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A THEORETICAL AND CRYSTALLOGRAPHIC STUDY OF THE GEOMETRIES AND CONFORMATIONS OF FLUORO-OLEFINS AS PEPTIDE ANALOGUES

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Abstract - The crystal structure of 2-cyclohexylidene-2-fluoroacetic acid (1) is reported. Geometry studies of related compounds using ab initio MO theory at the STO-3G level of approximation give structures in reasonable agreement with the structure of 1.

The conformational preference and barrier to rotation about the carbon-carbon single bond in methyl propenoate (3, X = H) and methyl 2-fluoropropenoate (3, X = F) have been calculated using the same method, with extensive geometry optimisation. It is found that both esters show a preference for the s-cis conformation rather than the s-trans as expected (26). The s-cis conformation is preferred over the s-trans by 2.1kJmol^{-1} in 3, X = H and 2.2 kJmol^{-1} in 3, X = F. The effect of fluorine substitution on the conformational preference is therefore minimal. Fluorine substitution in 3 reduces the calculated barrier to internal rotation by ca. 7 - 10%. This can be accounted for on the basis of the total fluorine-oxygen electrostatic interaction energy using the excess charges calculated using the STO-3G basis set, and appear to be due to a simple polar destabilisation of the minimum energy conformation. cis-1-Fluoropropene and Z-2-fluoro-2-butene have been studied for comparison with "standard" peptide geometries. The comparison of corresponding structural parameters is moderate. Comparison of calculated dipole moments suggests that the fluoro-olefin unit would be a more appropriate model for the peptide bond than simple olefin units.

INTRODUCTION : FLUORO-OLEFINS AS PEPTIDE ANALOGUES

The van der Waal's radius of covalent fluorine is close to 1.35A, compared to 1.1A for hydrogen and 1.8A for chlorine. Fluorine is therefore probably the only element capable of replacing hydrogen in organic molecules with minimal steric consequences. In contrast, the high electronegativity of fluorine (3.9[1]) may have profound electronic effects. The importance of these two opposing factors in drug design is well illustrated by reference to the well-known metabolic effects of fluoroacetic acid (2 - 4) and the 5-fluoro uracil anti-tumour agents (5,6).

The importance of peptides in living systems hardly requires mention, and the consequent examination of stereochemically similar materials for use as drugs has beem amply discussed (7,8). In particular, two groups of workers have independently suggested the replacement of peptide bonds with olefin units in enkephalin analogues (9,10), the primary structural effects of such a substitution are small (9). In addition, the olefin bond is likely to increase resistance to enzymic degradation (9). However, the olefin bond is of very low polarity and, while it has been suggested (10b) that this might be useful in increasing lipophilicity, the effect on intramolecular forces might be extreme. We therefore propose the replacement of olefinic hydrogen with fluorine. The high electronegativity of fluorine should introduce a pronounced polarity in the olefin unit in a direction analogous to the effect of oxygen in the peptide unit. The structural effects

of the fluorination of olefins are therefore of interest.

The structures of all the vinyl fluorides have been determined by electron diffraction methods (11), and most have been studied by microwave spectroscopy (12 - 14). The results of all these studies are in good agreement. In addition, the structures of cis- and trans-1-fluoro-1-propene and 2-fluoro-1-propene have been examined by microwave methods (15 - 17), including determinations of barriers to internal rotation. In most cases, the structures found demonstrate a striking tendency toward an increase of the C=C-X bond angle as X changes from hydrogen to fluorine. This effect is most pronounced in 1,1-difluoroethene and cis-1,2-difluoroethene. Speculation regarding possible attractive fluorine-fluorine interactions has led many workers to calculate geometries for the difluoroethylenes by molecular orbital (MO) methods (18 - 25) in attempts to account for the observations. In general, though the origin of the effect is only poorly understood, the effect itself is at least qualitatively reproduced by MO theory. The conceptually simpler "molecular mechanics" or "force-field" studies so far carried out (26 - 30) do not so far appear to reproduce the observed trends reliably, despite recent promising developments (31).

