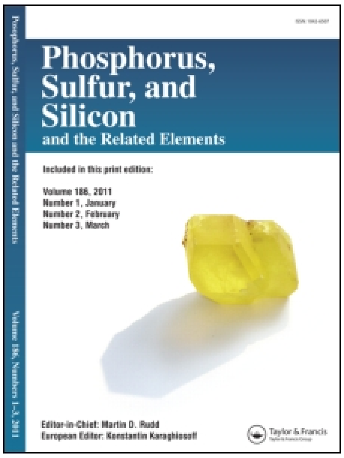

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SYNTHESIS OF CHIRAL BIS-(2-CHLOROETHYL) AMINO-SUBSTITUTED 1,3,$2^{3}\gamma^{3}$ (or $^{4}\gamma^{5}$)BENZODIAZAPHOSPHORINONES; RESOLUTION, OXIDATION REACTIONS AND X-RAY STRUCTURE DETERMINATIONS OF INDIVIDUAL ENANTIOMERS

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SYNTHESIS OF CHIRAL BIS-(2-CHLOROETHYL)AMINO-SUBSTITUTED 1,3,2$\sigma^3\lambda^3$ (or $\sigma^4\lambda^5$)BENZODIAZAPHOSPHORINONES; RESOLUTION, OXIDATION REACTIONS AND X-RAY STRUCTURE DETERMINATIONS OF INDIVIDUAL ENANTIOMERS

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(Received 14 May 1997)

The chiral N-methyl-N′-(1-phenylethyl)-substituted anthranilamides R-(+)-**3** (R_C-enantiomer) and S-(−)-**3** (S_C-enantiomer) were formed by reaction of N-methylisatoic anhydride, **1**, with R-(+)- and S-(−)-1-phenylethylamine, R-(+)-**2** and S-(−)-**2**. Reaction of R-(+)-**3** and S-(−)-**3** with phosphorus trichloride led to mixtures of diastereomers of 5,6-benzo-2-chloro-1-methyl-3-(1-phenylethyl)-1,3,2$\sigma^3\lambda^3$-diazaphosphorin-4-ones, (R_C,S_P)-**4**/(R_C,R_P)-**4** and (S_C,R_P)-**4**/(S_C,S_P)-**4**. Attempted separation of the diastereomers of **4** by several methods failed. Reaction of the mixtures of (R_C,S_P)-**4**/(R_C,R_P)-**4** and (S_C,R_P)-**4**/(S_C,S_P)-**4** with bis-(2-chloroethyl)amine hydrochloride in the presence of triethylamine again led to mixtures of diastereomers of 5,6-benzo-2-[bis-(2-chloroethyl)amino]-1-methyl-3-(1-phenylethyl)-1,3,2$\sigma^3\lambda^3$-diazaphosphorin-4-one, (R_C,S_P)-**5**/(R_C,R_P)-**5** and (S_C,R_P)-**5**/(S_C,S_P)-**5**. By recrystallization it was possible to isolate the pure diastereomers (R_C,S_P)-**5** and (S_C,R_P)-**5**. Oxidation reactions on (R_C,S_P)-**5** and (S_C,R_P)-**5** by the hydrogen peroxide-urea 1:1-adduct ($(NH_2)_2C(:O)\cdot H_2O_2$) or elemental sulfur led to the formation of the corresponding 2-oxo- and 2-thio-substituted 5,6-benzo-1,3,2$\sigma^4\lambda^5$-diazaphosphorin-4-ones, (R_C,R_P)-**6**, (S_C,S_P)-**6**, (R_C,R_P)-**7** and (S_C,S_P)-**7** as pure diastereomers in each case. All compounds were characterized unambiguously by n.m.r.-spectroscopy, mass spectrometry and elemental analysis. Optical rotations were determined for most of the reaction products described. For compounds (R_C,S_P)-**5**, (R_C,R_P)-**6**, (S_C,S_P)-**6** and (R_C,R_P)-**7**, X-ray crystal structure analyses were conducted. In all cases the absolute configuration at phosphorus was determined. The enantiomers of **6** crystallize in different space groups because only the (R_C,R_P) form contains solvent of crystallization.

*Corresponding author.

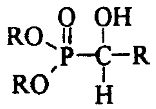
†Dedicated to Professor Heinz Harnisch on the occasion of his 70th birthday.

Keywords: 1,3,2-Benzodiazaphosphorinones; Bis-(2-chloroethyl)amino Group; Enantiomers; Diastereomers; Oxidation Reactions; X-Ray Crystal Structure Determinations.

INTRODUCTION

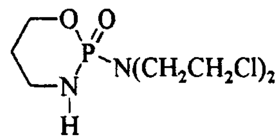
The design and development of chiral $\sigma^3\lambda^3$- and $\sigma^4\lambda^5$-P derivatives is being actively pursued with a view to application in biological processes and in transition metal-catalysed asymmetric synthesis. Recently, α-hydroxy phosphonates (**A**, Figure 1) were found to be biologically active and have been shown to inhibit the enzymes renin,[1] EPSP synthetase,[2] and HIV protease.[3] The absolute configuration at the stereogenic α-carbon in substituted phosphonic acids has been shown to be important for the biological activity.[4–6] The synthesis of the enantiomeric forms of the family of known anticancer drugs, based on the 1,3,2-oxazaphosphorine skeleton (Cyclophosphamide® (**B**, Figure 1), Ifosfamide® (**C**, Figure 1), Trofosfamide® (**D**, Figure 1)) show different activity, and it has been demonstrated[7–10] that the (S)-(−)-isomers are more effective antitumor agents than the racemic mixtures. Aside from pharmaceutical applications, aminophosphines (**E**, Figure 1) are successfully used as ligands in transition metal-mediated asymmetric synthesis.[11–14]. It is known that systems containing P-N single bonds are stable to hydrogenation and most other conditions for asymmetric catalysis. With this in mind, Wills[14] has developed a new class of optically pure chiral $\sigma^4\lambda^5$-1,3,2-diazaphosphorine (**F**, Figure 1) and 1,2-azaphosphole (**G**, Figure 1) derivatives as excellent catalysts for the reduction of ketones by borane. These P-N-containing ligands were employed in the asymmetric catalysis of palladium-mediated allylic substitution via a palladium-allyl intermediate.[14]

In 1993, we reported the preparation, isolation and characterization of 5,6-benzo-2-chloro-1,3-dimethyl-1,3,2-$\sigma^3\lambda^3$-diazaphosphorin-4-one[15] (**H**, Figure 1). In the present report, we describe the continuation of our investigations, using the "chiral pool" method.[14] This was employed for the synthesis of new chiral 1,3,2$\sigma^3\lambda^3$-benzodiazaphosphorinone derivatives, containing two chiral centres (P- and C-atom) in the molecule. We have used enantiomerically pure (R)-(+)- and (S)-(−)-1-phenylethylamine ((R)-(+)-**2** and (S)-(−)-**2**) to obtain the enantiomerically pure amides (R)-(+)-**3** and (S)-(−)-**3**. By resolution, the diastereomerically pure 1,3,2$\sigma^3\lambda^3$-diazaphosphorinones (R_C,S_P)-**5** and (S_C,R_P)-**5** were isolated. Starting from them, diastereomerically pure (R_C,R_P)-**6**, (S_C,S_P)-**6**, (R_C,R_P)-**7** and (S_C,S_P)-**7** were obtained. The formation and reactivity of these chiral compounds are described.

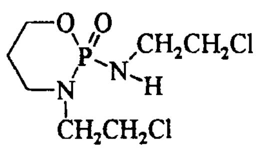


A

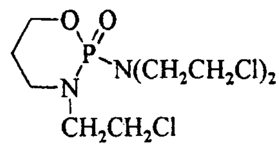
R = alkyl, aryl



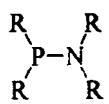
B



C

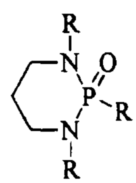


D



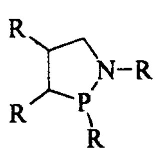
E

R = alkyl



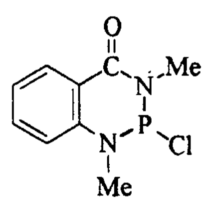
F

R = alkyl, aryl



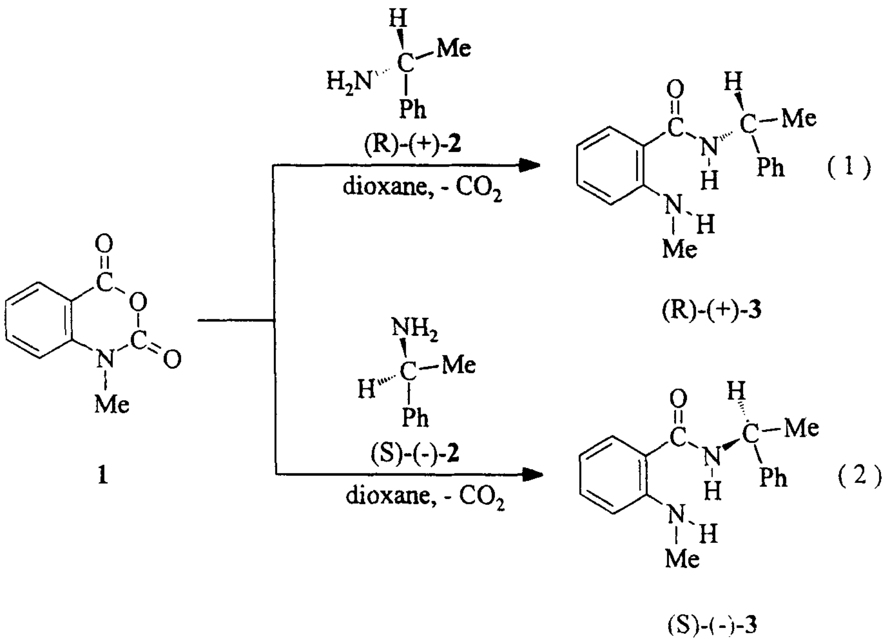
G

R = alkyl, aryl



H

FIGURE 1 Molecular skeleton of α-hydroxy-phosphonates (**A**), Cyclophosphamide (**B**), Ifosfamide (**C**), Trofosfamide (**D**), Aminophosphines (**E**), 1,3,2-Diazaphosphorines (**F**), 1,2-Azaphospholes (**G**) and 1,3,2-Diazaphosphorinone (**H**).

