Triptycene quinones in synthesis: preparation of triptycene bis-cyclopentenedione

Spyros Spyroudis* and Nikoletta Xanthopoulou

Laboratory of Organic Chemistry, Department of Chemistry,University of Thessaloniki, Thessaloniki 54124, Greece
E-mail: sspyr@chem.auth.gr

Dedicated to Professor Anastasios Varvoglis on his 65th birthday

(received 23 Dec 02; accepted 28 Mar 03; published on the web 06 May 03)

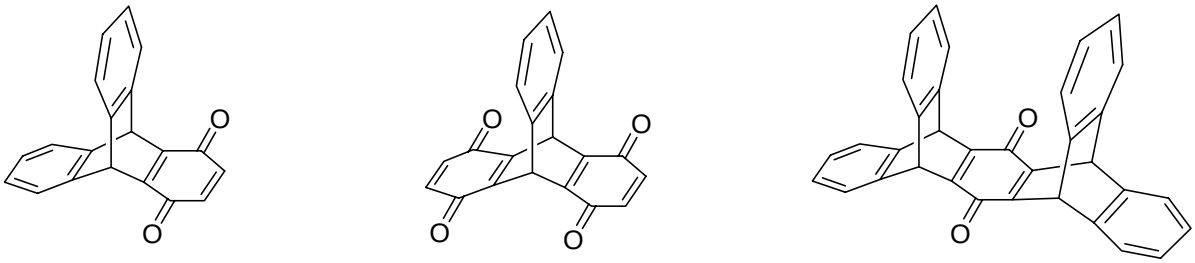
Abstract

The preparation of triptycene bis-quinone **2** starting from a Diels-Alder reaction of 1,4-dimethoxyanthracene and p-benzoquinone is described. This compound was transformed to triptycene bis-cyclopentenedione **16** through a double hydroxyquinone – iodonium ylide formation- ring contraction sequence.

Keywords: Triptycene, quinones, cyclopentenediones, phenyliodonium

Introduction

Triptycene quinones are triptycene derivatives in which at least one benzo group has been replaced by a quinonoid ring. Some representative structures of triptycene quinones are shown in Figure 1 below.



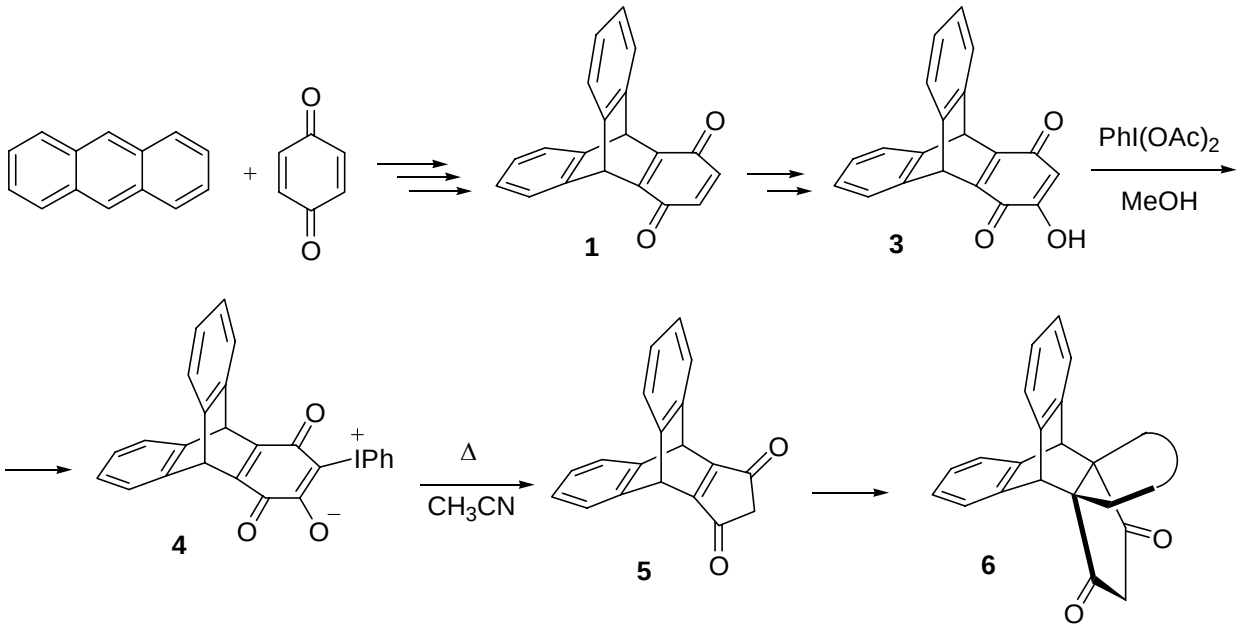
triptycene quinone, **1** triptycene bis-quinone, **2** pentiptycene quinone, **3**

Figure 1. Structures of triptycene quinones.

Such compounds combining the rigid structure of triptycene with the redox potential of quinones find several applications in Chemistry. Triptycene quinones serve as building blocks for the construction of three-dimensional supramolecules[1] and liquid crystalline derivatives,[2] for the synthesis of electron-transfer compounds with porphyrins[3] and tetrathiafulavalene[4] serving as donors, and for the preparation of polymeric chemosensors.[5] More recently pentiptycene quinones of type **3** were reported to form materials with monolayer assembly structure,[6] to find application as fluorescent chemosensors for metal ions,[7] and serve as building blocks for the construction of novel chain and channel networks.[8]

Triptycene quinones exhibit also interesting biological activity: a variety of them decrease the viability of leukemic cells in vitro,[9] triptycene quinones with methoxy substituents exhibit antioxidant and anti-inflammatory properties,[10] while the reaction of triptycene diquinones with amines was reported to afford derivatives with potent anticancer and antimalarial activities.[11]

In relation to our interest in hydroxyquinones[12] we recently reported[13] the synthesis of triptycene hydroxyquinone **3** and its conversion through phenyliodonium chemistry to triptycene cyclopentenedione, **5**. The latter reacts as a dienophile and dipolarophile affording polycyclic adducts **6** bearing the triptycene moiety (Scheme 1).

