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Conformational Analysis by Thermal Variation of Rotatory Power. Monosubstituted Cyclohexene Enantiomers

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The conformer rotatory powers of six 4-substituted cyclohexenes have been calculated by extension of the Brewster procedure and used to estimate the conformational free energy differences. The corresponding conformational rotivities are utilized to analyze the thermal variations of the rotatory power of 4-F, 4-Cl, and 4-D cyclohexenes. This technique yields coherent results for 4-fluoro- and 4-chlorocyclohexene and an up-to-date outcome for 4-deuteriocyclohexene, the equatorial conformer of which is more stable than the axial one (about 10 cal mol^{-1} enthalpy difference). The 4*S* enantiomers of the monosubstituted cyclohexenes were synthesized from a 4*R* ester, which was crystallized from the diastereoisomeric mixture resulting from the reaction between racemic 4-hydroxycyclohexene and 10-camphorsulfonic acid (1*S*,4*R*).

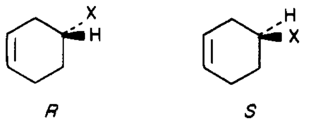
Determination of the thermal variation of rotatory power (tvrp), with solvent effect taken into account, makes it possible to determine the enthalpy difference between monosubstituted cyclohexene conformers as well as their rotivities $\Omega = [\alpha]/(n^2 + 2)$. We have previously[1,2] studied the conformational equilibrium of (4*R*)-4-methylcyclohexene[3] ($\Delta H° = -1.45$ kcal mol^{-1}). The corresponding rotivity of its equatorial conformer supports Brewster's calculations of the rotatory power of 4-substituted cyclohexenes.[4] The 4-methylcyclohexene axial conformer rotivity obtained by the Brewster procedure has been introduced into our tvrp analysis, which then gives estimates for the conformational entropy and free energy differences of $\Delta S° = -1$ cal mol^{-1} deg^{-1} and $\Delta G° = -1.15$ kcal mol^{-1}.

We have extended this technique to other substituents with low (F, Cl) or essentially zero (CN, D) conformational free energies to determine the corresponding conformational enthalpies and entropies and the conformer rotivities for comparison with values calculated by Brewster's method.

Three chiral 4-substituted cyclohexenes have been described in the literature, the substituents being methyl,[5] cyano,[6] and carboxyl.[6-8] We now report the synthesis of pure enantiomers of the fluoro, chloro, and deuterio derivatives. The absolute configurations of these compounds have been established through a steric correlation starting from a 4-cyanocyclohexene enantiomer and ending at the corresponding 4-carboxycyclohexene.

Experimental Section

Synthesis. The cyclohexene derivatives used or synthesized in this work are the following:



1, X = OH; **3**, X = $OSO_2C_{10}H_{15}O$; **4**, X = D; **5**, X = F; **6**, X = Cl, **7**, X = C≡N; **8**, X = $CONH_2$; **9**, X = COOH

Starting organic compounds (Fluka) were 10-camphorsulfonic acid (1*S*,4*R*) (**2**) ($C_{10}H_{15}OSO_3H$) and 1,4-cyclohexanediol. Compound **2** was characterized by its melting point (193 °C (lit. mp 195 °C)) and its rotatory power $[\alpha]^{20}_{D}$ +21.5° (*c* 10, H_2O), the latter 100% enantiomeric purity.[9]

Cyclohexen-4-ol (1*R* + 1*S*) was obtained by heating 1,4-cyclohexanediol with iodine and simultaneous distillation of the reaction products: 7-oxabicyclo[2.2.1]heptane (bp 119 °C (713 Torr)) and **1**, the latter being redistilled (bp 90 °C (45 Torr), yield 50%).

The esterification of **1** with the acid chloride of **2** (**2** + $SOCl_2$ without any enantiomeric-purity change) was performed at −5 °C in the presence of pyridine. After extraction of the reaction mixture, pyridine was removed through its toluene azeotrope. The **3*R*** + **3*S*** diastereoisomeric mixture was crystallized from methanol (mp 55 °C). The *R*/*S* configurations assigned to each compound refer only to the cyclohexenic asymmetric carbon, omitting carbon configurations of the camphorsulfonic moiety.

The 50.309-MHz ^{13}C NMR spectrum of the **3*R*** + **3*S*** mixture presents 20 lines for 16 carbons. Thus only four carbons have different chemical shifts relative to Me_4Si that distinguish the two diastereoisomers (official numbering of the cyclohexene moiety):

	C(1)	C(2)	C(3)	C(5)
3*R*	126.860	122.760	31.805	28.440
3*S*	126.800	122.815	31.720	28.520

After 10 successive crystallizations from methanol, we recovered the **3*R*** diastereoisomer, the melting point (73.5 °C) of which remained unchanged after further recrystallization; the specific rotation was $[\alpha]^{25}_{5461}$ +71.14° (*c* 0.31, CCl_4); the configuration will be established further. The ~100% diastereoisomeric purity was established through the complete absence of ^{13}C NMR signals assigned to the **3*S*** diastereoisomer. Compounds **2** and **3*R*** have equal enantiomeric purity.

