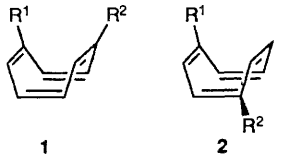
Structural Equilibria Determined by Attractive Steric Interactions. 1,6-Dialkylcyclooctatetraenes and their Bond-shift and Ring Inversion Investigated by Dynamic NMR Spectroscopy and Molecular Mechanics Calculations

J. Edgar Anderson * and Peter A. Kirsch
Chemistry Department, University College, Gower Street, London WC1E 6BT, UK

1,6-Dialkylcyclooctatetraenes equilibrate with their 1,4-dialkylcyclooctatetraene isomers by a bond-shift process which is slow on the NMR timescale at ambient temperature. The relative stability of these isomers is measured from NMR signal intensities, and attractive alkyl–alkyl steric interactions in the 1,6-isomer are invoked to explain its predominance. Molecular mechanics calculations bear out this explanation. Various features of attractive steric interactions appear from these results and are discussed. Barriers to the bond-shift and to some ring inversion processes are reported.

Attractive van der Waals forces due to dispersion (induced dipole–induced dipole) interactions between atoms are present in all molecules, but their effect on the molecular structure is usually overwhelmed by repulsive interactions. In contrast to extensive studies of steric strain within molecules, very little is known about attractive forces. This report is part of an effort to correct this by adapting the conformational equilibrium technique so widely used for studying strain. We investigate the position of an equilibrium which is unbalanced owing putatively to attractive interactions which are more important on one side of the equilibrium than on the other. The equilibrium concerned is the bond-shift equilibrium **1** ⇌ **2** between 1,6- and 1,4-dialkylcyclooctatetraenes.[1–7] Separate signals for the two isomers are seen in the NMR spectra at ambient temperature and measurement of their intensity leads directly to the position of the equilibrium.

The relationship of each group R with its immediate molecular environment — a substituted double bond — is the same for all four groups in **1** and **2**, the only difference being that



1 **2**

the two groups R are closer together in **1**. Insofar as there is more of **1** at equilibrium, it is more stable than **2**, (if entropy differences are unimportant, see below) and this stability has been attributed[1] to greater attractive interactions between groups R in **1**. Streitweiser and his colleagues have thus measured the attractive interactions in **1d**[1] and **1e**[2], and we have studied **1a**.[7] The corresponding dinitrocyclooctatetraene **1f** and two derivatives[6a] and the bis-hydroxyethyl derivative[6b] have also been studied, but the interaction of groups, while again attractive may be more complicated than that between two alkyl groups. Molecular mechanics calculations have been carried out for **1d**,[4,5] **1a**[4,7] and **1g**[4], and *ab initio* calculations for **1d**,[5] the latter matching experiment poorly when allowance was not made for electron correlation, putatively attractive interactions. Table 1 summarises all these results, and shows that there is reasonable agreement between experiment and calculation.

We now report measurements and calculations for diethyl- and diisopropyl-cyclooctatetraenes, and some further results for the di-*tert*-butyl and dimethyl compounds. In the course of synthesizing **1a–1d**, **1i** was obtained as a by-product. Results for this and for **1h** are included in Tables when available.

Results

NMR Spectra.—The assignment of signals in the NMR spectra of such equilibria has been discussed,[7] and is unequivocal, based on strikingly different coupling patterns for olefinic protons. Proton and carbon-13 chemical shifts for mixtures of the 1,4- and 1,6-dialkylcyclooctatetraenes are listed in Tables 7 and 8 in the Experimental section. Integration of appropriate signals shows that in each case there is an excess of the 1,6-dialkylcyclooctatetraene. The various equilibrium constants thus measured are shown in Table 1. Measurements of the equilibrium were carried out at several temperatures for each of the compounds **1a**, **1b**, **1c** and **1d**, taking care to allow sufficient time for equilibration at each temperature studied. Table 2 shows the enthalpy and entropy differences between isomers as derived from the temperature dependence of the equilibrium.

The limited range of temperatures at which the equilibrium could be studied, and an estimated 5% uncertainty in the equilibrium constants resulting from spectral integration, explain the relatively poor correlation coefficients shown in Table 2. The trend of the results suggests that the enthalpy of the 1,4-isomer is higher than that of the 1,6-isomer, and so too the entropy, except in the dimethyl case **1a**.

