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C-Phosphorylation of N-Methylpyrrole

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ABSTRACT: *The phosphorylation of N-methylpyrrole with phosphorus (III) halides has been studied. Migration of the dibromophosphino group from the second to the third position of N-methylpyrrole, leading to the 3-dibromophosphine, has been found. Methods for the synthesis of 2,4-bisphosphorylated pyrroles have been developed.* © 1999 John Wiley & Sons, Inc. Heteroatom Chem 10:213–221, 1999

INTRODUCTION

As we reported previously, halides of trivalent phosphorus in the presence of a base can be applied as efficient reagents to phosphorylate a variety of electron-rich compounds derived from pyrrole [1], indole [2], furan [3], thiophene [4], and indolizine [5]. Among these heteroaromatics, pyrrole and indolizine are most reactive with respect to electrophiles and to phosphorus (III) halides in particular. For indolizines, this high reactivity permitted us to obtain 1,3-diphosphorylated derivatives both of symmetric and unsymmetric structure and, more interestingly, to discover an isomerization of 1-phosphorylated to 3-phosphorylated indolizines occurring surprisingly readily.

Here, it is our intention to study the possibility for such migrations to occur in 1-methylpyrrole derivatives and also to synthesize 2,4-diphosphorylated pyrrole derivatives. It should be noted that 2 → 3 migrations of acyl and sulfinyl groups occurring in acid media are currently known for pyrrole derivatives [6–10], and, with regard to phosphorus-containing groups, 1 → 2 migration of the tetrafluorophosphorane group has been reported [11].

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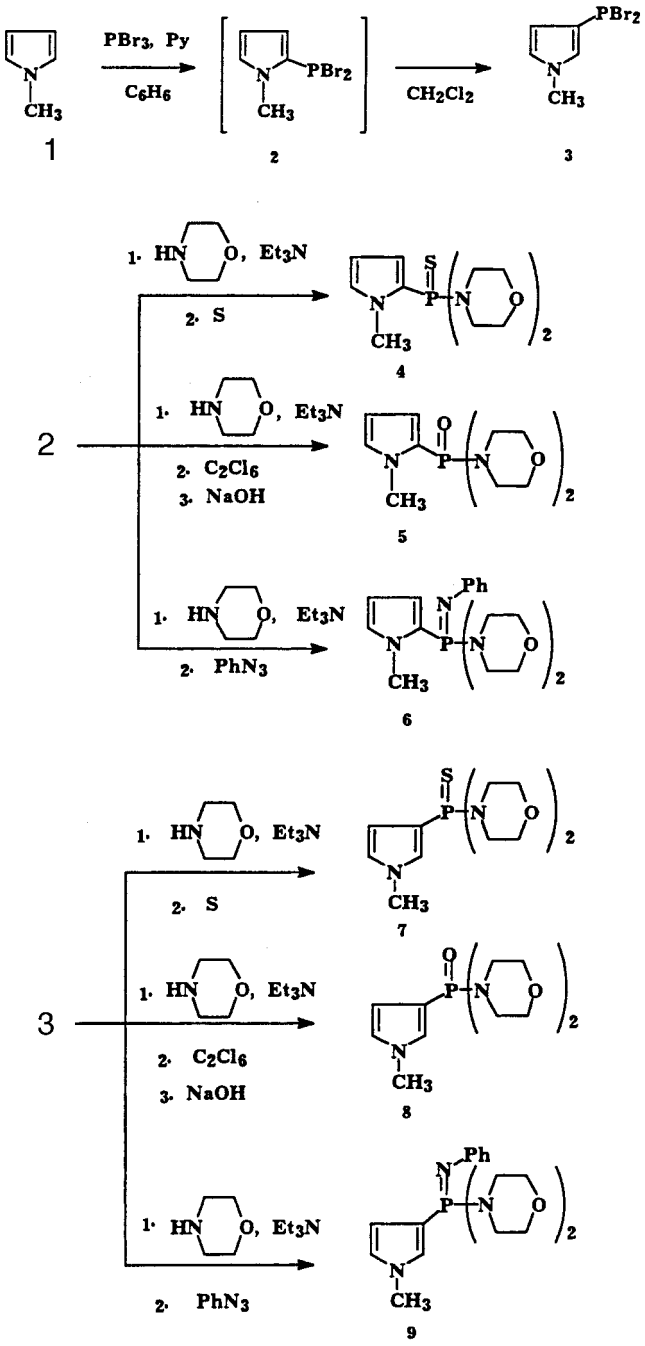
RESULTS AND DISCUSSION

We have found that the 2-dibromophosphino derivative **2** [12], initially formed in the phosphorylation of N-methylpyrrole **1** with phosphorus tribromide, completely isomerizes into the 3-dibromophosphino derivative **3** at room temperature. The rate of this process is markedly affected by the nature of the solvent. If dissolved in methylene chloride (5 mL), dibromophosphino derivative **2** (0.01 mol) isomerizes to compound **3** in 2 hours. In benzene solution, 1 month is needed for the reaction to be complete. The isomerization proceeds, even in hexane solution; however, it is still slower. Evidently, the greater reaction rate in methylene chloride is attributable to the fact that this solvent better dissolves hydrochlorides of organic bases that catalyze the conversion concerned [13]. The nature of the isomerization will be treated in more detail in the next article.

As distinct from the 2-dibromophosphino derivative **2,** the 3-dibromophosphino compound **3** is a crystalline solid reasonably stable in the absence of atmospheric moisture. Its structure has been corroborated by ^{31}P, ^{1}H, and ^{13}C NMR spectra, the most illustrative ^{13}C signal (a doublet at δ 120.86, $J(CP)$ = 116.2 Hz) arising from the third carbon atom.

