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THE JOINT ACTION OF TRISDIMETHYLAMINOPHOSPHINE (TDAP) AND CARBON TETRACHLORIDE ON SOME VICINAL DIOLS

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Abstract—The joint action of trisdimethylaminophosphine and carbon tetrachloride on vicinal diols affords either *trans* epoxides or spirophosphoranes. The mutarotation of these spirophosphoranes is described by ^{1}H NMR and ^{31}P NMR spectra. The mechanism of reaction providing either epoxides or spirophosphoranes is discussed.

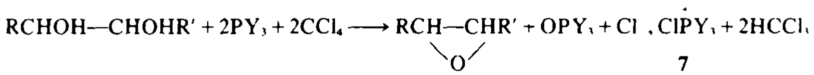
In a preliminary note[1] we described the formation of either epoxides or tetraoxyspirophosphoranes in the reaction of TDAP on α-glycols in the presence of carbon tetrachloride. This reaction is unlike the general case of 1-*n*-glycols where the activation of one hydroxyl group via alkoxytris(dimethylamino) phosphonium (ATDP) salts is readily obtained.[2] We describe here this reaction in full and give some interpretation concerning the orientation of the reaction.

RESULTS

Substrates providing epoxides

The slow addition of TDAP to a cold solution of carbon tetrachloride and substrates such as phenylethane diol **1**, *meso*-hydrobenzoin **2**, or o,o'-dimethoxy-*meso*-hydrobenzoin affords the *trans* epoxide resulting in the gross dehydration of the glycol. Two molar equivalents of TDAP are required for complete reaction; the phosphorus products are recovered as one equivalent of HMPA and one equivalent of chlorotrisdimethylamino phosphonium chloride **7**, isolated as the stable hexafluorophosphate salt.[3] These results substantiate the following stoichiometric equation (Scheme 1).

In no case can the ATDP salt be detected (TLC and ^{31}P NMR).



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1: R = Ph, R' = H
2: R = R' = Ph *meso*
3: R = R' = OMeOPh *meso*

4: (70%)
5: *trans* (97%)
6: *trans* (66%)

Scheme 1.

Substrates providing spirophosphoranes

Under the same conditions, these substrates require 1.2–2 equivalents of TDAP, according to the structures, for complete reaction. The reaction is followed by TLC; the starting material is replaced by a less polar spot, corresponding to a product that can be isolated after hydrolysis and extraction with hexane. The products are characterised by a ^{31}P NMR signal in the range $+25$ to $+40$ ppm with respect to phosphoric acid (Table 1).[4] The ^{1}H NMR spectra exhibit P–N(CH$_3$)$_2$ doublets, integrating for six protons instead of eighteen in the ATDP salts. Depending on the structure of the ligand glycol, one or several stereoisomers around the phosphorus atom can be distinguished.

Cycloalkane α-glycol ligands

With *cis* cyclohexane diol **11** a single phosphorane **8a** is isolated at once. Heating at 50°C during 20 h or dissolution in methanol overnight at room temperature induces the appearance of two other isomers observable in both ^{31}P and ^{1}H NMR, until an equilibrium is reached where isomeric **11c** predominates (Table 2). These observations are consistant with the existence of three pairs of stereoisomers (Scheme 2).[5] The tertiary protons in each ring become equivalent because of the fast interconversions of both cyclohexane chairs and the phosphorus bipyramid. The phosphorus bipyramid can flip either by the Berry pseudo rotations (BPR)[6] or by the turnstile (TS) interconversions[7,8] of low energy, where neither apical nitrogen, nor the diequatorial 5-membered ring is allowed. Thus by NMR spectroscopy it appears to be a square base pyramid.[9]

The ^{1}H NMR spectrum of the pure isomer **11a** exhibits a broad double triplet at 3.75 ppm. The spin decoupling from the methylene ring protons gives rise to one sharp doublet $^3J_{H-P} = 12.5$ Hz showing that the molecule is symmetric; this excludes the *cis–trans* configuration, leaving this isomer either with the *cis–cis* or the *trans–trans* configuration. It is likely that isomer **11b**, which has physical properties between **11a** and **11c** and which seems to be their kinetic intermediate has the *cis–trans* configuration. It should be possible to decide whether **11a** or **11c** is *cis–cis* or *trans–trans*; examination of molecular models gives no obvious information concerning the more hindered isomer.

