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# One-step synthesis of *rccc*- and *rctt*-diastereomers of novel calix[4]resorcinols based on a *para*-thiophosphorylated derivative of benzaldehyde

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ABSTRACT

Novel calix[4]resorcinols with four 2-thioxo-1,3,2-dioxaphosphorinane fragments included in aromatic substituents have been synthesized via a one-step condensation of resorcinol and its derivatives with a new *para*-thiophosphorylated benzaldehyde. It has been found that the diastereomeric ratio depends substantially on the reaction conditions, in particular, the solvents and catalysts used. The macrocyclic products obtained are *rctt*- and/or *rccc*-isomers, which were isolated and the structures determined by NMR and single crystal X-ray diffraction studies.



The design of phosphorus-containing macrocyclic compounds including calixarenes is an important area of development in contemporary organoelement chemistry.[1] The introduction of functional groups with a phosphorus atom of varying coordination in the macrocycle allows the synthesis of substances with three-dimensional architecture. Organophosphorus fragments having high coordination ability can enhance substantially the particular properties of a macromolecule or give it completely new features. For example, modification of the calix[4]arene matrix with functional groups containing phosphorus and sulfur atoms allows a remarkable improvement of the extraction ability of the derivatives obtained compared to their unsubstituted precursors, with respect to soft metal ions, specifically, $Ag^{+}$, $Co^{2+}$, $Cu^{2+}$, $Zn^{2+}$, $Pb^{2+}$, and $Hg^{2+}$.[2]

A general method for the synthesis of calix[4]resorcinols involves the acid-catalyzed condensation of resorcinol or its derivatives with aliphatic or aromatic aldehydes.[3] The macrocyclic compounds formed can exist as four diastereomers, namely, *rccc*, *rcct*, *rctt*, and *rttt*, which are differentiated by the spatial orientation of the substituents of the calixarene matrix relative to the macrocyclic cavity. The ratio of diastereomers usually depends on the nature of the initial aldehyde and the reaction conditions. For example, condensation of resorcinol with long-chain aliphatic aldehydes gives predominantly the *rccc*-isomer in high yields, and the use of aromatic aldehydes leads to a mixture of *rccc*- and *rctt*-isomers.

Recently, we realized for the first time the highly effective single-step synthesis of P = S-substituted calix[4]resorcinols containing four diethyl thiophosphate or 2-thioxo-1,3,2-dioxaphospholane groups on the aromatic substituents, which was based on the condensation of new thiophosphorylated derivatives of benzaldehyde with resorcinol or its derivatives in acidic media.[4] It was shown that the reactions proceeded stereoselectively in moderate to high yields with formation of only the isomer of calixarene in *chair* conformation with *rctt*-configuration of the thiophosphorylated substituents. It should be noted that the introduction of thiophosphoryl groups on the calixarene framework has so far been a labor-consuming process, and involved predominantly the addition of a sulfur atom to trivalent phosphorus atoms, which had been previously introduced on the upper rim of calix[4]resorcinols or cavitands via O-phosphorylation.[2b,5]

In order to design thiophosphorylated calix[4]resorcinols as functionalized partners in the reaction with resorcinol and its derivatives, we used for the first time 2-(4-formylphenoxy)-2-thioxa-5,5-dimethyl-1,3,2-dioxaphos-phorinane (**3**), which was synthesized in a yield of 88% by the reaction of 2-chloro-2-thioxo-1,3,2-dioxaphosphorinane (**1**), synthesized according to a known

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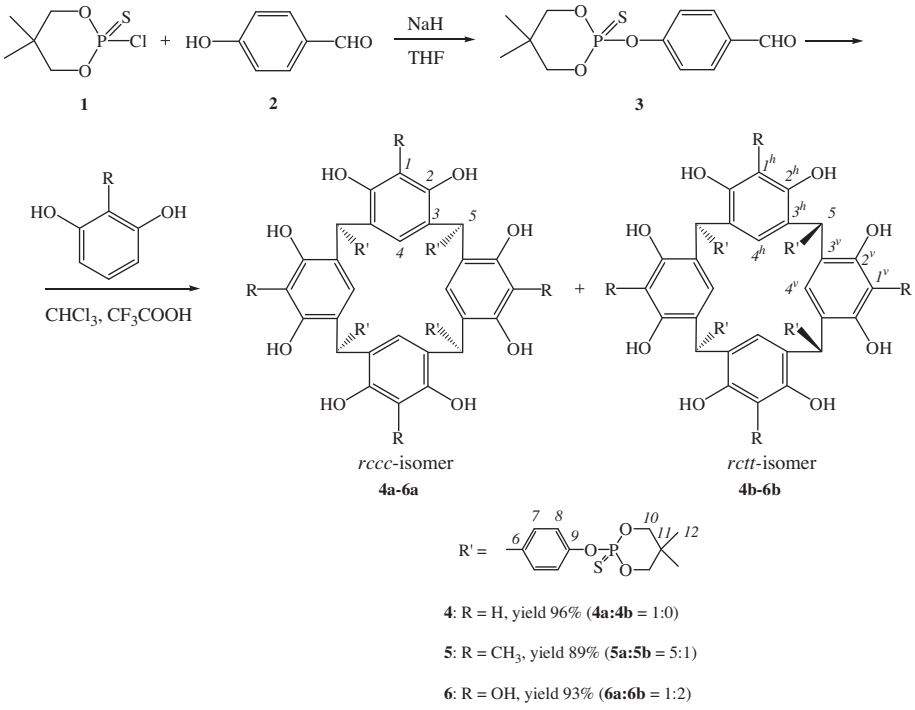


