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CONFORMATIONAL ANALYSIS—133

3,3-DIMETHYL-2,4-PENTANEDIONE. THE IMPORTANCE OF INDUCTION AND SOLVATION[1,2]

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Abstract—The conformations of the title compound have been analyzed in detail with respect to steric interaction energies, charge interaction energies, and solvation energies in heptane and benzene. Using previously developed methods, which include induction by dipoles in polarizable bonds, and the solvation of molecular dipoles and quadrupoles, predictions regarding the conformational equilibrium are made. These were tested by experimental determination of the dipole moment of the molecule in heptane and benzene, and are in agreement with the predictions. More simplified calculations lead to qualitatively erroneous results.

In 1961 Rogan and Ellis published a paper in which they discussed the conformations of 3,3-dimethyl-2,4-pentanedione.[3] The UV spectrum of the compound in hydrocarbon solvent is considerably different from that expected from two simple CO groups, and the IR spectrum shows a doublet CO stretching frequency. On this basis they concluded that there were probably two conformations in equilibrium. The conformations they considered are A–D. And they concluded that C and D were probably the conformations in the equilibrium.

In 1961 it was not clear for even the simple molecule acetone which way the torsional barrier about the C–C bond was oriented. It is now known that in acetone, hydrogens on the alpha carbons eclipse the CO in the ground state.[4] Utilizing this key fact, molecular mechanics calculational procedures for ketones have been developed,[5] which would seem to permit us to study now in a more detailed way the conformations of the compound in question. Inspection of models shows that in addition to the conformations considered by Rogan and Ellis, we also need to consider two more conformations, which we will call E and F.

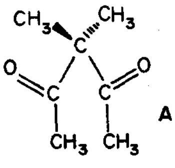
While molecular mechnics has been very useful for determining conformations and energies of hydrocarbons, and of a number of monofunctional molecules, polyfunctional molecules have been studied only slightly.[6] For these latter cases, treatment of charge interactions and solvation are problems which have not been explored in much depth.[6-8]

It would be desirable to have experimental information concerning the conformations of the molecule at hand. Since we are looking for an equilibrium, crystallographic data, even if available, would be of little use. Electron diffraction and/or microwave spectroscopy might be useful in determining the conformations, but no such data have been reported. The UV spectrum of the compound does show an interaction between the CO groups, but this is of no help for conformational considerations, and the doublet CO frequency could be due to an equilibrium between conformations, or it could be a result of Fermi resonance.[9]

The only easily accessible experimental quantity that we could see that would clearly be of use was the dipole moment, and accordingly it was measured in heptane and in benzene solutions. These numbers give us only limited structural information, but it proves to be sufficient to make a decision between accuracy of two different calculational procedures currently in use in molecular mechanics.

In the present work we considered conformations A–E. These were constrained by symmetry axes or planes so that the energy of each conformation could be calculated.[10] Relative energies (enthalpies) obtained are listed in Table 1. Not all of these conformations necessarily correspond to energy minima. Since we want to look at equilibria, we also need to consider entropy. The symmetry numbers and the calculated entropies due to symmetry and mixing in are given in Table 2. The free energies shown in Table 3 were obtained by combining the data in Tables 1 and 2.

Our earliest scheme for treating polar molecules allowed for the dipole–dipole interaction according to the classical method of Jeans, and such calculations can be carried out for the gas phase.[6] We here chose 1.5 as an effective dielectric constant for the gas phase.[11] If the dipoles are immersed in a solvent, the charge interaction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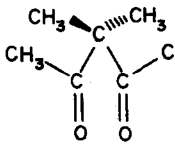
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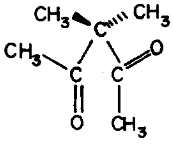
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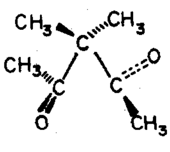
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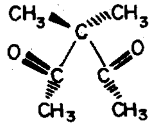
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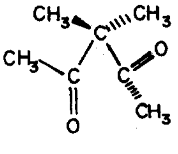
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Table 1. Conformations, energies (kcal/mole) and dipole moments (Debyes) of 3,3-dimethyl-2,4-pentanedione from the molecular mechanics program

