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Direct Synthesis of Isoxazolidinylphosphines by Cycloaddition of Nitrones to Diphenylphosphinoethenes and X-Ray Structure of 7,7-Dimethyl-1-Oxo-1-Phenyl-3-Diphenylphosphinyl-Hexahydro-1H-pyrrolo [1,2-c] [1,3,2] Oxazaphosphorine

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Abstract: *The 1,3-dipolar cycloaddition reaction of N-alkyl nitrones with diphenylvinylphosphines affords directly isoxazolidinylphosphines in satisfactory yields and in regio- and stereoselective manner. The parent diphenylvinylphosphine was found to favor the formation of 5-phosphinoisoxazolidines whereas diphenylpropenyl-phosphine gave instead the 4-phosphinoisoxazolidine regioisomer. However, in reactions utilizing an alkylarylvinylphosphine and/or N-arylnitrone, oxidation of the phosphine by the nitrone reagent was found to precede the cycloaddition. An attempted conversion of the bicyclic isoxazolidine derived from 2,2-dimethyl-dihydro-2H-pyrrole 1-oxide and diphenylvinylphosphine to the perhydropyrrolo[1,2-c] [1,3,2]oxaza-phosphorine ring system was accomplished through the use of the corresponding phosphine oxide derivative and provided a single diastereoisomer of the desired pyrrolooxazaphosphorinane characterized ultimately in the form of its dioxide hydrate by the X-ray diffraction technique.*

INTRODUCTION

Formation of heterocyclic rings with simultaneous introduction of substituent groups in stereocontrolled manner is of key importance to synthetic chemists. In recent years inter- and intramolecular 1,3-dipolar cycloadditions of nitrones to substituted olefins have been of considerable synthetic and mechanistic interest, especially since the resulting isoxazolidine ring can serve as precursor

to useful 1,3-aminoalcohols.[1,2]

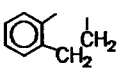
Recent disclosures from our laboratories[3-6] have also demonstrated feasibility of 1,3-dipolar cycloaddition of nitrones to phosphinylethenes as a powerful tool for regio-[5] and stereocontrolled[6] construction of isoxazolidines bearing P^V substituents either at 5 or at 4 position. In the context of potential utility of this kind of highly functionalized molecules[7] we thought it also worthwhile to examine the cycloaddition of nitrones to vinylphosphines as a possible direct route to the analogous P^{III} derivatives. However, in view of the available literature data such a strategy was by no means readily apparent since both acyclic[8] and cyclic[9,10] nitrones were reported to undergo facile deoxygenation upon treatment with triphenylphosphine under thermal conditions. In this paper we would like to report on our successful achievement of this strategy[11] as well as to present an exemplary synthesis of a novel phosphinyl-substituted bicyclic 1,3,2-oxazaphosphorinane which resulted from this study.

RESULTS AND DISCUSSION

The cycloaddition reactions were carried out by stirring a mixture of the corresponding nitrone and the vinyl phosphine in benzene solution under nitrogen atmosphere at room temperature or at reflux. The progress of the cycloadditions was monitored by means of the ^{31}P NMR.

Scheme 1

1 R–R'=–$CH_2CH_2C(Me)_2$– **4** R''= H **6a,b**

2 R–R'=  **4** R''= H **7a,b**

3 R = Ph R'= Me **4** R''= H **8a,b** **9**

1 R–R'=–$CH_2CH_2C(Me)_2$– **5** R''= Me **10**

Three (**1-3**, Scheme 1) out of the four nitrones selected for this study underwent the cycloaddition to diphenylvinylphosphine (**4**) with virtually complete exclusion of the oxygen transfer from N to P, even though the reactions with nitrones **2** and **3** required prolonged heating at reflux in order to be driven to completion. The resulting phosphinoisoxazolidines albeit air sensitive, could be conveniently isolated by crystallization of the crude reaction mixtures or by a quick passage through a short pad of silica gel without considerable concomitant oxidation to the corresponding phosphine oxides.

Phosphinoisoxazolidines **6-9** were assigned the structures shown in Scheme 1 on the basis of their ^1H, ^{13}C and ^{31}P NMR data. As for the previously studied phosphinylisoxazolidines[3-5] the ^{13}C NMR spectra were of particular value for regiochemical assignments although this time the additional APT spectra were required to make the assignment unequivocal. In contrast to the phosphinyl group

phosphine exerts only small deshielding effect on the α-carbon atom and at the same time $^1J_{PC}$ in phosphines are small and comparable with $^2J_{PC}$.[12] These features precluded immediate differentiation of the C4 and C5 in the two regioisomeric arrays, but the pertinent APT spectra indicated clearly that the most deshielded C5 carbon in **6-8** (δ 75-80 ppm) carried only one proton while the same C5 carbon in **9** (δ 70 ppm) was bonded with two protons. Accordingly, the C4 carbons in **6-8** (δ 40-45 ppm) were identified as methylene and the C4 in **9** (δ 49 ppm) as methine carbon, respectively. The different regiochemistry of **6-8** and **9** was also manifested in the corresponding ^{1}H NMR spectra which showed considerably larger differentiation of protons at C5 and C4 in **6-8** than in **9**. The former showed signals of C5 and C4 protons at 5.15-4.65 and 2.75-1.95 ppm, respectively, while the corresponding protons in **9** resonated at 4.45-4.05 and 3.60-3.40 ppm, respectively.

