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## Structural investigations and modeling of cavities in clathrates

Li Pang<sup>a</sup>, Edwin A. C. Lucken<sup>a</sup>, Jacques Weber<sup>a</sup> and Gérard Bernardinelli<sup>b,\*</sup>

<sup>a</sup>Département de Chimie Physique, Université de Genève, 30 quai E. Ansermet, 1211 Genève 4, Switzerland

<sup>b</sup>Laboratoire de Cristallographie, Université de Genève, 24 quai E. Ansermet, 1211 Genève 4, Switzerland

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### SUMMARY

A molecular-graphics study has been performed in order to build and visualize the shape of cavities within different clathrates from X-ray diffraction data [e.g. Dianin's compound, Werner complexes  $\text{Ni}(\text{SCN})_2(3\text{-methylpyridine})_4$ ,  $\text{Fe}(\text{acetylacetonate})_3$  and  $\text{Ni}(\text{ethylxanthate})_2(4,4'\text{-dimethyl-2,2'-bipyridyl})$  complexes]. The algorithm of the solvent-accessible surfaces representation has been applied to a part of the whole crystal structure rather than to isolated host molecules, by using the MOLCAD molecular modeling package. This type of modelization has been found very efficient both to study the shape properties of the host cavities (cage or channel types) and to approach the structural features of the host/guest interactions.

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### INTRODUCTION

Inclusion compounds or, more specifically, clathrates are molecular compounds with two essential components: one is the host molecule which forms a solid lattice characterized by lacunae in which can be included the other, the guest molecule. Since more and more new systems of inclusion compounds have been discovered and their crystal structures have been determined, the recognition of the shapes and sizes of the lacunae is essential to explain or predict whether the geometry of a given cavity is appropriate for the inclusion of a given guest molecule. Although several algorithms have been devoted to the determination of the geometrical parameters of the cavities in clathrates [1,2], a clear and unambiguous visualization of the lacunae in crystals remains a poorly exploited field. We present here such a representation for different clathrates presenting a wide range of cavities (half-full, full, or double-filled cage and channel with one or two independent guest molecules) for which the crystal structures have been previously studied in relation to nuclear quadrupole resonance results [3,4].

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\* To whom correspondence should be addressed.

## MATERIALS AND METHODS

The structural models have been generated using the MOLCAD package [5] running on a Silicon Graphics Iris-4D/70GTB system. The configuration of the workstation is characterized by 80-bit planes, 16 MB of CPU memory and 780 MB of hard-disk space, which makes it an ideal tool for real-time generation and manipulation of space-filling representations or 3D solid models of molecular surfaces. This is specially true for the modelization of the structural features of host lattices such as the clathrates studied in the present work, as clear pictures, obtained using the usual rendering techniques available on such equipment, and subsequent manipulation of the 'molecular' envelope of the host compound are required for visualizing the various cavity sites suitable for guest inclusion.

MOLCAD is an interactive graphics program for building and manipulating several types of molecular models, ranging from skeleton, ball-and-stick and space-filling representations of structures to molecular surfaces (dot, triangulated, 3D solids) and properties, such as molecular orbitals, electrostatic potentials or reactivity indices [6,7]. The main advantages of this package lie in its comfortable user interface designed with pop-up menus and its high-quality graphics capabilities. In our case, a clear and non-ambiguous representation of cavities within the host lattice was indispensable for understanding and rationalizing the host/guest interactions. To this end, we found it most convenient to use molecular models made of an adequately clipped 3D solid Connolly surface [8, 9], simultaneously displaying the ball-and-stick structural model within the molecular envelope. Indeed, in view of the large size of the clathrate models generated, dot- and meshsurfaces are confusing when trying to locate the possible cavities within the structure, and clearly the properly clipped solid surface is a very good solution for displaying the details of molecular volume and steric characteristics of intricate solids compounds, as previously shown by a molecular graphics investigation of zeolites [10]. Although the definition of the molecular surface as a solid model is rather arbitrary by itself, as it is based on the generation of atomic spheres with van der Waals radii, this concept is an important tool for studying molecular recognition problems such as host/guest interactions in inclusion compounds.

