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# Synthesis of Dimethyl 4-Thiazolidinylphosphine Oxides via Addition of Dimethylphosphine Oxide to 3-Thiazolines

Harald Gröger, Davoud Tehranfar, and Jürgen Martens*

*Fachbereich Chemie, Universität Oldenburg, Postfach 2503, D-26111 Oldenburg, Germany*

Jens R. Goerlich, Holger Thönnessen, Peter G. Jones, and Reinhard Schmutzler*

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

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## ABSTRACT

*The addition of dimethylphosphine oxide and its trimethylsiloxyphosphorus(III) derivative, generated in situ, to 3-thiazolines was found to yield dimethyl 4-thiazolidinylphosphine oxides via three different synthetic routes. The structures of two products were confirmed by X-ray analysis; common features include approximate envelope conformations of the five-membered rings and hydrogen bonding of the form N–H···O=P.* *© 1997 John Wiley & Sons, Inc.* *Heteroatom Chem* **8***: 207–215, 1997.*

## *INTRODUCTION*

Although the biological activity of α-aminophosphorus compounds [1–6] and their utility, e.g. as herbicides (e.g., Glyphosate) [1,2], have been described in detail, until now most of the work has been focussed on the synthesis and investigation of α-aminophosphonic acids and their derivatives [7–17], whereas much less is known about the corresponding α-aminophosphine oxides [18–20]. In the course of our studies of the addition of dimethylphosphine oxide to C=O and C=N double bonds [20–23] and of the synthesis of 4-thiazolidinylphosphonates and derivatives [24–26], we now wish to describe the syntheses of several new 3-thiazolines and their dimethylphosphine oxide adducts. Such α-aminophosphine oxides may be interesting substitutes for proline and other cyclic amino acids in the C-terminal position of peptides.

## *RESULTS AND DISCUSSION*

According to a method described in the literature [7,38], the 3-thiazolines **1a**–**h** were synthesized from α-chloro- or α-bromoaldehydes, ammonia, sodium hydrogen sulfide, and a second carbonyl component (Scheme 1).

The reactivity of C=O and C=N double bonds toward nucleophiles is strongly influenced by the electron density at the carbon atom [27,28]. Because of the electron richness of the 3-thiazoline system and the lower polarity of the C=N compared to that of the C=O bond, no reaction occurred when mixtures of 3-thiazolines with dimethylphosphine

*To whom correspondence should be addressed.
Dedicated to Professor Louis D. Quin on the occasion of his retirement from the University of Massachusetts.


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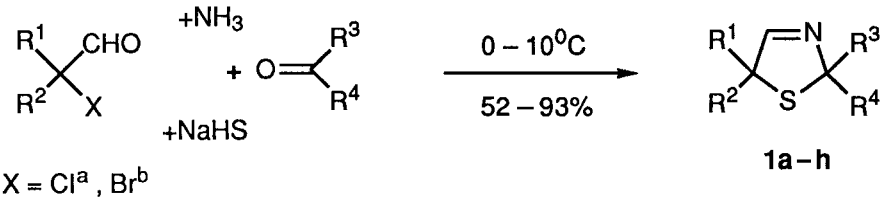
**SCHEME 1** Synthesis of 3-Thiazolines **1a**–**1h**




| *1* | $R^1$ | $R^2$ | $R^3$ | $R^4$ | *Yield*[c] | *Ref.* |
|---|---|---|---|---|---|---|
| **a** | $CH_3$ | $CH_3$ | $CH_3$ | $CH_3$ | 71 | [23] |
| **b** | $CH_3$ | $CH_3$ | -$(CH_2)_4$- | | 52 | [7] |
| **c** | $CH_3$ | $CH_3$ | -$(CH_2)_5$- | | 56 | [7] |
| **d** | $C_2H_5$ | $C_2H_5$ | $C_2H_5$ | $C_2H_5$ | 75 | — |
| **e** | $C_2H_5$ | $C_2H_5$ | -$(CH_2)_4$- | | 53 | — |
| **f** | -$(CH_2)_5$- | | $CH_3$ | $CH_3$ | 93 | [35] |
| **g** | -$(CH_2)_5$- | | $CH(CH_3)_2$ | H | 90 | — |
| **h** | -$(CH_2)_5$- | | -$(CH_2)_4$- | | 50 | — |

[a] In the case of **1a**–**e**.
[b] In the case of **1f**–**h**.
[c] In %.

oxide were stirred at room temperature, whereas the spontaneous addition of the latter to the C=O bond in aldehydes and ketones is well known [22,29].

In our case, the addition of dimethylphosphine oxide to the C=N bond in **1a**–**h** was achieved using three methods (Scheme 2). The use of equimolar amounts of potassium *tert*-butylate as a base [30,31] led to the generation of phosphinate anions, which added readily to the C=N bond (method **A**). In the case of **1f**, the resulting potassium salt was isolated as a colorless, hygroscopic solid [32]. Subsequent treatment with water furnished the free adducts **2e**–**h**.

As known for the preparation of dialkylphosphite adducts of 3-thiazolines [7], an alternative route to 4-thiazolidinyldimethylphosphine oxides **2** was provided by the thermally induced addition of dimethylphosphine oxide to the C=N bond in the case of **1b**,**c**,**e** and g (method **B**).

Good yields of adducts **2a**,**c**,**d** and g (Table 1) were obtained under mild reaction conditions when dimethylphosphinous trimethylsilyl ester [33,34] was generated in the first step, followed by treatment with 3-thiazolines and subsequently with water (method **C**) [35].

The chiral 3-thiazoline **1g** was employed in order to investigate the diastereoselectivity in addition reactions of dimethylphosphine oxide. We expected the best diastereoselectivities in the case of methods **A** and **C**, because of the relatively mild reaction conditions. Surprisingly, we found in all cases similar diastereomeric ratios with *dr* values between 63:37 and 69:31. The best result with *dr* = 69:31 was obtained using method **A** (Scheme 3).