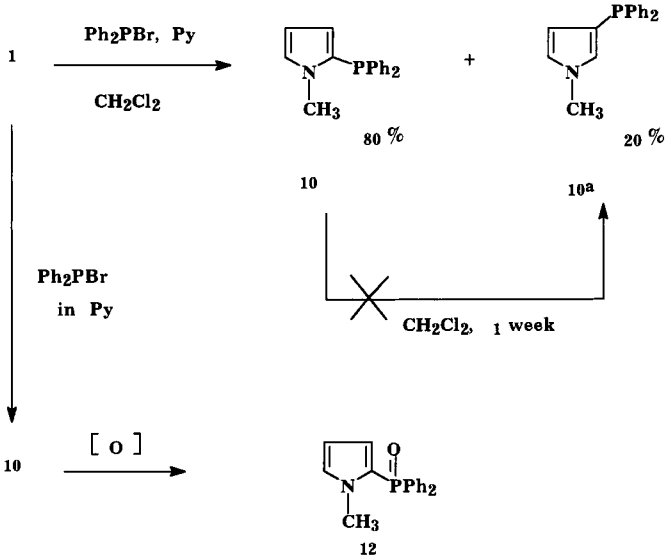
The dibromophosphines **2** and **3** gave rise to a variety of phosphorylated pyrroles, including thio-

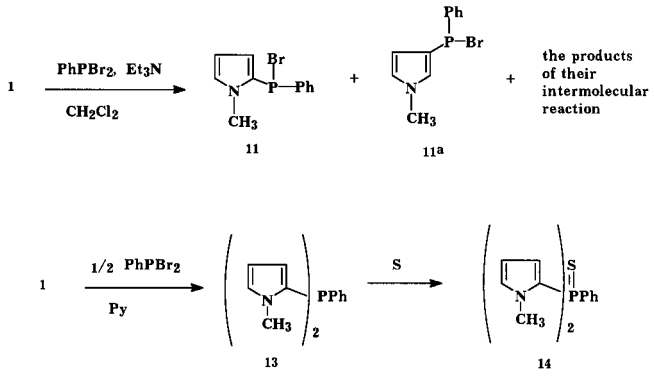
phosphonates (**4**, **7**), phosphonates (**5**, **8**), and iminophosphonates (**6**, **9**). The structures of the compounds obtained were proved by ^{31}P and ^{1}H NMR spectroscopy (Tables 1–3).



As regards isomerizations in indolizine molecules, dichlorophosphino, dibromophosphino, and diphenylphosphino groups have been shown to migrate [5]. In the case of N-methylpyrrole, we failed to extend the 2 → 3 isomerization found to other phosphorus-containing groups. Phosphine **10** does not isomerize to **10a** on standing in methylene chloride for a week. The reaction of N-methylpyrrole with dibromophenylphosphine in methylene chloride furnishes a mixture of the 2- and 3-bromophosphino derivatives **11** and **11a**, as well as the products of an intermolecular reaction. The isomerization with phosphorus trichloride could not be studied, as N-methylpyrrole was not sufficiently active to be phosphorylated with this reagent.

Previously, we reported [1] that the phosphorylation of N-methylpyrrole with diphenylbromophosphine in a 1:2 molar ratio takes place regioselectively to give 2,5-(1-methylpyrrolyl)bis(diphenyl)phosphine. Performed in pyridine, this reaction is likewise regioselective, and yields 2-(1-methylpyrrolyl)diphenylphosphine **10**, the β-isomer being absent. Phosphine **10** was identified by ^{31}P NMR spectra [δ (^{31}P) −29.49] and characterized after conversion into the oxide **12**, whose structure was also proved spectroscopically, from ^{31}P and ^{1}H NMR data (Tables 1 and 2). The regioselectivity is retained in the reaction of N-methylpyrrole with diphenylbromophosphine in pyridine (2:1 molar ratio). The product, di(1-methylpyrrolyl-2)phenylphosphine **13**, was identified by ^{31}P NMR spectra [δ (^{31}P) −52.61] and characterized after conversion of it into sulfide **14**. The latter compound was identified by ^{31}P and ^{1}H NMR spectroscopy (Tables 1 and 2).

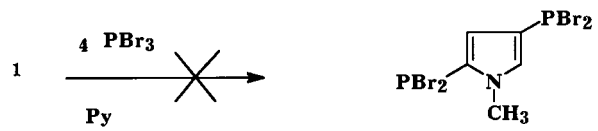




Contrary to the evidence reported in our preliminary communication [1], the reaction of phosphorus tribromide with N-methylpyrrole taken in a 1:3 ratio cannot be carried out regioselectively and leads to a mixture of trispyrrolylphosphines, none of which could be isolated as an individual compound. In these molecules, the phosphorus atom is bonded to the pyrrolyl ring in positions 1 and 2.

The regioselectivity is also lost if the phosphorylation with diphenylbromophosphine is conducted in methylene chloride rather than in pyridine.

