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α-Phosphoryl Sulfoxides VIII.[1,2] Stereochemistry of α-Chlorination of α-Phosphoryl Sulfoxides

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Abstract: Chlorination of α-phosphoryl sulfoxides **1** with iodobenzene dichloride and sulfuryl chloride in the presence and in the absence of pyridine and stereochemical investigations of this reaction using (+)-(S)-α-dimethoxyphosphorylmethyl p-tolyl sulfoxide **1a** are described. It was found that conversion of **1** to the corresponding α-chloro-α-phosphoryl sulfoxides **2** occurs under the stereochemical control of the sulfinyl group and leads to diastereomeric mixtures. The extent of asymmetric induction at the α-carbon atom and racemization of the chiral sulfinyl centre in **1** depend on the reaction conditions. The structure of the major diastereomer formed in the chlorination of (+)-(S)-**1a** i.e. (+)-$(S)_C(S)_S$-α-chloro-α-dimethoxyphosphorylmethyl p-tolyl sulfoxide **2a** was determined by X-ray analysis. The structure was solved by direct methods and refined to R=0.081. The experimental data on chlorination of α-phosphoryl sulfoxides **1** point to retention of the configuration at both chiral centres (C and S) and this stereochemistry can be rationalized assuming addition-elimination mechanism involving the formation of a positively charged ylide as intermediate.

INTRODUCTION

α-Halogenation of sulfoxides was one of the most extensively studied electrophilic substitution reactions at the chiral or prochiral α-carbon atom. Sulfoxides having at least one hydrogen at the α-carbon atom can be

converted into the corresponding α-halogeno sulfoxides upon treatment with a variety of electrophilic halogenating reagents. Iodobenzene dichloride, sulfuryl chloride, nitrosyl chloride, chlorine, bromine, hypochlorites, N-chlorobenzotriazole, N-chloro and N-bromosuccinimide in the presence of bases are usually used for this purpose.[3] The presence of bases should prevent the alternative Pummerer reaction of sulfoxides. It was found, however, that α-halogeno sulfoxides can be obtained when sulfuryl chloride or chlorine in the absence of bases are used. They are also formed in the acid catalyzed reaction with N-chlorosuccinimide.

The stereochemical course of α-halogenation of sulfoxides is strongly dependent on the reaction conditions. Thus, halogenation of sulfoxides in the presence of bases, which are soluble in the reaction medium like pyridine, is highly stereoselective but not regioselective. For example, halogenation of methyl benzyl sulfoxide under these conditions yields an equimolar mixture of products of the methyl and methylene group chlorination.[4] In the case of simple sulfoxides with a chiral or prochiral carbon one of the two possible diastereomers is formed.[5] On the contrary, halogenation carried out in the absence of bases or in the presence of bases insoluble in the reaction medium such as potassium carbonate is regioselective but usually not very stereoselective.[6]

Furthermore, it was found that a clear relationship exists between the stereochemical courses at sulfur and the α-carbon atom during halogenation of dialkyl or aralkyl sulfoxides. Generally, α-halogenation proceeds with simultaneous inversion or retention of configuration at both centres. The reaction mechanism proposed by Montanari[7,8] to explain the stereochemistry of α-halogenation of sulfoxides involves in a key step the concerted halogen migration and hydrogen abstraction in the transiently formed halogenosulfoxonium salts. An elimination-addition mechanism via "inverted ylids" proposed originally by Klein[9] may also be used to explain the stereochemical course of α-halogenation of sulfoxides.

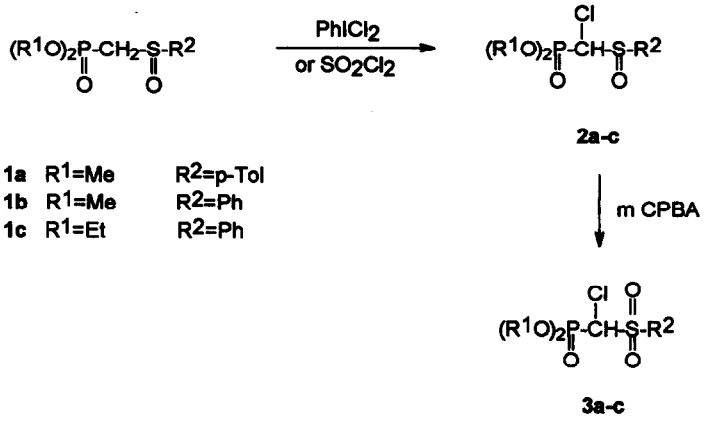
In the present paper we describe the synthesis of α-chloro α-phosphoryl sulfoxides as well as the stereochemistry of chlorination of chiral dimethoxyphosphorylmethyl p-tolyl sulfoxide. α-Phosphoryl sulfoxides, which recently became easily available in racemic and optically active forms, are interesting model compounds for the study on α-halogenation at least for two reasons. The first is that they contain the methylene protons of relatively high acidity due to the presence of two electron-withdrawing phosphoryl and sulfinyl groups. Secondly, it seemed interesting to study the effect of the dialkoxyphosphoryl group at the α-carbon atom on the stereochemical course of α-chlorination of sulfoxides, especially in view of the significant role of conformational and electronic factors in the mechanism of that reaction.

RESULTS

Synthesis of α-Chloro-α-Phosphoryl Sulfoxides

The chlorination reaction of α-phosphorylmethyl aryl sulfoxides **1a-c** was carried out in a methylene chloride solution using iodobenzene dichloride as a controlled source of chlorine or sulfuryl chloride at -40°C and 0°C, respectively. It was found that α-chloro-α-phosphoryl sulfoxides **2a-c** are produced in the chlorination reaction

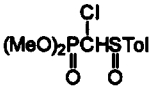
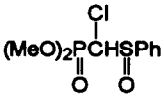
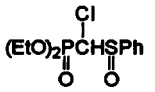
both when the reaction is performed in the presence of pyridine used in an excess or in its absence.



1a R^1=Me R^2=p-Tol
1b R^1=Me R^2=Ph
1c R^1=Et R^2=Ph

The analytically pure α-chloro-α-phosphoryl sulfoxides **2** were isolated from the reaction mixture by column chromatography. The structure of the chlorination products was confirmed by the ^{1}H NMR spectra and elemental analysis.