Compound **3*R*** was treated with different nucleophilic reagents ($LiB(C_2H_5)_3D$; KF; LiCl; NaCN) in order to perform bimolecular nucleophilic substitution reactions with configurational inversion. The experimental conditions allow this process to be stereospecific.[10-13] The reaction products were purified by preparative gas chromatography (GLPC).

The **3*R*** diastereoisomer was treated with the following: (a) lithium triethylborodeuteride in THF[14] at 0 °C; GLPC over 5% tricresyl phosphate column; **4*S***, $[\alpha]^{25}_{5461}$ +0.70° (*c* 3.022, octane); (b) potassium fluoride in triethylene glycol at 60 °C;[11] GLPC on Carbowax 6000 column; **5*S***, $[\alpha]^{25}_{5461}$ −46.28° (*c* 0.26, cyclohexane);

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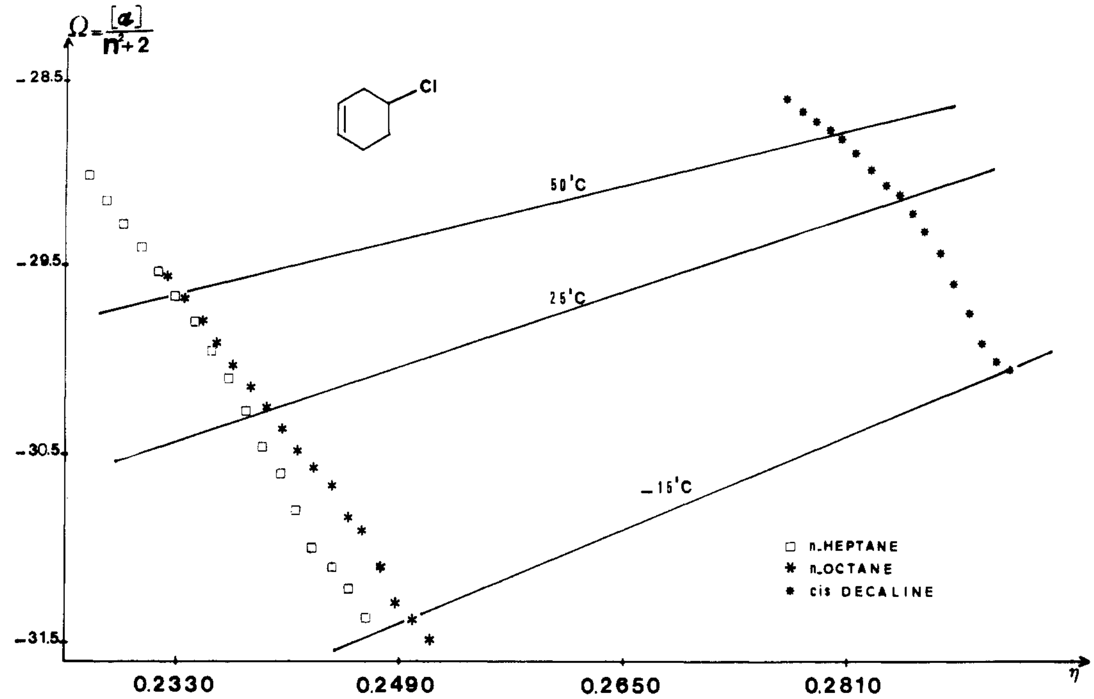

Figure 1. Solvent and temperature effects on the rotivity of 4-chlorocyclohexene (**6*S***).

