Synthesis of Substituted 3-(β,β-Dimethylhydrazino)-2-methoxy-2-oxo-1,2-oxaphospholanes†

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Z. Naturforsch. 40b, 407–415 (1985); received November 5, 1984

3-(β,β-Dimethylhydrazino)-1,2-oxaphospholanes, Diastereoselectivity, Configuration,
Mechanism, Equilibration

Cyclisation of δ-(N,N-dimethylhydrazono)alkyl phosphites afforded the title compounds in moderate to high yields. The ring closure was highly diastereoselective leading to an excess of the diastereomers with the β,β-dimethylhydrazino and MeOP groups in the trans configuration. The structure and relative configurations of diastereomeric pairs were established by ¹H and ¹³C NMR spectroscopy. A mechanism of cyclisation was proposed.

Introduction

Since the discovery of streptomycin [1] many other antibiotics containing an aminosugar moiety [2] have been isolated from natural sources and proved useful against a broad spectrum of microorganisms. As a part of our program directed towards the synthesis of monosaccharides in which the anomeric carbon is replaced by a phosphorus atom [3], we were interested in the construction of the 1,2-oxaphospholane ring having exocyclic C=N bonds. The addition of dialkyl phosphites to the C=N bond of Schiff bases [4], hydrazones [5] and related compounds has been recognized as a useful approach to the P—C—N fragment of α-aminoalkanephosphonates [6, 7]. Inokawa and co-workers [8] took advantage of the addition of dialkyl phosphites to sugar tosylhydrazones for the preparation of P-containing carbohydrates.

Recently, we have shown that the cyclisation of dimethyl-(1,1-dimethyl-3-oxobutyl) phosphite (1) led to the diastereomeric 1,2-oxaphospholan-3-ols 2A and 2B together with a substantial amount of the dihydroxyphosphonate 3 (eq. (1)) [9]. Structurally related dimethyl-(3-oxoalkyl) phosphites reacted similarly [3, 10].

On the basis of these results it could be anticipated that the derivatives of 1 containing C=N bonds, such as hydrazones or Schiff bases of a general formula 4, should also undergo a facile ring closure to afford the substituted 3-amino-1,2-oxaphospholanes (5) (eq. (2)). To verify this assumption, β-hydroxy-N,N-dimethylhydrazones 8, readily available from lithio-N,N-dimethylhydrazones and ketones [11], were selected as starting materials. Here, we would like to present the synthesis of diastereomeric 3-(β,β-dimethylhydrazino)-1,2-oxaphospholanes 10 and 11, as well as to discuss the stereochemistry of these compounds and to propose a mechanism of the cyclisation of 9.

* Reprint requests to Dr. A. E. Wróblewski.
† Stereochemistry of 1,2-oxaphospholanes IV. Part III [10]; part II [3]; part I [9].

0340–5087/85/0300–0407/$ 01.00/0

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Results

The starting β-hydroxy-N,N-dimethylhydrazones 8 were prepared in two ways: either by the condensation of acetaldol (7a) or diacetone alcohol (7b) with N,N-dimethylhydrazine, or by the addition of α-lithiated acetophenone N,N-dimethylhydrazone to the selected carbonyl compounds 6 [11] (eq. (3)). Yields of pure 8 in both cases were satisfactory to good. However, 8c and 8e were used crude for further transformation due to the expected decomposition during purification [11b]. When the preparation of 8b free of starting 7b was attempted, it was found that 8 can undergo the retroaldol reaction. In a sample of 8b warmed above 80°, a substantial amount of acetone N,N-dimethylhydrazone was detected by g.l.c. Two sugar N,N-dimethylhydrazones 8f and 8g were crystalline and thus useful for the characterization of the parent tetrose derivatives. The hydrazones 8a–g were quantitatively converted into the phosphites 9a–g under standard conditions [12]. Crude 9, with the exception of 9d, showed single resonances in the 31P NMR spectra and for this reason were considered sufficiently pure to be used in the next step of the synthesis. In the spectrum of 9d two signals of equal intensity, representing E and Z isomers, were found. The 1H NMR spectrum of 9d supported such an assignation.