The temperature dependence of the equilibria in **1d**[1,2,3] and **1a**[7] has been reported previously. The results quoted for **1d** in refs. 1 and 2 present a problem in that while the text says that the 1:2 population ratio at 25 °C is 2, in broad agreement with our result, an accompanying Table gives the equilibrium constant at that temperature as 0.702 and slightly increasing values of this constant at temperatures up to 50 °C. Perhaps the numbers in the Table represent the natural logarithm of the equilibrium constant. Paquette and his co-workers[3] report that the equilibrium constant for **1d** is temperature-independent over the temperature range 20–40 °C.

A qualitative observation allows us to be quite sure that for the compound **1d**, the gradual increase in the proportion of the 1,4-isomer with temperature is real. A sample of **1d**, newly trapped in a recipient cooled in acetone/solid CO_2 as it emerged from a gas–liquid chromatograph with port temperature 240 °C, and presumably reflecting the equilibrium at some temperature near to the port temperature, showed a ratio of 1,6:1,4 isomers of about 1.05.

The various results can be summarised as follows: around room temperature the 1,6-isomer is more populated than the 1,4-isomer. The larger the alkyl group, the more the 1,6-isomer with the alkyl groups close together, is favoured, but the proportion of the 1,4-isomer increases slightly with temperature.

Table 1 The 1,4/1,6-disubstituted cyclooctatetraene equilibrium. In all cases the 1,6-isomer is more stable.

	Substituents		Experimental					Calculated (gas phase)	
Compound	R^1	R^2	Solvent	T/°C	Ref.	Equilibrium constant	$-\Delta G_o^c$	$-\Delta H_o^c$	Ref.
1a	Me	Me	C_6D_6	20	7	1.15	0.08	0.043	7
			$CDCl_3$	−21	*f*	1.35		0.02	4
				−10	*f*	1.30			
				0	*f*	1.25			
				10	*f*	1.26			
				20	*f*	1.29			
				30	*f*	1.33			
				39	*f*	1.29			
1b	Et	Et	C_6D_6	20	*f*	1.52	0.24	0.22	*f*
			$CDCl_3$	−21	*f*	1.73			
				−11	*f*	1.69			
				−1	*f*	1.71			
				9	*f*	1.52			
				19	*f*	1.59			
				30	*f*	1.43			
				40	*f*	1.58			
				50	*f*	1.39			
1c	Pr^i	Pr^i	C_6D_6	20	*f*	1.84	0.36	0.46	*f*
			$CDCl_3$	−11	*f*	1.96			
				0	*f*	1.88			
				15	*f*	1.87			
				30	*f*	1.85			
				39	*f*	1.63			
				50	*f*	1.54			
				60	*f*	1.55			
1d	Bu^t	Bu^t	$CDCl_3$	25	1	1.42[a]	0.43	1.07	4
				25	3	2.08	0.48	1.17	5
				2	*f*	2.36			
				25	*f*	1.93	0.39		
				40	*f*	1.77			
				45	*f*	1.72			
				50	*f*	1.72			
				55	*f*	1.66			
1e	Ph	Ph	$CDCl_3$	25	2	1.35	0.18	*d*	
1f	NO_2	NO_2	$CDCl_3$	20	6*a*	2.86	0.01	*d*	
1g	Me	Bu^t			*d*			0.33	4
1h	Ph	Bu^t	$CDCl_3$	20	*f*	1.95	0.39		
1i	Me	Bu	$CDCl_3$	20	*f*	1.62		*d*	
1j	CH_2CH_2OH[e]		D_2O	0	6*b*	1.60			

[a] See text. [b] Ratio is 1,6:1,4. [c] In kcal mol^{-1}. [d] Has not been determined. [e] Both substituents are CH_2CH_2OH. [f] This work.

Table 2 Experimental enthalpy and entropy differences for the **2** ⇌ **1** equilibrium for dialkylcyclooctatetraenes[a,b]

Compound and alkyl group	$-\Delta H_o$/ kcal mol^{-1}	$-\Delta S_o$/ e.u.[c]	Correlation coefficient	$-\Delta G_o$ 20 °C/ kcal mol^{-1}
2a–1a Methyl	0.05	+0.3	0.064	0.08
2b–1b Ethyl	0.52	−1.0	0.851	0.24
2c–1c Isopropyl	0.61	−1.0	0.837	0.36
2d–1d *tert*-Butyl	1.14	−2.5	0.952	0.39[c]

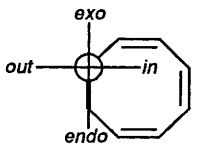
[a] Calculated from $\log_{10}k_{eq} = -\Delta H_o\,(2.3RT)^{-1} + \Delta S_o\,(2.3R)^{-1}$. The 1,6-isomer is the more stable in each case and has the lower entropy, except for the methyl compound. [b] 1 cal = 4.184 J; 1 e.u. = 1 cal mol^{-1} K^{-1}. [c] 25 °C in deuteriochloroform solution whereas other results are for benzene solution.

