A New Synthesis of α-Phosphinoyl Cycloalkanones by Phosphinylation of Cycloalkanone Enolates. Crystal and Molecular Structure of 2-(Diphenylphosphinoyl)-3-[tris(methylthio)methyl]cyclopentanone and 2-(Diphenylphosphinoyl)-3-carbomethoxycyclopentanone

Marian Mikołajczyk* and Piotr Kiełbasiński

Center of Molecular and Macromolecular Studies, Polish Academy of Sciences, Department of Organic Sulfur Compounds, 90-363 Lodź, Sienkiewicza 112, Poland

Michał W. Wieczorek and Jarosław Błaszczyk

Institute of General Chemistry, Technical University, 90-924 Łódź, Żwirki 36, Poland

Alfred Kolbe

Chemistry Section, University Halle-Wittenberg, 402-Halle, Weinbergweg 16, German Democratic Republic

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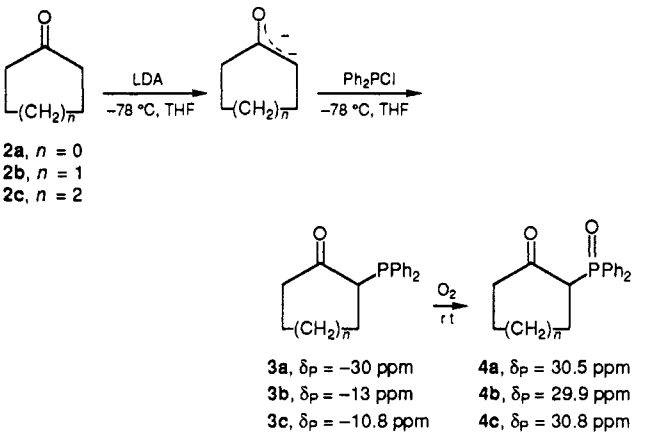
A new one-pot synthesis of 2-(diphenylphosphinoyl)cycloalkanones is described which involves the reaction of cyclic enolate anions with chlorodiphenylphosphine followed by oxidation with air. In an effort to synthesize sarkomycin, 2-(diphenylphosphinoyl)-3-[tris(methylthio)methyl]cyclopentanone (**9**) was prepared by tandem 1,4-addition of the lithio derivative of trimethyl trithioorthoformate to cyclopentenone and C-phosphinylation of the enolate anion formed. Methanolysis of **9** catalyzed by mercury salts gave 2-(diphenylphosphinoyl)-2-carbomethoxycyclopentanone (**10**). The Horner–Wittig reaction of **10** with formaldehyde under various experimental conditions failed. Both 2,3-disubstituted cyclopentanones **9** and **10** obtained are trans isomers as indicated by NMR and X-ray analysis. The cyclopentanone **9** was found to exist in the solid state in an envelope (C_S) conformation with the diaxial disposal of exocyclic substituents; the $Ph_2P(O)$ group is occupying the flap of the envelope. The five-membered ring in **10** adopts in the crystal a half-chair (C_2) conformation with both exocyclic substituents being axial.

Introduction

In recent years α-phosphoryl ketones have become valuable intermediates in organic synthesis, particularly as substrates in the Horner–Wittig olefination reactions.[1] The preparation of acyclic α-phosphoryl ketones is rather simple and may be accomplished by acylation of α-phosphonate carbanions.[2] However, α-phosphoryl cycloalkanones cannot be prepared in this way. The most reasonable method of the synthesis of α-phosphoryl cycloalkanones, which would consist in phosphorylation of the cyclic enolate anions, produces isomeric enol phosphates.[3] Another possible synthesis involving the reaction between α-halogeno ketones and trialkyl phosphites gives a mixture of α-phosphoryl ketones (Michaelis–Arbusov reaction) and enol phosphates (Perkov reaction), the latter being usually predominantly formed.[4] Nevertheless, some successful approaches to α-phosphoryl cycloalkanones have been reported in the literature. Thus, Herzig and Gasteiger obtained α-phosphoryl cyclohexanones in the reaction of trialkyl phosphites with 1-chlorocyclohexene oxide.[5] Recently, Wiemer et al. have succeeded in the synthesis of α-phosphoryl cycloalkanones either by phosphorylation of the dilithiated derivatives of cyclic ketones[6] or by the base-induced rearrangement of the corresponding enol phosphates.[7] A severe drawback of the latter method is, however, the lack of regioselectivity of the rearrangement.

Scheme I



2a, $n = 0$
2b, $n = 1$
2c, $n = 2$

3a, $\delta_P = -30$ ppm
3b, $\delta_P = -13$ ppm
3c, $\delta_P = -10.8$ ppm

4a, $\delta_P = 30.5$ ppm
4b, $\delta_P = 29.9$ ppm
4c, $\delta_P = 30.8$ ppm

In this paper we describe a new approach to the previously unknown α-phosphinoyl cycloalkanones based on the direct phosphinylation of cyclic enolate anions as well as an attempt to synthesize sarkomycin, utilizing α-phosphinoyl cyclopentanones as intermediates.

Results and Discussion

Synthesis of α-Diphenylphosphinoyl Cycloalkanones. In a continuation of our studies on the synthesis of cyclopentanoid antibiotics[8] we became interested in an easy access to α-phosphoryl cyclopentanones starting from cyclopentanone. Searching for a reagent which

(1) Walker, B. J. In *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G., Ed.; Academic Press: London, 1979; p 155.
(2) Aboujaoude, E. E.; Collignon, N.; Savignac, P. *J. Organomet. Chem.* **1984**, *264*, 9. Aboujaoude, E. E.; Collignon, N.; Teulade, M.-P.; Savignac, P. *Phosphorus Sulfur* **1985**, *25*, 57.
(3) Lichtenthaler, F. U. *Chem. Rev.* **1961**, *61*, 607.
(4) Cadogan, J. I. G. In *Organophosphorus Reagents in Organic Synthesis*; Cadogan, J. I. G., Ed.; Academic Press: London, 1979; p 1.
(5) Herzig, C.; Gasteiger, J. *Chem. Ber.* **1982**, *115*, 601.
(6) Sampson, P.; Hammond, G. B.; Wiemer, D. F. *J. Org. Chem.* **1986**, *51*, 4342.
(7) Calogeropoulou, T.; Hammond, G. B.; Wiemer, D. F. *J. Org. Chem.* **1987**, *52*, 4185.
(8) Mikołajczyk, M.; Bałczewski, P. *Synthesis* **1987**, 659 and references therein. For a summary see: Mikołajczyk, M. In *Reviews on Heteroatom Chemistry*; Oae, S., Ed.; Myu: Tokyo, in press.

