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On the Conformational Varieties of Adrenaline: the Free Molecule and the Molecule in the Crystal

BY J. CAILLET, P. CLAVERIE AND B. PULLMAN

Institut de Biologie Physico-Chimique, Laboratoire de Biochimie Théorique, associé au CNRS, 13 rue P. et M. Curie, 75005 Paris, France

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Refined quantum-mechanical computations invariably predict that the preferred conformers of free androgenic phenethylamines or hallucinogenic indolalkylamines should correspond to values of the torsion angles $\tau_1 \simeq \pm 90°$ and τ_2 close to ± 60 or 180°. X-ray crystallographic studies indicate that most such compounds exist in these conformations (in particular with $\tau_1 \simeq 90$, $\tau_2 \simeq 180°$) in the crystals. In some cases, however, the crystalline conformer corresponds to $\tau_1 \simeq 0$, $\tau_2 \simeq 180°$, an arrangement which does not even correspond to a local energy minimum on the conformational energy map for the free molecule. Such is, for example, the case for adrenaline in adrenaline hydrogen tartrate. Computations carried out for the lattice energy of this crystal and of the hypothetical crystals constructed with the usual conformers, by a procedure which uses intermolecular potential functions, show that the lattice energy of the 'experimental' crystal largely compensates for the loss in conformational energy of the constituent unit and represents a more stable arrangement than those obtained with conformers associated with $\tau_1 \simeq \pm 90°$.

1. Introduction

Many fundamental pharmacological compounds are composed of a conjugated ring with an attached ethylamine side chain (Pullman, 1976). Typical examples are the androgenic phenethylamines or the hallucinogenic indolalkylamines. In such molecules an essential conformational problem concerns the mutual orientation of the side chain and the ring. It is generally defined (Pullman, 1976) by reference to two torsion angles τ_1 and τ_2, illustrated in Fig. 1 for adrenaline. The first of these angles defines the overall orientation of the plane of the side chain with respect to the plane of the ring, the second the orientation of the cationic head with respect to the ring.

We recall that with the usual convention (Pullman, 1976) the torsion angle τ about the bond *B–C* in the sequence of atoms *A–B–C–D* is the angle through which the far bond *C–D* is rotated relative to the near bond *A–B*. The *cis*-planar position of bonds *A–B* and *C–D* corresponds to $\tau = 0°$. The torsion angles are considered positive for a right-handed rotation: when looking along the bond *B–C*, the far bond *C–D* rotates clockwise relative to the near bond *A–B*. Alternatively, the positive angles are defined as 0 to 180°, measured for a clockwise rotation, and negative angles as 0 to $-180°$, measured for a counterclockwise rotation.

Conformational energy maps constructed for a large series of phenethylamines (Pullman, Coubeils, Courrière & Gervois, 1972; Pullman, Berthod & Courrière, 1974) and indolalkylamines (Pullman, Courrière & Berthod, 1974; Port & Pullman, 1974) by refined quantum-mechanical procedures lead to the prediction that the most stable conformations of these molecules, in the free state, should be associated with $\tau_1 \simeq \pm 90$ and $\tau_2 = \pm 60$ or 180°, *i.e.* should correspond to a perpendicular arrangement of the C(1), C(7), C(8) plane of the side chain with respect to the plane of the

ring ($\tau_1 = 90°$) and a *gauche* ($\tau_2 = 60°$) or *trans* ($\tau_2 = 180°$) orientation of the cationic head with respect to the ring. A typical map of this kind constructed by the PCILO method (Pullman, Berthod & Courrière, 1974) is presented for adrenaline in Fig. 2. [Essentially similar results are found by *ab initio* computations (Pullman, Berthod & Courrière, 1974).] The global energy minimum at $\tau_1 = -90$, $\tau_2 = -60°$ represents a 'perpendicular-*gauche*' conformer. Similar conformers are represented by the local energy minima at $\tau_1 = 90$, $\tau_2 = -60°$; $\tau_1 = -90$, $\tau_2 = 60°$; and $\tau_1 = 90$, $\tau_2 = 60°$. On the other hand the local minima at $\tau_1 = \pm 90$, $\tau_2 = 180°$ represent 'perpendicular-*trans*' conformers.

