Molecular Mechanics and Dipole Moments as a Useful Combination in Conformational Analysis of Open-chain Compounds. Application to α-Adamantyl-β-diketones

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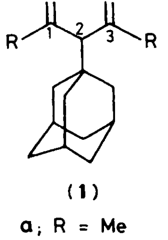
Molecular mechanics calculations predict the preferred conformations for 3-(1-adamantyl)pentane-2,4-dione (**1a**) and for 4-(1-adamantyl)-2,2,6,6-tetramethylheptane-3,5-dione (**1b**) and also give dipole moment values for both compounds which are in good agreement with the measured values.

Conformational analysis of open-chain compounds has been limited by their inherent conformational complexity. The advent of molecular mechanics methods[1] opened new avenues in conformational analysis, although it is desirable to compare the computational results with experimental data.

Some of us have recently reported a synthetic method, based on the use of cobalt(II) complexes of β-dicarbonyl compounds, which enabled us to incorporate 1-adamantyl units into the central α-position to afford α-(1-adamantyl)-β-dicarbonyl compounds (**1**).[2] Four of the five compounds of type (**1**) reported showed three or four carbonyl i.r. stretching bands indicating the possible existence of two or more equally populated conformations in slow equilibria on the i.r. time-scale.

Thus, the i.r. spectrum of (**1a**) (KBr disc) shows a very strong band at 1691 cm^{-1} and a shoulder at 1720 cm^{-1} whereas the Raman spectrum of neat (**1a**) shows a major band at 1716 cm^{-1} and a weaker one at 1690 cm^{-1}. We assign the higher frequency band to the symmetric stretching vibration and the lower frequency band to the corresponding asymmetric vibration. These data suggest that the vibrations of both carbonyl groups are coupled. However the i.r. spectrum in chloroform shows at least four carbonyl bands. This multiplicity, also observed in cyclohexane and $(CD_3)_2SO$, is attributed to the presence of rotational isomers.[3]

Different behaviour was observed for (**1b**). The i.r. [KBr disc; chloroform, cyclohexane, and $(CD_3)_2SO$] and the Raman spectra (neat solid and in chloroform) show a major band at *ca.* 1715 cm^{-1} and a weaker band at 1674—1680 cm^{-1},



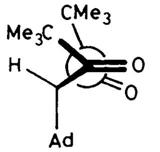
(**1**)
a; R = Me
b; R = Bu^t

Table 1. Results for the Newman projections (A)—(D) across an imaginary line linking C^1 and C^3 for one of the enantiomeric conformations of (**1a**). Relative energies, populations, dihedral angles C^{Ad}–C^2–C=O (ω_1 and ω_2), angles between dipoles (α), and dipole moments (μ) as calculated by the MM2 program.

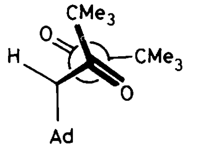
	Structure			
ε 2.02 (Cyclohexane)	(A)	(B)	(C)	(D)
Relative energy/kJ mol^{-1}	1.50	0.84	0.00	14.42
Population (%)	24.08	31.55	44.24	0.13
ω_1(C^{Ad}–C^2–C^1=O)/°	−2.81	90.19	105.60	126.73
ω_2(C^{Ad}–C^2–C^3=O)/°	74.13	27.71	13.80	−83.92
α(O=C^1 · · · C^3=O)/°	50.50	170.15	174.30	35.76
μ/Debye	4.68	0.91	0.26	4.33
ε 2.28 (Benzene)				
Relative energy/kJ mol^{-1}	1.25	0.79	0.00	14.13
Population (%)	25.84	31.22	42.90	0.14
ω_1(C^{Ad}–C^2–C^1=O)/°	−4.53	89.83	106.61	127.01
ω_2(C^{Ad}–C^2–C^3=O)/°	73.21	26.35	13.92	−84.01
α(O=C^1 · · · C^3=O)/°	48.65	169.85	174.94	35.59
μ/Debye	4.70	0.90	0.27	4.33

Table 2. Results for the Newman projections (E)—(G) across an imaginary line linking C^1 and C^3 for one of the enantiomeric conformations of (**1b**), as in Table 1.

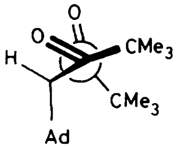
	Structure		
ε 2.02 (Cyclohexane)	(E)	(F)	(G)
Relative energy/kJ mol^{-1}	0.00	0.96	63.45
Population (%)	59.60	40.40	0.00
ω_1(C^{Ad}–C^2–C^1=O)/°	−45.34	95.72	144.48
ω_2(C^{Ad}–C^2–C^3=O)/°	89.00	40.42	−75.29
α(O=C^1 · · · C^3=O)/°	32.92	174.90	51.17
μ/Debye	5.47	0.42	4.90
ε 2.28 (Benzene)			
Relative energy/kJ mol^{-1}	0.00	1.80	63.87
Population (%)	66.28	33.27	0.00
ω_1(C^{Ad}–C^2–C^1=O)/°	−44.04	95.76	144.19
ω_2(C^{Ad}–C^2–C^3=O)/°	88.68	40.31	−75.55
α(O=C^1 · · · C^3=O)/°	32.36	174.90	50.98
μ/Debye	5.47	0.43	4.90