The slow configurational interconversion may proceed either through two consecutive BPR or TS of high energy or through an irregular process involving ring opening.[7] The isomerization barrier for the transformation can be estimated roughly from the data of Table 2. The assumption of a first order law for the disappearance of **11a** leads to a rate constant k_1 of about 3.3×10^{-5} at 27°C; hence a value for the activation energy $\Delta G^* = 24$ kcal mol^{-1}. This data is appreciably lower than that expected

Table 1.

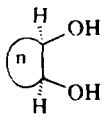
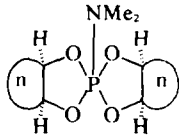
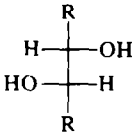
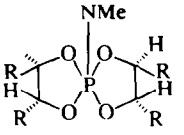
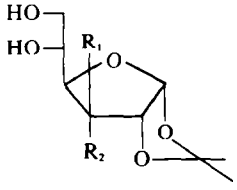
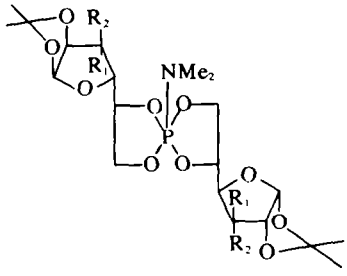
Substrates		Spirophosphoranes	Yield	^{31}P NMR δ/ppm
				
8: n = 6	**11**:		64%	+37
9: n = 7	**12**		86%	
10: n = 8	**13**		83%	+36.6 +38.3 +39.2
				
			Yield	^{31}P NMR δ/ppm
14: R = COOEtL (+)	**20**		48%	
15: R = COOiPrL (+)	**21**		90%	+25.2
16: R = COOBuL (+)	**22**		93%	
17: R = COOiPrDL	**23**		73%	+23.7 +25.2
18: R = φ(dl)	**24**		88%	+31.3 +33.2
19: R = φ(l)	**25**		57%	+32.2
				
			Yield	^{31}P NMR δ/ppm
26: $R_1 = OCH_2\phi$, R_2 = H	**28**		94%	+26.5 +27.2
27: R_1 = H, $R_2 = OCH_2\phi$	**29**		75%	+28.4

Table 2.

	^{31}P NMR δ/ppm	^{1}H NMR δ/ppm	%t = 0	%t = 10 h	%t = 20 h
11a	+37	2.85	100	30	16
11b	+35	2.75	—	25	21
11c	+32	2.63	—	45	63

from Trippett's evaluations; the apicophilicity of the NMe_2 group is about 7 kcal mol^{-1} lower than that of the benzoyl group;[10,11] for this last group ΔG* data is available on a very close related structure and estimated at about 21 kcal mol^{-1}; the actual value lower by 4 kcal mol^{-1} is a strong indication for another mechanism; an irregular pathway involving methanol is not unlikely (Scheme 5).