X-ray crystal structure studies of these types of molecule generally indicate the presence in the solid state of the very conformers predicted to be dominant in the free state (Pullman, 1976; Carlström, Bergin & Falkenberg, 1973). In particular most of the phenethylamines exist in the 'perpendicular-*trans*' conformation in the crystalline state. Indolalkylamines are generally found in either the 'perpendicular-*trans*' or the 'perpendicular-*gauche*' conformation. This indicates that in the majority of cases the crystal packing forces do not perturb the intrinsic conformational preference of the free molecules.

Some compounds of this class nevertheless behave in the crystal in a somewhat exceptional way by assuming a conformation with $\tau_1 \simeq 0$ and $\tau_2 \simeq 180°$, *i.e.* a 'planar-*trans*' conformation. Such is, for example, the case of adrenaline (epinephrine) in (−)-adrenaline hydrogen (+)-tartrate (Carlström, 1973) for which $\tau_1 = -3$ and $\tau_2 = -179°$. [Although the molecule is in the usual 'perpendicular-*trans*' conformation in the crystal of (−)-adrenaline (Andersen, 1975).] Other examples of such an exceptional conformation in phenethylamines or indolalkylamines are 6-hydroxydopamine hydrochloride (Andersen, Mostad & Rømming, 1975); serotonin in the serotonin–creatinine sulphate complex (Karle, Dragonette & Brenner, 1965) [but not in serotonin–picrate monohydrate (Thewalt & Bugg, 1972)]; 5-methoxy-*N*,*N*-dimethyltryptamine hydrochloride (Falkenberg & Carlström, 1971); melatonin (Wakahara, Fujiwara & Tomita, 1972; Quarles, Templeton & Zalkin, 1974); and psilocin (Petcher & Weber, 1974).

The occurrence of such 'planar-*trans*' conformers is the more puzzling as they do not correspond to even local energy minima on the conformational energy maps constructed for the free species. On the other hand they are usually only a few kcal mol^{-1} above the global energy minimum.

It seems obvious that the adoption of this particular 'planar-*trans*' conformation must be ascribed to the effect of packing forces and this paper presents an investigation of this problem for adrenaline. We have employed the procedure for the evaluation of crystal lattice energies from intermolecular potential functions described by Caillet & Claverie (1974, 1975) and applied in these publications for a comparative study of relative configurations of neighbouring molecules in the crystal with the optimal configurations of isolated binary complexes.

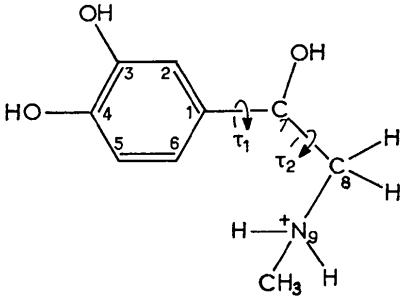


Fig. 1. Torsion angles τ_1 and τ_2 in adrenaline. $\tau_1 = \tau$[C(6)–C(1)–C(7)–C(8)], $\tau_2 = \tau$[C(1)–C(7)–C(8)–N(9)].

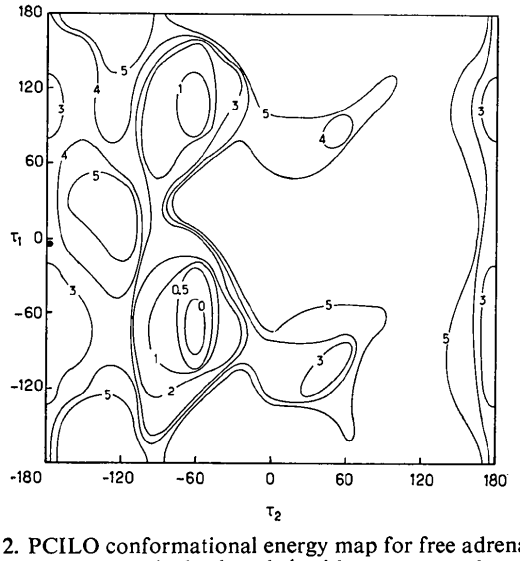


Fig. 2. PCILO conformational energy map for free adrenaline. Isoenergy curves in kcal mol^{-1} with respect to the global energy minimum taken as energy zero (Pullman, Berthod & Courrière, 1974).

