Pergamon

*Tetrahedron Letters*, Vol. 35, No. 11, pp. 1685-1688, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(94)E0115-E

# Synthesis and Configurational Analysis of Phosphorus Bridged Cavitands

**Tino Lippmann,[a] Enrico Dalcanale,*[b] and Gerhard Mann*[1]**

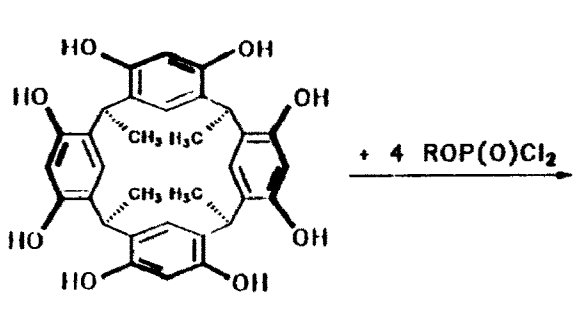
[a] Fachbereich Chemie, Universität Leipzig, Talstr. 35, D-04103, Germany

[b] Dipartimento di Chimica Organica ed Industriale, Universita di Parma, Viale delle Scienze, I-43100, Italy

**Abstract:** A novel family of diastereomeric cavitands, obtained by incorporation of four phosphate groups on a resorcinol derived calix[4]arene has been studied.

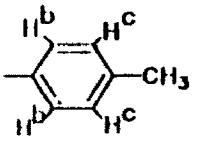
Cavitands are synthetic organic compounds with enforced concave surfaces of molecular dimensions.[2] Their ability to act as receptor for neutral and charged species has already been proved in the solid state, in solution,[3,4] and in the gas phase.[5] Cavitands bearing rigidly preorganized P=O groups attracted our attention as probes to study the influence of multiple hydrogen bonding patterns on molecular recognition phenomena. This paper reports synthesis, configurational analysis and preliminary complexation properties of phosphorus(V) bridged cavitands derived from resorcinol cyclic tetramers.

Reaction of all-cis-tetramethylcalix[4]arenoctol **1** with p-methylphenyldichloro phosphate in dry acetone, using triethylamine as base, gave a mixture of six diastereoisomers **2a-f** [6] in 80% isolated yield as shown by HPLC analysis (Table 1).




1

R =



2

2a: iiii
2b: iiio
2c: iioo
2d: ioio
2e: iooo
2f: oooo

In the reaction four dioxaphosphacin rings with four stereogenic centers at the phosphorus(V)atoms were formed by bridging the eight phenolic functions present in formula **1**.

Table 1. TLC and HPLC analysis of diastereoisomers **2a-f**

| Isomer | Ratio [%] | HPLC Merck Si-60 $CHCl_3$/n-hexane 6/4 $t_R$ [min] | TLC Silica $CH_2Cl_2$/acetone 40/1 $R_f$ |
|---|---|---|---|
| iiii | < 1 | 4.18 | - |
| iiio | 17 | 8.31 | 0.41 |
| iioo | 18 | 8.31 | 0.52 |
| ioio | 18 | 5.84 | 0.65 |
| iooo | 38 | 13.99 | 0.32 |
| oooo | 8 | 29.48 | 0.23 |

The reaction leads to all the six possible diastereoisomers having different orientations of the P=O groups either outwards (o) or inwards (i) with respect to the cavity. In a related system with phosphorus (III) derivatives Puddephatt et al. reported the selective formation of a single isomer with the lone pairs directed inwards and the phenyl groups outwards.[7] In our case the aryloxy groups can easily accomodate themselves in the inward positions because they can orient themselves upwards with respect to the cavity. The identification of the different isomers was done after preparative chromatographic isolation of five of them by $^{31}$P-NMR and $^{1}$H-NMR spectroscopy (Table 2).[8]

The NMR signal patterns reflect the symmetry of the different isomers and the orientation of the substituents OR at the stereogenic centers. As demonstrated by Cram et al. hydrogens directed inwards with respect to the cavity show a strong high-field shift.[9] Configuration of all isomers was deduced from the number of signals and the $^{1}$H-NMR shift for $H^b$ and $H^c$ which present significant differences when the substituents OR are directed inwards or outwards with respect to the cavity. The assignment is also in accordance with the chromatographic behaviour of the different diastereoisomers since the oooo isomer has on silica the highest retention time due to the presence of four P=O groups able to give rise to a strong interaction with the hydroxy groups of the stationary phase.

$^{31}$P-NMR titration of cavitands **2b,c,d** in $CDCl_3$ solution with cyclohexylammonium chloride [10] by means of computer-assisted non-linear least-squares fitting procedure [11] leads to the $K_a$ value of 1370 $dm^3mol^{-1}$ for the 1:1 complex between **2b** and the guest. Upon addition of the guest the $^{31}$P resonances belonging to the three P=O pointing inward (-18.56 and -18.72 ppm. Table 2) were shifted downfield more extensively than that of the P=O pointing outward (-25.75 ppm), thus confirming the

configurational attribution given above. In the other two cases either complexation was absent (**2d**) or very small (**2c**). The three preorganized P=O groups pointing toward the cavity in compound **2b** have the right geometry for a three-point hydrogen bonding interaction with alkylammonium ions.[12] Changing this geometry drastically reduces or even eliminates the binding ability of the host.

