CHAPTER 4

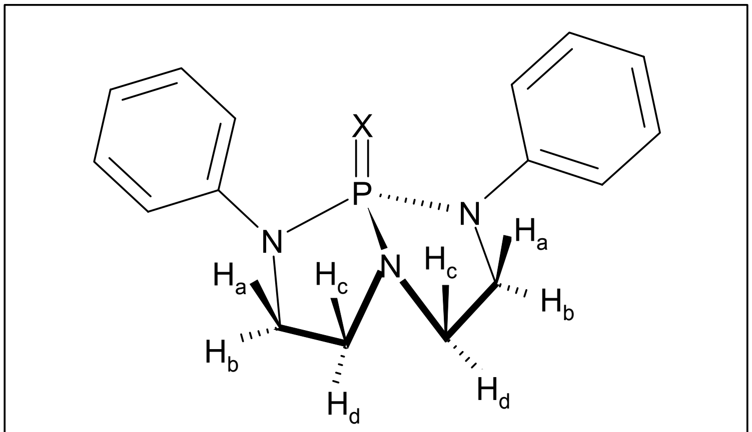
4. STRUCTURAL ANALYSIS

4.1 NMR Analysis

4.1.1 Introduction

The bicyclic system **11a** as well as its phosphoryl analogue **3a** showed similar and interesting ^{1}H NMR spectra (**Figure 4.2 and 4.3**), with one distinct difference in the aliphatic region.

There is high non-equivalency of the individual hydrogen atoms of the ring methylene protons. This suggest a high degree of rigidity on the NMR time scale which made it possible to compare dihedral angles determined from solution state NMR with those of X-ray diffraction data.



3a: X=O
11a: X=S

Figure 4. 1 Orientation of the methylene ring protons in **3a**, **11a**.

In the ^{1}H NMR spectrum of bicyclic compound **3a** only four sets of multiplets for the eight aliphatic hydrogens were observed. For the aliphatic protons of these compounds there is a dramatic separation into low-field and high-field spectral regions. The appearance of four sets of multiplets is due to the molecular plane

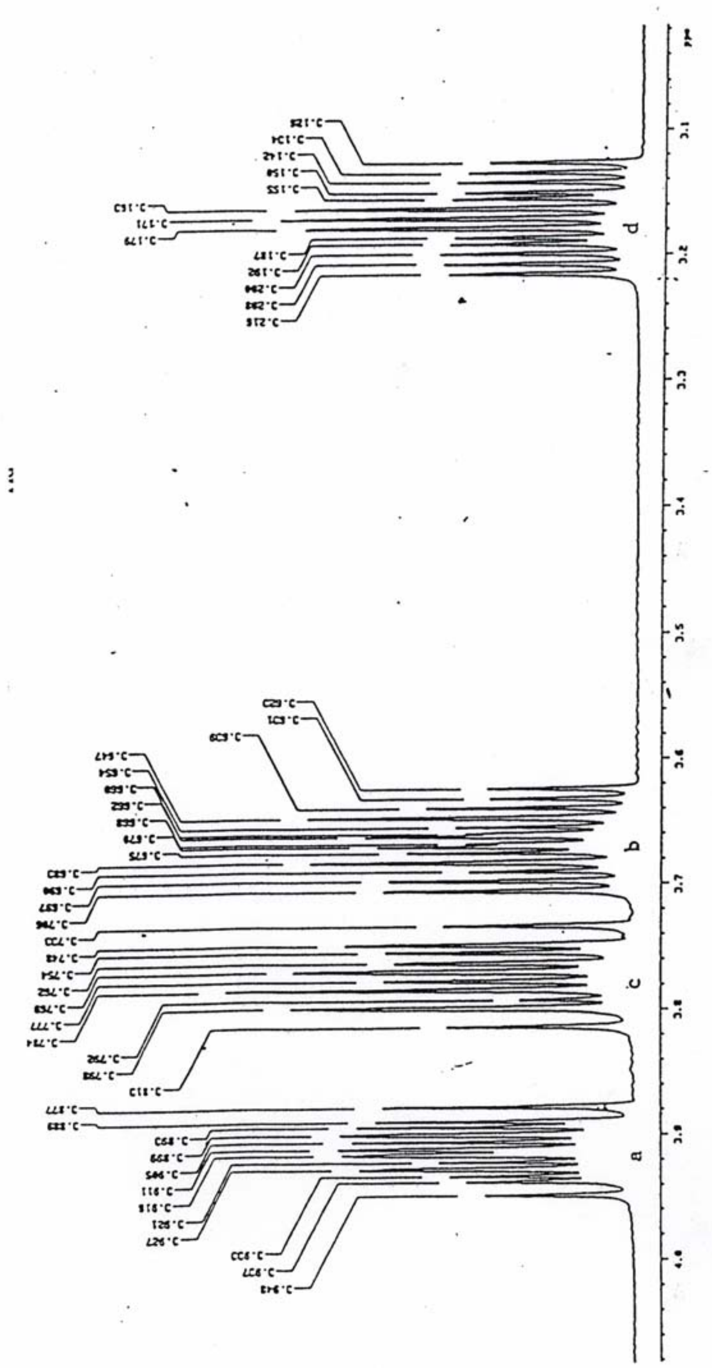


Figure 4. 2 ^{1}H NMR spectrum of P=O bicyclic compound, **3a**.