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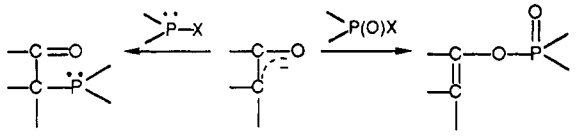
should allow the formation of the phosphorus–carbon bond, we turned our attention to the series of publications of Lutsenko and co-workers.[9] These authors have exhaustively investigated the reaction between acyclic enolate anions and tricoordinated phosphorus halogenides and found that the use of chlorodialkylphosphines leads in some cases to the exclusive C-phosphinylation. Although they were able to isolate the β-oxo phosphines formed, they did not attempt their oxidation to the corresponding β-oxo phosphine oxides.

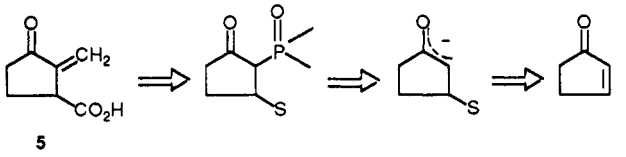
Having this in mind, we decided to use in our work chlorodiphenylphosphine (1) that is commercially available and much more easy to handle in comparison with chlorodialkylphosphines. It was gratifying to find that the exclusive phosphinylation at the carbon atom took place when the enolate anions of cyclopentanone **2a**, cyclohexanone **2b**, and cycloheptanone **2c** were treated with chlorodiphenylphosphine **1** at −78 °C in tetrahydrofuran solution (Scheme I). The ^{31}P NMR chemical shifts of the major products formed (for **3a** δ_P = −30 ppm, for **3b** δ_P = −13 ppm and for **3c** δ_P = −10.8 ppm) are in a typical region for phosphines and far away from diphenylphosphinites.[10,11] The β-oxo phosphines **3** appeared in our hands to be extremely air-sensitive, particularly under the reaction conditions. For this reason, they were oxidized to the corresponding β-oxo phosphine oxides **4** by simply bubbling air through the reaction solution. After the usual workup and purification, the phosphine oxides **4a**, **4b**, and **4c** were obtained in 82%, 60%, and 61% yields, respectively. Their structure was unequivocally confirmed by spectroscopic methods. It is worthy of note that the presence of the direct coupling constant $^1J_{C-P}$ equal to ca. 60 Hz in ^{13}C NMR spectra of **4** is the best evidence for C-phosphinylation of cyclic enolate anions by **1**.

Our results in combination with those reported by Lutsenko[9] clearly illustrate a dramatic difference in reactivity of two nucleophilic centers of the ambident enolate anion, depending on the nature of phosphorus halogenides used as electrophilic reaction partners. Whereas the phosphorylation of the enolate anion with phosphoryl halogenides, >P(O)X, occurs exclusively at the oxygen atom,[3] phosphorus(III) halogenides, >PX, react predominantly at the carbon atom which is a soft nucleophilic center of the anion.



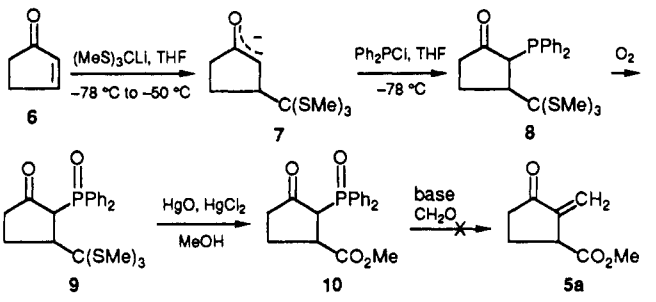
It is notable that a similar behavior toward tetra- and trivalent phosphorus halogenides shows the ambident α-sulfoxide carbanion. Thus, its reaction with phosphoryl halogenides occurs at the oxygen atom as a hard nucleophilic center and is followed by the Pummerer-type reaction affording phosphoric acid, pyrophosphate and α-halogeno sulfide.[13] By contrast, chlorodiphenylphosphine reacts with α-sulfinyl carbanion at the carbon atom to give α-sulfinylphosphine which undergoes easy isomerization to α-sulfenylphosphine oxide.[14]

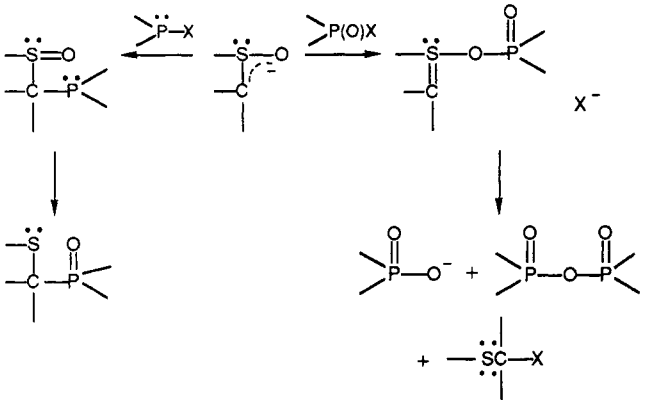
Scheme II



S = carboxylic group synthon

Scheme III





The results briefly presented above indicate that, in contrast to phosphoryl halogenides in which the phosphoryl phosphorus atom is a hard electrophilic center, halogenophosphines are soft electrophilic reagents. This is due to the presence of the lone electron pair on phosphorus, decreasing electrophilicity of the phosphorus atom. For the same reason trivalent P-compounds act also as nucleophilic reagents and exhibit the so-called biphilic reactivity.

