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Phosphorus-Containing Heterocyclic Compounds Derived from N-Vinylpyrroles

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ABSTRACT

C-phosphorylation of N-vinylpyrroles with phosphorus(III) halides is shown to occur both at position **2** *of the pyrrole ring and at the vinyl group. The properties of the resulting phosphorus-containing heterocyclic compounds and bis-phosphorylated N-vinylpyrroles are reported.* © 1997 John Wiley & Sons, Inc. Heteroatom Chem **8:**495–499, 1997

INTRODUCTION

Previously, we showed that phosphorus(III) halides in basic media act as efficient phosphorylating agents with respect to heteroaromatic compounds of the pyrrole, furan, thiophene [1], indolizine [2], imidazopyridine [3], imidazole [4], and pyrazole [5] series. Up to now, C-phosphorylation of heterocyclic compounds with phosphorus(III) halides has not been used as a pathway to new heterocyclic systems.

It seemed probable that cyclizations like this could be carried out with N-vinylpyrroles in whose molecules electrophilic substitution can proceed both at the aromatic ring and at the vinyl group [6]. The present study was aimed to evaluate the above hypothesis as well as to effect the preparation of bis(phosphorylated) N-vinylpyrroles.

Previously, a phosphorus-containing heterocyclic system derived by the treatment of N-vinylpyrrole with phosphorus pentachloride had been isolated in poor yield [7].

RESULTS AND DISCUSSION

On mixing of equimolar amounts of phenyldibromophosphine or phenyldichlorophosphine with N-vinylpyrrole in pyridine, the ^{31}P NMR spectrum of the reaction mixture displays a signal at δ −47 probably corresponding to formation of phosphine **2.** Within the next two weeks, the signal attenuates, whereas a new one given by phosphine **3** appears at δ −29 and grows in intensity. The signal assignments are in accord with the data of Ref. [7] and are also based on the trends in ^{31}P NMR spectra for phosphines in passing from the C(sp^3)–P to the C(sp^2)–P bond. An attempt to isolate phosphines **3** in individual form failed, and they were subsequently transformed into phosphine oxides **4** and phosphine sulfide **5** by con-

Dedicated to Prof. William McEwen on the occasion of his seventy-fifth birthday.