2. Method

The evaluation of lattice energies from simple intermolecular potential functions (involving essentially atom–atom terms) has been accomplished successfully in several recent works (Caillet & Claverie, 1974, 1975; Momany, Carruthers, McGuire & Scheraga, 1974; Momany, Carruthers & Scheraga, 1974; Hagler, Huler & Lifson, 1974; Huler & Warshel, 1974; Shipman, Burgess & Scheraga, 1975; Burgess, Shipman & Scheraga, 1975; and references therein). A detailed description of our own method may be found in Caillet & Claverie (1975); thus we only recall here the main practical features in §2(*a*)–(*d*), and describe in §2(*e*) the modification applied for very short interatomic distances which was not described in Caillet & Claverie (1974, 1975).

We evaluate the interaction energy as the sum of three long-range contributions (electrostatic, polarization and dispersion) and a short-range repulsive contribution. At large intermolecular distances (several molecular diameters), the usual simplified formulae (each molecule reduced to a single centre of force) may be used for the long-range contributions, while the short-range one may be neglected. At short distances (neighbouring molecules in the lattice) more refined formulae must be used.

(a) Electrostatic energy

For the calculation of this term, we need to know the net atomic charges of the two interacting molecules. This energy is then given by

$$E_{qq}=\sum_{i}^{(1)}\sum_{j}^{(2)}q_iq_j/R_{ij}\,. \tag{1}$$

We note that $\sum_{i}^{(n)}$ extends to all atoms belonging to molecule n; q_i and q_j are the net charges obtained from quantum-mechanical calculations on the isolated molecules.

(b) Polarization energy

The polarization energy is calculated as a sum of atom polarization contributions:

$$E_{\text{pol}}^{(1)}=-\tfrac{1}{2}\sum_{i}\alpha_i(\mathscr{E}_i)^2\,, \tag{2}$$

where $\mathscr{E}_i$ is the electric field created at atom i of molecule 1 by all other molecules, and α_i is the mean polarizability attributed to atom i. The mean polarizability of an atom is obtained by sharing the mean polarizability of the bond ij between the atoms i and j, according to the weights attributed to the atoms; these weights are obtained from the number of electrons involved in the bonds and the number of electrons on the atoms (lone pairs) (Caillet & Claverie, 1975).

This mode of calculating the polarization energy enables us to use the atom–atom distances already calculated for the electrostatic energy and thus to reduce the computation time.

(c) Dispersion and repulsion energy

These contributions are calculated from the semi-empirical Kitaigorodsky formula which also involves atom–atom terms, *i.e.* the same atom–atom distances previously calculated.

The Kitaigorodsky formula is a sum of atom–atom interactions:

$$E^{\text{KIT}}=\sum_{i}^{(1)}\sum_{j}^{(2)}E(i,j)\,, \tag{3}$$

where each atom–atom contribution $E(i,j)$ is the sum of a dispersion and a repulsion term:

$$E(i,j)=k_ik_j\left[-\frac{A}{z}+(1-\varrho_i/N_i^{\text{val}})\,(1-\varrho_j/N_i^{\text{val}})\times C\exp(-\alpha z)\right], \tag{4}$$

with $z=R_{ij}/R_{ij}^{o'}$ and $R_{ij}^{o'}=\sqrt{[(2R_i^w)\,(2R_j^w)]}$, where R_i^w and R_j^w are the van der Waals radii of atoms i and j. The parameters α, A and C are kept independent of the atomic species i and j. The values used are (Caillet & Claverie, 1975): $A=0{\cdot}214$ kcal mol^{-1}, $C=47\times10^3$ kcal mol^{-1}, $\alpha=12{\cdot}35$; and for the van der Waals radii: $R_{\text{H}}=1{\cdot}2$, $R_{\text{C(aliphatic)}}=1{\cdot}7$, $R_{\text{C(aromatic)}}=1{\cdot}77$, $R_{\text{N}}=1{\cdot}60$, $R_{\text{O}}=1{\cdot}50$ Å. The factors $(1-\varrho_i/N_i^{\text{val}})$ correspond to the influence of the electronic populations on the repulsion: ϱ_i is the net charge already used in (1), and N_i^{val} is the number of valence electrons.

