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REACTIONS OF N-METHYL 1,3-DIAMINOPROPANE WITH $N_3P_3Cl_6$ AND *GEM*-$N_3P_3Cl_4Ph_2$ LEADING TO SPIROCYCLIC PRODUCTS

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Abstract—The reactions of $N_3P_3Cl_6$ (**1**) and *gem*-$N_3P_3Cl_4Ph_2$ (**9**) with N-methyl 1,3-diaminopropane affords monospiro and dispiro products. With **1** trispiro products have also been isolated. The synthesis of these spirocyclic products and their characterization by proton and phosphorus NMR are discussed.

The chemistry of cyclophosphazenes has been expanding vigorously in recent years primarily due to the versatile nucleophilic substitution reactions on the six- and eight-membered halogenocyclophosphazenes and the utility of this chemistry as a model for the more complex polyphosphazenes.[1] In contrast to the reactions of chlorocyclophosphazenes with monofunctional reagents those with difunctional reagents proceed by a pairwise replacement of chlorine atoms. In most instances monospirocyclic products have been isolated.[2] The other possible products such as ansa,[3] intermolecular bridged or open chain[4] remain rare and have only been isolated earlier in lower yields or only in selected reactions. Even among spirocyclic derivatives the number of di- and trispiro derivatives are very few.[5] Recently it has been reported that the reaction of $N_3P_3Cl_6$ (**1**) with N-methyl 1,3-diaminopropane afforded primarily an intermolecular bridged product. This surprising result prompted us to reinvestigate this reaction. In a preliminary communication earlier,[6] we have reported that the above reaction proceeds by the normal spirocyclic pathway. We report here the full details of our results on the reactions of $N_3P_3Cl_6$ (**1**) and *gem*-$N_3P_3Cl_4Ph_2$ (**9**) with N-methyl 1,3-diaminopropane. The salient results of this investigation are (a) the reaction proceeds regioselectively by the spirocyclic pathway, (b) in addition to the monospiro derivative, it was possible to isolate the dispiro [with **1** and **9** and trispiro derivatives (with **1**)] also.

EXPERIMENTAL

$N_3P_3Cl_6$ (Aldrich) was recrystallized from light petroleum ether (60–80°C); N-methyl 1,3-diaminopropane (Aldrich) was used as received. $N_3P_3Cl_4Ph_2$ (**9**) and $N_3P_3Cl_2Ph_2[N(CH_3)CH_2CH_2CH_2NH]$ (**10**) were prepared according to literature procedures.[7,8] Anhydrous dimethyl amine was liberated from an aqueous solution (40% w/v) by treatment with KOH followed by allowing the liberated amine to dry further over KOH towers before being collected in a trap cooled at −78°C. Sodium hydride was obtained as a dispersion in mineral oil. The other solvents and reagents were purified by standard procedures.[9] Proton and phosphorus NMR spectra were recorded on a Bruker 400 MHz instrument. Some proton NMR spectra were also recorded at 60 or 80 MHz. The chemical shifts are reported in ppm relative to Me_4Si in $CDCl_3$ (proton) and 85% H_3PO_4 (ext) (phosphorus). Mass spectra were measured on a Kratos MS 80 RFA instrument (E.I./70 eV).

Preparation of $N_3P_3Cl_4[N(CH_3)CH_2CH_2CH_2NH]$ (**2**)

$N_3P_3Cl_6$ (**1**) (1.00 g, 2.9 mmol) was dissolved in dry tetrahydrofuran (50 cm^3). N-Methyl 1,3-diam-