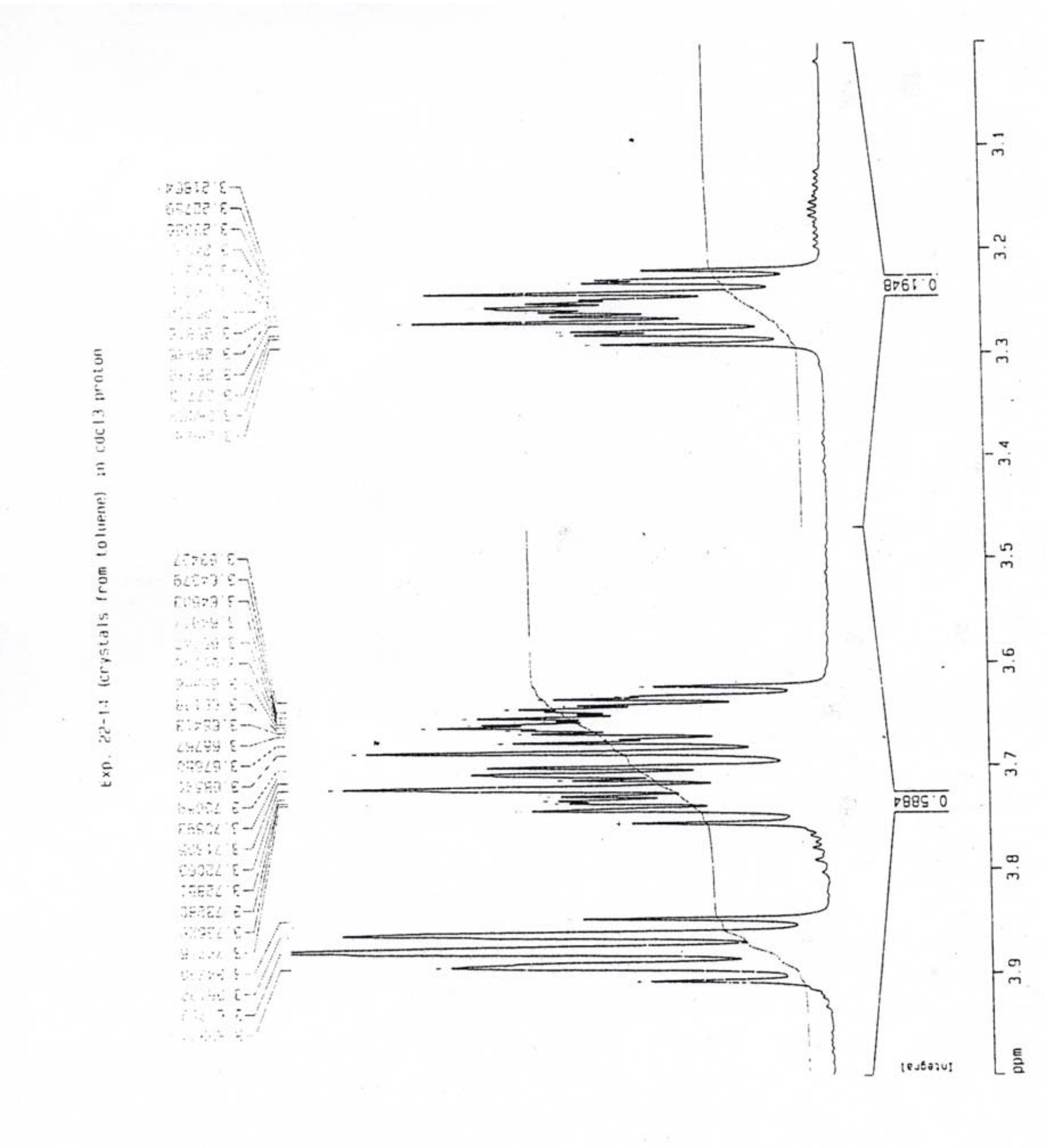


Figure 4. 3 ^{1}H NMR spectrum of P=S bicyclic compound, **<u>11a</u>**.

of symmetry. The plane of symmetry divides the protons into two groups of four protons of the vicinal system, which gives an ABCDX spin system, where X represents the ^{31}P nucleus. The existence of only one ABCDX splitting pattern in the aliphatic region, i.e. the two N-CH_2-CH_2-N moieties, suggests that the two halves of the molecule are equivalent in terms of the NMR time scale.

Conformational equilibria and other dynamic processes influence the coupling constants of many molecules. The observed data are then average values that are formed on the basis of the mole fractions *p*, from the data of the individual conformers. In the simplest case of an equilibrium between two conformers A and B, **Equation 4.1** holds.

$$J_{exp} = p_A J_A + p_B J_B \qquad \textbf{Equation 4. 1}$$

Vicinal proton-proton couplings in saturated compounds have been studied extensively both experimentally and theoretically. Coupling constants, which are frequency difference in Hertz (Hz) between multiplets, unlike chemical shifts, are not affected or dependent on the strength of the magnetic field. It has been shown that the sign of $^3J_{HH}$ is always positive and the magnitude depends basically on four factors.

i) dihedral bond angles
ii) electronegativity of the substituents on the H-C-C-H moiety
iii) bond length between the two carbon atoms bearing the protons
iv) H-C-C valence angles, θ.

One of the most important factors that affect vicinal coupling relationships is the dihedral angle[1]. Valence bond theory has been of great success in qualitatively describing trends in $^3J_{HH.}$ The dihedral angle (torsion angle) can be defined as the angle of rotation about a carbon-carbon bond viewed end on with lower numbered carbon nearest to the viewer and hydrogen eclipsed; a clockwise rotation of the carbon farthest away corresponds to a positive dihedral angle. The dependence of the coupling constant on dihedral angle can be approximately determined by the theoretically derived Karplus equation[2] as in **equations 4.2** and **4.3** and some of its variations. By employing an appropriate set of parameters, the Karplus equation can be used to describe some of the heterocyclic system conformations in terms of the dihedral angles. Normally the sign of the coupling constant has no effect on the appearance of the NMR spectra[3] and therefore has no effect on the Karplus equation:

$$^{3}J_{HH} = 8.5\cos^{2}\theta - 0.28 \quad \text{for } \theta = 0° - 90° \qquad \text{Equation 4. 2}$$

$$^{3}J_{HH} = 9.5\cos^{2}\theta - 0.28 \quad \text{for } \theta = 90° - 180° \qquad \text{Equation 4. 3}$$

where the value of theta (θ) is the dihedral angle.

The relationship between the dihedral angle and vicinal coupling constant is of particular importance in the stereochemistry of groups attached to cyclic systems, e.g. triterpenoids, steroids, etc. In cyclohexane ring, the hydrogens are axial or equatorial, forming with their neighbours a dihedral angle of 60° or 180°, thus rendering the application of the Karplus equation and some of its variations a straightforward procedure to find out the stereochemistry of the products through coupling constant between vicinal hydrogens, which could otherwise not be determined easily.

Since the dihedral angle is the largest when the vicinal protons are diaxial with respect to one another, the coupling constant are accordingly larger, but when the vicinal protons are in an axial equatorial or equatorial-equatorial relationship, the dihedral angle is about 60 degrees or less and the coupling constant are correspondingly smaller[4].

An estimation of coupling constant of dihedral angles constant by Karplus equation does not necessarily end up with only saturated systems, but also in olefins, where a modified Karplus equation predicts larger trans-coupling than cis-coupling.

One more factor that influences the determination of ^{3}J is the presence of a heteronuclear atom that has a magnetic nucleus. The presence of the heteronuclear atom in the organic molecule can introduce additional signals in the spectrum, since this nucleus will take up spin with respect to the applied field in the same way a neighbouring proton does. Vicinal heteronuclear coupling constants also depend on the dihedral angles. Karplus-like curves have been developed for $^{3}J_{(HCOP)}$ and $^{3}J_{(NCCH)}$. In molecules where non-bonding electrons are localized in a specific direction, as in some nitrogen and phosphorus containing compounds, geminal couplings are also dependant on the angular orientation.

The Karplus equation is not limited to the conformation analysis of six-membered ring heterocyclic systems but to a large number of five-membered ring phosphorus heterocyclic systems which have also been analyzed by NMR techniques. The Karplus equation can be applied to confirm the conformation and configuration of heterocyclic systems since the coupling is transmitted through nitrogen (also oxygen and sulphur) provided that no exchange of protons attached to the heteroatom occurs.

The complexities of the structural analysis of the five-membered phosphorus heterocycles is the question of planarity or pyramidality of the nitrogens in the PNR moiety. The 1,2,3-dioxaphospholanes, 2-oxo and 2-thio-1,2,3-oxazaphosporinane[5] systems are examples of compounds which follow a similar Karplus-like relationship.

The most stable conformations of cyclopentane are the envelope and the half-chair. The implications in the conformational analysis of cyclopentanes are the barriers between the two conformations which make it impossible to freeze out to individual conformers. It is for this reason that cyclopentanes and hetero-cyclocpentanes are totally different from cyclohexane derivatives in which their chair conformation is located in a deep energy valley. In cyclopentane there is little if any energy difference between the envelope and the half-chair. The molecule is thus in rapid state of conformational flux through conformational interchange. Internal substitution of the five-member ring with a heteroatom seems to introduce a small energy barrier in the conformational circuit. A few studies on heterocyclic five-membered rings have been reviewed by Fuschs and Riddel.[6,7] Both oxygen and nitrogen-containing rings, like cyclopentane itself, seem to interchange conformations freely. Equilibrium and NMR studies have been carried out for 2,4 disubstituted and 2,4,5-trisubstituted-1,3-dioxolanes[8].

