

## Molecular Mechanics Calculations on Alkanes and Non-conjugated Alkenes

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A new force field has been developed for the calculation of geometric and thermodynamic properties of alkanes and non-conjugated alkenes. The force field is a significant improvement on those of its kind in current usage and reproduces the heats of formation and hydrogenation of 60 diverse alkanes and alkenes with an average absolute difference of  $0.55 \text{ kcal mol}^{-1}$  between observed and calculated enthalpies. The corresponding figures for geometric properties are  $0.009 \text{ \AA}$ ,  $0.6^\circ$ , and  $0.9^\circ$ , in bond lengths, bond angles, and torsion angles, respectively over a set of 93 observations. Particular attention has been paid to the structural and thermodynamic properties of molecules which are not adequately reproduced by previous force fields.

MOLECULAR mechanics calculations have, in recent years, proved extremely useful for the investigation of a diversity of topics associated with organic chemistry, including molecular conformations, molecular thermodynamic properties, reaction mechanisms, kinetics, vibrational spectra and the interpretation of dynamic n.m.r. spectra.<sup>1-3</sup> The reliability of these calculations

<sup>1</sup> J. D. Dunitz and H. B. Burgi in 'MTP International Review of Science, Physical Chemistry Series Two,' Butterworths, London, 1976, vol. 11, ch. 4.

depends on the quality of the force field employed, which in turn depends upon the extent and precision of the experimental data used to parameterise the force field.

In developing a force field a set of trial force constants is systematically adjusted in order to obtain the best

<sup>2</sup> C. Altona and D. H. Faber, *Topics Current Chem.*, 1974, **45**, 1.

<sup>3</sup> E. M. Engler, J. D. Andose, and P. von R. Schleyer, *J. Amer. Chem. Soc.*, 1973, **95**, 8005.

fit between sets of observed and calculated quantities. The observed quantities usually comprise structural parameters derived from electron diffraction (bond lengths and angles, torsion angles, and non-bonded

mental data; but perhaps not too surprising in view of the enormity of such a task (to say nothing of the computer time involved!). We are not at this stage concerned with vibrational frequencies and our force field

TABLE 1  
Force field parameters

Atom key

1 = H, 2 = C(sp<sup>2</sup>), 3 = C(sp<sup>3</sup>)

Force constants are in kcal mol<sup>-1</sup> Å<sup>-2</sup> or in kcal mol<sup>-1</sup> deg<sup>-2</sup>; energies are in kcal mol<sup>-1</sup>

Bond stretching		Type 1	Type 2	$\frac{1}{2}k_1$	$l_0$					
		1	2	346.0	1.089					
		1	3	331.2	1.100					
		2	2	670.0	1.335					
		2	3	319.5	1.501					
		3	3	316.8	1.520					
van der Waals		Type 1	Type 2	$r_1^*$	$r_2^*$	$\epsilon$				
		1	1	3.10	0.0	0.016 0				
		1	2	3.53	0.0	0.033 0				
		1	3	3.35	0.0	0.029 9				
		2	2	4.00	0.0	0.076 0				
		2	3	3.60	0.0	0.080 0				
		3	3	3.85	0.0	0.120 0				
Angle bending		Type 1	Type 2	Type 3	$\frac{1}{2}k_\theta$	$k'_\theta$	$^*\theta_1^0$	$\theta_2^0$	$\theta_3^0$	$\theta_4^0$
		1	2	1	0.005 5	0.009 6	118.6			
		1	2	2	0.006 0	0.0	121.7	120.4		
		1	2	3	0.006 0	0.0		117.5		
		2	2	3	0.012 0	0.009 6		122.3	121.0	
		3	2	3	0.023 3	0.009 6			116.4	
		1	3	1	0.007 2	0.009 6	108.2	109.1		
		1	3	2	0.008 8	0.009 6	110.5	110.0	110.2	
		1	3	3	0.008 8	0.009 6	109.0	109.2	109.2	
		2	3	2	0.009 0	0.009 6		111.0	110.1	109.5
		2	3	3	0.009 0	0.009 6		110.4	110.1	109.5
		3	3	3	0.012 0	0.009 6		110.4	110.1	109.5
Torsion		Type 1	Type 2	Type 3	Type 4	$\frac{1}{2}k_\omega$	$s$	$n$		
		1	2	2	1	6.250 0	-1.0	2.0		
		1	2	2	3	6.250 0	-1.0	2.0		
		3	2	2	3	6.250 0	-1.0	2.0		
		1	2	3	1	0.136 7	1.0	3.0		
		1	2	3	2	0.136 7	1.0	3.0		
		1	2	3	3	0.136 7	1.0	3.0		
		2	2	3	1	0.062 9	-1.0	3.0		
		2	2	3	2	0.062 9	-1.0	3.0		
		2	2	3	3	0.062 9	-1.0	3.0		
		3	2	3	1	0.062 9	1.0	3.0		
		3	2	3	2	0.062 9	1.0	3.0		
		3	2	3	3	0.062 9	1.0	3.0		
		1	3	3	1	0.110 0	1.0	3.0		
		1	3	3	2	0.110 0	1.0	3.0		
		1	3	3	3	0.110 0	1.0	3.0		
		2	3	3	2	0.020 0	1.0	3.0		
		2	3	3	3	0.062 9	1.0	3.0		
		3	3	3	3	0.062 9	1.0	3.0		
Out-of-plane bending		Type 1	Type 2	Type 3	Type 4	$\frac{1}{2}k_x$				
		3	2	2	1	0.002 0				
		3	2	2	3	0.002 0				

\* Superscript indicates the degree of substitution at the central atom.

distances) and heats of formation or vibrational frequencies culled from as large and varied a sample as possible of the types of molecule under consideration. It is perhaps regrettable that no one force field is adequately parameterised on the basis of all three kinds of experi-

\* Hereafter 'alkene force field' should be interpreted as including an alkane capability.

is parameterised solely on the basis of geometric and thermodynamic data.

During the two or three years since currently extant alkane/alkene \* force fields were developed<sup>4,5</sup> a

<sup>4</sup> N. L. Allinger and J. T. Sprague, *J. Amer. Chem. Soc.*, 1972, **94**, 5734.

<sup>5</sup> O. Ermer and S. Lifson, *J. Amer. Chem. Soc.*, 1973, **95**, 4121.

TABLE 2

(a) Calculated and experimental heats of formation,  $\Delta H_f^\circ$  (gas, 25 °C) and calculated steric energies,  $E_s$  (kcal mol<sup>-1</sup>)

Compound	$E_s$	$\Delta H_f^\circ(\text{gas})_{\text{calc.}}$	$\Delta H_f^\circ(\text{gas})_{\text{obs.}}$	$\Delta_{\text{C-O}}$	Ref.
Ethylene	0.11	12.67	12.47	0.20	d, e
Propene	0.44	4.91	4.88	0.03	d, e
But-1-ene	0.80	-0.01	-0.11	0.10	d, e
<i>cis</i> -But-2-ene	1.99	-1.62	-1.77	0.15	d, e
<i>trans</i> -But-2-ene	0.68	-2.93	-2.83	-0.10	d, e
Isobutene	0.85	-3.61	-4.15	0.54	d, e
2-Methylbut-1-ene	1.48	-8.26	-8.55 ± 0.18	0.29	d
3-Methylbut-1-ene	1.98	-6.19	-6.61 ± 0.18	0.42	d
2-Methylbut-2-ene	2.53	-10.01	-10.15	0.14	d, e
2,3-Dimethylbut-1-ene	2.47	-14.72	-15.19 ± 0.50	0.47	d
2,3-Dimethylbut-2-ene	4.91	-16.56	-16.42 ± 0.25	-0.14	d
3,3-Dimethylbut-1-ene	2.68	-14.50	-14.51 ± 0.25	0.01	d
Pent-1-ene	1.02	-5.08	-5.33 ± 0.31	0.25	d
<i>cis</i> -Pent-2-ene	2.23	-6.67	-6.86	0.19	d, e
<i>trans</i> -Pent-2-ene	0.98	-7.92	-7.76	-0.16	d, e
2-Methylpent-2-ene	2.66	-15.17	-15.13	-0.04	d, e
2-Methyl- <i>trans</i> -pent-2-ene	3.02	-14.81	-15.09 ± 0.32	0.28	d
3-Methyl- <i>cis</i> -pent-2-ene	2.67	-15.16	-14.89 ± 0.36	-0.27	d
4-Methyl- <i>trans</i> -pent-2-ene	2.11	-14.15	-14.70 ± 0.35	0.55	d
4-Methyl- <i>cis</i> -pent-2-ene	2.60	-13.66	-13.74 ± 0.29	0.08	d
4,4-Dimethylpent-1-ene	2.16	-20.31	-19.32	-0.99	d, e
2,4,4-Trimethylpent-1-ene	3.43	-27.97	-26.37 ± 0.30	-1.60	d
Penta-1,4-diene	0.96	25.15	25.25 ± 0.25	-0.10	d
<i>trans</i> -Hex-2-ene	1.18	-13.01	-12.88 ± 0.39	-0.13	d
<i>cis</i> -Hex-2-ene	2.40	-11.79	-125.1 ± 0.33	0.72	d
Hexa-1,5-diene	1.29	20.19	20.05	0.14	d, e
Methylcyclopentane	8.13	-25.66	-25.50	-0.16	e
Cyclopentene	7.70	8.75	8.22	0.53	d-f
1-Methylcyclopentene	7.76	-0.12	-0.6 ± 0.5	0.48	d
3-Methylcyclopentene	7.81	1.51	2.00 ± 0.5	-0.49	d
Cyclohexane	3.45	-28.27	-29.50 ± 0.15	1.23	d
Methylcyclohexane	3.47	-35.61	-36.98 ± 0.25	1.37	d
Cyclohexene	2.78	-1.45	-1.18	-0.27	d, e
1-Methylcyclohexene	2.84	-10.32	-10.34 ± 0.20	0.02	d
Cyclohexa-1,4-diene	3.17	26.43	26.3	0.13	f
Cycloheptane	8.33	-28.69	-28.22 ± 0.18	-0.47	d
Cycloheptene	5.98	-3.54	-2.07	-1.47	d-f
<i>cis</i> -Cyclo-octene	7.88	-6.93	-6.47	-0.46	d-f
<i>trans</i> -Cyclo-octene	18.60	3.79	4.1 <sup>a</sup>	-0.31	f
Norbornane	19.47	-11.72	-12.42 ± 0.70	0.70	g
Norborna-2,5-diene	31.32	55.11	54.80 ± 0.55 <sup>b</sup>	0.31	h
5-Ethylidenenorborn-2-ene	25.22	34.79	34.82 ± 0.43	-0.03	i
Adamantane	11.63	-29.61	-30.65 ± 0.98	1.04	g
1-Methyladamantane	11.34	-38.90	-40.57 ± 0.34	1.67	8 <sup>b</sup>
2-Methyladamantane	12.91	-35.69	-35.66 ± 0.62	-0.03	8 <sup>b</sup>
1,3,5-7-Tetramethyladamantane	10.23	-67.05	-67.15 ± 0.80	0.10	8 <sup>b</sup>
Protoadamantane	21.79	-19.45	-20.54 ± 0.60	1.09	8 <sup>b</sup>
Diamantane	17.69	-33.06	-32.60 ± 0.58	-0.46	8 <sup>b</sup>
4-Methyldiamantane	17.33	-42.43	-43.53 ± 0.30	1.10	8 <sup>b</sup>
3-Methyldiamantane	18.76	-39.31	-37.60 ± 0.58	-1.71	8 <sup>b</sup>
1-Methyldiamantane	19.30	-40.46	-39.85 ± 0.85	-0.61	8 <sup>b</sup>
Perhydrotriquinacene	17.77	-23.46	-24.47 ± 0.86	1.01	8 <sup>a</sup>
Bicyclo[3.3.1]nonane	11.08	-30.69	-30.46 ± 0.55	-0.23	j
Bicyclo[3.3.2]decane	18.97	-28.08	-25.3 ± 1.7	-2.78	j

