Conformational Studies on Small Molecules*

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1 Introduction

In recent years, conformational analysis has attracted a great deal of attention and much effort. Various experimental methods have been applied to a large number of chemical species to determine the orientations about single bonds which are the most stable, and the many implications regarding reactivity, *etc.* have been widely discussed.[1–5]

For small molecules such as 1,2-disubstituted ethanes it was Mizushima[6] in the 1930s who showed that these tended to occur as *trans* and *gauche* forms (see Figure 1). Since these differ merely by a rotation of about 120° around the carbon–carbon single bond, which, for small substituents at least, does not require the molecule to surmount a very large potential energy barrier, it is not normally possible to separate these rotational isomers, rotamers, or conformers in the liquid or gaseous phases.

Besides the intrinsic interest which chemists have in structure, there are a number of good reasons for studying the conformations of molecules. One is the biological importance of this phenomenon.[7] As is well known, the exact way a protein chain folds into a compact, biologically active molecule, such as an enzyme, involves very specific conformational choices. If the chain is unfolded into an extended form, the biological activity is normally lost. In a number of cases it has been shown that such an uncoiled protein, when given the proper environment, *i.e.* solvent, temperature, pH, will spontaneously refold to its active form.

Naturally, it would be desirable to be able to predict the conformations, angular distortions, relative energies, barrier heights, *etc.* from sound and convincing theoretical or empirical bases. This is clearly a complicated problem,

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* Based upon Centenary Lecture delivered at Glasgow, Sheffield, and Bristol during March 1971.

[1] See, for example, the review of the work of Barton and Hassel (Nobel awards, 1969) by E. L. Eliel, *Science*, 1969, **166**, 718.

[2] O. Hassel and B. Ottar, *Acta Chem. Scand.*, 1947, **1**, 929.

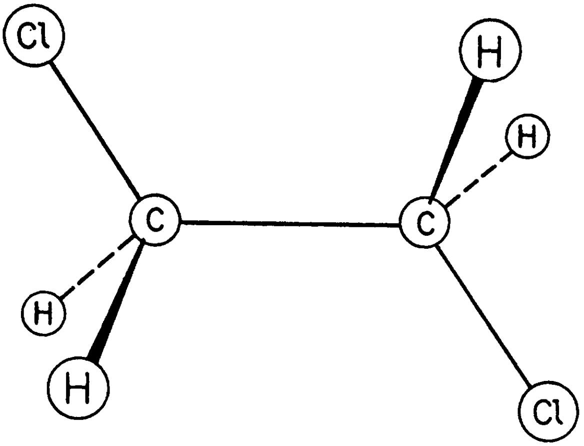
[3] D. H. R. Barton, 'The Principles of Conformational Analysis', in 'Les Prix Nobel en 1969', Norstedt and Soner, Stockholm, 1970, pp. 119—129.

[4] E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, 'Conformational Analysis', Interscience, New York, 1965.

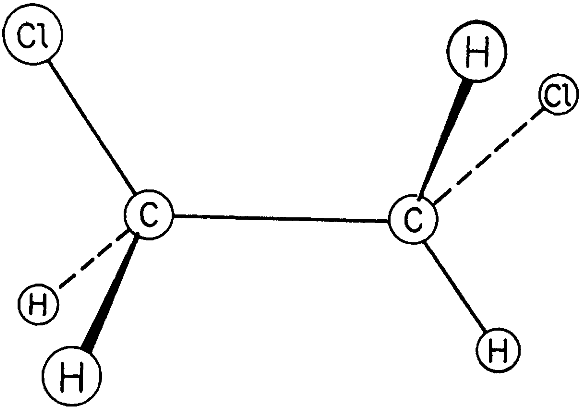
[5] M. Hanack, 'Conformational Theory', Academic Press, New York, 1965.

[6] S. Mizushima, 'Structure of Molecules and Internal Rotation', Academic Press, New York, 1954, p. 24.

[7] J. T. Edsall, in 'Structural Chemistry and Molecular Biology', ed. A. Rich and N. Davidson, W. H. Freeman and Co., San Francisco, 1968, p. 89.



(a) *trans*



(b) *gauche*

Figure 1 (a) trans *and* (b) gauche *rotamers of 1,1-dichloroethane*

but many systems have been set up for the purpose of doing this.[8] One reason for collecting more experimental data on small rotamer species is to provide

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[8] See, J. E. Williams, P. J. Stang, and P. von R. Schleyer, *Ann. Rev. Phys. Chem.*, 1968, **19**, 531.

checks on these published computational methods, and, where they meet these tests, to enable the predictive methods to be extended to wider classes of molecules.

A more basic aim is to acquire fundamental information about non-bonded forces within molecules. Even though our knowledge of bonded forces is far from adequate, it is considerably more advanced than our understanding of non-bonded forces; this situation needs improvement.

2 Experimental Techniques

A great many experimental techniques have been used to gain information about rotamers. Mizushima[6] and others found that i.r. and Raman spectroscopy were particularly useful. Often the crystalline form has a simpler spectrum than the liquid or gas, leading to the assumption that the crystal contains only one form while the extra lines in the other phases are assignable to the other form (or forms). This view was strengthened by the observation that the two sets of lines in the liquid or gas have different temperature coefficients of intensity. Incidentally, measurements of such intensity coefficients (which are hard to make accurately) give values for the energy difference between the rotameric forms.

Electron diffraction studies[6,9,10] and the change with temperature of the average dipole moment[6] have also been employed, and have been particularly important in the early history of the subject. Still another method uses acoustic dispersion or absorption measurements.[11,12]

In more recent years the most used tool has surely been n.m.r., particularly over a range of (low) temperatures. For many compounds, by lowering the temperature the rate of interconversion of the rotamer forms can be reduced sufficiently so that two sets of n.m.r. lines can be observed, one set for each rotamer. At higher temperatures, these first broaden, then merge, and finally sharpen to one set of lines representing the rapidly interconverting molecule. From such measurements, and others related to them, values for the free energy of activation at the barrier between rotamer forms can be found and some inferences (not always conclusive) drawn about the conformations present.[13] This technique is responsible for much of our present knowledge about conformations, but has been confined to liquids and solutions.

However, microwave spectroscopy can give much more detailed and more certain information about rotamers than any of the other methods.[14] It has serious limitations: it can be applied so far only to rather simple molecules and has, in the past, required considerable effort for each molecule. For this reason

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[9] O. Bastiansen, ref. 7, p. 640.

[10] Y. Morino and K. Kuchitsu, *J. Chem. Phys.*, 1958, **28**, 175.

[11] M. Eigen and L. de Maeyer, in 'Techniques of Organic Chemistry', ed. A. Weissberger, Interscience, New York, 1963, 2nd edn., vol. VIII/2, p. 895.

[12] E. Wyn-Jones and W. J. Orville-Thomas, 'Molecular Relaxation Processes', Chem. Soc. Special Publ., 1966, No. 20, p. 209.

[13] H. Booth, 'Applications of ^{1}H N.M.R. to the Conformational Analysis of Cyclic Compounds', *Progr. N.M.R. Spectroscopy*, ed. J. W. Emsley, J. Feeney, and L. H. Sutcliffe, Pergamon Press, Oxford, 1969, ch. 3.

[14] V. W. Laurie, *Accounts, Chem. Res.*, 1970, **3**, 331.

it has been mainly of value in providing detailed information on some basic molecules, useful as a check on theories or as a source of fitted parameters for empirical theories.

There are several approaches to a problem like this which can be defended. The most obvious is to assemble all the pertinent information from all sources, all techniques, and then attempt a grand synthesis which will account for everything. Attractive as this approach sounds, it has serious drawbacks. First, few have the energy, or the breadth of understanding, to undertake such a project in view of the massive amount of literature. Secondly, it is a rare person who can critically examine many different fields and reject the unreliable or patently false data that unfortunately are all too abundant. It takes only a few wrong numbers to destroy any attempt at explanation. Finally, it is often easy to introduce enough parameters so that a large but finite amount of data is fitted with a meaningless theory.

An alternative is to adopt a very parochial viewpoint and attempt to construct a theory which is based entirely, or almost entirely, on information from one technique alone, information which is carefully assessed and judged to be reliable. If this can be done, then the conclusions can be compared with those drawn independently by others from other sources of information. If various techniques in a truly independent way lead to the same conclusions, we can properly have vastly more confidence in them than otherwise.

3 The Microwave Method

In microwave spectroscopy a given molecule is under observation only during the time between two collisions, since almost all collisions cause transitions to other rotational states. Rotamer species rapidly interconvert, but mostly this reaction requires collisions. The result is that the microwave spectrum of a compound which occurs in two or more conformations normally contains the transitions of all the rotameric forms present in sufficient abundance, just as in the case of a mixture of stable, non-reactive species. Further, the high resolving power available lessens the chances that lines of one rotamer will cover up lines of another, although this does sometimes happen. An exceptional situation occurs when quantum mechanical tunnelling is important. This will be discussed later.

Consequently, it is possible in suitable cases to analyse the spectra of the separate rotamers and in principle to obtain for each form all the information usually extractable from the microwave spectrum of a single, pure species. This includes structure, particularly the value of the dihedral angle, dipole moments, low vibration frequencies, especially the torsional frequency, barriers to internal rotation of methyl groups, *etc.*[15] Particularly interesting is the collection of information which can lead to the determination of a potential function for rotation about the single bond from one rotamer to the others.

