Conformation of Sterically Hindered 4-Methyl-2-oxo-2-trityl-1,3,2-dioxaphosphorinane in the Solid State and the Solution

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Abstract The *cis*- and *trans*-2-methyl-2-oxo-2-trityl-1,3,2-dioxaphosphorinanes were obtained in the Arbuzov reaction of 2-methoxy-4-methyl-1,3,2-dioxaphosphorinane with trityl chloride. The NMR spectra (^1H , ^{13}C and ^{31}P) in solution indicated that *trans* isomer exists in the form of two noncongruent molecules and it adopts two different conformations: a halfchair and a sofa, while the *cis* isomer exists as the mixed half/chair–sofa conformer. The compounds crystallise as a pure chiral forms and as a racemates. The solid state structural studies show that NMR data are consistent with the single crystal X-ray analysis, but the conformation existing in the crystal structure is more complex than it can be supposed on sole NMR determination. Crystal data: *cis*-isomer chiral form: space group $P3_2$, $a = 8.782$, $b = 8.782$, $c = 21.680$, $\alpha = 90.00$, $\beta = 90.00$, $\gamma = 120.00$, $V = 1448.0$; *cis*-isomer racemate:

space group $Pca2_1$, $a = 16.773$, $b = 8.491$, $c = 27.006$, $\alpha = 90.00$, $\beta = 90.00$, $\gamma = 90.00$, $V = 3846.2$; *trans*-isomer racemate: space group Cc , $a = 16.133$, $b = 8.388$, $c = 16.158$, $\alpha = 90.00$, $\beta = 117.20$, $\gamma = 90.00$, $V = 1944.8$; *trans*-isomer chiral form: space group $P1$, $a = 8.397$, $b = 9.003$, $c = 14.944$, $\alpha = 80.76$, $\beta = 74.38$, $\gamma = 63.31$, $V = 971.1$).

Keywords Dioxaphosphorinane · Crystal structure · NMR

Introduction

The organophosphorus compounds are renowned for their diverse physiological activities. Among these the phosphate moiety is an important pharmacophore in the pharmaceutical chemistry [1–6] and can be used as a building block for antibiotics [7–10], herbicides [11, 12], insecticides [13], fungicides [14] and anti-viral agents [15]. Additionally, the phosphonic acids and their derivatives may be considered as long life analogues of transition states for tetrahedral intermediates in amide/ester hydrolysis [16]. Among others, these compounds also possess enzyme inhibition properties and consequently they can serve as antibacterial and anticancer drugs [17–31]. Phosphorylated alkenes are also synthetically useful [32–35] and are commonly used in organic synthesis [36–40].

In recent years, several six-membered ring phosphonates and phosphoramides have been reported as potent prodrugs against liver diseases such as hepatic B and C and also as antitumor agents [41]. Conformations of six-membered rings themselves and in reference to their biological activity has been lately widely studied and reviewed [42]. The cyclic phosphonates are required intermediates in

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multiple organic reactions [43–48] and they are used as chiral synthons [49]. Bisphosphonate compounds are still under study by pharmaceutical and other industrial companies because of their potential medical [49] or technical applications (e.g. pentaerythritol diphosphonate is capable of being used as a fire retardant agent and as a plasticizer [50]).

The 1,3,2-dioxaphosphorinane derivatives, an important class of organophosphorus heterocycles, are interesting compounds because of their biological activities, particularly in reference to the design of enzyme inhibitors [51–58]. As a part of organophosphorus compounds the 1,3,2-dioxaphosphorinanes are also very important in pesticide and medicinal science, owing to their wide biological activities and stereochemistry [59]. The conformation of heterocyclic 1,3,2-dioxaphosphorinane ring of the cyclic phosphate and phosphonate esters has been the subject of vigorous research in the past [60–62]. The interest in these molecules was stimulated, at least in part, due to their possible significance as models to study conformations of biologically important compounds such as cyclic-3',5'-nucleoside monophosphates and also cyclic nucleotides (e.g. cAMP) which contain a dioxaphosphorinane moiety and play important roles in hormone action and cell communication [63–67]. The conformation of the latter compounds is an important issue in view of their function as secondary messengers in cell physiology, and their stereochemically-dependent interactions with intracellular targets. Since 2-oxo-dioxaphosphorinanes tend to be crystalline solids, a systematic study of the effect of substituent groups on the conformation of the ring have been carried out by X-ray diffraction [59, 68, 69]. Substituent effects have also been studied by NMR [70–74] and dipole measurements [75].