(b) Calculated and observed heats of hydrogenation,  $-\Delta H$ , and calculated steric energy differences (kcal mol<sup>-1</sup>)

	$E_s$	$-\Delta H_{\text{calc.}}$	$-\Delta H_{\text{obs.}}$	$\Delta_{\text{C-O}}$	Ref.
<i>cis,cis</i> -Cyclo-octa-1,5-diene → <i>cis</i> -cyclo-octene	2.22	29.71	30.70 ± 0.07	-0.99	34
<i>cis,cis,cis</i> -Cyclonona-1,4,7-triene → <i>cis</i> -cyclononene	-2.76	52.22	53.26 ± 0.06	1.04	34
<i>cis,cis</i> -Cyclodeca-1,6-diene → <i>cis</i> -cyclodecene	-4.31	23.18	23.06 <sup>c</sup>	0.12	34
<i>trans,trans</i> -Cyclodeca-1,6-diene → <i>trans</i> -cyclodecene	-4.55	22.94	23.62 <sup>c</sup>	-0.68	34
<i>trans,trans</i> -Cyclodeca-1,6-diene → cyclodecane	-7.28	47.70	47.63 <sup>c</sup>	0.07	34
<i>cis,cis</i> -Cyclodeca-1,6-diene → cyclodecane	-9.46	45.52	43.73 <sup>c</sup>	1.79	34
Standard deviation over 60 compounds				0.79	

<sup>a</sup> The experimental  $\Delta H_f^\circ$  includes 1 kcal mol<sup>-1</sup> added to correct for work done in dissolution. <sup>b</sup> Mean of 3 experimental heat of formation values. <sup>c</sup> Sample sufficient for one determination only of the diene.  $\Delta_{\text{C-O}} = \Delta H_f^\circ(\text{gas})_{\text{calc.}} - \Delta H_f^\circ(\text{gas})_{\text{obs.}}$  in the heat of formation cases.  $\Delta_{\text{C-O}} = -\Delta H_{\text{calc.}} - (-\Delta H)_{\text{obs.}}$  in the heat of hydrogenation cases. Standard deviation for the experimental heats of formation are reported when the information is available. <sup>d</sup> J. D. Cox and G. Pilcher, 'Thermochemistry of Organic and Organometallic Compounds,' Academic Press, New York, 1970. <sup>e</sup> D. R. Stull, E. F. Westrum, jun., and G. C. Sinke, 'The Chemical Thermodynamics of Organic Compounds,' Wiley, New York, 1969. <sup>f</sup> S. W. Benson, F. R. Cruickshank, D. M. Golden, G. R. Haugen, H. E. O'Neal, A. S. Rodgers, R. Shaw, and R. Walsh, *Chem. Rev.*, 1969, **69**, 279. <sup>g</sup> R. H. Boyd, S. N. Sanwai, S. Shary-Tehrany, and D. McNally, *J. Phys. Chem.*, 1971, **75**, 1264. <sup>h</sup> R. Walsh and J. M. Wells, *J. Chem. Thermodynamics*, 1975, **7**, 149. <sup>i</sup> M. P. Kozina, L. P. Timofeeva, S. M. Skuratov, N. A. Belikova, E. M. Milvitskaya, and A. F. Platé, *J. Chem. Thermodynamics*, 1971, **3**, 563. <sup>j</sup> W. Parker, W. V. Steele, and I. Watt, *J. Chem. Thermodynamics*, 1977, **9**, 307.

TABLE 3

## Experimental and calculated structural parameters

Compound	Structure		Exp.	Calc.	Calc. — Exp.	Ref.
Ethylene		$l_{12}$ $l_{23}$ $\theta_{123}$	1.335 1.090 121.7	1.336 1.089 121.3	0.001 -0.001 -0.4	a
Propene		$l_{12}$ $l_{23}$ $\theta_{123}$	1.336 1.501 124.3	1.337 1.505 123.6	0.001 0.004 -0.7	b
<i>cis</i> -But-1-ene		$\theta_{123}$ $\theta_{234}$	126.7 114.8	125.5 115.4	-1.2 0.6	c
<i>skew</i> -But-1-ene		$\theta_{123}$ $\theta_{234}$	125.4 112.1	123.6 111.5	-1.7 -0.6	c
Isobutene		$\theta_{423}$	115.3	116.2	0.9	d
<i>trans</i> -But-2-ene		$l_{23}$ $l_{12}$ $\theta_{123}$	1.508 1.347 123.8	1.506 1.338 123.6	-0.002 -0.009 -0.2	e
2-Methyl- <i>skew</i> -But-1-ene		$\phi_{1234}$	$72.7 \pm 5.0$	71.5	-1.2	f
2,3-Dimethylbut-2-ene		$l_{12}$ $l_{24}$ $\theta_{123}$	1.511 1.353 113.2	1.511 1.346 114.4	0.000 -0.007 1.2	g
Cyclopentene		$\phi_{1534}$	156.7	160.9	4.2	h
Cyclohexene		$\phi_{1234}$ $\phi_{2345}$ $\phi_{3456}$	-15.2 44.9 -60.2	-15.3 45.4 -62.2	-0.1 0.5 -2.0	i
<i>cis,cis</i> -Cyclodeca-1,6-diene		$l_{12}$ $l_{23}$ $\theta_{123}$ $\theta_{345}$ $\phi_{1234}$ $\phi_{2345}$	1.326 1.506 128.2 114.1 -114.7 58.2	1.340 1.510 127.0 113.6 -115.5 59.5	0.014 0.004 -1.2 -0.5 -0.8 1.3	42
Norbornadiene		$l_{12}$ $l_{23}$ $\theta_{174}$ $\langle l_{17} \rangle$ $\phi_{2145}$	1.535 1.343 94.1 1.544 115.6	1.510 1.337 94.3 1.526 116.3	-0.025 -0.006 0.2 -0.018 0.7	4, j
Bicyclo[2.2.2]oct-2-ene		$\phi_{2143}$ $\phi_{1234}$	121.2 0.0	120.4 0.0	-0.8 0.0	k

TABLE 3 (Continued)

