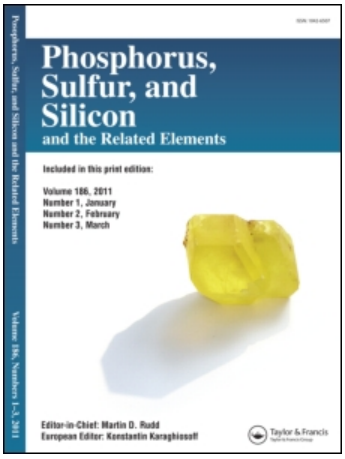

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THE STEREOCHEMISTRY OF THE DICHLOROCYCLOPROPANATION REACTION OF 2,5-DIHYDRO-LH-PHOSPHOLE1-OXIDES

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THE STEREOCHEMISTRY OF THE DICHLOROCYCLOPROPANATION REACTION OF 2,5-DIHYDRO-1H-PHOSPHOLE 1-OXIDES

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The structure of the products from the dichlorocyclopropanation reaction of a number of P-C- and P-O-substituted dihydrophosphole oxides is substantiated and characterized by X-ray analysis and NMR spectroscopy. An explanation is given for the outcome of the reactions yielding the trans-isomer solely or both of the two possible diastereoisomers. The reactivity of the latter two species is briefly discussed.

Key words: dichlorocyclopropanation; dihydrophosphole oxides; diastereoisomers; stereoselectivity; X-ray analysis; reactivity;

INTRODUCTION

Recently we have developed a method for the ring enlargement of the easily available dihydrophosphole oxides to di- or tetrahydrophosphinine-derivatives. The first step of this procedure is the addition of dichlorocarbene to the double bond of the starting material,[1,2] while the second step involves the opening of the dichlorocyclopropane ring formed. The possibilities for the realization of the second step together with the mechanistic implications have already been reported.[3–5] This paper provides information on the stereochemistry of the first step, namely on the cyclopropanation reaction.

RESULTS AND DISCUSSION

As the dichlorocarbene unit may attack the double bond of the 2,5-dihydro-3-methyl-1H-phosphole 1-oxides (**1**) from the two sides of the diastereotopic surface, adducts **2** may be formed theoretically in two diastereoisomeric forms (**A** and **B**) (Scheme I). According to our earlier experiences only one isomer is formed in the reaction of the 1-phenyl- and 1-alkyl-dihydrophosphole oxides (**1a-c**) with dichlorocarbene.[1] From the ^{31}P, ^{13}C and ^{1}H NMR spectra, however, we have not been able to decide on the stereostructure of the product (**2**).

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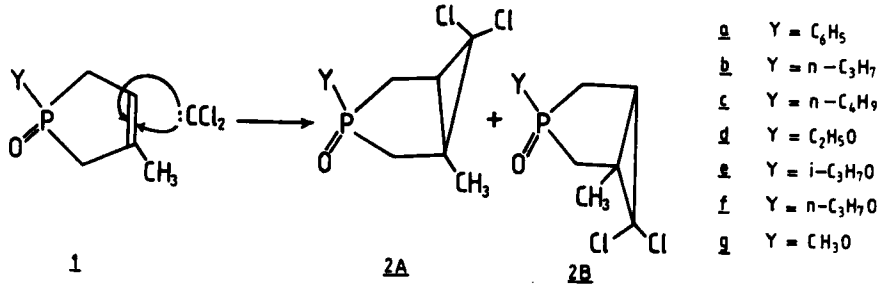


Scheme I.