## *X-RAY STRUCTURE DETERMINATIONS*

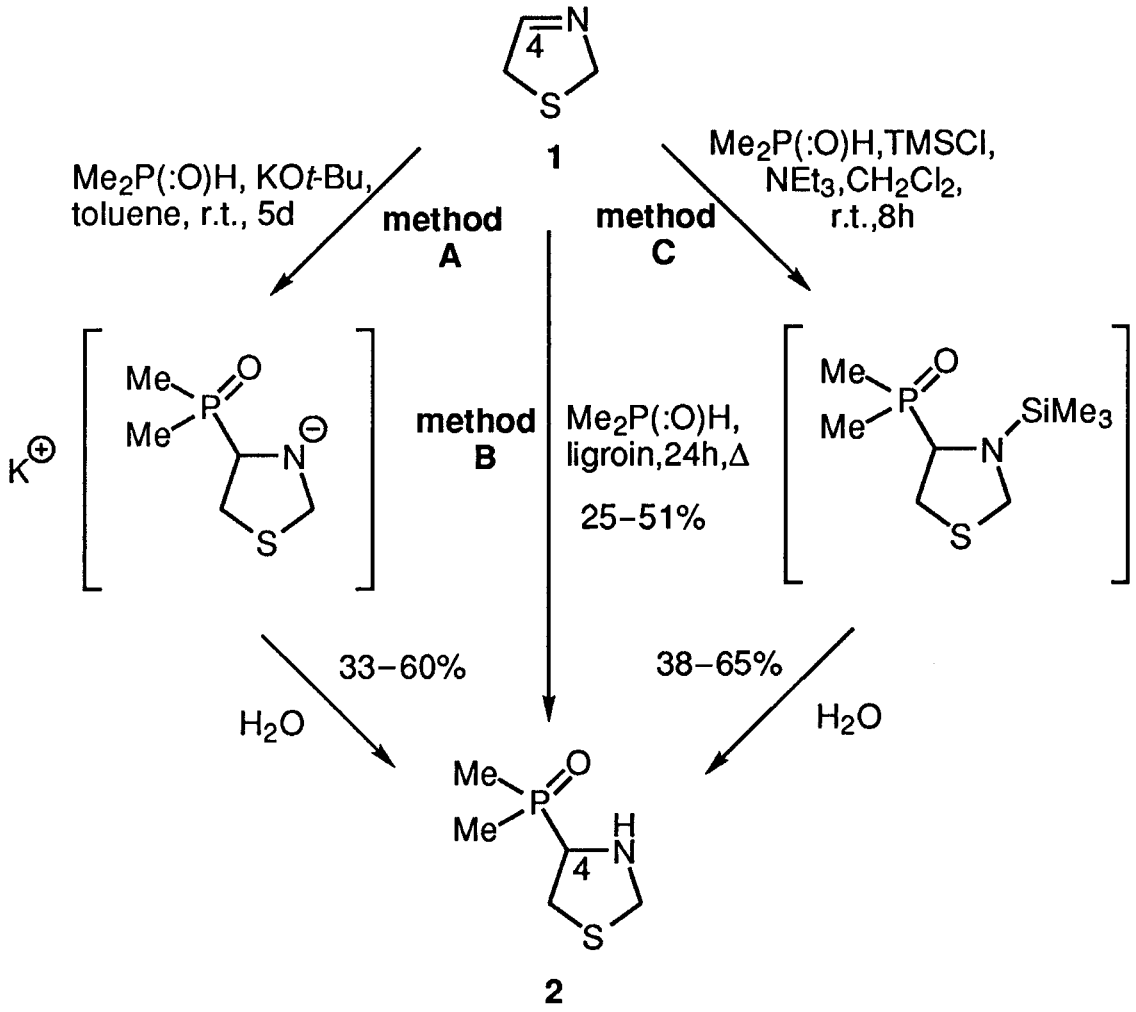
Compound **2c** (Figure 1) crystallizes in the orthorhombic space group *Fdd*2 [36]. The heterocyclic system displays an approximate envelope conformation, with C3 56 pm outside a plane through S, N, C4, and C7 (mean deviation 4.7 pm). The cyclohexyl group displays the expected chair conformation.

The phosphorus atom shows the expected distorted tetrahedral coordination, with the largest compression for the angle C2–P–C3 [102.6(2)°]. The largest bond angles at phosphorus, arising from the increased steric demand of the P=O double bond, are observed for O–P–C2 and O–P–C1 [113.6(2)°].

Weak intermolecular hydrogen bonding of the type N–H1···O [N···O 316.4(4) pm, N–H1···O 157(4)°, O at 1/4 + $x$, 1/4 − $y$, 1/4 + $z$] links the molecules in chains parallel to the $x$ axis.

Compound **2h** (Figure 2) crystallizes in the orthorhombic space group $Pca2_1$, with two independent molecules in the asymmetric unit [36]. Because they differ only slightly, only one of the two independent molecules will be discussed (Table 2).

In contrast to **2c**, the nitrogen atom is situated 57 pm outside the plane of the remaining four atoms of the heterocycle (mean deviation 3 pm). The cyclo-




**SCHEME 2** Preparation of the Dimethyl 4-Thiazolidinylphosphine Oxides **2**

pentyl group also displays an envelope conformation, with C14 60 pm outside a plane through the remaining atoms (mean deviation 1.4 pm).

As for **2c**, chains of hydrogen-bonded molecules are observed (here parallel to the *y* axis): N–H1···O (0.5 + *x*, −*y*, −*z*) with N···O′ 317.8(3) pm, N–H1···O′ 163(2)° and N′–H1′···O (−0.5 + *x*, 1 − *y*, *z*) with N′···O 311.9(3) pm, N′–H1′···O 166(3)°.

## *EXPERIMENTAL*

Melting points were determined in an open capillary tube on a Dr. Linström instrument and are uncorrected. Elemental analyses were carried out on a Carlo Erba Stumentalione analyzer (MOD 1104). The $^{1}H$, $^{13}C$, and $^{31}P$ NMR spectra were recorded on a Bruker AM 300 spectrometer, in $CDCl_3$ as a solvent. The mass spectrometric data were recorded on a Finnigan-MAT 212 spectrometer (Datasystem SS 300). Compounds **1a** [7], **1b** [7], **1c** [7], and **1f** [38], and 2-chloro-2-ethylbutanal [39] and α-bromocyclohexyl carboxaldehyde [40] were prepared as described in the literature.

