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Diazo Coupling of [2.2]Metacyclophanes

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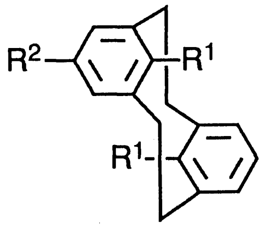
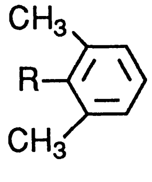
[2.2]Metacyclophanes(=MCPs) which carry hydroxy, methoxy or methyl group at the inner position exhibited a stronger reactivity toward diazonium salts than the corresponding phenol, anisole or toluene, respectively. Such a reactivity was also estimated in connection with the UV spectra of the azo benzene component.

Although [2.2]MCPs and related compounds have been worthy of interest among organic chemist,1) there are few investigation on their chemical natures. Since we found out a useful and practical preparation route of MCPs,2) we have been reporting their unique reactivity toward electrophilic reagents. For instance, in nitration of 8,16-dimethyl[2.2]MCP3) the one aromatic ring was only nitrated to afford 5-nitro-8,16-dimethyl[2.2]MCP under any conditions, which may be attributed to reduction of π-electron density of one aromatic ring by the nitro group on the other aromatic ring. And it is reported2a-b,4) that bromination of MCPs gave different types of products depending on the reaction conditions or the structures of MCPs. However, a precise link between an electronic nature of [2.2]MCPs and their reactivities is still obscure and a systematic study on characteristics of MCPs in electrophilic substitution reactions has not been done. In the present

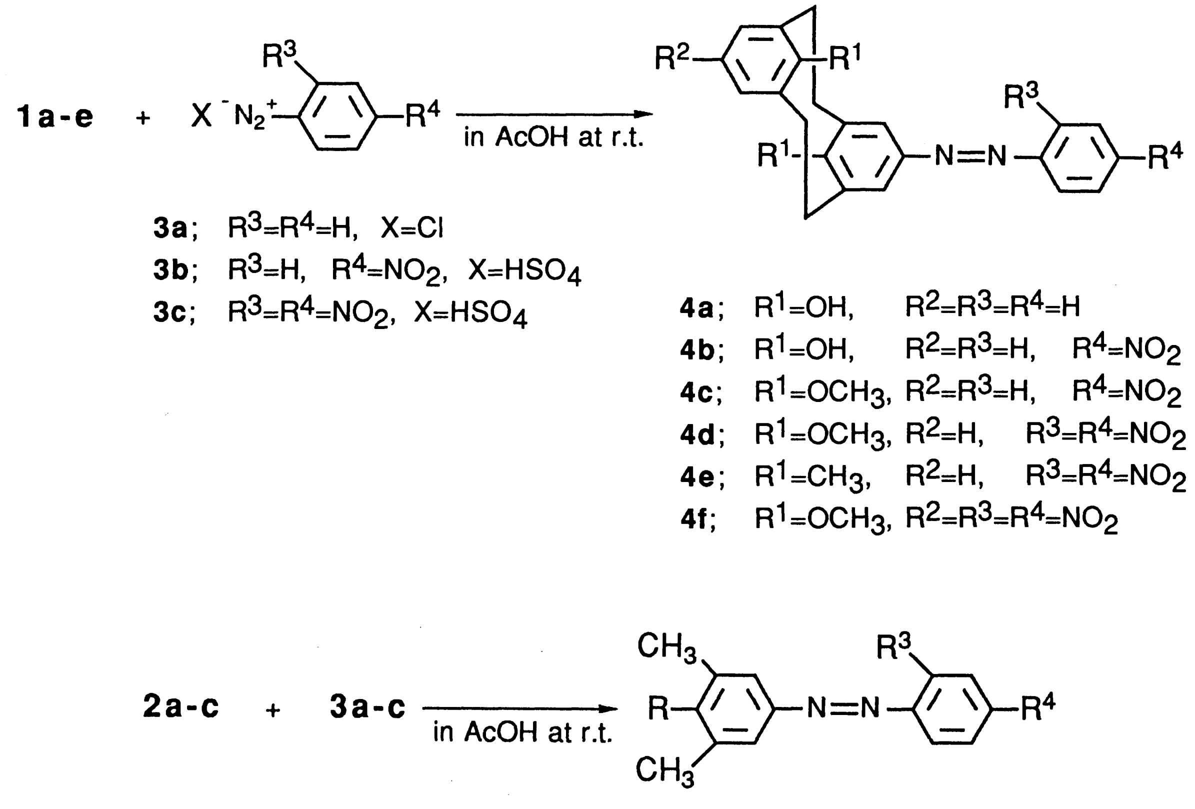


1a; R^1=OH, R^2=H
1b; $R^1=OCH_3$, R^2=H
1c; $R^1=CH_3$, R^2=H
1d; $R^1=OCH_3$, $R^2=NO_2$
1e; $R^1=CH_3$, $R^2=NO_2$



2a; R=OH
2b; $R=OCH_3$
2c; $R=CH_3$

paper, thus, we choose diazonium salts as electrophilic reagents because they are not so strong electrophiles and are supposedly influenced by a slight difference of MCP's reactivity for electrophilic substitution. Furthermore absorption spectra of azo benzene unit possibly give an information concerning a MCP's reactivity.



3a; R^3=R^4=H, X=Cl
3b; R^3=H, R^4=NO_2, X=HSO_4
3c; R^3=R^4=NO_2, X=HSO_4

4a; R^1=OH, R^2=R^3=R^4=H
4b; R^1=OH, R^2=R^3=H, R^4=NO_2
4c; R^1=OCH_3, R^2=R^3=H, R^4=NO_2
4d; R^1=OCH_3, R^2=H, R^3=R^4=NO_2
4e; R^1=CH_3, R^2=H, R^3=R^4=NO_2
4f; R^1=OCH_3, R^2=R^3=R^4=NO_2

5a; R=OH, R^3=H, R^4=NO_2
5b; R=OH, R^3=R^4=NO_2
5c; R=OCH3, R^3=H, R^4=NO_2
5d; R=OCH3, R^3=R^4=NO_2

Scheme 1.