(d) Representation of the hydrogen bond

When one of the atoms (i,j) is hydrogen and the other C, O or N, we use the following refined formula: we choose two distances R_m and R_M $(R_m<R_M)$; then for $R>R_M$ we use the normal parameters A,C,α; for $R<R_m$, we use modified parameters A',C',α' $(A'<A,\ C'<C,\ \alpha'>\alpha)$; and for $R_m<R<R_M$ we use interpolated values of these parameters according to:

$$K(x)=(K+K')/2+(0{\cdot}375x^5-1{\cdot}25x^3+1{\cdot}875x)\,(K-K')/2\,, \tag{5}$$

where K stands for one of the symbols A,C,α and $x=[R-(R_M+R_m)/2]/[(R_M-R_m)/2]$. We used the values (Caillet & Claverie, 1975): $R_m=1{\cdot}8$ Å, $R_M=2{\cdot}6$ Å, $A'=A/5$, $C'=C/2{\cdot}7$, $\alpha'=13{\cdot}8$ (for atoms heavier than C,O,N larger values of R_m and R_M should be used to correspond to their larger van der Waals radii). It must be emphasized that no information concerning the existence (or non-existence) of a hydrogen bond between given pairs of atoms is introduced *a priori*.

(e) Very short-range interaction

The dispersion energy $-A/z^6$ and the polarization energy tend to $-\infty$, as $-1/R^6$ when R goes to zero, so that the use of (2) and (4) at a very short distance would result in an enormous spurious attraction. Theoretically, these contributions should go to finite limits when R goes to zero, while the repulsion term should go to $+\infty$ as $1/R$ (the nuclear repulsion becoming predominant). Now, such very short distances may actually occur in the course of minimization processes, and it is therefore necessary to modify the formulae in an appropriate way. We define a critical value z_c corresponding to the first inflexion point (vanishing of second derivative) of the curve $-A/z^6+Ce^{-z}$ (Fig. 3). Then, for $z<z_c$, we use (1) $(a_dz^2+b_d)$ instead of $1/z^6$ (with $a_d=-3/z_c^8$ and $b_d=4/z_c^6$); (2) $(a_r/z+b_r)$ instead of $\exp(-\alpha z)$ [with $a_r=\alpha z_c^2\exp(-\alpha z_c)$ and $b_r=(1-\alpha z_c)\exp(-\alpha z_c)$]; (3) for the electric field $(\mathbf{R}/R)/R^2$ involved in the polarization energy, we put

$1/R^2 = 1/(R_{ij}^0 z)^2$, and we use $(a_p z^2 + b_p)$ instead of $1/z^2$ (with $a_p = -1/z_c^4$ and $b_p = 2/z_c^2$).

All these very short-range expressions were defined so as to ensure the continuity of the functions and their first derivatives at the critical value z_c.

The total lattice energy is calculated from these intermolecular potentials as indicated in Caillet & Claverie (1974, 1975).

3. Results and discussion

The methodology adopted in the present case consisted of applying the program for calculating the minimum energy of a crystal as described above for three different conformations of adrenaline, with different parameters for the crystal cell or for the positions of the molecules in the cell.

