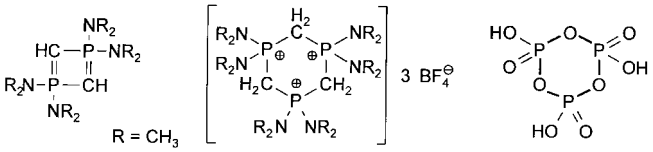
Cyclotrimethylenetriphosphinic Acid**

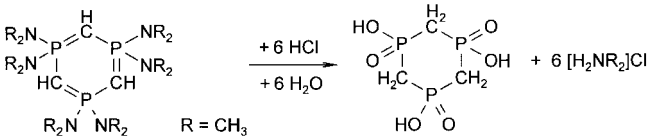
Ekkehard Fluck,* Gernot Heckmann,* and Stefan Plank

The reaction of bis(dimethylamino)difluoromethylphosphorane with two equivalents of *n*-butyllithium gives 1,1,3,3-tetrakis(dimethylamino)-1λ^5,3λ^5-diphosphete (**1**)[1–3] and 1,1,3,3,5,5-hexakis(dimethylamino)-1λ^5,3λ^5,5λ^5-[1,3,5]triphosphinine (**2**).[4–6] Whereas **1** readily hydrolyzes in water to give



1 **3** **5**

water-soluble, acyclic products,[7, 8] the water-insoluble compound **2** is stable to hydrolysis for a long period of time. In the reaction with $HBF_4 \cdot Et_2O$ in diethyl ether, **2** forms crystalline 1,1,3,3,5,5-hexakis(dimethylamino)-1λ^5,3λ^5,5λ^5-triphosphinantriium tetrafluoroborate (**3**) in 79.3 % yield.[9] The protonation of **2** can also be achieved by using other acids, for example with HCl in an aqueous medium, without cleavage of the six-membered ring of **3**. After heating the acidic solution for some time, the dimethylamino groups are successively hydrolytically eliminated resulting finally in the cyclotrimethylenetriphosphinic acid (**4**). The dimethylammonium chloride formed



2 **4**

in the course of the hydrolysis can be removed from the NaOH solution by heating the mixture and **4** can be isolated in the form of colorless sodium 1,3,5-trioxo-1λ^5,3λ^5,5λ^5-[1,3,5]triphosphinane-1,3,5-triolate (**4a**) in addition to NaCl.

The title compound **4** corresponds to the cyclotriphosphoric acid **5**,[10a] in which the three endocyclic oxygen atoms are substituted by methylene groups. Similar heterocycles with alternating P – C sequences, but with λ^3-phosphorus atoms, have been described in the form of 1λ^3-phospha-3,5-diphosphoniacyclohexanedihalogenides by Karsch.[10b] Compound **4** is stable to hydrolysis both in acidic and in alkaline media, even on heating. The structures of **4** and **4a** have been determined by the multiple-resonance NMR spectra.

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The $^{13}C\{^1H\}$ NMR spectrum, as expected, displays the twelve lines of the X part of an A_2BX spin system, which is characteristic for six-membered heterocycles with three symmetrically arranged P – C units (Figure 1).[5, 9, 12, 13] The missing symmetry of this X-part, which is apparent in the four lines