Experimental

Synthesis

(4S)-2-Chloro-4-methyl-1,3,2-dioxaphosphorinane (CMDOP) was obtained from (S)-(+)-butane-1,3-diol and PCl_3 in CH_2Cl_2 as solvent [76]. Yield of distilled product 58%. ^{31}P NMR (diethyl ether) $\delta = 151.0$ ppm.

(4S)-2-Methoxy-4-methyl-1,3,2-dioxaphosphorinane (MMDOP). Into the solution of the CMDOP (0.9 g, 5.8 mmol) in diethyl ether (6 mL) was added the mixture of anhydrous methanol (0.19 g, 5.8 mmol) and triethylamine (0.7 g, 15% excess) at -5°C . The resulting mixture was stirred at room temperature for 10 min and the precipitated hydrochloride was filtered off. The solution was concentrated to give crude product (0.6 g, 69%). This was

used for further reactions without purification. ^{31}P NMR $\delta = 129.3$ ppm (*trans*-isomer, 70%), $\delta = 133.0$ ppm (*cis*-isomer, 30%). The analogous reaction performed in the presence of 20% excess triethylamine at -10°C gave the mixture of 85% *cis*- and 15% *trans*-isomers.

(4S)-2-Triphenylmethyl-2-oxo-4-methyl-1,3,2-dioxaphosphorinane. Trityl chloride (1.1 g, 4 mmol) and the MMDOP (0.6 g, 4 mmol, 70% *trans*) in dry acetonitrile (6 mL) was heated at reflux for 15 min. The solvent was evaporated and the residue was crystallized from diethyl ether to give 0.9 g of the product containing 87.5% of the *trans*-isomer (**2a**) and 12.5% of the *cis*-isomer (**1b**). Analogous reaction with 85% *cis*-phosphite gave the mixture containing 83% *cis*-isomer (**1a**) and 17% *trans*-isomer (**2b**).

The mixtures were separated chromatographically on the silica gel (chloroform–diethyl ether–ethyl acetate, 50:40:2; *trans* R_F 0.23, *cis* R_F 0.15). The pure *cis*-isomers (**1a** and **1b**) were crystallized from acetonitrile (about 5 cm^3) at ambient temperature. Each of the *trans*-isomers (**2a** and **2b**) was crystallized from about 6 cm^3 of acetone at room temperature. In all cases the crystal grow after 3–6 h.

NMR Spectra

NMR experiments were performed in Varian VXR 200 MHz. Final compounds were dissolved in CDCl_3 , C_6D_6 and $\text{C}_5\text{D}_5\text{N}$ deuterated solvents. Chemical shifts were reported in ppm relative to TMS for ^1H , ^{13}C NMR spectra and to 85% H_3PO_4 in H_2O for ^{31}P NMR spectra. Crystalline samples were used for solid state NMR measurements. The solid-state CP MAS NMR experiments were performed on above mentioned spectrometer, equipped with an MAS probehead using 4 mm ZrO_2 rotors. The NMR data are given in Tables 1, 2, 3.

Table 1 ^1H NMR chemical shifts for tritylphosphonates **1** and **2** in solution at 298 K

Compound	Solvent	δA	δB	δC	δD	δE	δF
<i>Cis</i> - 1	CDCl_3	3.73	4.34	1.65	2.11	3.67	1.29
	C_6D_6	3.09	3.73	0.69	1.43	3.29	0.88
<i>Trans</i> - 2	CDCl_3	4.54	4.08	1.50 ^a	1.50	4.78	1.08
	C_6D_6	4.13	3.39	0.56	1.10	4.37	0.64

^a Precise values were not determined due to isochronicity of protons C and D

Table 2 ^{13}C NMR chemical shifts of **1a**, **b** and **2a**, **b** in solution and in solid state