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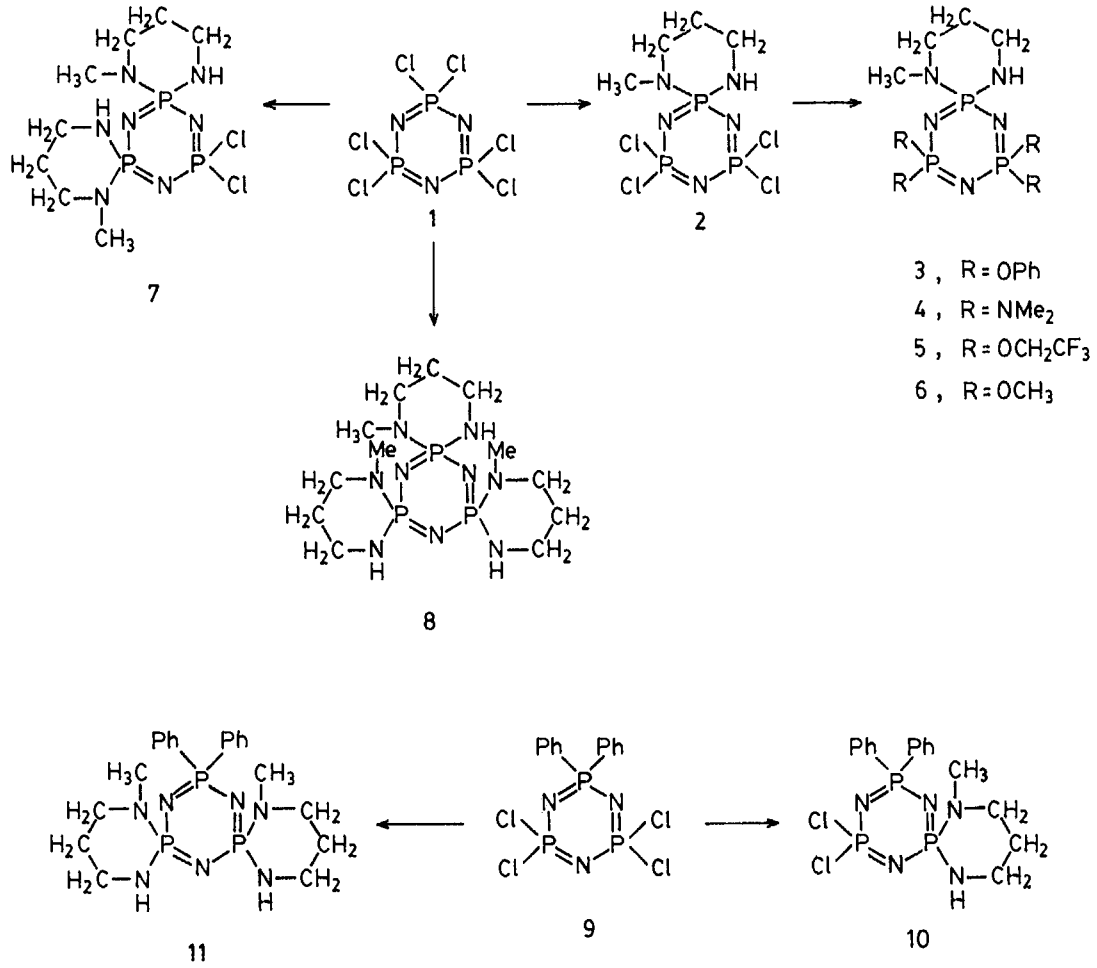

inopropane (0.51 g, 5.6 mmol) also dissolved in THF (20 cm^3) was added dropwise. A white precipitate of N-methyl 1,3-diaminopropane hydrochloride separated immediately. The reaction mixture was stirred for 1 h to ensure completion of reaction. The hydrochloride was filtered off and the solvent was removed from the filtrate *in vacuo* to afford a white solid. This was redissolved in benzene (100 cm^3), washed with water (2 × 25 cm^3), dried (Na_2SO_4), filtered, and the solvent removed from the filtrate to afford a solid which was recrystallized from a 1 : 1 mixture of benzene and petroleum ether to give **2**.

Yield: (0.81 g, 74.1%); m.p 153–54°C.

Mass: Found: 361. Calc. for $C_4H_{10}N_5{}^{35}Cl_4P_3$ (*m/z*): 361 (M^+).

Analysis: Found: C, 12.9; H, 2.9; N, 19.8. Calc. for $C_4H_{10}N_5Cl_4P_3$: C, 13.1; H, 2.8; N, 19.3%.

^{1}H NMR: 1.82 (m, 2H); 2.53 (d, 3H); 2.71 (s, 1H); 3.08 (m, 2H); 3.23 (m, 2H).