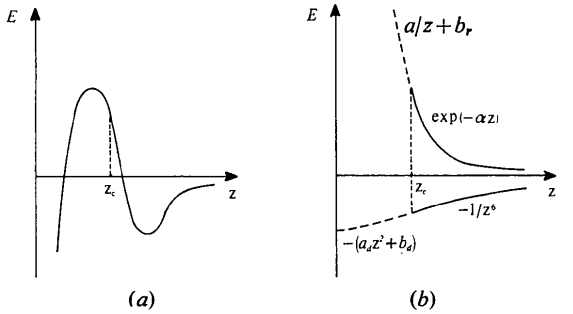
(*a*) '*Planar-trans*' *conformation* ($\tau_1 = 0$, $\tau_2 = 180°$)

For the first evaluation of the crystal energy, adrenaline was kept in a conformation very close to the experimental one ($\tau_1 = -3$, $\tau_2 = -179°$).

The initial positions of the adrenaline and tartrate molecules in the cell were the experimental ones (minimization A_1 of Table 1). The purpose of this first calculation was to check the minimization procedure against experiment. We have left the molecule free to move in a crystal cell in which only the angular cell parameters (α, β, γ) are kept constant. In this case, the minimum energy is evaluated to be $-201{\cdot}2$ kcal mol^{-1}. The molecules are only slightly displaced by an angle of rotation of 8–9° with respect to their experimental position in the crystalline surroundings. The cell parameters found at the end of the minimization are also very close to their initial experimental values (Table 1). The theoretical method thus satisfactorily matches the experimental geometry.

(*b*) '*Perpendicular-gauche*' *conformation* ($\tau_1 = -90$, $\tau_2 = -60°$)

A second evaluation of the crystal energy has been made with the torsion angles of adrenaline correspond-



(*a*) (*b*)

Fig. 3. The modification of the atom–atom potential at very short distances. (*a*) The curve $-A/z^6 + C\exp(-\alpha z)$. (*b*) The modified curves (---) for dispersion and repulsion for $z < z_c$. The value z_c corresponds to the first inflexion point of the curve (*a*).

Table 1. *Results of the minimization of the lattice energy for three conformations of adrenaline and comparison with the conformational energy of the isolated molecule*

All energies are expressed in kcal mol^{-1} of the complex: adrenaline + tartrate. The direction cosines of the rotation axes and the translations are given with respect to an orthonormal coordinate system defined from the lattice cell **a**,**b**,**c**. Since these vectors are orthogonal in the case under study, the unit vectors defining the coordinate system are simply **a**/*a*,**b**/*b*,**c**/*c*. The reference positions chosen for the tartrate and the aromatic ring of the adrenaline are the experimental ones. The lengths are expressed in Å and the angles in degrees (°).

	Adrenaline		Tartrate
Conformation A_1 ($\tau_1 = 0°$, $\tau_2 = 180°$), experimental minimum			
Cell parameters		$a = 7{\cdot}6$	
		$b = 25{\cdot}6$	
		$c = 7{\cdot}08$	
Rotation angle	9·0		7·85
Rotation axis	−0·81		−0·92
	−0·53		−0·37
	0·23		0·12
Translations	0·06		0·18
	−0·61		−0·30
	0·34		0·75
Conformation A_2, second minimum			
Cell parameters		$a = 7{\cdot}16$	
		$b = 26{\cdot}37$	
		$c = 8{\cdot}40$	
Rotation angle	18·37		38·77
Rotation axis	−0·97		−0·97
	0·14		−0·016
	−0·21		0·22
Translations	1·38		1·31
	0·28		−0·73
	−4·35		0·29
Conformation B_1 ($\tau_1 = -90°$, $\tau_2 = -60°$)			
Cell parameters		$a = 7{\cdot}4$	
		$b = 26{\cdot}8$	
		$c = 7{\cdot}8$	
Rotation angle	35·3		37·0
Rotation axis	−0·6		−0·92
	0·79		0·21
	0·10		0·32
Translations	0·08		1·12
	0·31		−0·59
	−0·22		4·04
Conformation B_2, second minimum			
Cell parameters		$a = 11{\cdot}68$	
		$b = 17{\cdot}57$	
		$c = 7{\cdot}58$	
Rotation angle	88·31		34·50
Rotation axis	0·57		0·28
	−0·82		0·44
	−0·10		−0·85
Translations	−0·12		2·09
	−2·40		−0·68
	−0·12		−3·82
Conformation C ($\tau_1 = 90°$, $\tau_2 = 180°$)			
Cell parameters		$a = 9{\cdot}68$	
		$b = 17{\cdot}81$	
		$c = 8{\cdot}22$	
Rotation angle	−87·0		81·17
Rotation axis	0·12		0·69
	−0·22		0·11
	−0·97		−0·71
Translations	4·9		0·54
	−4·3		−0·38
	−3·6		−3·6

