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Phosphorylated Resorcinol-based Cyclophanes

Leonid N. Markovsky,* Vitalii I. Kal'chenko, Dmitrii M. Rudkevich and Aleksandr N. Shivanyuk

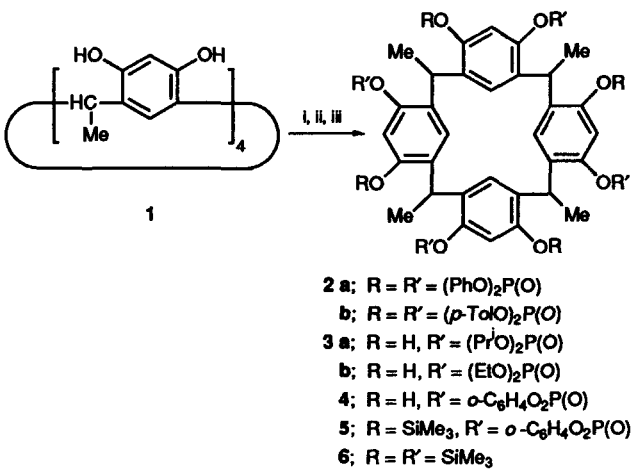
Institute of Organic Chemistry, Ukrainian Academy of Sciences, 253660 Kiev, Ukraine. Fax: +7 044 552 8308

Complete and partial O-functionalization of the octahydroxytetramethyl[1_4]metacyclophane with phosphoryl groups has been carried out, and reversible intramolecular addition of hydroxy or trimethylsilyloxy groups to the neighbouring P=O bonds with the formation of spirophosphorane fragments has been shown to be typical of the 3,10,17,24-tetrahydroxy(tetrakistrimethylsiloxy)-5,12,19,26-tetrakis-*o*-phenylenephosphoryloxy-1,8,15,22-tetramethyl [1_4]metacyclophane.

Octahydroxycyclophane **1**[1] is a promising 'host' molecule, able to form complexes with neutral molecules. Direct replacement of the hydroxyl hydrogen in molecules **1** enables one to effectively regulate the specificity and selectivity of guest bonding both by providing the most suitably substituted form of the molecular cavity for complexation and by changing the physicochemical properties of the functionalized cyclophanes.[2]

A series of O-functionalized octahydroxycyclophanes containing alkyl, acyl, heteryl and silyl groups has already been synthesized.[2–5] Some of their complexes with organic 'guest' molecules, namely CH_2Cl_2, $CHCl_3$, CCl_4, MeCN, MeOH, CS_2, ketones, benzene and its derivatives as well as dioxygen, have been obtained and characterized.[2,4–7]

The aim of this communication is to describe the O-functionalization of octahydroxy[1_4]metacyclophane **1**, obtained by the condensation of resorcinol with acetaldehyde, with phosphoryl groups in which the oxygen atoms possess good cation- and proton-acceptor properties.



2 a; R = R' = $(PhO)_2P(O)$
b; R = R' = $(p\text{-TolO})_2P(O)$
3 a; R = H, R' = $(Pr^iO)_2P(O)$
b; R = H, R' = $(EtO)_2P(O)$
4; R = H, R' = $o\text{-}C_6H_4O_2P(O)$
5; R = $SiMe_3$, R' = $o\text{-}C_6H_4O_2P(O)$
6; R = R' = $SiMe_3$

Scheme 1 *Reagents and conditions*: i, >P(O)Cl, Et_3N, tetrahydrofuran (THF), 20°C; ii, >P(O)H, CCl_4, Et_3N, THF, 20°C; iii, Me_3SiCl, Et_3N, THF, 20°C