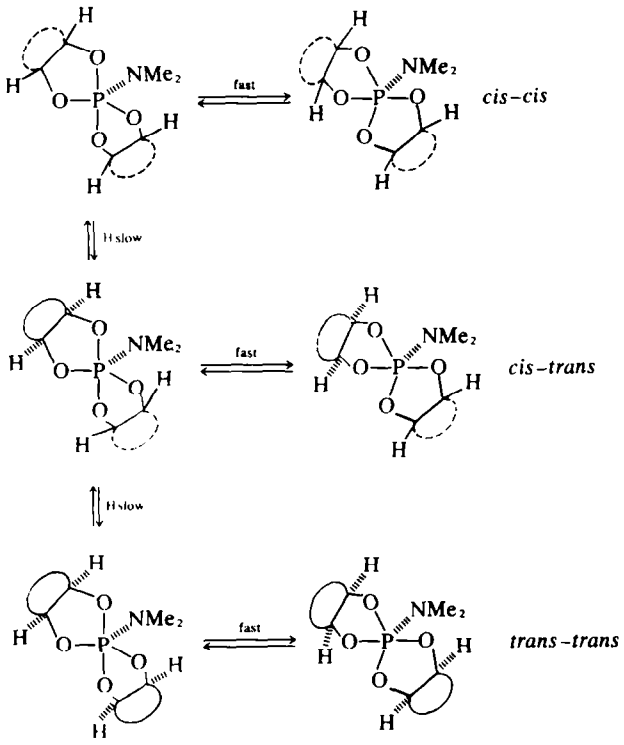
In the case of *cis*-cycloheptane and cyclo-octanediols the three isomers are observed immediately after isolation.

Threo-tartaric ester and threo-hydrobenzoin ligands

1-(+)-*threo*-tartaric esters afford the corresponding spirophosphoranes, requiring a 1.2 molar excess of TDAP. The bulk of the alkyl group of the esters influences the product yields (Table 1). The methyl ester gives a phosphorane observed by its +23 ppm signal in the ^{31}P NMR at −40°C, this phosphorane rearranges very readily at room temperature to an unidentified product (probably a phosphate δ ^{31}P = −15 ppm). *Threo*-hydrobenzoin behaves regularly to give a crystalline and rather stable spirophosphorane.[1] In all cases only one expected isomer is observed but when the (dl) racemic mixtures are used two diastereoisomers are observed in the ^{31}P NMR, corresponding to the expected *meso* (dP1) and the racemic pair (dPd; 1P1) (Scheme 3). Only ^{31}P NMR can distinguish between these two isomers. In ^{1}H NMR the proton signal of the NMe_2 groups are strictly equivalent.

Hexafuranose derivatives as ligands

Both 3-O-benzyl-1,2-O-isopropylidene-α-D-gluco-[12] and α-D-allofuranoses, from which we expected an epoxide, actually afford mixtures of stereoisomers. Three pairs of quickly interconverting bipyramids are expected. Both ^{31}P and ^{1}H NMR show three different species



Scheme 2.

corresponding to the *cis-cis*, *cis-trans* and *trans-trans* configurations (Scheme 4). It is not possible in this case to definitely assign any signals.

DISCUSSION

In every case, it is likely that the primary product is an α-hydroxy ATDP salt, Anselmi *et al.*[13] have noticed the easy formation of epoxides from these salts in weakly basic conditions employing a betain. Depending to the structure of the substrate, the oxyphosphonium and alcoolate groups of the betain are either in synclinal **B**, or in antiperiplanar conformation **C** (Scheme 5).

The formation of an epoxide **D** derives from the γ-elimination of **C**. The phosphorane **E**, formed by the cyclisation of **B**, enables the formation of the spirophosphorane **F**. Ramirez *et al.*[14] studied the formation of epoxides by the reaction of phosphines with aldehydes, showing the poor stability of derivatives such as **E**, when the phosphines are non-cyclic. Thus, the substitution reaction by the diol on **E** to form the spirophosphorane **F** is likely to be very fast. The lose of steric strain on formation of **D** or **E** from their respective intermediates is about the same, the fastest reaction is always that giving *trans* cyclic derivatives.

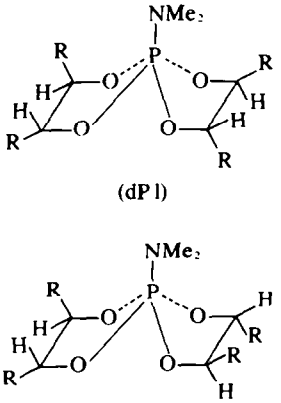
In the phosphorane formation from racemic diols, the reaction **E** → **F** is not selective toward any enantiomer. The two diastereoisomers are formed in equal quantities.