Table 1. Synthesis of α-Chloro-α-Phosphoryl Sulfoxides **2**

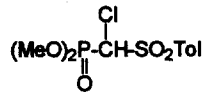
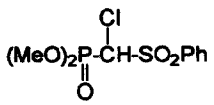
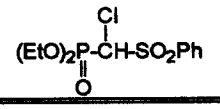
No	Product	Reaction conditions	Yield[%]*	Ratio of diastereomers
2a		$PhICl_2$/Py	56	3.2:1
		$PhICl_2$/-	60	2.9:1
		SO_2Cl_2/Py	44	2.75:1
		SO_2Cl_2/-	57	3.25:1
2b		$PhICl_2$/Py	51	2.5:1
2c		$PhICl_2$/Py	54	2.7:1
		SO_2Cl_2/Py	56	2.4:1
		SO_2Cl_2/-	63	2.4:1

*Yield of the analytically pure product.

The α-chloro-α-phosphoryl sulfoxides **2** were additionally characterized by oxidation to the corresponding α-chloro-α-phosphoryl sulfones **3** using m-chloroperbenzoic acid in chloroform solution. The yields and physical properties of α-chloro-α-phosphoryl sulfoxides **2** and sulfones **3** prepared are summarized in Table 1 and 2.

Since the α-carbon atom in α-phosphoryl sulfoxides **1a-c** is a prochiral centre, α-chloro sulfoxides **2a-c** contain in their molecules two asymmetric centres and therefore may exist in two diastereomeric forms. The diastereomers of α-chloro sulfoxides **2a-c** can be distinguished on the basis of their ^{1}H-NMR spectra. Two doublets for the methine proton and the doubling of signals of the diastereotopic alkoxy groups at the phosphorus atom are observed. Considering the spectrum readability, the signals of the methine proton are of greater analytical value. Analysis of the spectra of the crude reaction products revealed that chlorination of α-phosphoryl sulfoxides yields, in contrast to the chlorination of simple alkylaryl and dialkyl sulfoxides, a mixture of two diastereomers. The ratio of diastereomeric α-chloro sulfoxides **2a-c** was determined by integrating the methine proton signals in the ^{1}H-NMR spectra. It was found that for a given α-phosphoryl sulfoxide **1** the diastereomer ratio in the α-chloro-α-phosphoryl sulfoxide **2** obtained is practically constant irrespective of the chlorinating reagent and reaction medium. The ratios of the obtained diastereomers of α-chloro sulfoxides **2a-c** are given in Table 1. In all cases the major diastereomers were isolated from the diastereomeric mixtures by crystallization or by column chromatography.

Table 2. Synthesis of α-Chloro-α-Phosphoryl Sulfones **3**

No	Product	Yield[%]*	n_D^{20}/M.p.
3a		89	101-102°
3b		88	1.5382
3c		91	1.5300

* Yield of the analytically pure product.

Chlorination of (+)-(S)-Dimethoxyphosphorylmethyl p-Tolyl Sulfoxide 1a

Conversion of α-phosphoryl sulfoxides **1** to the corresponding α-chloro derivatives **2** is particularly interesting

from the stereochemical point of view, since in this reaction a new chiral centre at the α-carbon atom is formed under the stereochemical control of the sulfinyl group.

The (+)-(S) enantiomer of dimethoxyphosphorylmethyl p-tolyl sulfoxide **1a** of 97% optical purity and with specific rotation $[\alpha]_D$+144 was chosen as a model compound for studying the stereochemistry of chlorination. The chlorination reaction was performed using iodobenzene dichloride and sulfuryl chloride in the presence of pyridine as well as in its absence. In all cases, like for the racemic compounds, the mixtures of the diastereomeric α-chloro sulfoxides **2a** of almost identical composition were obtained.

The optical rotation of a mixture of diastereomeric α-chloro sulfoxides **2a** was measured after purification by column chromatography conducted in such a way as to preserve the ratio of diastereomers. The determined values of optical rotation differed considerably as shown in Table 3.

Table 3. α-Chlorination of (+)-(S)-Dimethoxyphosphorylmethyl p-Tolyl Sulfoxide **1a**

No	Chlorinating agent	Sulfoxide **2a**		
		$[\alpha]_D^{25}$ after chromatography	Ratio of diastereomers	$[\alpha]_D^{25}$ after epimerization
a	$PhICl_2$/Py	+63	3.3:1	+74
b	$PhICl_2$/-	+131	2.75:1	+165
c	SO_2Cl_2/-	+185	3.25:1	+209
d	SO_2Cl_2/Py	+180	2.8:1	-

The fact that a mixture of diastereomeric α-chloro sulfoxides **2a** of constant composition but with various values of optical rotation was obtained points to a partial racemization of the chiral sulfinyl group depending on the reaction conditions, the racemization being highest when iodobenzene dichloride in the presence of pyridine was used, and much lower when sulfuryl chloride was applied as chlorinating agent. In all cases, however, the α-chloro sulfoxide **2a** with optical rotation $[\alpha]_D$+243 was isolated from the diastereomeric mixture in the course of triple recrystallization from benzene. The value of optical rotation given above did not vary after successive crystallizations. The ^{1}H-NMR spectrum of the compound obtained in this way showed that it was one pure diastereomer which prevails in the reaction mixture.

In order to determine the optical purity at the sulfur atom of this diastereomer, it was subjected to reduction with zinc in methanol which led to the initial (+)-(S) α-phosphoryl sulfoxide **1a** with $[\alpha]_D$+139. Dehalogenations of the mixtures of diastereomeric α-chloro sulfoxides **2a** having specific rotations +69, +131, +180 were also carried out and the starting α-phosphoryl sulfoxide **1a** with optical rotation +49, +95 and +121 respectively, was obtained.

Table 4. Reduction of Optically Active α-Chloro-α-Phosphoryl Sulfoxides **2a**

No	$[\alpha]_D^{25}$		Optical purity at the sulfur atom (%)		
	2a	**1a**	**1a**	**2a***	**2a****
a	+63	+49	33	35	31
b	+131	+95	64	67	68
c	+185	-	-	-	86
d	+180	+121	81	85	-
e	+243	+139	93	98	-

*Values calculated after taking into consideration correction due to partial racemization of α-phosphoryl sulfoxide **1a** under reduction conditions.

Values calculated based on the values of optical rotation of **2a after epimerization at α carbon.