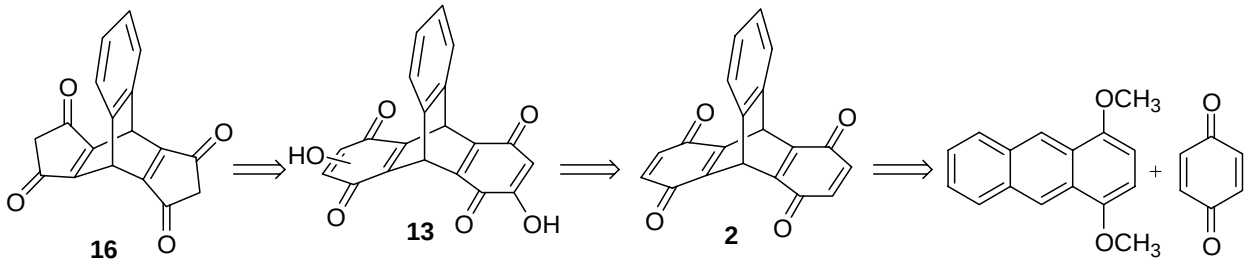


Scheme 1. Preparation of triptycene cyclopentenedione **5**.

The successful preparation of **5** prompted us to investigate the possibility of preparing the triptycene bis-cyclopentenedione **16** by applying the same methodology. We herein wish to report the results of our efforts.

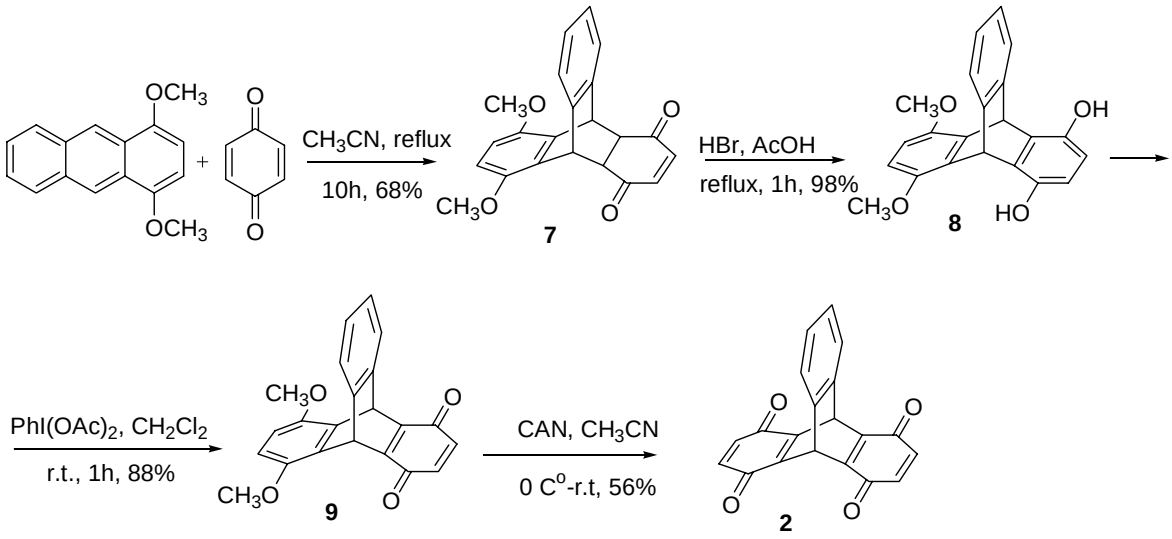
Results and Discussion

The synthesis of **16** was based on the retrosynthetic route shown in Scheme 2, having as key steps the preparation of triptycene dihydroxy-bis-quinones **13** and hence bis-quinone **2**, which was reported in the literature albeit without experimental details for its preparation.[14]



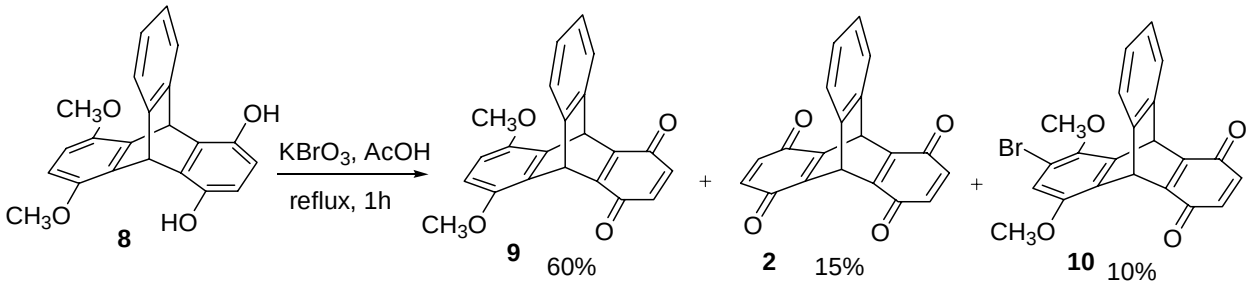
Scheme 2. Retrosynthetic route to triptycene bis cyclopentenedione **16.**

Triptycene bis-quinone **2** was prepared in three steps starting with a Diels-Alder reaction of 1,4-dimethoxyanthracene and 1,4-benzoquinone. The former is not commercially available and was prepared from quinizarin also in three steps (methylation and two subsequent reductions with $NaBH_4$) following a literature method.[15] The Diels- Alder reaction did not work well in the solvents usually used for cyclization (toluene or xylene) but in refluxing acetonitrile the dehydro adduct **7** was isolated in reasonable yield. This adduct was acid-isomerised almost quantitatively to the corresponding hydroquinone derivative **8** which was effectively oxidized by (diacetoxyiodo) benzene to dimethoxy triptycene quinone **9**. Finally, **9** was oxidatively-demethylated by ceric ammonium nitrate (CAN) to the desired bis-quinone **2** (Scheme 3).