Compound	Structure		Exp.	Calc.	Calc. — Exp.	Ref.
Bicyclo[2.2]octa-2,5-diene		$\phi_{2145}$ $\phi_{1784}$	123.4 0.0	123.4 0.0	0.0 0.0	<i>k</i>
Cyclohexa-1,4-diene		$l_{12}$ $l_{16}$ $\theta_{234}$ $\theta_{345}$ $\phi_{1244}$	1.334 1.496 113.3 123.5 0.0	1.338 1.509 113.2 123.4 0.0	0.004 0.013 -0.1 -0.1 0.0	<i>l</i>
Pin-2-ene		$l_{12}$ $\theta_{176}$ $\theta_{123}$ $\theta_{217}$ $\theta_{1,2,10}$ $\phi_{4365}$	1.34 $112 \pm 3$ $118 \pm 3$ $118 \pm 3$ 126 $146 \pm 8$	1.34 108 118 119 125 142	0.00 -4 0 1 -1 -4	<i>m</i>
Cyclohexane		$l_{CC}$ $\theta_{CCC}$ $\phi_{CCCC}$	1.528 111.3 55.2	1.530 111.3 55.2	0.002 0.0 0.0	<i>n, o</i>
Cyclodecane ( $C_{2h}$ average)		$\theta_{345}$ $\theta_{456}$ $\theta_{567}$ $\phi_{10,1,2,3}$ $\phi_{1234}$ $\phi_{2345}$ $r[H(6) \cdots H(9)]$ $r[H(2) \cdots H(6)]$	118.0 118.1 114.7 -152 55 66 2.08 1.94	117.9 117.6 114.9 -152 55 68 2.07 1.94	-0.1 -0.5 0.2 0 0 2 -0.01 0.00	18, <i>p</i>
Adamantane		$\theta_{123}$ $\theta_{234}$ $\langle l_{CC} \rangle$	110.0 109.2 1.534	110.0 109.2 1.536	0.0 0.0 0.002	<i>q</i>
Diamantane		$\langle l_{CC} \rangle$ $\langle \theta_{CCC} \rangle$ $\theta_{11,12,13}$ $\theta_{5,13,12}$ $\theta_{8,5,13}$ $\theta_{561}$	1.535 109.5 108.8 110.2 110.2 108.7	1.537 109.4 109.2 110.0 109.9 109.0	0.002 -0.1 0.4 -0.2 -0.3 0.3	<i>r</i>
<i>cis,cis</i> -Cyclo-octa-1,5-diene		$l_{12}$ $l_{23}$ $l_{34}$ $\theta_{123}$ $\theta_{234}$ $r(C1 \cdots C5)$ $r(C1 \cdots C6)$ $r(C2 \cdots C6)$ $r(C3 \cdots C7)$ $r(C4 \cdots C7)$ $r(C4 \cdots C8)$	1.341 1.502 1.554 127.8 116.8 3.30 3.05 3.32 3.82 3.19 3.13	1.340 1.512 1.530 127.8 115.8 3.39 3.08 3.31 3.81 3.19 3.05	-0.001 0.010 -0.024 0.0 -1.0 0.09 0.03 -0.01 -0.01 0.00 -0.08	27, <i>s</i>
<i>trans,trans,trans</i> -Cyclododeca-1,5,9-triene ( $D_3$ average)		$l_{23}$ $l_{34}$ $l_{45}$ $\phi_{234}$ $\theta_{245}$ $\phi_{1234}$ $\phi_{2345}$ $\phi_{12345}$	1.54 1.49 1.32 111.1 124.1 63.4 -116.5 178.0	1.53 1.51 1.34 112.1 123.5 61.6 -115.0 177.9	-0.01 0.02 0.02 1.0 -0.6 -1.8 1.5 -0.1	

considerable body of potentially useful experimental data has been gathered which should facilitate the definition of an improved alkene force field. These recent data include a small but useful sample pertaining to the usually neglected medium-sized ring dienes which has been incorporated into the new force field in order that such compounds may be investigated with a degree of confidence in the outcome.\* The remainder of our set of reference observations is drawn from the structural and thermodynamic constants of a large and varied group of saturated and unsaturated hydrocarbons.

Before describing the derivation of our alkene force field we noted that two aspects, in particular, of the subject required attention. (a) It is well known that a proper choice of non-bonded potential functions is crucial to the success of any force field parameterisation<sup>1-3</sup> and it is in just this area that recent calculations<sup>7</sup> and experimental work<sup>8,9</sup> have revealed shortcomings in some current parameterisations; particularly where repulsive H...H interactions are concerned. (b) Professor P. von R. Schleyer has provided us with a list of polycyclic hydrocarbons whose heats of formation are poorly reproduced by current alkene force fields,† in order that we might attempt to improve upon this situation. Both these topics are discussed in more detail in succeeding sections.

Finally, we have tried to keep the force field as simple as possible and to this end have adopted the same functional form (although with different force constants) as that of Schleyer's alkane force field.<sup>3</sup> There is a small price to be paid for this simplicity but we have found that the neglect of cross terms, such as the stretch-bend,<sup>10</sup> does not detract seriously from the utility of our force field. Indeed, in the examples to be discussed there were no major differences between the results obtained with our force field and with the Lifson-Ermer CFF which is based on an entirely different philosophy.

*The Force Field.*—The steric energy ( $E_s$ ) of a molecule is defined as the sum of the contributions from each of the terms describing potential energy as a function of molecular deformations from an arbitrary reference

\* Favini has performed extensive calculations on the six- to ten-membered-ring cycloalkenes and cycloalkadienes but unfortunately the force field and minimisation procedures used, throughout, are only approximate. Nevertheless, although the relative enthalpies of the various conformations may not be reliable the geometrical descriptions are sufficiently accurate to serve as a starting point for more refined calculations. The key to this series of publications appears in ref. 6 of the present paper.  
† We thank Professor Schleyer for this information.

geometry [equation (1)];  $l$ ,  $\theta$ ,  $r$ , and  $\omega$  are bond lengths, bond angles, 1—4 and higher interatomic distances, and torsion angles, respectively. The improper torsion angle

$$E_s = \sum_l \frac{1}{2} k_l (l - l_0)^2 + \sum_\theta \frac{1}{2} k_\theta (\Delta\theta^2 - k'_\theta \Delta\theta^3) + \sum_\omega \frac{1}{2} k_\omega (1 + s \cos \omega) + \sum_r \epsilon \{ -2/\alpha^6 + \exp[12(1 - \alpha)] \} + \sum_\chi \frac{1}{2} k_\chi (180 - \chi)^2 \quad (1)$$

$$\alpha = r/(r_1^* + r_2^*); \quad \Delta\theta = \theta - \theta_0$$

$\chi$  describes out-of-plane bending at the trigonal atoms.<sup>11</sup> The values of the force constants  $k_l$ ,  $k_\theta$ ,  $k'_\theta$ ,  $k_\omega$ ,  $\epsilon$ ,  $k_\chi$  and the equilibrium geometric parameters  $l_0$ ,  $\theta_0$ ,  $s$ ,  $n$ , and  $r^*$  are given in Table 1. The force constants were obtained by trial-and-error adjustment of the initial estimates, which were taken from the literature,<sup>3,5</sup> until satisfactory agreement was obtained with the enthalpies of formation and hydrogenation listed in Table 2 and the conformational data of Table 3. Notice that by taking initial values for the force constants from previously published work there is no implication that such values are directly transferable from one force field to another, but rather that they are likely to be of the correct order of magnitude and therefore will allow a start to be made on the process of refinement. Notice also, that although the functional form of Schleyer's force field is retained, the force field described herein is completely independent and indeed gives radically different results for some key molecules (see Results and Discussion section).

Enthalpies of formation are calculated by adding the steric energy to the sum of the appropriate group enthalpy increments. Values for the latter are given in Table 4 and were obtained from the steric energies and experimental enthalpies by a linear least-squares procedure.

The assumptions inherent in the partition of potential energy into various components due to easily visualised deformations, the derivation of force constants, and the rationale behind the method of calculating enthalpies

<sup>6</sup> G. Buemi, F. Zuccarello, and G. Favini, *J. Mol. Struct.*, **1974**, **21**, 41.

<sup>7</sup> (a) D. N. J. White and M. J. Bovill, *J. Mol. Struct.*, **1976**, **33**, 273; (b) See note 19 in R. H. Boyd, *J. Amer. Chem. Soc.*, **1975**, **97**, 5353; (c) S. Fitzwater and L. S. Bartell, *ibid.*, **1976**, **98**, 5107.

<sup>8</sup> T. Clark, T. McO. Knox, H. Mackle, and M. A. McKervey, *J.C.S. Chem. Comm.*, **1975**, 666.

<sup>9</sup> T. Clark, T. McO. Knox, H. Mackle, M. A. McKervey, and J. J. Rooney, *J. Amer. Chem. Soc.*, **1975**, **97**, 3835.

<sup>10</sup> O. Ermer, *Tetrahedron*, **1974**, **30**, 3103.

<sup>11</sup> A. Warshel, M. Levitt, and S. Lifson, *J. Mol. Spectroscopy*, **1970**, **33**, 84.

