
THE EMPIRICAL CONFORMATIONAL SURFACE OF THE Co(ETHYLENEDIAMINE) RING

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The conformational surface of the Co(en) chelate ring was studied by the method of structural correlations. The reduction of dimensionality of the conformation problem was achieved by employing the pseudorotation concept. The empirical potential surface was obtained by statistical treatment of 743 independent conformations from the Cambridge Structural Database. The theoretical potential surface was obtained by molecular mechanics. The minimal-energy conformation is gauche with the Co atom on the two-fold axis. Conformational flexibility also includes an envelope conformation with the N atom bent out of the plane. The transition between the mirror-image symmetrical conformations can occur by a pseudorotation pathway and is accompanied by increased planarity of the ring. The transition state is an envelope conformation with an out-of-plane Co atom.

Development of the method of molecular modelling, based on molecular mechanics, molecular graphics, etc. permits computer design of compounds with predetermined properties¹⁻². As detailed knowledge of the stereochemistry of the individual structural fragments simplifies molecular modelling and decreases the difficulty of the calculation, this work is a study of the stereochemistry of the five-membered ethylenediamine chelate ring which is the basic structural unit in a great many synthetic and natural chelate compounds, in an attempt to obtain a suitable model. Complexes of trivalent cobalt, for which a great deal of experimental data is available, were selected for this analysis. The conformational surface of the Co(en) five-membered ring was mapped using statistical analysis of the experimental data on the conformations in crystal structures. This technique, which is extension of the Bürgi³ and Dunitz⁴ "principle of structural correlations", assumes that the most frequent conformation corresponds to the energy minimum on the Born-Oppenheimer potential surface. The intra- and intermolecular forces in the vicinity of the Co(en) ring act as perturbing forces on the idealized conformation and the frequency of occurrence (probability density) of the individual conformations maps the conformational surface.

Detailed specification of the geometry of a five-membered ring requires either 15 Cartesian coordinates or a set of internal coordinates represented by the bond

lengths, bonding angles and torsion angles. Five deviations of atoms from the mean plane or five torsion angles are usually sufficient for conformational description. A marked reduction in the dimensionality of the conformational problem can be attained by employing the pseudorotational concept⁵⁻⁸. Torsion angles in a general five-membered ring can be described by the equations⁹:

$$\phi_i = c_i \Phi_m \cos(P + 4\pi i/5 + \varepsilon_i), \quad i = 1, 2, 3, 4, 5 \quad (1)$$

in which c_i and ε_i are constants determined by the type of ring (types of atoms, bond lengths and bonding angles), which are dependent on the method of calculation as not all the constants are independent. Φ_m is the amplitude of the ring puckering and P is the phase angle of puckering, characterizing the conformations of the individual rings. Parameters c_i and ε_i are determined by the least squares method from a sufficiently large set of experimental torsion angles^{9,10}. The pseudorotational conformational surface of the five-membered ring has two dimensions and can be depicted by a two-dimensional diagram.

EXPERIMENTAL DATA AND CALCULATIONS

The torsion angle values were obtained from the Cambridge Structural Database. The database was searched on the basis of the molecular fragment (Fig. 1) and the torsion angles were calculated using the GEOM78 program¹¹. From the set of torsion angles were excluded Co(en) rings containing atoms bonded by a double bond (either directly in the ring or in the immediate vicinity, such as complexes of peptides, N,N'-salicylidenedimine, etc., derivatives of pyridine, pyrrole, etc.). In addition, structures with $R > 10\%$ and chelate rings with anomalies (with C-C outside the range 0.150–0.156 nm and C-N outside 0.144–0.152 nm) in their bond lengths were also excluded. Of the total number of 504 structures and 911 rings, a total of 460 crystal structures and 763 Co(en) chelate rings were selected. As the energy of the chelate ring cannot depend on the atom numbering and on the chirality, the following conformations have equal energies:

$$\begin{aligned} E(\Phi_1, \Phi_2, \Phi_3, \Phi_4, \Phi_5) &= E(\Phi_5, \Phi_4, \Phi_3, \Phi_2, \Phi_1) = \\ &= E(-\Phi_1, -\Phi_2, -\Phi_3, -\Phi_4, -\Phi_5) = E(-\Phi_5, -\Phi_4, -\Phi_3, -\Phi_2, -\Phi_1). \end{aligned} \quad (2)$$