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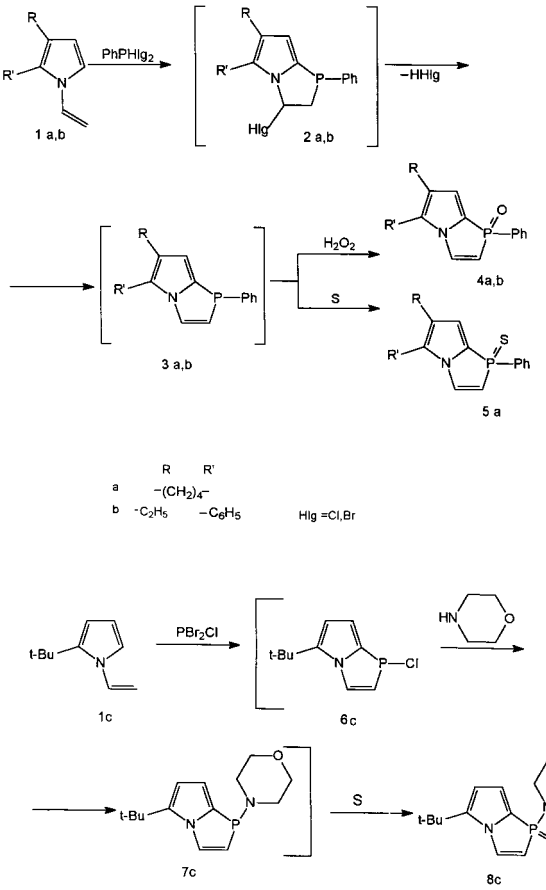
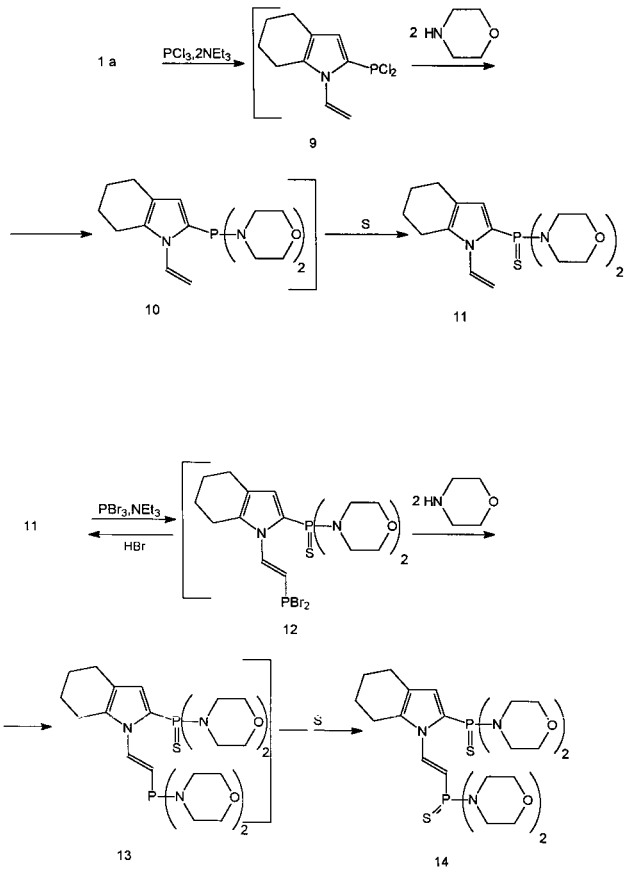
ventional methods. Phosphines **3** also were reacted with phenyl azide, but the corresponding phenyliminophosphines could not be isolated due to their immediate hydrolysis to oxides **4** caused even by moisture of the air. Such high hydrolyzability is likely to result from the phosphorus atom positioned in a five-membered ring that, in the course of hydrolysis, favors the formation of a five-coordinate intermediate with a trigonal bipyramidal phosphorus atom [8].



Within 20 minutes after addition of the pyridine solution of N-vinylpyrrole **1c** to the mixture of phosphorus tribromide and trichloride in a 2:1 ratio, a peak at δ 44 arises in the ^{31}P NMR spectrum, which corresponds to chlorophosphine **6c** being transformed into amide **7c.** Compounds **6c** and **7c** being extremely labile, are revealed by ^{31}P NMR spectroscopy, whereas phosphine sulfide **8c** can be isolated as an individual compound. N-Vinylpyrroles **1a,b** undergo the above conversions to yield unstable products, even in the case wherein phosphorus(V) derivatives would be formed.

The reaction of equimolar amounts of N-vinylpyrrole **1a** with phosphorus trichloride can be stopped at the stage of the formation of dichlorophosphine **9,** observable in the ^{31}P NMR spectrum, and unambiguously identified in the same manner as for amide **10,** i.e., in the form of thiophosphonate **11.**



Thiophosphonate **11** reacts in pyridine in the presence of triethylamine with an equimolar amount of phosphorus tribromide to give dibromophosphine **12** that shows two ^{31}P NMR signals at δ 150.7 and 60.7, respectively and is identified further as thiophosphonate **14.**

The bond between the dibromophosphino group and the appropriate carbon atom in the molecule of dibromophosphine **12** being very labile, the initial thiophosphonate **11** results on heating the solution of compound **12** in the presence of pyridine hydrobromide. Such a lability of C–P bonds inherent in the vinylogues of phosphonic amides has already been pointed out by us in previous articles [2,9,10].

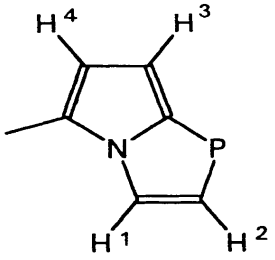
The phosphorus-containing compounds obtained represent crystalline solids, their structures being confirmed by ^{1}H, ^{31}P, and ^{13}C NMR spectra (see Tables 1, 2, and 3).

