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Synthesis and Configurational Analysis of Mixed-bridged Phosphate Cavitands

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Mixed-bridged cavitands derived from tetramethylresorcinarene having, respectively, methylene, ethylene and *p*-tolyl phosphate bridging groups are synthesized. The *in–out* isomers of each cavitand are separated and characterized. The diastereoselectivity in favour of the *in* isomer in the phosphate bridging reaction is determined by the nature of the bridging units already present on the macrocycle. The X-ray crystal structure of a fourfold-bridged phosphate cavitand in the *ioio* configuration reveals the spatial disposition of the phosphate bridges with the convergence of two P = O groups toward the centre of the cavity.

Keywords: Mixed-bridged phosphate cavitands, diastereoselectivity, in-out isomerism, solid state structure

INTRODUCTION

Cavitands, defined as synthetic organic compounds having enforced cavities of molecular dimensions, are well known molecular receptors [1]. In the design of cavitands the choice of the bridging groups connecting the phenolic hydroxyls of the resorcinarene skeleton is pivotal, since it determines shape, dimensions and complexation properties of the resulting cavity. Up to now most of the research in the field has focused on the preparation of symmetrically fourfold-bridged cavitands [2], neglecting the synthetically more demanding mixed-bridged analogues [3]. From the point of view of molecular recognition however, mixed-bridged cavitands are attractive for the presence of different functionalities in a well-defined spatial orientation on the rim of a cavity. In this respect the introduction of P = O groups, which can act as hydrogen bond acceptors, is particularly appealing, since the directionality of hydrogen bonding can be effectively used to impart selectivity in complexation [4]. On the other side, the presence of P(V) stereocenters brings configurational properties into play, such as the relative orientation of the P = O groups with respect to the cavity, which determines the number of possible diastereoisomers.

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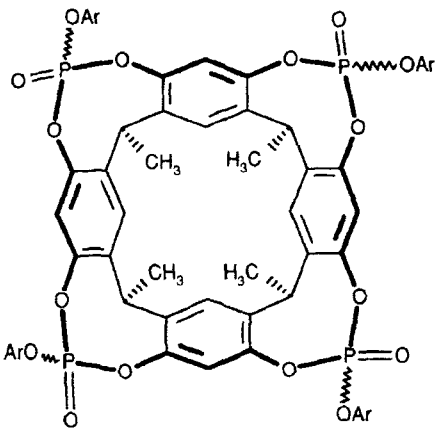
We recently reported the synthesis of different diastereomeric cavitands of structure **I** by incorporation of four phosphate groups on resorcinarene molecular platforms [5]. The reaction led to all the six possible diastereoisomers having different orientation of the P = O groups



STRUCTURE I

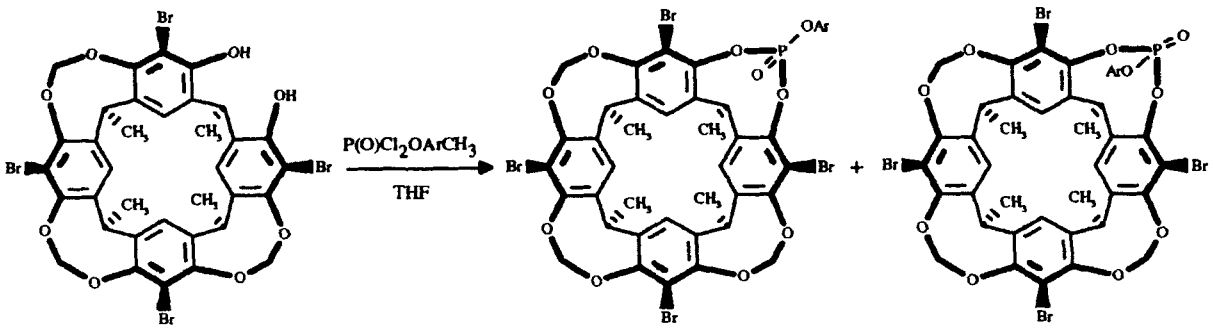
either inward (*i*) or outward (*o*) with respect to the cavity [6]. The configuration at the four stereocenters has been attributed on the basis of ^{13}C-NMR relaxation experiments [5].

In this paper we report synthesis and configurational analysis of three mixed-bridged cavitands which possess either one or two bridging phosphate groups. The crystal structure of one of the isomers of structure **I**, namely the *ioio* one, is also described to show the spatial disposition of the phosphate groups on the resorcinarene skeleton.

RESULTS AND DISCUSSION

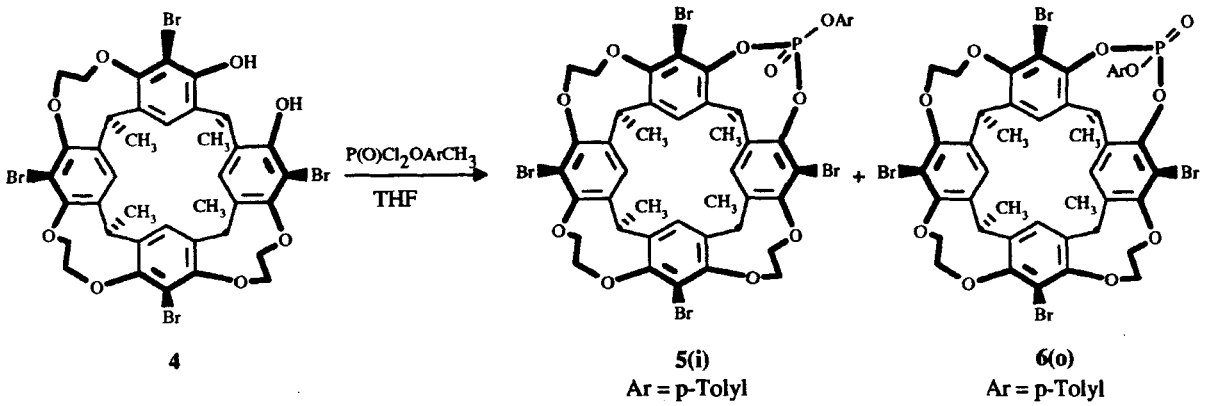
Synthesis and Configurational Analysis of Mixed-bridged Cavitands