For cyclocbutane and cyclopentane derivatives, because of their great flexibility, the dihedral angles are less well defined and an unambiguous assignment of the configuration on the basis of the ^3J values is, in general, not possible.

The proton-proton coupling constants of a rigid system can be determined from the solution state NMR spectrum and used to calculate the dihedral angles with the Karplus[9] equation.

4.1.2 Experimental

A study was already conducted on **3a**[10] to calculate the dihedral angles from the coupling constants. A similar study was done on the thiophosphoryl analogue **11a** in order to compare the structures of the two systems in terms of NMR data as well as X-ray diffraction data.

Full ^{1}H, ^{13}C and ^{31}P NMR assignments were made for the two bicyclic systems. The ^{1}H NMR spectrum of **3a** is of first order (chemical shifts are large compared to the coupling constants) and therefore relatively easy to calculate the coupling constants and make assignments to the different protons. The spectrum of **11a** is of second order (the chemical shifts are of the same magnitude as the coupling constants). This type of spectrum is much more complicated to analyze because the chemical shifts and coupling constants can no longer both be measured directly from the spectrum. It was therefore necessary to do a complete analysis of the system[11].

4.1.3 Results and Discussion

On the NMR scale the molecules under consideration are symmetrical and have a highly rigid conformation due to the two fused five-membered rings. Our results indicated that the molecules are flexible to a great extent and that numerous conformations of a stable molecule is possible in these cases.

The dihedral angles obtained from single crystal XRD results reported in the next section, as well as the calculated dihedral angles are listed in **table 4.1**. From the crystal structures it is clear that the two halves (two five-membered rings) of the molecules **3a** and **11a** are remarkably different as far as the dihedral angles are concerned. There is a remarkable difference in the vicinal proton orientation for each ring. The NMR data represent an average of the two rings, so they appear identical on the NMR-scale.

Our results indicate that the method of comparing the dihedral angles determined from NMR data using the Karplus equation with the dihedral angles from x-ray diffraction data is in this case very approximate. There is very little correlation between the experimental and the calculated dihedral angles for compounds **3a** and **11a**.

		P=O			P=S		
Bond		J value (Hz)	Dihedral angle (θ) XRD	Dihedral angle (θ) Calc	J value (Hz)	Dihedral angle (θ) XRD	Dihedral angle (θ) Calc
$J_{a\text{-}b^*}$	gem	11.8	-	-	11.35	-	-
$J_{c\text{-}d^*}$	gem	9.3	-	-	-9.31	-	-
$J_{a\text{-}c^*}$	cis	6.3	37.6	49.5	4.72	33.8	39.7
$J_{a\text{-}d^*}$	trans	6.2	157.5	145.7	6.22	-86.0	146.2
$J_{b\text{-}c^*}$	trans	3.3	83.4	145.7	6.22	154.2	145.7
$J_{b\text{-}d^*}$	cis	3.3	36.4	49.5	7.32	34.4	19.4

Table 4.1 Experimental (from both NMR and single crystal XRD data) and calculated values for dihedral angles for the bicyclic compounds **3a** and **11a**. *The subscripts a,b,c,d refers to the atomic labels in Fig. 4.1 on page 71.

Coupling constants should be integrated over the whole rotation circuit of the molecules rather than just summed over the most stable conformation. A wide range of coupling constants arise from the different conformations of the systems under investigation, but only one set of coupling constants were used to calculate the dihedral angles. Therefore an average value of the dihedral angles which resulted from our NMR data is not in agreement with the observed crystal structure.

As the NMR data arise from molecules in solution state and single crystal XRD data arise from molecules in the solid state it is expected that the results may be different.

4.2 Crystal Structure Analysis

4.2.1 Introduction

> *I held them in every light. I turned*
> *them in every attitude, I surveyed*
> *their characteristics. I dwelt upon*
> *their peculiarities. I pondered upon*
> *their conformation.*
>
> *- Edgar Allan Poe*[*]

Any aspect of science which depends upon a knowledge of the atomic positions in a molecule can profitably make use of X-ray crystallography. Where crystals of known chemical composition have been obtained, single crystal X-ray diffraction can be used to obtain their molecular structure. X-ray diffraction can derive precise structural information of the molecule, atom by atom as well as where the atoms are positioned in relation to each other. In the best cases X-ray diffraction is equivalent to taking a three dimensional photograph of the molecule.

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[*] *Edgar Allan Poe (1809 – 1849) was an American poet and writer.*

The inherent periodicity of a crystal makes it possible to be used as a diffraction grating for an X-ray beam of wavelength comparable to interatomic distances. X-rays most commonly used for X-ray crystallography is between 0.5 and 2.5 Å.[12] The magnitude of the interatomic distances involved in organic molecules is typically 1.54 Å for a C-C single bond.

The solution of a crystal structure depends upon recombining the diffracted X-rays to synthesize an image of the molecular structure by Fourier Transformation. A crystal structure is considered solved when it is possible to construct, from the diffraction data, a three dimensional electron density map showing the contents of the unit cell. The unit cell is the building block of the crystal lattice.

The crystal structures of the *N*-aryl substituted phosphoryl derivatives were available from previous studies, so it was possible to compare the structural features of some of the phosphoryl and thiophosphoryl analogues.

4.2.2 Experimental

The crystal structures of compounds **0** , **8** , **1f** and **11a** were determined.

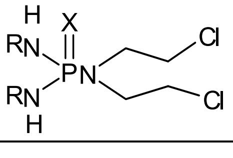
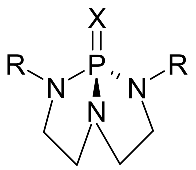
“username” of compound	Number of compound	Structure
Substrate	0 X=O 8 X=S	$Cl_2P(X)(NCH_2CH_2Cl)_2$
Triamidate	1f X=O, R=Bz	
Bicyclic	11a X=S, R=Ph	

Figure 4. 4 Triamidates for which crystal structures were determined.

Crystallographic data acquisition and refinement details of compounds **0**, **8**, **1f**, **11a** are listed in **table 4.2**.

