A New Synthesis of *P*-Substituted 2,3-Dihydro-1,3-dimethyl-1,3,2λ^3-benzodiazaphosphorin-4(1*H*)-ones and Alkylaminodifluorophosphanes with Chlorodifluorophosphane. – Synthesis and Structure of {*cis*-Bis[bis(2-chloroethyl)aminodifluorophosphane]dichloro}platinum(II)☆

Hans-Jürgen Plinta, Ion Neda, Axel Fischer, Peter G. Jones, and Reinhard Schmutzler*

Institut für Anorganische und Analytische Chemie der Technischen Universität,
Postfach 3329, D-38023 Braunschweig (Germany)

Received January 2, 1995

Key Words: 2,3-Dihydro-1,3-dimethyl-1,3,2-benzodiazaphosphorin-4-(1*H*)-ones, 2-trimethylsiloxy-, 2-oxo-, and 2-fluoro-substituted / Equilibrium reaction / Aminodifluorophosphanes / Platinum complex

2,3-Dihydro-1,3-dimethyl-2-oxo-1,3,2λ^4-benzodiazaphosphorin-4(1*H*)-one **1** reacted with diethylaminotrimethylsilane to give solely the 2-trimethylsiloxy-λ^3-diazaphosphorinone **2**. The reaction of **2** with the 2-chloro-λ^3-diazaphosphorinone **3** yielded the P–O–P-bridged compound **4** in an equilibrium reaction with elimination of trimethylchlorosilane. The synthesis of the *P*-difluorophosphite-substituted λ^3-benzodiazaphosphorinone **6** was effected by the reaction of chlorodifluorophosphane (**5**) with **1** in the presence of triethylamine in a 1:1 molar ratio, or in the reaction of **5** with **2** or **4**. The reaction of **5** with **6** led, with elimination of μ-oxo-bis(difluorophosphane), to the P(III)Cl species **3**. **5** reacted with *N,N'*-dimethylanthranilamide in the presence of triethylamine in a 2:1:2 molar ratio to give the *N,N'*-bis(difluorophosphane) derivative **9**, as evidenced by low temperature (−30°C) ^{19}F- and ^{31}P-NMR data. At room temperature the 2-fluoro-λ^3-diazaphosphorinone **10** was formed from **9** with intramolecular elimination of phosphorus trifluoride. 2-Chloroethyl- or bis(2-chloroethyl)aminodifluorophosphane **11** and **12** were obtained in the reaction of **5** with 2-chloroethyl- or bis(2-chloroethyl)amine hydrochloride in the presence of triethylamine in a 1:1:2 molar ratio. **12** reacted with (COD)$PtCl_2$ (COD = 1,5-cyclooctadiene) in a 2:1 molar ratio to give the {*cis*-bis[bis(2-chloroethyl)aminodifluorophosphane]dichloro}platinum(II) complex **13**. The characterization of **2**, **4**, **6**, and **11**–**13** is based on their NMR and mass spectra. The structures of **10** and **13** were established by single-crystal X-ray analysis. **10** crystallizes with two independent molecules. Both six-membered heterocycles display an envelope conformation with the phosphorus atoms 36.9 and 50.4 pm, respectively, out of the plane. The phosphorus atoms have pyramidal coordination geometry. The cis-configuration at platinum(II) in the complex **13** was confirmed; two ligands (**12**) are coordinated to Pt^{II} via phosphorus. The platinum atom has a distorted square-planar coordination geometry.

Introduction

In recent years a number of phosphorylated 1,3,5,2-triazaphosphorin-4,6-diones[1–6] and 1,3,2-benzodiazaphosphorin-4(1*H*)-ones[6–10] with 3-, 4-, and 5-coordinated phosphorus have been reported. The substituents at phosphorus were halogen atoms and alkyl, aryl, and dialkylamino groups.

The study of alkylating 2-chloroethylamino-substituted phosphorus compounds is of interest because of their potential cytostatic properties[11]. The development of new potential cytostatics is of steadily growing importance in medicine[11–13].

P–F compounds are of interest because of a useful peculiarity that distinguishes them with respect to their physiological effects from other halogen-containing phosphorus compounds: their hydrolysis is slowed down. For example, fluorophosphates are incorporated into oligodeoxyribonucleosides in such a way that they can control the growth of viruses and cells[14–17]. There is increasing interest in the possible control of selectivity and activity of active substances and of their physical, chemical, and biological properties by the introduction of fluorine or fluorine-containing groups in specific positions. The influence of fluorine on biological activity is still not well understood. It is evident that the use of chlorodifluorophosphane as a reactant can provide new fluorine-containing groups as synthons for the synthesis of active compounds.

The discovery of the cyclostatic activity of the so-called "cis-platinum"[18] is important in respect to this problem. An increased cyclostatic effect (synergistic effect) of the *cis*-bis[bis(2-chloroethyl)aminodifulorophosphane]dichloro-platinum(II)complex described in this work could be expected, because of its structural similarity to *cis*-platinum.

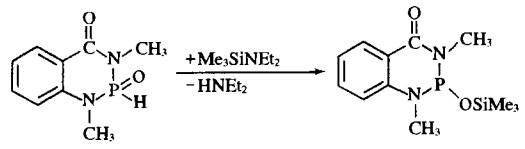
Results and Discussion

Synthesis of the 1,3,2λ^3-Benzodiazaphosphorin-4(1*H*)-ones 2 and 4

The existence of the *P*-trimethylsiloxy-substituted and the P–O–P bridged[19] 1,3,5-triaza-2λ^3-phosphorin-4,6-diones stimulated our interest in studying the possible synthesis of the corresponding 1,3,2λ^3-benzodiazaphosphorin-4(1*H*)-ones. The synthesis of an (O=)P–O–P(=O)-bridged λ^4-diazaphosphorinone has been described by Coppola[20].

  0009–2940/95/0707–0695 $ 10.00+.25/0

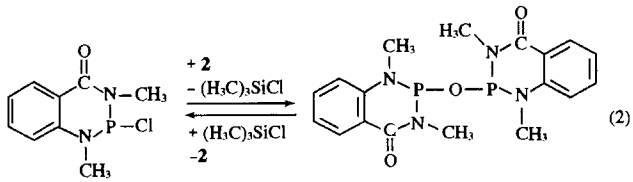
The reaction of 2,3-dihydro-1,3-dimethyl-2-oxo-1,3,2λ⁴-diazaphosphorin-4(1*H*)-one **1** with diethylaminotrimethylsilane resulted in the formation of the 2-trimethylsiloxy-substituted λ³-diazaphosphorinone **2** [eq. (1)].