Two MO calculations on fluoropropenes have concentrated on the reproduction of the observed barriers to internal rotation (32, 33). It was concluded that ab initio MO theory can be used to predict barriers to internal rotation in the monofluoropropenes with accuracy, provided that a reliable experimental geometry or fully optimised geometry is employed. Wolfe et al., (20) included geometry optimisation studies on three monofluoropropenes in an investigation of the factors affecting fluoro-olefin geometries, concluding that ab initio MO theory at the STO-3G level of approximation (34) led to a good agreement of calculated and experimental geometries.

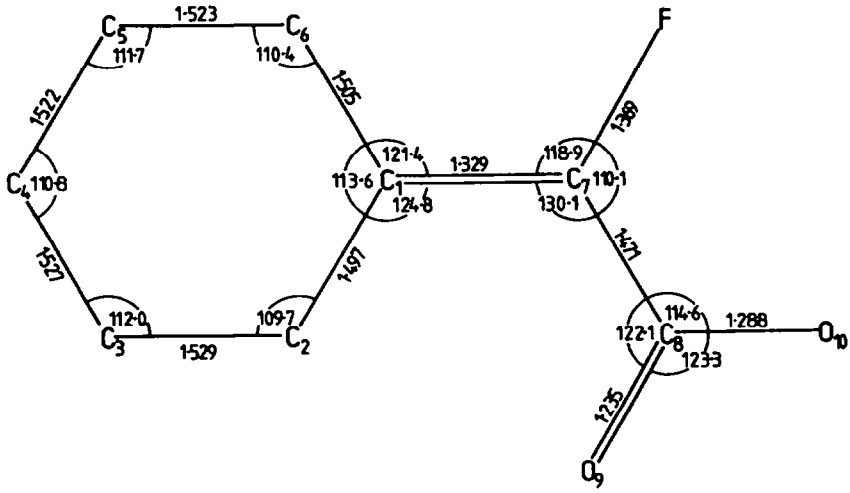
In this study we have used a combination of molecular orbital calculations and X-ray crystallography to investigate the structural and conformational properties of α-fluoro-α,β-unsaturated acids as model fluoro-olefins.

RESULTS AND DISCUSSION

THE CRYSTAL STRUCTURE OF 2-CYCLOHEXYLIDENE-2-FLUOROACETIC ACID (1).

The crystal structure of 1 is summarised in Figure 1 and the accompanying table.

Figure 1: The crystal structure of 2-cyclohexylidene-2-fluoroacetic acid 1 . [b]



Dihedral angles in 2-cyclohexylidene-2-fluoroacetic acid.[a]

$C_6C_1C_2C_3$	55.9	$C_1C_2C_3C_4$	-54.7
$C_7C_1C_2C_3$	-120.0	$C_2C_3C_4C_5$	54.7
$C_2C_1C_6C_5$	-56.0	$C_3C_4C_5C_6$	-54.2
$C_7C_1C_6C_5$	120.0	$C_4C_5C_6C_1$	54.3
$C_2C_1C_7C_8$	-3.8	$C_1C_7C_8O_9$	-12.8
$C_2C_1C_7F$	174.6	$C_1C_7C_8O_{10}$	167.4
$C_6C_1C_7C_8$	-179.4	$FC_7C_8O_9$	168.6
$C_6C_1C_7F$	-0.9	$FC_7C_8O_{10}$	-11.2

[a] The dihedral angle ABCD is positive for clockwise rotation of A from D looking along BC.

b The standard deviations of the above parameters are 0.003 Å (bond lengths), 0.2° (bond angles) and 0.3° (dihedral angles).

