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A dynamic look on molecular symmetry

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32 **ABSTRACT**

33 J. H. van't Hoff's seminal paper variously titled as either: Chemistry in Space, The
34 Placement of Atoms in Space or other with similar wording, depending on the language
35 it was published in, suggested that the structure of a molecule would be independent of
36 its physical state: solid, liquid, vapor, gaseous or in solution. But this is definitely not
37 true so much so that during the last decades many examples have accumulated showing
38 that the structure of a molecule in a crystalline solid can differ substantially from its
39 structure in solution. This would have important consequences not only on how
40 molecules are structurally described and the way they react, but also that molecular
41 symmetry may not be a static property and has to be considered from a dynamic point
42 of view. In order to add additional evidence to this conception we took advantage of a
43 family of trans-1,4-di- and tetra-substituted cyclohexane derivatives that appear to have
44 a centre of symmetry, but show a substantial dipole moment in solution. In the present
45 work we used the trans-1,4-dicarboxymethylcyclohexane and its 1,4-dibrominated
46 derivative and were able, through dipole moment determinations IR, Raman, NMR
47 studies and computational calculations with the SpinWorks, MOPAC and MOLDEN
48 programs, to confirm our assumption that the molecular symmetry as well as the
49 molecular structure are dependent on the environment.

50 **Keywords:** cyclohexanes, dipole, spectra, calculations, symmetry, exclusion

51 .

52

53 **INTRODUCTION**

54 **The starting point**

55 Well over one hundred years ago J. H. van't Hoff made the chemical world
56 aware of the fact that atoms occupy definite places in space.¹ This certainly
57 revolutionized the conception of what molecules could look like but had one limitation
58 that only became apparent much later. It can be summarized in one question. What
59 space did van't Hoff refer to? Perhaps it was vacuum, but now we know that molecules
60 are very seldom isolated in a vacuum and are usually found in solid, liquid (pure or in
61 solution), vapor or gaseous media, under conditions of temperature and pressure that
62 can vary extensively. These conditions range from near isolation close to absolute zero,
63 to crystalline solids or solutions, of various concentrations, at different temperatures and
64 pressures. The structure of molecules are studied in general through individual methods:
65 spectroscopic, dielectric, crystallographic, theoretical and computational, in various
66 environmental situations. They certainly give interesting and useful results but in all
67 cases lead to views of the molecules that are not broad enough to cover all the possible
68 alternatives of what may be considered to be a comprehensive understanding of their
69 behavior in what could be called "the real world". This is of particular importance
70 because molecules are actually "living beings" that will very likely behave differently
71 depending on the way they are looked at or the reactions in which they are involved.

72

73 All the above mentioned methods of study imply what is in essence the result of
74 looking at molecules under certain conditions that change depending on the procedure.
75 In other words they may be either alone, in bulk or as part of a reaction, so much so that
76 it becomes important to consider the environment they are surrounded by, because the
77 placement of their atoms in space, namely the structure, can vary substantially. In this

78 respect quite recent work both on the protomers of benzocaine^{2a} considering the static
79 vs dynamic protein structures as revealed by X-ray vs NMR experiments^{2b} showed the
80 marked influence of the environment on the properties of molecules.

81

82 These considerations lead to a different approach in the study of molecular
83 structures that was somehow anticipated by George F Wright³ when he stated in 1964
84 *“It would seem that as chemistry becomes more sophisticated the necessity for*
85 *designation of a substance in respect of its environment will increase”*. This approach
86 further suggests that the structure of molecules should be studied through the
87 simultaneous use of several methods that look at the molecular structures under
88 different conditions and environments, so that external influences leading also to
89 changes in molecular symmetry can be properly evaluated.

90

91 For a detailed study of this suggestion and on the basis of our previous work on a
92 trans-1,4-tetrasubstituted cyclohexane⁴ we chose trans-1,4-dimethoxycyclohexane and
93 its trans-1,4-dibrominated derivative and used the results of the variety of physical
94 methods listed above. The reason for this choice was the fact that these compounds
95 belong to a family of cyclohexane derivatives⁵ that appeared to be centrosymmetric but
96 showed a substantial dipole moment determined through dielectric measurements.