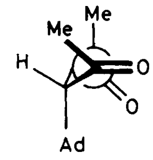
(E)



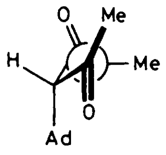
(F)



(G)



(A)



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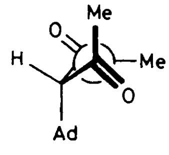
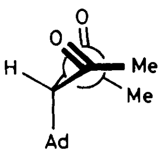


(C)



(D)

no multiplicity being observed. However, this does not preclude the existence of rotamers in fast equilibrium on the i.r. time-scale. Although there have been some i.r. studies on the keto forms of β-dicarbonyl compounds,[4] this technique alone cannot give definite conformational analysis results.

All the above considerations prompted us to perform a more quantitative study. Since no enol forms were observed for (**1a**) and (**1b**), both in CDCl$_3$ and in cyclohexane (^{1}H n.m.r. monitoring), we decided to tackle the problem by molecular mechanics (MM) and dipole moment studies. Dipole moments were determined in cyclohexane (ε 2.02) and in benzene (ε 2.28). Calculations were performed with Allinger's MM2 program,[5,6] which, although it routinely operates with a dielectric constant value ε of 1.5, other values can be introduced.

The torsional energy surface for the rotation around both C^2–CO bonds in (**1a**) was obtained by MM calculations using Allinger's MM2 program[5] and the two-bond drive technique. Initially we drove C^{Ad}–C^2–C^1=O and C^{Ad}–C^2–C^3=O dihedral angles from ±180° to ∓180° at 15° steps, considering the molecule to be in a vacuum (ε 1.5 in the MM2 program) and also in media of dielectric constants 2.02 and 2.28. Once the surface had been calculated, we drove the same dihedral angles again at 5° steps around the minima obtained in the previous calculations.

Table 1 shows results for the eight conformers of (**1a**) corresponding to energy minima (four pairs of enantiomers). Assuming the overall dipole moment (μ_T) to be a vectorial addition of individual μ values, values of $\mu_T = 2.15$ (*in vacuo*), 2.36 (in cyclohexane), and 2.45 D (in benzene) were calculated.

Table 2 shows results for analogous treatment of (**1b**): μ_T 3.41 (*in vacuo*), 4.23 (in cyclohexane), and 4.46 D (in benzene).

Calculated dipole moments are higher in media of higher dielectric constant, indicating as expected the greater contribution of the most polar conformers in solvents of higher dielectric constants. Note also that although the populations of the different calculated conformations depend significantly on the dielectric constant, the geometry of each conformation is practically independent of the polarity of the medium.

We have adopted the point-dipole approach to calculate the

Table 3. Dipole moments (Debye) calculated (MM2) and measured (Halverstadt–Kumler, μ^{HK}, and Guggenheim–Smith, μ^{GS}) in cyclohexane and in benzene at 25 °C for (**1a**) and (**1b**).

	ε 1.5	In cyclohexane (ε 2.02)				In benzene (ε 2.28)			
	μ^{MM2}	μ^{HK} [a]	μ^{HK} [b]	μ^{GS}	μ^{MM2}	μ^{HK} [a]	μ^{HK} [b]	μ^{GS}	μ^{MM2}
(**1a**)	2.15	2.46	2.40	2.50	2.36	2.84	2.79	2.86	2.45
(**1b**)	3.41	4.15	4.09	4.18	4.23	4.36	4.31	4.38	4.46

[a] The contribution of the atomic polarization was considered to be 5% of the electronic polarization in the HK method. [b] The contribution of the atomic polarisation was considered to be 15% of the electronic polarization in the HK method.

dipole moments with the MM2 program. The limitations of this approach have been stated by Allinger[7] and a sounder method (IDME) is being sought.[8]

The experimental dipole moments of compounds (**1**) have been evaluated in cyclohexane and in benzene at 25 °C by the Halverstadt–Kumler[9] and Guggenheim–Smith[10] methods. Table 3 shows the calculated and measured dipole moments. In both cases the differences between the values are <5% except for (**1a**) in benzene (13% difference for low absolute values).

MM2 calculates populations from energy values, thus neglecting the entropy contribution. However, entropy differences between conformations possessing the same symmetry, as applies in our cases, should be very small since in such situations the major contributions to entropy arise from groups of atoms.[11] Therefore, entropy contributions can be considered to cancel out for all the conformations. The agreement between our calculated and experimental data can be considered as good and we conclude that (**1a**) and (**1b**) most probably exist in cyclohexane and in benzene in the conformations (A)—(D) and (E)—(G), respectively, or very similar conformations. Energy minimization is achieved in some of them mainly by minimizing the dipole–dipole repulsive interactions and in others by minimizing the unfavourable steric interactions.

We believe that this combination of techniques should be tested for more compounds containing two polar groups.

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