Triptycene Quinones in Synthesis: Preparation of Triptycene Cyclopentenedione and Its Reactivity as a Dienophile

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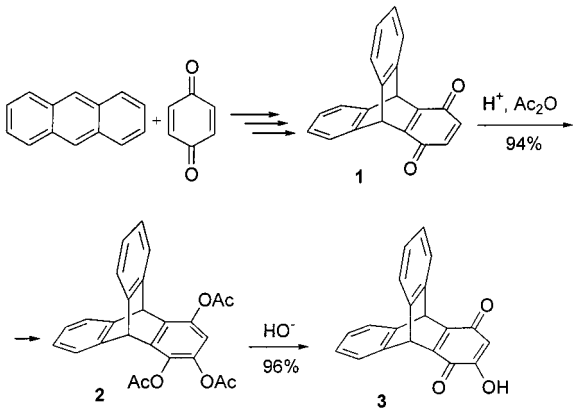
Abstract: Triptycenene quinone **1** was converted to triptycene cyclopentenedione **5** through hydroxyquinone−phenyliodonium ylide formation and thermal ring contraction of the latter. Cyclopentenedione **5** reacts as a dienophile and as a dipolarophile with dienes and nitrile oxides, affording polycyclic adducts bearing the triptycene moiety.

The term triptycene quinones refers to derivatives of triptycene in which at least one benzo group has been replaced by a quinoid ring. Although the synthesis of triptycene quinone, **1**,[1] as well as its bis-[2] and tris-quinone[3] homologues, has been described for some years now, a limited number of papers on their chemistry have appeared until recently.

Triptycene quinones, combining the rigid structure of triptycene with the redox properties of the quinone ring, exhibit interesting electrochemical properties[4] and intramolecular charge-transfer characteristics.[5] They are potential reagents for the preparation of liquid crystalline triptycene derivatives,[6] polymeric chemosensors,[7] and materials with monolayer assembly structure,[8] and they form three-dimensional supramolecular structures.[9] Triptycene quinone and derivatives also find applications as acceptors, with porphyrin derivatives[10] and tetrathiafulvalene[11] serving as donors, for the synthesis of electron-transfer compounds. Finally, in a preclinical study[12] it was shown that a variety of triptycene derivatives, triptycene quinones being among them, decrease the viability of leukemic cells in vitro.

Scheme 1



This diversity in the properties of triptycene quinones was one of the two reasons that prompted us to prepare the corresponding triptycene hydroxyquinone derivatives and investigate their reactivity. The second reason was the importance of the hydroxyquinone moiety.

Hydroxylated quinones that have one or more hydroxy groups directly attached to the quinone ring are found in nature in wide variety, and most of them exhibit interesting biological activity.[13] The synthesis and reactivity of this class of compounds have recently been reviewed.[14]

The preparation of 9,10-dihydro-2-hydroxy-9,10-[*o*]-benzenoanthracene-1,4-dione, triptycene hydroxyquinone (OH-TPQ), **3**, is outlined in Scheme 1. The corresponding 9,10-dihydro-9,10-[*o*]benzenoanthracene-1,4-dione, triptycenequinone (TPQ) **1**, was prepared in three steps from the Diels−Alder reaction of *p*-benzoquinone and anthracene, following a recently published procedure.[10] TPQ was converted to the triacetoxy derivative **2** under Thiele−Winter acetoxylation conditions[15] and the latter afforded the desired hydroxy derivative **3** on alkaline hydrolysis and oxidation.

The triptycene hydroxyquinone prepared in this manner was used for the synthesis of 1,2-[9′,10′](9′,10′-dihydroanthraceno)cyclopent-1-ene-3,5-dione, i.e., triptycene cylopentenedione, **5**, considering the importance of cyclopentene-1,3-diones as building blocks in organic synthesis.[16] The hydroxyquinone **3** was converted to phenyliodonium ylide **4** in 96% yield, and the latter afforded the cyclopentenedione **5** in yields ranging 35−50% upon thermal decomposition in refluxing acetonitrile (Scheme 2).

The reaction proceeds through the formation of carbene, Wolff rearrangement to ketene, reaction of the latter with H_2O present in the solvent and thermal decarboxylation of the formed acid to **5**. This reaction pathway was proposed for the analogous conversion of

