Metacyclophanes and Related Compounds. 6. Reduction of [2.2]Metaparacyclophanequinone[1]

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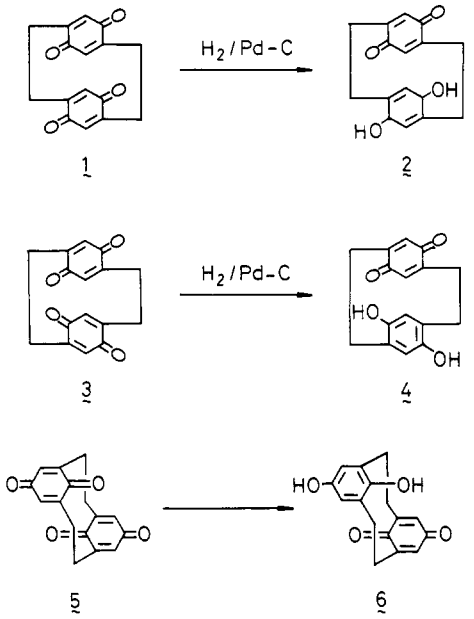
Abstract: The title compound (**24**) was prepared from 2,6-bis(chloromethyl)-4-*tert*-butylanisole (**7**) and 2,5-bis(mercaptomethyl)-1,4-dimethoxybenzene (**8**) in five steps. When **24** was reduced with Zn powder in acetic acid, initially, the corresponding tetrahydroxy derivative **26** was formed, but it soon converted by air to the corresponding quinhydrone type of complex, **25**, which shows a band due to a charge-transfer complex at 490 nm (log ϵ 2.83).

Although many [2.2]paracyclophanequinones,[2-8] [3.3]metacyclophanequinones,[9] and [2.2]metacyclophanequinone[10] have been prepared, [2.2]metaparacyclophanequinones have not been synthesized previously.

In addition Staab and Rebafka[5,6] reported that the partial hydrogenation of [2.2]paracyclophanequinones **1** and **3** afforded the interesting intermolecular quinhydrones **2** and **4** as black and dark violet crystals, respectively, whereas the quinhydrone **6** obtained from **5** was almost colorless as a solid but was colored in solution.[1]

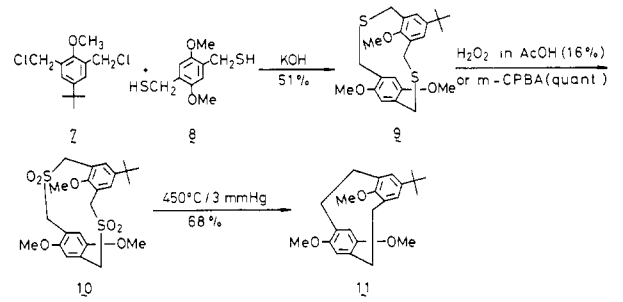


We undertook the present work in order to prepare the title compound and to obtain information about the color of the corresponding quinhydrone.

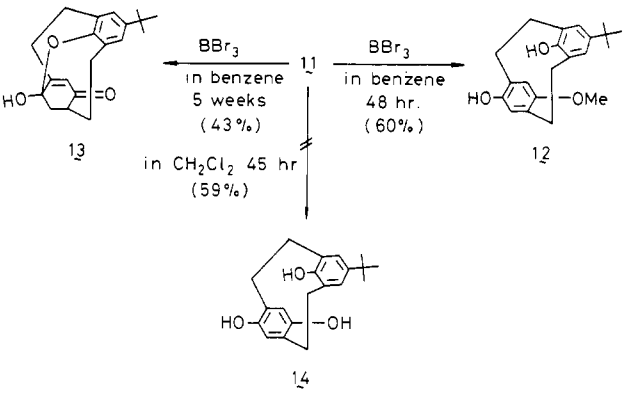
Results and Discussion

When **7**[11] was treated with **8**[12] according to the reported method,[11] **9** was obtained in 51% yield. Oxidation of **9** with H_2O_2 in AcOH afforded **10** in only 16% yield, but oxidation of **9** with *m*-CPBA gave **10** in almost quantitative yield.

