[11] Work currently in progress in these laboratories has led to the synthesis of the 4-α-ethyl derivative of this glycoside **9** and thence to the 4-α-ethyl derivative of the 6-deoxygulal **11** (MEM blocking group in place of MOM) (W. Noall, unpublished results). The use of this gulal derivative for further synthesis of polyether ketone **3** is under investigation.

[12] The authors are grateful to Dr. W. Leimgruber of Hoffmann-La Roche for supplying a generous sample of lasalocid A which was degraded to the polyether ketone **3** by the procedure of Dr. Westley.[4]

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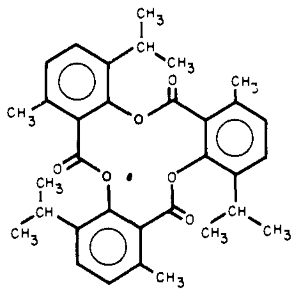
Received October 18, 1979

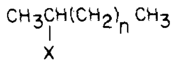
Enantiomer Recognition and Guest–Host Configurational Correlation in Crystals of Tri-*o*-thymotide Clathrate Inclusion Compounds

Sir:

Chiral recognition by host molecules or molecular assemblies has attracted considerable attention in recent years.[1] We describe chiral recognition aspects in single crystals of tri-*o*-thymotide (TOT) clathrate inclusion complexes.[2] In the latter, a large variety of guest molecules may be accommodated in cavities (channels or cages) which are built up by TOT molecules during crystallization from media containing the guest.

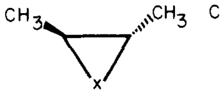


TOT

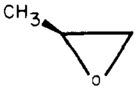


$CH_3\underset{\displaystyle X}{C}H(CH_2)_n\,CH_3$

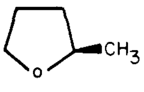
	1a	b	c	d	e	f
x)	Cl	Br	Cl	Br	Br	Br
n)	1	1	5	5	6	9



2a X = S
b X = O



3



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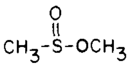

$CH_3-\overset{\displaystyle O}{\overset{\|}{S}}-OCH_3$

5

TOT generally undergoes "spontaneous resolution" on crystallization in clathrate structures (cage clathrate, trigonal crystals, space group $P3_121$ or $P3_221$; channel clathrate, hexagonal crystals, space group $P6_1$ or $P6_5$).[3,4] Any such single crystal thus contains only *P* or only *M* configurated TOT species and provides a chiral environment about included guest molecules. When such clathrates are formed from solutions containing a racemic mixture of guest species, the two guest enantiomers should be included to a different extent by a growing crystal of given handedness and, indeed, such qualitative results have been described in the past.[6] To better understand the nature of chiral molecular recognition, we have undertaken a chemical and crystallographic study of the TOT clathrates and herein evaluate the degree of chiral recognition that is possible with some of these complexes, the scope of guest structure that may be included and resolved, and the possibility of correlating guest configuration with TOT chirality.

Single crystals of clathrate were grown from solutions of TOT in a large excess of the desired guest by slow cooling or slow evaporation. When larger crystals were desired, individual clathrate crystals were suspended in saturated guest solutions of TOT which were then slowly cooled; this procedure could be repeated more than once and crystals weighing up to 0.5 g were routinely prepared. The crystals were characterized by measurement of their unit cell constants and space groups; the TOT:guest ratios were established by NMR spectra and VPC analyses of solutions prepared from dissolved crystals and by density measurements.

The enantiomeric excess of the included guest, i.e., the degree of optical resolution, and the configuration of the predominant enantiomer were determined by direct polarimetric observations of solutions of the guests, by NMR analysis with chiral shift reagents, or by VPC analysis of the guest on a chiral phase (using recently developed, efficient analytical resolution techniques for *N*-trifluoroacetyl-2-aminoalkanes,[7] cyclic ethers,[1e,8] and episulfides[9]). For each guest, crystals containing excess *R* enantiomer and crystals containing excess *S* enantiomer were generally examined, and for each crystal the sign of rotation of the TOT was established; such "enantiomeric" experiments provided an estimate of reproducibility as well as a check that errors due to impurities were not introduced. This study is particularly feasible with TOT because it has a sufficiently high barrier to enantiomerization, $M \rightleftharpoons P$ ($\sim$21 kcal/mol),[10] and specific rotation ($[\alpha]_D > 70°$) in solution to enable measurement of its sign of rotation after dissolving only a small crystal chip in cold solvent.[3a]

Table I displays our results. The higher enantiomer selectivity generally observed in the cage clathrates compared with that in the channel complexes is intuitively understandable in terms of the more complete envelopment of the guest in the cages; however, a deeper insight awaits crystal structure analyses of representative complexes which will indicate guest geometry and guest–host contacts. It might have been thought[11] that sharp differences in chiral discrimination would occur in channel complexes when the length of the included guest matched the unit cell length, c = 29 Å, of the channel or a multiple of the asymmetric unit along the channel, $c/6$. However, on the basis of the results with **1e** (estimated length, 14.1 Å, $\sim c/2$) compared with those of **1d** (12.8 Å) and **1f** (17.8 Å), there appears to be little if any such dependence.