	0	**8**	**1f**	**11a**
Empirical formula	$C_4H_8NPOCl_2$	$C_4H_8NPSCl_2$	$C_{18}H_{23}N_3O_1P_1Cl_2$	$C_{16}H_{18}N_3PS$
Molecular weight	258.9	275.0	399	315.36
Crystal dimension,		0.48 x 0.36 x 0.28	0.48 x 0.57 x 0.62	0.55 x 0.42 x 0.26
	Monoclinic	Monoclinic		Triclinic
Space group	$P2_1/c$	$P2_1/c$	$P2_1/n$	P-1
Cell dimensions:				
a, Å	9.088(3)	13.2840	9.369(4)	8.2311(14)
b, Å	8.492(3)	5.9693	9.866(2)	10.4883(18)
c, Å	13.129(4)	14.1940	21.479(6)	10.6538(9)
α,°	90.00	90.000	90.000	115.417(11)
β, °	101.238(6)	104.024	94.85(3)	91.825(10)
γ,,°	90.000	90.000	90.000	105.479(14)
Z	4	4	4	2
Volume, Å^3	993.8(5)	1092.0(4)	1978.2	789.2(2)
D (cal), g.cm^{-1}	1.730	1.67	1.34	1.327
μ, cm^{-1}			3.68	0.303
Radiation (*λ*, Å)	0.71073	0.71073	0.7107	0.71073
T, ° C	293(2)		295	293(2) K
F(000)	520.0	552.00	824	332
Scan Range (*θ* °)		$3 \leq \theta \leq 30.05$	$3 \leq \theta \leq 30$	2.15to29.96
Zone collected:				
H	-7:12	-18:18	-13:13	-11:11
K	-11:11	-6:7	-13:0	-14:14
L	-17:17	-16:17	0:30	-14:14
Reflections collected		7213	6198	9131
Unique reflections used (> 3 *σ* (**I**))	2462	2679	3345	3558
R_{int}	0.0317	0.0178	0.0880	0.0880
Parameters refined	133	133	233	
Max. positional shift/esd	0.002	15.000	0.011	0.390
Residual electron density (eÅ^3):				
Maximum	0.296	0.474	0.87	0.390
Minimum	-0.414	-0.295	-0.52	-0.276
U_{iso}(H), Å^2			0.090(4)	
R	0.0345	0.0331	0.0787	0.0397
$_wR^2$	0.0955	0.0830	0.0514	0.1093

Table 4.2 Crystallographic data acquisition and refinement details of compound **0**, **8**, **1f**, **11a**.

PO triamidate, 1f $(PhCH_2NH)_2P(O)$ $N(CH_2CH_2Cl)_2$

All diffraction measurements were obtained at room temperature and the data were collected on an Enraf Nonius CAD4 diffractometer with MoK_{σ} radiation Accurate unit cell parameters were obtained by least squares methods from the position of 25 centered reflections for each crystal. Data were corrected for Lorentz and polarization effects and absorption corrections were applied.[13] Intensity checks were carried out every second hour and an orientation control every 400 reflections. Three standard reflections were used to check orientation and crystal stability at regular intervals, and the decay during data collection was 4.1% (corrected). The structure was solved by direct methods.[14, 15] Refinement was by full matrix least squares methods, using $\sigma^2(F_{obs})$ weights[15]. All the non-hydrogen atoms were refined anisotropically. All hydrogen atoms, except the experimentally located and refined H10 and H18, were placed in calculated positions and were included in the refinement with common isotropic thermal parameters. Atomic scattering factors were taken from the literature.[16] A perspective view of the molecule, prepared with ORTEP[17], is represented in **Figure 4.5.**

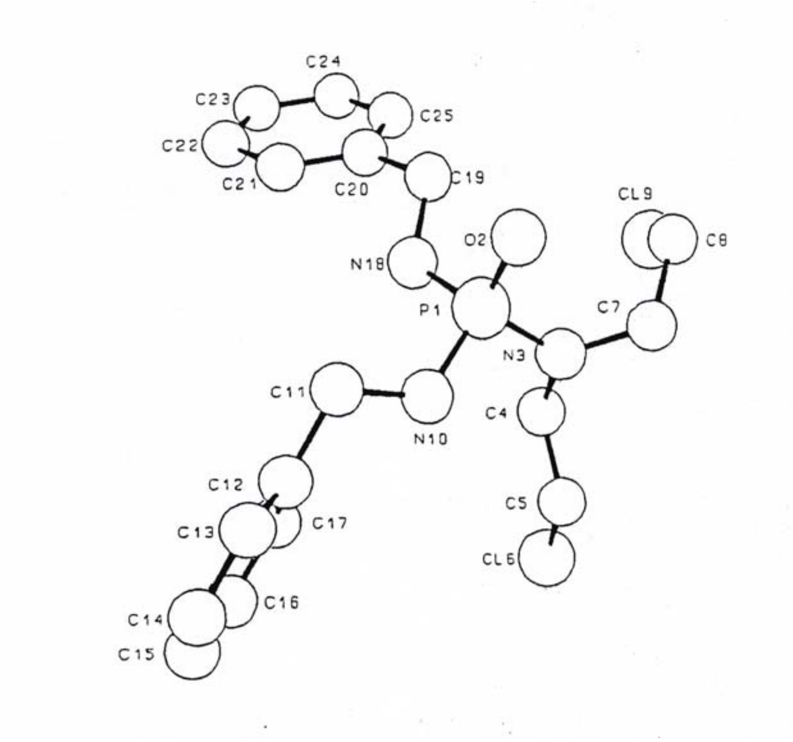


Figure 4.5 ORTEP drawing of 1f.

Atom	x/c	y/c	z/c	U_{eq} $=1/3\ \Sigma_i\ \Sigma_j\ U_{ij}\ a_i^*\ a_j(a_i.a_j)$
P(1)	3156(1)	7519(1)	2384(1)	33(1)
O(2)	3423(3)	6142(3)	2646(1)	44(1)
N(3)	4650(3)	8107(3)	2131(2)	37(1)
C(4)	4734(5)	9521(4)	1908(2)	43(1)
C(5)	4766(6)	9579(4)	1224(2)	63(1)
Cl(6)	5019(2)	11288(1)	985(1)	76(1)
C(7)	5977(4)	7335(5)	2212(2)	49(1)
C(8)	6731(5)	7329(5)	2857(3)	76(2)
Cl(9)	7232(2)	8951(2)	3157(1)	104(1)
N(10)	1990(4)	7716(4)	1782(2)	40(1)
C(11)	447(4)	7489(5)	1810(2)	57(1)
C(12)	-419(5)	8124(5)	1267(2)	47(1)
C(13)	-1325(5)	7419(6)	869(2)	57(1)
C(14)	-2120(6)	7992(6)	375(3)	67(2)
C(15)	-1941(7)	9386(7)	276(3)	90(2)
C(16)	-1040(7)	10097(6)	671(3)	97(2)
C(17)	-287(6)	9521(6)	1151(3)	72(2)
N(18)	2540(3)	8534(3)	2897(2)	34(1)
C(19)	3110(5)	8452(4)	3541(2)	46(1)
C(20)	2476(5)	9517(4)	3948(2)	39(1)
C(21)	1019(5)	9780(4)	3875(2)	48(1)
C(22)	473(7)	10765(5)	4265(3)	74(2)
C(23)	1353(8)	11402(6)	4716(3)	87(2)
C(24)	2779(7)	11114(6)	4776(3)	81(2)
C(25)	3359(6)	10150(5)	4404(2)	59(1)

Table 4. 3 Fractional atomic coordinates (x 10^4) and equivalent thermal factors (x 10^3 Å^2) for **<u>1f</u>**.