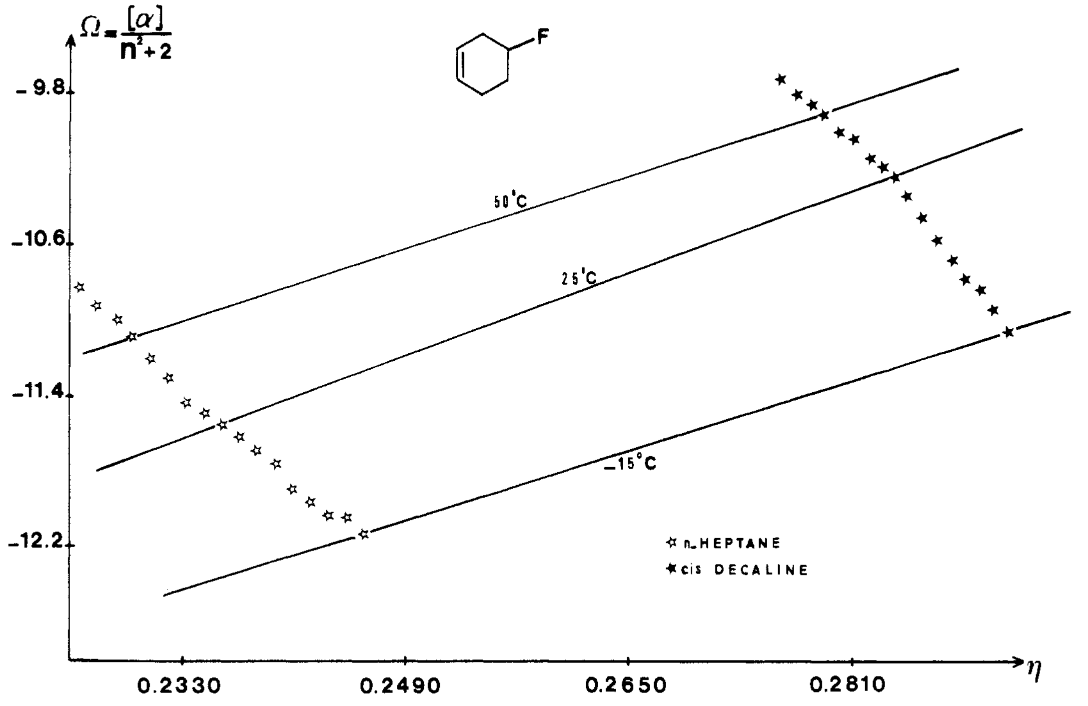

Figure 2. Solvent and temperature effects on the rotivity of 4-fluorocyclohexene (**5*S***).

(c) lithium chloride in refluxing anhydrous acetone for 48 h; GLPC on Carbowax 6000 column; **6*S***, $[\alpha]^{25}_{5461}$ −118.32° (*c* 0.524, cyclohexane); (d) potassium cyanide in dimethyl sulfoxide with heating for 90 min at 50 °C; GLPC on SE-30 column; **7*S***, $[\alpha]^{25}_{5461}$ −120.56° (*c* 0.214, cyclohexane).

Doering and Mastrocola[6] synthesized **7*S***, $[\alpha]^{25}_{5461}$ −103.95° (*c* 0.8, cyclohexane), from a sample of **9*S***, $[\alpha]_{5461}$ −101.85° (*c* 0.7, CCl_4). They inferred that the maximum possible value for the rotatory power of **7*S*** was $[\alpha]^{25}_{5461}$ −132.6°. The low reliability of such calculations[15] must be emphasized when the rotatory power is so dependent on solvent and concentration: **9*R***, $[\alpha]_{5461}$ +140.7° (purum, tube 1-dm path length),[8] $[\alpha]_{5461}$ +123° (*c* 1.01, CCl_4);[8] **9*S***, $[\alpha]_{5461}$ −110° (*c* 7, methanol),[7] $[\alpha]_{5461}$ −121° (*c* 1.54, CCl_4).[8] Therefore, our **7*S*** rotatory power is within the uncertainty field of the propounded value.

To specify the absolute configuration of compounds **3*R*–7*S***, we converted **7*S*** into 1,2,3,6-tetrahydrobenzamide **8*S*** (mp 152 °C; $[\alpha]^{25}_{5461}$ −92.47° (*c* 1.08, $CHCl_3$)) by treatment with an aqueous alkaline solution of 20 N hydrogen peroxide. Compound **9*S*** obtained after acid hydrolysis ($[\alpha]^{25}_{5461}$ −89.4° (*c* 0.246, methanol)) had an optical purity near 80%. Absolute configuration of compound **9*S*** was established by steric relationship.[7]

Rotivity Measurements. Rotivities were determined as in our previous experiments.[1-3] For each solvent, measurements were made at 17 temperatures in the range −15 to +65 °C at 5-deg intervals. For **4*S***, we obtained the values reported in Table I (solvent C, octane). The experimental data for **5*S*** (solvents B, *n*-heptane, and G, *cis*-decalin) and **6*S*** (solvents B, C, and G) are reported in Tables S-II and S-III (see paragraph at end of paper regarding supplementary material). Graphs of solvent and tem-

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Table I. Rotivities $\langle\Omega\rangle$ of 4-Deuteriocyclohexene (4*S*) at Different Temperatures in Solvent Octane

t, °C	10^2C, g cm^{-3}	n	$[\alpha]$	$\langle\Omega\rangle$	η
−15	3.168	1.417 84	0.358	0.089	0.251 92
−10	3.151	1.415 47	0.455	0.114	0.250 66
−5	3.134	1.413 09	0.478	0.119	0.249 40
0	3.117	1.410 72	0.481	0.121	0.248 14
5	3.100	1.408 34	0.516	0.129	0.246 88
10	3.083	1.405 97	0.519	0.130	0.245 62
15	3.066	1.403 59	0.609	0.153	0.244 35
20	3.049	1.401 23	0.678	0.171	0.243 08
25	3.032	1.398 86	0.704	0.178	0.241 81
30	3.015	1.396 49	0.774	0.196	0.240 54
35	2.998	1.394 13	0.845	0.214	0.239 27
40	2.981	1.391 76	0.849	0.216	0.238 00
45	2.964	1.389 39	0.911	0.232	0.236 72
50	2.947	1.387 04	0.927	0.236	0.235 45
55	2.930	1.384 67	0.933	0.238	0.234 17
60	2.913	1.382 31	0.949	0.243	0.232 89
65	2.896	1.379 96	0.978	0.250	0.231 61

perature effects on the rotivity are shown in Figures 1 and 2.