Cyclisations of the vigorously reacting phosphites 9a and 9b were carried out with water using tetrahydrofuran (THF) as a solvent (eq. (4)), while in
the case of the less reactive phosphites 9c, 9d and 9g
the reaction was carried out in the heterogeneous system. In the $^{31}$P NMR spectra of the crude reaction mixtures resonances of diastereomeric 1,2-oxaphospholanes were observed in the +40 ppm region. Signals in the +140 ppm region characteristic of phosphites had disappeared [13a]. Furthermore, careful examination of these spectra revealed two important features of the cyclisation: (i) an excess of the diastereomer having the hydrogen bond P=O•••H—N (10) over 11 (Table I), (ii) a low amount of the acyclic compounds 12, to which signals in the +20 ppm region [13b] were assigned. Column chromatography on silica gel was successfully employed to separate the diastereomeric pairs 10b/11b, 10c/11c, and 10d/11d. The relative configurations of the pure isomers thus obtained were established by means of $^1$H and $^{13}$C NMR spectroscopy (see Discussion). The reaction of 9e with water gave no 1,2-oxaphospholanes as shown by the $^{31}$P NMR spectrum of the crude reaction mixture. Instead of the cyclisation, the elimination of dimethyl phosphite from 9e occurred, and chalcone N,N-dimethylhydrazone was identified by $^1$H NMR as the main reaction product. The phosphites 9f and 9g reacted with water in a different manner. 1,2-Oxaphospholanes were not found in the crude product obtained from 9f, but four diastereomers 10—11g were formed from 9g (Table I). The reason for the different reactivity of 9f and 9g will be discussed later on. Numerous attempts at purification/separation of 10—11g were unsuccessful due to the instability of these compounds.

When a mixture of diastereomers 10—11a was subjected to column chromatography no material was recovered even with methanol from silica gel. Further studies indicated that these compounds are unstable. From a sample of distilled 10—11a left at room temperature for several months a white solid precipitated. The $^{31}$P NMR spectrum of this solid showed two resonances at +34.0 and +30.4 ppm in the ratio of 5:1. The same signals were also detected in the crude reaction mixture of 10—11a (Table I). On the basis of $^1$H and $^{13}$C NMR spectra the structure 13a was established for the two components of this solid (see Discussion). Therefore, one can expect that hydrolysis occurred during chromatography, and 13a was absorbed on silica gel. Finally, although 10b was stable enough to be chromatographed on silica gel, 13b was also formed when liquid 10b had been left at room temperature for several months. Generally, the substituted 3-(β,β-dimethylhydrazino)-3-methoxy-3-oxo-1,2-oxaphospholanes described in this paper underwent deterioration when kept at room temperature. Hydrolysis of the MeOP group is, so far, the only recognized transformation of this class of compounds.

Recently, we have also shown that pure 2A or 2B could be equilibrated at room temperature in the presence of 10 mol-% MeONa/MeOH to the 45:55 mixture of these compounds [9]. Under the same conditions 10b remained intact. However, refluxing

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*Composition of the crude products calculated from the $^{31}$P NMR spectrum;*  
*b two additional signals at δ$_{31p}$ 34.0 and 30.5 ppm found.*
Facile cyclisation of $\text{9g}$ and the lack of reactivity of $\text{9f}$ could be explained on the grounds of $\text{13b}$ (eq. (5)). Prolonged treatment of $\text{10b}$ (15 h) with MeONa/MeOH led to a 62:38 mixture of the diastereomers but at the same time the amount of $\text{13b}$ increased to 13%.

