

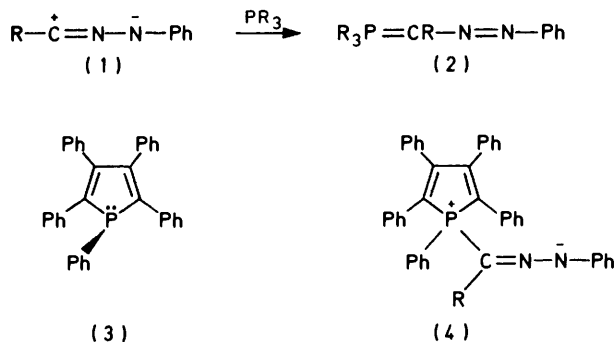
Reactions of Diphenylnitrilimine with Phosphites and Diazaphospholenes

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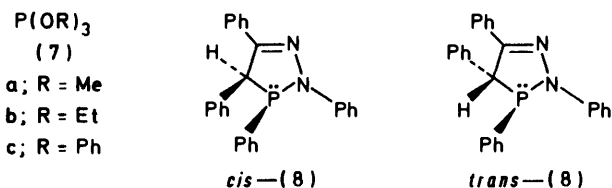
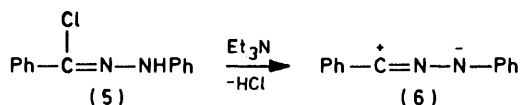
Reaction of diphenylnitrilimine (6) with phosphites (7) leads to the formation of α -phenylhydrazonophosphonates (9), whose configurational assignment about the C=N bond has been determined.

$\alpha\beta$ -Bis(phenylhydrazono)phosphine oxide (10I) [or (10II)] is obtained by the reaction of (6) with diazaphospholen *cis*-(8) [or *trans*-(8)], a mixture of (10I and III) [or (10II and IV)] being formed only after work-up. Configurational assignments about the two C=N bond have been determined and the relative configuration of the two chiral centres in (10I–IV) has been tentatively assigned. The stereospecificity of this reaction is explained in terms of spirocyclic pentaco-ordinate phosphorus intermediates whose formation may be favoured by ligand subset symmetry.

It has been found^{1,2} that addition of 1,3-dipolar nitrilimines (1) to phosphine leads to azophosphorus ylides (2). Formation of the betaine adduct (4) has been observed³ from reaction of pentaphenylphosphole (3) with nitrilimines (1); further cyclization of the azomethylene group with the ring phosphorus did not take place.



We now report that analogous reactions of diphenylnitrilimine (6) with the phosphites (7) and the diazaphospholens (8) give the corresponding α -phenylhydrazonophosphonates (9) and $\alpha\beta$ -bis(phenylhydrazono)phosphine oxides (10), respectively. Diphenylnitrilimine (6) was generated *in situ* by dehydrochlorination of the hydrazonyl halide (5) with triethylamine.



Thus, when equimolecular amounts of (7) and (5) were allowed to react in the presence of excess of triethylamine in dry benzene at room temperature for several hours, phosphonates (9) were isolated in 70% yield after work-up.

The two diastereoisomers (9) can be conveniently isolated in pure form by silica gel chromatography. The configurational assignment about the C=N bond has been determined essentially by ¹H n.m.r. (see Table I). The differences in the chemical shift of the NH

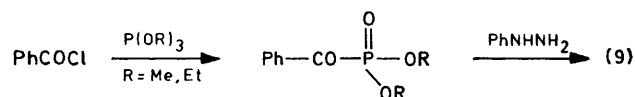
TABLE I

¹H N.m.r. spectral data (CDCl₃) for (9)
[PhNHN=CPhP(O)(OR)₂]

Compound	$\delta(\text{POR})$ (J_{POR}/Hz)	$\delta(\text{ArH})$	$\delta(\text{NH})$ (J_{PNH}/Hz)
(9Ia)	3.80 (d, 11)	6.80–8.00	12.25 (d, 3)
(9IIa)	3.82 (d, 11)	6.50–7.80	8.35 (s) ^a
(9Ib)	4.25 (m), 1.37 (m)	6.50–8.15	12.25 (d, 3)
(9IIb)	4.27 (m), 1.37 (m)	6.60–7.80	8.45 (s) ^a
(9Ic)		6.65–8.25	11.95 (d, 4)
(9IIc)		6.60–7.70	8.35 (s) ^a

