

**ELECTROSTATIC EFFECTS ON CONFORMATIONAL EQUILIBRIA:  
SOLVATION ENTHALPIES AND THE REACTION FIELD THEORY**

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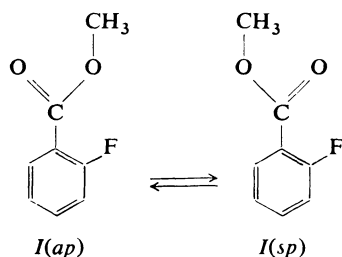
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Solvation enthalpies of isomeric methyl 2-, 3-, and 4-fluorobenzoates in solvents n-hexane and nitromethane were determined calorimetrically. The enthalpy of the conformational equilibrium  $ap \rightleftharpoons sp$  of methyl 2-fluorobenzoate was estimated from the temperature dependence of IR spectra and served to calculate the solvation enthalpies of the two conformers, although with a considerable uncertainty. All the results together were discussed in terms of two theories: a) the simple electrostatic approach predicting the reaction enthalpy from the coulombic interaction of atomic charges in an apparently homogeneous medium, and b) the extended reaction-field theory expressing the solvation energy as a sum of dipole, quadrupole, cavity, and dispersion terms. In addition, quantum chemical calculations on various levels were carried out. Comparison with experiments revealed that the reaction-field theory, even if extended, reproduces only the general trend in the solvation enthalpies. Of the individual terms particularly the dispersion term is likely to be responsible for the bad fit: it is significant but cannot be satisfactorily predicted by the present theory. Also the cavity term is misrepresented by theory while it is in fact unimportant for isomeric molecules. The simple electrostatic approach predicts the reaction enthalpy in the gas phase relatively well, *i.e.* with a similar precision as semiempirical quantum chemical methods. In solvents this approach works worse, but still better than a two-step calculation consisting of the electrostatic gas-phase value and of the reaction-field solvation enthalpy; the latter procedure cannot be generally recommended. Summarizing, our results are in favour of simple theories which yield approximate results of the same quality as the more sophisticated ones, sometimes even better.

The effect of electrostatic energy on conformational equilibria has been investigated on several model systems<sup>1-3</sup> but most frequently on aromatic compounds existing

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in two coplanar conformations<sup>4-9</sup>. Among the systems investigated by us<sup>6-9</sup>, methyl 2-fluorobenzoate (*I*) was most suitable<sup>6,8</sup> for two reasons: The electrostatic effect is sufficiently strong (in contradistinction to 3-substituted derivatives<sup>4,7</sup>) and the non-bonded interactions (*i.e.* steric effects) compensate with a good approximation. Under such conditions the simple electrostatic theory, representing the solvent together with a solute molecule as a homogeneous continuum, works reasonably well. We obtained a good agreement of the experimental Gibbs energy of the equilibrium  $I(ap) \rightleftharpoons I(sp)$  in nonpolar solvents with electrostatic calculations, when using the solvent bulk permittivity and the point-charges approximation<sup>6</sup>, less satisfactory was the point-dipoles approximation<sup>9</sup>.



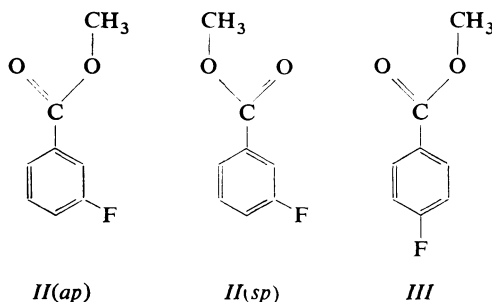
In polar solvents, this equilibrium was predicted at least qualitatively within the framework of the same theory but any more accurate value of the effective permittivity could not be obtained<sup>8</sup>. This is one shortcoming of the approach. Some authors obviated it by applying the electrostatic formula for the gas phase<sup>2,3,10,11</sup> and calculating the solvation energy separately<sup>10-16</sup> in terms of a more sophisticated theory. The reaction-field theory<sup>12-14</sup> expresses the solvent-solute interaction as a function of solute dipole, quadrupole, or even octupole<sup>16</sup>; its extension adds still a dispersion energy term<sup>15,16</sup> and solvent-solvent interaction<sup>15,16</sup> (*i.e.* cavity term). There is, however, little agreement as to which terms may or must not be neglected, and as to the values of certain parameters.

Another problem is which experimental quantity should be used for comparison with theory. The simple coulombic energy calculations, with the permittivity equal to unity, concern the isolated molecule and correspond thus to potential energy  $\Delta E_p$ , with some approximation also to  $\Delta H^0$  or  $\Delta G^0$  at absolute zero. At a finite temperature  $\Delta H^0$  was claimed to be a better approximation<sup>17</sup> than  $\Delta G^0$  since it is probably less temperature dependent. The coulombic energy calculated for a solution cannot be related to any thermodynamic quantity in a straightforward way: the reason is in the not well defined effective permittivity. The great uncertainty in the latter makes also the choice of the experimental quantity less important. In practical applications  $\Delta G^0$  was used more frequently<sup>4-9</sup> than  $\Delta H^0$  (ref.<sup>3</sup>). Note also the serious discrepancies among the experimental results themselves<sup>10</sup>. On the contrary, the

reaction-field theory considers the solute molecule in a force field the potential of which is added to the chemical potential. The calculated energy is thus  $\Delta G^0$  (compare the reasoning in ref.<sup>13</sup>) and must be converted into  $\Delta H^0$  if necessary<sup>12</sup>.

Our first intention was to determine  $\Delta H^0$  of the equilibrium  $I(ap) \rightleftharpoons I(sp)$  and solvation enthalpies  $\Delta H_{\text{soliv}}$  of the two rotamers, to be compared with electrostatic and reaction-field calculations. Since  $\Delta H^0$  could not be estimated with the required reliability, we extended the investigation to isomeric methyl 3-fluorobenzoate (*II*) and 4-fluorobenzoate (*III*). These model compounds present no conformational problems: The equilibrium  $II(ap) \rightleftharpoons II(sp)$  is very near to 1 : 1, while no rotamers are possible in the case of *III*. We determined solvation enthalpies of *I–III* in one nonpolar and one polar solvent (n-hexane and nitromethane), and estimated the less dependable values for the rotamers *I(ap)* and *I(sp)* basing on the temperature dependence of IR spectra in n-decane and decahydronaphthalene. All the values are confronted with the extended reaction-field theory, analyzing the individual terms of the solvation energy. In the case of the equilibrium  $I(ap) \rightleftharpoons I(sp)$  it was also possible to compare the direct electrostatic calculation with the indirect way which involves the solvation energy adopted from the reaction-field theory. We further attempted to improve the electrostatic calculations taking into account the charges on all atoms instead only on the most polar bonds. These charges were calculated by various quantum chemical methods.

Comparison of all the compounds *I–III* together means in other terms that we investigate – in addition to the equilibrium  $I(ap) \rightleftharpoons I(sp)$  – also the experimentally inaccessible equilibria  $II \rightleftharpoons III$  and  $I \rightleftharpoons III$ . Such approach may be considered artificial but the theory does not assume that the equilibrium should be reached by a certain rate. On the other hand, the obvious merit of our approach is in obtaining directly the solvation enthalpies which can be compared with theory immediately.