**Scheme 1.** Synthesis of thiophosphorylated calix[4]resorcinols **4**–**6**.

procedure,[6] and 4-hydroxybenzaldehyde (**2**) in the presence of sodium hydride in anhydrous THF (Scheme 1).[7] The crystal structure of compound **3** was established by means of single crystal X-ray diffraction.[8,9]

Subsequent condensation of equimolar amounts of resorcinol and aldehyde **3** in chloroform containing trifluoroacetic acid (60–65 °C, ca. 35 h) resulted in the formation of only the *rccc*-isomer of calix[4]resorcinol **4a** in a yield of 96% (method A).[10] Reaction of compound **3** with 2-methylresorcinol under similar conditions took place with the formation of a mixture of *rccc*- and *rctt*-isomers **5a** and **5b**, respectively, in a 5:1 ratio and a total yield of 89%.[11] Finally, in an analogous reaction, pyrogallol gave a mixture of *rccc*- and *rctt*-isomers **6a** and **6b** in a 1:2 ratio and a total yield of 93%; however, the *rctt*-isomer **6b** predominated (Scheme 1).[12] It should be noted that increasing the reaction time did not affect substantially the ratio and total yield of the isomers, which precipitated from the reaction mixture. Owing to the different solubilities, the isomers were isolated in pure form by means of consecutive recrystallization from acetone and ethanol, and then characterized.

It is interesting to note the effect of the nature of the solvents and catalysts used on the isomeric ratios of the calix[4]resorcinols. For example, substitution of the mixture of chloroform and trifluoroacetic acid for ethanol, water, and concentrated hydrochloric acid in the reactions of resorcinol or 2-methylresorcinol with aldehyde **3** (not shown in Scheme 1) gave rise to stereoselective formation of only the *rctt*-isomers **5b** and **6b**, respectively, in *chair* conformation, in moderate yields of up to 56% (method B).[13,14]

It should be noted that the *rccc*-isomers of thiophosphorylated calix[4]resorcinols were synthesized for the first time in the reactions with functionalized derivatives of benzaldehydes. The assignments of the signals of compounds **4a**–**6a** in the NMR spectra were performed by means of $^{1}H$, $^{13}C$, HSQC, and HMBC experiments. Each group of these compounds corresponds to one resonance in the NMR spectra; this indicates the existence of highly symmetric *cone* conformation in the solutions of these compounds; the multiplet signals of the dioxaphosphorinane fragments being the only exception.

An interesting feature of compounds **4a**–**6a** was the strong dependence of their dynamic behavior versus solvent. As was mentioned above, calix[4]resorcinols can exist in conformations of various symmetries. The conformation is one of the main factors which determines the function of these macromolecules in supramolecular systems.[15] When a calix[4]resorcinol has small nonbulky (e.g., aliphatic) substituents, an averaged spectrum on the NMR time-scale is observed, which is ascribed to the *cone* conformation; although it is the consequence of rapid *boat 1*–*cone*–*boat 2* conformational interconversion (Fig. 1). When there are bulky substituents present, in some cases the frozen *boat* conformation is detected in the NMR spectra.[3a,c,16] Several reports on the effect of the polarity of the solvent on the dynamic characteristics of calix[4]resorcinols in solutions relate the solvent effect mainly to its polarity and ability to break hydrogen bonds between the hydroxyl groups of resorcinol rings.[17]

In our case, a large difference is observed in the $^{1}H$ NMR spectra in the two solvents, which are similar by their properties, namely, DMSO-$d_6$ and acetone-$d_6$. At 303 K in acetone-$d_6$, the observed $^{1}H$ NMR spectrum of compound **4a** is characteristic of the *cone* conformation; that is, each group of protons corresponds to one signal. In DMSO-$d_6$, a similar spectrum could only be obtained at 373 K, while that at 303 K shows coalescence of the peaks due to the H4 protons (Fig. 2).

Values of the barriers of *boat 1*–*cone*–*boat 2* interconversion ($\Delta G^{\#}$) can be calculated with the use of Eyring equations.[18] Unfortunately, it is impossible to determine directly from conducted