Tri-bridged resorcinarenes **1** and **4** [7] having respectively methylene and ethylene bridges, and A,C-methylene-di-bridged resorcinarene **7** [8] served as starting materials for the synthesis of the cavitands reported here.[‡] Treatment of **1** with *p*-tolyl phosphate dichloride provided the isomeric cavitands **2(i)** and **3(o)** in 52% and 13% isolated yield respectively (Scheme 1). The same reaction performed on the ethylene tri-bridged derivative **4** afforded cavitands **5(i)** and **6(o)** in 35% and 30% yield (Scheme 2). The diastereomer attribution is based on the chemical shift differences of the ^{31}P and ^{1}H resonances of the phosphate groups, as already shown for four-fold-bridged phosphate cavitands of structure **I** and confirmed by the reported crystal structure. The chemical shifts of the aromatic tolyl hydro-



SCHEME 1

[‡]The term *cavitand* refers only to a tetra-bridged resorcinarene. For partly-bridged resorcinarenes we follow the nomenclature used in reference 3a.



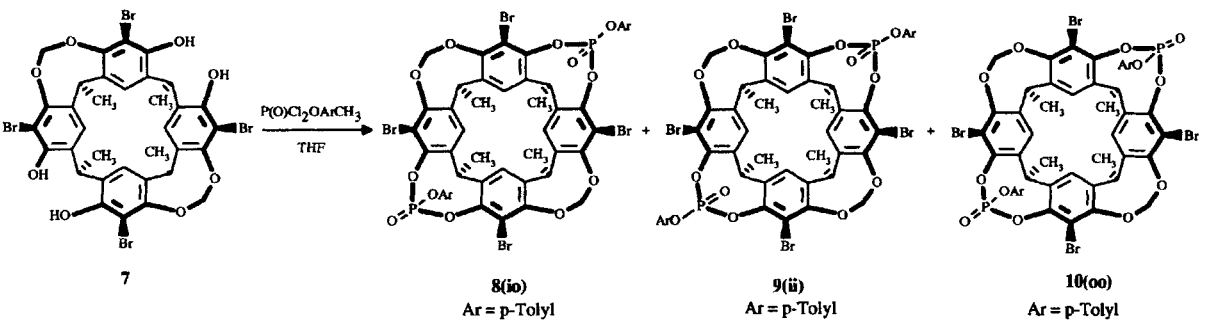
SCHEME 2

gens are particularly diagnostic: the inward facing protons experience a significant upfield shift with respect to the corresponding outward ones. The attribution is confirmed by ^{31}P resonances which are always at higher field for the *out* isomers (see experimental section) [5].

In the case of **7** the bridging reaction led to all three possible isomeric cavitands **8 (io)**, **9 (ii)** and **10 (oo)** in 56% overall yield (Scheme 3). The number of resonances of phosphorous atoms and *p*-tolyl protons allowed the univocal identification of **8 (io)** isomer. Discrimination between the symmetrically equivalent isomers **9 (ii)** and **10 (oo)** is based on the ^{1}H and ^{31}P chemical shift differences discussed above.

When the substrates are tri-bridged resorcinarenes the isomer distribution in the cavitands formed is always shifted toward the *in* one. However, the high diasterostereoselectivity of the phosphate bridging reaction observed in the case of **1** (ratio **2(i)/3(o)** = 4) is in contrast with the very small one observed for **4** (ratio **5(i)/6(o)** < 1.2). These wide different results can be explained considering the relative opening of the resulting cavities in the two molecules. An inward facing tolyl group can be better accomodated in the wider cavity of **4** with respect to the narrower one of **1**. Thus the product diastereostereoselectivity of the phosphate bridging reaction is controlled by the nature of the bridging units already present on the macrocyclic substrate.

The product distribution observed in the case of cavitands **8–10** [24% **8(io)**; 14% **9(ii)** and **10(oo)**] perfectly matches the 1:2:1 theoretical statistical distribution. This indicates that the residual conformational mobility present in **7** is sufficient to exclude any configurational bias.



SCHEME 3

X-ray Crystal Structure of the Tetraphosphate *ioio* Cavitand

The molecular structure of the macrocycle is illustrated in Figures 1a,b. The atomic numbering scheme identically adopted in each of the four phosphate subunits A, B, C, D is depicted in Scheme 4. The atomic fractional coordinates are listed in Table I, and the most relevant bond distances and angles are reported in Table II.

