Evaluation of the transannular interaction of 5-substituted [2.2]metacyclophanes carrying a diazonio group on their outer position

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A diazonio group has been introduced into the outer (13-)position of 5-substituted [2.2]metacyclophanes (MCPs) (3). The absorption maxima of the substituted [2.2]MCP diazonium salts are bathochromically shifted from those of unsubstituted reference compounds. Stability constants (log K_s) of the complexation between the [2.2]MCP diazonium salts have been measured in order to estimate their cationic character. When log K_s for [2.2]MCP diazonium salts which carry the functional groups are plotted against Brown–Okamoto's substituent constant (σ_p^+) for them, a linear relationship is obtained. This result establishes that the electronic effect of the functional group is transmittable between two aromatic rings in [2.2]MCPs through a transannular interaction.

Cyclophane compounds provide intriguing models for investigation of intramolecular and transannular electronic effects of a particular orientation of two π systems in forced proximity. We have been very interested in a transannular interaction between two aromatic rings in [2.2]metacyclophane (MCP) systems because this interaction must be responsible for the unusual reactivity of [2.2]MCPs.[1]
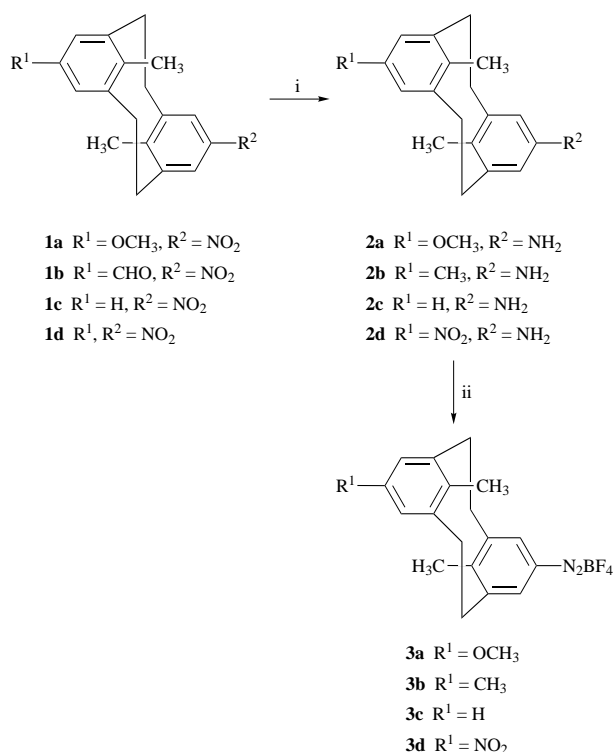
Recently, we prepared various [2.2]metacyclophanes in order to evaluate a transannular interaction between their two aromatic π systems.[2] From these investigations the existence of an interaction in a neutral [2.2]MCP molecule has become apparent. However, evaluation of a transannular interaction between the two aromatic rings of an MCP cation or anion was very limited, because their compounds are unstable. We previously reported simple and efficient methods for preparation of [2.2]MCP diazonium salts.[3] Thus, it occurred to us to synthesize the MCPs which have a diazonio group on one aromatic ring and the various substituents on the opposite ring in order to make clear the transannular interaction of MCP diazonium cations from their physical data.

Results and discussion

Preparation of MCP diazonium salts

Amino[2.2]MCPs (2) were prepared from the corresponding nitro[2.2]MCPs (1) under different reductive conditions, described below (Scheme 1).

Nitro[2.2]MCP (R¹ = H) (1c) and methoxynitro[2.2]MCP (R¹ = OCH₃) (1a) were reduced with hydrogen gas in the presence of 10% Pd/C according to a previously reported procedure[4] to give amino[2.2]MCPs (2a and c, respectively) in quantitative yield. Interestingly, methylnitro[2.2]MCP (R¹ = CH₃) (2b) can be prepared from nitro[2.2]MCP (R¹ = CHO) (1b) under similar conditions (99% yield). Reduction of benzaldehyde under these conditions gives only benzylalcohol, although the reason for this unusual reactivity is not clear at present. On the other hand, aminonitro[2.2]MCP (R¹ = NO₂) (2b) was obtained by partial reduction[5] with methanolic sodium hydrogensulfide (45% yield).[6] Diazonium salts (3a–d) were converted from the corresponding amino[2.2]MCPs (2a–d) in good yields using isopentyl nitrite in EtOH (Scheme 1). The formation of these salts was confirmed by ¹H NMR and IR spectroscopy and elemental analyses.