Reaction of **2** with an excess of sodium phenoxide (acetonitrile, reflux, 11 h), dimethylamine (chloroform, reflux, 4 h), sodium trifluoroethoxide (acetonitrile, reflux, 8 h), or sodium methoxide (acetonitrile, reflux, 24 h) afforded compounds $N_3P_3(OPh)_4[N(CH_3)CH_2CH_2CH_2NH]$ (**3**), $N_3P_3(NMe_2)_4[N(CH_3)CH_2CH_2CH_2NH]$ (**4**), $N_3P_3(OCH_2CF_3)_4[N(CH_3)CH_2CH_2CH_2NH]$ (**5**) and $N_3P_3(OMe)_4[N(CH_3)CH_2CH_2CH_2NH]$ (**6**), respectively. The data for these compounds is as follows:

(**3**) Oil, 25.2%.
Mass: Found: 593. Calc. for $C_{28}H_{30}N_5O_4P_3$: (*m/z*) 593 (M^+).
^{1}H NMR: 1.62 (m, 2H); 1.78 (d, 3H); 3.00 (m, 4H); 7.22 (m, 20H).

(**4**) M.p. 68°C; 87.6%.
Mass: Found: 397. Calc. for $C_{12}H_{34}N_9P_3$: (*m/z*) 397 (M^+).
^{1}H NMR: 2.00 (m, 2H); 2.60 (m, 2H); 3.00 (m, 4H).

(**5**) Oil, 78.9%.
Mass: Found: 617. Calc. for $C_{12}H_{18}N_5F_{12}O_4P_3$: (*m/z*) 617 ($M^+$).

^{1}H NMR: 1.78 (m, 2H); 2.50 (d, 3H); 3.20 (m, 4H); 4.47 (m, 8H).

(**6**) Oil, 71.0%.

Mass: Found: 345. Calc. for $C_8H_{22}N_5O_4P_3$: (m/z) 345 (M^+).

^{1}H NMR: 1.76 (m, 2H); 2.52 (d, 3H); 3.20 (m, 4H); 3.67 (m, 12H).

Preparation of $N_3P_3Cl_2[N(CH_3)CH_2CH_2CH_2NH]_2$ (**7**)

To a solution of $N_3P_3Cl_6$ (5.00 g, 14.4 mmol) in hexane/dichloromethane (v/v 7:3) (90 cm^3) was added the diamine (5.33 g, 60.4 mmol) dissolved in the same solvent mixture (60 cm^3) in a dropwise manner over a period of 20 min. The mixture was stirred at room temperature for 11 h. The course of the reaction was monitored by TLC (20% petroleum ether: 80% ethyl acetate/I_2 vapour). At the end of the reaction the amine hydrochloride was filtered and washed with the same solvent mixture (50 cm^3). The organic layer was washed with water (3×50 cm^3), dried (Na_2SO_4), filtered, and the solvent removed from the filtrate to afford a crude product. It was purified by chromatography (silica gel; eluant, 90% ethyl acetate: 10% hexane).

Yield: 2.98 g, 54.9%, m.p. 199–201°C.

Mass: Found: 377. Calc. for $C_8H_{20}N_7Cl_2P_3$: (m/z) 377 (M^+).

^{1}H NMR: 1.78 (m, 4H); 2.55 (d, 6H); 3.06 (m, 4H); 3.26 (m, 4H).

Analysis: Found: C, 25.8; H, 5.7; N, 25.3. Calc. for $C_8H_{20}N_7Cl_2P_3$: C, 25.4; H, 5.3; N, 25.9%.

Preparation of $N_3P_3[N(CH_3)CH_2CH_2CH_2NH]_3$ (**8**)

To $N_3P_3Cl_6$ (5.00 g, 14.4 mmol) dissolved in a 7:3 (v/v) mixture of n-hexane/dichloromethane (90 cm^3) was added the diamine dissolved in the same solvent mixture (60 cm^3) dropwise over a period of 20 min. The reaction mixture was stirred for 48 h. The course of the reaction was monitored by TLC (100% ethyl acetate/I_2 vapour). The reaction mixture was filtered, the filtrate washed with water (3×50 cm^3). dried (Na_2SO_4) and the solvent removed from the filtrate to afford a product (4.5 g) which was shown by TLC to contain small amounts of **7** also. It was purified by chromatography (silica gel; eluant, 95% ethyl acetate: 5% acetone mixture) to give **8**.