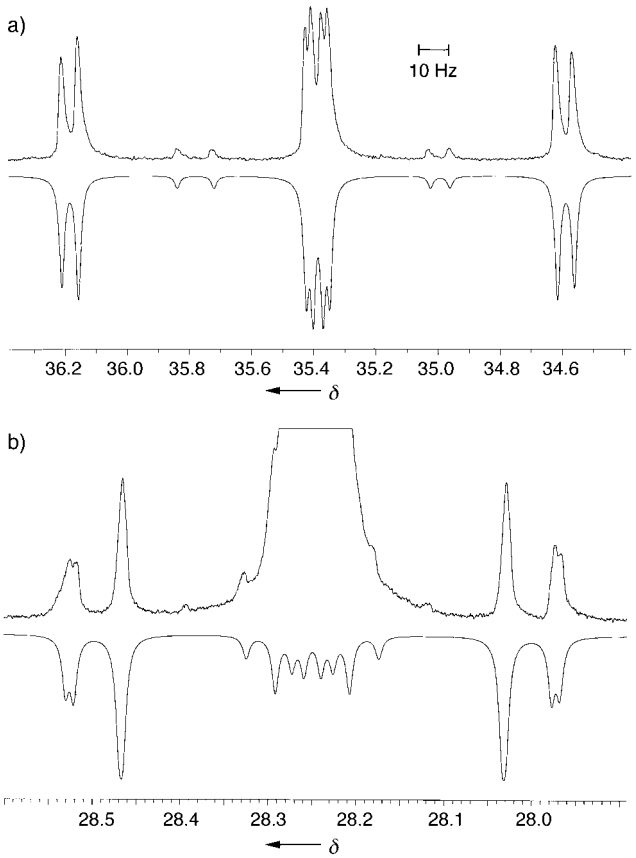

Figure 1. a) 100.614 MHz $^{13}C\{^1H\}$ NMR spectrum of **4a** with simulated part of spectra and b) ^{13}C satellites in the 161.983 MHz $^{31}P\{^1H\}$ NMR spectrum of **4a** with corresponding simulation, in each case at 85 °C in aqueous NaOH (line width at the height of the two most intensive ^{13}C satellites: 16 Hz).[11]

with lowest intensity, allows the sign of the geminal coupling constant $^2J(P_A,P_B)$ as well as the isotopic shift $^1\Delta^{31}P_A(^{13}C^X)$ (see ref. [5]; for the numbering see Table 1) to be determined.[11] The singlet in the $^{31}P\{^1H\}$ NMR spectrum is flanked by ^{13}C satellites, which can be assigned to the A_2B part (Figure 1). The ^{31}P NMR signal of **4** and **4a**, respectively, is significantly shifted to higher field in comparison to the signals of the starting material **2** ($\delta = 65.6$),[5] of the cation **3** ($\delta = 45.2$),[9] of the cyclic acid 1,3-dioxo-1λ^5,3λ^5-[1,3]diphosphinane-1,3-diol (which contains two 1,3-positioned phosphorus atoms; $\delta = 43.5$),[14] and of the central phosphorus atom P_α of the open-chain phosphinic acid $O{=}P_\alpha(OH)[CH_2P(O)(OH)_2]_2$ ($\delta = 37.3$);[15] in comparison with the corresponding signal of **5** ($\delta = 20.7$),[16] the ^{31}P NMR signal of **4** is, however, shifted downfield by about 15 ppm. Several salts of the acid 2,4,6-trioxo-2λ^5,4λ^5,6λ^5-[1,2,4,6]oxatriphosphinane-2,4,6-triol, which is bismethyleneanalogous to **5,** are known.[15, 17, 18] NMR data are, however, only available for the sodium salt (CH_2 multiplet at $\delta(^1H) = 2.22$).[18]

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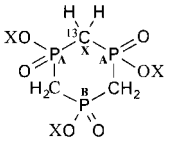
Table 1. NMR data of **4** (in 37% HCl) and **4a** (in aqueous NaOH); concentration in each case 0.1 M L^{-1}.[11]



X = H: **4**
X = Na: **4a**

	δ				^nJ [Hz]	
	4	**4a**	*n*		**4**	**4a**
^{31}P:	34.92	28.25	1	P_AC^X	85.3	79.2
^{13}C:	31.56	35.38	1	$P^{17}O$	–	89
^{17}O:	106	121	1	^{13}CH	127[a]	117[b]
^{1}H:	2.177	1.637	2	P_AP_B	+14.3	+9.6
			3	P_BC^X	−3.6	−3.2

[a] Determined from ^{13}C satellites of the singlet in the ^{1}H{^{31}P-CW} spectrum. [b] Determined from the ^{13}C{^{1}H} multiplet of the monodeuterated methylene group (see text).

^{13}C DEPT experiments on **4** and **4a** confirm that in each case only methylene carbon atoms are present in the heterocycle. The vicinal coupling constants of the PCPC ring units are negative as in **2** and **3**. The small value of $^2J(P_A,P_B) = +14.3$ Hz—compared with the significantly higher values of the geminal coupling in the P=CH–P triads of the triylide **2** (+73.0 Hz), of several diamino-λ^5-[1,3]diphosphinines (44.3–164.2 Hz),[19] and of the 1,1,3,3,5,5-hexakis(dimethylamino)-1,2-dihydro-3λ^5,5λ^5-[1,3,5]triphosphininium cation (72.8 Hz)[12]—indicates single bonds in the ring, as also confirmed by the similarly low ^2J(P,P) values of the λ^5-PCH_2-λ^5-P groups of **3** (4.0 Hz) and of the phosphorylphosphonylmethylene OP-$[N(CH_3)_2]_2CH_2PCH_3(O)N(CH_3)_2$ (5.7 Hz; hydrolysis product of **1**).[7, 8, 20] The existence of O=P–O atom sequences in the title compound and its sodium salt were verified by ^{17}O NMR experiments.[11] The ^{17}O NMR signals lie in the range of the signals of the phosphoryl oxygen atoms of the sodium phosphate as well as of the methyl-, dimethyl- and of the trimethylphosphate; in contrast to the singlet of the acid ($\Delta\nu_{1/2} = 410$ Hz), **4a**, as expected, displays a $^1J(^{31}P,^{17}O)$ splitting of 89 Hz.[21] There are no signals of dimethylamino groups visible in the ^{1}H and ^{13}C{^{1}H} NMR spectra.