Some of the limitations of the microwave method are being a little eased by

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[15] J. E. Wollrab, 'Rotational Spectra and Molecular Structure', Academic Press, New York, 1967.

various current developments. The availability of commercial microwave spectrometers greatly speeds the collection of data and may make possible improved accuracy of intensity measurements. This greater speed and ease should lead to quicker analyses and also encourage more studies of vibrational satellites and isotopic forms. The extended use of microwave–microwave double resonance and, more recently, of radio frequency–microwave double resonance has also aided the assignment of difficult spectra. Computer averaging techniques provide greater sensitivity, which can often be critical. In addition to these experimental developments, there have been several extensions of the theory of the rotational spectra of molecules with an internal degree of freedom.[16–19]

Table 1 lists some of the molecules for which two or more rotamers have been identified and studied by microwave spectroscopy. It is based upon the list compiled by Morino and Hirota[20] but contains more recent entries, kindly supplied by Dr. F. Wodarczyk. Also shown is the nature of the rotamers, such as *cis*, *gauche*, *etc.*, with the more stable form underlined, where known. Besides these molecules, a great many have been studied in which only one form was observed, although there are reasons to believe that a second form exists, perhaps with insufficient dipole moment or too high an energy [see Table 1 (ii)]. A considerable number of additional species are known to be under investigation currently in many laboratories.

Table 1 *Molecules studied by microwave spectroscopy*

(i) *Molecules with at least two stable forms identified*

The following molecules are arranged according to the bond about which hindered rotation leading to the different rotameric forms takes place. The designation of the stable forms refers to the relative orientations of the underlined functional groups. More stable form is underlined.

Molecule		*Dihedral angle* (°)	*Stable forms*		*Ref.*
C—C (sp^3–sp^3)					
n-Propyl fluoride	$\underline{CH_3}CH_2CH_2\underline{F}$	117	*trans*	$\underline{\textit{gauche}}$	*a*
n-Propyl chloride	$\underline{CH_3}CH_2CH_2\underline{Cl}$	110	*trans*	*gauche*	*b*
n-Propyl bromide	$\underline{CH_3}CH_2CH_2\underline{Br}$		*trans*	*gauche*	*c*
n-Propyl iodide	$\underline{CH_3}CH_2CH_2\underline{I}$		*trans*	*gauche*	*d*
n-Propanol	$\underline{CH_3}CH_2CH_2\underline{OH}$	116	*trans*	*gauche*	*e*
n-Propyl cyanide	$\underline{CH_3}CH_2CH_2\underline{CN}$		*trans*	*gauche*	*f*
n-Propylacetylene	$\underline{CH_3}CH_2CH_2\underline{C{:}CH}$	115	*trans*	$\underline{\textit{gauche}}$	*g*

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[16] R. Meyer and E. B. Wilson, *J. Chem. Phys.*, 1970, **53**, 3969.

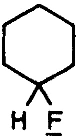
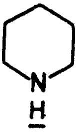
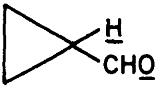
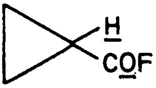
[17] J. V. Knopp and C. R. Quade, *J. Chem. Phys.*, 1970, **53**, 1.

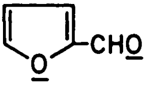
[18] H. M. Pickett, *J. Chem. Phys.*, 1972, **56**, 1715.

[19] A. Bauder, E. Mathier, R. Meyer, M. Ribeaud, and H. H. Gunthard, *Mol. Phys.*, 1968, **15**, 597.

[20] Y. Morino and E. Hirota, *Ann. Rev. Phys. Chem.*, 1969, **20**, 139.

Table 1 (*cont.*)

Molecule		*Dihedral angle* (°)	*Stable forms*		*Ref.*
n-Propyl isocyanide	$\underline{CH}_3CH_2CH_2\underline{NC}$		*trans*	*gauche*	*h*
n-Butyraldehyde	$\underline{CH}_3CH_2CH_2\underline{CHO}$	101	*trans*	*gauche*	*i*
Cyclohexyl fluoride			axial	$\underline{\text{equatorial}}$	*j*
C—N					
Piperidine			axial	$\underline{\text{equatorial}}$	*k*
Ethylamine	$\underline{CH}_3CH_2NH_2\underline{:}$		*trans*	*gauche*	*l*
C—O					
Ethanol	$\underline{CH}_3CH_2\underline{OH}$	126	*trans*	*gauche*	*m*
Isopropanol	$(CH_3)_2C\underline{H}O\underline{H}$		*trans*	*gauche*	*n*
Ethyl formate	$\underline{CH}_3CH_2O\underline{C}HO$	95	$\underline{\textit{trans}}$	*gauche*	*o*
Ethyl nitrate	$\underline{CH}_3CH_2O\underline{N}O_2$	95	$\underline{\textit{trans}}$	*gauche*	*p*
C—S					
Ethanethiol	$\underline{CH}_3CH_2S\underline{H}$		*trans*	*gauche*	*q*
Ethyl methyl sulphide	$\underline{CH}_3CH_2S\underline{CH}_3$		*trans*	*gauche*	*r*
Isopropanethiol	$(CH_3)_2C\underline{H}S\underline{H}$		$\underline{\textit{trans}}$	*gauche*	*s*
C—C (*sp*²–*sp*³)					
3-Fluoropropene	$\underline{CH}_2{=}CHCH_2\underline{F}$	125	$\underline{\textit{cis}}$	*gauche*	*t*
3-Chloropropene	$\underline{CH}_2{=}CHCH_2\underline{Cl}$	122	*cis*	*gauche*	*u*
Allyl cyanide	$\underline{CH_2{=}C}HCH_2\underline{CN}$		$\underline{\textit{cis}}$	*gauche*	*v*
But-1-ene	$\underline{CH_2{=}C}HCH_2\underline{CH}_3$		*cis*	$\underline{\textit{gauche}}$	*w*
Propionaldehyde	$\underline{CH}_3CH_2CH\underline{O}$	131	*cis*	*gauche*	*x*
Propionyl fluoride	$\underline{CH}_3CH_2C\underline{O}F$	120	$\underline{\textit{cis}}$	*gauche*	*y*
Fluoroacetyl fluoride	$\underline{F}CH_2CO\underline{F}$	180	$\underline{\textit{cis}}$	*trans*	*z*
Chloroacetaldehyde	$\underline{Cl}CH_2CH\underline{O}$		*cis*	*trans*	*aa*
Cyclopropane-carbaldehyde		180	$\underline{\textit{cis}}$	$\underline{\textit{trans}}$	*bb*
Cyclopropanecarbonyl fluoride		180	$\underline{\textit{cis}}$	*trans*	*cc*

Molecule		*Dihedral angle* (°)	*Stable forms*		*Ref.*
C—C (sp^2–sp^2)					
Acryloyl fluoride	$\underline{CH_2{=}CH}C\underline{O}F$	180	*sym-cis*	*sym-trans*	*dd*
Acrylic acid	$\underline{CH_2{=}CH}C\underline{O}OH$	180	*cis*	*trans*	*ee*
2-Furfuraldehyde		180	*cis*	*trans*	*ff*
Miscellaneous					
Nitrous acid	$\underline{H}ON\underline{O}$	180	*cis*	*trans*	*gg*
Methyl nitrite	$\underline{CH_3}ON\underline{O}$		*cis*	*trans*	*hh*
Methylhydrazine	$\underline{CH_3}N\underline{H}N\underline{H}_2$		inner	outer	*ii*
Acetaldoxime	$\underline{CH_3}CH{=}N\underline{O}H$	180	*cis*	*trans*	*jj*

(ii) *Molecules with one rotameric form identified*

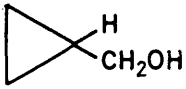
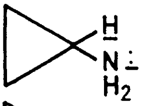
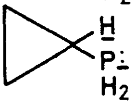
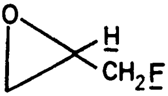
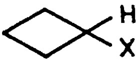
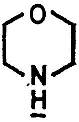
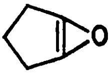
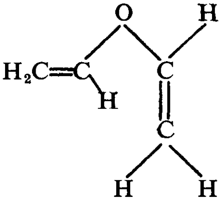
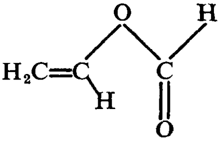
Molecule		*Form found*	*Ref.*
1-Chloro-2-fluoroethane	$\underline{F}CH_2CH_2\underline{Cl}$	*gauche*	*kk*
1,2-Difluoroethane	$\underline{F}CH_2CH_2\underline{F}$	*gauche*	*ll*
1,1,2-Trifluoroethane	$\underline{H}F_2CCH_2\underline{F}$	*gauche*	*mm*
2-Halogenoethanols (X = F, Cl, or Br)	$\underline{X}CH_2CH_2\underline{O}H$	*gauche*	*nn*
Ethylene glycol	$H\underline{O}CH_2CH_2\underline{O}H$	*gauche*	*oo*
Cyclopropylmethanol		—	*pp*
Cyclopropylamine		*trans*	*qq*
Cyclopropylphosphine		*trans*	*rr*
1-Fluoro-2,3-epoxypropane		*gauche*	*ss*
Halogenocyclobutanes (X = F or Cl)		equatorial	*tt*
Morpholine		equatorial	*uu*

Table 1 (*cont.*)