Yield: 3.96 g, 70%; m.p. 160–167°C.

Mass: Found: 393. Calc. for $C_{12}H_{30}N_9P_3$: (m/z) 393 (M^+).

^{1}H NMR: 1.77 (m, 6H); 2.45 (d, 3H); 2.52 (d, 6H), 2.7 (s,b, 3H); 3.03 (m, 6H); 3.20 (m, 6H).

Analysis: Found: C, 36.1; H, 7.8; N, 31.8. Calc. for $C_{12}H_{30}N_9P_3$: C, 36.7; H, 7.7; N, 32.1%.

Preparation of $N_3P_3Ph_2[N(CH_3)CH_2CH_2CH_2NH]_2$ (**11**)

To a stirred solution of N-methyl 1,3-diaminopropane (1.34 g, 15.3 mmol) and triethylamine (3.12 g, 30.6 mmol) in dry chloroform (35 cm^3) was added a solution of $N_3P_3Ph_2Cl_4$ (**9**) (3.00 g, 7.0 mmol) in chloroform (50 cm^3), in a dropwise manner at room temperature over a period of 20 min. Then the reaction mixture was heated under reflux for 86 h. After allowing the mixture to come to ambient temperature it was washed with water (3×30 cm^3) and dried (Na_2SO_4). Removal of solvent afforded the product which was shown to be a mixture of $N_3P_3Cl_2Ph_2[N(CH_3)CH_2CH_2CH_2NH]_2$ and **11**. Pure **11** was obtained by chromatography over silica gel using ethyl acetate and acetone as eluants. Product **10** eluted first 1.51 g, 48.5% yield. Product **11** was obtained next.

Yield: 0.56 g, 17.4%, m.p. $\geqslant$ 200° C.

Mass: Found: 461. Calc. for $C_{20}H_{30}N_7P_3$: (m/z) 461 (M^+).

^{1}H NMR: 1.90 (m, 4H); 2.6 (d, 6H); 3.2 (m, 4H), 3.8 (m, 4H); 7.4, 7.8, 7.9 (m, 12H).

Analysis: Found: C, 51.7; H, 6.3; N, 21.0. Calc. for $C_{20}H_{30}N_7P_3$: C, 52.1; H, 6.5; N, 21.2%.

RESULTS AND DISCUSSION

Synthetic aspects

Schemes 1 and 2 summarize the reactions of $N_3P_3Cl_6$ (**1**) and *gem*-$N_3P_3Cl_4Ph_2$ (**9**) with N-methyl 1,3-diaminopropane respectively. In general the reactions of **1** are much faster than that of **9**. The dispiro and trispiro derivatives with **1** are obtained in good yields using a mixture of dichloromethane and hexane as solvent. While the monospiro derivative with **9** is obtained in reasonable yield, the next stage of substitution is sluggish and only moderate yields of **11** could be isolated. To our knowledge this is the first example of a dispiro derivative of the six membered cyclophosphazene ring containing the geminally substituted phenyl groups.

Structures of the products by NMR

Product **10** has been reported earlier and has been shown to have a spirocyclic structure.[8] A spirocyclic structure for product **2** is easily assigned by a combination of phosphorus NMR and mass spectrometry. First, the mass spectrum rules out the