Molecular Mechanics Calculations for Diethyl and Diisopropyl Derivatives.—Various conformational minima exist for each alkyl–cyclooctatetraene bond, so calculations using Allinger's MM2-82 program[8a] were first carried out for cyclooctatetraene with a single ethyl or isopropyl substituent to show the energy variation with rotation conformation, without the perturbing influence of a second alkyl substituent. Calculations were then carried out for the two isomers of the diethyl and diisopropyl compounds.

Each conformation can be concisely described by the dihedral angle which the unique, indicator bond, (C–H in the case of an isopropyl group, or C–CH_3 in the case of the ethyl group) makes with the double bond to which it is attached. A qualitative description of the conformation is useful however, so the terms *exo*, *endo*, *out*, and *in*, are defined as in **3**. As far as attractions across the ring are concerned, whether methyl groups are located *in* or *out* is much more important than whether they are *exo* or *endo*.

As far as interactions between the alkyl group and its immediate surroundings, the double bond, are concerned, the preferred conformations of an ethyl group are calculated to be those with the methyl group near-to-orthogonal to the double bond, but whether *out* or *in* makes little difference. The rotational transition state has the methyl group eclipsing the double bond *i.e. endo*.

Thr preferred conformations of isopropylcyclooctatetraene have both methyls of the isopropyl group as far as possible from the plane of the double bond. Thus the methine hydrogen is near the plane either *anti*-periplanar to the double bond *i.e. exo*,



3

or nearly *syn*-periplanar but directed over the ring somewhat, *endo-in*. Once again, calculations show that the least stable conformations occur when a methyl group eclipses the double bond, and it is this destabilisation that dominates the conformational analysis of these monosubstituted compounds.

Calculations for the diethyl-compounds **1b** and **2b** are summarised in Table 3. Conformations divide into three sets IN,IN *etc.* which are separated by the rotational barrier to a methyl group passing through the plane. In the 1,6-isomer several minima separated by small barriers are found within sets, depending as rotation of the ethyl groups brings the attracting methyl groups nearer to each other. This significantly modifies the conformational enthalpy which is nonetheless mainly due to alkyl group–double bond repulsions.

No such local minima are found in the 1,4-isomer, for which perturbations due to attractive interactions are very small. The last column in Table 3 shows the calculated enthalpy difference between equivalent versions of the 1,6- and 1,4-isomers, and as expected these are largest when methyls are directed inwards and attractions of methyl groups are maximised.

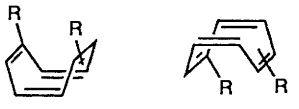
The lowest enthalpy in each set is in bold in the Table and was used to calculate the likely population of rotational forms for both the 1,4- and 1,6-isomer. These are shown as percentages adding up to 100% for each isomer in the Table. Using the same six values, the **2b**–**1b** equilibrium constant was calculated to be 1.46 at 20 °C (1.52 experimentally) which corresponds to a 59:41 ratio of isomers. Such calculations neglect entropy differences between conformations, see Discussion.

Calculations for the diisopropyl compounds **1c** and **2c** are summarised in Table 4. Once again the possible rotational conformational minima divide into three sets separated by the barrier to the biggest group eclipsing the double bond, and the biggest difference in stability is seen when the unique hydrogen is directed outwards *i.e.* the methyl groups are nearer to each other and attractions are maximised. Populations were calculated as before, and these are shown as percentages in Table 4. The same values were used to calculate the **2c**–**1c** equilibrium constant of 2.22 at 20 °C (1.84 experimentally) which corresponds to a 69:31 ratio of isomers.

Molecular mechanics calculations of any structure include terms for the pairwise interactions of all atoms, so the interactions between the alkyl groups, atom by atom, can be extracted from the calculations and summed. These 49 (7 × 7, diethyl) and 100 (10 × 10, diisopropyl) for the significant conformations of Table 4 are listed in Table 5, and are all attractive. The difference in stability of a particular conformation is always similar in size to the difference in the sum of pairwise attractive interactions (compare the first and last columns in each case). Other calculated terms are not always the same (since for example, dihedral angles are different, see Table 4) but the sums of all other terms do more or less match in the two isomers. Other programs might evaluate attractive interactions differently (see Discussion), but the present calculations do suggest that it is plausible to attribute the difference in energy of the 1,4- and 1,6-isomers to attractive steric interactions in the latter compound.