Discussion

Structural and configurational studies

The structures of the 1,2-oxaphospholanes obtained were established on the basis of the NMR spectral data. In the $^{31}\text{P}$ NMR spectra (Table I) two $^{31}\text{P}$-signals (four in the cases of $\text{10-11a}$ and $\text{10-11g}$) of diastereomers in the region $+38$ to $+44$ ppm, characteristic of the 1,2-oxaphospholane ring [9], were observed. The formation of the diastereomeric products was also conclusive from the stereochemical point of view, because the achiral phosphites $\text{9b-d}$ were transformed into the 1,2-oxaphospholanes containing two chiral centers. This feature was also clearly demonstrated in the $^1\text{H}$ NMR spectra. The spectra of the phosphites $\text{9}$ showed the $\text{H—C—O—P}$ couplings only, while in the spectra of $\text{10b-d}$ and $\text{11b-d}$ the $\text{H—C—C—P}$ couplings appeared additionally. The $\text{C—P}$ couplings to all ring carbons found in the $^{13}\text{C}$ NMR spectra confirmed the cyclisation of $\text{9}$ to 1,2-oxaphospholane derivatives. The $^1\text{H}$ and $^{13}\text{C}$ NMR spectra of $\text{13a}$ and $\text{13b}$ showed neither the $\text{CH}_3\text{OP}$ doublet nor the additional resonances of the $\text{Me—N}$ group.

The relative configurations of the diastereomeric pairs $\text{10b-11b}$, $\text{10c-11c}$, and $\text{10d-11d}$ were deduced mostly from the $^1\text{H}$ NMR spectra. In $\text{11b}$ the $\text{CH}_3—\text{C(3)}—\text{P}$ group was deshielded by the $\text{P=O}$ bond [14] with respect to that in $\text{10b}$. This differentiation was attributed to the cis configuration of the $\text{CH}_3—\text{C(3)}$ ans $\text{P=O}$ groups in $\text{11b}$. Furthermore, the $^{13}\text{C}$-resonance of the $\text{CH}_3—\text{C(3)}$ nucleus of $\text{10b}$ was shifted upfield by 1.56 ppm relative to that in $\text{11b}$.

As before [9], we assumed that the steric compression by the $\text{CH}_3\text{OP}$ group is operative, and it was concluded that in $\text{10b}$ the $\text{CH}_3—\text{C(3)}$ and $\text{CH}_3\text{O—P}$ groups are in the cis configuration. The introduction of the phenyl substituents into the 1,2-oxaphospholane ring made further assignments straightforward. In $\text{10c}$ and $\text{10d}$ the signals of the $\text{CH}_3—\text{OP}$ groups were shifted upfield by ca. 0.5 ppm in comparison to that of $\text{11c}$ and $\text{11d}$, respectively. On the basis of this effect [15], the cis arrangements of the $\text{CH}_3\text{O—P}$ and $\text{Ph—C(3)}$ groups in $\text{10c}$ and $\text{10d}$ were established.

Mechanistic considerations

The stereochemical results described in this paper together with our previous observations [3, 9, 10] allow us to suggest the following mechanism for the cyclisation of the $\delta$-hydrazonoalkyl phosphites $\text{9}$. The formation of the $\text{P—C}$ bond involves a water-promoted nucleophilic attack by the trivalent phosphorus on the $\text{C= N}$ bond to afford $\text{14}$, which is subsequently transformed into the non-charged species $\text{15}$ (Scheme 1). In $\text{15}$ the $\text{P—C}$ bond occupies the energetically unfavourable apical position [16]. Two independent pseudorotations with the methoxy groups acting as pivots give the stable intermediates $\text{16A}$ and $\text{16B}$ having all substituents around phosphorus located in the energetically favourable positions [16, 17]. The elimination of methanol from the apical positions of $\text{16A/16B}$ affords a pair of diastereomers, $\text{10}$ and $\text{11}$, respectively, while breaking of the appropriate endocyclic $\text{P—O}$ bond gives the ring-opened products $\text{12}$. In our experiments a significant excess of $\text{10}$ over $\text{11}$ was observed for $\text{b, c}$, and $\text{d}$. These results allow us to suggest that the decomposition of $\text{16}$ is a diastereodifferentiating process and $\text{16A}$ reacts faster than $\text{16B}$ because the hydrogen bond $\text{P=O—H—N}$ is being formed.