possibility of an open chain or an intermolecular bridged compound. The mass spectrum, besides showing the prominent parent ion peaks also is of the four chlorine isotope pattern for **2**. Second, since the difunctional reagent is unsymmetrical, spirocyclic and ansa structures are readily distinguished by phosphorus NMR.[4a,6,10] As can be easily visualized an ansa structure for **2** would mean that all the three phosphorus nuclei in the cyclotriphosphazene would be chemical shift non-equivalent and the phosphorus spectrum would have been of the three-spin type (ABC, ABX or AMX). An AB_2 type of spectrum as obtained in the present instance is consistent only with a spirocyclic structure. Since isochronous phosphorus chemical shifts are known in cyclophosphazene literature,[8,11] confirmation of the assignment of structure for **2** is obtained by preparing its derivatives **3**, **4**, **5** and **6**, all of which show an AB_2 type of phosphorus NMR spectrum. These data are presented in Table 1. Further in the proton NMR of the derivatives **4**, **5** and **6**, only one type of resonance is seen for $N(CH_3)_2$, OCH_2CF_3 or OCH_3. If the structure of **2** was *ansa*, clearly more signals would have been seen for **4**, **5** and **6**. Finally, the phosphorus chemical shift and the coupling constant values obtained for **2–6** are consistent with a number of spirocyclic structures known in the literature.[2a]

In dispiro compounds such as $N_3P_3Cl_2[HN(CH_2)_3NH]_2$[12] or $N_3P_3Cl_2[O(CH_2)_3O]_2$,[4a] only one isomer is possible. However, dispiro compounds derived from an unsymmetrical difunctional reagent, as in the present instance can be in *cis* and *trans* orientations.[12–14] Figure 1 shows the proton NMR spectrum of **7** and Fig. 2 shows the phosphorus NMR spectrum of **7**. As can be seen in the proton NMR only *one* N—CH_3, two N—CH_2 and one C—CH_2 environments are seen consistent with the presence of only *one* isomer in a major quantity.

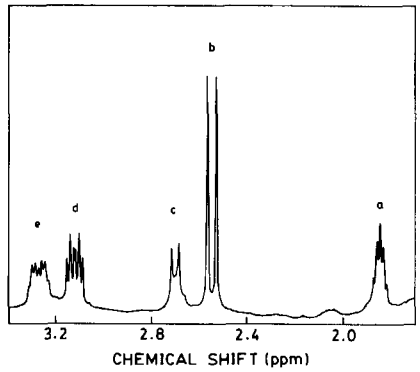

Fig. 1. Proton NMR spectrum (400.14 MHz) of $N_3P_3Cl_2[HN(CH_2)_3N(CH_3)]_2$ (**7**) showing N—CH_3 resonance (b). For other assignments see text.

Table 1. ^{31}P NMR data

Compound	Structure	δPCl_2 ppm	δP(spiro) ppm	δPR_2 ppm	J_{P-N-P} Hz	Reference
$N_3P_3Cl_4[HN(CH_2)_3N(CH_3)]$ (**2**)	Monospiro	20.3	9.8	—	39.1	This work
$N_3P_3(OC_6H_5)_4[HN(CH_2)_3N(CH_3)]$ (**3**)	Monospiro	—	19.3	8.6	58.5	This work
$N_3P_3(N(CH_3)_2)_4[HN(CH_2)_3N(CH_3)]$ (**4**)	Monospiro	—	19.3	25.0	37.2	This work
$N_3P_3(OCH_2CF_3)_4[HN(CH_2)_3N(CH_3)]$ (**5**)	Monospiro	—	19.9	16.3	59.3	This work
$N_3P_3(OCH_3)_4[HN(CH_2)_3N(CH_3)]$ (**6**)	Monospiro	—	19.8	18.8	51.0	This work
$N_3P_3Cl_2[HN(CH_2)_3N(CH_3)]_2$ (**7**)	Dispiro[a]	11.2	21.6	—	39.5	This work
$N_3P_3[HN(CH_2)_3N(CH_3)]_3$ (**8**)	Trispiro[b]	—	16.5(2)[c] 24.9(1)[c]	—	37.3	This work
$N_3P_3Cl_2(Ph)_2[HN(CH_2)_3N(CH_3)]$ (**10**)	Monospiro	20.7	15.0	20.2	17.2 20.1 19.5	This work and 8
$N_3P_3(Ph)_2[HN(CH_2)_3N(CH_3)]_2$ (**11**)	Dispiro	—	10.9	19.0	26.0	This work
$N_3P_3Cl_2[HN(CH_2)_3O]_2$	Dispiro	12.7	23.8	—	50.5	12
$N_3P_3[N(CH_3)CH_2CH_2O]_3$	Trispiro	—	33.6(1)[c] 25.4(2)[c]	—	58.6	14
$N_3P_3[O(CH_2)_3O]_3$	Trispiro	—	14.1	—	—	4a

[a] These values are for the major *cis* isomer (see text); other lines are seen in small intensities at ~9.0 and 22.1 ppm and are probably due to the *trans* isomer.