To conclude, the phosphorylation of N-vinylpyrroles with phosphorus(III) halides provides a synthetic access to a variety of condensed phosphorus(V)-containing heterocycles.

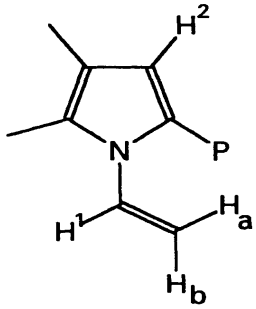
TABLE 1 Synthetic Data, Results of Elemental Analysis, and ^{31}P NMR Spectral Characteristics for Compounds **4, 5, 8, 11, 14**

Compound	*Melting Point (°C)*	*Yield (%)*	*Molecular Formula*	*^{31}P NMR, ppm solvent*	*Elemental Analysis Found (calculated)*	
					N	*P*
4a	189–190	66	$C_{16}H_{16}NOP$	22,0 CH_2Cl_2	5,01 (5,10)	11,12 (11,50)
4b	142–143	37	$C_{20}H_{18}NOP$	21,3 CH_2Cl_2	4,40 (4,20)	9,60 (9,30)
5a	130–131	59	$C_{16}H_{16}NSP$	26,1 C_5H_5N	4,95 (4,90)	10,81 (10,40)
8c	119–121	54	$C_{14}H_{21}N_2OSP$	47 CH_2Cl_2	9,53 (9,10)	10,42 (10,10)
11	146–148	56	$C_{18}H_{27}N_3O_2SP$	60 CH_2Cl_2	11,14 (10,60)	8,13 (8,30)
14	172–174	42	$C_{18}H_{43}N_5O_4S_2P_2$	75,1;62,4 CH_2Cl_2	12,00 (12,30)	5,34 (5,50)

TABLE 2 ^1H NMR Spectral Data for Compounds **4, 5, 8, 11,** and **14** in $CDCl_3$