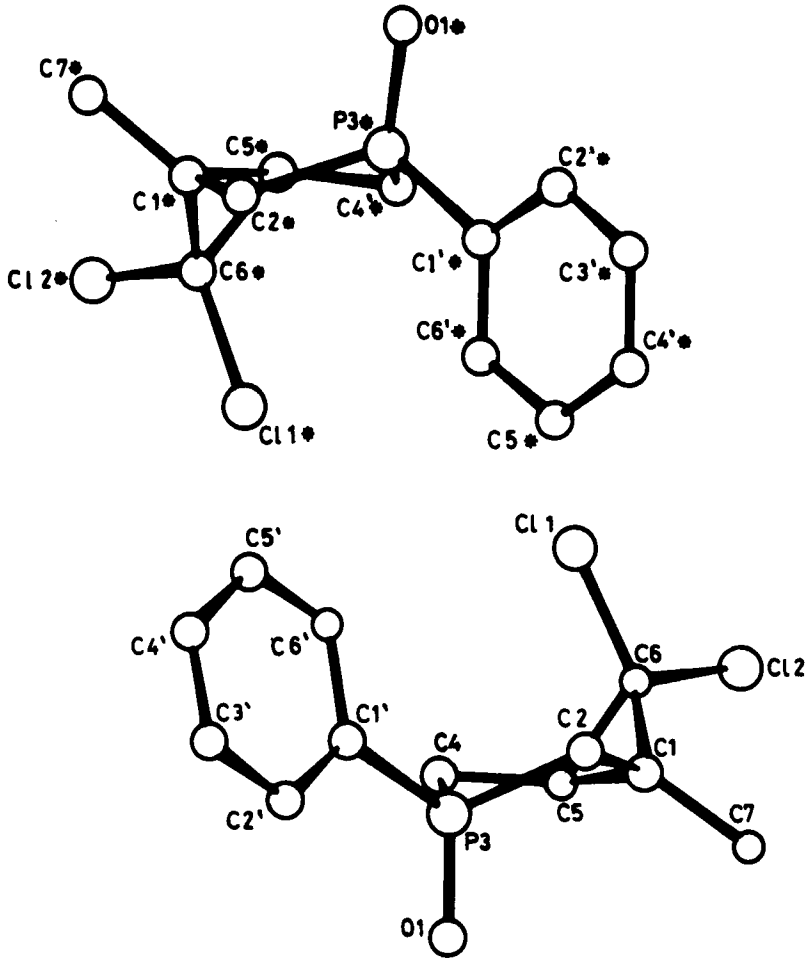


FIGURE 1 Perspective view of the symmetry independent molecules for **2a** showing the crystallographic numbering. The H atoms have been omitted for clarity.

It was the X-ray examination that helped to solve the problem. Single-crystal X-ray analysis of the phenyl-derivative (**2a**) has revealed that the cyclopropane ring and the oxygen atom of the phosphoryl group are on the opposite side of the five-membered hetero ring indicating that the particular isomer we have belongs to series **A**. It can also be stated, that each cell unit consists of two symmetry independent molecules with not only similar configuration, but with rather similar conformation as well (Figure 1). Each hetero ring has the same pucker, resulting in an almost perfect envelope shape[6] with the phosphorus atom on the flap, placing this latter in trans position to the cyclopropane ring. Atomic coordinates of non-H atoms are listed in Table I.[7]

As an analogy we mention the experience of Arbuzov et al., that the epoxidation of dihydrophosphole oxide-derivatives leads also to the trans-product.[8] The orientation was substantiated to be directed by electronic effects.

In our case the exclusive formation of isomer **2Aa** may also be governed mainly by electronic effects beside the steric reasons. Due to the electronic repulsion of

TABLE I

Final fractional coordinates for non-H atoms with e. s. d. s in parentheses

Atom	x/a	y/b	z/c
Cl(1)	1.0244(2)	0.4203(1)	0.4249(1)
Cl(2)	1.2978(2)	0.2787(1)	0.35485(9)
O(1)	0.8176(5)	0.0304(2)	0.6490(2)
C(1)	1.1408(6)	0.1813(3)	0.5249(3)
C(2)	1.0441(6)	0.2081(4)	0.6052(3)
P(3)	0.8199(1)	0.1587(1)	0.60437(7)
C(4)	0.8020(6)	0.2006(3)	0.4808(2)
C(5)	1.0020(6)	0.1788(3)	0.4528(2)
C(6)	1.1224(7)	0.2758(4)	0.4340(3)
C(7)	1.3111(7)	0.0910(5)	0.5471(4)
C(1′)	0.6503(6)	0.2470(3)	0.6485(3)
C(2′)	0.5513(7)	0.1928(4)	0.7248(3)
C(3′)	0.4243(8)	0.2612(5)	0.7604(3)
C(4′)	0.3926(8)	0.3801(5)	0.7216(4)
C(5′)	0.4902(9)	0.4344(5)	0.6466(4)
C(6′)	0.6178(8)	0.3693(4)	0.6098(3)
Atom	x/a	y/b	z/c
Cl(1*)	0.4824(2)	0.6064(1)	0.89357(9)
Cl(2*)	0.2324(2)	0.7539(1)	0.75208(9)
O(1*)	0.7371(4)	0.9805(2)	0.9316(2)
C(1*)	0.3871(6)	0.8507(3)	0.8721(2)
C(2*)	0.4770(6)	0.8230(3)	0.9671(2)
P(3*)	0.7125(1)	0.8558(1)	0.94310(7)
C(4*)	0.7293(6)	0.8174(3)	0.8381(2)
C(5*)	0.5335(6)	0.8437(3)	0.8013(2)
C(6*)	0.4021(6)	0.7524(4)	0.8304(3)
C(7*)	0.2234(7)	0.9451(5)	0.8494(3)
C(1′*)	0.8676(6)	0.7533(4)	1.0273(2)
C(2′*)	0.9926(7)	0.7972(4)	1.0716(3)
C(3′*)	1.1112(7)	0.7227(5)	1.1361(3)
C(4′*)	1.1111(8)	0.6026(6)	1.1587(4)
C(5′*)	0.9911(8)	0.5566(4)	1.1161(4)
C(6′*)	0.8668(7)	0.6318(4)	1.0507(3)