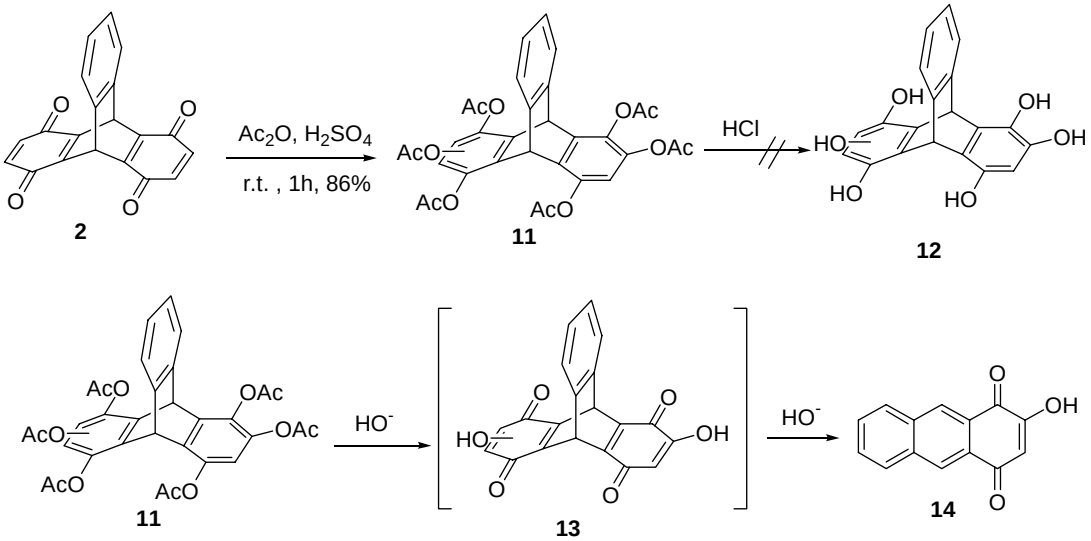
Scheme 3. Preparation of triptycene bis-quinone **2**.

As was mentioned earlier, $PhI(OAc)_2$ was found to be very effective for the oxidation of hydroquinone **8** to quinone **9.** The use of a more conventional oxidant, like potassium bromate, also gave the desired **9** in 60% yield, along with 15% of bis-quinone **2** and 10% of the bromo derivative **10**, thus complicating the reaction (Scheme 4).



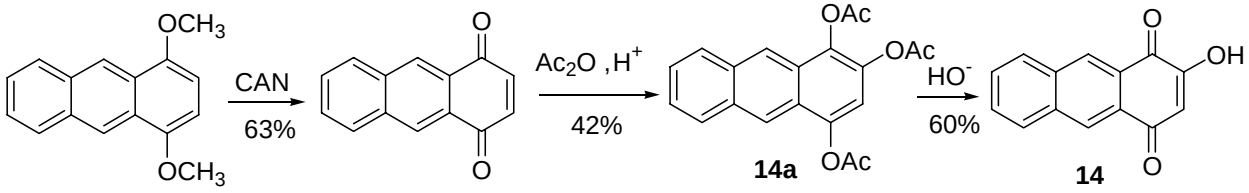
Scheme 4. Alternative preparation of **2**.

In the next step bis-quinone **2** was converted under Thiele-Winter conditions to a mixture (1:1 estimated by ^{1}H-NMR spectroscopy) of the two possible hexaacetoxy triptycene isomers **11**. Acid hydrolysis under various conditions did not lead to hexahydroxy isomers **12**, as complex mixtures of partially acetoxylated compounds were always isolated. In contrast, hydrolysis under basic conditions afforded 2-hydroxy-1,4-anthraquinone **14** as the only isolable product (Scheme 5). It is possible that **11** is converted to dihydroxy bis-quinone isomers **13**, as in a typical reaction for the preparation of hydroxy quinones from 1,2,4-triacetoxybenzenes.[12] Bis-quinone **13** affords **14** through a retro Diels-Alder reaction. This tendency of triptycene quinones to undergo retro Diels-Alder reactions under basic conditions has also been observed with other triptycene quinonic derivatives.[16]