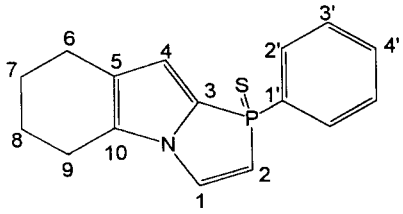
4,5,8,14



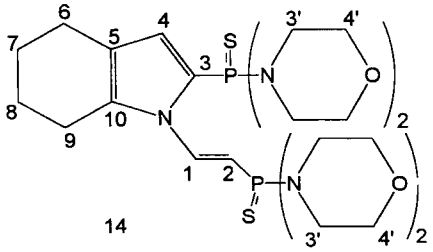
11

Compound	*^1H NMR Spectral Characteristics*
4a	$-CH_2-CH_2-$ 1.8(M) 4H, $-CH_2-$ 2.5(M) 2H, $-CH_2-$ 2.6(M) 2H, H^2 5.6 (d.d J_{pM} = 18Γμ, J_{HH} = 6.3 Hz) 1H, H^1 7.7 (d.d J_{pM} = 13.8 Hz. J_{HH} = 6.3 Hz) 1H, H^3 6.5(s) 1H, Ar-7.2–7.6(M) 5H
4b	CH_3- 1.1(t) 3H, $-CH_2-$ 2.5(d) 2H, H^2 5.7(d.d J_{pM} = 18.6 Hz, J_{HH} = 6.9 Hz) 1H, H^3 6.7(M) 1H, H^1 7.7(d.d J_{pM} = 13.8 Hz, J_{HH} = 6.9 Hz), 1H, Ar- 7.2–7.6(M) 10H
5a	$-CH_2-CH_2-$ 1.8(M) 4H, $-CH_2-$ 2.5(M) 2H, $-CH_2-$ 2.7(M) 2H, H^2 5.7(d.d J_{pM} = 22 Hz, J_{HH} = 5.8 Hz) 1H, H^3 6.5(s) 1H, H^1 7.8(d.d J_{pM} = 15 Hz, J_{HH} = 5.8 Hz) 1H, Ar- 7.3–7.5(M) 5H
8c	$3CH_3$- 1.3(s) 9H, $-N(CH_2)_2-$ 3.1(M) 4H, $O(CH_2)_2-$ 3.6(M) 4H, H^2 5.5(d.d J_{pM} = 18.6 Hz, J_{HH} = 6.5 Hz) 1H, H^4 5.9(M) 1H, H^3 6.5(M) 1H, H^1 7.5(d.d J_{pM} = 31.2 Hz, J_{HH} = 6.5 Hz) 1H
11	$-CH_2-CH_2-$ 1.7(M) 4H, $-CH_2-$ 2.5(M) 2H, $-CH_2-$ 2.7(M) 2H, $-N(CH_2)_2-$ 3.2(M) 4H, $O(CH_2)_2-$ 3.7(M) 4H, H_b 4.99(μ J_{MHb} = 9 Hz) 1H, H_a 5.03(d J_{MHa} = 16 Hz) 1H, H^2 6.4(d J_{pM} = 3.6 Hz) 1H, H^1 7.7(d.dJ_{MHa} = 16 Hz, J_{MHb} = 9 Hz) 1H
14	$-CH_2-CH_2-$ 1.7(M) 4H, $-CH_2-$ 2.4(M) 2H, $-CH_2-$ 2.6(M) 2H, $-N(CH_2)_2-$ 3.1(M) 8H, $O(CH_2)_2-$ 3.6(M) 8H, H^2 5.6(d.d J_{pM} = 13.5 Hz, J_{HH} = 15.9 Hz) 1H, H^3 6.6(d J_{pH} = 4.8 Hz) 1H, H^1 8.3(d.d J_{pM} = 18.6 Hz, J_{MH} = 15.9 Hz) 1H

TABLE 3 ^{13}C NMR Spectal Data for Compounds **5a, 14** in $CDCl_3$



5a



14

N	*C*[1]	*C*[2]	*C*[3]	*C*[4]	*C*[5]	*C*[6,7,8,9]	*C*[10]	*C*[2′]	*C*[3′]	*C*[4′]
5a	131.7 (2.9)	110.12 (77.6)	123.6 (115)	116.4 (12.5)	124.5 (9.7)	23.032 22.855 22.361 21.077	130.8 (12.6)	130.8 (12.6)	128.4 (13.6)	134.5
14	143.78 (23)	104.83 (127.5)	122.98 (148.5)	124.55 (16.2)	122.5 (13.3)	23.391 22.913 22.33 21.441	135.88 (6.8)	—	45.544 44.618	69.94

EXPERIMENTAL

The ^{31}P, ^{1}H, and ^{13}C NMR spectra were recorded on a Varian 300 spectrometer using TMS as an internal standard for ^{1}H and ^{13}C signals and 85% H_3PO_4 as an external standard for ^{31}P signals.

Solution of 6,7-(Butanediyl-1,4)-4-phenyl-4,4'-dihydropyrrolo[1,2-a] [1,3]azaphosphole **3**

A mixture of 4,5,6,7-tetrahydro-N-vinylindole (3.3 mmol), phenyldichlorophosphine (3.3 mmol), and pyridine (30 ml) was allowed to stand under argon at 20°C for two weeks. Within the first 20 minutes, an individual signal at δ −47 was observed in the ^{31}P NMR spectrum that was attributed to phosphine **2a.** In the two weeks that followed, the signal was attenuating while a new peak at δ −29 was growing stronger.

6,7-(Butanediyl-1,4)-4-phenyl-4-oxo-4,4'-dihydropyrrolo[1,2-a] [1,3]azaphosphole **4a**

A 25% aqueous solution of hydrogen peroxide (5 mmol) was added to the phosphine solution **3a** (3.3 mmol). After the pyridine had been evaporated, the residual solid was dissolved in methylene chloride (40 mL), washed with water, and left for 2 hours over a dehydrating agent (Na_2SO_4). This was followed by filtering the solution and evaporating the filtrate. The oily residue was triturated with pentane and then recrystallized from toluene (20 mL). MS (m/e) 269 (M^+).

