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Synthesis and Conformational Behavior of Syn- and Anti-8-methoxycarbonyl-(Z)-[6]paracycloph-3-enes

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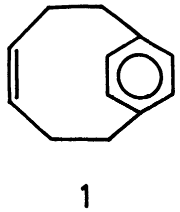
Syn- and anti-8-methoxycarbonyl-(Z)-[6]paracycloph-3-enes were synthesized and the barrier for the conformational inversion of the bridge was determined to be $\Delta G^{\neq}(298)=103$ kJ mol^{-1}.

One of the most intriguing aspects of small-bridged [n]para-$^{1)}$ and [n]metacyclophanes$^{2)}$ is the dynamic conformational behavior of the oligomethylene bridges. Recently, we reported the synthesis of (Z)-[6]paracycloph-3-ene (1)$^{3,4)}$ which is expected to have more strained benzene ring than that of [6]paracyclophane.$^{6)}$ However the dynamic behavior of the bridge of 1 was not elucidated by the NMR method (up to 150 °C). In this connection, we report here the synthesis of 8-methoxycarbonyl derivatives of 1, syn- and anti-8-methoxycarbonyl-(Z)-[6]paracycloph-3-enes (2S) and (2A) and the study of the conformational inversion of the bridge of them.



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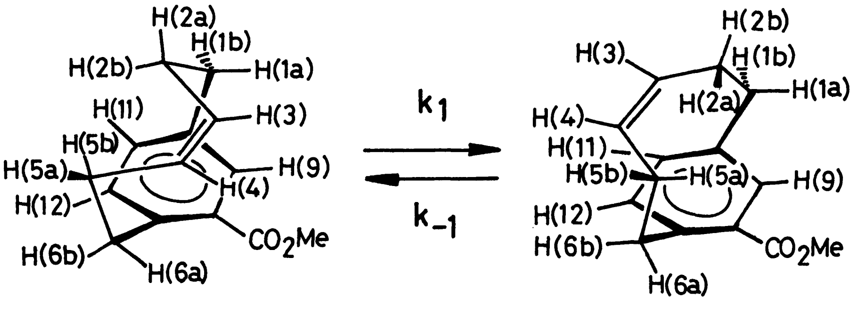
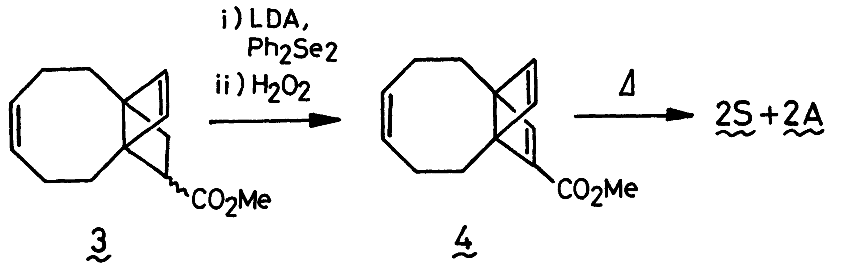
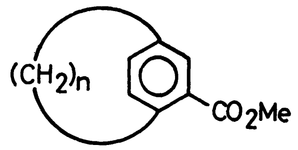


2S 2A

Phenylselenenylation (LDA, Ph_2Se_2, THF, -78 °C) followed by oxidation (H_2O_2, pyr, CH_2Cl_2, 0 °C) of the [6.2.2]propelladiene 3$^{3)}$ gave the propellatriene 4,$^{7)}$ the Dewar benzene type isomer of 2S and 2A, in 48% overall yield. As expected,$^{6b,d)}$ thermal valence isomerization of 4 took place readily [E_a(cyclohexane)=104 kJ mol^{-1}, log A=12.8] to afford ca. 1:1 mixture of 2S and 2A quantitatively. The conformers 2S and 2A were separated by silica-gel chromatography and the structural assignment of them was made on the basis of the following observations in the NMR spectra:$^{7)}$ (i) The aromatic proton H(9) of 2S appeared at higher field than that of 2A ($\Delta\delta=0.24$) whereas H(11) and H(12) of