(1)

1 **2**

The P–O–P bridged compound **4** was obtained from the reaction of **2** with the 2-chloro-λ³-benzodiazaphosphorinone **3** in a 1:1 molar ratio [eq. (2)].



(2)

3 **4**

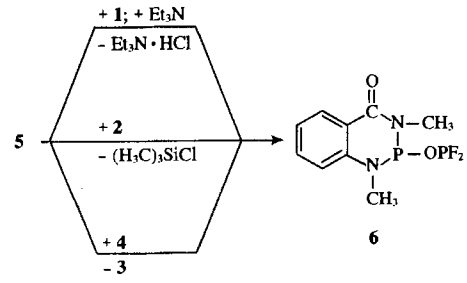
The course of the reaction was followed by recording the ^{31}P-NMR spectrum every 24 hours. After ca. 3 d at 50 °C, an equilibrium between **2**, **3**, and **4**, and trimethylchlorosilane was established. The observed integral ratio 1:1 for **2**:**4** in the ^{31}P-NMR spectrum was unchanged after another 5 days. Through repeated removal of trimethylchlorosilane and part of the solvent at reduced pressure it was possible to shift the equilibrium almost completely in the direction of the product (integral ratio **4**:**2** = 12:1).

The NMR and mass spectrometric investigation of compounds **2** and **4** showed the expected correlation between the δ(^{1}H), δ(^{13}C), and δ(^{31}P) values and the mass spectrometric fragmentation[7–10,19]. In the mass spectra, molecular ion peaks were of low intensity (1% for **2** and 10% for **4**) reflecting, especially, the instability of the P–OSi(CH$_3$)$_3$ bond. In the IR-spectrum the P–O–P stretching vibration was observed as a weak band at ν = 884 cm^{-1}[21]. For the complete NMR and mass spectrometric characterisation of **2** and **4**, see the Experimental Section.

Synthesis of the λ³-Benzodiazaphosphorin-4(1*H*)-ones 6 and 10

In the reaction of PF_2Cl **5** with 2,3-dihydro-1,3-dimethyl-2-oxo-1,3,2λ⁴-benzodiazaphosphorin-4(1*H*)-one **1** in the presence of triethylamine in a 1:1:1 molar ratio, or in the reaction of **5** with **2** or **4** in an equimolar ratio, the *P*-difluorophosphito-substituted compound **6**, which was unstable at room temperature, was obtained in good yield [eq. (3)].

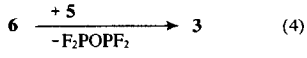
6 could be characterised by NMR spectroscopy at −20 °C. The observed δ(^{1}H), δ(^{13}C), δ(^{19}F), and δ(^{31}P) values are in good agreement with literature data[7–10]. The δ(^{31}P) value of the OPF_2 group in **6** is characteristic of aromatic difluorophosphites[22,23].



(3)

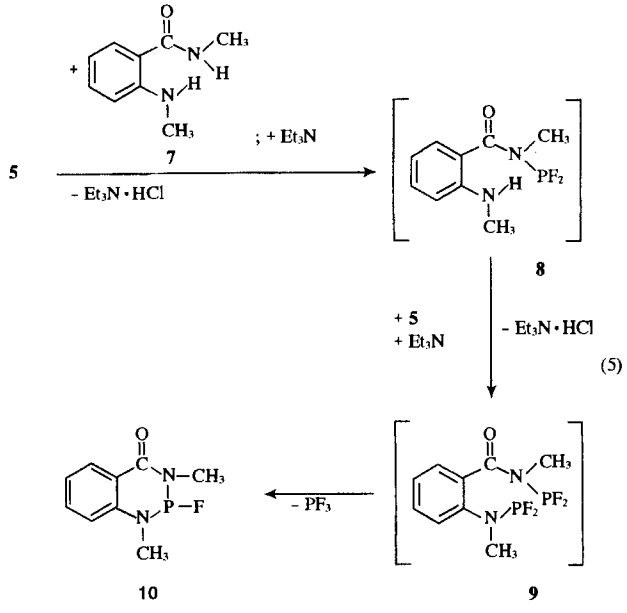
5 **6**

Reaction of **5** with **6** in an equimolar ratio led, with elimination of μ-oxo-bis(difluorophosphane)[24], to **3**[10] [eq. (4)].



(4)

A new synthesis of the 2-fluorosubstituted 1,3,2λ³-benzodiazaphosphorinone **10**[8], under mild conditions at room temperature, consists in the reaction of **5** with *N*,*N*′-dimethylanthranilamide **7** in the presence of triethylamine in a molar ratio 2:1:2 [eq. (5)].



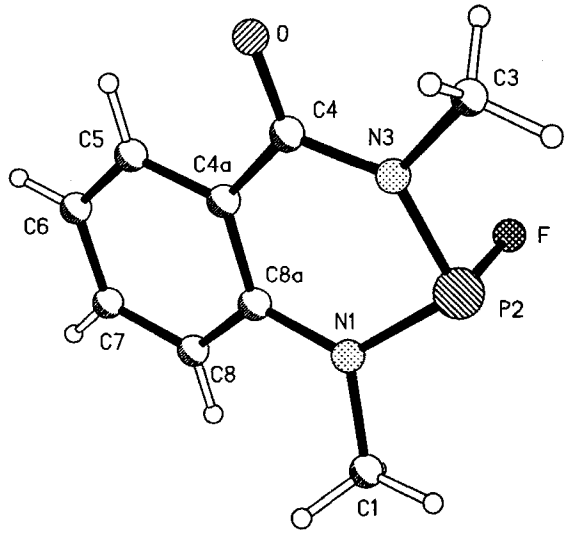
(5)

10 **9**

The previously described compound **10**[8] was obtained in good yield. The *N*,*N*′-bis(difluorophosphane)-substituted intermediate compound **9** could be observed by NMR spectroscopy in solution (CD_2Cl_2 capillary) at −30 °C. At room temperature a cyclisation reaction with elimination of PF_3 and formation of **10**[25,26] took place. The formation of phosphorus trifluoride may be explained by an entropy increase in a closed system[26–28]. The existence of the monodifluorophosphane-substituted intermediate **8** is postulated on the basis of the formation of **9**. Compound **8** could not be observed NMR-spectroscopically because of the rapid formation of **9** under the reaction conditions [eq. (5)]. A related intramolecular cyclisation reaction of 1,2-bis(difluorophosphito)benzene with elimination of phosphorus trifluoride and formation of 2-fluoro-1,3,2λ³-benzodioxaphosphole was observed by Krüger[25].