Results and Discussion

Specific Rotatory Power and Conformational Equilibrium. Each 4-substituted cyclohexene is in equilibrium between two conformers E ⇄ A (mole fractions w_E and w_A), and the main goal of this study is to determine the thermodynamic parameters of each equilibrium.

For such optically active molecules, the experimental specific rotatory power $\langle[\alpha]\rangle$ is

$$\langle[\alpha]\rangle = w_E[\alpha]_E + w_A[\alpha]_A \qquad (1)$$

The free energy difference between conformers,

$$\Delta G^\circ_T = G^\circ_A - G^\circ_E = -RT \ln [([\alpha]_E - \langle[\alpha]\rangle)/(\langle[\alpha]\rangle - [\alpha]_A)] \qquad (2)$$

is obtained from the experimental value $\langle[\alpha]\rangle$ and from $[\alpha]_E$ and $[\alpha]_A$ estimated by addition of increments calculated from the list of molecular rotation increments $[M]_D$ published by Brewster.[4] In $k(XY)$ increments, X and Y terms correspond to two atoms associated with an X–C–C–Y dihedral angle, the sign of which fixes that of $k(XY)$. For the equatorial conformer of a 4-X-substituted cyclohexene, the six dihedral angles of the C(4)–C(5) central bond lead to the following increment:

$$[M]^E_D = \pm k(CC - 2CH + HH + XH - XH) = \pm k(C - H)^2$$

In the same way, the six dihedral angles built around C(5)–C(6) or C(3)–C(4) bonds lead to

$$[M]^E_D = \pm k(C - H)(C^* - H) \qquad (C^* = C\ sp^2)$$

Thus, the molecular rotatory power $\Sigma[M]^E_D$ of such a structure is independent of the nature of X (terms XH being eliminated); it represents only cyclic chirality.

According to Brewster, $\Sigma[M]^E_D = \pm 160°$. A negative sign designates 4*S* enantiomers when the X priority number, in the sense of sequential rules, is 1 or 3 as in our compounds.

For axial conformers, a substituent increment must be added to the cycle contribution (opposite sign relative to the equatorial ones owing to cycle inversion). This axial substituent increment is the sum of two terms corresponding to its gauche position relative to C(2)–C(3) and C(5)–C(6) bonds. The signs are those of the corresponding dihedral angles. When the second of these terms is given from the $k(C - H)(X - H)$ rotatory power estimated by Brewster,[4] we calculate the first term $[M]_D = -k(C^* - H)(X - H)$ through the following relationships established as Brewster does for 1,2-ethanediol:[4]

$$k(C^* - H)(X - H) = k(C - H)(C^* - H)k(X - H)^2/k(C - H)(X - H) \qquad (3)$$

$$k(X - H)^2 = [k(C - H)(X - H)]^2/k(C - H)^2 \qquad (4)$$

As $k(C - H)^2 = 60$ and $k(C - H)(C^* - H) = 140$, the specific molecular rotatory power of the 4*S* axial conformers is

$$\Sigma[M]^A_D = 160 - {}^4\!/\!_3 k(C - H)(X - H) \qquad (5)$$

For each substituent, the corresponding values are reported in Table II. Owing to the difference between Brewster's reference wavelength and that of our experiments, $[M]_{5461}$ values have been calculated through the simplified Drude equation $[M]\lambda^2$ = constant.

For the fluorine substituent, two different values of $k(C - H)(F - H)$ are available, Brewster's[4] (−10) and that which can be calculated from the helicoidal rotatory power model (+30).[16]

For the deuterium substituent, the conformational rotatory power $k(C - H)(D - H)$ can be calculated from the R atomic refractions according to the Brewster relationship:[4]

$$k(C - H)(D - H) = 160(R_C^{1/2} - R_H^{1/2})(R_D^{1/2} - R_H^{1/2}) = -1.13$$

For each compound studied in this work as well as for (4*S*)-4-carboxycyclohexene and (4*S*)-4-methylcyclohexene, we have calculated (Table III) the conformational free energy difference ΔG°_X of corresponding groups by using experimental rotatory power values $\langle[\alpha]\rangle$ and those of specific rotatory powers $[\alpha]_E$ and $[\alpha]_A$ (Table IV).

It is a simple new way to estimate ΔG°_X. As good agreements are observed with the values previously reported from other experimental methods, we must emphasize the remarkable efficiency of Brewster's procedures and the accuracy of the parameters. As an example, an error of 50 cal mol^{-1} on ΔG°_{Cl} would not change the $[\alpha]_A$ value by more than 6%.

For 4-deuteriocyclohexene, the result ($\Delta G^\circ_D \simeq -2$ cal mol^{-1}) is in good agreement with a recent report of Anet and Kopelevich[22] on selectively deuteriated cyclohexane-d_{10}. The only disagreement comes from 4-fluorocyclohexene, but it may be noticed that the Brewster increment value (−10) is an a priori calculated one. To fit $G^\circ_A - G^\circ_E = 14$ cal mol^{-1}, it would be necessary to raise the fluorine increment to +60, a value that could be used in future calculations.