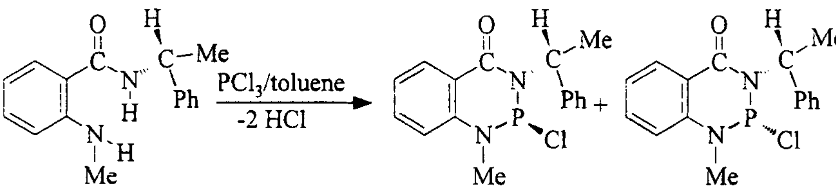


RESULTS AND DISCUSSION

According to Eqns. (1) and (2), compounds (R)-(+)-**3** and (S)-(−)-**3** were obtained in 92% yield by reaction of N-methylisatoic anhydride, **1**, with R-(+)-1-phenylethylamine, (R)-(+)-**2**, and S-(−)-1-phenylethylamine, (S)-(−)-**2**, using dioxane as a solvent. As expected, both ^{1}H- and ^{13}C-n.m.r. spectra of the enantiomers (R)-(+)-**3** and (S)-(−)-**3** are almost identical with regard to chemical shifts and coupling constants. For example, both ^{3}J(HH)-coupling constants (CH_3CHPh) at the chiral carbon atoms in compounds (R)-(+)-**3** and (S)-(−)-**3** are 6.91 Hz. The only difference between (R)-(+)-**3** and (S)-(−)-**3** is observed in their optical rotations: for (R)-(+)-**3**, the $[\alpha]_D^{25}$ value is +115.5° (c = 1.0, CH_2Cl_2); for (S)-(−)-**3** it is −115.5° (c = 1.0, CH_2Cl_2).

When (R)-(+)-**3** and (S)-(−)-**3** were refluxed in toluene with phosphorus trichloride (Eqns. (3) and (4)), the diastereomeric mixtures (R_C,S_P)-**4**/(R_C,R_P)-**4** and (S_C,R_P)-**4**/(S_C,S_P)-**4**, respectively, were formed.

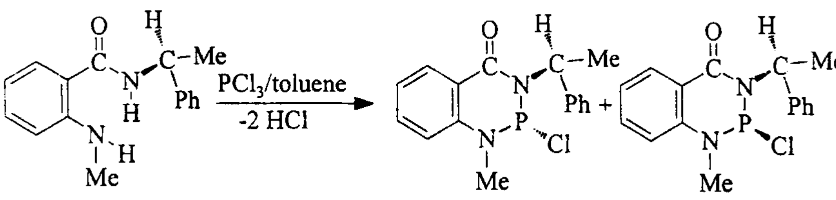
The ^{1}H-n.m.r. spectrum of the mixture of (R_C,S_P)-**4** and (R_C,R_P)-**4** was found to exhibit identical values for both diastereomers, whereas in the ^{31}P-n.m.r. spectra two signals of similar chemical shift [δ = 118 and 121 ppm], associated with the expected presence of two diastereomers, were observed. The orientation of the chlorine atom, bonded to the pyramidal, tricoordinated phosphorus atom



(3)

(R)-(+)-3 (R_C,S_P)-**4** (R_C,R_P)-**4**

mixture of diastereomers



(4)

(S)-(-)-3 (S_C,R_P)-**4** (S_C,S_P)-**4**

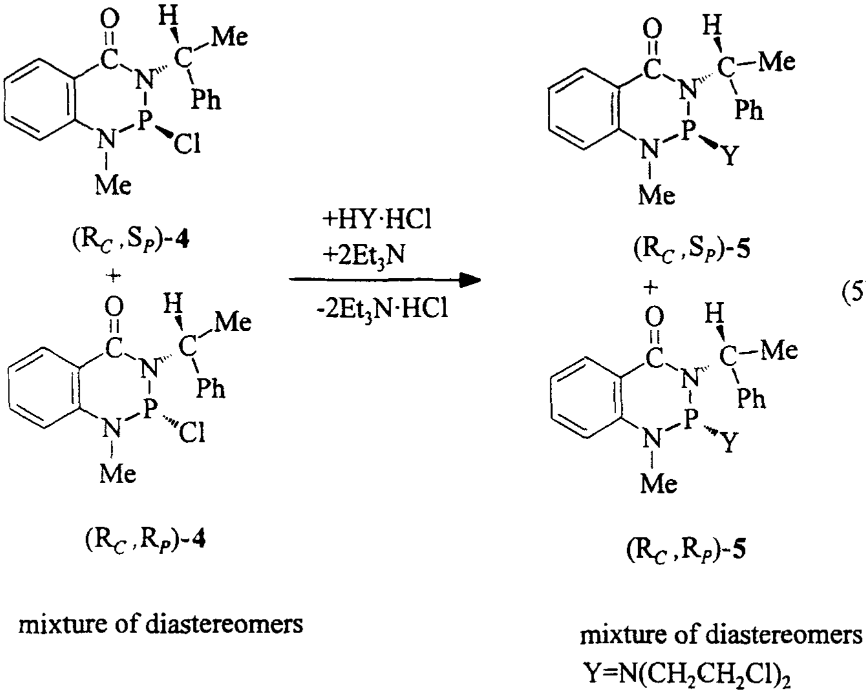
mixture of diastereomers

is presumably critical in determining the ratio of diastereomers, which was determined after refluxing the reaction mixture for 4 h in toluene as (R_C,S_P)-**4**/(R_C,R_P)-**4** = 3:1, by integration of the ^{31}P-n.m.r. signals.

The mixture of diastereomers (R_C,S_P)-**4**/(R_C,R_P)-**4** was characterized unequivocally by n.m.r.-spectroscopy, mass spectrometry and elemental analysis, but the diastereomers could not be separated by physical methods, e.g. column chromatography or recrystallization; thus, the direct determination of the relative configurations was not possible. Most probably, the less sterically crowded isomer bearing the chlorine atom and the substituent Ph(CH)Me in *trans* position should be the main product. This assumption was later confirmed.

Results comparable to those described above were observed for the other diastereomeric mixture, consisting of the products (S_C,R_P)-**4**/(S_C,S_P)-**4**. The $\delta(^{31}P)$-n.m.r. values of the reaction products were almost identical, as were the ^{1}H-n.m.r. resonances.

^{13}C-N.m.r spectra of both diastereomeric mixtures, (R_C,S_P)-**4**/(R_C,R_P)-**4** and (S_C,R_P)-**4**/(S_C,S_P)-**4**, were recorded, but most of the signals could not be assigned because of the similarity of the $\delta(^{13}C)$ values of all isomers.



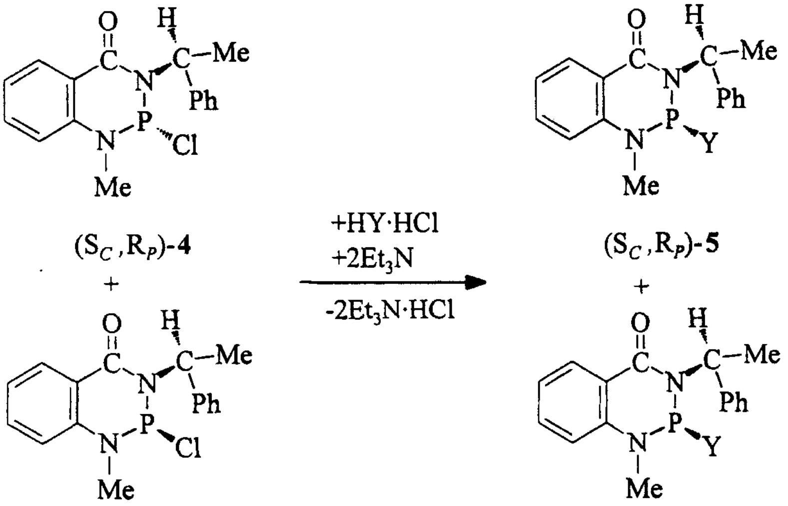
(5)

In an attempt to resolve indirectly the diastereomers of (R_C,S_P)-**4**/(R_C,R_P)-**4** and (S_C,R_P)-**4**/(S_C,S_P)-**4**, both isomeric mixtures were allowed to react with bis-(2-chloroethyl)amine hydrochloride/triethylamine (Eqns. (5) and (6)):

In this way, the diastereomeric mixture (R_C,S_P)-**5**/(R_C,R_P)-**5** was formed in good yield from (R_C,S_P)-**4**/(R_C,R_P)-**4**. By recrystallization of (R_C,S_P)-**5**/(R_C,R_P)-**5** from diethyl ether, it was possible to isolate the pure isomer (R_C,S_P)-**5**. Compound (R_C,R_P)-**5** remained in the mother liquor, together with a small amount of (R_C,S_P)-**5** and some impurities that could not be identified by spectroscopic methods. It was not yet possible to isolate pure (R_C,R_P)-**5**.