The conformational space (e.g. on the pseudorotational ring) has planar mm symmetry (the symmetry of an idealized ring is C_2). Thus a data set of 2972 rings was obtained for statistical analysis.

Constants c_i and ε_i for the Co(en) ring were determined by the CHELAT program¹⁰. Details of the calculation are given in ref.⁹ but the constraints $c_1 = c_5 = 1$ and $\varepsilon_1 = \varepsilon_5 = 0$ were replaced by the constraints due to Díez et al.¹²:

$$2/5 \sum_{i=1}^5 c_i \cos(\varepsilon_i + 4\pi i/5) \cos(4\pi i/5) = 1 \quad (3)$$

$$2/5 \sum_{i=1}^5 c_i \sin(\varepsilon_i + 4\pi i/5) \sin(4\pi i/5) = 1 \quad (4)$$

$$\sum_{i=1}^5 c_i \sin(\varepsilon_i + 4\pi i/5) \cos(4\pi i/5) = 0 \quad (5)$$

$$\sum_{i=1}^5 c_i \cos(\varepsilon_i + 4\pi i/5) \sin(4\pi i/5) = 0 \quad (6)$$

The results are listed in Table I and, for comparison, the constants derived from the bond lengths and angles assuming infinitesimal deviation from the reference geometry^{10,13} are also given. The calculation was carried out using the mean bond lengths Co-N 192.1 pm, N-C 150.5 pm, C-C 153.2 pm and mean bonding angles θ N-Co-N 88.7°, Co-N-C 107.5° and N-C-C 106.8°, normalized so that their sum was 540° ($\theta'_i = \theta_i \cdot (540/\sum \theta_i)$).

In fixing c_i and ε_i , parameters Φ_m and P were calculated for each chelate ring. Their distribution is depicted in Fig. 2. This distribution was also expressed numerically so that the conformational ring was divided into small intervals and the density of the conformation occurrence (probability density) was calculated. A more precise value is obtained for small intervals, while large fluctuations occur at small densities. The distribution is deformed at large intervals (it decreases in the region of the maximum and increases at small values). An interval of 4° (square 16 deg²) was found to be a suitable compromise but further smoothing was necessary at low values. The overall algorithm of the calculation of the probability density was as follows: provided that the conformational occurrence on a square of 16 deg² was greater than 10, the calculated value was retained. When the frequency in the interval was 5–9, the average value for the given square and four neighbouring squares was used. For lower frequencies, the values for 9 squares were averaged.

The probability density was transformed to energy on the basis of analogy with the Boltzmann law,

$$N_i/N = \exp(-E_i/kT) / \sum \exp(-E_i/kT) \quad (7)$$

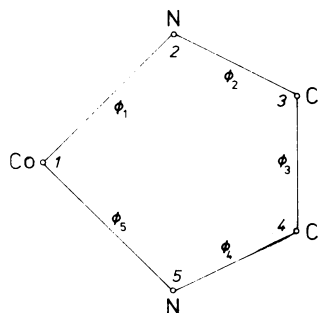


FIG. 1

The molecular fragment of the Co(en) chelate ring and atom numbering

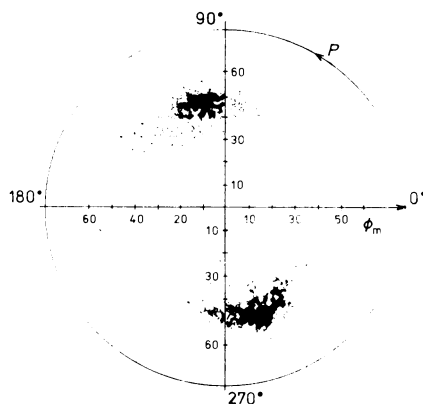


FIG. 2

The conformation wheel for the Co(en) chelate ring. Distribution of experimentally determined conformations