Molecule		*Form found*	*Ref.*
1,2-Epoxycyclopentene		boat	*vv*
Prop-2-yn-1-ol	$\underline{\mathrm{HC{\equiv}C}}\mathrm{CH_2O}\underline{\mathrm{H}}$	*gauche*	*ww*
Prop-2-yne-1-thiol	$\underline{\mathrm{HC{\equiv}C}}\mathrm{CH_2S}\underline{\mathrm{H}}$	*gauche*	*xx*
Allyl alcohol	$\underline{\mathrm{CH_2{=}CH}}\mathrm{CH_2}\underline{\mathrm{O}}\mathrm{H}$	*gauche*	*yy*
Prop-2-ene-1-thiol	$\underline{\mathrm{CH_2{=}CH}}\mathrm{CH_2}\underline{\mathrm{S}}\mathrm{H}$	*gauche*	*zz*
Allylamine	$\underline{\mathrm{CH_2{=}CH}}\mathrm{CH_2}\underline{\mathrm{N}}\mathrm{H_2}$	N *cis*, lone pair *trans*	*aaa*
Methyl ethyl ketone	$\underline{\mathrm{CH}}_3\mathrm{COCH_2}\underline{\mathrm{CH}}_3$	*trans*	*bbb*
Fluoroacetone	$\mathrm{CH_3C}\underline{\mathrm{O}}\mathrm{CH_2}\underline{\mathrm{F}}$	*trans*	*ccc*
Glycolaldehyde	$\mathrm{H}\underline{\mathrm{O}}\mathrm{CH_2CH}\underline{\mathrm{O}}$	planar *cis*	*ddd*
Acraldehyde	$\underline{\mathrm{H_2C{=}C}}\mathrm{HCH}\underline{\mathrm{O}}$	*sym-trans*	*eee*
1-Methylacraldehyde	$\mathrm{CH_2{=}C(CH_3)CHO}$	*sym-trans*	*fff*
Methyl vinyl ketone	$\mathrm{CH_3C}\underline{\mathrm{O}}\mathrm{C}\underline{\mathrm{H{=}CH_2}}$	*sym-trans*	*ggg*
Formic acid	$\underline{\mathrm{H}}\mathrm{COO}\underline{\mathrm{H}}$	*trans*	*hhh*
trans-Crotonaldehyde	$\mathrm{CH_3}\underline{\mathrm{C}}\mathrm{H{=}CHCH}\underline{\mathrm{O}}$	*sym-trans*	*iii*
Methyl formate	$\underline{\mathrm{CH}}_3\mathrm{OCH}\underline{\mathrm{O}}$	*cis*	*jjj*
Methyl vinyl ether	$\underline{\mathrm{CH}}_3\mathrm{O}\underline{\mathrm{CH{=}CH_2}}$	*cis*	*kkk*
Divinyl ether		non-planar, structure as shown	*lll*
Vinyl formate		as shown	*mmm*
Glyoxal	$\mathrm{HC}\underline{\mathrm{O}}\mathrm{CH}\underline{\mathrm{O}}$	*trans* (no spectrum)	
Biacetyl	$\mathrm{CH_3C}\underline{\mathrm{O}}\mathrm{C}\underline{\mathrm{O}}\mathrm{CH_3}$	*trans* (no spectrum)	*nnn*
Buta-1,3-diene	$\mathrm{H_2C{=}}\underline{\mathrm{C}}\mathrm{HCH{=}}\underline{\mathrm{C}}\mathrm{H_2}$	*trans* (no spectrum)	
Fluoroprene	$\mathrm{H_2}\underline{\mathrm{C}}\mathrm{{=}CHFC{=}}\underline{\mathrm{C}}\mathrm{H_2}$	*sym-trans*	*ooo*
Isoprene	$\mathrm{H_2}\underline{\mathrm{C}}\mathrm{{=}CH(CH_3)C{=}}\underline{\mathrm{C}}\mathrm{H_2}$	*sym-trans*	*ppp*
1,1-Difluorobutadiene	$\mathrm{F_2}\underline{\mathrm{C}}\mathrm{{=}CHCH{=}}\underline{\mathrm{C}}\mathrm{H_2}$	*sym-trans*	*qqq*

Molecule		*Form found*	*Ref.*
1,1-Difluoro-3-methylbutadiene	$F_2\underline{C}{=}CHC(CH_3){=}\underline{C}H_2$	*sym-trans*	*rrr*
cis-Penta-1,3-diene *trans*-Penta-1,3-diene	$H_2\underline{C}{=}CHCH{=}\underline{C}HCH_2$	*sym-trans*	*sss*
Propionic acid	$\underline{CH}_3CH_2C\underline{O}OH$	*cis*	*ttt*

[a] E. Hirota, *J. Chem. Phys.*, 1962, **37**, 283; [b] T. N. Sarachman, *J. Chem. Phys.*, 1963, **39**, 469; [c] T. N. Sarachman, 23rd Symposium on Molecular Structure and Spectroscopy, The Ohio State University, Columbus, Ohio, 1968, paper N7; S. Armstrong, *Appl. Spectroscopy*, 1969, **23**, 575; [d] T. N. Sarachman, 24th Symposium on Molecular Structure and Spectroscopy, The Ohio State University, Columbus, Ohio, 1969, paper U9; [e] L. M. Imanov, A. A. Abdurakhmanov, and R. A. Ragimova, *Optics and Spectroscopy*, 1967, **22**, 456; *ibid.*, 1969, **26**, 75; *Phys. Letters* (*A*), 1970, **32**, 123; [f] E. Hirota, *J. Chem. Phys.*, 1962, **37**, 2918; [g] F. Wodarczyk and E. B. Wilson, *J. Chem. Phys.*, 1972, **56**, 166; D. Damiani and A. M. Mirri, *Chem. Phys. Letters*, 1971, **10**, 351; [h] M. J. Fuller, personal communication; [i] P. L. Lee and R. H. Schwendeman, 25th Symposium on Molecular Structure and Spectroscopy, The Ohio State University, Columbus, Ohio, 1970, paper C10; [j] L. Pierce and R. Nelson, *J. Amer. Chem. Soc.*, 1966, **88**, 216; L. Pierce and J. F. Beecher, *J. Amer. Chem. Soc.*, 1966, **88**, 5406; [k] C. C. Costain, P. J. Buckley, and J. E. Parkin, *Chem. Comm.*, 1968, 668; [l] Y. S. Li, 24th Symposium on Molecular Structure and Spectroscopy, The Ohio State University, Columbus, Ohio, 1969, paper 01; [m] L. M. Imanov and Ch. O. Kadzhar, *Optics and Spectroscopy*, 1963, **14**, 157; J. Michielsen-Effinger, *Ann. Soc. sci. Bruxelles, Ser. III*, 1964, **78**, 223; *J. Phys.* (*Paris*), 1969, **30**, 336; M. Takano, Y. Sasada, and T. Satoh, *J. Mol. Spectroscopy*, 1968, **26**, 157; Y. Sasada, M. Takano, and T. Satoh, *J. Mol. Spectroscopy*, 1971, **38**, 33; [n] S. Kondo and E. Hirota, *J. Mol. Spectroscopy*, 1970, **34**, 97; A. A. Abdurakhmanov, M. N. Elchiev, and L. L. Imanov, *Izvest. Akad. Nauk Azerb. S.S.R.*, *Ser. fiz.-mat. i tekh. Nauk*, 1970, 58; [o] J. M. Riveros and E. B. Wilson, *J. Chem. Phys.*, 1967, **46**, 4605; [p] D. G. Scroggin and J. M. Riveros, personal communication; [q] Ch. O. Kadzhar, A. A. Abbasov, and L. M. Imanov, *Optics and Spectroscopy*, 1968, **24**, 334; *Izvest. Akad. Nauk Azerb. S.S.R.*, *Ser. fiz.-mat. i tekh. Nauk*, 1968, 71; M. Hayashi, W. Ohno, and H. Murata, Symposium on Molecular Structure, *Chem. Soc. Japan*, 1968, Tokyo, paper 1A8; [r] S. Yamada, M. Hayashi, and H. Murata, Symposium on Molecular Structure, *Chem. Soc. Japan*, Tokyo, 1968, paper 1A7; [s] J. H. Griffiths, Symposium on Molecular Structure and Spectroscopy, The Ohio State University, Columbus, Ohio, 1970, paper C3; [t] E. Hirota, *J. Chem. Phys.*, 1965, **42**, 2071; P. Meakin, D. O. Harris, and E. Hirota, *J. Chem. Phys.*, 1969, **51**, 3775; [u] E. Hirota, *J. Mol. Spectroscopy*, 1970, **35**, 9; [v] K. V. L. N. Sastry, V. M. Rao, and S. C. Dass, *Canad. J. Phys.*, 1968, **46**, 959; [w] S. Kondo, E. Hirota, and Y. Morino, *J. Mol. Spectroscopy*, 1968, **28**, 471; [x] S. S. Butcher and E. B. Wilson, *J. Chem. Phys.*, 1964, **40**, 1671; [y] O. L. Stiefvater and E. B. Wilson, *J. Chem. Phys.*, 1969, **50**, 5385; [z] E. Saegebarth and E. B. Wilson, *J. Chem. Phys.*, 1967, **46**, 3088; [aa] R. G. Ford, personal communication; [bb] H. N. Volltrauer and R. H. Schwendeman, *J. Chem. Phys.*, 1971, **54**, 260; [cc] H. N. Volltrauer and R. H. Schwendeman, *J. Chem. Phys.*, 1971, **54**, 268; [dd] J. J. Keirns and R. F. Curl, jun., *J. Chem. Phys.*, 1968, **48**, 3773; [ee] K. Bolton, N. L. Owen, and J. Sheridan, *Nature*, 1968, **218**, 266; [ff] F. Moennig, H. Dreizler, and H. D. Rudolph, *Z. Naturforsch.*, 1965, **20**, 1323; [gg] A. P. Cox and R. L. Kuczowski, *J. Amer. Chem. Soc.*, 1966, **88**, 5071; A. P. Cox, A. H. Brittain, and D. J. Finnigan, *Trans. Faraday Soc.*, 1971, **67**, 2179; [hh] W. D. Gwinn, R. J. Anderson, and D. Stelman, Symposium on Gas Phase Molecular Structure, Austin, Texas, 1968, paper M2; D. Stelman, *Diss. Abs.*, 1965, **25**, No. 64-9094; [ii] R. P. Lattimer and M. D. Harmony, *J. Chem. Phys.*, 1970, **53**, 4575; [jj] R. S. Rogowski and R. H. Schwendeman, *J. Chem. Phys.*, 1969, **50**, 397; [kk] I. A. Mukhtarov, *Doklady Akad. Nauk S.S.S.R.*, 1957, **115**, 486; *Izvest. Akad. Nauk S.S.S.R. Ser. fiz.*, 1958, **22**, 1154; *Optika i Spektroskopiya*, 1959, **6**, 260; *Izvest. Akad. Nauk Azerb. S.S.R.*, *Ser. fiz.-mat. i tekh. Nauk*, 1964, **6**, 37; [ll] S. S. Butcher, R. A. Cohen, and T. C. Rounds, *J. Chem. Phys.*, 1971, **54**, 4123; [mm] I. A. Mukhtarov, *Doklady Akad. Nauk S.S.S.R.*, 1963, **148**, 566; *ibid.*, 1963, **151**, 1076; *Optika i Spektroskopiya*, 1963, **14**, 728; *ibid.*, 1964, **16**, 360; *ibid.*, 1964, **16**, 910; [nn] R. G. Azrak and E. B. Wilson, *J. Chem. Phys.*, 1970, **52**, 5299; K. S. Buckton and R. G. Azrak, *J. Chem. Phys.*, 1970, **52**, 5652; [oo] H. Mollendal, personal communication; [pp] W. V. F. Brooks, K. V. L. N. Sastry, Symposium on Molecular Structure and Spectroscopy, The