Facile cyclisation of $\text{9g}$ and the lack of reactivity of $\text{9f}$ could be explained on the grounds of...
Finally, we would like to comment on hydrolysis of the substituted (β,β-dimethylhydrazino)-2-methoxy-2-oxo-1,2-oxaphospholanes. The formation of 13 via the exocyclic cleavage of the MeO—P group in 10–11a, 10b, and most likely 10–11g is in contrast with the ring opening of 2-methoxy-2-oxo-1,2-oxaphospholane observed by Denis and Westheimer [22], but it is consistent with the recent results of Macomber [23] for hydrolysis of 5,5-dimethyl-2-methoxy-2-oxo-1,2-oxaphospholene-3. Taking into account the stability of 2A towards hydrolysis [24] and lack of the third methyl substituent in the hydrazino group in 13b it is possible that under the comparable conditions the 3-(β,β-dimethylhydrazino) analogue 10b undergoes the hydrazino-nitrogens assisted hydrolysis. However, this suggestion requires further studies.

Experimental
The instrumentation and general procedures were the same as described earlier [9]. G.l.c. analysis of 8b was carried out on 3% XE 60 on a Chromosorb W column at 90° under N₂ pressure of 1.7 atm.

Acetaldol N,N-dimethylhydrazone (8a)
To a solution of freshly distilled acetaldol (10.7 g, 0.121 mole) in benzene (50 ml) cooled in an ice-water bath, N,N-dimethylhydrazine (10.5 ml, 0.135 mole) was added dropwise. The reaction mixture was stirred at 20 °C for 4 h. Water was separated and the benzene solution was dried over MgSO₄. The crude product was distilled to give 8a (14.0 g, 89%) as a colorless oil of b.p. 65 °C/2 mm.

\[ ^1H \text{NMR (CDCl}_3 \text{)} \delta (\text{ppm}): 1.18 (d, J = 6.4 \text{ Hz}, 3H, \text{CH}_3-\text{CH}), 2.32 (dd, J = 5.0 \text{ Hz}, J = 6.4 \text{ Hz}, 2H, \text{CH}_3), 2.72 (s, 6H, Me₂N), 3.97 (q, J = 6.4 \text{ Hz}, \text{MeO}) \]

Stereochemistry. From the crystallographic data published for 1,2-oxaphospholanes [18–20] P—C bond lengths of ca. 1.8 Å could be expected for 10–11g and 10–11f. In 9g the substituents able to close the 1,2-oxaphospholane ring occupy the equatorial and axial positions of the 1,3-dioxane ring. The distance between the P and C reactant centers is 1.9 Å as measured from the corresponding Dreiding model. For the closure of the 1,2-oxaphospholane and 1,3-dioxane ring system of the cis configuration only a slight twist of the 1,3-dioxane chair in 10–11g is required to compensate the ring strain. On the other hand, in 9f the substituents occupy the equatorial positions of the conformationally rigid 1,3-dioxane ring. The reacting centers are 2.2 Å apart. This distance is sufficient enough to prevent cyclisation. Such a rationale is in agreement with general observations that cis-fused 5- and 6-membered rings are readily formed [21].
A magnetically stirred slurry of diacetone alcohol (5.0 ml, 40 mM), N,N-dimethyldihydrazine (3.0 ml, 40 mM), chloroform (30 ml) and anhydrous MgSO\textsubscript{4} (2 g) was refluxed for 10 h. After removal of drying agent and solvent a fraction of b.p. 42–50 °C/2 mm was collected, which contained ca. 5% (by g.l.c.) of untreated diacetone alcohol. This fraction was treated with N,N-dimethylhydrazine (1 ml) as above to give after distillation 8b (4.0 g, 63%) as a colorless oil of b.p. 35–36 °C.

3-Hydroxy-3-methylbutyrophenone
N,N-dimethylhydrazone (8c)

To a solution of BuLi (7.5 ml, 12 mM) in THF (30 ml) cooled to −70 °C acetoephone N,N-dimethyldihydrazine [25] (1.62 g, 10 mM) was added dropwise. After 30 min acetone (0.75 ml, 10 mM) was injected. The reaction mixture was stirred at −70 °C for 30 min and allowed to warm to 20 °C. Ether (100 ml) was added and the organic layer was washed consecutively with cold water, NH\textsubscript{4}Cl aq., water and dried. Evaporation of solvents left crude 8c (2.2 g, 99%) as a yellowish oil.

IR (KBr): 3430, 1600.