The X-ray structure analysis of **10** reveals two independent molecules with minor conformational differences; one molecule is shown in Figure 1. The heterocyclic systems of both molecules display an "envelope"-type conformation, in which N1, N3, C4, C4a, and C8a (or the corresponding primed atoms) are coplanar to a good approximation (mean deviations from the planes are 4.0 and 4.3 pm). The phosphorus atoms lie 36.9 and 50.4 pm, respectively, out of the plane. A similar ring conformation was observed for the analogous 2-fluoro-3-methyl-1,3,2λ^3-benzoxazaphosphorinone[29]. The phosphorus atom in **10** displays a pyramidal coordination geometry; P2 (P2′) lies 77.1 (78.0 pm) out of the plane formed by the atoms in α-position[29].

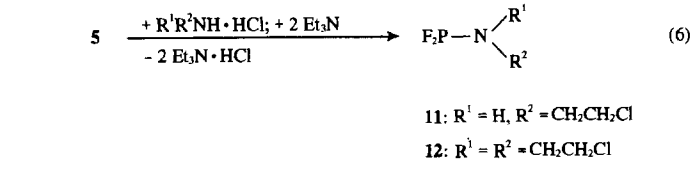
Figure 1. One of the two independent molecules of compound **10** in the crystal[a]



[a] Atom radii are arbitrary; selected bond lengths [pm] and angles [°]: N(1)–P(2) 166.6(2), P(2)–N(3) 170.2(2), P(2′)–F′ 161.1(2), P(2)–F 161.66(14), N(1′)–P(2′) 167.1(2), P(2′)–N(3′) 169.4(2); C(1)–N(1)–P(2) 114.98(13), F–P(2)–N(3) 98.71(7), C(4)–N(3)–P(2) 128.27(13), C(1′)–N(1′)–P(2′) 115.45(13), F′–P(2′)–N(3′) 99.18(8), C(4′)–N(3′)–P(2′) 127.31(13), F–P(2)–N(1) 102.09(8), N(1)–P(2)–N(3) 99.59(8), C(3)–N(3)–P(2) 114.90(13), F′–P(2′)–N(1′) 100.81(8), N(1′)–P(2′)–N(3′) 99.02(8), C(3′)–N(3′)–P(2′) 116.40(13).

Synthesis of the Aminodifluorophosphanes 11 and 12

The reaction of chlorodifluorophosphane **5** with 2-chloroethylamine hydrochloride or bis(2-chloroethyl)amine hydrochloride in the presence of triethylamine in a 1:1:2 molar ratio furnished **11** and **12** under mild conditions in good yield, according to eq. (6).



(6)

11: $R^1 = H$, $R^2 = CH_2CH_2Cl$

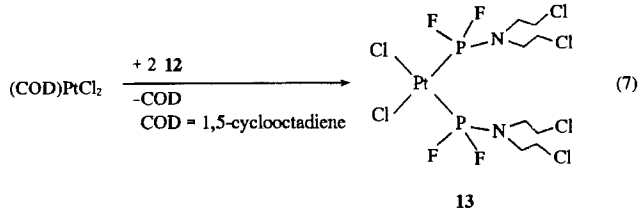
12: $R^1 = R^2 = CH_2CH_2Cl$

The synthesis of the aminodifluorophosphanes of type $RNHPF_2$ [R = $(CF_3)_2COSiMe_3$ and $C_6H_4OSiMe_3$] from the reaction of **5** or bromodifluorophosphane with the corresponding aminotrimethylsilyl compounds is known[25].

Compounds **11** and **12** were characterised by NMR and mass spectrometry. The ^{1}H-, ^{13}C-, ^{19}F-, and ^{31}P-NMR data correspond to the literature values for aminodifluorophosphanes[30]. In the mass spectra, a molecular ion of low intensity (2%) could be observed only for **11**. The base peak for both compounds was the fragment $[M - CH_2Cl]^+$. For other fragments, see the Experimental Section.

Reaction of 12 with (COD)PtCl$_2$

The reaction of **12** with (COD)PtCl$_2$ (COD = 1,5-cyclooctadiene) in a 2:1 molar ratio yielded the complex {*cis*-bis[bis(2-chloroethyl)aminodifluorophosphane]dichloro}-platinum(II) **13** in good yield, in accord with eq. (7).



(7)

13

The ^{1}H- and ^{13}C-NMR data of **13** differ only insignificantly from those of compound **12**. In the ^{31}P-NMR spectrum, a triplet due to the bis(aminodifluorophosphane) groups in **13** [δ = 89.98; $^{|1+3|}J$(PF) = 1137.19 Hz] was observed. The pronounced high-field shift, compared to the value of the free ligand **12** [δ(^{31}P) = 143.10], suggests the presence of a σ/π-synergism[31,32].

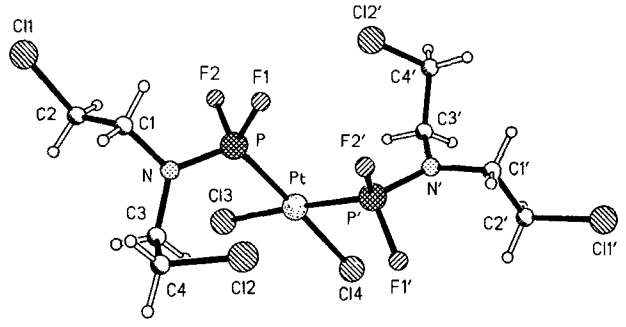
The value of the $^1J(^{31}P^{195}Pt)$ coupling constant, 5902.94 Hz, indicates a *cis* arrangement of ligands at platinum in the square-planar platinum(II) complex **13**[22,33]. The identity of **13** was confirmed by ^{19}F-NMR spectroscopy and elemental analysis.

In the mass spectrum of **13** no molecular ion was observed. The base peak corresponded to the fragment $[L - CH_2Cl]^+$. Other fragments resulted from the consecutive loss of chloride anions and an aminodifluorophosphane ligand (Experimental Section).