### *3-Thiazolines* **1a–h***: General Procedure*

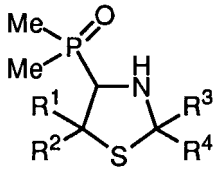
At a temperature between 0 and 10°C and with vigorous stirring, the α-chloro- or α-bromo aldehyde (0.30 mol), dissolved in 30 mL of dichloromethane, was added dropwise over 0.5 hours to a mixture of aqueous ammonia (25%, 65 mL), the corresponding second carbonyl compound (0.35 mol) and sodium hydrogen sulfide monohydrate (0.35 mol). Subsequently, dichloromethane (100 mL) was added, and the mixture was stirred overnight. The organic phase was separated, and the aqueous phase was extracted with dichloromethane (2 × 50 mL). Evaporation of the solvent of the dried recombined organic phases under reduced pressure led to the formation of a yellow oil, which was distilled in vacuo to give a col-

**TABLE 1** NMR Data of the Dimethylphosphine Oxide Adducts of the 3-Thiazolines **2a**–**2h**[a]

| | $\delta$ ($^1H$), J (Hz) | $\delta$ ($^{13}C$), J ($H_2$) | $\delta$ ($^{31}P$) |
|---|---|---|---|
| **2a** | 1.48–1.64 (m, 18H, $CH_3$), 3.07 (d, 1H, $^2J$ = 7.2 Hz, C4–H) | 16.95 (d, $^1J$ = 69.2 Hz, $CH_3PO$), 17.42 (d, $^1J$ = 67.1 Hz, $CH_3PO$), 28.81, 29.05 [C5($\underline{C}H_3)_2$], 31.97, 32.72 [C2($\underline{C}H_3)_2$], 62.31 (C5), 69.70 (d, $^1J$ = 71.7 Hz, C4), 74.08 (d, $^3J$ = 18.3 Hz, C2) | 41.02 |
| **2b** | 1.31–2.12 [m, 20H, $CH_3$, $(CH_2)_4$], 2.91 (d, 1H, $^2J$ = 7.2 Hz, C3–H) | 16.79 (d, $^1J$ = 68.8 Hz, $CH_3PO$), 17.27 (d, $^1J$ = 66.9 Hz, $CH_3PO$), 23.58, 24.04, 25.41, 40.98, 43.51 [$(CH_2)_4$], 28.73, 29.11 [C2($\underline{C}H_3)_2$], 60.78 (C2), 70.04 (d, $^1J$ = 72.1 Hz, C3), 83.13 (d, $^3J$ = 18.3 Hz, C5) | 41.20 |
| **2c** | 1.24–1.86 [m, 22H, $CH_3$, -$(CH_2)_5$-], 3.06 (d, 1H, $^1J$ = 7.1 Hz, C3–H) | 16.98 (d, $^1J$ = 69.7 Hz, $CH_3PO$), 17.47 (d, $^1J$ = 67.1 Hz, $CH_3PO$), 23.53, 25.16, 25.41, 40.98, 41.42 [$(CH_2)_5$], 28.97 [C2($\underline{C}H_3)_2$], 59.74 (C2), 68.64 (d, $^1J$ = 71.9 Hz, C3), 79.57 (d, $^3J$ = 17.5 Hz, C5) | 41.12 |
| **2d** | 0.84–1.09 (m, 12H, $CH_2\underline{C}H_3$), 1.58 (d, 3H, $^2J$ = 12.6 Hz, $CH_3\underline{P}O$), 1.59 (d, 3H, $^2J$ = 12.6 Hz, $CH_3\underline{P}O$), 1.63–2.02 (m, 8H, $C\underline{H}_2CH_3$), 2.56 (br d, 1H, $^3J$ = 9.1 Hz, NH), 3.17 (br dd, 1H, $^3J$ = 12.4 Hz, $^2J$ = 8.6 Hz, C4–H) | 9.33, 9.65, 9.87, 10.05 (4 × $CH_2\underline{C}H_3$), 17.26 (d, $^1J$ = 68.0 Hz, 2 × $CH_3PO$), 27.67, 32.43, 32.64, 33.85 (4 × $\underline{C}H_2CH_3$), 64.32 (d, $^1J$ = 72.0 Hz, C4), 70.37 (C5), 81.70 (d, $^3J$ = 17.4 Hz, C2) | 41.36 |
| **2e** | 1.00 (t, $^2J$ = 7.7 Hz, 3H, $CH_2\underline{C}H_3$), 1.03 (t, $^2J$ = 7.0 Hz, 3H, $CH_2\underline{C}H_3$), 1.43–2.14 [m, 18H, -$(CH_2)_4$-, $C\underline{H}_2CH_3$, $(CH_3)_2PO$], 3.06 (d, $^2J$ = 8.3 Hz, 1H, C3–H) | 9.99 (2 × $CH_2\underline{C}H_3$), 17.18 (d, $^1J$ = 66.9 Hz, $CH_3PO$), 17.27 (d, $^1J$ = 65.5 Hz, $CH_3PO$), 23.72, 24.14, 40.82, 43.46 [$(CH_2)_4$], 28.03, 32.80 [C2($\underline{C}H_2)_2$], 65.43 (d, $^1J$ = 72.7 Hz, C3), 71.31 (C2), 82.48 (d, $^3J$ = 18.3 Hz, C5) | 41.13 |
| **2f** | 1.27–1.64 [m, 22 H, $CH_3$, -$(CH_2)_5$-], 2.33 (d, $^3J$ = 0.28 Hz, 1H, NH), 3.08 (d, $^2J$ = 9.03 Hz, 1H, C4–H) | 16.78 (d, $^1J$ = 69.2 Hz, $CH_3PO$), 17.77 (d, $^1J$ = 67.6 Hz, $CH_3PO$), 23.45, 25.39, 27.50, 36.31, 39.38 [$(CH_2)_5$], 31.92, 32.52 [C2($\underline{C}H_3)_2$], 69.89 (d, $^1J$ = 73.1 Hz, C4), 70.53 (C5), 73.14 (d, $^3J$ = 19.5 Hz, C2) | 42.76 |
| **2g** | major diastereomer: 0.91–2.12 [m, 23H, $C\underline{H}(CH_3)_2$, $CH_3$, -$(CH_2)_5$-], 2.75 (d, $^2J$ = 7.9 Hz, 1H, C4–H), 4.33 (d, $^3J$ = 6.8 Hz, 1H, C2–H) | major diastereomer: 16.73 (d, $^1J$ = 68.4 Hz, $CH_3PO$), 17.84 (d, $^1J$ = 67.6 Hz, $CH_3PO$), 19.83, 20.39 [$CH(\underline{C}H_3)_2$], 23.41, 25.37, 27.40, 35.55, 39.27 [-$(\underline{C}H_2)_5$-], 33.80 [$\underline{C}H(CH_3)_2$], 67.18 (C5), 72.11 (d, $^1J$ = 73.2 Hz, C4), 74.75 (d, $^3J$ = 16.8 Hz, C2) | major diastereomer: 41.54 |
| | minor diastereomer: 0.91–2.12 [m, 23H, $C\underline{H}(CH_3)_2$, $CH_3$, -$(CH_2)_5$-], 2.85 (d, $^2J$ = 8.5 Hz, 1H, C4–H), 4.15 (d, $^3J$ = 9.0 Hz, 1H, C2–H) | minor diastereomer: 16.57 (d, $^1J$ = 67.9 Hz, $CH_3PO$), 17.75 (d, $^1J$ = 67.9 Hz, $CH_3PO$), 19.64, 20.25 [$CH(\underline{C}H_3)_2$], 23.76, 25.48, 27.28, 35.51, 38.92 [-$(\underline{C}H_2)_5$-], 37.25 [$\underline{C}H(CH_3)_2$], 67.88 (C5), 69.25 (d, $^1J$ = 74.0 Hz, C4), 74.80 (d, $^3J$ = 16.8 Hz, C2) | minor diastereomer: 42.63 |
| **2h** | 1.16–2.18 [m, 24H, $CH_3$, -$(CH_2)$-], 2.54–2.69 (m, 1H, NH), 2.89–2.96 (m, 1H, C14–H) | 16.84 (d, $^1J$ = 68.2 Hz, $CH_3PO$), 17.88 (d, $^1J$ = 67.7 Hz, $CH_3PO$), 23.69, 23.73, 24.20, 25.50, 27.58, 36.55, 39.51, 41.04, 43.51 [-$(CH_2)$-], 69.23 (C6), 70.52 (d, $^1J$ = 73.3 Hz, C14), 82.39 (d, $^3J$ = 19.03 Hz, C12) | 41.69 |