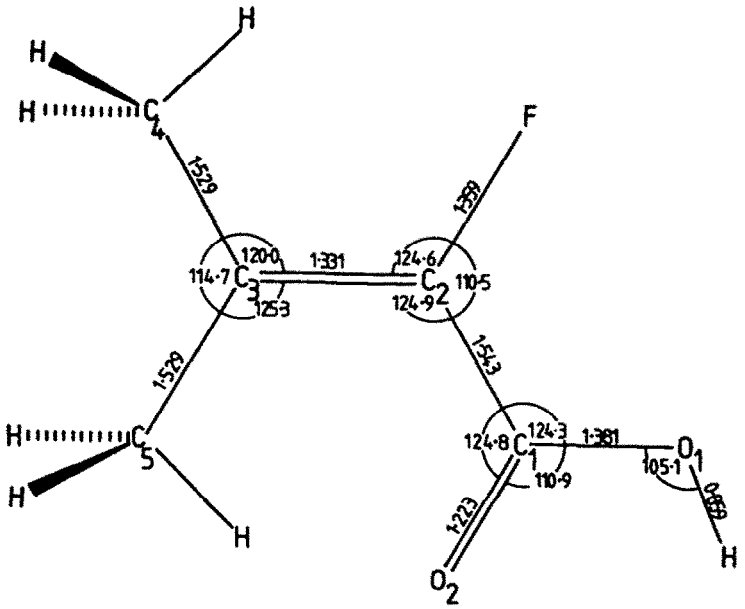
The geometry of the cyclohexane ring compares well with a published geometry of methylenecyclohexane calculated by force-field methods (35), and shows the expected slightly flattened chair conformation. The disposition of substituents about the double bond, however, shows considerable deviation from "standard" (36) geometries. For example, the C_1-C_7-C_8 bond angle is abnormally large (ca. 130°), while the C_1-C_7-F bond angle is considerably smaller than expected. These distortions suggest the presence of a considerable steric interaction between the carbonyl oxygen and the cyclohexane ring at C_2. Of additional interest, the carbonly oxygen is eclipsed with the alkene double bond, that is, in the s-cis conformation, rather than the s-trans conformation generally expected in 1,3-diene-like structures (37). Consideration of crystallographic data for similar materials (38,39) suggests that this is the usual conformation in solid α,β-unsaturated esters and acids and not an effect associated with fluorine substitution.

To gain some insight into the possible factors contributing to the geometry of 1, a number of MO studies have been carried out on model compounds. These used the program GAUSSIAN 70 (34), operating with STO-3G basis sets (40) throughout. This basis set was chosen both to permit calculations on relatively large molecules, and because of the reliability of structures calculated by this method (20).

THE GEOMETRY OF 2-FLUORO-3-METHYLBUT-2-ENOIC ACID (2).

2-Fluoro-3-methylbut-2-enoic acid (2) (Figure 2) provides a suitable model for interactions existing in 1. All the geometric parameters, with the exception of the methyl group C-H bond lengths and C-C-H and H-C-H bond angles, were optimised in turn. This process was continued until computed increments in bond lengths dropped below 0.01A and bond angle increments dropped below 0.1°. The conformation of the carbonyl group was chosen to duplicate that found in the crystal structure of 1, that is, the s-cis conformation was assumed. A search for a non-planar minimum energy conformation was carried out by a separate optimisation of the C=C-C=O and the methyl group H-C_5-C_3=C_2 dihedral angles. Each dihedral angle was displaced from coplanarity by 10° such that the in-plane hydrogen on C_5 was above the plane of the diagram in Figure 2, while the carbonyl oxygen was below the plane. Two iteration cycles on each dihedral angle reduced both angles to within 0.1° of the co-planar orientation. The carbonyl group was therefore assumed co-planar with the alkene bond for the remainder of the study, while both methyl groups were fixed with one hydrogen eclipsing the C=C double bond as shown. It is noteworthy that the variation of energy with the orientation about these two single bonds is quite small; the carbonyl group may be rotated by 5° at a cost of ca. 6 $Jmol^{-1}$,

Figure 2: The optimised structure of 2-fluoro-3-methyl-2-butenoic acid



while the methyl group may be rotated the same amount at the expense of 12 $Jmol^{-1}$. It follows that small deviations from planarity are to be anticipated in such systems; this is indeed the case in 1, where the C_1-C_7-C_8=O_9 dihedral angle approaches 13°.