Analogous results were obtained from the reaction of (S_C,R_P)-**4**/(S_C,S_P)-**4** (cf. Eqn. (6)). Compound (S_C,R_P)-**5** could be isolated by recrystallization, leaving (S_C,S_P)-**5** in the mother liquor. The $\delta(^{31}P)$-n.m.r. values of both compounds [δ = 82 ppm] lie in the expected range. The characteristic $\delta(^1H)$ values and the $^3J(PH)$ coupling constants for the CH_3NP-groups of (R_C,S_P)-**5** and (S_C,R_P)-**5** were nearly identical, as were all other $\delta(^1H)$ and $\delta(^{13}C)$ values (cf. Experimental Part).

Because single crystals could be obtained for (R_C,S_P)-**5**, an unambiguous characterization (including the absolute configuration) was possible by X-ray



(S_C,R_P)-**4** + (S_C,S_P)-**4**

mixture of diastereomers

+HY·HCl, +2Et_3N, -2Et_3N·HCl

(S_C,R_P)-**5** + (S_C,S_P)-**5** (6)

mixture of diastereomers

Y=$N(CH_2CH_2Cl)_2$

crystal structure analysis. This showed that the bis-(2-chloroethyl)amino substituent bonded to phosphorus and the Ph(CH)Me-substituent bonded to one of the nitrogen atoms, are indeed in *trans* position (cf. Figure 2), as suggested above. The results of the X-ray investigation are discussed later in more detail.

Following the isolation of pure (R_C,S_P)-**5** and (S_C,R_P)-**5**, it was possible to investigate oxidation reactions at the phosphorus atoms, and the influence of the oxidation on the n.m.r. spectroscopic data of the resulting products. In general, oxidation reactions of tertiary phosphines with hydrogen peroxide or with elemental sulfur are exothermic, leading to tertiary phosphine oxides or sulfides.[16,17] Thus, (R_C,S_P)-**5** and (S_C,R_P)-**5** were allowed to react with the hydrogen peroxide-urea 1:1-adduct and with elemental sulfur, as shown in Eqns. (7)–(10):

The reactions with hydrogen peroxide-urea 1:1-adduct were first attempted at room temperature in dichloromethane as a solvent. Because no reaction was observed by ^{31}P-n.m.r. spectroscopy, the reaction mixtures were subsequently refluxed for 2h, forming (R_C,R_P)-**6** and (S_C,S_P)-**6** in good yields. The lack of reaction at room temperature is probably attributable to steric hindrance at the phosphorus atom, resulting from the bulky neighbouring substituents. The use

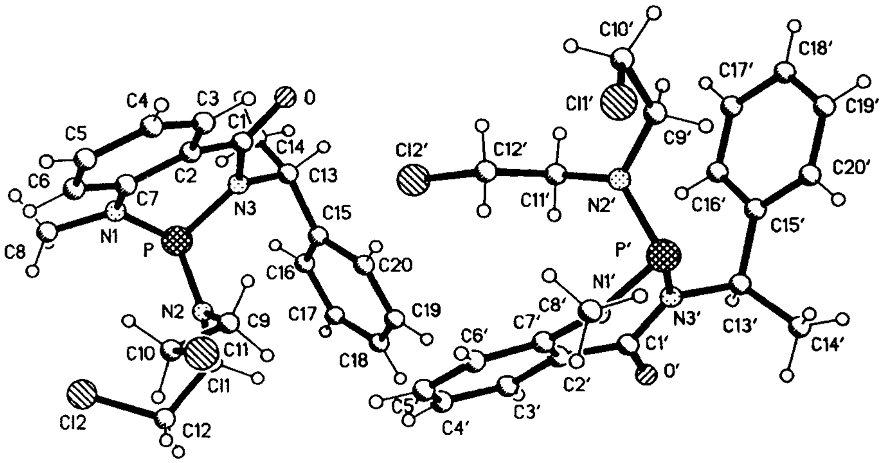
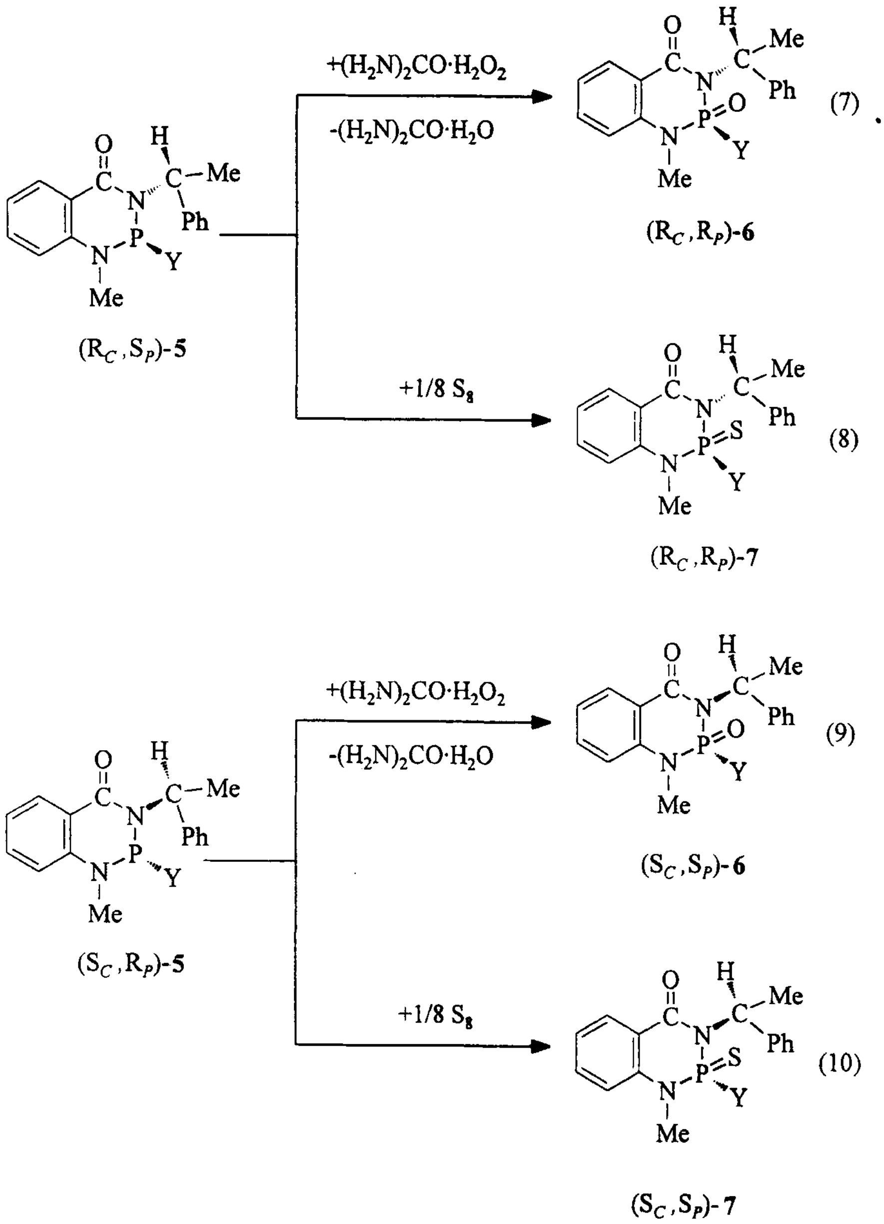


FIGURE 2 The asymmetric unit of compound (R_C,S_P)-**5** in the crystal. Radii are arbitrary. Selected bond lengths [pm] and angles [°]: P-N(2) 167.5(2), P-N(1) 170.8(2), P-N(3) 174.1(2), O-C(1) 122.2(3), N(1)-C(7) 140.0(3), N(1)-C(8) 146.8(3), N(2)-C(11) 146.4(3), N(2)-C(9) 146.7(3), N(3)-C(1) 137.8(3), N(3)-C(13) 149.4(3). N(2)-P-N(1) 106.62(11), N(2)-P-N(3) 105.59(10), N(1)-P-N(3) 96.01(10), C(7)-N(1)-C(8) 118.6(2), C(7)-N(1)-P 124.6(2), C(8)-N(1)-P 114.0(2), C(11)-N(2)-C(9) 117.3(2), C(11)-N(2)-P 116.7(2), C(9)-N(2)-P 125.1(2), C(1)-N(3)-C(13) 116.5(2), C(1)-N(3)-P 128.5(2), C(13)-N(3)-P 114.5(2). The values for the second independent molecule are closely similar.

of the pure enantiomers (R_C,S_P)-**5** and (S_C,R_P)-**5** as starting compounds led, accordingly, in each case to only one isomer ((R_C,R_P)-**6** and (S_C,S_P)-**6**, respectively).

Both reaction products **6** were characterized by the usual methods (cf. Experimental Part) and did not show any pecularities. Single crystals of both (R_C,R_P)-**6** and (S_C,S_P)-**6** were isolated. For a discussion of the X-ray results, *vide infra*.

The use of elemental sulfur as oxidizing agent for the $\sigma^3\lambda^3$-phosphorus atoms of (R_C,S_P)-**5** and (S_C,R_P)-**5** caused still more problems. Although, in general, exothermic reactions were expected,[16,17] no reaction was observed when (R_C,S_P)-**5** or (S_C,R_P)-**5** were stirred with elemental sulfur at room temperature, or were refluxed in dichloromethane as a solvent. Only refluxing the reactants in toluene as a high-boiling solvent for 8 h led, according to Eqns. (8) and (10), to the corresponding phosphine sulfides (R_C,R_P)-**7** and (S_C,S_P)-**7**. Drastic reaction conditions were required to form (R_C,R_P)-**7** and (S_C,S_P)-**7** in good yields. The low reactivity of (R_C,S_P)-**5** and (S_C,R_P)-**5** towards elemental sulfur is probably also due to steric effects. All n.m.r. spectroscopic and mass spectrometric data of (R_C,R_P)-**7** and (S_C,S_P)-**7** were in good agreement with their proposed structures.