Table 1 (*cont.*)

Ohio State University, Columbus, Ohio, 1968, paper E5; [qq] D. K. Hendricksen and M. D. Harmony, *J. Chem. Phys.*, 1969, **51**, 700; [rr] L. A. Dinsmore, C. O. Britt, and J. E. Boggs, *J. Chem. Phys.*, 1971, **54**, 915; [ss] S. C. Dass, A. Bhannik, W. V. F. Brooks, and R. M. Lees, *J. Mol. Spectroscopy*, 1971, **38**, 281; [tt] H. Kim and W. D. Gwinn, *J. Chem. Phys.*, 1966, **44**, 865; [uu] J. J. Sloan and R. Kewley, *Canad. J. Chem.*, 1969, **47**, 3453; [vv] W. J. Lafferty, *J. Mol. Spectroscopy*, 1970, **36**, 84; [ww] E. Hirota, *J. Mol. Spectroscopy*, 1968, **26**, 335; C. O. Kadzhar, G. A. Abdullaev, and L. M. Imanov, *Izvest. Akad. Nauk Azerb. S.S.R., Ser. fiz.-mat. i tekh. Nauk*, 1969, **3**, 26; K. Bolton, N. L. Owen, and J. Sheridan, *Nature*, 1968, **217**, 164; [xx] K. Bolton and J. Sheridan, *Spectrochim. Acta*, 1970, **A26**, 1001; [yy] A. N. Murty and R. F. Curl, jun., *J. Chem. Phys.*, 1967, **46**, 4167; [zz] K. V. L. N. Sastry, S. C. Dass, W. V. F. Brooks, and A. Bhaumik, *J. Mol. Spectroscopy*, 1969, **31**, 54; [aaa] G. Roussy, J. Demaison, I. Botskor, and H. D. Rudolf, *J. Mol. Spectroscopy*, 1971, **38**, 535; [bbb] L. Pierce, C. K. Chang, M. Hayashi, and R. Nelson, *J. Mol. Spectroscopy*, 1969, **32**, 449; [ccc] E. Saegebarth and L. C. Krisher, *J. Chem. Phys.*, 1970, **52**, 3555; [ddd] K. M. Marstokk and M. Mollendal, *J. Mol. Structure*, 1970, **5**, 205; [eee] E. A. Cherniak and C. C. Costain, *J. Chem. Phys.*, 1966, **45**, 104; P. Wagner, J. Fine, J. W. Simmons, and J. H. Goldstein, *J. Chem. Phys.*, 1957, **26**, 634; K. Kuchitsu, T. Fukuyama, and Y. Morino, *J. Mol. Structure*, 1969, **4**, 41; [fff] M. Suzuki and K. Kozima, *J. Mol. Spectroscopy*, 1971, **38**, 314; [ggg] P. D. Foster, V. M. Rao, and R. F. Curl, jun., *J. Chem. Phys.*, 1965, **43**, 1064; [hhh] M. Suzuki and K. Kozima, *Bull. Chem. Soc. Japan*, 1969, **42**, 2183; [iii] D. R. Lide, jun., *Trans. Amer. Cryst. Assoc.*, 1966, **2**, 106; M. Suzuki and K. Kozima, *Bull. Chem. Soc. Japan*, 1969, **42**, 2183; S. L. Hsu and W. H. Flygare, *Chem. Phys. Letters*, 1969, **4**, 317; [jjj] R. F. Curl, jun., *J. Chem. Phys.*, 1959, **30**, 1529; [kkk] P. Cahill, L. P. Gold, and N. L. Owen, *J. Chem. Phys.*, 1968, **48**, 1620; [lll] C. Hirose and R. F. Curl, jun., *J. Mol. Spectroscopy*, 1971, **38**, 358; [mmm] V. M. Rao and R. F. Curl, jun., *J. Chem. Phys.*, 1964, **40**, 3688; [nnn] D. R. Lide, jun., *Trans. Amer. Cryst. Assoc.*, 1966, **2**, 106; [ooo] D. R. Lide, jun., *J. Chem. Phys.*, 1962, **37**, 2074; [ppp] D. R. Lide, jun. and M. Jen, *J. Chem. Phys.*, 1964, **40**, 252; S. L. Hsu, M. Kemp, J. Pochan, R. Benson, and W. H. Flygare, *J. Chem. Phys.*, 1969, **50**, 1482; [qqq] R. A. Beaudet, *J. Chem. Phys.*, 1965, **42**, 3758; [rrr] Y. S. Huange and R. A. Beaudet, *J. Mol. Spectroscopy*, 1970, **34**, 1; [sss] S. L. Hsu and W. H. Flygare, *J. Chem. Phys.*, 1970, **52**, 1053; [ttt] O. L. Stiefvater, 21st Symposium on Molecular Structure and Spectroscopy, The Ohio State University, Columbus, Ohio, 1966.

4 The Molecular Model

The observed spectra can often, but not always, be interpreted as two (or sometimes three) different rigid rotor spectra, each with its own set of moments of inertia and each with its own satellite lines arising from low-lying vibrationally excited states. The two sets of ground-state moments of inertia may be related to one another by a simple rigid rotation of one part of the molecular model relative to the other part, about the single bond between them. More often some additional changes of structure, not usually very large, have to be introduced as well on going from one rotamer to the other. In other words, the rigid–rigid one-degree-of-freedom model is often not completely adequate, except as a first approximation.

To the extent that values for the bond distances and other angles can be assumed known, and that the rigid–rigid model is adequate, the values of the dihedral angle for the various rotamers can be calculated to fit the observed moments of inertia (Figure 2). When the rigid–rigid model is not quite adequate, distortions of other angles can be somewhat arbitrarily introduced and the dihedral angles still estimated to fit the six moments of inertia. Table 1 shows some diheral angles determined in this manner; (where one form is planar or has some special symmetry, this can sometimes be verified by independent arguments). If enough isotopic species were studied, the structures of the various

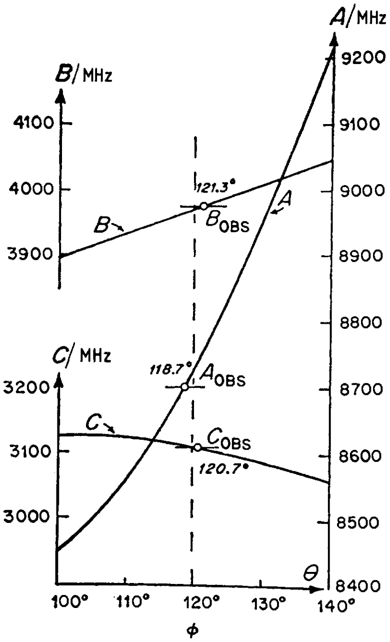


Figure 2 *Plot of predicted rotational constants* versus *dihedral angle (for propionyl fluoride), compared with experimental values*

rotamers could presumably be determined without any assumption concerning distances or angles, but little work of this degree of completeness has been attempted.[21]

Rough supporting information on the dihedral angles can be obtained from the dipole moment components along the three principal axes, obtainable from the microwave spectra *via* the Stark effect. Conventional bond moment values can be combined vectorially and plotted as a function of the dihedral angle. Comparison with the observed values then gives estimates for the dihedral angles.

Among the various vibrational satellites observed, usually one set (often the strongest set) can be assigned to molecules in the first excited state of torsional motion, and perhaps several other sets to the second, third, *etc.* excited levels of this same (approximate) normal co-ordinate (Figure 3). These are particularly interesting and useful. Intensity measurements on these, relative to the same rotational transition for molecules in their ground vibrational state, give the relative populations of the excited states, and hence, from the Boltzmann factor $e^{-\Delta E/RT}$, the energy of excitation ΔE (corrections having been made for any differences in statistical weight).

These same torsional energy values can sometimes be observed directly in the

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[21] But see E. Hirota, *J. Chem. Phys.*, 1965, **42**, 2071.