the partial negative charge of the oxygen atom in the phosphoryl group and the π-electrons of the double bond the electron density of the latter is concentrated to the side opposite to the oxygen atom and so the electrophilic dichlorocarbene unit can attack from this side easier. The dominance of the same diastereoisomer can again be forcasted by considering the energy relationship of the two possible transition states: the repulsive interactions between the lone pairs of electrons of the phosphoryl-oxygen and those of the appropriate chlorine atom in the carbene unit is practically missing in the transition state leading to **2Aa**, while in the other leading to **2Ba** is considerable. Figure 2 shows the situation for the two possible diastereoisomers (**A** and **B**) of the product (**2a**).

The same situation exists for the reaction of other alkyl-substituted dihydrophosphole oxides (**1b,c**) with dichlorocarbene suggesting again the formation of the trans-adducts (**2Ab,c**). Going even further it can be stated, that the addition of dichlorocarbene to P-C substituted dihydrophosphole oxides (**1a-c**) takes place with hundred per cent stereoselectivity affording isomer **A**.

Recently we have described the preparation of the adducts of 1-alkoxy-dihydrophosphole oxides with dichlorocarbene (**2d-f**) as intermediates for dihydrophosphinine oxides.[2] Elemental analysis, mass and IR spectroscopic examinations confirmed the gross structure of the adducts (**2d-f**), but as it turned out eventually from the duplication of the signals in the ^{31}P, ^{13}C and ^{1}H NMR spectra products **2d-f** contained both of the two possible diastereoisomers (**A** and **B**) (Scheme I). The relative ^{31}P NMR intensities of the isomers referred to a ratio of ~58:42.

It can be seen in Figure 2 that in the adducts **2Ad-f**, as well as in the activated complexes leading to them an additional repulsive interaction appears between the loan electron pairs of the oxygen atom of the alkoxy-group and one of the chlorine atoms in the dichlorocyclopropane moiety, and so their formation are not favoured as much extent as they are in the case of adducts **2Aa-c**. Still isomer **A** might be dominating in the mixture of the products (**2d-f**), because in this case the chlorine-phosphoryl-oxygen interaction is missing.

In the case of adduct **2d** we were able to obtain isomer **A** separately in clean form by column chromatography, the ^{13}C NMR spectrum of which was very useful

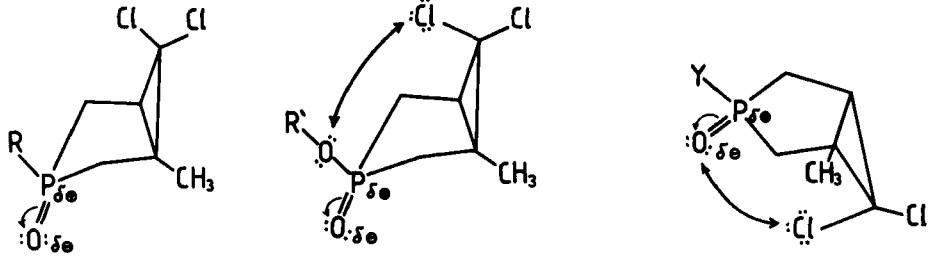


FIGURE 2 Situation for the two possible diastereoisomers (**A** and **B**) of the product **2**.

