

Selective Inclusion and Orientation of Chloroform in the Molecular Cavity of a 30-Membered Hexalactam Host

Fritz Vögtle,^{a*} Heinrich Puff,^b Edmund Friedrichs,^b and Walter M. Müller^a

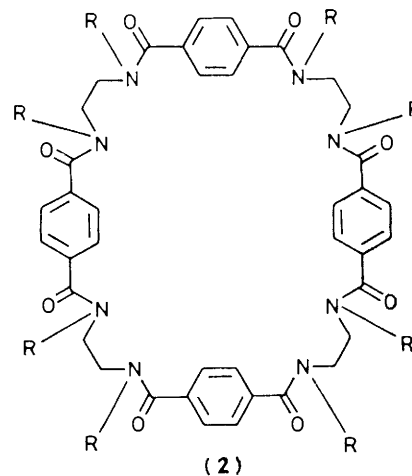
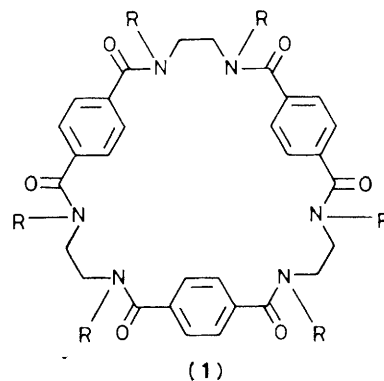
^a *Institut für Organische Chemie und Biochemie, and* ^b *Anorganisch-Chemisches Institut, der Universität Bonn, Gerhard-Domagk-Strasse 1, D-5300 Bonn 1, Federal Republic of Germany*

X-Ray structural studies reveal that one chloroform guest molecule is embedded in the molecular cavity formed by the synthetic large-ring host molecule (1) and is orientated in an unique key-lock-type arrangement in such a way that the hydrogen atom of the chloroform projects into the centre of the macro-ring.

In our efforts to synthesize neutral host cavities analogous to those in cyclodextrins, capable of including uncharged organic guest molecules,^{1,2} we isolated a novel compound formed by the inclusion of chloroform into the [6.6.6]cyclophane (1). The hexabenzyl-substituted hexalactam trimer (1)² (25% yield, m.p. 255–257 °C) and the tetramer (2) (3.3% yield, m.p. 143–145 °C)† are formed in a high-dilution cyclization reaction between readily available starting materials (terephthaloyl dichloride and *N,N'*-dibenzylethylenediamine). At present adducts of (2) with uncharged molecules have not been obtained, but (1) takes up chloroform when the latter is used as eluant for chromatography, or as a recrystallization solvent. The inclusion compound remains stable after several hours of drying at 50 °C and 12 Torr or after recrystallization from ethyl acetate.

On examination by mass spectroscopy chloroform is released, and the molecular ion of the host is observed (*m/z* 1110). The crystal morphology of the adduct changes when it is heated at 160 °C. Between 188 and 193 °C chloroform is evolved, and at 205 °C a new crystal form (needles) appears whose m.p. (255–257 °C) is the same as that of the free host (1). The structure of the inclusion complex has been determined by X-ray crystallography.

Crystal data for the (1)·CHCl₃ adduct (C₇₂H₆₆N₆O₆·CHCl₃): *M* = 1229, rhombohedral, *a* = *b* = *c* = 1506.0(3) pm, $\alpha = \beta = \gamma = 96.80(3)^\circ$, *U* = 3.337 nm³, space group *R*3̄, *Z* = 2, *D*_{3d} = 1.22 g cm⁻³. A total of 2785 independent reflections ($\theta \leq 55^\circ$) were measured on a four-circle diffractometer (CAD 4, Enraf Nonius) using Cu-*K*_α radiation [of these 1424 had $|F_0| < 3\sigma(|F_0|)$] and were classed as unobserved]. The structure was solved by direct methods. The values of 8 two-phase structure semi-invariants were estimated by the



R = CH₂Ph

† The new compounds described showed correct elemental analyses.