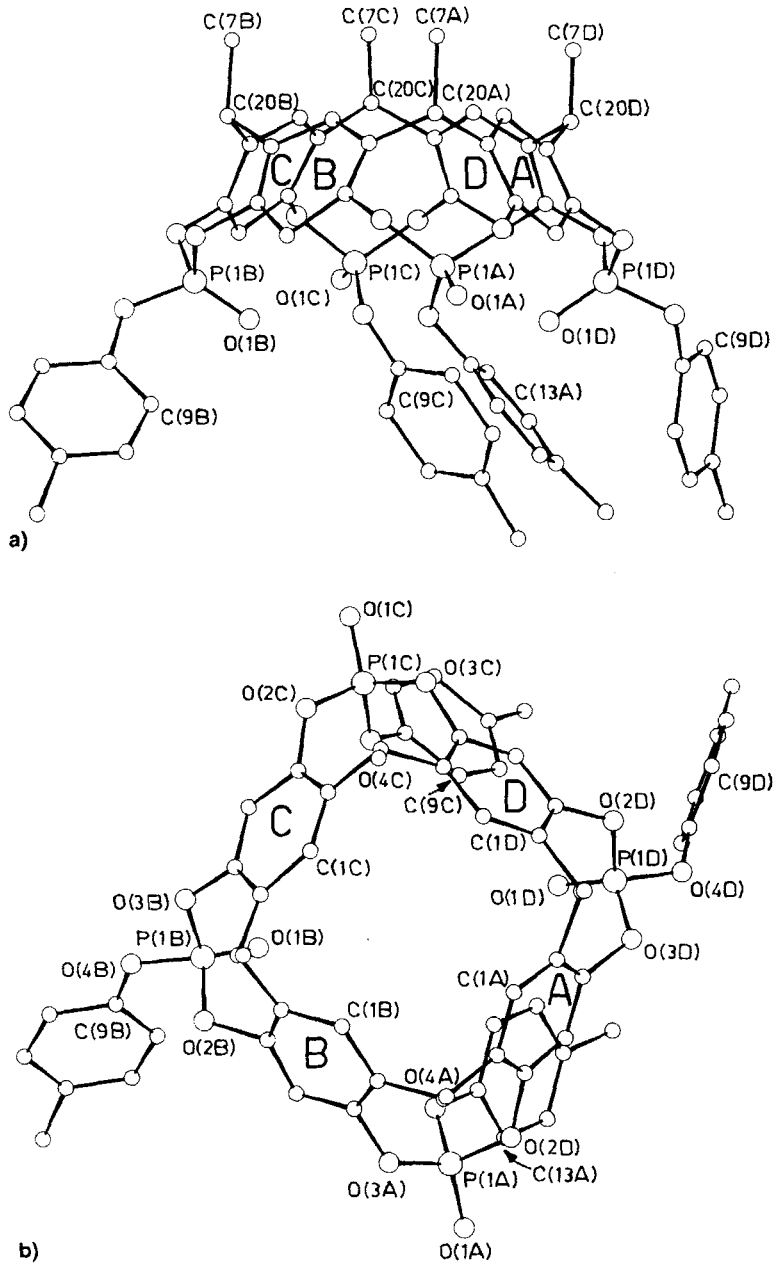
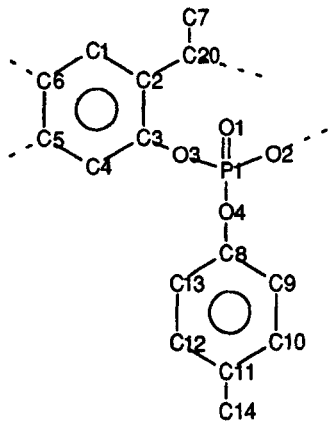


FIGURE 1 Side (a) and bottom (b) views of the molecular structure of the *ioio* isomer of **I** showing the partial atom-labeling scheme.



SCHEME 4

The macrocycle is blocked in the cone configuration with the four methyl feet located on the minor opening of the cavity (C(7)), almost perpendicular to the least-square plane through the four C(20) bridges taken as reference molecular plane R (dihedral angles: A-R 121.6(3), B-R 122.7(4), C-R (120.8(3), D-R 122.4(4)°). The complete and unequivocal description of the molecular conformation of the macrocycle can be given by using the conformational parameters [9], which give the values reported in Table III if the macrocycle is oriented as in Figure 1a and running around it counterclockwise. The intramolecular space available is

TABLE I Fractional atomic coordinates ($\times 10^4$) and equivalent isotropic thermal parameters ($Å^2 \times 10^4$) for the non-hydrogen atoms of **cavitand I** *(ioio)*

	x/a	*y/b*	*z/c*	U_{eq}[a]
P(1A)	9810	−1679 (5)	−1328	758(24)
O(1A)	10124(5)	−2109(12)	−1701(6)	980(66)
O(2A)	9419(4)	−973(11)	−1814(5)	656(51)
O(3A)	10067(4)	−940(11)	−681(5)	695(52)
O(4A)	9529(5)	−2561(12)	−1013(6)	794(62)
C(1A)	8578(5)	909(15)	−1297(8)	650(78)
C(2A)	9017(6)	447(15)	−1323(8)	745(93)
C(3A)	9020(5)	−509(14)	−1711(7)	578(74)
C(4A)	8604(5)	−1038(13)	−2009(6)	549(69)
C(5A)	8188(5)	−565(12)	−1955(8)	573(47)
C(6A)	8154(3)	420(12)	−1610(7)	521(45)
C(7A)	9461(7)	2251(13)	−929(8)	725(92)
C(8A)	9255(9)	−3385(19)	−1410(10)	971(122)
C(9A)	8806(9)	−3523(18)	−1339(13)	1075(139)
C(10A)	8514(8)	−4344(17)	−1710(12)	948(116)
C(11A)	8690(9)	−4993(23)	−2151(13)	1193(155)
C(12A)	9151(9)	−4883(25)	−2178(15)	1361(161)
C(13A)	9439(10)	−4038(20)	−1843(12)	1154(135)
C(14A)	8356(12)	−5736(26)	−2597(17)	2083(235)
C(20A)	9468(6)	987(13)	−938(5)	809(95)
P(1B)	9567(2)	−2139(5)	1825(3)	704(23)
O(1B)	9276(4)	−2779(11)	1288(6)	802(58)
O(2B)	9950(4)	−1326(12)	1605(6)	771(56)
O(3B)	9299(3)	−1347(10)	2231(5)	659(49)
O(4B)	9898(5)	−2722(14)	2509(7)	1079(75)
C(1B)	9467(6)	789(16)	296(9)	668(79)
C(2B)	9579(6)	266(13)	944(9)	577(76)
C(3B)	9827(6)	−715(14)	936(7)	691(84)
C(4B)	9998(6)	−1215(17)	434(7)	656(80)
C(5B)	9878(5)	−556(16)	−160(8)	580(75)
C(6B)	9627(6)	434(14)	−252(6)	685(87)
C(7B)	9425(6)	2008(12)	1570(9)	721(90)
C(8B)	10200(7)	−3584(18)	2474(10)	771(95)
C(9B)	10211(10)	−4254(20)	1924(12)	1475(163)
C(10B)	10538(9)	−5110(23)	2051(15)	1684(203)
C(11B)	10903(11)	−5368(25)	2604(16)	1794(231)
C(12B)	10879(9)	−4586(25)	3100(17)	1755(198)