As follows from the above structural assignment and as could have been expected on the basis of perturbation theory[13] (as well as by comparison with the extensive literature on 1,3-dipolar cycloadditions to monosubstituted olefins[1]), the single regioisomers obtained with cyclic nitrones **1** and **2** were the 5-phosphinoisoxazolidines, and the same 5-phosphino regioisomer predominated significantly in the 87:13 mixture of products obtained with the acyclic nitrone **3**. The degree of stereoselectivity in the studied cycloadditions turned out to be meaningful only in the reaction with nitrone **1** which afforded a 6:1 (exo/endo) mixture of the two diastereoisomers of **6**. The corresponding stereoisomeric ratio of 5-phosphinoisoxazolidines formed in reactions involving nitrones **2** and **3** was only 2:1. In contrast, the minor regioisomeric 4-phosphinoisoxazolidine **9** was formed with complete stereoselectivity and was assigned the *trans* configuration.

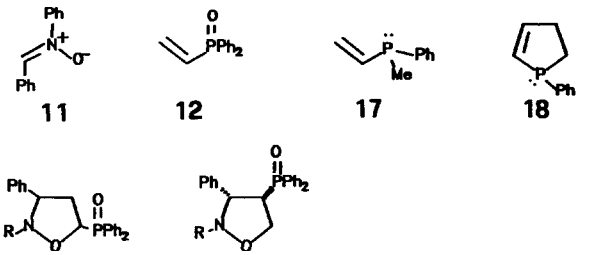
In a recent study[5] on the closely related nitrone cycloadditions to vinylphosphine oxides, showing analogous preference for the formation of the 5-phosphinylisoxazolidines, we have demonstrated that the preference could be directed towards formation of the 4-phosphinylisoxazolidines by placement of a terminal substituent at the dipolarophile double bond. To verify if this kind of regiochemical control could also apply to the studied cycloadditions to vinyl phosphines, we carried out the reaction of nitrone **1** with diphenylpropenylphosphine **5** (Scheme 1). As it appeared, the reaction led to the formation of a single phosphinoisoxazolidine **10**, even though a mixture of regioisomers could have been rather expected as a result of directive competition of the two groups electrodonating in nature.

Compound **10** was assigned the shown structure on the basis of its ^{1}H and ^{13}C NMR spectra. In the former the more deshielded signal (4.49 ppm) was a doublet of quintet, attesting the presence of the methyl group at C5. In the latter the bridgehead carbon and the adjacent one of the pyrrolidine ring were found coupled with phosphorus with J_{PC} = 22.9 and 2.1 Hz respectively, indicating the presence of the phosphorus atom at C4 of the isoxazolidine ring. It also followed that **10** was an exo product with the methyl and phosphine substituents in the *cis* relationship reflecting geometry of the starting olefin **5**.

In addition, the regiochemical outcome of the cycloaddition of **1** to **5** provides an experimental indication that in comparison with the methyl, the electron-releasing ability of the diphenylphosphino group towards the double bond is very poor. This observation is in accord with the calculation results of Schade and Schleyer,[14] which indicated that there is only a very weak P-C π interaction in vinylphosphines, due to considerable resistance of the phosphorus atom to planarization,. Similar conclusion derives also from more recent spectroscopic studies.[15]

The studied cycloaddition reactions of nitrones to vinyl phosphines, shown above to be both effective and selective in the production of 5- and 4-phosphinoisoxazolidines, suffer however from some structural limitations in regard to the two reactants. When *C,N*-diphenylnitrone (**11**) was reacted with **4**, oxidation of the phosphine occurred rather than cycloaddition.

Chart 1



The main products of the reaction were the corresponding phosphine oxide **12** and the products of nitrone reduction. Phosphinylisoxazolidines **13** and **14** (Chart 1) were also formed in the ratio observed previously in the reaction of **11** with **12**,[3,5] indicating that oxidation preceded the cycloaddition. Products of cycloaddition of **11** to **4** were formed in negligible amounts and could only be detected in the ^{31}P NMR spectrum of the crude reaction mixture. When 2 equivalents of nitrone **11** were used in this reaction, isoxazolidines **13** and **14** were obtained in high yield as the only phosphorus containing products. This reaction demonstrated that replacement of a *N*-methyl group in **3** for the *N*-phenyl in **11** was already sufficient to dramatically change the reactivity of the nitrone towards the vinylphosphine from a dipole to an oxidant one. The divergent behaviour of **11** in respect to **1-3** can be ascribed to the higher polarity of the N-O bond in **11** that renders its oxygen more accessible for phosphorus rather than to a diminished reactivity of **11** since it has been reported to be much more reactive as a dipole than **3**.[16] To confirm this suggestion, a competition experiment was performed employing nitrones **3** and **11** and vinylphosphine **4** in 1:1:1 ratio. The products of this reaction were identified as the phosphinyl-isoxazolidines **13-16**, and once again they were formed from each nitrone in the same regio and stereoisomeric ratios as previously observed in reactions of **12**.[3,5] It could have been concluded, therefore, that the oxidation of **4** to **12** by nitrone **11** was the fastest reaction and that subsequently the preferential cycloaddition of the two nitrones to **12**, being more reactive as a dipolarophile than **4**, occurred. The phosphinoisoxazolidines were only detected in minor amounts in the ^{31}P NMR spectrum of the crude reaction mixture.