#### Footnotes to Table 3.

- <sup>a</sup> K. Kuchitsu, *J. Chem. Phys.*, **1966**, **44**, 906. <sup>b</sup> D. R. Lide and D. Christensen, *J. Chem. Phys.*, **1961**, **35**, 1374. <sup>c</sup> S. Kondo, E. Hirota, and Y. Morino, *J. Mol. Spectroscopy*, **1968**, **28**, 471. <sup>d</sup> L. H. Scharpen and V. W. Laurie, *J. Chem. Phys.*, **1963**, **39**, 1732. <sup>e</sup> A. Almeningen, I. M. Anfinsen, and A. Haaland, *Acta Chem. Scand.*, **1970**, **24**, 43. <sup>f</sup> T. Shimanouchi, Y. Abe, and K. Kuchitsu, *J. Mol. Struct.*, **1968**, **2**, 82. <sup>g</sup> I. Tokue, T. Fukuyama, and K. Kuchitsu, *J. Mol. Struct.*, **1974**, **23**, 33. <sup>h</sup> J. Laane and R. C. Lord, *J. Chem. Phys.*, **1967**, **47**, 4941. <sup>i</sup> J. F. Chiang and S. H. Bauer, *J. Amer. Chem. Soc.*, **1969**, **91**, 1898. <sup>j</sup> A. Yokozeki and K. Kochitsu, *Bull. Chem. Soc. Japan*, **1971**, **44**, 2356. <sup>k</sup> A. Yokozeki and K. Kochitsu, *Bull. Chem. Soc. Japan*, **1971**, **44**, 1783. <sup>l</sup> G. Dallinga and L. H. Toneman, *J. Mol. Struct.*, **1967**, **1**, 117. <sup>m</sup> B. A. Arbutov and V. A. Naumov, *Doklady Akad. Nauk S.S.R.*, **1964**, **158**, 376. <sup>n</sup> H. J. Geise, H. R. Buys, and F. C. Mijlhoff, *J. Mol. Struct.*, **1971**, **9**, 447. <sup>o</sup> M. Davis and O. Hassel, *Acta Chem. Scand.*, **1970**, **17**, 1181. <sup>p</sup> J. D. Dunitz, 'Perspectives in Structural Chemistry,' ed. J. D. Dunitz and J. A. Ibers, Wiley, New York, **1968**, vol. 2, p. 27. <sup>q</sup> I. Hargittai, *Chem. Comm.*, **1971**, 1499. <sup>r</sup> I. L. Karle and J. Karle, *J. Amer. Chem. Soc.*, **1965**, **87**, 919. <sup>s</sup> M. D. Glick and L. F. Dahl, *J. Organometallic Chem.*, **1965**, **3**, 200. <sup>t</sup> A. Immirzi and G. Allegra, *Atti Accad. naz. Lincei, Rend. Classe Sci. fis. mat. nat.*, **1967**, **43**, 338.

of formation have been discussed at length in recent reviews,<sup>1-3</sup> to which reference should be made for further clarification.

TABLE 4  
Group enthalpy increments (kcal mol<sup>-1</sup>)

		E.s.d.
=CH <sub>3</sub>	6.28	0.19
=CH	8.46	0.07
=C	9.79	0.32
-CH <sub>3</sub>	-10.26	0.11
-CH <sub>2</sub>	-5.29	0.04
-CH	-2.38	0.06
-C	-1.12	0.23

*Minimisation.*—Energy minimisation is accomplished by means of a two-stage iterative Newton-Raphson procedure which we have found to be one of the few completely effective optimisation algorithms used in molecular mechanics calculations.

The first stage is an approximation to the general quasi-Newton iteration [equation (2)] where  $x$  are the

$$x_{k+1} = x_k - F^+ \nabla E_s(x) \quad (2)^*$$

cartesian co-ordinates and  $E_s$  is the steric energy of the molecule under consideration. Setting  $F = \partial^2 E_s / \partial x_i \partial x_j$ ;  $i, j \leq 3$  for each atom is very effective for bringing a crude, trial conformation into the vicinity of the minimum, but efficiency is poor thereafter. At this stage recourse is made to the quadratically convergent Newton-Raphson procedure, where  $F = \partial^2 E_s / \partial x_i \partial x_j$ ;  $i, j = 1, 3n$  and  $n$  is the number of atoms, which converges rapidly on the minimum (or maximum!). Typically 100 iterations of stage one will reduce the components of  $\nabla E$  to 0.1 kcal mol<sup>-1</sup>Å<sup>-1</sup> and three subsequent iterations of stage two to 10<sup>-8</sup> kcal mol<sup>-1</sup>Å<sup>-1</sup> for a thirty-atom molecule, at the expense of a minute or two of computer time.

The merits of the above procedure have been discussed previously<sup>13</sup> but we stress that second-derivative procedures give access to both minimisation and maximisation (for calculating transition state structures) in addition to the means of distinguishing between the two possibilities.<sup>14</sup>

In order to facilitate future improvements in the force field, numerical first and second derivatives were used throughout the following calculations. The values of the first derivatives did not exceed 10<sup>-8</sup> kcal mol<sup>-1</sup>Å<sup>-1</sup> at the minimum or maximum in any of the calculations.

## RESULTS AND DISCUSSION

A complete discussion of all the calculations performed with the new force field would be very lengthy, so we have restricted comment to those cases where something may be added to an existing controversy or where completely novel results are being described.

\* Where  $F^+$  is the generalised inverse<sup>12</sup> of  $F$ .

<sup>12</sup> A. Warshel and S. Lifson, *J. Chem. Phys.*, 1970, **53**, 582.

<sup>13</sup> D. N. J. White and O. Ermer, *Chem. Phys. Letters*, 1975, **31**, 111.

<sup>14</sup> O. Ermer, *Tetrahedron*, 1975, **31**, 1849.

<sup>15</sup> J. B. Hendrickson, *J. Amer. Chem. Soc.*, 1967, **89**, 7036, 7043, 7047.

*Cyclodecane.*—The boat-chair-boat (BCB)<sup>15</sup> conformation is calculated to be the most favourable and is preferred to the twist chair-chair (TCCC)<sup>3</sup> variant by 0.5 kcal mol<sup>-1</sup>. There is an overwhelming variety of experimental evidence in support of our conclusion<sup>7</sup> and indeed the BCB conformation persists in the solid, liquid, and gaseous states and even survives the replacement of ring carbon by oxygen atoms<sup>16</sup> or the introduction of an oxo-group.<sup>17</sup> The Ermer-Lifson force field (CFF)<sup>5</sup> yields the same result as our calculations although Schleyer's (SFF)<sup>3</sup> and Allinger's (AFF)<sup>4</sup> force fields do not. This discrepancy, which we have discussed,<sup>7</sup> arises because AFF and SFF overestimate the repulsive nature of the six very short (*ca.* 1.9 Å) H···H non-bonded interactions in the BCB conformation of cyclodecane. The corresponding non-bonded distances in the TCCC conformation are longer and the improper scaling of the H···H potentials to the rest of the force field results in an apparently lower steric energy for this conformation. We have found that a minor revision of the H···H potential in SFF leads to the BCB conformation being preferred.<sup>7</sup>

As a result of a high precision neutron diffraction study of cyclodecane its molecular geometry is defined within very narrow limits<sup>18</sup> and it is gratifying that our force field reproduces the experimental geometry almost exactly (Table 3).

*Polycyclic Alkanes.*—As mentioned previously, Professor Schleyer has pointed out that AFF and SFF do not properly reproduce the enthalpies of formation of the group of polycyclic hydrocarbons shown in Table 5—despite giving excellent results for a variety of other hydrocarbons. We have therefore calculated these quantities with our new force field; the results are shown in Table 5 together with those from AFF and SFF. We have obtained a significantly improved overall result although we were not able to isolate any particular reason for this. Only in the case of manxane could no improvement be obtained over earlier results and our calculated  $\Delta H_f$  value is closer to that obtained from SFF than the experimental value. It is not possible at this stage to decide whether our calculated 'error' of 6 kcal mol<sup>-1</sup> lies in the force field, the experimental value, or perhaps both. It may be significant however that SFF generally gives reasonable heats of formation and their result for manxane is, exceptionally, in 'error' by 4 kcal mol<sup>-1</sup>.

In addition to the polycyclic hydrocarbons mentioned above it appears that AFF and SFF predict 2,8- and 2,4-ethanonoradamantane to be isoenergetic,<sup>19</sup> when in fact the latter is more stable by *ca.* 2 kcal mol<sup>-1</sup>. Our calculations correctly indicate the 2,4-isomer as the minimum energy form but the enthalpy difference is underestimated at 0.5 kcal mol<sup>-1</sup>. Although this is an im-

<sup>16</sup> I. W. Bassi, R. Scordamaglia, and L. Fiore, *J.C.S. Perkin II*, 1975, 1129.

<sup>17</sup> P. Groth, *Acta Chem. Scand.*, 1976, **A30**, 294.

<sup>18</sup> O. Ermer, J. D. Dunitz, and I. Bernal, *Acta Cryst.*, 1973, **B29**, 2278.

<sup>19</sup> S. A. Godleski, P. von R. Schleyer, and E. Osawa, *J.C.S. Chem. Comm.*, 1976, 38.

provement on previous results there is clearly scope for further change. This will probably have to be made at the expense of a more complex force field as it proved impossible to increase the calculated difference by parameter revision without upsetting the results for other compounds.

*cis-But-2-ene*.—Ermer and Lifson have proposed that *cis*-but-2-ene has  $C_{2v}$  symmetry on the basis of calculations with their CFF<sup>5</sup> and this conclusion appears to be

between the inner pair of hydrogen atoms is rather short and overemphasis of the repulsion between them would lead not only to opening up of the C=C-C angles but also twisting of the methyl groups in an attempt to relieve the strain.

