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Synthesis of 8,16-Dimethyl- and 8,16-Dimethoxy-5,13-di-*t*-butyl[2.2]metacyclophane-1,2,9,10-tetraone

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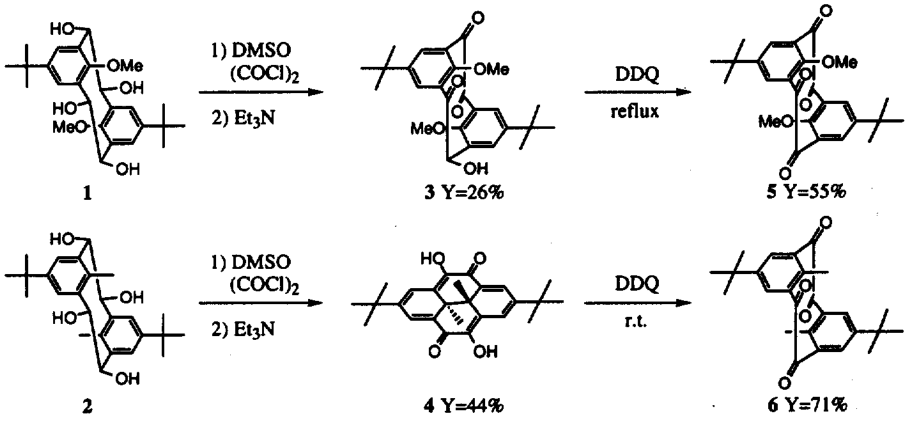
Abstract: Swern oxidation of 8,16-dimethoxy- and 8,16-dimethyl-5,13-di-*t*-butyl-1,2,9,10-tetrahydroxy[2.2]metacyclophane, **1** and **2**, afforded 5,13-di-*t*-butyl-10-hydroxy-8,16-dimethoxy[2.2]metacyclophane-1,2,9-trione **3** and **4**. By subsequent oxidation with DDQ, 8,16-dimethoxy- and 8,16-dimethyl-5,13-di-*t*-butyl[2.2]metacyclophane-1,2,9,10-tetraones, **5** and **6**, were obtained.

[2.2]Metacyclophanes with added strain on the bridges, such as [2.2]metacyclophane-dienes[1] and [2.2]metacyclophane-ketones, show interesting reactivity. Thus, metacyclophane-1,10-dione exhibits a pronounced tendency towards adduct formation with nucleophiles; even its hydrate forms easily.[2] Ring expansion of the [2.2]metacyclophane-diones to the corresponding [3.2]metacyclophane-diones by using either diazomethane[3] or methylidenephosphorane under mild conditions are very unique reactions. [2.2]Metacyclophane-1-one,[4] -1,2-dione[5] and -1,10-dione[6] have been prepared. Here, the synthesis, physical and structural properties of the novel [2.2]metacyclophane-1,2,9,10-tetraones are described.



Scheme 1

[2.2]Metacyclophane-1,2,9,10-tetraols (**1**,**2**) are readily accessible by a simple, one step reductive pinacol-type coupling of benzene-1,3-dicarbaldehydes, using either samarium iodide[7] or, preferably aluminum.[7] Oxidation of **1** and **2** is not easy, as most reagents such as DDQ, $KMnO_4$ or $BaMnO_4$ lead to 1,2-diol cleavage, yielding predominantly the corresponding 1,3-benzenedicarbaldehydes. Oxidation can be achieved by a modified Swern procedure[8] which uses oxalyl chloride-DMSO (9.0 mmol:19.8 mmol) in CH_2Cl_2 (4 mL), followed by addition of the substrate (0.22 mmol) in CH_2Cl_2 (5 mL) and DMSO (2 mL) and subsequent addition of Et_3N (44.2 mmol). The reaction gives the hydroxy[2.2]metacyclophane-trione **3** in 26% yield. When the Swern oxidation is carried out on **2**, **4** is isolated in 44% yield. The interconvertibility of the [2.2]metacyclophane and the dihydropyrene frame is well known from other reactions.[1,9] Here, functionalities within the metacyclophane bridge are incorporated in the dihydropyrene frame; that **4** does not exhibit any aromaticity as opposed to the corresponding dihydropyrene[10] is

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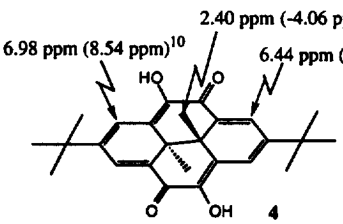
evidenced by the shifts of both the protons of the frame as well as of the methyl groups (Fig. 1). Both **3** and **4** were subjected to further oxidation by using DDQ[11] to give the desired tetraones **5** and **6**[12] in 55% and 71% yield, respectively (Scheme 1).