Interestingly, in the same manner in which *N*-aryl substitution makes nitrones more prone to release the oxygen atom for oxidation, a reverse substitution of one phenyl group with an alkyl group in vinylphosphine can be sufficient to render the phosphorus lone pair more readily available for the nitrone oxygen in the oxidation reaction. Indeed, vinylphosphines **17** and **18** (Chart 1) underwent quantitative oxidation to the corresponding phosphine oxides even when reacted with **1** at room

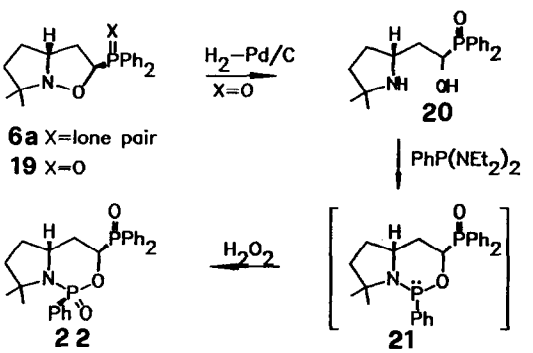
temperature.

In conclusion, the 1,3-dipolar cycloaddition of nitrones to vinylphosphines is a viable process and affords directly isoxazolidinylphosphines in satisfactory yields and with considerable regio- and stereoselectivity provided that use of *N*-aryl nitrones and *P*-alkyl vinylphosphines as the reaction components is avoided.

As a possible application of the synthesized diphenylphosphinoisoxazolidines, other than using them directly as ligands for transition metals, we envisaged their transformation into novel 1,3,2-oxazaphosphorinanes that could be realized by sequential reductive ring-opening of the isoxazolidine and reaction of the resulting aminoalcohol with dichloro- or diaminophosphines. Our attention was attracted to this molecules by the known pharmacological properties of oxaza-phosphorinanes[17] as well as their utility as ligands.[18] Moreover, an additional phosphorus substituent could render these molecules even more attractive as ligands by making them bidentate and possessing two nonequivalent phosphine sites.

Unfortunately, our attempts to afford the ring-opening of **6a** with preservation of its phosphine functionality by mild hydrogenation with Raney-Ni or palladium over carbon failed. Since the inertness of **6a** towards hydrogenolysis derived probably from sequestering of the catalyst by the phosphine moiety, we turned our attention to the ring-opening of the corresponding phosphinylisoxazolidine **19**[3,5] which was easily available from the analogous cycloaddition of **1** to **12**. At the same time, employment of **19** did not preclude the possibility to obtain the phosphino derivative, since convenient procedures exist for conversion of phosphine oxides to phosphines.[19]

Scheme 2



Hydrogenation of **19** in the presence of Pd/C gave cleanly the desired aminoalcohol **20** (Scheme 2), which was subsequently reacted with bis(diethylamino)phenylphosphine to afford the phosphinyl-oxazaphosphorinane **21** in good overall yield. In a ^{31}P NMR spectrum **21** displayed the expected pair of doublets at 112.38 and 30.83 ppm, with $^{3}J_{PP} = 2$ Hz, but due to its pronounced propensity to oxidation it was not isolated in the P^{III} form. We found it more convenient to oxidize **21** *in situ* by treatment with H_2O_2 and to use the resulting dioxide **22** for final characterization. Dioxide **22** was obtained as a single diastereoisomer exhibiting another pair of doublets in the ^{31}P NMR spectrum, δ 29.35 and 17.95 ppm,

$^3J_{PP}$ = 29.5 Hz, and was assigned the *trans* stereochemistry on the basis of the following single-crystal X-ray diffraction analysis of **22**·H_2O.

A view of the molecular structure of **22**·H_2O with atom labelling is displayed in Figure 1. Figure 2 shows the stereoscopic view of its unit cell packing and Table 1 collects the crystal data and experimental parameters. The pertinent positional parameters, bond lenghts and bond angles are given in Tables 2, 3, and 4, respectively.

Inspection of Fig. 1 reveals that diphenylphosphinyl substituent and O1 phosphoryl oxygen reside on the opposite sides of the oxazaphosphorinane ring in a trans stereochemical relationship. The found conformation of the oxazaphosphorinane ring is a twist one with the asymmetry parameters[20] in relation to a two-fold axis $\Delta C_2(C2) = 14.3°$, $\Delta C_2(C1\text{-}O3) = 13.4°$ and $|\Phi|_{av.} = 40.8°$, respectively. In known structures the 1,3,2-oxazaphosphorinane ring possess either chair, half chair or twist conformation.[21] Literature data indicate also the dependance of the conformation of this ring on the N and P substituents.[21,22] The investigated structure constitutes the first example of an oxazaphosphorinane ring condensed with the five-membered pyrrolidine ring. This pyrrolidine ring is found in **22** to exist in two envelope conformations. The occupancy factor for C5 atom in the major-component molecule is 0.63(1) and the asymmetry parameters of its deformed envelope are $\Delta C_S(C4) = 4.7°$ and $|\Phi|_{av.} = 23.1°$. The minor-component molecule has the envelope conformation with $\Delta C_S(C6) = 2.5°$ and $|\Phi|_{av.} = 17.9°$. The observed conformational lability of the pyrrolidine ring in **22** may be associated with the unfavourable 1,3-syn steric interactions of the two quaternary centres of C6 and P1. As indicated by the sum of the nitrogen bond angles equal to 356.7° the nitrogen bridgehead in **22** is nearly planar.