Y=N$(CH_2CH_2Cl)_2$

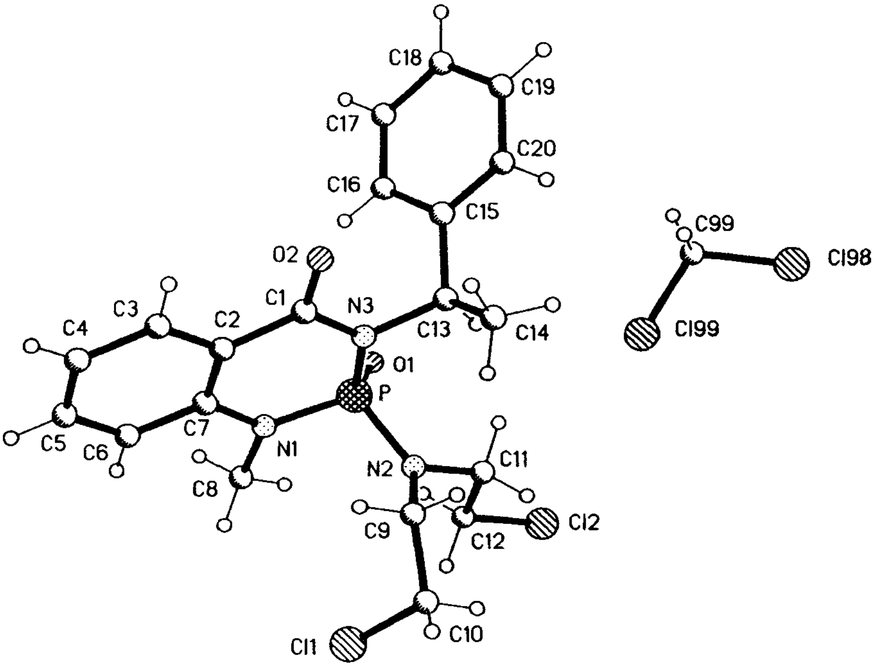


FIGURE 3 The formula unit of compound (R_C,R_P)-**6**·CH_2Cl_2 in the crystal. Radii are arbitrary. Selected bond lengths [pm] and angles [°]: P-O(1) 147.1(2), P-N(2) 164.5(2), P-N(1) 164.7(2), P-N(3) 168.1(2), O(2)-C(1) 122.4(3), N(1)-C(7) 140.3(3), N(1)-C(8) 147.8(3), N(2)-C(9) 147.0(4), N(2)-C(11) 147.3(3), N(3)-C(1) 138.9(3), N(3)-C(13) 149.6(3); O(1)-P-N(2) 109.20(11), O(1)-P-N(1) 115.90(11), N(2)-P-N(1) 107.45(11), O(1)-P-N(3) 112.97(11), N(2)-P-N(3) 108.52(10), N(1)-P-N(3) 102.37(10), C(7)-N(1)-C(8) 118.6(2), C(7)-N(1)-P 126.4(2), C(8)-N(1)-P 114.8(2), C(9)-N(2)-C(11) 117.0(2), C(9)-N(2)-P 120.5(2), C(11)-N(2)-P 119.7(2), C(1)-N(3)-C(13) 117.5(2), C(1)-N(3)-P 128.5(2), C(13)-N(3)-P 113.9(2).

For (R_C,R_P)-**7**, an X-ray crystal structure determination was conducted and the results are compared to those of (R_C,S_P)-**5**, (R_C,R_P)-**6** and (S_C,S_P)-**6** in the following.

X-Ray Crystal Structure Determinations of Compounds (R_C,S_P)-5, (R_C,R_P)-6, (S_C,S_P)-6, and (R_C,R_P)-7:

X-ray crystal structure analyses were conducted for the above compounds (Figures 2–5). No isomerization of the starting compounds was observed during the oxidation reactions. The absolute configuration of all four compounds was established unambiguously, based on the anomalous scattering of the heavier atoms (P, S, Cl). All compounds crystallise in chiral space groups (Table II and Experimental Part). Compound (R_C,S_P)-**5** contains two independent molecules

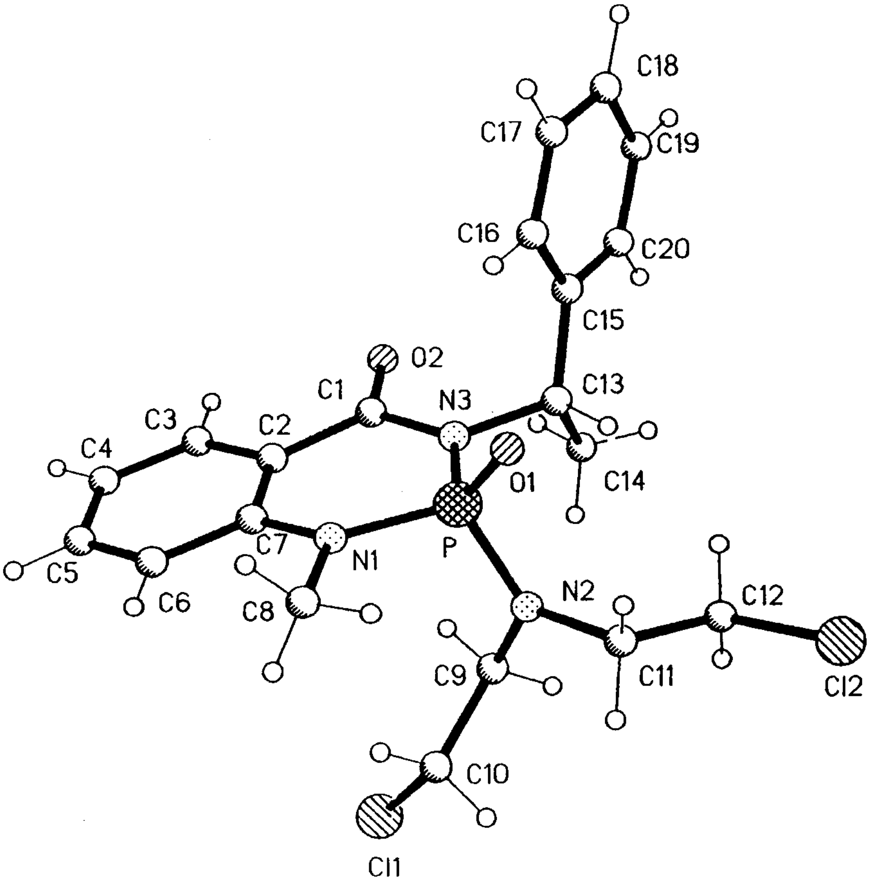


FIGURE 4 The molecule of compound (S_C,S_P)-**6** in the crystal. Radii are arbitrary. Selected bond lengths [pm] and angles [°]: P-O(1) 147.28(11), P-N(2) 164.72(13), P-N(1) 165.18(14), P-N(3) 168.17(12), O(2)-C(1) 122.4(2), N(1)-C(7) 140.4(2), N(1)-C(8) 148.4(2), N(2)-C(9) 146.5(2), N(2)-C(11) 146.7(2), N(3)-C(1) 138.9(2), N(3)-C(13) 149.6(2); O(1)-P-N(2) 109.89(7), O(1)-P-N(1) 115.39(7), N(2)-P-N(1) 107.56(7), O(1)-P-N(3) 113.89(6), N(2)-P-N(3) 107.16(6), N(1)-P-N(3) 102.35(6), C(7)-N(1)-C(8) 119.09(13), C(7)-N(1)-P 126.44(11), C(8)-N(1)-P 114.44(11), C(9)-N(2)-C(11) 118.41(13), C(9)-N(2)-P 119.88(10), C(11)-N(2)-P 121.63(11), C(1)-N(3)-C(13) 118.24(12), C(1)-N(3)-P 128.42(10), C(13)-N(3)-P 113.33(9).

per asymmetric unit. Curiously, compound (R_C,R_P)-**6** crystallises as a dichloromethane solvate while (S_C,S_P)-**6** does not; this may be due to slight differences in crystallization conditions.

A least-squares fit of the independent molecules of (R_C,S_P)-**5** (Figure 6) shows that they are closely similar; the mean deviation of the atoms P, O, N1–3, C1–7 is only 2 pm. Solely the second component of the disordered chloroethyl group shows appreciable deviations. Similarly, the heterocyclic moieties of (R_C,R_P)-**6**