*Cycloheptene*.—There seems little doubt that the  $C_s$  chair is the most stable form of cycloheptene and, further, that the  $C_2$  twist conformation is only slightly less stable than the chair.<sup>4,5</sup> We calculate an enthalpy difference

TABLE 5

Heats of formation (kcal mol<sup>-1</sup>) of polycyclic alkanes

Molecule	$\Delta H_f^0(\text{gas})_{\text{obs.}}$	$\Delta(\text{SFF})$	$\Delta(\text{AFF})$	$\Delta(\text{WBFF})$	Ref.
Adamantane	$-31.76 \pm 0.32$ $-30.65,^a -30.57^b$ $-32.96^c$	-0.74	-2.06	1.04	8, b
1-Methyladamantane	$-40.57 \pm 0.34$	-1.25	-2.32	1.67	8, b
2-Methyladamantane	$-35.66 \pm 0.62$	-2.28	-3.38	-0.03	8, b
1,3,5,7-Tetramethyladamantane	$-67.15 \pm 0.80$	-3.11	-3.06	0.10	8, b
Protoadamantane	$-20.54 \pm 0.60$	-0.59	-2.09	1.09	8, b
Diamantane	$-32.60 \pm 0.58$	-4.77	-5.53	-0.46	8, b
4-Methyldiamantane	$-43.53 \pm 0.30$	-3.29	-3.68	1.10	8, b
3-Methyldiamantane	$-37.60 \pm 0.58$	-5.31	-5.75	-1.71	8, b
1-Methyldiamantane	$-39.85 \pm 0.85$	-3.71	-4.58	-0.61	8, b
Perhydrotriquinacene	$-24.47 \pm 0.86$	0.73	4.73	1.01	8, a
Bicyclo[3.3.1]nonane	$-30.46 \pm 0.55$	0.09	-0.18	-0.23	d
Bicyclo[3.3.2]decane	$-25.3 \pm 1.8$	-0.87	0.10	-2.78	d
Mean deviation		2.23	3.12	0.98	

$\Delta = \Delta H_f^0(\text{gas})_{\text{calc.}} - \Delta H_f^0(\text{gas})_{\text{obs.}}$

AFF = Allinger's force field; SFF = Schleyer's force field; WBFF = White-Bovill's force field.

<sup>a</sup> Footnote g Table 2. <sup>b</sup> R. S. Butler, A. S. Carson, P. G. Laye, and W. V. Steele, *J. Chem. Thermodynamics*, 1971, **3**, 277. <sup>c</sup> M. Mansson, N. Rapport, and E. F. Westrum, jun., *J. Amer. Chem. Soc.*, 1970, **92**, 7276.

supported by a microwave analysis.<sup>20</sup> Allinger, on the other hand, calculates that a  $C_2$  conformation with slightly twisted methyl groups is to be preferred.<sup>4</sup> Our results (Figure 1) indicate a  $C_{2v}$  conformation almost identical to the CFF prediction. There are two factors which might lead to this difference. In the first place both Ermer and Lifson and ourselves use a full-matrix Newton-Raphson minimisation procedure whereas Allinger uses only the first step of our two-stage procedure.<sup>21</sup> Our own experience has indicated that the torsion angles do not, in general, have their optimum values at the end of stage one.<sup>12</sup> Secondly there is no doubt that Allinger's

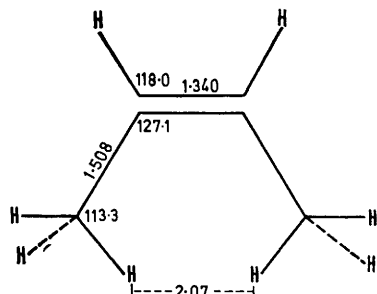


FIGURE 1 Calculated structure of *cis*-but-2-ene ( $C_{2v}$  symmetry)

unduly 'hard' H...H potentials contribute significantly to the calculated result. The distance of 2.07 Å

<sup>20</sup> S. Kondo, Y. Sakurai, E. Hirota, and Y. Morino, *J. Mol. Spectroscopy*, 1970, **34**, 231.

between these two forms of 1.5 kcal mol<sup>-1</sup>, whereas AFF and CFF yield a value of ca. 0.5 kcal mol<sup>-1</sup>. Our calculated geometry for the  $C_s$  chair is shown in Figure 2. The

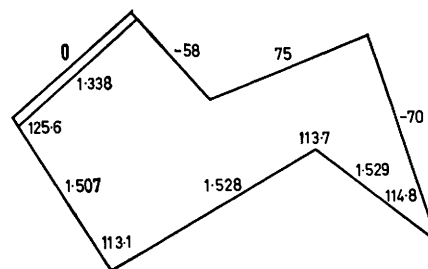


FIGURE 2 Calculated minimum energy conformation of cycloheptene ( $C_s$  symmetry)

only point of concentration seems to be whether the  $C_s$  boat conformation is an energy maximum or minimum.<sup>5</sup> Our calculations give qualitatively the same result as CFF (energy maximum) in that we calculate the  $C_s$  boat to be an extremely shallow minimum closely flanked by a pair of maxima about 0.04 kcal mol<sup>-1</sup> above the minimum (*i.e.* a saddle point).

*cis,cis-Cyclo-octa-1,5-diene* (COD-1,5).—Following the publication of Anet's dynamic n.m.r. work on COD-1,5<sup>22</sup>

<sup>21</sup> See appendix, N. L. Allinger and G. A. Lane, *J. Amer. Chem. Soc.*, 1974, **96**, 2937.

<sup>22</sup> F. A. L. Anet and L. Kozerski, *J. Amer. Chem. Soc.*, 1973, **95**, 3407.



a number of molecular mechanics calculations have been performed in an attempt to interpret the n.m.r. results.<sup>23-25</sup>

The first point concerns the establishment of a minimum energy conformation for COD-1,5. There seems to be universal agreement that the  $C_2$  symmetric twist-boat conformation is the energy minimum,<sup>23-26</sup> but calculated values for the  $C(sp^2)-C-C-C(sp^2)$  torsion angles (*i.e.* the degree of twist) range from 27 to 55°. Experimental values of 45°\* and 65° have been obtained from an electron diffraction study of the hydrocarbon,<sup>27</sup> and an X-ray crystal structure analysis of a dibromo-derivative,<sup>28</sup> respectively. Our calculated value of 52° (Figure 3) is

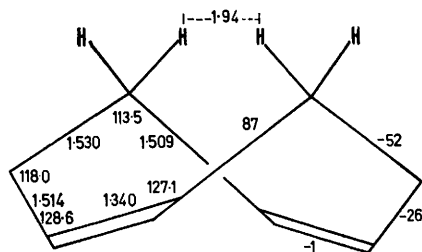


FIGURE 3 Calculated twist-boat conformation of *cis,cis*-cyclo-octa-1,5-diene ( $C_2$  symmetry)

in excellent agreement with the electron diffraction results (Table 3).

The various twist-boat interconversion pathways have been described in detail elsewhere;<sup>23-25</sup> interest in these processes centres on establishing which correspond to the barrier heights measured by Anet.<sup>22</sup> Anet<sup>23</sup> and Ermer<sup>25</sup> calculate that the route through the  $D_2$  skew conformation is the lowest energy process, followed by those through the  $C_{2v}$  boat and  $C_{2h}$  chair with approximately equal barrier heights. Allinger,<sup>24</sup> on the other hand, calculates that the route through the  $C_{2v}$  boat is the minimum energy pathway, followed by that through the chair and finally the route through the skew as the maximum energy interconversion route.

Because of the marked difference between these results we decided to investigate this system closely. We realised that it was unlikely that such a dichotomy arose from differences amongst the various force fields, because of the usually similar results obtained for other calculations, but rather that differences in the methods of generating the transition states held the key to the problem.

In the first instance we used the method of Wiberg and Boyd<sup>29</sup> in order to map the energy changes from the twist-boat to the boat and skew conformations and

\* This value is only approximate because of assumptions made about the molecular geometry in order to facilitate interpretation of the electron diffraction results.

† Allinger's calculations were performed with AFF-73,<sup>24</sup> whereas we used AFF-72.<sup>4</sup> Although full details of AFF-73 are not available it appears to be a slightly improved version of AFF-72. These do not affect our arguments above.

<sup>23</sup> F. A. L. Anet and R. Anet in 'Dynamic Nuclear Magnetic Resonance Spectroscopy,' ed. F. A. Cotton and L. M. Jackman, Academic Press, New York, 1975, p. 571

generated the transition state between twist-boat and chair conformations with a molecule building program. In all three cases we used a larger number of constraints on the system that was actually necessary. For example, in mapping from the twist-boat to the skew all nine torsion angles around each of the  $C(sp^3)-C(sp^3)$  bonds were driven instead of only the  $C(sp^2)-C-C-C(sp^2)$  torsion angles. In this case we obtained the same order of preference for the various interconversion pathways as Allinger, and similar values for the barrier heights.