4,7-Diphenyl-4-oxo-4,4'-dihydropyrrolo[1,2-a] [1,3]azaphosphole **4b**

The compound was synthesized analogously to **4a** and recrystallized from toluene–heptane (1:1).

6,7-(Butanediyl-1,4)-4-phenyl-4-thio-4,4'-dihydropyrrolo[1,2-a] [1,3]azaphosphole **5a**

Sulfur (3.3 mmol) was added to the phosphine solution **3a** (3.3 mmol). A signal at δ 60 was registered in the ^{31}P NMR spectrum. After evaporation of the pyridine, the solid obtained was dissolved in methylene chloride (40 mL), washed with water, and maintained over calcinated Na_2SO_4 for 2 hours. Then the mixture was filtered, and the filtrate was evaporated. The resultant oily residue was triturated with pentane and recrystallized from methanol (30 mL). MS (m/e) 285 (M^+).

Adding sulfur to the pyridine solution of phosphine **2a** proceeded likewise and involved much the same procedure.

5-tert-Butyl-4-morpholino-4-thio-4,4'-dihydropyrrolo[1,2-a] [1,3]azaphosphole **8c**

A mixture of phosphorus tribromide (2.4 mmol) and phosphorus trichloride (4.8 mmol) was added with

stirring to a solution of 2-*tert*-butyl-N-vinylpyrrole (7.2 mmol) in pyridine (40 mL). A ^{31}P NMR signal was observed at δ 44. Then triethylamine (21.6 mmol) and morpholine (7.2 mmol) were added, which resulted in a ^{31}P NMR signal at δ 32. On addition of sulfur (7.2 mmol), a signal at δ 47 was noticed. This was followed by evaporating the pyridine, dissolving the solid obtained in methylene chloride (40 mL), washing the solution with water, and keeping it over a dehydrating agent (Na_2SO_4) for 2 hours. After filtration of the solution and evaporation of the filtrate, the resultant oily residue was triturated with pentane and recrystallized from methanol (30 mL). MS (m/e) 296 (M^+).

(4,5,6,7-Tetrahydro-N-vinylindol-2-yl)-thiophosphonic Dimorpholide **11**

Phosphorus trichloride (4.07 mmol) was added with stirring to a solution of 4,5,6,7-tetrahydro-N-vinylindole (4.07 mmol) in pyridine (35 mL) containing triethylamine (12.21 mmol). A signal at δ 130 was detected in the ^{31}P NMR spectrum. On addition of morpholine (24.42 mmol) to the reaction mixture, a signal at δ 82 arose. This was followed by the addition of sulfur (4.07 mmol) and, accordingly, by the registration of a signal at δ 60. Pyridine was evaporated, and the residual solid was dissolved in methylene chloride (40 mL). The solution was washed with water and allowed to stand over a dehydrating agent (Na_2SO_4) for 2 hours. After filtration of the solution and evaporation of the filtrate the oily residue obtained was triturated with pentane and recrystallized from isopropyl alcohol (25 mL). MS (m/e) 381 (M^+).

(4,5,6,7-Tetrahydro-N-(dimorpholidothiophosphinovinyl)indol-2-yl)-thiophosphonic Dimorpholide **14**

Phosphorus tribromide (2.62 mmol) was added with stirring to a solution of (4,5,6,7-tetrahydro-N-vinylindol-2-yl)-thiophosphonic dimorpholide (2.62 mmol) in pyridine (35 mL) containing triethylamine (7.86 mmol). Two signals at δ 60.7 and 150.7 were observed in the ^{31}P NMR spectrum. On treatment of the reaction mixture with morpholine (13.1 mmol) immediately followed by addition of sulfur (2.62 mmol), signals at δ 62 and 75 were registered. After evaporation of pyridine, the solid obtained was dissolved in methylene chloride (40 mL), washed with water, and left to stand over a dehydrating agent (Na_2SO_4) for 2 hours. Then filtration of the solution and evaporation of the filtrate followed. The resultant oily residue was triturated with pentane and recrystallized first from isopropyl alcohol (25 mL) and then from toluene (15 mL).

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