An Attempt at the Synthesis of Sarkomycin. Our successful synthesis of β-oxo phosphine oxides **4** encouraged us to apply them for synthetic purposes. Particularly interesting seemed to us the synthesis of sarkomycin (**5**). This compound belonging to the family of cyclopentanoid antibiotics recently attracted considerable attention of many research groups mainly due to its antitumor activity.[15]

The strategy of the synthesis of **5**, based on retrosynthetic analysis outlined in Scheme II, was to utilize tandem 1,4-addition reaction of the carboxylic group synthon to cyclopentenone and regioselective C-phosphinylation of

(9) Novikova, E. S.; Kurkin, A. N.; Lutsenko, I. F. In *Khimiya i primenenye fosforoorganicheskikh soedineniy*; Kabachnik, M. I., Ed.; Izdatelstvo "Nauka": Leningrad, 1987; p 65 and references therein.

(10) Although the nature of minor byproducts was not investigated in details, in the case of the reaction of cyclopentanone enolate with Ph_2PCl, a byproduct was isolated in a very low yield which, on the basis of spectroscopic analyses, was ascribed a structure of 2,5-bis(diphenylphosphinoyl)cyclopentanone; δ_P = 31.5 ppm, m/e = 484 (M^+).

(11) For example, the chemical shifts for $EtPPh_2$ and Ph_2P–OEt are δ_P = −13 ppm and δ_P = 109 ppm, respectively.[12]

(12) Mark, V.; Dungan, C.; Crutchfield, M.; Van Wazer, J. In *Topics in Phosphorus Chemistry*; Interscience: New York, 1967; Vol. 5, p 226.

(13) Mikołajczyk, M.; Zatorski, A. *Synthesis* **1973**, 669.

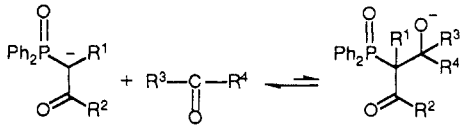
(14) Vedejs, E.; Mastalerz, H.; Mejer, G. P.; Powell, D. W. *J. Org. Chem.* **1981**, *46*, 5253.

(15) Helmchen, G.; Ihring, K.; Schindler, H. *Tetrahedron Lett.* **1987**, *28*, 183 and references therein.

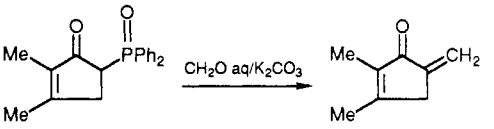
the enolate anion formed. This should provide a key cyclopentanone intermediate with the α-phosphinoyl group as a precursor of the exocyclic methylene moiety in **5**.

Experimental implementation of the above synthetic concept is shown in Scheme III. Trimethyl trithioorthoformate was used as the carboxylic group synthon whose anion was found to react with 2-cyclopentenone (**6**) in an 1,4-fashion, giving the transient enolate anion **7**. Its reaction with chlorodiphenylphosphine (**1**) gave the β-oxo phosphine **8**, which upon oxidation with air afforded 2-(diphenylphosphinoyl)-3-[tris(methylthio)methyl]cyclopentanone (**9**). It is interesting to note that all the transformations from **6** to **9** were performed in an one-pot procedure, and the total yield of **9** after column chromatography was 40%. The next step involving methanolysis of the trithioorthoester moiety in the presence of mercury(II) oxide and mercury(II) chloride produced 2-(diphenylphosphinoyl)-3-carbomethoxycyclopentanone (**10**) in 75% yield. To complete the synthesis of sarkomycin methyl ester (**5a**), the Horner–Wittig reaction of **10** with formaldehyde was carried out. In spite of the fact that a broad variety of bases was used and the reaction was performed under various conditions,[16] it turned out that the β-oxo phosphine oxide **10** did not undergo the Horner–Wittig reaction. This is in contrast to the corresponding β-oxo phosphonates, which are known to undergo it very easily.[17] Moreover, we found that the other cyclic β-oxo phosphine oxides **4a**, **4b**, and **9** prepared in this work behave similarly. Though in all cases the formation of small amounts of diphenylphosphinic acid was observed, no desired *exo*-methylene products could be detected. Most probably the substrates were decomposed during the reaction as indicated by the ^{31}P NMR spectra, which revealed appearance of a broad band in the region of δ_P = 30 ppm. Similarly, negative results were observed when **4a**, **4b**, **9**, and **10** were subjected to the Horner–Wittig reaction with more reactive benzaldehyde or with isobutyraldehyde.

In this context, it should be mentioned that Torr and Warren[18] have also found that acyclic β-oxo phosphine oxides do not react with carbonyl compounds under the Horner–Wittig reaction conditions. These authors tried to explain this fact by assuming that the balance between carbanion reactivity and formation of a new P–O bond must be unfavorable for phosphine oxides and therefore the equilibrium between substrates and the oxyanion formed must be shifted to the left side.



On the other hand, however, in one of our syntheses of methylenomycin B we were able to perform successfully the Horner–Wittig reaction using 2,3-dimethyl-5-(diphenylphosphinoyl)-2-cyclopentenone as a substrate.[19]



The results presented above indicate that the reasons for different reactivity of various types of β-oxo phosphine oxides are not yet completely understood. Undoubtedly, of some importance must be the structure and stability of the starting anion.

Spectral Properties of Cyclic β-Oxo Phosphine Oxides 9 and 10. Since all the cyclic β-oxo phosphine oxides obtained in this work are new compounds and, apart from their reluctance to undergo the Horner–Wittig reaction, may find other synthetic applications, we decided to examine their structure and conformation.

In the first instance, we attempted to establish the cis–trans geometry of the exocyclic substituents at C(2) and C(3) in the cyclopentanones **9** and **10** by spectroscopic methods. Thus, the ^1H NMR spectrum of **10** revealed that the proton at C(2) appears as a double doublet due to the coupling with phosphorus ($^2J_{H-P}$ = 12.22 Hz) and with the proton at C(3) ($^3J_{H-H}$ = 6.37 Hz). On the other hand, the proton at C(2) in **9** appears in the ^1H NMR spectrum as a doublet only with $^2J_{H-P}$ = 14.87 Hz. This means that no coupling is observed between protons at C(2) and C(3). Accordingly, the proton at C(3) appears in the spectrum as a simple double doublet due to its coupling with the cis and trans protons at C(4) ($^3J_{H-H}$ = 8.8 and 17.1 Hz). The lack of a coupling between protons at C(2) and C(3) in **9** strongly suggests that in the most favorable conformation of the cyclopentanone ring the torsional angle H2–C2–C3–H3 should be very close to 90°. Moreover, the values of the vicinal coupling constants, $^3J_{H2-H3}$, presented above are not diagnostic in determining the cis–trans geometry of the exocyclic substituents in **9** and **10**. Since it is quite reasonable to assume that both compounds have the same configuration, the different coupling constants $^3J_{H2-H3}$ may result from a different conformation of the cyclopentanone ring in each case. Nevertheless, the lack of the NOE effect between H2 and H3 in **10** strongly suggests the trans configuration of both **9** and **10**.