Atom	x/c	y/c	z/c	U_{eq} $=1/3\ \Sigma_i\ \Sigma_j\ U_{ij}\ a_i^*\ a_j(a_i.a_j)$
H(4A)	5696(5)	9984(4)	2124(2)	90(4)
H(4B)	3810(5)	10073(4)	2039(2)	90(4)
H(5A)	5637(6)	8961(4)	1085(2)	90(4)
H(5B)	3765(6)	9201(4)	1004(2)	90(4)
H(7A)	5732(4)	6297(5)	2084(2)	90(4)
H(7B)	6705(4)	7752(5)	1898(2)	90(4)
H(8A)	6027(5)	6868(5)	3170(3)	90(4)
H(8B)	7690(5)	6724(5)	2847(3)	90(4)
H(10)	2252(56)	7472(55)	1504(22)	90(4)
H(11A)	243(4)	6412(5)	1807(2)	90(4)
H(11B)	122(4)	7924(5)	2238(2)	90(4)
H(13)	-1430(5)	6342(6)	944(2)	90(4)
H(14)	-2855(6)	7396(6)	72(3)	90(4)
H(15)	-2524(7)	9884(7)	-115(3)	90(4)
H(16)	-926(7)	11173(6)	597(3)	90(4)

H(17)	434(6)	10128(6)	1454(3)	90(4)
H(18)	1852(47)	9099(46)	2766(22)	90(4)
H(19A)	2876(5)	7460(4)	3719(2)	90(4)
H(19B)	4256(5)	8593(4)	3562(2)	90(4)
H(21)	325(5)	9247(4)	3530(2)	90(4)
H(22)	-651(7)	11022(5)	4209(3)	90(4)
H(23)	916(8)	12132(6)	5023(3)	90(4)
H(24)	3471(7)	11648(6)	5121(3)	90(4)
H(25)	4484(6)	9897(5)	4470(2)	90(4)

Table 4. 4 Coordinates of the hydrogen atoms ($\times 10^4$) and isotropic thermal factors ($\times 10^3$ Å) for **1f**

PS Bicyclic, 11a

The data were collected on an Enraf-Nonius CAD4 diffractometer using Mo K_α radiation and an ω-2θ scan. The structure was solved by direct methods using SHELX97-2[18] in conjunction with WinGX[19]. Hydrogen atoms were introduced in calculated positions using the SHELX instruction HFIX 44 for the aromatic hydrogens and HFIX 24 for the hydrogens on the secondary carbon atoms. A drawing of **11a**[20] prepared using Platon is presented in **Figure 4.6**.

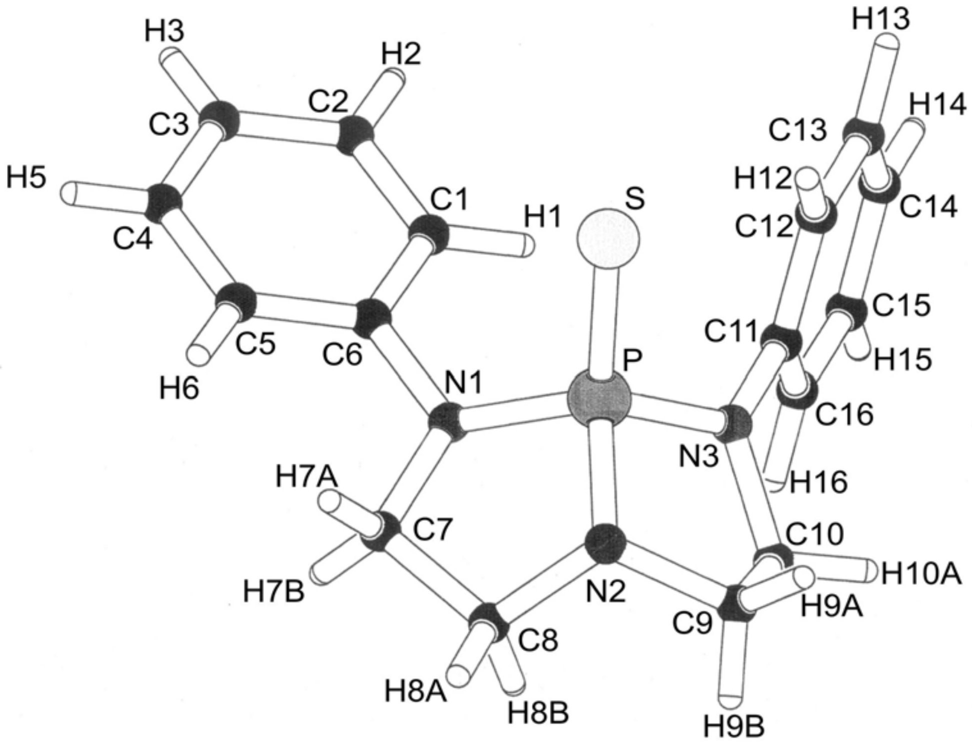


Figure 4.6 Platon drawing of **11a**.

Atom	X/c	y/c	z/c	U_{eq} $=1/3\ \Sigma_i\ \Sigma_j\ U_{ij}\ a_i{}^*a_j(a_i.a_j)$
P	8741(1)	7652(1)	685(1)	36(1)
S	10949(1)	8411(1)	1849(1)	49(1)
N(3)	7750(2)	8920(1)	972(1)	40(1)
N(1)	7516(2)	6042(1)	600(1)	42(1)
N(2)	8551(2)	7040(1)	-1061(1)	48(1)
C(11)	7320(2)	9837(1)	2270(1)	38(1)
C(4)	7502(2)	5726(2)	1772(2)	41(1)
C(16)	8556(2)	10752(2)	3464(2)	50(1)
C(10)	6913(3)	8744(2)	-363(2)	57(1)
C(12)	5642(2)	9841(2)	2349(2)	53(1)
C(5)	7222(2)	6734(2)	3046(2)	49(1)
C(14)	6439(3)	11625(2)	4781(2)	61(1)
C(7)	7330(3)	4834(2)	-820(2)	58(1)
C(3)	7712(3)	4418(2)	1662(2)	57(1)
C(15)	8101(2)	11628(2)	4712(2)	58(1)
C(8)	7375(3)	5514(2)	-1805(2)	67(1)
C(9)	8044(3)	8117(2)	-1405(2)	60(1)
C(1)	7355(3)	5118(3)	4067(2)	74(1)
C(6)	7157(3)	6425(2)	4185(2)	62(1)
C(2)	7637(3)	4125(2)	2816(2)	73(1)
C(13)	5217(3)	10731(2)	3594(2)	68(1)

Table 4. 5 Fractional atomic coordinates (x 10^4) and equivalent thermal factors (x 10^3 Å^2) for **<u>11a</u>**.

Atom	x/c	y/c	z/c	U_{eq} $=1/3\ \Sigma_i\ \Sigma_j\ U_{ij}\ a_i{}^*\ a_j(a_i.a_j)$
H(16)	9750(30)	10779(2)	3426(2)	59
H(10A)	6880(3)	9652(14)	-290(2)	69
H(10B)	5806(18)	8092(10)	-625(4)	69
H(12)	4754(19)	9205(14)	1514(18)	64
H(5)	7072(4)	7653(19)	3137(3)	58
H(14)	6134(8)	12241(15)	5650(20)	73
H(7A)	6278(16)	4070(12)	-1043(4)	69
H(7B)	8238(14)	4422(7)	-883(2)	69
H(3)	7891(5)	3784(16)	880(20)	68
H(15)	8980(20)	12260(14)	5558(19)	69
H(8A)	7780(7)	4938(10)	-2670(15)	80
H(8B)	6220(19)	5523(2)	-2072(5)	80
H(9A)	7439(10)	7639(8)	-2339(15)	72
H(9B)	9023(16)	8886(13)	-1324(2)	72
H(1)	7300(4)	4921(6)	4790(20)	88
H(6)	6978(5)	7102(17)	5030(20)	75
H(2)	7778(5)	3250(20)	2739(3)	87
H(13)	3950(30)	10728(2)	3636(3)	81

Table 4. 6 Coordinates of the hydrogen atoms (x10^4) and isotropic thermal factors (x 10^3 Å) for **<u>11a</u>**.