Cycloalkanediols

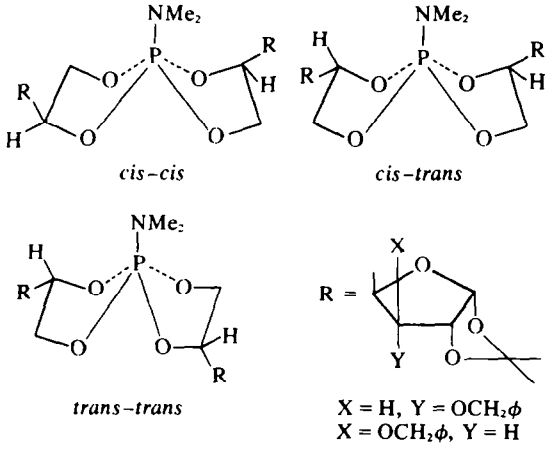
In this case, the formation of the phosphorane is the only allowed reaction. On the other hand, it is surprising that the *trans* cyclohexanediol remains unaffected under the conditions of the reaction.

Sugar derivatives

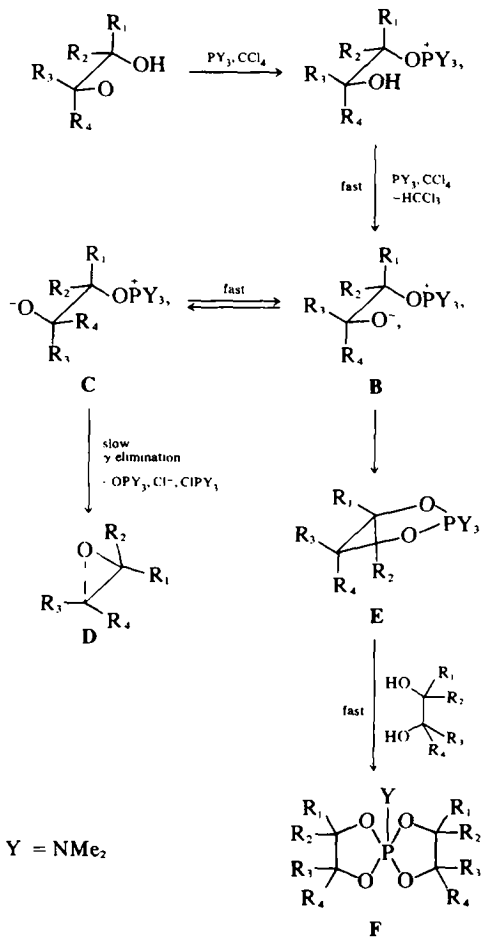
We expected these substrates to behave in the same



Scheme 3.



Scheme 4.



Scheme 5.

manner as phenylethane diol. A careful inspection of molecular models is necessary to explain the result. The conformation of the intermediate betaïn is affected by two parameters, the torsion angles of the C_4–C_5 and the C_5–C_6 bonds. The three staggered conformers about C_4–C_5 are represented by Scheme 6. One can see that in conformations A_1 and A_2, the distance of the negative betaïn oxygen and the furanose ring oxygen is about 2.8 Å. The Van der Waals radius of neutral oxygen being 1.4 Å these conformations are probably prohibited with respect to both steric hindrance and electrostatic repulsion.

Concerning the C_5–C_6 conformation, in conformation A_3 needed for the epoxide formation, the distance between the oxyphosphonium and the ring oxygens is 2.6 Å, whereas in conformations such as A_4 and A_5 which give a phosphorane, it is 3.8 Å.

EXPERIMENTAL

The m.ps were not corrected. The NMR spectra were recorded on a MINIMAR JEOL or a BRUCKER 90 MHz using TMS as internal standard. Chemical shifts are given in ppm (δ). ^{31}P NMR spectra were recorded on a BRUCKER 90 MHz, using D_3PO_4 as internal standard. Specific rotations were determined with a Perkin Elmer 141 polarimeter. Thin layer chromatograms were run on silica gel Merck (kieselgel G).