The solid surfaces presented here have been obtained, using the Gouraud rendering capability of the Iris, from Connolly envelopes smoothed by a test sphere with a radius defined by the user. To visualize the lacunae inside a molecular structure, the cavities should have at least one open extremity to permit such a test sphere to enter and build up the surfaces, otherwise a part of the molecules must be removed.

## DISCUSSION

The representation of van der Waals surfaces and solvent-accessible envelopes is generally applied in drug design modeling to find an adequate substrate susceptible of being linked to a receptor site of an isolated molecule or protein [11], the cavities being an integral part of the molecule. In the case of clathrates, the cavities are essentially an intermolecular phenomenon where the lacunae are formed through the 3D lattice of host molecules. Thus, the atomic positions of whole or neighbouring unit cells must be generated from those of the asymmetric unit by using the symmetry operations of the space group. The host molecules to be generated should be carefully chosen in such a way as to obtain a clearly visible picture of the cage or channel forms of the cavities.

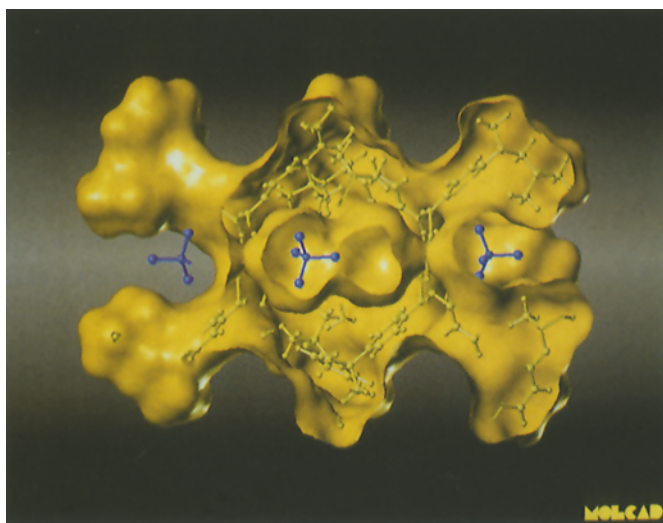


Fig. 1.  $\text{CCl}_4$ /Dianin's compound with a half-filled cage cavity.

It is evident that during the production of an effective cavity surface, the guest molecules should be removed from the surface calculation and subsequently reintroduced to visualize and manipulate the whole structure.

#### *Cage type*

In clathrates where the cavities are entirely surrounded by the host molecules, a cage is formed

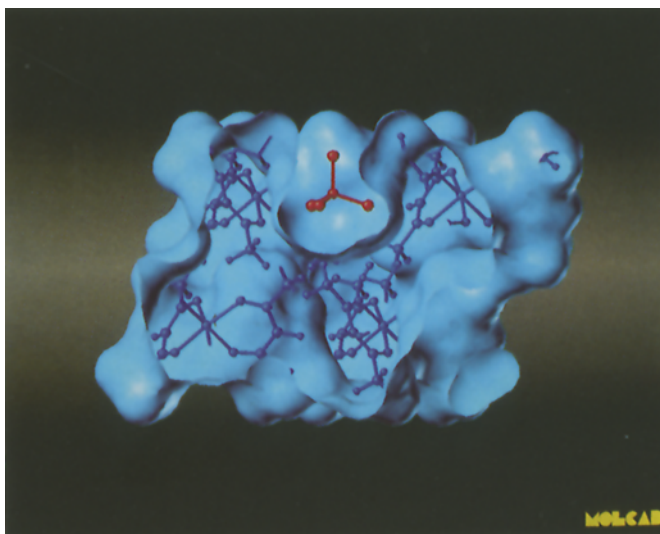


Fig. 2.  $\text{Fe}(\text{acetylacetonate})_3$  complex with one  $\text{CCl}_4$  guest molecule per cavity. The  $\text{Fe}(\text{acetylacetonate})_3$  located at the top of the cage has been removed.