*PO substrate, **0***

All diffraction measurements were obtained at room temperature and the data were collected on an Enraf Nonius CAD4 diffractometer with MoK$_\sigma$ radiation. Atomic coordinates of compound **0** are listed in **tables 4.7** and **4.8**. A molecular drawing of the crystal structure is shown in **Figure 4.7.**

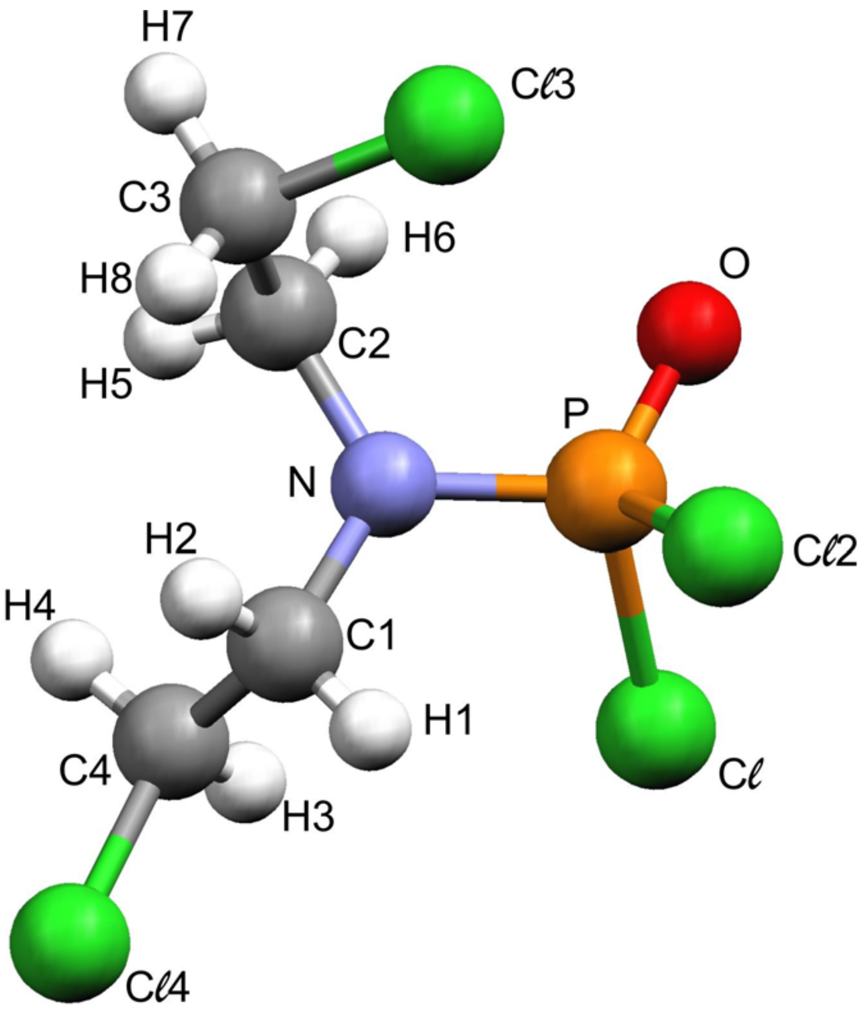


Figure 4.7 Molecular drawing of $Cl_2P(O)N(CH_2CH_2Cl)_2$, **0**

Atom	x/c	y/c	z/c	U_{eq} $=1/3\ \Sigma_i\ \Sigma_j\ U_{ij}\ a_i{}^*a_j(a_i.a_j)$
P	2010(1)	1764(1)	4658(0)	38(1)
Cl2	1867(1)	-575(1)	4412(1)	57(1)
Cl	4101(1)	2156(1)	4423(1)	55(1)
Cl3	2703(1)	5643(1)	5590(1)	62(1)
Cl4	3518(1)	-1344(1)	8020(1)	66(1)
N	2019(2)	1993(2)	5882(1)	37(1)
O	875(2)	2633(2)	3939(1)	50(1)
C2	1139(3)	3256(3)	6253(2)	41(1)
C1	3044(3)	1066(3)	6666(2)	39(1)
C3	2026(3)	4713(3)	6621(2)	50(1)
C4	2201(3)	-166(3)	7158(2)	49(1)

Table 4.7 Fractional atomic coordinates (x 10^4) and equivalent thermal factors (x 10^3 Å^2) for **0**.

Atom	x/c	y/c	z/c	U_{eq} $=1/3\ \Sigma_i\ \Sigma_j\ U_{ij}\ a_i{}^*\ a_j(a_i.a_j)$
H1	3754(30)	5459(29)	6347(20)	49(7)
H2	3487(32)	1772(32)	7195(21)	58(8)
H3	1677(32)	-848(31)	6658(21)	55(8)
H4	1439(33)	311(32)	7536(23)	62(8)
H5	696(27)	2885(27)	6805(19)	41(6)
H6	275(30)	3511(3)	5690(2)	51(7)
H7	1328(30)	5488(31)	6861(20)	54(7)
H8	2923(32)	4463(30)	7153(22)	56(8)

Table 4.8 Coordinates of the hydrogen atoms (x10^4) and isotropic thermal factors (x 10^3 Å) for **0**.

PS substrate, 8

All diffraction measurements were obtained at room temperature and the data were collected on an Enraf Nonius CAD4 diffractometer with MoK$_\sigma$ radiation. Atomic coordinates of compound **8** are listed in **tables 4.9** and **4.10**. A molecular drawing of the crystal structure is shown in **Figure 4.8.**