TABLE II

^{31}P and ^{13}C NMR data for the **A** and **B** diastereoisomers of 3-alkoxy-6,6-dichloro-1-methyl-3-phosphabicyclo[3.1.0]hexane 3-oxides (**2d-f**)[a,b]

Compound Y		^{31}P NMR	^{13}C NMR (J_{P-C}) C_1	C_2	C_4	C_5	C_6	C_1—CH_3	$C_{2'}$	$C_{3'}$	
3′ 2′ 1′ **2d**	**A**	86.9	30.9	30.3	24.5	31.9	71.6	21.1	60.2	16.1	
CH_3—CH_2—O—			(12.4)	(90.2)	(90.1)	(10.3)	(12.4)	(8.1)	(6.6)	(5.9)	[c]
	B	82.9	[d]	31.7	25.7	32.6	71.0	21.3)	61.6	15.9	
				(96.6)	(91.6)	(12.4)	(12.4)	(8.1)	(7.3)	(4.4)	
CH_3 2′ 1′ **2e**	**A**	85.4	[d]	30.9	25.2	31.9	71.7	21.1	69.2	23.8	
CH—O—				(90.1)	(90.1)	(11.8)	(13.6)	(7.3)	(6.6)	(3.7)	
3′ /	**B**	80.9	[d]	32.3	26.4	32.5	71.1	21.3	70.2)	23.3	
CH_3				(92.3)	(91.6)	(11.7)	(13.6)	(8.1)	(6.5)	(4.4)	
4′ 3′ 2′ 1′ **2f**	**A**	86.5	30.0	29.7	23.9	31.4	71.3	20.5	65.0	22.9	
			(12.5)	(90.9)	(89.4)	(12.5)	(13.9)	(6.6)	(6.6)	(5.9)	$C_{4'}$
CH_3—CH_2—CH_2—O—	**B**	82.7	30.7	31.2	25.4	32.1	70.8	20.8	66.3	22.8	9.1
			(14.7)	(91.6)	(91.6)	(12.5)	(11.7)	(7.3)	(6.6)	(4.1)	

[a] $CDCl_3$ solution, J given in Hz.
[b] Samples containing the two diastereoisomers were subjected to NMR measurements.
[c] Data were confirmed by the spectrum of the separated isomer.
[d] Not resolved.

TABLE III

^1H NMR data for the **A** and **B** diastereoisomers of 3-alkoxy-6,6-dichloro-1-methyl-3-phosphabicyclo[3.1.0]hexane 3-oxides (**2d-f**)[a,b]

Compound		^1H NMR δ(multiplicity, integral, J_{HH}) —CH—CH_3	C_1—CH_3	$P(CH_2)_2$, CH	O—C—H
2d	**A**	1.36 (t, $^3J_{HH}$ = 7) [c] 3H,	1.56 (s,) [c] 3H	1.76–2.90 (m, 5H)	3.84–4.28 (m, 2H)[e]
	B	1.34 (t, $^3J_{HH}$ = 7)	1.64 (s,)		
2e	**A**	1.36 (d, $^3J_{HH}$ = 7) [c] 6H,	1.56 (s,) [c] 3H	1.76–2.75 (m, 5H)	4.36–4.84 (m, 1H)
	B	1.32 (d, $^3J_{HH}$ = 7)	1.63 (s,)		
2f	**A**	0.96 (t, $^3J_{HH}$ = 8) [c] 3H,	1.55 (s,) [c] [f]	1.35–2.60 (m[f])[g]	3.95(q, $^3J_{HH}$ = $^3J_{PH}$ = 6) 2H
	B	0.94 (t, $^3J_{HH}$ = 8)	1.62 (s,)		3.97(q, $^3J_{HH}$ = $^3J_{PH}$ = 7

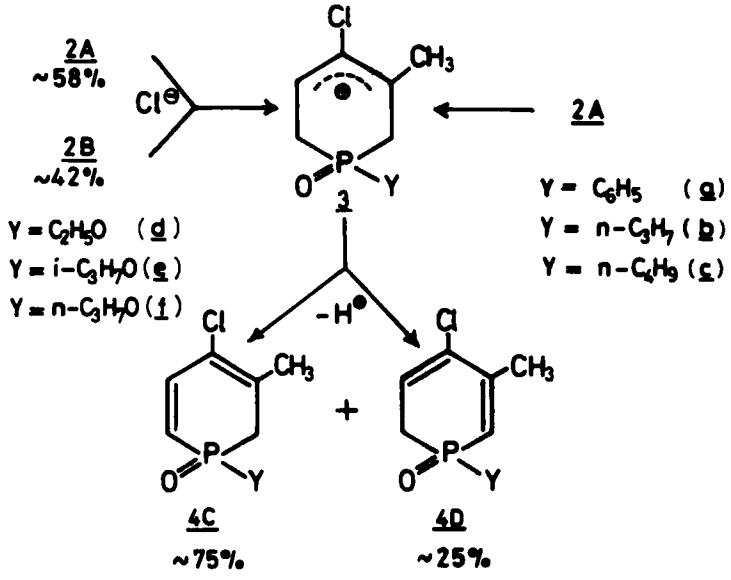
[a] $CDCl_3$ solution, J given in Hz.
[b] Samples containing the two diastereoisomers were subjected to NMR measurements.
[c] May be reversed.
[e] For the **2Ad** isomer separated: 4.07 (quint, 2H, $^3J_{HH}$ = $^3J_{PH}$ = 7).
[f] The signals are overlapped, total intensity 10H.
[g] Includes also the signal of the $OCH_2CH_2CH_3$.