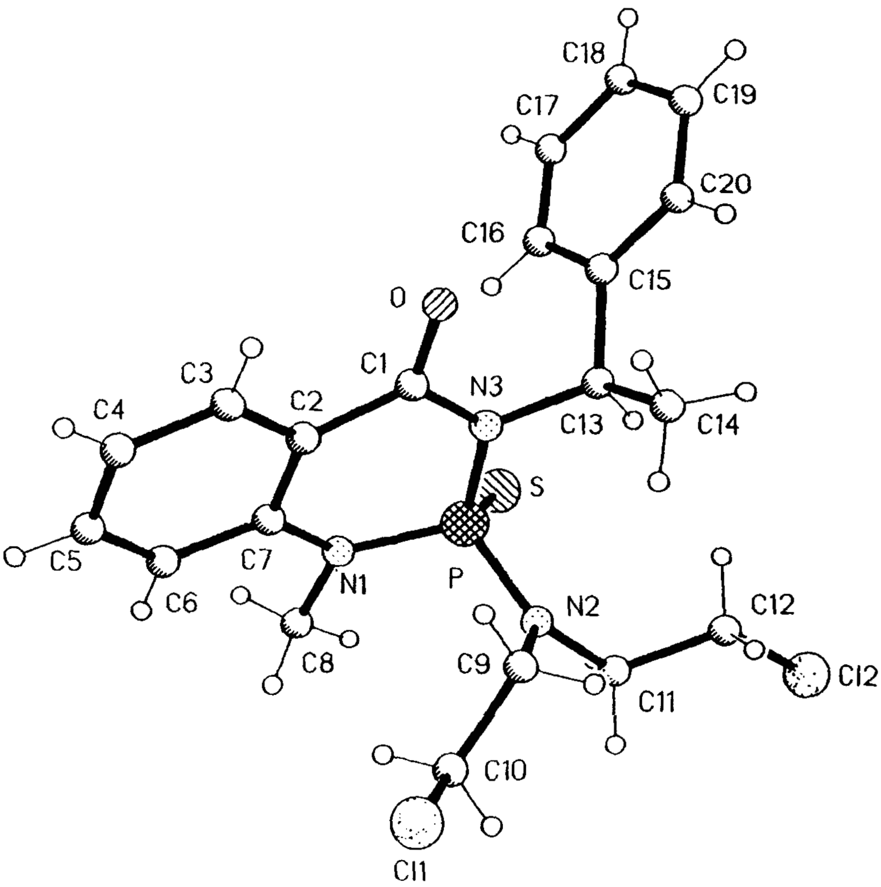


FIGURE 5 The molecule of compound (R_C,R_P)-**7** in the crystal. Radii are arbitrary. Selected bond lengths [pm] and angles [°]: P-N(2) 164.6(3), P-N(1) 164.8(3), P-N(3) 168.7(3), P-S 193.08(13), O-C(1) 121.9(4), N(1)-C(7) 140.8(4), N(1)-C(8) 148.4(5), N(2)-C(11) 147.1(5), N(2)-C(9) 147.9(5), N(3)-C(1) 139.8(4), N(3)-C(13) 148.9(5); N(2)-P-N(1) 107.4(2), N(2)-P-N(3) 106.9(2), N(1)-P-N(3) 102.5(2), N(2)-P-S 110.97(12), N(1)-P-S 114.56(12), 0N(3)-P-S 113.84(11), C(7)-N(1)-C(8) 118.2(3), C(7)-N(1)-P 126.2(2), C(8)-N(1)-P 115.3(3), C(11)-N(2)-C(9) 117.0(3), C(11)-N(2)-P 124.3(3), C(9)-N(2)-P 118.7(2), C(1)-N(3)-C(13) 117.3(3), C(1)-N(3)-P 127.7(3), C(13)-N(3)-P 114.8(2).

and inverted (S_C,S_P)-**6** can be fitted to a mean deviation of 6 pm, but the phenyl and chloroethyl groups have different conformations (Figure 7). The energy balance between the two forms must be small enough to be influenced by the presence or absence of co-crystallised solvent.

The six-membered heterorings of the $\sigma^4\lambda^5$-phosphorus compounds show a planar conformation, with mean deviations of (R_C,R_P)-**6** 1.3 pm, (S_C,S_P)-**6** 3.2

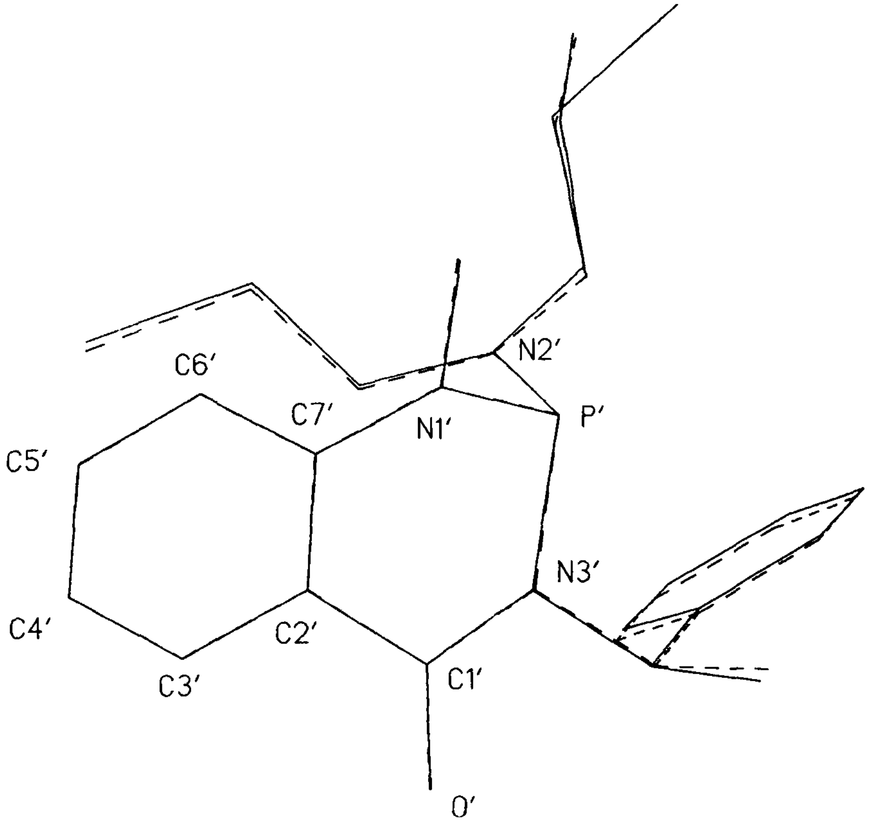


FIGURE 6 Least-squares fit of the two independent molecules of (R_C,S_P)-**5**.

pm and (R_C,R_P)-**7** 4.7 pm. In contrast, the heteroring of compound (R_C,S_P)-**5** displays a 1,2-coplanar conformation, in which the phosphorus atom and N3 lie outside the plane formed by N1, C1, C2 and C7 (P by 80 pm, N3 44 pm).

The $\sigma^3\lambda^3$-phosphorus atom of (R_C,S_P)-**5** displays the expected pyramidal conformation, in which P lies 73 pm outside the plane of its α substituents. The angles vary from 96.01(10)° (N1-P-N3) to 106.62(11)° (N2-P-N1). The other compounds contain a tetrahedrally coordinated phosphorus atom, with the largest angle at P between the chalcogen atom and N1 [114.56(11)° ((R_C,R_P)-**7**) to 115.90(11)°((R_C,R_P)-**6**)]; such angle deformations are normal for P=O and P=S systems. In all three compounds the smallest angle is the endocyclic angle N1-P-N3 [102.35(6)° ((S_C,S_P)-**6**) to 102.44(14)°((R_C,R_P)-**7**)].

The $\sigma^4\lambda^5$-phosphorus compounds show two types of P-N bonds. While the P-N1 and P-N2 bond lengths differ insignificantly [164.5(2) pm (P-N2 (R_C,R_P)-**6**)

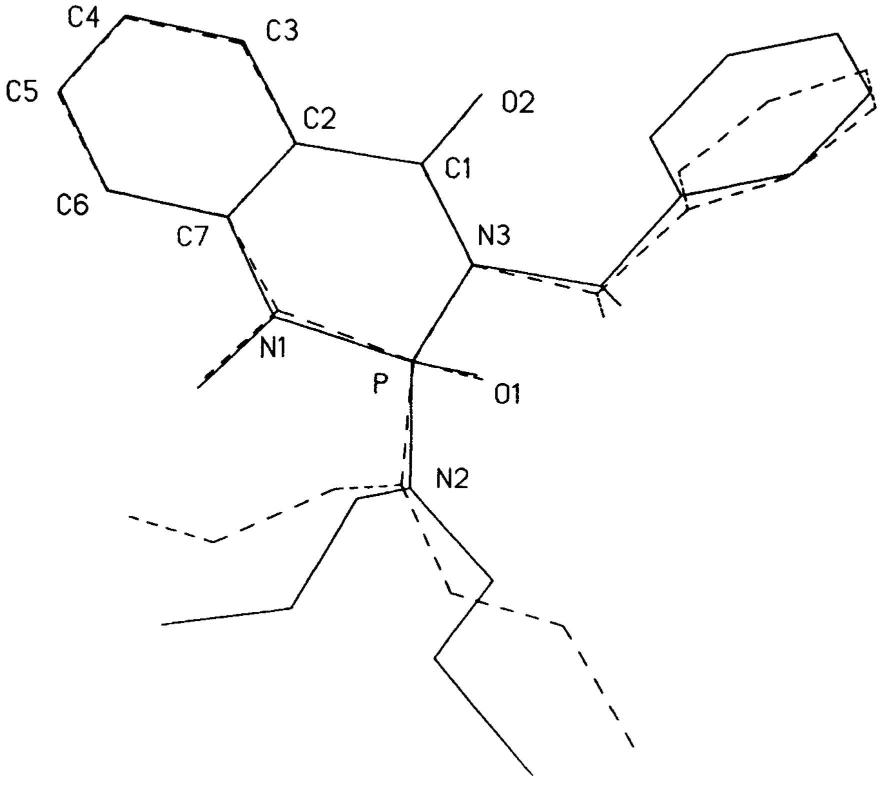


FIGURE 7 Least-squares fit of the structures of (R_C,R_P)-**6** and inverted (S_C,S_P)-**6**; the latter is represented by dashed bonds.

to 165.2(1) pm (P-N1 (S_C,S_P)-**6**)], the P-N3 distance is 3–4 pm longer [168.1(2) pm ((R_C,R_P)-**6**) to 168.7(3) pm ((R_C,R_P)-**7**)]. Compound (R_C,S_P)-**5** shows three different P-N bond lengths: P-N2 167.5(2) pm, P-N1 170.8(2) pm and P-N3 174.1(2) pm. The P-N distances in the $\sigma^3\lambda^3$-phosphorus compound (R_C,S_P)-**5** are longer than in the corresponding $\sigma^4\lambda^5$ phosphorus compounds. The pattern of P-N bond lengths may be rationalised on the basis of more ready delocalisation of the resonance form $N^+ = P\text{-}O^-$ and less N-P double bond character for the N atom adjacent to the carbonyl group.