The molecules of hydrating water link the molecules of **22** by a system of hydrogen bonds O4-H1...O1 (-x+1.5, -y+0.5, -z+1) and O4-H2...O2, forming the chains along y axis. The pertinent H1...O1 and H2...O2 distances are 2.13(3) and 2.06(3) Å, respectively, and the angles O4-H1...O1 and O4-H2...O2 are 159(3)° and 158(3)°, respectively.

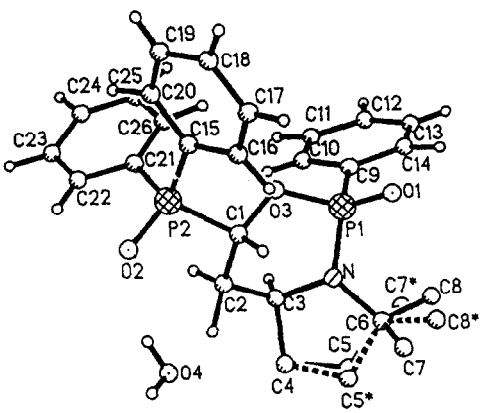


Figure 1. A view of oxazaphosphorinane **22** with atom numbering.

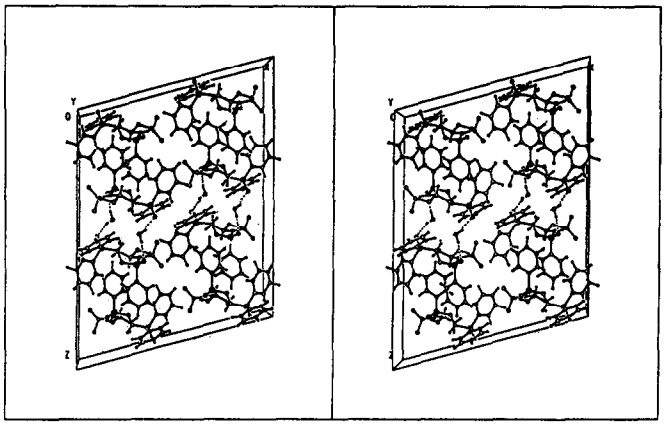


Figure 2. The unit cell packing for **22**

EXPERIMENTAL

All reactions were carried out under nitrogen. Melting points (uncorrected) were measured with a Kofler apparatus. NMR spectra were recorded in $CDCl_3$ on Varian FT-80 A (^{13}C, 20 MHz; ^{31}P, 32.203 MHz) and on Varian Gemini 200 (^1H NMR, 200 MHz) spectrometers. In ^{13}C NMR spectra only signals of the aliphatic region and only couplings with phosphorus are reported. The chemical shifts for ^1H and ^{13}C NMR spectra are given in ppm from TMS; for ^{31}P NMR spectra in ppm from H_3PO_4 85%. Ratios of diastereomeric products were obtained by integration of the corresponding ^{31}P NMR signals of the crude mixtures. The isoxazolidinylphosphine oxides used for comparison and for the synthesis of **22** were available from our previous study.[5] Nitrones were synthesized by standard procedures according to the literature.[1]

Cycloaddition of 2,2-dimethyl-3,4-dihydro-2H-pyrrole 1-oxide (**1**) *to diphenylvinylphosphine* (**4**) - A solution of 144 mg (1.2 mmol) of nitrone **1** and 212 mg (1 mmol) of diphenylvinylphosphine[23] (**4**) in 3 mL of dry benzene was left at room temperature for 6 days. ^{31}P NMR monitoring reveals the presence of two isomers in 6:1 ratio. Crystallization of the viscous oil obtained after solvent removal from ligroin 100-150°C gave 202 mg (62% yield) of the major isomer **6a** as white crystals.

6a: m.p.: 119-120°C. Anal. Calcd for $C_{20}H_{24}NOP$ C, 73.82; H, 7.43; N, 4.30. Found C, 73.79; H, 7.58; N, 4.68. ^{31}P NMR: δ -8.77. ^1H NMR: δ 7.57-7.44 (m, 4H), 7.38-7.29 (m, 6H), 4.67 (dd, J = 10.1, 5.9 Hz, 1H), 3.90 (m, 1H), 2.40 (ddt, J = 10.2, 7.0, 12.4 Hz, 1H), 2.12 (m, 1H), 1.96 (dt, J = 12.2, 6.0 Hz, 1H), 1.78 (m, 1H), 1.62 (m, 1H), 1.46 (m, 1H), 1.40 (s, 3H), 1.08 (s, 3H). ^{13}C NMR: δ 77.06 (d, J = 5.8 Hz), 68.97, 63.44 (d, J = 4.8 Hz), 41.97 (d, J = 19.4 Hz), 36.51, 31.17, 26.82, 24.03.