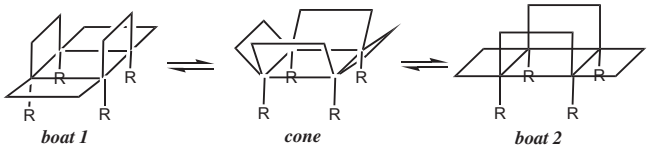


**Figure 1.** *Boat 1*–*cone*–*boat 2* interconversion.

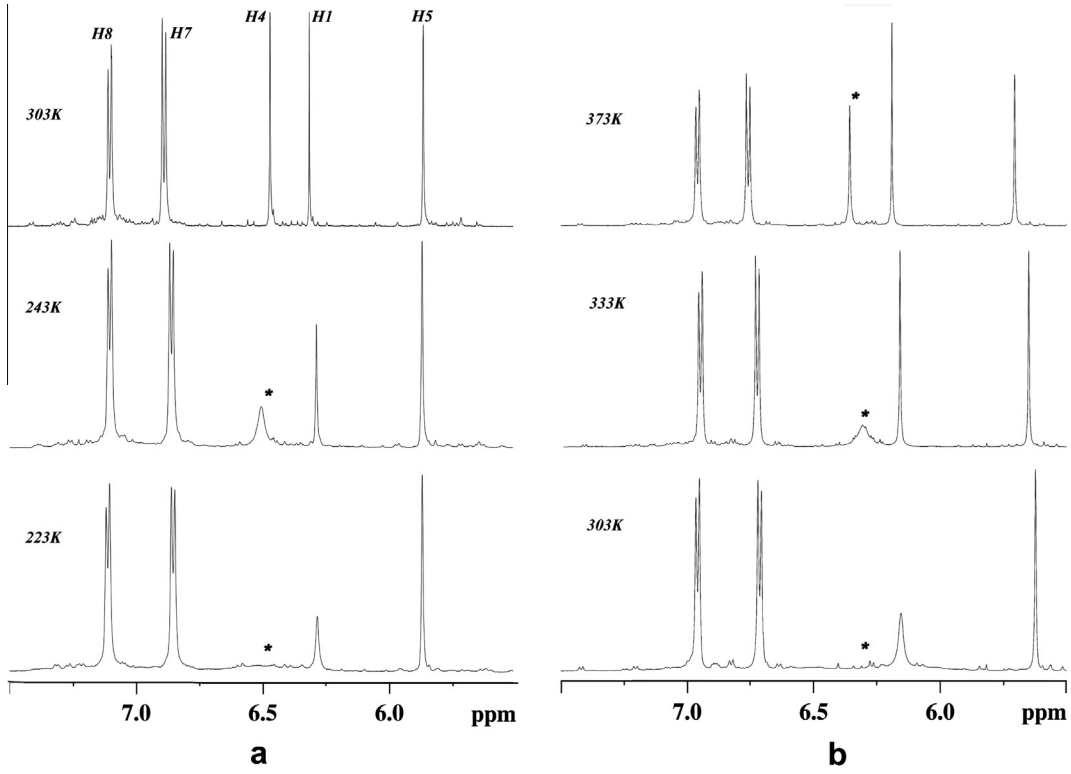


**Figure 2.** Temperature-dependent $^1$H NMR spectra of the aromatic protons signals of **4a** at 600 MHz in acetone-$d_6$ (a) and DMSO-$d_6$ (b). The peak of H4 is marked by asterisk.

experiments the difference of chemical shifts $\delta_\nu$ for the states being in chemical exchange. In compound **4a**, this is the difference of chemical shifts of H4 protons for two opposite resorcinol rings oriented vertically relative to macrocyclic cavity and two other opposite resorcinol rings oriented horizontally. And H4 protons oriented horizontally to resorcinol rings undergo the deshielding effect of aromatic currents of two opposite resorcinol rings oriented vertically. The magnitude of deshielding effect determines the difference of chemical shifts and is related to the value of aromatic currents of resorcinol rings. As the spectrum corresponding to the completely frozen *boat* conformation was not obtained in any of the solvents used, the difference in the chemical shifts for this conformation was considered to be 1 ppm = 600 Hz, as in earlier work,[5] where NMR structural data were given for calix[4]resorcinols in *boat* configuration. The barriers for the *boat 1–cone–boat 2* interconversion for **4a** calculated from the temperatures of coalescence correspond to $\Delta G$ = 59.5 kJ/mol for $T_C$ = 303 K (DMSO-$d_6$) and $\Delta G$ = 44.4 kJ/mol for $T_C$ = 223 K (acetone-$d_6$).

The large difference observed for the barrier of *boat 1–cone–boat 2* interconversion depending on the used solvent, more specifically, DMSO-$d_6$ or acetone-$d_6$ ($\Delta\Delta G$ = 15 kJ/mol), can be related to the nature of DMSO, particularly its large dipole moment and ability to form hydrogen bonds with proton donor compounds. It is known that *cone* conformation in calixresorcinol is stabilized by the cyclic intramolecular hydrogen bond. While some hydroxyl groups of resorcinol fragments are involved in it, others are free and directed out of the calixresorcinol cavity and, consequently, can form additional hydrogen bonds. The system is dynamic and all hydroxyl groups are involved in *flip–flop* exchange between bonded and free state.[19] DMSO molecules, while solvating calixresorcinol, are embedded in the system of hydrogen bonds stabilizing the existing equilibrium forms of conformers, thus increasing the barrier of *boat 1–cone–boat 2* interconversion.

It is interesting to note that thiophosphorylated calix[4]resorcinols **4a** and **5a** adopt a boat conformation in the crystal state (Fig. 3a, b).[8,20,21] It should be mentioned that the conformation of molecule **5a** is highly distorted.

The $^1$H NMR spectra of compounds **4b**–**6b** in the *chair* conformation display doubling of their proton and carbon signals for the resorcinol fragments; this attests to the different, vertical ($v$) and horizontal ($h$), arrangements of opposite resorcinol rings with respect to the macrocyclic plane as was the case for analogous thiophosphorylated calix[4]resorcinols in our previous publications.[4] The *chair* conformation of calixarene **6b** was confirmed by single crystal X-ray diffraction (Fig. 3c).[8,22]

The crystal and molecular structures of the obtained compounds are of interest considering that classical hydrogen bonding takes part in their formation. The results of structure analysis and the relationship between their instability and the features of the molecular packing will be reported in due course.

In conclusion, we have demonstrated that new benzaldehyde **3** is a useful starting material for the one-step preparation of novel calix[4]resorcinols with four 2-thioxo-1,3,2-dioxaphosphorinane fragments attached to the aromatic substituents. The syntheses proceed with moderate to high yields enabling intentionally desired *rccc*- and/or *rctt*-isomers to be prepared depending on the experimental conditions. An interesting feature of the synthesized compounds is the strong dependence of their dynamic behavior on NMR time-scale versus the solvent used.