MCPs **1a-c** were prepared from anisole or tert-butyl toluene in 6-8 steps according to the reported method.[2a,c] **1d** and **1e** were obtained by nitration of **1b** with $Cu(NO_3)_2$ and **1c** with fuming HNO_3, respectively. The reactions of the MCPs **1a-c** and the aromatic compounds **2a-c** regarded as referential substrates of the corresponding cyclophanes with diazonium salts **3a-c** were carried out in AcOH at room temperature(Scheme 1 and Table 1). As expected the reaction of hydroxy MCP **1a** with **3a-b** proceeded smoothly within a few minutes, however, it was found that one aromatic ring only underwent the coupling to give **4a-b**. The reaction of **1a** with most reactive **3c** afforded a complex mixture which is indicated to contain a small amount of a bis-azocyclophane, however, separation and purification of products are unsuccessful at the present time.

Table 1. Yields of diazo coupling(%)

Diazonium salt	Substrate							
	1a	**1b**	**1c**	**1d**	**1e**	**2a**	**2b**	**2c**
3a	**4a**(30)	-a)	-a)			-a)	-a)	-a)
3b	**4b**(90)	**4c**(95)	-a)	-a)	-a)	**5a**(85)	-a)	-a)
3c	-b)	**4d**(89)	**4e**(15)	**4f**(8)	-a)	**5b**(92)	**5d**c)	-a)

a) No reaction. b) Complex mixture. c) A small amount of **5d** was obtained.

Although methoxy MCP **1b** reacted with nitro-substituted diazonium salts **3b-c** to give **4c-d** in good yields, respectively, it did not afford any azo compounds with **3a**. On the other hand **1c** only reacted with **3c** among diazonium salts used here. In those cases bis-azocyclophanes were not formed neither. Under the similar reaction conditions **2a** and **2b** coupled with **3b-c** and **3c**, respectively, however, no reaction was observed between **2c** and any diazonium salts even in a longer reaction time(2 h). From these results it was recognized that the cyclophanes **1a**, **1b**, and **1c** obviously possess a stronger reactivity toward the diazonium salts than the corresponding **2a**, **2b**, and **2c**, respectively. However such an enhancement is not so large because **1b** and **1c** cannot react with **3a** considered as a weaker electrophile. Furthermore **1c** only reacts with the strong electrophilic diazonium salt **3c** in low yield. In general the aromatic rings undergoing an attack by the diazonium salts should contain a strong electron-releasing group or diazonium salts should contain an electron-withdrawing group for electrophilic attack to occur. From those points of view such an enhancement in azo coupling of cyclophane compounds might be explained in terms of the increase of π-electron density of the aromatic ring to be attacked. However, it is very hard for one more diazonium salt to attack another aromatic ring of the cyclophanes. These results imply the diazo group should intramoleculary reduce the π-electron density of the another aromatic ring in the cyclophanes since the diazo group has the character of an electron attraction. The existence of such a π-electron interaction between two aromatic rings is also supported by the diazo coupling of nitro MCP **1d.** The result is also shown in Table 1. As described here **1b** reacts with **3b** and **3c** to afford **4c** and **4d** in good yields, respectively. On the contrary **1d** was completely recovered in the reaction with **3b**. And the yield of the reaction between **1d** and the most reactive diazonium salt **3c** is only 8%. In this case it seems that a reduction of π-electron density by the nitro group on the another aromatic ring causes such a low reactivity of the cyclophanes. As expected the nitro MCP **1e** did not react with the most reactive **3c**. These facts strongly suggest there exists reduction or increment of π-electron density via through-space interaction between two aromatic rings of [2.2]metacyclophane skeleton. It is expected that such a deviation of π-electron density reflects the absorption spectra of azo benzene component. Thus UV spectra of the products were measured in benzene. The spectral data are summarized in Table 2. Although **5a** shows an absorption peak at 390 nm, it is shifted to 440 nm in the corresponding MCP **4b**. Such a red shift($\Delta\lambda$=33 nm) was also seen in the spectra of **4c** and **5c** which was prepared by methylation of **5a**. Furthermore the 42 nm red-shift was observed in the spectra of **4d** and **5d**. It is probable that this shift is deduced to the effect of cyclophane skeleton working as an electron-releasing group.[5] Introduction of an electron-withdrawing group like a nitro group into MCPs is responsible for a blue shift as indicated by the 23 nm shift of λmax in the spectra for **4d** and **4f**. In this case the nitro group seems to diminish a whole electron-donating nature of [2.2]MCP. Those results highly reveal a through-space interaction in two aromatic rings. A few significant characteristics for an electronic nature of [2.2]MCPs are summarized as follows. [2.2]MCPs exhibit a stronger reactivity in the diazo coupling, nevertheless, once they couple with one diazonium salt, they never undergo the attack of another diazonium salt. The UV spectra of the azobenzene portion are affected by the chemical nature of another aromatic ring which is remote from it by the ethylene unit. All results obtained here can be explained by a through-space interaction between two aromatic rings of [2.2]MCPs. Studies on diazo coupling of [2.n]MCPs are in progress in our laboratories.

Table 2. λmax of azo compounds[a)]

Azo compound[b)]	λmax/nm
4a	372
4b	440
4c	394
4d	418
4e	430
4f	395
5a	390
5b	445
5c	361
5d	376

a) In benzene at 27 °C. b) ca. 3×10^{-5} M.

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