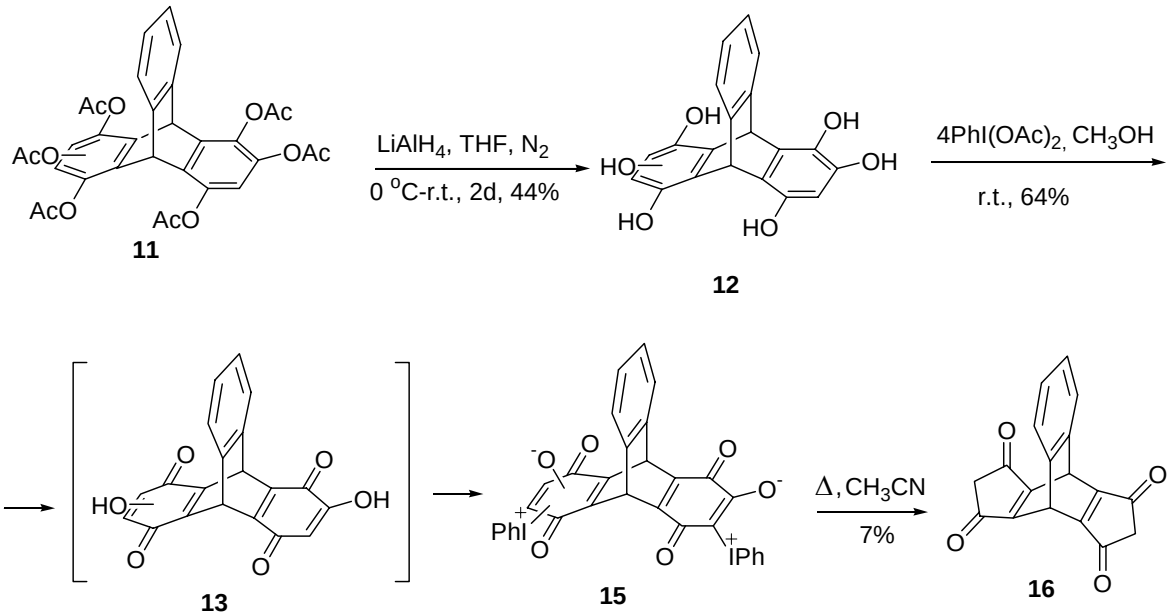
Scheme 5. Unsuccessful attempts for the preparation of dihydroxy bis-quinones **13**.

In order to confirm the formation of **14**, this hydroxy quinone was prepared by an independent method: available 1,4-dimethoxyanthracene was oxidatively demethylated to 1,4-anthraquinone, which in turn was transformed to 1,2,4-triacetoxyanthracene **14a** which was hydrolyzed to **14** (Scheme 6).



Scheme 6. Independent route to 2-hydroxy-1,4-anthraquinone **14**.

Finally, the acetoxy groups of **11** were smoothly removed by $LiAlH_4$ to afford a reasonable yield of hexahydroxytriptycene isomers **12**. This mixture was converted in a tandem oxidation-aryliodination reaction to the corresponding mixture of bis-ylide isomers **15** using four equivalents of $PhI(OAc)_2$. This mixture was subjected to thermal decomposition in refluxing acetonitrile and the target molecule triptycene bis-cyclopentenedione **16** was isolated in 7% yield (Scheme 7).



Scheme 7. Synthesis of triptycene bis-cyclopentenedione **16**.

Triptycene bis-cyclopentenedione **16** exists in solution in its tetraketo form, analogously to triptycene cyclopentenedione **17.**[13] The two compounds exhibit similar spectroscopic ^{1}H-NMR and ^{13}C-NMR data, the main difference being the anisotropy of the protons of the methylene groups in **16** (Figure 2).

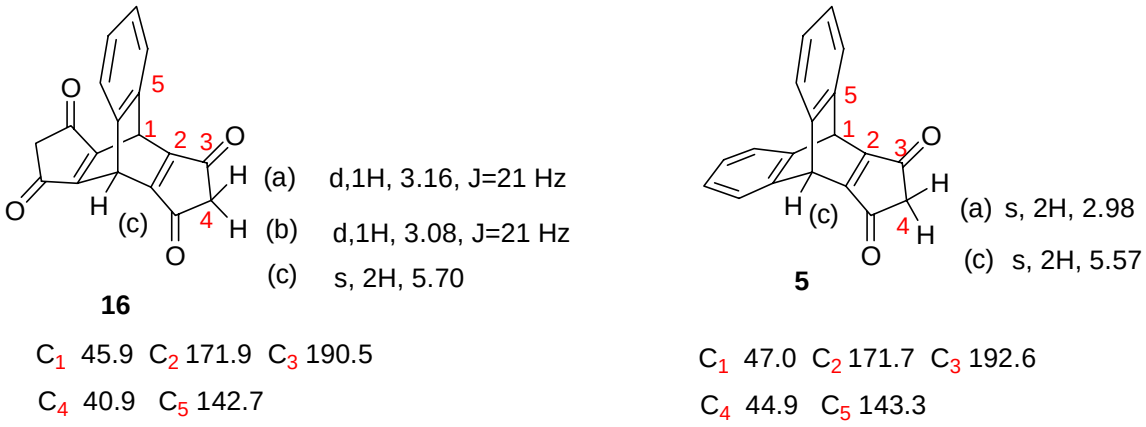
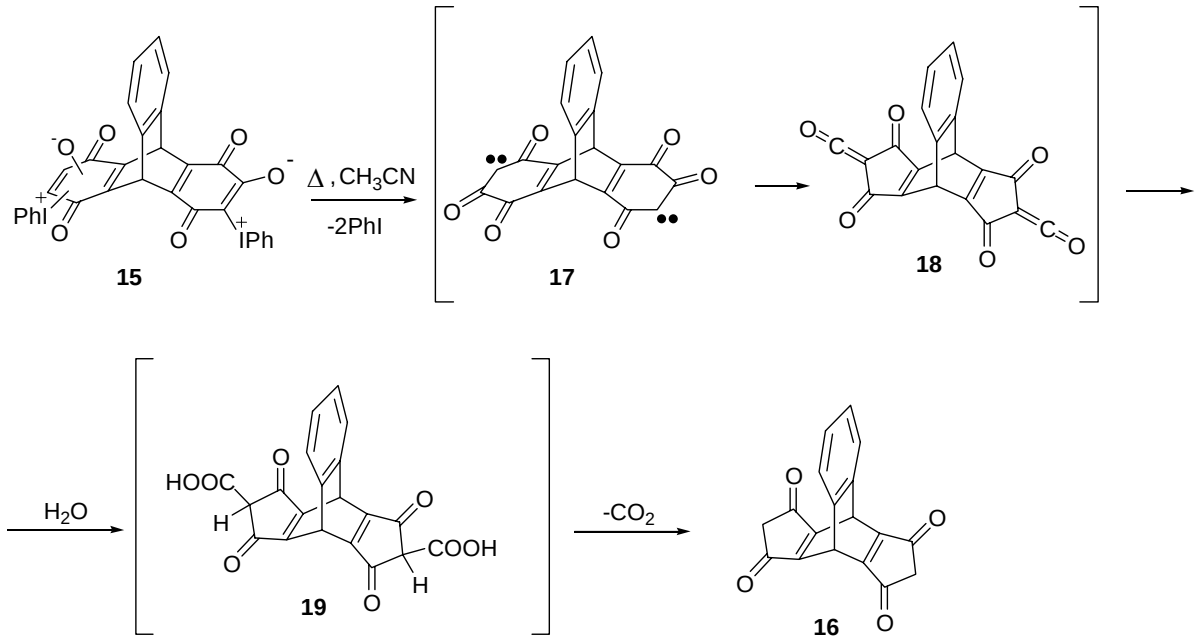