Unlike the indolizines [5], N-methylpyrrole, when treated with excess phosphorus tribromide in pyridine, does not yield the bis(dibromophosphino) derivative **15.**



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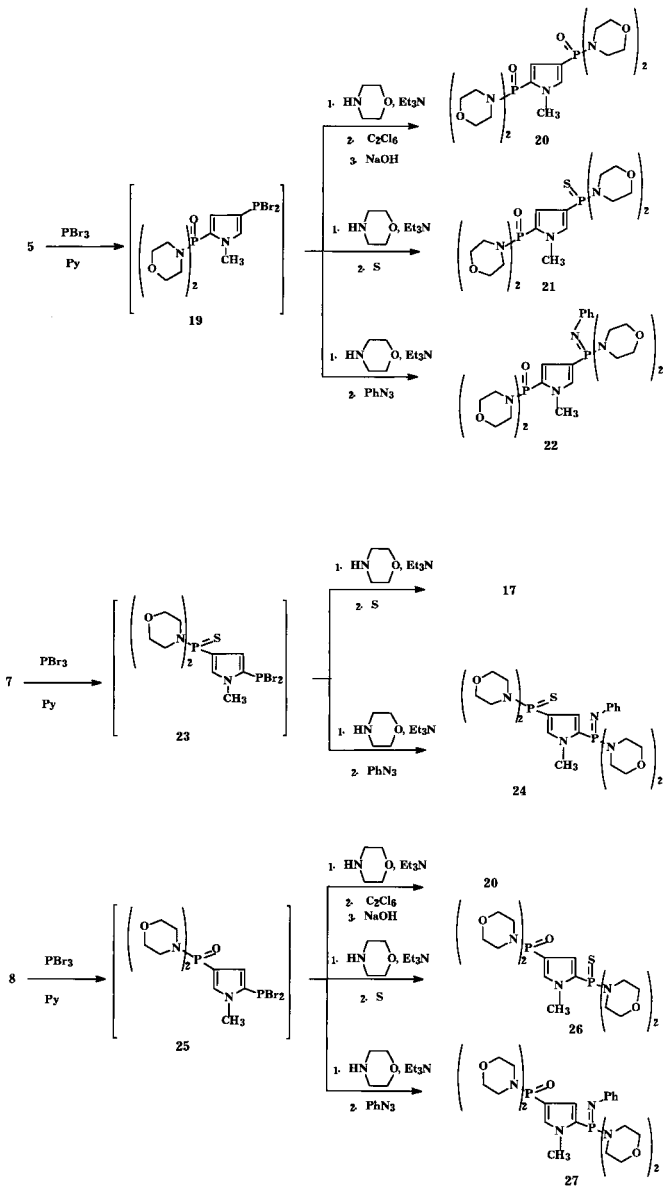
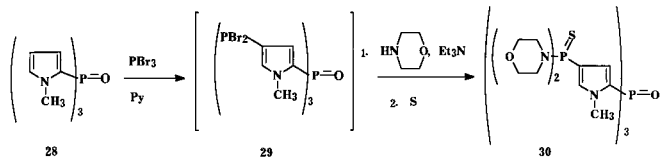
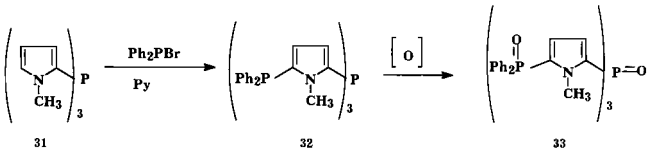
In 2- and 3-phosphorylated pyrroles containing a pentavalent phosphorus atom, for example, in compounds **4, 5, 7,** and **8,** a second phosphorylation occurs regioselectively at position 4 for 2-phosphorylated and at position 5 for 3-phosphorylated pyrrole derivatives. Such an orientation of electrophilic attack is typical of N-alkylpyrroles containing electron-acceptor substituents of medium strength [13]. By reaction of the 2- and 3-phosphorylated pyrroles **4, 5, 7,** and **8** with phosphorus tribromide in pyridine, compounds **17, 18, 20, 21, 22, 24, 26,** and **27** were synthesized, and their structures were corroborated by ^{31}P and ^{1}H NMR spectra (Tables 1 and 2).



The above-mentioned regioselectivity is retained in passing to systems of more complex structure. The phosphorylation of tris(1-methylpyrrolyl-2)phosphine oxide **28** with phosphorus tribromide in pyridine involved the position 4 of the pyrrole ring, to provide the dibromophosphino derivative **29** that was identified by ^{31}P NMR spectroscopy [δ (^{31}P) -2.39 and $+132.79$] and characterized after conversion into the thiophosphonate **30.** The identity of compound **30** was confirmed by ^{31}P and ^{1}H NMR spectral evidence (Tables 1 and 2).



We were unable to phosphorylate tris(1-methylpyrrolyl-2)phosphine oxide **28** with diphenylbromophosphine, which proved to be too weak a phosphorylating agent in this case. However, diphenylbromophosphine in pyridine was found to phosphorylate tris(1-methylpyrrolyl-2)phosphine **31** at position 5. The reaction resulted in phosphine **32** being isolated as the only product. By treatment with hydrogen peroxide, tris(5-diphenylphosphino-1-methylpyrrolyl-2)phosphine **32** was oxidized to the phosphine oxide **33.** The structures of products **32** and **33** were supported by ^{31}P and ^{1}H NMR spectral data (Tables 1 and 2).



EXPERIMENTAL

A Varian Gemini-200 instrument was used to record the ^{31}P and ^{13}C NMR spectra. The ^{13}C signals were registered with respect to tetramethylsilane as an internal standard, and the ^{31}P signals, to the external standard, 85% H_3PO_4.

Isomerization of 2-Dibromophosphino-1-methylpyrrole **(2)** *into 3-Dibromophosphino-1-methylpyrrole* **(3).** To a solution of phosphorus tribromide (2.71 g, 0.01 mole) in methylene chloride (3 mL), a solution of N-methylpyrrole (0.81 g, 0.01 mole) and pyridine (0.79 g, 0.01 mole) in methylene chloride (2 mL) was added. The reaction mixture was maintained at room temperature for 1 hour. The signals at δ 145.70 for 3 and δ 109.74 for 2 were observed in a 1:2 ratio in a ^{31}P NMR spectrum. After 1 hour, the extent of the isomerization was 95.5%.