Table 2. Selected $^{31}P$ § and $^{1}H$ NMR& data for compounds **2b-f**

| isomer (symmetry) | $^{31}P$ | $^{1}H^{a}$ | $^{1}H^{b,c}$ (in) | $^{1}H^{b,c}$ (out) |
|---|---|---|---|---|
| **2b** iiio (Cs) | -18.56 (2P) | 6.57 (s, 2H) | 6.86 (d, 2H) | 7.13 (d, 4H) |
| | -18.72 (1P) | 6.88 (s, 2H) | 6.97 (d, 2H) | 7.16 (d, 4H) |
| | -25.75 (1P) | | | 7.17 (d, 2H) |
| | | | | 7.23 (d, 2H) |
| **2c** iioo (Cs) | - 17.57 (2P) | 6.50 (s, 2H) | 6.66 (d, 4H) | 7.15 (d, 4H) |
| | -25.77 (2P) | 6.56 (s, 1H) | 6.70 (d, 4H) | 7.18 (d, 4H) |
| | | 6.96 (s, 1H) | | |
| **2d** ioio (C2v) | -17.79 (2P) | 6.57 (s, 4H) | 6.75 (d, 4H) | 7.11 (s, 8H) |
| | -25.87 (2P) | | 6.81 (d, 4H) | |
| **2e** iooo (Cs) | -16.39 (1P) | 6.61 (s, 2H) | 5.95 (d, 2H) | 7.19 (d, 2H) |
| | -25.45 (2P) | 6.66 (s, 2H) | 6.17 (d, 2H) | 7.21 (d, 2H) |
| | -26.02 (1P) | | 6.81 (d, 4H) | |
| | | | 6.89 (d, 4H) | |
| **2f** oooo (C4v) | -25.62 (4P) | 6.62 (s, 4H) | 6.41 (d, 8H) | |
| | | | 6.66 (d, 8H) | |

§ 200 MHz in $CDCl_3$ at 25°C; external standard $H_3PO_4$ (85%).
& 400 MHz in $CDCl_3$ at 25°C.

This novel family of diastereoisomeric cavitands is well suited for the evaluation of multiple point hydrogen bonding interactions in molecular recognition phenomena. The influence of different R substituents on the relative ratio of different diastereoisomers and on their complexation properties is under study.

**Acknowledgement.** This work was supported by the Vigoni Program, a German-Italian joined research project. We thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support. Centro Interfacoltà di Misure of the University of Parma provided the facilities for NMR and mass spectroscopy.

## References and Notes

1. Present address: Prof. Dr. G. Mann, Supramolecular Chemistry Laboratory, Gottleubaer Str. 15, D-04349 Leipzig, Germany.
2. Cram, D. J. *Nature* **1992**, *356*, 29-36.
3. Soncini, P.; Bonsignore, S.; Dalcanale, E.; Ugozzoli, F. *J. Org. Chem.* **1992**, *57*, 4608-4612.
4. Lippmann, T.; Wilde, H.; Pink, M.; Schäfer, A.; Hesse, M.; Mann, G. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1195-1197.
5. Vincenti, M.; Pelizzetti, E.; Dalcanale, E.; Soncini, P. *Pure Appl. Chem.* **1993**, *65*, 1507-1512.
6. Systematic name (IUPAC nomenclature):1,21,23,25-tetramethyl-5,9,13,17-tetra(4`-methylphenoxy) 2,20:3,19-dimetheno-1H,21H,23H,25H-bis/1,3,2$\lambda^5$/dioxaphosphacino/5,4-i:5`,4`-i`/benzo /1,2-d:5,4-d`/bis/1,3,2$\lambda^5$/benzodioxaphosphocin.
7. Xu, W.; Rourke, P.; Vittal, J. J.; Puddephatt, R. J. *J. Chem. Soc.*; *Chem.Commun.* **1993**, 145-147. Xu, W.; Vittal, J. J.; Puddephatt, R. J. *J. Am. Chem. Soc.* **1993**, *115*, 6456-6457.
8. All new compounds gave satisfactory analytical and spectral data.
9. Cram, D. J.; Karbach, S.; Kim, H. E.; Knobler, C. B.; Maverick, E. F.; Ericson, J. L.; Helgeson, R.C. *J. Am. Chem. Soc.* **1988**, *110*, 2229-2273. Tucker, J. A.; Knobler, C. B.; Trueblood, K. N.; Cram, D. J.*J. Am. Chem. Soc.* **1989**, *111*, 3688-3699.
10. $^{31}$P-NMR titration (200MHz): [host]=5x10$^{-4}$mol dm$^{-3}$; [guest]=0.5-15.0x10$^{-4}$mol dm$^{-3}$. The determination involved analysis of the movements of two distinct macrocycle resonances.
11. Whitlock, B. J.; Whitlock, H. W. *J. Am. Chem. Soc.* **1990**, *112*, 3910-3915. Wilcox, C. S. in *Frontiers in Supramolecular Chemistry and Photochemistry*; Schneider, H. J., Dürr, H., Eds.; VCH Publishers: New York, **1991**; pp 123-143.
12. Savage, P. B.; Holmgren, S. K.; Gellman, S. H. *J. Am. Chem. Soc.* **1993**, *115*, 7900-7901.

(*Received in Germany* 10 *December* 1993; *accepted* 13 *January* 1994)