Scheme I

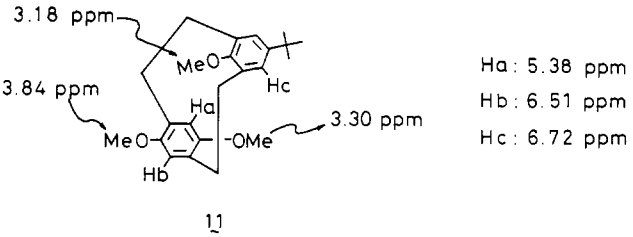


Scheme II



Trimethoxyclcophane **11** was obtained in 68% yield from **10** by gas-phase pyrolysis at 450 °C and 3-mmHg pressure (Scheme I).

The ^1H NMR ($CDCl_3$) spectrum of **11** shows aromatic protons at 5.38, 6.51, and 6.72 ppm and methoxy protons at 3.18, 3.30, and 3.84 ppm as singlets. Their signals can be assigned as below.



11

When **11** was treated with BBr_3 in benzene or CH_2Cl_2, **12** or **13** was obtained but not the expected **14** (Scheme II).

Compound **13** was also obtained by the treatment of **12** with BBr_3 in benzene. This result suggests that **12** is initially formed and then converted to **13** by further reaction with BBr_3 in benzene.

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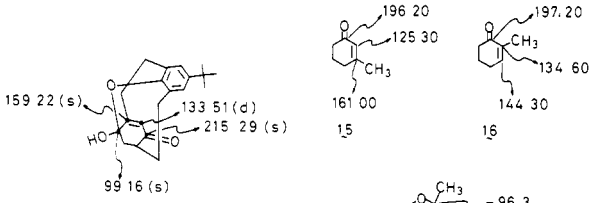
The ^1H NMR ($CDCl_3$) spectrum of **12** shows methoxy protons at 3.32 ppm and hydroxy protons at 4.50 and 4.73 ppm as singlets. This spectral data supports the proposed structure of **12**.

The IR (KBr) spectrum of **13** shows ν_{OH} at 3340 cm^{-1} and $\nu_{C=O}$ at 1645 cm^{-1}. This means that **13** is an α,β-unsaturated carbonyl compound. The ^1H NMR ($CDCl_3$) spectrum of **13** shows an olefinic proton at 5.41 ppm and aromatic protons at 6.90 ppm as singlets. The former signal is assigned to the internal olefinic proton, since the proton is shifted upfield as a result of shielding by the ring current of the opposite aromatic ring.

The ^{13}C NMR spectrum of **13** shows a carbonyl carbon at 215.29 ppm, olefinic carbons at 133.51 and 159.29 ppm, and a hemiketal carbon at 99.16 ppm.

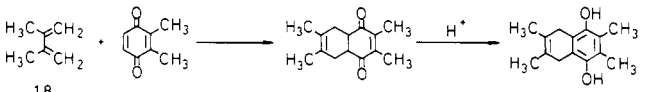


13 15 16 17

These signals are assigned by comparison with those of related compounds such as **15**,[13] **16**,[13] and **17**.[14]

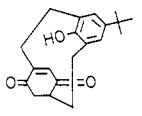
The structure assigned **13** is supported by its elemental analysis, the above spectral data, and the chemical conversions discussed below.

Some Diels–Alder adducts of benzoquinones with dienes can be converted from the diketo form to the corresponding enol form by treatment with a proton acid.[15] For example,



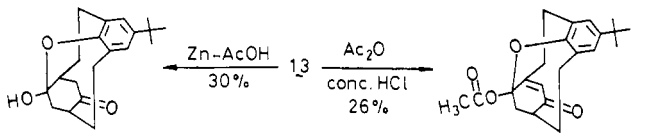
18 19 20 21

When **13** was treated with concentrated hydrochloric acid, it was recovered unchanged in almost quantitative yield. This finding suggests that the alternative structure **13′** is unlikely.



13

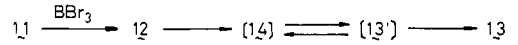
When **13** was treated with acetic anhydride in the presence of concentrated hydrochloric acid, the acetate **22** was obtained. Reduction of **13** with Zn powder in acetic acid afforded **23** in 30% yield.