TABLE I (Continued)

	x/a	y/b	z/c	U_{eq} [a]
C(13B)	10525(9)	−3818(23)	3074(10)	1227(136)
C(14B)	11228(9)	−6231(21)	2726(23)	2720(304)
C(20B)	9424(4)	744(12)	1561(9)	732(91)
P(1C)	7282(2)	−1753(5)	1194(3)	692(22)
O(1C)	6941(4)	−2153(12)	1547(6)	887(62)
O(2C)	7664(5)	−1014(10)	1685(5)	724(55)
O(3C)	7044(4)	−986(11)	596(5)	715(53)
O(4C)	7588(4)	−2632(11)	910(6)	661(55)
C(1C)	8536(5)	747(14)	1212(8)	586(74)
C(2C)	8094(4)	415(12)	1238(7)	495(72)
C(3C)	8101(7)	−626(14)	1544(9)	688(93)
C(4C)	8493(6)	−1226(15)	1918(9)	685(85)
C(5C)	8913(6)	−778(13)	1854(9)	679(87)
C(6C)	8954(3)	245(12)	1549(8)	601(83)
C(7C)	7702(6)	2223(11)	913(10)	836(98)
C(8C)	7394(8)	−3544(16)	561(11)	839(111)
C(9C)	7425(7)	−3676(17)	−105(10)	908(110)
C(10C)	7233(7)	−4594(21)	−498(13)	1028(122)
C(11C)	6954(12)	−5426(21)	−291(12)	1251(160)
C(12C)	6955(8)	−5252(18)	384(12)	1013(120)
C(13C)	7152(7)	−4373(17)	805(11)	957(116)
C(14C)	6758(9)	−6388(19)	−704(14)	1424(153)
C(20C)	7646(4)	972(10)	884(5)	376(61)
P(1D)	7469(2)	−1874(6)	−1972(3)	766(25)
O(1D)	7720(5)	−2616(11)	−1446(6)	808(62)
O(2D)	7113(4)	−1096(12)	−1742(6)	823(61)
O(3D)	7764(4)	−1116(10)	−2311(5)	745(55)
O(4D)	7165(6)	−2403(15)	−2608(7)	1143(84)
C(1D)	7628(6)	907(15)	−368(7)	596(51)
C(2D)	7515(5)	418(14)	−1008(6)	564(76)
C(3D)	7266(5)	−577(16)	−1115(8)	644(87)
C(4D)	7100(6)	−957(15)	−570(7)	727(90)
C(5D)	7230(7)	−527(15)	85(8)	677(89)
C(6D)	7492(5)	453(13)	190(5)	538(75)
C(7D)	7662(8)	2093(15)	−1611(9)	1170(134)
C(8D)	6843(11)	−3170(23)	−2587(9)	945(136)
C(9D)	6394(9)	−2918(19)	−2573(14)	1101(139)
C(10D)	6084(7)	−3786(19)	−2568(12)	1080(130)
C(11D)	6182(7)	−4916(17)	−2596(11)	872(108)
C(12D)	6632(8)	−5204(19)	−2610(15)	1310(158)
C(13D)	6934(8)	−4311(22)	−2584(12)	1165(141)
C(14D)	5797(7)	−5743(17)	−2619(13)	1178(135)
C(20D)	7679(4)	836(14)	−1599(7)	572(74)
S(1G)	1113(3)	2058(12)	9914(6)	1715(60)
O(1G)	867(9)	2997(21)	9644(13)	2274(150)
C(1G)	915(10)	1479(34)	10563(16)	2293(257)
C(2G)	837(8)	1129(18)	9322(11)	1509(160)
S(1L)	3613(4)	699(7)	5022(6)	1358(44)
O(1L)	3598(8)	1932(11)	5061(10)	1039(82)
C(1L)	4201(8)	334(19)	5206(13)	1193(136)
C(2L)	3527(12)	244(27)	5726(16)	2140(221)
O(1W) [b]	896(23)	3564(55)	5283(34)	1796(311)
O(2W)	3511(26)	3245(38)	10064(35)	4699(276)
O(3W) [b]	1060(20)	3128(49)	5287(29)	1890(221)

[a] Equivalent Isotropic U defined as one-third of the trace of the orthogonalized U_{ij} tensor.
[b] *Disordered atoms wit S. O. F. 0.5.*

determined by the orientation of the O(1) atoms at the phosphate groups. Although all the phosphorus atoms are constrained toward the exterior of the cavity, two of their attached oxygen atoms, O(1B) and O(1D) point inward, whereas O(1A) and O(1C) point outward the