97

98 We expect that this approach will lead to a better understanding of the structure of
99 molecules and a clearer view of their symmetrical characteristics. To do so we will
100 proceed by steps starting with the dipole moment determinations because they gave the

101 first indication that there could be a different view of both molecular structure and
102 symmetry.

103 The first step. The molecules and their dipole moments

104 Since molecular structure is often closely related to molecular symmetry an
105 examination of this property provides a good starting point for the analysis of this
106 problem. In other words how the influence of the environment would affect the structure
107 of a molecule. This study becomes especially pertinent because it is known that the
108 absence of a centre of symmetry in a molecule is responsible for the existence of a
109 dipole moment, when it is determined in solution. Furthermore substantial dipole
110 moment values found in a number of compounds.^{3, 6-11} of apparently centrosymmetric
111 molecules have led over the years to reevaluate this notion. It has even been suggested
112 that this nonzero dipole moment was due to an abnormally high atom polarization. This
113 is a consideration difficult to accept since the latter property is temperature independent
114 while the dipole moment, resulting from orientation polarization, is clearly temperature
115 dependent. This fact had received considerable attention and was the cause of extensive
116 discussions⁶⁻⁹ with substantial evidence suggesting that the nonzero dipole moment
117 could, at the very least, be the result of the loss of centrosymmetry⁸. Consequently in
118 1,4-di and tetra substituted cyclohexanes that, in the solid state appear as
119 centrosymmetric molecules by several methods of analysis (crystallographic and
120 spectroscopic), a substantial dipole moment was determined when examined in
121 solution.⁵

122

123 The centre of symmetry

124 If the centre of symmetry, present or absent, seems to be the key to a possible
125 solution it is worthwhile to examine it further in some detail, especially since it is
126 widely accepted as being associated with the absence or existence of a dipole moment.

127

128 On the other hand the absence of a centre of symmetry, as the cause for a dipole
129 moment, can have a number of origins. Important ones are the rotations and orientations
130 of substituent groups on the 1 and 4 carbon atoms in certain cyclohexanes, as is the case
131 of diacid derivatives like esters and amides, and a deformation of the molecular ring.
132 The former cause was discussed and described in detail by E. Salz *et al.*,¹² that
133 considered (sic) *the sterically favored conformations of this molecule are those in*
134 *which the ester groups are coplanar with the C-H bonds, so that the carbonyl bond is*
135 *cis to the neighboring C-H bond designating this the 0,0 conformation.* However they
136 do indicate that the dipole of the ester group forms a substantial angle with this C-H
137 bond. They further conclude that the dipole moment results from the deformation in the
138 bond angles of the ester groups and consider as very low any influence of the "aliphatic
139 ring" (the central cyclohexane ring). Similar results described in the work by D. Y.
140 Yoon et al.¹³ involved dipole moment determinations and force-field calculations.

141

142 Kozima and Yoshino¹⁴ observed and discussed this problem comparing the
143 Raman spectra of solid and liquid samples of trans-1,4-dihalocyclohexanes and found
144 that there is a substantial change in the spectra when going from solid to liquid, leading
145 them to consider that in the solid the structure of the molecules is rigid and has, when in
146 solution, what they call (sic) "*a dynamic configuration*". They also considered that
147 there is a change in the molecular symmetry due to the fact that the C_{2h} point group

148 assigned to the molecule in the solid disappears in solution. A conclusion drawn from
149 the difference in the Raman spectra.

150

151 In the detailed discussion of these authors there is no mention of the centre
152 of symmetry that exists in the C_{2h} point group, although they do mention the symmetry
153 species belonging to it, namely A_u , A_g , B_u and B_g , as can be seen in a Character Table of
154 this Point Group explaining the absence of a dipole moment. The authors use this
155 evidence to justify a zero dipole moment. However in their paper they reported both the
156 determined total polarization, that they indicate as $P_{2\infty}$, and the molar refraction (R_D).
157 These values, with the classical Debye equation [$\mu = 0.01281 \times 10^{-18} (P_{2\infty} - R_D)^{1/2}$] lead to
158 the respective dipole moments at 298K. For the trans-1,4-dichlorocyclohexane $\mu = 0.47$
159 D and for the trans-1,4-dibromocyclohexane $\mu = 0.40$ D. Thus invalidating their
160 assumption of a zero, or even, near zero dipole moment.