Figure 2. ^{1}H NMR and ^{13}C NMR data for triptycene bis- and mono-cyclopentenediones, **16** and **5**.

We believe the reaction pathway to be essentially the same as that proposed for the thermal decomposition of aryliodonium ylides of 2-hydroxy-1,4-benzoquinones:[17] bisketene **18** is produced by Wolff rearrangement of bis-carbene **17** resulting from extrusion of PhI.



Scheme 8. Proposed reaction pathway for the preparation of **16**.

Highly reactive **18** undergoes hydrolysis with water present in the solvent and the resulting acid **19** decarboxylates to the desired triptycene bis-cyclopentenedione **16** (Scheme 8). This reaction pathway leads also to the preparation of **5** from the thermal degradation of the corresponding mono ylide. The formation of the intermediate ketene is supported by its trapping with methanol to form the corresponding ester.[13]

In conclusion we presented a reaction sequence for the preparation of triptycene bis-cyclopentenedione **16** based on hydroxyquinone-ylide formation chemistry. This compound, as well as its precursors, might serve as building blocks for the construction of polycyclic structures bearing the triptycene moiety.

Experimental Section

General Procedures. Melting points were determined on a Stuart Scientific Melting Point Apparatus SMP3 (230 Volts) and are uncorrected. ^{1}H-NMR and ^{13}C-NMR spectra were recorded with a Bruker AM 300 (300 MHz and 75 MHz for ^{1}H and ^{13}C, respectively) in ca 5% solution of $CDCl_3$ using Me_4Si as the internal standard. Mass spectra were recorded with a spectrometer VG-250 in 70eV, ESI. Elemental analyses were carried out in a Perkin-Elmer 2400-II elemental analyst.

5,8–Dimethoxy-4a,9,9a,10–tetrahydro-9,10-[1,2]benzenoanthracene-1,4-dione, (7). To a solution of 1,4-dimethoxy-anthracene (2.26 g, 9.5 mmol) in CH_3CN (40 mL) 1,4-benzoquinone (4.2 g, 38.8 mmol) was added and the mixture was refluxed for 10 h. After cooling, the yellow-green precipitate formed was filtered and dried in a desiccator for 24 h to afford **7** (2.23 g, 68%), mp 220 ^{o}C dec. ^{1}H-NMR δ 2.17 (s, 2H), 3.80 (s, 6H), 6.54 (s, 2H), 6.58 (s, 2H), 7.00-7.11 (m, 2H), 7.42-7.51 (m, 2H). MS (70 eV); m/z (%): 347 (M+1, 100), 239 (77), 224 (70), 208 (31), 180 (48), 152 (68). Anal. Calcd for $C_{22}H_{18}O_4$: C, 76.28%; H, 5.24%. Found C, 76.01%; H, 5.50%.

5,8-Dimethoxy-9,10-dihydro-9,10-[1,2]benzenoanthracene-1,4-diol, (8). A suspension of 5,8-dimethoxy-4a,9,9a,10-tetrahydro-9,10-[1,2]benzenoanthracene-1,4-dione, **7** (0.75 g, 2.16 mmol) in CH_3COOH (50 mL) was refluxed until the solid was completely dissolved (20-30 min). Hydrobromic acid (48% solution, 20 drops) was added and the resulting mixture was poured onto water (10 mL). The white precipitate formed was filtered and dried in a desiccator for 24 h to yield **3** (0.74 g, 98%), mp >200 ^{o}C dec. ^{1}H -NMR ($CDCl_3$+DMSO-d_6) δ 3.80 (s, 6H), 6.27 (s, 2H), 6.34 (s, 2H), 6.55 (s, 2H), 6.96-7.01 (m, 2H), 7.35-7.42 (m, 2H). MS (70 eV); m/z (%): 348 (M+2, 100), 330 (36), 316 (94), 298 (34), 284. Anal. Calcd for $C_{22}H_{18}O_4$: C, 76.28%; H, 5.24%; Found: C, 76.68%; H, 4.99%.