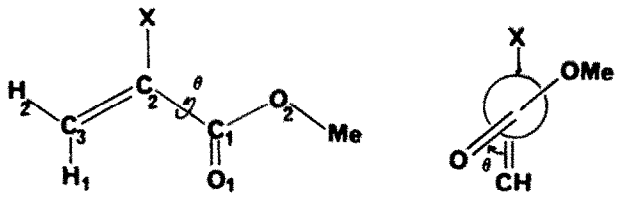
Comparison of the optimised structure of 2 (Figure 2) with the experimentally determined structure of 1 shows that, in general, calculated single bond lengths are exaggerated by ca. 0.02A, as expected (41). The calculated values of the C_4-C_3-C_5, O_2-C_1-C_2 and F-C_2-C_1 angles agree well with the corresponding angles in 1; however, the deviation from symmetry observed in 1 is only moderately well reproduced. This may be due to the different environment of the carbonyl groups in the two cases; 1 exists in the solid as a hydrogen-bonded dimer, whereas computational limitations forced treatment of 2 as the monomer. Clearly, this must also affect the validity of any argument concerning steric interactions between C_5 (in 2) and the carbonyl oxygen. Nonetheless, consideration of the gross orbital overlap population ("bond order") between the centres of interest is instructive. The overlap population between C_5 and the carbonyl oxygen is calculated at ca. -4×10^{-3}. The overlap population between the in-plane hydrogen on C_5 and the carbonyl oxygen is also negative, though smaller in magnitude. This may be taken to indicate a repulsive interaction between the carbonyl group and the nearby methyl group. Another possible source of distortion about C_2 is interaction between the ester oxygen (O_1 in 2) and the fluorine on C_2. The overlap population between these two centres is positive, and decreases with distance beyond ca. 2.3A, indicating an attractive fluorine-oxygen interaction. This compares well with a non-bonded poptential proposed for the fluorine-fluorine interaction in fluoroethanes (31). This apparent attractive interaction may account in part for the small F-C_2-C_1 angle in 2.

GEOMETRIES AND CONFORMATIONAL PROPERTIES OF METHYL PROPENOATE AND METHYL 2-FLUORO-PROPENOATE

Methyl 2-fluoro-2-propenoate (3, X = F) (Figure 3) provides a simple model for examination of the barriers to internal rotation and conformational preferences

Figure 3

Numbering scheme and torsional angle θ in 3



of more complex α,β-unsaturated α-fluoroesters. In addition, experimental data on the structures of methyl propenoate (3, X = H) (42) and propenoic acid (38,39) are available for comparison with calculated geometries.

There is substantial experimental evidence to show that the conformation of simple carboxylic acid esters is weighted heavily towards the s-cis rotamer, in which the O-alkyl single bond eclipses the carbonyl oxygen (43 - 46). Accordingly, this conformation was assumed throughout the following geometry study. All other parameters were iterated on with the exception of the C-H bond lengths and angles within the methyl group (tetrahedral geometry assumed, with r_{C-H} = 1.09A). Iteration was continued until the total energy change summed over all geometric parameter increments in a single iterative cycle dropped below 0.1 $kJmol^{-1}$. The use of an energy convergence criterion was considered appropriate in this case since the final results were to be used in a calculation of the barrier to internal rotation. This energy criterion was met when no bond length increment exceeded 0,002A and bond angle increments were all less than 0,05°.

Table 1: Experimental and calculated geometries for methyl acrylate and acrylic acid.