Bond-shift and Ring Inversion Processes.—On raising the temperature, all NMR signals broaden and eventually coalesce as the interconversion **1** ⇌ **2** becomes fast on the NMR timescale. The energy of activation for the bond-shift process at the coalescence temperature was determined from such NMR spectra as before[7] and the results are listed along with literature values for other compounds in Table 6.

A second dynamic process can be observed in the NMR spectrum of ethyl and isopropyl derivatives of cyclooctatetraene in the form of doubling of some alkyl group signals on lowering the temperature. Methylene protons of the ethyl group and methyl protons of the isopropyl group become diastereotopic as the interconversion of chiral ring conformations **4** ⇌ **5**



4 5

becomes slow on the NMR timescale. Barriers to this process were determined from the coalescence of decoupled signals and are slightly different for the 1,4- and 1,6-isomers of each compound. Results are shown in Table 6 along with literature values of ring inversion barriers for similar compounds.

Discussion

Experimental results and calculations agree that the 1,6-disubstituted compounds are more stable than their 1,4-disubstituted isomers and apparently this difference can be attributed to the enthalpy of attraction of the alkyl groups, which are nearer to each other, and thus attracting more strongly, in the former case.

The equilibria are temperature-dependent for each of the dimethyl, diethyl, diisopropyl and di-*tert*-butyl cyclooctatetraenes, see Table 1, in a way that shows that beyond experimental error, the 1,6-isomer has a lower enthalpy than the 1,4-isomer and that the entropy is significantly lower as well, at least in the ethyl, isopropyl, and *tert*-butyl compounds.

Calculations suggest that for diethylcyclooctatetraene at least, there are more conformational minima for the 1,6-isomer which thus has higher conformational entropy. The minima in the 1,4-isomer are presumably much wider and flatter so this form has a higher rotational and vibrational entropy. There is no obvious way of deciding the balance of importance of these two effects (although molecular dynamics simulations might be helpful[8c]) so we will concentrate on the experimental indications that the 1,4-disubstituted isomer has the higher entropy.

This result suggests that somehow the attractive forces in the 1,6-isomer reduce the number of states available, which is as inherently reasonable for attractive forces as for repulsive ones. The difference between the 1,6- and 1,4-isomers is between the presence or virtual absence of a force and it is not surprising that the latter case represents a higher entropy.

In the calculations of the conformational energy of the diethyl compound there are some interesting points. The conformations preferred always have the methyl groups aproximately orthogonal to the double bond. However in the 1,4-isomer the *in,in* version is slightly less stable than the *out,out* by less than 0.1 kcal mol^{-1} while in the 1,6-isomer, the *in,in* conformation, which puts the methyl groups close together, is more stable than the *out,out* by 0.34 kcal mol^{-1}.

In the calculations of diisopropyl compounds, the isopropyl groups in the 1,4-isomer once again adopt conformations very similar to that in the monosubstituted case. The 1,6-isomer conformations mirror those of the 1,4-isomer in their *order* of stability, but each is between 0.4 and 0.7 kcal mol^{-1} more stable.

For the two isomers of either compound, dihedral angles are slightly different in conformations of the same name, and the differences are greater where methyl groups point in and thus

Table 3 Calculated energy (kcal/mol^{-1}) of various conformations[a] of 1,6- and 1,4-diethylcyclooctatetraenes and percentage populations.[b] Dihedral angles (°) are for the C–CH_3 bond with its attached double bond.[c]

	1,6-Isomer			1,4-Isomer[d]			
Conformation[c]	Dihedral angles/°	Energy/kcal mol^{-1}	Occupancy (%)	Dihedral angles/°	Energy/kcal mol^{-1}	Occupancy (%)	ΔE[e]/kcal mol^{-1}
IN,IN			35			23	
endo-in, exo-in	+74 −106	**11.967**					
endo-in, endo-in	+71 −87	12.002		+78 −79	**12.347**		0.435
exo-in, exo-in	+118 −121	12.008					
exo-in, exo-in	+131 −168	12.559					
exo-in, endo-in	+170 −81	12.567					
IN,OUT and OUT,IN			23 (both)			25 (both)	
endo-in, endo-out	+80 +79	**12.213**		+81 +77	**12.399**		0.186
exo-in, endo-out	+111 +79	12.334					
OUT,OUT			19			27	
endo-out, endo-out	−77 +79	**12.306**		−78 +79	**12.341**		0.035

[a] Some particularly high rotational energy minima have not been included. Most stable conformation in each 'set' (see text) is in bold. [b] Calculated from only the most stable conformation (in bold) in each set assuming entropies are equal, and adding up to 100% for each isomer. [c] See **3**. Dihedral angle is 0° when methyl eclipses the double bond, and has limits 0 ± 90° and 180 ± 90° for the descriptions *endo* and *exo* respectively. [d] Only three minima are found, see text. [e] Difference between energies of the 1,4- and 1,6-isomers.