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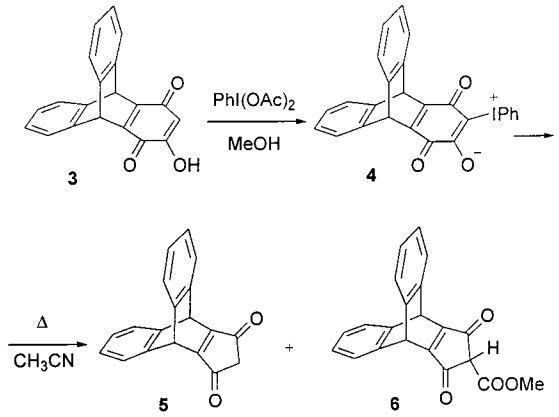
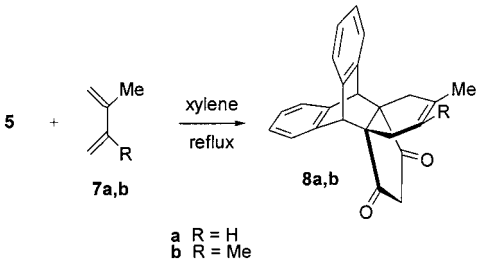
Scheme 2



Scheme 3



iodonium ylides of hydroxybenzoquinones to cyclopentenediones[17] and is strongly supported by the formation of carboxymethyl derivative **6**. The latter is always a byproduct of the reaction (yield 5−10%) and undoubtedly arises from the reaction of the intermediate ketene with methanol.

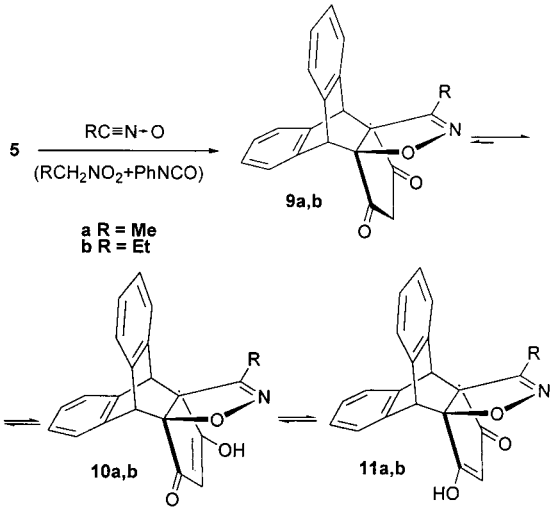
Methanol is the solvent of choice for the preparation of iodonium ylide **4**. The use of other solvents (CH_3CN, CH_2Cl_2) provides unsatisfactory results in this case. The relative instability of **4** prevents the effective removal of methanol (e.g., by recrystallization) and hence the undesired formation of **6**.

The reactivity of cyclopentenedione **5** as a dienophile was then examined. Although the parent cyclopentene-1,3-dione reacts with furan under mild conditions (furan as solvent, rt, 1−2 weeks) to afford the Diels−Alder adduct,[18] no such reaction was observed with **5** under the same conditions. Furan did not react with **5** even on heating at 80 °C, the possible reason being steric hindrance in combination with the poor diene character of furan. No cycloaddition reaction was also observed with a variety of dienes such as cylopentadiene, 1,4-dimethylbutadiene, anthracene, and 1,4-dimethoxyanthracene. In all the cases, unreacted **5** was quantitatively recovered.

On the contrary, **5** reacted with less hindered dienes, such as isoprene **7a** and 2,3-dimethylbutadiene **7b**, to afford the Diels−Alder adducts **8a**,**b** in 51% and 53% yields, respectively (Scheme 3).

The adducts **8a**,**b** exist in solution ($CDCl_3$−DMSO-d_6) exclusively in their keto forms, as deduced by ^{1}H NMR. The reaction of triptycene cyclopentenedione, **5**, with a typical class of 1,3-dipoles, such as nitrile oxides, was also investigated. The nitrile oxides, prepared in situ from

Scheme 4



phenyl isocyanate and the corresponding nitroalkane, easily reacted with **5** to give a complex mixture of products. Upon alkaline extraction of the crude reaction mixture, the cycloaddition products **9a**,**b** were isolated in 11% and 15% yields, respectively (Scheme 4).

Both compounds exist in solution ($CDCl_3$ or $CDCl_3$−DMSO-d_6) in their two enolic forms **10** and **11**, in a ratio of 1:1. Sometimes in more concentrated solutions a small amount of the keto form **9** is also detectable by ^{1}H NMR spectroscopy.

The above findings indicate that triptycene cyclopentenedione might serve as dienophile and dipolarophile for the construction of complex molecules bearing the interesting triptycene moiety.