Compound	Solvent conditions	δMe	δC4	δC5	δC6	$\delta\text{CP}^{\text{a}}$	$\delta\text{C1}'$	$\delta\text{C2}', 3', 4'$
<i>Cis</i> - 1	CDCl_3	22.8 (8.7)	76.4 (8.8)	33.1 (12.0)	66.8 (8.4)	63.8 (136.0)	141.4 (5.3)	130.9 (6.7); 127.9; 127.0 (1.7)
	Solid, racemic 1b	22.5	76.6	33.1 ^a	69.1 ^a	64.2 (135.0)	141.0	127.6; 130.0 ^a
	Solid 1a (4S, Rp)	22.2	76.2	33.0	70.3	64.7 (136.0)	142.3; 139.4	141.4; 125.8–132.2 ^b
<i>Trans</i> - 2	CDCl_3	22.3 (8.0)	73.5 (7.4)	32.9 (5.1)	65.3 (7.4)	62.8 (135.0)	141.2 (5.4)	130.9 (6.6); 127.9; 127.0 (1.8)
	Solid, racemic 2a	22.7	73.6	32.8 ^a	^c	63.9 (134.0)	141.1 ^d	127.7; 132.3
	Solid 2b (4S, Sp)	21.5	74.0	32.5–36.0 ^a	66.5 ^a	63.5 (135.0)	140.3; 140.9 ^e	126.0–134.0 ^f
		25.6				63.9 (135.0)	142.0; 144.0	

^a Broad signal^b Three ill resolved signals^c Signal not observed^d Line width^e Two doublets^f Relative intensity 1:1:3:1**Table 3** ^1H – ^1H coupling constants for tritylphosphonates **1** and **2** in solution at 297 K

Compound	Solvent	J_{AB}	J_{AC}	J_{BC}	J_{CD}	J_{BD}	J_{CE}	J_{DE}	J_{AD}	J_{BP}	J_{EP}	J_{CP}	J_{DP}	J_{EF}
<i>Cis</i> - 1	C_6D_6	10.7	3.7	4.5	14.2	4.7	3.6	9.3	9.8	9.1	8.0	2.6	1.5	6.3
	CDCl_3	10.8	3.7	3.5	14.7	4.8	3.0	9.8	8.7	9.8	6.0	3.0	1.1	6.3
	Py-d_5	10.6	3.7	4.4	14.3	4.9	3.9	9.3	9.2	10.3	7.6	2.8	1.3	6.4
<i>Trans</i> - 2	C_6D_6	11.2	2.4	2.0	14.3	4.6	2.8	11.2	2.4	20.3	1.1	2.4	1.0	6.2
	CDCl_3	10.6	^a	3.0	^a	4.0	^a	^a	2.7	19.6	1.1	^a	^a	6.2

^a Coupling constant has been not determined due to isochronicity of protons C and D, resulting in virtual coupling, complicating the multiplets A and C

X-ray Crystallography

Colourless rectangular prism shape crystals of 4-methyl-2-oxo-2-trityl-1,3,2-dioxaphosphorinane were mounted in turn on a KM-4 automatic four-circle diffractometer equipped with proportional counter detector, and used for data collection. X-ray intensity data were collected with graphite monochromated $\text{CuK}\alpha$ or $\text{MoK}\alpha$ radiation (Table 2), with ω – 2θ scan mode. The unit cells parameters were determined from least-squares refinement of the setting angles of 99 strong reflections. Details concerning crystal data and refinement are given in Table 4. Examination of three reflections monitored after each 100 measured reflections showed no loss of the intensity for all measurements. Lorentz, polarization, and numerical absorption [77] corrections were applied. The structures were solved by direct methods. All the non-hydrogen atoms were refined anisotropically using full-matrix, least-squares technique on F^2 . All the hydrogen atoms were found from difference Fourier synthesis after four cycles of anisotropic refinement, and refined as “riding” on the adjacent atom with individual isotropic displacement factor equal 1.2 times the value of equivalent displacement factor

of the parent atoms. The hydrogen atom positions were idealised after each cycle of refinement. The methyl groups were allowed to rotate about their local three-fold axes. The methyl group of **2a** shows static disorder over two positions of $\text{C}_3\text{O}_2\text{P}$ ring. The refinement of this disorder model with occupation parameters free to refine (the sum of the both parameters was constrained to be 1) leads to 0.527(18) : 0.473(18) participation of domains in final refinement cycle. The SHELXS97 [78], SHELXL97 [79] and SHELXTL [80] programs were used for all the calculations. Atomic scattering factors were those incorporated in the computer programs. Selected interatomic bond distances and angles are listed in Table 5, and geometrical parameters of intermolecular interactions are listed in Table 6.

