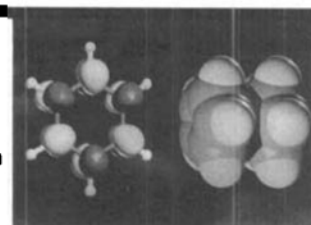


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- [9] A. Niederhauser, G. Bart, M. Neuenschwander, *Helv. Chim. Acta* 1973, 56, 2427.
- [10] M. Neuenschwander, U. Lienhard, H.-P. Fahrni, B. Hurni, *Helv. Chim. Acta* 1978, 61, 2428.
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- [16] Übersichtsartikel vgl. E. Negishi, *Pure Appl. Chem.* 1981, 53, 2333; H. Felkin, G. Swierczewski, *Tetrahedron* 1975, 31, 2735.
- [17] Vgl. z.B. F. Wudl, S.P. Bitler, *J. Am. Chem. Soc.* 1986, 108, 4685; V. Ratovelomanana, G. Linstumelle, *Tetrahedron Lett.* 1981, 22, 315; E. Negishi, N. Okukado, S.F. Lovich, F.-T. Luo, *J. Org. Chem.* 1984, 49, 2629.
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A Simple Procedure for Exploring the Conformational Possibilities of Flexible Molecules

Roman Eminger and Silvio Fallab*

During the last decade molecular mechanics has become a popular tool for structurally orientated chemists which fruitfully complements experimental methods. It can either be used to estimate relative internal molecular energies or to predict the structure of unknown species. In both cases, some starting structure which may be derived from experimental data must be optimized by minimizing an energy function of a number n of variables p_i , either cartesian atomic coordinates or internal molecular coordinates such as torsional angles.

Since even for small n and for moderately sized molecules such functions $E = f(p_1, p_2, \dots)$ have extraordinarily large

numbers of minima, the results of the seemingly straightforward procedure must always be interpreted with caution. Pictorially speaking, it means finding the lowest spot in a wildly fissured mountainous landscape where each small hole represents a local minimum. How can one know, whether the minimum found is the global one, and whether its coordinates correspond to the 'best' structure? A different starting geometry may have led to an even lower minimum.

This multiple-minimum problem has been the topic of various research groups in recent years. Apart from locating the most stable form of a molecular system, it is often desirable to evaluate as well the geometries and energies of other less stable configurations or conformations. The strategies which have been developed to explore potential-energy hypersurfaces of molecular systems can be divided into two broad categories: *i*) deterministic searches in which the degrees of freedom are varied systematically by cho-

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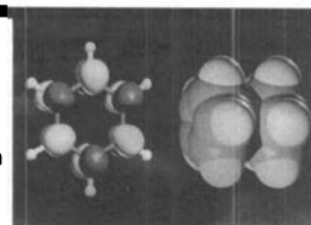
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search runs. Since the objective of a conformation search is not only to detect some low-energy forms but also to make conformation sampling as complete as possible, the main problem – as in all stochastic procedures – lies in estimating search convergence.

A different kind of random search method, known as the ellipsoid algorithm, can be employed to find conformations which satisfy certain molecular constraints, e.g., experimentally derived distance constraints. *Billeter et al.* have first applied it to the determination of peptide conformations [4]. Starting from a randomly chosen set of dihedral angles, low-energy conformations could be predicted efficiently by defining the structure determining H-bonds in terms of distance constraints for the N- and O-atoms involved. The method has also been successfully applied to cyclic molecules. By simply requiring interatomic distances to be larger than the respective sum of the *van der Waals* radii, a number of new 18-crown-6 conformations have been found [5]. This new search procedure, however, is predominantly aimed at the global minimum or – as in the case of peptides – at a specific structure type rather than at the complete set of low-energy conformations. A special case of deterministic search applicable to macrocyclic molecules has been published by *Müller* and coworkers [6]. Their algorithm is based on an approximate *Fourier* representation of the atomic coordinates of the ring.