23 13 22

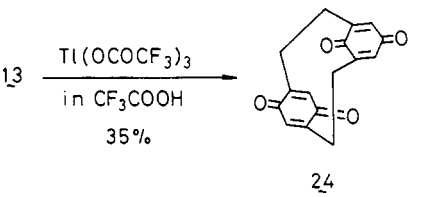
The structures assigned **22** and **23** are supported by elemental analyses and spectral data.

Although the reaction pathway to **13** is still obscure, the tentative pathway is proposed as follows.



11 12 [14] [13′] 13

Oxidation of **13** with $Tl(OCOCF_3)_3$ in CF_3COOH afforded the desired [2.2]metaparacyclophanebisquinone (**24**) in 35% yield.



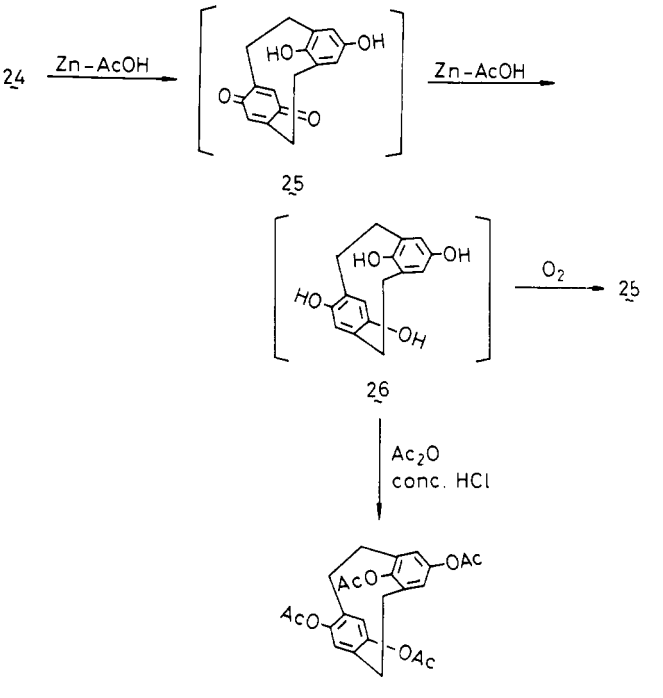
24

When zinc powder was added to a solution of **24** in acetic acid, the solution began to change color immediately and went from yellow to dark violet in a few minutes. The color of the solution changed to colorless after the excess zinc powder was removed by filtration; the filtrate gradually changed from colorless to dark violet, from which the desired quinhydrone **25** was isolated as purplish black crystals in 32% yield.

Partial hydrogenation of **24** in the presence of PtO_2 in ethanol also afforded **25** in 56% yield. The change of color during the reduction was observed in this case as well.

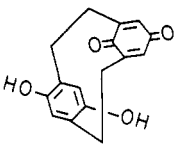
The above finding means that at first partial hydrogenation of **24** occurs to give the colored **25**, which is reduced in a few minutes to afford colorless **26**. However, compound **26** is apparently labile to air and so reconverted to **25**.

In fact, when the intermediate colorless solution was treated with acetic anhydride, tetraacetate **27** was obtained.



24 25 26 25 27

The ^1H NMR spectrum of **25** shows olefinic protons at 5.95 and 6.28 ppm as singlets, and aromatic protons at 6.18 and 6.32 ppm as doublets (J = 2.5 Hz). On the basis of the above data, the other possible quinhydrone structure **25′** seems less likely.



25

As shown in Figure 1, the spectrum of **25** shows a band due to a charge-transfer complex at 490 nm (log ϵ 2.83).