Table 4 Calculated energy (kcal/mol^{-1}) of various conformations of 1,6- and 1,4-diisopropylcyclooctatetraenes and calculated populations.[b] Dihedral angles (°) are for the unique isopropyl group C–H bond with its attached double bond.[a]

	1,6-Isomer			1,4-Isomer[d]			
Conformation[c]	Dihedral angles/°	Energy/kcal mol^{-1}	Occupancy (%)	Dihedral angles/°	Energy/kcal mol^{-1}	Occupancy (%)	ΔE/kcal mol^{-1}[c]
ENDO,ENDO			38			35	
endo-in, endo-in	+24 −37	**13.911**		+33 −33	**14.417**		0.506
endo-in, endo-out	+39 +48	14.525		+33 +38	15.149		0.624
endo-out, endo-out	−49 +16	15.216		−40 +39	15.883		0.667
EXO,ENDO and ENDO,EXO			23 (both)			24 (both)	
exo, endo-out	+172 +34	14.718		+178 +39	15.380		0.662
endo-in, exo	+34 −177	**14.197**		+33 +178	**14.647**		0.450
EXO,EXO							
exo, exo	−179 +175	**14.429**	16	+178 +177	**14.836**	17	0.407

[a] See 3. Value is 0° when the unique hydrogen group eclipses the double bond, and has limits of 0 ± 90° and 180 ± 90° for the descriptions *endo* and *exo* respectively. [b] See footnote *b* in Table 3. [c] Difference between energies of 1,4- and 1,6-isomers.

Table 5 Calculated sum[a] of pairwise attractive interactions (kcal mol^{-1}) of the atoms of the alkyl groups in equivalent conformations of dialkylcyclooctatetraenes compared with differences in total steric energies

Difference in total energy[b]	Name of conformation	Pairwise interactions 1,6-isomer	Pairwise interactions 1,4-isomer	Difference[c] in pairwise interactions
Diethyl compound				
0.435	*endo-in, endo-in*	−0.524	−0.052	0.472
0.186	*endo-in, endo-out*	−0.304	−0.052	0.252
0.035	*endo-out, endo-out*	−0.122	−0.046	0.076
Diisopropyl compound				
0.506	*endo-in, endo-in*	−0.573	−0.074	0.499
0.450	*endo-in, exo*	−0.658	−0.084	0.574
0.407	*exo, exo*	−0.511	−0.092	0.419

[a] Sum of 49 and 100 pairwise interactions for the diethyl and diisopropyl compounds respectively. [b] The 1,6-compound is the more stable. [c] The 1,6-compound has the greater sum of attractive interactions.

influence each other, in the 1,6-conformation. The order of stabilities of conformations for the two isomers is so similar as to suggest that the greater stability of the 1,6-set of conformations comes simply from the proximity of the second substituent, rather than from any change that alkyl groups induce in each other's conformation.

The size of the alkyl groups methyl, ethyl, isopropyl, and *tert*-butyl as reflected by conformational free energy differences of the present equilibria at room temperature is interesting, see last column of Table 2. The *tert*-butyl group is not markedly larger than an isopropyl group which would agree with the two extra methyl groups being largely *out* and thus in positions of minimum steric attraction of the distant alkyl group. This contrasts with repulsive steric interactions where *tert*-butyl often has an effect markedly larger than isopropyl[20–24] as the extra methyl group is inevitably located in the position of maximum steric compression avoided by the two methyls of the isopropyl group.

The result for the *tert*-butyl, phenyl compound **1h–2h** is of some interest. Hirota and his colleagues have demonstrated[25] in many acyclic systems that *tert*-butyl and phenyl groups have a preference to be gauche to each other, which has been attributed to C–H • • • pi bonding. The free energy difference for **1h–2h** is 0.39 kcal mol^{-1}, almost the same as in the di-*tert*-butyl case. The phenyl group is presumably coplanar with the double bond of the ring, with none of its atoms within the cyclooctatetraene ring periphery, in contrast to how *tert*-butyl methyl groups are arranged, yet the attractive interactions are as great as in the di-*tert*-butyl case. This might imply

Table 6 Barriers (kcal mol^{-1}) to bond-shift and ring inversion processes in substituted cyclooctatetraenes (COT)[a]