Results and Discussion

In the solid state the 4-methyl-2-oxo-2-trityl-1,3,2-dioxaphosphorinane exists in four forms: two (**1a**, **1b**) adopting formal *cis* configuration (**1**) and two (**2a**, **2b**) possessing a

Table 4 Crystal data and structure refinement details for studied compounds

Compound	1a	1b	2a	2b
Crystal system, space group	Trigonal, $P3_2$ (No. 145)	Orthorhombic, $Pca2_1$ (No. 29)	Monoclinic, Cc (No. 9)	Triclinic, $P 1$ (No. 1)
Wavelength	$\lambda(\text{CuK}\alpha) = 1.54179$	$\lambda(\text{MoK}\alpha) = 0.71069$	$\lambda(\text{MoK}\alpha) = 0.71073$	$\lambda(\text{CuK}\alpha) = 1.54178$
Unit cell dimensions ($\text{\AA}$, $^\circ$)	$a = 8.7820(10)$ $b = 8.7820(10)$ $c = 21.680(4)$ $\alpha = 90.00$ $\beta = 90.00$ $\gamma = 120.00$	$a = 16.773(3)$ $b = 8.491(1)$ $c = 27.006(5)$ $\alpha = 90.00$ $\beta = 90.00$ $\gamma = 90.00$	$a = 16.133(3)$ $b = 8.388(2)$ $c = 16.158(3)$ $\alpha = 90.00$ $\beta = 117.20(3)$ $\gamma = 90.00$	$a = 8.397(2)$ $b = 9.003(2)$ $c = 14.944(3)$ $\alpha = 80.76(3)$ $\beta = 74.38(2)$ $\gamma = 63.31(2)$
Volume ($\text{\AA}^3$)	1448.0(4)	3846.2(11)	1944.8(9)	971.1(4)
Z, Calculated density (Mg/m^3)	3, 1.302	8, 1.307	4, 1.292	2, 1.294
Absorption coefficient (mm^{-1})	1.424	0.164	0.162	1.416
$F(000)$	600	1600	800	400
Crystal size (mm)	$0.107 \times 0.099 \times 0.093$	$0.036 \times 0.027 \times 0.022$	$0.118 \times 0.109 \times 0.100$	$0.126 \times 0.093 \times 0.079$
θ range for data collection ($^\circ$)	5.82–74.89	1.51–25.00	2.81–25.02	3.07–74.91
Index ranges	$0 \leq h \leq 10, -10 \leq k \leq 9, -27 \leq l \leq 26$	$-11 \leq h \leq 19, -10 \leq k \leq 10, -32 \leq l \leq 32$	$-19 \leq h \leq 19, -9 \leq k \leq 9, -19 \leq l \leq 10$	$-10 \leq h \leq 10, -11 \leq k \leq 10, -18 \leq l \leq 18$
Reflections collected/unique	6043/3824 [$R_{\text{int}} = 0.0198$]	18152/6660 [$R_{\text{int}} = 0.0114$]	5010/3422 [$R_{\text{int}} = 0.0419$]	8002/8002 [$R_{\text{int}} = 0.000$]
Completeness	100% to $\theta = 67^\circ$	99% to $\theta = 25^\circ$	100% to $\theta = 25^\circ$	100% $\theta = 67^\circ$
Min. and max. transmission	0.856 and 0.869	0.994 and 1.000	0.977 and 0.985	0.863 and 0.872
Data/restraints/parameters	3824/1 ^a /246	6660/1 ^a /487	2084/2 ^a /256	8002/3 ^a /490
Goodness-of-fit on F^2	1.042	1.035	1.056	1.099
Final R indices ($I > 2\sigma(I)$)	$R1 = 0.0287$, $wR2 = 0.0802$	$R1 = 0.0197$, $wR2 = 0.0557$	$R1 = 0.0464$, $wR2 = 0.1130$	$R1 = 0.0390$, $wR2 = 0.1236$
R indices (all data)	$R1 = 0.0288$, $wR2 = 0.0803$	$R1 = 0.0267$, $wR2 = 0.0641$	$R1 = 0.0610$, $wR2 = 0.1240$	$R1 = 0.0392$, $wR2 = 0.1238$
Flack parameter	0.015(13)	0.004(6)	0.005(16)	0.03(2)
Largest diff. peak and hole ($\text{e \AA}^{-3}$)	0.183 and -0.166	0.258 and -0.239	0.158 and -0.350	0.365 and -0.277

