46.9, 46.8, 46.8, 46.3, 46.1.

**(±)Tetramethyl 6-amino-9,10-ethanoanthracene-2,3,*trans*-11,12-tetracarboxylate (13ab)** A solution of the nitro tetraester **12ab** (2.0 g, 4.14 mmol) in 140 mL of EtOH was heated under gentle reflux in the presence of dilute aqueous HCl (2 N, 5.6 mL) and Fe powder (5.6 g, 100 mmol) with vigorous stirring. The reduction process was monitored by TLC, and stopped when TLC showed complete conversion. The mixture was cooled and poured into 100 mL of saturated aqueous $NaHCO_3$ and extracted with $CH_2Cl_2$. The extracts were dried over $MgSO_4$ and evaporated to give 1.86 g (4.10 mmol, 99%) of amine **13ab** as a yellow solid, ($R_f$ 0.60, EtOAc) which was sufficiently pure (as indicated by NMR spectroscopy) for the next step. IR (KBr pellet) 3450, 3375, 1626 $cm^{-1}$. $^1H$ NMR ($CDCl_3$) δ 3.30-3.35 (m, 1H), 3.43-3.46 (m, 1H), 3.62-3.66 (m, 6H), 3.86-3.87 (m, 6H), 4.66-4.69 (br s, 2H), 6.38-6.44 (m, 1H), 6.61 (d, $J$=2.2 Hz, 0.5H, $H_5$ of isomer **13a**), 6.69 (d, $J$=2.2 Hz, 0.5H, $H_5$ of isomer **13b**), 6.98 (d, $J$=7.9 Hz, 0.5H, $H_7$ of isomer **13a**), 7.07 (d, $J$=7.9Hz, 0.5H, $H_7$ of isomer **13b**), 7.58-7.64 (m, 2H). $^{13}C$ NMR ($CDCl_3$) δ 172.5, 172.4, 172.3, 172.2, 168.3, 168.2, 167.9, 167.8, 146.5, 145.7, 145.4, 145.3, 144.8, 144.0, 142.0, 140.1, 130.8, 130.5, 130.2, 130.0, 129.7, 128.7, 125.5, 125.3, 124.9, 124.7, 124.2, 123.8, 112.9, 112.8, 112.2, 111.4, 52.6, 52.6, 52.5, 52.4, 47.8, 47.3, 46.6, 46.4, 45.7, 45.5.

**Dimethyl 6-aminoanthracene-2,3-dicarboxylate (14)** Amino tetraester **13ab** (906 mg, 2.00 mmol) was added to 10 mL of $Ph_2O$. The flask was purged with $N_2$, and the mixture was brought to reflux. Reflux was maintained for 4 hr. The mixture became homogeneous and the liberated dimethyl fumarate deposited on the walls of the flask and the condenser as white crystals. The solution was cooled slightly, and transferred from the flask to another beaker *via* Pasteur pipet, with care taken not to carry any dimethyl fumarate crystals along with the desired solution. On cooling to room temp, a yellow ppt was formed, which was removed *via* filtration and rinsed with $CCl_4$ to give 526 mg (1.70 mmol, 85%) of diester **14** as a yellow solid, $R_f$ 0.65 (EtOAc), mp 216-218 °C. $^1H$ NMR ($CDCl_3$) δ 3.96 (d, 6H), 7.06 (d, $J_{5,7}$=2.3 Hz, 1H, $H_5$), 7.09 (dd, $J_{7,8}$=9.5 Hz, $J_{7,5}$=2.3 Hz, 1H, $H_7$), 7.89 (d, $J_{8,7}$=9.5 Hz, 1H, $H_8$), 8.16 (s, 1H), 8.27 (s, 1H), 8.35 (s, 1H), 8.39 (s, 1H). $^{13}C$ NMR (DMSO-$d_6$) δ 168.0, 167.4, 147.8, 135.6, 131.6, 130.8, 128.0, 127.8, 127.4, 126.7, 124.0, 122.5, 122.0, 118.6, 102.6, 52.4, 52.4. FAB-MS calcd for $C_{18}H_{15}NO_4$($M+H^+$) 310.1079; found 310.1079. Anal. calcd for $C_{18}H_{15}NO_4 \cdot ¼ H_2O$ C: 68.89, H: 4.98, N: 4.46; found C: 69.08, H: 4.91, N: 4.31.