## Acknowledgments

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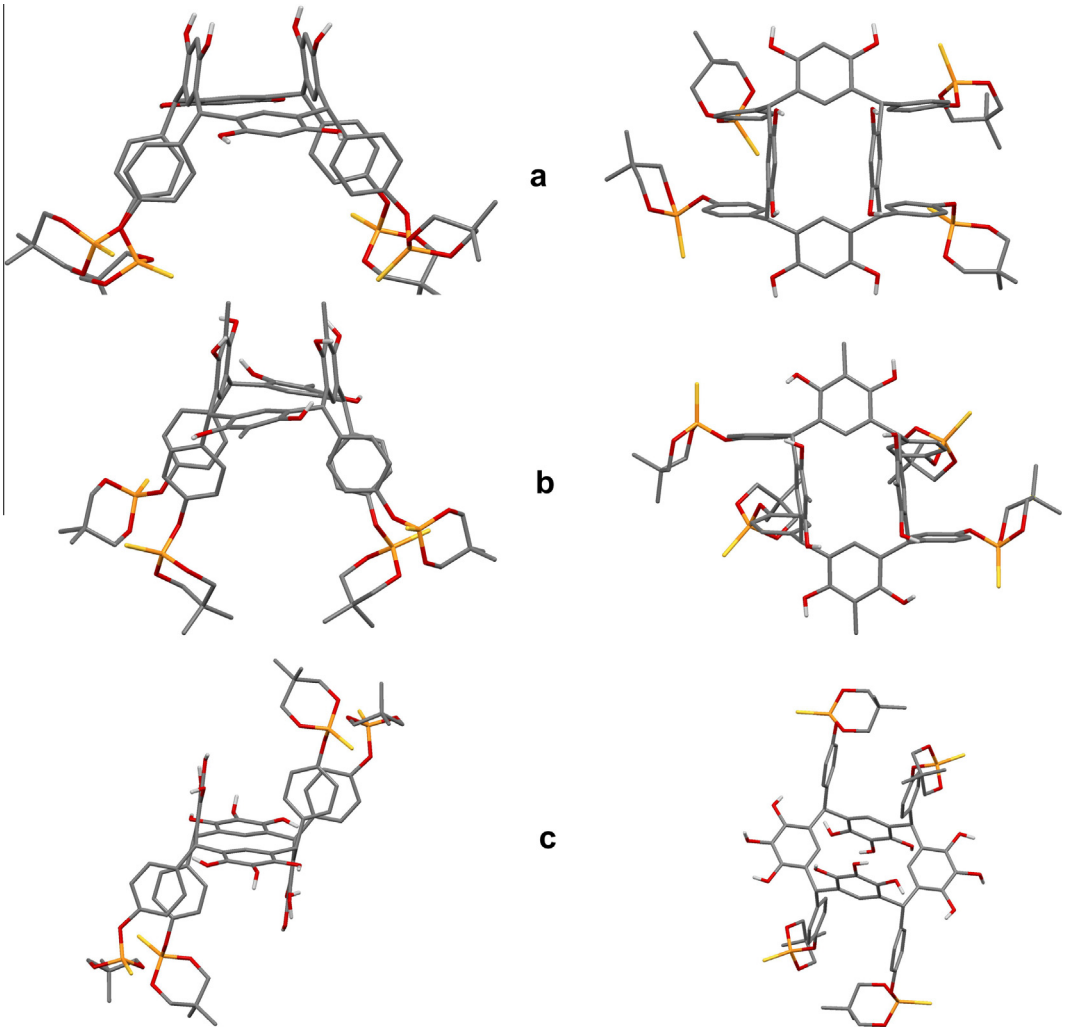


**Figure 3.** Two projections of the calix[4]resorcinol molecules in the crystals of **4a** (a), **5a** (b), and **6b** (c). Hydrogen atoms (excluding H-atoms of the hydroxyl groups) and solvent molecules are omitted for clarity.