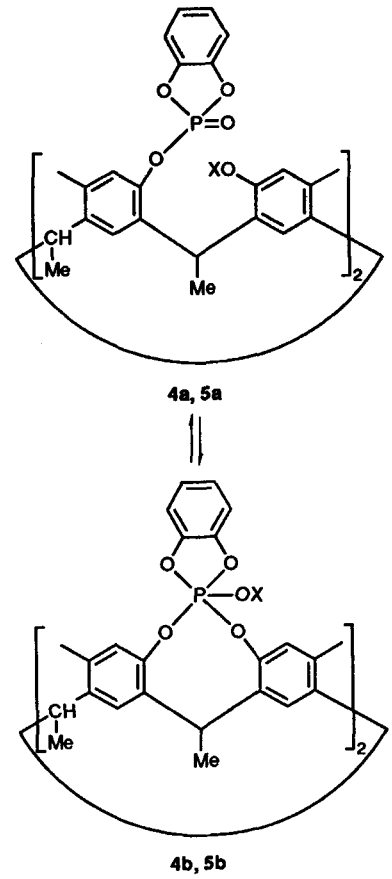
On reaction with traditional phosphorylating agents, the hydrogen atoms of the hydroxy groups in compound **1** are replaced, the reaction process being dependent upon the structure of the cyclophane. Thus, a twofold excess of diphenyl or ditolyl-chlorophosphate in the presence of triethylamine leads to complete replacement of the hydrogen atoms of the hydroxy groups, and 3,5,10,12,17,19,24,26-octakisdiaryloxyphosphoryloxy-1,8,15,22-tetramethyl[1_4]metacyclophanes **2** are formed in 70–80% yields. At the same time, under these conditions, the sterically bulky diisopropylchlorophosphate reagent phosphorylates only half of the hydroxy groups in compound **1** to 3,10,17,24-tetrahydroxy-5,12,19,26-tetrakisdiisopropoxyphosphoryloxy-1,8,12,22-tetramethyl[1_4]metacyclophane **3a**.[8]

The reaction of octol **1** with the three-component system dialkylphosphite–CCl_4–Et_3N (octol:phosphite = 1:16) leads to tetraphosphorylated cyclophanes **3** (Scheme 1) (50–60% yields).†

Tetrakis-*o*-phenylenephosphoryloxy[1_4]metacyclophane **4a** has been obtained in 95% yield by the reaction of octol **1** with four mol. equiv. of *o*-phenylenechlorophosphate in the presence of Et_3N.

One set of signals for all the proton groups in the ^1H NMR spectra of compounds **2a,b** observed at ambient temperature shows a 'crown' conformation, which is known to be flexible in the absence of stabilizing hydrogen bonds and is in fast equilibrium with the 'boat' conformation.[9–11]

On the contrary, the ^1H NMR spectra of cyclophanes **3a,b** exhibit a double set of signals for the benzene rings, whereas a double set of signals is observed for the methyl groups of the diethoxyphosphoryl fragments with a quadruple set for the methyl protons of the diisopropoxyphosphoryl fragments. Such spectroscopic evidence indicates both the destruction of the 'crown' conformation by the bulky dialkoxyphosphoryl substituents and its transformation into the less symmetrical 'chair' form for **3b** and, probably, the 'diamond' form for **3a**.



Scheme 2 Ring–chain phosphate–phosphorane equilibrium

The ^{31}P NMR spectra are not sensitive to the conformational changes in the molecules and only one signal for the phosphorus atom is observed for compounds **2** and **3**.

The spatial proximity of the phosphoryl fragments and the hydroxy groups of the neighbouring benzene rings in compound **4a** leads to reversible intramolecular nucleophilic addition of the OH groups to P=O bonds and formation of the spirophosphorane structure **4b** (Scheme 2).[12,13] The equilibrium position between the tautomers **4a** (chain) and **4b** (ring) depends on the temperature and the nature of the solvent (Table 1).

The ^{31}P NMR spectrum of the tautomeric mixture **4a⇄4b** shows one signal at δ 10.32 for tetracoordinate phosphorus and three neighbouring signals (δ −16.46, −17.48, −18.63) for pentacoordinate phosphorus, the ratio of intensities within this group of signals being dependent on temperature. Thus, at 24°C it is 1:3:1, whereas at 100°C it is 2:2.7:1. On cooling the system to 24°C the ratio is restored to its initial level.

Table 1 Position of the ring–chain equilibrium **4a⇄4b**

Solvent	*T*/°C	[4a]/[4b]
$PhNO_2$	24	0.89
	60	0.86
	80	0.84
	100	0.97
THF	24	0.40
DMF[a]	24	0.33
Et_3N	24	∞

[a] DMF = *N*,*N*-dimethylformamide.

† ^1H and ^{31}P NMR data and elemental analyses confirm the structures of the new compounds synthesized.