Experimental Section

9,10-Dihydro-1,2,4-tris-acetoxy-9,10-[*o*]benzenoanthracene (1,2,4-triacetoxytriptycene, 2). To a stirred solution of triptycenequinone (**1**, 0.5 g, 1.8 mmol) in Ac_2O (20 mL) was added dropwise H_2SO_4 (0.1 mL) at room temperature, and stirring was continued for 40 min. The yellow mixture was then poured onto 45 mL of ice−water and stirred for an additional 1 h. The off-white precipitate was filtered under vacuum and washed several times with water to afford **2** in 98% yield: mp 220−222 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.22 (3H, s), 2.43 (3H, s), 2.44 (3H, s), 5.41 (1H, s), 5.43 (1H, s), 6.70 (1H, s), 7.01−7.05 (4H, m) and 7.34−7.38 (4H, m); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 168.5, 167.8, 143.9, 143.8, 140.4, 136.1, 125.6, 125.5, 122.1, 124.0, 113.6, 48.9, 48.4, 20.9, 20.54, 20.48; MS *m*/*z* 428 (M^+, 31), 386 (44), 302 (96), 284 (99), 202 (100), 178 (50), 152 (25). Anal. Calcd for $C_{26}H_{20}O_6$: C, 72.88; H, 4.70. Found: C, 73.07; H, 4.67.

9,10-Dihydro-2-hydroxy-9,10-[*o*]benzenoanthracene-1,4-dione (3). A solution of NaOH in water (20%, 3 mL, 15 mmol) was added dropwise to a solution of **2** (0.5 g, 1.17 mmol) in 16 mL of CH_3OH. The color of the solution changed from bright yellow to light green and finally to purple. Stirring at room temperature was continued for about 1 h, and then the solution was acidified with 20% HCl (pH = 1). Water (30 mL) was added, and the orange precipitate was filtered to afford **3** in 97% yield. The crude product was used without further purification for the next step. An analytical sample was obtained by recrystallization from MeOH: mp 130−132 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.78 (1H, s), 5.82 (1H, s), 5.92 (1H, s), 7.02−7.05 (4H, m), 7.41−7.44 (4H, m); MS *m*/*z* 300 (M^+, 75), 230 (52), 202 (45), 178 (100), 152 (35). Anal. Calcd for $C_{20}H_{12}O_3$: C, 79.99; H, 4.02. Found: C, 80.12; H, 4.11.

9,10-Dihydro-2-oxido-3-phenyliodonio-9,10-[*o*]benzenoanthracene-1,4-dione (4). To a stirred solution of **3** (310 mg, 1.05 mmol) in CH_3OH (6 mL) was added dropwise a solution of PhI(OAc)$_2$ (430 mg, 1.33 mmol) in CH_3OH (6 mL) at 0 °C. The ice

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bath was removed, and stirring was continued for 1.5 h. The solvent was removed in the rotary evaporator using a cool bath, and the precipitate was triturated with diethyl ether to afford an orange precipitate that was filtered and washed repeatedly with diethyl ether. The ylide **4** was isolated in 96% yield, and it was kept in the refrigerator. It is relatively unstable, and no fully satisfactory elemental analysis could be obtained: mp 105−108 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.84 (1H, s), 5.94 (1H, s), 7.02−7.07 (4H, m), 7.35−7.49 (4H+3H, m), 7.88 (2H, d, J = 9 Hz). Ms *m*/*z* 204 (100), 127, 77.

Thermal Decomposition of Ylide 4. A solution of **4** (410 mg, 0.82 mmol) in CH_3CN (30 mL) was refluxed for 4 h. The solvent was evaporated, and the residue was subjected to column chromatography (silica gel, hexanes−EtOAc, 5:1) to afford, after iodobenzene, **1,2-[9′,10′](9′,10′-dihydroanthraceno)cyclopent-1-ene-3,5-dione**, **5**, as an off-white solid in yield ranging 33−50%: mp 230−236 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): 2.98 (s, 2H), 5.57 (s, 2H), 7.02−7.06 (m, 4H), 7.39−7.42 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) 192.6, 171.7, 143.3, 125.8, 124.8, 47.0, 44.9; MS *m*/*z* 272 (M^+, 73), 230 (45), 215 (15), 202 (100), 178 (11). Anal. Calcd for $C_{19}H_{12}O_2$: C, 83.81; H, 4.44. Found: C, 83.68; H, 4.54. The next fraction was the ester **1,2-[9′,10′](9′,10′-dihydroanthraceno)-4-carboxymethylcyclopent-1-ene-3,5-dione**, **6**, in 5−10% yield: yellowish crystals; mp 212−214 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) 3.76 (s, 3H), 5.73 (s, 1H), 5.80 (s, 1H), 5.83 (s, 1H), 6.98−7.01 (m, 4H), 7.38−7.41 (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz) 47.1, 47.5, 56.4, 105.7, 124.2, 124.3, 125.4, 143.5, 143.6, 149.9, 152.9, 158.3, 178.1, 183.3; MS *m*/*z* 330 (M^+, 13), 299 (82), 272 (58), 202 (100), 178 (11). Anal.Calcd for $C_{21}H_{14}O_4$: C, 76.35; H, 4.27. Found: C, 75.93; H, 4.11.