Thermal Variation of Rotatory Power. For chiral molecules that exhibit a conformational equilibrium between two conformers E ⇄ A, a thermal variation analysis of the average rotivity $\langle\Omega_0\rangle$ is possible:

$$\langle\Omega_0\rangle = (\Omega_0^E - \Omega_0^A)w_E + \Omega_0^A \qquad (6)$$

$$w_E = \exp(-\Delta S^\circ/R)/[\exp(-\Delta S^\circ/R) + \exp(-\Delta H^\circ/RT)]$$

The $\langle\Omega_0\rangle$ values are obtained from the experimental rotatory power measured in different saturated hydro-

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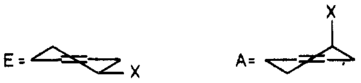
Table II. Calculated Rotatory Powers of Different 4*S*-Substituted Cyclohexene Conformers



X	$k(C-H)(X-H)$ (5894 Å)	$[M]^E_D$ (5894 Å)	$[M]^E_{5461Å}$[a]	$[\alpha]^E_{5461Å}$[b]	$[M]^A_D$[c] (5894 Å)	$[M]^A_{5461Å}$[a]	$[\alpha]^A_{5461Å}$[b]
Cl	170	−160	−186	−159	−67	−78	−67
F	−10	−160	−186	−186	+173	+201	+201
	+30	−160	−186	−186	+120	+140	+140
CN	160	−160	−186	−174	−53	−62	−58
COOH	90	−160	−186	−148	+40	+47	+37
CH_3	60	−160	−186	−194	+80	+93	+97
D	−1.13	−160	−186	−224.5	+161.5	+188	+226.7

[a] $[M]_{5461Å}$ calculated from $[M]_D$ through the relation $[M]_{5461Å} = [M]_D(5894)^2/(5461)^2$. [b] $[\alpha]_{5461Å} = 100[M]_{5461Å}/MW$ (MW = molecular weight). [c] Calculated from eq 5.

Table III. Conformational Free Energy Difference $\Delta G°_X$ (kcal mol^{-1} at 298 K)

X	$\langle[\alpha]\rangle$ (5461 Å)	$G°_A - G°_E = -\Delta G°_X$	
		this work[f]	literature
Cl	−118.32[a]	0.14	0.200 (116 K) rmn[c] [17] 0.200 (213 K) rmn[d] [18] 0.100 (303 K) 0.310 (128 K) rmn[e] [19]
F	−46.28[a]	0.34 (−10) 0.17 (+30)	0.014 (107 K), rmn[c] [17]
CN	−120.56[a]	0.09	0 (303 K) rmn[d] [18]
COOR	−110[g] (R = H)	0.8 (R = H)	0.8 (R = CH_3) rmn[d] [20]
	−121 (R = H)	1.0 (R = H)	
CH_3	−153.12[b]	1.07	1.0 (298 K) kinetic[21] 1.15 (298 K) tvrp[3]
D	+0.70[b]	0.002	0.006 rmn,[d] cyclohexane ring[22]

[a] Solvent C_6H_{12}. [b] Solvent C_8H_{18}. [c] Low-temperature integration of signals. [d] Compound partially deuteriated. [e] Solvent CF_2Cl_2. [f] Values calculated from eq 2; for $[\alpha]^E$ and $[\alpha]^A$, cf. Table II. [g] −110 (*c* 7, CH_3OH) (ref 7); −121 (*c* 1.54, CCl_4) (ref 8).

Table IV. Intrinsic Rotivities Ω_0 of 5*S* and 6*S* vs. Temperature

t, °C	**5*S*** $\langle\Omega_0\rangle$[a]	**5*S*** $\langle\Omega_0\rangle$[b]	**6*S*** $\langle\Omega_0\rangle$[a]
−15	−20.192	−22.648	−39.326
−10	−19.775	−21.833	−38.790
−5	−19.623	−20.994	−38.377
0	−19.272	−20.539	−37.966
5	−18.926	−19.813	−37.323
10	−18.424	−19.060	−36.723
15	−18.104	−18.323	−36.264
20	−17.787	−17.580	−35.656
25	−17.492	−16.968	−35.139
30	−17.219	−16.579	−35.682
35	−16.949	−16.254	−34.236
40	−16.485	−15.688	−33.810
45	−16.122	−15.245	−33.414
50	−15.742	−14.847	−33.058
55	−15.402	−14.566	−32.701
60	−15.123	−14.253	−32.354
65	−14.787	−13.871	−31.957

[a] $\langle\Omega_0\rangle$ values calculated from values of $\langle\Omega\rangle$ in solvent heptane. [b] $\langle\Omega_0\rangle$ values calculated from values of $\langle\Omega\rangle$ in solvent *cis*-decalin.