1a R¹ = OCH₃, R² = NO₂
1b R¹ = CHO, R² = NO₂
1c R¹ = H, R² = NO₂
1d R¹, R² = NO₂

2a R¹ = OCH₃, R² = NH₂
2b R¹ = CH₃, R² = NH₂
2c R¹ = H, R² = NH₂
2d R¹ = NO₂, R² = NH₂

3a R¹ = OCH₃
3b R¹ = CH₃
3c R¹ = H
3d R¹ = NO₂

Scheme 1   *Reagents and conditions*: i, for **a**, **b** and **c**; 10% Pd/C, H₂, C₆H₆, room temp., 2 h; for **d**; NaSH, MeOH–toluene, reflux, 12 h; ii, for **a**, **b** and **c**; conc. HCl, C₅H₁₁ONO, conc. HBF₄, 0 °C, 10 min; for **d**; conc. HBr, C₅H₁₁ONO, conc. HBF₄, 0 °C, 10 min

Properties of [2.2]MCP diazonium salts

We measured several physical characteristics of the salts (3a–d) which are summarized in Table 1.

¹H NMR spectra. Plots of the chemical shifts of internal methyl protons *versus* Brown–Okamoto's constant (σ_p^+)[7] for the substituent (R¹) are shown in Fig. 1. Use of Brown–Okamoto's constant (σ_p^+) takes into account the ability of the diazonium group of the MCP salt to withdraw electrons from the ring by resonance effects, and these resonance structures are stabilized by the transannular electron-releasing effect of the opposite ring carrying the substituent (R¹). Internal methyl

Table 1 Selected physical data for [2.2]MCP diazonium salts

| Diazonium salt	R^1	$\sigma^+(R^1)$	δ^a	ν/cm^{-1} (N_2^+)	λ_{max}/nm	$\log(K_s/mol\ dm^{-3})$
3a	OCH_3	-0.778	0.57, 0.90	2252	447	3.50
3b	CH_3	-0.311	0.61, 0.81	2258	409	3.73
3c	H	0.00	0.70, 0.82	2260	391	4.12
3d	NO_2	0.790	0.77, 0.85	2275	356	4.58

^{a} Chemical shifts of internal methyl protons.
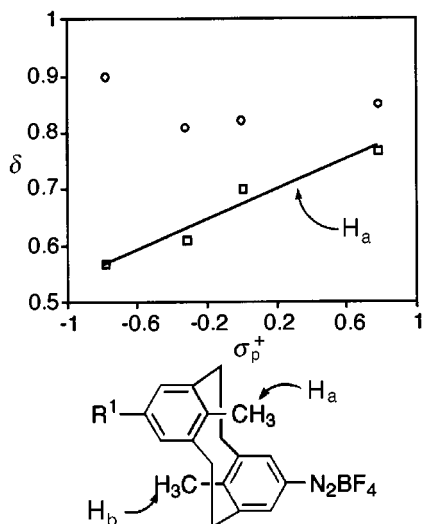
Fig. 1 Plots of chemical shifts of internal methyl protons *vs.* Brown–Okamoto's constants (σ_p^+) for substituent R^1
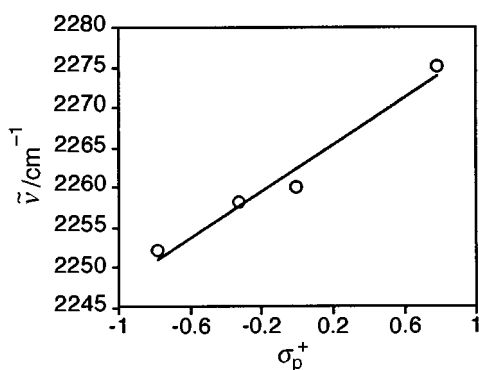
Fig. 2 Plots of wavenumbers of N_2^+ groups *vs.* Brown–Okamoto's constants (σ_p^+) for substituent R^1

protons of these salts resonate in two different regions, one of them appears in the upfield region which exhibits a good correlation with σ_p^+ (*r* value = 0.98) and the other appears in the downfield region where the correlation with σ_p^+ values is poor. This tendency explains why methyl protons appearing in the upfield region (H_a) are only affected by the substituent effect of the outer (13-)substituent, and why methyl protons appearing in downfield region (H_b) are affected by not only the substituent effect of the outer (13-)substituent but also by the ring current effect of the aromatic ring carrying various substituents on their outer (13-)position. These protons are assigned in Fig. 1.

