Intramolecular [2+2] Photocycloaddition. 15.[1] Synthesis of 1,2-Ethano-9,10-methano[2.2]paracyclophanes

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Synopsis. The title compounds were prepared in 30% yield by the sequence of photocycloaddition of styrene derivatives, followed by bromination and elimination. The isomer ratio of the products was 5 : 4.

Cyclophanes fused by small rings are special interest in theoretical and experimental studies of strained aromatic hydrocarbons. One such compound in this family is *exo*-1,2; 9,10-bismethano[2.2]paracyclophane (**1**), whose preparation from [3.3]paracyclophane was reported by Truesdale.[2] Higher homologs (**2,3**) in which the cyclophanes are fused by cyclobutane ring have been described by Müller,[3] Meier,[4] and Nishimura et al.[5] In these cases the fused ring was incorporated using inter- and intramolecular photocycloaddition.

Since only a few examples in this interesting family exist and the earlier findings[2] regarding the selectivity of the elimination steps cannot be interpreted in a straightforward manner, we were prompted to make novel and unsymmetrical 1,2-ethano-9,10-methano[2.2]paracyclophane. We now wish to report its successful synthesis using intramolecular photocycloaddition reaction[5] as well as the transformations utilized earlier by Truesdale.[2]

The styrene derivatives **4** have been cyclized to paracyclophanes **5** by our method.[5] *cis*-1,2-Ethano [2.3]paracyclophane **5a** was brominated in refluxing CCl_4 with excess amount of NBS, followed by treatment with butyllithium in THF at −78 °C to afford a mixture of the desired compounds **6** and **7** in 30% yield. This mixture was purified by column chromatography (SiO_2, hexane); we have, however, not yet separated **6** and **7** by recrystallization, HPLC (reversed phase C-18, MeOH), or capillary GC (SE-30, 200 °C). Attempts were unsuccessful to cyclize other cyclophanes **5** (n=4—6) at the tether by the same method as that mentioned above. These observations are consistent with the Baldwin ring-closure rule, which states that the 3-Exo-Tet route is the most facile among the n-Exo-Tet routes ($3 \leqslant n \leqslant 7$).[6]

The presence of *exo*-**6** and *endo*-**7** isomers in the reaction mixture was evident from NMR spectroscopy (^{1}H, ^{13}C,[7] NOESY, and COSY). Simple integration of peaks (Ha(2H), Hd, and He) showed that the ratio of the two isomers (*exo*-**6** : *endo*-**7**) was 5 : 4 (see Fig. 1). Both **6** and **7** show resonance peaks that are typical of the *cis*-cyclobutane ring methines δ=4.12 (m, 2H).[8] The chemical shift of the cyclopropane ring protons in **6** and **7** are equivalent (δ=2.45(m, 2H), 1.97 (sextet, 7.8 and 14.6, 1H), and 1.19 (q, 7.8 and 14.6, 1H)). The data for the cyclopropane ring protons are consistent with those reported by Truesdale.[2] On the other hand, the aromatic proton chemical shifts in **6** and **7** are different. The spectrum for the *exo* isomer (**6**) should show a larger chemical shift difference between its ortho protons($\Delta\delta_{ab}$ and $\Delta\delta_{ac}$) than would be predicted for the corresponding $\Delta\delta_{de}$ and $\Delta\delta_{fg}$ in the case of the *endo*-isomer, because of the unequal shieldings of the aromatic protons by the C–C bonds of the small fused rings. Compared with

