Medium-sized cyclophanes. Part 54.[1] Bromination of 5-*tert*-butyl-8-methoxy[2.2]metaparacyclophane-1,9-diene and dehydrobromination of the bromine adduct

J. Chem. Research (S), 2001, 14–15
J. Chem. Research (M), 2001, 0148–0160

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Bromination of 5-*tert*-butyl-8-methoxy[2.2]metaparacyclophane-1,9-diene **1** with bromine affords the *cis*-adduct to the bridged double bond; when treated with potassium *tert*-butoxide in refluxing THF, the *cis*-adduct *endo,exo*-**2** gives a mixture of [2.2]metaparacyclophan-9-ene-1-one (**4**) and 2-one (**5**) in 59% yield.

Keywords: cyclophanes, bromination

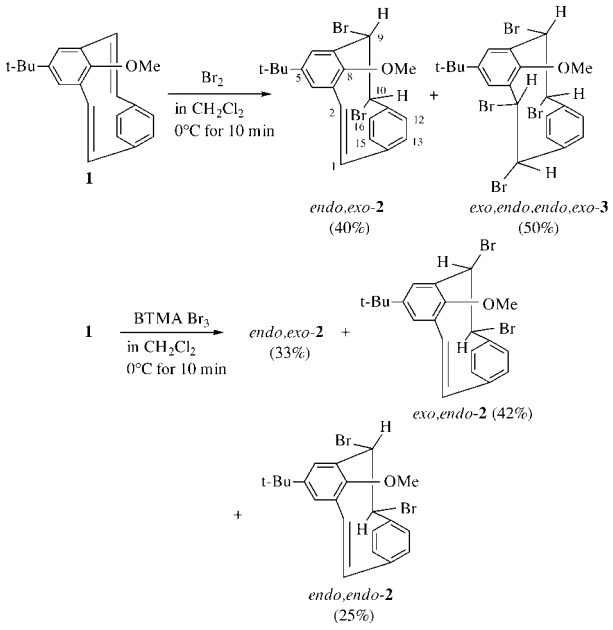
Cram *et al*. have reported that bromination of [2.2]paracyclophan-1-ene with bromine affords the corresponding *cis*-adduct.[2] We have previously reported[3] that the reaction of 5,13-di-*tert*-butyl-8,16-dimethyl[2.2]metacyclophan-1-ene with bromine affords 4,5,9,10-tetrabromo-2,7-di-*tert*-butyl-*trans*-10b,10c-dimethyl-10b,10c-dihydropyrene in good yield, but not the adduct to the bridged double bond. This novel transannular reaction might be attributed to 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. Subsequently, we have reported that di-*tert*-butyl-dimethyl[2.n]metacyclophan-1-enes were treated with an equimolar amount of benzyltrimethylammonium tribromide (BTMA Br_3) in dichloromethane[4] to afford the *cis*-adducts to the bridged double bond in good yield. This result indicated the first success in the introduction of two bromo groups into the methylene groups of dimethyl[n.2]metacyclophanes.

However, bromination of [2.2]MPCP-1,9-diene (MPCP = metaparacyclophane) has not yet been reported in spite of the possibility of the different behaviour for the bromination reagent. Thus there is substantial interest in investigating the bromination of the internally substituted [2.2]MPCP-1,9-dienes, which might afford single mono- and di-brominated products to the bridged double bonds because of the formation of 14π dihydropyrene derivatives being impossible. We report here the addition of bromine to 5-*tert*-butyl-8-methoxy[2.2]-MPCP-1,9-diene **1** and the assignment of the structures of bromine adducts. The attempted dehydrobromination of the bromine adduct **2** with potassium *tert*-butoxide is also described.

Results and discussion

The preparation of 5-*tert*-butyl-8-methoxy[2.2]MPCP-1,9-diene **1** was carried out following the reported procedure[5] starting from 6-*tert*-butyl-9-methoxy-2,11-dithia[3.3]-MPCP.[6,7] The assignment of structure for **1** was readily apparent from its ^{1}H-NMR spectrum. Thus the ^{1}H-NMR spectrum of **1** showed an upfield shift at δ 3.26 for the methoxy protons due to the ring current[8,9] of the opposite *para* benzene ring and a set of doublets (*J* 9.8 Hz) at δ 6.68 and 7.06 for olefinic protons.