The X-ray structure analysis of **13** (Fig. 2) shows that two ligands **12** (mutually cis) coordinate through the phosphorus atom, consistent with the Pearson concept[22,32,34]. The platinum atom displays slightly distorted square planar coordination geometry; it lies only 1.1 pm out of the mean ligand plane (P, P′, Cl3, and Cl4; mean deviation 0.3 pm). The greater steric demand of the aminodifluorophosphane ligands is reflected in the wide P–Pt–P′ angle of 98.63(7)°. The aminodifluorophosphane ligands lie trans to each other; the torsion angle N–P···P′–N′ (174.7°) shows that N and N′ are approximately antiperiplanar. As has been observed previously, platinum-phosphorus bonds involving fluorophosphane ligands are short[35–37] [here 218.5(2) and 218.8(2) pm] and indicate σ/π-synergistic effects[31,32]; cf. the ^{31}P-NMR discussion of **13**. The activity-related carbon–chlorine bond lengths are not significantly different [177.0(8), 178.0(10) pm; cf. 179.4, 178.4 pm in 4-hydroper-

oxycyclophosphamide[38]]. Similar values (178, 179 pm and 176.9, 179.8 pm) are observed for racemic CP and CP hydrate[39] (CP = cyclophosphamide), whereas the values are appreciably greater in (+)-CP (181, 182 pm). The heterolysis of the C–Cl bonds in **13**, which is important with respect to the potential cancerostatic activity, should be possible in vivo.

Figure 2. The molecule of compound **13** in the crystal[a]



[a] Atom radii are arbitrary; selected bond lengths [pm] and angles [°]: Pt–P' 218.5(2), Pt–Cl(3) 232.1(2), Cl(1)–C(2) 178.5(8), Cl(1')–C(2') 177.0(8), Pt–P 218.8(2), Pt–Cl(4) 232.6(2), Cl(2)–C(4) 178.6(9), Cl(2')–C(4') 178.0(10); P'–Pt–P 98.63(7), P–Pt–Cl(3) 86.03(7), P–Pt–Cl(4) 176.77(7), N'–P'–Pt 118.4(2), P'–Pt–Cl(3) 175.33(7), P'–Pt–Cl(4) 84.53(7), N–P–Pt 120.1(2).

We are grateful to *BASF AG, BAYER AG, DEGUSSA AG,* and *HOECHST AG* for generous gifts of chemical used in this research, and to Dr. *H. M. Schiebel* and Frau *D. Döring* for recording mass spectra. The support of the *Fonds der Chemischen Industrie* is gratefully acknowledged. I. Neda thanks the *Bundesanstalt für Arbeit* for ABM support.

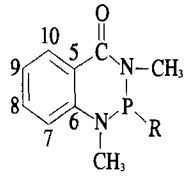
Experimental

All experiments were carried out with exclusion of air and moisture; solvents were purified and dried according to the usual methods[40]. "In vacuo" refers to a pressure of 0.05 Torr at 25 °C, unless otherwise stated. – NMR: Spectrometer Bruker AC-200 (^{1}H at 200.1 MHz; ^{13}C at 50.3 MHz; ^{19}F at 188.3 MHz; ^{31}P at 81 MHz); reference substances were $SiMe_4$ (TMS) ext. (^{1}H, ^{13}C), $CFCl_3$ ext. (^{19}F), and 85% H_3PO_4 ext. (^{31}P); high-field shifts are given negative, low-field shifts positive signs. – MS: Spectrometer Finnigan MAT 8430 (70 eV); melting points were determined in sealed capillaries on a Büchi 510 instrument. – IR [in cm^{-1}]: Spectrometer Beckman IR-4260 (spectra were recorded in CH_2Cl_2 solution, using NaCl cells). – Elemental analyses: Analytical laboratory of the Institut für Anorganische und Analytische Chemie der Technischen Universität, Braunschweig.

Materials: 1,3-dimethyl-2,3-dihydro-2-oxo-1,3,2λ^4-benzodiazaphosphorin-4(1*H*)-one **1**[41], diethylaminotrimethylsilane[42], 2-chloro-2,3-dihydro-1,3-dimethyl-1,3,2λ^3-benzodiazaphosphorin-4(1*H*)-one (**3**)[10], chlorodifluorophosphane (**5**)[43], *N,N'*-dimethylanthranilamide (**7**)[43], η^4-1,5-cyclooctadienedichloroplatinum(II)[44]. Commercial products: 2-chloroethylamine hydrochloride and bis(2-chloroethyl)amine hydrochloride (Fa. Janssen Chimica).

Preparation of 2,3-Dihydro-1,3-dimethyl-2-trimethylsiloxy-1,3,2λ^3-benzodiazaphosphorin-4(1H)-one (**2**): Diethylaminotrimethylsilane (2.76 g, 19.0 mmol) was added dropwise with stirring during 15 min to a solution of **1** (3.99 g, 19.0 mmol) in 70 ml of toluene. Stirring was continued for 1 d, then the solvent and other volatile products were removed in vacuo. The identity of diethylamine was confirmed by ^{1}H-NMR spectroscopy. The product was obtained as an oily liquid, which was not purified further; yield 4.35 g (15.4 mmol, 81%) **2**. – ^{1}H NMR ($CDCl_3$): δ = –0.09 [s, 9H, $(H_3C)_3Si$]; 3.13 and 3.17 [2 d, 3H + 3H, ^3J(HP) = 12.32, 13.96 Hz, CH_3NP, $CH_3NC(=O)$]; 6.79–8.21 [m, 4H, C_6H_4]. – ^{13}C NMR ($CDCl_3$): δ = 0.76 [s, 3 C, $(H_3C)_3Si$]; 32.63 and 35.23 [2 d, 1 C + 1 C, ^2J(CP) = 39.99, 45.65 Hz, CH_3NP, $CH_3NC(=O)$]; 114.51–133.08 [5 s, 5 C, aromatic C-5 and C-7–C-10 (for numbering scheme, see Figure 3]; 144.56 [d, 1 C, ^2J(CP) = 8.35 Hz, aromatic C-6]; 163.71 [d, 1 C, ^2J(CP) = 6.79 Hz, C(=O)NP]. – ^{31}P NMR ($CDCl_3$): δ = 102.85 (s). – EI-MS; *m/z* (%): 282 (1) [M^+]; 210 (100) [$M^+ - Si(CH_3)_3 + H$]; 209 (2) [$M^+ - Si(CH_3)_3$]; 164 (24) [$C_6H_4C(=O)NCH_3P^+$]; 133 (34) [$C_6H_4C(=O)NCH_3^+$]; 105 (22) [$C_6H_4NCH_3^+$]; 104 (28) [$C_6H_4C(=O)^+$]; 77 (31) [$C_6H_5^+$]; 73 (30) [$Si(CH_3)_3^+$]. – $C_{12}H_{19}N_2O_2PSi$ (282.39): calcd. C 51.04, H 6.80, N 9.92; found C 50.82, H 6.61, N 9.51.

