CHEMISTRY LETTERS, pp. 711-714, 1990. © 1990 The Chemical Society of Japan

The Potential Energy Calculation for Conglomerate Crystals

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The potential energy calculation for the hypothetical crystal structures of two chiral salts was carried out by using the program WMIN. The calculation revealed that the most stable structure of the chiral salts belonged to the space group $P2_12_12_1$, which was in agreement with the real structure.

Some chiral amines can be transformed from racemic compounds into conglomerates when they are converted into salts with an achiral acid. We have discussed the structural relationship between the chiral amines and achiral acid in these systems.[1,2] In order to predict the structure of an achiral acid suitable for the transformation of a chiral amine into a conglomerate salt, a quantitative evaluation of the potential energy for hypothetical racemic compound and conglomerate crystals should be effective. After Kitaigorodsky had proposed a simple potential,[3] many calculations[4] have been applied in the field of structural chemistry, particularly in the aid of X-ray analysis. The potential energy of crystal system can be evaluated by using this potential calculation. When a compound, of which the crystal structure is unknown, is taken, hypothetical crystal structures may be made up, and their potential energies may be calculated. Among them, the hypothetical structure with the lowest potential energy may represent the real structure, because the real structure should have the lowest energy.

In this paper, we wish to report the potential energy calculation of two conglomerate salts by using the program WMIN[5] as a fundamental approach for the prediction of an achiral acid, which can transform a chiral amine into a conglomerate salt.

All the computations were carried out on HITACHI M-680H and M-682H computers in the Computer Centre of the University of Tokyo. The program WMIN[5] was used for all the potential energy calculations. The following atom-atom non-bonded potential was used for the calculation.

$$V_{ij} = \frac{q_i q_j}{r_{ij}} - \frac{A_{ij}}{r_{ij}^{6}} + \frac{B_{ij}}{r_{ij}^{12}}$$

where q represents the point charge on each atom, r represents the distance between two atoms, and A and B represent constants taken from the reference.[6]

The molecules in the crystal were treated as rigid through all the potential energy calculations.

At first, in order to evaluate the usefulness of the calculation, we calculated the potential energy of a few racemic compounds. Usually, the optically pure form of racemic compounds crystallizes in a different space group from that of their racemic modifications. The structural analysis of some racemic compounds in both racemic modification and optically pure form has been reported. For example, optically pure alanine, trans-1, 2-

cyclohexanedicarboxylic acid, and valine crystallize in the space group of $P2_12_12_1$,[7] $P2_1$,[8] and $P2_1$,[9] respectively, whereas their racemic modifications crystallize in $Pna2_1$,[10] $C2/c$,[11] and $P2_1/c$,[12] respectively. The potential energy calculations for these compounds were performed by using coordinates of X-ray structural analysis reported.

It is known that the crystal energy has to be used in order to compare the energy of a racemic compound crystal with that of a conglomerate crystal.[13] In the cases mentioned above, the crystal energy of the racemic modifications should be lower than that of the optically pure forms. The results on the calculation for the crystal energy are listed in Table 1.

Table 1 shows that each racemic modification has lower energy than its optically pure form. The result is in good agreement with the fact that these compounds are racemic compounds. Then, this calculation method is considered to be applicable to the comparison of the hypothetical crystal structures of chiral compounds.

Table 1. The crystal energy calculation of racemic compounds

Compound	Space group	Energy / kcal·mol^{-1}
Alanine	$Pna2_1$	-48.9816
	$P2_12_12_1$	-47.6217
trans-1, 2-Cyclohexanedicarboxylic acid	$C2/c$	-32.9950
	$P2_1$	-32.9060
Valine	$P2_1/c$	-48.1269
	$P2_1$	-46.8009