Substituted cyclooctatetraene	Bond-shift barrier (T/K)	Ref.	Ring inversion barrier (T/K)	Ref.
COT	13.7 (263)	9		
COT-OR	14.9–16.2	10	12.4–12.7	10
COT-F	12 (240)	11		
COT-Ph	15.7 (304)	This work		
COT-C(Me)$_2$OH[a]	17.4 (314)	12	14.7 (271)	12
COT-Pr^i			14.8 (248)	13
COT-1,2(Me)$_2$	21.1 (395)	14		
COT-1,3(CH$_2$)$_7$	19.8 (298)	15	18.1 (298)	15
COT-1,3(CH$_2$)$_8$	18.4 (298)	15	16.4 (298)	15
COT-1,3(CH$_2$)$_9$	17.9 (298)	15	16.2 (298)	15
COT-1,2Me,CO$_2$Me	19.5 (261)	16		
COT-1,5(CH$_2$)$_8$	23.6 (298)	17		
COT-1,6Me,Bu	17.2 (324)	This work		
COT-1,6(Me)$_2$[b]	17.3 (325)	7		
COT-1,6(Et)$_2$	17.8 (322)	This work	15.7 (316)	This work
COT-1,4(Et)$_2$	17.8 (322)	This work	14.3 (288)	This work
COT-1,6Et,Bu	18.0 (327)	This work		
COT-1,6(Pr^i)$_2$	19.0 (359)	This work	16.6 (294)	This work
COT-1,4(Pr^i)$_2$	19.0 (359)	This work	15.7 (276)	This work
COT-1,6Ph,Bu^t	21.3 (404)	This work		
COT-1,6(Bu^t)$_2$[b]	22.6 (298)	1		
COT-3Me,1,2(CH$_2$)$_4$	25.9 (298)	18	23.5 (298)	18
COT-1,2,3(Me)$_3$	26.8 (363)	19		
COT-1,2,3,4(Me)$_4$	33.7 (433)	19		

[a] The compound studied was in fact hexadeuteriated on the ring. [b] The result is for the mixture of the 1,4- and 1,6-isomers.

stabilisation in the phenyl compound beyond what can be attributed to van der Waals attraction, that is Hirota's kind of C–H • • • pi interaction. Calculations suggest however that in the di-*tert*-butyl case, there is repulsion between the two nearest hydrogens of the two *tert*-butyl groups so the discrepancy between the results for **1d** and **1h**, if it is indeed real, does not have an unequivocal explanation.

It is an interesting speculation whether the **1**–**2** equilibrium might be solvent dependent. The alkyl groups of the 1,6-isomer are less exposed to the solvent than those of the 1,4-isomer so that in a lipophobic solvent the former might be additionally favoured. For the diethyl compound we observed the bond-shift equilibrium in a medium of 50% deuterium oxide–50% deuteriated tetrahydrofuran but the equilibrium constants were not appreciably different from those found for deuteriobenzene solution.

The use of molecular mechanics calculations in the study of attractive steric interactions deserves comment. Bond lengths calculated by molecular mechanics can be compared with experimental measurements and parameters can be adjusted to optimise a comparison. The energy of interaction of two atoms in a molecule, and by extension of two groups, is small and unmeasurable, and adjusting parameters to reproduce an experimentally observed separation of two distant atoms is impractical. Molecular mechanics programs therefore usually take van der Waals attractions and repulsions as varying with the inverse sixth and twelfth powers of the internuclear distance respectively. For each pair of atom types a value is chosen for the internuclear distance and the energy at the minimum energy point so as to optimise broadly the fit with what can be determined experimentally, *viz.* conformational energies, heats of formation, torsional angles, bond angles, and bond lengths.

Choice of program thus leaves much room for variation in the calculation of the interaction between two alkyl groups, whether repelling each other or attracting. The variation should be less however when observing what different programs predict for the difference in the size of the interaction in two structures being compared.

We used Allinger's MM2-82 program.[8a] Since this work was completed Allinger's MM3 program[8b] has become available and incorporates changes in van der Waals parameters tending to soften hydrogens, and giving a better fit of total energy, albeit marginally so for simple compounds. We have not used MM3 because further calculations will little embellish the present experimental results. A larger body of results, such as the present, may eventually illuminate such calculations.