161

162 The same 1,4-dihalocyclohexanes were studied, through NMR, by G. Wood and
163 E. P. Woo¹⁵, concentrating on the conformational equilibrium, and accepting as a result
164 that they are essentially in the chair conformation but they make no considerations on
165 their ring structures or their dipole moments.

166

167 These results suggest that a comparison of the IR and Raman spectra especially
168 in the finger print region could indicate that, according to the Mutual Exclusion Rule
169 (MER)¹⁶, in solution these molecules are not centrosymmetric and would explain the
170 non-zero dipole moment resulting from dielectric determinations.

171 Therefore a detailed examination of the NMR spectra could lead to
172 understanding the possible deformation of the cyclohexane ring and calculations with a
173 program like MOPAC would also assist in identifying the ring vibrations that lead to the
174 deformation that is the origin of the determined dipole moment.

175

176 At this point the question is whether the deviation from centrosymmetry is
177 permanent or transient depending on the environment and resulting a consequence of
178 the dynamic character of symmetry.

179

180 In quest for an answer

181 Both trans-1,4-dicarboxymethylcyclohexane (I) and trans-1,4-dibromo1,4-
182 dicarboxymethylcyclohexane (II) were chosen to examine this problem because both
183 compounds are soluble in solvents that are used in every kind of physical study from
184 dipole moment determinations at two temperatures to IR and Raman, both in solution
185 and in solids, and NMR spectroscopy. It is expected that this will take into
186 consideration the medium in which these molecules are examined.

187

188 The importance of this dual approach stems from the fact that dipole moments
189 are a bulk property, but spectroscopy is molecule-based. Therefore it should provide a
190 better view of the dynamic characteristics of both the structure and symmetry of the
191 molecules considered.

192 **EXPERIMENTAL PART**

193 **1. Dipole moment determinations**

The dipole moments were determined at two temperatures (298 and 308 K) from single solution permittivity measurements using the Mechetti-Baron equation as previously described¹⁷⁻¹⁸, with CCl₄ as solvent, in a newly developed instrument¹⁹. The permittivities of the solvent and the sample containing solution are calculated from the measured frequencies. A nonpolar solvent is essential here and CCl₄ was used because, from previous experience⁴ it appeared to interact less with the solute. Solvent permittivities (ϵ_1), solvent and solute densities (d_1 and d_2 in g ml⁻¹), solute refractive index (n_2), solute p/p concentration, and solution permittivities (ϵ_{12}) are shown in Table 1. Therein it can be seen, through their systematic increase, the important influence of temperature on the dipole moment values.

204

205 Table 1

206

207 **2. IR and Raman both in the solid and in solutions**

IR and Raman spectra were obtained on both compounds in the solid and in CCl₄ solutions. Preliminary spectra on the samples in CCl₄ were obtained on a Perkin-Elmer Model 1600 FTIR instrument. The spectra (S1 and S2), although not very conclusive, did indicate the possible application of the (MER) to study the structure of these molecules. Especially due to the coincidence of several the frequencies in the C-H stretchings region (2953, 2910 and 2866cm⁻¹) and also of the 1737cm⁻¹ of the carbonyl band. However since the lower frequency region is not as clear better spectra, of both IR and Raman, were obtained on a Bruker IFS 66 FTIR Instrument, with the Bruker FRA 106 and are shown in Figures 1 and 2. Although superficially they appear to look similar, there are differences to be considered. Keeping in mind that the MER refers to normal modes, since there are two carbonyl groups it should be considered that although the peaks coincide, one corresponds to a symmetric stretching, that is the result of a change in polarizability typical of Raman spectra and the other to an unsymmetrical stretching

221 typical of the IR spectra resulting from a change in polarization, that is reflected in the
222 change in the dipole moment.

223
224 Figure 1. IR (top) and Raman (bottom) spectra of the protondiester in carbon
225 tetrachloride

226
227 Figure 2. Expansion of the IR (top) and Raman (bottom) spectra of the protondiester in
228 carbon tetrachloride.