In the next series of calculations we used the Wiberg-Boyd algorithm, but with the minimum number of constraints, and obtained the same order of preference as Anet and Ermer!! Although Allinger gives no indication of his procedure for defining the various interconversion pathways it seemed clear that too many constraints were applied. In order to check this conclusion we repeated these calculations using AFF whereupon the route through the skew emerged as the minimum energy pathway.†

Finally, we repeated the calculations yet again using the Newton-Raphson maximisation procedure to define the three transition states. The results were very similar to those obtained by using the Wiberg-Boyd algorithm with minimal constraints except that the energies of the transition states were some 0.02 kcal mol<sup>-1</sup> lower, probably as a consequence of *complete* molecular relaxation (*i.e.* no artificial constraints). This lends additional support to the conclusion that a second-derivative minimisation/maximisation procedure, such as the Newton-Raphson, is the only safe optimisation algorithm for molecular mechanics calculations;<sup>12</sup> our calculated barrier heights are compared with Ermer's and Anet's in Table 6 along with the experimental results.

TABLE 6

Calculated and experimental barrier heights (kcal mol<sup>-1</sup>) for the various *cis,cis*-cyclo-octa-1,5-diene conformational interconversions

	Anet <sup>23</sup>	Ermer <sup>25</sup>	White and Bovill	Experiment <sup>22</sup>
$\Delta V_{\text{chair}}$	7.2	5.9*	4.6	
$\Delta V_{\text{boat}}$	6.6	5.7*	4.5	4.9*
$\Delta V_{\text{skew}}$	4.2	4.2*	2.3	4.4*

\* Values are  $\Delta G$ .

*Cyclonona-1,5-dienes* (CND-1,5).—The structures of two *cis,cis*-, two *cis,trans*-, and three *trans,trans*-conformers of CND-1,5 have been calculated and the results are shown in Figure 4. The minimum energy conformation is the *cis,cis*-isomer of Figure 4(a) and results of

<sup>24</sup> N. L. Allinger and J. T. Sprague, *Tetrahedron*, 1975, **31**, .21.

<sup>25</sup> O. Ermer, *J. Amer. Chem. Soc.*, 1976, **98**, 3964.

<sup>26</sup> G. Favini, F. Zuccarello, and G. Buemi, *J. Mol. Struct.*, 1969, **3**, 385.

<sup>27</sup> L. Hedberg and K. Hedberg, Abs. Papers, Nat. Meeting Amer. Cryst. Ass., 1964, Bozeman, Montana.

<sup>28</sup> R. K. Mackenzie, D. D. MacNicol, H. H. Mills, R. A. Raphael, F. B. Wilson, and J. A. Zabkiewicz, *J.C.S. Perkin II*, 1972, 1632.

<sup>29</sup> K. B. Wiberg and R. H. Boyd, *J. Amer. Chem. Soc.*, 1972, **94**, 8426.

equilibration<sup>30</sup> together with n.m.r. experiments<sup>31</sup> are in complete agreement with our conclusion as to the favoured isomer but give no indication as to its conform-

and -1,6-dienes have not been studied previously in any great detail although the results of qualitative molecular mechanics calculations have been published<sup>6</sup> and

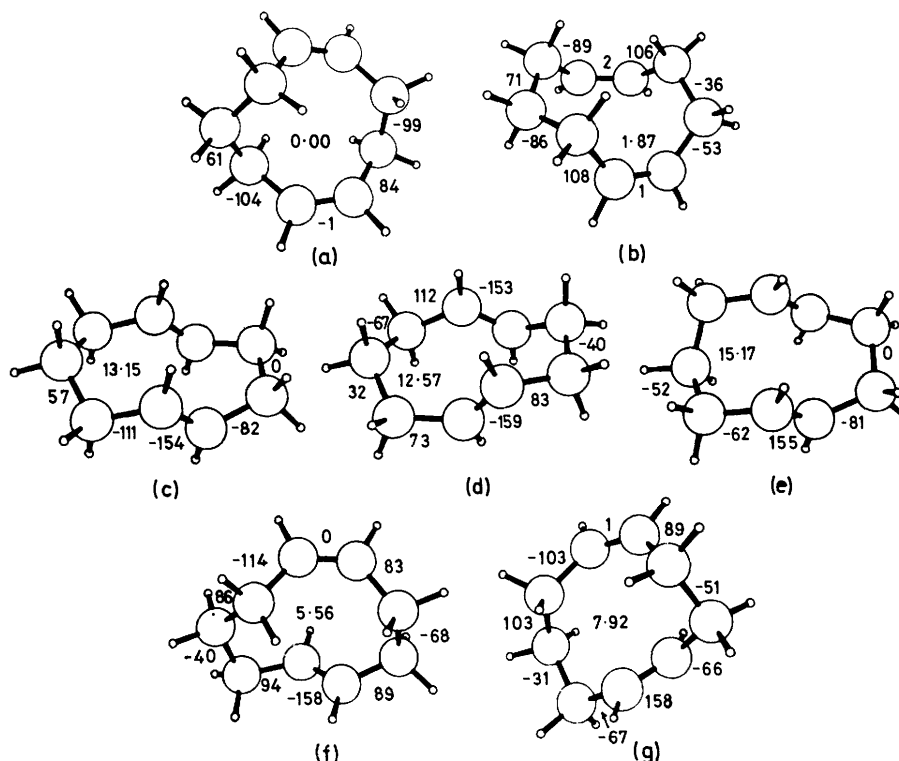


FIGURE 4 Cyclonona-1,5-diene conformations; peripheral values are torsion angles and the inner value is the steric energy (kcal mol<sup>-1</sup>) above the minimum. Symmetry is C<sub>1</sub> except as noted: (a) C<sub>2</sub>, (c) C<sub>2</sub>, (e) C<sub>2</sub>.

ation. However, Favini<sup>32</sup> also calculates the *cis,cis*-isomer of Figure 4(a) to be the global minimum, and his calculated geometry is very similar to ours. It may also be pertinent that this conformation bears a strong resemblance to the known global minimum energy conformation of cyclodeca-1,6-diene [Figure 10(a)]. There are very few experimental structural data available for the CND-1,5's, but a recent X-ray crystal structure analysis of byssochlamic acid<sup>33</sup> has shown that the *cis,cis*-CND-1,5 ring has a conformation very similar to that of Figure 4(b); the two conformations are compared in Figure 5.

We calculate the minimum energy *cis,cis*-conformation to be 5.6 kcal mol<sup>-1</sup> more stable than the lowest energy *cis,trans*-conformation; *cf.* a value of 4.3 kcal mol<sup>-1</sup> derived from recent measurements of heats of hydrogenation.<sup>34</sup> Some calculated and observed heats of hydrogenation are shown in Table 2.

*Cyclodecadienes.*—The conformations of cyclodeca-1,5-

<sup>30</sup> D. Devaprabhakara, C. G. Cardenus, and P. D. Gardner, *J. Amer. Chem. Soc.*, 1963, **85**, 1553.

<sup>31</sup> R. Vaidyanathaswamy and D. Devaprabhakara, *J. Org. Chem.*, 1967, **32**, 4143.

<sup>32</sup> F. Zuccarello, G. Buemi, and G. Favini, *J. Mol. Struct.*, 1971, **8**, 549.

<sup>33</sup> I. C. Paul, G. A. Sim, T. A. Hamor, and J. M. Robertson, *J. Chem. Soc.*, 1963, 5502.

<sup>34</sup> R. B. Turner, B. J. Mallon, M. Tichy, W. von E. Doering, W. R. Roth, and G. Schröder, *J. Amer. Chem. Soc.*, 1973, **95**, 8605.

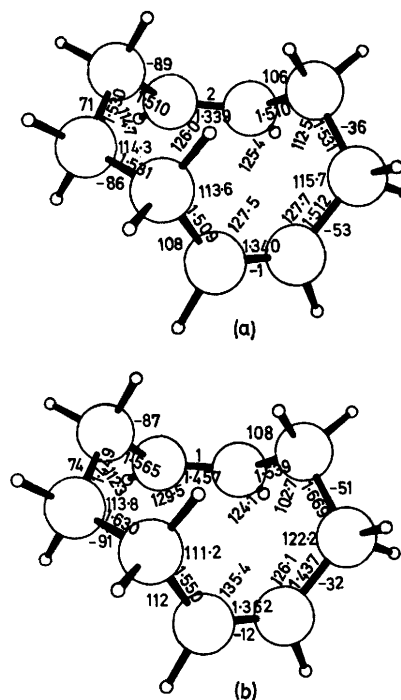


FIGURE 5 The calculated (a) and observed (b) structures of the *cis,cis*-cyclonona-1,5-diene ring as found in byssochlamic acid. Bond lengths and angles inner and torsion angles peripheral values

the *cis-cis*-cyclodeca-1,6-dienes have been studied by Allinger<sup>35</sup> and by Ermer.<sup>5</sup> The partial results of our work on the cyclodeca-1,6-dienes, using a development version of the present force field, have been the subject

cranolides,<sup>37</sup> with one *cis,trans*- and two *trans,trans*- conformations observed *via* X-ray crystal structure analyses. We have calculated the geometry and relative enthalpies of one *cis,trans*-, two *cis-cis*-, and five *trans*-

