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Conformation of *cis,cis*-Cycloocta-2,7-dienone Ethylene Ketal

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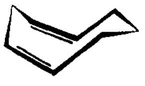
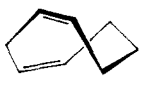
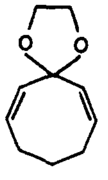
cis,cis-Cycloocta-2,7-dienone ethylene ketal (1) exists virtually entirely in a chiral twist boat conformation, unlike the parent *cis,cis*-1,4-cyclooctadiene. The barrier ($\Delta G^{\ddagger}$) to pseudorotation (which is also a conformational enantiomerization) has been measured by 348-MHz ^{1}H NMR spectroscopy and is 6.0 kcal/mol.

A recent investigation has shown that *cis,cis*-1,4-cyclooctadiene[1] exists as a conformational mixture of a relatively rigid boat–chair (BC) and a more or less flexible twist boat (TB), with the latter being the major conformation. Iterative force-field calculations show that the barrier to pseudorotation in the twist boat is only 3.8 kcal/mol. Thus, it is not surprising that direct evidence for this process could not be obtained by dynamic NMR methods.


BC


TB

An examination of molecular models shows that appropriate substituents on 1,4-cyclooctadiene should produce large predictable effects on the equilibrium between the boat–chair and twist boat, if the conformational ideas previously put forward for the parent compound are correct. The ethylene ketal of cycloocta-2,7-dienone (1)[2] is particularly well suited for this purpose since it is readily accessible and has the same chemical symmetry as does the parent compound. The oxygen substituents on the eight-membered ring are much larger than hydrogen atoms and can produce large changes in transannular repulsions. Nevertheless, the oxygens are small enough so as not to perturb seriously vicinal nonbonded interactions.



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Results and Discussion

The ^{1}H NMR spectrum of 1 shows three bands for the methylene groups at room temperature (Table I). The resonances of the ethylene ketal moiety and of the allylic protons broaden below about −130 °C and give rise to broad 1:1 doublets at −148 °C. As expected, there is only a small chemical shift difference of the ethylene ketal protons, as these are quite far from the chiral twist-boat moiety. The band of the unique homoallylic methylene group remains unchanged. No dynamic NMR effect is observed in the ^{13}C spectra of 1 between room temperature and −160 °C.[3]

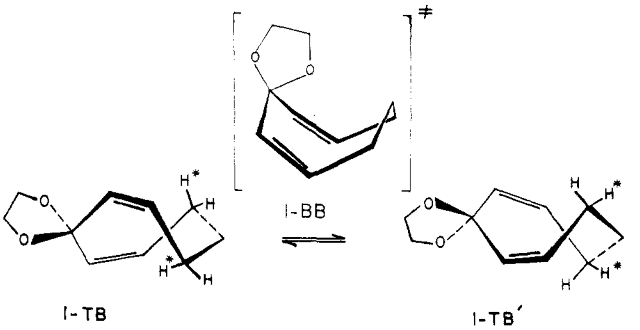
The presence of dynamic NMR effects only for the allylic and ethylene ketal proton resonances is strong evidence for a conformation with C_2 symmetry, i.e., for the twist-boat conformation (I-TB). It is possible, of course, that the conformation is actually unsymmetrical but that suitable conformational processes are rapid at −160 °C. It is indeed possible that the global energy minimum in 1 is a conformation which is slightly distorted from the symmetrical one. Force-field calculations on the parent diene do show local energy minima on each side of the symmetrical twist boat,[1] which is the global minimum for that compound. In any case, the NMR evidence is clearly consistent with a twist boat, which can be more or less symmetrical, as long as it is flexible.

Table I. ^{1}H NMR Chemical Shifts in *cis,cis*-Cycloocta-2,7-dienone Ethylene Ketal (1)

	chemical shifts^a			
T, °C	CH	5-CH$_2$	4,6-CH$_2$	9,10-CH$_2$
rt^b	5.8	1.57	2.28	4.0
-101^c		1.57	2.28	4.01
-147^c		1.57^d	2.07,^{e} 2.47^e	3.94,^{f} 4.14^f

^{a} In parts per million from tetramethylsilane. ^{b} In CDCl$_3$. ^{c} In CHFCl$_2$-CHF$_2$Cl (1:3) at 348 MHz. ^{d} $\Delta\nu_{1/2}$ = 25 Hz. ^{e} $\Delta\nu_{1/2}$ = 40 Hz. ^{f} $\Delta\nu_{1/2}$ = 30 Hz.

The experimental data on 1 can be fitted to a boat–chair only if very unlikely chemical shift coincidences are postulated for both the homallylic protons and the ethylene ketal carbons. The chemical shifts of 1 do not show any significant temperature-dependent chemical shifts, apart from those involved in the dynamic NMR effects already mentioned. Thus, it appears that 1 is conformationally homogeneous, unlike the parent 1,4-cyclooctadiene. The *conformational process responsible for the observed dynamic NMR effect in 1 is almost certainly the interconversion of two enantiomeric twist boats (I-TB and I-TB′) via a boat–boat (I-BB) transition state. From a line-shape analysis carried out on the allylic proton band at −140 °C, a $\Delta G^{\ddagger}$ of 6.0 kcal/mol can be calculated. This barrier is substantially higher than the corresponding barrier in the parent 1,4-cyclooctadiene, where, as mentioned previously, it is too small to measure by dynamic NMR methods and where force-field calculations give a value of 3.8 kcal/mol. Although we have not carried out a force-field calculation of the barrier in 1, a difference of 2.2 kcal/mol between 1 and the parent diene is reasonable if the boat–boat is the transition state. In the boat–boat the distance between



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[2] E. W. Garbisch, *J. Org. Chem.*, 30, 2109 (1965); *Chem. Ind. (London)*, 1715 (1964).