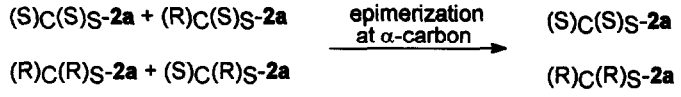
The effect of the reduction conditions on the optical rotation value of **1a** was determined in an independent experiment in which α-phosphoryl sulfoxide **1a**, $[\alpha]_D$+144, was treated with sulfuric acid in methanol solution. The decrease of optical rotation of **1a** to the value of $[\alpha]_D$+137 was observed. The above results as well as the ^{1}H-NMR spectra indicate unequivocally that the isolated diastereomer **2a**, $[\alpha]_D$+243 is optically pure at both chiral centres. The results presented in Table 4 also establish optical purity of the chiral sulfinyl centre in α-chloro-α-phosphoryl sulfoxides **2a** obtained under different reaction conditions. Thus, optical purity at the sulfur atom of the α-chloro sulfoxide **2a** obtained using iodobenzene dichloride in the presence of pyridine was 35%, whereas in the absence of pyridine it was 67%. On the contrary, chlorination with sulfuryl chloride leads to the α-chlorosulfoxide **2a** with 85% optical purity. The optical purities at the sulfur atom in **1a**, determined from the reduction experiments are summarized in Table 4.[10]

It deserves noting that in all cases the zinc reduction yielded the dextrorotatory α-phosphoryl sulfoxide **1a** i.e. with the same configuration S as that of the starting α-phosphoryl sulfoxide **1a**. This result is a proof of a prevailing retention of configuration at the sulfur atom during chlorination of α-phosphoryl sulfoxides **1** under all reaction conditions tested.

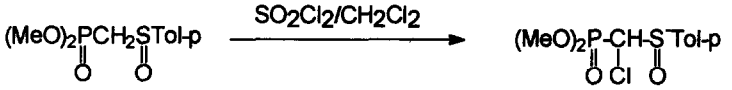
The ratio of diastereomeric α-chloro sulfoxides **2a** was determined from the ^{1}H-NMR spectra obtained directly after isolation of the products from reaction mixtures. In the spectra of the same compounds taken after two weeks the signals corresponding to the prevailing diastereomer were only observed while those to the other diastereomer disappeared. This phenomenon is due to conversion of the less thermodynamically stable diastereomer of the α-chloro sulfoxide **2a** to the more stable one. The epimerization takes place at the optically

active α-carbon atom, most probably via the carbanionic species since the proton at this carbon atom is exceptionally acidic due to the presence of three substituents stabilizing the α-phosphonate carbanion, i.e. the phosphoryl and sulfinyl groups and chlorine atom. The values of optical rotations of the α-chloro-α-phosphoryl-sulfoxide diastereomers **2a** obtained in this way changed and increased somewhat with respect to the corresponding diastereomeric mixtures (see Table 3, last column).

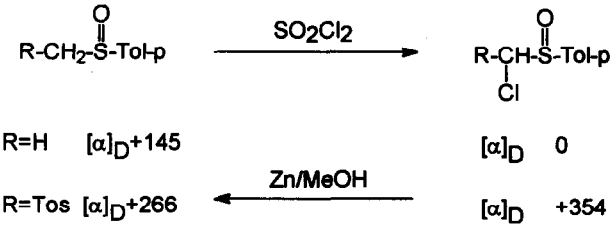
The phenomenon of isomerization of diastereomers of **2a** (see below) makes it possible to determine independently the optical purity at the sulfur atom, since, in effect, we have to deal with an enantiomeric mixture and the value of optical rotation of one pure enantiomer is known. The values of optical purity at the sulfur atom of α-chloro sulfoxides **2a** calculated based on isomerization are listed in Table 4 together with the values determined by the reduction method. It is necessary to stress a good agreement between the values of optical purity calculated by both methods.



Durst found that chlorination of simple sulfoxides with sulfuryl chloride in the absence of a base, though efficient and convenient thanks to the simple procedure, is non-stereospecific and yields both possible diastereomers in equal amounts.[11]



On the other hand, the (+)-(S) enantiomer of **1a** yields the chlorination product of high optical purity (86%) at the sulfur centre. In order to compare the influence of substituents at the α-carbon atom on the stereochemical course of chlorination two additional experiments were caried out using optically active methyl p-tolyl sulfoxide $[\alpha]_D$+145 and tolylsulfonylmethyl p-tolyl sulfoxide $[\alpha]_D$+266. The chlorination reaction was carried out according to the procedure elaborated for α-phosphoryl sulfoxides and in both cases the corresponding α-chloro sulfoxides were obtained.



In the case of unsubstituted methyl p-tolyl sulfoxide racemic α-chloromethyl p-tolyl sulfoxide was obtained, whereas chlorination of the sulfoxide with the α-tosyl group afforded a mixture of the corresponding diastereomers in a ratio 3.5:1, $[\alpha]_D$+354. Moreover, reduction of this mixture with zinc and methanol gave back the starting sulfoxide with the same optical rotation what indicates that chlorination occurs with a full retention at sulfur.

Therefore, the presence of the α-phosphoryl group in sulfoxides as well as the α-tosyl substituent has a strong effect on their chemical reactivity and, as can be seen from the above results, changes completely the reaction stereochemistry and most probably the mechanism of chlorination.

Crystal and Molecular Structure of (+)-(S)$_C$(S)$_S$-α-Chloro-α-Dimethoxyphosphorylmethyl p-Tolyl Sulfoxide **2a**

In order to determine the absolute configuration of the newly formed chiral centre at the α-carbon atom in the major diastereomer (+)-**2a** isolated from the chlorination reaction of (+)-(S)-**1** we determined its crystal and molecular structure. Since the absolute configuration S at the sulfinyl sulfur atom in (+)-**2a** has been found to be preserved during chlorination, a simple X-ray analysis should allow to deduce the absolute configuration at the α-carbon atom by internal comparison of two chiral centres. The structure of the α-chloro-α-phosphoryl sulfoxide (+)-**2a**, $[\alpha]_D$+243, mp. 106-107°, has been solved by direct methods and refined by full-matrix least-squares to the final value R=0.081.

The molecular structure of the sulfoxide (+)-**2a** investigated here with the numbering system is shown in Fig.1. The most important result of the X-ray analysis is that the absolute configuration at the α-carbon atom is S. Fig.2 shows the Newman projection around the C(1)-S bond which clearly reveals that this sulfoxide adopts the conformation with the antiperiplanar arrangement of the dimethoxyphosphoryl group at C and p-tolyl group at S.