3-Dibromophosphino-1-methylpyrrole **(3).** To a stirred solution of N-methylpyrrole 1.78 g (0.022 mole) and pyridine 1.74 g (0.022 mole) in methylene chloride (5 mL), a solution of phosphorus tribromide 5.96 g (0.022 mole) in methylene chloride (5 mL) was added at 5°C over 10 minutes. The reaction mixture was allowed to stand at room temperature for 5 hours. (Resonance at δ 146.60 was detected in the ^{31}P NMR spectrum.) After addition of benzene (70 mL), the mixture was filtered and the filtrate evaporated to 2/3 of its initial volume. The product was precipitated with hexane.

2-Dimorpholinothiophosphonato-1-methylpyrrole **(4).** To a stirred solution of N-methylpyrrole 1.62 g (0.020 mole) and pyridine 1.58 g (0.020 mole) in benzene (10 mL), a solution of phosphorus tribromide 5.42 g (0.020 mole) in benzene (10 mL) was added at 10°C [δ (^{31}P) 109.36]. The reaction mixture was left to stand at this temperature for 30 minutes, and then a solution of morpholine 3.48 g (0.040 mol) and triethylamine 6.06 g (0.060 mol) in benzene (60 mL) was added. One hour later the mixture was filtered. After addition of sulfur 0.64 g (0.020 mole) to the filtrate, the mixture was refluxed for 1 hour. After evaporation of it to dryness, the resulting oil was treated with ethanol. The product was crystallized from octane.

2-Dimorpholinophosphonato-1-methylpyrrole **(5).** To a stirred solution of phosphorus tribromide 5.42 g (0.020 mole) in benzene (10 mL), a solution of N-methylpyrrole 1.62 g (0.020 mole) and pyridine 1.58 g (0.020 mole) in benzene (10 mL), was added at 10°C [δ (^{31}P) 109.34]. The reaction mixture was left to stand at this temperature for 30 minutes, and then a solution of morpholine 3.48 g (0.040 mole) and triethylamine 6.06 g (0.060 mole) in benzene (80 mL) was added. One hour later the mixture was filtered, and a solution of hexachloroethane 4.74 g (0.020 mole) in benzene (20 mL) was added to the filtrate. This was refluxed for 1 hour. The phosphonic salt was dissolved in methylene chloride (80 mL) and treated with 5% aqueous sodium hydroxide (20 mL). The organic layer was separated, dried over anhydrous sodium sulfate, and evaporated to dryness. The product was crystallized from octane.

2-Dimorpholinophenyliminophosphonato-1-methylpyrrole **(6).** To a stirred solution of phosphorus tribromide 5.42 g (0.020 mole) in benzene (10 mL), a solution of N-methylpyrrole 1.62 g (0.020 mole) and pyridine 1.58 g (0.020 mole) in benzene (10 mL), was added at 10°C [δ (^{31}P) 109.34]. The reaction mixture was left to stand at this temperature for 30 minutes, and then a solution of morpholine 3.48 g (0.040 mole) and triethylamine 6.06 g (0.060 mole) in benzene (80 mL) was added. One hour later the mixture was filtered. After addition of phenyl azide 2.38 g (0.020 mole) to the filtrate, it was refluxed for 5 hours. Then the mixture was evaporated to dryness, and the resulting oil was treated with hexane. The product was crystallized from a 1:1 mixture of CH_3OH and H_2O.

3-Dimorpholinothiophosphonato-1-methylpyrrole **(7).** To 1-methylpyrrolyl-3-dibromophosphine **(3)** 5.96 g (0.022 mole) [δ (^{31}P) 146.60], a solution of morpholine 3.83 g (0.044 mole) and triethylamine

TABLE 1 Yield, Analytical, and ^{31}P NMR Spectroscopic Data of Compounds **3–33**

No	*Yield (%)*	*Mp (°C)*	*Formula*	*δ(31P) (Solvent)*	*Found % (Calcd %) P*	*N*	*S or Br*
3	95	54–58	$C_5H_6NBr_2P$	145.7 ($CHCl_3$)	11.32 (11.44)	5.10 (5.17)	59.10 (59.04)
4	73	113	$C_{13}H_{22}N_3O_2PS$	61.8 ($CHCl_3$)	10.00 (9.84)	13.29 (13.33)	10.20 (10.13)
5	61	109	$C_{13}H_{22}N_3O_3P$	15.5 (CH_2Cl_2)	10.30 (10.37)	14.14 (14.07)	—
6	70	120	$C_{19}H_{27}N_4O_2P$	13.5 (CH_3OH) 3.8 (C_6H_6)	8.34 (8.29)	14.85 (14.97)	—
7	75	123	$C_{13}H_{22}N_3O_2PS$	69.5 ($CHCl_3$)	9.71 (9.84)	13.12 (13.33)	10.24 (10.13)
8	60	110–111	$C_{13}H_{22}N_3O_3P$	22.5 (CH_2Cl_2)	10.29 (10.37)	14.00 (14.07)	—
9	74	131	$C_{19}H_{27}N_4O_2P$	12.7 ($CHCl_3$)	8.40 (8.29)	15.06 (14.97)	—
12	45	99–100	$C_{17}H_{16}NOP$	19.28 (CH_3CN)	11.05 (11.03)	5.05 (4.98)	—
14	68	149–150	$C_{16}H_{17}N_2PS$	15.2 ($CHCl_3$)	10.38 (10.33)	9.30 (9.33)	10.87 (10.67)
17	75	186	$C_{21}H_{37}N_5O_4P_2S_2$	60.2; 65.9 ($CHCl_3$)	11.14 (11.27)	12.92 (12.73)	11.71 (11.64)
18	52	248–250	$C_{27}H_{42}N_6O_4P_2S$	20.0; 58.9 ($CHCl_3$)	10.24 (10.20)	13.74 (13.82)	5.31 (5.26)
20	15	oil	$C_{21}H_{37}N_5O_6P_2$	15.3; 21.3 (CH_2Cl_2)	12.03 (11.99)	13.67 (13.54)	—
21	64	192	$C_{21}H_{37}N_5O_5P_2S$	15.2; 67.4 ($CHCl_3$)	11.31 (11.63)	13.27 (13.13)	6.39 (6.00)
22	52	136–137	$C_{37}H_{42}N_6O_5P_2$	11.3; 15.4 ($CHCl_3$)	10.52 (10.47)	14.18 (14.19)	—
24	57	260–261	$C_{27}H_{42}N_6O_4P_2S$	5.9; 67.7 (CH_2Cl_2)	10.13 (10.20)	13.50 (13.82)	5.54 (5.26)
26	60	98–103	$C_{21}H_{37}N_5O_5P_2S$	21.2; 60.1 ($CHCl_3$)	11.31 (11.63)	13.24 (13.13)	6.47 (6.00)
27	44	142–143	$C_{27}H_{42}N_6O_5P_2$	5.3; 22.0 ($CHCl_3$)	10.41 (10.47)	14.20 (14.19)	—
28	82	139–141	$C_{15}H_{18}N_3OP$	0.1 (C_6H_6)	11.00 (11.03)	15.02 (14.95)	—
30	64	255–260	$C_{39}H_{63}N_9O_7PS_3$	67.5; −0.6 ($CHCl_3$)	3.40 (3.44)	14.05 (13.97)	10.65 (10.64)
32	54	163–171	$C_{51}H_{45}N_3P_7$	−71.4; −29.8 (CH_2Cl_2)	23.24 (23.21)	4.50 (4.49)	—
33	90	244–246	$C_{51}H_{45}N_3O_4P_7$	−0.93; 18.9 ($CHCl_3$)	21.72 (21.70)	4.20 (4.21)	—