Virtually all deterministic and stochastic methods published so far are based on the variation of the starting geometry. We wish to report an entirely different procedure for exploring the conformational space of a flexible molecular system. Instead of changing the starting geometry in each run, we vary the optimizing tool. As the well known SIMPLEX minimizer and the ellipsoid algorithm mentioned above, PATTERN MOVE (= PM), a somewhat related procedure suggested by *Hooke* and *Jeeves* [7] may be used to avoid trapping in undesirable local minima. One by one, the variables, e.g. torsional angles, are modified by a user chosen increment, which in the beginning of the process must be large enough to overcome every conceivable energy barrier. If the incremented parameter yields a lower energy, the conformational change is immediately carried out and the successful increment is stored. At the end of these single parameter changes, an additional 'pattern move' corresponding to the sequence of successful increments is performed. In the next cycle, the increment is reduced by an appropriately chosen factor. In optimization experiments with metal complexes [8], PM showed a much better convergence behaviour than SIMPLEX.

In contrast to the SIMPLEX method, the regions of conformation space covered by the PM algorithm not only depend on the increment chosen, but also on the order in which the variables are modified. Our search

method is based on this special property of PM. By randomly changing parameter sequences, quite different energy minima corresponding to chemically relevant conformations are found. To show that the new procedure which will be referred to as PMPP (*Pattern Move Parameter Permutation*), can be successfully used for conformational search purposes, two applications to different classes of molecular systems are described: 1) cycloalkanes and 2) metal complexes of flexible multidentate ligands.

1. *Cyclooctane* has been chosen as a test molecule because of its high number of symmetrical conformers well documented either by molecular mechanics methods [9] or *ab initio* calculations [10]. Of the 10 symmetry types discussed by *Hendrickson* [11], 7 are easily detected by PMPP: C_s , C_2 , D_2 , D_{4d} , C_{2v} , D_{2d} , S_4 . Our search procedure did not produce C_{2h} which, according to *Ferguson* and *Raber* [9], is not existent. Both of the remaining two have a symmetry plane intersecting a C–C bond, which would imply an energetically unfavourable zero dihedral angle. In each search run, PM optimization starts with the same planar zigzag C_8 chain. The energy function to be minimized consists of 3 terms: *i*) u_{nc} representing the sum of noncovalent atomic interactions, *ii*) u_t the torsional strain of 8 CC–CC fragments and *iii*) u_r an artificial potential ensuring ring closure of the C_8 chain. The C–C–C bond angle and the C–C bond length were fixed at mean values found in medium ring size cyclic hydrocarbons, 115° and 154 pm, respectively. The CC–CC torsional barrier was set to 10 kJ [12].

Practically every search run results in a well defined conformer. Energy convergence at the level of 0.001 kJ is reached after 60–80 PM cycles. The original rotational increment of 190° applied to the open zigzag chain was reduced by a factor of 0.6 after each cycle. It may be advantageous to split the optimization process into two phases: 1) a rough sampling phase in which the ring is formed under a reduced set of energy constraints and 2) final energy minimization including all the terms. When using the

complete function in the first phase, only 6 of the symmetry forms enumerated above are produced. The highly symmetrical D_{4d} and D_{2d} conformers are found only when all the H-interactions are omitted, and extended atom parameters are used for the methylene groups. In this way, early entanglement of the artificially stiff C–H bonds is prevented.

When a D_{4d} conformation generated in the absence of H-interactions is subjected to final energy minimization, the result is very sensitive to the PM parameters used. D_{4d} symmetry is retained only if the rotational increment Δ tor is small, e.g. 1° . At larger values of Δ tor, depending on parameter sequences, the C_{2v} or the D_2 conformer is formed which points to a shallow minimum for the D_{4d} structure.

The energies of D_{4d} , D_2 , C_{2v} , and C_s geometries are all within 4 kJ of the global minimum thought to be represented by C_s . The C_2 , S_4 , and D_{2d} forms are somewhat higher in energy: 6, 47, and 48 kJ, respectively. Our results are in good agreement with earlier molecular-mechanics studies [9] as well as with *ab initio* calculations [10]. In addition to the structures reported in the literature [11], our search procedure revealed the existence of a C_i - and a second C_2 -conformer whose energies are 41 and 78 kJ, respectively, above the global minimum. Whether these new minima correspond to stable molecular systems is uncertain, however.