TABLE II Selected bond distances (Å) and angles (°) for compound **I(*ioio*)**

P(1A)–O(1A)	1.44(2)	P(1A)–O(2A)	1.57(1)
P(1A)–O(3A)	1.61(1)	P(1A)–O(4A)	1.56(2)
O(2A)–C(3A)	1.37(2)	O(3A)–C(5B)	1.39(2)
O(4A)–C(8A)	1.40(2)	C(1A)–C(2A)	1.43(2)
C(1A)–C(6A)	1.39(2)	C(2A)–C(3A)	1.39(2)
C(2A)–C(20A)	1.52(2)	C(3A)–C(4A)	1.39(2)
C(4A)–C(5A)	1.39(2)	C(5A)–C(6A)	1.39(2)
C(5A)–O(3D)	1.45(2)	C(6A)–C(20D)	1.50(2)
C(7A)–C(20A)	1.51(2)	C(8A)–C(9A)	1.39(4)
C(8A)–C(13A)	1.39(4)	C(9A)–C(10A)	1.40(3)
C(10A)–C(11A)	1.38(4)	C(11A)–C(12A)	1.39(4)
C(11A)–C(14A)	1.47(4)	C(12A)–C(13A)	1.39(4)
C(20A)–C(6B)	1.51(2)	P(1B)–O(1B)	1.43(1)
P(1B)–O(2B)	1.64(1)	P(1B)–O(3B)	1.59(1)
P(1B)–O(4B)	1.64(1)	O(2B)–C(3B)	1.51(2)
O(3B)–C(5C)	1.39(2)	O(4B)–C(8B)	1.38(3)
C(1B)–C(2B)	1.42(2)	C(1B)–C(6B)	1.38(2)
C(2B)–C(3B)	1.39(2)	C(2B)–C(20B)	1.55 (3)
C(3B)–C(4B)	1.38(2)	C(4B)–C(5B)	1.41(2)
C(5B)–C(6B)	1,39(2)	C(7B)–C(20B)	1.51(2)
C(8B)–C(9B)	1.38(3)	C(8B)–C(13B)	1.38(3)
C(9B)–C(10B)	1.39(4)	C(10B)–C(11B)	1.39(4)
C(11B)–C(12B)	1.39(5)	C(11B)–C(14B)	1.39(4)
C(12B)–C(13B)	1.39(4)	C(20B)–C(6C)	1.51(2)
P(1C)–O(1C)	1.46(1)	P(1C)–O(2C)	1.58(1)
P(1C)–O(3C)	1.55(1)	P(1C)–O(4C)	1.59(1)
O(2C)–C(3C)	1.47(3)	O(3C)–C(5D)	1.40(2)
O(4C)–C(8C)	1.35(2)	C(1C)–C(2C)	1.39(2)
C(1C)–C(6C)	1.40(2)	C(2C)–C(3C)	1.39(2)
C(2C)–C(20C)	1.50(2)	C(3C)–C(4C)	1.42(2)
C(4C)–C(5C)	1.39(3)	C(5C)–C(6C)	1.39(2)
C(7C)–C(20C)	1.50(2)	C(8C)–C(9C)	1.39(3)
C(8C)–C(13C)	1.39(3)	C(9C)–C(10C)	1.39(3)
C(10C)–C(11C)	1.42(4)	C(11C)–C(12C)	1.39(4)
C(11C)–C(14C)	1.46(3)	C(12C)–C(13C)	1.39(3)
C(20C)–C(6D)	1.50(1)	P(1D)–O(1D)	1.44(1)
P(1D)–O(2D)	1.56(1)	P(1D)–O(3D)	1.54(1)
P(1D)–O(4D)	1.52(1)	O(2D)–C(3D)	1.39(2)
O(4D)–C(8D)	1.33(4)	C(1D)–C(2D)	1.39(2)
C(1D)–C(6D)	1.40(2)	C(2D)–C(3D)	1.39(2)
C(2D)–C(20D)	1.49(2)	C(3D)–C(4D)	1.40(2)
C(4D)–C(5D)	1.39(2)	C(5D)–C(6D)	1.39(2)
C(7D)–C(20D)	1.50(2)	C(8D)–C(9D)	1.37(4)
C(8D)–C(13D)	1.39(4)	C(9D)–C(10D)	1.39(3)
C(10D)–C(11D)	1.39(3)	C(11D)–C(12D)	1.39(3)
C(11D)–C(14D)	1.50(3)	C(12D)–C(13D)	1.39(3)
O(3A)–P(1A)–O(4A)	103.1(7)	O(2A)–P(1A)–O(4A)	103.3(7)
O(2A)–P(1A)–O(3A)	110.2(5)	O(1A)–P(1A)–O(4A)	117.0(8)
O(1A)–P(1A)–O(3A)	112.9(6)	O(1A)–P(1A)–O(2A)	109.7(7)
P(1A)–O(2A)–C(3A)	130.8(1)	P(1A)–O(3A)–C(5B)	127.0(1)
P(1A)–O(4A)–C(8A)	121.8(1)	O(3B)–P(1B)–O(4B)	94.9(7)
O(2B)–P(1B)–O(4B)	99.9(8)	O(2B)–P(1B)–O(3B)	105.0(7)
O(1B)–P(1B)–O(4B)	122.6(8)	O(1B)–P(1B)–O(3B)	115.3(7)
O(1B)–P(1B)–O(2B)	115.9(8)	P(1B)–O(2B)–C(3B)	120.3(1)
P(1B)–O(3B)–C(5C)	117.1(1)	P(1B)–O(4B)–C(8B)	122.2(1)
O(3C)–P(1C)–O(4C)	107.3(7)	O(2C)–P(1C)–O(4C)	102.3(7)
O(2C)–P(1C)–O(3C)	106.3(7)	O(1C)–P(1C)–O(4C)	119.5(8)
O(1C)–P(1C)–O(3C)	110.0(8)	O(1C)–P(1C)–O(2C)	110.5(8)
P(1C)–O(2C)–C(3C)	125.6(1)	P(1C)–O(3C)–C(5D)	128.8(1)
P(1C)–O(4C)–C(8C)	121.1(1)	O(3D)–P(1D)–O(4D)	98.6(9)
O(2D)–P(1D)–O(4D)	101.4(9)	O(2D)–P(1D)–O(3D)	106.7(7)
O(1D)–P(1D)–O(4D)	117.6(8)	O(1D)–P(1D)–O(3D)	116.5(8)
O(1D)–P(1D)–O(2D)	114.0(9)	P(1D)–O(2D)–C(3D)	116.6(1)
C(5A)–O(3D)–P(1D)	124.5(1)	P(1D)–O(4D)–C(8D)	122.6(2)

TABLE III Conformational parameters (°) of compound **I(*ioio*)** according to Ref. [9]

	ϕ	κ
A-D	91(2)	-91(2)
D-C	86(2)	-80(2)
C-B	87(2)	-89(2)
B-A	84(2)	-87(2)

TABLE IV Intramolecular hydrogen bonds in compound **I(*ioio*)**

Donor···Acceptor	(Å)	Donor-H···Acceptor	(°)
C(13A)···O(1A)	3.04(3)	C(13A)-H···O(1A)	119(2)
C(9B)···O(1B)	3.27(3)	C(9B)-H···O(1B)	126(2)
C(9C)···O(1D)	3.32(3)	C(9C)-H···O(1D)	136(1)
C(9D)···O(2D)	3.22(3)	C(9D)-H···O(2D)	103(1)

intramolecular cavity. The distance between O(1B) and O(1D) of two opposite P = O groups is 6.29(1) Å, while the distance between O(1A) and O(1C) is 12.81(1) Å (Figs. 1a,b). This makes the shape of the molecule strongly asymmetric: it resembles that of a truncated cone with the minor opening, at the C(7) atoms, almost circular and the major one, at the phosphate oxygens, strongly elliptic (Fig. 1b). The orientation of the *p*-tolyl groups is determined by four intramolecular hydrogen bonds involving the tolyl *ortho* hydrogens and the phosphate O(1) and O(2) atoms (Tab. IV). In this way the inward pointing *p*-tolyl moieties contribute to extend the walls of the cavity instead of closing it. The molecular packing is consistent with the van der Waals radii with one DMSO and two water molecules which fill the voids of the crystal lattice. Another DMSO molecule is axially faced on the minor entrance of the macrocycle with its oxygen atom held by a tetrafurcate hydrogen bond with the circular array of the hydrogens on the C(1) atoms of the four benzene rings (intermolecular $O_{DMSO} \cdots H_{Ph}$ distances from 2.67(2) to 2.85(2) Å.