6.67 g (0.066 mole) in benzene (40 mL) was added with stirring. Two hours later sulfur 0.70 g (0.022 mole) was added, and the mixture was refluxed for 1 hour. After filtration and evaporation of the filtrate to dryness, the resulting oil was treated with ethanol. The product was crystallized from octane.

3-Dimorpholinophosphonato-1-methylpyrrole **(8).** To 1-methylpyrrolyl-3-dibromophosphine **(3)** 5.96 g (0.022 mole) (δ (^{31}P) 146.60), a solution of morpholine 3.83 g (0.044 mole) and triethylamine 6.67 g (0.066 mole) in benzene (80 mL) was added. After 2 hours, the mixture was filtered, and a solution of hexachloroethane 5.21 g (0.022 mole) in benzene (20 mL) was added to the filtrate. The phosphonic salt was dissolved in methylene chloride (80 mL) and treated with 5% aqueous sodium hydroxide (20 mL). The organic layer was separated, dried over anhydrous sodium sulfate, and evaporated to dryness. The product was crystallized from octane.

TABLE 2 ^{1}H NMR Data of the Heterocycles **3–33,** δ, Multiplicity, (J, Hz), $CDCl_3$

No.	*2-H*	*3-H*	*4-H*	*5-H*	*N-CH$_3$*	*Morpholine*	*Others*
3	7.11 s	—	6.22 d J(PH) = 1.5	6.77 s	3.70 s		
4	—	6.13 (J(PH) = 7.0), J(HH) = 3.0)	6.56 (J(HH) = 3.0, J(HH) = 4.0 J(PH) = 1.0)	6.84	3.96 s	3.00–3.20 m (CH_2-N) 3.66 t (J(HH) = 4.4, CH_2-O)	
5	—	6.14 J(PH) = 6.2, J(HH) = 2.7)	6.51 s[a]	6.85 s[a]	3.92 s	3.00–3.20 m (CH_2-N) 3.65 t(J(HH) = 4.5, CH_2-O)	
6	—	6.17 (J(PH) = 6.0, J(HH) = 2.4)	6.60 s[a]	6.83 s[a]	3.87 s	3.00–3.40 m (CH_2-N) 3.50–3.70 m (CH_2-O)	6.69 t(J(HH) = 7.5, p-H) 6.73 d(J(HH) = 8.4, o-H) 7.08 t(J(HH) = 7.5, m-H)
7	7.18 d (J(PH) = 1.8)	—	6.21 d (J(PH) = 1.5)	6.66 d (J(PH) = 1.8)		3.10–3.20 m (CH_2-N) 3.60–3.70 m (N-CH_3, CH_2-O)	
8	7.05 d (J(PH) = 1.5)	—	6.16 d (J(PH) = 1.5)	6.65 d (J(PH) = 1.8)	3.66 s	3.00–3.20 m (CH_2-N) 3.62 t(J(HH) = 4.5, CH_2-O)	
9	7.14 s*	—	6.23 s[a]	6.65 s[a]	3.65 s	3.00–3.20 m (CH_2-N) 3.62 t(J(HH) = 4.2, CH_2-O)	6.69 t(J(HH) = 7.6, p-H) 6.87 d(J(HH) = 8.4, o-H) 7.11 t(J(HH) = 7.6, m-H)
12	—	6.00 s	5.85 s	6.79 s	3.87 s		7.05–7.80 m (Ph)
14	—	6.08 s[a]	5.91 s[a]	6.89 s[a]	3.84 s		7.10–7.90 m (Ph)
17	—	6.66 s[a]	7.31 s[a]	3.97 s	2.90–3.30 m (CH_2-N) 3.67 t(J(HH) = 4.4, CH_2-O)		
18	—	6.70 s[a]	—	7.32 s[a]	3.95 s	2.92–3.30 m (CH_2-N) 3.65 t(J(HH) = 4.4, CH_2-O)	6.71 t(J(HH) = 7.5, p-H) 6.85 d(J(HH) = 8.6, o-H) 7.11 t(J(HH) = 7.5, m-H)
20	—	6.65 s[a]	—	7.30 s[a]	3.91 s	2.90–3.27 m (CH_2-N) 3.67 t(J(HH) = 4.5, CH_2-O)	
21	—	6.62 s[a]	—	7.32 s[a]	3.93 s	2.95–3.25 m (CH_2-N) 3.67 t(J(HH) = 4.4, CH_2-O)	
22	—	6.61 s[a]	—	7.32 s[a]	3.94 s	2.95–3.30 m (CH_2-N) 3.64 t(J(HH) = 4.4, CH_2-O)	6.72 t(J(HH) = 7.5, p-H) 6.84 d(J(HH) = 8.7, o-H) 7.11 t(J(HH) = 7.5, m-H)
24	—	6.69 s[a]	—	7.30 s[a]	3.97 s	2.95–3.20 m (CH_2-N) 3.67 t(J(HH) = 4.5, CH_2-O)	6.70–6.83 m(o, p-H) 7.11 t(J(HH) = 7.8, m-H)
26	—	6.68 s[a]	—	7.20 s[a]	3.99 s	3.00–3.25 m(CH_2-N) 3.67 t(J(HH) = 4.4, CH_2-O)	
27	—		—	7.42 s[a]	3.89 s	2.70–3.20 m(CH_2-N) 3.30–3.75 m(CH_2-O)	6.45–6.80 m(H(3)-Het, o,p-H Ph) 7.02 t(J(HH) = 7.8, m-H)
28	—	6.14 dt (J(HH) = 2.0, J(HH) = 3.5, J(PH) = 3.5	6.07 t (J(HH) = 3.5)	6.39 m (J(HH) = 3.5, J(HH) = 2.0, J(PH) = 2.0	3.60 s		
30	—	6.18 s[a]	—	7.38 s[a]	3.86 s	2.95–3.35 m (CH_2-N) 3.68 t(J(HH) = 4.4, CH_2-O)	
33	—		5.97 t (J(PH) = 4.0, H(3)H(4))	—	3.98 s		7.40–7.80 m(o, m, p-H)