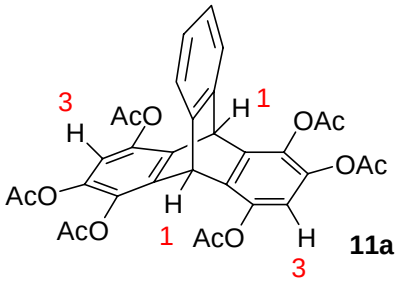
5,8-Dimethoxy-9,10-dihydro-9,10-[1,2]benzenoanthracene-1,4-dione, (9). To a solution of 5,8-dimethoxy-9,10-dihydro-9,10-[1,2]benzenoanthracene-1,4-diol, **8** (0.243 g, 0.70 mmol) in

CH_2Cl_2 (8 mL) a solution of (diacetoxyiodo)benzene (0.237 g, 0.73 mmol) in CH_2Cl_2 (8 mL) was added with stirring at room temperature. Stirring was continued for one h. The solution was concentrated to dryness and purified by column chromatography (silica gel) using a mixture of hexanes – ethyl acetate (5:1) as eluant to afford 0.21 g of **9** (yield 88%), mp 271-272 ^oC. ^1H -NMR δ 3.81 (s, 6H), 6.24 (s, 2H), 6.55 (s, 2H), 6.59 (s, 2H), 7.00-7.05 (m, 2H), 7.42-7.50 (m, 2H). ^{13}C-NMR δ 41.2, 56.3, 109.3, 124.5, 125.2, 133.4, 135.2, 144.1, 149.5, 152.7, 183.5 (C=O). MS (70 eV); m/z (%): 344 (M^+, 100), 330 (40), 286 (25), 176. Anal. Calcd for $C_{22}H_{16}O_4$: C, 76.73%; H 4.68%. Found C, 76.41%; H, 4.67%.

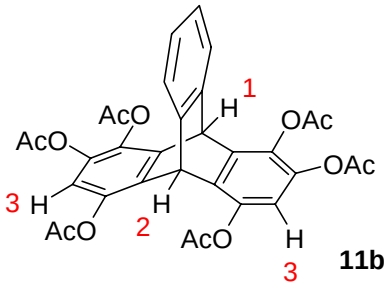
9,10-Dihydro-9,10- [1,2]benzenoanthracene-1,4,5,8-tetrone, (2). To a magnetically stirred solution of 5,8-dimethoxy-9,10-dihydro-9,10-[1,2]benzenoanthracene-1,4-dione, **9** (0.73 g, 2.1 mmol) in CH_3CN (70 mL) at 0 ^oC a solution of ceric ammonium nitrate, CAN, (3.4 g, 6.2 mmol) in H_2O (60 mL) was added drop wise. Stirring was continued for two hours at room temperature, excess CH_3CN was removed in the rotary evaporator and the resulting solution was extracted with CH_2Cl_2 (3 x 40 mL). The solution was concentrated to dryness and purified by column chromatography (silica gel) using a mixture of hexanes-ethyl acetate (5:1) as eluant to afford 0.38 g of **2** (yield 57%), yellow crystals, mp 220 ^oC dec. ^1H -NMR δ 6.18 (s, 2H), 6.65 (s, 4H), 7.07-7.10 (m, 4H), 7.47-7.50 (m, 4H) . ^{13}C-NMR δ 42.2, 125.5, 126.0, 135.5, 151.6, 182.2 (C=O). MS (70 eV); m/z (%): 314 (M^+, 100), 286 (15), 258 (25), 232 (60), 208 (75) 176 (24). Anal. Calcd for $C_{20}H_{10}O_4$: C, 76.43%; H, 3.20%. Found C, 76.30%; H, 3.00%.

Oxidation of 8 with $KBrO_3$. A solution of 5,8-dimethoxy-9,10-dihydro-9,10-[1,2]benzenoanthracene-1,4-diol, **8** (0.3 g, 0.96 mmol) in CH_3COOH (20 mL) was refluxed till the hydroquinone was dissolved. A solution of $KBrO_3$ (1.6 g, 9.4 mmol) in H_2O (10 mL) was added using a dropping funnel, followed by the addition of another 10 mL of H_2O and reflux was continued for 10 min. After cooling at rt the resulting solid was filtered and subjected to column chromatography (silica gel, hexanes-ethyl acetate, 5:1) to afford in order of eluance a) Dimethoxyquinone, **9** (0.17 g, 60% yield) b) **6-Bromo-5,8-dimethoxy-9,10-dihydro-9,10-[1,2]benzenoanthracene-1,4-dione, (10),** (0.037 g, yield 10%). ^1H NMR δ 3.81 (s, 3H), 3.85 (s, 3H), 6.15 (s, 1H), 6.19 (s, 1H), 6.62 (s, 2H), 6.78 (s, 1H), 6.92-7.08 (m, 2H), 7.42-7.50 (m, 2H). ^{13}C NMR δ 41.1, 42.65, 56.20, 62.20, 113.5, 124.6, 124.7, 135.3,135.4, 143.3, 151.6, 183.2 (C=O) and c) diquinone **2** (0.046g, 15% yield).

Thiele-Winter preparation of 1,2,4,5,6,(7),8–hexacetoxy-9,10–dihydro-9,10-[1,2] benzenoanthracenes (or 1,2,4,5,6,(7),8-hexacetoxytriptycenes), (11). To a magnetically stirred solution of 9,10-dihydro-9,10- [1,2]benzenoanthracene-1,4,5,8-tetrone, **2** (0.38 g, 1.2 mmol) in acetic anhydride (65 mL) a catalytic amount (0.8 mL) of H_2SO_4 was added drop wise and stirring was continued for 24 h. The mixture was poured onto ice-water (200 mL), stirring was continued for one hour and the resulting solid was filtered, washed repeatedly with water and dried in a desiccator to afford **11** as off-white solid (0.64 g, yield 86%), mp 194-198 ^oC dec. The 1:1 ratio of the two isomers (**11a** and **11b**) was estimated by integration of the peaks of the bridge protons in ^1H NMR (Figure 3).