**6-Aminoanthracene-2,3-dimethanol (2)** In a 25-mL flask, flushed with $N_2$, were placed **14** (154.5 mg, 0.500 mmol), THF (10 mL), and a magnetic stir bar. The solution was cooled to 0 °C, and 0.7 mL of Red-Al® (65 wt % in toluene) was added dropwise (*ca.* 10 min). The mixture was then kept at 0 °C for 45 min. The reaction was cautiously quenched by the slow addition of 5 mL of aqueous $Na_2SO_4$, whereupon much gas was evolved. To the mixture was then added 5 mL of aqueous Rochelle salt, and the mixture was stirred for 1 h. The mixture was then diluted with 5 mL of $H_2O$ and 15 mL of EtOAc, and stirring was continued. After 1 h, the mixture was diluted with an additional 5 mL of $H_2O$ and 15 mL of EtOAc. The mixture was filtered, the

$H_2O$ layer was extracted with 3x5 mL EtOAc. The extracts were combined and dried over $MgSO_4$. The solvent was evaporated to give 63.5 mg (0.25 mmol, 50%) diol **2** as a brown solid, mp >310 °C. Purification by chromatography was attempted; however, column fractions discolored noticeably, suggesting facile decomposition. $^1$H NMR (DMSO-$d_6$) δ 4.67 (t, $J$=5.6 Hz, 4H), 5.21 (t, $J$=5.6 Hz, 1H), 5.18 (t, $J$=5.6 Hz, 1H), 5.49 (s, 2 H), 6.86 ($J_{5,7}$=2.2 Hz, 1H, $H_5$), 6.99 (dd, $J_{7,8}$=8.8 Hz, $J_{7,5}$=2.2 Hz, 1H, $H_7$), 7.77 (d, $J_{8,7}$=8.9 Hz, 1H, $H_8$), 7.81 (s, 1H), 7.83 (s, 1H), 7.97 (s, 1H), 8.21 (s, 1H). $^{13}$C NMR (DMSO-$d_6$) δ 145.8, 137.8, 135.5, 133.6, 131.3, 128.9, 127.7, 126.4, 125.3, 125.3, 124.1, 120.6, 120.4, 103.0, 61.0, 61.0. FAB-MS: The compound did not give a molecular ion. Anal. A satisfactory elemental analysis could not be obtained.

**2,3-bis(acetoxymethyl)-6-(acetamido)anthracene (15)** Amino diol **2** (76.0 mg, 300 μmol) was dissolved in 5 mL (62 mmol, 207 eq) pyridine, and 2 mL (21 mmol, 70 eq) $Ac_2O$ was added. The solution was stirred at room temp for 1 h. The solvent was removed, and 10 mL water was added to the residue. The solid that formed was isolated by filtration and purified by column chromatography ($SiO_2$; 4:1 EtOAc : hexane) to give 91.1 mg (240 μmol, 80%) of triacetate **15** as a yellow solid, $R_f$ 0.40 (EtOAc), mp 218-220 °C. $^1$H NMR (DMSO-$d_6$) δ 2.07-2.16 (m, 9H); 5.31 (s, 4H), 7.55 (dd, $J_{7,5}$=1.8 Hz, 1H, $H_7$), 8.02-8.06 (m, 3H), 8.48-8.49 (m, 3H), 10.22 (s, 1H). $^{13}$C NMR (DMSO-$d_6$) δ 170.2, 168.8, 136.6, 132.2, 131.8, 131.0, 130.8, 129.4, 128.9, 128.8, 128.3, 125.9, 125.0, 121.2, 113.6, 63.8, 63.8, 24.2, 20.7. FAB-MS calcd for $C_{22}H_{22}NO_5$ ($M+H^+$) 380.1498; found 380.1497. Anal. calcd for $C_{22}H_{21}NO_5 \cdot ¼ H_2O$ C: 68.83, H: 5.64, N: 3.65; found C: 68.82, H: 5.66, N: 3.60.

**5-Nitroanthraquinone-2,3-dicarboxylic acid (17)** To a mixture of 2 mL of conc $H_2SO_4$ and 2 mL of fuming $HNO_3$ at 0 °C, was added 1.18 g (3.98 mmol) of 2,3-anthraquinonedicarboxylic acid **16**.[23] The solid did not all dissolve. The mixture was gradually warmed to about 55 °C, by which time all the solid had dissolved.The mixture was stirred at 55 °C for 1 h. The mixture was then cooled to room temp and poured onto ice, whereupon a yellow ppt formed. The mixture was filtered and the ppt was washed with water. After drying, 1.09 g (3.19 mmol, 80%) of nitro compound **17** was obtained as a yellow solid, $R_f$ 0.40 ($CH_3CN$), mp 298-300 °C (lit.[12] 296 °C). A sample was recrystallized from HOAc, mp 312-314 °C. IR (KBr pellet) 1536, 1314 cm$^{-1}$. $^1$H NMR (DMSO-$d_6$) δ 8.12 (t, $J_{7,8}$=$J_{7,6}$=7.9 Hz, 1H, $H_7$), 8.21-8.24 (dd, $J_{8,7}$=7.9 Hz, $J_{8,6}$=1.1 Hz, 1H, $H_8$), 8.27 (s, 1H), 8.34 (s, 1H), 8.42-8.45 (dd, $J_{6,7}$=7.9 Hz, $J_{6,8}$=1.1 Hz, 1H, $H_6$). $^{13}$C NMR (DMSO-$d_6$) δ 179.9, 179.1, 167.2, 167.2, 148.4, 137.5, 137.5, 135.9, 134.4, 134.2, 133.9, 129.3, 128.1, 126.7, 126.7, 123.8.

