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[2.2]Metacyclophanes Having Hydroxy Groups on the Bridge

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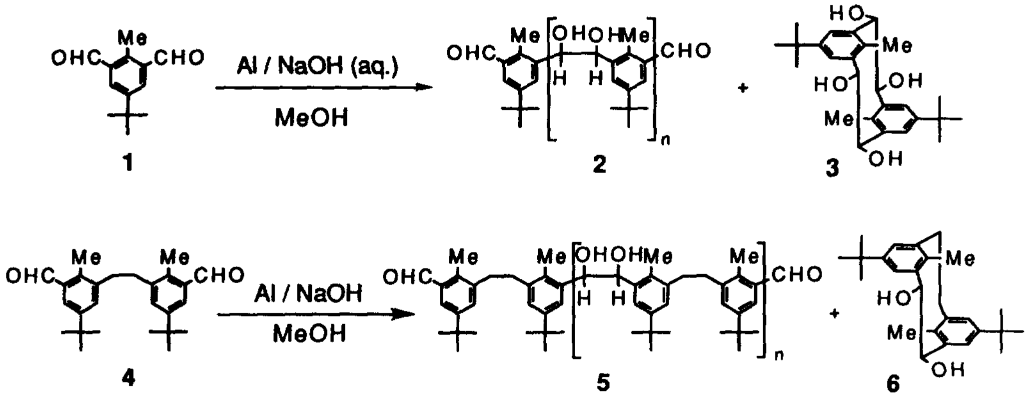
Abstract: The aluminium-mediated pinacol coupling of 5-t-butyl-2-methyl-1,3-benzenedicarboxaldehyde produced 5,13-di-t-butyl-8,16-dimethyl-1,2,9,10-tetrahydroxy[2.2]metacyclophane as a single stereoisomer in a fairly good yield. Also, a 1,2-dihydroxy derivative was prepared by the intramolecular coupling of 1,2-bis(5-t-butyl-3-formyl-2-methylphenyl)ethane.

Inter- and intramolecular metal-mediated coupling of aromatic aldehydes have been extensively explored.[1] The McMurry reaction was successfully used to prepare [3.2]metacyclophane-10-enes;[2] however, the synthesis of hindered [2.2]meta- and [2.2]paracyclophanes via reductive coupling of aromatic carbonyl compounds has not been described. We report herein the first example of the practical synthesis of [2.2]metacyclophanes having hydroxy groups on the bridge the pinacol coupling.

When 5-t-butyl-2-methyl-1,3-benzenedicarboxaldehyde (**1**) was subjected to the conditions of the Al/ aq. NaOH/methanol reductive system,[1c,3] a novel tetrahydroxy[2.2]metacyclophane **3**[4] was obtained, accompanied by the intermolecularly coupled oligomer **2**. Metacyclophane **3** was easily separated from **2**, just by washing with dichlorometane. The aluminium-mediated intramolecular pinacol coupling reaction of 1,2-bis(5-t-butyl-3-formyl-2-methylphenyl)ethane (**4**) yielded dihydroxy[2.2]metacyclophane **6**[4], although the reaction temperature had to be raised for the coupling to succeed due to the poor solubility of the substrate **4** in the solvent system (Scheme 1 and Table 1).

A very interesting aspect observed in these reactions is that they proceeded with high stereoselectivity, probably due to steric factors. Metacyclophane **3** and **6** were obtained each as a single stereoisomer, as



Scheme 1. Pinacol Coupling Reaction of Dialdehydes **1** and **4**.

Table 1. Pinacol Coupling Reaction[a]

Substrate	Al	MeOH	10% aq. NaOH	Temp.	Cyclophane (%)	Oligomer (%)
1; 1.10 g	0.55 g	25 ml	10 ml	r.t.[b]	**3** (33)	**2** (60)[c]
1; 1.10 g	0.55 g	25 ml	10 ml	55 °C	**3** (26)	**2** (63)[c]
4; 1.14 g	0.55 g	30 ml	10 ml	60 °C	**6** (18)	**5** (50)[c]

a) Reaction time; 3 h. b) During addition of a NaOH solution, the temperature of the reaction mixture increased by about 8°C. c) Weight/weight percent yields are given.

evidenced by their ^{1}H NMR spectra, which showed OH and methine protons on their bridges as singlet peaks. The X-ray crystallographic analysis of **3** (Fig. 1) disclosed that the hydroxy groups are in equatorial positions.[5]

In conclusion, a very simple and convenient preparation of bridge-substituted [2.2]metacyclophanes was achieved via the aluminium-mediated pinacol coupling reaction of aromatic dialdehydes.