The bond distances and angles are listed in Table 5 and 6, respectively. They do not show significant deviations from the expected values. The geometry at phosphorus as well as at sulfur is close to tetrahedral.

DISCUSSION

On the basis of the presented data, it is known that chlorination of α-phosphoryl sulfoxides occurs with prevailing retention of the configuration at the sulfur atom, but these results do not allow us to define the stereochemistry at the carbon atom. The crystal structure of the major diastereomer of α-chloro sulfoxide was determined by X-ray analysis, and the S absolute configuration assigned to the chiral carbon atom. It means that chlorination of α-phosphoryl sulfoxides occurs either with retention at the carbon atom with abstraction of pro-S hydrogen or with inversion of configuration when pro-R hydrogen is abstracted. According to the study received up to now, steric course involving retention and inversion of configuration at the sulfur and carbon atom, respectively, was not noticed. Therefore, it is more probable that chlorination of α-phosphoryl sulfoxides occurs with retention at both chiral centres.

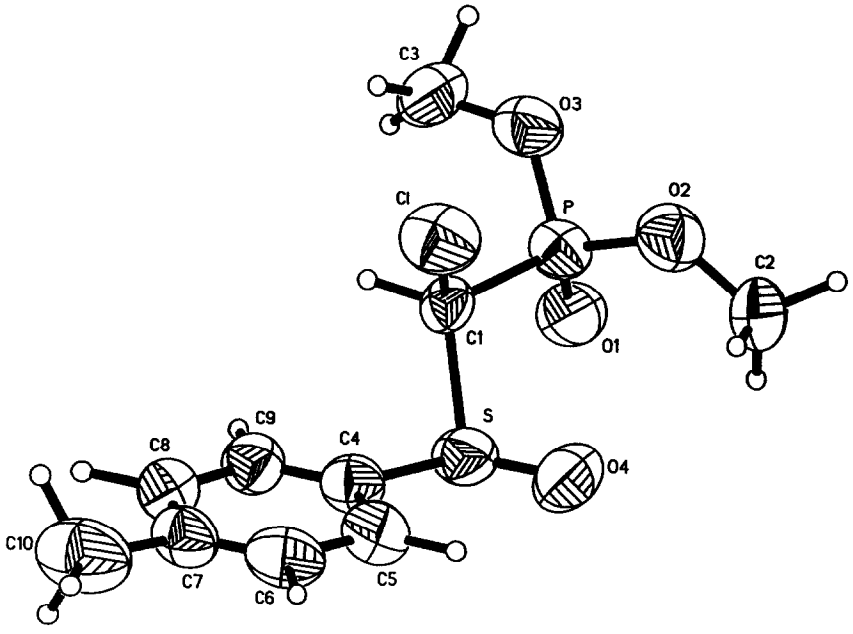


Fig.1. Three-dimensional view of (+)-$(S)_C(S)_S$-**2a**

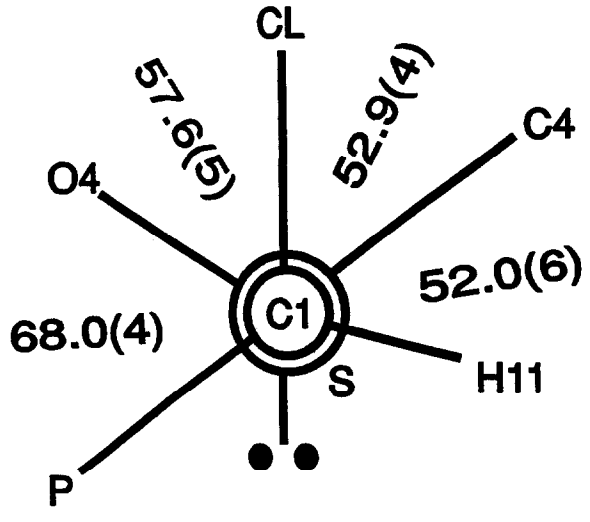


Fig.2. Newman projection around the C(1)-S bond.

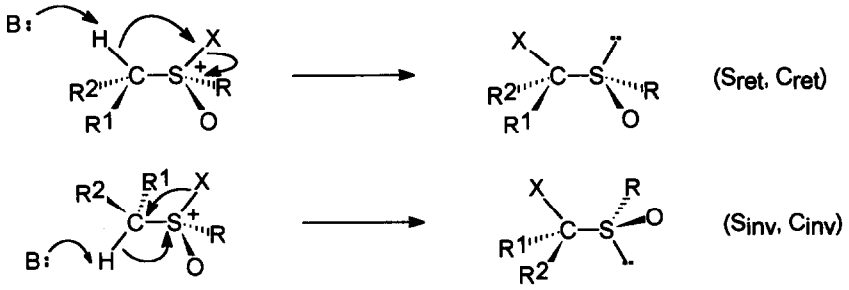
Table 5. Bond lengths (Å)

0(1)-P	1.442(6)	0(2)-P	1.536(7)
0(3)-P	1.572(6)	C(1)-P	1.832(7)
C(2)-0(2)	1.437(12)	C(3)-0(3)	1.383(12)
0(4)-S	1.454(8)	C(1)-S	1.854(7)
C(4)-S	1.805(8)	C(1)-Cl	1.744(7)
C(5)-C(4)	1.389(10)	C(9)-C(4)	1.356(12)
C(6)-C(5)	1.408(14)	C(7)-C(6)	1.324(14)
C(8)-C(7)	1.332(11)	C(10)-C(7)	1.532(14)
C(9)-C(8)	1.392(12)		
H(21)-C(2)	1.08	H(22)-C(2)	1.08
H(23)-C(2)	1.08	H(31)-C(3)	1.08
H(32)-C(3)	1.08	H(33)-C(3)	1.08
H(11)-C(1)	1.08	H(51)-C(5)	1.08
H(61)-C(6)	1.08	H(81-C(8)	1.08
H(91)-C(9)	1.08	H(101)-C(10)	1.08
H(102)-C(10)	1.08	H(103)-C(10)	1.08

Table 6. Bond angles (°)