## References and notes


1. (a) Antipin, I. S.; Kasakova, E. Kh.; Habicher, W. D.; Konovalov, A. I. *Russ. Chem. Rev.* **1998**, *67*, 905; (b) Cherenok, S.; Kalchenko, V. *Top. Heterocycl. Chem.* **2009**, *20*, 229; (c) Dutasta, J.-P. *Top. Curr. Chem.* **2004**, *232*, 55; (d) Pinalli, R.; Dalcanale, E. *Acc. Chem. Res.* **2013**, *46*, 399; (e) Knyazeva, I. R.; Burilov, A. R.; Pudovik, M. A.; Habicher, W. D. *Russ. Chem. Rev.* **2013**, *82*, 150.
2. (a) Wang, H.; Li, Z.; Liu, Y. *Sci. Chin. B Chem.* **2007**, *50*, 654; (b) Bibal, B.; Declercq, J.-P.; Dutasta, J.-P.; Tinantb, B.; Valad, A.-G. *Tetrahedron* **2003**, *59*, 5849.
3. (a) Tunstad, L. M.; Tucker, J. A.; Dalcanale, E.; Weiser, J.; Bryant, J. A.; Sherman, J. C.; Helgeson, R. C.; Knobler, C. B.; Cram, D. J. *J. Org. Chem.* **1989**, *54*, 1305; (b) Thoden van Velzen, E. U.; Engbersen, J. F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1994**, *116*, 3597; (c) Högberg, A. G. S. *J. Org. Chem.* **1980**, *45*, 4498; (d) Yamakawa, Y.; Ueda, M.; Nagahata, R.; Takeuchi, T.; Asai, M. *J. Chem. Soc., Perkin Trans. 1* **1998**, 4135; (e) Prosvirkin, A. V.; Kazakova, E. Kh.; Gubaidullin, A. T.; Litvinov, I. A.; Gruner, M.; Habicher, W. D.; Konovalov, A. I. *Russ. Chem. Bull., Int. Ed.* **2005**, *54*, 2550.
4. (a) Knyazeva, I. R.; Burilov, A. R.; Fazleeva, G. M.; Nuretdinov, I. A.; Gryaznova, T. V.; Budnikova, Yu G.; Khrisanforova, V. V.; Gubaidullin, A. T.; Gabidullin, B. M.; Syakaev, V. V.; Pudovik, M. A.; Konovalov, A. I. *Phosphorus, Sulfur Silicon Relat. Elem.* **2011**, *186*, 1972; (b) Knyazeva, I. R.; Sokolova, V. I.; Gruner, M.; Habicher, W. D.; Voronina, J. K.; Burilov, A. R.; Pudovik, M. A. *J. Incl. Phenom. Macrocycl. Chem.* **2012**. http://dx.doi.org/10.1007/s10847-012-0190-0.
5. Maslennikova, V. I.; Serkova, O. S.; Gruner, M.; Goutal, S.; Bauer, I.; Habicher, W. D.; Lyssenko, K. A.; Antipin, M. Yu; Nifantyev, E. E. *Eur. J. Org. Chem.* **2004**, 4884.
6. Ren, J.-L.; Cheng, B.-W.; Zhang, J.-S. h.; Zang, H.-J.; Kang, W.-M.; Ding, Ch.-K. *Jiegou Huaxue* **2008**, *27*, 70.
7. *Experimental procedure for the preparation of and spectroscopic data of compound* ***3***: A solution of 4-hydroxybenzaldehyde (**2**) (8.34 g, 68.3 mmol) in THF (60 mL) was added dropwise to a suspension of NaH (1.64 g, 68.3 mmol) in THF (120 mL) at 10 °C and the mixture was stirred at rt for 60 min. Then, a solution of 2-chloro-2-thioxo-1,3,2-dioxaphosphorinane (**1**) (13.70 g, 68.3 mmol) in THF (70 mL) was added and the resulting suspension was stirred with heating (~65 °C) under a nitrogen atmosphere. The progress of the reaction was monitored by TLC. After 6 h, the precipitate was filtered and washed with benzene. The solvent was evaporated and the crude residue was purified by column chromatography using dichloromethane as eluent. The pure compound **3** was obtained as a white solid (17.11 g, 88% yield, $R_f$ = 0.58), mp 103–104 °C. $^{31}$P NMR (166.9 MHz, $CDCl_3$): $\delta$ = 53.2 ppm. $^1$H NMR (600.1 MHz, $CDCl_3$): $\delta$ = 0.94 (s, 3H, $CH_3$), 1.35 (s, 3H, $CH_3$), 4.04 (m, 2H, $OCH_2$), 4.32 (m, 2H, $OCH_2$), 7.38 (d, $^3J_{HH}$ = 8.49 Hz, $^4J_{PH}$ = 1.3 Hz, 2H, P–O–$C_{ar}$–$CH_{ar}$), 7.92 (d, $^3J_{HH}$ = 8.49 Hz, 2H, $CH_{ar}$–$C_{ar}$–CHO), 9.99 (s, 1H, CHO) ppm. IR (film) $\nu_{max}$: 820 cm$^{-1}$ (P=S). Anal. Calcd for $C_{12}H_{15}O_4PS$: C, 50.35; H, 5.24; P, 10.84; S, 11.19. Found: C, 50.63; H, 5.21; P, 10.70; S, 11.44. ESI-MS: $m/z$ = 287 $[M+H]^+$ (calcd M = 286).
8. Crystals of compound **3**, suitable for X-ray analysis, were obtained by slow evaporation of a $CHCl_3$ solution. Suitable monocrystals of compounds **4a**, **5a**, and **6b** were grown in acetone/EtOH/DMSO solution. The X-ray diffraction data for **3**, **4a**, **5a**, and **6b** were collected on a Bruker Smart APEX II CCD diffractometer in the ω-scan mode using graphite monochromated Mo Kα ($\lambda$ = 0.71073 Å) radiation. The crystals of compounds **4a**, **5a**, and **6b** decomposed rapidly when exposed to air. Therefore specimens of **4a** and **5a** were subjected to a nitrogen gas cooling stream immediately after being mounted and were kept at a temperature of 150 K during the experiment. The single crystal of **6b** was loaded into a thin-walled capillary, partially filled with supernatant solution and the experiment was carried out at 296(2) K. Crystals of **3** were stable, the experiment was performed at 296(2) K. All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were inserted at calculated positions and refined as riding atoms, except those of the hydroxyl groups, which were located from difference maps and refined using a riding model. Crystallographic data (except structure factors) reported in this paper have been deposited at the Cambridge Crystallographic Data Centre with supplementary publication numbers CCDC 908161, 908159, 908160, and 908162 for **3**, **4a**, **5a**, and **6b**, respectively. Copies of these data can be

obtained free of charge upon application to the CCDC (12 Union Road, Cambridge CB2 1EZ, UK. Fax: (internat.) +44 1223/336 033; E-mail: deposit@ccdc.cam.ac.uk).