Table 1 (*cont.*)

Conformation	Total lattice energy	Lattice energy with respect to B_2	Conformational energy with respect to B	Lattice energy + conformational energy with respect to B_2
A_1	−201·2	−15·9	+4	−11·9
A_2	−213·4	−28·1	+4	−24·1
B_1	−175·8	9·5	0	9·5
B_2	−185·3	0	0	0
C	−191·8	−6·5	+3	−3·5

ing to the energy minimum of the PCILO calculation.

Minimization B_1: The initial positions of the molecules are defined by the experimental coordinates for the tartrate and the *aromatic ring* of adrenaline. During the minimization, the variable cell parameters change very little, but the positions of the molecules become very different. The energy minimum amounts to −175·8 kcal mol^{-1} and is thus less favourable than in the previous case.

Minimization B_2: When dealing with such a 'hypothetical' crystal for which no experimental information exists, it is convenient to perform several minimizations with different initial conditions, in order to reduce the probability of finding only a local minimum different from the lowest. The lattice energy corresponding to the initial conditions of the minimization B_1 was highly repulsive (1512 kcal mol^{-1} complex), thus indicating an important steric hindrance and this implies the possibility of the molecules becoming 'geared' together during the minimization, thus arriving at some local minimum and not the deepest one. Therefore, we performed another minimization with the same initial coordinates of the complex (from which all others are deduced by symmetry operations and translations), but with enlarged initial cell parameters ($a=11$, $b=32$, $c=10{\cdot}5$ Å). The initial value of the lattice energy is now −60·5 kcal/mol complex, a quite reasonable value, which shows that the previous steric hindrance has actually been removed. The final energy obtained is −185·3 kcal/mol complex, *i.e.* about 10 kcal mol^{-1} lower than the result of minimization B_1, which therefore appears as a local minimum (the final positions of the molecules are indeed quite different for B_1 and B_2: see Table 1).

(*c*) *'Perpendicular-trans' conformation* ($\tau_1=90$, $\tau_2=180°$)

The third conformation adopted for adrenaline corresponds to a local energy minimum of Fig. 2 with the side chain perpendicular to the aromatic ring but the cationic head *trans* with respect to it. The initial coordinates of the tartrate and of the aromatic ring of adrenaline are the experimental ones. The initial cell parameters are $a=11$, $b=32$, $c=10{\cdot}5$ Å. We employed such an enlarged cell in order to avoid the occurrence of steric hindrance when using the initial positions defined above. The minimization leads to a lattice energy of −191·8 kcal mol^{-1} which is thus intermediate between A_1 and B_1 or B_2.

(*d*) *Minimization* A_2

In order to check the validity of the minima calculated for the two last 'crystals' obtained with input conformations of adrenaline different from the experimental, we have performed a minimization for the near experimental conformation ($\tau_1=0$, $\tau_2=180°$) but starting with initial positions of the tartrate and of the aromatic ring of adrenaline corresponding to the minimum obtained for the theoretically most stable 'perpendicular-*gauche*' conformation ($\tau_1=-90$, $\tau_2=-60°$) and with enlarged cell parameters: $a=11$, $b=32$, $c=10{\cdot}5$ Å to allow an easy reorientation of the molecules. With a starting energy of −96·35 kcal mol^{-1}, we have obtained after minimization an energy of −213·4 kcal mol^{-1} associated with positions for the two molecules much closer to the experimental ones than the initial ones (rotation of 39° for the tartrate molecule and of 18° for the adrenaline molecule: see Table 1).