This relationship was modified to

$$q = \exp(-E/U)/c \quad (8)$$

$$\ln q = -E/U - \ln c,$$

where q is the probability density, c is a constant including term $\sum \exp(-E_i/U)$ and normalization of the probability density. U is an undefined constant (analogous to kT , where k is the Boltzmann constant), whose physical meaning is difficult to define, reflecting the character of the deformation forces. The energy scale is normalized by selecting zero energy for the most stable conformation:

$$\ln q_{\max} = 0 - \ln c. \quad (9)$$

The energy is then given by Eq. (10) (when constant U is not known, this is the relative energy):

$$E/U = -\ln q + \ln q_{\max}. \quad (10)$$

The energy conformational surface is depicted in Fig. 3. This surface is approximated by an analytical function. The approximation was based on Eq. (9) of ref.¹⁴, which was modified by the trial-and-error method to yield the best agreement between the calculated and empirical energies. The best agreement was found for the function

$$V(q, \omega) = Aq^3 + Bq^2 + Cq + Dq^3 \sin 2\omega + Eq^2 \sin 2\omega + Fq \sin 2\omega + G, \quad (11)$$

where $q = \Phi_m^2$, $\omega = P - 108^\circ$. The calculation was carried out using 77% of the lowest values of the empirical energy (a total of 228 net lattice points).

The optimized function was limited to 7 parameters. The following parameters were obtained by the method of least squares (standard deviations are given in brackets):

$$\begin{aligned} A &= -5.07 \cdot 10^{-9} (6.504 \cdot 10^{-9}), B = 2.580 \cdot 10^{-4} (0.46 \cdot 10^{-4}), \\ C &= -1.1167 (0.0995), D = 0.272 \cdot 10^{-6} (0.038 \cdot 10^{-6}), \\ E &= -11.992 \cdot 10^{-4} (1.712 \cdot 10^{-4}), F = 1.833 (0.189), G = 1.414.00 (64.62). \end{aligned}$$

The standard error $V(q, \omega)$ is 49.97 (the energy values used for calculation of the parameters lie in the range 0–770). The energies are adjusted on an arbitrary scale so that the probability

TABLE I

The pseudorotational constants c_i (dimensionless) and ε_i (in $^\circ$) for the Co(en) chelate ring. A — Derived from the torsion angles of 743 chelate rings respecting the conformational space symmetry, B — derived from the mean bond lengths and angles

c_i	A	B	ε_i	A	B
c_1	0.9300	0.9499	ε_1	0.0436	-0.4917
c_2	1.0560	1.0421	ε_2	5.1748	3.9365
c_3	1.0367	1.0210	ε_3	0.0	0.0
c_4	1.0560	1.0421	ε_4	-5.1748	-3.9363
c_5	0.9300	0.9499	ε_5	-0.0436	0.4919

density $0.01/16 \text{ deg}^{-2}$ corresponds approximately to an energy value of 1 000). The correlation coefficient is 0.965 (0.017).

In order to evaluate the suitability of Eq. (10) for transformation of the probability density to energy, the potential surface was calculated by molecular mechanics. The MBLD88 program was used in the calculation (a modernized version of the program formed by combination of the MOLBLD4¹⁵ and MBDL¹⁶ programs). The potential fields and model for $[\text{CoCl}_4(\text{en})]$ were taken from DeHayes and Busch¹⁶. The program was modified so that it was possible to fix the torsion angles given by the pseudorotational parameters Φ_m and P by the "DRIVE" method of Wiberg and Boyd¹⁷ and so that the pseudorotational parameters between the individual parameters change continuously with no sudden change in conformation (movement in an approximate spiral along a pseudorotational surface starting from the conformation corresponding to the energy minimum). The potential surface is depicted in Fig. 4. The extreme conformations were optimized independently. The conformation with the minimum energy has $\Phi_m = 52.3^\circ$, $P = -72^\circ$ and $E = 2.34 \text{ kJ mol}^{-1}$. For the planar conformation $\Phi_m = 0$, where P is not defined, $E = 38.97 \text{ kJ mol}^{-1}$ was calculated and, for the transition state, ${}^1E \Phi_m = 42.78$, $P = 18^\circ$ and $E = 27.29 \text{ kJ mol}^{-1}$.