11a



11b

Figure 3

Both bridge protons (H-1) in **11a** appear as a singlet at 5.50 δ, whereas in **11b** H-1 gives a singlet at 5.53 δ and H-2 a singlet at 5.45 δ. H-3 appears as two singlets for both isomers at 6.78 and 6.79 δ. The methyl groups give broad singlets at 2.23 and 2.40 (1:2) δ and the aromatic protons resonate at 7.01-7.06 (m) and 7.31-7.36 (m). MS (70 eV); m/z (%): 602 (M^+, 33), 560 (37), 518 (25), 207 (50), 135 (100).

Attempts for hydrolysis of 11. All attempts of acid-hydrolysis of **11** to the corresponding hexahydroxy derivative **12** failed. In all cases (HCl acid of different concentration, CH_3OH as solvent, prolonged periods of reaction at room temperature, heating etc.) complex mixtures of partially hydrolyzed products were isolated. Sometimes even the presence of methoxy groups (probably from the solvent) were detected by ^{1}H-NMR spectroscopy in the products.

Complicated mixtures of products were also the results of hydrolysis with aqueous NaOH. In this case the only isolable product (after column chromatography in 10-15% yields) was **2-hydroxy-1,4-anthraquinone 14**, mp 238-241 °C, lit.[18] mp 243 °C. ^{1}H NMR δ 6.48 (s, 1H), 7.70 (m, 2H), 8.05 (m, 2H), 8.65 (s, 1H), 8.67 (s, 1H), 8.95 (s, br, 1H, OH).

Alternative preparation of 2-hydroxy-1,4-anthraquinone (14). To a magnetically-stirred solution of 1,4-dimethoxyanthracene (0.48 g, 2 mmol) in CH_3CN (50 mL) at 0 °C a solution of CAN (3.3 g, 6 mmol) in water (45 mL) was added, the ice bath was removed and stirring was continued for 2 hours. Excess CH_3CN was removed in the rotary evaporator and the resulting suspension was extracted with CH_2Cl_2 (3 x 50 mL). The solvent was evaporated to dryness and the residue was chromatographed on column (silica gel, hexanes-ethylacetate 5:1) to afford 0.264 g, 63% yield, of **1,4-anthraquinone**, mp 214-217 °C dec, lit.[19] 219-223 °C dec. ^{1}H –NMR δ 7.07 (s, 2H), 7.68-7.71 (m, 2H), 8.05-8.08 (m, 2H), 8.61 (s, 2H). MS (70 eV); m/z (%): 208 (M^+, 60), 180 (75), 153 (95), 127 (100), 76 (66). To a magnetically-stirred solution of 1,4-anthraquinone (0.26 g, 1.25 mmol) in acetic anhydride (40 mL) a catalytic amount (0.7 mL) of H_2SO_4 was added dropwise and stirring was continued for 30 min. The mixture was poured onto ice-water (100 mL), stirring was continued for an additional hour and the resulting solid was filtered, washed repeatedly with water and dried in a desiccator to afford **1,2,4-triacetoxyanthracene (14a)** (0.185 g, 42% yield), mp 188-190 °C , lit.[18] mp 191 °C. ^{1}H –NMR δ 2.22 (s, 3H), 2.46 (s, 3H), 2.67 (s, 3H), 6.88 (s, 1H), 7.09-7.13 (m, 2H), 7.41-7.45 (m, 2H), 8.26 (s, 1H). To a magnetically-stirred solution of **15** (0.04 gr, 0.12 mmol) in CH_3OH (5 mL) a

solution of 20% NaOH (1 mL) was added and stirring was continued for 2 hours. The resulting solution was acidified with 20% HCl acid, poured onto water (10 mL) and the precipitated solid was filtered and dried to afford **2-hydroxy-1,4-anthraquinone 14** (0.015 g, 60%), in all respects identical to that isolated from the basic-hydrolysis of hexaacetoxytriptycenes **11**.

Preparation of 1,2,4,5,6,(7),8-hexahydroxy-9,10-dihydro-9,10-[*1,2*]benzenoanthracenes (or 1,2,4,5,6,(7),8-hexahydroxytriptycenes), (12). A 100 mL three-necked flask, equipped with a reflux condenser and a pressure-equalizing dropping funnel, was charged with a suspension of $LiAlH_4$ (0.33 g, 8.7 mmol) in anhydrous THF (10 mL) under Ar. A degassed solution of hexacetoxytriptycenes **11** (0.6 g, 1 mmol) in anhydrous THF (20 mL) was added from the dropping funnel at 0 ^oC with stirring, during a period of 30 min. The cooling bath was removed, the reaction mixture was allowed to reach rt and finally it was refluxed for 6 hours. After cooling the resulting mixture was carefully poured onto ice-H_2SO_4 (10%, 30 mL). The reaction flask was rinsed thoroughly with ether and the combined ether-THF suspension was filtered through a thick layer of celite. The organic solvents were removed with the rotary evaporator, the water suspension was extracted with ether (5 x 30 mL) and dried with Na_2SO_4. Ether was removed to afford 1,2,4,5,6,(7),8-hexahydroxytriptycenes **12** (0.15 g, 44%) mp > 300 ^oC. ^1H -NMR ($CDCl_3$+DMSO-d_6) δ both isomers give a complex set of singlets for bridge and aromatic protons (of the trihydroxy moieties) at 5.94, 6.02, 6.06, 6.08 (4H, total) , 6.9 (m, 2H) , 7.29 (m, 2H) . MS (70 eV); m/z (%): 350 (M^+, 37), 332 (8), 224 (12), 210 (23), 196 (29) 155 (50), 126 (100). Anal. Calcd for $C_{20}H_{14}O_6$: C, 68.57%; H, 4.03%. Found C, 68.28%; H, 4.40%.