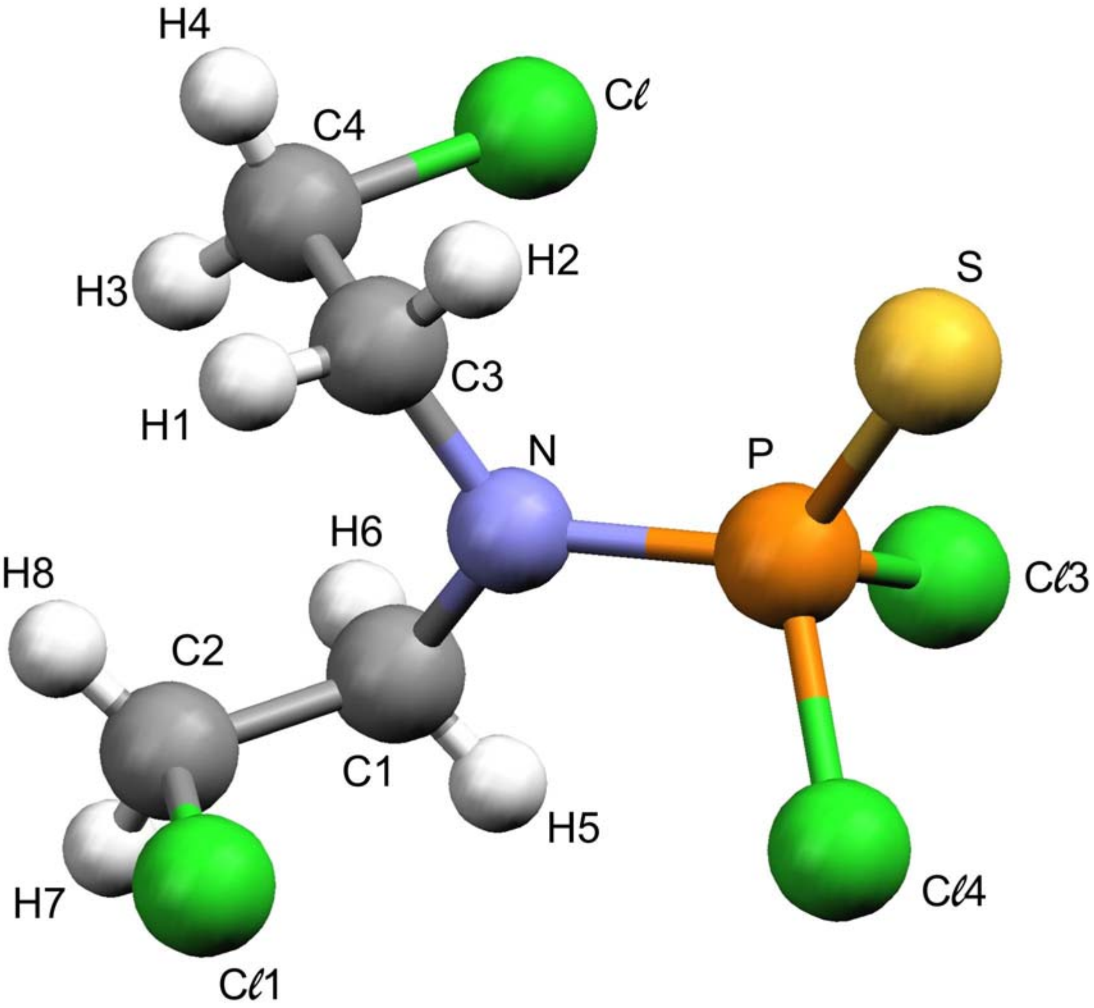


Figure 4.8 Molecular drawing of $Cl_2P(S)N(CH_2CH_2Cl)_2$, **8**

Atom	x/c	y/c	z/c	U_{eq} $=1/3\ \Sigma_i\ \Sigma_j\ U_{ij}\ a_i{}^*a_j(a_i.a_j)$
P	2658(5)	1065(11)	1541(5)	43(19)
Cl	593(6)	2798(15)	-632(7)	74(3)
Cl1	4240(6)	2796(13)	-49(7)	64(2)
Cl3	4059(6)	441(16)	2265(6)	69(3)
Cl4	2712(9)	4450(13)	1495(7)	79(3)
N	2534(14)	214(3)	352(15)	39(4)
S	1768(6)	-44(14)	2288(6)	58(2)
C2	3567(2)	-699(5)	-870(2)	50(6)
C1	3189(19)	1089(5)	-267(2)	44(5)
C3	1673(18)	-1025(5)	-202(2)	45(6)
C4	1020(20)	260(6)	-1078(2)	57(7)

Table 4.9 Fractional atomic coordinates (x 10^4) and equivalent thermal factors (x 10^3 Å^2) for **8**.

Atom	x/c	y/c	z/c	U_{eq} $=1/3\ \Sigma_i\ \Sigma_j\ U_{ij}\ a_i{}^*\ a_j(a_i.a_j)$
H1	1860(20)	-234(5)	490(2)	49(8)
H2	1330(20)	-1460(5)	285(19)	39(7)
H6	2860(20)	2150(50)	-780(20)	47(7)
H5	3700(20)	1820(50)	180(20)	45(7)
H8	3090(20)	-1410(60)	-1360(2)	52(9)
H3	1330(30)	710(60)	-1660(30)	60(10)
H7	4010(20)	20(50)	-1220(20)	51(7)
H4	480(30)	-570(60)	-1320(30)	71(10)

Table 4.10 Coordinates of the hydrogen atoms (x10^4) and isotropic thermal factors (x 10^3 Å) for **8**

4.2.3 Results and Discussion

The ^{1}H NMR spectra of the two substrates, compounds **0** and **8** were very similar which indicated comparable geometries/conformation in solution state for the two compounds. However the chemical reactivities are very different. The phosphoryl compound is moderately reactive and undergo nucleophilic displacement at the phosphoryl centre quite easily. The thiophosphoryl analogue is very resistant to nucleophilic attack but not completely resistant. More harsh reaction conditions were necessary to displace the two chlorines at the thiophosphoryl centre. It was expected that a more detailed structural analysis of the two systems, will shed some light on the different chemical reactivities. Selected bond distances, bond angles and torsion angles are listed in **Table 4.11**.

The X-ray diffraction data revealed a few structural differences between the two compounds.

- The nitrogen atom in the thiophosphoryl analogue **8** is comparable with the nitrogen atom in the phosphoryl analogue **0**; both are planar.
- No intramolecular hydrogen bonding; no intermolecular hydrogen bonding.
- The bond angles in the $Cl_2P(X)N$ moieties are slightly different:
- The angle Cl-P=S are slightly smaller than the Cl-P=O bond angle; the S=P-N angle in slightly bigger than the O=P-N bond angle. (We expected a *perfect* tetrahedral geometry for both, but it seems that the sulphur atom is ‘bended’ away from the mustard moiety);
- The bond angles involving nitrogen are different (C-N-C)
- The torsion angles involving the $Cl_2P(X)N$ moiety are comparable
- The torsion angles of the two chloroethyl chains are different

Compounds **0** and **8** represent comparable geometry, and any differences in chemical reactivity should reflect the difference between the phosphoryl and thiophosphoryl center, and not the different geometries of the compounds.

Bond Distances /Å			
	0		**8**
P=O	1.4562(17)	P=S	1.8890(10)
P-N(1)	1.6177(19)	P-N(1)	1.7316(22)
P-Cl(2)	2.0126(10)	P-Cl(4)	2.0232(11)
P-Cl	2.0114(10)	P-Cl(3)	1.9318(10)
N(1)-C(1)	1.4740(28)	N(1)-C(3)	1.4276(10)
N(1)-C(2)	1.4753(29)	N(1)-C(1)	1.4733(31)
Bond Angles / °			
Y=P-N(1)	116.68(10)	Y=P-N(1)	121.30(7)
Cl-P-Cl	99.91(4)	Cl-P-Cl	99.96(5)
O-P-Cl(2)	112.37(8)	S-P-Cl(4)	113.55(5)
O-P-Cl	112.84(8)	S-P-Cl(3)	106.65(5)
C(1)-N(1)-C(2)	117.86(18)	C(1)-N(1)-C(3)	111.44(21)
C(1)-N(1)-P	120.64(15)	C(3)-N(1)-P	124.27(17)
C(2)-N(1)-P	121.11(15)	C(1)-N(1)-P	123.10(16)
Torsion Angles / °			
O-P-N-C(1)	175.04(16)	S-P-N-C(3)	11.49(23)
Cl-P-N-C(1)	-56.55(17)	Cl(3)-P-N-C(3)	135.16(19)
Cl(2)-P-N-C(1)	49.57(18)	Cl(4)-P-N-C(3)	-118.77(19)
O-P-N-C(2)	-12.26(21)	S-P-N-C(1)	177.97(16)
Cl-P-N-C(2)	116.14(16)	Cl3-P-N-C(1)	-58.36(20)
Cl(2)-P-N-C(2)	-137.73(16)	Cl(4)-P-N-C(1)	47.72(20)
C(1)-N-C(1)-C(3)	75.26(26)	C(3)-N-C(1)-C(2)	-54.70(28)
P-N-C(2)-C(3)	-97.63(23)	P-N-C(1)-C(2)	137.27(20)
N-C(2)-C(3)-Cl(3)	64.27(25)	N-C(1)-C(2)-Cl(1)	-56.07(26)
C(2)-N-C(1)-C(4)	78.84(26)	C(1)-N-C(3)-C(4)	-53.26(30)
P-N-C(1)-C(4)	-108.23(22)	P-N-C(3)-C(4)	114.60(24)
Cl(4)-C(4)-C(1)-N	175.44(17)	Cl-C(4)-C(3)-N	-56.80(27)

Table 4.11 Selected bond distances, bond angles and torsion angles for **0** and **8**. Atomic labels are according to the structures in **Fig 4.7** and **4.8** respectively.