In rings with unequal bond lengths, the concepts of envelope and twist conformations lost their original meaning of C_s and C_2 symmetrical conformations as defined for cyclopentane. Thus a more general definition will be introduced (conformations C_2 and C_s are special cases). An envelope conformation is a conformation in which one torsion angle equals zero:

$$\theta_i = 0 \Rightarrow \cos(P + 4\pi i/5 + \varepsilon_i) = 0. \quad (12)$$

On the other hand, a twist conformation is a conformation in which the torsion angle attains the maximal value on the pseudorotational pathway:

$$\Phi_i = \max \Rightarrow \cos(P + 4\pi i/5 + \varepsilon_i) = \pm 1. \quad (13)$$

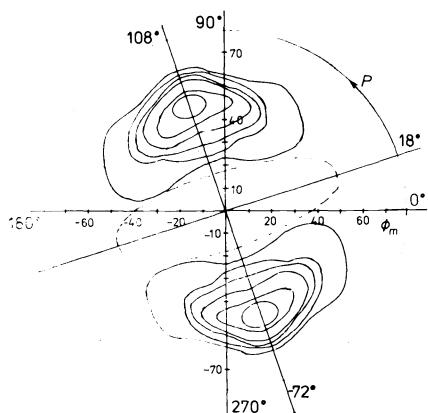


FIG. 3
The empirical potential surface for the Co(en) chelate ring. The energy values are on an arbitrary scale

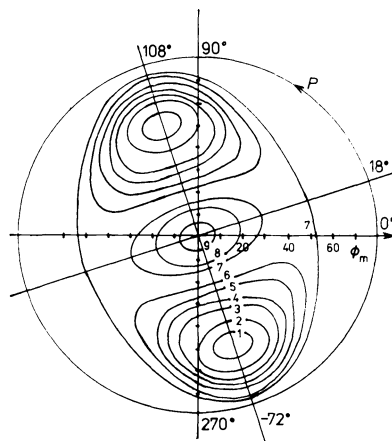


FIG. 4
The molecular-mechanical potential surface for the Co(en) chelate ring. The energy values are given in kJ mol^{-1}

The phase angle values corresponding to these extreme conformations plotted together with the conformational symbols on the conformational ring (adopted from ref.¹⁸) is used as reference nomenclature for the ring for assignment of the individual conformations and the absolute conformation¹⁹. For example, representation ${}_1E$ is related to the conformation in which atoms 2, 3, 4 and 5 lie in the plane and atom 1 lies below the plane. Symbol 1E refers to the conformation with atom 1 above the plane. Symbol 1_5T designates the "symmetrical" twist conformation with atom 1 above and atom 5 below the plane formed by atoms 2, 3 and 4. Symbol ${}_2T^3$ designates the "asymmetrical" twist conformation in which the deviation of atom 2 from the plane is greater than the deviation of atom 3. The borderline between conformations δ and λ (ref.¹⁹) corresponds to envelope conformations ${}_1E$ and 1E (envelope Co). The ring nomenclature is depicted in Fig. 5.