[a] $CDCl_3$; $\delta$ (ppm); J (Hz).

**SCHEME 3** Synthesized Dimethyl 4-Thiazolidinylphosphine Oxides **2**




**2a – 2h**

| *2* | $R^1$ | $R^2$ | $R^3$ | $R^4$ | *Method*[a] | *Yield*[b] | *dr*[c] |
|---|---|---|---|---|---|---|---|
| **a** | $CH_3$ | $CH_3$ | $CH_3$ | $CH_3$ | C | 50 | — |
| **b** | $CH_3$ | $CH_3$ | $-(CH_2)_4-$ | | B | 37 | — |
| **c** | $CH_3$ | $CH_3$ | $-(CH_2)_5-$ | | B | 51 | — |
| | | | | | C | 65 | — |
| **d** | $C_2H_5$ | $C_2H_5$ | $C_2H_5$ | $C_2H_5$ | C | 50 | — |
| **e** | $C_2H_5$ | $C_2H_5$ | $-(CH_2)_4-$ | | A | 38 | — |
| | | | | | B | 25 | — |
| **f** | $-(CH_2)_5-$ | | $CH_3$ | $CH_3$ | A | 35 | — |
| **g** | $-(CH_2)_5-$ | | $CH(CH_3)_2$ | H | A | 33 | 69:31 |
| | | | | | B | 36 | 68:32 |
| | | | | | C | 38 | 63:37 |
| **h** | $-(CH_2)_5-$ | | $-(CH_2)_4-$ | | A | 60 | — |

[a]The different methods are described in the Experimental section.
[b]In %.
[c]*dr* = diastereomeric ratio (determined from the $^{31}$P-NMR spectra of the crude products).