In principle, the method can just as well be applied to larger systems. Without attempting an exhaustive search, the same kind of optimization experiments were carried out with C_{16} - and C_{17} -alkanes. Cycloheptadecane has been the object of a recent publication, in which different search procedures were compared [13]. The main difficulty lies in the enormous number of conformers which must be analyzed and compared. In the case of cyclohexadecane, each of the first 130 runs produced a new conformer with an energy varying over 120 kJ above the minimum found in this limited search. 15 among them had either a plane of symmetry or a C_2 -axis. The lowest in energy

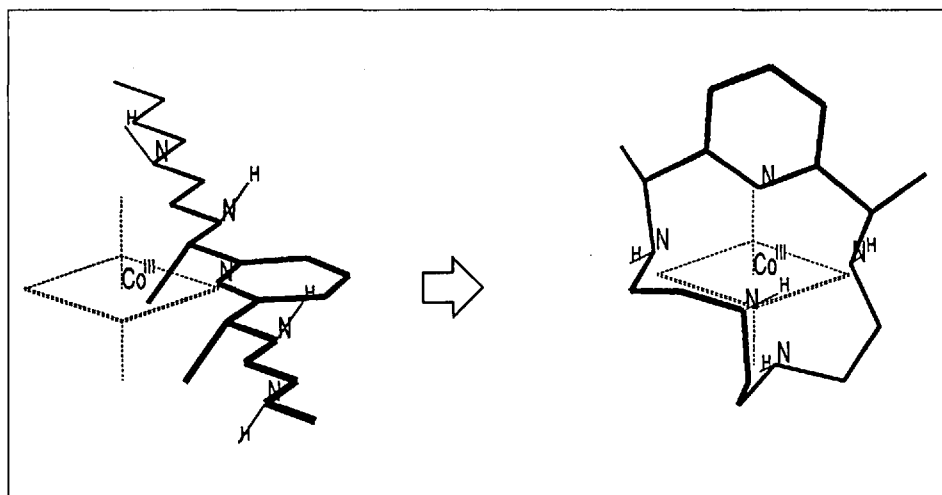


Fig. 1

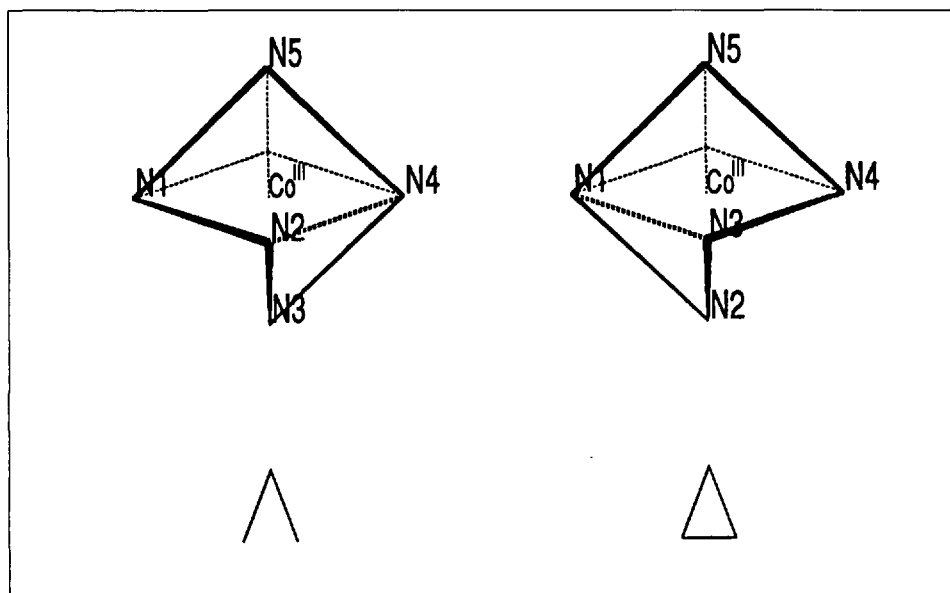


Fig. 2

was a C_1 -conformer. The highest symmetry found was D_2 with an energy of 100 kJ above the minimum.

