Medium-sized cyclophanes, 63.[1] Synthesis and structure of [2.2]metacyclophane-1,2-diol and conversion into [2.2]metacyclophane-1,2-dione by Swern oxidation

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McMurry cyclisation of 1,2-bis(5-*t*-butyl-2-methyl-3-formylphenyl)ethane **2** afforded *anti*-[2.2]metacyclophan-1-ene **3** and *anti*-[2.2]metacyclophane-1,2-diols **4**, which were converted into the corresponding 1,2-dione **6** by Swern oxidation.

Keywords: cyclophanes, [2.2]metacyclophane-1,2-diol, McMurry reaction, Swern oxidation, strained molecules

For many years various research groups have been attracted by the chemistry and spectral properties of the [2.2]MCP ([2.2]MCP = [2.2]metacyclophane) skeleton.[2,3] Its conformation, which was elucidated by X-ray measurements,[4] is frozen into a chair-like non-planar form. Many attempts have been made directly to introduce functional groups into the methylene groups of [2.2]MCPs, but these have failed because of the deviation of the benzyl carbon atom from the plane of the benzene ring.[5]

Cram *et al.* have reported that bromination of [2.2]paracyclophan-1-ene with bromine affords the corresponding *cis*-adduct.[6] Previously, we have reported that di-*t*-butyldimethyl[2.*n*]MCP-1-enes[7] were treated with an equimolar amount of benzyltrimethylammonium tribromide (BTMA Br_3) in methylene dichloride to afford the *cis*-adducts to the bridged double bond.[8,9] This result indicates the first success in the introduction of two bromo groups into the methylene groups of dimethyl[*n*.2]MCPs. We have extended the novel reaction mentioned above and reported on the acetolysis of bromine adducts with silver acetate in acetic acid and the conversion to dimethyl[2.*n*]MCP-1,2-diones *via* hydrolysis followed by Swern oxidation of the dihydroxy derivatives.[10] However, we have not yet succeeded to prepare [2.2]MCP-1,2-diones *via* the bromination of dimethyl[2.2]MCP-1-enes due to the novel transannular reaction arising from the electronic interaction between two benzene rings, the proximity of the 8,16-positions and the release of the considerable strain energy to form the more stable annulene π-electron system, 10b,10c-dihydropyrene. Thus, the reaction of 5,13-di-*t*-butyl-8,16-dimethyl[2.2]MCP-1-ene with bromine affords 4,5,9,10-tetrabromo-2,7-di-*t*-butyl-*trans*-10b,10c-dimethyl-10b,10c-dihydropyrene in good yield, but not the adduct to the bridged double bond, which can be converted to the corresponding [2.2]MCP-1,2-dione.[8]

On the other hand, in cyclophane chemistry, the reductive coupling of carbonyl compounds by low-valent titanium, the McMurry reaction,[11] has been used before by Mitchell *et al.*[12] to synthesise cyclophanes with glycol units as bridges, by Tanner and Wennerström,[13] and recently by Hopf *et al.*[14] and Grützmacher *et al.*[15] in cyclisation of suitable dialdehydes to yield unsaturated cyclophanes. Thus, there is substantial interest in developing a more convenient preparation of [2.2]MCP-1-enes or 1,2-diols than the conventional sulfur method.[16] We report here on a convenient preparation of *anti*-[2.2]MCP-1-ene **3** and [2.2]MCP-1,2-diols **4** by McMurry reaction and first success for conversion to 1,2-dione by Swern oxidation.[17]

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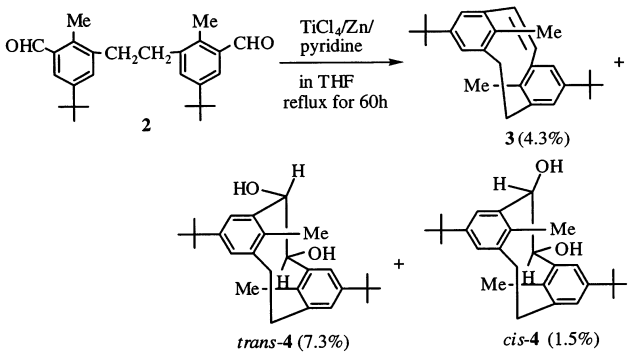
Results and discussion