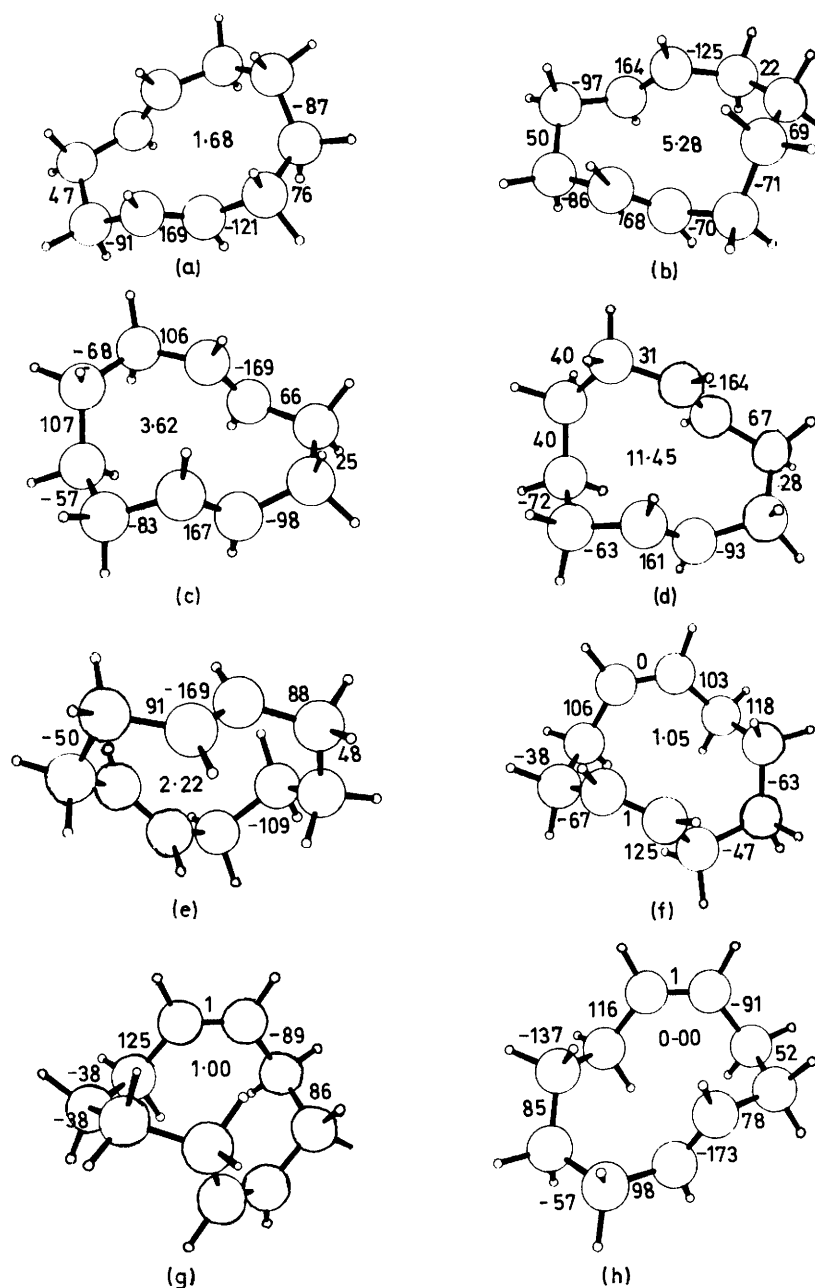


FIGURE 6 Cyclodeca-1,5-diene conformations; symmetries are (a)  $C_2$ , (e)  $C_2$ , (g)  $C_2$

of a preliminary communication.<sup>36</sup> Details of our final results appear in the following paragraphs.

(a) *Cyclodeca-1,5-diene* (CDD-1,5). Our interest in this system stems from the fact that the CDD-1,5 ring is fairly widespread amongst naturally occurring germa-

<sup>35</sup> N. L. Allinger, M. T. Tribble, and J. T. Sprague, *J. Org. Chem.*, 1972, **37**, 2423.

<sup>36</sup> D. N. J. White and M. J. Bovill, *Tetrahedron Letters*, 1975, 2239.

*trans*-conformers of CDD-1,5; the results are shown in Figure 6. The minimum energy conformation is the *cis,trans*-isomer shown in Figure 6(h) and its geometry is compared with that obtained from an X-ray crystal structure analysis of eupafornonin<sup>38</sup> in Figure 7. There

<sup>37</sup> G. A. Sim in 'Molecular Structure by Diffraction Methods,' Chem. Soc. Specialist Periodical Reports, 1974, vol. 2, p. 131; vol. 3, p. 163.

<sup>38</sup> A. T. McPhail and K. D. Onan, *J.C.S. Perkin II*, 1976, 578.

appears to be no experimental evidence regarding the minimum energy conformation of CDD-1,5 but the agreement of the calculated geometrical parameters for the *cis,trans*-isomer with the X-ray results is excellent, despite fairly heavy substitution of the CDD-1,5 ring in the latter instance. There are three other conformations within 2 kcal mol<sup>-1</sup> of the calculated global minimum; the two approximately isoenergetic *cis,cis*-isomers and the *trans,trans*-isomer shown in Figure 6(a). A conformation very similar to that of the lowest energy *trans,trans*-isomer has been observed in a series of germacranolides of which costunolide<sup>39</sup> is a good representative. The conformer in Figure 6(a) has C<sub>2</sub> symmetry, whilst the macrocycle in costunolide has only approximate C<sub>2</sub>

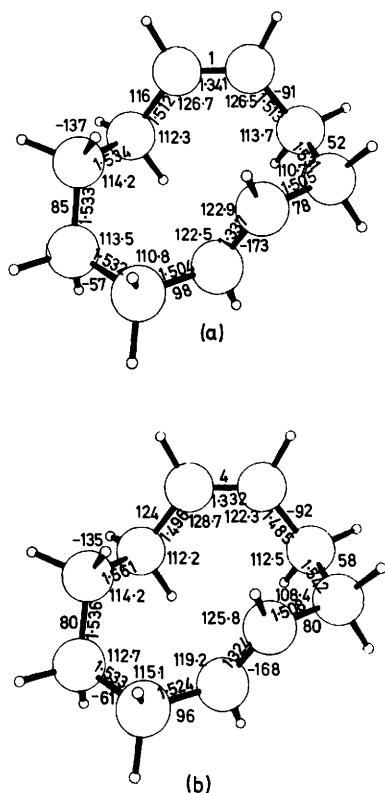


FIGURE 7 Calculated minimum energy conformation of cyclodeca-1,5-diene (a) compared with the geometry of the ten-membered ring of eupafornin (b)

symmetry because of its various substituents. Nevertheless, there is good agreement between our calculated geometry and the C<sub>2</sub>-averaged result from the X-ray crystal structure analysis,<sup>39</sup> which are compared in Figure 8. There are also some experimental data regarding the conformation of Figure 6(e) and the calculated ring torsion angles are compared with those from an X-ray crystal structure analysis of shiromodiol<sup>40</sup> in Figure 9. A detailed comparison cannot be made because one of the double bonds is replaced by a *trans*-fused epoxide system

<sup>39</sup> M. J. Bovill, P. J. Cox, P. D. Cradwick, M. H. P. Guy, G. A. Sim, and D. N. J. White, *Acta Cryst.*, 1976, **B32**, 3203.

<sup>40</sup> R. J. McClure, G. A. Sim, P. Coggon, and A. T. McPhail, *Chem. Comm.*, 1970, 128.

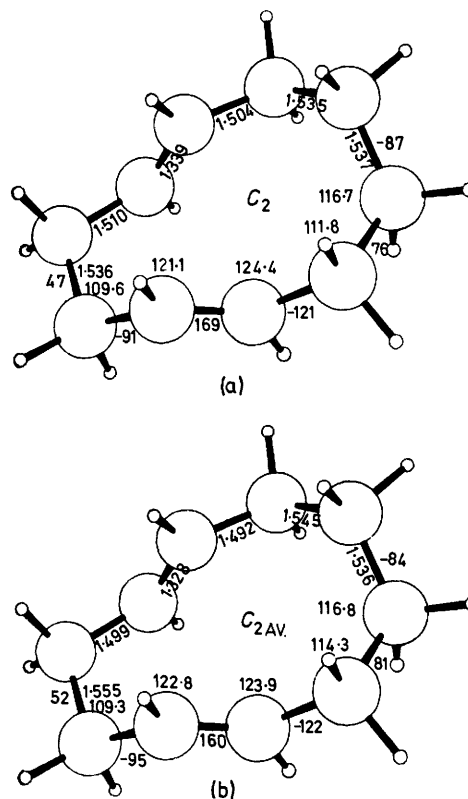


FIGURE 8 Geometry of the calculated (a) minimum energy conformation of *trans,trans*-cyclodeca-1,5-diene compared with the C<sub>2</sub> averaged geometry of the macrocycle in costunolide (b)

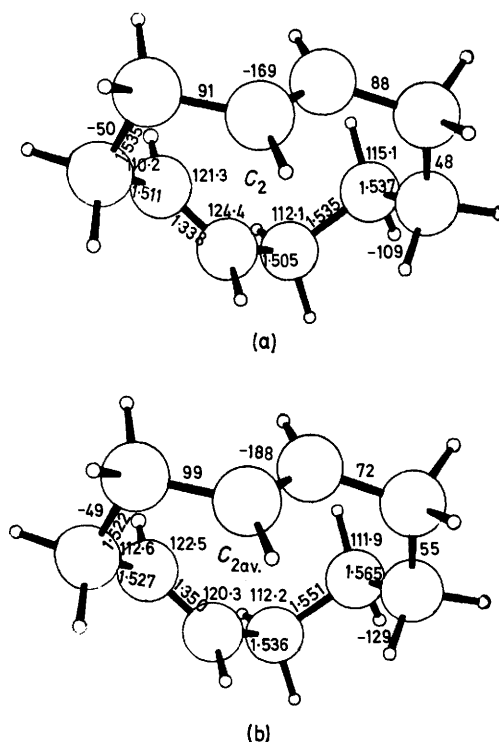


FIGURE 9 Calculated (a) and observed (b) geometries of the shiromodiol-type cyclodecadiene ring

in the natural product; but the two conformations are qualitatively similar.