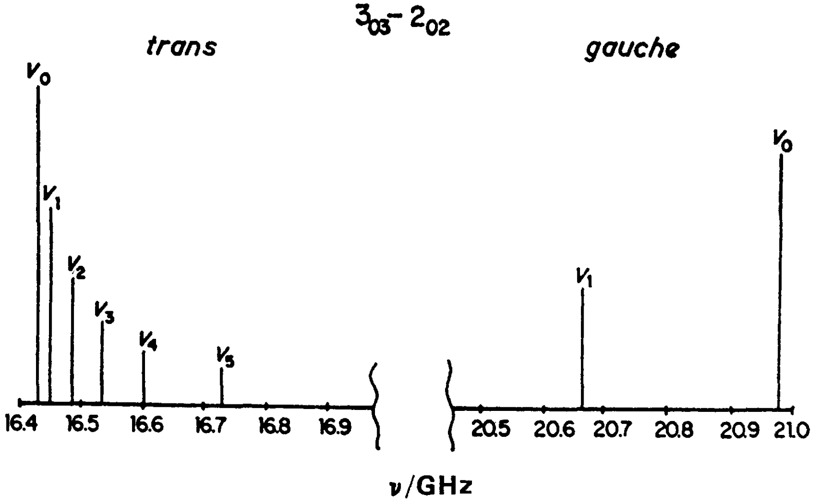

Figure 3 *Vibrational satellite transitions for torsional mode (for ethyl formate)*

far-i.r. spectrum and it is very desirable to have information from both techniques to avoid errors of interpretation in both types of spectra, errors which have occured in the past.

The torsional energies essentially yield the curvature of the torsional potential energy function at the minimum position corresponding to a particular rotamer. If sufficiently accurate information on the higher excited states can be obtained, anharmonicity can be estimated and the deviation of the lower part of the potential wells from parabolic shape approximated (usually only rather roughly).

The energy difference between different rotamers can be obtained in principle —and approximately in practice—by measuring the relative intensities of two rotational transitions, one from each rotamer, and taking into account the linewidths, linestrengths, and statistical weights of the two transitions, and the dipole moment components of the two rotamers. Neither the rotational or vibrational partition function is involved in this calculation since one is concerned here with the relative populations of two specific rotational levels.

5 Fitting the Potential Energy Function

In the one-vibration approximation, the potential energy is treated as a function of one variable. In the further approximation of two connected rigid parts, the one variable is taken to be the dihedral angle of internal rotation, ϕ. The potential energy $V(\phi)$ can then be expanded in a Fourier series

$$V(\phi) = \tfrac{1}{2}\Sigma V_n(1 - \cos n\phi) \qquad (1)$$

(for the common case where there is a plane of symmetry at $\phi = 0$). This series must be limited in practice to a small number of terms. This limitation amounts to a physical assumption concerning the nature of $V(\phi)$; namely, that the function is a relatively smooth and simple one, without sharply peaked barriers, for example. This assumption is important because most of the experimental information is drawn from molecules which are in rather low energy states, so that much accuracy cannot be expected for parts of the potential of much higher energy. Since steric repulsions are normally thought to change rapidly with distance, it might be imagined that very sharp peaks could occur as non-bonded atoms essentially came in 'contact'. However, the deformation of bond angles does not require much energy and will take place in such a manner as to reduce and often round off sharp peaks. Figure 4 shows the parts of the potential function on which one can most easily get information.† When quantum mechanical tunnelling is observable, additional restrictions on the relevant peak can be formulated.

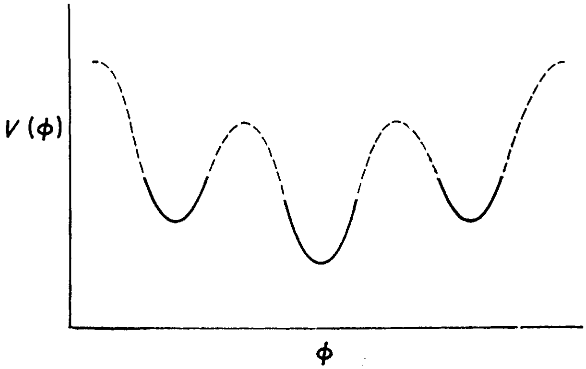

Figure 4 *Typical potential energy curve as function of dihedral angle; heavy portions are more reliably determined*

The dihedral angle, the torsional frequencies of the two rotamers (when there are just two non-equivalent forms), and the energy difference permit the fitting of four Fourier coefficients and it is still an open question as to how sufficient this is. In some cases the anharmonicity of one or two forms has also been estimated, permitting approximate values for five or six Fourier coefficients to be obtained. Figure 5 shows the $V(\phi)$ thereby calculated for propionyl fluoride.[22] The great problem is that of accuracy and a knowledge of accuracy.

In some cases a valuable additional piece of information is obtainable. When the potential function has two (or more) equivalent minima, as for example two symmetrically related *gauche* forms, quantum mechanical tunnelling may be noticeable. This will split the otherwise doubly (or triply) degenerate energy levels into two levels. With a suitable dipole moment, transitions from one to

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† Note added in proof: recent studies by I. Warren have shown that high-energy portions of the potential energy are indeed very poorly determined.

[22] O. L. Stiefvater and E. B. Wilson, *J. Chem. Phys.*, 1969, **50**, 5385.

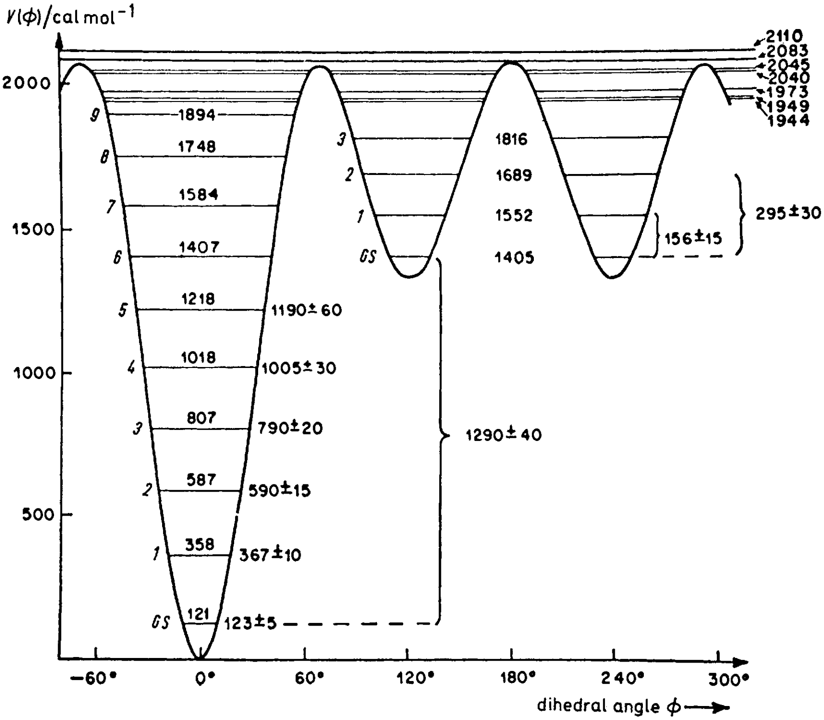

Figure 5 *Potential energy function fitted to propionyl fluoride data, showing observed and calculated torsional energy levels (observed values carry error estimates)*

the other of these components, combined with a change in rotational energy, may appear in the microwave region. The contribution of the tunnelling may range from negligible to very large. When it is small, the effect may show as a doubling of certain types of rotational lines. This was observed in the case of allyl fluoride,[23] and yields the extent of the tunnelling splitting.

The great value of this information is that it is substantially influenced by the barriers between the equivalent forms, even though the molecules being observed are in low-lying states. An approximate formula[24] for the tunnelling splitting Δ_n for the nth pair of split levels is

$$\Delta_n = h\nu/\pi \, A_n^2$$

$$A_n = \exp\,[(2\pi/h) \int_0^{x_1} [2m(V - E_n)]^{1/2}\,dx$$

where $h\nu$ is the difference $(E_{n+1} - E_n)$ (treated as approximately independent

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[23] P. Meakin, D. O. Harris, and E. Hirota, *J. Chem. Phys.*, 1969, **51**, 3775.

[24] D. M. Dennison and G. E. Uhlenbeck, *Phys. Rev.*, 1932, **41**, 313.

of n), E_n is the mean energy of the slightly split nth pair, V is the potential energy as function of co-ordinate x, m is the effective mass, and x_1 is the first point for $x > 0$ where $V = E_n$. This shows that the tunnelling is dependent upon the square root area in the non-classical region, *i.e.*

$$\int_0^{x_1} \sqrt{2m(V - E_n)}\,\mathrm{d}x$$

In other examples the transition from one tunnelling state to the other is not allowed, but the tunnelling nevertheless influences the spectrum because of a more complicated effect, the coriolis coupling of the internal motion and the overall rotation. This effect is influenced by the tunnelling and has been of great value for three-fold symmetric barriers, notably in the case of methyl group internal rotation. It can also, however, have an observable effect in the two-fold case,[17,18,25–28] from which the tunnelling splitting can be extracted and then used to obtain barrier information.

If the tunnelling splitting is small compared with the rotational transition frequencies, the rotational spectra, ignoring the splitting, may still approximate that of a rigid rotor. In other cases, the contribution of the tunnelling may dominate. These latter can be very difficult to analyse.

Most of the above considerations are still of value if the model is somewhat generalized so that ϕ is no longer simply the dihedral angle between two rigid parts, but is a more generalized co-ordinate which mixes in some deformations of the two halves as they rotate relative to one another. A beginning has been made towards a theoretical treatment of such a model, from which one might ultimately hope to extract information about the deformations which take place during the internal motion.[16] Conversely if theoretical predictions of these 'bending back' effects are available, their influence on the microwave spectrum can be predicted and then tested.