Figure 3. Numbering scheme for the assignment of the aromatic ^{13}C-NMR resonances in compounds **2**, **4**, and **6**



Preparation of the P–O–P-Bridged Compound (**4**): A mixture of **2** (2.46 g, 8.7 mmol) and **3** (2.0 g, 8.7 mmol), dissolved in 30 ml of toluene, was stirred at 50 °C. The reaction was followed by recording the ^{31}P-NMR spectrum every 24 h. After 3 days an equilibrium between **2**, **3**, **4**, and trimethylchlorosilane was established. The integration ratio **2**:**4** was 1:1. Trimethylchlorosilane, formed in the course of the reaction, together with part of the solvent, was removed in vacuo (5 Torr, 50 °C) every 2 h until the equilibrium was strongly shifted in the direction of the products (integral ratio **4**:**2** = 12:1). Finally, the remaining volatile reaction products were removed in vacuo and the residue was washed three times with 20 ml of diethyl ether. The product was obtained as a colourless solid, which was dried in vacuo; m.p. 162 °C; yield 2.58 g (6.4 mmol, 74%) **4**. – ^{1}H NMR ($CDCl_3$): δ = 2.92 and 3.16 [2 d, 6H + 6H, ^3J(HP) = 12.81, 12.89 Hz, 2 × CH_3NP, 2 × $CH_3NC(=O)$]; 6.72–8.23 [m, 8H, 2 × C_6H_4]. – ^{13}C NMR ($CDCl_3$): δ = 32.99 and 35.79 [2 d, 2 C + 2 C, ^2J(CP) = 39.90, 46.0 Hz, 2 × CH_3NP, 2 × $CH_3NC(=O)$]; 114.89–133.68 [5 s, 10 C, 2 × aromatic C-5 and C-7–C-10 (for numbering scheme, see Figure 3)]; 144.33 [d, 2 C, ^2J(CP) = 8.07 Hz, 2 × aromatic C-6]; 163.60 [s, 2 C, 2 × C(=O)NP]. – ^{31}P NMR ($CDCl_3$): δ = 103.33 (s). – EI MS; *m/z* (%): 402 (10) [M^+]; 386 (8) [$M^+ - CH_3 - H$]; 210 (94) [$C_6H_4(NCH_3)_2C(=O)P(=O) + H^+$]; 193 (100) [$C_6H_4(NCH_3)_2C(=O)P^+$]; 152 (26) [$C_6H_4NCH_3P(=O)^+$]; 136 (18) [$C_6H_4NCH_3P^+$]; 133 (21) [$C_6H_4C(=O)NCH_3^+$]; 105 (24) [$C_6H_4NCH_3^+$]; 57 (43) [$C(=O)NCH_3^+$]. – IR ($CD_2Cl_2$): $\tilde{\nu}$ = 884 (w) cm^{-1} (P–O–P). – $C_{18}H_{20}N_4O_3P_2$ (402.36): calcd. C 53.73, H 5.02, N 13.93; found C 53.80, H 5.03, N 13.72.

Preparation of the P-Difluorophosphito-Substituted 1,3,2λ^3-Benzodiazaphosphorin-4(1H)-one (**6**). General Procedure for Routes A, B, and C: In a heavy-wall glass tube equipped with a Teflon® stopcock was placed the phosphoryl compound **1** and triethylamine in a 1:1 molar ratio (route A), the *P*-trimethylsiloxy-substituted compound **2** (route B), or the P–O–P-bridged compound **4** in dichloromethane (route C). At –196 °C chlorodifluorophosphane **5** was condensed into the glass tube in a 1:1 molar ratio, the reaction mixture was warmed to –20 °C during 1 h and stirred

for 1 h at this temperature. The volatile by-products of the reaction were removed in vacuo. To the residue 15 ml of diethyl ether was added at −20 °C, the solution was filtered, and the filtrate was stored at the same temperature. In the case of compounds **4** and **5** (route C) a colourless solid precipitated, which was filtered off and identified as compound **3**. Finally, the solvent was removed from the filtrate in vacuo and compound **6**, unstable at room temperature, was obtained as a colourless oil. It was stored at −20 °C. − ^{1}H NMR (CD_2Cl_2, −20 °C): δ = 3.01 and 3.21 [2 d, 3H + 3H, ^3J(HP) = 12.90, 13.31 Hz, CH_3NP, $CH_3NC(=O)$]; 6.84−8.20 [m, 4H, C_6H_4]. − ^{13}C NMR (CD_2Cl_2, −20 °C): δ = 33.14 and 36.08 [2 d, 1 C + 1 C, ^2J(CP) = 38.23, 45.44 Hz, CH_3NP, $CH_3NC(=O)$]; 114.99−133.81 [5 s, 5 C, aromatic C-5 and C-7−C-10 (for numbering scheme, see Figure 3]; 144.22 [d, 1 C, ^2J(CP) = 7.87 Hz, aromatic C-6]; 163.60 [s, 1 C, C(=O)NP]. − ^{19}F NMR (CD_2Cl_2, −20 °C): δ = −38.01 [dd, 2 F, ^1J(FP) = 1347.51 Hz and ^3J(FP) = 22.35 Hz, F_2POP]. − ^{31}P NMR (CD_2Cl_2, −20 °C): δ = 110.91 [dt, 1 P, ^1J(PF) = 1347.58 Hz, ^2J(POP) = 13.56 Hz, $POPF_2$]; δ = 103.11 [dt, 1 P, ^2J(PP) = 13.61 Hz, ^3J(PF) = 22.21 Hz, $POPF_2$]. − As a consequence of the instability of **6** towards moisture and warming to room temperature, no mass spectrum and elemental analysis were obtained.