and can be filled by a variable number of guest molecules. The case of Dianin's compound (Fig. 1) shows that only one half of the cage is occupied by a  $\text{CCl}_4$  guest molecule. The hour-glass-shaped cavity has threefold symmetry and a centre of inversion on which the axial chlorine atom of the  $\text{CCl}_4$  guest molecule is located.

In the  $\text{Fe}(\text{acetylacetonate})_3/\text{CCl}_4$  complex the threefold symmetric cage is entirely filled by one guest molecule in a fairly compact way. Thus, when we try to build up the solid surface, no cavity appears whatever the radius of the test sphere chosen. To visualize a part of the cage (Fig. 2), the host molecule on the top of the cavity has been removed. In such a case it is clear that the representation of the solid surface of the cavity is not true to life. The tighter fit of carbon tetrachloride into the cavity of the acetylacetonate complex compared to that of Dianin's compound has already been deduced from the fact that in the latter complex the guest molecule starts to undergo rapid reorientation about its threefold axis at 105 K while for the former complex this does not occur until 185 K [3].

A case of a multi-filled cage cavity is well illustrated by the Werner clathrate  $\text{Ni}(\text{SCN})_2(3\text{-methylpyridine})_4/\text{CCl}_4$  and shows clearly the effectiveness of this type of graphics representation to the investigation of host/guest interactions. Indeed, this compound crystallizes in the orthorhombic  $Fddd$  space group and an investigation using a conventional ball-and-stick model of the

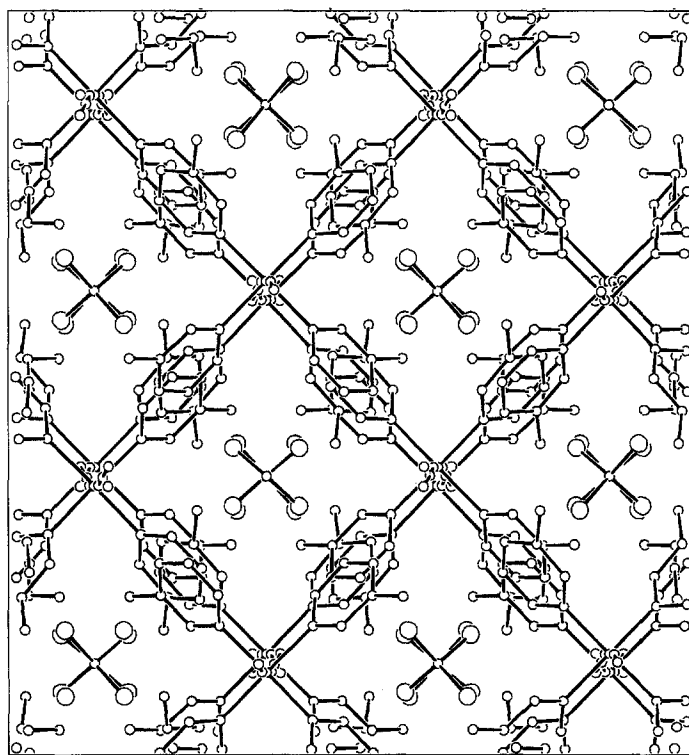


Fig. 3. View along the [100] direction of the structure of  $\text{Ni}(\text{SCN})_2(3\text{-methylpyridine})_4/\text{CCl}_4$  Werner complex in a conventional ball-and-stick representation.