Attempted bromination of 5-*tert*-butyl-8-methoxy[2.2]MPCP-1,9-diene **1** with 2 equiv. of bromine carried out in dichloromethane at 0°C for 10 min led to the expected bromine adducts **2** and **3** to the bridged double bond in 40 and 50% yields, respectively. In contrast, compound **1** was treated with an equimolar amount of benzyltrimethylammonium tribromide (BTMA Br_3) in dichloromethane, which was recently found to be a convenient solid brominating reagent,[10] to afford a mixture of isomers of the corresponding mono-adduct **2** in quantitative yield (Scheme 1). Interestingly, depending on the brominating reagents different selectivity has been observed. The structures of the products obtained in the present work were determined from their elemental analyses and spectral data. The ^{1}H NMR spectrum of mono-adduct *endo,exo*-**2** in $CDCl_3$ shows a pair of doublets (*J* 5.5 Hz) at δ 5.43 and 5.63 for methine protons and a doublet (*J* 2.0 Hz) at δ 7.38 ppm for one aromatic proton of the *meta*-benzene ring (H_6) which is in a strongly deshielding region of the 9-*endo*-Br atom on an ethylene bridge. A similar finding was observed for one aromatic proton of the inside *para*-benzene ring (H_{16}) which is in a strongly deshielding region of the 10-*exo*-Br atom on the ethylene bridge at δ 6.63 ppm as a doublet (*J* 8.6 Hz). These data strongly support the two Br atoms being in the 9-*endo*- and 10-*exo*-arrangement and, therefore, *endo,exo*-**2** is found to be the *cis*-adduct to the bridged double bond. This assignment is also applied to the bisadduct **3**. Thus, the ^{1}H NMR spectrum of **3** in $CDCl_3$ shows a pair of doublets (*J* 5.8 Hz) at δ 5.39 and 5.70 for methine protons and three singlets at δ 6.75 ($H^{15,16}$), 7.05 ($H^{12,13}$) and 7.46 ($H^{4,6}$), which indicate a symmetrical structure for **3**. It was also observed that both aromatic protons



Scheme 1

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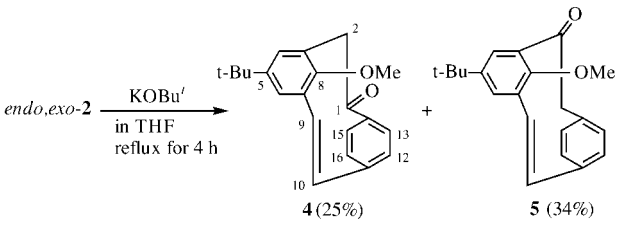
of the *meta*-benzene ring ($H_{4,6}$) strongly deshielded at δ 7.46 by two *endo*-Br atoms on ethylene bridges. On the basis of the spectral data, **3** is assigned the structure 1-*exo*,2-*endo*,9-*endo*,10-*exo*-tetrabromo-5-*tert*-butyl-8-methoxy[2.2]MPCP (*exo,endo,endo,exo*-**3**).

In contrast, the ^{1}H NMR spectrum of *endo,endo*-**2** in $CDCl_3$ shows a pair of doublets (*J* 9.8 Hz) at δ 4.74 and 5.21 for methine protons, for which the coupling constant is larger than that of *cis*-adduct *endo,exo*-**2** (*J* 5.5 Hz), and a strongly deshielded aromatic proton of the outside *para*-benzene ring (H_{12}) at δ 7.64 ppm attributable to the 10-*endo*-Br atom on ethylene bridge. These data strongly support the two Br atoms being in the 9-*endo*- and 10-*endo*-arrangement and, therefore, *endo,endo*-**2** is found to be the *trans*-adduct to the bridged double bond compared to *endo,exo*-**2**. Furthermore, for *endo,endo*-**2** the internal methoxy protons were observed at a slightly lower field (δ 3.35 ppm) than that of *endo,exo*-**2** (δ 3.29) due to the 10-*endo*-Br atom on ethylene bridge. Similarly, *exo,endo*-**2** is assigned the 9-*exo*- and 10-*endo*-arrangement attributable to *cis*-addition to the double bond.