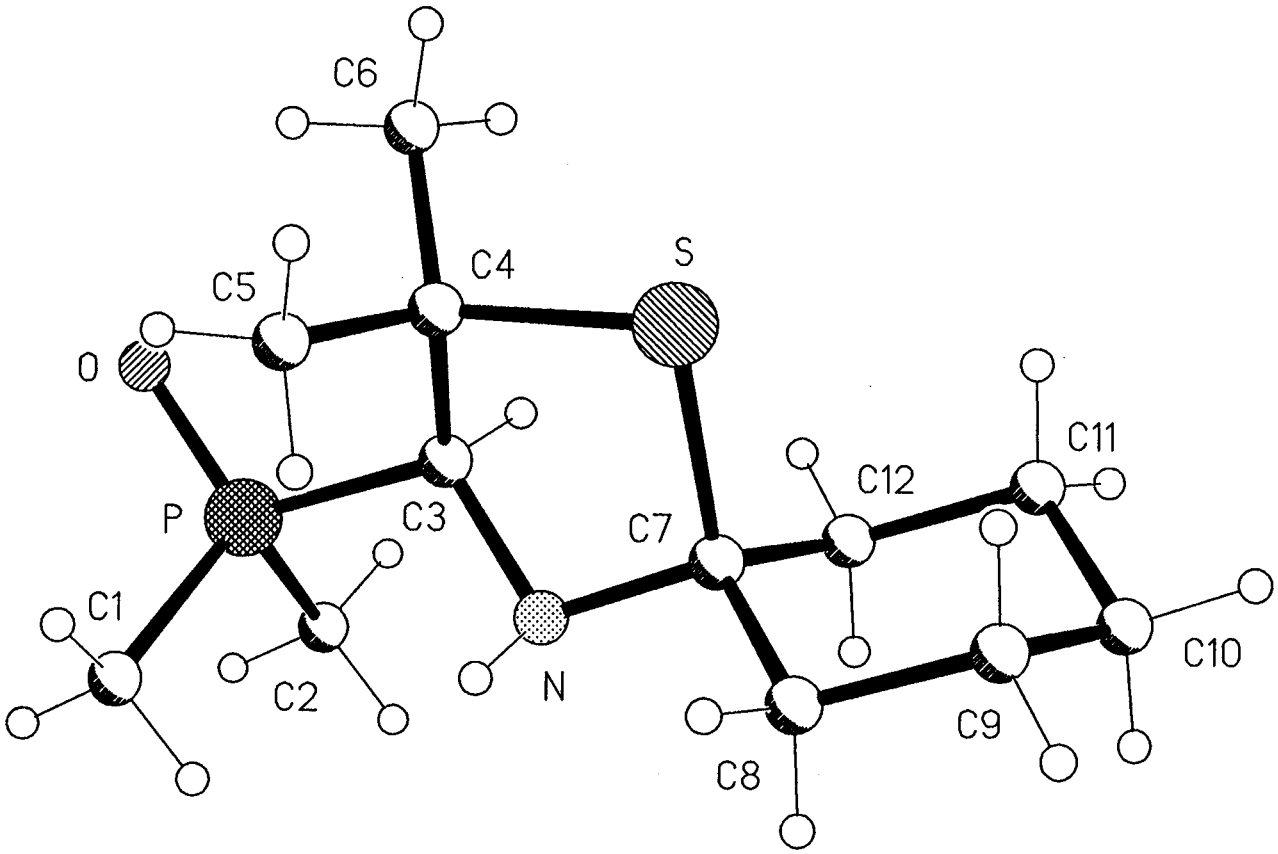



**FIGURE 1** Molecular structure of compound **2c**.

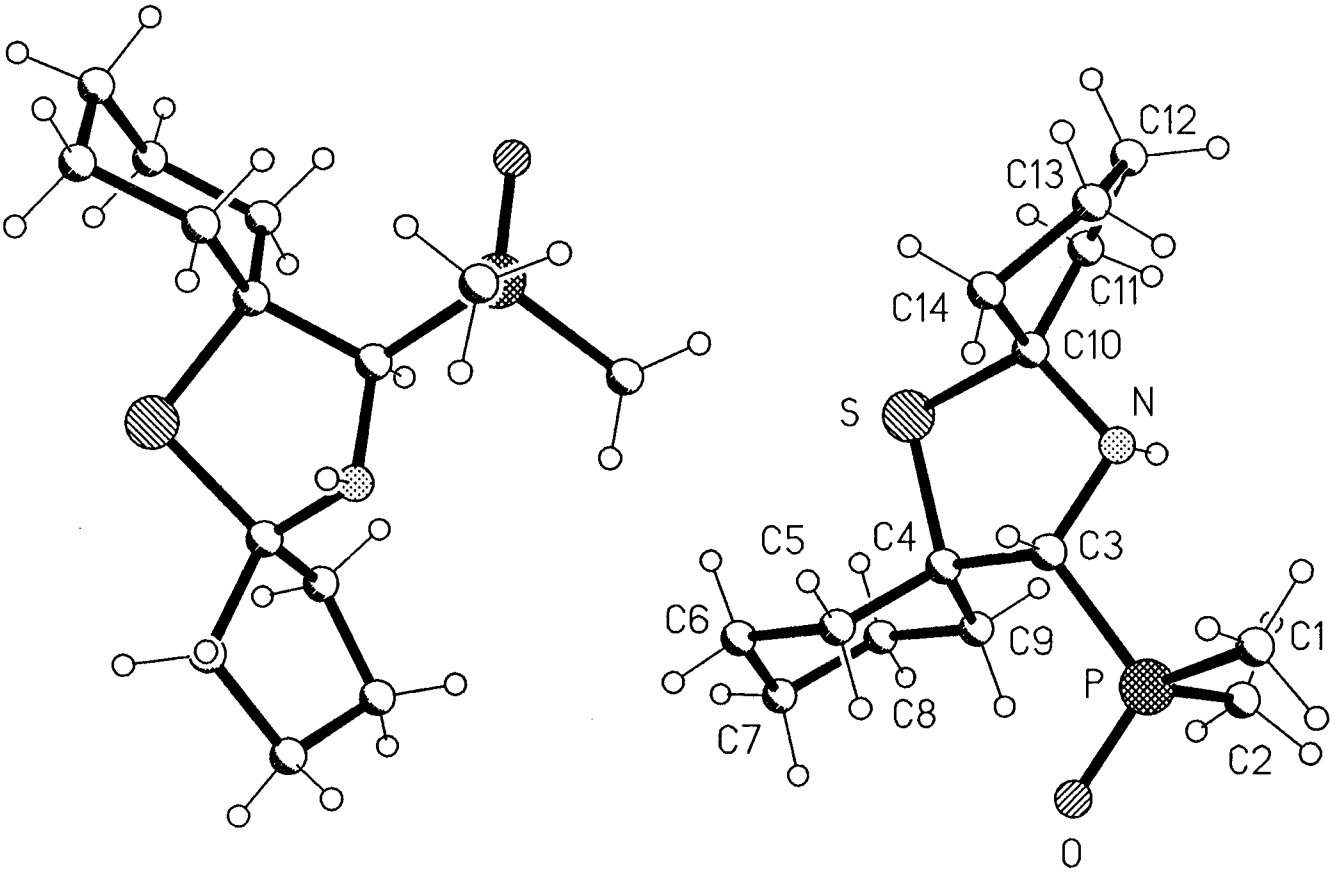



**FIGURE 2** Molecular structure of compound **2h** (two independent molecules).

orless liquid. The elemental analyses of **1** were not obtained because of the unpleasant smell of the 3-thiazolines **1**. The confirmation of the structure is based on spectroscopic data and on the characterization of the dimethylphosphine oxide adducts **2**.

### *2,2,5,5-Tetraethyl-3-thiazoline* (**1d**)

Prepared from 30.1 g (0.35 mol) of 3-pentanone and 40.4 g (0.30 mol) of 2-chloro-2-ethylbutanal; yield 29.9 g (75%); bp 58–60°C (0.08 mbar). $^1$H NMR ($CDCl_3$): $\delta$ = 0.87–0.95 [m, 12H, 4 × $CH_3$], 1.63–1.89 [m, 8H, 4 × $CH_2$], 6.82 [s, 1H, C4-H]. $^{13}$C NMR ($CDCl_3$): $\delta$ = 9.43, 9.45 [4 × $CH_3$], 31.71, 34.93 [4 × $CH_2$], 74.62 [C5], 97.37 [C2], 164.34 [C4]. MS (CI-isobutane): *m/z* (%) = 200 (100) [$MH^+$]. $C_{11}H_{21}NS$ (199.3).