## EXPERIMENTAL

*Materials:* Methyl 2-fluorobenzoate (*I*) was characterized previously<sup>6</sup>. Methyl 3-fluorobenzoate (*II*), b.p. 84–85°C/2.7 kPa,  $n_D^{20}$  1.4928, and methyl 4-fluorobenzoate (*III*), b.p. 85°C/2.7 kPa,  $n_D^{20}$  = 1.4935, were prepared in the same way<sup>6</sup> from commercially available acids, their purity

was checked by GLC. Since methyl 4-fluorobenzoate contained 1.1% of the 2-isomer, the measured enthalpies were corrected appropriately; the correction is, however, insignificant compared to the experimental error. The solvents, n-hexane, n-decane, decahydronaphthalene, and nitromethane, were purified by standard procedures. The hydrocarbons were dried with sodium metal, nitromethane with phosphorus pentoxide. The purity was checked by GLC; decahydronaphthalene contained 53% of the *trans*-isomer.

*Spectral measurements:* The IR spectra in the region  $1680\text{--}1780\text{ cm}^{-1}$  were registered on a Perkin-Elmer 621 instrument on a  $20\times$  expanded scale. NaCl cells were used, thickness 1 mm (concentration  $0.01\text{ mol l}^{-1}$  in decahydronaphthalene solution) or 0.16 mm (concentration  $0.09\text{ mol l}^{-1}$  in decane or nitromethane solution). Temperature was measured with a copper-constantan thermocouple. Measurements were always done at nine different temperatures, beginning with 302 K up to 368 K (in nitromethane), or up to 417 K (in decane), or 430 K (in decahydronaphthalene), respectively. The correction for concentration change with temperature was carried out using tabulated values of densities. In the case of decahydronaphthalene an extrapolation of the density data was necessary, based on the analogy with n-decane. No correction was applied for the change of the optical path with temperature. Note that these corrections are irrelevant for the resulting values of  $\Delta H^0$  in any case — the values of  $\Delta G^0$  are affected only if they have been calculated with the assumption of temperature independent absorption coefficients<sup>18</sup>.

The band separation and calculation of integrated absorption intensities was accomplished using a program based on Lorentz-type band shape<sup>6</sup>. If the data of the same series (*i.e.* differing in temperature only) are processed by this program, the results are markedly improved by the constraint that the band half-widths and wave numbers must shift regularly with temperature. Hence we processed the data twice: Firstly the wave numbers ( $\nu$ ), half-widths ( $\Delta\nu_{1/2}$ ), and integrated absorption intensities ( $A$ ) of the two bands, as well as the base-line values, were obtained by free computer fitting. Then the values of half-widths were smoothed out linearly with respect to temperature and the resulting values input into the second fitting. The values of wave numbers were always reasonably linear with temperature and need not be smoothed out. The principal spectral data are listed in Table I.

In calculating the thermodynamic quantities from infrared data the integrated absorption coefficients of the two rotamers were first taken as different and temperature dependent. They were expressed as  $\alpha_1 f_1(T)$  and  $\alpha_2 f_2(T)$ , respectively. When the analytical concentration is constant at different temperatures, the integrated absorption intensities  $A_1$ ,  $A_2$  are given through the mole fractions  $x_1$  and  $x_2$ :

$$A_1 = x_1 \alpha_1 f_1(T) \quad (1a)$$

$$A_2 = x_2 \alpha_2 f_2(T) \quad (1b)$$

Combining with the thermodynamic equation

$$-RT \ln \frac{x_2}{x_1} = \Delta H^0 - T \Delta S^0 \quad (2)$$

we get

$$\ln \frac{A_1}{A_2} = \frac{\Delta H^0}{R} T^{-1} + \ln \frac{\alpha_1}{\alpha_2} + \ln \frac{f_1(T)}{f_2(T)} - \frac{\Delta S^0}{R} \quad (3)$$

For determining  $\Delta H^0$  we assumed that the ratio of absorption coefficients (as well as  $\Delta S^0$ ) is temperature independent<sup>19</sup>, i.e.  $f_1(T) = f_2(T)$ . Then  $\Delta H^0$  is obtained from a linear regression of  $\ln(A_1/A_2)$  upon  $T^{-1}$ .

In order to determine  $\Delta G^0$ ,  $x_1$  and  $x_2$  are calculated from Eq. (2) and from the condition  $x_1 + x_2 = 1$ . By substituting the resulting values into Eqs (1a,b) one gets:

$$A_1 = \alpha_1 f_1(T) e^{\Delta H^0(T^{-1} - T_0^{-1})/R} / [e^{\Delta H^0(T^{-1} - T_0^{-1})/R} + e^{-\Delta G^0/RT_0}] \quad (4a)$$

$$A_2 = \alpha_2 f_2(T) e^{-\Delta G^0/RT_0} / [e^{\Delta H^0(T^{-1} - T_0^{-1})/R} + e^{-\Delta G^0/RT_0}] \quad (4b)$$

TABLE I

Infrared spectral data and derived conformer population of methyl 2- and 3-fluorobenzoates (I, II)

Compound	I		II		
	Solvent	n-decane	decahydro-naphthalene	nitromethane	decahydro-naphthalene
$\nu(\text{C=O})$ <i>ap</i> $\text{cm}^{-1}$ (302 K)		1 729.9	1 728.8	1 722.0	1 737.0
<i>sp</i> $\text{cm}^{-1}$ (302 K)		1 748.2	1 747.0	1 732.7	<sup>a</sup>
$\frac{1}{2} \Delta\nu_{1/2}$ <i>ap</i> $\text{cm}^{-1}$ (302 K)		3.69	3.53	7.03	3.1
<i>sp</i> $\text{cm}^{-1}$ (302 K)		3.48	3.49	5.65	<sup>a</sup>
<i>A ap</i> $\text{cm}^{-2} \text{ l mol}^{-1}$ (302 K)		7 989	9 000	7 768	11 661
<i>sp</i> $\text{cm}^{-2} \text{ l mol}^{-1}$ (302 K)		4 228	5 246	7 599	<sup>a</sup>
$\Delta H^0$ $\text{kJ mol}^{-1}$		1.32	0.44	3.24	—
$\Delta G^0$ $\text{kJ mol}^{-1}$ (298 K) <sup>b</sup>		1.60	1.36	0.04	—
$N_{\text{ap}}\%$ (298 K) <sup>b,c</sup>		66	63	50	—
$s \cdot 10^2$ <sup>b,d</sup>		0.58	0.86	0.68	—
$\Delta G^0$ $\text{kJ mol}^{-1}$ (298 K) <sup>e</sup>		-5.27	<sup>g</sup>	-2.16	—
$N_{\text{ap}}\%$ (298 K) <sup>e,c</sup>		11	<sup>g</sup>	29	—
$s \cdot 10^2$ <sup>e,d</sup>		0.56	<sup>g</sup>	0.66	—
$\alpha_1/\alpha_1$ <sup>e</sup>		11.2	-3.32	1.93	—
$\Delta G^0$ $\text{kJ mol}^{-1}$ (298 K) <sup>f</sup>		1.32	0.44	3.24	—
$N_{\text{ap}}\%$ (298 K) <sup>f,c</sup>		63	54	79	—
$s \cdot 10^2$ <sup>f,d</sup>		0.58	0.86	0.69	—
$\alpha_1/\alpha_1$ <sup>f</sup>		1.12	1.45	0.28	—

<sup>a</sup> Bands not resolved; <sup>b</sup> calculated with the assumption  $\alpha_1 = \alpha_2$ , see Experimental; <sup>c</sup> population of the *ap* rotamer; <sup>d</sup> residual standard deviation in  $\ln A$ , the figures represent also the per cent. relative error in  $A$ ; <sup>e</sup> calculated with the assumed temperature independence of  $\alpha$ , see Experimental; <sup>f</sup> assumption  $\Delta G^0 = \Delta H^0$ ; <sup>g</sup> no solution ( $\alpha_1/\alpha_2$  negative).