229

230 This is important when considering the MER because, as said above, it refers to
231 normal modes. Therefore a superficial resemblance, although useful could be
232 misleading due to the existence of the just mentioned fact of a C=O symmetric
233 stretching in the Raman spectrum and an unsymmetrical stretching in the IR spectrum,
234 There is a clear the differences in intensities in both cases (see Table S1). Furthermore
235 in the low frequency region (1400 to 500cm^{-1}) where the ring vibrations should appear,
236 the picture is not clear enough to indicate deformation.

237

238 **Calculation of IR and Raman spectra**

239 Infra-red and Raman spectra were calculated using the Gaussian03 software
240 package.²⁰ The DFT calculations were done using the B3LYP functional at the 6-
241 311++G(d,p) basis level. The calculations were done with all symmetry considerations
242 turned off in the program. As is typical, the calculated values are somewhat higher than
243 those observed and the unscaled values are presented in Table S1.

244

245 The blanks in this Table mean that the activity is very small. The absence of any
246 essential coincidence in the absorptions of both spectra indicates that in the solid state

centrosymmetry is maintained, suggesting that there is an exclusion between the normal modes. Although the calculations tend to overestimate the frequencies they do help to interpret the experimental data.

Additional insight into the problem of a possible ring deformation can be obtained from these tables through the MOPAC²¹ and MOLDEN²² programs. With the former the molecular structure and IR spectra can be calculated and the latter helps to analyze them. This allowed to identify the type of ring vibration a particular frequency corresponds to, either stretching, bending or wagging. Especially because depending on their intensities shown on the Table S1 their contributions to the dipole moment can become apparent.

To identify the bonds corresponding to each frequency the ring carbon atoms are numbered as shown in Figure 3. The MOPAC calculations were carried out with the input shown in the Table S2, considering that the plane containing the ester groups on C₂ and C₆ form a 0 degrees dihedral angle, indicated as (HCC=0:0). So that the calculations are in line with the work by E. Salz et al.¹². The MOPAC output shows the molecule to belong to the C_s symmetry Point Group, that would justify the determined dipole moment and it also provides the IR frequencies shown in Table S3. The corresponding vibrations are intense enough to participate in the existence of the non-zero dipole moment determined in solution. The resulting spectrum obtained through the MOLDEN program is shown in Figure S3.

Figure 3. Nomenclature for the protons in the protondiester and labels of the ring protons that correspond to the coupling constants in Table 8

Considering only the six ring C-C bonds 12 normal mode vibrations would be

expected, that should appear in the low frequency region, between 1200 and 500cm⁻¹ for the stretching and bending and lower for the wagging (below 400cm⁻¹) (see Table S4) Comparing these results with those on Table S1, although there is no strict coincidence with the MOPAC calculated numbers (see Table S4) they do correspond to the movements of the six carbons of the cyclohexane ring. If the six ring carbon atoms are considered, 12 normal modes should be expected (3N-6). (Table 2).

Table 2

The calculated IR ring vibrations and those calculated with MOPAC, showing a reasonable coincidence, are shown in Table 2.

The Z coordinates of carbons 2 and 6 in the MOPAC Cartesian Input Coordinates compared with the Cartesian Output Coordinates provide additional information (see Tables S5 and S6), because they change from exactly zero to a different value. This indicates that, when the molecules are allowed to move their structure reached a conformation with a non-zero dipole moment.

The existence of a possible centrosymmetric conformation belonging to the C_{2h} symmetry Point Group with a different, Heat of Formation cannot be ruled out. The calculations were then repeated rotating the carbomethyl groups by 20 degrees all the way from 0 to 360° and the Heat of Formtion (Hf) vs degrees (see Figure S4). They are listed together with the dipole momento values and collected in Table 3. There it can be

seen that H_f varies between a maximum of $H_f = -179.74$ and a minimum of $H_f = -184.03$ kcal/mole.

Table 3

A MOPAC calculation with strict symmetry conditions resulted in a conformation belonging to the C_{2h} Point Group with $H_f = -188.32$ kcal/mol and $\mu = 0.00D$, suggesting the existence of also a stable conformation with a lower H_f .