### *2,2-Diethyl-1-thia-4-aza[4.4]non-3-ene* (**1e**)

Prepared from 29.4 g (0.35 mol) of cyclopentanone and 40.4 g (0.30 mol) of 2-chloro-2-ethylbutanal; yield 31.3 g (53%); bp 67–70°C (0.005 mbar). $^1$H NMR ($CDCl_3$): $\delta$ = 0.88 [t, $^3J$ = 7.4 Hz, 6H, 2 × $CH_3$], 1.68 [q, $^3J$ = 7.4 Hz, 4H, 2 × $C\underline{H}_2CH_3$], 1.65–2.11 [m, 8H, -$(CH_2)_4$-], 6.68 [s, 1H, C3–$\underline{H}$]. $^{13}$C NMR ($CDCl_3$): $\delta$ = 9.81 [2 × $CH_3$], 24.33, 31.91, 43.78 [6 × $CH_2$], 76.02 [C2], 96.97 [C5], 163.78 [C3]. MS (CI-isobutane): *m/z* (%) = 198 (100) [$MH^+$]. $C_{13}H_{19}NS$ (197.3).

### *2-Isopropyl-1-thia-3-aza-spiro[4.5]dec-4-ene* (**1g**)

Prepared from 5.3 g (0.074 mol) of isobutyraldehyde and 11.7 g (0.063 mol) of α-bromocyclohexyl aldehyde; yield 10.9 g (90%); bp 72–74°C (0.004 mbar). $^1$H NMR ($CDCl_3$): $\delta$ = 0.82–2.11 [m, 11H, C$\underline{H}$$(CH_3)_2$, -$(CH_2)_5$-], 0.89 [d, 3H, $^3J$ = 6.7 Hz, $CH_3$], 0.97 [d, 3H, $^3J$ = 6.8 Hz, $CH_3$], 5.46 [dd, 1H, $^4J$ = 2.6 Hz, $^3J$ = 5.5 Hz, C2–H], 7.00 [d, 1H, $^4J$ = 2.6 Hz, HC=N]. $^{13}$C NMR ($CDCl_3$): $\delta$ = 18.06, 19.58 [2 × $CH_3$], 23.93, 25.08, 37.35 [5 × $CH_2$], 34.61 [$\underline{C}$H$(CH_3)_2$], 71.05 [C5], 88.66 [C2], 167.18 [C=N]. MS (CI-isobutane): *m/z* (%) = 198 (100) [$MH^+$]. $C_{11}H_{19}NS$ (197.3).

### *7-Thia-13-aza-dispiro[5.1.4.2]tetradec-13-ene* (**1h**)

Prepared from 6.8 g (0.081 mol) of cyclopentanone and 13.1 g (0.069 mol) of α-bromocyclohexyl alde-

**TABLE 2** Crystallographic Data

| Compound | **2c** | **2h** |
|---|---|---|
| Formula | $C_{12}H_{24}NOPS$ | $C_{14}H_{26}NOPS$ |
| $M_r$ | 261.35 | 287.39 |
| Crystal size (mm) | 0.90 × 0.50 × 0.15 | 0.80 × 0.50 × 0.30 |
| Space group | *Fdd*2 | $Pca2_1$ |
| Temperature (°C) | −100 | −130 |
| Cell constants: | | |
| *a*(pm) | 2172.8(4) | 1701.7(2) |
| *b*(pm) | 3617.7(7) | 1134.90(14) |
| *c*(pm) | 709.97(14) | 1556.1(2) |
| *V*(nm³) | 5.581(2) | 3.0051 |
| *Z* | 16 | 8 |
| $D_x$ (Mg m$^{-3}$) | 1.244 | 1.270 |
| *F*(000) | 2272 | 1248 |
| $\mu$ (mm$^{-1}$) | 0.329 | 0.312 |
| $2\theta_{max}$(°) | 50 | 55 |
| No. of reflections: | | |
| measured | 3837 | 5788 |
| independent | 2461 | 4575 |
| $R_{int}$ | 0.0332 | 0.0240 |
| $wR(F^2)$ (all refl.) | 0.0983 | 0.0762 |
| *R*(*F*) (obs. refl.) | 0.0422 | 0.0291 |
| No. of parameters | 153 | 337 |
| Flack *x* parameter | 0.10(12) | −0.05(6) |
| *S* | 1.001 | 1.044 |
| Max. $\Delta/\sigma$ | <0.001 | <0.001 |
| Max. $\Delta\rho$(e nm$^{-3}$) | 186 | 355 |

hyde; yield 7.1 g (50%); bp 83–85°C (0.01 mbar). $^1$H NMR ($CDCl_3$): $\delta$ = 1.14–2.18 [m, 18H, -$(CH_2)_4$-, -$(CH_2)_5$-], 6.92 [s, 1H, HC=N]. $^{13}$C NMR ($CDCl_3$): $\delta$ = 24.08, 24.41, 25.09, 37.74, 44.24 [9 × $CH_2$], 72.11 [C6], 95.63 [C12], 164.60 [C=N]. MS (CI-isobutane): *m*/*z* (%) = 210 (100) [$MH^+$]. $C_{12}H_{21}NS$ (209.3).

## *Dimethylphosphine Oxide Adducts 2: General Procedures*

*Method A.* 3-Thiazoline **1** (5 mmol) and potassium *tert*-butylate (0.56 g, 5 mmol) were dissolved in dry toluene (50 mL) and a dimethylphosphine oxide solution (3.67 mL, 5 mmol, and 1.5 M in toluene) was slowly added dropwise at room temperature. After having been stirred for 5 days, the reaction mixture was hydrolyzed with water (10 mL) and neutralized with hydrochloric acid (1N). The organic phase was separated, and the aqueous phase was washed with toluene (3 × 10 mL). The combined organic extracts were dried with magnesium sulfate and separated from the solvent in vacuo. A colorless, viscous oil was formed, which crystallized at room temperature or, better, at 4°C in a refrigerator. The crystals were washed with petroleum ether 40/60 and dried in vacuo.

*Method B.* The 3-thiazoline **1** (5 mmol) and dimethylphosphine oxide (0.40 g, 5 mmol) were dissolved in 30 mL of ligroin and refluxed for 24 hours. Subsequently, the hot reaction mixture was separated from the oily residue and was left to crystallize at −28°C. Crystals formed after several days and were filtered off, washed with petroleum ether (40/60), and dried in vacuo.