Data common for all compounds: empirical formula— $\text{C}_{23}\text{H}_{23}\text{O}_3\text{P}$; formula weight = 378.38 g/mol; measurement temperature = 291.0(3) K; refinement method—full-matrix least-squares on F^2

^a Floating origin restraints

formal *trans* conformation (**2**). All these forms crystallise in non-centrosymmetric space groups, but only **1a** and **2b** are chiral (Table 4). The crystals of **1b** and **2a** contain internal glide planes what leads to racemic compounds. Additionally, the methyl group of **2a** is disordered over two sites (with almost equal participation of domains), what also leads to conclusion that, from a strict point of view, the asymmetric unit of **2a** contains a racemate. The chiral

centres P1 and C1 have different configuration in **1** and the same configuration in **2**, and for chiral crystals **1a** and **2b** it is R, S and S, S respectively. The forms **1b** and **2b** possess two molecules located in the asymmetric unit, while asymmetric unit of **1a** and **2a** is occupied by only one molecule. In both cases of the doubled asymmetric unit content, both molecules possess the same configuration of chiral centres.

Six-membered rings possess twelve potential symmetry elements which must be considered in order to determine the solid state conformation of the ring, and this can be done by calculation of two types of asymmetry parameters [81]:

$\Delta C_2 = \sqrt{\frac{\sum_{i=1}^m (\phi_i - \phi'_i)^2}{m}}$ for twofold axis, and $\Delta C_s = \sqrt{\frac{\sum_{i=1}^m (\phi_i + \phi'_i)^2}{m}}$ for mirror plane, where m is the number of the symmetrical pairs of the torsion angles and the ϕ_i and ϕ'_i are values of the symmetry-dependent torsion angles taken into account. Placement of asymmetry parameters for the solid state determined compounds (**1a**, **1b**, **2a**, **2b**) is shown in Fig. 1. The most preferred conformation of the puckered heteroatom rings is the half-chair slightly distorted toward sofa (rings of **1a**, **2a** and **2b** containing P1 atom). The other three rings exhibit half-chair, sofa and sofa strongly distorted toward half-chair conformations, respectively for **1b** (ring containing P1 atom), **2b** (ring containing P51 atom) and **1b** (ring containing P51 atom). The study of solid state conformations of the structurally characterised dioxaphosphorinanes found in Cambridge Structure Database [82] (112 compounds) shows that the most preferred conformation is a distorted one between sofa and twist (72 structures) and the second most populated conformation is the transition one between sofa and half-chair (32 structures). The studied compounds represent mainly the less preferred conformations (the mixed one: sofa/half-chair) and two rings exhibit rare, almost ideal sofa or nearly perfect half-chair conformation. The total puckering amplitude [83] of the studied heteroatomic six-membered rings falls in the range 0.470 (**1b**)–0.525 (**2b**) with $\theta \subset < 16.74\text{--}168.11^\circ >$ and $\varphi \subset < 15.13\text{--}339.83^\circ >$.

There are no classical hydrogen bonds in the structures of 4-methyl-2-oxo-2-trityl-1,3,2-dioxaphosphorinane due to the absence of hydrogen bonds donors (Figs. 2, 3, 4, 5), however some intermolecular C–H...O short contacts (Table 6) can be classified as weak hydrogen bonds [84, 85]. Additionally, stacking interactions between aromatic rings of studied compounds do not exist.

Beside the structural analysis, the conformation of discussed cyclic derivatives can be the most conveniently deduced from the angular dependence of the magnitude of $^1\text{H}\text{--}^1\text{H}$, $^1\text{H}\text{--}^{31}\text{P}$ and $^{13}\text{C}\text{--}^{31}\text{P}$ vicinal coupling constants. However, frequently the question arises whether the conformation in the solid state corresponds to the one found in the solution. ^{13}C and ^{31}P CP-MAS NMR technique provides means of verifying this point by the comparison of the chemical shifts of signals in the solution and the solid state spectra. In addition the line multiplicity in MAS NMR can serve as a means of detection of multiple conformations or crystallographically nonequivalent molecules in the solid lattice. In present case, the ^{13}C SS NMR (crystalline form) racemic isomer *cis*-**1b** shows existence of three nonequivalent (conformationally) molecules, but only one molecule for the crystalline form of enantiomerically pure compound (*cis*-**1a**). Racemic isomer *trans*-**2a** in crystalline form demonstrates rather broad spectrum indicating an existence of a few nonequivalent molecules or a significant portion of disorder in the lattice. Enantiomeric form *cis*-**1a** shows existence of two nonequivalent molecules (1:1).