In order to calculate the potential energy of the hypothetical crystal structures of an unknown organic salt, the hypothetical crystal structures were built up as follows: MMP2[14] calculation was performed to get the most stable structures of an organic amine and an organic acid, respectively. Then, they were connected with each other by a hydrogen bond with ordinary distance of hydrogen bonding, which is based on reported X-ray analysis data,[1] and the pair was treated as one molecule. The pair was regarded as an asymmetric unit in a hypothetical crystal, and the gravity center of the pair was located at every lattice point, which was led by division of an unit cell along each axis in a constant interval of one tenth.[15] Furthermore, the pair was rotated by the step of 60 degrees around three axis on each lattice point.[15] For all cases, the pair was transformed in an unit cell by symmetry operation(s) of a space group, and a hypothetical crystal (C_n, $1 \leq n \leq 216000 = 10 \times 10 \times 10 \times 6 \times 6 \times 6$), which consists of three neighboring unit cells along each axis, was built. The shortest atomic distance d_n between the pairs in C_n was calculated. The pairs in the crystal with the longest d_n is considered to be least overlapped each other. This crystal structure was used as the initial structure for the energy minimization by the program WMIN.

The potential energies of 1-phenylethylammonium cinnamate and 1-(4-isopropylphenyl)ethylammonium cinnamate, which are known to have a space group of $P2_12_12_1$,1) were calculated for the hypothetical structure, which was determined as mentioned above, by using the lattice constants, *a*, *b*, *c*, α, β, and γ, of X-ray analysis of 1-phenylethylammonium cinnamate. The crystal energies13) are listed in Table 2. The crystal energies are in good agreement with those (with a remark in Table 2) calculated by using each X-ray analysis datum. It should be especially emphasized that the calculation on the potential energy of 1-(4-isopropylphenyl)ethyl-ammonium cinnamate by using lattice constants quite different from actual ones gave a satisfactory result. Furthermore, both of the resulting crystal structures were very close to those of X-ray analysis. Therefore, our method for the construction of a hypothetical structure is considered to be valid.

Next, the potential energies of the hypothetical structures belonged to centrosymmetric space groups were calculated. Organic compounds usually crystallize in limited space groups. For examples, racemic compounds crystallize almost in three space groups, $P2_1/c$, $P\bar{1}$, and $C2/c$.16, 17) Then, the potential energy calculations were carried out for centrosymmetric hypothetical crystals in these space groups. The crystal energies13) are also listed in Table 2. All centrosymmetric crystals have higher energy than noncentrosymmetric one, of which the space group is $P2_12_12_1$. The results are interpreted that the crystals of the space group $P2_12_12_1$ is more stable than those of the space groups, $P2_1/c$, $P\bar{1}$, and $C2/c$, and the result is in good agreement with the fact that the real structures of both salts are conglomerates.

Table 2. The hypothetical crystal energy calculations of conglomerate salts

Salt	Space group	Energy / kcal·mol^{-1}
1-Phenylethylammonium cinnamate	$P2_12_12_1$a)	-145.7912
	$P2_12_12_1$	-146.8862
	$P2_1/c$	-140.1745
	$P\bar{1}$	-126.9491
	$C2/c$	-122.8722
1-(4-Isopropylphenyl)ethylammonium cinnamate	$P2_12_12_1$a)	-151.0279
	$P2_12_12_1$	-152.0704
	$P2_1/c$	-148.5221
	$P\bar{1}$	-139.2070
	$C2/c$	-142.6652

a) Used coordinates of X-ray analysis.1)

The potential calculations of hypothetical crystals can give an information whether a molecule, of which the crystal structure is unknown, crystallizes in centrosymmetric or noncentrosymmetric space group. The information is considered to be valuable for the fundamental approach in the prediction of an achiral acid, which can transform a chiral amine into a conglomerate salt.

The potential energy calculations for some racemic modifications, of which the crystal structures are unknown, is now in progress.

The work was supported by Grant-in Aid for Scientific Research on Priority Areas (Multiplex Organic Systems, No. 01649006) from the Ministry of Education, Science and Culture of Japan.

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(Received January 26, 1990)