3,3-Diphenyl-3-hydroxypropiophenone
N,N-dimethylhydrazone (8d)

This compound was obtained from acetoephone N,N-dimethyldihydrazine (2.8 g, 17.2 mM) and benzophenone (3.1 g, 17.0 mM) in a similar way as described for 8c. Evaporation of solvents left a solid which after crystallization from benzene/hexane gave 8d (2.86 g, 48%) of m.p. 125–126 °C.

IR (KBr): 3406, 1610.

3-Hydroxy-3-phenylpropiophenone
N,N-dimethylhydrazone (8e)

This compound was prepared from acetoephone N,N-dimethyldihydrazine (5.2 g, 32 mM) and benzaldehyde (3.4 ml, 32 mM) as described for 8c. Evaporation of solvents left crude 8e (7.9 g, 92%) as a yellowish oil.

IR (KBr): 3400, 1610.

Diacetone alcohol N,N-dimethyldihydrazone (8b)

A magnetically stirred slurry of diacetone alcohol (5.0 ml, 40 mM), N,N-dimethyldihydrazine (3.0 ml, 40 mM), chloroform (30 ml) and anhydrous MgSO\textsubscript{4} (2 g) was refluxed for 10 h. After removal of drying agent and solvent a fraction of b.p. 42–50 °C/2 mm was collected, which contained ca. 5% (by g.l.c.) of untreated diacetone alcohol. This fraction was treated with N,N-dimethyldihydrazine (1 ml) as above to give after distillation 8b (4.0 g, 63%) as a colorless oil of b.p. 35–36 °C.

3-Hydroxy-3-phenylpropiophenone
N,N-dimethylhydrazone (8f)

This compound was obtained from acetoephone N,N-dimethyldihydrazine (2.8 g, 17.2 mM) and benzaldehyde (3.4 ml, 32 mM) as described for 8c. Evaporation of solvents left crude 8f (2.2 g, 85%) as a yellowish oil.

2,4-O-Benzylidene-D-threose
N,N-dimethylhydrazone (8g)

This hydrazone was obtained from crude 2,4-O-benzylidene-D-threose [27] (2.7 g, 13.0 mM) and N,N-dimethyldihydrazine (0.99 ml, 13.0 mM) in ethanol (25 ml), treated similarly as described for 8f. After chromatography on the silica gel column and crystallization from chloroform-hexanes 8g was obtained as colorless needles of m.p. 97–98 °C and [\(\alpha\)\text{D}]\text{18} –66.8° (c 1.57, chloroform).

IR (KBr): 3430, 1620.

Analysis for C\textsubscript{9}H\textsubscript{18}N\textsubscript{2}O\textsubscript{3}

Calcd C 51.04 H 8.57 N 14.89
Found C 51.24 H 8.60 N 14.86.

2,4-O-Ethylidene-D-erythrose
N,N-dimethylhydrazone (8f)

To a solution of crude 2,4-O-ethylidene-D-erythrose [26] (2.0 g, 13.7 mM) in ethanol (25 ml), N,N-dimethyldihydrazine (1.1 ml, 14.5 mM) was added and the reaction mixture was left overnight. Solvent was evaporated and a solid was extracted with benzene (3×20 ml). Benzene was evaporated leaving 8f (2.2 g, 85%) as a yellow solid. After filtration through a pad of silica gel and crystallisation from chloroform-hexanes 8f was obtained as colorless needles of m.p. 97–98 °C and [\(\alpha\)\text{D}]\text{18} –66.8° (c 1.57, chloroform).

IR (KBr): 3420, 1620.

Analysis for C\textsubscript{9}H\textsubscript{18}N\textsubscript{2}O\textsubscript{3}

Calcd C 51.04 H 8.57 N 14.89
Found C 51.24 H 8.60 N 14.86.

2,4-O-Benzylidene-D-threose
N,N-dimethylhydrazone (8g)

This hydrazone was obtained from crude 2,4-O-benzylidene-D-threose [27] (2.7 g, 13.0 mM) and N,N-dimethyldihydrazine (0.99 ml, 13.0 mM) in a similar way as described for 8f. After chromatography on the silica gel column and crystallization from chloroform-hexanes 8g was obtained. This hydrazone was described as described for 8f. After chromatography on the silica gel column and crystallization from chloroform-hexanes 8g was obtained.