Compound:	Acrylic acid				Methyl Acrylate.	
Method:[a]	X-ray		ED		ED	STO-3G
	-150°[e]	-90°[d]	(a)	(b)	(c)	
Bond lengths (A):						
$r(C_1-C_2)$	1.47	1.46	1.44	1.44	1.44[f]	1.52
$r(C_1-O_1)$	1.26	1.24	1.22	1.22	1.22[f]	1.22
$r(C_1-O_2)$	1.28	1.32	1.43	1.36	1.36	1.39
$r(C_2-C_3)$	1.30	1.33	1.36	1.36[f]	1.36[f]	1.31
r(Me-O)	-	-	-	-	1.46	1.44
Bond angles:						
$O_1-C_1-O_2$	122	123	125	125	125[f]	123.4
$O_1-C_1-C_2$	122	124	120	120	120[f]	125.9
$O_2-C_1-C_2$	116	113	115	115	115[f]	110.7
$C_1-C_2-C_3$	121	121	120	120[f]	120[f]	121.7
Me-O-C_1	-	-	-	-	115±5	111.9

[a] ED: Electron diffraction. [b]Ref. 32a. [c]Ref. 32b
[d] Ref. 27 [e] Ref. 28.
[f] Assumed value.

Table 1 compares the optimised structure of methyl propenoate with experimtnally determined structures of methyl propenoate (42) and propenoic acid (38, 39). In general, the agreement is good, supporting the use of the STO-3G basis set in this instance.

The results of full geometry optimisations at five equally-spaced values of the dihedral angle (defined as in Figure 3) are given in Tables 2 and 3 for 3, X = H and 3, X = F respectively. In addition, the variation of the total energy in each case is given by:

X = H : E_{tot} = 10.3-1.04cos (θ)-9.29cos (2θ)
X = F : E_{tot} = 9.83-1.02cos (θ)-8.74cos (2θ)

(from least-squares fitting to the calculated points). The deviation of any point from either curve is well within the 0.1 $kJmol^{-1}$ convergence limit for the geometry calculations.

It is immediately clear that the minimum energy conformation in both cases is the s-cis conformation. Further, the preference for the s-cis conformer is ca.

Table 2: The calculated geometry of Methyl Propenoate (3 ,X=H).

θ=	0	45	90	135	180
Bond lengths:					
$r(C_1-C_2)$	1.5150	1.5206	1.5280	1.5218	1.5151
$r(C_1-O_1)$	1.2187	1.2175	1.2164	1.2177	1.2189
$r(C_1-O_2)$	1.3939	1.3944	1.3947	1.3946	1.3944
$r(C_2-H)$	1.0827	1.0836	1.0845	1.0838	1.0834
$r(C_2-C_3)$	1.3116	1.3102	1.3087	1.3102	1.3113
$r(C_3-H)^a$	1.0832	1.0829	1.0827	1.0828	1.0829
$r(C_4-O_2)$	1.4402	1.4405	1.4411	1.4407	1.4397
Bond angles:					
$(O_1-C_1-O_2)$	123.37	123.27	123.16	123.18	123.08
$(O_1-C_1-C_2)$	125.91	126.29	126.34	125.73	125.09
$(O_2-C_1-C_2)$	110.72	110.44	110.50	111.09	111.83
$(C_1-C_2-C_3)$	121.66	122.37	123.10	122.98	123.69
(C_1-C_2-H)	115.75	115.61	115.42	115.27	114.33
(C_3-C_2-H)	122.59	122.02	121.48	121.75	121.98
$(C_2-C_3-H_1)$	121.27	121.90	122.08	121.99	121.70
$(C_2-C_3-H_2)$	122.26	121.98	122.08	121.87	121.83
$(H_1-C_3-H_2)$	116.47	116.12	115.84	116.14	116.47
$(C_4-O_2-C_1)$	111.94	111.96	111.95	111.88	111.86
Total energies:					
E (kJ mol^{-1})	0.0	9.53	19.61	11.03	2.05

Table 3: Optimised geometries of Methyl 2-Fluoropropenoate (3 ,X=F):