2a:[8] m.p. 152–154°C; ^1H NMR ([$^2H_6$]acetone) δ 1.28 (d, 12H, CH_3, *J* 7.2 Hz), 4.76 (q, 4H, CH, *J* 7.2 Hz), 6.95–7.35 (m, 88H, arom.); ^{31}P NMR (acetone) δ −18.23.

2b: m.p. 135–136°C; ^1H NMR ([$^2H_6$]acetone) 1.21 (d, 12H, CH_3, *J* 7.0 Hz), 2.12 (s, 48H, CH_3–C_6H_4), 4.85 (q, 4H, CH, *J* 7.0 Hz), 6.80–7.10 (m, 72H, arom.); ^{31}P NMR (acetone) δ −16.57.

3a:[8] m.p. 216–218°C; ^1H NMR ([$^2H_6$]DMSO, DMSO = dimethyl sulfoxide) 1.27 [d, 12H, $(CH_3)_2CH$, *J* 6.4 Hz], 1.32 [d, 12H, $(CH_3)_2CH$, *J* 6.4 Hz], 1.33 [two d, 24H, $(CH_3)_2CH$, *J* 6.4 Hz], 1.38 (d, 12H, CH_3, *J* 7.2 Hz), 4.55 (q, 4H, CH, *J* 7.2 Hz), 4.70 [octet, 8H, $(CH_3)_2CH$, *J* 6.4 Hz], 6.07 (s, 2H, arom.), 6.75 (s, 2H, arom.), 6.90 (s, 2H, arom.), 7.27 (s, 2H, arom.), 8.53 (s, 4H, OH); ^{31}P NMR(DMSO) δ −7.38.

3b: m.p. 262–264°C; ^1H NMR ([$^2H_6$]DMSO) 1.21 (two, t, 24H, CH_3CH_2, *J* 7.0 Hz), 1.36 (d, 12H, CH_3, *J* 7.0 Hz), 4.05 (q, 16H, CH_3CH_2, *J* 7.0 Hz), 4.48 (q, 4H, CH, *J* 7.0 Hz), 6.22 (s, 4H, arom.), 6.91 (s, 2H, arom.), 7.07 (s, 2H, arom.), 8.90 (s, 4H, OH); ^{31}P NMR(DMSO) δ −5.27.

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The spectra observed can reflect conformational transitions and partial intermolecular cyclizations, as well as the formation of isomers with a different number of spirocyclic fragments in a molecule. In fact, the computer modelling[14] of the ring–chain equilibrium **4a**⇌**4b** shows that even the formation of two spirocyclic fragments can distort the 'crown' conformation, thus impeding further intramolecular cyclizations.

Similar ring–chain equilibrium is observed in 3,10,17,24-tetrakistrimethylsiloxy-1,8,15,22-tetramethyl[1_4]metacyclophane **5a**, obtained by the reaction of octakistrimethylsiloxycyclophane **6**‡ with four mol. equiv. of *o*-phenylenechlorophosphate (toluene, 95°C). In this case the ^{31}P NMR spectrum shows singlets at δ 7.38 (**5a**) and −18.23 (**5b**) in the ratio 10:1 (toluene). In a solution of pyridine, which is capable of association with pentacoordinate phosphorus,[13] the equilibrium shifts towards the spirocyclic tautomer and reaches the 1:1 ratio of [**5a**]/[**5b**].

Preliminary investigations have shown that cyclophanes **2a,b** are active carriers of cations of the alkali metals (and those of the alkaline earths to a certain extent) and form complexes with toluene, phenol, *m*-cresol, *etc.*

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‡ **4**: m.p. 110–120°C; ^{1}H NMR($CDCl_3$) δ 1.71 (m, 12H, CH_3), 4.75 (q, 4H, CH, *J* 7.2 Hz), 6.35–7.40 (m, 24H, arom.).

6: m.p. >260°C; ^{1}H NMR($CDCl_3$) δ 0.02 [s, 36H, $(CH_3)_3Si$], 0.34 [s, 36H, $(CH_3)_3Si$], 1.37 (d, 12H, CH_3, *J* 7.2 Hz), 4.53 (q, 4H, CH, *J* 7.2 Hz), 6.00–6.20 (m, 8H, arom.).

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