Formation of epoxides

To a solution of diol (1 eq) and carbon tetrachloride (2 eq) in methylene chloride, cooled to −40°C, was added two equivalents of TDAP in the same solvent. After the addition, the solvent was removed *in vacuo*, the residue hydrolysed, extracted with pentane and dried ($MgSO_4$). The epoxide obtained after evaporation of the solvent was purified by distillation or recrystallisation.

2-Phenyloxirane **4**. Yield: 70% identified by comparison with lit.[15]

Trans-2,3-diphenyloxirane **5**. Yield: 97% identified by comparison with lit.[16]

Trans-2,3-(di-o,o'-methoxyphenyl)-oxirane **6**. Yield: 66%; m.p. = 150–152°C; TLC (R_f ~ 0.6, AcOEt:cyclohexane 30:70); NMR ($CDCl_3$): δ: 6.7–7.4 (m, Ar); 4.18 (s, CH); 3.78 (s, CH_3).

Formation of spirophosphoranes

To a solution of diol (1 eq) and carbon tetrachloride (4 eq) in methylene chloride, cooled to −40°C, was added dropwise a solution of TDAP in the same solvent, till the diol disappearance (TLC). The solvent was removed *in vacuo* and the residue hydrolysed (pH = 14), extracted with either pentane or a mixture ether:pentane 1:1, and dried ($MgSO_4$). After evaporation of the solvent, the crude product was pure enough for analysis.

2,3,7,8 - *Di* - (*perhydrobenzo*) - 5 - *dimethylamino* - 1,4,6,9 - *tetraoxa* - 5 - *phospha* - *spiro*[4,4]*nonane* **11**. Yield: 64%; m.p. = 140°C; TLC (R_f ~ 0.7, AcOEt); NMR (CCl_4) δ: 3.5–4 (m, J = 12.5 Hz, CH); 2.85 (d, J = 9.5 Hz, CH_3); 1.1–1.9 (m, CH_2); ^{31}P NMR (acetone) δ: +37; (Found: C, 55.44; H, 8.58; N, 4.62. $C_{14}H_{26}NPO_4$ requires: C, 55.61; H, 8.49; N, 4.50%).

2,3,7,8 - *Dicycloheptyl* - 5 - *dimethylamino* - 1,4,6,9 - *tetraoxa* - 5 - *phospha* - *spiro*[4,4]*nonane* **12**. Yield: 86%; TLC (R_f ~ 0.7, AcOEt:cyclohexane 50:50); NMR (CCl_4) δ: 3.6–4.3 (m, CH); 2.77, 2.69, 2.65 (3 d, J = 9.5 Hz, CH_3); 0.9–2.1 (m, CH_2).

2,3,7,8 - *Dicyclooctyl* - 5 - *dimethylamino* - 1,4,6,9 - *tetraoxa* - 5 - *phospha* - *spiro*[4,4]*nonane* **13**. Yield: 83%; TLC (R_f = 0.7, AcOEt:cyclohexane 50:50); NMR (CCl_4) δ: 3.5–4.1 (m, CH); 2.71, 2.67, 2.66 (3 d, J = 9.5 Hz, CH_3); 1.1–2 (m, CH_2); ^{31}P NMR (acetone) δ: +36.67, +38.33; +39.83.

2,3,7,8 - *Tetracarboethoxy* - 5 - *dimethylamino* - 1,4,6,9 - *tetraoxa* - 5 - *phospha* - *spiro*[4,4]*nonane* **20**. Yield: 48%; NMR ($CDCl_3$) δ: 4–4.6 (m, CH); 4.25 (q, J = 7 Hz, CH_2); 2.75 (d, J = 10.5 Hz, N–CH_3); 1.3 (t, J = 7 Hz, CH_2–CH_3).

2,3,7,8 - *Tetracarboisopropyloxy* - 5 - *dimethylamino* - 1,4,6,9 - *tetraoxa* - 5 - *phospha* - *spiro*[4,4]*nonane* **21**. Yield: 90%; TLC (R_f = 0.6, AcOEt:cyclohexane 50:50); $[\alpha]_D^{21} = -2.1°$ (c = 8, AcOEt); NMR (CCl_4) δ: 5.05 (h, J = 6.3 Hz, CH–CH_3); 4.15–4.28 (m, CH–O); 2.8 (d, J = 10.5 Hz, N–CH_3); 1.28 (d, J = 6.3 Hz, CH–CH_3); ^{31}P NMR (acetone) δ: +25.19.