^a Broad singlet which might be a doublet with a very small coupling constant.

proton resonance suggest that (9I) has the *Z*-configuration. The NH of (9I) is strongly intramolecularly bonded as indicated by its low resonance value (see Table I) and i.r. spectra (see Experimental section); this



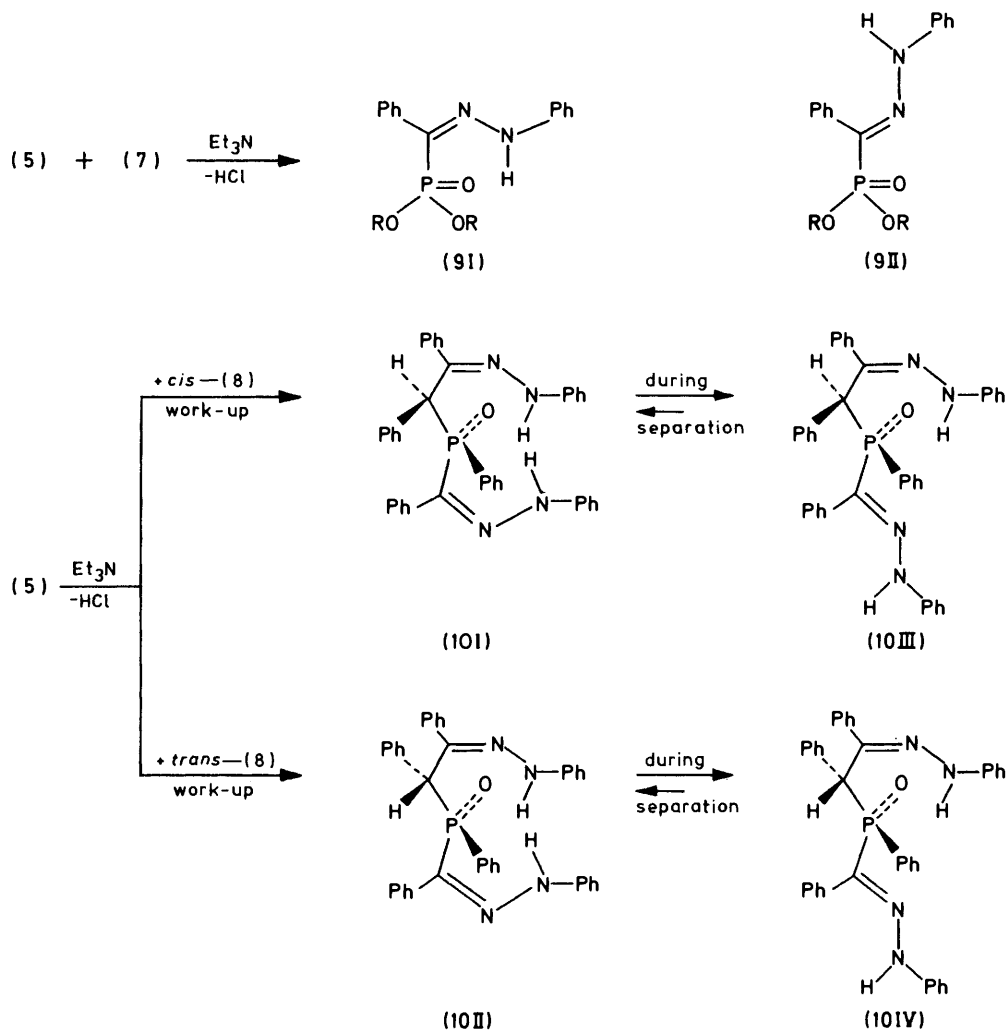
SCHEME 1

requires that it has the *Z*-configuration. The u.v. spectra show the maximum for (9Ia) (ϵ 21 850) displaced by +44 nm relative to isomer (9IIa) (ϵ 14 940); the isomer which absorbs with greater intensity at a longer wavelength has the *Z*-configuration.

It is noteworthy that isomers (9I and II) were found to be quite stable in neutral organic solutions (CHCl₃, CH₂Cl₂, C₆H₆) at room temperature for several hours, whereas slow interconversion was observed in acidic media.