The starting compound 1,2-bis(5-*t*-butyl-2-methylphenyl) ethane **1**[18] has been prepared according our previous paper by using the *t*-butyl group as a positional protective group on the aromatic ring.[16] Although the $TiCl_4$-catalysed formylation of compound **1** with dichloromethyl methyl ether[19] at 20°C for 2 h led to complete two-fold formylation, a mixture of the desired 1,2-bis(5-*t*-butyl-3-formyl-2-methylphenyl)ethane **2** and other isomers was obtained. The desired product **2** was isolated in pure by the fractional recrystallisation from hexane in only 39% yield.

1,2-Bis(5-*t*-butyl-3-formyl-2-methylyphenyl)ethane **2** was subjected to reductive coupling by the McMurry reaction following the Grützmacher's procedure[15] (Scheme 1). Thus, the reductive coupling reaction of **2** carried out using $TiCl_4$–Zn in refluxing THF under high dilution conditions afforded the desired compound *anti*-5,13-di-*t*-butyl-8,16-dimethyl[2.2]-MCP-1-ene **3** in only 4.3% yield along with the corresponding diols *trans*-**4** and *cis*-**4** in 8.8% yield. The more favourable formation of [2.2]MCP-diols seems to be due to the much more strained structure of **3** than diols **4** containing the saturated C–C linkage. Thus, during the McMurry reaction the dehydration of the diol to form the double bond might be quite difficult.



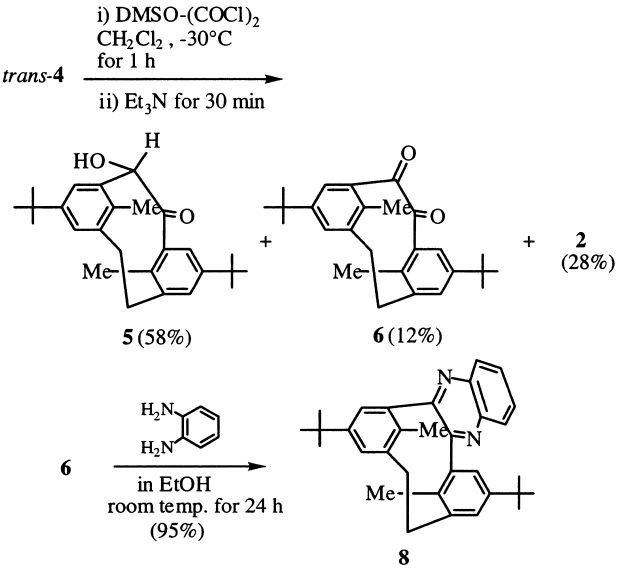
Scheme 1

The assignment of **3** was carried out by the comparison of the authentic sample.[8] The structures of products *trans*-**4** and *cis*-**4** were also determined on the basis of their elemental analyses and spectral data. Thus, we previously assigned[20] the ^{1}H NMR signals of 1-*exo*,5,13-trichloro-8,16-dimethyl [2.2]MCP. We have assigned the ^{1}H NMR signals of **4** in a similar fashion. For example, the ^{1}H NMR spectrum of *trans*-**4** shows an internal methyl resonance as a singlet at δ 0.58, a bridge methine signal as a singlet at δ 4.63, and two aromatic