The conformation of 2-oxo-1,3,2-dioxaphosphorinane ring system was found to depend on the nature and on the bulkiness of the ring substituents [86]. In general the electron-withdrawing substituents with their known preference for axial position were found to enhance the

Table 5 Selected structural data for studied compounds (Å, °)

	<i>Cis-1a</i>	<i>Cis-1b</i>	<i>Trans-2a</i>	<i>Trans-2b</i>
O1–P1	1.5762(11)	1.570(6)	1.563(3)	1.575(2)
O2–P1	1.5771(12)	1.43(3)	1.566(3)	1.582(2)
O3–P1	1.4643(12)	1.552(4)	1.466(3)	1.463(2)
P51–O51	–	1.565(16)	–	1.571(2)
P51–O52	–	1.47(3)	–	1.580(3)
P51–O53	–	1.575(14)	–	1.462(3)
O3–P1–O1	112.02(7)	105.32(15)	113.7(2)	113.48(14)
O3–P1–O2	113.35(7)	112.6(14)	114.2(2)	114.13(16)
O1–P1–O2	106.31(7)	113.7(13)	104.60(18)	104.27(13)
O51–P51–O52	–	114.2(17)	–	104.87(14)
O51–P51–O53	–	105.6(4)	–	114.44(16)
O52–P51–O53	–	112.0(11)	–	113.88(17)
P1–O1–C1–C2	–41.60(18)	–6.73(12)	53.83(7)	–58.93(4)
O1–C1–C2–C3	61.7(2)	42.58(19)	–59.46(8)	59.78(4)
C1–C2–C3–O2	–50.58(2)	–58.04(11)	54.93(7)	–54.94(5)
C2–C3–O2–P1	16.33(2)	38.28(7)	–45.43(6)	48.35(5)
C3–O2–P1–O1	4.53(16)	–4.72(17)	35.83(4)	–41.9(3)
O2–P1–O1–C1	9.49(11)	–12.15(6)	–39.72(5)	46.7(3)
P51–O51–C51–C52	–	–17.85(7)	–	–47.44(5)
O51–C51–C52–C53	–	50.95(8)	–	57.5(5)
C51–C52–C53–O52	–	–58.95(8)	–	–58.2(5)
C52–C53–O52–P51	–	35.07(8)	–	45.34(4)
C53–O52–P51–O51	–	–5.05(17)	–	–29.4(3)
O52–P51–O51–C51	–	–5.22(15)	–	31.96(4)

chair-twist boat equilibrium, but the MeO substituent in axial position and *t*-Bu in equatorial position leads to the chair conformation [87]. On the other hand, the bulky substituent, such as a trityl group at 2-position of the 6,4-dimethyl substituted ring, causes significant ring flattening due to steric repulsions [88]. Two bulky ring substituents cause the transition into the boat conformation, as is the case of 2,6-bis-*tert*-butyl-substituted ring [89].

Unusually large difference in the chemical shifts of ^{31}P atoms, observed for **1** and **2** solutions (amounting up to 10 ppm in CDCl_3 at 273 K), shows that three types of conformations of the title compound exist. The ^1H NMR spectra were recorded in two different solvents: chloroform-*d* and benzene-*d*₆. In deuterated chloroform chemical shifts of protons are in lower field (larger δ) than in deuterated benzene because benzene has a strong diamagnetic anisotropy [90] and it causes observed resonance of a given

Table 6 Hydrogen bonds in studied compounds (Å, °)