Conformation	Eff. Dielec. Const. 1.5			Eff. Dielec. Const. 8.0	
	ΔE	μ	Dipole-Dipole Energy	ΔE	μ
A	8.46	3.07	2.25	8.07	3.07
B	4.90	5.40	4.38	4.50	5.39
C	3.99	2.73	0.54	4.97	2.71
D	0.12	0.17	1.89	0	0.27
E	3.53	4.95	3.22	2.35	5.03
F	0	4.31	1.21	0.34	4.45

Table 2. Entropy differences of conformations of 3,3-dimethyl-2,4-pentanedione

Isomer	σ	Sm	$-R\ln\sigma$	Total Relative Entropy
A	2	0	-1.38	-1.38
B	2	0	-1.38	-1.38
C	1	0	0	0
D	2	+1.38	-1.38	0
E	1	0	0	0
F	1	1.38	0	+1.38

energy can be divided by the dielectric constant of the solvent to obtain an approximate charge interaction energy in the particular solvent.[12] These calculations were carried out for effective dielectric constants of 1.5 (gas phase) and 8 (benzene), and the results are summarized in Table 1.

First, the calculations indicate that only two conformations that are of relatively low energy contribute appreciably to the conformational mixture. One of these (D) was predicted to be important by Rogan and Ellis, and the other one (F) was one they did not even consider. Their conformation C, which they believed to be the other stable one, is not, according to our calculations. The calculations described above permit one to calculate dipole moments for the conformational mixtures in media of dielectric constants of 1.5 and 8 as 3.63 and 3.14 D, respectively. The measured dipole moment of the compound in heptane is 2.42 D, and in benzene 2.77 D. Thus, the absolute values of the numbers calculated are not in very good agreement with experiment, and correspond to errors of 0.5–1.0 kcal/mole. More worrisome, the shift of the dipole moment with solvent calculated is in the opposite direction from that observed experimentally, and clearly this is a problem that must be resolved.

We now know that in simple ketones the CO oxygen is eclipsed by a substituent on the alpha carbon when the molecule is at a torsional minimum.[4] Conformations A and C do not meet this condition, and, barring any large steric or electrostatic interactions, these should correspond to energy maxima rather than energy minima, and indeed they are found to be quite unfavorable. Gross steric interactions occur in conformation A, and it can be also eliminated on those grounds. The remaining conformations all correspond to torsional energy minima. To be at an energy minimum, a carbonyl has the option of eclipsing either the C–C bond which leads to the other carbonyl, or a C–C bond leading to either of the Me groups. Both CO's have the first arrangement in conformation B. In conformation F (a *dl* pair) one CO eclipses the bond to the other CO, while the second one eclipses a Me. In conformations D and E, both CO's eclipse methyls; either both CO's eclipse the same Me (E), or they eclipse different Me's (D).

Next we may consider the electrostatic situation. The dipole moment is quite large for B (5.40 D), and the dipoles are clearly parallel and close together, which really excludes this conformation as a low energy one. Conformations D, E and F do not have any of these serious energetic problems. They each seem to have reasonable steric and dipole interactions, and correspond to torsional energy minima. So these are the conformations we might actually expect to observe.

Table 1 gives the energies and dipole moments of these conformations as calculated for the compound in a medium of dielectric constant 1.5. As expected, conformations D and F are indeed the more favorable ones. Conformation E proves to be somewhat higher in energy because of the dipole–dipole interaction. The calculated dipole moments of the conformations change slightly with solvent, because the electrostatic interaction energy is different, and the minimization of the energy leads to a slightly different geometry, but the differences are insignificant. On the other hand, the dipole–dipole interaction energy is greatly reduced when the dielectric constant of the medium becomes as high as 8, so that conformations B and E, in which there were large dipole–dipole interactions, are stabilized by a relatively

Table 3. Free energies of the conformations of 3,3-dimethyl-2,4-pentanedione (kcal/mole)

