A FACILE SYNTHESIS OF [m.m]METACYCLOPHADIONES

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Abstract: The [m.m]metacyclophadiones have been successfully synthesized from ω -(m-bromo-phenyl)alkan-2-one (**2a-f**) by the photoinduced S_{RN}1 reaction. The anti structure has been suggested for all the [m.m]phanes whose m number are less than seven.

The conformation and dynamic behavior of mobile [m.n]phanes has been of theoretical interest for more than two decades¹). An [m.n]phane with keto group in its bridging chain is one of the current synthetic targets because the keto group can be easily converted to $-CD_2$ -group which can simplify the coupling pattern of the complicated ¹H-spin system of the carbon chain in the ¹H NMR spectrum of the parent hydrocarbon, and the resulting simple spin system can clarify the dynamic process of the mobile phane.

The overall yields in the wide variety of synthetic method so far developed²⁻⁶) for ketocyclophanes were generally not satisfactory because they involved the multi-step reaction sequences. We now report a facile one-step preparation of [m.m]metacyclophadiones (m=3-8) by the photoinduced S_{RN}^{1} reaction⁷) of ω -(m-bromophenyl)-3.3-dimethylalkan-2-one (**2a**-f) in the presence of KO^tBu in liquid ammonia.



la-f (n=0-5)

2a-f (n=0-5) **3a-e** (n=1-5)

The starting methylketones (2) were easily prepared by conventional methods. The methylketone of the shortest chain (2a) was prepared from m-bromobenzylbromide (3a) by two steps (i; MeI,KO^tBu, ii;MeLi,H⁺). The longer chain methylketones (2b-f) were synthesized from corresponding dibromide (3a-e) by treatment with isobutyronitryl in the presence of LDA followed by methylation with methyllithium.

These ketones were then subjected to the photoinduced S_{RN} 1 reaction. A mixture of ketone (2) and sixfold excess of K0^tBu in liquid ammonia was irradiated at -33°C for 15-60 minutes. The crude products were purified by silica gel column chromatography to give tetramethy1[m.m]-metacyclophadione (1) in 21-33% yields (Table 1).

The double S_{RN} 1 reaction, namely an intermolecular reaction followed by intramolecular cyclization, could give the [m.m]phanes successfully, however, the initial intramolecular

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cyclization which gives a single looped [m]metacyclophane could not be observed even in the reaction of the longest chain case (2f).

In the ¹H NMR spectra of **la.** the signal due to the inner arvl hydrogens (Hi) appeared at high field when compared to the corresponding signal of m-xylene ($\Delta \delta =$ -1.01 ppm). Although to a lesser extent. similar up-field shift was observed both in 1b and 1c ($\Delta\delta$; -0.36, -0.31ppm, respectively). These up-field shifts clearly suggest the predominance of the anti structure $^{6,8)}$ in these metacyclophanes. In comparison to these up-field shifts 1d has a very small shift value (-0.05ppm), however, which may be a sign of the anti structure since the crystallographic analysis has disclosed clearly the anti structure in the crystalline state⁹⁾ (Fig. 1).

Table 1. Yields of ${\rm S}_{\rm RN}$ reaction and $^{1}{\rm H}$ NMR chemical shifts of the aromatic hydrogens in la-f.

Compounds	Yields(%)	¹ H NM Hi	R ([§] CDC1 ₃) Others
1a [3.3] 1b [4.4] 1c [5.5] 1d [6.6] 1e [7.7] 1f [8.8] (m-xylene)	33 25 23 21 22 24	5.86 6.51 6.56 6.82 6.84 6.88 (6.87)	7.30-7.60 6.90-7.30 7.00-7.35 6.90-7.30 6.90-7.35 6.80-7.30



Fig. 1. ORTEP drawing of 1d.

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- 9) The crystal_odata of 1d are as follows; Monoclinic, P2₁/n, a=13.531(4), b=13.304(5), c=6.647(2) Å, β=97.93 (2)°, Z=2, R=0.097 (909 reflections). All the computations were carried out using the UNICS3 program system [T. Sakurai and K. Kobayashi, Rep. Inst. Phys. & Chem. Res., 55, 69 (1979)]. Final crystallographic coordinates have been deposited in the Cambridge Crystallographic Data Center.

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