A. Contributions to the Potential Energy.—One of the ultimate objects of these studies is to acquire information about the forces which lead to the potential $V(\phi)$. It is presumably sufficient to start with the Born–Oppenheimer approximation for separating the electronic from the nuclear motion. The potential $V(\phi)$ then represents the electronic energy of the system with the nuclei fixed in a sequence of positions measured by the co-ordinate ϕ. This electronic energy includes all the coulombic attractions and repulsions of the electrons and nuclei and also the electronic kinetic energy, these being related by the virial theorem:[29]

$$2\langle T\rangle + \langle V_\mathrm{e}\rangle + \Sigma_i\, x_i \frac{\partial E_\mathrm{e}}{\partial x_i} = 0$$

[25] S. S. Butcher and C. C. Costain, *J. Mol. Spectroscopy*, 1965, **15**, 40.

[26] D. O. Harris, H. W. Harrington, A. C. Luntz, and W. D. Gwinn, *J. Chem. Phys.*, 1966, **44**, 3467.

[27] L. H. Sharpen and V. W. Laurie, *J. Chem. Phys.*, 1968, **49**, 3041.

[28] L. H. Sharpen, *J. Chem. Phys.*, 1968, **48**, 3552.

[29] J. C. Slater, *J. Chem. Phys.*, 1933, **1**, 687.

where $\langle T \rangle$ and $\langle V_e \rangle$ are expectation values of the kinetic and potential energies of the electrons (including internuclear repulsion), E_e is the Born–Oppenheimer electronic energy, and the x_i are the nuclear co-ordinates.

At this point it becomes of possible advantage to break down the forces on the nuclei into parts to be evaluated empirically, parts such as steric repulsion, dipole–dipole interaction, *etc.* This procedure has been widely used for decades,[30–32] but often with unnecessary apologies for using 'classical mechanics' instead of quantum mechanics.

In this review the following types of forces will be considered:

1 Double bond character due to resonance
2 Hydrogen bonding
3 'Barrier forces'
4 Steric repulsion
5 Electrostatic forces such as dipole–dipole
6 Valence bond stretching and bending forces
7 Inductive forces
8 Dispersion or van der Waals forces

It seems quite reasonable to seek parameterized forms for these forces with parameters adjusted to fit the experimental data. Such a project requires means to calculate structures, energies, *etc.*, from the postulated force laws and trial parameters, so that they may be compared with experiment. There is no difficulty in principle in doing this, but in practice rather large and elaborate computer programs are required. These seek, for example, for configurations of minimum energy—the equilibrium configurations—by various minimization schemes.

Since this area has recently been well reviewed,[8] no detailed analysis of these schemes will be given here. Instead, a discussion of some of their basic assumptions and ways of validating them will be offered.

The forces listed earlier all have physical reality (although perhaps some areas of indefinite overlap). Thus, when two atoms are forced too close together, there is no doubt that they will repel each other. Qualitatively, therefore, all of the current attempts at calculating structures, conformations, isomerization energies, *etc.* by compounding empirical force laws must have some measure of validity, especially in extreme cases. The difficulty comes when there is a close balance of forces so that the correctness of the overall calculation depends critically on the quantitative accuracy of the force laws.

At the quantitative level, a basic and often unstated assumption is involved: that the force laws and parameters used are truly transferable from one molecule to another. This is a reasonable assumption to try, but it has not yet been directly verified. A second and obvious assumption is that the various force laws used are sufficiently correct in form.

At this point it is well to agree on the criteria by which one should judge the

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[30] T. L. Hill, *J. Chem. Phys.*, 1946, **14**, 465.
[31] F. H. Westheimer and J. E. Mayer, *J. Chem. Phys.*, 1946, **14**, 733.
[32] F. H. Westheimer, in 'Steric Effects in Organic Chemistry', ed. M. S. Newman, J. Wiley and Sons, New York, 1956, ch. 12.

success of a computational procedure such as those under discussion. They all involve, either very directly or in a hidden way, a very large number of adjustable parameters. Therefore, it is perhaps not too surprising if a fairly large number of known experimental values can be reasonably well fitted with a suitable choice of values for the parameters. It is not easy to see how the number of parameters can be much reduced; there remains the possibility of increasing the amount of experimental data to be fitted and this is exactly one reason for more microwave studies of rotameters.

It may be worthwhile to look at some of the experimental information to see if it is susceptible to any qualitative interpretations. Without a large mass of data, any attempt at rationalization, whether qualitative or quantitative, is hazardous because we are very sure that many different types of forces can be important, and this makes it too easy to invent *ad hoc* explanations for each molecular example. Nevertheless, one might hope to select examples in which it is reasonable to expect that most of the forces in our list are small, thus permitting an interpretation in terms of a few major contributors.

(i) *Barrier forces*. In the absence of double-bond character, hydrogen bonding, large electrostatic effects, and strong steric repulsions due to a close approach, the three-fold term

$$\tfrac{1}{2}V_3(1 - \cos 3\phi)$$

is often the largest. Further, there is a slight suggestion in the available data that this term depends mainly on the nature of the axial bond.[33] In many of the computer systems, there is included a fixed three-fold *barrier potential* depending upon the nature of the axial bond only. Naturally, it should be possible to analyse these barrier potentials into more basic components and many efforts have been made to do so. For the simplest case, that of ethane, a considerable variety of approximate SCF–MO treatments have given numerical results reasonably close to the experimental barrier, despite the fact that the barrier is the difference between two energies, each vastly larger than the difference.[34–37] Furthermore, the breakdown into components such as electron–nuclear repulsion, electron–electron repulsion, *etc.* seems to differ considerably from one approximation to another despite the fact that their resultant, the total barrier, does not.[38] This makes it difficult at the present to discuss the origins of barriers in physical terms. Therefore, we shall assume that barriers exist and hope that they do constitute a transferable portion of the potential, until the further accumulation of data shows this to be untenable.

The barrier force alone, viewed in this simplified way, would lead to 120° angles between the rotamers and little energy difference. We shall provisionally assume that deviations from this condition indicates the presence of other

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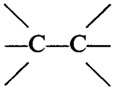
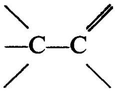
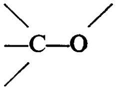
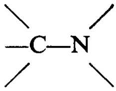
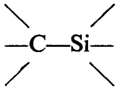
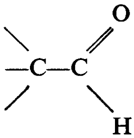
[33] E. Saegebarth and E. B. Wilson, *J. Chem. Phys.*, 1967, **46**, 3088.
[34] R. M. Pitzer and W. N. Lipscomb, *J. Chem. Phys.*, 1963, **39**, 1995.
[35] R. M. Pitzer, *J. Chem. Phys.*, 1964, **41**, 2216.
[36] W. H. Fink and L. C. Allen, *J. Chem. Phys.*, 1967, **46**, 2261.
[37] L. Pedersen and K. Morokuma, *J. Chem. Phys.*, 1967, **46**, 3941.
[38] I. R. Epstein and W. N. Lipscomb, *J. Amer. Chem. Soc.*, 1970, **92**, 6094.

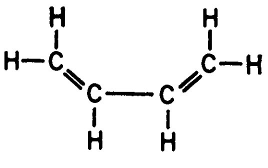
forces, *e.g.* steric or electrostatic. Table 2 gives some barrier values which very tentatively might be transferred to more complicated molecules.

Table 2 *Some prototype three-fold barriers* /cal mol^{-1} [a]

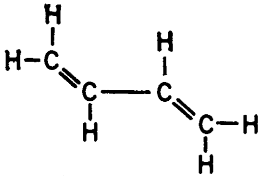
	C_2H_6	2928[b]
	$CH_3CH{=}CH_2$	1978
	CH_3OH	1070
	CH_3NH_2	1980
	CH_3SiH_3	1670
	CH_3CHO	1167

[a] From J. E. Wollrab, 'Rotational Spectra and Molecular Structure', Academic Press, New York, 1967, appendix 9; [b] S. Weiss and G. E. Leroi, *J. Chem. Phys.*, 1968, **48**, 862.

(ii) *Double bond character*. The energy barrier between *cis*- and *trans*-isomers for typical ethylenic compounds is much higher than the barriers between normal rotational isomers. There are many species in which the bond about which the rotation can occur is not a pure single bond but has some double bond character, because of conjugation or resonance. An example where this effect would be expected is butadiene, in which the central bond is shorter than a normal single

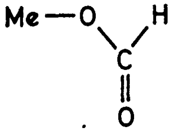


cis



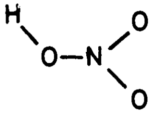
trans

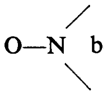
bond and two forms, differing by 180° rotation, would be expected. Some substituted butadienes have been studied by microwave spectroscopy and only the *trans*-forms found.[39] Likewise in methyl formate[40] the central O—C bond



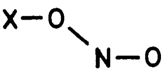
would be expected to acquire some double bond character. Again, despite several searches, no microwave evidence for a second form has been reported. It is interesting to note that Pauling's qualitative picture, which uses 'banana bonds' to represent a double bond, predicts the preference for *sym-trans* over *sym-cis*.[41,42]

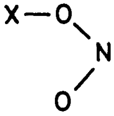
In nitric acid[43]



the planar form is found, as expected for an  $O{-}N$ bond with some double bond character, and two forms differing by 180° presumably occur but are equivalent.

In CH_3ONO and HONO two forms are found[44,45]





differing by a 180° rotation around the central O—N bond.

Many other examples of this effect have been studied, by other techniques such

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[39] S. L. Hsu, M. K. Kemp, J. M. Pochan, R. C. Benson, and W. H. Flygare, *J. Chem. Phys.*, 1969, **50**, 1482.

[40] R. F. Curl, jun., *J. Chem. Phys.*, 1959, **30**, 1529.

[41] L. Pauling, *Proc. Nat. Acad. Sci. U.S.A.*, 1958, **44**, 211.

[42] J. D. Dunitz and P. Strickler, ref. 7, p. 595.