Eqs (4a,b) should in principle allow to obtain  $\Delta H^0$ ,  $\Delta G^0$ ,  $\alpha_1$ ,  $\alpha_2$  simultaneously by least-squares fitting of the values of  $A_1$ ,  $A_2$  in the dependence on  $T$ ; the functions  $f_1(T)$  and  $f_2(T)$  must be assumed to have a simple form, e.g. linear. However, with actually available data no convergence was obtained unless one of the following additional constraints was adopted: a) The integrated absorption coefficients are equal at any temperature<sup>20</sup>, i.e.  $\alpha_1 = \alpha_2$  and  $f_1(T) = f_2(T)$ . b) The integrated absorption coefficients are different but independent of temperature, i.e.  $\alpha_1 \neq \alpha_2$  and  $f_1(T) = f_2(T) = 1$ . In this case the ratio  $\alpha_1/\alpha_2$  can be obtained<sup>18</sup> by a linear regression of  $\alpha_1$  vs  $\alpha_2$ . c) The entropy difference between rotamers is neglected, so that  $\Delta G^0$  simply equals  $\Delta H^0$ .

We calculated  $\Delta G^0$  and the population of rotamers with one of the three assumptions a–c and using Eq. (4); the unknown parameters were determined by computer fitting, minimizing the sum of squares in  $\ln A$ . The results are given in Table I. According to the residual standard deviations (in  $\ln A$ ) all the hypotheses a–c would be equally acceptable. However, that sub b) can be rejected as it requires unacceptable values of  $\alpha_1/\alpha_2$ , in one case even negative. Note that the calculations of  $\Delta G^0$  were not improved when some points — deviating in the  $\ln(A_1/A_2)$  vs  $T^{-1}$  plot — were dropped.

*Calorimetric measurements:* The enthalpies of solution ( $\Delta H_{\text{sol}}$ ) were determined in a Calvet calorimeter (Setaram, Lyon) using asymmetric two-part vessels of stainless steel with aluminium foil<sup>21</sup>. The vapour area was minimized by adding mercury, and a correction for the heat of vaporization was determined from blank experiments. The final concentration of solute did not exceed 1.5% by weight. Signal from the calorimeter was monitored, digitalized and integrated<sup>22</sup> using a Wang 2200 C calculator. The results are listed in Table II, their accuracy is better than  $\pm 2\%$ .

TABLE II  
Thermodynamic data of isomeric methyl fluorobenzoates (kJ mol<sup>-1</sup>)

Isomer	I <sup>a</sup>	II <sup>a</sup>	III
	2-F	3-F	4-F
Enthalpy of solution $\Delta H_{\text{sol}}$ (298.15 K)			
in n-hexane	9.87	8.30	8.43
in nitromethane	3.10	4.11	4.14
Enthalpy of vaporization $\Delta H_v$			
at 368.15 K (experiment)	53.6	51.2	51.2
at 298.16 K (extrapolated)	57.7	55.4	55.3
Critical temperature K (estimated <sup>25</sup> )	693.5	676.3	677.7
Enthalpy of solvation $\Delta H_{\text{solv}}$ (298.15 K)			
in n-hexane	-47.8	-47.1	-46.9
in nitromethane	-54.6	-51.3	-51.2

<sup>a</sup> Experimental values valid for the actually populated mixture of rotamers, see Discussion.

The enthalpies of vaporization ( $\Delta H_v$ ) were determined by means of a calorimeter of the isothermal adiabatic type with detachable vessel, operating on the principle of complete evaporation of the liquid<sup>2,3</sup>. Experiments were carried out at the temperature 368.15 K and the results extrapolated to 298.15 K using the Watson relation<sup>2,4</sup>:

$$\Delta H_{v_1} = \Delta H_{v_2} \left( \frac{1 - T_1/T_c}{1 - T_2/T_c} \right)^{0.38} \quad (5)$$

The critical temperature  $T_c$  was estimated according to Lydersen<sup>2,5</sup>. The results are given in Table II. The accuracy of the experiment was estimated to be within 0.2%, the error caused by the extrapolation may be 0.5–0.8%. The final values are thus reliable to 0.4 kJ mol<sup>-1</sup>. Since, however, the effect of extrapolation is virtually constant for the three isomers, the relative values should be reliable to 0.1 kJ mol<sup>-1</sup>.

The enthalpies of solvation,  $\Delta H_{solv}$ , were obtained from the relation

$$\Delta H_{solv} = \Delta H_{sol} - \Delta H_v \quad (6)$$

Their values are given in Table II. In the case of *ortho* and *meta* isomers they relate to a population of rotamers at 298 K. The values of  $\Delta H_{solv}$  for individual rotamers can be calculated only indirectly with certain assumptions. An attempt in this direction is described in Results.

*Measurement of dipole moments:* The dipole moments were determined either by the method of Halverstadt–Kumler (compounds *II* and *III*) like in our previous communication<sup>6</sup>, or by the method of Guggenheim–Smith (compound *I*) as used in our laboratory more recently<sup>2,6</sup>. The results are listed in Table III. Dipole moments expected for individual conformers and their mixtures were calculated from bond moments as previously<sup>6,9</sup>.

TABLE III  
Dipole moments of isomeric methyl fluorobenzoates (298 K)

Compound	Solvent	$\alpha^a$ $\beta^a$	$P_2^0$ $R_D^b$	$\mu(5)^c$ $\mu(15)^c$	$\mu_{calc}$
<i>I</i>	CCl <sub>4</sub>	6.19	—	7.3	7.57 <sup>e</sup>
		0.177 <sup>d</sup>	—	—	
<i>II</i>	benzene	3.01	125.6	6.9	6.51 <sup>f</sup>
		−0.307	37.7	6.7	
<i>III</i>	benzene	2.27	103.6	5.9	5.31
		−0.321	37.7	5.7	

<sup>a</sup> Slopes of the plots  $\epsilon_{12}$  vs  $w_2$  and  $d_{12}^{-1}$  vs  $w_2$ , respectively; <sup>b</sup> calculated from increments; <sup>c</sup> units 10<sup>-30</sup> C m, correction for the atomic polarization 5% or 15% of the  $R_D$  value, respectively; <sup>d</sup> the slope ( $\gamma$ ) of the plot  $n_{12}^2$  vs  $w_2$ , determination by the Guggenheim–Smith method; <sup>e</sup> calculated from bond moments for a 66 : 34 mixture of rotamers *I(ap)* and *I(sp)*; <sup>f</sup> calculated for a 50 : 50 mixture of rotamers *II(ap)* and *II(sp)*.