[3] The olefinic bands of 1 are close to the solvent resonances, and no attempt to observe them was made.

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the inward-pointing hydrogens on C-3 and C-7 is only 1.92 Å,[1] and thus the steric repulsion between these two hydrogens is already quite significant in the parent compound.

It can be predicted on the basis of the present data that 3,3-dimethyl-*cis*-1,4-cyclooctadiene[4] and 3,3,7,7-tetramethyl-*cis*-1,4-cyclooctadiene will both exist very predominantly in twist-boat conformations and that the barriers to ring inversion in these compounds will be considerably greater than that in 1. The boat–boat of the above tetramethyl derivative should be extremely strained, and it is likely that ring inversion in the compound will proceed via a boat–chair, which is itself of fairly high energy. However, it appears unlikely that the latter barrier will be high enough for that diene to exist in isolable enantiomeric forms at room temperature.

Experimental Section

The *cis,cis*-cycloocta-2,7-dienone ethylene ketal was prepared from cyclooctanone according to the procedure described by Garbisch.[2] The compound was purified by preparative VPC on a Carbowax 20M column. Its ^{1}H NMR spectrum (348 MHz) in $CDCl_3$ at room temperature exhibits absorption bands at δ 1.57 (5-CH_2), 2.28 (4,6-CH_2), 4.0 (9,10-CH_2), and 5.8 (CH protons). The ^{13}C NMR spectrum (63.1 MHz) in $CDCl_3$ at room temperature show bands at δ 23.9 (4,6-$^{13}CH_2$), 25.9 (5-$^{13}CH_2$), 65.2 (9,10-$^{13}CH_2$), 113.0 (3,7-^{13}CH), 106.3 (1-^{13}C), and 117.7 (2,8-^{13}CH).

^{13}C NMR spectra were measured on a superconducting solenoid NMR spectrometer operating at 59 kG.[5] The ^{1}H NMR spectra were obtained on a superconducting solenoid NMR spectrometer operating at 82 kG.[6] Tetramethylsilane was used as internal reference for both ^{13}C and ^{1}H NMR spectra.

Acknowledgment. This work was supported by the National Science Foundation.

Registry No. 1, 72708-69-1.

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Kinetics and Mechanism of the Ene Reaction of Dimethyl Mesoxalate with Alkenes[1a]

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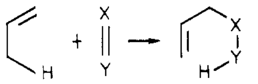
The kinetics of the ene reaction of dimethyl mesoxalate with 1-pentene, 1-hexene, 3-methyl-1-butene, 3-methyl-1-pentene, (*E*)-2-pentene, and (*Z*)-2-pentene have been studied. The reaction was found to be second order, first order with respect to each reactant. Thermodynamic parameters, viz., enthalpy ($\Delta H^* = 75$–96 kJ mol^{-1}) and entropy ($\Delta S^* = -120$ to -170 J mol^{-1} K^{-1}) of activation, as well as the lack of a significant effect of solvent polarity on the rate of the reaction, indicated a concerted mechanism. Analysis of the ΔH^* values obtained in terms of a loose transition state suggested that the transition state is product-like ("late") in character.

The reaction between an alkene containing an allylic hydrogen atom and an electron-deficient multiple bond (enophile), leading to a 1:1 adduct according to eq 1, is known as the ene synthesis.[2a–c]



(1)

In spite of the relative simplicity of the ene reaction a complete and consistent picture of its mechanism is still lacking. For different ene reactions just about all possible mechanisms have been put forward. The suggestions include a free-radical mechanism involving an intermediate diradical[3,4] or a radical pair, if a promoting transfer of a hydrogen atom is involved,[5,6] as well as an ionic mechanism,[7] and finally the often advanced concerted mechanism via a six-membered cyclic transition state.[8–10]

The concerted ene reaction is a pericyclic process and as such it can be considered in terms of orbital symmetry rules and the frontier orbital or the Dewar–Zimmermann method. As the transition state of the ene reaction has no elements of symmetry, the approaches are not rigorous. Their justification in relation to the specific ene reaction requires additional support from experimental evidence.

Kinetic methods have so far found a rather limited[11,12] application in the study of the ene reaction mechanism, and the recent prevalence of concerted mechanism proposals is based largely upon stereochemical evidence, viz., asymmetric induction,[13,14] cis configuration of the newly formed C–C and C–H bonds,[15] stereoselective migration

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[1] (a) This research was supported by the Polish Academy of Sciences through Project MR-I.12.1. (b) Warsaw Agricultural University, Institute of Chemistry and Agricultural Chemistry, 02-528 Warszawa, Poland.

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