2,3,7,8 - *Tetracarbobutyloxy* - 5 - *dimethylamino* - 1,4,6,9 - *tetraoxa* - 5 - *phospha* - *spiro*[4,4]*nonane* **22**. Yield: 93%; TLC (R_f = 0.5, AcOEt:cyclohexane 30:70); NMR (CCl_4) δ: 3.9–4.5 (m, CH–O and CH_2–COO); 2.78 (d, J = 10 Hz, N–CH_3); 1.15–1.9 (m, CH_2 butyle); 0.75–1.15 (m, CH_3 butyle).

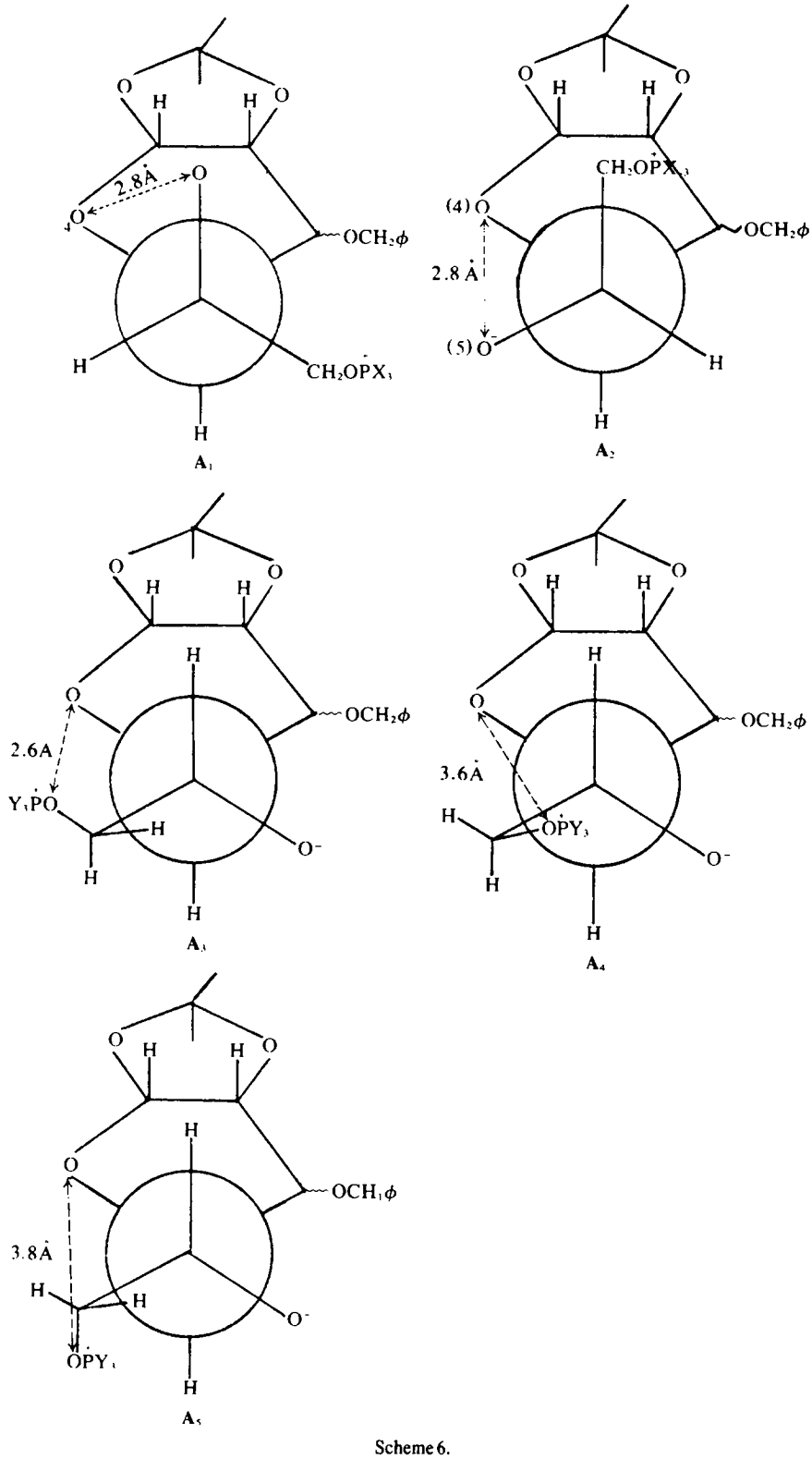
2,3,7,8 - *Tetracarboisopropyloxy* - 5 - *dimethylamino* - 1,4,6,9 - *tetraoxa* - 5 - *phospha* - *spiro*[4,4]*nonane* (*racemic and meso*) **23**. Yield: 73%; NMR ($CDCl_3$) δ: 5.07 (h, J = 6.3 Hz, CH isopropyle); 4.1–4.6 (m, CH–O); 2.77 (d, J = 10.5 Hz, N–CH_3); 1.27 (d, J = 6.3 Hz, CH_3 isopropyle); ^{31}P NMR (acetone) δ: +23.72; +25.19.