*Solvation energy calculations:* The basic idea which we can refer as extended reaction-field theory, is partitioning of the solvation enthalpy,  $\Delta H_{\text{solv}}$ , into the following contributions:<sup>12-16,27</sup>

$$\Delta H_{\text{solv}} = \Delta E_{\text{elst}} + \Delta E_{\text{cav}} + \Delta E_{\text{disp}} + \Delta E_{\text{spec}} \quad (7)$$

The terms  $\Delta E_{\text{elst}}$ ,  $\Delta E_{\text{disp}}$ , and  $\Delta E_{\text{spec}}$  characterize the electrostatic, dispersion, and specific interactions, respectively;  $\Delta E_{\text{spec}}$  is neglected when strong specific interactions are excluded by a proper choice of compounds and solvents. The term  $\Delta E_{\text{cav}}$  represents the energy required to create a cavity of sufficient size within the solvent. Its sign is positive in contrast to the other negative terms.

The electrostatic energy of the solute-solvent interaction,  $\Delta E_{\text{elst}}$ , was partitioned further in terms of the reaction-field theory proper in the form given by Abraham<sup>12-14</sup>:

$$\begin{aligned} \Delta E_{\text{elst}} &= \Delta E_{\text{dip}} + \Delta E_{\text{qdr}} + \Delta E_{\text{dp}} - \frac{d}{dT} (\Delta E_{\text{dip}} + \Delta E_{\text{qdr}} + \Delta E_{\text{dp}}) = \\ &= kx/(1 - lx) + 3hx/(5 - x) + bf[1 - \exp(-bf/16RT)] - T d \Delta E/dT \quad (8) \end{aligned}$$

The meaning of the variables  $b$ ,  $f$ ,  $h$ ,  $k$ ,  $l$ , and  $x$  is the same as given previously<sup>27</sup>. The first two terms in Eq. (8) express the dipolar and quadrupolar contributions to the solute electric field from the solute dipole (involved in  $k$ ) and quadrupole (in  $h$ ). The solvent permittivity is involved in its functions  $x$ . The solute polarizability is accounted for by  $l$ , function of the refractive index. The third term in Eq. (8), so called direct polar term, arises from generalized integration of the solute dipolar and quadrupolar interactions with the solvent dipoles. Hence it equals zero when the bulk solvent permittivity is less than 2, and becomes actually significant only in the most polar solvents. It was often neglected<sup>10,13,15</sup>, in our program it is included together with  $\Delta E_{\text{dip}}$  (Table IV). The last term in Eq. (8), originally substantiated not quite clearly<sup>12</sup>, is best understood as an entropy correction. It converts the value of  $\Delta G^0$  as determined by the preceding terms into  $\Delta H^0$ .

The calculation of the cavity term,  $\Delta E_{\text{cav}}$ , was based on an expression<sup>28</sup> taken from the Scaled Particle Theory (SPT) as given in Eq. (9).

$$\Delta E_{\text{cav}} = \left\{ -\ln(1 - y) + \frac{3y}{1 - y} R_a + \left[ \frac{3y}{1 - y} + \frac{9}{2} \left( \frac{y}{1 - y} \right)^2 \right] R_a^2 + \frac{yP}{\rho kT} R_a^3 \right\} RT \quad (9)$$

The equation was devised for  $\Delta G$ , we used it with some approximation for  $\Delta H$ . The meaning of variables  $R_a$ ,  $P$ , and  $y$  was the same as previously<sup>27</sup>.

The dispersion term,  $\Delta E_{\text{disp}}$ , involves both attractive and repulsive nonbonded interactions. The calculation was based on the improved theory<sup>29</sup> as given in Eq. (10) where constants  $K_r$  and  $\delta$  were taken as 0.5 and 0.436, respectively.

$$\Delta E_{\text{disp}} = -(1 - \delta) K_r^{3/2} N_v \alpha_u \alpha_v [I_u I_v / (I_u + I_v)] r_{uv}^{-6} \quad (10)$$

The meaning of all variables was the same as described previously<sup>27</sup>. Since the factor  $(1 - \delta)$  represents an empirical conversion of enthalpy into Gibbs energy, it was dropped in our calculations relating directly to enthalpy.

The values of individual terms according to Eq. (7)–(10) for solvents n-hexane, n-decane, and nitromethane are given in Table IV. Their sums, corresponding to the theoretically anticipated



$\Delta H_{\text{solv}}$ , are given in Table V as relative values, related to methyl 4-fluorobenzoate ( $\delta \Delta H_{\text{solv}} = 0$ ). Concerning the parameters in our calculations, those characterizing the particular solute molecules or conformers were chosen as listed in Table VI. They all are calculated values, except the refractive index  $n_D^{20}$  for which the experimental value was substituted, irrespective of the conformation. The ionization potentials were approximated by the energy of HOMO orbitals.

The centre of the spherical cavity was located always in the centre of gravity of the molecule and the coordinate axes were oriented in the direction of the principal central axes of rotation. Since the quadrupole moment depends upon the choice of coordinates, it was always related to this coordinate system.

*Quantum chemical calculations:* The CNDO/2, INDO, *ab initio* STO-3G, and MNDO methods were applied in standard parametrization, see ref.<sup>30-33</sup>, respectively. The geometry of the two conformers of methyl 2-fluorobenzoate was fully optimized except the conformation of the  $\text{CH}_3$  group (45 degrees of freedom), both by the gradient CNDO/2 method<sup>34</sup> and by MNDO method<sup>33</sup>. The results are listed in Table VII, together with our previous results<sup>8</sup> obtained with non-optimized geometry.

TABLE IV

Individual terms of the reaction-field theory for solvation of isomeric methyl fluorobenzoates (in  $\text{kJ mol}^{-1}$ , 298.15 K)

Isomer	$\Delta E_{\text{dip}} + \Delta E_{\text{dp}}^a$	$\Delta E_{\text{qdr}}^a$	$-T(d \Delta E/dT)^a$	$\Delta E_{\text{cav}}^a$	$\Delta E_{\text{dip}}^a$
n-Hexane					
<i>Isp</i>	-0.442	-0.014	-0.146	39.88	-102.96
<i>Iap</i>	-0.142	-0.015	-0.050	39.87	-103.26
<i>IIsp</i>	-0.331	-0.005	-0.109	40.10	-102.00
<i>IIap</i>	-0.003	-0.035	-0.012	40.10	-101.95
<i>III</i>	-0.093	-0.018	-0.037	39.85	-102.34
n-Decane					
<i>Isp</i>	-0.372	-0.010	-0.111	43.98	-96.86
<i>Iap</i>	-0.119	-0.010	-0.037	43.96	-97.15
<i>IIsp</i>	-0.281	-0.003	-0.081	44.63	-96.51
<i>IIap</i>	-0.002	-0.025	-0.007	44.63	-96.45
<i>III</i>	-0.079	-0.013	-0.026	44.35	-96.83
Nitromethane					
<i>Isp</i>	-2.112	-0.741	-1.172	56.57	-179.49
<i>Iap</i>	-0.678	-0.361	-0.495	56.55	-180.05
<i>IIsp</i>	-1.573	-0.487	-0.833	56.89	-177.70
<i>IIap</i>	-0.013	-0.405	-0.360	56.89	-177.61
<i>III</i>	-0.440	-0.333	-0.408	56.54	-178.32

<sup>a</sup> The terms are defined in Eqs (7)–(10).