CONCLUSIONS

The results reported above indicate that a significant diastereoselectivity in the phosphate bridging reaction can be achieved only when the partly bridged resorcinarene substrate presents a conformationally rigid and sufficiently narrow cavity. A wider cavity and some degree of conformational mobility in the resorcinarene precursor highly reduce or even eliminate any diastereoselectivity.

The X-ray crystal structure of the *ioio* isomer of a fourfold-bridged phosphate cavitand **I** shows two important features of this class of molecules:

- the distance between the two opposite inward facing P = O is 6.29(1) Å, too far apart to allow complexation of metal cations (Fig. 1a);
- the *p*-tolyl moieties in the inward orientation contribute to extend the walls of the cavity instead of closing it (Fig. 1b).

EXPERIMENTAL SECTION

General Methods

ACS grade reagents were used without further purification. THF was freshly distilled before use from sodium ketyl. *p*-tolyl phosphate dichloride was synthesized by conventional methods [10] and distilled before use. Analytical TLC was performed on Merck silica gel 60 F_{254} precoated plates. Preparative TLC employed glass-backed silica gel plates with a concentration zone (Merck 60 F_{254}). Column chromatography was performed using silica gel (ICN, 63-200 mesh ASTM). ^{1}H-NMR spectra were recorded at 400 and 300 MHz. ^{31}P-NMR spectra were recorded at 161.9 and 81.0 MHz. Chemical shifts are given in part per million ($\delta_{TMS} = 0$) using as internal reference the residual solvent resonances of deuteriated solvents (7.25 ppm for chloroform). ^{31}P-NMR chemical shifts were measured relative to H_3PO_4(85%) as the internal standard. IR spectra were recorded with a FTIR instrument. Mass spectra were recorded on a single-stage quadrupole mass spectrometer using the DCI technique. Elemental analyses

were performed by the service of Parma University.

Tri-bridged resorcinarenes **1**, **4** and A,C-di-bridged analogue **7** were prepared according to published procedures [7, 8].

7,11,15,28-Tetrabromo-1,21,23,25-tetramethyl-5-(4′-methylphenoxy)-2,20:3,19-dimetheno-1H,21H,23H,25H-[1,3]dioxacino[1,2-d]benzo[4,5-g′][1,3]dioxacino [1′,2′-d′]benzo[4′,5′-g″][1,3] dioxacino [1″,2″-d″]benzo[4″,5″-g‴][1,3,2λ^5] dioxaphosphocin 2(i) and 3(o)

To a stirred solution of resorcinarene **1** (200 mg, 0.22 mmol) in 80 mL dry THF triethylamine (0.3 mL, 2.20 mmol) was added with a syringe at once. A solution of *p*-tolyl phosphate dichloride (0.19 mL, 1.10 mmol) in 30 mL dry THF was then added dropwise over 1 h. The reaction mixture was stirred for one day at room temperature. The solid triethylammonium chloride formed was filtered off. The solvent of the remaining solution was removed in vacuo and the resulting solid was dried at the vacuum pump. Purification by column chromatography on silica gel with 7/3 hexane/ethyl acetate as eluant afforded **2** and **3** as white solids in 65% overall yield: **2 (isomer i**, 52%), white solid, mp 300°C (dec.), TLC R_f 0.57; **3 (isomer o**, 13%), white solid, mp 300°C (dec.), TLC R_f 0.3.

2(i): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.74 (d, 3H, J = 7.5 Hz), 1.79 (d, 9H, J = 7.5 Hz), 2.37 (s, 3H, Ar-CH_3 *out*), 4.57 (d, 1H, J = 7.5 Hz), 4.60 (d, 2H, J = 7.5 Hz), 4.89 (dq, 1H, J_1 = 7.5 Hz, J_{HP} = 3 Hz), 5.05 (q, 1H, J = 7.5 Hz), 5.10 (q, 2H, J = 7.5 Hz), 5.90 (d, 2H, J = 7.5 Hz), 6.01 (d, 1H, J = 7.5 Hz), 7.17 (s, 2H), 7.19 (s, 2H), 7.21 (d, 2H, Ar-H *out*, J = 8.6 Hz), 7.36 (dd, 2H, Ar-H *out*, J_1 = 8.6 Hz, J_{HP} = 1.2 Hz); ^{31}P NMR ($CDCl_3$, 161.9 MHz) δ −21.24 (s, P=O *in*); MS (CI) m/z 1048 (M^-, 100%); IR (CH_2Cl_2) 1310 cm^{-1} ν(P=O). Anal. Calcd. for $C_{42}H_{33}Br_4O_{10}P$: C, 48.09; H, 3.15 Found: C, 47.98; H, 3.08.

3(o): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.75 (d, 3H, J = 7.5 Hz), 1.77 (d, 9H, J = 7.5 Hz), 2.28 (s, 3H, Ar-CH_3 *in*), 4.32 (d, 1H, J = 7.5 Hz), 4.38 (d, 2H, J = 7.5 Hz), 5.00 (dq, 1H, J_1 = 7.5 Hz, J_{HP} = 3 Hz), 5.07 (q, 1H, J = 7.5 Hz), 5.12 (q, 2H, J = 7.5 Hz), 5.89 (d, 2H, J = 7.5 Hz), 6.00 (d, 1H, J = 7.5 Hz), 6.89 (d, 2H, Ar-H *in*, J = 8.6 Hz), 7.00 (d, 2H, Ar-H *in*, J = 8.6 Hz), 7.23 (s, 2H), 7.25 (s, 2H); ^{31}P NMR ($CDCl_3$, 81 MHz) δ −23.9 (s, P=O *out*); MS (CI) m/z 1048 (M^-, 100%); IR (CH_2Cl_2) 1310 cm^{-1} ν(P=O). Anal. Calcd. for $C_{42}H_{33}Br_4O_{10}P$: C, 48.09; H, 3.15. Found: C, 47.94; H, 3.20.