Conformation	ΔH (Table 1)	ΔS° (Table 2)	ΔG°[a]
Eff. Dielect. Const. 1.5			
A	8.46	-1.38	9.28
B	4.90	-1.38	5.72
C	3.99	0	4.40
D	0.12	0	0.53
E	3.52	0	3.93
F	0	+1.38	0
Eff. Dielect. Const. 8.0			
A	8.07	-1.38	8.55
B	4.50	-1.38	4.98
C	4.97	0	5.04
D	0	0	0.07
E	2.35	0	2.42
F	0.34	+1.38	0

(a) ΔG° is relative to the conformation of lowest standard free energy.

large amount, and the other conformation less so. Qualitatively, however, there is little change. Conformation D is now the most stable, followed rather closely by F. Conformation E is third in stability, although the energy remains sufficiently high that it will not contribute significantly to the equilibirum.

The following points seem significant. In a medium of low dielectric constant, conformations D and F are similar in energy. As the dielectric constant of the medium increases, the stability of D relative to F increases. Hence, one can predict by the dipole–dipole interaction method that the dipole moment of the compound should decrease as the dielectric constant of the medium increases, due to this shift in conformational populations. This is exactly opposite to what is observed experimentally, where the dipole moment increases as the dielectric constant increases.

Obviously, a more sophisticated method for dealing with the electrostatic interaction in the molecule is needed here. Such a method was previously described,[8] and consists of two parts. First, the dipoles in a given conformation are each allowed to induce in the remaining bonds in the conformation small moments, which are related to the polarizability and spacial arrangement of the molecule. An induced charge distribution for the molecule is thus obtained. This general approach is that of Smith and Eyring,[13] as modified and described earlier.[7]

Once the total charge distribution in the molecule is available, this charge distribution is immersed in a solvent of appropriate dielectric constant, and, following the method of Abraham,[14] the solvation energy for the charge distribution is approximated as the sum of the molecular dipole and quadrupole solvation terms.

To calculate the electrostatic energies, the total conformational energies calculated by the molecular mechanics program were the starting point, and the procedure was as follows. Since all charge energies will be dealt with separately, the dipole–dipole interaction term is subtracted out from the molecular mechanics energy. The charge interaction[7] and solvation terms[8] which have then been calculated separately are added to the molecular mechanics steric energy, to give a total conformational energy, for the particular conformation in the medium of given dielectric constant. This information is summarized in Table 4.

First, for the values in heptane, we note the following. Conformation D is slightly more stable than conformation F (in contrast to the more simple prediction made earlier). Conformations E and C are next in energy, but sufficiently high that their contribution to the equilibrium is negligible. When the molecule is dissolved in benzene, conformation D remains of lowest energy, but that of conformation F is now quite similar. The prediction here is that conformation D predominates in heptane, but the equilibrium shifts more towards F in benzene. This is consistent with what is observed experimentally, and it is opposite to the simple prediction

Table 4. Data for the energy calculations on 3,3-dimethyl-2,4-pentanedione conformations by MSE method (kcal/mole)[a]

Property	CONFORMATION					
	A	B	C	D	E	F
Dipole Moment (D)	2.71	5.47	2.69	0.22	4.96	4.61
E_s	6.71	2.84	3.94	-1.27	0.89	-0.72
E_c	-23.81	-20.85	-25.89	-24.32	-22.91	-24.30
E^V	-17.11 (8.48)	-18.01 (7.57)	-21.94 (3.64)	-25.59 (0)	-22.02 (3.57)	-25.02 (0.57)
H	-1.11	-2.01	-0.80	-0.93	-1.70	-1.27
E^S	-18.21 (8.31)	-20.02 (6.50)	-22.74 (3.78)	-26.52 (0)	-23.42 (3.10)	-26.28 (0.24)

(a) Numbers in parentheses are relative to the indicated zero value.

E_s = steric energy from molecular mechanics program minus the dipole interaction term.

E_c = charge interaction.

Energy of conformation in the gas phase (or heptane), $E^V = E_s + E_c$.

H = heat of solvation in benzene relative to heptane.