To obtain further evidence for the ring deformation, several sets of NMR spectra were obtained in $CDCl_3$ solutions, three at 200MHz on a Bruker 200 instrument on the diester (two on the plain and one on the dibrominated) and five, on the plain and dibrominated diester, run at 300 on a Bruker AV 600 Avance I using a 5 mm probe equipped with a z axis gradient and on a Bruker AV 500 Avance I spectrometer with a 5 mm BBO inverse detection probe.

The ring protons are labeled so that they correspond to the coupling constants listed on Table 4.

The irradiated and calculated diprotodiester at 200MHz are shown in Figure 4 wherein the Chemical shifts of the former are indicated. With these values and the coupling constants listed in Table 4 the irradiated spectrum was calculated with the SpinWorks4²³ program.

Figure 4. Experimental (upper) and Simulated (lower) of the 200MHz irradiated spectra. The complete diprotodiester spectrum at 600MHz is shown in Figure 5

357 Figure 5. 600 MHz Complete spectrum of the protondiester.

358 Further calculations of this spectrum were done considering that in it there are
359
360 2-bond and 3-bond proton-proton coupling constants for the protondiester. The notation
361
362 $^2J_{BC}$ indicates a 2-bond (geminal) coupling between two protons on the same carbon,
363
364 whereas $^3J_{BC'}$ indicates that this is a proton on a different carbon atom (C) and it is a 3-
365
366 bond (vicinal) coupling between protons on adjacent carbons. The values of the
367
368 couplings between the *B* and *C* protons were obtained from a simulation of a
369
370 homodecoupling experiment (Table 4), and the couplings to the *A* proton were based on
371
372 literature values²⁴.
373
374

375 In Figure 5 the band at high frequency signal (near 2 ppm) corresponds to the *A*
376 protons, the next band near 1.83 ppm corresponds to the *C* (equatorial protons) and the
377 band at low frequency (near 1.2 ppm) corresponds to the axial protons, labeled *B* in
378 Figure 3.

379

380 In this spectrum the traces near 1.2 and 1.8ppm did not afford any significant
381 information since they corresponded to eight protons (four axial and four equatorial) on
382 the sides of the cyclohexane ring. They are difficult to evaluate considering the
383 numerous interactions between them, so that finding their coupling constants would
384 prove to be very difficult (see the experimental and simulated spectra of both regions in
385 Figures S5 and S6).

386 Therefore only the axial A protons signal, near 2 ppm, on the 1,4-carbon
387 atoms were simulated. The full spectrum (10 spins) was then simulated using only 2-
388 bond and 3-bond couplings, because these two protons are actually coupled to the sides

389 of the ring and it they should be very sensitive to the ring symmetry. The spectrum is
390 shown in Figure 6 and the simulated coupling constants are those shown in Table 4.

391 Figure 6. The experimental spectrum is the upper trace and the lower trace is the
392 simulated spectrum with the coupling constants shown in Table 4.
393

394 Some of the coupling constants are a little hazy, but they do help to analyze
395 the spectra. We did a homo decoupling of the protons on carbons 1 and 4 and it gave us
396 the spectrum shown on Figure 7. Here the difference in the size of the equatorial and
397 axial peaks can be seen again. A situation quite similar to that observed in the 200MHz
398 spectra, providing an additional confirmation of the absence of a centre of symmetry.

399 Figure 7. The bottom spectrum corresponds to the Band C protons when the A protons
400 are decoupled. Top spectrum: simulation of the four protons on one side of
401 the ring, treated as an AA'BB' spin spectrum. The iterated values of the
402 coupling constants are given in Table 4.
403

404 These spectra gave us all the *BC* couplings and their values are consistent with those
405 listed in the literature²⁴

406

407 Dibrominated diester

408 To complete the picture the experimental 200 MHz proton spectrum of the
409 dibromodiester derivative was obtained at 30° C (Fig. 8). The ratio of the high-
410 frequency to the low-frequency band is 3:4. We assign the low-frequency band to the
411 ring protons in intermediate exchange, by analogy to published work⁴ on the
412 dibromodicyano derivative.