Interestingly, when **4a** is heated to 90 °C in D_2O for 48 h, the three methylene groups of the sodium salt are partially deuterated; each of the methylene groups displays only one deuterium atom. The degree of deuteration is 90%; doubly deuterated methylene groups were not detected. This extraordinary finding arose from ^{13}C{^{1}H} and ^{1}H{^{31}P} NMR experiments.[11] The ^{13}C{^{1}H} NMR spectrum displays a triplet structure ($^1J(P_A,C^X)$) at 365 K, which is due to C^XD coupling and within the limits of the precision of the measurement consists of broadened signals in the ratio 1:1:1:2:2:2:1:1:1 ($\Delta\nu_{1/2} \approx 8$ Hz); in each case the three outer lines show the same splitting as the two outer line pairs of the nondeuterated species (see Figure 1). This splitting pattern is only consistent with monodeuterated methylene groups in **4a**, as was also confirmed by simulations. The partly recognizable ^{13}C lines of the nondeuterated isotopomer allow the determination of the ^{2}H-induced isotope shift, whose value also indicated the presence of CHD groups.[11] From the two ^{1}H{^{31}P} NMR spectra at 300 K and 363 K, which show a sharp singlet (CH_2 groups) and a second signal at 363 K, which is almost split into the triplet ($\Delta\nu_{1/2} = 3.8$ Hz; at 300 K: 1.8 Hz), an integral ratio of 1:9 was determined in each case by line form analysis; thus, a degree of deuteration of 90% (±2%) can be assumed. The ^{2}H-induced isotope shift is −0.02 ppm.[11]

NMR spectroscopic studies of **4** and **4a** at lower temperatures, which could disclose information about the ring conformation and ring inversion of the saturated six-membered ring, were only possible to a limited extent due to the employed solvent (see Table 1) and did not produce any significant results. The width at half intensity of the singlet in the ^{31}P{^{1}H} NMR spectrum of **4a** at 300 K is 1.4 Hz; at −10 °C only a broadening to 5.4 Hz was displayed.

Experimental Section

Compound **2** (1.00 g, 2.52 mmol) was treated with hydrochloric acid (20 mL, 37%), and the reaction mixture was heated. The ^{31}P{^{1}H} NMR spectrum of the resulting mixture only displayed the signals of **3**.[9] The solution was heated under ^{31}P{^{1}H} NMR control to 80 °C until all dimethylamino groups were eliminated from the cation of **3** (after ca. 48 h). After removal of the residual hydrochloric acid under vacuum, **4** remained in addition to $[(CH_3)_2NH_2]Cl$ in the molar ratio 1:6 as a colorless powder. The powder was dissolved in water (30 mL), treated with sodium hydroxide solution (0.91 g, 22.70 mmol), and heated under reflux to remove the dimethylammonium ion and form the sodium salt **4a.** After about 48 h only the signals of the anion **4a** were visible in the ^{31}P{^{1}H}, ^{13}C{^{1}H}, and ^{1}H NMR spectra of the reaction solution. **4a**: IR (Nujol, CsBr plates, only significant absorptions; see ref. [24]): $\tilde{\nu} = 1193$ (ms, sh), 1164 (s, $\nu_{as}(PO_2)$), 1078 (ms, $\nu_s(PO_2)$), 1011 (s, $\delta(CH_2)$), 822 (s, $\nu_{as}(P_3C_3$ ring)), 485 cm^{-1} (m, $\delta_s(PO_2)$); all bands are srongly broadened.

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[11] NMR spectra: Bruker AM 400 (^{1}H: 400.134 MHz); ^{1}H{^{31}P}: Bruker AM 200 (^{1}H: 200.132 MHz); [D_8]toluene capillary as external lock (5-mm-Ø-NMR tubes). Digital resolution (Hz/pkt), scan number, reference: ^{13}C{^{1}H}: 0.15, 52500, TMS; ^{31}P{^{1}H}: 0.08, 1200, H_3PO_4 (85%, external); ^{1}H: 0.3, 32, TMS; ^{17}O (373 K): 3.0, 660000, H_2O.