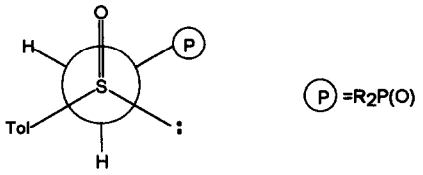
0(2)	-P	-0(1)	116.2(4)	0(3)	-P	-0(1)	116.7(4)
0(3)	-P	-0(2)	99.3(3)	C(1)	-P	-0(1)	110.0(3)
C(1)	-P	-0(2)	109.3(4)	C(1)	-P	-0(3)	104.4(3)
C(2)	-0(2)	-P	123.1(6)	C(3)	-0(3)	-P	121.6(6)
C(1)	-S	-0(4)	107.2(4)	C(4)	-S	-0(4)	107.1(4)
C(4)	-S	-C(1)	97.6(3)	S	-C(1)	-P	108.6(4)
Cl	-C(1)	-P	112.1(4)	Cl	-C(1)	-S	113.8(4)
C(5)	-C(4)	-S	117.0(7)	C(9)	-C(4)	-S	119.5(6)
C(9)	-C(4)	-C(5)	123.3(9)	C(6)	-C(5)	-C(4)	113.7(9)
C(7)	-C(6)	-C(5)	125.0(9)	C(8)	-C(7)	-C(6)	118.1(9)
C(10)	-C(7)	-C(6)	122.5(9)	C(10)	-C(7)	-C(8)	119.2(10)
C(9)	-C(8)	-C(7)	122.5(9)	C(8)	-C(9)	-C(4)	117.4(8)

The mechanism proposed by Montanari[8] (Scheme 1) to explain the prevailing retention of configuration in the halogenation of methyl aryl sulfoxides assumes a concerted migration of a halo cation from sulfur to carbon. This mechanism requires also the halo oxosulfonium ion to adopt a syn-periplanar conformation. However, a syn-periplanar conformation is unfavoured by steric factors, particularly when substitution at the α-carbon is increased. For instance, when the methyl group is replaced by the ethyl one, the α-halogenation occurs with prevailing inversion of configuration at the sulfinyl group. This stereochemistry is due to enhanced stability of an anti-periplanar conformation of the halo oxosulfonium salt.



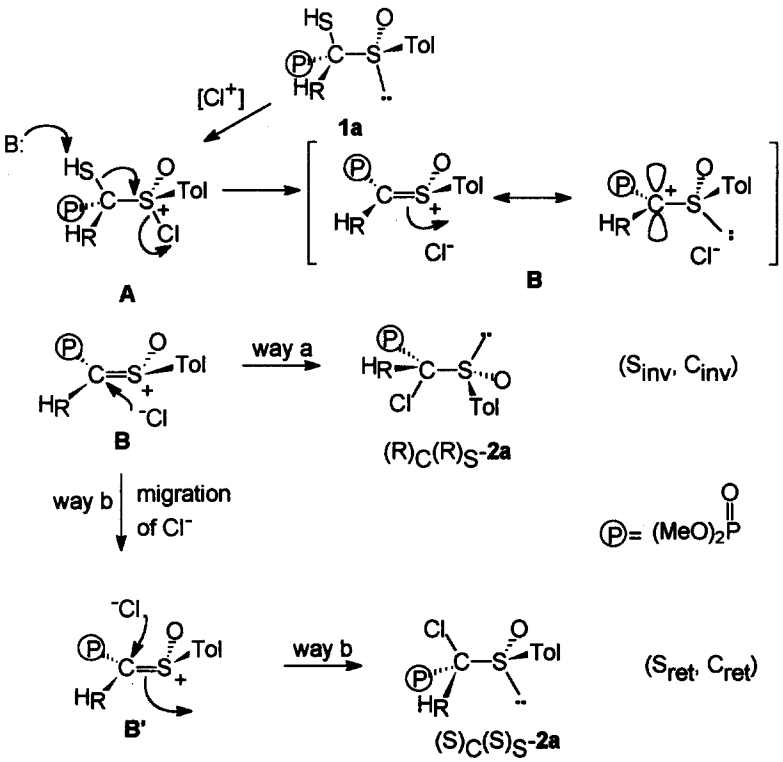
Scheme 1

It seems far less probable that α-phosphoryl sulfoxides exist in a syn-periplanar conformation since the α-carbon atom is connected with a bulky dialkoxyphosphoryl moiety. In fact, X-ray analysis of diphenoxyphosphorylmethyl phenyl sulfoxide revealed that it adopts a conformation in which the bulky diphenoxyphosphoryl and phenyl groups are in anti-periplanar orientation around the sulfur-methylene carbon bond.[12] Moreover, the CD spectra[2] of a series of (+)-α-phosphoryl sulfoxides of general formulae, $R^1_2P(X)CHR^2S(O)Tol\text{-}p$ (where R^1=MeO, EtO, Ph, Me_2N, X=O,S, R^2=H, Me) strongly suggest that a predominant (if not exclusive) solution conformation is the same i.e. both the phosphoryl group and aromatic ring are antiperiplanar as shown below.



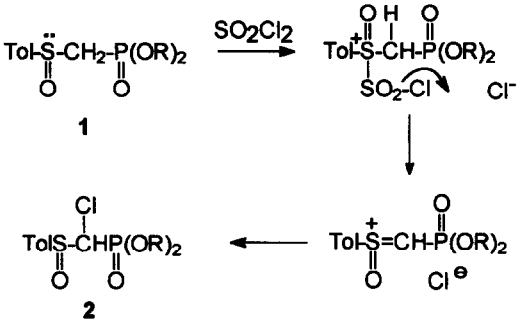
However, the observed stereochemistry of the chlorination of α-phosphoryl sulfoxides may be explained by assuming the formation of the positively charged ylide **B** via stereoselective anti elimination of a proton and chloride anion from the chlorosulfoxonium salt **A** formed in the first reaction stage. In the elimination reaction the chloride leaves with the pair of electrons and another pair of electrons from the C-H bond is introduced into

the C-S bond as shown in Scheme 2. It is important to note that the positively charged ylide **B** is not planar and sulfur maintains its original configuration after anti elimination. Moreover, the sharing of two electrons by sulfur and the vacant p orbital on carbon introduces a barrier to rotation around the C-S bond. The configuration at sulfur and carbon in the chlorination product is determined during the addition of the chloride anion to the ylide **B**. The attack of **B** by the chloride anion from the same side (way a) where it was eliminated (under the PH_RCS plane) will lead to the α-chlorosulfoxide **2a** in which both chiral centres (S and C) have inverted configuration with respect to the starting sulfoxide **1a**. This step involves inversion at sulfur in the intermediate **B** due to introduction of the lone electron pair anti to the forming C-Cl bond. On the other hand, the migration of the chloride anion from one side the PH_RCS plane to the other leads to the configurationally different ylide structure **B'**. The attack of the chloride anion at the carbon atom in **B'** will result in the formation of α-chlorosulfoxide **2a** with retention of configuration at both chiral centres. The overall steric course of the chlorination reaction will depend on a difference between energy barrier for inversion at sulfur in the first case (way a), and the energy barrier necessary to overcome the electrostatic attraction between two ions of opposite charges for their partial separation that will permit a migration of anion, in the second case (way b).