*Electrostatic calculations:* The relative electrostatic energy of the two planar *ap* and *sp* conformers was calculated using point-charges approximation according to Eq. (11), where  $r_{ij}$  is the distance between the charges  $q_i$  and  $q_j$ .

$$2.303RT \log K = \frac{N_A}{4\pi\epsilon_0} \sum_{i,j} \left[ \left( \frac{q_i q_j}{r_{ij} \epsilon_{ef}} \right)_{sp} - \left( \frac{q_i q_j}{r_{ij} \epsilon_{ef}} \right)_{ap} \right] \quad (11)$$

The effective atomic charges were obtained by resolution of bond moments of polar bonds only, as described previously<sup>6-9</sup>, or alternatively for all atoms of the molecule from the CNDO/2, INDO, STO-3G, and MNDO electron distribution in combination with Mulliken population analysis (like in ref.<sup>7</sup>). The effective permittivity  $\epsilon_{ef}$  was taken equal to unity for the gas phase (results in Table VII), or equal to the bulk permittivity of the solvent<sup>35</sup> (results in Table VIII).

TABLE V

Comparison of enthalpies of solvation of isomeric methyl fluorobenzoates with the reaction-field theory (in  $\text{kJ mol}^{-1}$ , 298.15 K)

Isomer	Experimental		Calculated $\delta \Delta H_{\text{solv}}$ rel.	Calculated terms				
	abs. ( $\Delta H_{\text{solv}}$ )	rel. ( $\delta \Delta H_{\text{solv}}$ )		dip	qdr	$-T d\Delta E/dT$	cav	dis
n-Hexane								
<i>III</i>	-46.9	0	0	0	0	0	0	0
<i>II</i>	-47.1	-0.2	0.52	-0.07	0.00	-0.02	0.25	0.37
<i>I(ap)</i>	(-47.6)	(-0.7)	-0.96	-0.05	0.00	-0.01	0.02	-0.92
<i>I(sp)</i>	(-50.0)	(-3.1)	-1.05	-0.35	0.00	-0.11	0.03	-0.62
<i>I mean</i>	-48.9	-2.0	-1.01	-0.20	0.00	-0.06	0.02	-0.77
Nitromethane								
<i>III</i>	-51.2	0	0	0	0	0	0	0
<i>II</i>	-51.3	-0.1	0.37	-0.35	-0.11	-0.19	0.35	0.67
<i>I(ap)</i>	(-53.9)	(-2.7)	-2.08	-0.24	-0.03	-0.09	0.01	-1.73
<i>I(sp)</i>	(-57.6)	(-6.4)	-3.98	-1.67	-0.41	-0.76	0.03	-1.17
<i>I mean</i>	-55.8	-4.6	-3.03	-0.96	-0.22	-0.43	0.02	-1.45
Transfer from n-hexane to nitromethane								
<i>III</i>	-4.3	0	0	0	0	0	0	0
<i>II</i>	-4.2	0.1	-0.15	-0.28	-0.11	-0.17	0.10	0.30
<i>I(ap)</i>	(-6.3)	(-2.0)	-1.12	-0.19	-0.03	-0.08	-0.01	-0.81
<i>I(sp)</i>	(-7.6)	(-3.3)	-2.93	-1.32	-0.41	-0.65	0.00	-0.55
<i>I mehn</i>	-6.9	-2.6	-2.02	-0.76	-0.22	-0.37	0.00	-0.68

TABLE VI  
Parameters needed for reaction-field calculations of isomeric methyl fluorobenzoates

Isomer	$n_D^{20}$	Dipole moment <sup>a</sup> 10 <sup>-30</sup> Cm	$IP^a$ eV
III	1.4935	4.92	12.255
II(sp)	1.4928	9.30	12.198
II(ap)	1.4928	0.85	12.185
I(sp)	1.5032	10.71	12.038
I(ap)	1.5032	6.07	12.119

<sup>a</sup> Calculated values (INDO).

TABLE VII  
Quantum chemical and electrostatic description of the conformational equilibrium  $ap \rightleftharpoons sp$  of methyl 2-fluorobenzoate (I) in the gas phase (in kJ mol<sup>-1</sup>, 298 K)

Geometry	Method	$\Delta E_{tot}$ $N_{ap}$ %	Dip. moment 10 <sup>-30</sup> Cm		$\Delta E_{elst}$ <sup>a</sup> $N_{ap}$ %
			<i>ap</i> <i>sp</i>	effective	
Standard <sup>b</sup>	CNDO/2	3.16 <sup>c</sup> (78)	5.57 10.07	6.82	3.96 (83)
	INDO	3.73 <sup>c</sup> (82)	6.07 10.71	7.13	3.73 (82)
	STO-3G	-1.86 <sup>c</sup> (32)	2.87 6.70	5.76	0.61 (56)
CNDO/2 <sup>d</sup>	CNDO/2	3.26 (79)	9.40 11.94	9.99	-24.81 (0)
	STO-3G	-3.47 (20)	5.57 7.34	7.02	-14.44 (0)
MNDO <sup>d</sup>	MNDO	1.97 (69)	7.57 12.76	9.49	- 9.63 (0)
		Bond moments	-	5.40 10.60	6.64
Experiment		3.7 <sup>e</sup> (82)	- -	7.3-7.7 <sup>f</sup>	3.7 <sup>e</sup> (82)

<sup>a</sup> Calculated from Eq. (11) and from atomic charges as given by the respective quantum chemical method; <sup>b</sup> as in ref.<sup>6</sup>; <sup>c</sup> calculated by us previously<sup>8</sup>; <sup>d</sup> fully optimized geometry; <sup>e</sup> extrapolated value<sup>8</sup>; <sup>f</sup> in tetrachloromethane and in benzene, respectively.

## RESULTS

*Thermodynamics of the conformational equilibrium.* The equilibrium  $I(ap) \rightleftharpoons I(sp)$  was previously investigated<sup>6,8</sup> by means of dipole moments and infrared spectroscopy. The low precision of the former approach and practical impossibility of measurement at variable temperatures made us dependent on infrared data, *viz.* on the integrated absorption intensities of the carbonyl band. Determination of thermodynamic parameters by this technique is impaired in virtue of the actually unknown integrated absorption coefficients,  $\alpha_1$  and  $\alpha_2$ . In order to determine  $\Delta H^0$ ,

TABLE VIII

Direct and indirect electrostatic treatment of the conformational equilibrium  $ap \rightleftharpoons sp$  of methyl 2-fluorobenzoate (*I*) in solution at 298 K ( $\Delta E$  in kJ mol<sup>-1</sup>, in parentheses  $N_{sp}$  %)