In all compounds the coordination of the nitrogen atoms is nearly planar. The angle sums vary from 357.2 (N1 of (R_C,S_P)-**5** and N2 of (R_C,R_P)-**6**) to 360° (N1 and N3 of (S_C,S_P)-**6** and N2 of (R_C,R_P)-**7**). The largest angles at N1 and N3 are the endocyclic angles C7-N1-P [124.4(2)° ((R_C,S_P)-**5**) to 126.4(1)° ((S_C,S_P)-**6**)] and C1-N3-P [127.7(3)° ((R_C,R_P)-**7**) to 128.5(2)° ((R_C,S_P)-**5**)]. The 2-chloroethyl groups of compounds (S_C,S_P)-**6** and (R_C,R_P)-**7** both exhibit antiperiplanar con-

TABLE I Torsion angles of the 2-chloroethyl groups.

	(R_C,S_P)-5	(R_C,R_P)-6	(S_C,S_P)-6	(R_C,R_P)-7
N2-C9-C10-C11	−170.8(2)°	−65.5(3)°	168.3(1)°	173.7(3)°
N2′-C9′-C10′-C11′	65.3(6)°			
N2′-C9′-C10″-C11″	170.7(4)°			
N2-C11-C12-C12	65.3(3)°	−178.0(2)°	171.0(1)°	−171.4(3)°
N2′-C11′-C12′-C12′	−170.4(2)°			

formation. In the other compounds the 2-chloroethyl groups are arranged antiperiplanar or gauche (cf. Table I).

The phenyl groups C15 to C20 form a dihedral angle to the plane of the heterocycles from 76° ((R_C,S_P)-**5**) to 86° ((R_C,R_P)-**7**), i.e. the rings are essentially perpendicular.

EXPERIMENTAL

All experiments were conducted with exclusion of air and moisture in sealed systems in a nitrogen atmosphere. Solvents were purified and dried according to the usual methods.[18,19] N.m.r.-spectra: Bruker AC 200 (^{1}H at 200.1 MHz, ^{13}C at 50.3 MHz, ^{31}P at 81.0 MHz). Reference substances: TMS ext. (^{1}H); $CDCl_3$ int. (^{13}C); 85% H_3PO_4 ext. (^{31}P). High-field shifts were given negative, low field shifts positive signs. All n.m.r.-spectra were recorded in $CDCl_3$ as a solvent. Mass spectra were recorded on a Finnigan MAT 8430 spectrometer, employing the EI-method. IR-spectra: All IR-spectra were recorded on $CHCl_3$-solutions on a Nicolet FT-IR-spectrometer. Elemental analyses were conducted at Analytisches Laboratorium des Instituts für Anorganische und Analytische Chemie der Technischen Universität Braunschweig. Optical rotations were determined at the Institut für Organische Chemie der Technischen Universität Braunschweig, using a Perkin-Elmer 241 polarimeter.

The abbreviation "i.v." refers to a pressure of *ca.* 0.1 mm Hg.

Starting Compounds:

All starting compounds were commercially available.

Formation of compounds (R)-(+)-3 and (S)-(−)-3:

Solutions of 17.72 g (0.10 mole) of N-methylisatoic anhydride, **1**, and 12.20 g (0.11 mole) of R-(+)-1-phenylethylamine, (R)-(+)-**2** (forming (R)-(+)-**3**), or S-(−)-1-phenylethylamine, (S)-(−)-**2** (forming (S)-(−)-**3**), in 250 ml of 1,4-

TABLE II Crystal data for compounds (R_C,S_P)-**5**, (R_C,R_P)-**6**, (S_C,S_P)-**6** and (R_C,R_P)-**7**.

Compound	(R_C,S_P)-**5**	(R_C,R_P)-**6**·CH_2Cl_2	(S_C,S_P)-**6**	(R_C,R_P)-**7**
Formula	$C_{20}H_{24}Cl_2N_3OP$	$C_{21}H_{26}Cl_4N_3O_2P$	$C_{20}H_{24}Cl_3N_3O_2P$	$C_{20}H_{24}Cl_3N_3OPS$
M_r	424.31	525.22	440.29	456.35
Crystal size (mm)	0.60 × 0.40 × 0.40	0.85 × 0.70 × 0.40	0.95 × 0.50 × 0.40	0.80 × 0.45 × 0.40
Temperature (°C)	−130	−100	−100	−130
Crystal system	triclinic	orthorhombic	orthorhombic	orthorhombic
Space group	P1	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
Cell constants				
a (pm)	794.8(2)	1139.45(8)	1078.8(8)	1116.0(2)
b (pm)	921.0(2)	1316.56(10)	1118.44(12)	1176.3(2)
c (pm)	1424.5(3)	1641.5(2)	1717.7(2)	1661.1(3)
α(°)	80.22(3)	90	90	90
β(°)	86.65(3)	90	90	90
γ(°)	88.82(3)	90	90	90
U (nm^3)	1.0258(4)	2.4625(4)	2.0725(4)	2.1808(8)
Z	2	4	4	4
D_X ($Mg\ m^{-3}$)	1.246	1.272	1.412	1.390
μ (mm^{-1})	0.277	0.456	0.412	0.483
F(000)	402	972	920	952
$2\theta_{max}$ (°)	50	55	55	50
No. of reflns.:				
measured	7228	5286	6329	4162
independent	6740	4998	4741	3835
R_{int}	0.021	0.024	0.011	0.026
$wR(F^2$, all refl.)	0.082	0.103	0.067	0.094
$R(F, > 4\sigma(F))$	0.032	0.039	0.026	0.041
No. of parameters	510	282	255	255
S	1.03	1.07	1.05	1.06
Flack *x* parameter[20]	−0.02(4)	−0.06(6)	−0.03(4)	−0.08(8)
max. Δ/σ	<0.001	<0.001	<0.001	<0.001
max. Δρ ($e\ nm^{-3}$)	195	712	188	228

dioxane were stirred at 60°C for 3h. Subsequently, the solvents were removed i.v. The remaining colourless solids were obtained in a state of high purity. Analytical samples of (R)-(+)-**3** and (S)-(−)-**3** were obtained by recrystallization from diethyl ether.

Compound (R)-(+)-3:

Yield: 23.62 g (93%); m.p.: 108–110°C; $[\alpha]_D^{25}$ = +115.5°(c = 1.0, CH_2Cl_2).

^{1}H-N.m.r.: δ = 1.55 (d, 3H, ^{3}J(HH) = 6.90 Hz, CH_3CH); 2.83 (s, 3H, CH_3NH); 5.24 (m, 1H, CH_3CH); 6.28–7.48 (m, 11H, 2× NH and 9× $H_{aromatic}$).-^{13}C-N.m.r.: δ = 21.89 (s, 1C, CH_3CH); 29.49 (s, 1C, CH_3NH); 48.81 (s, 1C, CH_3CH); 110.98–150.60 (m, 12C, $C_{aromatic}$); 168.95 (s, 1C, C(:O)NH).-EI-MS: m/z (%): 254 (99) $[M]^+$; 150 (14) $[M\text{-}CH(CH_3)C_6H_5+H]^+$, 134 (44) $[C_6H_4C(:O)NHCH_3)]^+$; 120 (80) $[C_6H_5CH(CH_3)NH]^+$; 105 (100) $[CH(CH_3)C_6H_5]^+$; 104 (30) $[C_6H_4C(:O)]^+$; 77 (42) $[C_6H_5]^+$.-IR ($CHCl_3$): ν = 3315 (vs, NH); 1623 (vs, C(:O)).

$C_{16}H_{18}N_2O$(254.33) calcd. C 75.56 H 7.13 N 11.01 %; found C 75.37 H 7.14 N 10.97 %

Compound (S)-(−)-3:

Yield: 23.37 g (92%); m.p.: 107 − 109°C; $[\alpha]_D^{25}$ = −115.5° (c = 1.0, CH_2Cl_2).

^{1}H-N.m.r.: δ = 1.55 (d, 3H, ^{3}J(HH) = 6.92 Hz, CH_3CH); 2.84 (s, 3H, CH_3MH); 5.24 (m, 1H, CH_3CH); 6.28–7.48 (m, 11H, 2× NH and 9× $H_{aromatic}$). - ^{13}C-N.m.r.: δ = 21.89 (s, 1C, CH_3CH); 29.49 (s, 1C, CH_3); 48.81 (s, 1C, CH_3CH); 110.98–150.60 (m, 12C, $C_{aromatic}$); 168.95 (s, 1C, C(:O)NH)-EI-MS: m/z (%): 254 (90) $[M]^+$; 150 (14) $[M\text{-}CH(CH_3)C_6H_5 + H]^+$; 134 (38) $[C_6H_4C(:O)NHCH_3]^+$ 120 (100) $[C_6H_5CH(CH_3)NH]^+$; 105 (90) $[CH(CH_3)C_6H_5]^+$; 104 (26) $[C_6H_4C(:O)]^+$; 77 (35) $[C_6H_5]^+$. - IR ($CHCl_3$): ν = 3318 (vs, NH); 1624 (vs, C(:O)).

$C_{16}H_{18}N_2O$ (254.33) calcd. C 75.56 H 7.13 N 11.01 % found C 75.83 H 7.28 N 11.02 %

Formation of the mixture of diastereomers (R_C,S_P)-4/(R_C,R_P)-4 and (S_C,R_P)-4/(S_C,S_P)-4:

Solutions of 12.72 g (0.05 mole) of (R)-(+)-**3** or (S)-(−)-**3** and 8.24 g (0.06 mole) of phosphorus trichloride in 300 ml of toluene were refluxed for 4h. Subsequently, the solutions were filtered through a sintered glass disc. The solvents and volatile compounds were removed i.v. Attempts to recrystallize the remaining colourless oils from various solvents failed. In neither case was it possible to purify the diastereomeric mixtures, ((R_C,S_P)-**4**/(R_C,R_P)-**4** or (S_C,R_P)-**4**/(S_C,S_P)-**4**), nor to isolate one of the diastereomers; decomposition of the reaction products was observed.