Table V. Calculated Intrinsic Rotivities of 5*S* and 6*S* Conformers from [α] Values of Table II

	5*S*			**6*S***	
	E	A[c]	A[d]	E	A
$[\alpha]_{5461Å}$	−186	+201	+140	−159	−67
Ω[a]	−45.3	+49	+34	−39	−16.3
Ω_0[b]	−159.5	+228	+166	−67.4	+9.25

[a] $\Omega = [\alpha]/(n^2 + 2)$; $n = 1.45$. [b] Ω_0 estimation from eq 7; **5*S***, $K = -0.355$, $L = -8.54$; **6*S***, $K = -0.38$, $L = -27.02$. [c] Hypothesis $k(C - H)(F - H) = -10$. [d] Hypothesis $k(C - H)(F - H) = +30$.

carbon solvents[1-3] by using Beckmann and Cohen's equation:[23]

$$\langle\Omega\rangle = \langle[\alpha]\rangle/(n^2 + 2) = \langle\Omega_0\rangle + P(n^2 - 1)/(n^2 + 2)$$

In a recent report, Vul'fson and Nikolaev[24] show that, contrary to Beckmann and Cohen's theory, the solvent effect on $\langle\Omega\rangle$ does not stem from a direct influence of the medium dielectric constant on optical activity. Yet, they agree with our procedure to take into account the solvent effect on rotivities $\langle\Omega\rangle$ when conformational studies are performed on the thermal variation of optical activity. They emphasize our conclusion about the necessity of using the intrinsic rotivity $\langle\Omega_0\rangle$ to get significant results. Owing to the conclusions of Vul'fson and Nikolaev,[24] we forsake the term "vacuum rotivity" for $\langle\Omega_0\rangle$, which we have previously used[1] owing to Beckmann and Cohen's theory.

A least-squares analysis of the experimental graph $\langle\Omega_0\rangle = f(T)$ allows calculation of the thermodynamic parameters $\Delta H°$ and $\Delta S°$ and intrinsic conformer rotivities Ω_0^E and Ω_0^A. Nevertheless, we have shown that the experimental accuracy is not sufficient to simultaneously obtain these four parameters.[1] Owing to the good results of the preceding section, we plan to use the specific rotatory powers that have been determined to support the tvrp studies of **4*S***, **5*S***, and **6*S***. The 4-cyano derivative has not been studied owing to the predicted vibronic coupling of this compound. As we have previously shown,[2] such a coupling can contribute significantly to the tvrp, precluding any analysis in terms of conformational variations.

The tvrp's have been measured in three solvents for **6*S*** (Figure 1) and in two solvents for **5*S*** (Figure 2). The results are typical of compounds with a two-conformer equilibrium. With molecules locked in one conformation, the experimental points would be along the line bringing together the 25 °C points which only relate to the solvent effect. As each solvent graph in Figures 1 and 2 is nearly perpendicular to this line, it is obvious that a more important effect, the variation of the conformational populations, is superposed upon the solvent effect.

The intrinsic rotivities of **5*S*** and **6*S*** (Table IV) have been calculated through the relationship

$$\langle\Omega_0\rangle_T = (\langle\Omega\rangle_T K + \eta_T L)/(K + \eta_T) \qquad (7)$$

with

$$\eta_T = (n^2 - 1)/(n^2 + 2) \quad \text{and} \quad \langle\Omega_0\rangle = K\langle P\rangle + L$$

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To calculate specific rotivities Ω_0^E and Ω_0^A from specific rotatory powers $[\alpha]_E$ and $[\alpha]_A$, determined in the previous section, we postulate that Brewster's values correspond to an average refractive index ($n = 1.45$). Equation 6 and experimental parameters K and L have been utilized to calculate rotivities Ω_0 from rotivities Ω ($n = 1.45$) (Table V).

For 4-chlorocyclohexene **6*S***, a least-squares analysis of the $\langle\Omega_0\rangle = f(T)$ experimental curve is readily carried out when one of the two parameters $\Delta S°$ or Ω_0^A is fixed. The first case ($\Delta S° = 1.5, 2.0, 2.65$) illustrates that the Ω_0^E values resulting from these calculations (−77, −76, −66) depend on the assumed $\Delta S°$ values and are in agreement with Ω_0^E issuing from Brewster's procedure (Table V). The alternative minimization, which uses as a fixed value the Ω_0^A from Table V, leads to the three other parameters, with their uncertainties (twice the standard deviation) within parentheses.

$$\textbf{6}\boldsymbol{S}\text{:}\ \Omega_0^E = -68.7\ (22),\ \Delta H° = 0.86\ (0.3)\ \text{kcal mol}^{-1},\ \Delta S° = 2.3\ (0.2)\ \text{cal mol}^{-1}\ \text{deg}^{-1}$$

The free energy difference $\Delta G° = 0.17$ (0.36) kcal mol^{-1} that results from these parameters is in agreement with the experimental value (Table III). On the other hand, one may emphasize that the Ω_0^E value is concordant with that of Table V, which confirms the conformer identification as with 4-methylcyclohexene.[3]

In the case of 4-fluorocyclohexene **5*S***, it is not possible to carry out the minimization if only one of the four parameters is fixed. This problem reflects the low conformer enthalpy difference, which does not allow important population changes with temperature. Therefore, the experimental accuracy is not sufficient to determine three parameters simultaneously. Nevertheless, if we use Ω_0^E and Ω_0^A of Table V as fixed values, the two-parameter minimization leads to $\Delta H°$ and $\Delta G°$ in kcal mol^{-1} and $\Delta S°$ in cal mol^{-1} deg^{-1}:

$$\textbf{5}\boldsymbol{S}\text{:}\ \Delta H° = 0.131\ (0.006),\ \Delta S° = -0.64\ (0.02),\ \Delta G° = 0.322\ (0.012)$$

$$\Delta H° = 0.147\ (0.007),\ \Delta S° = -0.006\ (0.02),\ \Delta G° = 0.149\ (0.013)$$

The two sets of values correspond to the $k(C-H)(F-H)$ hypothesis (−10 and +30, respectively).