Since the X-ray structure of the bicyclic compound **3a** had been determined before[21], it was now possible to compare the molecular parameters of the two systems i.e. **3a** and **11a**, closely related bicyclic structures. Selected bond angles and bond distances for both compounds are listed in **Table 4.12**. Selected torsion angles for these compounds are listed in **Table 4.1**.

Bond Lengths /Å					
	3a	**11a**		**3a**	**11a**
P=Y	1.926(2)	1.437(2)	N(2)-C(8)	1.470(2)	1.451(3)
P-N(1)	1.682(2)	1.676(3)	N(2)-C(9)	1.476(2)	1.475(2)
P-N(2)	1.674(3)	1.661(2)	N(3)-C(11)	1.426(2)	1.420(3)
P-N(3)	1.665(3)	1.653(3)	N(3)-C(10)	1.476(2)	1.473(2)
N(1)-C(4)	1.422(2)	1.407(3)	C(7)-C(8)	1.498(3)	1.497(3)
N(1)-C(7)	1.467(2)	1.470(2)	C(9)-C(10)	1.516(3)	1.504(2)
Bond Angles /°					
Y=P-N(1)	113.3(1)	114.4(2)	C(8)-N(2)-P	110.5(1)	109.2(2)
Y=P-N(2)	121.1(1)	121.3(1)	C(9)-N(2)-P	108.2(1)	110.9(1)
Y=P-N(3)	114.2(1)	112.7(1)	C(11)-N(3)C(10)	119.3(1)	121.2(2)
N(1)-P-N(2)	95.4(1)	96.3(2)	C(11)-N(3)-P	127.6(1)	126.0(1)
N(1)-P-N(3)	114.9(1)	114.4(2)	C(10)-N(3)-P	111.3(1)	111.1(1)
N(2)-P-N(3)	95.8(1)	95.7(1)	N(1)-C(7)-C(8)	106.0(1)	104.5(1)
C(4)-N(1)-C(7)	119.1(1)	120.6(1)	N(2)-C(8)-C(7)	107.3(1)	107.1(1)
C((4)-N(1)-P	122.8(1)	127.4(2)	N(2)-C(9)-C(10)	106.9(1)	109.0(1)
C((7)-N(1)-P	109.6(1)	110.3(1)	N(3)-C(10)-C(9)	103.2(1)	106.3(2)
C(8)-N(2)-C(9)	114.2(1)	115.9(1)			

Table 4. 12 Selected Bond Lengths and Bond Angles for **3a** and **11a**.

It is clear that all parameters that describe the geometry of the 2,5,8-triaza-$1\lambda^5$-phosphabicyclo[3.3.0]octane system are in both cases approximately the same. The bond distances of the thiophosphoramidate (S=P-N) function does not show any unusual features, with the average P-N bond distance of 1.674 Å, a typical value reported[22] for the amides of phosphoric acid. The length of the thiophosphoryl bond (P=S, 1.926 Å) is also very typical. According to the Cambridge Structural Data Base, the average value of the P=S bond distance in 74 listed compounds of the (N,N',N'')P=S type is 1.929 Å. Compounds **3a** and **11a** represent similar geometry, and any differences in chemical reactivity should therefore reflect the difference between the phosphoryl and thiophosphoryl center, and not the different geometries of the bicyclic skeleton.

Both X-ray diffraction and NMR analysis supported the comparable molecular conformations for systems **3a** and **11a**.

4.3 References

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1. D.H. Williams, I. Flemming, *Spectroscopic methods in organic chemistry,* 3rd Edition, McGraw-Hill Book, London, (1980).
2. H. Gunther, *NMR Spectroscopy,* John Wiley and sons, Chichester, 2nd Edition, 115 (1992).
3. L.M. Jackman, S. Sternhell, *Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, 2nd Edition, Pergamon Press, Elmsford, New York, 270-277 (1969).
4. Atta-ur-Rahman, *Nuclear Magnetic Resonance*, Springer-Verlag, New York, 82, (1986).
5. J. Nielsen, O. Dahl, *J. Chem. Soc. Perkin Trans.,* 2, 553 (1984).
6. B. Fuchs, *Top. Steroechem.,* 10, 1, (1978).
7. F.G. Riddel, *The Conformational Analysis of Heterocyclic compounds,* Academic, New York (1980).
8. W.E. Willy, G.Binsch, E.L. Eliel, *J. Am. Chem. Soc.,* 92, 5394 (1970).
9. M.J. Karplus, *Amer. Chem. Soc.,* 85, 2870 (1963).
10. R.M. Mampa, M.Sc. Dissertation*, X-ray and NMR Spectroscopic studies of selected Heterocyclic Compounds of Phosphorus and Nitrogen* (2000).
11. F. Scheinmann, *An Introduction to spectroscopic methods for the identification of organic compounds,* Vol.1, First Edition, 23 (1970).
12. A. Guinier, *X-Ray Diffraction,* W.H. Freeman and Company (1963).
13. A.C.T. North, D.C. Phillips, F.S. Matthews, *Acta Crystallogr.*, Sect A, **24**, 351

(1968).

14. G.M. Sheldrick, SHELX86. *A program for the solution of crystal structures.* University of Göttingen: Göttingen, Germany (1986).
15. G.M. Sheldrick, SHELX76. *Program for crystal structure determination.* University of Cambridge (1976).
16. *International tables for X-ray crystallography,* Kynoch press., Birmingham (1974) Volume 4; D. T. Cromer and D. Liberman, *J. Chem. Phys.,* 4, *1891 (1970).*
17. C.K. Johnson, ORTEP. Report ORNL-3794. Oak Ridge National Laboratory, Tennessee, USA (1965).
18. G. Sheldrick, SHELXL-97: A program for Crystal Structure Refinement; University of Göttingen: Göttingen, Germany (1997).
19. L.J. Farrugia, *J. Appl. Cryst.,* **32**, 837 (1999).
20. S. Laurens, V.V.H. Ichharam, T.A. Modro, *Heteroatom Chemistry,* 12 (5), 327 (2001).
21. S. Bourne, X.Y. Mbianda, T.A. Modro, L.R. Nassimbeni, H. Wan, *J. Chem. Soc., Perkin Trans. 2,* 83, (1998).
22. M.P. du Plessis, T.A. Modro, L.R. Nassimbeni, *J. Org. Chem. ,* **47**, 2313 (1982).