[43] A. P. Cox and J. M. Riveros, *J. Chem. Phys.*, 1965, **42**, 3106; D. J. Millen and J. R. Morton, *J. Chem. Soc.*, 1960, 1523.

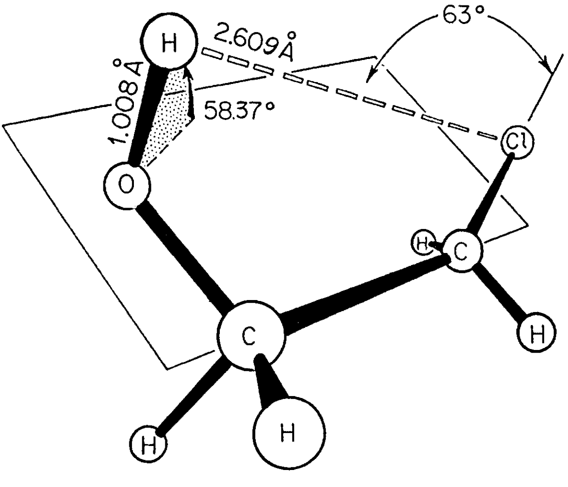
[44] D. Stelman, *Diss. Abs.*, 1965, **25**, No. 64-9094.

[45] A. P. Cox, A. H. Brittain, and D. J. Finnigan, *Trans. Faraday Soc.*, 1971, **67**, 2179.

as n.m.r., as well.[46] It is important to note that the two-fold contribution to the barrier can be dominant even when there is only a small amount of double bond character.

(iii) *Hydrogen bonding*. Internal hydrogen bonding is another force which has been postulated to be important in determining the conformations of appropriate molecules. It is generally considered that hydrogen bonding can play a role when the hydrogen is bonded to oxygen or nitrogen and when the geometry is such that it can approach at the proper distance to another oxygen, nitrogen, a halogen, or perhaps to electrons from a double bond or a conjugated ring. Many studies have been made of such systems using the i.r. (especially the shift of the OH stretching frequency) and n.m.r. spectra as criteria.[47] These can give a semi-quantitative ordering of the strength of the hydrogen bond.

Microwave spectroscopy has begun to be applied to some of these molecules. Thus Murty and Curl[48] studied allyl alcohol and found that the conformation they could identify (presumably therefore the dominant one) was the one which brought the O—H hydrogen close to the C=C double bond. Similarly, a rather detailed study of 2-chloroethanol[49] ($ClCH_2CH_2OH$) shows that, of the nine conformations which might be expected in terms of the normal C—C and C—O three-fold barrier potentials, one equivalent pair in which the hydrogen is close



gauche - $ClCH_2CH_2OH$

Figure 6 *Structure found for main species of chloroethano*

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[46] T. H. Siddall and W. E. Stewart, *Progr. N.M.R. Spectroscopy*, 1969, **5**, 33.

[47] G. C. Pimentel and A. L. McClellan, 'The Hydrogen Bond', W. H. Freeman and Co., San Francisco, 1960.

[48] A. N. Murty and R. Curl, *J. Chem. Phys.*, 1967, **46**, 4176.

[49] R. G. Azrak and E. B. Wilson, *J. Chem. Phys.*, 1970, **52**, 5299.

to the chlorine is definitely observed. No lines were assigned to any other conformations, which may, however, be present in small amounts, as indicated by i.r. studies.[50-52] The geometry is not favourable for a very strong hydrogen bond, because the Cl—H—O group is very non-linear (Figure 6) and in fact the OH shift in the i.r. is quite small. It may not be surprising, therefore, that the chlorine quadrupole hyperfine structure leads to a practically cylindrically symmetric field gradient tensor, oriented along the C—Cl bond, just as if the 'H-bonding' had no influence on the electron cloud around the chlorine. If there were much covalent character to Cl · · · H or much charge transfer, one would expect these to influence the field gradient. Moreover, the C—Cl and O—H bonds are very nearly parallel, just the orientation one would expect from the electrostatic interaction of the normal C—Cl and O—H dipoles.

This result naturally cannot be generalized to all internal hydrogen bonds. For example, a different situation seems to hold for 2-formyl 6-hydroxyfulvene, now under investigation by Pickett.[53] The observation of alternating intensities suggested an effectively symmetric O · · · H · · · O bond which would then permit the molecule to have two equivalent resonating structures as shown in Figure 7, an arrangement which should be considerably favoured by the resonance energy. However, a small barrier could still exist at the central hydrogen position, through which the hydrogen could rapidly tunnel. The preliminary results with the deuteriated species suggest the latter situation.

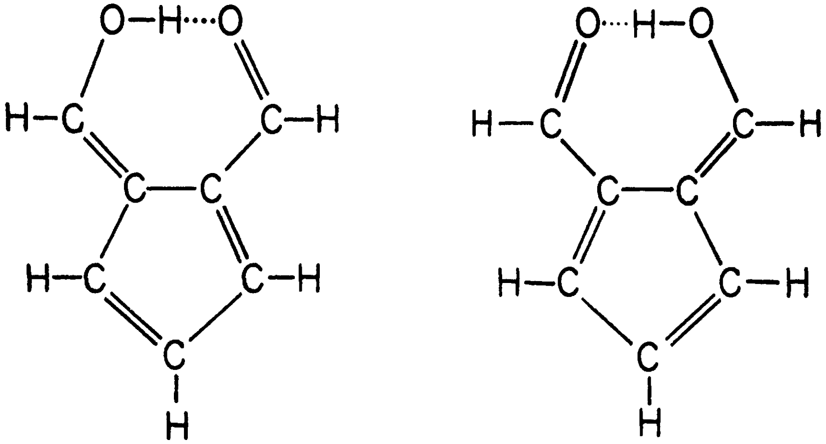

Figure 7 *Two resonant forms for hydrogen bonded 2-formyl-6-hydroxyfulvene*

Other molecules showing conformations compatible with weak internal

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[50] M. Kuhn, W. Luettke, and R. Mecke, *Z. analyt. Chem.*, 1959, **170**, 106.
[51] P. J. Krueger and H. D. Mettee, *Canad. J. Chem.*, 1964, **42**, 326.
[52] P. Buckley, P. Giguere, and M. Schneider, *Canad. J. Chem.*, 1969, **47**, 901.
[53] H. M. Pickett, personal communication.

hydrogen bonding include, CH_2FCH_2OH,[54] CH_2BrCH_2OH,[49] $CF_3CH_2NH_2$,[55] $NH_2CH_2CH_2OH$,[56] and $CH{\equiv}CCH_2OH$.[57]

(iv) *Steric repulsion.* It is of course obvious that steric repulsion must exist but it is more difficult to agree on its quantitative laws. Qualitatively, and to some extent quantitatively, steric repulsion should produce several effects in the microwave spectra of rotamers. The potential energy as a function of internal rotation should be influenced, especially where two atoms approach each other within the sum of their van der Waals radii. This effect appears quite definite in the case of ethyl formate[58] (Figure 8) and also ethyl nitrate,[59] for example, for which the dihedral angle for the *gauche* form was found at 95° instead of 120° and the derived potential energy curve goes to high but not well defined values in the *cis* (180°) configuration.

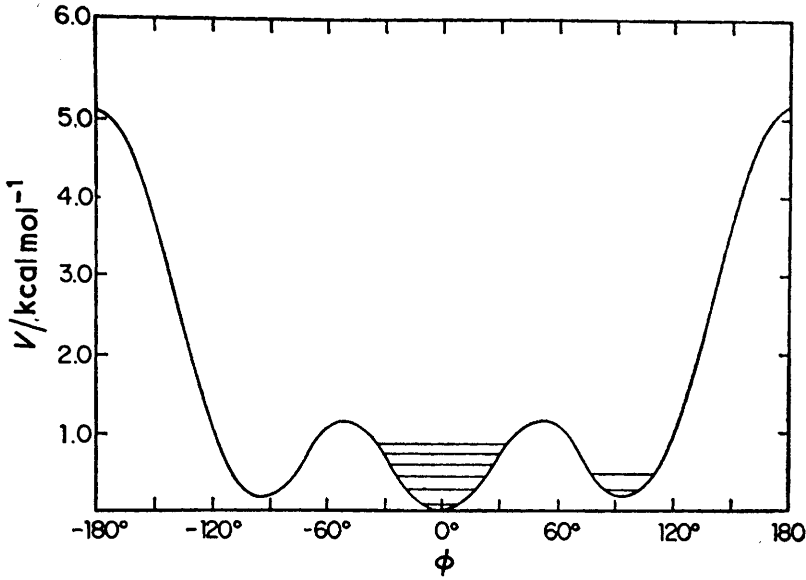

Figure 8 *Approximate potential function for ethyl formate showing small dihedral angle and high* cis *energy, presumably due to steric repulsion*

Another effect expected is an opening up of certain bond angles in the rotamer with the stronger steric repulsions. Not many really complete structural studies have been made, but the moment of inertia data for ethyl formate,[58] fluoro-

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[54] K. S. Buckton and R. G. Azrak, *J. Chem. Phys.*, 1970, **52**, 5652.

[55] I. Warren and E. B. Wilson, *J. Chem. Phys.*, 1972, **56**, 2137.

[56] R. E. Penn, presented at the Symposium on Molecular Structure and Spectroscopy, Ohio State University, Columbus, Ohio, 1968, paper N11.

[57] E. Hirota, *J. Mol. Spectroscopy*, 1968, **26**, 335.

[58] J. M. Riveros and E. B. Wilson, *J. Chem. Phys.*, 1967, **46**, 4605.