7,12,17,31-Tetrabromo-9,10,14,15,19,20-hexahydro-1,24,26,28-tetramethyl-5-(4′-methylphenoxy)-2,23:3,22-dimetheno-1H,24H,26H,28H-[1,4]dioxonino [1,2-e]benzo[4,5-h′] [1,4]dioxonino [1′,2′-e′]benzo[4′,5′-h″] [1,4]dioxonino [1″,2″,-e″]benzo[4″,5″-h‴][1,3,2λ^5] dioxaphosphocin 5 and 6

Compounds **5** and **6** were prepared following the same procedure as for **2** and **3**, starting from resorcinarene **4** (200 mg, 0.21 mmol). Purification of the crude by column chromatography on silica gel with CH_2Cl_2 as eluant afforded two isomeric products in 65% overall yield: **5 (isomer i**, 35%), white solid, mp 207°C, TLC R_f 0.55; **6 (isomer o**, 30%), white solid, mp 282°C, TLC R_f 0.4.

5(i): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.60 (d, 3H, J = 7.5 Hz), 1.66 (d, 6H, J = 7.5 Hz), 1.81 (d, 3H, J = 7.5 Hz), 2.35 (s, 3H, Ar-CH_3 *out*), 3.8–3.9 (m, 4H), 3.96–4.01 (m, 2H), 4.32–4.53 (m, 6H), 4.87 (dq, 1H, J_1 = 7.5 Hz, J_{HP} = 2.5 Hz), 5.45 (q, 1H, J = 7.5 Hz), 5.52 (q, 2H, 7.5 Hz), 7.19 (d, 2H, Ar-H *out*, J = 8.4 Hz), 7.26 (s, 2H), 7.35 (d, 2H, Ar-H *out*, J = 8.4 Hz), 7.42 (s, 2H); ^{31}P NMR ($CDCl_3$, 161.9 MHz) δ −20.0 (s, P=O *in*);

MS (CI) m/z 1090 (M^+, 100%); IR (CH_2Cl_2) 1300 cm^{-1} ν(P=O). Anal. Calcd. for $C_{45}H_{39}Br_4O_{10}P$: C,49.50;H,3.57. Found: C,49.42; H,3.49.

6(o): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.67 (d, 9H, J = 7.5 Hz), 1.87 (d, 3H, J = 7.5 Hz), 2.24 (s, 3H, Ar-CH_3 *in*), 3.71 (ddd, 2H, J_1 = 12.7 Hz, J_2 = 5.4 Hz, J_3 = 1.8 Hz), 3.80 – 3.91 (m, 4H), 4.37 (ddd, 2H, J_1 = 12.7 Hz, J_2 = 7.8 Hz, J_3 = 2.2 Hz), 4.44 – 4.54 (m, 4H), 5.01 (dq, 1H, J_1 = 7.2 Hz, J_{HP} = 1.6 Hz), 5.49 (q, 1H, J = 7.5 Hz), 5.51 (q, 2H, J = 7.5 Hz), 6.87 (d, 2H, Ar-H *in*, J = 8.4 Hz), 6.96 (d, 2H, Ar-H *in*, J = 8.4 Hz), 7.32 (s, 2H), 7.47 (s, 2H); ^{31}P NMR ($CDCl_3$, 161.9 MHz) δ – 24.0 (s, P=O *out*); MS (CI) m/z 1090 (M^+, 100%); IR (CH_2Cl_2) 1310 cm^{-1} ν(P=O). Anal. Calcd. for $C_{45}H_{39}Br_4O_{10}P$: C,49.50; H,3.57. Found: C,49.34; H,3.51.

7,11,15,28-Tetrabromo-1,21,23,25-tetramethyl-5,13-bis(4′-methylphenoxy)-2,20:3,19-dimetheno-1H,21H,23H,25H-[1,3]dioxacino[1,2-d]benzo[4,5-g′] [1,3,2λ 5]dioxaphosphocino [1′,2′-d′]benzo[4′,5′-g″] [1,3]dioxacino [1″,2″-d″] benzo[4″,5″,-g‴][1,3,2λ^5] dioxaphosphocin 8(io), 9(ii), 10(oo)

Compounds **8**–**10** were prepared following the same procedure used for **2** and **3**, starting from resorcinarene **7** (200 mg, 0.23 mmol). Purification of the crude by column chromatography on silica gel with CH_2Cl_2/ethylacetate (98:2) as eluant afforded, **8**, **9**, **10** as three isomeric products in 56% over all yield: **8** (**isomer io**, 28%), white solid, mp 320°C (dec.), TLC R_f 0.53; **9** (**isomer ii**, 14%), white solid, mp 260°C (dec.), TLC R_f 0.47: **10** (**isomer oo**, 14%), white solid, mp 250°C (dec.), TLC R_f 0.42.

8(io): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.77 (d, 6H, J = 7.5 Hz), 1.78 (d, 6H, J = 7.5 Hz), 2.25 (s, 3H, Ar-CH_3 *in*), 2.35 (s, 3H, Ar-CH_3 *out*), 4.47 (d, 4H, J = 7.5 Hz), 4.90 (dq, 1H, J_1 = 7.5 Hz, J_{HP} = 2.5 Hz), 5.05 (dq, 1H, J_1 = 7.5 Hz, J_{HP} = 2.5 Hz), 5.10 (q, 2H, J = 7.5 Hz), 5.86 (d, 4H, J = 7.5 Hz), 6.99 (s, 4H, Ar-H *in*), 7.18 (d, 2H, Ar-H *out*, J = 8.3 Hz), 7.23 (s, 2H), 7.26 (s, 2H), 7.33 (d, 2H, Ar-H *out*, J = 8.3 Hz); ^{31}P NMR ($CDCl_3$, 81 MHz) δ – 24.5 (s, 1P, P=O *out*), – 18.9 (s, 1P, P=O *in*); MS (CI) m/z 1188 (M^+, 100%); IR (CH_2Cl_2) 1310 cm^{-1} ν(P=O). Anal. Calcd. for $C_{48}H_{38}Br_4O_{12}P_2$: C,48.48; H,3.22. Found: C,47.88; H,3.56.