[b] These values are for the major *trans* isomer (see text); other lines in smaller intensities are seen at 16.9 and 23.4 ppm and are probably due to the *cis* isomer.

[c] The values in parentheses represent the intensities of the two multiplets.

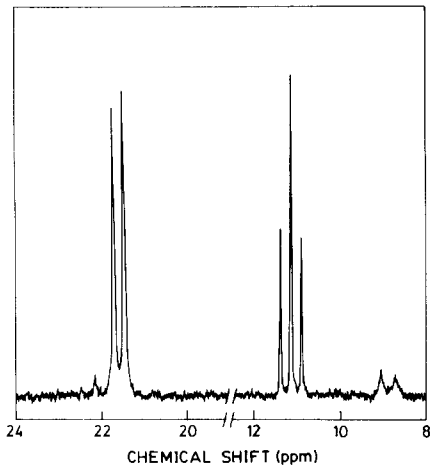

Fig. 2. Phosphorus NMR spectrum (161.78 MHz) of **7**.

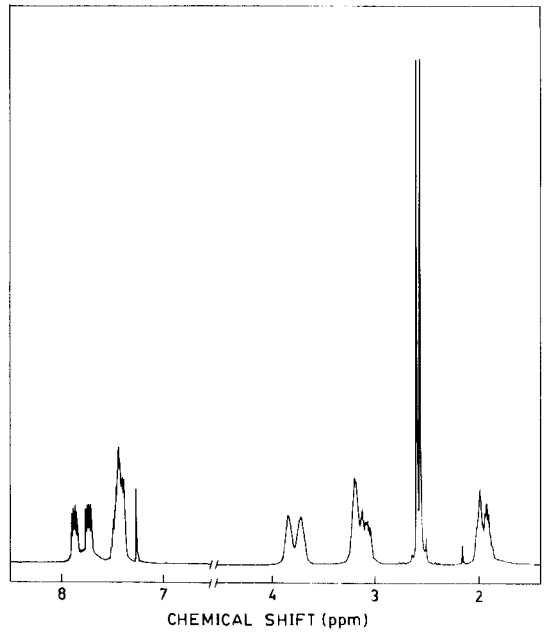

Fig. 3. Proton NMR spectrum (400.14 MHz) of **11**.

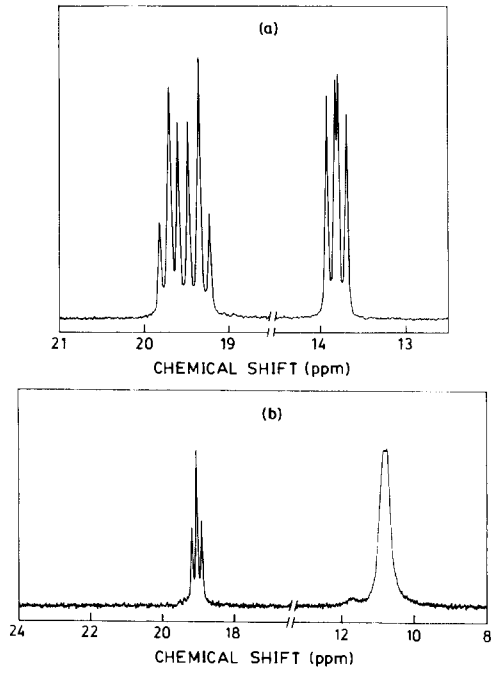

Fig. 4. Phosphorus NMR spectrum (161.98 MHz) of (a) compound **10** and (b) compound **11**.