5 n=6
6 n=5

2A at higher field than those of **2S** ($\Delta\delta$=0.15-0.21) in the ^{1}H NMR spectra due to the shielding effect of the bridge double bond. (ii) Similarly, the aromatic carbon C(8) of **2S** located syn to the bridge double bond appeared at lower field than that of **2A** being anti to the bridge ($\Delta\delta$=3.2) in the ^{13}C NMR spectra due to steric compression. From the chemical shifts and the coupling constants of the benzyl protons H(1a), H(1b), H(6a), and H(6b) in the ^{1}H NMR spectra,7) it is deduced that **2S** and **2A** have the conformations shown in Fig. 1 in which the bridge double bond is apart from the benzene ring.8) As shown in Fig. 2, **2S** and **2A** exhibited remarkable bathochromic shift (ca. 15 nm) in the long-wave-length region of the UV spectra compared with that of 8-methoxycarbonyl[6]paracyclophane (**5**).6d) This indicates the increase of out-of-plane deformation of the benzene ring in the formers relative to that in the latter.8) While no apparent difference was observed between the spectra of **2S** and **2A** despite considerable difference in the steric arrangement, the interaction between two π systems may also contribute to some extent to the above shift.

Interestingly, it was found that the mutual isomerization between **2S** and **2A** took place slowly at ambient temperature. Therefore, the elucidation of the dynamic behavior of the bridge has become feasible. The rate constants of the isomerization of **2S** to **2A** and **2A** to **2S** in methanol were determined by measurement of the change by HPLC and are listed in Table 1. At the temperatures examined,

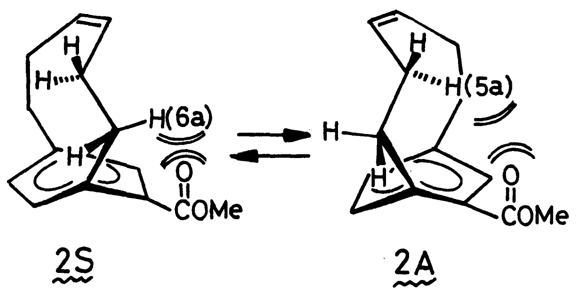


Fig. 1. Plausible conformations for **2S** and **2A**.

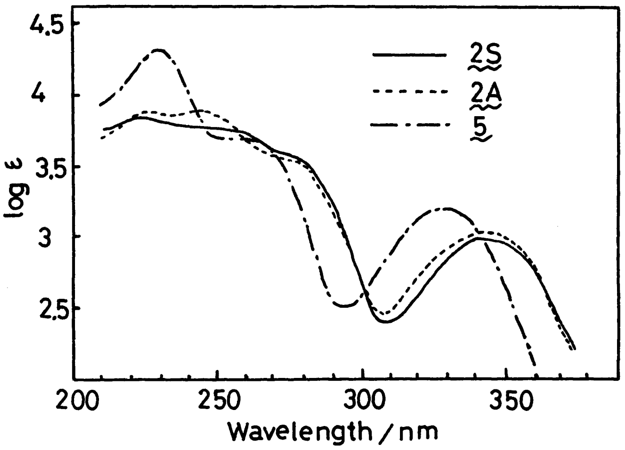


Fig. 2. UV spectra of **2S**, **2A**, and **5** in ethanol.

Table 1. Kinetic data for isomerization between **2S** and **2A**[a]

Temp °C	k_1(**2S**→**2A**)[b] s^{-1}	k_{-1}(**2A**→**2S**)[b] s^{-1}	K(**2S**/**2A**)[c]	$\Delta H^{\neq}$[d] kJ mol^{-1}	$\Delta S^{\neq}$[d] $\text{J mol}^{-1}\ \text{K}^{-1}$
25.0	$(5.58 \pm 0.12) \times 10^{-6}$	$(5.64 \pm 0.07) \times 10^{-6}$	0.97 ± 0.01	104 (103)	2.5 (0.8)
38.0	$(2.91 \pm 0.02) \times 10^{-5}$	$(3.01 \pm 0.06) \times 10^{-5}$	0.96 ± 0.03		
50.0	$(1.53 \pm 0.06) \times 10^{-4}$	$(1.55 \pm 0.07) \times 10^{-4}$	0.97 ± 0.02		

a) 2×10^{-3} mol dm^{-3} in methanol. *b*) The rate constanys were calculated using the usual expression for a reversible first-order reaction (ref. 9). *c*) Observed equilibrium ratio of **2S**/**2A**. *d*) Values for **2S**→**2A**. Those for **2A**→**2S** are given in parentheses.