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$\delta(^{17}O)$ of the aqueous HCl (37%) for **4**: $\delta = 27.5$;[22] of the aqueous NaOH for **4a**: $\delta = 5.3$; $\Delta\nu_{1/2}$ in each case 55 Hz. $\delta(^1H)$ of the HCl (37%) for **4**: $\delta = 7.00$; of the aqueous NaOH at **4a**: $\delta = 3.77$. Spectra simulations: Bruker WIN-DAISY, version 4.0. Deconvolution: Bruker WIN1D-NMR, version 6.0. Measurement temperature: **4** 300 K; **4a** 358 K; **4a** deuterated in D_2O 365 K. Isotope shifts: $^1\Delta^{31}P_A(^{13}C^X) = -0.009$ relative to [per-^{12}C]-isotopomer; $^{13}CH_2/^{13}CHD$ $^1\Delta^{13}C(^2H) = -0.38$; CH_2/CHD $^1\Delta^1H(^2H) = -0.020$ [from $^1H\{^{31}P\}$ spectra].[20, 23]

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Evolving Opportunities in Structure Solution from Powder Diffraction Data—Crystal Structure Determination of a Molecular System with Twelve Variable Torsion Angles**

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In general, determination of crystal structures from single-crystal diffraction data can be carried out in a routine and straightforward manner. However, many crystalline solids can be obtained only as microcrystalline powders and are not suitable for investigation by single-crystal diffraction methods. In the past, this problem has limited the ability to determine the structural properties of such materials. There is clearly a pressing need to develop and exploit techniques for solving crystal structures from *powder* diffraction data.[1–3] However, although traditional techniques for structure solution from powder diffraction data have been applied successfully in several cases, these techniques have certain intrinsic limitations,[2] and organic molecular crystals represent a particularly challenging case. For these reasons, our recent research has focused on the development and implementation of new methodologies for structure solution from powder diffraction data, and has led to new "direct-space" approaches for structure solution which overcome some of these difficulties. Such direct-space techniques are particularly suited to the case of molecular crystal structures. Herein, we demonstrate the current state-of-the-art in the solution of molecular crystal structures from powder diffraction. To our knowledge, the structure reported here is the most complex molecular crystal structure, solved directly from powder diffraction data, that has so far been reported in the literature.

Direct-space approaches[2, 4, 5] for structure solution from powder diffraction data are based on sampling trial crystal structures in direct space. Structural models are generated independently of the powder diffraction data, with the "quality" of each structural model assessed by comparison between the powder diffraction pattern calculated for the structural model and the experimental powder diffraction pattern. In our work, this comparison is based on the profile R factor R_{wp},[6] as used in Rietveld refinement. We emphasize that R_{wp} considers the whole digitized intensity profile, and thus uses the raw powder diffraction data directly "as measured". Peak overlap is implicitly taken care of, and the need to extract integrated intensities $I(hkl)$ for individual reflections from the powder diffraction pattern is circumvented. In effect, our direct-space approach searches the $R_{wp}(\mathbf{X})$ hypersurface to find the best structure solution (lowest R_{wp}), where $\{\mathbf{X}\}$ represents the set of variables that define the structure. In direct-space strategies for structure solution, the structure is defined by a "structural fragment", which represents an appropriate collection of atoms within the asymmetric unit. The variables in $\{\mathbf{X}\}$ represent the position, orientation, and intramolecular geometry of the structural fragment. The position is specified by the coordinates $\{x, y, z\}$ of the center of mass or a predefined pivot atom, the orientation is specified by rotation angles $\{\theta, \phi, \psi\}$ around a set of orthogonal axes, and the intramolecular geometry is specified by a set of variable torsion angles $\{\tau_1, \tau_2, \ldots, \tau_n\}$. In general, the bond lengths, bond angles, and any known torsion angles (i.e. if aspects of the molecular conformation are known a priori) are fixed in the structure solution calculation, and are taken either from standard values for the type of molecule under study or from the known geometry of a similar molecule. Previous research has demonstrated the success of Monte Carlo,[4, 7–13] simulated annealing,[5, 14–16] and genetic algorithm[17–22] methods for searching R factor hypersurfaces to locate the global minimum (structure solution). Most of these direct-space approaches have considered hypersurfaces based on the profile R factor R_{wp} (as in this paper), although hypersurfaces based on other definitions of agreement factor have also been considered.[16, 20–22] In all of these methods for global optimization, the main limitation is the number of variables in $\{\mathbf{X}\}$ (the number of degrees of freedom which define the hypersurface) and early applications of direct-space approaches for structure solution focused on examples of essentially rigid molecules, with at most a few variable torsion angles. The generalization of direct-space

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