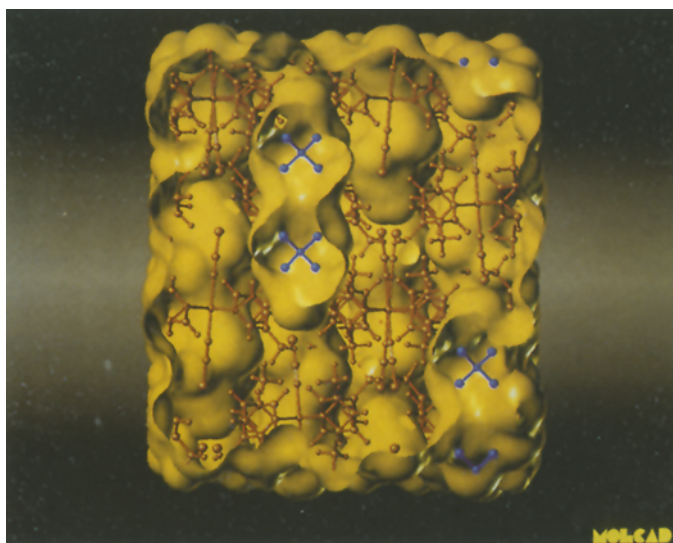


Fig. 4.  $\text{Ni}(\text{SCN})_2(3\text{-methylpyridine})_4/\text{CCl}_4$  Werner complex showing the double-filled cage cavity.

unit cell (Fig. 3) could lead one to suppose that we are in the presence of a channel type clathrate (the channel being oriented along the  $[100]$  direction). This approach led Nassimbeni et al. [12] to describe the isostructural clathrate of chloroform as being of channel type. In fact, a solid-surface representation of the crystal structure on the  $ac$  plane (Fig. 4) shows unequivocally that two guest molecules are located in a cage closed at both extremities by the methyl groups linked to the pyridine part of the host molecules. The cage possesses three twofold axes passing through its centre and for given  $y$ - and  $z$ -coordinates, only one cage is located along the  $[100]$  direction. It appears clearly that the cage involved in this clathrate is large enough to accept more voluminous guest molecules or to lead to disordered structures as shown recently [4] on the same host with different guest molecules.

#### *Channel type*

The solid-surface representation of clathrate compounds is certainly the most effective method of investigation to localize the shapes, sizes and directions of channels in a complicated molecular structure. This task can be accomplished with some difficulty if the guest molecules are aligned in one direction by manipulation of a ball-and-stick model but the building of the solid surface shows the solution immediately. This case is illustrated by the crystal structure of the  $\text{Ni}(\text{ethyl-xanthate})_2(4,4'\text{-dimethyl-2,2'-bipyridyl})$  (Fig. 5) where three different channels are oriented along the three unit-cell axis directions. Two inequivalent  $\text{CCl}_4$  guest molecules are located in pairs or individually in distinct channels. An adequate clipping of the model (Fig. 6) permits the visualization of the interlacing of the channels in the structure.

A more complex case arises when the cavities form a zigzag shape channel since no alignment of the guest molecules or apparent hole can be detected in the molecular packing. This is the case of the triclinic form of the Werner clathrate  $\text{Ni}(\text{SCN})_2(3\text{-methylpyridine})_4/\text{CHCl}_3$  where the chloroform guest molecules are distributed in a non-linear channel (Fig. 7).