413 Figure 8. NMR spectrum of the dibrominated diester.

414 In this case as in our previous cited work⁵ the experimental traces show just one peak
415 for both types of protons, namely the axial and equatorial ones, suggesting a fast

416 exchange.

417

418 **DISCUSSION**

419 The first indication that that these molecules are in a dynamic movement affecting
420 their symmetry when not in the crystalline state, is the appreciable dipole moment
421 change when determined at two temperatures (298 and 308 K), as can be seen in Table
422 1. The difference is substantial and similar to that encountered in our previous work on
423 the 1,4-dibromo-1,4-dicyanocyclohexane⁴. These results have the advantage of having
424 been obtained with a much more precise procedure as the one used previously²⁵ that did
425 produce a substantial dipole moment value (2.08D in benzene).

426

427 W. Kwestroo, F. A. Meijer and E. Havinga²⁶ did a limited review, among other
428 compounds, on trans-1,4-dibromocyclohexane reporting a $\mu = 0.57\text{D}$ at 298 in CCl_4 . B.
429 Franzus and D. E. Hudson²⁷, confirmed these results, finding $\mu = 0.55\text{ D}$ (in heptane),
430 but also calculated the dipole moment with the Kozima and Yoshino values finding $\mu =$
431 0.4 D . This coincides with our above indicated results and is a confirmation that, in
432 solution, these molecules are not centrosymmetric.

433

434 Furthermore previous work on trans-1,4-di and tetra-substituted
435 cyclohexanes^{4,5,25} has provided conclusive evidence that, at least in solution the
436 non-zero dipole moment of these molecules is the result of the presence of a substantial
437 amount of non-centrosymmetric structures, when they are examined at normal
438 temperature and pressure, namely 298K and one atmosphere. Regardless of the fact that
439 X-Ray studies of several of these compounds showed that in the crystalline state the

440 molecules are centrosymmetric⁴⁻²⁸⁻³¹, this is a clear indication that in solution there is an
441 orientation polarization responsible for the determined dipole moment.

442

443 Consequently the determination of dipole moments in solution, at least at two
444 temperatures, appears to be a very useful indicator that, when a molecule is allowed a
445 certain degree of freedom and is not constrained as in the crystalline state, its structure
446 will vary extensively and become open to a dynamic analysis of its movements. This
447 was the case of our previous study on 1,4.dibromo-1,4.dicyanocyclohexane⁴, here we
448 found evidence of the loss of the centrosymmetry observed in the crystalline state²⁸.

449

450 The first indication of a dynamic nature of the molecular symmetry came from
451 the IR and Raman spectra in CCl₄ of the simple diprotonated diester (Figures S1 and
452 S2). Therein it can be seen that it substantially follows the MER because the main
453 absorptions, especially those of the carbonyl group, coincide exactly at 1737cm⁻¹. This
454 is evidence that the centre of symmetry disappeared when the compound went into
455 solution. The close frequencies in the carbonyl stretching in both spectra indicates a
456 symmetric and an asymmetric normal mode, one IR active and one Raman active.

457

458 Careful observation of the spectra on Figures 1 and 2 confirms this and supports
459 the assumption that in solution the MER is valid and that there is no longer a centre of
460 symmetry in this molecules, although it exists in the crystalline solid³¹.

461

462 This situation is similar to that in the trans-1,4-cyclohexanedicarboxylic acid.
463 The spectra, available in the literature³², were obtained on the solid with no coincidence
464 of the major peaks, indicating that central symmetry is maintained. (Figures S7 and S8).
465 Crystallographic study³³ of this compound found in the unit cell the existence of two
466 centrosymmetric molecules belonging to the C_i point group.

467
468 Furthermore the evolution of the cyclohexane ring itself, as well as that of some
469 isotopic derivatives, has been studied in detail by Wiberg and Shrake³⁴, both in the
470 liquid and solid states through IR and Raman. They handle their spectra considering that
471 the molecules belong to the D_{3h} point group that lacks a centre of symmetry.

472
473 Turning now to the NMR studies, the calculations of Gibbs Energies by Wood
474 and Woo¹⁵ for both the dibromo and dichloro cyclohexane derivatives, as discussed in
475 the Introduction, suggested a certain amount of ring deformation caused by the dynamic
476 movements of the molecules.