This conclusion is corroborated by the phosphorus-31 NMR which shows a triplet and a doublet as expected for a two spin dispiro system. Small amounts of additional lines are seen which probably are due to impurities of the other dispiro isomer. Interestingly, the δPCl_2 is shifted upfield relative to δP spiro. This is unusual although previously such chemical shifts are reported for $N_3P_3Cl_2[HN(CH_2)_3O]_2$.[12] From phosphorus and proton NMR data alone it is difficult to assign the stereochemistry unambiguously for **7**. In the only similar case where a crystal structure is known for an analogous dispiro compound $N_3P_3Cl_2[N(CH_3)CH_2CH_2O]_2$, the major isomer at the dispiro stage turns out to be *cis*.[14] Based on this literature precedence we are tentatively assigning a *cis* structure for **7** although the final confirmation must await a crystal structure determination. Similarly the other dispiro derivative $N_3P_3Ph_2[N(CH_3)CH_2CH_2CH_2NH]_2$ also is present as a single stereoisomer as evident by its proton (Fig. 3) and phosphorus NMR (Fig. 4) data.

The trispiro product **8** is clearly a mixture of the two stereoisomers. Owing to their close R_f values it was not possible to effect a separation of these products. However, the reaction is stereoselective with the major product being of the *trans* geometry. The *trans* configuration would be expected to show two N—CH_3 doublets in the proton NMR whereas the *cis* product should show only one. The presence of two doublets with virtual coupling in the proton NMR (Fig. 5) for the N—CH_3 protons is a strong evidence in favour of a *trans* structure for the major stereoisomer. The phosphorus NMR of this product (Fig. 6) comprises a major triplet and doublet arising out of the AX_2 spin system of the *trans* compound. Although the *cis* product would have been expected to show a single phosphorus environment, small non-equivalences among the phosphorus nuclei are perhaps responsible for the additional minor peaks at 23.4 and 16.9 ppm. This type of behaviour is quite analogous to the only other such example known in literature, $N_3P_3[N(CH_3)CH_2CH_2O]_3$.[14] In conclusion, in this study, the reactions of $N_3P_3Cl_6$ and *gem*-$N_3P_3Cl_4Ph_2$

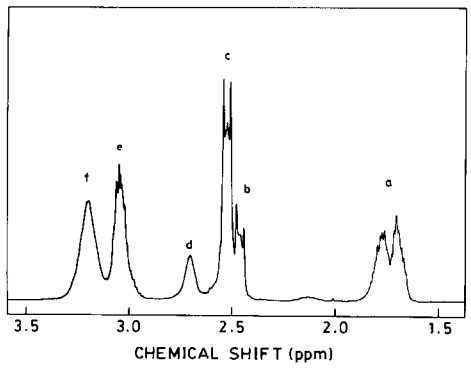

Fig. 5. Proton NMR spectrum (400.14 MHz) of trispiro compound **8** showing the N—CH_3 resonances in 1:2 intensity ratio (peaks b and c); for other assignments see text.

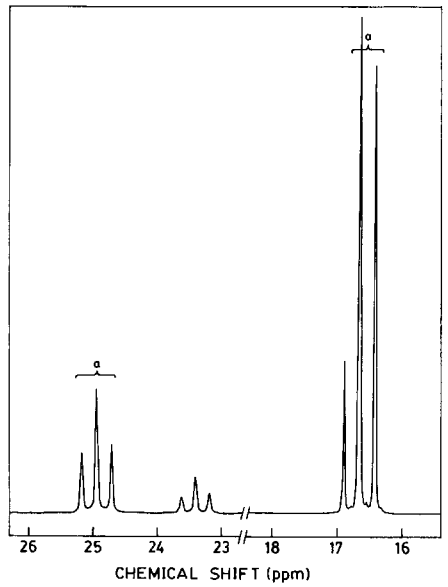

Fig. 6. Phosphorus NMR spectrum (161.98 MHz) of **8**. Peaks marked (a) are due to the major *trans* isomer. Other peaks are due to the minor *cis* isomer.

with N-methyl 1,3-diaminopropane proceed by the spirocyclic pathway affording monospiro, dispiro as well as trispiro derivatives. The reactions are clearly regio- and stereoselective, although the exact reasons for the stereoselectivity are not clearly understood at this time.

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