θ=	0	45	90	135	180
Bond lengths:					
$r(C_1-C_2)$	1.5303	1.5378	1.5452	1.5383	1.5324
$r(C_1-O_1)$	1.2182	1.2167	1.2160	1.2169	1.2177
$r(C_1-O_2)$	1.3908	1.3909	1.3915	1.3917	1.3915
$r(C_2-F)$	1.3548	1.3561	1.3576	1.3569	1.3561
$r(C_2-C_3)$	1.3168	1.3156	1.3140	1.3153	1.3164
$r(C_3-H)^b$	1.0806	1.0803	1.0800	1.0803	1.0804
$r(C_4-O_2)$	1.4405	1.4412	1.4417	1.4413	1.4405
Bond angles:					
$(O_1-C_1-O_2)$	123.30	124.18	123.88	123.94	123.96
$(O_1-C_1-C_2)$	125.12	125.51	125.78	125.47	124.87
$(O_2-C_1-C_2)$	110.58	110.31	110.34	110.59	111.17
$(C_1-C_2-C_3)$	121.89	122.54	123.32	123.26	123.92
(C_1-C_2-F)	114.95	114.55	114.07	113.96	113.30
(C_3-C_2-F)	123.16	122.91	122.61	122.78	122.78
$(C_2-C_3-H_1)$	120.25	120.90	121.30	120.94	120.66
$(C_2-C_3-H_2)$	121.91	121.59	121.36	121.49	121.45
$(H_1-C_3-H_2)$	117.84	117.51	117.34	117.57	117.89
$(C_4-O_2-C_1)$	111.86	111.50	111.96	111.84	111.79
Relative energy :					
E (kJmol^{-1})	0.0	9.21	18.59	10.42	2.21

2.1 kJmol^{-1} in each case. This value is very close to the values obtained by George et al., (47,48) for the energy difference between two rotamers (assumed s-trans and non-s-trans) of methyl propenoate and trans-methyl but-2-enoate. It was assumed by these workers that the preferred form was the s-trans form on the basis of experience with α,β-unsaturated ketones and aldehydes (49). Sheriden and co-workers, however, noted that no firm conclusion regarding the vapour-phase conformational preference of methyl propenoate was possible from their work (45), and other workers have concluded that the preferred conformation of several α,β-unsaturated esters is s-cis (50). We conclude that simple α,β-unsaturated carboxylic acid esters prefer the s-cis conformation by 1-2 kJmol^{-1}, and that arguments based on the conformational preferences of simple dienes and α,β-unsaturated aldehydes and ketones may not be extended to α,β-unsaturated esters.

The barriers to rotation in 3, X = H and 3, X = F are calculated to be 19.8 kJmol^{-1} and 18.5 kJmol^{-1} respectively (these values are the differences between the maxima and minima of the calculated curves). It appears that fluorine substitution has only a slight effect on the barrier to internal rotation. The origin of this effect appears to be primarily a simple dipolar interaction. Table 4 shows the excess charge distribution on oxygen and fluorine calculated for 3, X = F using the STO-3G basis set for the arrangements with $\theta = 0^\circ$ and $\theta = 90^\circ$ (minimum and maximum energy arrangements respectively), together with the fluorine-oxygen distances and the total electrostatic interaction energy in each case. The difference in the total electrostatic interaction energies is 1.2 kJmol^{-1}, very close to the calculated difference in the barrier heights for 3, X = H and 3, X = F. The difference in the barrier heights may thus be ascribed almost entirely to an electrostatic destabilisation of the minimum energy conformer rather than a stabilisation of the $\theta = 90^\circ$ arrangement.

Table 4: Electrostatic energies of conformations of 3, X=F.