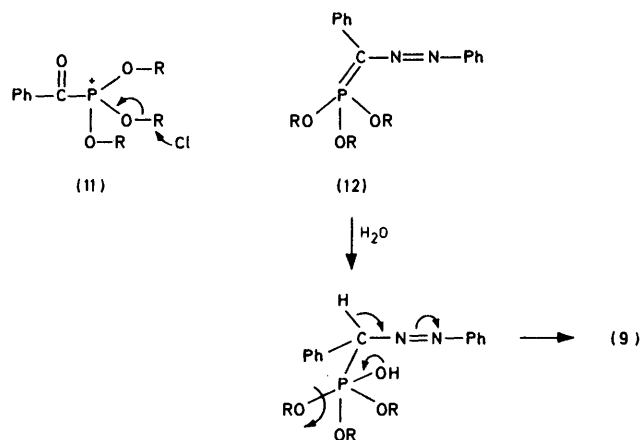
The phosphonates (9a and b) were also identified by comparison with authentic samples prepared independently by the route in Scheme 1, of which the first step is a Michaelis–Arbuzov reaction.⁴ Compound (9c) is not available by this procedure.

In the Michaelis–Arbuzov rearrangement⁴ the inter-



SCHEME 2

mediate is the phosphonium salt (11) which leads to the α -oxophosphonate after S_N2 displacement by chloride ion on the alkoxy-carbon atom. This is not possible for aromatic phosphites.⁵ A plausible mechanism for



the reaction involves formation of the unstable aza-ylide (12) from which (9) may be formed on addition of water

during work-up. For this reason in our reaction we can obtain compounds (9) even with aromatic phosphites.

When pure diazaphospholene *cis*-(8)⁶ was treated in benzene solution with an equimolar amount of (6) (generated *in situ*) a mixture of $\alpha\beta$ -bis(phenylhydrazono)phosphine oxides (10I and III) was obtained in 75% yield. T.l.c. showed the reaction to be complete within two days at room temperature; moreover t.l.c. analysis of the mixture showed only the presence of (10I). After work-up which consisted of filtration of triethylamine hydrochloride and evaporation of the solvent, a mixture of (10I and III) in the ratio of 80:20 (as determined by ¹H n.m.r. analysis) was obtained.

On the other hand, for the same reaction conditions *trans*-(8) gave only isomer (10II) (by t.l.c. analysis), and the reaction was noticeably slower (5 days). After work-up considerable formation of the other isomer (10IV) was observed, a mixture of (10II and IV) in the ratio *ca.* 65:35 being obtained. The formation of (10III) [or (10IV)] and their different ratios in the reaction mixtures can be explained by isomerization of (10I) [or (10II)] during work-up.

When pure (10I) was dissolved in benzene in the presence of triethylamine and water, isomerization to (10III) was observed. Under the same conditions, the interconversion of (10II and IV) was found to be more rapid. Further isomerization was also noted during the chromatographic separation.

Each of the four diastereoisomers (10) was isolated in pure form by silica gel chromatography and characterized essentially by ^1H n.m.r. (see Table 2).

TABLE 2

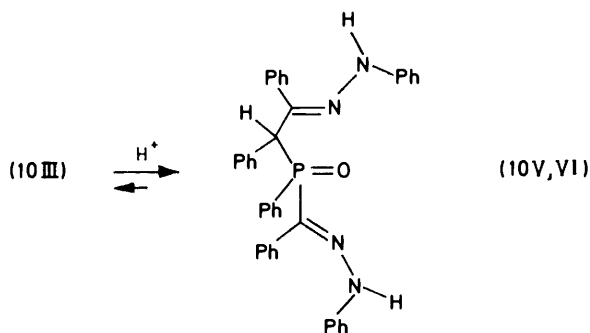
^1H N.m.r. spectral data (CD_2Cl_2)^a for (10)
 $[\text{PhNH}_\beta\text{N}=\text{CPhCHPhP}(\text{O})\text{PhCPh}=\text{NNH}_\alpha\text{Ph}]$

Compound	$\delta(\text{PCH})$ (J_{PCH}/Hz)	$\delta(\text{ArH})$	$\delta(\text{NH}_\beta)$	$\delta(\text{NH}_\alpha)$ (J_{PNH}/Hz)
(10I)	5.30 (d, 15)	6.70—8.00	10.85 (s)	11.85 (d, 3)
(10II)	5.22 (d, 11)	6.75—8.05	10.90 (s)	12.10 (d, 3)
(10III)	6.15 (d, 17)	6.90—7.80	10.90 (s)	8.50 ^c
(10IV)	5.75 (d, 16)	6.60—8.15	11.90 (s)	8.30 ^c
(10V)	4.97 (12)	6.65—7.55	<i>b</i>	8.27 ^c
(10VI)	5.11 (14)	6.60—7.65	<i>b</i>	8.02 ^c

^a Concentrations of 3—5 mol % phenylhydrazone were used. Chemical shifts are from Me_4Si . ^b Masked by aromatic protons. ^c Broad.