9(ii): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.77 (d, 6H, J = 7.4 Hz), 1.78 (d, 6H, J = 7.4 Hz), 2.34 (s, 6H, Ar-CH_3 *out*), 4.70 (d, 4H, J = 7.4 Hz), 4.90 (dq, 2H, J_1 = 7.5 Hz, J_{HP} = 2.5 Hz), 5.10 (q, 2H, J = 7.4 Hz), 5.88 (d, 4H, J = 7.4 Hz), 7.17 (d, 4H, Ar-H *out*, J = 8.5 Hz), 7.19 (s, 4H) 7.36 (d, 4H, Ar-H *out*, J = 8.5 Hz); ^{31}P NMR ($CDCl_3$, 81 MHz) δ – 20.2 (s, P=O *in*); MS (CI) m/z 1188 (M^+, 100%); IR (CH_2Cl_2) 1300 cm^{-1} ν(P=O). Anal. Calcd. for $C_{48}H_{38}Br_4O_{12}P_2$: C,48.48; H,3.22. Found: C,48.71; H,3.10.

10(oo): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.84 (d, 6H, J = 7.5 Hz), 1.89 (d, 6H, J = 7.5 Hz), 1.90 (s, 6H, Ar-CH_3 *in*), 4.25 (d, 4H, J = 7.5 Hz), 4.94 (dq, 2H, J_1 = 7.5 Hz, J_{HP} = 2.6 Hz), 5.23 (q, 2H, J_1 = 7.5 Hz), 5.87 (d, 4H, J = 7.5 Hz), 5.98 (d, 4H, Ar-H *in*, J = 8.3 Hz), 6.41 (d, 4H, Ar-H *in*, J = 8.3 Hz), 7.41 (s, 4H); ^{31}P NMR ($CDCl_3$, 81 MHz) δ – 24.5 (s, P=O *out*); MS (CI) m/z 1188 (M^+, 100%); IR (CH_2Cl_2) 1310 cm^{-1} ν(P=O). Anal. Calcd. for $C_{48}H_{38}Br_4O_{12}P_2$: C,48.48: H,3.22. Found: C,47.91; H,3.61.

Crystal Structure Data of $C_{60}H_{52}O_{16}P_4$•2DMSO•2H_2O (*ioio* isomer of compound I)

A colourless single crystal of approximate dimensions of 0.2 × 0.3 × 0.4 mm., grown from DMSO, was mounted on a glass rod without protection from the air. Crystal data are given in

TABLE V Experimental data for the X-ray diffraction studies

Formula	$C_{60}H_{52}O_{16}P_4 \cdot 2(CH_3)_2SO \cdot 2H_2O$
cryst syst	monoclinic
space group	*C c*
cell parameters at 295 K [a]	
a,Å	29.720 (8)
b, Å	11.950 (4)
c, Å	20.322 (6)
β,deg	104.39 (2)
V, Å^3	6991 (4)
Z	4
Dcalc, g cm^{-3}	1.278
F(000)	2816
mol wt	1345.24
linear abs coeff, cm^{-1}	2.364
diffractometer	Enraf Nonius CAD4
radiation	Mo Kα (0.7107 Å)
2θ range, deg	6 ÷ 56
unique data	8436 (± h, + k, + l)
unique data with $I \geq 2\sigma(I)$	2187
agreement between equivalent obsd reflcns	0.07
No. of variables in each block	174, 186, 186, 265
max Δ/σ on last cycle	0.07
$R = \Sigma\|\Delta F\|/\Sigma\|F_o\|$	0.072
$R_w = \Sigma w^{1/2}\|\Delta F\|/\Sigma w^{1/2}\|F_o\|$	0.072
GOF = $[\Sigma w^{1/2}\|\Delta F\|^2/(NO-NV)]^{1/2}$	1.85
max in final ΔF Fourier mape e Å^{-3}	0.285

[a] Unit cell parameters were obtained by least-squares analysis of the setting angles of 30 centered reflections found in a random search on the reciprocal space.

Table V. All the intensities were calculated from profile analyses according to the Lehmann and Larsen method [11]. During the systematic data collection the intensities of two standard reflections, collected every 100 to monitor crystal decay and instrumental linearity, showed a linear decrease. The intensities were corrected for Lorentz and polarization but not for absorption effects. The structure was solved by Direct Methods using SIR92 [12]. The best FOM Emap showed the coordinates of all non-hydrogen atoms of the macrocycle. Two DMSO solvent molecules and two water molecules (one of them disordered over two different positions) were found in the asymmetric unit when the structure was completed by Fourier ΔF map. The crystal structure was refined by blocked full-matrix least-squares methods on *F* using SHELX76 [13]. Parameters refined were: the overall scale factor, the atomic coordinates and anisotropic thermal parameters for all the non-hydrogen atoms with the exception of C(5A), C(6A), C(1D) and the oxygen atoms of the water molecules for which isotropic thermal parameters were assumed. All the hydrogen atoms were placed at their calculated positions with the geometrical constraint C-H 1.0 Å and refined "riding" on their corresponding carbon atoms. The atomic scattering factors of the non-hydrogen atoms were taken from Cromer and Waber [14], the values of $\Delta f'$ and $\Delta f''$ were those of Cromer [15]. The geometrical calculations were obtained by PARST [16]. All the calculations were carried out on the GOULD ENCORE91 of the Centro di Studio per la Strutturistica Diffrattometrica of C.N.R., Parma. List of the thermal parameters for the non-hydrogen atoms (Tab. SI), list of the atomic coordinates of the hydrogen atoms (Tab. SII) and a full list of the bond distances and angles (Tab. SIII) have been deposited with the Cambridge Crystallographic Data Centre.

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