The cyclic β-oxo phosphine oxides were also characterized by means of IR spectroscopy. To our surprise, the IR spectra of **4a**, **9**, and **10** appeared to be almost identical. The positions and intensities of the bands are collected

Table II. Selected Bond Lengths (Å) in 9 and 10

bond in 9		bond in 10	
P–O(2)	1.490 (2)	P–O(1)	1.486 (1)
P–C(2)	1.844 (2)	P–C(2)	1.829 (2)
P–C(6)	1.808 (3)	P–C(6)	1.797 (3)
P–C(12)	1.807 (3)	P–C(12)	1.805 (3)
C(1)–O(1)	1.205 (3)	C(1)–O(2)	1.202 (3)
C(1)–C(2)	1.524 (4)	C(1)–C(2)	1.524 (3)
C(1)–C(5)	1.506 (4)	C(1)–C(5)	1.503 (4)
C(2)–C(3)	1.543 (3)	C(2)–C(3)	1.545 (3)
C(3)–C(4)	1.561 (3)	C(3)–C(4)	1.543 (4)
C(3)–C(18)	1.551 (4)	C(3)–C(18)	1.505 (3)
C(4)–C(5)	1.526 (4)	C(4)–C(5)	1.517 (4)
C(18)–S(1)	1.845 (3)	C(18)–O(3)	1.187 (3)
C(18)–S(2)	1.819 (3)	C(18)–O(4)	1.338 (3)
C(18)–S(3)	1.841 (2)		

(16) The following conditions were applied: K_2CO_3 in MeOH, EtOH, or THF, aqueous CH_2O; LDA and paraformaldehyde, gaseous CH_2O or THF solution of CH_2O, PTC–solid K_2CO_3, Bu_4NBr, aqueous CH_2O in CH_2Cl_2; KOtBu and THF solution of CH_2O in CH_2Cl_2; Et_3N or iPr_2NEt or piperidine or DBU and THF solution of CH_2O; DBU + LiCl + 12-crown-4 and CH_2O in THF, KF/Al_2O_3 and aqueous CH_2O.

(17) (a) Mikołajczyk, M.; Grzejszczak, S.; Midura, W.; Zatorski, A. *Phosphorus Sulfur* **1983**, *18*, 175, (b) Mikołajczyk, M.; Zatorski, A. Polish Patent 141 948, 15 Jan, 1988, Appl. 247247, 13 Apr, 1984. (c) Castagnino, E.; Corsano, S.; Strappaveccia, G. P. *Tetrahedron Lett.* **1985**, *26*, 93. (d) Corbel, B.; Hernot, D.; Haelters, J.-P.; Sturtz, G. *Tetrahedron Lett.* **1987**, *28*, 6605. (e) Mikołajczyk, M.; Żurawiński, R.; Kiełbasiński, P. *Tetrahedron Lett.* **1989**, *30*, 1143.

(18) Torr, R. S.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1173.

(19) Mikołajczyk, M.; Zatorski, A., unpublished results cited in Vlahov, R., Ed. *Proceedings of the Third International Conference on Chemistry and Biotechnology of Biologically Active Natural Products*; Sofia: Bulgaria, 1985, Vol. 2, p 254.

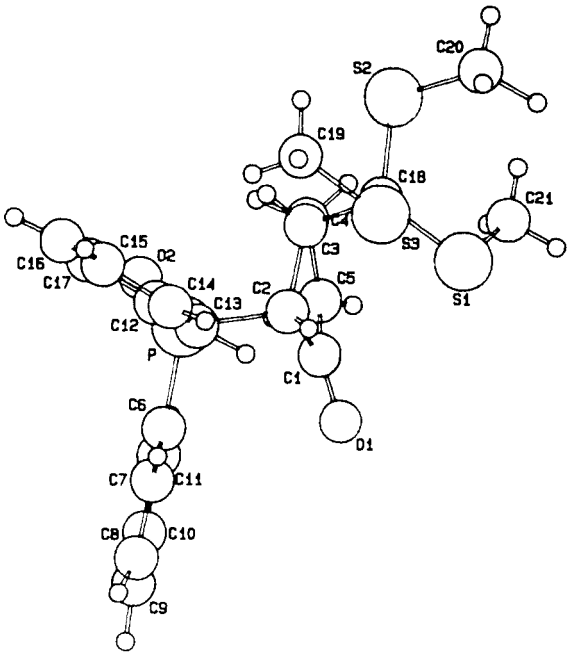


Figure 1. A three-dimensional view of 2-(diphenylphosphinoyl)-3-[tris(methylthio)methyl]cyclopentanone (**9**).

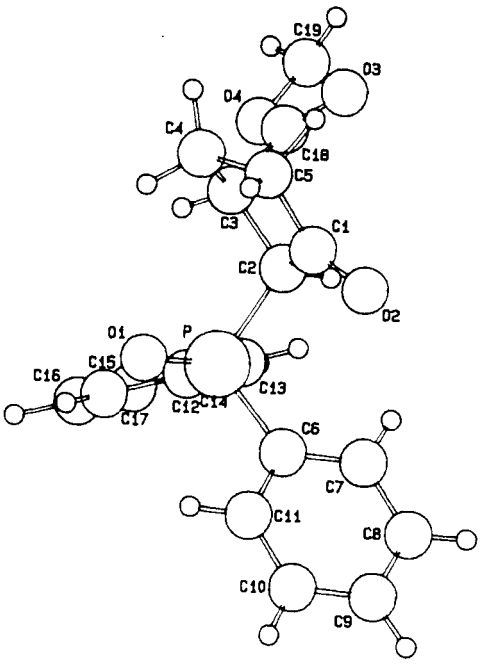


Figure 2. A three-dimensional view of 2-(diphenylphosphinoyl)-3-carbomethoxycyclopentanone (**10**).