protons as a pair of doublets at δ 7.17 and 7.57 (J = 2.0 Hz); the latter protons are in a strongly deshielding region of the oxygen atom of *endo*-OH on ethylene bridge. The structure of the *anti*-confomer is also readily assigned from the chemical shift of the methyl protons at δ 0.58. Thus the internal methyl protons should show an upfield shift due to the ring current of the opposite aromatic ring.[21,22] These data strongly support that the two OH groups are *endo*- and *endo*-arrangement and therefore, *trans*-**4** is found to be *trans*-diol. In contrast, the ^{1}H NMR spectrum of *cis*-**4** shows two internal methyl protons as singlets at δ 0.55, and 0.82, two bridged methine protons as a set of multiplets around δ 4.92–4.96 and 5.25–5.3, and four aromatic protons as two sets of doublets at δ 7.08, 7.19 (J = 2.0 Hz) and 7.21, 7.40 (J = 2.0 Hz). We observed one methyl group to be deshielded by the *exo*-OH group on the ethylene bridge resulting in a downfield shift (0.82 ppm). This observation strongly supports one of the OH groups being in an *exo*-arrangement. A deshielded aromatic proton was observed in the NMR spectrum of *cis*-**4** at δ 7.40 which is almost the same as that for the *endo*-Br arrangement of 10,11-dibromo-6,14-di-*t*-butyl-9,17-dimethyl[3.2]MCP in which one aromatic proton lies in a strongly deshielded region of the *endo*-Br atom on the ethylene bridge (δ 7.69).[9a] On the basis of the spectral data, *cis*-**4** is assigned the structure, 1-*endo*-2-*exo*-dihydroxy-5,13-di-*t*-butyl-8,16-dimethyl[2.2]MCP.

Although Mitchell *et al.* reported[12] the first preparation of benzo[2.2]MCP-1,2-dione from oxidation of the corresponding benzo[2.2]MCP-1,2-diol, the physical and chemical properties have not established so far. Thus, there is substantial interest in the oxidation of [2.2]MCP **4** having a 1,2-diol to afford [2.2]MCP-1,2-dione. An attempted oxidation of the *trans*-diol *trans*-**4** to the 1,2-dione **6** with pyridinium chlorochromate carried out in a methylene dichloride solution under the same reaction conditions as previously reported[23] failed. Only the cleavage reaction product, the dialdehyde **2**, was obtained in a quantitative yield. This finding seems to support the strained nature of the diketone **6**. Fortunately, Swern oxidation[17] of *trans*-**4** succeeded in affording the desired [2.2]diketone **6** in only 12% yield along with [2.2]monoketone **5** and ring cleavage reaction product **2** in 58 and 28% yields, respectively. This reaction mixture was treated again under the same Swern oxidation conditions to afford **6** along with the partial oxidation product **5** in the ratio of 80:20. Careful recrystallisation from hexane-CH_2Cl_2, 10:1 afforded *anti*-5,13-di-*t*-butyl-8,16-dimethyl[2.2]MCP-1,2-dione **6** as orange prisms. However, this diketone **6** was found to be quite labile under treatment by silica gel column chromatography and on refluxing in toluene afforded 1,2-bis(5-*t*-butyl-3-carboxy-2-methylphenyl)ethane (**7**) in quantitative yield. Thus, a trapping reaction of diketone **6** with *o*-phenylenediamine was attempted, in which the crude diketone **6** was treated with *o*-phenylenediamine in ethanol at room temperature for 24 h to afford in almost quantitative yield the desired [2.2]MCP **8** having a quinoxaline skeleton (Scheme 2).

The structure of the diketone **6**, was assigned on the basis of elemental analyses and spectral data. Thus, the ^{1}H NMR spectrum of **6** shows an internal methyl resonance as a singlet at δ 0.66 and all four aromatic protons as a singlet at δ 7.42 which are in a strongly deshielding region of oxygen atom of carbonyl group on ethylene bridge. The structure of the *anti*-confomer is also readily assigned from the chemical shift of the methyl protons at δ 0.66. The higher frequency of C=O stretching vibration in the IR spectrum for **6** (1686 cm^{-1}) in comparison with that for the reference compound benzil **9** (1662 cm^{-1}) presumably reflects the deviation of the carbonyl group from the plane of the benzene ring rather than conjugation between the carbonyl group and the benzene ring.



Scheme 2

This finding is similar to those for the strained [2.2]paracyclophan-1-ones[6,24] and [2.2]metacyclophan-1-ones,[23] for which absorptions are toward wavelengths characteristic of unconjugated ketones.

In conclusion, we have demonstrated the preparation of [2.2]MCP-1-ene **3** and [2.2]MCP-1,2-diols **4** by a McMurry cyclisation of 1,2-bis(5-*t*-butyl-3-formyl-2-methylphenyl)-ethane **2**. Also, [2.2]MCP-1,2-diols **4** were converted to the 1,2-dione **6** by Swern oxidation. Further studies on the chemical properties of the 1,2-dione **6** are now in progress.

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