The electronic spectrum of **25** indicates a larger charge-transfer interaction than for **6** but less than for **2** and **4**. This would be expected since the overlap between the quinone and hydroquinone rings of **25** is larger than that of **6** but less than those of **2** and **4**. λ_{max} for these compounds are the following: **2**, 495; **4**, 515; **25**, 490; **6**, 459 nm. Consequently, there seems to be close rela-

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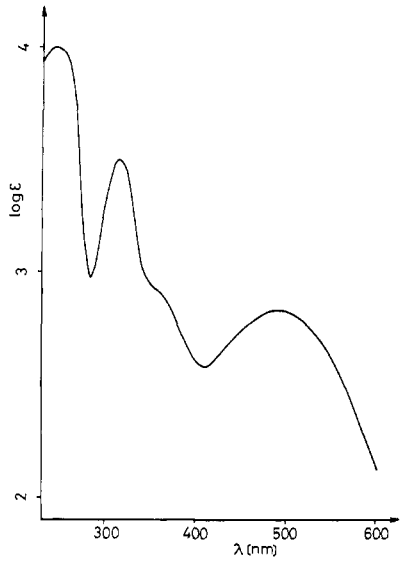

Figure 1. Electronic spectra of **25** (in THF).

tionship between such overlap and the λ_{max} of the quinhydrones **2**, **4**, **25**, and **6**.

Experimental Section

All melting points are uncorrected. NMR spectra were determined at 100 MHz with Nippon Denshi JEOL FT-100 NMR spectrometer with Me_4Si as an internal reference. IR spectra were measured as KBr pellets with a Nippon Bunko IR-A-102 spectrometer. Mass spectra were obtained with a Nippon Denshi, JMS-01SA-2 spectrometer at 75 eV, by using a direct-inlet system.

Preparation of 9. A solution of 16.1 g (70 mmol) of **8** and 18.3 g (70 mmol) of **7** in 350 mL of benzene and a solution of 7.7 g (137 mmol) of potassium hydroxide in 200 mL of water were added dropwise simultaneously from two Hershberg funnels with stirring under nitrogen to a solution of 1.1 g of potassium hydroxide in 4 L of ethanol. When the addition was complete (2 days), the mixture was concentrated, and the residue was extracted with dichloromethane. After the dichloromethane extract was washed with water, dried, and concentrated to leave a residue, it was chromatographed over Al_2O_3 using a 1:1 hexane–benzene mixture for elution. The first eluate fraction provided a crystalline solid, which, after recrystallization from 5:1 hexane–benzene mixture, gave 14.8 g (50.5%) of **9**: colorless prisms (hexane–benzene); mp 187–190 °C; IR (KBr) 2950, 1505, 1470, 1400, 1250, 1210, 1090, 1040, 1010, 870, 860, 745, 685 cm^{-1}; NMR ($CDCl_3$) δ 1.25 (9 H, s), 3.06–4.61 (8 H, m), 3.32 (3 H, s), 3.40 (3 H, s), 3.80 (3 H, s), 6.02 (1 H, s), 6.56 (1 H, s), 7.04 (2 H, s); mass spectrum, *m/e* 418 (M^+).

Anal. Calcd for $C_{23}H_{30}O_3S_2$: C, 65.99; H, 7.22. Found: C, 66.08; H, 7.28.

Oxidation of 9. Method A. A mixture of 8.5 g (20.3 mmol) of **9**, 34 mL of 35% hydrogen peroxide, and 135 mL of acetic acid was refluxed for 14 h. The reaction mixture was poured into a cold solution of 80 g of sodium hydroxide in 300 mL of water, and the resulting paste was allowed to cool to room temperature. When the crude sulfone was filtered off and washed with a small amount of ethanol, 1.56 g (16%) of pale orange crystals **10** were obtained.

Method B. A mixture of 6.0 g (14.3 mmol) of **9**, 15.5 g (71.8 mmol) of 80% *m*-chloroperbenzoic acid, and 600 mL of CH_2Cl_2 was stirred at room temperature for 22 h. The reaction mixture was washed with 10% Na_2CO_3 and water, dried over Na_2SO_4, and concentrated in vacuo to leave 6.90 g (quantitative) of **10**: colorless solid; mp >300 °C; IR (KBr) 2950, 1600, 1510, 1480, 1460, 1310, 1300, 1260, 1220, 1170, 1110, 1040, 1000, 90, 870, 780, 750, 700, 680 cm^{-1}; NMR ($CDCl_3$) δ 1.27 (9 H, s), 3.36 (6 H, s), 3.90 (3 H, s), 3.70–5.08 (8 H, m), 6.26 (1 H, s), 6.75 (1 H, s), 7.55 (1 H, d), 7.66 (1 H, d); mass spectrum, *m/e* 482 (M^+).