IR (KBr): 3406, 1610.

Analysis for C\textsubscript{9}H\textsubscript{18}N\textsubscript{2}O\textsubscript{3}

Calcd C 51.04 H 8.57 N 14.89
Found C 51.24 H 8.60 N 14.86.

2,4-O-Benzylidene-D-threose
N,N-dimethylhydrazone (8g)

This hydrazone was obtained from crude 2,4-O-benzylidene-D-threose [27] (2.7 g, 13.0 mM) and N,N-dimethyldihydrazine (0.99 ml, 13.0 mM) in a similar way as described for 8f. After chromatography on the silica gel column and crystallization from chloroform-hexanes 8g was obtained. This hydrazone was obtained. This hydrazone was obtained. This hydrazone was obtained.
Preparation of the phosphites 9a–g.

General procedure

To the solution of 8a (13.0 g, 0.1 mole) and triethylamine (14.3 ml, 0.11 mole) in benzene (80 ml), O–O-dimethyl phosphorochloridite [28] (13.5 g, 0.0105 mole) was added dropwise at 7°C. The reaction mixture was stirred for 2 h, filtered, and the filtrate evaporated. The crude product was used directly or was distilled to give 9a (15.4 g, 69%) as a colorless oil of b.p. 66–88 °C/0.2 mm.

1H NMR (CDCl3): 1.28 (d, J = 6.2 Hz, 3H, CH3–CH), 2.46 (t, J = 5.8 Hz, 2H, CH2), 2.72 (s, 6H, Me2N), 3.47 (d, J = 10.0 Hz, 6H, MeOPOMe), 4.40 (dx, J = 9.0 Hz, J = 6.2 Hz, 1H, HCOP), 6.63 (t, J = 5.6 Hz, 1H, HC=N).

31P NMR (CDCl3): 39.4.

In a similar manner the following phosphites were prepared:

9b: colorless oil, yield 71%, b.p. 65–67 °C/0.1 mm.

1H NMR (CDCl3): 1.41 (s, 6H, Me2C), 2.03 (s, 3H, CH3C=), 2.41 (s, 6H, Me2N), 2.46 (s, 2H, CH2), 3.43 (d, J = 10.0 Hz, 6H, MeOPOMe).

31P NMR (CDCl3): 136.0.

9c: yellow oil, crude.

1H NMR (CDCl3): 1.35 (s, 6H, Me2C), 2.47 (s, 6H, Me2N), 3.21 (d, J = 10.0 Hz, 6H, MeOPOMe), 3.31 (m, 2H, CH2), 7.1–7.9 (m, 5H, Ph).

31P NMR (CDCl3): 135.0.

9d: yellow viscous oil, crude.

1H NMR (CDCl3): 2.13 and 2.28 (2 s, 6H, MeNMe), 3.03 and 3.17 (2 d, J = 10.0 Hz, 6H, MeOPOMe), 4.30 (s, 2H, CH2), 7.0–7.8 (m, 15H, Ph).

31P NMR (CDCl3): 137.6 and 137.4.

9e: yellow viscous oil, crude.

1H NMR (CDCl3): 2.38 (s, 6H, Me2N), 3.13 and 3.17 (2 d, J = 10.3 Hz, 6H, MeOPOMe), 3.38 (d, J = 7.0 Hz, 2H, CH2), 5.40 (dt, J = 9.0 Hz, J = 7.0 Hz, 1H, HCOP), 7.0–7.7 (m, 10H, Ph).

31P NMR (CDCl3): 139.9.

9f: yellow viscous oil, crude.

1H NMR (CDCl3): 1.28 (d, J = 6.0 Hz, 3H, CH1–CH2), 2.82 (s, 6H, Me2N), 3.40 and 3.43 (2 d, J = 10.0 Hz, 6H, MeOPOMe), 3.3–4.3 (m, 4H, H2–3,4a,4b), 4.74 (q, J = 6.0 Hz, 1H, HC–CH3), 6.37 (d, J = 6.0 Hz, 1H, H-1).

31P NMR (CDCl3): 139.6.

9g: yellow viscous oil, crude.