Method <sup>a</sup>	In n-hexane			In nitromethane		
	direct <sup>b</sup>	indirect		direct <sup>b</sup>	indirect	
	elst.	elst. <sup>c</sup>	qu. chem. <sup>d</sup>	elst.	elst. <sup>c</sup>	qu. chem. <sup>d</sup>
Bond moments	2.02 (69)	3.70 (82)	—	0.11 (51)	1.89 (68)	—
CNDO/2	2.10 (70)	3.87 (83)	3.07 (77)	0.11 (51)	2.06 (69)	1.26 (62)
INDO	1.98 (69)	3.74 (82)	3.64 (81)	0.10 (51)	1.93 (68)	1.83 (67)
STO-3G	0.33 (53)	0.52 (55)	-1.95 (31)	0.02 (50)	-1.29 (38)	-3.76 (18)
CNDO/2 optim.	-13.20 (0)	-24.90 (0)	3.17 (78)	-0.69 (43)	-26.71 (0)	1.36 (63)
STO-3G optim.	-7.68 (4)	-14.53 (0)	-3.56 (19)	-0.40 (46)	-16.34 (0)	-5.37 (10)
MNDO optim.	-5.12 (11)	-9.72 (2)	1.88 (68)	-0.27 (47)	-11.53 (1)	0.07 (51)
Experimental $\Delta H^0$	—	1.32 (63) <sup>e</sup>	—	—	~ 0 (50)	—

<sup>a</sup> Methods of charge calculation as given in Table VII; <sup>b</sup> calculated from Eq. (11) with the solvent bulk permittivity instead of  $\epsilon_{ef}$ ; <sup>c</sup> calculated from  $\Delta E_{elst}$  from Table VII by adding the difference of respective  $\delta \Delta H_{solv}$  (calc.) from Table V; <sup>d</sup> calculated from  $\Delta E_{tot}$  from Table VII by adding the difference of respective  $\delta \Delta H_{solv}$  (calc.) from Table V; <sup>e</sup> in Table I the value of 66% was preferred assuming that  $\Delta G^0 = 1.60 \neq \Delta H^0$ , the difference is insignificant.

the presumption is sufficient that the ratio  $\alpha_1/\alpha_2$  does not change with temperature. This is assumed quite commonly<sup>20</sup> but need not always apply<sup>19</sup>, particularly in polar solvents. In order to encompass a broad temperature interval, we investigated the conformational equilibrium in three solvents of sufficiently high boiling point (Table I). The values of  $\Delta H^0$  in the non-polar solvents decane and decahydronaphthalene could be acceptable, although the difference between them is too high. On the contrary,  $\Delta H^0$  in nitromethane is evidently wrong owing to the non-constancy of  $\alpha_1/\alpha_2$ . According to the apparent value  $3.24 \text{ kJ mol}^{-1}$  the more polar rotamer should be destabilized in a polar solvent; in addition unacceptable solvation enthalpies would result (see the next section). Even the difference against  $\Delta G^0$  would be too high.

The values of  $\Delta G^0$  have only indirect significance in this study since they are needed to calculate solvation enthalpies of the pure rotamers. For this purpose, an error in  $\Delta G^0$  is much less important than an error in  $\Delta H^0$ ; on the other hand, the values of  $\Delta G^0$  are still more difficult to get from IR spectral data. We obtained reasonable results for all three solvents with the simple assumption<sup>20</sup> that  $\alpha_1 = \alpha_2$  at any temperature (Table I). In particular, the values in nonpolar solvents agree surprisingly well with previous dipole moment measurement in benzene<sup>6</sup>, as well as with present measurement in tetrachloromethane (Table IV). Important is also the regular trend obtained by this approach in a variety of solvents<sup>8</sup>. In solvent decane  $\Delta G^0$  is also very near to  $\Delta H^0$ . As an alternative we attempted to improve the  $\Delta G^0$  values by accounting for possibly unequal coefficients  $\alpha_1$  and  $\alpha_2$  by the procedure of Hartman and coworkers<sup>18</sup>. The attempt failed since the found ratio  $\alpha_1/\alpha_2$  was in one case negative, in another inconceivably high (Table I). The failure of this procedure has been noted several times, *e.g.*<sup>19,36</sup>. The assumption that  $\alpha_1$  and  $\alpha_2$  are invariable with temperature is evidently still less realistic than that they are variable but always equal. The last alternative is to assume simply that  $\Delta G^0$  at ambient temperature equals to  $\Delta H^0$ . According to our results (Table I) it may be approximately fulfilled in decane but certainly not in polar solvents, see also the very different value of  $\Delta G^0$  and  $\Delta H^0$  measured in dimethylformamide<sup>37</sup> as another example. Finally, we tried to estimate  $\Delta G^0$  and  $\Delta H^0$  in a more general way by computer fitting of Eqs (4), taking into account unequal coefficients  $\alpha_1$  and  $\alpha_2$  as well as their possible temperature dependence. Our experimental data were, however, insufficiently precise to determine so many parameters: the resulting standard deviation was virtually equal for a broad variation of parameter values. Similar experience was made with other data and a different optimization procedure<sup>19</sup>.

In concluding this section we have chosen the values of  $\Delta H^0 = 1.32$  and  $\Delta G_{298}^0 = 1.60 \text{ (kJ mol}^{-1}\text{)}$  in decane as most reliable and representative for nonpolar solvents. The latter value corresponds to the ratio  $ap : sp = 66 : 34$ . Our most relevant argument for this choice was the coincidence of IR and dipole moment results. In nitromethane – and in solvents of similar polarity – we prefer to assume

an approximately equal population of rotamers, *i.e.*  $\Delta H^0 = \Delta G^0 \simeq 0$ . This estimation is based on the whole pattern of solvent dependence<sup>8</sup>.

*Solvation enthalpies.* The solvation enthalpy  $\Delta H_{\text{sol}v}$ , corresponding to the transfer of one mol of solute from the gas phase into an (infinitely) diluted solution, is obtained in principle by subtracting the enthalpies of solution  $\Delta H_{\text{sol}1}$  and of vaporization  $\Delta H_v$ , Eq. (6). This can be done simply for methyl 4-fluorobenzoate (*III*). The values obtained (Table II) are the most dependable experimental enthalpy values of this paper.

On the other hand, the experimental  $\Delta H_{\text{sol}v}$  of methyl 2-fluorobenzoate (*I*) is a complex quantity since the rotamer population is changed in the course of solvation and/or vaporization. Let us assume that the equilibrium mixture in hexane contains 66% of the *ap*-rotamer, as given above, and in the gas phase 82% (an extrapolated or theoretical value<sup>8</sup>). The composition of the liquid phase need not be known explicitly, let us denote the fraction of the *ap*-rotamer through  $x$ . In the process of dissolution the fraction  $x$  is dissolved in the form of the *ap*-rotamer, the fraction  $(1 - x)$  is dissolved as the *sp*-rotamer, in addition the fraction  $(0.66 - x)$  isomerizes  $I(\text{sp}) \rightarrow I(\text{ap})$ :

$$\Delta H_{\text{sol}1} = x \Delta H_{\text{sol}1,\text{ap}} + (1 - x) \Delta H_{\text{sol}1,\text{sp}} + (0.66 - x)(-\Delta H_{\text{Hx}}^0). \quad (12)$$