9. *Crystallographic data for* **3**: $C_{12}H_{15}O_4PS$, $M$ = 286.27, monoclinic, $a$ = 12.109(3) Å, $b$ = 16.653(4) Å, $c$ = 6.7274(15) Å, $\beta$ = 96.401(3)°, $V$ = 1348.2(5) Å$^3$, $T$ = 296(2) K, space group $Cc$, $Z$ = 4, $\mu$ = 0.362 mm$^{-1}$, 7388 reflections measured ($R_\sigma$ = 0.0338), 3037 independent reflections ($R_{int}$ = 0.0298), $R_1$ = 0.0752 (all data), $wR_2$ = 0.1973 (all data), $R_1$ = 0.0688 ($I > 2\sigma_I$), $wR_2$ = 0.1925 ($I > 2\sigma_I$), GoF = 1.345.
10. *Experimental procedure for the preparation of and spectroscopic data of compound* ***4a*** *(Method A):* a mixture of resorcinol (0.38 g, 3.50 mmol) and aldehyde **3** (1 g, 3.50 mmol) in $CHCl_3$ (26 mL) and trifluoroacetic acid (3 mL) was stirred under heating at 60–65 °C for 35 h under a nitrogen atmosphere. The precipitate formed was filtered, washed sequentially with $CHCl_3$ and $Et_2O$. The washing procedure was repeated until only a colorless filtrate was observed. After drying in vacuo (40 °C, 0.06 Torr) pure **4a** as its *rccc*-isomer in *cone* conformation was obtained (1.27 g, 96%) as a pale yellow powder, mp >190 °C (dec). $^{31}$P NMR (166.9 MHz, acetone-$d_6$): $\delta$ = 54.3 ppm. $^1$H NMR (600.1 MHz, acetone-$d_6$): $\delta$ = 1.02 (s, 12H, H12), 1.34 (s, 12H, H12), 4.14 (m, 8H, H10), 4.55 (m, 8H, H10), 5.87 (s, 4H, H5), 6.31 (s, 4H, H1), 6.47 (s, 4H, H4), 6.90 (d, $^3J_{HH}$ = 8.80 Hz, 8H, H7), 7.11 (d, $^3J_{HH}$ = 8.80 Hz, $^4J_{PH}$ = 1.3 Hz, 8H, H8), 7.61(s, 8H, OH) ppm. $^{13}$C NMR (150.9 MHz, acetone-$d_6$): $\delta$ = 21.4 (s, C12), 22.6 (s, C12), 33.6 (s, C11), 43.2 (s, C5), 79.3 (s, C10), 104.2 (s, C1), 121.3 (s, $^3J_{PC}$ = 4.3 Hz, C8), 122.4 (s, C6), 131.3 (s, C7), 133.1 (s, C4), 144.2 (s, C3), 149.9 (s, $^3J_{PC}$ = 6.5 Hz, C9), 154.8 (s, C2) ppm. IR $\nu_{max}$: 828 (P=S); 969, 1002 (P–O–C); 3100–3600 (OH) cm$^{-1}$. Anal. Calcd for $C_{72}H_{76}O_{20}P_4S_4$: C, 57.14; H, 5.03; P, 8.20; S, 8.47. Found: C, 57.15; H, 4.93; P, 8.22; S, 8.50. ESI-MS: $m/z$ = 1513 [M+H]$^+$ (calcd M = 1512).
11. *Experimental procedure for the preparation of and spectroscopic data of compounds* ***5a*** *and* ***5b****:* a mixture of **5a** and **5b** in a 5:1 ratio (by $^{31}$P NMR spectroscopy) and combined yield of 0.59 g (89%) were obtained according to the method A by treatment of 2-methylresorcinol (0.22 g, 1.75 mmol) with aldehyde **3** (0.50 g, 1.75 mmol). Sequential recrystallization from acetone and EtOH gave pure *rctt*- and *rccc*-isomers. *Rctt*-isomer **5b**, *chair* conformation: white powder, yield 0.10 g (15%), mp >240 °C (dec). $^{31}$P NMR (166.9 MHz, DMSO-$d_6$): $\delta$ = 55.3 ppm. $^1$H NMR (600.1 MHz, DMSO-$d_6$): $\delta$ = 0.91 (s, 12H, H12), 1.22 (s, 12H, H12), 1.93 (s, 6H, C1-C$H_3^h$), 2.08 (s, 6H, C1-C$H_3^v$), 4.03 (m, 8H, H10), 4.36 (m, 8H, H10), 5.35 (s, 2H, H4$^h$), 5.67 (s, 4H, H5), 6.15 (s, 2H, H4$^v$), 6.67 (d, $^3J_{HH}$ = 8.01 Hz, 8H, H7), 6.83 (d, $^3J_{HH}$ = 8.01 Hz, 8H, H8), 7.46 (s, 4H, OH$^v$), 7.68 (s, 4H, OH$^h$) ppm. IR $\nu_{max}$: 829 (P=S); 965, 1001 (P–O–C); 3050–3600 (OH) cm$^{-1}$. Anal. Calcd for $C_{76}H_{84}O_{20}P_4S_4$: C, 58.16; H, 5.36; P, 7.91; S, 8.16. Found: C, 58.12; H, 5.34; P, 7.83; S, 7.92. ESI-MS: $m/z$ = 1569 [M+H]$^+$ (calcd. M = 1568). *Rccc*-isomer **5a**, *cone* conformation: pale yellow powder, yield 0.43 g (65%), mp >195 °C (dec). $^{31}$P NMR (166.9 MHz, DMSO-$d_6$): $\delta$ = 55.3 ppm. $^1$H NMR (600.1 MHz, DMSO-$d_6$): $\delta$ = 0.92 (s, 12H, H12), 1.23 (s, 12H, H12), 1.92 (s, 12H, C1-C$H_3$), 4.07 (m, 8H, H10), 4.39 (m, 8H, H10), 5.81 (s, 4H, H5), 6.10 (s, 4H, H4), 6.75 (d, $^3J_{HH}$ = 7.86 Hz, 8H, H7), 6.95 (d, $^3J_{HH}$ = 7.86 Hz, 8H, H8), 7.52 (s, 8H, OH) ppm. IR $\nu_{max}$: 828 (P=S); 968, 1002 (P–O–C); 3100–3600 (OH) cm$^{-1}$. Anal. Calcd for $C_{76}H_{84}O_{20}P_4S_4$: C, 58.16; H, 5.36; P, 7.91; S, 8.16. Found: C, 58.03; H, 5.34; P, 7.84; S, 8.13. ESI-MS: $m/z$ = 1569 [M+H]$^+$ (calcd M = 1568).