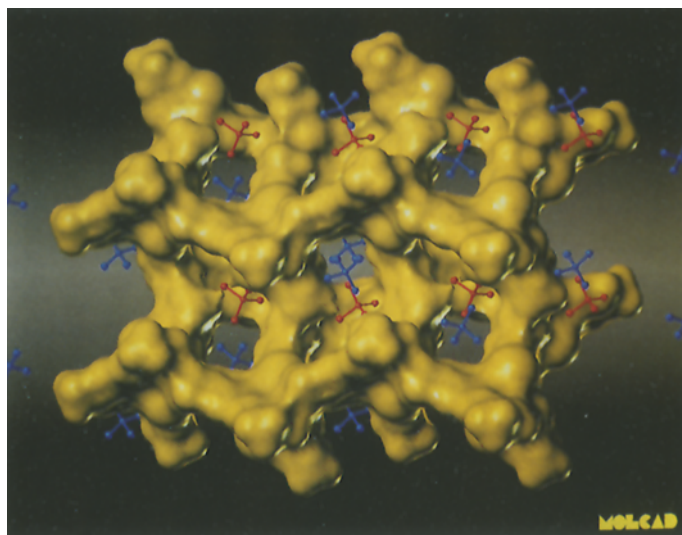


Fig. 5. Channel type clathrate of  $\text{Ni}(\text{ethylxanthate})_2(4,4'\text{-dimethyl-2,2'-bipyridyl})$  with two independent  $\text{CCl}_4$  guest molecules (in red and blue).

## CONCLUSIONS

The recognition and location of the shapes and dimensions of the cages or channels containing the guest molecules in clathrates using the current tools of structural analysis is a time-consuming

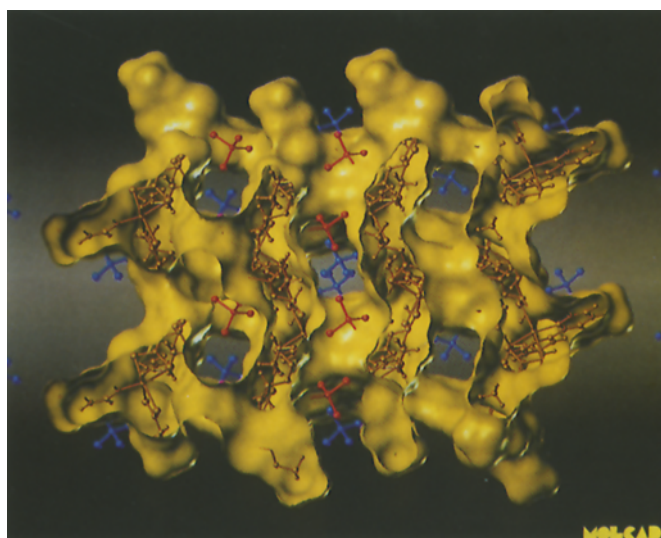


Fig. 6. Clipped solid-surface representation of the  $\text{Ni}(\text{ethylxanthate})_2(4,4'\text{-dimethyl-2,2'-bipyridyl})/\text{CCl}_4$  clathrate showing the interlacing of the channels.

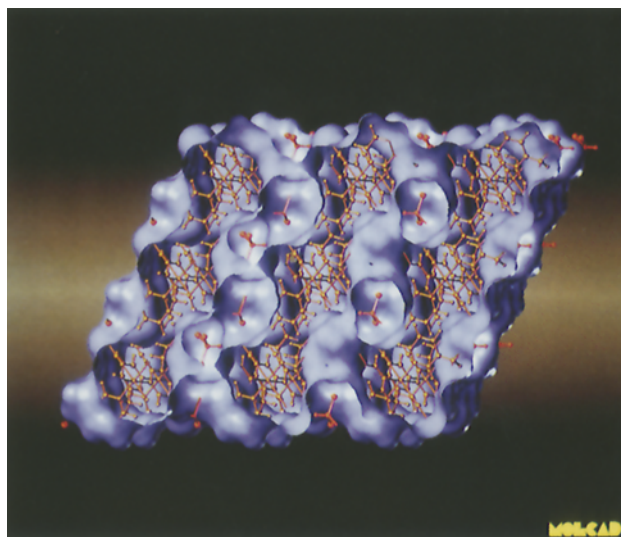


Fig. 7. Zigzag-shaped channels observed in the triclinic form of the  $\text{Ni}(\text{SCN})_2(3\text{-methylpyridine})_4/\text{CHCl}_3$  clathrate.

process which often gives rise to uncertain results. The approach by computer-aided molecular graphics presented here renders this recognition both rapid and unambiguous.

## ACKNOWLEDGEMENTS

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