Scheme 2

The most striking result of the present paper is the different behaviour of tolyl sulfoxides containing methyl, α-phosphorylmethyl and α-tosylmethyl groups when SO_2Cl_2 is used. Although the mechanism of the sulfoxide chlorination by SO_2Cl_2 was not investigated, a possible reaction course is shown in Scheme 3 which involves the formation of an intermediate with a S-S bond.



Scheme 3

If an elimination-addition mechanism is at work, the different behaviour of the substrates could be interpreted on the basis of different barrier of rotation around the C-S bond.

EXPERIMENTAL

All melting points are uncorrected. Solvents and commercial reagents were distilled and dried by conventional methods before use. ^{1}H-NMR spectra were recorded at 60MHz with R12B Perkin-Elmer Spectrometer and Varian A-60 Spectrometer and at 90MHz with a Bruker HX90 Spectrometer. Column chromatography was done on Merck silica gel, 100-200 mesh. Optical activity measurements were made with a Perkin-Elmer 241 MC photopolarimeter in acetone or chloroform solution.

Optically Active Methyl p-Tolyl Sulfoxide

Optically active (+)-(S)-methyl p-tolyl sulfoxide, $[\alpha]_D^{25}$+145 (c 1.6 acetone) was obtained according to the literature.[13]

Optically active Dimethoxyphosphorylmethyl p-Tolyl Sulfoxide 1a

Optically active (+)-(S)-dimethoxyphosphorylmethyl p-tolyl sulphoxide **1a**, $[\alpha]_D^{25}$+144 (c 1.0 acetone) (97% ee), was obtained according to the procedure described by us previously.[14]

Chlorination of α-Phosphoryl Sulfoxides 1 to α-Chloro-α-Phosphoryl Sulfoxides 2

α-Chloro-α-Dimethoxyphosphorylmethyl p-Tolyl Sulfoxides 2a

A. Chlorination with Iodobenzene Dichloride and Pyridine. A solution of iodobenzene dichloride (0.715g, 0.0026mol) in anhydrous pyridine (8ml) was added dropwise at -40° to a stirred solution of the sulfoxide **1a** (0.524g, 0.002mol) in anhydrous dichloromethane (4ml). The mixture was kept at -40° for 1h, and then at room temperature for 1h. Chloroform (30ml) was added and pyridine was removed with aqueous sulfuric acid; the chloroform solution was then washed with water, dried and evaporated to give a mixture of the diastereomers **2a** in a 3.2:1 ratio as indicated by NMR spectrum.

Analytically pure sample of **2a** was obtained by column chromatography (benzene-acetone 5:1) in 56% yield (0.3g), **2a** was then recrystallized from benzene three times to give 0.087g (26%) of a predominant diastereomer, m.p.106-7°, ^{1}H-NMR ($CDCl_3$) δ 2.4 (s, 3, $\underline{CH_3}$-C_6H_4). 3.81, 3.89 (dd, 6, $\underline{CH_3}OP$, $J_{P\text{-}C}$11.2Hz), 4.61 (d, 1, P(O)$\underline{CH}$Cl, $J_{P\text{-}C}$11.7Hz), 7.42 (A_2B_2, 4, aromatic); minor diastereomer: 3.75, 3.83 (dd, 6, CH_3OP, $J_{P\text{-}C}$11.08, 11.3Hz), 4.72 (d, 1, P(O)$\underline{CH}$Cl, $J_{P\text{-}C}$9.5Hz). Anal.Calcd. for $C_{10}H_{14}O_4ClPS$: C, 40.48; H, 4.76; Found: C, 40.57; H, 4.69.

B.Chlorination with Iodobenzene Dichloride without Pyridine. A solution of iodobenzene dichloride (0.715g, 0.026mol) in anhydrous dichloromethane (10ml) was added dropwise at -40° to a stirred solution of the sulfoxide **1a** (0 524g, 0.002mol) in anhydrous dichloromethane (10ml). The mixture was kept at -40° for 1h, then was allowed to warm to room temperature and washed with water. The solvent was evaporated off to give a mixture of diastereomers **2a** in a 2.9:1 ratio. Column chromatography afforded 0.356g of **2a** (60%).

C. Chlorination with Sulfuryl Chloride. Sulfuryl chloride (0.325g, 0.0024mol) was added dropwise to a stirred solution of 0.524g (0.002mol) of **1a** in 10ml of methylene chloride at 0°. The mixture was kept at 0° for 30min and then worked up as described above (B). The ratio of diastereomers was found to be 3.25:1. Purification by chromatography afforded **2a** in 57% yield (0.34g).

D. Chlorination with Sulfuryl Chloride and Pyridine To a solution of 0.524g (0.002mol) of **1a** in methylene chloride (3ml) and pyridine (0.5g) a solution of 0.27g (0.002 mol) of sulfuryl chloride in methylene chloride (2ml) was added at 0°. After 30min the reaction mixture was warmed to room temperature. After evaporation of methylene chloride and sulfur dioxide, the residue was dissolved in chlororoform (50ml). Pyridine was removed with aqueous sulfuric acid; the chloroform solution was then washed with water, dried and evaporated to give the product (diastereomeric ratio 2.75:1). Column chromatography yielded 0.26g (44%) of **2a**.

Physical and spectral properties of **2a** obtained according to the procedures B, C, D were identical with those obtained according to the procedure A.

α-Chloro-α-Dimethoxyphosphorylmethyl Phenyl Sulfoxide 2b. The reaction of **1b** with iodobenzene dichloride was carried out according to the procedure A and the crude product was obtained as a 2.5:1 diastereomeric mixture. This mixture was chromatographed to give the pure **2b** in 51% yield.
Recrystallization afforded a pure diastereomer of **2b** m.p. 110-11°. ^{1}H-NMR ($CDCl_3$) δ 3.81, 3.91 (dd, 6, $\underline{CH_3}OP$, J_{P-C}11Hz), 4.79 (d, 1, P(O)$\underline{CH}Cl$, J_{P-C}11.5Hz), 7.53 (m, 5, aromatic); minor diastereomer: 3.68, 3.73 (d.d, 6, $\underline{CH_3}OP$, J_{P-C}11.2Hz), 4.88 (d, 1, P(O)$\underline{CH}Cl$, J_{P-C}9.6Hz). Anal.Calcd. for $C_9H_{12}O_4ClPS$, C, 38.28; H, 4.30; Found C, 38.4; H, 4.30.