6b: ^{31}P NMR: δ -7.76.

Cycloaddition of 3,4-dihydro-isoquinoline-N-oxide (**2**) *to diphenylvinylphosphine* (**4**) - A solution of 147 mg (1 mmol) of nitrone **2** and 212 mg (1 mmol) of phosphine **4** in 5 mL of dry benzene was refluxed for 24 h. ^{31}P NMR reveales the presence of two isomers in 2:1 ratio. After evaporation of the solvent, crystallization of the crude residue from ligroin 100-150°C afforded 164 mg (45% yield) of a mixture of two isomers. Anal. (mixture of isomers) Calcd for $C_{23}H_{22}NOP$ C, 76.86; H, 6.17; N, 3.89. Found C, 76.82; H, 6.40; N, 4.02.

7a: m.p.: 128-130°C. ^{31}P NMR: δ -7.01. ^{1}H NMR: δ 7.68-7.48 (m, 4H), 7.43-7.30 (m, 6H), 7.20-7.05 (m, 3H), 6.98-6.94 (m, 1H), 5.16 (dt, J = 9.2, 6.0 Hz, 1H), 4.28 (t, J = 8.3 Hz, 1H), 3.19 (dt, J = 3.4, 10.1 Hz, 1H), 3.30 (m, 1H), 3.04 (m, 1H), 2.86 (dt, J = 16.1, 3.6 Hz, 1H), 2.66-2.44 (m, 2H). ^{13}C NMR: δ 76.37 (d, J = 9.6 Hz), 62.68 (d, J = 2.5 Hz), 47.78, 41.48 (d, J = 15.5 Hz), 28.13.

7b: ^{31}P NMR: δ -3.02. ^{1}H NMR: δ (the only hydrogens discerned) 4.97 (ddd, J = 10.9, 7.0, 1.8 Hz, 1H), 4.61 (dd, J = 10.4, 6.5 Hz, 1H), 2.70-2.45 (m, 2H). ^{13}C NMR: δ 79.02 (d, J = 12.9 Hz), 63.09 (d, J not discerned), 49.88, 41.72 (d, J = 21.2 Hz), 28.46.

Cycloaddition of N-methyl-C-phenylnitrone (**3**) *to diphenylvinylphosphine* (**4**) - A solution of 135 mg (1 mmol) of nitrone **3** and 212 mg (1 mmol) of phosphine **4** in 5 mL of dry benzene has been refluxed for 48 h. ^{31}P and ^{13}C NMR monitoring of the crude reaction mixture revealed the presence of three isomers in 61:26:13 ratio assigned as two 5-substituted adduct **8a,b** and the 4-substituted adduct **9** respectively. Chromatography of the reaction mixture on a short pad of silica gel (eluant diethyl ether) gave 235 mg (63% yield) of a colorless viscous oil containing the three isomers in a ratio similar to the above.

8a: ^{31}P NMR: δ -6.36. ^{1}H NMR: δ 7.75-7.20 (m, 15H), 5.16-5.04 (m, 1H), 3.42 (m, 1H), 2.75-2.30 (m, 2H), 2.63 (s, 3H). ^{13}C NMR: δ 76.01 (d, J = 7.0 Hz), 72.16 (d, J = 3.9 Hz), 44.04, 43.27 (d, J = 3.1 Hz).

8b: ^{31}P NMR: δ -9.62. ^{1}H NMR: δ (the only hydrogens discerned) 3.70-3.58 (m, 1H), 2.72 (s, 3H). ^{13}C NMR: δ 77.22 (d, J = 6.3 Hz), 72.85 (d, J = 1.0 Hz), 45.05, 43.02 (d, J = 12.9 Hz).

9: ^{31}P NMR: δ -7.13. ^{1}H NMR: δ (the only hydrogens discerned) 4.52-4.40 (m, 1H), 4.12-4.02 (m, 1H), 3.60-3.40 (m, 2H), 2.67 (s, 3H). ^{13}C NMR: δ (the only carbons discerned) 69.67 (d, J = 18.9 Hz), 49.16 (d, J = 11.4 Hz).

Cycloaddition of 2,2-dimethyl-3,4-dihydro-2H-pyrrole 1-oxide (**1**) *to Z-diphenylpropenylphosphine* (**5**) - A solution of nitrone **1** (113 mg, 1 mmol) and *Z*-diphenylpropenylphosphine[24] (**5**) (225 mg , 0.88 mmol; the phosphine contained 12% of not reactive *E*-diphenylpropenylphosphine) in degassed toluene was heated at reflux for 36 h. After concentration and chromatography on alumina (eluant petroleum ether-diethyl ether 2:1, R_f = 0.5) 150 mg (50% yield) of isoxazolidine **10** were obtained as white crystals.