	θ=0	θ=90
Distances		
r(F-O_1)	3.58	3.22
r(F-O_2)	2.59	3.14
Excess charges[a]		
F	-0.121	-0.124
O_1	-0.256	-0.249
O_2	-0.246	-0.245
Electrostatic energy (kJmol^{-1})		
	28.0	26.8

[a] calculated using the STO-3G basis set

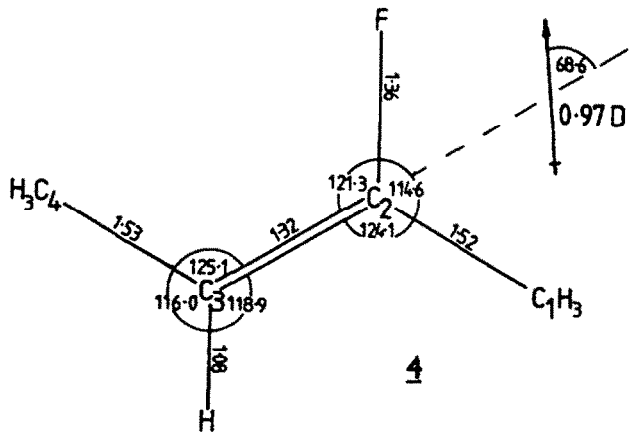
[b] Calculated using $E_{tot}=S(N_0Q_1Q_2/4\pi\varepsilon_0 r)$
$=1.388\times10^3(q_1q_2/r)$
when q_i is in eu and r in A.

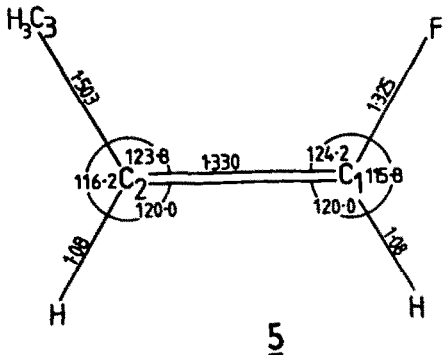
COMPARISON OF CALCULATED FLUOROALKENE GEOMETRIES WITH STANDARD PEPTIDE GEOMETRIES

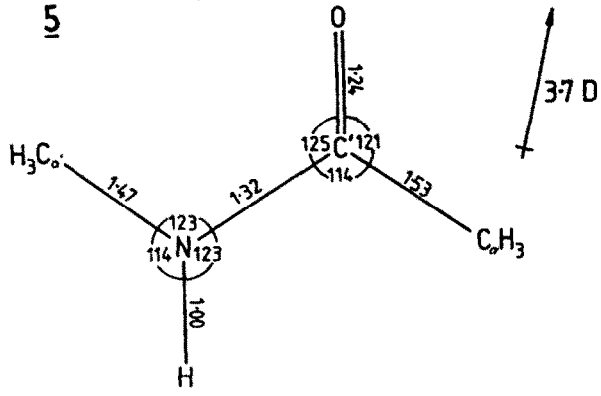
Since our interest in the fluoro-olefin unit arises from the possibility of constructing peptide analogues incorporating fluoroalkene units in place of peptide bonds, the structures of two simple fluoroalkenes have been examined using ab initio MO theory. Z-2-Fluorobut-2-ene (4) and cis-1-fluoropropene (5) were chosen for study; 4 provides a model N-methylacetamide analogue, while 5 may be compared with experimental (15) and previously calculated (32, 33) structures as well as N-methylformamide.

For the calculations on 4, the geometry about C_1 and C_4 (Figure 4) were assumed tetrahedral as before, with the C-H bond lengths fixed at 1.09A. It was also assumed that the methyl group conformation included one C-H bond eclipsed with the alkene double bond. All the remaining structural parameters were optimised

Figure 4: Comparison of theoretical fluoro-olefin geometries and typical peptide geometries.







sequentially until bond length and bond angle increments dropped below 0.02A and 0.1° respectively. The calculation of the geometry of 5 optimised the C_1-F, C_1=C_2 and C_2-C_3 bond lengths and the C_2-C_1-F and C_1=C_2-C_3 bond angles, using the same termination criterion.