Table III. Selected Bond Angles (deg) in 9 and 10

angles in 9		angles in 10	
P-C(2)-C(1)	109.8 (2)	P-C(2)-C(1)	110.8 (1)
P-C(2)-C(3)	110.0 (2)	P-C(2)-C(3)	109.8 (1)
P-C(2)-H(21)	108.3 (2)	P-C(2)-H(21)	108.0 (1)
C(2)-P-C(6)	107.3 (1)	C(2)-P-C(6)	107.35 (9)
C(2)-P-C(12)	105.4 (1)	C(2)-P-C(12)	104.44 (9)
C(2)-P-O(2)	112.0 (2)	C(2)-P-O(1)	112.29 (9)
C(6)-P-O(2)	111.8 (1)	C(6)-P-O(1)	112.63 (9)
C(12)-P-O(2)	112.5 (1)	C(12)-P-O(1)	112.13 (9)
O(1)-C(1)-C(2)	124.5 (2)	O(2)-C(1)-C(2)	124.8 (3)
O(1)-C(1)-C(5)	127.4 (3)	O(2)-C(1)-C(5)	125.7 (2)
C(1)-C(2)-C(3)	105.2 (2)	C(1)-C(2)-C(3)	105.2 (2)
C(2)-C(3)-C(4)	103.9 (2)	C(2)-C(3)-C(4)	104.4 (2)
C(3)-C(4)-C(5)	107.7 (3)	C(3)-C(4)-C(5)	106.1 (3)
C(4)-C(5)-C(1)	106.6 (2)	C(4)-C(5)-C(1)	106.1 (2)
C(5)-C(1)-C(2)	108.2 (2)	C(5)-C(1)-C(2)	109.5 (2)
C(2)-C(3)-C(18)	112.6 (2)	C(2)-C(3)-C(18)	109.9 (2)
C(4)-C(3)-C(18)	113.0 (2)	C(4)-C(3)-C(18)	112.4 (2)

in Table I (see Supplementary Material). The observable differences, though also small, can be detected in the CH region. Evidently, the arrangement formed by the five-membered ring, whose conformation is stabilized by the C=O and P=O groups and two aromatic rings, is very stable and forms an entity in itself. Moreover, the detailed analysis of the IR spectra of **9** strongly suggests that the bulky tris(methylthio)methyl group should occupy an axial position in the five-membered ring.

Crystal and Molecular Structure of 9 and 10. In order to assure the trans configuration of **9** and **10** deduced from NMR examination as well as to get better insight into the conformation of the five-membered cyclopentanone rings,[20] we have carried out X-ray investigations on crystals of both compounds.

The solid-state structures with the atom numbering for **9** and **10** are shown in Figure 1 and Figure 2, respectively. The principal bond lengths and angles are listed in Tables II and III. Figure 3 shows the Newman projections in **9** along P–C(2) and C(2)–C(3) bonds and the corresponding

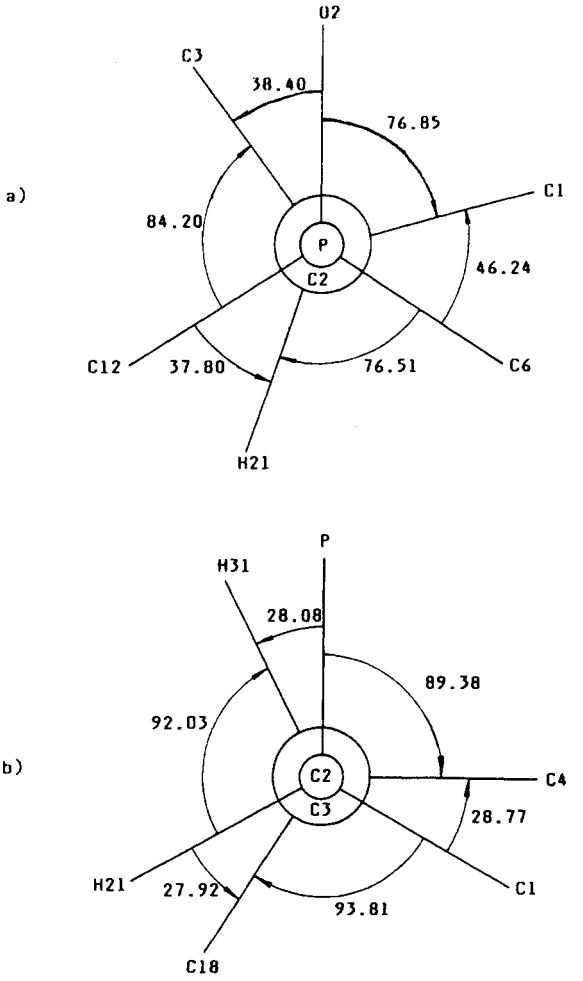


Figure 3. Newman projections around the C(2)–P and C(2)–C(3) bonds showing the relevant torsion angles (deg) in **9**.

torsional angles. Figure 4 shows the same projections for **10**. The geometry of the five-membered ring in both compounds is characterized by the internal torsional angles (Table IVa) and the ring deformation values and asym-

(20) For a review on the conformation of five-membered ring, see: Fuchs, B. *Topics in Stereochemistry*; Eliel, E. L., Allinger, N. L., Eds.; J. Wiley and Sons: New York, 1978; Vol. 10, p 1.

Table IV. Cyclopentanone Ring Geometry Parameters in 9 and 10

	9	10
(a) Internal Torsional Angles (deg)		
C(1)–C(2)–C(3)–C(4)	28.77	−24.56
C(2)–C(3)–C(4)–C(5)	−20.71	30.10
C(3)–C(4)–C(5)–C(1)	4.51	−23.81
C(4)–C(5)–C(1)–C(2)	13.98	8.27
C(5)–C(1)–C(2)–C(3)	−24.17	10.42

	9	10		9	10
(b) Ring Deformation and Asymmetry Parameters (deg)					
ΔC_s(C1)	25.31	36.7	ΔC_2(C1)	33.76	1.6
ΔC_s(C2)	4.90	28.9	ΔC_2(C2)	46.53	29.2
ΔC_s(C3)	16.99	10.2	ΔC_2(C3)	41.53	45.6
ΔC_s(C4)	32.33	12.4	ΔC_2(C4)	20.67	44.6
ΔC_s(C5)	36.27	30.7	ΔC_2(C5)	8.09	17.7

metry parameters (Table IVb).