**5-Aminoanthraquinone-2,3-dicarboxylic acid (18)** A suspension of 2.17 g (6.36 mmol) **17** in 35 mL EtOH was heated to reflux. A solution of 1.5 g (6.24 mmol, 0.98 equiv) of $Na_2S$ in 10 mL $H_2O$ was added dropwise within a 20 min period. The mixture was refluxed for 5 h. The reaction mixture was cooled to room temp. The mixture was diluted with a five-fold amount of water. The solution was acidified carefully with dilute HCl (6 M). The deep purple ppt was filtered, washed with $H_2O$, and dried, to afford 1.47 g (4.72 mmol, 74%) of crude diacid **18** as a dark purple solid. IR (KBr pellet) 3431, 3313, 1535 (N-H) cm$^{-1}$. $^1$H NMR

(DMSO-$d_6$) δ 7.23 (dd, $J_{6,7}$=8.4 Hz, $J_{6,8}$=0.9 Hz, 1H, $H_6$), 7.42 (dd, $J_{8,7}$=7.2 Hz, $J_{8,6}$=0.9 Hz, 1H, $H_8$), 7.54 (dd, $J_{7,6}$=8.4 Hz, $J_{7,8}$=7.2 Hz, 1H, $H_7$), 8.30 (s, 1H), 8.35 (s, 1H). Because of the high polarity of this compound, it was taken on to the next step without further purification.

**5-Aminoanthracene-2,3-dicarboxylic acid (3)** To 30 mL 20% $NH_4OH$ was added sequentially 558 mg (1.79 mmol) of quinone **18** and 2.2 g (34 mmol, 19 equiv) of activated Zn powder. The blood-red mixture was refluxed, and the color of the mixture faded as the reaction proceeded. As soon as the color had fully discharged, the mixture was filtered while still hot. The filtered solid was returned to the flask, and refluxed in 30 mL 20% $NH_4OH$ for 1 h. The mixture was filtered again, and the combined filtrates were cooled to 0 °C. The filtrate was carefully acidified to pH 4-5 with 6 N HCl. The ppt that formed was isolated by filtration, washed with $H_2O$, and dried to afford 387 mg (1.38 mmol, 77%) of **3** as a tan solid, $R_f$ 0.30 ($CH_3CN$), which was found quite pure by $^1H$ NMR. An analytical sample was obtained by recrystallization from MeCN/MeOH/$Me_2CO$: mp >310 °C. $^1H$ NMR (DMSO-$d_6$) δ 6.70-6.73 (dd, $J_{7,8}$=$J_{7,6}$=8.2 Hz, 1H, $H_7$), 7.32 (m, 2H), 8.33 (d, 2H), 8.54 (s, 1H), 8.90 (s, 1H); $^{13}C$ NMR (DMSO-$d_6$) δ 169.0, 168.6, 145.0, 133.9, 131.1, 129.9, 129.9, 129.7, 128.6, 128.3, 128.2, 126.9, 124.1, 122.8, 115.4, 105.8. Anal. calcd for $C_{16}H_{11}NO_4$ • 0.4 $H_2O$ C: 66.6 H: 4.12 N: 4.86; found C: 66.79 H: 4.14 N: 4.81.

**5-Aminoanthracene-2,3-dimethanol (1)** In a 25-mL flask, flushed with $N_2$, was placed diacid **3** (385 mg, 1.37 mmol), THF (3 mL), and a magnetic stir bar. Next 4 mL $BH_3$•THF (1 M in THF) was added dropwise (*ca.* 1h) to the stirred mixture at 0 °C. The mixture was then kept at 0 °C for about an hour. The mixture was allowed to warm to room temp, and stirred for 12 h. To the mixture was carefully added 50% (v/v) aqueous THF (8 mL) to quench excess borane. The solution was saturated with anhydrous $K_2CO_3$. The layers were separated, and the water layer was extracted with THF three times. The organic layers were combined, and dried over anhydrous $MgSO_4$. The solvent was evaporated, and the residue was then subjected to column chromatography (silica gel) with EtOAc as eluant. The fractions were evaporated to give 116 mg (0.458 mmol, 33%) of diol **1** as a brown solid, $R_f$ 0.20 (EtOAc), mp 208-210 °C. $^1H$ NMR (DMSO-$d_6$) δ 4.69-4.72 (t, $J$=5.0 Hz, 4H), 5.24-5.36 (q, $J$=5.0 Hz, 2H), 5.87 (s, 2H), 6.57-6.61 (dd, $J$=6.8, 2.0 Hz, 1H), 7.16-7.26 (m, 2H), 7.92 (s, 1H), 7.95 (s, 1H), 8.29 (s, 1H), 8.66 (s, 1H). $^{13}C$ NMR (DMSO-$d_6$) δ 144.5, 138.0, 137.3, 132.4, 130.3, 129.3, 126.3, 126.1, 125.1, 124.9, 124.4, 122.9, 120.4, 115.5, 60.9, 60.8. FAB-MS calcd for $C_{16}H_{15}NO_2$: 253.1103; found 253.1102. Anal. calcd for $C_{16}H_{15}NO_2$ • ¼ $H_2O$ C: 74.54, H: 6.07, N: 5.43; found C: 74.65, H: 6.12, N: 5.35.

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