*Method C.* Trimethylchlorosilane (0.35 mL, 2.75 mmol) was added dropwise in an inert gas atmosphere at 0°C to a solution of dimethylphosphine oxide (0.20 g, 2.5 mmol) and triethylamine (0.39 mL, 2.75 mmol) in dry dichloromethane (50 mL) so that the temperature did not exceed 5°C. After having been stirred for 15 minutes, the 3-thiazoline component 1 (2.5 mol), dissolved in 10 mL of dry dichloromethane, was added dropwise. Stirring at room temperature was continued for another 8 hours, water (50 mL) was added to the reaction mixture, and the organic phase was separated. The aqueous phase was washed with dichloromethane (2 × 15 mL), and the combined organic phases were dried with magnesium sulfate. After removal of the solvent in vacuo, the crystalline residue was washed with petroleum ether (40/60) and dried in vacuo.

## *Dimethyl 2,2,5,5-Tetramethyl-4-thiazolidinylphosphine Oxide* (**2a**)

Prepared via method C from 0.36 g (2.5 mmol) of 2,2,5,5-tetramethyl-3-thiazoline [23] **1a**; colorless crystals; yield 0.28 g (50%); mp 73–74°C. MS (CI, isobutane): *m*/*z* (%) = 222 (100) [$MH^+$]. $C_9H_{20}NOPS$ (221.2); calcd: C, 48.85; H, 9.11; N, 6.33; found: C, 48.32; H, 9.04; N, 5.80.

## *Dimethyl 2,2-Dimethyl-1-thia-4-aza-spiro[4.4]non-3-ylphosphine Oxide* (**2b**)

Prepared via method B from 0.85 g (5 mmol) of 2,2-dimethyl-1-thia-4-aza-spiro[4.4]non-3-ene [7] **1b**; colorless crystals; yield 0.46 g (37%); mp 107–108°C. MS (CI, isobutane): *m*/*z* (%) = 248 (100) [$MH^+$]. $C_{11}H_{22}NOPS$ (247.3); calcd: C, 53.42; H, 8.97; N, 5.66; found: C, 53.05; H, 8.89; N, 5.40.

## *Dimethyl 2,2-Dimethyl-1-thia-4-aza-spiro[4.5]dec-3-ylphosphine Oxide* (**2c**)

Prepared via method B from 0.92 g (5 mmol) and via method C from 0.46 g (2.5 mmol) of 2,2-dimethyl-1-thia-4-aza-spiro[4.5]dec-3-ene [7] **1c**; colorless crystals; yield 0.66 g (51%; method B); 0.43 g (65%; method C); mp 148–149°C. MS (CI, isobutane): *m*/*z*

(%) = 262 (100) [$MH^+$]. $C_{12}H_{24}NOPS$ (261.3); calcd: C, 55.15; H, 9.26; N, 5.36; found: C, 55.02; H, 9.36; N, 5.22.

### *Dimethyl 2,2,5,5-Tetraethyl-4-thiazolidinylphosphine Oxide* (**2d**)

Prepared via method C from 0.50 g (2.5 mmol) of 2,2,5,5-tetraethyl-3-thiazoline **1d**; colorless crystals; yield 0.35 g (50%); mp 92–93°C. MS (CI, isobutane): *m/z* (%) = 278 (100) [$MH^+$]. $C_{13}H_{28}NOPS$ (277.4); calcd: C, 56.29; H, 10.17; N, 5.05; found: C, 56.19; H, 10.32; N, 4.96.

### *2,2-Diethyl-1-thia-4-aza-spiro[4.4]non-3-yl Dimethylphosphine Oxide* (**2e**)

Prepared via methods A or B from 0.99 g (5 mmol) of 2,2-diethyl-1-thia-4-aza-spiro[4.4]non-3-ene **1e**; colorless crystals; yield 0.52 g (38%; method A); 0.34 g (25%; method B); mp 139–140°C. MS (CI, isobutane): *m/z* (%) = 276 (100) [$MH^+$]. $C_{13}H_{26}NOPS$ (275.3); calcd: C, 56.70; H, 9.52; N, 5.09; found: C, 56.31; H, 9.22; N, 4.56.

### *Dimethyl 2,2-Dimethyl-1-thia-3-aza-spiro[4.5]dec-4-ylphosphine Oxide* (**2f**)

Prepared via method A from 0.92 g (5 mmol) 2,2-dimethyl-1-thia-3-aza-spiro[4.5]decene **1f**. The resulting salt was isolated, characterized by $^1H$- and $^{31}P$-NMR spectroscopy, and hydrolyzed in a second step; colorless crystals; yield 0.46 g (35%); mp 118–120°C. MS (CI, isobutane): *m/z* (%) = 262 (100) [$MH^+$]. $C_{12}H_{24}NOPS$ (261.3); calcd: C, 55.15; H, 9.26; N, 5.36; found: C, 55.03; H, 9.25; N, 5.25.

### *Dimethyl 2-Isopropyl-1-thia-3-aza-spiro[4.5]dec-4-ylphosphine Oxide* (**2g**)

Prepared via methods A and B from 0.99 g (5 mmol) and via method C from 0.50 g (2.5 mmol) 2-isopropyl-1-thia-3-aza-spiro[4.5]decene **1g**; colorless crystals; yield 0.46 g (33%; method A); 0.50 g (36%; method B); 0.26 g (38%; method C). MS (CI, isobutane): *m/z* (%) = 276 (90) [$MH^+$], 198 (100) [$MH^+$ -$(CH_3)_2PHO$]. $C_{13}H_{26}NOPS$ (275.3); calcd: C, 56.70; H, 9.52; N, 5.09; found: C, 56.59; H, 9.62; N, 4.98.

### *Dimethyl 7-Thia-13-aza-dispiro[5.1.4.2]tetradec-14-ylphosphine Oxide* (**2h**)

Prepared via method A from 1.05 g (5 mmol) 7-thia-13-aza-dispiro[5.1.4.2]tetradecene **1h**; colorless crystals; yield 0.86 g (60%); mp 167–168°C. MS (CI, isobutane): *m/z* (%) = 288 (100) [$MH^+$]. $C_{14}H_{26}NOPS$ (287.4); calcd: C, 58.51; H, 9.12; N, 4.87; found: C, 58.80; H, 9.19; N, 4.66.