Anal. Calcd for $C_{23}H_{30}O_7S_2$: C, 57.24; H, 6.27. Found: C, 57.05; H, 6.18.

Pyrolysis of 10. Pyrolysis of disulfone **10** was carried out in an apparatus consisting of a horizontal tube (15 mm in diameter) passing through two adjacent tube furnaces, each of which was 20 cm long. The first furnace provided a temperature that would induce sublimation of the disulfone; the second was used at a higher temperature (500 °C) that would assure pyrolysis. A vacuum pump was connected at the exit from the second furnace. Two grams (4.78 mmol) of **10** was pyrolyzed at 450 °C under reduced pressure (2–3 mmHg) in the above apparatus as follows. The sample of **10** was placed in the first furnace, and small glass beads were packed into the second furnace. The product that sublimed was collected and chromatographed on silica gel (300 mesh) with hexane–benzene (1:1) to yield 1.2 g of yellow residue. Recrystallization from methanol gave 1.0 g (68%) of **11**: colorless solid; mp 91.5–92.5 °C; IR (KBr) 2900, 1500, 1460, 1390, 1230, 1205, 1180, 1100, 1040, 1015, 880, 850, 800, 710, 700, 660; NMR ($CDCl_3$) δ 1.26 (9 H, s), 2.10–3.70 (8 H, m), 3.18 (3 H, s), 3.30 (3 H, s), 3.84 (3 H, s), 5.38 (1 H, s), 6.51 (1 H, s), 6.72 (2 H, s); mass spectrum, *m/e* 354 (M^+).

Anal. Calcd for $C_{23}H_{30}O_3$: C, 77.93; H, 8.53. Found: C, 77.90; H, 8.59.

Dealkylation of 11 with BBr_3. Preparation of 12. To a stirred solution of 1.0 g (2.82 mmol) of **11** in 100 mL of dry benzene at room temperature was added dropwise a solution of 4 mL (42 mmol) of BBr_3 in 20 mL of dry benzene over a period of 1 h. After the reaction mixture was permitted to stand for 46 h at room temperature, it was washed with water, dried over Na_2SO_4, and concentrated in vacuo to leave a 0.96 g of crude **12**. Recrystallization from hexane–benzene (10:1) gave 550 mg (60%) of **12**: colorless needles (hexane–benzene); mp 128–141 °C; IR (KBr) 3600, 3150, 2960, 2940, 1500, 1470, 1440, 1410, 1280, 1205, 1100, 1020, 885, 800, 740 cm^{-1}; NMR ($CDCl_3$) δ 1.26 (9 H, s), 2.10–3.42 (8 H, m), 3.32 (3 H, s), 4.50 (1 H, s), 4.73 (1 H, s), 5.40 (1 H, s), 6.56 (1 H, s), 6.64 (1 H, s), 6.66 (1 H, s); mass spectrum, *m/e* 326 (M^+).

Anal. Calcd for $C_{21}H_{26}O_3$: C, 77.27; H, 8.03. Found: C, 77.36; H, 7.76.

Preparation of 13. Method A. To a solution of 500 mg (1.41 mmol) of 8,12,15-trimethoxy-5-*tert*-butyl[2.2]metacyclophane (**11**) in 50 mL of dry benzene at room temperature was added dropwise a solution of 1.2 mL (12.6 mmol) of BBr_3 in 10 mL of dry benzene over a period of 1 h. After the reaction mixture was permitted to stand for 5 weeks at room temperature, it was washed with water, dried over Na_2SO_4, and concentrated in vacuo to leave a resin that after column chromatography (silica gel 300 mesh) afforded crude **13**. Recrystallization from hexane–benzene (1:1) gave 190 mg (43%) of **13**.