Analysis of Figure 1 and X-ray data for **9** quoted in Table IV reveals that the cyclopentanone ring exists in an envelope (C_s) conformation with the axial exocyclic tris(methylthio)methyl and diphenylphosphinoyl groups, the latter being situated on the flap of the envelope. It is interesting to note that diaxial conformation of **9** was indicated by IR spectra. Another interesting feature of the solid-state structure of **9** is that the torsional angle H(21)–C(2)–C(3)–H(31) (see Figure 3) is equal to 92.03°. This observation explains the lack of a coupling between protons at C(2) and C(3) in the ^{1}H NMR spectra and may be best interpreted in terms of the same, strongly predominant (if not exclusive) conformation of **9** in a solution.

An X-ray analysis of the cyclopentanone **10** showed it to exist in the crystal in a half-chair (C_2) conformation with the trans-diaxial disposal of both exocyclic substituents at C(2) and C(3). In this case the torsional angle H(21)–C(2)–C(3)–H(31) is greater than that in **9** and equal to 98.85°, which is reflected in the observable coupling constant, $^3J_{H-H}$ = 6.37 Hz. The Newman projections indicate also that the phosphinoyl oxygen atom O(1) is almost symmetrically situated between the ring carbon atoms C(1) and C(3), and the nonbonding distances between them are 3.227 and 3.226 Å, respectively. Similar situation is observed for the hydrogen atom H(21) with respect to C(6) and C(12) where the corresponding distances are 2.979 and 3.013 Å.

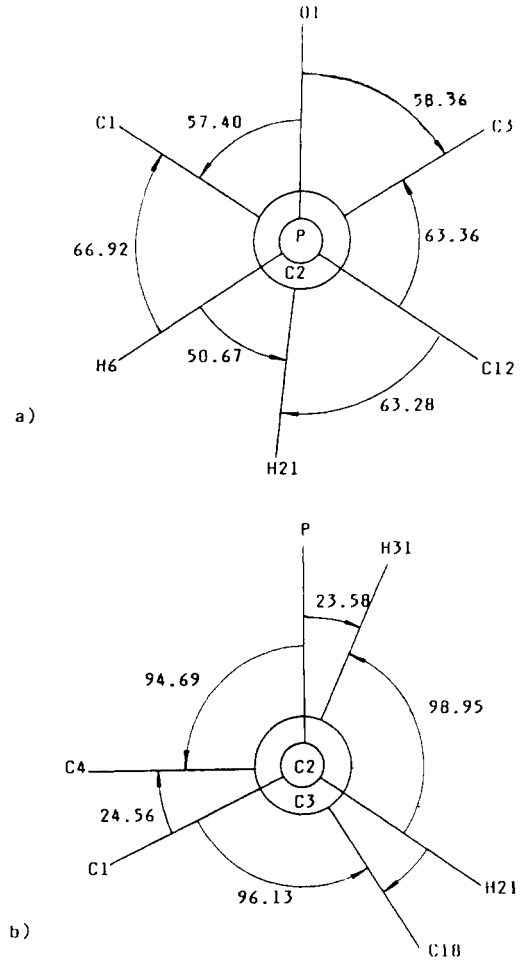


Figure 4. Newman projections around the C(2)–P and C(2)–C(3) bonds showing the relevant torsion angles (deg) in **10**.

Experimental Section

^{1}H and ^{13}C NMR spectra were measured with a Bruker MSL 300 instrument if not otherwise stated. ^{31}P NMR spectra were measured with a FT JEOL FX-60 instrument. Mass spectra were obtained with an LKB-2091 instrument. IR spectra were recorded with a Specord instrument. Melting points are uncorrected.

2-(Diphenylphosphinoyl)cyclopentanone (4a). To a solution of LDA (0.0225 mol), prepared from 4 g of iPr_2NH and 19 mL of 1.2 M BuLi in THF (30 mL), cyclopentanone **2a** (1.68 g, 0.02 mol) in 10 mL of THF was added under argon at −78 °C. After about 30 min chlorodiphenylphosphine (4.41 g, 0.02 mol) was added, and the solution was allowed to reach room temperature. The ^{31}P NMR spectrum of the reaction solution revealed the signal at δ = −30 ppm, which was ascribed to **3a**. Dry air was bubbled through this solution at room temperature for about 30 min. Saturated aqueous solution of NH_4Cl and brine were added, and the layers were separated. The aqueous layer was extracted twice with THF. The combined organic layers were washed with brine and dried over $MgSO_4$. After evaporation of solvents a white solid was obtained which was washed with ether to give 5 g (88%) of pure **4a**, after crystallization from EtOAc: mp 154–157 °C; ^{1}H NMR ($CDCl_3$) δ 1.75–2.6 (m, 6, CH_2's), 3.4 (ddd, 1, $^2J_{P-H}$ = 13.53 Hz, J_{H-H} = 7.67 Hz, J_{H-H} = 9.1 Hz, CHP), 7.3–8.15 (m, 10, Ph); ^{31}P NMR ($CDCl_3$) δ 30.5; ^{13}C NMR ($CDCl_3$) δ 21.48 (d, J_{P-C} = 6.4 Hz, C4), 25.04 (C3), 39.74 (C5), 49.24 (d, $^1J_{P-C}$ = 63.9 Hz, C2), 128.2–128.6 and 130.7–133.1 (several signals, Ph), 212.62 (d, J_{P-C} = 2.9 Hz, C=O); MS *m/e* (rel intensity) 284 (M^+, 56), 229 (43), 202 (74), 201 (100), 125 (79), 83 (3), 77 (47), 55 (9), 51 (23), 47 (30).

Anal. Calcd for $C_{17}H_{17}O_2P$: C, 71.83; H, 6.03; P, 10.90. Found: C, 71.95; H, 6.23; P, 10.75.