Mixture of diastereomers (R_C,S_P)-4/(R_C,R_P)-4:

Yield: 13.55 g (85%); b.p.: >200°C/0.05 mm Hg (oil).

^{1}H-N.m.r.: δ = 1.86 (d, 3H, ^{3}J(HH) = 6.89 Hz, CH_3CH); 3.23 (d, 3H, ^{3}J(HP) = 17.76 Hz, CH_3NP); 6.05 (m, 1H, CH_3CH); 6.93–8.26 (m, 9H, $H_{aromatic}$)-^{31}P-N.m.r.: δ = 118.46 and 120.78 (2s)-EI-MS: Only hydrolysis products were observed.

$C_{16}H_{16}ClN_2OP$ (318.74) calcd. C 60.29 H 5.06 N 8.79 %; found C 60.24 H 5.39 N 8.66 %

Mixture of diastereomers (S_C,R_P)-4/(S_C,S_P)-4:

Yield: 13.39 g (84%); b.p.: >200°C/0.05 mm Hg (oil).

^{1}H-N.m.r.: δ = 1.87 (d, 3H, ^{3}J(HH) = 6.87 Hz, CH_3CH); 3.24 (d, 3H, ^{3}J(HP) = 17.68 Hz, CH_3NP); 6.03 (m, 1H, CH_3CH); 6.89–8.19 (m, 9H, $H_{aromatic}$)-^{31}P-N.m.r.: δ = 121.37 and 122.83 (2s)-EI-MS (contaminated with hydrolysis products): m/z (%): 318 (50) $[M]^+$; 179 (100) $[C_6H_4CONCH_3]^+$.

$C_{16}H_{16}ClN_2OP$ (318.74) calcd. C 60.29 H 5.06 N 8.79 %; found C 60.22 H 5.17 N 8.85 %

Formation of the mixture of diastereomers (R_C,S_P)-5/(R_C,S_P)-5 and (S_C,R_P)-5/(S_C,S_P)-5:

Freshly prepared samples (in each case 12.72 g, 0.04 mole) of the racemic mixtures, (R_C,S_P)-**4**/(R_C,R_P)-**4** or (S_C,R_P)-**4**/(S_C,S_P)-**4**, and equimolar amounts of bis-(2-chloroethyl)amine hydrochloride (7.14 g, 0.04 mole) were dissolved in 300 ml of dichloromethane. At 0°C, 8.08 g (0.08 mole) of triethylamine was added dropwise. The reaction mixtures were allowed to warm up to r.t. and were stirred for 1d. Subsequently, the solvents and volatile compounds were removed i.v. The residues were extracted with 3 × 150 ml of diethyl ether. The combined extracts were concentrated i.v. to a volume of *ca.* 70 ml and cooled to −20°C for 1d. During this time, colourless solids precipitated, were filtered off through a sintered glass disc and were dried i.v. Recrystallization of the solid mixtures,

(R_C,S_P)-**5**/(R_C,R_P)-**5** or (S_C,R_P)-**5**/(S_C,S_P)-**5**, from diethyl ether allowed the isolation of pure (R_C,S_P)-**5** and (S_C,R_P)-**5**. Crystals suitable for an X-ray crystal structure determination were obtained for (R_C,S_P)-**5**.

Compound (R_C,S_P)-5:

Yield: 8.14 g (48%); m.p.: 140–142°C; $[\alpha]_D^{25} = +359.7°$ (c = 1.0, CH_2Cl_2).

^{1}H-N.m.r.: δ = 1.75 (d, 3H, $^3J(HH)$ = 7.12 Hz, CHCH_3); 2.25–3.10 (m, 8H, N(CH_2CH_2Cl)$_2$); 3.13 (d, 3H, $^3J(HP)$ = 14.58 Hz, NCH_3); 6.30 (m, 1H, C*H*Ph); 6.75–8.25 (m, 9H, $H_{aromatic}$)-^{13}C-N.m.r.: δ = 18.61 (d, 1C, $^3J(CP)$ = 9.76 Hz, *C*H$_3$CHNP); 36.84 (d, 1C, $^2J(CP)$ = 43.33 Hz, *C*H$_3$NP); 42.71 (d, 2C, $^3J(CP)$ = 3.22 Hz, PN(CH$_2$*C*H$_2$Cl)$_2$); 51.35 (d, 2C, $^2J(CP)$ = 19.37 Hz, PN(*C*H$_2$CH$_2$Cl)$_2$); 51.47 (d, 1C, $^2J(CP)$ = 27.28 Hz, PN*C*HCH$_3$); 113.68–145.58 (m, 12C, $C_{aromatic}$); 164.16 (d, 1C, $^2J(CP)$ = 6.94 Hz, *C*(:O)NP)-^{31}P-N.m.r.: δ = 82.42 (s).-EI-MS: m/z (%): 423 (8) $[M]^+$; 283 (34) $[M\text{-}N(CH_2CH_2Cl)_2]^+$; 179 (100) $[M\text{-}C_6H_5CH(CH_3)\text{-}N(CH_2CH_2Cl)_2+H]^+$; 105 (22) $[C_6H_5CH(CH_3)]^+$; 104 (8) $[C_6H_4C(:O)]^+$; 77 (9) $[C_6H_5]^+$. -IR ($CHCl_3$): (ν = 1635 (vs, C(:O)).

$C_{20}H_{24}Cl_2N_3OP$ (424.31) calcd. C 56.61 H 5.70 N 9.90 %; found C 56.67 H 5.79 N 9.90 %

Compound (S_C,R_P)-5:

Yield: 8.31 g (49%); m.p.: 139–142°C; $[\alpha]_D^{25} = -360.7°$ (c = 1.0, CH_2Cl_2).

^{1}H-N.m.r.: δ = 1.75 (d, 3H, $^3J(HH)$ = 6.75 Hz, CHCH_3); 2.30–3.00 (m, 8H, N(CH_2CH_2Cl)$_2$); 3.12 (d, 3H, $^3J(HP)$ = 14.58 Hz, NCH_3); 6.30 (m, 1H, C*H*Ph); 6.75–8.12 (m, 9H, $H_{aromatic}$). - ^{13}C-N.m.r.: δ = 18.52 (d, 1C, $^3J(CP)$ = 9.66 Hz, *C*H$_3$CHNP); 36.79 (d, 1C, $^2J(CP)$ = 43.86 Hz, *C*H$_3$NP); 42.65 (d, 2C, $^2J(CP)$ = 3.35 Hz, PN(CH$_2$*C*H$_2$Cl)$_2$); 51.24 (d, 2C, $^2J(CP)$ = 19.47 Hz, PN(*C*H$_2$CH$_2$Cl)$_2$); 51.32 (d, 1C, $^2J(CP)$ = 27.14 Hz, PN*C*HCH$_3$); 113.61–145.46 (m, 12C, $C_{aromatic}$); 164.08 (d, 1C, $^2J(CP)$ = 6.81 Hz, *C*(:O)NP). - ^{31}P-N.m.r.: δ = 82.21 (s). -EI-MS: m/z (%): 423 (8) $[M]^+$; 283 (30) $[M\text{-}N(CH_2CH_2Cl)_2]^+$; 179 (100) $[M\text{-}C_6H_5CH(CH_3)\text{-}N(CH_2CH_2Cl)_2+H]^+$; 105 (12) $[C_6H_5CH(CH_3)]^+$; 104 (4) $[C_6H_4C(:O)]^+$; 77 (4) $[C_6H_5]^+$. -IR ($CHCl_3$): ν = 1639 (vs, C(:O)).

$C_{20}H_{24}Cl_2N_3OP$ (424.31) calcd. C 56.61 H 5.70 N 9.90 %; found C 56.75 H 5.78 N 9.78 %

Formation of compounds (R_C,R_P)-6 and S_C,S_P)-6:

To stirred solutions of 0.85 g (2.00 mmole) of (R_C,R_S)-**5** or (S_C,R_P)-**5** in 30 ml of dichloromethane were added 0.56 g (6.00 mmole) of hydrogen peroxide-urea 1:1-adduct and the reaction mixtures were refluxed for 2h. Subsequently, the mixtures were cooled to room temperature and were filtered through a sintered glass disc. The filtrates were washed with 2 × 5 ml of water. The organic layers were separated and dried over sodium sulfate for 12h. After filtration, the solvents were removed i.v. and the residues were recrystallized from dichloromethane/diethyl ether (volume ratio 1:1).

Compound (R_C,R_P)-6:

Yield 0.69 g (78%); m.p.: 138–140°C; $[\alpha]_D^{25}$ = +239.6° (c = 1.0, CH_2Cl_2). ^{1}H-N.m.r.: δ = 1.94 (d, 3H, $^3J(HH)$ = 7.07 Hz, CHCH_3); 2.90–3.55 (m, 8H, N(CH_2CH_2Cl)$_2$); 3.21 (d, 3H, $^3J(HP)$ = 8.14 Hz, NCH_3); 5.70 (m, 1H, CHPh); 6.90–8.20 (m, 9H, $H_{aromatic}$).-^{13}C-N.m.r.: δ = 17.50 (s, 1C, CH$_3$CH); 30.26 (d, 1C, $^2J(CP)$ = 3.88 Hz, CH$_3$NP); 42.17 (d, 2C, $^3J(CP)$ = 1.23 Hz, PN(CH$_2$$CH_2$Cl)$_2$); 50.02 (d, 2C, $^2J(CP)$ = 5.00 Hz, PN(CH$_2$CH$_2$Cl)$_2$); 52.70 (d, 1C, $^2J(CP)$ = 3.52 Hz, PNCHCH$_3$); 112.72–142.14 (m, 12C, $C_{aromatic}$); 163.37 (d, 1C, $^2J(CP)$ = 4.18 Hz, C(:O)NP).-^{31}P-N.m.r.: δ = 8.99 (s).-EI-MS: m/z (%): 439 (38) $[M]^+$; 286 (100) $[M-CH_2ClCH_3CHC_6H_5+H]^+$; 195 (98) [M-$C_6H_5CH(CH_3)$-N(CH$_2CH_2$Cl)$_2$]$^+$; 105 (34) $[C_6H_5CH(CH_3)]^+$; 77 (16) $[C_6H_5]^+$. -IR ($CHCl_3$): ν = 1670 (vs, C(:O)); 1234 (vs, P(:O)).