α-Chloro-α-Diethoxyphosphorylmethyl Phenyl Sulfoxide 2c Chlorination of **1c** was carried out as described above.
According to the procedure A **2a** was obtained as a mixture of diastereomers in a 2.7:1 ratio. Column chromatography (benzene-acetone 2:1) afforded the pure product in 54% yield, n_D^{20}=1.5167.
Isolated pure diastereomer: ^{1}H-NMR ($CDCl_3$) δ 1.38 (t, 6, $\underline{CH_3}CH_2O$), 4.33 (q, 4, $CH_3\underline{CH_2}O$), 4.72 (d, 1, P(O)$\underline{CH}Cl$, J_{P-C}13Hz, 7.7 (m, 5, aromatic); minor diastereomer: 4.95 (d, 1, P(O)$\underline{CH}Cl$, J_{P-C}11Hz). Anal.Calcd. for $C_{11}H_{17}O_4PSCl$: C, 42.38; H, 5.49; Found: C, 41.79; H, 5.60.
According to the procedure C, the crude product **2c** was obtained as a diastereomeric mixture in a 2.39:1 ratio and yield after purification was 63%.
According to the procedure D, **2a** was obtained in a ratio 2.4:1. Standard purification yielded 56% of **2c**.

Oxidation of α-Chloro-α-Phosphoryl Sulfoxides 2 to α-Chloro-α-Phosphoryl Sulfones 3

α-Chloro-α-Dimethoxyphosphorylmethyl-p-Tolyl Sulfone 3a. A solution of the sulfoxide **2a** (0.29g, 0.001mol) in chloroform (10ml) was oxidized with equimolar quantity of m-chloroperbenzoic acid at room temperature for 24h. Work-up afforded the sulfone **3a** which was purified by crystallization from benzene, m.p. 101-102°. Yield of **3a** was 89% (0.27g). ^{1}H-NMR ($CDCl_3$): δ 2.35 (s, 3, $\underline{CH_3}C_6H_4$), 3.84 (d, 6, $\underline{CH_3}OP$, J_{P-C}11.3Hz), 4.98 (d, 1, P$\underline{CH}Cl$, J_{P-C}13.2Hz), 7.6 (m, 4, aromatic). Anal.Calcd. for $C_{10}H_{11}O_5PSCl$; C, 38.41; H, 4.51; Found C, 38.17; H, 4.30.

α-Chloro-α-Dimethoxyphosphorylmethyl Phenyl Sulfone 3b. Oxidation of **2b** with m-chloroperbenzoic acid afforded the corresponding sulfone **3b** which was purified by column chromatography (ether-light petroleum 1:1), yield 89%. ^{1}H-NMR ($CDCl_3$): δ 3.92 (d, 6, CH_3OP, J_{P-C}11Hz), 4.88 (d, 1, P$\underline{CH}Cl$, J_{P-C}13Hz), 8.0 (m, 5, aromatic). Anal.Calcd. for $C_9H_{12}O_5PSCl$: C, 36.19; H, 4.05; Found: C, 36.3; H, 4.06.

α-Chloro-α-Diethoxyphosphorylmethyl Phenyl Sulfone 3c. Oxidation of **2c** with m-chloroperbenzoic acid afforded the sulfone **3c**, which was purified by column chromatography (ether-light petroleum 1:1), n_D^{20}1.5300, yield 91%, ^{1}H-NMR ($CDCl_3$) δ 1.35 (t, 6, $\underline{CH_3}CH_2OP$, J_{H-H}7.0Hz), 4.30 (q, 4, J_{H-H}7.0Hz, $CH_3\underline{CH_2}OP$), 4.98 (d, 1, P-$\underline{CH}Cl$, J_{P-C}13.0Hz), 7.85 (m, 5, aromatic). Anal.Calcd. for $C_{11}H_{16}O_5PSCl$, C 40.44; H, 4.94; Found C, 40.28; 4.70.

Optically Active α-Chloro-α-Phosphoryl Sulfoxides **2a**

Chlorination of (+)-(S)-dimethoxyphosphorylmethyl p-tolyl sulfoxide **1a** $[\alpha]_D^{25}$+144 (c, 1.0 acetone) with iodobenzene dichloride and sulfuryl chloride in the presence or absence of pyridine, was carried out as described for the racemic **1a**. Specific rotations and ratios of a diastereomeric mixture of **2a** and yields (after purification) were dependent on the chlorination conditions and are as follows: procedure A - 3.3:1, $[\alpha]_D^{25}$+131, 61%, procedure B - 2.8:1 $[\alpha]_D^{25}$+131, 61%, procedure C - 3.25:1, $[\alpha]_D^{25}$+185, 59%., procedure D - 2.75:1, $[\alpha]_D^{25}$+180, 45%. After three times repeated crystallization from benzene the pure major diastereomer of **2a** $[\alpha]_D$+243 (c, 1.6, $CHCl_3$) was isolated.

Table 7. Positional parameters (x10^4) for the nonhydrogen atoms

	x/a	y/b	z/c
P	-1647(3)	1187(3)	6960(1)
0(1)	-635(8)	605(8)	7444(3)
0(2)	-2295(9)	-229(9)	6554(3)
0(3)	-3545(8)	2108(9)	7072(3)
C(2)	-1426(14)	-1898(13)	6514(5)
C(3)	-3673(14)	3556(14)	7411(5)
S	2090(3)	1969	6492(1)
Cl	-1340(3)	3389(4)	5946(1)
0(4)	2001(10)	493(9)	6115(4)
C(1)	-292(10)	2799(9)	6575(3)
C(4)	3003(10)	3767(12)	6095(3)
C(5)	3675(11)	3406(14)	5564(3)
C(6)	4452(13)	4853(16)	5293(4)
C(7)	4558(11)	6430(13)	5509(4)
C(8)	3890(11)	6683(12)	6022(4)
C(9)	3112(12)	5354(12)	6336(4)
C(10)	5265(16)	7986(18)	5174(5)

Table 8. Anisotropic temperature factors ($Å^2x10^3$) in the form:

$exp[-2\Pi(h^2a^2U_{11} + k^2b^2U_{22} + l^2c^2U_{33} + 2hkabU_{12} + 2hlacU_{13} + 2klbcU_{23})]$.