1H NMR (CDCl3): 2.77 (s, 6H, Me2N), 3.50 (d, J = 10.5 Hz, 6H, MeOPOMe), 3.95–4.55 (m, 4H, H–2,3,4a,4b), 5.60 (s, 1H, HCOP), 6.65 (d, J = 6.0 Hz, 1H, H–1), 7.2–7.7 (m, 5H, Ph).

31P NMR (CDCl3): 146.8.

Synthesis of substituted 1,2-oxaphospholanes 10–11.

General procedure

To the phosphites 9a–g, neat or as a solution in dry THF (ca. 4 M), an equimolar amount of water was added dropwise at room temperature. The reaction mixtures were stirred until the 31P NMR resonance of the phosphites disappeared. The crude products were distilled in vacuo or purified on silica gel. Column chromatography on silica gel was also employed for separation of diastereomers 10 and 11.

10a/11a: colorless oil, yield 83%, b.p. 100–105 °C/0.1 mm.

31P NMR (CCl4): 43.0, 42.3, 40.9, 39.2.

IR (neat): 3210, 1770, 1260.

10b: yield 55%, m.p. 42–43 °C, b.p. 79–81 °C/0.05 mm.

1H NMR (CDCl3): 1.40 and 1.56 (2 s, 6H, Me2C), 1.45 (d, J = 15.5 Hz, 3H, CH2–C–3), 1.8–2.5 (m, 2H, CH2), 2.52 (s, 6H, Me2N), 3.80 (d, J = 10.7 Hz, 3H, MeOP).

13C NMR (CDCl3): 20.54 (d, J = 3.3 Hz, CH1–C–3), 30.26 and 30.52 [29] (2 d, H2–C–C–5–CH3), 47.24 (d, J = 7.0 Hz, C–4), 50.04 (s, Me2N), 52.00 (d, J = 6.6 Hz, H2COP), 58.00 (d, J = 130.5 Hz, C–3), 79.62 (d, J = 7.3 Hz, C–5).

31P NMR (CDCl3): 42.9.

IR (neat): 3230, 1670, 1260.

Analysis for C10H14PSO3

Calcd C 45.75 H 8.96 N 11.86 P 13.11


11b: yield 7%, colorless oil.

1H NMR (CDCl3): 1.44 (s, 6H, Me2C), 1.59 (d, J = 15.8 Hz, 3H, CH2–C–3), 1.9–2.2 (m, 2H, CH2), 2.48 (s, 6H, Me2N), 3.82 (d, J = 10.4 Hz, MeOP).

13C NMR (CDCl3): 22.10 (d, J = 4.4 Hz, H2C–C–3), 31.10 (s, H2C–C–5–CH3), 49.84 (d, J = 10.3 Hz, C–4), 50.35 (s, Me2N), 52.62 (d, J = 7.4 Hz, H2COP), 58.31 (d, J = 129.4 Hz, C–3), 79.04 (d, J = 6.6 Hz, C–5).

31P NMR (CDCl3): 41.7.

10c/11c: very sick yellowish oil, yield 36%, b.p. 160–170 °C (bath)/0.1 mm.

10c: colorless oil.

1H NMR (CDCl3): 1.47 and 1.71 (2 s, 6H, Me2C), 2.06 (s, 6H, Me2N), 2.4–3.2 (m, 2H, CH2), 3.50 (d, J = 10.6 Hz, 3H, MeOP), 7.2–7.5 (m, 5H, Ph).

31P NMR (CDCl3): 39.4.
11c: colorless oil.

$^1$H NMR (CDCl$_3$): 1.39 and 1.60 (2 s, 6 H, Me$_2$C), 2.07 (s, 6 H, Me$_2$N), 2.45–3.0 (m, 2 H, CH$_2$), 4.00 (d, $J = 10.6$ Hz, 3 H, MeOP), 7.2–7.5 (m, 5 H, Ph).

$^{31}$P NMR (CDCl$_3$): 38.9.

10d: yield 31%, m.p. 155–156°C.

$^1$H NMR (CDCl$_3$): 1.41 (s, 6 H, Me$_2$N), 3.43 (d, $J = 10.6$ Hz, 3 H, MeOP), 3.4–4.3 (m, 2 H, CH$_2$), 6.8–7.7 (m, 15 H, Ph).