12. *Experimental procedure for the preparation of and spectroscopic data of compounds* ***6a*** *and* ***6b****:* a mixture of **6a** and **6b** in a 2:1 ratio (by $^{31}$P NMR spectroscopy) and combined yield of 1.28 g (93%) were obtained according to method A by treatment of pyrogallol (0.44 g, 3.50 mmol) with aldehyde **3** (1 g, 3.50 mmol). Sequential recrystallization from acetone and EtOH gave pure *rctt*- and *rccc*-isomers. *Rctt*-isomer **6b**, *chair* conformation: dark-pink powder, yield 0.61 g (44%), mp >220 °C (dec). $^{31}$P NMR (166.9 MHz, DMSO-$d_6$): $\delta$ = 55.3 ppm. $^1$H NMR (600.1 MHz, DMSO-$d_6$): $\delta$ = 0.90 (s, 12H, H12), 1.20 (s, 12H, H12), 4.02 (m, 8H, H10), 4.35 (m, 8H, H10), 5.23 (s, 2H, H4$^h$), 5.69 (s, 4H, H5), 6.97 (s, 2H, H4$^v$), 6.64 (d, $^3J_{HH}$ = 8.13 Hz, 8H, H7), 6.82 (d, $^3J_{HH}$ = 8.13 Hz, 8H, H8), 7.56 (s, 4H, OH$^v$), 7.67 (s, 4H, OH$^h$) ppm. IR $\nu_{max}$: 830 (P=S); 967, 1001 (P–O–C); 3100–3600 (OH) cm$^{-1}$. Anal. Calcd for $C_{72}H_{76}O_{24}P_4S_4$: C, 54.82; H, 4.82; P, 7.87; S, 8.12. Found: C, 54.75; H, 4.80; P, 7.57; S, 8.16. ESI-MS: $m/z$ = 1577 [M+H]$^+$ (calcd M = 1576). *Rccc*-isomer **6a**, *cone* conformation: dark-pink powder, yield 0.21 g (15%), mp >200 °C (dec). $^{31}$P NMR (166.9 MHz, DMSO-$d_6$): $\delta$ = 55.8 ppm. $^1$H NMR (600.1 MHz, DMSO-$d_6$): $\delta$ = 1.01 (s, 12H, H12), 1.33 (s, 12H, H12), 4.11 (m, 8H, H10), 4.52 (m, 8H, H10), 5.84 (s, 4H, H5), 6.02 (s, 4H, H4), 6.87 (d, $^3J_{HH}$ = 7.86 Hz, 8H, H7), 7.08 (d, $^3J_{HH}$ = 7.86 Hz, $^4J_{PH}$ = 1.3 Hz, 8H, H8) ppm. IR $\nu_{max}$: 828 (P=S); 968, 1002 (P–O–C); 3100–3600 (OH) cm$^{-1}$. Anal. Calcd for $C_{72}H_{76}O_{24}P_4S_4$: C, 54.82; H, 4.82; P, 7.87; S, 8.12. Found: C, 54.63; H, 4.90; P, 7.81; S, 8.13. ESI-MS: $m/z$ = 1577 [M+H]$^+$ (calcd M = 1576).
13. *Experimental procedure for the preparation of and spectroscopic data of compound* ***4b*** *(Method B):* a mixture of resorcinol (0.19 g, 1.75 mmol) and aldehyde **3** (0.50 g, 1.75 mmol) in EtOH (6.5 mL), $H_2O$ (6.5 mL), and concentrated HCl (3 mL) was stirred under heating at 60–65 °C for 18 h. The precipitate was filtered and washed sequentially with EtOH and $Et_2O$. After drying in vacuo (40 °C, 0.06 Torr) pure **4b** as the *rctt*-isomer in *chair* conformation was obtained (0.35 g, 54%) as a cream powder, mp >200 °C (dec). $^{31}$P NMR (166.9 MHz, acetone-$d_6$): $\delta$ = 54.2 ppm. $^1$H NMR (600.1 MHz, DMSO-$d_6$): 0.90 (s, 12H, H12), 1.20 (s, 12H, H12), 4.02 (m, 8H, H10), 4.35 (m, 8H, H10), 5.56 (s, 2H, H4$^h$), 5.59 (s, 4H, H5), 6.16 (s, 2H, H1$^v$), 6.31 (s, 2H, H4$^v$), 6.34 (s, 2H, H1$^h$), 6.63 (d, $^3J_{HH}$ = 7.89 Hz, 8H, H7), 6.82 (d, $^3J_{HH}$ = 7.89 Hz, 8H, H8), 8.56 (s, 4H, OH$^v$), 8.64 (s, 4H, OH$^h$). IR $\nu_{max}$: 828 (P=S); 969, 1003 (P–O–C); 3100–3600 (OH) cm$^{-1}$. Anal. Calcd for $C_{72}H_{76}O_{20}P_4S_4$: C, 57.14; H, 5.03; P, 8.20; S, 8.47. Found: C, 57.30; H, 5.07; P, 8.37; S, 8.26. ESI-MS: $m/z$ = 1513 [M+H]$^+$ (calcd M = 1512).