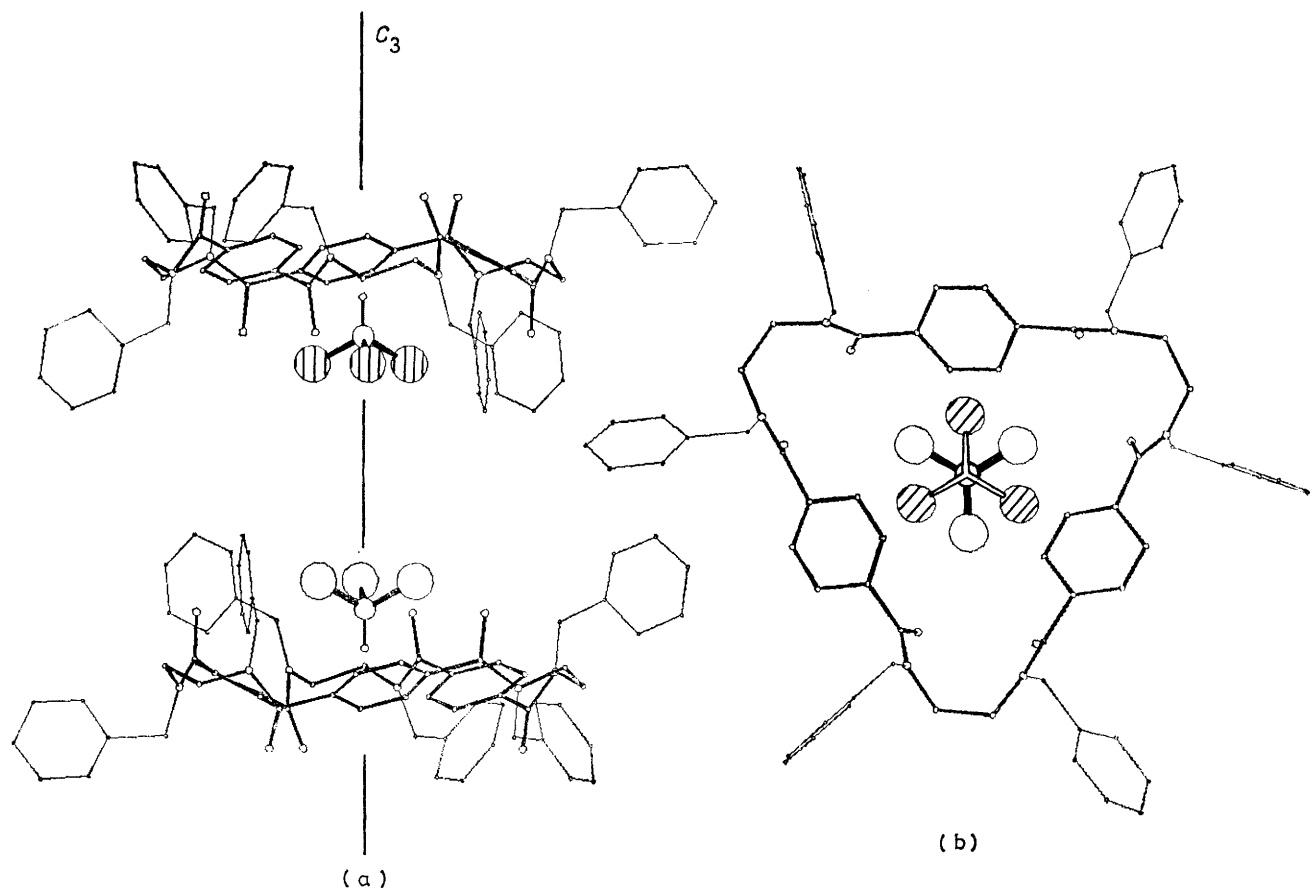


Figure 1. X-Ray structure of the (1)·CHCl₃ inclusion compound. (a) View across the central plane of the macrocyclic ring. (b) View down the trigonal axis perpendicular to the central plane.

formulae of Hauptman³ and added to the starting set. The positions of the non-hydrogen atoms were refined anisotropically to R 0.149.‡ The structure is shown in Figures 1 and 2.

The CHCl₃ guest is orientated and fixed in the niche of the host, with its C-H bond directed towards the cavity centre along the trigonal axis of the host structure. The planes formed by the chlorine atoms of each CHCl₃ molecule above and below the host are approximately parallel to the least-squares plane through the nitrogen atoms in the macro-ring. The distance from the hydrogen atom of the chloroform molecule to this central plane is 83 pm. The two chloroform molecules shown in Figure 1(b) are orientated in a staggered arrangement. The *p*-phenylene units of the host are inclined by an angle of 17.1° to the plane perpendicular to the threefold axis.