the equilibrium constants (K) between **2S** and **2A** were nearly unity in contrast to the corresponding [6]paracyclophane **5**[6d] and the [5] homologue **6**[10] with methoxycarbonyl group (K=0.25-0.3). This may be interpreted by compensation for the steric strain due to nonbonded repulsion between H(6a) and the ester group in **2S** with that in **2A** between H(5a) and the same group as depicted in Fig. 1. From the above data, the barrier for the inversion of the bridge, $\Delta G^{\neq}$(298, **2S**→**2A**)= $\Delta G^{\neq}$(298, **2A**→**2S**)= 103 kJ mol^{-1} (24.6 kcal/mol), was obtained. The barrier is thus considerably high and is associated with the enthalpy factor. It is therefore concluded that the bridge of **2S** and **2A** is much more rigid than those of (E)-[8]paracycloph-4-enes[5c,e] and other small-bridged cyclophanes with saturatd methylene chains.[1,2]

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7) All new compounds gave satisfactory analytical and spectral data. The NMR data for **2S**, **2A**, and **4** follow:

2S: ^{1}H NMR (360 MHz, CD_2Cl_2) δ 1.10-1.21 (2H, m, H(2b)+H(5b)), 1.86-1.97 (2H, m, H(2a)+H(5a)), 2.36 (1H, ddd, ^{2}J=12.0, ^{3}J=12.0, ^{3}J=3.1 Hz, H(1a)), 2.79 (1H, ddd, ^{2}J=12.0, ^{3}J=4.2, ^{3}J=3.1 Hz, H(1b)), 2.92 (1H, ddd, ^{2}J=12.1, ^{3}J=3.5, ^{3}J=3.5 Hz, H(6b)), 3.26 (1H, ddd, ^{2}J=12.1, ^{3}J=12.1, ^{3}J=3.4 Hz, H(6a)), 3.88 (3H, s), 4.62-4.78 (2H, m, H(3)+H(4)), 7.34 (2H, 2s, H(11)+H(12)), 7.69 (1H, br s, H(9)); ^{13}C NMR ($CDCl_3$) δ 167.7 (s, C=O), 148.5 (s, C(7)), 143.2 (s, C(10)), 136.4 (d, C(9)), 136.2 (s, C(8)), 134.6, 133.7 (d, C(11)+C(12)), 131.6, 131.4 (d, C(3)+C(4)), 51.8 (q, Me), 36.0, 34.7 (2C), 34.0 (t, C(1)+C(2)+C(5)+C(6)).

2A: ^{1}H NMR (360 MHz, CD_2Cl_2) δ 0.82-0.95 (2H, m, H(2a)+H(5a)), 1.89-2.00 (2H, m, H(2b)+H(5b)), 2.28 (1H, ddd, ^{2}J=12.1, ^{3}J=12.1, ^{3}J=2.9 Hz, H(1b)), 2.33 (1H, ddd, ^{2}J=12.1, ^{3}J=12.1, ^{3}J=3.1 Hz, H(6b)), 2.90 (1H, ddd, ^{2}J=12.1, ^{3}J=3.6, ^{3}J=3.6 Hz, H(1a)), 3.76 (1H, ddd, ^{2}J=12.1, ^{3}J=3.6, ^{3}J=3.6 Hz, H(6a)), 3.89 (3H, s), 4.69-4.81 (2H, m, H(3)+H(4)), 7.13 (1H, B of ABX, $^{3}J_{AB}$=7.7, $^{5}J_{BX}$=0 Hz, H(11)), 7.19 (1H, A of ABX, $^{3}J_{AB}$=7.7, $^{4}J_{AX}$=1.6 Hz, H(12)), 7.93 (1H, X of ABX, $^{4}J_{AX}$=1.6, $^{5}J_{BX}$=0 Hz, H(9)); ^{13}C NMR ($CDCl_3$) δ 167.4 (s, C=O), 145.2 (s, C(7)), 142.5 (s, C(10)), 139.0, 137.6 (d, C(11)+C(12)), 134.7 (d, C(9)), 133.0 (s, C(8)), 132.5, 131.4 (d, C(3)+C(4)), 51.8 (q, Me), 36.6, 35.7, 34.2, 33.1 (t, C(1)+C(2)+C(5)+C(6)).

4: ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.8-2.2 (8H, m), 3.71 (3H, s), 5.5-5.8 (2H, m), 6.45 (1H, d), 6.61 (1H, d), 7.22 (1H, s); ^{13}C NMR ($CDCl_3$) δ 163.5 (s), 156.0 (d), 146.3 (s), 145.0 (d), 143.9 (d), 132.2 (d), 131.5 (d), 67.6 (s), 66.5 (s), 51.4 (q), 30.3 (t), 28.9 (t), 22.5 (t), 22.3 (t).

8) Preliminary results on X-ray analysis of 8,11-dimethoxycarbonyl-(Z)-[6]paracycloph-3-ene support these deductions about the conformation and deformation of this system; unpublished results.

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