2. A pentaazacyclopentadecane-cobalt(III) complex, the structure of which has been reported by Drew *et al.* [14], was chosen to demonstrate the applicability of PMPP to an entirely different class of molecules. Optimizing coordination spheres requires an additional set of geometric constraints. Depending on the nature of the metal centre, ligand atoms must form a specific polyhedron. As reflected by the large variability of bond lengths and bond angles at metal centres, the geometry of a coordination sphere is not as well defined as the covalent framework of an organic molecule. This justifies the different treatment of coordinate bonds: ligands are considered as independently floating entities constrained to optimal positions by a penalty function u_{ml} , which takes the specific strengths and the geometrical factors of M-L bonds into account. Parameters for this kind of force field, which is based on a program devised for modeling metal-proteins [15], have been optimized using a series of low-molecular-weight complexes, in which steric ligand-ligand

interactions are important [8]. Ligand bond lengths and bond angles remain fixed at average values observed in X-ray studies of crystallized complexes. The total energy to be minimized in this case consists of 4 terms: u_{nc} , u_t , u_r , and u_{ml} and the parameter list is enlarged by 6 variables for global translation and rotation of each independent ligand. The optimization process starts at an artificial high energy structure in which the ligand forms an open zigzag chain (Fig. 1). The outstretched conformation leads to a high u_r as well as a high u_{ml} . The best results were obtained when noncovalent interactions were omitted completely from the sampling phase. Ca. 40% of the search runs are trapped in chemically meaningless local minima. Only those structures which showed reasonable coordination of the pentadentate ligand were subjected to final energy minimization using the complete function.

Before discussing the results and comparing them to the experimental, some stereochemical considerations are appropriate. Because of the strong preference of Co^{III} for octahedral coordination, topologically speaking there is only one way for the pentadentate ligand to wrap around the metal

centre. It must be shaped as a more or less deformed square pyramid, and the N-atom must be *cis*-oriented to the unoccupied site. Considering the different chemical nature of the coordinated groups, the square pyramid can exist in two enantiomeric forms (Fig. 2).

Independent of the coordination geometry the cyclic pentaaza ligand (L = 2,13-dimethyl-3,6,9,12,18-pentaazabicyclo-[12.3.1]octadeca-1(18),14,16-triene) can itself exhibit several configurations, because each of the secondary-amine N-atoms, when coordinated, is an asymmetric centre. From the topological symmetry of the molecule, it can easily be deduced that seven distinct nonenantiomeric combinations can be constructed. Not all of them, however, may be sterically possible and molecular-mechanics experiments should indicate which of them are the most probable.

During the final energy minimization phase, a chloride was fixed in the sixth coordination site at a distance of 230 pm. Referring to the Λ configuration of Fig. 2, only the [N1, N2, N3, N4]-configurations *SRRS* and *SRRR* proved to be chemically feasible. All the other possibilities led to energies far above the minimum, pointing to incomplete or unsatisfactory coordination. Obviously, configurations at secondary amino groups occupying the central position of a facial fragment are of prime importance. The N4-configuration has only a minor influence on the overall energy.

Since each of the N-H bonds can, in principle, point toward the empty position or away from it, the number of theoretically possible stereoisomers will be doubled. Our search algorithm does not allow inversion at the chiral centres and, therefore, all these steric possibilities have to be tested separately.

Regardless of the chirality induced by the coordinate bonds, the ligand has two chiral C-atoms. The Me groups can be on the same (*RS*, *SR*) or on opposite sides (*RR*, *SS*) of the pyridine ring. With respect to the chiral metal centre, this gives rise to four diastereoisomeric forms (Fig. 3).