$C_{20}H_{24}Cl_2N_3O_2P$ (440.31) calcd. C 54.56 H 5.49 N 9.54 %; found C 54.66 H 5.56 N 9.50 %

Compound (S_C,S_P)-6:

Yield: 0.68 g (77%); m.p.: 138–140°C; $[\alpha]_D^{25}$ = −238.0° (c = 1.0, CH_2Cl_2). ^{1}H-N.m.r.: δ = 1.94 (d, 3H, $^3J(HH)$ = 7.09 Hz, CHCH_3); 2.90–3.55 (m, 8H, N(CH_2CH_2Cl)$_2$); 3.21 (d, 3H, $^3J(HP)$ = 8.30 Hz, NCH_3); 5.70 (m, 1H, CHPh); 6.90–8.20 (m, 9H, $H_{aromatic}$).-^{13}C-N.m.r.: δ = 17.51 (s, 1C, CH$_3$CH); 30.28 (d, 1C, $^2J(CP)$ = 4.08 Hz, CH$_3$NP); 42.20 (d, 2C, $^3J(CP)$ = 1.19 Hz, PN(CH$_2$$CH_2$Cl)$_2$); 50.03 (d, 2C, $^2J(CP)$ = 4.81 Hz, PN(CH$_2$CH$_2$Cl)$_2$); 52.71 (d, 1C, $^2J(CP)$ = 3.47 Hz, PNCHCH$_3$); 112.73–142.14 (m, 12C, $C_{aromatic}$); 163.37 (d, 1C, $^2J(CP)$ = 4.18 Hz, C(:O)NP).-^{31}P-N.m.r.: δ = 9.01 (s).-EI-MS: m/z (%): 439 (50) $[M]^+$; 286 (100) $[M-CH_2ClCH_3CHC_6H_5+H]^+$; 195 (90) [M-$C_6H_5CH(CH_3)$-N(CH$_2CH_2$Cl)$_2$]$^+$; 105 (34) $[C_6H_5CH(CH_3)]^+$; 77 (16) $[C_6H_5]^+$.-IR ($CHCl_3$): ν = 1670 (vs, C(:O)); 1236 (vs, P(:O)).

$C_{20}H_{24}Cl_2N_3O_2P$ (440.31) calcd. C 54.56 H 5.49 N 9.54 %; found C 54.48 H 5.54 N 9.39 %

Formation of compounds (R_C,R_P)-7 and (S_C,S_P)-7:

To stirred solutions of 0.85 g (2.00 mmole) of (R_C,S_P)-**5** or (S_C,R_P)-**5** in 30 ml of toluene were added 0.064 g (2.00 mmole) portions of elemental sulfur and the reaction mixtures were refluxed for 8h. Subsequently, the mixtures were cooled to room temperature and were filtered through a sintered glass disc. The solvents were removed i.v. and the residues were recrystallized from dichloromethane/diethyl ether (volume ratio 1:1).

Compound (R_C,R_P)-7:

Yield: 0.74 g (81%); m.p.: 145–147°C; $[\alpha]_D{}^{25} = +194.7°$ (c = 1.0, CH_2Cl_2).
^{1}H-N.m.r.: δ = 1.95 (d, 3H, ^{3}J(HH) = 6.96 Hz, CHCH_3); 3.30 (d, 3H, ^{3}J(HP) = 10.64 Hz, PNCH_3); 3.45–3.65 (m, 8H, N(CH_2CH_2Cl)$_2$); 5.65 (m, 1H, C*H*Ph); 6.95–8.10 (m, 9H, $H_{aromatic}$).-^{13}C-N.m.r.: δ = 17.46 (s, 1C, *C*H$_3$CH); 32.69 (d, 1C, ^{2}J(CP) = 7.23 Hz, *C*H$_3$NP); 41.71 (d, 2C, ^{3}J(CP) = 1.81 Hz, PN(CH$_2$*C*H$_2$Cl)$_2$); 50.50 (d, 2C, ^{2}J(CP) = 4.68 Hz, PN(*C*H$_2$CH$_2$Cl)$_2$); 54.11 (d, 1C, ^{2}J(CP) = 6.78 Hz, PN*C*HCH$_3$); 113.38–142.31 (m, 12C, $C_{aromatic}$), 163.00 (s, 1C, *C*(:O)NP).-^{31}P-N.m.r.: δ = 68.04 (s).-EI-MS: m/z (%): 455 (20) $[M]^+$; 211 (100) $[M\text{-}C_6H_5CH(CH_3)\text{-}N(CH_2CH_2Cl)_2+H]^+$; 105 (22) $[C_6H_5CH(CH_3)]^+$; 77 (9) $[C_6H_5]^+$. -IR ($CHCl_3$): ν = 1667 (vs, C(:O)); 758 and 646 (ms, P(:S)).

$C_{20}H_{24}Cl_2N_3OPS$ (456.38) calcd. C 52.64 H 5.30 N 9.21 S 7.03 %; found C 52.56 H 5.45 N 9.46 S 6.99 %

Compound (S_C,S_P)-7:

Yield: 0.74 g (81%); m.p.: 143–145°C; $[\alpha]_D{}^{25} = -185.7°$ (c = 1.0, CH_2Cl_2).
^{1}H-N.m.r.: δ = 1.95 (d, 3H, ^{3}J(HH) = 7.02 Hz, CHCH_3); 3.30 (d, 3H, ^{3}J(HP) = 10.67 Hz, NCH_3); 3.45–3.65 (m, 8H, N(CH_2CH_2Cl)$_2$); 5.65 (m, 1H, C*H*Ph); 6.95–8.10 (m, 9H, $H_{aromatic}$).-^{13}C-N.m.r.: δ = 17.46 (s, 1C, *C*H$_3$CH); 32.69 (d, 1C, ^{2}J(CP) = 7.32 Hz, *C*H$_3$NP); 41.70 (d, 2C, ^{3}J(CP) = 1.68 Hz, PN(CH$_2$*C*H$_2$Cl)$_2$); 50.50 (d, 2C, ^{2}J(CP) = 4.85 Hz, PN(*C*H$_2$CH$_2$Cl)$_2$); 54.11 (d, 1C, ^{2}J(CP) = 6.71 Hz, PN*C*HCH$_3$); 113.38–142.31 (m, 12C, $C_{aromatic}$); 163.00 (s, 1C, *C*(:O)NP).-^{31}P-N.m.r.: δ = 67.76 (s).-EI-MS: m/z (%): 455 (25) $[M]^+$; 211 (100) $[M\text{-}C_6H_5CH(CH_3)\text{-}N(CH_2CH_2Cl)_2+H]^+$; 105 (28)

$[C_6H_5CH(CH_3)]^+$; 77 (16) $[C_6H_5]^+$. -IR ($CHCl_3$): ν = 1666 (vs, C(:O)); 758 and 646 (ms, P(:S)).

$C_{20}H_{24}Cl_2N_3OPS$ (456.38) calcd. C 52.64 H 5.30 N 9.21 S 7.03 %; found C 52.72 H 5.36 N 9.05 S 7.12 %

X-ray Crystal Structure Determinations of (R_C,S_P)-5, (R_C,R_P)-6, (S_C,S_P)-6, and (R_C,R_P)-7:

Data collection and reduction:

Crystals were mounted on glass fibres in inert oil and transferred to the cold gas stream of the diffractometer (Stoe STADI-4 for (R_C,S_P)-**5** and (R_C,R_P)-**7**, Siemens P4 for (R_C,R_P)-**6** and (S_C,S_P)-**6**, both with Siemens LT-2 low temperature attachment). The cell constants for (R_C,S_P)-**5** and (R_C,R_P)-**7** were refined from $\pm\omega$ angles of 52 (64) reflections in the 2θ range 20–23°. The orientation matrix for (R_C,R_P)-**6** and (S_C,S_P)-**6** was refined from setting angles of 63 reflections in the 2θ range 5–25° (monochromated Mo K_α radiation). In all cases a full set of Friedel opposite reflections was collected.

Structure solution and refinement:

The structures were solved by direct methods and refined anisotropically on F^2 (program system: SHELXL-93, G.M.Sheldrick, University of Göttingen). H atoms were included using a riding model or rigid methyl groups. Weighting schemes of the form $w^{-1} = [\sigma^2(F_O^2) + (aP)^2 + bP]$ were employed, with $P = (F_O^2 + 2F_c^2)/3$. The atoms C10′–C11′ of the 2-chloroethyl group of (R_C,S_P)-**5** are disordered and were refined on two positions. Crystal data are presented in Table II. Absolute configurations were determined by the method of Flack[20] and the origin for (R_C,S_P)-**5** was fixed by the method of Flack & Schwarzenbach.[21] Full details of the structure determinations have been deposited at the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-76344 Eggenstein-Leopoldshafen, Germany, from where this material may be obtained on quoting the full literature citation and the reference numbers CSD 406928 [(R_C,S_P)-**5**], CSD 406929 [(R_C,R_P)-**6**], CSD 406930 [(S_C,S_P)-**6**], and CSD 406931 [(R_C,R_P)-**7**].

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