IR spectra. A good correlation was obtained between the absorption wavenumbers ($\tilde{\nu}$) of the diazonio groups (N_2^+) and σ_p^+ (Fig. 2). The absorption wavenumbers for the N_2 triple bond of the salt **3d** was observed at 2275 cm^{-1} which is shifted about 15 cm^{-1} higher than that of the salt **3c**. This can be explained by the fact that when the substituent (R^1) is an electron withdrawing group, the resonance structure may be unstabilized. Its N_2 triple bond character is stronger than that of the salt **3c**. However, the absorption wavenumbers of the N_2 triple bond of the salts **3a** and **3b** were observed at 2252 and 2258
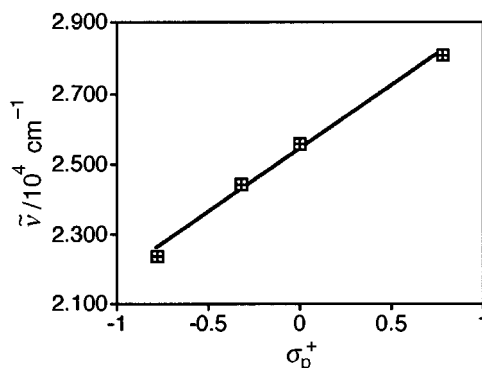
Fig. 3 Plots of absorption wavenumbers *vs.* Brown–Okamoto's constants (σ_p^+) for substituent R^1

cm^{-1}, respectively. The N_2 triple bond character of MCP salts carrying an electron releasing group (**3a**, **3b**) is weaker than that of the salt **3c**, because the resonance structures are stabilized in the opposite way; when the substituent (R^1) is an electron releasing group, the resonance structure may be stabilized. Thus, IR absorption wavenumbers of diazonio groups (N_2^+) of MCP salts show interesting behavior.

Absorption spectra. The data for the absorption spectra of the salts **3a–d** are summarized in Table 1. Energy gaps between the HOMO and the LUMO of MCP π systems can be estimated by their absorption maximum wavenumbers. When the outer substituent (R^1) of the salt has electron-releasing character such as **3a** or **3b**, these absorption maxima appeared in the higher energy region (differences between **3a** and **3b** and the salt **3c** are *ca.* 3.2×10^3 and 1.1×10^3 cm^{-1}, respectively). On the contrary, when the salt carried an electron-withdrawing group, such as **3d**, the absorption maximum was observed in the lower energy region (the difference between **3d** and the salt **3c** is *ca.* 2.5×10^3 cm^{-1}). When the differences in absorption maxima of these salts (**3a–d**) were plotted against σ_p^+, a good correlation was obtained (*r* = 0.99) (Fig. 3). This implies that the energy gap between the HOMO and the LUMO of MCP π systems is affected by not only the substituent effect but also the cationic diazonio substituent. It is part of the strong evidence in support of the existence of transannular interaction between the two aromatic rings on MCP.

pK_s measurement. Stability constants ($\log K_s$) for the complexation between 18-crown-6 ether and MCP diazonium salts were determined according to a previously published method[3] to evaluate their cationic character.

Log K_s for MCP salts in 1,2-dichloromethane at 20 °C are in the range 3.50–4.68. However, Hashida and Matsui reported that log K_s of the *p*-toluenediazonium salt **4** is 5.10.[8] It is clear that stability constants for MCP salts are smaller than that of **4**. These data suggest that the electrophilicities of MCP diazonium cations are much reduced by the electron-releasing effect of the opposite aromatic ring. In other words, the positive charge of the MCP diazonium cation is more effectively dispersed on the aromatic ring than that of the *p*-toluenediazonium cation (Fig. 4). The Brown–Okamoto's plots for the substituted MCP diazonium salts (**3a–d**) show a good correlation with a least-squares treatment, giving the equation log $K_s = 0.71\sigma_p^+ + 4.03$ with a correlation coefficient (*r*) of 0.990 (Fig. 5). Note that from this slope the cationic character

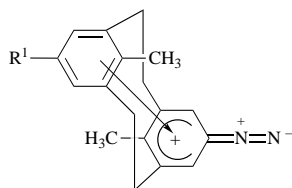**Fig. 4** Effective positive charge dispersion in the MCP diazonium cation

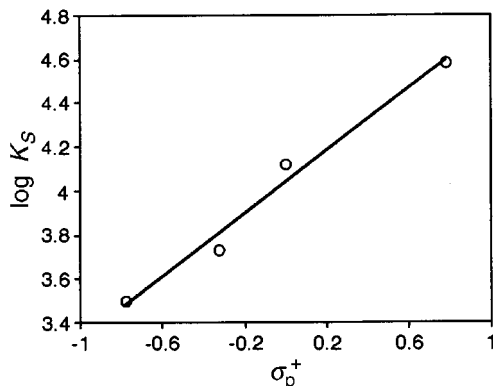**Fig. 5** Plots of stability constants (log K_s) vs. Brown–Okamoto's constants (σ_p^+) for substituent R^1

of these salts is affected by both the inductive effect and the resonance effect of the outer substituent, since both effects are considered in the Brown–Okamato's constant (σ_p^+).