2-(Diphenylphosphinoyl)cyclohexanone (4b). With LDA (0.0225 mol) (prepared as above), cyclohexanone **2b** (1.96 g, 0.02 mol), and Ph_2PCl (4.41 g, 0.02 mol) as starting materials in a similar procedure as for **4a**, **3b** was revealed by ^{31}P NMR (δ = −13 ppm). Oxidation of **3b** to **4b** required bubbling dry air through the reaction solution for 1 h. After the usual workup and evaporation of solvents, 5.7 g (95.6%) of the crude product was obtained. Crystallization from EtOAc gave 3.58 g (60%) of pure **4b** (the remaining solution contained still **4b**, as evidenced by TLC, but no attempts to isolate it were made): mp 126–130 °C; ^{1}H NMR ($CDCl_3$) δ 1.5–2.8 (m, 8, CH_2's), 3.42–3.6 (m, 1, CHP), 7.4–8.00 (m, 10, Ph); ^{31}P NMR ($CDCl_3$) δ 29.9 ppm; ^{13}C NMR ($CDCl_3$) δ 23.3 (d, J_{P-C} = 3.22 Hz), 27.6, 28.72 (d, J_{P-C} = 3.37 Hz), 43.6, 52.7 (d, J_{P-C} = 59.9 Hz, CHP), 128.9–129.5 and 131.7–132.6 (several signals, Ph), 208 (C=O); MS *m/e* (rel intensity) 298 (M^+, 79), 229 (37), 219 (20), 202 (100), 201 (90), 155 (24), 125 (10), 77 (47).

Anal. Calcd for $C_{18}H_{19}O_2P$: C, 72.47; H, 6.42; P, 10.38. Found: C, 72.32; H, 6.57; P, 10.29.

2-(Diphenylphosphinoyl)cycloheptanone (4c). With LDA (0.0113 mol), prepared as above, cycloheptanone **2c** (1.12 g, 0.01 mol), and Ph_2PCl (2.205 g, 0.01 mol) as starting materials in the identical procedure as for **4a**, **3c** was revealed by ^{31}P NMR (δ = −10.8 ppm). Oxidation of **3c** to **4c** was performed by bubbling dry air through the reaction solution for ca. 1 h. After the usual workup and evaporation of solvents, 2.9 g (92.9%) of the crude oily product was obtained. Ether was added, and the crude product was crystallized to give 1.9 g (60.9%) of practically pure **4c** (the remaining solution contained still **4c**, as evidenced by TLC,

Table V. Summary of Crystal Data and Data Collection

	9	10
formula	$C_{21}H_{25}O_2PS_3$	$C_{19}H_{19}PO_4$
M_r	436.595	342.331
space group	$P2_1/c$	$P2_1/c$
a, Å	9.013 (1)	11.590 (1)
b, Å	9.582 (1)	17.523 (1)
c, Å	24.651 (1)	8.713 (1)
β, deg	95.75 (1)	99.83 (1)
V, Å^3	2118.3 (3)	1743.4 (5)
Z	4	4
D_c, g cm^{-3}	1.369 (1)	1.304 (1)
D_m, g cm^{-3}	1.365 (1)	1.301 (1)
radiation	Cu Kα	Cu Kα
μ, mm^{-1}	39.9	15.5
2θ range, deg	$2.0 < 2\theta < 150$	$2.0 < 2\theta < 150$
F rejection criterion	$3\sigma(I)$	$3\sigma(I)$
number of reflections		
measured	4626	3306
observed	4119	2795
R	0.039	0.038
R_w	0.044	0.037

but no isolation was attempted), after crystallization from small amounts of acetone: mp 132–135 °C; ^{1}H NMR ($CDCl_3$) (60 MHz) δ 0.9–3.2 (m, 10 H, CH_2's), 3.3–4.1 (m, 1 H, CHP), 7.2–8.0 (m, 10 H, Ph); ^{31}P NMR ($CDCl_3$) δ 30.8 ppm; ^{13}C NMR (25.126 MHz) ($CDCl_3$) δ 23.9 (d, J_{P-C} = 3.76 Hz), 26.2, 27.95 (d, J_{P-C} = 13.1 Hz), 30.2, 43.4, 56.47 (J_{P-C} = 58.2 Hz, CHP), 128–133.6 (several signals, Ph), 209.85 (C=O); MS m/e (rel intensity) 312 (59, M$^+$), 258 (10), 229 (27), 219 (86), 202 (100), 201 (79), 155 (9), 125 (8), 77 (37).

Anal. Calcd for $C_{19}H_{21}O_2P$: C, 73.06; H, 6.78; P, 10.24. Found: C, 72.04, H, 6.56; P, 10.33.

2-(Diphenylphosphinoyl)-3-[tris(methylthio)methyl]-cyclopentanone (9). To a solution of trimethyl trithioorthoformate (1.54 g, 0.01 mol) in THF (35 mL) was dropped *n*-butyllithium (10 mL, 0.012 mol) under argon at −78 °C followed by 0.5 mL of HMPT. After 10 min 2-cyclopentenone (**6**) was added dropwise at −78 to −50 °C. The solution was stirred for 1.5 h at −50 °C and then cooled to −78 °C, and chlorodiphenylphosphine (2.205 g, 0.01 mol) was quickly added. The reaction mixture was allowed to reach room temperature. Dry air was bubbled through the crude reaction solution at room temperature for 0.5 h. Brine was added, and the layers were separated. The aqueous layer was extracted twice with THF. The combined organic layers were washed twice with brine and dried over $MgSO_4$. After evaporation of solvents 4.6 g of brown oil was obtained, which was purified by column chromatography on silica gel using ether as an eluent to give 1.744 g (40%) of pure **9** as a white solid (TLC, silica gel Merck; ether, R_f = 0.25), after crystallization from EtOAc: mp 129–132 °C; ^{1}H NMR ($CDCl_3$) δ 2.04 (s, 9, SCH_3), 2.0–2.6 (m, 4, CH_2's), 3.31 (dd, 1, $J_{H3-H4'}$ = 8.8 Hz, $J_{H3-H4''}$ = 17.1 Hz, CHC(SMe)$_3$), 4.03 (d, 1, $^2J_{P-H}$ = 14.9 Hz, CHP), 7.45–8.6 (m, 10, Ph); ^{31}P NMR ($CDCl_3$) δ 28.4; ^{13}C NMR ($CDCl_3$) δ 14.03 (SCH_3), 23.5 (C4), 37.6 (C5), 47.9 (C3), 56.1 (d, J_{P-C} = 53.4 Hz, C2), 128.2–132.4 (several signals, Ph), 212.7 (C=O); MS m/e (rel intensity), 436 (M$^+$, 1), 389 (40, M$^+$ − SMe), 375 (11), 201 (25), 183 (100), 153 (9), 141 (18), 77 (19).