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
P	53(1)	56(1)	56(1)	2(1)	0(1)	-4(1)
0(1)	65(3)	63(4)	74(4)	10(3)	11(3)	1(3)
0(2)	70(3)	70(4)	79(4)	4(4)	-15(3)	-4(3)
0(3)	58(3)	75(4)	79(4)	-7(3)	9(3)	-3(3)
C(2)	81(6)	62(5)	114(8)	-22(6)	-9(6)	-6(5)
C(3)	73(6)	68(6)	119(8)	4(6)	19(6)	18(5)
S	53(1)	61(1)	84(1)	19(1)	4(1)	4(1)
Cl	79(1)	100(2)	72(1)	22(1)	-15(1)	5(1)
0(4)	79(5)	56(3)	168(8)	5(5)	42(5)	11(4)
C(1)	54(4)	41(3)	51(4)	8(3)	-1(3)	4(3)
C(4)	51(4)	65(5)	52(4)	6(4)	5(3)	2(4)
C(5)	61(5)	81(6)	56(4)	-1(5)	2(4)	-3(5)
C(6)	57(5)	111(9)	64(5)	8(6)	11(4)	4(6)
C(7)	55(4)	68(5)	63(5)	18(5)	7(4)	-6(4)
C(8)	58(4)	58(5)	80(5)	3(5)	3(4)	0(4)
C(9)	59(5)	64(5)	73(5)	6(4)	10(4)	2(4)
C(10)	82(7)	123(10)	98(8)	32(8)	12(6)	-3(7)

Reduction of Optically Active α-Chloro-α-Phosphoryl Sulfoxides **2a**

Zinc dust (0.16g, 0.0025mol) was added to a solution of α-chloro-α-phosphoryl sulfoxide **2a** (0.15g, 0.0005mol) in methanol (5ml) in the presence of a drop of concentrated sulfuric acid. The mixture was heated under reflux for 15min., diluted with chloroform, filtered and washed with aqueous sodium carbonate. Evaporation afforded the crude sulfoxide (+)-(S) **1a** which was purified by column chromatography (benzene-acetone 5:1) (65%). Specific rotations of **1a** depending on chlorinating agent are reported in Table 4.

Optical Stability of (+)-(S)-1a under Reduction Conditions

A mixture of **1a** (0.131g, 0.0005mol) $[\alpha]_D$+144 (97%ee) and zinc dust (0.16g, 0.0025m) in methanol (5ml) in the presence of a drop of concentrated sulfuric acid was refluxed for 15 min. After diluting with chloroform, solution was filtered, washed with aqueous sodium carbonate and evaporated. Purification afforded the pure sulfoxide **1a**, $[\alpha]_D^{25}$+137 (c, 1.04, acetone) (92%ee).

Chlorination of Optically Active Methyl-p-Tolyl Sulfoxide

Sulfuryl chloride (0.162g, 0.0012mol) was added dropwise to a stirred solution of 0.154g of methyl p-tolyl sulfoxide $[\alpha]_D$+145 in 5 ml of methylene chloride at -10°. The mixture was kept at 0° for 30 min and then solution was washed with water, dried and evaporated to give chloromethyl p-tolyl sulfoxide (90% yield) $[\alpha]_D^{25}$0 (c, 2.3 acetone).

Table 9. Hydrogen atom positional parameters (x10^4) with isotropic temperature factors (Å^{2}x10^3).

	x/a	y/b	z/c	U
H(21)	-2304(14)	-3013(13)	6452(5)	255(36)
H(22)	-352(14)	-2218(13)	6809(5)	255(36)
H(23)	-817(14)	-1527(13)	6120(5)	255(36)
H(31)	-5104(14)	3273(14)	7498(5)	255(36)
H(32)	-3589(14)	4565(14)	7099(5)	255(36)
H(33)	-3003(14)	3983(14)	7790(5)	255(36)
H(11)	-359(56)	4103(42)	6741(31)	66(25)
H(51)	3617(11)	2133(14)	5377(3)	149(27)
H(61)	4986(13)	4660(16)	4876(4)	149(27)
H(81)	3951(11)	7969(12)	6199(4)	149(27)
H(91)	2622(12)	5577(12)	6757(4)	149(27)
H(101)	5793(16)	8211(18)	4757(5)	255(36)
H(102)	6358(16)	8169(18)	5475(5)	255(36)
H(103)	4162(16)	8887(18)	5259(5)	255(36)

Crystal Structure of α-Chloro-α-dimethoxyphosphorylmethyl p-Tolyl Sulfoxide 2a

The compound was crystallized from acetone. A prismatic crystal with dimensions 0.1x0.13x0.14mm was sealed into a Lindemann glass capillary tube. Intensity data were collected on a Stoe Stadi-4 diffractometer (Mo-K_α=0.71069Å). Cell dimensions were determined by a least-squares fit to setting for 2θ reflections (hkl). Measurements were carried out with standard background counts (30s) and θ-2θ scan of fixed range (60s) for 3,5≤2θ≤55.0 with graphite monochromated MoK_α. With the application of the criterion I≥2 (I), 1485 of the 1788 unique reflections measured were considered to be observed.

Crystal Data. $C_{10}H_{14}O_4ClPS$, M=296.7, orthorombic $P2_12_12_1$, a=7.254(1), b=7.718(1), c=23.893(4)Å, V=1337.68(40)Å^3, Z=4, F(000)=616.00, D_c=1.48g•cm^{-3}, D_m=1.46 g•cm^{-3}, μ(MoK_α)=4.96 cm^{-1}.

The structure was solved by direct methods (SHELX 76, G.M.Sheldrick, programm TANG) and refined by full-matrix least-squares with anisotropic temperature factors for all the non-hydrogen atoms. The methyl H atoms, which were assigned with group isotropic temperature factors, were refined as part of rigid methyl groups. The remaining H atoms were allowed to refine freely with group isotropic temperature factors. The final value of R_W=0.0810 with R=0.0804 (1485 reflections and 169 parameters) was obtained.. The positional parameters and anisotropic temperature factors for non-hydrogen atoms are given in Tables 7 and 8. In Table 9 are hydrogen atoms positional parameters with isotropic temperature factors. The observed and calculated structure factors are deposited as supplementary publication.

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