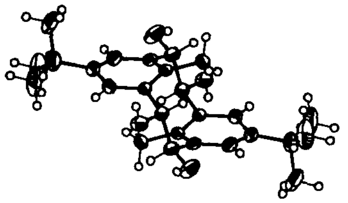


Fig. 1. ORTEP Drawing of **3**.

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References and Notes

1. a) Wirth, T. *Angew. Chem. Int. Ed. Eng.* **1996**, 35, 61-63. b) Khurana, J. M.; Sehgal, A.; Gogia, A.; Manian, A.; Maikap, G. C. *J. Chem Soc., Perkin Trans.1*, **1996**, 2213-2215. c) Tsukinoki, T.; Ishimoto, K.; Suzuki, H.; Mataka, S.; Tashiro, M. *Bull. Chem. Soc. Jpn.* **1993**, 66, 3419-3422.
2. Grützmacher, H. F.; Neumann, E. *Chem. Ber.* **1993**, 126, 1495-1497.
3. General procedure: Aluminium powder (150 mesh) was added to a solution of dialdehyde in methanol. The mixture was subjected to mechanical stirring and then the aqueous NaOH solution was added dropwise during a period of 15 min. Stirring was continued for 3 h. The mixture was filtered and the filtrate was extracted with ethyl acetate. The extract was washed with water, dried (magnesium sulfate) and evaporated to afford the crude product which was column chomatographed (silica gel, Wako C-300, eluant: hexane/ ethyl acetate mixtures) to give a mixture of cyclophane and oligomers. The mixture was washed with dichloromethane to give the cyclophane. Compounds **3** and **6** gave satisfactory elemental analysis.
4. Spectral data of **3**: Colorless needless (hexane/ethyl acetate, 1/1), mp 325-328 °C (dec); IR (KBr) 3412 cm^{-1}; ^{1}H NMR (DMSO-d_6) 7.53 (s, 4H), 5.45 (s, 4H), 4.31 (s, 4H), 1.25 (s, 18H), 0.51 (s, 6H); ^{13}C NMR (DMSO-d_6) 143.8, 136.1, 135.6, 120.8, 78.2, 33.8, 31.1, 13.7; MS (EI) m/z 412 (M$^+$). Spectral data of **6**: Colorless needless (hexane), mp 200 °C (dec); IR (KBr) 3430 cm^{-1}; ^{1}H NMR (DMSO-d_6) 7.50 (d, 2H, J= 1.98 Hz), 7.13 (d, 2H, J= 1.98 Hz), 5.47 (s, 2H), 4.33 (s, 2H), 2.86 (d, 2H, J= 9.9 Hz), 2.63 (d, 2H, J= 9.9 Hz), 1.24 (s, 18H), 0.47 (s, 6H); ^{13}C NMR (DMSO-d_6) 144.8, 137.0, 136.0, 135.8, 124.5, 120.0, 78.6, 35.3, 33.7, 31.1, 13.4; MS (EI) m/z 380 (M$^+$).
5. X-ray crystalographic analysis of **3**: Colorless needless, $C_{26}H_{36}O_4$, F. W.= 412.57, triclinic, a= 11.739 (2), b= 13.677 (2), c= 10.149 (2) Å, α= 102.80 (2), β= 108.83 (2), γ=70.900 (10)°, V= 1445.1 (4) Å^3, Z= 2, D_c= 1.151 g cm^{-3}, space group $P2_1/n$. Data were collected on an Enraf-Nonius CAD4 diffractometer, ω-2θ scan type, graphite-monochromated Cu Kα radiation, λ= 1.54184 Å. Of 4893 independent reflections collected in the range $2 < \theta < 65°$, 3876 with $I_0 > 2\sigma(I_0)$ were taken as observed. The crystal did not show any significant decay during the data collection. Positional parameters were determined by direct methods using SIR 92[6] and were reflected by full-matrix least-squares calculations with nonhydrogen atoms treated anisotropically using the scheme $w= 1/[\sigma^2(F_0^2)+(0.1028P)^2+1.1035P]$ were $P=(F_0^2+2F_c^2)/3$. All hydrogen atoms were located at ideal positions (SHELXL-93) and were included in refinement, but restrained to ride on the atom to which they are bonded. Isotropic thermal factors of H atoms were held fixed to 1.3 times U(eq) of the riding atoms. Final residuals R= 0.0619, R_w= 0.1746.
6. Altomare, M.; Burla, M.; Camalli, G.; Cascarano, C.; Giacovazzo, A.; Guagliardi, G.; Polidori, J. *J. Appl. Cryst.* **1993**, 26, 343-350.

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