10: m.p.: 109-110°C. Anal. Calcd for $C_{21}H_{26}NOP$ C, 74.31; H, 7.72; N, 4.13. Found C, 74.70; H,7.91; N, 4.04. ^{31}P NMR: δ -17.8. ^{1}H NMR: δ 7.60-7.24 (m, 10H), 4.49 (d quintet, J = 6.6, 2.9 Hz, 1H), 3.70 (m, 1H), 2.94 (q, J = 6.7 Hz, 1H), 1.75-1.20 (m, 3H), 1.27 (dd, J = 6.5, 3.6 Hz, 3H), 1.25 (s, 3H), 0.98 (s, 3H), 0.92-0.76 (m, 1H). ^{13}C NMR: δ 76.65 (d, J = 14.4 Hz), 67.92 (d, J = 22.9 Hz), 66.58, 53.25 (d, J = 12.8 Hz), 35.56, 31.73 (d, J = 2.1 Hz), 26.70, 23.45, 17.98 (d, J = 17.7).

Reaction of C,N-diphenylnitrone (**11**) *with diphenylvinylphosphine* (**4**) - A solution of 197 mg (1 mmol) of **11** and 212 mg (1 mmol) of phosphine **4** in 5 mL of dry benzene was refluxed 5 h under nitrogen. After this time, a ^{31}P NMR spectrum showed the presence of phosphine oxide **12** (26.45 ppm) and of the cycloadducts **13** and **14** in a 1.5:1 regioisomeric ratio. The reaction mixture, after concentration, was fractionated by column chromatography (eluant $CHCl_3$-MeOH 10:1). The fast eluting fraction (216 mg) contained a mixture of unreacted phosphine, *N*-phenylbenzaldehyde imine and azoxybenzene. The second fraction contained 138 mg of a 1:1.5 mixture of adducts **13** and **14**, and the third fraction contained 75 mg of diphenylvinylphosphine oxide **12**. In a reaction with two equivalents of nitrone **11** adducts **13** and **14** were obtained, after purification, in the same ratio in 76% overall yield.

Reaction of methylphenylvinylphosphine (**17**) *with 2,2-dimethyl-3,4-dihydro-2H-pyrrole 1-oxide* (**1**) - A solution of methylphenylvinylphosphine[25] (**17**) (300 mg, 2 mmol, ^{31}P NMR: δ -31.33) and 226 mg (2 mmol) of nitrone **1** in $CHCl_3$ (1 mL) was stirred at room temperature. Monitoring of the reaction by ^{31}P NMR revealed after ten minutes the formation of the corresponding vinylphosphine oxide (^{31}P NMR: δ 27.11). In one hour the reaction was complete.

Reaction of 3,4-dihydro-1-phenylphosphole (**18**) *with 2,2- dimethyl-3,4-dihydro-2H-pyrrole 1-oxide* (**1**) A solution of dihydrophosphole[26] **18** (162 mg, 1 mmol, ^{31}P NMR: δ -1.62) and 136 mg (1.2 mmol) of nitrone **1** in $CHCl_3$ (1 mL) was stirred at room temperature. Monitoring of the reaction by ^{31}P NMR revealed after one hour the formation of the oxidized dihydrophosphole (^{31}P NMR: δ 60.50). After 8 h the reaction was complete.

Synthesis of aminoalcohol **20** - A solution of 600 mg (1.75 mmol) of isoxazolidine **19** in MeOH (5 mL) was added of 400 mg of 10% Pd/C and stirred under hydrogen at atmospheric pressure for 24 h. After filtration of the catalyst on Celite and concentration of the solution, the oily residue was purified by flash chromatography (eluant CH_2Cl_2-MeOH 15:1) to give 520 mg (86% yield) of **20** as a colorless viscous oil.

20: Anal. Calcd for $C_{20}H_{26}NO_2P + 2H_2O$ C, 63.32; H, 7.38; N, 3.69. Found C, 63.51; H, 7.27; N, 4.29. IR ($CDCl_3$): 3210, 3062, 2977, 2800, 1605, 1591, 1437, 1214, 1157 cm^{-1}. ^{31}P NMR: δ 35.1. ^1H NMR: δ 9.70 (broad, 1H), 7.97-7.70 (m, 4H), 7.65-7.35 (m, 6H), 6.00 (broad, 1H), 5.14 (t, J = 11.0 Hz, 1H), 3.86 (broad q, J = 8.0 Hz, 1H), 2.40 (t, J = 12.9 Hz, 1H), 2.05-1.75 (m, 1H), 1.70-1.15 (m, 4H), 1.36 (s, 3H), 1.20 (s, 3H). ^{13}C NMR: δ 64.22, 63.38 (d, J = 95.5 Hz), 54.07, 37.04, 32.96, 28.51, 25.90, 25.37.

Synthesis of 7,7-dimethyl-1-oxo-1-phenyl-3-diphenylphosphinyl-hexahydro-1H-pyrrolo[1,2-c][1,3,2] oxazaphosphorine (**22**) - A solution of aminoalcohol **20** (100 mg, 0.29 mmol) and bis(diethylamino) phenylphosphine (75 mg, 0.3 mmol) in 2 mL of dry benzene was refluxed for 8 h. ^{31}P NMR monitoring showed two sets of signal at $\delta_P = 112.38$ ($J_{PP} = 2$Hz) and 30.83 ($J_{PP} = 2$ Hz) assigned to the phosphorinane **21**. Attempts to isolate **21** failed and for convenience the crude reaction mixture was oxidized with H_2O_2. Work up followed by flash chromatography ($CHCl_3$-MeOH 30:1) afforded 70 mg (50% yield) of pure **22** as white crystals.