14. *Experimental procedure for the preparation of and spectroscopic data of compound* ***5b****:* calix[4]resorcinol **5b**, chair conformation was obtained according to method B by treatment of 2-methylresorcinol (0.17 g, 1.40 mmol) and aldehyde **3** (0.40 g, 1.40 mmol). Pure **5b** was obtained (0.31 g, 56%) as a white powder, mp >240 °C. NMR ($^{31}$P, $^1$H) data of compound **5b** synthesized by methods A and B were identical. IR $\nu_{max}$: 829 (P=S); 967, 1001 (P–O–C); 3100–3600 (OH) cm$^{-1}$. Anal. Calcd for $C_{76}H_{84}O_{20}P_4S_4$: C, 58.16; H, 5.36; P, 7.91; S, 8.16. Found: C, 58.10; H, 5.45; P, 7.83; S, 8.15. ESI-MS: $m/z$ = 1569 [M+H]$^+$ (calcd M = 1568).
15. Vysotsky, M.; Schmidt, C.; Boehmer, V. In *Advances in Supramolecular Chemistry*; Gokel, W., Ed.; JAI Press: Greenwich, 2000; Vol. 7, pp 139–233.
16. (a) Abis, L.; Dalcanale, E.; Du vosel, S.; Spera, S. *J. Org. Chem.* **1988**, *53*, 5475; (b) Abis, L.; Dalcanale, E.; Duvosel, A.; Spera, S. *J. Chem. Soc., Perkin Trans. 2* **1990**, 2075; (c) Kaminsky, J.; Dvorakova, H.; Stursa, J.; Moravcova, J. *Czech. Chem. Commun.* **2011**, *76*, 1199.
17. (a) Schiel, Ch.; Hembury, G. A.; Borovkov, V. V.; Klaes, M.; Agena, C.; Wada, T.; Grimme, S.; Inoue, Y.; Mattay, J. *J. Org. Chem.* **2006**, *71*, 976; (b) Roncucci, P.; Pirondini, L.; Paderni, G.; Massera, Ch.; Dalcanale, E.; Azov, V. A.; Diederich, F. *Chem. Eur. J.* **2006**, *12*, 4775.
18. Activation free energies ($\Delta G^\#$) were determined using Eyring equations ($\Delta G^\#$ = 19.14 $T_C$·(9.97 + log ($T_C/\delta_\nu$)), J/mol, where, $T_C$–is the coalescence temperature and $\delta_\nu$ is the chemical shift difference of the exchanging resonances in the absence of chemical exchange.
19. (a) Schneider, H.-J.; Schneider, U. *J. Incl. Phenom. Mol. Recog. Chem.* **1994**, *19*, 67; (b) Mäkinen, M.; Jalkanen, J.-P.; Vainiotalo, P. *Tetrahedron* **2002**, *58*, 8591.
20. *Crystallographic data for* ***4a****:* $C_{72}H_{76}O_{20}P_4S_4$·$C_2H_6OS$, $M$ = 1591.58, triclinic, $a$ = 17.620(9) Å, $b$ = 17.810(9) Å, $c$ = 20.288(10) Å, $\delta$ = 65.596(7)°, $\beta$ = 86.321(7)°, $\delta$ = 73.022(7)°, $V$ = 5533(5) Å$^3$, $T$ = 150(2) K, space group $P\bar{1}$, $Z$ = 2, $\mu$ = 0.213 mm$^{-1}$, 62221 reflections measured ($R_\sigma$ = 0.1485), 23949 independent reflections ($R_{int}$ = 0.0677), $R_1$ = 0.2068 (all data), $wR_2$ = 0.3105 (all data), $R_1$ = 0.1037 ($I > 2\sigma_I$), $wR_2$ = 0.2711 ($I > 2\sigma_I$), GoF = 0.901.
21. *Crystallographic data for* ***5a****:* $C_{76}H_{84}O_{20}P_4S_4$, $M$ = 1569.55, monoclinic, $a$ = 27.5575(18) Å, $b$ = 24.7896(17) Å, $c$ = 20.5926(12) Å, $\beta$ = 124.420(3)°, $V$ = 11604.6(13) Å$^3$, $T$ = 150(2) K, space group $C\ 2/c$, $Z$ = 4, $\mu$ = 0.184 mm$^{-1}$, 32915 reflections measured ($R_\sigma$ = 0.0468), 12508 independent reflections ($R_{int}$ = 0.0298), $R_1$ = 0.0767 (all data), $wR_2$ = 0.1639 (all data), $R_1$ = 0.0542 ($I > 2\sigma_I$), $wR_2$ = 0.1523 ($I > 2\sigma_I$), GoF = 1.058.
22. *Crystallographic data for* ***6b****:* $C_{72}H_{76}O_{24}P_4S_4$·$8C_3H_6O$, $M$ = 2042.07, monoclinic, $a$ = 21.753(5) Å, $b$ = 22.615(6) Å, $c$ = 11.049(3) Å, $\beta$ = 103.853(3), $V$ = 5278(2) Å$^3$, $T$ = 296(2) K, space group $P2_1/c$, $Z$ = 2, $\mu$ = 0.227 mm$^{-1}$, 45928 reflections measured ($R_\sigma$ = 0.0300), 12068 independent reflections ($R_{int}$ = 0.0311), $R_1$ = 0.0658 (all data), $wR_2$ = 0.1220 (all data), $R_1$ = 0.0428 ($I > 2\sigma_I$), $wR_2$ = 0.1043 ($I > 2\sigma_I$), GoF = 1.028.