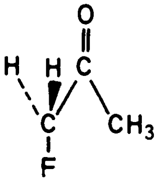
[59] D. Scroggin, Ph.D. Thesis, Harvard University, 1971.

acetyl fluoride,[33] and ethyl nitrate,[59] require some distortion from the rigid–rigid model in the direction qualitatively called for by steric forces. Thus the $\widehat{CCO}$ angle in fluoroacetyl fluoride appears to be about 6° larger in the form with F eclipsing O than in the other form, presumably because of F · · · O repulsion.

Quantitatively the situation is unsatisfactory, because of the number of different atom pairs which occur, each requiring two or more parameters. It is difficult to make meaningful comparisons between the many different non-bonded force laws currently being used in empirical calculations; they cannot properly be isolated from the other terms in the total potential energy expression. Thus some authors do and some do not employ valence-type interaction force terms, some use coulombic interactions between charges centred on atoms (even for hydrocarbons), one author measures the non-bonded interaction from an origin displaced along the bond from the hydrogen nucleus, *etc.* All of these alternatives will have an effect on the non-bonded repulsion terms. It is, therefore, necessary to base a judgment on the overall success of the various total treatments.

(v) *Electrostatic forces.* Another force which is surely important is that due to charges transferred from one part of the molecule to another. Dipole moments are reasonably well accounted for in terms of transferable bond dipole moments so it has long been supposed that dipole–dipole interactions can be important. Again there is qualitative information which can be comfortably explained in these terms.

For fluoroacetone,[60] only a form with F *trans* to O has been found, despite the



fact that a methyl group (and some examples of substituted methyls) attached to a doubly bonded carbon usually prefers to have an H (or X) atom eclipsing the O or C at the other end of the double bond (see allyl fluoride,[21] allyl chloride,[61] propionaldehyde,[62] propylene,[63] acetaldehyde,[64] and the more stable form of fluoroacetyl fluoride[33]). In none of these examples, however, is there such an obvious dipole–dipole repulsion favouring the *trans* conformation as one would expect between the C=O and C—F dipoles in fluoroacetone.

A series in which it is tempting to invoke dipole–dipole interaction,[65] even

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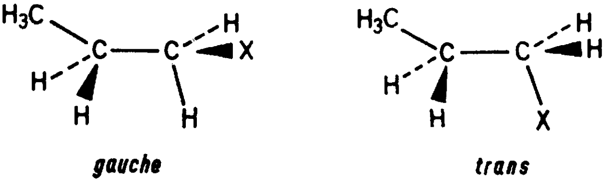
[60] E. Saegebarth and L. C. Krisher, *J. Chem. Phys.*, 1970, **52**, 3555.
[61] E. Hirota, *J. Mol. Spectroscopy*, 1970, **35**, 9.
[62] S. S. Butcher and E. B. Wilson, *J. Chem. Phys.*, 1964, **40**, 1671.
[63] D. R. Herschbach and L. C. Krisher, *J. Chem. Phys.*, 1958, **28**, 728.
[64] R. W. Kilb, C. C. Lin, and E. B. Wilson, *J. Chem. Phys.*, 1957, **26**, 1695.
[65] G. J. Szasz, *J. Chem. Phys.*, 1955, **23**, 2449.

though it is perhaps less certain, consists of the simpler n-propyl derivatives. It was pointed out some time ago,[66] from i.r. evidence, that some of these slightly prefer the *gauche* rather than the *trans* form, *i.e.*



Microwave studies have been made with X = F,[67] Cl,[68] Br,[69,70] CN,[71] C≡H,[72] OH,[73] and NC,[74] and all appear to favour *gauche* or to be nearly neutral (X = CH_3 is supposed to favour *trans*, from other evidence[75,76]). The dipole moments, especially the change from one form to the other in n-propylacetylene, suggest that CH_3—C has a small group moment with the CH_3 end positive.[72] The interaction of this with the negative dipole of the C—X group could be the force[65] counterbalancing the expected steric repulsion (for which there is some evidence from the dihedral and other angles). The dipole–dipole would be a longer-range force than the steric repulsion, so that it is possible to think of distinguishing their effects.

For point dipoles in a vacuum, the interaction potential is well known and many quantitative calculations were made in the past with this basis. Unfortunately there are three difficulties which cast considerable doubt on the reliability of such numerical results. First, it is not clear where the point dipoles should be located. Second, it is very dubious to assume that quadrupole and higher terms can be neglected (if indeed the multipole expansion converges, even in a practical sense). Finally, some workers assign a dielectric constant, somewhat arbitrarily chosen, to account for the effect of the intervening electron distribution. These difficulties suggest caution and reliance on empiricism; nevertheless, electrostatic forces are surely important.

(vi) *Other forces*. One expects dipole–induced-dipole forces, also van der Waals or dispersion attraction. In large molecules with flat ring substituents, such as

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[66] N. Sheppard, *Adv. Spectroscopy*, 1959, **1**, 228.
[67] E. Hirota, *J. Chem. Phys.*, 1962, **37**, 283.
[68] T. N. Sarachman, *J. Chem. Phys.*, 1963, **39**, 469.
[69] T. N. Sarachman, presented at the Symposium on Molecular Structure and Spectroscopy, Columbus, Ohio, 1968, paper N7.
[70] S. Armstrong, *Appl. Spectroscopy*, 1969, **23**, 575.
[71] E. Hirota, *J. Chem. Phys.*, 1962, **37**, 2918.
[72] F. Wodarczyk and E. B. Wilson, *J. Chem. Phys.*, 1972, **56**, 166.
[73] A. A. Abdurakhmanov, R. A. Ragimova, and L. M. Imanov, *Phys. Letters* (*A*), 1970, **32**, 123.
[74] M. Fuller, personal communication.
[75] K. Kuchitsu, *Bull. Chem. Soc., Japan*, **1959**, **32**, 748.
[76] R. A. Bonham and L. S. Bartell, *J. Amer. Chem. Soc.*, 1959, **81**, 3491.

DNA, these have been postulated to be of major importance. In small molecules this force should be small, and so far microwave data does not seem to have led to any definite information on the subject.

B. Fluoroacetyl Fluoride.—The conformations found for fluoroacetyl fluoride,[33] namely with the halogen in the methyl group *cis* or *trans* to the other fluorine, instead of the expected *trans* and skew conformations, pose a real puzzle (Figure 9). Clearly a rather large $(1 - \cos 2\phi)$ term is needed, with a positive coefficient, *i.e.* minima at the *cis* and *trans* angles. Otherwise stated, some attractive force making the *cis* position more stable, or some repulsive force raising the energy of the 90° angle, is required. Strong van der Waals attractions would do it, but the distances involved are such as to suggest repulsion rather than attraction. The normal three-fold barrier favours *trans* and is a maximum at *cis*. A dipole–dipole interaction could stabilize *trans* but only, it would appear, with a concomitant conversion of the *cis* minimum into a maximum.

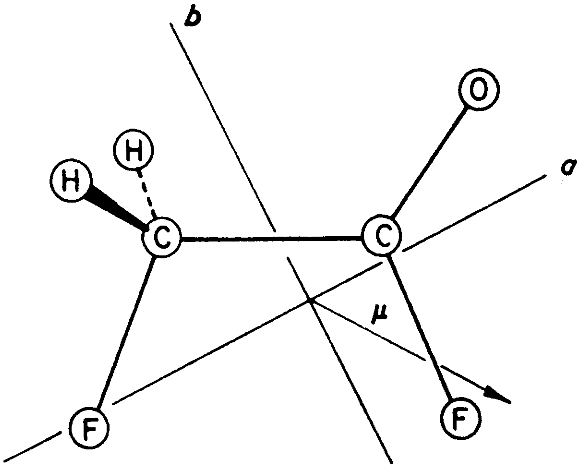

Figure 9 *Less stable form of fluoroacetyl fluoride*

One possibility is some double-bond character in the FCH_2—CH_2 bond, such as could arise from resonance forms involving F with a formal charge. Another idea which has been suggested is incipient hydrogen bonding C—H · · · O made favourable by the effect of the three electronegative atoms.

This situation may be a warning that nature is more complicated than we had hoped and that even transferability cannot always be expected. At any rate, none of the major quantitative empirical computer programs would seem capable of handling this example.*

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* It should be noted that a CNDO/2 calculation gave the correct conformations for this molecule (L. Saunders, personal communication). It would be interesting to test this approximation on many rotamer pairs.

6 Conclusion

The microwave method is being applied to more and more molecules and its power and accuracy is gradually increasing. It provides data which must be fitted by any calculational procedure which claims physical validity. There is a strong need to increase the accuracy further and to make more cross-comparisons with the results of other methods, such as i.r. Raman, n.m.r., *etc.*

The selected molecules discussed above suggest that there exist cases in which one or two of the commonly postulated intramolecular forces can qualitatively explain the microwave results. For these it should not be difficult to get semi-quantitative fits by parameter adjustment with conventional force laws. On the other hand, the real test of such quantitative formulae is for molecules with several forces opposing one another. Much more experimental data will have to be acquired before really satisfactory tests can be made, because of the necessarily large number of parameters. Furthermore, some of the examples suggest that, for some kinds of molecules at least, additional effects may have to be included in the treatment and that transferability is not yet guaranteed.

It would therefore appear wise to reserve judgment on the validity of predictions made with the aid of current empirical force laws, particularly outside of narrow molecular classes, except possibly in those cases where qualitative considerations alone seem convincing. In the meantime various types of *a priori* quantum mechanical calculations are advancing in power and in time may provide the predictive method of choice for simpler molecules.

Besides the very great debt I owe to the students and post-doctoral fellows who have worked on individual rotational isomer pairs, with whom I have had much beneficial discussion, I should especially like to thank Dr. O. Stiefvater and Dr. F. Wodarczyk. I am also grateful to the National Science Foundation for research support and to the John Simon Guggenheim Memorial Foundation for a fellowship.