Method B. A solution of 5.35 mL of BBr_3 (56.4 mmol) in dry CH_2Cl_2 (20 mL) was added dropwise during 20 min to a stirred solution of 2.5 g (7.05 mmol) of **11** in dry CH_2Cl_2 (75 mL) at 0 °C. After the reaction mixture was stirred at room temperature for 45 h, it was worked up as described above; the yield was almost colorless solid **13**. Recrystallization from hexane–benzene (1:1) gave 1.3 g (59%) of **13**: colorless needles (hexane–benzene); mp 177.5–181 °C; IR (KBr) 3340, 2970, 1645, 1480, 1140, 1100, 990, 910, 685 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.22 (9 H, s), 1.90–3.40 (11 H, m), 3.52 (1 H, s, exchanged with D_2O), 5.41 (1 H, s), 6.90 (2 H, s), 7.31 (6 H, s); ^{13}C NMR ($CDCl_3$) δ 24.48 (t), 30.12 (t), 31.18 (t), 31.64 (q), 32.52 (s), 34.87 (t), 37.81 (t), 41.33 (d), 99.16 (s), 123.47 (d), 124.78 (d), 132.80 (s), 133.51 (d), 133.86 (s), 148.54 (s), 150.47 (s), 159.22 (s), 215.29 (s); mass spectrum, *m/e* 312 (M^+); UV ($CHCl_3$) λ_{max} 243 nm (log ϵ 3.58).

Anal. Calcd for $C_{20}H_{24}O_3 + C_6H_6$: C, 79.96; H, 7.74. Found: C, 79.88; H, 7.74.

Acetylation of 13. To a solution of 50 mg (0.16 mmol) of **13** in 12.5 mL of acetic anhydride was added 0.5 mL of concentrated hydrochloric acid. After the reaction mixture was stirred for 5 h at room temperature, it was poured into 50 mL of water. The solution was permitted to stand for 2 h, and a pale yellow precipitate formed. This solid was collected and washed with water to give 33 mg (58%) of crude **22**. Recrystallization from hexane gave 15 mg (26%) of **22**: colorless prisms (hexane); mp 171–175 °C; IR (KBr) 2950, 1745, 1665, 1470, 1370, 1250, 1190, 1180, 1100, 1060, 1000, 930, 870, 845, 770 cm^{-1}; NMR ($CDCl_3$) δ 1.22 (9 H, s), 2.22 (3 H, s), 2.05–3.30 (11 H, m), 5.45 (1 H, s), 6.89 (2 H, s); mass spectrum, *m/e* 354 (M^+).

Anal. Calcd for $C_{22}H_{26}O_4$: C, 74.55; H, 7.39. Found: C, 74.32; H, 7.37.

Reduction of 13. A mixture of 100 mg (0.32 mmol) of **13**, 1.0 g (15.4 mmol) of zinc powder, and 10 mL of acetic acid was stirred at 100 °C in an oil bath for 2 h. After the reaction mixture was filtered, the filtrate was poured into 50 mL of water and extracted with CH_2Cl_2, and the CH_2Cl extracts were washed with water, dried over Na_2SO_4, and concentrated in vacuo to leave a pale yellow solid quantitatively. Recrystallization from hexane gave 30 mg (30%) of **23**: colorless prisms (hexane); mp 106–111 °C; IR (KBr) 3410, 2950, 1675, 1480, 1300, 1210, 1140, 1115, 1085, 1000, 920, 860, 840, 800, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (9 H, s), 2.30–3.50 (14 H, m), 6.85 (1 H, d), 6.95 (1 H, d, J = 3.5 Hz), 2.20 (1 H, s); ^{13}C NMR ($CDCl_3$) δ 24.51 (t), 26.09 (t), 26.56 (t), 31.59 (q), 34.45 (s), 37.38 (t), 38.96 (t), 40.01 (t), 43.23 (d), 43.52 (d), 99.33 (s), 123.85 (d), 125.13 (d), 133.09 (s), 135.14 (s), 149.53 (s), 209.20 (s); mass spectrum, *m/e* 314 (M^+).

Anal. Calcd for $C_{20}H_{26}O_3$: C, 76.40; H, 8.34. Found: C, 76.62; H, 8.36.