The UV spectra of **5** and **6** in CH_2Cl_2 show that the π–π^* transition of both **5** and **6** is shifted to longer wavelengths ($\Delta\lambda_{max}$=12nm[**5**];$\Delta\lambda_{max}$=16nm[**6**]) compared to the parent compounds, 5,13-di-*t*-butyl-8,16-dimethyl[2.2]metacyclophane[13] and 5,13-di-*t*-butyl-8,16-dimethoxy[2.2]metacyclophane.[13] In the ^{1}H-NMR spectrum of tetraone **6** a low field shift can be observed for the internal methyl protons in respect to those of the tetraol **2** (δ_H 0.65[**2**]→ 0.92 ppm[**6**]). Both facts indicate that there is an interaction between the benzo unit and the carbonyl group, but smaller than in conformationally non-constrained arylketones. This conclusion is supported by the X-ray crystal structure of **6** (Fig 2).[14] The X-ray of **6** also shows that the carbonyl groups are almost coplanar (dihedral angle between the carbonyls is 3.0°) and interestingly that the [2.2]metacyclophane chair-like structure in **6** is less distorted than in tetraol **2** or in comparable metacyclophanes with no additional substituents on the bridge.[15] The distances between the carbons in the 8- and 16- positions are shorter in **6** (2.59Å) than in **2** (2.77Å).[7] The strain of **6** rests in the bridges as evidenced by the non-planarity of the carbonyl groups (dihedral angle C3-C2-C1 / C3-O1-C1 is 4.7°).



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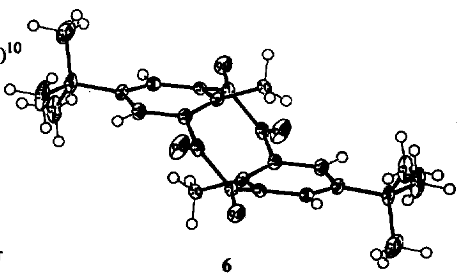
Values in parentheses are ^{1}H NMR data (δ_H CD_2Cl_2) for 2,7-di-*t*-butyl-10b,10c-dimethyl-10b,10c-dihydropyrene

Fig. 1 ^{1}H NMR data of **4**



6

Fig. 2 ORTEP Drawing of **6**

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12. **5**: 238-242°C (dec.) (benzene);ν(KBr) 2962, 1690, 1263 cm^{-1}; δ_H (270MHz,$CDCl_3$) 1.28 (s,18H), 3.16 (s,6H), 7.47 (s,4H); δ_C 31.24, 34.76, 63.29, 125.48, 132.01, 146.97, 160.73, 186.38; MS (EI) *m/z* 436 (M^+); UV (CH_2Cl_2) λ_{max} (nm) 227 (logε 4.4), 264 (logε 4.3). **6**: mp 230-240°C (dec.) (benzene);ν(KBr) 2960, 1682 cm^{-1}; δ_H ($CDCl_3$) 0.92 (s,6H), 1.34 (s,18H), 7.63 (s,4H); δ_C (67.8 MHz) 18.22, 31.05, 35.08, 130.06, 133.01, 140.55, 151.62, 187.99; MS (FAB, 3-nitrobenzyl alcohol) *m/z* 558 (MH^+·nitrobenzyl alcohol); UV λ_{max} (nm) 228 (logε 4.4), 262 (logε 4.2).
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14. Crystal data for **6**: $C_{26}H_{28}O_4$, M = 404.48, T = 183K, triclinic, a = 6.955(1), b = 11.806(1), c = 6.434(4) Å, α = 92.82(2)°, β = 91.58(2)°, γ =85.36(1)°, V = 525.8(3) Å^3, space group (P-1), Z = 1, μ = 0.507 mm^{-1}; 2127 independent reflections; 1571 with $I_o > 2\sigma(I_o)$ taken as observed. Final residuals R = 0.0719, R_w= 0.2094, where the weighting scheme is $w = 1/[\sigma^2 (F_o^2)+(0.2000P)^2+0.0000P]$, $P=(F_o^2+2F_c^2)/3$.
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