From the data reported in Tables 1 and 2 it can be noted that the NH protons of the α -hydrazone-groups of (9) and (10) have identical behaviour, thus suggesting that the α -hydrazone-groups in (10I and II) have the *Z*-configuration while in (10III and IV) they have the *E*-configuration. The configurational assignments of the β -hydrazone-groups of (10) are analogous.

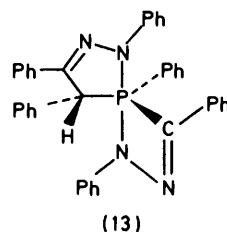
In all four isomers (10I—IV) the β -hydrazone-groups have the *Z*-configuration. Isomerization of (10III) [or (10IV)] under acidic conditions gave the new isomers (10V and VI) which show the new methine and β -NH proton resonances reported in Table 2. These values suggest an *E*-configuration for the β -hydrazone group in isomers (10V and VI).



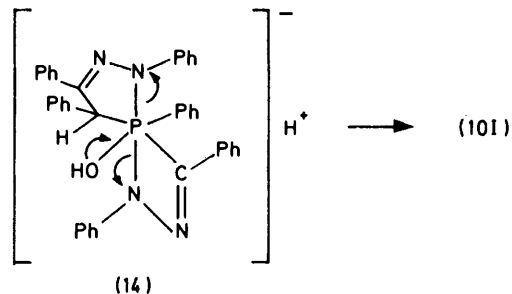
Analogous assignments have been reported⁷ in previous work on β -phenylhydrazonomethylphosphinates. In conclusion, the products (10I and II) have the *ZZ*-configuration (about the two $\text{C}=\text{N}$ bonds), (10III) and (10IV) have the *ZE*-configuration as depicted in Scheme 2, and (10V and VI) have the *EE*-configuration. The relative configuration of the two chiral centres is tentatively assumed (see Scheme 2) on the basis of the mechanism.

From the above results it is clear that there is inter-

vention by water at some stage of the reaction. In fact, when the reaction was carried out in C_6D_6 solution and monitored by ^1H n.m.r., the gradual disappearance of the methine proton of *cis*-(8) was observed and replaced by a broad doublet at δ 5.20 (d, J 14 Hz) which did not overlap with those from pure samples of (10I and III). No absorption of the NH protons was observed. This new product might be intermediate (13) (Scheme 3). Repeated attempts to isolate this intermediate were unsuccessful.



(13)



(14)

SCHEME 3

After two days, when traces of water were deliberately added to the reaction solution, the characteristic methine proton signal of (10I) was observed and after 1 h traces of (10III) also appeared. For this reason we suggest that the stereospecificity of this reaction might be due to formation of a spirocyclic phosphorane such as (13) from which (10I) is formed by reaction with water. The formation of (13) may be favoured by its stabilization due to ligand subset symmetry,⁸ *i.e.* two identical ligands in the apical subset, and three identical ligands in the equatorial subset.

Furthermore, it is reasonable to assume that the nucleophilic attack of water on (13) generates the hexacoordinate transition state or intermediate (14) which then collapses to (10I). This hexacoordinate structure should be important in nucleophilic reaction of the spirocyclic intermediate (13), since the presence of the two diaza-groups, which have considerable π -acceptor character, should confer considerable Lewis-acid behaviour on the phosphorus atom and make it the preferred site of nucleophilic attack. This behaviour has been found in several oxyphosphorane systems.⁹ Moreover, hexacoordinate phosphorus can be stable when incorporated into one (or preferably more) heterocyclic rings, thus reducing crowding.¹⁰ The proposed spirocyclic

intermediate such as (13) is consistent with the exclusive formation of isomer (10I) with the *ZZ*-configuration about the two C=N bonds. The other isomer (10III) is produced only after work-up and chromatographic separation.*

EXPERIMENTAL

I.r. spectra were recorded on a Perkin-Elmer model 257 spectrometer, u.v. spectra on a Perkin-Elmer model 402, and ^1H n.m.r. spectra on a JEOL C-60 HL spectrometer operating at 60 MHz (Me_4Si as internal standard). Microanalyses were performed on mixtures of isomers as well as on pure isomers. The results obtained were practically identical. M.p.s were determined on a Kofler hot-stage and are uncorrected. Phosphites were all redistilled in dry apparatus and stored under nitrogen. Hydrazoneyl halide (5) and diazaphospholens (8) were prepared as described in the literature.^{6,11}