The fact that *cis*-adducts *endo,exo*-**2** and **3** are exclusively obtained in the case of bromination with bromine indicates the presence of the four membered transition state[11] rather than the nonclassic bromonium ion intermediate[12] in the process of bromination. The absence of the nonclassic bromonium ion intermediate might be attributed to the strain of this intermediate. However, when the reactivity of the bromination reagent such as BTMA Br_3 is increased, *cis*-addition of [2.2]MPCP-1,9-diene with BTMA Br_3 might compete with *trans*-addition.

Treatment of *endo,exo*-**2** with potassium *tert*-butoxide in THF refluxing for 4h gave two isomeric ketones, 5-*tert*-butyl-8-methoxy[2.2]MPCP-9-ene-1-one (**4**) and 2-one (**5**) in 25 and 34% yields, respectively. No dehydrobrominated products such as 1-bromo-5-*tert*-butyl-8-methoxy[2.2]MPCP-1,9-diene or [2.2]MPCP-1-yne have been observed under the conditions used.



Scheme 2

The structures of the [2.2]MPCP ketones **4** and **5** were assigned on the basis of elemental analyses and spectral data. The low frequency of the carbonyl stretching vibrations in the IR spectrum (1701 cm^{-1} for **4** and 1708 cm^{-1} for **5**) in comparison to that of the reference compound deoxybenzoin (1685 cm^{-1}), presumably and in analogy to the corresponding paracyclophane analogue,[12] reflects expanded OCC bond angles rather than conjugation. The ^{1}H NMR spectrum of **4** in $CDCl_3$ shows a pair of doublets at δ 3.62, 3.81 (*J* 15.6 Hz) for bridged methylene protons and at δ 6.67, 7.14 (*J* 9.8 Hz) for olefinic protons. In contrast, the ^{1}H NMR spectrum of **5** in $CDCl_3$ shows an almost similar spectrum except for a pair of doublets at δ 3.22, 3.96 (*J* 15.6 Hz) for bridged methylene protons. Although these signals in the ^{1}H NMR spectrum both correspond to the isomeric ketones **4** and **5**, the chemical shifts for the methylene protons of **4** at δ 3.62, 3.81 (*J* 15.6 Hz) correspond to those for [2.2]metacyclophan-1-one [δ 3.72, 3.92 (*J* 15.6 Hz)],[14] but in the case of **5** the methylene protons are observed at δ 3.22 and 3.96 as a pair of doublets, in which the former *exo*-proton might be shielded by the ring current effect of the opposing meta-benzene ring and the latter *endo*-proton might be deshielded due to oxygen atom of the carbonyl group on ethylene bridge.[13]

Although the detailed mechanism of formation of **4** and **5** is not clear, one might assume the reaction pathway *via* nucleophilic substitution of **2** with *tert*-butoxy anion followed by HBr elimination rather than the formation of a [2.2]MPCP-1-yne intermediate followed by the addition of *tert*-butanol to the triple bond giving different results from those for the corresponding [2.2]paracyclophanes which afford the [2.2]paracyclophan-1-yne intermediate.[15]

In conclusion, we have found that the addition of bromine to 5-*tert*-butyl-8-methoxy[2.2]MPCP-1,9-diene **1** with bromine affords exclusively the *cis*-adduct **2** to the bridging double bond. However, this selectivity has not been observed in the case of BTMA Br_3 to afford a mixture of *cis*- and *trans*-adducts. We have isolated for the first time two isomeric ketones, 5-*tert*-butyl-8-methoxy[2.2]MPCP-9-ene-1-one (**4**) and 2-one (**5**) in the metaparacyclophane systems. Further studies on the chemical properties of [2.2]MPCPs **2** and **3** are now in progress.

Received 14 July 2000; accepted 5 November 2000
Paper 00/437

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