in assigning the spectra of the other samples (**2d-f**) containing both of the diastereoisomers (**A** and **B**). Beside this the ^{13}C NMR spectra obtained by "Attached Proton Test"-technic and the ^{13}C NMR data of the adducts (**2Aa-c**) described

earlier[1] helped the assignment. The ^{31}P, ^{13}C and ^{1}H NMR data for products **2d-f** have been collected in Table II and in Table III, respectively.

Similarly to the reaction of P-C substituted-dihydrophosphole oxides (**1a-c**) with dichlorocarbene the formation of only one diastereoisomer was observed in the dichlorocyclopropanation reaction of the 1-methoxy-derivative (**1g**).[1] From the above mentioned reasons we believe that the product (**2g**) belongs also to series **A** (trans isomer). Carrying out this reaction under more forcing conditions, used for the preparation of the other alkoxy substituted adducts (**2d-f**), the other isomer (**2Bg**) was also formed, but only in a quantity of ~25%. The higher preference for the formation of **2Ag** may be connected with the small steric requirement of the methoxy-group.

As the reactivity of the diastereisomers is concerned we have two observations to be mentioned. In the thermal transformation of the isomeric mixtures of the adducts (**2Ad-f** and **2Bd-f**) to the regioisomers (**C** and **D**) of the dihydrophosphinine oxides (**4d-f**) the ratio of the isomers changes from A:B = 58:42 to C:D = 76:24,[2] the latter ratio being similar to that (73:27) observed in the thermolysis of other adducts (**2a-c**) consisting of only one isomer (**A**).[3] The change in the ratio of the isomers is in good agreement with the involvement of a cationic intermediate (**3**) during the transformation[3,9] (Scheme II).



Scheme II.

The second observation of ours is that the rates of the thermolysis for the diastereoisomers of **2d** are different, namely isomer **B** seems to be more reactive. Interrupting the thermal transformation of the sample (**2d**) containing both isomer **A** and **B**, only isomer **A** could be detected and identified in the mixture.

EXPERIMENTAL

The ^{31}P, ^{1}H and ^{13}C NMR spectra were taken on a JEOL FX 100 MHz instrument, operating at 40.26, 100.0 and 25.0 MHz, respectively. Chemical shifts are downfield, relative to 85% phosphoric acid and to tetramethylsilane, respectively, and have a positive sign. All coupling constants are given in Hertz.

3-Substituted 6,6-dichloro-1-methyl-3-phosphabicyclo[3.1.0]hexane 3-oxides have been prepared as described earlier.[1,2]

X-ray Crystal Structure Determination for **2a**. Crystals of $C_{12}H_{13}Cl_2OP$ (Mw = 275,12) are triclinic; space group $P\bar{1}$, a = 7.320(1), b = 11.983(1), c = 15.463(2) Å, α = 71.82(1), β = 88.60(1), γ = 83.04(1)°, V = 1279.0(3) Å^3, Z = 4 /two molecules in the asymmetric unit/ D_c = 1.43 g·cm^{-3}. X-ray data were collected from a white prism crystal having approximate dimensions of 0.15x0.25x0.35 mm^3 by an Enraf-Nonius CAD-4 diffractometer using graphite monochromated Cu-K_α radiation (λ = 1.54184 Å, ω-2Θ scan in the range $3 < 2\Theta < 150°$, scan width (ω) 0.4 + 0.14 tg Θ). Out of the 5456 observations 4124 were unique and non zero. For the structure analysis and refinement 3064 reflections taken with $F_0^2 > 36$ (F_0^2) were applied. They were corrected for absorption by the program DIFABS.[10] Relative transmission coefficient ranged from 0.786 to 1.818 with an average value of 0.994. No decay correction had to be used. The structure was solved by direct methods and refined in anisotropic mode for 289 variables to a final R = 0.050 (R_w = 0.080, R_{tot} = 0.076, S = 2.47). The highest residual peak in the final difference electron density map was 0.35 (7) e.Å^{-3}. The hydrogen positions were generated from assumed geometries and added to the structure factor calculations without refinement. All calculations have been done by SDP-PLUS.[11]

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