With each of these, a limited number of

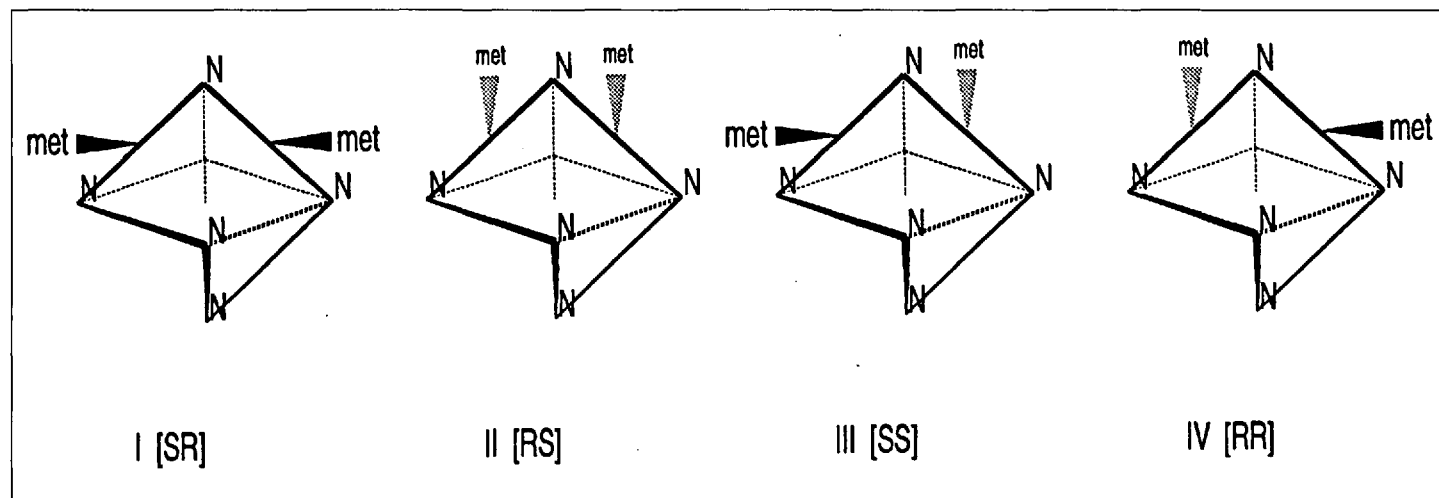


Fig. 3

low-energy structures were located which differ in chelate ring conformation. Those rings which include the pyridine N-atom have a weak envelope conformation with dihedral angles between -10° and $+10^\circ$, whereas the chelate rings $N(1)-N(2)$, $N(2)-N(3)$, and $N(3)-N(4)$ exhibit a pronounced gauche conformation. The global minimum was found with structure II and III. PMPP produced two conformers which differ only by 2 kJ. One of them (Fig. 1) has the same ring conformations ($\lambda\delta\lambda$) as the structure reported [14] which corresponds to the schematic drawing II (Fig. 3). Unfavourable orientation of the Me groups destabilizes structures I and IV by at least 80 kJ.

Conclusions

By using a nongradient minimization method described by Hooke and Jeeves [7] and a simple scheme for randomly shuffling parameter sequences, efficient conformation sampling can be achieved. In contrast to conventional conformation-search procedures, we use the same starting geometry in each run and modify the optimizing tool. To search the entire conformation space, defined in terms of flexible dihedral angles, the

energy must be high in the beginning of the optimization process and a large rotational increment must be applied. Instead of randomly collecting local minima, each PMPP cycle leads to vastly different areas of dihedral angle space. By gradually reducing parameter increments, a high probability of hitting a chemically significant energy minimum is ensured.

The method can be applied to any kind of flexible molecular system. When optimizing coordination spheres, the number of variables is increased by 6 degrees of freedom for each independent ligand molecule. Since optimization is often connected with tight molecular folding, omitting H-interactions in the first phase helps to avoid ligand conformations unfit for coordination. The sampling results are not very sensitive upon variations of bond lengths and bond angles which remain fixed during optimization. Our program is in part based on a general molecular-mechanics program provided by Prof. M. Dobler, ETHZ, which is gratefully acknowledged. It is written in PASCAL and its central part; the energy calculation, in OC-CAM. Computations were done on a workstation *Apollo DN 3000*, powered up by a transputer board with 4 parallel *T 800* processors.