The analysis of the **4*S*** tvrp data is a special case since $\Omega^E \simeq -\Omega^A$ (Table II), which reduces eq 6 to two parameters:

$$\langle\Omega\rangle \simeq (2w_E - 1)\Omega^E \tag{8}$$

From Beckmann and Cohen's equation for the equatorial conformer,

$$\Omega^E = \Omega_0^E + P^E\eta \tag{9}$$

at a given temperature, variation of the average rotivity with solvent is

$$\Delta\langle\Omega\rangle \simeq P^E(2w_E - 1)\Delta\eta$$

If we suppose $\Delta G° \simeq 10$ cal mol^{-1} at 300 K, $w_E \simeq 0.50$. Taking into account this approximate w_E value and the $\Delta\eta$ (5×10^{-2}) corresponding to our solvent range, and postulating that P^E is equal to that of 4-methylcyclohexene (51.5),[3] we estimate the maximum value of $\Delta\langle\Omega\rangle$ at about 2×10^{-2}, a figure that is scarcely detectable.

Consequently, tvrp analysis of 4-deuteriocyclohexene has been achieved in only one solvent (octane) between −15 and +65 °C. A relatively important variation of $\langle\Omega\rangle$ (10 times higher than that appearing in the solvent effect) was observed (Table I), which corresponds to a change in conformer populations.

From eq 8 and 9, we obtain

$$\langle\Omega\rangle_T = (2w_E - 1)_T(\Omega_0^E + P^E\eta_T) \tag{10}$$

If we consider, as Brewster does, that the molecular rotivity of an equatorial conformer does not vary with substituent, we can evaluate $\Omega_0^E \simeq -71$ from the intrinsic rotivity of 4-methylcyclohexene.[3]

Experimental values $\langle\Omega\rangle_T$ and η_T (Table I) lead to an evaluation of the equilibrium constant K_T; a least-squares analysis of the thermal variation of ln K_T allows the calculation of $\Delta H°$. The result obtained, $\Delta H° = H°_A - H°_E = +13$ cal mol^{-1} (±1.2) is in good agreement with that derived from the equilibrium constant expression:

$$K = (\Omega_0^E - \langle\Omega_0\rangle)/(\langle\Omega_0\rangle - \Omega_0^A)$$

$$\Delta H° = -(2RT^2/\Omega_0^E)(\mathrm{d}\langle\Omega_0\rangle/\mathrm{d}T)$$

with

$$\Omega_0^E \simeq -\Omega_0^A \quad \text{and} \quad |\langle\Omega_0\rangle| \ll |\Omega_0^E|$$

According to the previous discussion, since the solvent effect does not affect the measurement, we can combine the thermal variation of $\langle\Omega\rangle$ with that of the intrinsic average rotivity $\langle\Omega_0\rangle$.

$$(\mathrm{d}\langle\Omega_0\rangle/\mathrm{d}T) \simeq (\mathrm{d}\langle\Omega\rangle/\mathrm{d}T)$$

Results (Table I) allow an enthalpy difference evaluation of $\Delta H° = H°_A - H°_E = +10$ cal mol^{-1}; even if this value is only a rough estimate owing to the above hypothesis, its sign, which is given by $(\mathrm{d}\langle\Omega\rangle/\mathrm{d}T)$, proves that the equatorial conformer is more stable than the axial one.

The deuterium conformational enthalpy $\Delta H°_D = -\Delta H°$ is therefore negative as for all other substituents.

Conclusion

Our study shows coherent and complementary corrections between the empirical Brewster's procedure and our analysis of the thermal variation of the rotatory power. Accordingly, our method is useful for conformational analysis.

With the cyclohexene derivatives under investigation, different levels of integration of the two methods have been necessary. With 4-chlorocyclohexene, only one Brewster's parameter (Ω_0^A) was introduced in the tvrp analysis that provided the $\Delta H°$, $\Delta S°$, and Ω_0^E values. This last one agrees well with the Brewster's one. Owing to the low $\Delta H°$ of the 4-fluorocyclohexene, Brewster's Ω_0^E and Ω_0^A values were used to give $\Delta H°$ and $\Delta S°$.

The conformational equilibrium of 4-deuteriocyclohexene was analyzed easily owing to the weak solvent effect and to the relationship between the conformer rotivities. The sign of the thermal variation of the rotatory power proves that the deuterium conformation enthalpy is negative as with the other substituents; but $\Delta H°$ is reduced to a few calories/mole according to the tvrp analysis. In a recent paper,[22] Anet and Kopelevich have shown by NMR spectroscopy that deuterium prefers the equatorial position in a cyclohexane ring: $\Delta G° = G°_A - G°_E = 6.3 \pm 1.5$ cal mol^{-1}, in good agreement with our $\Delta H°$ value. These results (small equatorial conformational preference) seem to be opposite to the well-known reduced size of the deuterium atom relative to hydrogen; but it may be argued, as by Allinger et al.,[25] that it is the geminal hydrogen that prefers the axial position.