Table 1. Experimental data for the synthesis of compound **6**

Compound	**6**	**6**	**6**
Route	A	B	C
Reactants (g; mmol)	**1** (5.0; 23.8) Et_3N (2.41; 23.8) **5** (2.49; 23.8)	**2** (1.5; 5.3) **5** (0.55; 5.3)	**4** (1.5; 3.7) **5** (0.39; 3.7)
Solvent CH_2Cl_2 (ml)	50	25	25
Yield g (mmol, %)	3.45 (12.4, 52)	0.81 (2.9, 55)	0.5 (1.8, 49)
Further products g (mmol, %)	—	—	**3** 0.43 (1.9, 50)

Formation of 2-Chloro-2,3-dihydro-1,3-dimethyl-1,3,2λ^3-benzodiazaphosphorin-4(1H)-one (**3**) *from* **6** *and* PF_2Cl (**5**): A solution of **6** (1.0 g, 3.6 mmol) in 20 ml of dichloromethane was placed at −20 °C in a heavy-wall glass tube equipped with a Teflon® stopcock. At −196 °C chlorodifluorophosphane **5** (0.38 g, 3.6 mmol) was condensed into the tube and the reaction mixture was allowed to warm up to room temperature during 1 h, and then stirred for 3 h. The volatile product of the reaction was removed in vacuo and was identified at 0 °C [δ(^{19}F) = −41.24 (m) and δ(^{31}P) = 110.91 (m) in $CDCl_3$] as μ-oxo-bis(difluorophosphane)[24]. After removal of the solvent, 25 ml of diethyl ether was added to the residue and the product was recrystallised at −20 °C; m.p. 100 °C; yield 0.73 g (3.2 mmol, 89%) of **3**. Compound **3**[10] was characterised by NMR spectroscopy and mass spectrometry.

Preparation of N,N'-Bis(difluorophosphanyl)-N,N'-dimethylanthranilamide (**9**) *and of 2-Fluoro-2,3-dihydro-1,3-dimethyl-1,3,2λ^3-benzodiazaphosphorin-4(1H)-one* (**10**): The reactions and all the subsequent operations were conducted as described for **6** (routes A−C): Reactants: **7** (1.0 g, 6.1 mmol) and PF_2Cl (**5**, 1.27 g, 12.2 mmol) in 20 ml of dichloromethane. The intermediate product **9** was observed in solution by NMR spectroscopy at −30 °C (CD_2Cl_2 capillary): δ(^{19}F) = −71.14 and −68.21 [2 d, 2×2 F, ^1J(FP) = 1184.12 and 1202.44 Hz, 2 × PF_2]; δ(^{31}P) = 142.11 and 146.31 [2 t, 2 P, ^1J(PF) = 1183.99 and 1202.81 Hz, 2 × PF_2]. After stirring **9** for 1 d at room temperature compound **10** was formed with elimination of phosphorus trifluoride[26], which was observed by NMR-spectroscopy in a sealed NMR tube in CD_2Cl_2 as a solvent {δ(^{19}F) = −33.1 [d, 3 F, ^1J(FP) = 1401.04 Hz, PF_3]; δ(^{31}P) = 105.21 [q, 1 P, ^1J(PF) = 1401.01 Hz, PF_3]}[45]. After removal of all the volatile products in vacuo compound **10** was recrystallised from 10 ml of diethyl ether at −20 °C; m.p. 76 °C; yield 0.92 g (4.33 mmol, 71%) **10**. Compound **10** was characterised by NMR-spectroscopy and mass spectrometry[8] and by a single crystal X-ray structure analysis (Figure 1, Table 3).

Preparation of 2-Chloroethylaminodifluorophosphane (**11**) *and of Bis(2-chloroethyl)aminodifluorophosphane* (**12**). − *General method:* A solution of the primary or secondary amine hydrochloride and triethylamine in a 1:2 molar ratio in 30 ml of diethyl ether was placed in a heavy-wall glass tube equipped with a Teflon® stopcock. At −196 °C an equimolar quantity of chlorodifluorophosphane **5** was condensed in the glass tube. The reaction mixture was allowed to warm up to room temperature, was then stirred for 1 d and the solution was filtered [the precipitate is assumed to be triethylamine hydrofluoride, δ(^{19}F) = −125.15 (s) in $CDCl_3$[7]]. The solvent was removed in vacuo. Fractional distillation of the remaining liquid resulted in the isolation of the aminodifluorophosphanes, **11** and **12**, as colourless liquids in good yield. Experimental data, boiling points, and yields are listed in Table 2.

Table 2. Experimental data for the synthesis of compounds **11** and **12**

Aminodifluorophosphane	**11**	**12**
Reactants (g; mmol)	2-chloroethylamine hydrochloride (3.0; 25.9) **5** (2.76; 26.4) Et_3N (5.35; 52.9)	bis(2-chloroethyl)amine hydrochloride (3.0; 17.2) **5** (1.87; 17.9) Et_3N (3.52; 34.8)
b. p. °C (Torr)	31-32 (7)	40 (0.1)
Yield g (mmol, %)	2.71 (18.4, 71)	2.67 (12.7, 74)

Characterization of **11**: ^{1}H NMR ($CDCl_3$): δ = 3.25−3.57 [m, 4H, CH_2CH_2Cl]; 3.84−4.21 [m, 1H, HN]. − ^{13}C NMR ($CDCl_3$): δ = 39.41 [d, 1 C, ^3J(CP) = 1.77 Hz, CH_2Cl]; 46.08 [d, 1 C, ^2J(CP) = 7.49 Hz, CH_2NP]. − ^{19}F NMR ($CDCl_3$): δ = −67.80 [d, 2 F, ^1J(FP) = 1198.65 Hz, F_2P]. − ^{31}P NMR ($CDCl_3$): δ = 142.92 [t, 1 P, ^1J(PF) = 1199.10 Hz, PF_2]. − EI MS; *m/z* (%): 147 (2) [M^+]; 128 (2) [M^+ − F]; 98 (100) [M^+ − CH_2Cl]; 84 (3) [F_2PNH^+]; 78 (4) [$FPNCH_2^+$]; 69 (31) [PF_2^+]; 50 (3) [PF^+]. − $C_2H_5ClF_2NP$ (147.50): calcd. C 16.28, H 3.42, N 9.50; found C 16.25, H 3.45, N 9.53.

Characterization of **12**: ^{1}H NMR ($CDCl_3$): δ = 3.35−3.60 [m, 8H, 2 × CH_2CH_2Cl]. − ^{13}C NMR ($CDCl_3$): δ = 42.05 [d, 2 C, ^3J(CP) = 2.02 Hz, 2 × CH_2Cl]; 45.30 [d, 2 C, ^2J(CP) = 6.61 Hz, 2 × CH_2NP]. − ^{19}F NMR ($CDCl_3$): δ = −64.90 [d, 2 F, ^1J(FP) = 1210.67 Hz, F_2P]. − ^{31}P NMR ($CDCl_3$): δ = 143.10 [t, 1 P, ^1J(PF) = 1210.83 Hz, PF_2]. − EI MS; *m/z* (%): 160 (100) [M^+ − CH_2Cl]; 98 (5) [F_2PNCH_2 + H^+]; 78 (2) [$FPNCH_2^+$]; 69 (14) [PF_2^+]; 63 (8) [$CH_2CH_2Cl^+$]; 50 (2) [PF^+]. − $C_4H_8Cl_2F_2NP$ (210.00): calcd. C 22.88, H 3.85, N 6.67; found C 22.92, H 3.95, N 6.50.