Preparation of 2,7-dioxido-3,6-di(phenyliodonio)-9,10-dihydro-9,10-[*1,2*]benzenoanthracene-1,4,5,8-tetrone and 2,6-dioxido-3,7-di(phenyliodonio)-9,10-dihydro-9,10-[*1,2*]benzenoanthracene-1,4,5,8-tetrone mixture (15). A solution of (diacetoxyiodo)benzene (0.57 g, 1.76 mmol) in CH_3OH (8 mL) was added dropwise to a magnetically-stirred solution of hexahydroxytriptycenes **12** (0.15 g, 0.44 mmol) at 0 ^oC. The ice-bath was removed and stirring was continued for one hour at room temperature. The orange precipitate was filtered, the methanolic filtrate was evaporated in vacuum, keeping the temperature as low as possible, and the oily remnant was triturated with ether to afford a second crop of the product. The combined solids were washed repeatedly with ether to afford 0.37 g (57% yield) of **15** as a red-orange powder, mp 120-122 ^oC dec., kept all the time in the refrigerator. Anal. Calcd for $C_{32}H_{16}I_2O_6$: C, 51.23%; H, 2.15%. Found C, 51.66%; H, 1.91%.

Triptycene bis-cyclopentenedione (16). A suspension of bis-ylide **15** (0.36 g, 0.48 mmol) in CH_3CN (12 mL) was refluxed for 4 h. The clear solution was evaporated to dryness and the residue was chromatographed on column (silica gel, hexanes-ethyl acetate 5:1 to 2:1) to afford, after iodobenzene extrusion, triptycene bis-cyclopentenedione **16** as yellowish crystals (0.01 g, 7%), mp 106-108 ^oC. ^1H –NMR δ 3.08 (d, J = 21 Hz, 1H), 3.16 (d, J = 21 Hz, 1H), 5.70 (s, 2H), 7.08-7.12 (m, 2H), 7.47-7.52 (m, 2H). ^{13}C-NMR δ 40.9, 45.9, 126.5, 142.7, 171.9, 190.5 MS (70 eV); m/z (%): 289 ($M-1^+$, 7), 213 (60), 149 (78), 126 (100). Anal. Calcd for $C_{18}H_{10}O_4$: C, 74.48%; H 3.47%. Found C, 74.92%; H, 3.64%.

References

1. (a) Hashimoto, M.; Tagaki, H.; Yamamura, K. *Tetrahedron Lett*. **1999**, *40*, 6037. (b) Hashimoto, M.; Yamamura, K.; Yamane, J. *Tetrahedron* **2001**, *51*, 10253.
2. Norvez, S. *J. Org. Chem*. **1993**, *58*, 2414.
3. (a) Wiehe, A.; Senge, M. O.; Kurreck, H. *Liebigs Ann./Recueil* **1997**, 1951. (b) Wiehe, A.; Senge, M. O.; Schäfer, A.; Speck, M.; Tannert, S.; Kurreck, H.; Röder, B. *Tetrahedron*, **2001,** *51*, 10089.
4. Scheib, S.; Cava, M. P.; Baldwin, J. W.; Metzer, R. M. *J. Org. Chem*. **1998**, *63*, 1198.
5. Yang, J.-S.; Swager, T. M. *J. Am. Chem. Soc*. **1998**, *120*, 11864.
6. Yang, J.-S.; Lee, C.-C.; Yau, S.-L.; Chang, C.-C.; Lee, C.-C.; Leu, J.-M. *J. Org. Chem.* **2000**, *65*, 871.
7. Yang, J.-S.; Lin,C.-S; Hwang, C.-S. *Org. Lett.* **2001**, *3*, 889.
8. Yang, J.-S.; Liu, C.-P.; Lee, G.-H *Tetrahedron Lett.* **2001**, *41*, 7911.
9. Perchellet, E. M.; Magill, M. J.; Huang, X.; Brantis, C. E.; Hua, D. H.; Perchellet, J.-P. *Anti-Cancer Drugs* 1999, *10*, 749.
10. Xanthopoulou, N.J.; Kourounakis, A. P.; Spyroudis, S.; Kourounakis, P.N. *Eur. J. Med. Chem.*, accepted for publication.
11. Hua, D.H.; Tamura, M.; Huang, X.; Stephany, H, A.; Helfrich, B.A.; Perchellet, E.M., Sperfslage, B. J.; Perchellet, J-P.; Jiang, S.; Kyle, D. E.; Chiang, P.K. *J. Org. Chem.* **2002**, *67,* 2907.
12. Spyroudis, S. *Molecules* **2000**, *5*, 1291.
13. Spyroudis, S.; Xanthopoulou, N. *J. Org. Chem*. **2002**, *67*, 4612.
14. Iwamura, H.; Makino, K. *J. Chem. Soc., Chem. Commun.* **1978**, 720.
15. Criswell, T. R.; Klanderman, B. H. *J. Org. Chem*. **1974**, *39*, 770.
16. Xanthopoulou, N. Ph. D. Thesis to be submitted at the University of Thessaloniki.
17. Papoutsis, I.; Spyroudis, S.; Varvoglis, A. *Tetrahedron Lett.* **1994**, *35*, 8449.
18. Fieser, L. *J. Am. Chem. Soc.* **1928**, *50*, 465.
19. Cava, M., D.; Deava, A. A.; Muth, K. *J. Am. Chem. Soc.* **1959**, *81*, 6458.