22: m.p.: 96-97°C. Anal. Calcd for $C_{26}H_{29}NO_3P_2 + H_2O$ C, 64.59; H, 6.46; N, 2.89. Found C, 64.91; H, 6.49; N, 2.88. IR ($CDCl_3$): 3062, 2968, 1600, 1592, 1437, 1252, 1225, 1168, 1125 cm^{-1}. ^{31}P NMR: δ 29.35 (J_{PP} = 29.5 Hz), 17.95 (J_{PP} = 29.5 Hz). ^1H NMR: δ 7.95-7.65 (m, 6H), 7.60-7.15 (m, 9H), 5.46-5.33 (m, 1H), 3.57- 3.42 (m, 1H), 2.60-1.00 (m, 6H), 1.45 (s, 3H), 1.15 (s, 3H). ^{13}C NMR: δ 68.86 (dd, J = 89.4, 8.3 Hz), 62.48 (d, J = 4.9 Hz), 55.93 (dd, J = 6.6, 3.7 Hz), 40.79 (d, J = 9.8 Hz), 33.67 (d, J = 2.4 Hz), 31.88 (d, J = 8.1 Hz), 30.12, 28.21.

X-ray analysis - Crystals of **22** were obtained by slow crystallization from benzene. Accurate unit cell dimensions were obtained by the least-squares fit to the θ values of 25 reflections ($21° < \theta < 27°$) measured on an Enraf-Nonius CAD4 diffractometer. Diffraction data were collected using graphite-monochromated CuK_α radiation and the $\omega - 2\Theta$ scan mode. The scan speed varied with the intensity from 1 to 6°/min. After every 200 reflections three standard reflections were measured to check misorientation and radiation damage. No systematic intensity reduction was observed. The intensity data were corrected for Lorentz and polarization effects.

The structure was solved by direct methods using the SHELXS-86[27] program and was refined by full-matrix least squares. All non-hydrogen atoms were refined with anisotropic thermal parameters. Upon refining the structure very high temperature factors of C5, C7 and C8 atoms were observed. Two alternative positions of these atoms were found on the difference map and both were refined with anisotropic temperature factors. The occupancy factors for the resulting two conformations of the five-membered ring are 0.63(1) and 0.37(1), respectively for C5, C7, C8 and $C5^*$, $C7^*$, $C8^*$ atoms.

Table 1. The Crystal Data and Experimental Parameters for $22 \cdot H_2O$

Molecular formula	$C_{26}H_{29}NO_3 \cdot H_2O$
Mr	483.5
Space group	C2/c
a (Å)	21.509(2)
b (Å)	8.798(1)
c (Å)	27.286(3)
β(deg)	105.13(1)
V ($Å^3$)	4984.5(9)
Z	8
F(000)	2048
D_x (Mgm^{-3})	1.288
D_m (Mgm^{-3})	1.28
Radiation	CuK_α
$\mu(CuK_\alpha)/cm^{-1}$	18.45
Crystal size/mm	0.2,0.3,0.2
Θ range (deg)	1-75
Reflections measured	5089
Reflections with $I > 3\sigma(I)$	4718
R	0.055
R_w	0.071

Table 2. Positional Parameters ($x10^5$) for the P Atoms and ($x10^4$) for the O, N and C Atoms with Estimated Standard Deviations in Parentheses in **22**.

	x	y	z
P1	69280(2)	23103(5)	33810(2)
P2	87616(2)	25239(4)	44121(2)
O1	6549(1)	985(2)	3472(1)
O2	8998(1)	3377(2)	4897(1)
O3	7685(1)	2261(1)	3649(1)
O4	3187(1)	245(3)	445(1)
N	6730(1)	3921(2)	3601(1)
C1	7914(1)	3015(2)	4133(1)
C2	7837(1)	4719(2)	4075(1)
C3	7206(1)	5182(2)	3700(1)
C4	6852(1)	6457(3)	3893(1)
C5	6169(2)	6204(6)	3607(4)
C5*	6185(4)	5880(13)	3881(4)
C6	6065(1)	4487(3)	3556(1)
C7	5862(3)	3810(8)	4021(3)
C7*	5811(5)	5074(14)	2974(3)
C8	5601(3)	4078(12)	3070(3)
C8*	5600(4)	3314(12)	3674(6)
C9	6922(1)	2466(2)	2724(1)
C10	7379(1)	3329(2)	2571(1)
C11	7318(1)	3575(3)	2055(1)
C12	6802(1)	2965(3)	1698(1)
C13	6355(1)	2073(3)	1847(1)
C14	6415(1)	1825(3)	2357(1)
C15	8815(1)	496(2)	4490(1)
C16	8340(1)	-312(2)	4648(1)
C17	8437(1)	-1825(2)	4780(1)
C18	8999(1)	-2559(2)	4756(1)
C19	9465(1)	-1775(2)	4598(1)
C20	9375(1)	-245(2)	4462(1)
C21	9204(1)	3035(2)	3959(1)
C22	9714(1)	4054(3)	4116(1)
C23	10072(1)	4489(3)	3781(2)
C24	9917(1)	3931(4)	3296(1)
C25	9417(1)	2931(4)	3139(1)
C26	9057(1)	2447(2)	3467(1)