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If we refer to other recent studies of monodeuteriated six-membered rings, we must emphasize that the thermal variation of circular dichroism is weak with 3(*R*)-deuteriocyclohexanone,[26] more important for 5(*S*)-deuterio-2,2-dimethylcyclohexanone,[27] and very important for 3(*R*)-deuterio-2,2-dimethylcyclohexanone.[27] For these last two compounds, thermal variation analysis leads to $\Delta H° = H°_A - H°_E < 0$, but we argue that the thermal variation may have been induced, in large part, by a vibronic effect like the one we have found in camphor.[2] Therefore, the difference between the cyclohexene and cyclohexanone results is not significant.

Supplementary Material Available: Tables S-II and S-III of rotativities of **5*S*** at −15 to 65 °C in *n*-heptane and *cis*-decalin and of **6*S*** at −15 to 65 °C in these solvents and in octane (2 pages). Ordering information is given on any current masthead page.

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Pyrocondensation of Anthracene

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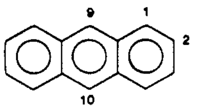
The predominant initial products in the thermal chemistry of anthracene are 2,9′-bianthracenyl and 9,10-dihydroanthracene. Over the range 350–500 °C, in the gas and liquid phase, this reaction follows second-order kinetics with $k/\mathrm{M}^{-1}\ \mathrm{s}^{-1} = 10^{7.37\pm0.27} \exp\{-22520\pm420/T\}$. The only other major product is 1,9′-bianthracenyl, which at low extents of reaction is formed at a rate one-seventh that of 2,9′-bianthracenyl. Anthracene selectively forms biaryls with the following compounds (relative rate constants for forming the major cross-biaryls are in parentheses): naphthalene (0.5), phenanthrene (0.2), biphenyl (0.2), diphenyl ether (0.2). A kinetic analysis of results leads us to propose that the initial step in these reactions is the reversible formation of a diradical via coupling of two ground-state molecules. This is followed by a rate-limiting, intramolecular H-transfer step resulting in a dihydrobiaryl molecule, which then rapidly loses two hydrogen atoms, probably by free radical reactions, to form the major biaryl products. Minor biaryl products are formed in a less selective manner in a reaction catalyzed by 9,10-dihydroanthracene. Aryl radicals are likely intermediates in these reactions.

Introduction

Upon heating, hydrocarbons tend to decompose along two parallel pathways: one leads to small, thermally stable molecules, the other to a complex, intractable carbonaceous residue. Most studies of hydrocarbon pyrolysis have examined the former pathway. There now exists a large body of detailed kinetic data in this area as well as well-developed predictive ability. This advanced state is most evident in the case of paraffin pyrolysis, which, despite its considerable mechanistic complexity, is one of the best understood classes of reactions in chemical kinetics.[1]

On the other hand, relatively few chemical studies of reactions leading toward carbonization have been reported. Moreover, these studies have only rarely been done with the intention of deducing exact reaction mechanisms. As a result, while some general features of these reactions are known, mechanistic details, such as intermediates and rate-controlling steps, are largely unknown. We are now engaged in a program intended to clarify some of the basic features of these reactions. We report here studies of the "model compound" anthracene (An).

We chose to study anthracene pyrolysis for the following reasons. (1) A previous theoretical analysis suggested that "polymerization" might follow a straightforward free-radical pathway.[2] (2) Anthracene has only one highly reactive position, the meso (9 or 10) position, and therefore promised to react in a relatively simple manner. (3) Thermodynamic and kinetic properties of probable reaction intermediates were known or roughly estimable.[2,3] (4) Bianthracenyl isomers can be analyzed by gas chromatography.



Results of previous work on An pyrolysis are summarized below.

Several survey studies of a range of aromatic compounds[4,5] have concluded that as a neat liquid, An is a relatively reactive unsubstituted polyaromatic hydrocarbon which begins to decompose in the range 400–450 °C. It decomposed at least 100 times slower as a gas than as a liquid.[4]

In the early 1960s both Lang and Buffleb[6] and Badger et al.[7] examined An pyrolysis in gas-phase flow reactors with the aim of identifying products. Both groups reported 2,2′-bianthracenyl as a major reaction product near 700 °C and also reported products apparently formed by condensation of other bianthracenes. Reaction extents were rather high (>10% reported by Badger et al.), and unidentified tars were formed.

Walker and co-workers[8] used UV absorption to measure An disappearance rates at 490–509 °C over the applied pressure range 0.34–2.07 kbar. They found first-order kinetics from ~20% to >99% decomposition as well as a significant pressure dependence ($V = -17\ \mathrm{cm}^3\ \mathrm{mol}^{-1}$). Their reported Arrhenius expression was $10^{9.4}$ exp{−

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