	D–H	H...A	D...A	D–H...A
<i>Cis-1a</i>				
C7–H7...O1	0.93	2.42	3.155(2)	135.9
C13–H13...O3	0.93	2.44	3.171(2)	136.1
C20–H20...O3#1	0.93	2.50	3.422(2)	171.7
<i>Cis-1b</i>				
C8–H8...O53#2	1.08	2.46	3.522(7)	168
C11–H11...O1	1.08	2.58	3.070(3)	107
C17–H17...O3	1.08	2.30	3.148(5)	134
C19–H19...O2	1.08	2.26	3.092(7)	133
C58–H58...O3	1.08	2.53	3.588(6)	167
C64–H64...O3#3	1.08	2.47	3.399(11)	143
C67–H67...O53	1.08	2.24	3.086(7)	133
C69–H69...O52	1.08	2.25	3.098(12)	134
C70–H70...O51#4	1.08	2.59	3.568(6)	150
<i>Trans-2a</i>				
C11–H11...O3	0.93	2.46	3.192(7)	135.8
C13–H13...O2	0.93	2.33	3.044(5)	133.7
C19–H19...O1	0.93	2.55	3.055(5)	114.1
<i>Trans-2b</i>				
C11–H11...O1	0.93	2.60	3.083(4)	113.1
C13–H13...O2	0.93	2.37	3.078(4)	132.9
C19–H19...O3	0.93	2.49	3.221(5)	136.0
C57–H57...O52	0.93	2.56	3.052(4)	113.2
C63–H63...O53	0.93	2.41	3.151(5)	136.1
C69–H69...O51	0.93	2.31	3.040(4)	135.6

Symmetry transformations used to generate equivalent atoms: #1: $+x, +y + 1, +z$; #2: $+0.5 - z, +y + 1, +0.5 + z$; #3: $+0.5 + x, -y, +z$; #4: $+0.5 + x - 1, +y, +0.5 + z$

protons to be shifted to a higher field (smaller δ). This difference appears to be dependent on the shape of the solvent molecules. Aromatic solvent, such as benzene is flat. There were difficulties to determine precise values of chemical shifts of protons C and D due to isochronicity of these signals. The signals of protons A and E in compound *cis* appear in a higher field than in the *trans* compound because of the influence of the shielding cone of trityl (increasing electron density over benzene rings) and the protons have a smaller chemical shift in the *cis* conformation than in the *trans* because there are no other elements which influence the signals.

The observed H–H coupling constants in *cis*-conformation are comparable (or almost identical) in the cases of J_{AC} , J_{BD} , J_{EF} , J_{CD} , J_{DP} , J_{DE} , J_{AB} . The long range coupling [91] (over more than three bonds) can be observed and it involves relatively small coupling constants like in the case of $^4J_{DP}$, $^4J_{CP}$ when the conformation is closely related to the conformation of cyclohexane. For compound possessing *cis*-conformation all coupling constant are well separated

in all used deuterated solvents. Some coupling constants (like $^3J_{BP}$ one) change with the polarity of the solvent and the solvent dielectric constant [92] (enlargement of this value is accompanied by increased coupling constant). Remaining constants change with the variation of the molecular geometry i.e. changes of interbond angles. Deuterated benzene (like deuterated pyridine), because of the flat shape, may create solute–solvent complexes in a solution, and in consequence they can influence the bonds and interbond angles, which leads to changes in a coupling constants. Deuterated pyridine additionally causes the paramagnetic shift and thus it may also have influence on coupling constants.

The compound possessing the *trans*-conformation does not produce the coupling constants of C and D protons in deuterated chloroform, due to their isochronicity, thus the solvent was changed to the less polar—deuterated benzene. The coupling constants between AB, BD and BP atoms are larger in benzene and between BC and AD atoms are smaller due to the conformation of the compound. These couplings are between axial and equatorial protons, and they exist through three bonds. On the basis of Karplus equation (correlation of changes of coupling constant with changes of dihedral angle [93]) it can be stated that two preferable groups of H–C–C–H torsion angles exist, one

Fig. 2 The molecular conformation of **1a** with atom numbering, plotted with 50% probability of displacement ellipsoids of non-hydrogen atoms. The hydrogen atoms were omitted for clarity

Fig. 1 Placement and values of the smallest asymmetry parameters for studied compounds: **a** *cis*-**1a**, **b** *cis*-**1b**, **c** *trans*-**2a** and **d** *trans*-**2b**

Fig. 3 The molecular conformation of **1b** with atom numbering, plotted with 50% probability of displacement ellipsoids of non-hydrogen atoms. The hydrogen atoms were omitted for clarity

Fig. 4 The molecular conformation of **2a** with atom numbering, plotted with 50% probability of displacement ellipsoids of non-hydrogen atoms. The hydrogen atoms were omitted for clarity. The hollow line and C4' atom indicates the disordered methyl group

for A–C, B–C, B–D and C–E pairs of protons and second one for DE–AD pairs of protons. The angle near to 60° gives the coupling constant about 4 Hz and angle close to 120° leads to the coupling constant equals about 6 Hz [91], thus it can be postulated that H–C–C–H torsion angles of the first mentioned group are slightly larger than 60° , and those ones of second group are about 120 – 140° .