$^{31}$P NMR (CDCl$_3$): 38.1.

IR (KBr): 3420, 1620, 1260.

Analysis for C$_{24}$H$_{27}$N$_2$O$_5$P

Caled C 68.02 H 6.44 N 6.53 P 7.36.

Found C 68.02 H 6.44 N 6.53 P 7.36.


$^1$H NMR (CDCl$_3$): 1.68 (s, 6 H, Me$_2$N), 3.4–4.1 (m, 2 H, CH$_2$), 4.06 (d, $J = 10.9$ Hz, 3 H, MeOP), 7.1–7.6 (m, 15 H, Ph).

$^{31}$P NMR (CDCl$_3$): 39.0.

IR (KBr): 3420, 1620, 1260.

Synthesis of the salts 13.

A representative procedure for 3-(β,β-dimethylhydrazino)-2-hydroxy-5-methyl-2-oxo-1,2-oxaphospholane (13a)

A mixture of diastereomers 10–11a (3.9 g, 18.7 mM) was kept at room temperature for 7 months. The residue was suspended in chloroform, filtrated and washed with chloroform to give 13a (1.22 g, 31%) as a white amorphous solid.

$^1$H NMR (CD$_2$OD): 1.32 and 1.34 (2 d, $J = 6.0$ Hz, 3 H, CH$_3$–C–5, ratio 5:1), 1.8–2.2 (m, 2 H, CH$_2$), 3.03 and 3.05 (2 s, 3 H, Me$_2$N, ratio 1:5), 3.5–3.7 (m, 1 H, H–C–3), 4.2–4.5 (m, 1 H, H–C–5).

$^{13}$C NMR (CD$_2$OD): major diastereomer: 22.33 (d, $J = 6.3$ Hz, CH$_3$–C–5), 39.45 (d, $J = 3.9$ Hz, C–4), 45.43 (s, Me$_2$N), 49.58 (d, $J = 122.6$ Hz, C–3), 72.85 (d, $J = 6.3$ Hz, C–5); minor diastereomer: 23.02 (d, $J = 6.8$ Hz, CH$_3$–C–5), 39.27 (d, $J = 3.9$ Hz, C–4), 45.71 (s, Me$_2$N), 51.11 (d, $J = 121.1$ Hz, C–3), 71.18 (d, $J = 5.8$ Hz, C–5).

$^{31}$P NMR (CD$_2$OH): 34.0 and 30.4 (ratio 5:1).

IR (KBr): 2700, 1620, 1260.

Analysis for C$_9$H$_{12}$N$_2$O$_5$P

Caled C 36.89 H 7.76 N 14.35 P 15.50.

Found C 36.89 H 7.76 N 14.35 P 15.50.

13b: yield 16%, white amorphous solid.

$^1$H NMR (CD$_2$OD): 1.36 and 1.43 (2 s, 6 H, Me$_2$C–5), 1.53 (d, $J = 12.5$ Hz, 3 H, MeC–3), 1.9–2.1 (m, 2 H, CH$_2$), 3.09 (s, 6 H, Me$_2$N).

$^{13}$C NMR (CD$_2$OD): 22.68 (d, $J = 4.4$ Hz, CH$_3$–C–3), 31.42 and 31.75 (29) (2 d, $J = 3.4$ Hz, H$_3$C–C–5–CH$_3$), 49.33 (s, Me$_2$N), 51.63 (d, $J = 5.9$ Hz, C–4), 57.79 (d, $J = 127.0$ Hz, C–3), 77.41 (d, $J = 4.4$ Hz, C–5).

$^{31}$P NMR (CH$_2$OH): 32.2.

IR (KBr): 2700, 2400, 1620, 1210.

The author is very much indebted to Professor R. Bodalski of this Institute for encouragement and stimulating discussions. Technical assistance of Mr. P. Graczyk in preparation of 8g, 9g and 10–11g is gratefully acknowledged. This work was partially supported by grant MR. I. 12. from the Polish Academy of Sciences.

[29] Chemical shifts as well as coupling constants to phosphorus could not be unequivocally determined from the 22.63 MHz spectrum.