Hydrogen atoms were located from a difference Fourier map and their positional and individual isotropic thermal parameters were refined. Only the hydrogen atoms of the methyl groups and disordered five-membered ring were omitted. The function $\Sigma w(|F_o| - |F_c|)^2$ was minimized and in the final cycles of calculations a weighting scheme $w = [\sigma^2(F_o + 0.005(F_o)^2]^{-1}$ was used. An empirical isotropic extinction correction was introduced and the parameter x was refined. Any peaks higher than 0.47 eA^3 were not observed on the final difference Fourier map. Most of the computations were performed with the SHELX-76 crystal structure determination program.[28]

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Table 3. Bond Lengths (Å) in **22**.

O1	---P1	1.480(2)	O3	---P1	1.602(2)
N	---P1	1.638(2)	C9	---P1	1.795(3)
O2	---P2	1.491(1)	C1	---P2	1.835(2)
C15	---P2	1.797(2)	C21	---P2	1.802(3)
C1	---O3	1.445(2)	C3	---N	1.486(3)
C6	---N	1.489(3)	C2	---C1	1.512(2)
C3	---C2	1.526(3)	C4	---C3	1.525(3)
C5	---C4	1.490(5)	C5*	---C4	1.514(10)
C6	---C5	1.527(6)	C6	---C5*	1.495(11)
C7	---C6	1.563(9)	C7*	---C6	1.623(9)
C8	---C6	1.481(7)	C8*	---C6	1.529(12)
C10	---C9	1.390(3)	C14	---C9	1.393(3)
C11	---C10	1.396(4)	C12	---C11	1.380(3)
C13	---C12	1.382(4)	C14	---C13	1.381(4)
C16	---C15	1.402(3)	C20	---C15	1.390(3)
C17	---C16	1.381(3)	C18	---C17	1.385(3)
C19	---C18	1.377(3)	C20	---C19	1.396(3)
C22	---C21	1.395(3)	C26	---C21	1.396(4)
C23	---C22	1.394(5)	C24	---C23	1.369(4)
C25	---C24	1.369(4)	C26	---C25	1.393(4)

Table 4. Bond Angles (°) in **22**.

O3	-P1	-O1	116.16(3)	N	-P1	-O1	114.37(3)
N	-P1	-O3	100.75(3)	C9	-P1	-O1	111.54(7)
C9	-P1	-O3	101.51(8)	C9	-P1	-N	111.41(6)
C1	-P2	-O2	108.73(8)	C15	-P2	-O2	113.48(8)
C15	-P2	-C1	107.96(9)	C21	-P2	-O2	111.41(7)
C21	-P2	-C1	107.57(11)	C21	-P2	-C15	107.48(10)
C1	-O3	-P1	117.9(1)	C3	-N	-P1	118.7(1)
C6	-N	-P1	126.5(1)	C6	-N	-C3	111.5(1)
O3	-C1	-P2	109.6(1)	C2	-C1	-P2	110.3(1)
C2	-C1	-O3	111.0(2)	C3	-C2	-C1	112.9(2)
C2	-C3	-N	111.9(1)	C4	-C3	-N	103.3(2)
C4	-C3	-C2	113.7(1)	C5	-C4	-C3	102.8(3)
C5*	-C4	-C3	107.6(5)	C6	-C5	-C4	107.3(4)
C6	-C5*	-C4	107.7(6)	C5	-C6	-N	102.0(2)
C5*	-C6	-N	102.2(4)	C7	-C6	-N	105.8(3)
C7*	-C6	-N	104.9(3)	C7	-C6	-C5	111.6(4)
C7*	-C6	-C5*	106.3(6)	C8	-C6	-N	113.6(3)
C8*	-C6	-N	115.1(4)	C8	-C6	-C5	111.7(5)
C8*	-C6	-C5*	116.7(6)	C8	-C6	-C7	111.6(4)
C8*	-C6	-C7*	110.4(6)	C10	-C9	-P1	121.4(2)
C14	-C9	-P1	119.2(2)	C14	-C9	-C10	119.2(2)
C11	-C10	-C9	120.2(2)	C12	-C11	-C10	119.9(2)
C13	-C12	-C11	120.4(2)	C14	-C13	-C12	119.8(2)
C13	-C14	-C9	120.7(2)	C16	-C15	-P2	120.8(2)
C20	-C15	-P2	119.3(1)	C20	-C15	-C16	119.4(2)
C17	-C16	-C15	119.8(2)	C18	-C17	-C16	120.8(2)
C19	-C18	-C17	119.8(2)	C20	-C19	-C18	120.3(2)
C19	-C20	-C15	120.0(2)	C22	-C21	-P2	117.6(2)
C26	-C21	-P2	122.7(2)	C26	-C21	-C22	119.7(2)
C23	-C22	-C21	120.0(2)	C24	-C23	-C22	119.9(2)
C25	-C24	-C23	120.4(2)	C26	-C25	-C24	121.2(3)
C25	-C26	-C21	118.8(2)				

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