Anal. Calcd for $C_{21}H_{25}O_2PS_3$: C, 57.77; H, 5.77; P, 7.09. Found: C, 57.75, H, 5.77; P, 7.41.

2-(Diphenylphosphinoyl)-3-carbomethoxycyclopentanone (10). The phosphinoxide **9** (0.872 g, 2 mmol) was dissolved in 40 mL of aqueous methanol (93% MeOH, 7% H_2O, vol). Yellow mercury(II) oxide (0.74 g, 3.4 mmol) and mercury(II) chloride (2.34 g, 8.6 mmol) were added, and the resulting suspension was stirred and refluxed under argon for 8 h and then left overnight at room temperature. The precipitate was filtered off and washed several times with CH_2Cl_2. From the combined filtrates solvents were evaporated to dryness. An aqueous solution of NH_4Cl and CH_2Cl_2 were added to the residue, the mixture formed was vigorously shaken, and the layers were separated. The aqueous layer was extracted twice with CH_2Cl_2. The combined organic layers were washed once with aqueous NH_4Cl and dried over $MgSO_4$. After evaporation of the solvent, 0.643 g (94%) of a crude product was obtained as a white-pink solid. Crystallization from small amounts of EtOAc gave 0.514 g (75%) of pure **10**, as white crystals; mp 147–150 °C; ^{1}H NMR ($CDCl_3$) δ 2.0–2.45 (m, 4, CH_2's), 3.53 (s, 3, OCH_3), 3.5–3.7 (m, 1, $CHCO_2Me$), 3.86 (dd, 1, $^2J_{P-H}$ = 12.2 Hz, J_{H2-H3} = 6.4 Hz, CHP), 7.3–8.0 (m, 10, Ph); ^{31}P NMR ($CDCl_3$) δ 30.5; ^{13}C NMR ($CDCl_3$) δ 26.04 (d, J_{P-C} = 5.4 Hz, C4), 38.96 (C5), 42.5 (C3), 52.3 (d, J_{P-C} = 62.5 Hz, C2), 52.4 (OCH_3), 128.4–132.2 (several signals, Ph), 174.2 (CO_2Me), 210 (C=O); MS m/e (rel intensity) 342 (M$^+$, 34), 311 (12, M$^+$ − OMe), 287 (29), 283 (49), 201 (100), 77 (37).

Anal. Calcd for $C_{19}H_{19}O_4P$: C, 66.66; H, 5.59; P, 9.05. Found: C, 66.63; H, 5.57; P, 8.96.

X-ray Analysis. Crystal data and some details of the structure refinements are given in Table V. Intensity data were collected using a CAD4 diffractometer in the range: for **10**, $1 < \theta < 70°$; for **9**, $1 < \theta < 75°$, with graphite monochromatized Cu Kα radiation (λ = 1.541 78 Å) in the $\omega/2\theta$ scan mode, lattice constants were refined by least-squares fit of 25 reflections in the θ range 16.2–27.8° for **10** and 11.6–28.0° for **9**. In **10**, no absorption correction was applied but in **9** was applied with maximum correction factor equal to 0.9998, minimum correction factor equal to 0.8696, average correction factor equal to 0.9373. A total of 3306 integrated reflections in **10** and 4626 reflections in **9** were collected up to $\sin\theta/\lambda$ = 0.7511 Å^{-1}, $\omega/2\theta$ scan technique, scan width: 0.78 + 0.14 tan θ)° for **10**; (0.85 + 0.14 tan θ) for **9**, range of measurement: $0 < h < 14$, $0 < k < 21$, $-10 < l < 10$ for **10** and $0 < h < 11$, $0 < k < 12$, $-30 < l < 30$ for **9**. A small decline in intensities of three standard reflections (6,0,2; 0,−9,−2; 2,8,−2) in **10** was −1.5% during 78.3 h and in **9**, where standard reflections are −2,0,−12; 0,4,−7; −1,5,−1, was −0.7% during 52.8 h. A total of 2795 observed reflections in **10** and 4119 in **9** [with criteria $I > 3\sigma(I)$] were used to solve the structure by direct methods and to refine it by full-matrix least-squares method using F's; H atoms combined with carbon were placed at idealized positions with fixed isotropic thermal parameter of carbon atom and refined. Refinement converged in **10** to R = 0.038, R_w = 0.037 with unit weight for 293 refined parameters, and in **9** to R = 0.039, R_w = 0.044 with unit weight for 328 refined parameters. Largest shift error in the last cycle was in **10**, 0.23, and in **9**, 0.15. Largest residual peak in final difference Fourier map was 0.279 eÅ^{-3} in **10** and 0.258 eÅ^{-3} in **9**. All calculations were carried out with the Enraf-Nonius SDP crystallographic computing package[21] scattering factors from *International Tables for X-ray Crystallography*.[22]

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Registry No. **2a**, 120-92-3; **2b**, 108-94-1; **2c**, 502-42-1; **3a**, 124604-15-5; **3b**, 124604-16-6; **3c**, 124604-17-7; **4a**, 124604-10-0; **4b**, 124604-11-1; **4c**, 124604-12-2; **6**, 930-68-7; **9**, 124604-13-3; **10**, 124604-14-4; Ph_2PCl, 1079-66-9; $(MeS)_3CH$, 5418-86-0.

Supplementary Material Available: Table I and further X-ray data for compounds **9** and **10**; tables of bond lengths and bond angles, general displacement parameter expressions (B's and U's), refined displacement parameter expressions (β's), and positional parameters (24 pages). Ordering information is given on any current masthead page.

(21) Frenz, B. A. *SDP Structure Determination Package*; Enraf-Nonius: Delft, 1984.

(22) *International Tables for X-ray Crystallography*; Kynoch Press: Birmingham, 1974.