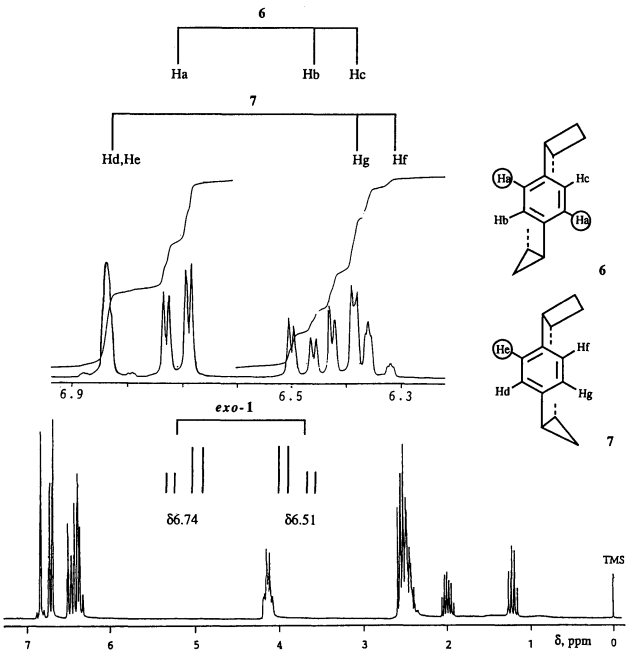
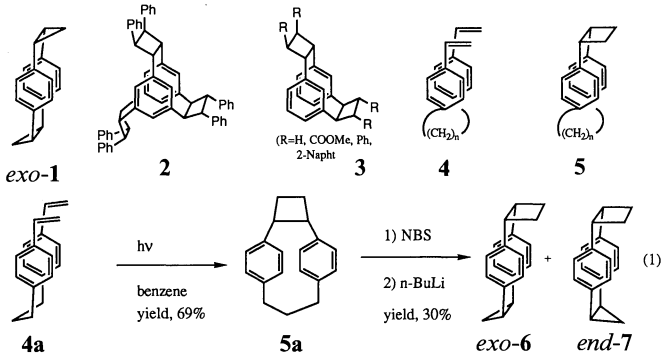


Fig. 1. 200 MHz ^{1}H NMR spectrum of a mixture of 1,2-ethano-9,10-methano[2.2]paracyclophanes *exo*-**6** and *endo*-**7**. The COSY spectrum shows two groups of signals, designated **6** and **7**. The NOESY spectrum shows three NOE interactions between aromatic hydrogens and fused-cycloalkane benzyl hydrogens. These affected aromatic hydrogens are indicated by circles in simplified structures **6** and **7**. All aromatic hydrogens are coupled with other aromatic hydrogens at the meta positions with a small coupling constant of 2.0; hydrogen Hf is coupled with Hd (J=1.2). The spectrum pattern of *exo*-**1** is also indicated (see Ref. 2).



Truesdale's NMR data, the shielding effects of the cyclobutane moiety is greater than that of cyclopropane. This is consistent with the dihedral angles of the cycloalkane C–C and C_{arom}–H bonds (calcd: cyclobutane moiety, ca. 6° and cyclopropane moiety, ca. 59°) in these compounds. Consequently, the resonances with the larger $\Delta\delta$ between the ortho hydrogens was assigned to **6**.

An MM2 calculation suggests that the two conformers of **5a** (n=3), which would be precursors of *exo*-**6** and *endo*-**7**, are of almost equal population. Thus, the bromination-and-elimination procedure[2] should give nearly equal amounts of isomers **6** and **7**, as was observed. On the other hand, Truesdale[2] obtained only one of the two possible isomers, namely the *exo* isomer, in the conversion of [3.3]paracyclophane to **1**. This observation appears to be consistent with data[9] from an NMR conformational analysis which suggests unequal stabilities for the two [3.3]paracyclophane conformers; it, however, is inconsistent with later results,[10,11] indicating that the ratio of the two conformers is about 1 : 1 at temperatures higher than −70°C.[11] One must, however, consider the resonance effect of the cyclopropane ring in the transformation to **1**. If this effect would play an important role in the elimination process, the high stereoselectivity observed by Truesdale would be reasonable. Resolution of this keen discrepancy observed in the transformation of the substrates containing the cyclopropane or cyclobutane moiety requires further experimentation.