Bond-shift and Ring Inversion Barriers.—The effect of substituents on the barrier to bond-shift in cyclooctatetraenes is quite complex[9–19] but remote substituents unlinked to each other are expected to cause it to increase, and this is borne out by the present results for the dialkyl compounds. It is convincingly argued[15,17] that the transition state for bond-shift is unlikely to have all atoms of the ring skeleton in one plane. During bond-shift, eclipsing of the substituent with the adjacent vinylic proton along a single bond of the ring no doubt increases, and the marked rise in the barrier on changing from the diisopropyl to the di-*tert*-butyl derivative (19.0 and 22.6 kcal mol^{-1}), that is, when a methyl group is necessarily directed along the single bond, shows the contribution to the bond-shift barrier of this eclipsing.

The ring inversion barriers also increase with substitution, which fits again with increased eclipsing interactions of the substituent during rotation about ring single bonds. Each C–C–C–C dihedral angle changes from about 70° to −70°. Eclipsing along all four single bonds, as implied by a planar transition state, may not be the easiest ring inversion pathway. Rotation about the various single bonds in some complex sequence involving successive planification of parts of the molecule may well achieve ring inversion with less overall eclipsing strain at any one point in the process. This would explain why the diisopropyl derivative has a ring inversion barrier little larger than the monoisopropyl compound whose barrier is very much more than the putative barrier of about 12 kcal mol^{-1} for cyclooctatetraene itself.

Table 7 Proton NMR chemical shift data for disubstituted cyclooctatetraenes

Compound	H2	H3	H4/6	H5	H7	H8	Alkyl
1,6-**1a**[a]		5.51 or	5.73		5.63	5.63	1.609
1,4-**2a**[a]	5.54	5.54		5.68 or	5.69		1.626
1,6-**1b**[a]		5.54 or	5.79		5.70	5.70	0.96, 1.80–2.06[c]
1,4-**2b**[a]	5.60	5.60		5.71 or	5.76		0.99, 1.80–2.06[c]
1,6-**1c**[b]		5.56 or	5.75		5.88	5.88	1.04,[d] 2.32
1,4-**2c**[b]	5.58	5.58		5.83 or	5.87		1.01,[d] 2.30

[a] In deuteriobenzene solution at 20 °C. [b] In deuteriochloroform solution at 25 °C. [c] On decoupling the methyl signal the methylene groups appear as AB-quartets (J 14.6) at 2.073 and 2.102 for the 1,4-isomer **2e** and at 2.070 and 2.142 for the 1,6-isomer **1e**. [d] The isopropyl methyl signals appear as two doublets (J 8.8) for each isomer at 0.991 and 0.994 for the 1,4-isomer **2f** and at 1.012 and 1.020 for the 1,6-isomer **1f**.

Table 8 Carbon-13 chemical shifts (δ) of disubstituted cyclooctatetraenes

Compound	C1	C2	C3	C4	C5	C6	C7	C8	C_a–C_d
1,6-**1a**	140.1	133.2	131.2		133.2	190.1	126.4		23.8
1,4-**2a**	138.9	127.1		138.9	135.0	130.0		135.0	23.5
1,6-**1b**	145.9	133.7	131.5		133.7	145.9	125.6		30.9, 13.6
1,4-**2b**	144.9	126.1		144.9	134.5	131.1		134.5	13.7, 30.8
1,6-**1c**	150.3	132.6	131.0		132.6	150.3	123.6		21.8, 22.2, 35.5
1,4-**2c**	149.2	124.0		149.2	132.4	131.5		132.4	21.8, 22.2, 35.4

Experimental

The diethyl and diisopropylcyclooctatetraenes **1b** and **1c** were prepared by alkylating Paquette's bridged sulfone[26] as used previously[7] to make dimethylcyclooctatetraene **1a**. The mixed butyl, alkylcyclooctatetraene was a by-product arising from alkylation of the intermediate sulfone by butyllithium.

The **1b**, **2b** mixture is a pungent clear yellow liquid emerging from a 10% w/w silicone oil column 10ft × 3/8 in at 200 °C with t_{ret} 600 s. (Found: M^+ 160.1270. Calc. for $C_{12}H_{16}$; M, 160.1252). The **1c**, **2c** mixture is a fragrant yellow oil with t_{ret} *ca.* 650 s under the same conditions (Found: M^+, 188.1578. Calc. for $C_{14}H_{20}$; M, 188.1565). The mixed 1,4- and 1,6-phenyl-*tert*-butylcyclooctatetraenes **1h**, **2h** were prepared by the method of Streitwieser and his collaborators,[27] (Found: M^+, 236.1552. Calc. for $C_{12}H_{20}$; M, 236.1565).

NMR spectra and equilibrium constants were obtained as described previously.[7] The only significant conformational variables are the torsional angles around the cyclooctatetraene to alkyl group bonds, which were not sought by Monte Carlo or molecular dynamics searches but by systematic driving of the two dihedral angles. That a minimum is true was verified by driving away from the minimum and finding a real barrier before the next minimum. No false minima were encountered.