Total conformational enthalpy, $E^S = E^V + H$.

Table 5. Standard free energies of the conformations of 3,3-dimethyl-2,4-pentanedione calculated by the MSE method

Conformation	ΔH^o	$\Delta S^{o\,b}$	$\Delta G^{o\,c}$
Eff. Dielect. Const. 1.5 (heptane)			
A	8.43	-1.38	8.89
B	7.57	-1.38	7.95
C	3.64	0	3.64
D	0.00	0	0.00
E	3.56	0	3.56
F	0.56	+1.38	0.16
Eff. Dielect. Const. 8.0 (benzene)			
A	8.31	-1.38	8.92
B	6.50	-1.38	7.09
C	3.78	0	3.95
D	0.00	0	0.17
E	3.10	0	3.27
F	0.24	+1.38	0.00

(a) These are the relative E^V values from Table 4.

(b) These are the relative E^S values from Table 4.

(c) Relative to the lowest standard free energy conformation.

made above. It is also predicted that conformation E will be much stabilized by the benzene solvent, but will still be insignificant in concentration. The calculated dipole moments by this scheme are 3.06 in heptane and 3.48 in benzene, which correspond to errors in the energies of the individual conformations of only 0.5 kcal/mole.

The calculations above provide the interesting result that the equilibrium between conformation D and F is calculated to shift in different directions with increasing dielectric constant of the solvent, depending on how the calculation is done. The reason for this peculiar behavior is as follows. In conformation D, the dipoles are relatively far apart (3.41 A), whereas in conformation F the distance is considerably smaller (2.87 A). However, the orientation between the dipoles is more or less tail-to-tail in D, so that overall dipole moment is small, but the interaction energy is relatively large (1.89 kcal/mole), compared with conformation F, where the ineraction is more head-to-tail, and the energy is smaller (1.22 kcal/mole). If one simply reduces the electrostatic energy by dividing the number by the dielectric constant, the higher energy (conformation D) is reduced more, and equilibrium shifts in that direction.

As mentioned previously, this is opposite to what is observed experimentally. Now, turning to the alternative method of calculation, after allowing for induction, the charge interaction energies prove to be essentially identical. The shift with solvation when solvating the very small dipole of D gives 0.00 kcal/mole of solvation energy. The quadrupole is large, however, and its solvation gives 0.93 kcal/mole. On the other hand, solvating conformation F gives 1.01 kcal/mole of dipole solvation energy, and 0.26 kcal/mole of quadrupole solvation energy. The solvation of the large dipole of F is therefore the determining quantity, but solvation of the quadrupoles must also be taken into account if a reasonably accurate result is wanted.

CONCLUSIONS

The example discussed here is one of very few known cases where the different methods for calculating the electrostatic energies of different conformations of a molecule give results which are *qualitatively* dependent on the calculational method used. While the differences are not very great, they are experimentally measurable, and the qualitatively correct result is obtained only by the procedure in which both induction within the molecule, and dipole and quadrupole solvation are taken into account. It is hoped that the scheme used herein will provide a better general method for attacking conformational problems which involve polar molecules and solvation.

EXPERIMENTAL

3,3-*Dimethyl-2,4-pentanedione*

2,4-Pentanedione was alkylated with excess MeI in acetone in the presence of excess K_2CO_3 at reflux for 5 days. Distillation gave the product, contaminated with some 3-methyl-2,4-pentanedione (by glc). Redistillation gave the product, pure by glc, which showed only 2 singlets in the proton NMR, 8.17 and 2.6.

The dipole moments were measured and the calculations were carried out according to previously described methods.[15] The values obtained were 2.42 D in heptane and 2.77 D in benzene.

Acknowledgement—The authors are indebted to Mr. W. D. Steffy for the dipole moment measurements.

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[10] The 1971 force-field (Ref. 5) was used in the present work. The 1973 force-field (Ref. 6) became available only after this work was begun. It would be expected to yield essentially the same results. The 1973 program (MMI) is available from the Quantum Chemistry Program Exchange, University of Indiana, Bloomington, IN 47401, U.S.A.

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