- [1] M. Saunders, *J. Am. Chem. Soc.* **1987**, *109*, 3150.
- [2] D.M. Ferguson, D.J. Raber, *J. Comput. Chem.* **1990**, *11*, 1061.
- [3] G. Chang, W.C. Guida, W.C. Still, *J. Am. Chem. Soc.* **1989**, *111*, 4379.
- [4] M. Billeter, T.F. Havel, K. Wüthrich, *J. Comput. Chem.* **1987**, *8*, 132.
- [5] M. Billeter, A.E. Howard, I.D. Kuntz, P.A. Kollman, *J. Am. Chem. Soc.* **1988**, *110*, 8385.
- [6] P.R. Gerber, K. Gubernator, K. Müller, *Helv. Chim. Acta* **1988**, *71*, 1429.
- [7] R. Hooke, T.A. Jeeves, *J. Ass. Comput. Mach.* **1961**, *8*, 212.
- [8] R. Eminger, S. Fallab, M. Zehnder, M. Dobler, submitted to *Helv. Chim. Acta*.
- [9] D.M. Ferguson, D.J. Raber, *J. Am. Chem. Soc.* **1989**, *111*, 4371.
- [10] K. Siam, O.V. Dorofeeva, V.S. Mastryukov, J.D. Ewbank, N.L. Allinger, L. Schäfer, *J. Mol. Struct.* **1988**, *164*, 93.
- [11] J.B. Hendrickson, *J. Am. Chem. Soc.* **1967**, *89*, 7036.
- [12] F.A. Momany, R.F. McGuire, A.W. Burgess, H.A. Scheraga, *J. Phys. Chem.* **1975**, *79*, 2361.
- [13] M. Saunders, K.N. Houk, Y.-D. Wu, W.C. Still, M. Lipton, G. Chang, W.C. Guida, *J. Am. Chem. Soc.* **1990**, *112*, 1419.
- [14] M.G.B. Drew, S. Hollis, P.C. Yates, *J. Chem. Soc., Dalton Trans.* **1985**, 1829.
- [15] A. Vedani, M. Dobler, J.D. Dunitz, *J. Comput. Chem.* **1986**, *7*, 701; A. Vedani, D.W. Huhta, *J. Am. Chem. Soc.* **1990**, *112*, 4759.

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Comparison of the Performances of the Gaussian and Cadpac *ab initio* Program Packages on Different Computers

Thomas Bally^{a)}*, Pierre-Alain Carrupt^{b)}, and Jacques Weber^{c)}

Abstract. Ten different benchmark tests have been performed for different versions of the *Gaussian* as well as for the *Cadpac ab initio* program package on nine different computers ranging from vector supercomputers to workstations. The test jobs form a set representative of the most frequent applications of *ab initio* quantum chemistry, *i.e.* single point and gradient calculations at the SCF and MP2 levels of theory as well as SCF second derivative calculations for both closed-shell and open-shell species (the molecule of bicyclobutane and its radical cation calculated using the 6-31G* basis set). The relative performances of the different programs and machines exhibit considerable variation as a function of the type of calculation and the present results should prove useful for the selection of the most efficient program and computer for a given application. Notably, modern RISC-based workstations were found to be similar or sometimes even superior in performance to most mainframes for calculations of the type represented by the test jobs.

Introduction

Quantum chemical calculations have undoubtedly become a major component of computational chemistry, with a vast number of applications devoted to a broad range of

compounds and properties [1]. Together with the impressive recent developments in computer hardware, the growing availability of adequate program packages is certainly to a good extent at the origin of this increasing popularity, although the use of these pro-

grams as 'black boxes' is generally not possible.

Among the commonly used quantum chemical models, the *ab initio* techniques occupy an important place, since they attempt to find solutions to the self consistent mean-field (SCF) problem of electronic structure 'from first principles' and subsequently introduce corrections to those by treating the problem of electron correlation by various techniques [2]. In contrast to the so-called semiempirical methods, they are apparently free of parameters although one should of course not underestimate the degree of arbitrariness introduced by the choice of the one-electron basis set in the SCF calculation and the N-electron basis set in post-SCF treatments.

Methodological aspects of the *ab initio* approach to electronic structure theory have recently been outlined in several excellent textbooks [1][3], which also offer guidance as to the best strategy to adopt in calculating different molecular properties with maxi-

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