Preparation of {cis-Bis[bis(2-chloroethyl)aminodifluorophosphane]dichloro}platinum(II) (**13**): Compound **12** (0.55 g, 2.6 mmol) was added dropwise to a solution of 0.50 g (1.3 mmol) (COD)$PtCl_2$ in 50 ml of dichloromethane during 5 min with stirring. The reaction mixture was stirred at room temperature for 2 d. Afterwards, 1/4 of the solvent was removed in vacuo. Then diethyl ether was added until the solution became turbid. At −20 °C after 1 d colourless crystals were obtained; m.p. 164 °C; yield 0.75 g (1.1 mmol, 84%) **13**. − ^{1}H NMR (CD_3CN): δ = 3.44−3.92 [m, 16H, 4 × CH_2CH_2Cl]. − ^{13}C NMR (CD_3CN): δ = 41.77 [s, 4 C,

4 × CH_2Cl]; 47.82 [d, 4 C, $^2J(CP)$ = 4.37 Hz, 4 × CH_2NP]. – ^{19}F NMR (CD_3CN): δ = −49.72 ["d", 4 F, $^{[1+3]}J(FP)$ = 1136.58 Hz, $^2J(^{19}F^{195}Pt)$ = 571.68 Hz, 2 × F_2P]. – ^{31}P NMR (CD_3CN): δ = 89.98 ["t", 2 P, $^{[1+3]}J(PF)$ = 1137.19 Hz, $^1J(^{31}P^{195}Pt)$ = 5902.94 Hz, 2 × F_2P]. – EI MS; *m/z* (%): 648 (93) [M^+ − Cl]; 613 (58) [M^+ − 2 Cl]; 404 (26) [M^+ − 2 Cl − L]; 369 (16) [M^+ − 3 Cl − L]; 209 (4) [L^+]; 174 (50) [L^+ − Cl]; 160 (100) [L^+ − CH_2Cl]; 138 (12) [L^+ − 2 Cl − H]; 111 (11) [L^+ − 2 CH_2Cl]; 70 (21) [PF_2 + H^+]; 69 (13) [PF_2^+]; 63 (27) [$CH_2CH_2Cl^+$]. – $C_8H_{16}Cl_6F_4N_2P_2Pt$ (685.98): calcd. C 14.01, H 2.36, N 4.08; found C 13.93, H 2.31, N 3.97.

Crystal Structure Analysis of **10** and **13**: See Table 3[46].

Table 3. Crystallographic data of compounds **10** and **13**

Compound	**10**	**13**
Formula	$C_9H_{10}FN_2OP$	$C_8H_{16}Cl_6F_4N_2P_2Pt$
M_r	212.2	686.0
Crystal habit	colourless crystal	colourless prism
Crystal size	0.8 × 0.75 × 0.6	0.35 × 0.3 × 0.25
Space group	$P2_1/c$	$P2_1/c$
Temperature (°C)	−100	20
Lattice constants:		
a (pm)	824.8(2)	782.0(2)
b (pm)	891.3(2)	1517.4(3)
c (pm)	2620.4(6)	1713.6(4)
β (°)	92.48(3)	99.15(2)
V (nm^3)	1.9246	2.0075
Z	8	4
D_x (Mg m^{-3})	1.464	2.270
F(000)	880	1296
μ (mm^{-1})	0.27	7.98
$2\Theta_{max}$ (°)	50	50
Number of reflections:		
measured	3481	3554
independent	3401	3537
R_{int}	0.026	0.075
$wR(F^2)$ (all reflections)	0.095	0.090
R(*F*) (observed reflections)	0.033	0.035
Number of parameters	257	209
S	1.04	1.09
Max. Δ/σ	0.001	0.002
Max. Δ (e nm^{-3})	223	1462

[☆] Dedicated to Professor *Wilhelm Preetz* on the occasion of his 60th birthday.

[1] T. G. Meyer, P. G. Jones, R. Schmutzler, *Z. Naturforsch., B: Org. Chem., Inorg. Chem.* **1992**, *47b*, 517–525.

[2] C. Müller, T. G. Meyer, M. Farkens, R. Sonnenburg, R. Schmutzler, *Z. Naturforsch., B: Org. Chem., Inorg. Chem.* **1992**, *47b*, 760–766.

[3] I. Neda, M. Farkens, A. Fischer, P. G. Jones, R. Schmutzler, *Z. Naturforsch., B: Org. Chem., Inorg. Chem.* **1993**, *48b*, 443–451.

[4] M. Farkens, I. Neda, A. Fischer, P. G. Jones, R. Schmutzler, *Z. Naturforsch., B: Org. Chem., Inorg. Chem.* **1993**, *48b*, 853–859.

[5] I. Neda, M. Farkens, A. Fischer, P. G. Jones, R. Schmutzler, *Z. Naturforsch., B: Org. Chem., Inorg. Chem.* **1993**, *48b*, 860–874.

[6] I. Neda, T. Kaukorat, R. Schmutzler, *Phosphorus, Sulfur and Silicon* **1993**, *80*, 173–179.

[7] I. Neda, H.-J. Plinta, R. Schmutzler, *Z. Naturforsch., B: Org. Chem., Inorg. Chem.* **1993**, *48b*, 333–340.

[8] I. Neda, A. Fischer, P. G. Jones, R. Schmutzler, *Phosphorus, Sulfur and Silicon* **1993**, *78*, 271–287.

[9] I. Neda, H.-J. Plinta, A. Fischer, P. G. Jones, R. Schmutzler, *J. Fluorine Chem.* **1995**, *71*. 65–74.

[10] I. Neda, T. Kaukorat, R. Schmutzler, *Phosphorus, Sulfur and Silicon* **1993**, *80*, 241–250.

[11] D. L. Hill, *A Review of Cyclophosphamide*; Charles C. Thomas, Springfield, Ill., U.S.A., **1975**.

[12] H. Arnold, F. Bourseaux, *Angew. Chem.* **1958**, *70*, 539–544.

[13] J. D. Hoeschele, H. D. H. Showalter, A. J. Kraker, W. L. Elliot, B. J. Roberts, J. W. Kampf, *J. Med. Chem.* **1994**, *37*, 2630–2636.