[a]Broad signals.

TABLE 3 ^{13}C NMR Data of the Hetrocycles **3, 4, 7,** δ, Multiplicity, (J, Hz), $CDCl_3$

No.	*2-C*	*3-C*	*4-C*	*5-C*	*Others*
3	127.82 d (J(PC) = 49.24)	120.86 d (J(PC) = 116.20)	113.12 d (J(PC) = 14.70)	125.32 d (J(PC) = 5.01)	36.48 s (N-CH_3)
4	120.78 d (J(PC) = 160, 83)	119.41 d (J(PC) = 15.38)	107.41 d (J(PC) = 11.21)	129.60 d (J(PC) = 10.63)	36.45 s (N-CH_3) 45.10 s (CH_2-O) 66.78 d (J(PC) = 7.17, CH_2-N)
7	131.43 d (J(PC) = 25,11)	113.06 d (J(PC) = 145.07)	110.83 d (J(PC) = 7.77)	123.79 d (J(PC) = 12.29)	36.29 s (N-CH_3) 44.81 s (CH_2-O) 66.88 d (J(PC) = 8.37, CH_2-N)

3-Dimorpholinophenyliminophosphonato-1-methylpyrrole **(9).** To 1-methylpyrrolyl-3-dibromophosphine **(3)** 5.96 g (0.022 mole) [δ (^{31}P) 146.60], a solution of morpholine 3.83 g (0.044 mole) and triethylamine 6.67 g (0.066 mole) in benzene (40 mL) was added. After 2 hours, the mixture was filtered. Phenyl azide 2.62 g (0.022 mole) was added to the filtrate, which was then refluxed for 5 hours. The mixture was evaporated to dryness, and the resulting oil was treated with ethanol. The product was crystallized from ethanol.

Reaction of N-Methylpyrrole with Diphenylbromophosphine in Methylene Chloride. To a solution of diphenylbromophosphine 0.53 g (0.002 mole) in methylene chloride (2 mL), a solution of N-methylpyrrole 0.16 g (0.002 mole) and pyridine 0.16 g (0.002 mole) in methylene chloride (3 mL) was added. The reaction mixture was maintained at room temperature for 48 hours. As evidenced by the ^{31}P NMR spectrum, about 20% of the 3-phosphorylated product **(10a)** had resulted (δ − 27.89). The reaction mixture was left for 1 week, the ^{31}P NMR resonance remaining unchanged.

Reaction of N-Methylpyrrole with Phenyldibromophosphine in Methylene Chloride. To a solution of phenyldibromophosphine 0.40 g (0.0015 mole) in methylene chloride (1 mL), a solution of N-methylpyrrole 0.0015 g (0.0015 mole) and triethylamine 0.15 g (0.0015 mole) in methylene chloride (1 mL) was added. The reaction mixture was allowed to stand at room temperature for 24 hours. Signals were observed in the ^{31}P NMR spectrum at δ 43.41 **(11a)**, 36.45 **(11)**, 2.19, −1.25, −3.57, −23.17, −27.52, −31.84, and −34.18.

2-(1-Methylpyrrolyl)diphenylphosphine Oxide **(12).** To a solution of N-methylpyrrole 4.05 g (0.05 mole) in pyridine (10 mL), a solution of diphenylbromophosphine 11.70 g (0.05 mole) in pyridine (5 mL) was added. The reaction mixture was maintained at room temperature for 24 hours [δ (^{31}P) −29.49], followed by filtration and evaporation of the filtrate to dryness. The resulting oil was dissolved in methylene chloride, and 30% aqueous hydrogen peroxide (3 mL) was added over 10 minutes. After having been allowed to stand for 10 minutes, the reaction mixture was neutralized with 4% aqueous sodium hydroxide and washed with water (2 × 30 mL). The organic layer was separated, dried over anhydrous sodium sulfate, and evaporated to dryness. The product was extracted with hexane.