DISCUSSION

The pseudorotational concept in the torsion angle space, generalized for rings with unequal bond lengths has been found to be useful for description of the conformation of the Co(en) chelate rings in spite of the fact that actual pseudorotation was not found in this ring. The torsion angles calculated from the two parameters Φ_m and P are reproducible with a mean error of $[\sum_{i=1}^5 (\Phi_i^o - \Phi_i^c)^2 (5 - 2)]^{1/2} 0.61^\circ$ (Φ_i^o is the observed and Φ_i^c the calculated value), which is comparable with the experimental error in the determination of the torsion angles by X-ray diffraction. The greatest lack of agreement (maximal error 2.45°) was found for very strained rings with high Φ_m value, which could be a result of the fact that the pseudorotational equation was derived for infinitesimal deviation from the planar conformation (e.g. for the more planar Co(Gly) rings, the mean error is 0.37° , ref.²⁰).

Parameters c_i and ε_i calculated both from the set of experimental torsion angles and from the approximation to planar conformation are in good agreement. The

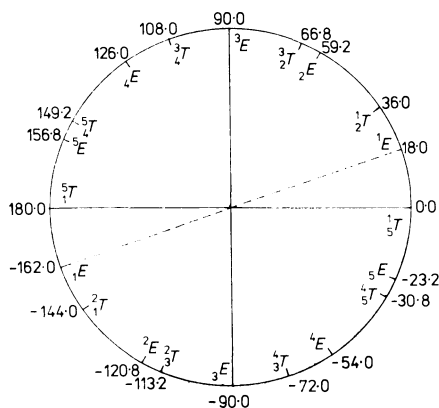


FIG. 5
The nomenclature for the Co(en) chelate ring

ε_i values produce a shift in phase angle P for the idealized conformation from the multiple of 18° that is typical for rings with identical bond lengths. In spite of the fact that a nomenclature ring must be drawn up in conformation determination, nonetheless the torsion angle method has obvious advantages over the method of Cramer and Pople⁶.

The probability density map indicated that the conformation of the Co(en) ring lies in two enantiomeric conformational ring regions. For symmetry reasons, the conformation with minimum energy has a phase angle of $P = 108^\circ$ (or -72°). The maximum probability density was found for $\Phi_m = 49.3^\circ$. The most stable conformation can be described by the symbols 3_4T and 4_3T . The Co(en) ring has a certain flexibility. The probability density half-width is 25° (measured on P at constant Φ_m) which also includes envelope conformations 3E and 4E or 3E and 4E . Atypical conformations are found for fused chelate rings, e.g. 1,4,7,10-tetraazacyclodecane and N,N,N',N'-tetrakis-(2-aminoethyl)-2,4-pentanediamine with $\Phi_m = 57^\circ$ or phase angle $P = -5^\circ$ (1_5T conformation).

The empirical and molecular mechanical potential surfaces are qualitatively and, to a considerable degree, also quantitatively similar. Thus, at least to a first approximation, Eq. (10) can be used for transformation of the probability density to energy in the rather complicated crystalline state and, in the rather large statistical set, the various intra- and intermolecular (lattice) forces can be considered independent. In contrast to Boltzmann statistics, U cannot be considered to be temperature-dependent. Constant U can be considered to be the mean deformation energy. The value of U will depend on the dominant type of crystal cohesive forces (ionic or van der Waals crystals).

The empirical potential surface tends to have a "triangular shape" and the difference in the energy minimum positions can be a result either of the imperfection of the force field in molecular mechanics or of the systematic effect of condensed five-membered chelate rings that predominate in the data set and the effect of substituents.

The two stable conformations are separated by an energy barrier. Conformation transition can occur by a pseudorotation pathway after partial increase in the planarity of the ring. The transition state is an envelope conformation in which the Co atom lies outside the plane of the other four atoms.

Comparison of the molecular mechanical and empirical surfaces permits (very approximate) enumeration of constant U in Eq. (10), yielding a value of 5 kJ mol^{-1} (the kT value for normal temperature is 2.5 kJ mol^{-1}). This high value indicates an important participation of the intramolecular energy in the overall deformation energy. From the point of view of this work, the recent discussion of the possibility of obtaining quantitative energy relationships from structural parameters²¹ seems unnecessarily pessimistic.

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