References

1 M. H. Lyttle, A. Streitwieser Jr and R. Q. Klutz, *J. Am. Chem. Soc.*, 1981, **103**, 3232.
2 M. H. Lyttle, Ph.D. Thesis, University of California, Berkeley, 1982.
3 L. A. Paquette, G. J. Hefferon, R. Samodral and Y. Hanzawa, *J. Org. Chem.*, 1983, **48**, 1262.
4 N. L. Allinger, M. Frierson and F. A. van Catledge, *J. Am. Chem. Soc.*, 1982, **104**, 4592.
5 C. Tosi, *J. Comput. Chem.*, 1984, **5**, 248.
6 (*a*) Z. V. Todres, G. Ts. Ovsepyan, V. I. Bakhmutov, A. Yu. Kosnikov, S. V. Lindeman and Yu. T. Struchkov, *Russ. J. Org. Chem.*, 1989, **25**, 67; (*b*) M. R. Gottesfeld, F. A. Masoudi and D. E. Hansen, *Tetrahedron Lett.*, 1992, **33**, 447.
7 J. E. Anderson and P. A. Kirsch, *J. Chem. Soc., Perkin Trans. 2*, 1990, 885.
8 (*a*) N. L. Allinger and H. L. Flanagan, *J. Comput. Chem.*, 1983, **4**, 399; (*b*) N. L. Allinger, Y. H. Yuh and J.-H. Lii, *J. Am. Chem. Soc.*, 1989, **111**, 8551; (*c*) H. A. Y. Yu and M. Karplus, *J. Am. Chem. Soc.*, 1990, **112**, 5706, and references therein.
9 F. A. L. Anet, *J. Am. Chem. Soc.*, 1962, **84**, 671.
10 (*a*) J. F. M. Oth, *Pure Appl. Chem.*, 1971, **25**, 573; (*b*) J. F. M. Oth and R. Merenyi, *Tetrahedron Lett.*, 1966, 3087.
11 D. E. Gwynn, G. M. Whitesides and J. D. Roberts, *J. Am. Chem. Soc.*, 1965, **87**, 2862.
12 F. A. L. Anet, A. J. R. Bourn and Y. S. Lin, *J. Am. Chem. Soc.*, 1964, **86**, 3576.
13 G. W. Buchanan, *Tetrahedron Lett.*, 1972, 665.
14 L. A. Paquette, *Pure Appl. Chem.*, 1972, **54**, 987.
15 L. A. Paquette, T.-Z. Wang, J. Luo, C. E. Cottrell, A. E. Clough and L. B. Anderson, *J. Am. Chem. Soc.*, 1990, **112**, 239.
16 F. A. L. Anet and L. A. Bock, *J. Am. Chem. Soc.*, 1968, **90**, 7130.
17 L. A. Paquette, M. P. Trova, J. Luo, A. E. Clough and L. B. Anderson, *J. Am. Chem. Soc.*, 1990, **112**, 228.
18 L. A. Paquette and T.-Z. Wang, *J. Am. Chem. Soc.*, 1988, **110**, 8192.
19 J. M. Gardlik, L. A. Paquette and R. Gleiter, *J. Am. Chem. Soc.*, 1979, **101**, 1617.
20 M. E. Squillacote and J. M. Neth, *Magn. Reson. Chem.*, 1987, **25**, 53, and references cited therein.
21 F. A. L. Anet and M. E. Squillacote, *J. Am. Chem. Soc.*, 1975, **97**, 3243.
22 H. Booth and J. R. Everett, *J. Chem. Soc., Perkin Trans. 2*, 1980, 255 and references therein.

23 B. van de Graaf, J. M. A. Baas and B. M. Wepster, *Recl. Trav. Chim. Pays-Bas*, 1978, **97**, 268.
24 E. Osawa, J. B. Collins and P. v. R. Schleyer, *Tetrahedron*, 1977, **33**, 2667.
25 M. Nishio and M. Hirota, *Tetrahedron*, 1989, **45**, 7201.
26 L. A. Paquette, S. V. Ley, R. H. Meisinger, R. K. Russell and M. Oku, *J. Am. Chem. Soc.*, 1974, **96**, 5806.
27 M. J. Miller, M. H. Lyttle and A. Streitwieser Jr., *J. Org. Chem.*, 1981, **46**, 1977.

Paper 2/02400D
Received 11*th May* 1992
Accepted 2*nd July* 1992