It is apparent that the electrophilicities of salts are affected by the electronic effect of the outer substituent on the aromatic ring through the transannular interaction.

Conclusions

The results obtained in this study reveal that a transannular interaction exists between the neutral aromatic ring and the aryl diazonium cation in the [2.2]MCP structure. Straight lines are obtained for plots of the Brown–Okamoto's constant (σ_p^+) of the outer (13-)substituent against physical data for MCP diazonium salts, for example, the absorption wavenumber ($1/\lambda_{max}$), the wavenumber of the triple bond of the diazonio group (v/cm^{-1}) and the stability constant for the complexation with 18-crown-6 ether (log K_s). It can also be concluded that an outer (13-)substituent on the opposite aromatic ring in the [2.2]MCP diazonium salt can affect the electrophilicity of the diazonio group. This result indicates that electronic effects of the outer (13−)substituents are transmitted to the 5-position diazonio group *via* a transannular interaction. Furthermore, it should be noted that the electronic interaction of these salts may be of the charge-transfer type, placing a positive charge on one MCP ring bearing the diazonio substituent. This could be explained by Brown–Okamoto's correlation (Fig. 3) and the large red shift of the maximum wavelength of MCP salts.

Experimental

All melting points were recorded on a Yanako hot-stage microscope apparatus and are uncorrected. ^{1}H NMR spectra were recorded on a Nippon Densi α-500 spectrometer in CDCl$_3$ or CD$_3$CN with Me$_4$Si as an internal reference. IR spectra were recorded on a Hitachi 260-30 spectrometer and a Nippon Bunko JASCO IR-700 spectrometer. Mass spectra were obtained on a Nippon Densi JEOL-DX-300 spectrometer at 75 eV using a direct inlet system. Column chromatography was carried out on silica gel (Wako gel, C-300). The amount of silica gel used was 5–50 g.

Reduction of nitro compounds 1a, 1b and 1c with H$_2$ using Pd/C as a catalyst

100 mg of 10% Pd/C was added to a solution of the nitro compound (0.15 mmol) in benzene (50 cm^3). After hydrogen gas had been bubbled into the mixture with stirring for 2 h at room temp., the Pd/C was filtered off. The filtrate was evaporated under reduced pressure to leave the residue, which was recrystallized from benzene to give product **2a**, **2b** or **2c**.

5-Amino-8,16-dimethyl-13-methoxy[2.2]metacyclophane 2a. Colourless prisms (42 mg, quant.); mp 166–169 °C; v_{max}(KBr)/cm^{-1} 3420, 3325 (NH$_2$); δ_H(500 MHz; CDCl$_3$) 0.66 (3H, s, internal CH$_3$), 0.79 (3H, s, internal CH$_3$), 2.70–2.95 (8H, m, bridged methylene), 2.90–3.50 (2H, br s, NH$_2$), 3.49 (3H, s, OCH$_3$), 6.52 (2H, s, aromatic), 6.69 (2H, s, aromatic); m/z 281 (M$^+$) (Found: C, 81.1; H, 8.3; N, 5.1. C$_{19}$H$_{23}$NO requires C, 81.1; H, 8.2; N, 5.0%).

5-Amino-8,13,16-trimethyl[2.2]metacyclophane 2b. Colourless prisms (40 mg, quant.); mp 224–228 °C; v_{max}(KBr)/cm^{-1} 3550, 3350 (NH$_2$); δ_H(500 MHz; CDCl$_3$) 0.55 (3H, s, internal CH$_3$), 0.81 (3H, s, internal CH$_3$), 2.21 (3H, s, external CH$_3$), 2.60–3.00 (8H, m, bridged methylene), 3.20–3.80 (2H, br s, NH$_2$), 6.52 (2H, s, aromatic), 6.90 (2H, s, aromatic); m/z 265 (M$^+$) (Found: C, 86.0; H, 8.7; N, 5.3. C$_{19}$H$_{23}$N requires C, 86.0; H, 8.6; N, 5.0%).

5-Amino-8,16-dimethyl[2.2]metacyclophane 2c. Colourless prisms (38 mg, quant.); mp 215–218 °C (from hexane) (lit.,[4] 215–218 °C).