Oxidation of 13 with TTFA. To a standard solution of 20 mL of trifluoroacetic acid (TFA) containing 1.4 mmol of $Tl(TFA)_3$ was added 1.0 g (3.2 mmol) of **13** at 0 °C, and the resulting deep red mixture was stirred at room temperature for 2.5 h. The reaction mixture was poured into ice water and extracted with CH_2Cl_2, and the CH_2Cl_2 extracts were washed with water and dried over Na_2SO_4. Concentration of the solution gave the yellow paste that on column chromtography (silica gel 300 mesh) afforded crude quinone **24**. Recrystallization from ethanol gave 300 mg (35%) of **24**: bright yellow prisms (ethanol); mp 196-205 °C; IR (KBr) 1670, 1655, 1435, 1280, 1235, 920 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.1-3.85 (8 H, m), 6.20 (1 H, m), 6.34 (1 H, m), 6.46 (1 H, m), 6.49 (1 H, m); ^{13}C NMR ($CDCl_3$) δ 26.85, 28.17, 29.19, 31.29, 131.08, 132.74, 133.86, 135.91, 149.65, 149.90, 151.70, 152.43, 185.51, 186.20, 187.91, 189.60; mass spectrum, *m/e* 268 (M^+); UV ($CHCl_3$) λ_{max} 251 nm (log ε 4.35).

Anal. Calcd for $C_{16}H_{12}O_4$: C, 71.63; H, 4.51. Found: C, 71.93; H, 4.49.

Reduction of [2.2]Metaparacyclophanequinone (24). Method A: AcOH-Zn Reduction. To a solution of 100 mg (0.37 mmol) of [2.2]-metaparaquinonophane (**24**) in 40 mL of acetic acid was added 1.0 g of zinc powder. Addition of zinc powder to the mixture produced a reddish brown to dark wine-red color immediately. The reaction mixture was stirred at room temperature for a few minutes. After the reaction miture became colorless, zinc powder was removed by filtration and the solvent of the filtrate was distilled away in vacuo to leave a very pale violet solid containing $(AcO)_2Zn$, which dissolve in water. The aqueous solution was allowed to stand for some time in contact with air. The solution turned reddish violet rapidly. It was extracted with ether several times, dried over Na_2SO_4, and concentrated in vacuo to leave 100 mg of dark violet solid. Reprecipitation with ether-hexane and washing with CH_2Cl_2 gave 32 mg (32%) of purplish black solid **25**.

Method B: Hydrogenation (PtO_2/H_2). Hydrogen gas was bubbled into the stirred mixture of 30 mg (0.11 mmol) of **24** and 10 mg of PtO_2 (Adams' catalyst) in 25 mL of ethanol at room temperature. The reaction mixture turned reddish brown from yellow quickly, and the brown color disappeared gradually. After the solution turned colorless, the catalyst was removed by filtration and the filtrate, which turned dark violet gradually, was concentrated in vacuo to leave a dark violet solid and was worked up described above; the yield was 17 mg (56%) of **25**: purplish black solid; mp 184 °C; IR (KBr) 3440, 3360, 2950, 1635, 1615, 1420, 1290, 1200, 1140, 900, 870 cm^{-1}; NMR (Me_2SO-d_6) δ 2.0-3.3 (8 H, m), 5.95 (1 H, s), 6.18 (1 H, d, *J* = 2.5 Hz), 6.28 (1 H, s), 6.32 (1 H, d, *J* = 2.5 Hz), 8.60 (1 H, s, exchanged with D_2O); mass spectrum, *m/e* 270 (M^+); UV (THF) λ_{max} 490 (log ε 2.83), 355 (log ε 2.92), 315 (log ε 3.50), 245 nm (log ε 4.00).

Anal. Calcd for $C_{16}H_{14}O_4 + {}^1/_4H_2O$: C, 69.94; H, 5.32. Found: C, 69.88; H, 5.33.