477
478 Hawkes and Utley³⁵ discussed and described the conformational difference
479 observed in the NMR spectra and consider them caused by the ring flattening suggested
480 by Joseph B. Lambert.³⁶⁻³⁷ In his 1967 paper he made a more general evaluation of
481 distorted-chair conformations in six-membered rings reporting the existence of distorted
482 ring conformations on the basis of spectral evidence on a number of 1,4 disubstituted
483 cyclohexanes. He found how the dihedral angle of the H-C-C-H bonds on the sides of
484 the ring change depending on the variety of substituents on the 1,4 carbon atoms.

485

486 In both just mentioned cases the authors analyzed the effect of substituents on
487 carbons 1 and 4 (2 and 6 in our numbering on Fig. 3) of the cyclohexane ring.
488 Especially the work by Lambert deals precisely with what happens to molecules in
489 solution. Suggesting that that the environment or “space” has to be considered in
490 structural studies.

491

492 Furthermore the influence of alkyl groups on the conformational isomerism of
493 bromo substituted alkoxy cyclohexanes was also found by Josué M. Silla *et al.*³⁸ through
494 NMR and theoretical calculations, providing additional evidence to our assumption.

495

496 So if the non-zero dipole moments found are attributed to ring deformation, the
497 structure of the rings has a distinct influence on the ring protons with an effect on their
498 NMR spectra. The ring protons are those on C₄ and C₉ and C₅ and C₁₀ (the numbers
499 correspond to those indicated in Figure 3), and offered good possibilities as we found in
500 our previous work.⁴ If the tetra substituted compounds do belong to the C_{2h} point
501 groups as found by Echeverria in their crystallographic studies,²⁸⁻²⁹ they should have a
502 centre of symmetry. As a result of this the plane perpendicular to the C₂ axis would
503 divide the molecules into two identical moieties so that if the A protons on C₂ and C₆
504 were irradiated the remaining eight ring hydrogen atoms would behave as a simple
505 perfectly symmetric four spin trace of the A₂B₂ type. This does not appear to be the
506 present situation and would indicate that the plane containing atoms C₂ and C₆ leaves
507 four hydrogen atoms on each side, two axial and two equatorial but it is not a plane of
508 symmetry dividing the molecule into two not equal halves. Therefore as we saw in our

509 previous work on the dibromodicyano derivative⁴ there is fast exchange at room
510 temperature and the two systems could only be seen at low temperatures. This situation is
511 clear in the dibromo derivative and in the diproto ones through irradiation of the
512 corresponding hydrogen atoms, as had been found by Baron , Medrano, Ferraro and
513 Buep⁵ in the trans-1,4-dicyanocyclohexane.

514

515 Furthermore in the 200MHz irradiated spectrum there is again a clear difference
516 in the size of the traces that can be caused by a difference in the nature of the influence
517 of the neighboring ester groups. Although they are in the equatorial conformation, as
518 was the case with the CN group, the carbomethyl moiety can rotate freely and, as shown
519 in previous work by Salz, Hummel, Flory and Plavsic¹² the direction of the dipole
520 moment appears to be closer to the equatorial protons than to the axial ones. This
521 creates an influence quite similar to that observed in a previous work on chloralides³⁹
522 wherein the close presence of a carbonyl as well as an oxygen atom affected the size
523 and chemical shifts of neighbouring and vicinal protons. Therefore, as in the case of the
524 cyano derivative⁵, where the equatorial CN group had a distinct influence on the vicinal
525 protons causing a clear difference in size, this difference in the spectrum can be
526 attributed to the absence of a centre of symmetry.

527

528 **CONCLUSIONS**

529 The dual approach suggested in the Introduction showed that the results of
530 dipole moment determinations as well as IR, Raman and NMR spectroscopy tend to
531 explain the apparent paradox of what is generally considered to be a centrosymmetric

532 molecule but has a substantial dipole moment, depending on the conditions it is being
533 studied. Essentially, as anticipated, our work implies a comparison between bulk
534 molecular measurements (dipole moments) and molecule based studies (spectroscopic).
535 Especially since in the latter case there are enough measurable vibrational modes to
536 justify the substantial dipole moments.