The resulting structures are shown in Figure 4, together with a structure for N-methylacetamide derived from the "standard" peptide geometries (51,52,53). It is, however, important to note that one determination of the structure of formamide in the gas phase found an appreciably non-planar geometry about nitrogen (54), as have many crystallographic studies of polypeptides.

The calculated geometry of 5 agrees well with the previous calculations (32,33) and with the available experimental data (15). The structure obtained for 4 parallels those observed (17) and calculated for 2-fluoropropene. Comparison of the two calculated structures with the "standard" peptide geometry shows many close similarities and some differences. For example, the C_1-C_2 and C_2-C_3 distances in 4 compare well with the corresponding C-C' and N-C' distances in

N-methylacetamide, but the angle between the two bonds in each case differs significantly.

A comparison of dipole moments is also of interest. The gas phase dipole moment of N-methylacetamide is reported as 3.71D (55). Calculations indicate that the dipole moment vector forms an angle of 44° - 54° with the C-N bond (56, 57) (Figure 4). This may be compared with the dipole moment calculated for 4 of 0.97D, at an angle of ca. 69° with the C=C bond in the sense indicated in Figure 4. This estimate of the dipole moment is probably low (35); the actual value is likely to be in the range 1.5 - 2.0D.

CONCLUSION

As fluorine substitution in olefins leads to only small changes in conformation with increase in polarity, fluoro-olefin units could be effective peptide analogues.

EXPERIMENTAL

All computations were performed on a CDC Cyber 7600 computer. 2-Cyclohexylidene-2-fluoroacetic acid (1) was prepared by aqueous alkaline hydrolysis of the ethyl ester, prepared according to the method of Machleidt and Wessendorff (58). A single crystal of the free acid was obtained from a solution in n-heptane by progressive evaporation.

The crystal data for (1) are formula $C_8H_{11}FO_2$, M.wt., 158.17, F(000) = 336. The crystals were monoclinic with cell dimensions $P2_1/n$ a:7.943(5), b:6.090(4), C:16.227(8) A, and beta 97.13(3) deg. The density was 1.35 $Mg.m^{-3}$. The mu (Mo-K-alpha) was 0.10 mm^{-1}, and absorption effects were ignored.

For the data collection, the temperature was $293^{\circ}K$ and wavelength 0.71069A. The total data observed was 1160 points and the rejection criterion was I > 2.5 x sigma (I). The weighting function used was $w = 1/(\sigma^2|F_o| + 0.001X|F_o|^2)$. The data were collected on a Nicolet R3m four-circle diffractometer fitted with a graphite monochromator.

The structure was determined by direct methods using 32 starting phase permutations. Refinement proceeded smoothly to convergence at R = 0.0465 with anisotropic refinement of all non-hydrogen atoms. The position of the hydrogen atom of the OH group was found from a difference map. The remaining hydrogen atom co-ordinates were calculated using known geometries. All calculations were carried out with the SHELXTL package of the R3m System (59).

The heavy atom co-ordinates and temperature factors obtained are given in Table 5.

TABLE 5. Atom coordinates ($x10^4$) and temperature factors ($Å^2 x10^3$)

atom	x	y	z	U
C(1)	3527(2)	629(3)	3937(1)	37(1)*
C(2)	4869(2)	2354(3)	4102(1)	41(1)*
C(3)	5528(2)	2993(3)	3289(1)	45(1)*
C(4)	6148(2)	1004(3)	2840(1)	50(1)*
C(5)	4772(2)	-739(3)	2701(1)	47(1)*
C(6)	4107(2)	-1379(3)	3510(1)	46(1)*
C(7)	1934(2)	840(3)	4096(1)	40(1)*
C(8)	1112(2)	2648(3)	4495(1)	43(1)*
O(9)	1935(2)	4131(3)	4876(1)	68(1)*
O(10)	-519(1)	2543(2)	4416(1)	60(1)*
F(11)	798(1)	-795(2)	3851(1)	59(1)*

* Equivalent isotropic U defined as one third of the trace of the orthogonalised U_{ij} tensor

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