Chiral guests having C_2 symmetry were expected to be differentiated to a high degree in cage clathrate cavities because the latter contain a twofold axis. Indeed, guests **2a** and **2b** afforded the expected cage clathrate crystals and the extracted guests had relatively high optical purities. This principle, the matching of guest molecular symmetry with the symmetry of the cavity, may be useful in the choice of appropriate host and guest species in other molecular recognition problems (cf. ref 5).

From the results presented, it appears that TOT enclathration may be used, at least within a related series of compounds, to establish *absolute* configurations by noting the sign of the TOT upon dissolution. Thus, all of the guests **1** having configuration *S* are preferentially enclathrated by (+)-TOT molecules. Similarly, (+)-TOT preferentially includes the *S,S* enantiomers of **2**. Such correlations may have application in configurational assignments where other approaches are problematic, e.g., when the formation of derivatives is difficult or the substance affords inherently weak chirality observations. Since the resolutions described here depend on the guest molecular geometry and not on specific functional groups, application to chiral hydrocarbons may also be envisaged.

With regard to preparative resolutions using TOT enclathration, it should be noted that, once single crystals of clath-

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Table I. Enantiomeric Excess and Correlation of Guest and Host Chirality in (+)-Tri-*o*-thymotide Clathrate Crystals[a]

guest	type	host: guest[b]	guest, % ee[c]	guest config
2-chlorobutane (**1a**)	cage	2:1	32[d]	(*S*)-(+)
2-bromobutane (**1b**)	cage	2:1	34[d]	(*S*)-(+)
2-chlorooctane (**1c**)	channel	2.6:1	4[e]	(*S*)-(+)[e]
2-bromooctane (**1d**)	channel	2.7:1	4[e]	(*S*)-(+)[e]
2-bromononane (**1e**)	channel	3:1	5[e]	(*S*)[e]
2-bromododecane (**1f**)	channel	3.8:1	5[e]	(*S*)[e]
trans-2,3-dimethylthiirane (**2a**)	cage	2:1	30[f]	(*S*,*S*)-(−)[f]
trans-2,3-dimethyloxirane (**2b**)	cage	2:1	47[f]	(*S*,*S*)-(−)[f]
propylene oxide (**3**)	cage	2:1	5	(*R*)-(+)[f]
2-methyltetrahydrofuran (**4**)	cage	2:1	2[f]	(*S*)-(+)[g]
methyl methanesulfinate (**5**)	cage	2:1	15[h]	(*R*)-(+)[h]

[a] With the exception of **3**, all chirality correlations rest on clathrates with excess *R* guest and with excess *S* guest, although only one TOT–guest pair is given. [b] Determined from crystal cell constants and measured density, VPC, and NMR analysis. [c] Maximum error limit, ±10% of value for ee >10%; for smaller ee, maximum absolute error ±1%. [d] Polarimetric measurement, based on $[\alpha]_D$ 37° for **1a** and 34° for **1b**; limit of error for **1a** may exceed 10% [D. D. Davis and F. R. Jensen, *J. Org. Chem.*, **35,** 10 (1970)]. [e] Guest converted, through inversion of configuration, into the corresponding amino compound by treatment with ethanolic ammonia. VPC analysis of *N*-trifluoroacetyl derivatives on chiral phase gives ee as well as configuration: B. Feibush and E. Gil-Av, *J. Gas Chromatogr.*, 257 (1967); S. Weinstein, B. Feibush, and E. Gil-Av, *J. Chromatogr.*, **126,** 97 (1976). [f] VPC analysis on chiral phase was kindly performed by Professor V. Schurig and co-workers;[8,9] guest configuration was established by comparison with authentic optically active guests prepared independently. [g] Polarimetric measurement of guest in chloroform at 6328 Å in a microcell (100-μL volume); cf. D. Gagnaire and A. Butt, *Bull. Soc. Chim. Fr.*, 312 (1961). [h] Polarimetric measurement and NMR analysis using tris(dicampholylmethanato-d_2)europium(III): M. D. McCreary, D. W. Lewis, D. L. Wernick, and G. M. Whitesides, *J. Am. Chem. Soc.*, **96,** 1038 (1974). Guest configuration assignment was made by analogy to ref 1g.