537

538 The IR spectra, both experimental and calculated, together with the
539 MOPAC and MOLDEN results indicate, not only a substantial deformation of the
540 cyclohexane ring that can be considered as responsible for the experimentally
541 determined dipole moments, but also that there exists, among others, a centrosymmetric
542 conformation and that in solution the molecule being studied is present in a variety of
543 conformations.

544

545 At this point the original question can be answered saying that the evidence
546 found supports the idea that, due to the dynamic character of symmetry, the description
547 of a molecule has to take into consideration its environment or, in the words of van't
548 Hoff, the space or medium in which it is immersed.

549

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TABLES

Table 1. Data Used in the Dipole Moment Calculations

Compd.	Temp.	ϵ_1	d_1	d_2	n_2	Conc.(p/p)	ϵ_{12}	μ (D)
I	298	2.2279	1.5943	1.111	1.435	0.00158	2.2367	2.45 ± 0.02
I	308	2.2079	1.5943	1.111	1.435	0.00295	2.2293	2.77 ± 0.02
II	298	2.2279	1.5943	1.717	1.513	0.00724	2.2427	3.78 ± 0.02
II	308	2.2079	1.5943	1.717	1.513	0.00313	2.2357	4.19 ± 0.02

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TABLE 2. Calculated ring vibrations (Table S2 and MOPAC)

VIBRATION No.		TYPE OF VIBRATION	TABLES S2 VALUES	MOPAC CALCULATED VALUES
IR	MOPAC			
1	2	Ring wagging	21.9	21.1
9	9	Ring wagging	197.6	184.4
13	13	Ring wagging	265.2	249.2
17	17	Ring wagging	407.7	448.9
19	20	Bond bending	497.8	510.5
27	27	Bond bending	889.6	847.1
30	30	Bond bending	919.7	905.1
32	31	Bond bending	998.9	995.7
35	35	Bond stretching	1058.2	1035.2
37	39	Bond stretching	1093.3	1114.9
40	40	Bond stretching	1170.8	1161.2
42	42	Bond stretching	1174.5	1172.5

TABLE 3. Hf vs angle vs μ

Angle Degrees	μ D	Hf kcal/mol
0	0.033	-182.7
20	0.026	-182.1
40	0.023	-180.8
60	0.017	-179.4
80	0.024	-178.9
100	0.038	-179.9
120	0.039	-181.3
140	0.026	-182.8
160	0.019	-183.7
180	0.039	-184
200	0.019	-183.7
220	0.026	-182.8
240	0.032	-181.3
260	0.032	-179.7
280	0.024	-178.9
300	0.017	-179.4
320	0.023	-180.8
340	0.026	-182.1
360	0.028	-182.7

Table 4. Coupling constants of the ring protons

Coupling	Type	Value (Hz)
$^3J_{AC}$	gauche	3
$^3J_{AB}$	trans	11
$^3J_{BB'}$	trans	12.1
$^2J_{BC}$	geminal	-13.7
$^3J_{BC'}$	gauche	4.5
$^3J_{CC'}$	gauche	3.5

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FIGURES

Figure 1. IR (top) and Raman (bottom) spectra of the protodiester in carbon tetrachloride

Figure 2. Expansion of the IR (top) and Raman (bottom) spectra of the protodiester in carbon tetrachloride.

Figure 3. Nomenclature for the protons in the protodiester and labels of the ring protons that that correspond to the coupling constants in Table 8

Figure 4. Experimental (upper) and Simulated (lower) of the 200MHz irradiated spectra.

Figure 5. 600 MHz Complete spectrum of the protondiester.

Figure 6. The experimental spectrum is the upper trace and the lower trace is the simulated spectrum with the coupling constants shown in Table 4.

Figure 7. The bottom spectrum corresponds to the Band C protons when the A protons are decoupled. Top spectrum: simulation of the four protons on one side of the ring, treated as an $AA'BB'$ spin system. The iterated values of the coupling constants are given in Table 4.

Figure 8. NMR spectrum of the dibrominated diester.

GRAFICAL ABSTRACT