5-Amino-8,16-dimethyl-13-nitro[2.2]metacyclophane 2d. A solution of dinitro compound **1d** (50 mg, 0.15 mmol) and sodium hydrogensulfide (100 mg) in methanol (30 cm^3) and toluene (30 cm^3) was refluxed for 12 h under a stream of argon. The reaction mixture was poured into water and the organic layer was dried (MgSO$_4$) and evaporated under reduced pressure. The residue was chromatographed on a silica gel column with toluene as an eluent to give the title compound **2d**, which was recrystallized from benzene (20 mg, 45%), mp 247–250 °C; v_{max}(KBr)/cm^{-1} 3420, 3328 (NH$_2$); δ_H(500 MHz; CDCl$_3$) 0.49 (3H, s, internal CH$_3$), 0.90 (3H, s, internal CH$_3$), 2.60–3.05 (8H, m, bridged methylene), 3.20–3.80 (2H, br s, NH$_2$), 6.53 (2H, s, aromatic), 8.00 (2H, s, aromatic); m/z 296 (M$^+$) (Found: C, 72.9; H, 6.9; N, 9.2. C$_{18}$H$_{20}$N$_2$O$_2$ requires C, 73.0; H, 6.8; N, 9.5%).

Diazotisation of 2a–c and 2d

To a stirred suspension of amino compound (0.15 mmol) in ethanol (5 cm^3) was added 0.5 cm^3 of 35% hydrochloric acid (in the case of **2a**–**c**) or 47% hydrobromic acid (in the case of **2d**) at room temp., and the mixture was stirred for 10 min. After the addition of isopentyl nitrite (0.1 cm^3, 1 mmol) at 0 °C, the reaction mixture was stirred for 10 min and 42% tetrafluoroboric acid (1 cm^3) was added. After stirring for 10 min, 50 cm^3 of absolute diethyl ether was added to the reaction mixture. The resulting precipitates were collected by filtration and washed with diethyl ether to give diazonium salts **3a**, **3b**, **3c** and **3d**, respectively.

8,16-Dimethyl-13-methoxy[2.2]metacyclophane-5-diazonium tetrafluoroborate 3a. Pale yellow powder (51 mg, 90%); mp 100–110 °C; v_{max}(KBr)/cm^{-1} 2282 (N$_2^+$); δ_H(500 MHz; [^{2}H$_3$]-acetonitrile) 0.57 (3H, s, internal CH$_3$), 0.90 (3H, s, internal CH$_3$), 3.76 (3H, s, OCH$_3$), 2.60–3.20 (8H, m, bridged methylene), 6.85 (2H, s, aromatic), 8.16 (2H, s, aromatic); (Found: C, 60.0; H, 5.3; N, 7.4. C$_{19}$H$_{21}$N$_2$OBF$_4$ requires C, 60.0; H. 5.6; N, 7.4%).

8,13,16-Trimethyl[2.2]metacyclophane-5-diazonium tetrafluoroborate 3b. Pale yellow powder (50 mg, 91%); mp 100–102 °C (decomp.); v_{max}(KBr)/cm^{-1} 2258 (N$_2^+$); δ_H(500 MHz; [^{2}H$_3$]-acetonitrile) 0.61 (3H, s, internal CH$_3$), 0.81 (3H, s, internal CH$_3$), 2.20 (3H, s, CH$_3$), 2.60–3.15 (8H, m, bridged methylene), 7.06 (2H, s, aromatic), 8.16 (2H, s, aromatic); (Found: C, 62.6; H, 5.8; N, 7.7. C$_{19}$H$_{21}$N$_2$BF$_4$ requires C, 62.7; H, 5.8; N, 7.7%).

8,16-Dimethyl[2.2]metacyclophane-5-diazonium tetrafluoroborate 3c. Pale yellow powder (47 mg, 90%); mp 100–102 °C (decomp.) (lit.,[3] >100 °C (decomp.).

8,16-Dimethyl-13-nitro[2.2]metacyclophane-5-diazonium tetrafluoroborate 3d. Pale green powder (36 mg, 60%); mp 98–103 °C (decomp.); ν_{max}(KBr)/cm^{-1} 2275 (N$_2^+$); δ_H(500 MHz; [^{2}H$_3$]acetonitrile) 0.77 (3H, s, internal CH$_3$), 0.85 (3H, s, internal CH$_3$), 2.80–3.17 (8H, m, bridged methylene), 8.13 (2H, s, aromatic), 8.26 (2H, s, aromatic); (Found: C, 52.3; H, 4.8; N, 10.3. C$_{18}$H$_{18}$N$_3$O$_2$BF$_4$·H$_2$O requires C, 52.3; H, 4.9; N, 10.2%).

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