Second equation for the two unknowns,  $\Delta H_{\text{sol}1,\text{ap}}$  and  $\Delta H_{\text{sol}1,\text{sp}}$ , results from the thermodynamic cycle (Fig. 1):

$$\Delta H_{\text{sol}1,\text{ap}} - \Delta H_{\text{sol}1,\text{sp}} = \Delta H_{\text{liq}}^0 - \Delta H_{\text{Hx}}^0. \quad (13)$$

The enthalpy of isomerization in the liquid phase,  $\Delta H_{\text{liq}}^0$ , need not be specified. Quite similarly, it holds for the vaporization process (Fig. 1):

$$\Delta H_v = x \Delta H_{v,\text{ap}} + (1 - x) \Delta H_{v,\text{sp}} + (0.82 - x)(-\Delta H_{\text{g}}^0) \quad (14)$$

and

$$\Delta H_{v,\text{ap}} - \Delta H_{v,\text{sp}} = \Delta H_{\text{liq}}^0 - \Delta H_{\text{g}}^0. \quad (15)$$

When one solves Eqs (12), (13) for  $\Delta H_{\text{sol}1,\text{ap}}$  and  $\Delta H_{\text{sol}1,\text{sp}}$ , and Eqs (14), (15) for  $\Delta H_{v,\text{ap}}$  and  $\Delta H_{v,\text{sp}}$ , the two components can be summed according to Eq. (6). Then  $\Delta H_{\text{liq}}^0$  and  $x$  cancel out and one gets:

$$\Delta H_{\text{sol}v,\text{ap}} = \Delta H_{\text{sol}1} - \Delta H_v - 0.34 \Delta H_{\text{Hx}}^0 + 0.18 \Delta H_{\text{g}}^0, \quad (16)$$

$$\Delta H_{\text{sol}v,\text{sp}} = \Delta H_{\text{sol}1} - \Delta H_v + 0.66 \Delta H_{\text{Hx}}^0 - 0.82 \Delta H_{\text{g}}^0. \quad (17)$$

The results are given in Table V and in Fig. 1. The values for nitromethane solvent were calculated in the same way with  $\Delta H_{\text{Nm}}^0 = \Delta G_{\text{Nm}}^0 = 0$ . (The apparent  $\Delta H_{\text{Nm}}^0$  value of  $3.24 \text{ kJ mol}^{-1}$ , discussed in the preceding section, would imply an inadmissible result: For the more polar *sp*-rotamer a less intensive solvation.) The results for nitromethane are listed in Table V, too, and visualized in Fig. 2. All the values for rotamers are much less reliable than those for methyl 4-fluorobenzoate but their possible uncertainty is difficult to estimate. This is expressed by parentheses in Table V. For the sake of more accurate comparison with theoretical values we calculated still the mean values of  $\Delta H_{\text{solv}}$  for the two rotamers of *I*. These are very little dependent on the assumed  $\Delta H^0$  and  $\Delta G^0$  of the conformational equilibrium and determined essentially by the experimental calorimetric enthalpies. However, they lack an immediate physical meaning.

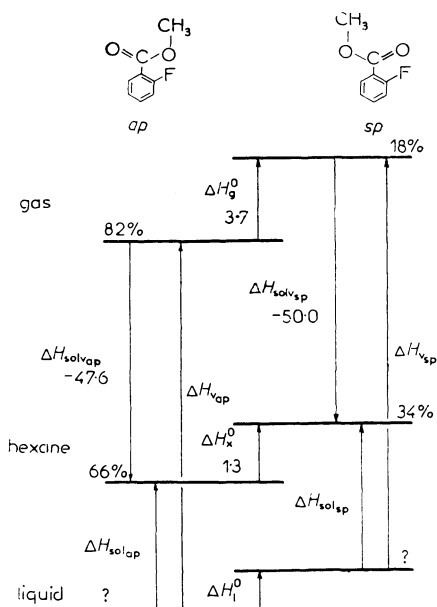


FIG. 1

Thermodynamic quantities, both experimentally determined and derived, connected with the conformational equilibrium  $I(\text{ap}) \rightleftharpoons I(\text{sp})$  in the gas phase, n-hexane solution, and liquid phase (survey of symbols and values)

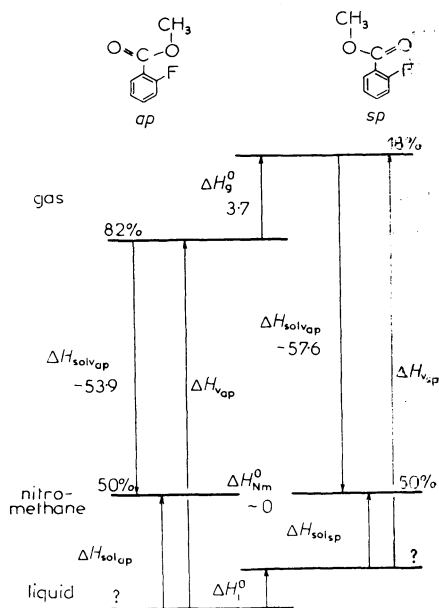


FIG. 2

Thermodynamic quantities connected with the conformational equilibrium  $I(\text{ap}) \rightleftharpoons I(\text{sp})$  as in Fig. 1 but in solvent nitromethane

With methyl 3-fluorobenzoate (*II*) similar problems arise in principle, due to the conformational equilibrium  $II(ap) \rightleftharpoons II(sp)$  and its solvent induced shifts. There are, however, good reasons to believe that the population of rotamers is nearly equal and little dependent on solvent. The dipole moment of *II* in benzene (Table III) agrees with this assumption; see also the dipole moment of methyl 3-chlorobenzoate and its small dependence on solvent<sup>4</sup>, further the small calculated energy difference for the two rotamers of 3-fluorobenzoic acid<sup>38</sup>. For this reason and with respect to the attainable accuracy, more sophisticated calculations for this isomer would be useless. We report in Table V only mean values for the two rotamers. The actual values can hardly differ by more than 0.1 kJ mol<sup>-1</sup>.

## DISCUSSION

*Confrontation of theories with experiments.* For a survey of experimentally determined or estimated thermodynamical quantities let us refer once more to Figs 1 and 2. Four types of these quantities are involved which can be compared with various theoretical concepts:

A) The reaction enthalpy  $\Delta H_g^0$  of the conformational equilibrium  $I(ap) \rightleftharpoons I(sp)$  in the gas phase can be confronted with simple electrostatic calculation according to Eq. (11) and with quantum chemical calculations on different levels.

B) The solvation enthalpies  $\Delta H_{solv}$  can be compared directly with the prediction of the extended reaction-field theory. However, a good agreement cannot be expected since this theory has not been devised for absolute values. The comparison can be done not only for the rotamers  $I(ap)$  and  $I(sp)$ , but also for the isomers *II* and *III*.

C) The relative values of solvation enthalpies  $\delta \Delta H_{solv}$ , representing the change of reaction enthalpy with solvation, are available for different equilibria, e.g.  $I(ap) \rightleftharpoons I(sp)$ ,  $I \rightleftharpoons III$ ,  $II \rightleftharpoons III$ . They can be compared immediately to the extended reaction-field theory and even the importance of individual theoretical terms can be assessed.