Experimental

General Methods. Elemental analysis was performed at the Microanalytical Center of Gunma University. NMR spectra were recorded on a Varian Gemini 200 FT NMR spectrometer with tetramethylsilane as an internal standard. GC analysis was performed on a Shimadzu GC-14A gas chromatograph. Reversed-phase HPLC was carried out using a Shimadzu LC-6A HPLC apparatus. Melting points are not corrected. The MM2 program was provided by Professor Dr. E. Osawa of Toyohashi University of Technology.

Materials. Styrene derivative **4** and *cis*-1,2-ethanol[2.n]-paracyclophane **5** were prepared as described by us elsewhere.[5] THF was distilled over Na under a nitrogen atmosphere after undergoing prolonged reflux. The other solvents were purified by distillation. The other materials and reagents were all of the highest grade commercially available, and were used without further purification.

Preparation of Paddlanes 6 and 7. A mixture of paracyclophane **5a** (0.17 g, 0.68 mmol), NBS (0.37 g, 3.4 mmol), and benzoyl peroxide (a trace amount) in CCl_4 (20 mL) was heated at reflux under a nitrogen atmosphere for 20 h. The reaction mixture was poured into 5% aqueous HCl (50 mL) and extracted with chloroform (4×20 mL). The combined organic layer was neutralized with aqueous $NaHCO_3$, washed three times with water, and dried over anhydrous $MgSO_4$. After evaporation of the solvent the crude product was used without further purification, because of its rather unstable nature.

The crude bromide was dissolved in dry THF (40 mL) under a nitrogen atmosphere, and cooled to −78°C. A butyllithium–hexane solution (15%, 3.0 mL, 4 equivalent) was added using a hypodermic syringe over a period of 20 min. After addition, the mixture was allowed to stand overnight at room temperature. The reaction mixture was poured into 5% aqueous HCl (50 mL) and extracted with benzene (4×20 mL). The combined organic layer was neutralized with aqueous $NaHCO_3$, washed three times with water, and dried over anhydrous $MgSO_4$. After evaporation of the solvent the crystalline product (mp 140—160°C) was collected on a column chromatograph (SiO_2, hexane). The yield was 50 mg (30%).

Elemental analysis as a mixture of isomers **6** and **7**: Anal. Calcd (Found), C, 92.63 (92.59); H, 7.37 (7.40).

Cyclophane 6: ^{1}H NMR δ(multiplicity, coupling constant J in Hz, intensity)=6.71(d*A*Bq, 8.1 and 2.0, 4H), 6.48 (A*B*q, 8.1 and 2.0, 2H), 6.41 (A*B*q, 8.1 and 2.0, 2H), 4.12 (m, 2H), 2.56 (m, 4H), 2.45 (m, 2H), 1.97 (sextet, 7.8 and 14.6, 1H), 1.19 (q, 7.8 and 14.6, 1H); ^{13}C NMR δ(intensity)=140.42 (2C), 138.48 (2C), 134.96 (2C), 132.40 (2C), 128.34 (2C), 127.32 (2C), 48.41 (2C), 24.68 (2C), 19.87 (2C), 4.10 (1C).

Cyclophane 7: ^{1}H NMR δ=6.86 (*A*Bq, 8.1 and 2.0, 2H), 6.81 (A*B*q, 8.1, 2.0, and 1.2, 2H), 6.41 (*A*Bq, 8.1 and 2.0, 2H), 6.34 (A*B*q, 8.1, 2.0, and 1.2, 2H), 4.12 (m, 2H), 2.56 (m, 4H), 2.45 (m, 2H), 1.97 (sextet, 7.8 and 14.6, 1H), 1.19 (q, 7.8 and 14.6, 1H); ^{13}C NMR δ=140.54 (2C), 138.52 (2C), 134.90 (2C), 131.08 (2C), 127.96 (2C), 126.92 (2C), 48.47 (2C), 24.81 (2C), 20.05 (2C), 4.32 (1C).

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