^{13}C NMR spectra were recorded in the solution (deuterated chloroform) and in the solid state. In solution the chemical shift of the methyl group and its coupling constants are comparable for both isomers. The similarity of the chemical shift of the CP^a and aromatic carbon atoms for *cis* and *trans* isomers can be also observed. Chemical shift and coupling constants of a C4 and C6 atoms in both conformers are different because of the shielding cone of trityl group in the conformers. Noteworthy is the fact that C5 atom chemical shift in both conformers is comparable but the coupling constant in *cis*-conformer is two times larger than in *trans*. This can be explained by the Karplus effect. In presented case, the change of the C₂O₂P ring conformation leads to the alteration of the torsion angles, and in consequence to the different coupling constants.

The ^{13}C CP-MAS NMR spectra recorded for **1b** racemic and **2a** racemic 4-methyl-2-oxo-2-trityl-1,3,2-dioxaphosphorinane show that the chemical shifts of the methyl group are comparable just like signals from aromatic carbon atoms. For C5 atoms the chemical shifts are very similar but the observed signals are broadened in both cases. The signal of C6 atom of **2a** is unobserved (in **1b** the broad signal appears) probably due to the close presence of the trityl group in this conformation. The chemical shift of C1' is comparable in both conformations but in **2a** the broadening of the signal line is observed. Additionally, the signals from C4 atoms are not observed in both cases.

The ^{13}C CP-MAS NMR spectra recorded for solid **1a** and **2b** were similar to these ones recorded without magic angle spinning (the MAS do not average the observed signals), and this fact, in case of **2b**, confirms the presence of two different conformations in solid state. In **1a** the couplings are not observed thus it can be supposed that

Fig. 5 The molecular conformation of **2b** with atom numbering, plotted with 50% probability of displacement ellipsoids of non-hydrogen atoms. The hydrogen atoms were omitted for clarity

there is only one independent conformation and in the case of aromatic carbon atoms three ill resolved lines related to C3' and C4' atoms can be found.

In the case of **2a** magic angle spinning did not give the signals averaging, thus it can be supposed that there are two conformations due to existence of doublets from methyl group, CP^a and C1 signals. Noteworthy is the fact that the signals of C5 and C6 atoms are considerably broadened in comparison to those ones observed in ¹³C CP-MAS NMR spectrum of **1a**. The signal originating from C1' atoms creates the two doublets and C2', 3', 4' atoms signals have the observed relative intensity 1:1:3:1.

Conclusion

The *cis*- and *trans*-2-methyl-2-oxo-2-trityl-1,3,2-dioxaphosphorinanes can be crystallised as pure enantiomers and racemates. In each conformer one of the obtained forms contains two molecules per asymmetric unit (racemic *cis* and chiral *trans*). In both cases asymmetric unit contains molecules with two different conformations of the puckered heteroatomic ring. The small but essential conformational differences existing for heteroatomic rings do not exhibit fully in NMR spectra, because only for the *trans* isomer the two noncongruent molecules appear in the spectra. It can be explained by existence of two distinctly different conformations in the *trans* isomer (sofa and distorted half-chair), while in *cis* isomer the different conformations show some closeness (all conformations can be described as more or less distorted half-chair).

Supplementary Data

Tables of crystal data and structure refinement, anisotropic displacement coefficients, atomic coordinates and equivalent isotropic displacement parameters for non-hydrogen atoms, H-atom coordinates and isotropic displacement parameters, bond lengths and interbond angles have been deposited with the Cambridge Crystallographic Data Centre under No CCDC806956, CCDC806957, CCDC806958, CCDC806959, respectively for compounds **1a**, **1b**, **2a** and **2b**.

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