D) The reaction enthalpies  $\Delta H_s^0$  (or Gibbs energies  $\Delta G_s^0$ ) of the conformational equilibrium  $I(ap) \rightleftharpoons I(sp)$  in solution can be treated either directly by calculating the electrostatic energy according to Eq. (11) for a given solvent, or indirectly by calculating the electrostatic energy for the gas phase and adding the solvation term from the reaction-field theory.

In these four cases the possibilities of theory are very different, so is also the reliability of the experimental results. For these reasons the above cases will be treated separately in the subsequent sections.

*Conformational equilibrium in the gas phase.* We have been unable to obtain directly an enthalpy value for this equilibrium. The value adopted for calculations



of  $\Delta H_{\text{soliv}}$  of the rotamers and quoted also in Table VII is a product of extrapolation of  $\Delta G^0$  measured in various solvents<sup>8</sup>. Hence the simple comparison of theory with experiment cannot be of decisive importance, proper attention is to be given also to the agreement of the theoretical methods with each other (Table VII). Striking is the good agreement of CNDO/2 and INDO methods, optimized or non-optimized, electrostatic calculation, and the extrapolation from experiments. The electrostatic calculation was most successful in the point-charges approximation<sup>7,9</sup> with charges from resolution of bond moments, the effective permittivity  $\epsilon_{\text{eff}} = 1$  is clearly preferable<sup>2-5,39</sup> to recommended higher values<sup>40</sup>. The STO-3G method fails even as to the sign of the effect. A secondary criterion can be the effective dipole moment, calculated by the individual methods for the anticipated population of rotamers, although the experimental value in the gas phase is not known. Again the agreement of the above named methods is good. Concerning the geometry optimization, it changes but little the CNDO/2 energy but makes the dipole moments worse; in STO-3G it has clearly a negative effect. Even MNDO with optimized geometry is unsatisfactory.

We have further tried more sophisticated electrostatic calculations, including not only the charges on the strongly polar bonds but on all atoms of the molecule, as recommended *e.g.* in ref.<sup>3</sup>. When these charges were taken from non-optimized CNDO/2 and INDO methods (in combination with the Mulliken population) similar results were obtained as with simpler procedures (Table VII, last column). On the contrary the CNDO/2, MNDO, and STO-3G methods with optimized geometry gave in this application completely puzzling results, wrong both in sign and in the order of magnitude. We can advance no simple explanation of this failure. Attention may be drawn to the non-realistic charges on hydrogen atoms and/or on the carboxyl carbon atom for which the Mulliken population might be partly responsible.

The conclusion of this section is apparently that the simplest electrostatic calculation and simpler semiempirical quantum chemical methods afford the best results.

*The extended reaction-field theory.* In contradiction to the preceding section, the experimental  $\Delta H_{\text{soliv}}$  are reliable values, with the exception of those for individual rotamers given in Table V in parentheses. A comparison of their absolute values (Table V, first column) with the extended reaction-field theory (sum of the terms in Table IV) would reveal big discrepancies the origin of which is evidently in the cavity and dispersion terms. The electrostatic effects themselves are negligible in this connection. In fact, the theory was devised just for relative values (differences between rotamers) with the assumption that some specific effects ( $\Delta E_{\text{spec}}$  in Eq. (7)) will cancel. Therefore, further consideration will be restricted to relative values  $\delta \Delta H_{\text{soliv}}$  (Table V, column 2) related to methyl 4-fluorobenzoate as reference. One can follow either the general trends within the series of isomeric structures, or merely qualitative

relations within a certain pair of isomers. A more quantitative agreement has been in fact not expected. Actually, comparison of the two columns of Table V is not encouraging on the first insight. The difference between isomers 2-F and 4-F is underestimated in the theory by 25–50%, that between 3-F and 4-F is predicted inversely. The difference between rotamers 2-*ap* and 2-*sp* is also underestimated, of course the experimental values are not quite dependable. Nevertheless, the general trend among the isomers is reproduced by theory. The relatively best prediction is achieved for the difference between the two solvents.

Analysis of individual terms of Eq. (7) and (8) revealed firstly the inadequacy of the calculated cavity energy  $\Delta E_{\text{cav}}$ . For all isomers this term is negligible, except for 3-F. For the latter compound it makes always the agreement with experiment worse. The most probable reason is the non-realistic calculation of the cavity size<sup>27</sup> for this molecule. In such cases a more efficient approximation could be advanced: to take the cavity simply as equal for the two rotamers or isomers, so that the term  $\Delta E_{\text{cav}}$  would cancel out. Of the remaining terms we have found none which could be completely omitted (Table V).  $\Delta E_{\text{qdr}}$  is negligible in n-hexane but of some importance in nitromethane, somewhat more important is the entropy correction. The terms  $\Delta E_{\text{dip}}$  and  $\Delta E_{\text{disp}}$  constitute comparable and significant parts of the gross energy, while the latter is theoretically less firmly based and may be considered the main source of the bad fit. A recent study of (*E*)- and (*Z*)-1,2-dichloroethenes<sup>16</sup> came to conclusions in qualitative agreement with ours. While the cavity term was little significant, the dispersion term was not evaluated. Without it an agreement with experiment could not be achieved, although still an octupole term was added<sup>16</sup>.

Note that the sequence of solvation enthalpies for 2-, 3-, and 4-fluorobenzoates follows the qualitative rule that the compound with a greater dipole moment is more solvated (compare Tables III and V). Even the relation of the rotamers *ap* and *sp* of 2-fluorobenzoate is predicted correctly by this rule. Quantitatively the dipole term  $\delta \Delta E_{\text{dip}}$  seems to be underestimated. Summarizing, we believe that the reaction-field theory proper is roughly valid as a reasonable approximation, the main weakness is in the added dispersion term. Before any improvement is advanced, further simple model systems have to be studied. In this respect the calorimetric technique is a promising approach.

*Conformational equilibrium in solution.* The experimental values of  $\Delta H_{\text{S}}^0$  for this equilibrium in n-hexane and nitromethane are less dependable than the foregoing  $\Delta H_{\text{solv}}$ . Nevertheless, the comparison with a variety of theoretical procedures (Table VIII) allows some conclusions. Simple electrostatic calculations are unobjectionable for solvent n-hexane since the permittivities of solvent and solute are virtually equal and determine unambiguously the effective permittivity  $\epsilon_{\text{ef}}$ . For solvent nitromethane any efficient procedure of calculating  $\epsilon_{\text{ef}}$  for interaction of dipoles is not known. We used the solvent bulk permittivity instead, as a very rough approximation,

merely the upper limit of possible values. The results obtained were acceptable in the case of either solvent, irrespective of whether the charges from bond moments, from CNDO/2, or INDO were taken. Note, however, that the results in nitromethane are much less telling since any sufficiently small calculated value would be in fact satisfactory. The STO-3G method and particularly all the variants with optimized geometry failed completely as a source of atomic charges (like for the gas phase). The indirect methods consisting of separate calculations of the gas phase reaction enthalpy and of the solvation enthalpy, yielded in general worse results, whether the gas phase value was taken from quantum chemical or from electrostatic calculations. The reason is mostly in the too low solvation enthalpy, making the final value too high. Reasonable results obtained *e.g.* for the combination of MNDO with solvation enthalpy, are due to compensation of errors of the two components. We can conclude that simple methods are useful but as inaccurate as can be anticipated, while more sophisticated methods yield often worse rather than better results.

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