Acetylation of 26. To a solution of 30 mg (0.11 mmol) of [2.2]-metaparaquinonophane (**24**) in 10 mL of acetic acid was added 0.5 g (7.7 mmol) of zinc powder. The reaction mixture was stirred at room temperature for a few minutes. After the bright yellow solution turned colorless, 10 mL of acetic anhydride and 8 drops of concentrated HCl were added to the reaction miture. The reaction mixture was stirred at 80 °C for 10 min, filtered, and poured into 100 mL of water. After the aqueous solution was stirred at room temperature for 1.5 h, it was extracted with CH_2Cl_2, washed with water, dried over Na_2SO_4, and concentrated in vacuo to leave 50 mg (100%) of crude **27**. Recrystallization from hexane-benzene (5:1) gave 30 mg (61%) of **27**: colorless prisms (hexane-benzene); mp 176-181 °C; IR (KBr) 2940, 1750, 1585, 1490, 1450, 1435, 1365, 1210, 1170, 1160, 1120, 1010, 955, 910, 800 cm^{-1}; NMR ($CDCl_3$) δ 1.25 (3 H, s), 2.13 (3 H, s), 2.26 (3 H, s), 2.32 (3 H, s), 2.0-3.15 (8 H, m), 6.06 (1 H, s), 6.59 (1 H, d, *J* = 3 Hz), 6.65 (1 H, d, *J* = 3 Hz), 6.91 (1 H, d); mass spectrum, *m/e* 440 (M^+).

Anal. Calcd for $C_{24}H_{24}O_8$: C, 65.45; H, 5.49. Found: C, 65.33; H, 5.54.

Registry No. **7**, 62224-04-8; **8**, 50874-28-7; **9**, 87207-25-8; **10**, 87207-26-9; **11**, 87207-27-0; **12**, 87207-28-1; **13**, 87207-29-2; **22**, 87207-30-5; **23**, 87207-31-6; **24**, 72652-39-2; **25**, 87207-32-7; **26**, 87207-33-8; **27**, 87207-34-9.

Termination of Biomimetic Cyclizations by the Allylsilane Function. Formation of the Steroid Nucleus in One Step from an Acyclic Polyenic Chain

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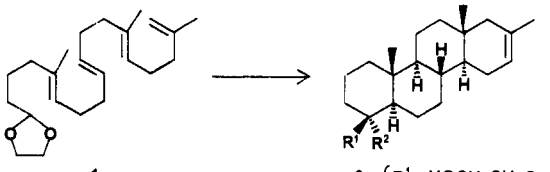
Abstract: The aim of this project was to modify the cyclization substrate **1**, which is known to undergo ring closure to give **2a** and **2b**, in such a way that a five- instead of six-membered ring D is formed, thus resulting in the construction of the complete steroid nucleus. The substrate **5** was first prepared as shown in Scheme I, but it gave a very complicated mixture of cyclization products. However, the substrate **18**, which was obtained as depicted in Scheme II, afforded the tetracyclic products **24** and **25** in >34% yield. The steroidal constitution of the nucleus of these products was established by their transformation into the known 17α- and 17β-vinylandrostenones **36**, which are convertible into progesterone.

The stannic chloride catalyzed cyclization of the tetraenic acetal **1** has been shown[1] to proceed highly regio- as well as stereoselectively to give, as the only detectable tetracyclic material, two readily separated crystalline products which proved to be the D-homosteroidal substances **2a** and **2b**, differing only in that they were epimeric at C-4 (steroid numbering). Up until now this case has represented the closest nonenzymatic analogy to the biological process for the production of tetracyclic triterpenoids from squalene. Thus in the one-step conversion **1** → **2**, four rings and seven chiral centers are formed in predominantly one stereochemical sense from an acyclic polyene chain—a process which



1

2a (R^1 = $HOCH_2CH_2O$-, R^2 = H)

2b (R^1 = H, R^2 = $HOCH_2CH_2O$-)

in this respect is comparable in complexity to the biological conversion of squalene into lanosterol.

It has been our aim, for some time, to modify the substrate **1** so that cyclization would give a tetracyclic product with a five-membered ring D, thus yielding the complete steroid nucleus. By

(1) Johnson, W. S.; Wiedhaup, K.; Brady, S. F.; Olson, G. L. *J. Am. Chem. Soc.* **1968**, *90*, 5277-5279; **1974**, *96*, 3979-3984.

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