(b) *Cyclodeca-1,6-diene* (CDD-1,6). The CDD-1,6 system is better defined experimentally than the 1,5-isomer, and a number of useful structural and thermodynamic measurements are available—most of which were used

with CCF<sup>5</sup> and 0.30 kcal mol<sup>-1</sup> with AFF<sup>4</sup>) between the two conformers.

Equilibration experiments<sup>41</sup> indicate that although the *cis,cis*-form is certainly the predominant configuration there were detectable amounts of a *cis,trans*-isomer in the equilibrium mixture at 25 °C and this seems to correspond

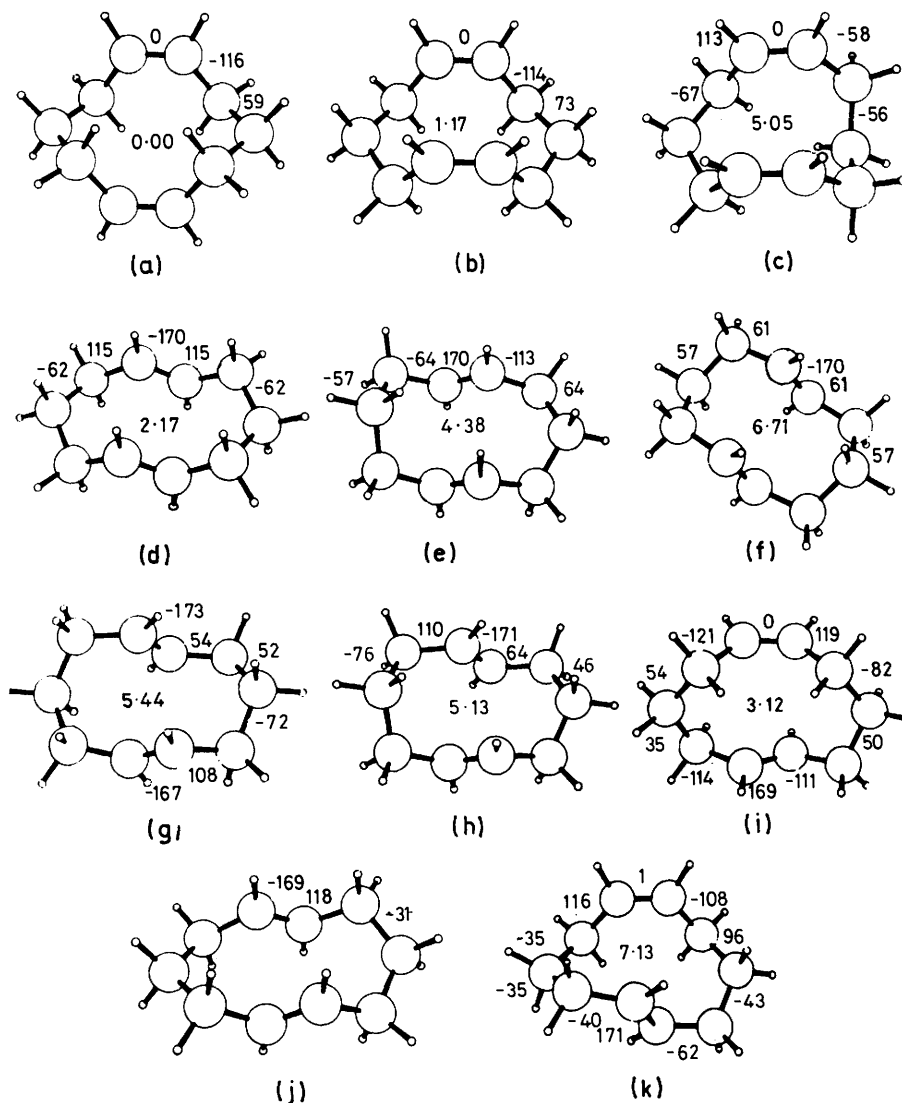


FIGURE 10 Calculated conformations of cyclodeca-1,6-diene with the following symmetries: (a)  $C_{2h}$ , (b)  $C_{2v}$ , (c)  $C_s$ , (d)  $C_{2h}$ , (e)  $C_s$ , (f)  $C_{2h}$ , (g)  $C_2$ , (h)  $C_2$ , (i)  $C_1$ , (j)  $D_2$ , (k)  $C_1$

in the development of this force field (see Tables 2 and 3). The geometries and relative enthalpies of eleven conformations of CDD-1,6 have been calculated with the present force field and the results are shown in Figure 10. The global minimum is calculated to be the *cis,cis*-chair conformation, in excellent agreement with thermochemical measurements,<sup>34,41</sup> and this has a molecular geometry almost exactly identical with that observed by gas-phase electron diffraction<sup>42</sup> (see Table 3). The *cis,cis*-boat form is, at best, barely present in the gas phase at 35 °C,<sup>42</sup> an observation which accords well with our calculated enthalpy difference of 1.2 kcal mol<sup>-1</sup> (*cf.* 0.16 kcal mol<sup>-1</sup>

with the conformation of Figure 10(i) which has a calculated enthalpy 3.12 kcal mol<sup>-1</sup> above that of the *cis,cis*-chair. No *trans,trans*-isomer was observed and therefore our calculated minimum energies for the *cis,cis*-chair and *cis,trans*-chair are probably 1–2 kcal mol<sup>-1</sup> too high (see heats of hydrogenation in Table 2) with respect to the *trans,trans*-isomer of Figure 10(d).

There is reasonable, if not conclusive, evidence as to the minimum energy conformation of *trans,trans*-CDD-

<sup>41</sup> J. Dale, *Angew. Chem. Internat. Edn.*, 1966, **5**, 1000.

<sup>42</sup> A. Alnennigen, G. G. Jacobsen, and H. M. Seip, *Acta Chem. Scand.*, 1969, **23**, 1495.

1,6. An X-ray crystal structure analysis of the 2,7-dibromo-3,8-dimethoxy-derivative<sup>43</sup> has shown that the

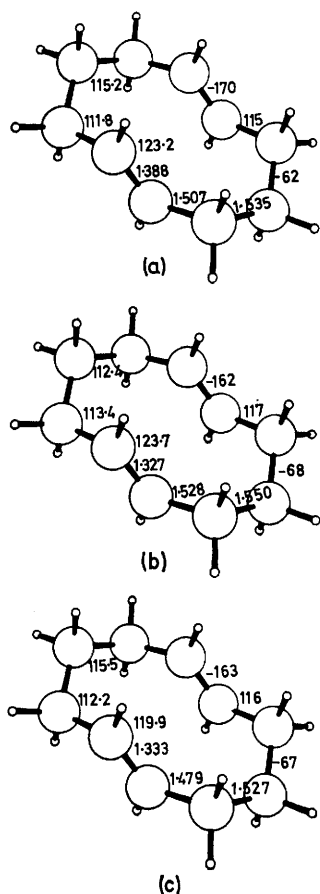


FIGURE 11 Calculated geometry (a) of the minimum energy *trans,trans*-cyclodeca-1,6-diene conformation compared with the  $C_{2h}$  average experimental values from X-ray crystal structure analyses of a substituted hydrocarbon (b) and 1,5-diazacyclodecane-6,10-dione (c)

ten-membered ring adopts a crown conformation with  $C_i$  symmetry. Furthermore, 1,5-diazacyclodecane-6,10-dione<sup>44</sup> exhibits this same crown conformation with ring torsion angles very similar to those of the CDD-1,6-derivative. The similarities between the minimum energy conformations of medium-sized ring alkenes and amides have been noted, previously,<sup>5,45</sup> and this, taken together with the fact that the same conformation occurs in two entirely different crystal structures, supports our calculation of the crown conformation of Figure 10(d) as the minimum energy *trans,trans*-variant. Our calculated conformation has  $C_{2h}$  symmetry whilst the substituents prevent the dibromo-dimethoxy-derivative from adopting this form although the departure from a  $C_{2h}$  conformation is not very great. The cyclic diamide has no symmetry, and whilst the departure from  $C_{2h}$  is larger than for the dibromo-dimethoxy-CDD-1,6 it is still a reasonable approximation to the same. The three conformations are shown in Figure 11 with the results of the two crystal structure analyses averaged to give a  $C_{2h}$  symmetric ring.

*Added in proof.* Professor N. L. Allinger has recently developed a new force field (MM2) which solves most of the alkane-related difficulties associated with AFF72 and 73 (personal communication). Full details of MM2 will appear in *J. Amer. Chem. Soc.* during 1977.

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<sup>43</sup> D. N. J. White, *Helv. Chim. Acta*, 1973, **56**, 1347.

<sup>44</sup> T. Srikrishnan and J. D. Dunitz, *Acta Cryst.*, 1975, **B31**, 1372.

<sup>45</sup> D. N. J. White and M. H. P. Guy, *J.C.S. Perkin II*, 1975, 43.