[14] F. Eckstein, W. Bruns, A. Parmeggiani, *Biochemistry* **1975**, *14*, 5225–5232.

[15] C. H. Agris, K. R. Blake, P. S. Miller, M. P. Reddy, *Biochemistry* **1986**, *25*, 6268–6275.

[16] W. Dabkowski, F. Cramer, J. Michalski, *Tetrahedron Lett.* **1987**, *28*, 3561–3562.

[17] W. Dabkowski, F. Cramer, J. Michalski, *Tetrahedron Lett.* **1988**, *29*, 3301–3302.

[18] B. Rosenberg, L. van Camp, J. E. Trasko, V. H. Mansour, *Nature*, **1969**, *222*, 385–386.

[19] I. Neda, M. Farkens, R. Schmutzler, *Z. Naturforsch., B: Org. Chem., Inorg. Chem.* **1994**, *49b*, 165–170.

[20] G. M. Coppola, *J. Heterocyclic Chem.* **1983**, *20*, 331–336.

[21] E. Pretsch, Th. Clerc, J. Seibl and W. Simon, *Tabellen zur Strukturaufklärung organischer Verbindungen mit spektroskopischen Methoden, 3. Aufl.*; Springer-Verlag, Berlin, Heidelberg, New York, London, Paris, Tokyo, **1986**, I–185, I–235, I–245.

[22] H.-J. Plinta, R. Gereke, A. Fischer, P. G. Jones, R. Schmutzler, *Z. Naturforsch., B: Org. Chem., Inorg. Chem.* **1992**, *48b*, 737–746.

[23] B.-W. Krüger, M. Sell, R. Schmutzler, *Z. Naturforsch., B: Org. Chem., Inorg. Chem.* **1983**, *38b*, 1074–1080.

[24] R. W. Rudolph, R. C. Taylor, R. W. Parry, *J. Am. Chem. Soc.* **1966**, *88*, 3729–3734.

[25] B.-W. Krüger, Dissertation, Technische Universität Braunschweig, **1978**.

[26] H.-J. Plinta, Diplomarbeit, Technische Universität Braunschweig, **1992**.

[27] I. Neda, H.-J. Plinta, R. Sonnenburg, A. Fischer, P. G. Jones, R. Schmutzler, *Chem. Ber.* **1995**, *128*, 267–273.

[28] P. W. Atkins, *Physikalische Chemie, 1. Aufl.*; VCH, Weinheim, **1990**, 831–854.

[29] A. Fischer, I. Neda, P. G. Jones, R. Schmutzler, *Phosphorus, Sulfur and Silicon* **1993**, *83*, 135–148.

[30] G. S. Reddy, R. Schmutzler, *Z. Naturforsch., B: Org. Chem., Inorg. Chem.* **1965**, *20b*, 104–109.

[31] F. Kober, *Grundlagen der Komplexchemie, 1. Aufl.*; Verlage Salle und Sauerländer, Frankfurt am Main, Berlin, München, Aarau, Salzburg, **1979**, S. 235–242.

[32] H.-J. Plinta, I. Neda, R. Schmutzler, *Z. Naturforsch., B: Org. Chem., Inorg. Chem.* **1993**, *39b*, 100–110.

[33] M. J. Baker, P. G. Pringle, *J. Chem. Soc. Chem. Commun.* **1993**, 314–317.

[34] R. G. Pearson, *J. Chem. Educ.* **1968**, *45*, 581–587.

[35] A. Fischer, I. Neda, P. G. Jones, R. Schmutzler, *Z. Naturforsch., B: Org. Chem., Inorg. Chem.* **1994**, *49b*, 1481–1493.

[36] L. Heuer, P. G. Jones, R. Schmutzler, *J. Fluor. Chem.* **1990**, *46*, 243–254.

[37] T. G. Meyer, P. G. Jones and R. Schmutzler, *Z. Naturforsch., B: Org. Chem., Inorg. Chem.* **1993**, *48b*, 875–885.

[48] B. A. Camerman, H. W. Smith, *Acta Cryst.* **1977**, *B33*, 678–683.

[39] J. C. Clardy, J. A. Mosbo, J. G. Verkade, *Phosphorus* **1974**, *4*, 151–156.

[40] D. D. Perrin, W. L. F. Armarego, *"Purification of Laboratory Chemicals"*; Pergamon Press, Oxford, New York, Beijing, Frankfurt, Sao Paulo, Sydney, Tokyo, Toronto, **1988**.

[41] G. M. Coppola, R. I. Mansukhani, *J. Heterocycl. Chem.* **1978**, *15*, 1169–1173.

[42] U. Wannagat, *Adv. Inorg. Chem. Radiochem.* (H. J. Emeléus and A. G. Sharpe eds.), **1964**, *6*, 225–278.

[43] W. Albers, W. Krüger, W. Storzer, R. Schmutzler, *Synth. React. Inorg. Met.-Org. Chem.* **1985**, *15*, 187–195.

[44] H. C. Clark, L. E. Manzer, *J. Organometal. Chem.* **1973**, *59*, 411–428.

[45] E. Fluck, *Die Kernmagnetische Resonanz und ihre Anwendung in der Anorganischen Chemie*; Springer-Verlag, Berlin, Göttingen, Heidelberg, **1963**, S. 250, 256.

[46] *Data collection and reduction of* **10**: The crystal was mounted in inert oil on a glass fibre and transferred to the cold gas stream of the diffractometer (Siemens R3 system with LT-2 low temperature attachment). Intensities were measured with ω scans using monochromated Mo-K_α radiation (λ = 71.073 pm). Cell constants were refined from diffractometer angles of 50

reflections in the 2Θ-range 20−23°. *Structure solution and refinement:* The structure was solved by direct methods and refined anisotropically on F^2 using the program SHELXL-93 (G. M. Sheldrick, University of Göttingen). Hydrogen atoms were included with rigid methyl groups or a riding model.

Data collection and reduction of **13**: Because of its instability at low temperature (presumably because of a phase transition) the data were recorded at room temperature. Stoe STADI-4 diffractometer, ω/Θ scans, cell constants refined from ±ω angles of 56 reflections in the 2Θ-range 20−23°. An absorption correction based on ψ scans yielded transmission factors 0.42−0.76. *Structure solution and refinement:* The structure was solved by the heavy-atom method and refined as above.

Full details of the structure determinations have been deposited at the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-76344 Eggenstein-Leopoldshafen, Germany. Any request for this material should quote a full literature citation and the reference number CSD-401539 (**10**), 401538 (**13**).

[95001]