Di(1-Methylpyrrolyl-2)phenylphosphine Sulfide **(14).** To a solution of N-methylpyrrole 4.05 g (0.05 mole) in pyridine (10 mL), a solution of phenyldibromophosphine 6.57 g (0.025 mole) in pyridine (5 mL) was added. The reaction mixture was maintained at room temperature for 24 hours [δ (^{31}P) −52.61] and was refluxed for 1 hour after addition of sulfur 1.60 g (0.05 mol). Then the mixture was filtered, the filtrate evaporated to dryness, and the resulting oil treated with acetonitrile. The product was crystallized from ethanol.

Reaction of Phosphorus Tribromide with 3 Moles of N-Methylpyrrole. To a stirred solution of N-methylpyrrole 3.65 g (0.045 mole) in pyridine (20 mL), a solution of phosphorus tribromide 4.07 g (0.015 mole) in pyridine (10 mL) was added at 0°C. The reaction mixture was left to stand at room temperature for 24 hours. Resonances at δ − 70.73, −71.56, and −72.12 were detected in the ^{31}P NMR spectrum.

Reaction of N-Methylpyrrole with 4 Moles of Phosphorus Tribromide. To a stirred solution of phosphorus tribromide 5.42 g (0.020 mole) in pyridine (10 mL), a solution of N-methylpyrrole 0.41 g (0.005 mole) in pyridine (10 mL) was added at 0°C. The reaction mixture was left to stand at room temperature for 48 hours. Resonances at δ 136.92, 133.12, 129.77, 126.75, 111.81, and 108.72 were detected in the ^{31}P NMR spectrum.

2,4-Tetramorpholinodithiophosphonyl-1-methylpyrrole **(17).** To a solution of compound **(4)** (or **7**) 9.45 g (0.030 mole) in pyridine (20 mL), a solution of phosphorus tribromide 8.13 g (0.030 mole) in pyridine was added. The reaction mixture was allowed to stand at room temperature for 4 days. The signals observed in the ^{31}P NMR spectrum were at δ 59.78 and 145.73 (or for compound **23,** 67.81 and 108.93). Then a solution of morpholine 5.22 g (0.060 mole) and triethylamine 9.09 g (0.090 mole) in benzene (50 mL) was added, and, 2 hours later, the mixture was filtered. After addition of sulfur 0.96 g (0.030 mole) to the filtrate, the mixture was refluxed for 1 hour. After evaporation of it to dryness, the resulting oil was treated with ethanol.

4-Dimorpholinophenyliminophosphonyl-2-dimorpholinothiophosphonyl-1-methylpyrrole **(18).** To a solution of compound **(4)** 9.45 g (0.030 mole) in pyridine (25 mL), a solution of phosphorus tribromide 8.13 g (0.030 mole) in pyridine (25 mL) was added. The reaction mixture was allowed to stand at room temperature for 4 days [δ (^{31}P) 60.07 and 146.34]. Then a solution of morpholine 5.22 g (0.060 mole) and triethylamine 9.09 g (0.090 mole) in benzene (100 mL) was added, and, 1 hour later, the mix-

ture was filtered. After addition of a solution of phenyl azide 3.57 g (0.030 mole) in benzene (10 mL) to the filtrate, it was refluxed for 10 hours and then evaporated to dryness. The resulting oil was treated with diethyl ether. The product was crystallized from toluene.

2,4-Tetramorpholinodiphosphonyl-1-methylpyrrole **(20).** To a solution of compound **(5)** (or **8**) 8.97 g (0.030 mole) in pyridine (20 mL), a solution of phosphorus tribromide 8.13 g (0.030 mole) in pyridine (10 mL) was added. The reaction mixture was allowed to stand at room temperature for 4 days. The resonances detected in the ^{31}P NMR spectrum were δ 15.80 and 145.94 (or for compound **25,** 20.17 and 109.31). Then a solution of morpholine 5.22 g (0.060 mole) and triethylamine 9.09 g (0.090 mole) in benzene (80 mL) was added. One hour later, the mixture was filtered and a solution of hexachloroethane 7.11 g (0.030 mol) in benzene (30 mL) was added to the filtrate. After 2 hours, treatment with 5% aqueous sodium hydroxide (20 mL) and extraction with methylene chloride (3 $\times$ 50 mL) were effected. The organic layer was separated, dried over anhydrous sodium sulfate, and evaporated to dryness, leaving the product as an oil.

2-Dimorpholinophosphonyl-4-dimorpholinothiophosphonyl-1-methylpyrrole **(21).** To a solution of compound **(5)** 8.97 g (0.030 mole) in pyridine (25 mL), a solution of phosphorus tribromide 8.13 g (0.030 mole) in pyridine (25 mL) was added. The reaction mixture was allowed to stand at room temperature for 4 days [δ (^{31}P) 15.40 and 146.71]. Then, a solution of morpholine 5.22 g (0.060 mole) and triethylamine 9.09 g (0.090 mole) in benzene (50 mL) was added, and, 1 hour later, the mixture was filtered. After addition of sulfur 0.96 g (0.030 mole) to the filtrate, the mixture was refluxed for 1 hour and then evaporated to dryness. The residue was treated with water, and the product was crystallized from octane.