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## *REFERENCES*

[1] G. Jäger, in K. H. Büchel (ed): *Pflanzenschutz und Schädlingsbekämpfung,* Georg Thieme-Verlag, Stuttgart, p. 188 (1977).
[2] J. E. Franz (Monsanto Co.): DAS 2152826 (1971); *Chem. Abstr., 77,* 1972, 165079k.
[3] L. Maier, *Phosphorus Sulfur, 14,* 1983, 295.
[4] B. Lal, A. N. Dohadwalla, N. K. Dadkar, A. D'Sa, N. J. de Souza, *J. Med. Chem., 27,* 1984, 1470.
[5] V. P. Kukhar', V. A. Solodenko, *Usp. Khim., 56,* 1987, 1504.
[6] V. P. Kukhar', V. A. Soloshonok, V. A. Solodenko, *Phosphorus, Sulfur and Silicon, 92,* 1994, 239.
[7] K. Drauz, H. G. Koban, J. Martens, W. Schwarze, *Liebigs Ann. Chem.,* 1985, 448.
[8] B. Dhawan, D. Redmore, *Phosphorus Sulfur, 32,* 1987, 119.
[9] L. Maier, *Phosphorus, Sulfur and Silicon, 53,* 1990, 43.
[10] L. Maier, *Phosphorus, Sulfur and Silicon, 62,* 1991, 29.
[11] L. Maier, P. J. Diehl, *Phosphorus, Sulfur and Silicon, 63,* 1991, 15.
[12] C. Hubert, B. Oussaid, G. Etemad-Moghadam, M. Koenig, B. Garrigues, *Synthesis,* 1994, 51.
[13] S. Hanessian, Y. L. Bennani, *Synthesis,* 1994, 1272.
[14] I. Hoppe, U. Schöllkopf, M. Nieger, K. Egert, *Angew. Chem., 97,* 1985, 1066; *Angew. Chem. Int. Ed. Engl., 24,* 1985, 1036.
[15] U. Groth, L. Richter, U. Schöllkopf, *Tetrahedron, 48,* 1992, 117.
[16] U. Groth, L. Richter, U. Schöllkopf, *Liebigs Ann. Chem.,* 1992, 903.
[17] U. Groth, L. Lehmann, L. Richter, U. Schöllkopf, *Liebigs Ann. Chem.,* 1993, 427.
[18] N. Kreutzkamp, K. Storck, *Naturwissenschaften, 47,* 1960, 497.
[19] L. Maier, *Phosphorus, Sulfur and Silicon, 63,* 1991, 237.
[20] J. R. Goerlich, I. Neda, M. Well, A. Fischer, P. G. Jones, R. Schmutzler, *Z. Naturforsch., 48b,* 1993, 1161.
[21] I. Neda, V. A. Pinchuk, A. Fischer, P. G. Jones, R. Schmutzler, Yu. G. Shermolovich, *J. Fluorine Chem., 70,* 1995, 127.
[22] M. Well, R. Schmutzler, *Phosphorus, Sulfur and Silicon, 72,* 1992, 171.
[23] J. R. Goerlich, R. Schmutzler, *Phosphorus, Sulfur and Silicon, 101,* 1995, 213.
[24] J. Martens, J. Kintscher, K. Lindner, S. Pohl, W. Saak, D. Haase, *Liebigs Ann. Chem.,* 1991, 305.

[25] H. Gröger, Y. Saida, S. Arai, J. Martens, H. Sasai, M. Shibasaki, *Tetrahedron Lett., 37,* 1996, 9291.
[26] H. Gröger, J. Martens, *Synth. Commun., 26,* 1996, 1903.
[27] J. March: *Advanced Organic Chemistry,* 4th ed., Wiley, New York, Chichester, Brisbane, Toronto, Singapore, p. 879 (1992).
[28] D. Redmore: in E. J. Griffith, M. Grayson (eds): *Topics in Phosphorus Chemistry,* Interscience, New York, vol. 8, p. 515 (1976).
[29] H.-J. Kleiner, *Liebigs Ann. Chem.,* 1974, 751.
[30] K.-D. Berlin, G. B. Butler, *Chem. Rev., 60,* 1960, 243.
[31] W. P. Jencks, H. F. Gilbert, *Pure Appl. Chem., 49,* 1977, 1021.
[32] Colorless, amorphous solid. Highly hygroscopic. Mp: 94°C. Elemental analysis (C,H,N) gave satisfactory results for $C_{12}H_{23}KNOPS$ (299.46). The negative charge is thought to be localized at the nitrogen atom because no NH-resonance was observed in the $^1$H-NMR spectrum. Further $^1$H- and $^{31}$P-NMR parameters are nearly the same as described for the free adduct **2f**.
[33] M. Volkholz, O. Stelzer, R. Schmutzler, *Chem. Ber., 111,* 1978, 890.
[34] F. Afarinkia, C. W. Rees, J. I. G. Cadogan, *Tetrahedron, 46,* 1990, 7175.
[35] L. Wozniak, J. Chojnowski, *Tetrahedron, 45,* 1989, 2465.
[36] X-ray Structure Determinations (Crystal data are given in Table 2). *Data collection and reduction:* Crystals were mounted on glass fibers in inert oil and transferred to the cold gas stream of the diffractometer (Stoe STADI-4 for **2h** and Siemens P4 for **2c**, both with LT-2 low-temperature attachment). The cell constants for **2h** were refined from $\pm\omega$ angles of 52 reflections in the $2\theta$ range 20°–23°. The orientation matrix for **2c** was refined from setting angles of 47 reflections in the $2\theta$ range 20°–25° (monochromated $MoK_\alpha$ radiation).

*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 as rigid methyl groups. The weighting scheme was of the form $w^{-1} = [\sigma^2(F_o^2) + (aP)^2 + bP]$, with $P = (F_o^2 + 2F_c^2)/3$. Absolute structures were determined using the method of Flack [37]. 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 number CSD 401787 (**2c**) and CSD 401788 (**2h**).
[37] H. D. Flack, *Acta Crystallogr., A39,* 1983, 876.
[38] M. Hatam, D. Tehranfar, J. Martens, *Synth. Commun., 25,* 1995, 1677.
[39] C. D. Stevens, B. T. Gillis, *J. Am. Chem. Soc., 79,* 1957, 3449.
[40] P. Duhamel, L. Duhamel, J. Y. Valnot, *Bull. Soc. Chim. Fr.,* 1973, 1465.