Nevertheless, the minimum thus found has to be considered as different from the 'experimental' one, found in calculation A_1 by starting from the experimental positions. The occurrence of such a 'non-experimental' minimum has already been noticed previously for nitrobenzene (Caillet & Claverie, 1975), and this phenomenon is probably quite general with complex molecules. Regarding the fact that the 'experimental' minimum is not the lowest in the present case, there may be a number of (mutually non-exclusive) explanations:

(1) systematic defects in the theoretical potential;

(2) preference for the 'experimental geometry' in micro-crystals, which would be kept when the crystal grows;

(3) the entropy term $-TS$ in the free energy expression $A=E-TS$, which could favour the 'experimental' geometry.

In Table 1 we have collected the different results and computed the energy differences with respect to the results corresponding to the theoretically most stable free conformer, 'perpendicular-*gauche*' ($\tau_1=-90$; $\tau_2=-60°$). In the column 'Conformational energy with respect to B', we indicate the energy difference corresponding to the isolated adrenaline molecule calculated by the PCILO method (Pullman, Coubeils, Courrière & Gervois, 1972). The last column corresponds to the sum of columns 'Lattice energy with respect to B_2' and 'Conformational energy with respect to B' and indicates that the stabilization due to the lattice energy of the crystal of conformer A is appreciably larger than the destabilization of the isolated molecule in the same conformation.

4. Conclusion

The present computations provide a quantitative explanation for the 'unusual' conformation adopted for adrenaline in the crystal of its hydrogen tartrate complex in terms of the strong stabilization of the crystal lattice which overcomes by far the loss of conformational energy with respect to the theoretically most stable conformer of the free molecule. Conceptionally the situation is thus analogous to that encountered in our previous study of the effect of the crystal environment on the stacking pattern of adenines (Caillet & Claverie, 1974): namely, the optimal geometry of the *isolated* subunit [binary complex in Caillet & Claverie (1974) or the free molecule in the present case] need not necessarily be identical to the optimal geometry in a crystal, corresponding to the interaction of such subunits. These examples stress the necessity of explicitly taking into account environmental factors in cases in which the experimental results are at variance with predictions referring to free molecules and show also the possibility of arriving at an agreement between the two aspects with the presently available methodologies and computational techniques.

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The Crystal Structure of *O*-Ethyl *S*-(11-Carboxyundecyl)dithiocarbonate

BY JONAS ABRAHAMSSON AND ROBERT PEARSON

Department of Structural Chemistry, Faculty of Medicine, University of Göteborg, Fack, S-400 33 *Göteborg* 33, *Sweden*

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O-Ethyl *S*-(11-carboxyundecyl)dithiocarbonate ($C_{15}H_{28}S_2O_3$) is triclinic ($P\bar{1}$) with $a=7{\cdot}534$, $b=4{\cdot}797$, $c=25{\cdot}304$ Å, $\alpha=90{\cdot}83$, $\beta=90{\cdot}72$ and $\gamma=79{\cdot}71°$. The bond distances and angles agree very well with those reported earlier for the homologue with a shorter carbon chain (C5). The conformations are also very similar in the two compounds. The ethyl end of one molecule just reaches S(2) of a neighbouring one. This results in a packing with only small regions of lateral hydrocarbon chain packing. The chain arrangement cannot be described by any known subcell.

Introduction

In a previous report from this laboratory the crystal structure of a hexanoic acid with an ethyldithiocarbonate group in the ω position was described (HES) (Abrahamsson & Innes, 1974). The present study has been undertaken to make possible a comparison with a homologue with a longer hydrocarbon chain, *i.e.* dodecanoic acid (DOS).

Crystal data

$C_{15}H_{28}S_2O_3$, triclinic, $a=7{\cdot}534$ (6), $b=4{\cdot}797$ (4), $c=25{\cdot}304$ (14) Å, $\alpha=90{\cdot}83$ (4), $\beta=90{\cdot}72$ (4), $\gamma=79{\cdot}71$ (4)°, $V=899{\cdot}57$ Å^3, M.W. 320·52, $Z=2$, $D_c=1{\cdot}18$,