Reaction of (5) with Phosphites (7).—An excess of Et_3N (1 ml) was added to a stirred solution of (5) (1.4 g, 6×10^{-3} mol) and trimethyl phosphite (7a) (0.74 g, 6×10^{-3} mol) in dry benzene (100 ml) and the mixture was set aside at room temperature for 24 h. Triethylamine hydrochloride was then filtered off and the filtrate evaporated under reduced pressure. The ^1H n.m.r. spectrum of the reaction product mixture showed the characteristic absorptions of (9Ia and IIa) in the ratio of *ca.* 2 : 3. The separation of the two isomers was carried out by chromatography on a silica gel column [cyclohexane-ether-ethyl acetate (4 : 3 : 3) as eluant]: (9Ia and IIa) were isolated in 70% yield. The isomer (9Ia) (R_F 0.56) had m.p. 96–97 °C, λ_{max} (benzene) 360 nm (ϵ 21 800); ν_{max} (CHCl_3) 3 160 (NH), 1 260 (P=O), and 1 015 (POC) cm^{-1} . The isomer (9IIa) (R_F 0.15) had m.p. 103–105 °C, λ_{max} (benzene) 316 nm (ϵ 15 000); ν_{max} (CHCl_3) 3 260 (NH), 1 240 (P=O), and 1 040 (POC) cm^{-1} . The ^1H n.m.r. data are reported in Table 1 (Found: C, 59.3; H, 5.5; N, 9.1. $\text{C}_{15}\text{H}_{17}\text{N}_2\text{O}_3\text{P}$ requires C, 59.2; H, 5.6; N, 9.2%). In a similar way were obtained (9Ib) (R_F 0.65), an oil, ν_{max} (CHCl_3) 3 200 (NH), 1 260 (P=O), and 1 010 (POC) cm^{-1} ; (9IIb) (R_F 0.20), an oil, ν_{max} (CHCl_3) 3 320 (NH), 1 240 (P=O), and 1 030 (POC) cm^{-1} (Found: C, 61.5; H, 6.2; N, 8.3. $\text{C}_{17}\text{H}_{21}\text{N}_2\text{O}_3\text{P}$ requires C, 61.4; H, 6.3; N, 8.4%); (9Ic) (R_F 0.75), an oil, ν_{max} (CHCl_3) 3 220 (NH), 1 270 (P=O), and 1 000 (POC) cm^{-1} ; (9Ic) (R_F 0.57), an oil, ν_{max} (CHCl_3) 3 315 (NH), 1 260 (P=O), and 1 000 (POC) cm^{-1} (Found: C, 70.2; H, 4.8; N, 6.3. $\text{C}_{25}\text{H}_{21}\text{N}_2\text{O}_3\text{P}$ requires C, 70.0; H, 4.9; N, 6.5%).

Reaction times for the formation of (9b and c) (70%) were 2 and 5 days, respectively. Attempts to isolate the intermediate (12) were not successful. No formation of (9) was observed in the absence of triethylamine. The ^1H n.m.r. data of (9b and c) are collected in Table 1. Products (9a and b) were also identified by comparison of their spectral data with those of an authentic sample prepared by reaction of phenylhydrazine with dimethyl benzoylphosphonate obtained by a Michaelis-Arbuzov reaction.⁴

Reaction of (5) with *cis*-(8).—To a solution of the diazaphospholen *cis*-(8) (0.784 g, 2×10^{-3} mol) in dry benzene (50 ml) was added the hydrazoneyl halide (5) (0.461 g, 2×10^{-3} mol) and an excess of triethylamine; the mixture was stirred under nitrogen at room temperature and the course of the reaction was followed by t.l.c.. Only form-

ation of the (1,2-diphenyl-2-phenylhydrazoneethyl)-(phenyl)(phenylhydrazonebenzyl)phosphine oxide isomer (10I) was observed.