rate have been prepared, they may be crushed and used to seed subsequent crystallizations to give polycrystalline material having an optical purity of 80–90% of that in a single crystal. Secondly, crystallization of TOT from partially resolved material yields clathrates which contain guests having appreciably enhanced optical purity over that of the starting material.[12]

Acknowledgments. We are grateful to Dr. G. Tsoucaris for his interest and support and to Professor H. Kagan for kindly providing facilities where part of this work was performed. We thank Professor E. Gil-Av, Dr. S. Weinstein, R. Charles, and M. Lachmi for advice and discussions and for the columns used to separate the enantiomeric N-TFA-2-aminoalkanes. We are indebted to Professor V. Schurig and W. Bürkle, for the analyses of guests **2–4** and for fruitful discussions. Chiral Eu(III) reagent was very kindly provided by Professor G. M. Whitesides. TOT was synthesized by Mrs. A. Jacob; we thank her and Mme F. Villain for technical assistance. This research received support from the CNRS (as part of ATP No. 2662 on "Chiral Structures" with the NCRD, Jerusalem) and the Israel Academy of Sciences.

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(2) Although first prepared in 1865, the structure of TOT was only established by Baker et al. [W. Baker, B. Gilbert, and W. D. Ollis, *J. Chem. Soc.*, 1443 (1952)], who demonstrated the clathrate inclusion properties. Powell[6] first recognized the chiral aspects of TOT complexes and their possible use for guest resolutions and configurational assignments. For a recent review of clathrate phenomena and comprehensive references to earlier reviews and literature, see D. D. Mac Nicol, J. J. McKendrick, and D. R. Wilson, *Chem. Soc. Rev.*, **7**, 65 (1978).

(3) (a) A. C. D. Newman and H. M. Powell, *J. Chem. Soc.*, 3747 (1952); (b) D. Lawton and H. M. Powell, *ibid.*, 2339 (1958); (c) D. J. Williams and D. Lawton, *Tetrahedron Lett.*, 111 (1975); (d) S. Brunie, A. Navaza, G. Tsoucaris, J. P. Declercq, and G. Germain, *Acta Crystallogr., Sect. B*, **33,** 2545 (1977).

(4) Although almost all of the TOT clathrates reported thus far belong to one of these two (chiral) types, TOT clathrates having achiral crystal structures have recently been prepared and characterized;[5] the choice of clathrate structure depends primarily on the nature of the guest.

(5) (a) R. Arad-Yellin, S. Brunie, B. S. Green, M. Knossow, and G. Tsoucaris, *Mol. Cryst. Liquid Cryst.*, **50**, 275 (1979); (b) R. Arad-Yellin, S. Brunie, B. S. Green, M. Knossow, and G. Tsoucaris, *J. Am. Chem. Soc.*, **101,** 7529 (1979).

(6) H. M. Powell, *Nature* (*London*), **170**, 155 (1952); *Endeavour*, **15**, 20 (1956).

(7) S. Weinstein, B. Feibush, and E. Gil-Av, *J. Chromatogr.*, **126**, 97 (1976).

(8) V. Schurig and W. Bürkle, *Angew. Chem., Int. Ed. Engl.*, **17,** 132 (1978).

(9) V. Schurig, unpublished results.

(10) W. D. Ollis, J. F. Stoddart, and I. O. Sutherland, *Tetrahedron*, **30**, 1903 (1974).

(11) (a) D. Lawton and H. M. Powell, *J. Chem. Soc.*, 2350 (1950); (b) W. Schlenk, *Justus Liebigs Ann. Chem.*, 1162 (1973).

(12) The last two points may also be of interest in connection with speculations on the abiotic origin and amplification of optical activity.

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Received July 6, 1979

Crystal Lattice Control of Unimolecular Photorearrangements. Differences in Cyclohexenone Photochemistry in Solution and the Solid State. Solution Results

Sir:

We have recently demonstrated in the case of a β,γ-unsaturated ketone[1] that irradiation in the solid state leads to results different from those observed in solution owing to the fact that the molecular distortions and deformations necessary for the solution rearrangement process are too great to be permitted by the molecular rigidity of the crystal lattice. As a result, alternative least motion unimolecular processes occur in the latter medium. Implicit in these results was the assumption that reaction occurs from the same ketone conformational isomer in solution as in the solid state.

In this and the following paper,[2] we report an example of a second way in which crystal lattice restraints can affect unimolecular photoreactivity, namely by limiting reaction to one stable conformational isomer of a given substrate in contrast to the liquid phase where a minor higher energy conformational isomer is the reacting species. The class of molecules we have chosen to study possesses the basic tetrahydro-1,4-naphthoquinol structure common to compounds **2** and **3** (Scheme I). We first describe the solution photochemistry of several of these compounds, and in the following paper[2] we compare and

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