2-Dimorpholinophosphonyl-4-dimorpholinophenyliminophosphonyl-1-methylpyrrole **(22).** To a solution of compound **(5)** 11.96 g (0.040 mole) in pyridine (25 mL), a solution of phosphorus tribromide 10.84 g (0.040 mole) in pyridine (25 mL) was added. The reaction mixture was allowed to stand at room temperature for 4 days [δ (^{31}P) 14.43 and 145.49]. Then, a solution of morpholine 6.96 g (0.080 mole) and triethylamine 12.12 g (0.120 mole) in benzene (100 mL) was added, and, 1 hour later, the mixture was filtered. After addition of a solution of phenyl azide 4.76 g (0.040 mole) in benzene (10 mL) to the filtrate, it was refluxed for 5 hours and then evaporated to dryness. The product was extracted with octane.

2-Dimorpholinophenyliminophosphonyl-4-dimorpholinothiophosphonyl-1-methylpyrrole **(24).** To a solution of compound **(7)** 9.45 g (0.030 mole) in pyridine (25 mL), a solution of phosphorus tribromide 8.13 g (0.030 mole) in pyridine (25 mL) was added. The reaction mixture was allowed to stand at room temperature for 4 days [δ (^{31}P) 66.73 and 108.93]. Then, a solution of morpholine 5.22 g (0.060 mole) and triethylamine 9.09 g (0.090 mole) in benzene (100 mL) was added, and, 1 hour later, the mixture was filtered. After addition of a solution of phenyl azide 3.57 g (0.030 mole) in benzene (10 mL) to the filtrate, it was refluxed for 5 hours and then evaporated to dryness. The residue was treated with ethanol, and the product was crystallized from ethanol.

4-Dimorpholinophosphonyl-2-dimorpholinothiophosphonyl-1-methylpyrrole **(26).** To a solution of compound **(8)** 8.97 g (0.030 mole) in pyridine (25 mL), a solution of phosphorus tribromide 8.13 g (0.030 mole) in pyridine (25 mL) was added. The reaction mixture was allowed to stand at room temperature for 4 days [δ (^{31}P) 18.07 and 107.21]. Then, a solution of morpholine 5.22 g (0.060 mole) and triethylamine 9.09 g (0.090 mole) in benzene (80 mL) was added, and, 1 hour later, the mixture was filtered. After addition of sulfur 0.96 g (0.030 mole) to the filtrate, the mixture was refluxed for 1 hour and then evaporated to dryness. The product was crystallized from octane.

2-Dimorpholinophenyliminophosphonyl-4-dimorpholinophosphonyl-1-methylpyrrole **(27).** To a solution of compound **(8)** 8.97 g (0.030 mole) in pyridine (25 mL), a solution of phosphorus tribromide 8.13 g (0.030 mole) in pyridine (15 mL) was added. The reaction mixture was held at room temperature for 4 days [δ (^{31}P) 20.70 and 109.83]. Then, a solution of morpholine 5.22 g (0.060 mole) and triethylamine 9.09 g (0.090 mole) in benzene (100 mL) was added, and, 1 hour later, the mixture was filtered. After addition of a solution of phenyl azide 3.57 g (0.030 mole) in benzene (10 mL) to the filtrate, it was refluxed for 5 hours and then evaporated to dryness. The product was crystallized from octane.

Tris(1-methylpyrrolyl-2)phosphine Oxide **(28).** To a stirred solution of tris(1-methylpyrrolyl-2)phosphine 1.63 g (0.006 mole) in methylene chloride (20 mL), a 30% aqueous solution of hydrogen peroxide

(1 mL) was added at 10°C over 20 minutes. After having been allowed to stand at room temperature for 30 minutes, the reaction mixture was washed with water (2 × 30 mL). The organic layer was separated, dried over anhydrous sodium sulfate, and evaporated to dryness. The product was crystallized from diethyl ether.

Tris(*4-dimorpholinothiophosphonyl-1-methylpyrrolyl-2*)*phosphine Oxide* **(30).** To a solution of phosphine oxide **(28)** 3.03 g (0.01 mole) in pyridine (10 mL), a solution of phosphorus tribromide 8.13 g (0.03 mole) in pyridine (5 mL) was added. The reaction mixture was allowed to stand at room temperature for 24 hours. Peaks at δ 1.40 and 142.90 in a 1:3 intensity ratio were observed in the ^{31}P NMR spectrum. Then a solution of morpholine 5.22 g (0.06 mole) and triethylamine 9.09 g (0.09 mole) in benzene was added. One hour later, sulfur 0.96 g (0.03 mole) was added, and the mixture was refluxed for 4 hours. After filtration and evaporation of the filtrate to dryness, the resulting oil was treated with water (5 mL). The product was crystallized from ethanol.

Tris(*5-diphenylphosphino-1-methylpyrrolyl-2*)*phosphine* **(32).** To a solution of tris(1-methylpyrrolyl-2)phosphine 5.15 g (0.019 mole) in pyridine (20 mL), a solution of diphenylbromophosphine 18.55 g (0.070 mole) in pyridine (10 mL) was added. The reaction mixture was left to stand at room temperature for 3 days and was kept at 80°C for another 10 hours. After evaporation of the pyridine under reduced pressure, the product was extracted with diethyl ether (50 mL), and the precipitate was filtered off under argon.

Tris(*5-diphenylphosphionyl-1-methylpyrrolyl-2*)*phosphine Oxide* **(33).** To a stirred solution of compound **(32)** 5.47 g (0.012 mole) in methylene chloride (100 mL), a 30% aqueous solution of hydrogen peroxide (10 mL) was added at 10°C over 20 minutes. After having been allowed to stand at room temperature for 30 minutes, the reaction mixture was washed with water (2 × 10 mL). The organic layer was separated, dried over anhydrous sodium sulfate, and evaporated to dryness. The resulting oil was triturated with water. The product was crystallized from a mixture of methanol (23.5 g) and water (15.5 g).

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