After 48 h, work-up, which consisted of filtration of the hydrochloride and evaporation of the solvent, gave a (10I–III) mixture in the ratio *ca.* 80 : 20. This mixture was chromatographed on a silica gel column. Elution with 2 : 1 hexane-ether gave products (10I) in 45% and (10III) in 25% yield. Pure (10I), R_F 0.70, was crystallized from n-hexane and had m.p. 65–67 °C; ν_{max} (CHCl_3) 3 220 (NH) and 3 180 (NH) cm^{-1} . Pure (10III), R_F 0.14, was crystallized from n-hexane and had m.p. 207–209 °C; ν_{max} (CHCl_3) 3 320 (NH) and 3 210 (NH) cm^{-1} . ^1H N.m.r. data of (10I and III) are reported in Table 2.

When this reaction was repeated in C_6D_6 it was examined periodically by ^1H n.m.r. spectroscopy. The doublet due to the starting phosphine *cis*-(8), δ 4.82 (J 21 Hz), was slowly replaced by a new broad doublet at δ 5.20 (J 14 Hz) which did not overlap with those from pure samples of (10I and III). No absorption due to NH was observed. When traces of water was deliberately added to the solution the doublet and the signal for the corresponding NH protons of (10I) immediately appeared.

After 30 min the absorptions for (10I) gradually decreased and new absorptions due to the isomer (10III) appeared, the ratio between (10I and III) being *ca.* 80 : 20. After 4 h the ratio became 60 : 40. A further decrease in (10I) and increase in (10III) was observed after several hours. Finally a 20 : 80 ratio of (10I and III) resulted after 70 h.

Reaction of (5) with *trans*-(8).—Compound (5) (0.461 g, 2×10^{-3} mol) and triethylamine in excess were added to a solution of *trans*-(8) (0.784 g, 2×10^{-3} mol) in dry benzene (50 ml) under nitrogen and the resulting mixture was left at room temperature. The reaction appeared to be noticeably slower (60 h) than that above, only one of the possible isomers (10II) being noted by t.l.c. Work-up as above yielded a mixture of (10II and IV) in the ratio 65 : 35 (by ^1H n.m.r. analysis). Chromatography on a silica gel column (2 : 1 hexane-ether as eluant) afforded (10II) in 35% and (10IV) in 40% yield, thus indicating that further isomerization of (10II) to (10IV) had occurred during chromatography. Isomer (10II), R_F 0.50, was recrystallized from n-hexane and had m.p. 225–228 °C; ν_{max} (CHCl_3) 3 230 (NH) and 3 190 (NH) cm^{-1} . Isomer (10IV), R_F 0.25, had m.p. 225–228 °C (from n-hexane); ν_{max} (CHCl_3) 3 320 (NH) and 3 210 (NH) cm^{-1} . ^1H N.m.r. data of (10II and IV) are reported in Table 2.

From control experiments it was observed that isomer ratios were dependent on the time used in work-up. Longer work-up times gave predominant formation of (10III) from *cis*-(8) or (10IV) from *trans*-(8).

When isomers (10I and II) were kept at room temperature in benzene to which traces of water and triethylamine were added, some isomerization into (10III and IV), respectively, was observed. Starting from (10I) a 40 : 60 ratio of (10I and III) was obtained after 50 h, while starting from (10II) a (10II : IV) ratio of *ca.* 20 : 80 was observed after 50 h. Slower isomerization of (10I) [or (10II)] into (10II) [or (10I)] was also detected.

Isomerization of (10III) under Acidic Conditions.—A benzene solution of isomer (10III) (0.5 g) was saturated with hydrogen chloride and left at room temperature for 24 h, after which time a *ca.* 1 : 1 mixture of isomers (10V and VI) was obtained in 60% yield. A similar result was obtained

* Although *cis*-(8) is used here as an illustration for the proposed mechanism, *trans*-(8) would lead to an analogous conclusion.

with isomer (10IV). Separation of the isomers was accomplished by chromatography on a silica gel column (elution with 1:1:1 cyclohexane-ethyl acetate-ether). Isomer (10V), R_F 0.45, had m.p. 187—189 °C; ν_{\max} (CHCl₃) 3 320 (NH) cm⁻¹. Isomer (10VI), R_F 0.25, had m.p. 190—192 °C; ν_{\max} (CHCl₃) 3 320 (NH) cm⁻¹. ¹H N.m.r. data are reported in Table 2.

In all the isomers of (10), strong bands in the i.r. region (KBr) were caused by the P=O stretching vibrations (1 220—1 280 cm⁻¹) and by PPh stretching (1 440 cm⁻¹). Strong bands were also found at 1 600 and 1 500 cm⁻¹.

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