Diels−Alder Reactions of 5 with Dienes. (a) Reaction with Isoprene. A solution of **5** (70 mg, 0.26 mmol) and isoprene (1.36 g, 20 mmol) in xylene (8 mL) was refluxed for 4.5 h. The solvent was concentrated to a small volume (calcd 2 mL), and the white solid formed was collected by filtration to afford **4,5-[9',10']](9',10'-dihydroanthraceno)-4,5-(1"-methyl-cyclohexen-1"-o)cyclopentano-1,3-dione**, **8a**, in 51% yield: mp 225−230 °C; ^{1}H NMR ($CDCl_3$−DMSO-d_6, 300 MHz) δ 1.54 (s, 3H), 1.58 (m, br 1H), 1.70 (d, J = 14 Hz, 1H), 2.33 (d, J = 14 Hz, 1H), 2.44 (dd, J_1 = 14 Hz, J_2 = 6 Hz, 1H), 4.17 (s, 2H), 4.78 (s, 2H), 7.00 (m, 2H), 7.10 (m, 2H), 7.16 (m, 2H), 7.29 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 202.6, 141.0, 140.5, 140.3, 134.5, 125.4, 125.3, 125.0, 123.6, 118.6, 108.6, 57.4, 57.1,50.6, 42.9, 40.3, 33.8, 28.7, 22.3; HRMS calcd for $C_{24}H_{21}O_2$ (M + 1) 341.1536, found 341.1536.

(b) Reaction with 2,3-Dimethyl-1,3-butadiene. A solution of **5** (30 mg, 0.11 mmol) and 2,3-dimethyl-1,3-butadiene (0.3 g, 1.1 mmol) in xylene (5 mL) was refluxed for 4.5 h. The white solid formed was collected by filtration to afford **4,5-[9',10']](9',-10'-dihydroanthraceno)-4,5-(1",2"-dimethylcyclohexen-1"-o)cyclopentano-1,3-dione**, **8b**, in 53% yield: mp 210−215 °C; ^{1}H NMR ($CDCl_3$−DMSO-d_6, 300 MHz) 1.49 (s, 6H), 1.72 (d, J = 14 Hz, 2H), 2.29 (d, J = 14 Hz, 2H), 4.18 (s, 2H), 4.80 (s, 2H), 7.00 (m, 2H), 7.10 (m, 2H), 7.17 (m, 2H), 7.29 (m, 2H); ^{13}C NMR ($CDCl_3$−DMSO-d_6, 75 MHz) δ 198.3, 141.7, 141.1, 125.9, 125.8, 125.6, 124.3, 109.5, 58.1, 51.0, 42.7, 36.1, 18.8; MS *m*/*z* 354 (M^+, 100), 52 (40), 202 (30), 178 (85). Anal. Calcd for $C_{25}H_{22}O_2$: C, 84.72; H, 6.25. Found: C, 84.31; H, 6.01.

Reaction of Triptycene Cyclopentene-1,3-dione with Nitrile Oxides. To a stirred solution of triptycene cyclopentene-1,3-dione, **5** (0.15 g, 0.55 mmol), in benzene (5 mL) were added successively the corresponding nitroalkane ($EtNO_2$ or $PrNO_2$, 0.6 mmol), PhN=C=O (0.55 g, 0.50 mL, 1.1 mmol), and 1−2 drops of Et_3N. Stirring was continued at room temperature for 24 h. After evaporation of the solvent, the solid residue was dissolved in CH_2Cl_2 (10 mL), the organic layer was washed with 5% NaOH (3 × 5 mL), and the combined basic solution was filtered and acidified. The precipitate formed was filtrated, dried under vacuum, and recrystallized from CH_2Cl_2/hexanes to afford the cycloaddition product.

Reaction with MeC≡N → O. 4,5-[9',10']](9',10'-Dihydroanthraceno)-4,5-(3"-methylisoxazolo)cyclopentano-1,3-dione, 10, 11a: yield 11%; mp 208−211 °C dec; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.03 and 1.92 (s, CH_3), 4.71 and 4.94 (s, br, bridge), (7.15−7.47, m, aromatic and vinylic), 9.46 and 11.96 (s, OH). Anal. Calcd for $C_{21}H_{15}NO_3$: C, 76.58; H, 4.59; N, 4.25. Found: C, 76.73; H, 4.32; N, 4.17.

Reaction with EtC≡N → O. 4,5-[9',10']](9',10'-Dihydroanthraceno)-4,5-(3"-ethylisoxazolo)cyclopentano-1,3-dione, 10, 11b: yield 15%; mp 220−222 °C dec; **10b** and **11b** ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.07 and 1.12 (t, J = 6 Hz), 2.25 and 2.32 (q, J = 6 Hz), 4.72 and 4.94 (s, br, bridge), (7.15−7.47, m, aromatic and vinylic), 9.38 and 12.18 (s, OH); HRMS calcd for $C_{22}H_{16}NO_3$ (M − 1) 342.1136, found 342.1130.

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