2,3,7,8 - *Tetraphenyl* - 5 - *dimethylamino* - 1,4,6,9 - *tetraoxa* - 5 - *phospha* - *spiro*[4,4]*nonane* (*racemic and meso*) **24**. Yield: 88%; m.p. = 176–180°C; TLC (R_f = 0.7, AcOEt:cyclohexane 30:70); NMR ($CDCl_3$) δ: 7.29 (s, Ar); 4.45–4.87 (m, CH–O); 3.08 (d, J = 10 Hz, N–CH_3); ^{31}P NMR (CH_2Cl_2) δ: +31.36; +33.24; (Found: C, 72.60; H, 6.20; N, 3.10. $C_{30}H_{30}NPO_4$ requires: C, 72.16; H, 6.01; N, 2.80%).

2,3,7,8 - *Tetraphenyl* - 5 - *dimethylamino* - 1,4,6,9 - *tetraoxa* - 5 - *phospha* - *spiro*[4,4]*nonane* **25**. Yield: 57%; m.p. = 115°C; $[\alpha]_D^{21} = -42.3°$ (c = 1.3, DMF); NMR ($CDCl_3$) δ: 7.27 (s, Ar); 4.4–4.75 (m, CH–O); 3.02 (d, J = 10 Hz, N–CH_3); ^{31}P NMR (DMF) δ: +32.17; (Found: C, 72.18; H, 6.19; N, 3.02. $C_{30}H_{30}NPO_4$ requires: C, 72.16; H, 6.01; N, 2.80).

Spirophosphorane **28**. Yield: 94%; TLC (R_f = 0.65, AcOEt:cyclohexane 60:40); NMR ($CDCl_3$) δ: 7.3 (m, Ar); 5.92–5.88 (2 d, J = 3.5 Hz, H_1); 3.6–4.7 (m, CH and CH_2); 2.75, 2.72, 2.67 (3 d, J = 10 Hz, N–CH_3); 2.75, 2.72, 2.67 (3 d, J = 10 Hz, N–CH_3); 1.48–1.29 (2 s, CH_3 isopropyle). ^{31}P NMR (acetone) δ: +26.5; +27.2; +28.4.

Spriophosphorane **29**. Yield: 75%; TLC (R_f = 0.75,



Scheme 6.

AcOEt: cyclohexane 50:50); NMR ($CDCl_3$) δ: 7.46 (s, Ar); 5.82 (d, J = 3.5 Hz, H_1); 3–4.8 (m, CH and CH_2); 2.72, 2.67 (2 d, J = 9.5 Hz, N–CH_3); 1.58–1.36 (2 s, CH_3 isopropyle).

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