The structure of the (1)·CHCl₃ inclusion complex is reminiscent of that of certain hexahost clathrates,⁴ but differs basically from them in having a large host cavity and in the key-lock manner of attachment of the guest to the cavity centre (Figures 1b, 2). In this respect it also differs significantly from the interesting dioxan clathrate described recently.⁵

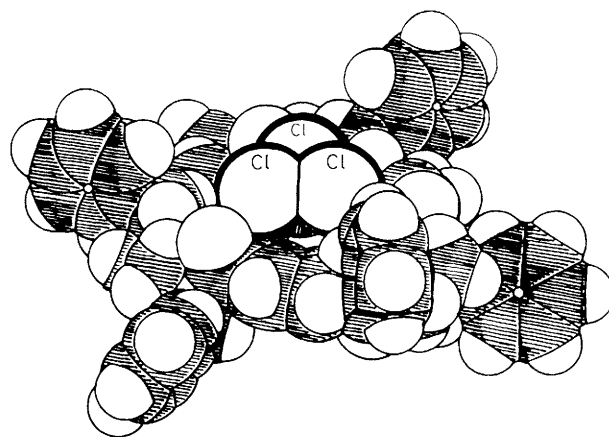


Figure 2. Space-filling illustration of the key-lock-like arrangement of the CHCl₃ guest in the niche of the host (1).

The selectivity of the CHCl₃ inclusion is shown by the fact that similar solvents, *e.g.* CHBr₃, CH₂Cl₂, and CCl₄, do not act as guests for (1), and, further, no stoichiometric solvent adducts seem to be formed by the tetramer (2).

Compound (1) is an example of a new host type that has the general advantage that the six substituents of the macro-ring and the *p*-phenylene rings can be replaced easily by other structural units, thus modifying its properties. The (1)·CHCl₃ inclusion complex described here seems to be as yet the only example,⁶ other than the molecular inclusion complexes of the

‡ The electron difference map shows minor residual electron densities ($1.1 \times 10^3 e \text{ nm}^{-3}$) separated by more than 317 pm from the nearest C-atom. These may be due to randomly oriented solvent molecules and could not be assigned to a definite species.

The atomic co-ordinates for this analysis are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation of this communication.

cyclodextrins just mentioned and those investigated by Gutsche, Andreotti, *et al.*,⁷ of uncharged host–uncharged guest inclusion, but with a hitherto unobserved arrangement reminiscent of receptor–substrate complexes (Figure 2). It is hoped that a new strategy for the design of specific host–guest orientations and interactions will arise from this work.

Received, 12th August 1982; Com. 962

References

- 1 F. Vögtle, *Chimia*, 1981, **35**, 483.
 - 2 F. Vögtle and W. M. Müller, *Angew. Chem.*, 1982, **94**, 138; *Angew. Chem., Int. Ed. Engl.*, 1982, **21**, 147; *Angew. Chem. Suppl.*, 1982, 185–192.
 - 3 H. Hauptman, in 'Theory and Practice of Direct Methods in Crystallography,' eds. M. F. C. Ladd and R. A. Palmer, Plenum Press, New York and London, 1980, p. 187; space group $R\bar{3}$ treated as $P\bar{1}$.
 - 4 D. D. MacNicol, J. J. McKendrick, and D. R. Wilson, *Chem. Soc. Rev.*, 1978, **7**, 65; E. Weber, W. M. Müller, and F. Vögtle, *Tetrahedron Lett.*, 1979, 2235.
 - 5 S. J. Abbott, A. G. M. Barrett, C. R. A. Godfrey, S. B. Kalindjian, G. W. Simpson, and D. J. Williams, *J. Chem. Soc., Chem. Commun.*, 1982, 796.
 - 6 In contrast, the benzene clathrate reported by H. Stetter and E.-E. Roos, *Chem. Ber.*, 1955, **88**, 1390, has proved to be not a molecular complex, but a lattice inclusion complex with the benzene molecule being located outside the host cavities. We thank Dr. R. Hilgenfeld and Prof. Dr. W. Saenger, Freie Universität Berlin, for this information before publication.
 - 7 G. D. Andreotti, R. Ungaro, and A. Pochini, *J. Chem. Soc., Chem. Commun.*, 1979, 1005; C. D. Gutsche, B. Dhawan, K. H. No, and R. Muthukrishnan, *J. Am. Chem. Soc.*, 1981, **103**, 3782.
-