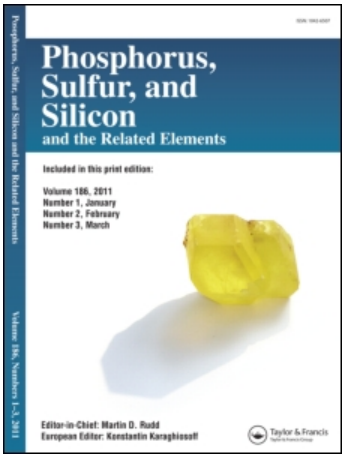

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DIRECT TRANSFORMATION OF PHOSPHINIC ACIDS IN THE 3-PHOSPHOLENE SERIES TO PHOSPHINAMIDES

Jerzy Szewczyk[a]; John R. Lloyd[a]; Louis D. Quin[a]
[a] Gross Chemical Laboratory, Duke University, Durham, North Carolina

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DIRECT TRANSFORMATION OF PHOSPHINIC ACIDS IN THE 3-PHOSPHOLENE SERIES TO PHOSPHINAMIDES

JERZY SZEWCZYK, JOHN R. LLOYD and LOUIS D. QUIN*

Gross Chemical Laboratory, Duke University, Durham, North Carolina 27706

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Tris(*N*,*N*-dialkylamino)phosphines undergo a transamination reaction with phosphinic acids containing the 3-phospholene ring. Yields of phosphinamides ranged from 66 to 93% for five different combinations. Products were characterized by ^{13}C and ^{31}P NMR. Transamination was not effected with diphenylphosphinic acid or methylphosphonic acid, but a low conversion of diethyl phosphate to its amide was achieved. With *p*-toluenesulfonic acid, tris(*N*,*N*-dimethylamino)phosphine was converted to a stable salt. The mechanism of the reaction with the phospholene acids was determined by ^{31}P NMR studies to proceed through formation of a mixed anhydride $R_2P(O)—O—P(NR'_2)_2$; the displaced dialkylamino group then attacks at phosphoryl to give the phosphinamide.

In 1963, Burgada[1] announced a one-step method for the conversion of carboxylic acids to their *N*,*N*-dialkylamides. This consists of heating the acid with a tris-(*N*,*N*-dialkylamino)phosphine.

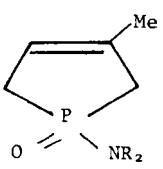
$$3\ RCOOH + P(NR'_2)_3 \rightarrow 3\ RCONR'_2 + H_3PO_3$$

We have had great success with this method in previous research,[2] where we converted cyclic dicarboxylic acids to their bis-(*N*,*N*-dimethyl)amides in yields of 85–90%. We have now found that this reaction can have utility with phosphorus-based acids; phosphinic acids in the 3-phospholene series were converted to phosphinamides in good yield. Some exploratory studies on the transamination with other types of acids have also been performed, but with less promising results.

Scope of the Reaction

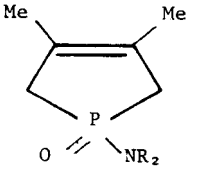
Five different phosphinamides have been prepared, with yields ranging from 66 to 95%, from phospholene acids. Both tris(*N*,*N*-dimethylamino)- and tris(*N*,*N*-diethylamino) phosphines were used as reagents. By varying the ratio of reactants, it was found that all three of the dialkylamino groups of the aminophosphine were available for transfer to the phosphinic acid. For the *N*,*N*-dimethyl compound, best results (up to 95%) were obtained when the molar ratio of the phosphine to the acid was 1 : 1 (at room temperature) or 1 : 2 (in refluxing benzene). For the *N*,*N*-diethyl compounds, yields of 70–75% were obtained with 1 : 2 or 1 : 3 mixtures in refluxing benzene. The products were purified by column chromatography and then vacuum distillation.

*Author to whom all correspondence should be addressed.



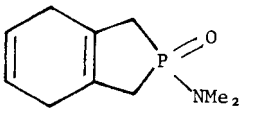
1, R=CH_3

2, R=C_2H_5



3, R=CH_3

4, R=C_2H_5



5

Data for the synthesis of **1–4** are provided in Table I, with their spectral data in Table II. Compound **5** is described in the Experimental Section.

The successful extension of this process to other types of phosphorus-based acids could be of considerable significance. The only other method for one-step phosphorus acid to amide transformation involves coupling of phosphoric acid or dialkyl phosphates with an amine through the triphenylphosphine-carbon tetrachloride product[3] or the tris(*N*,*N*-dimethylamino)phosphine-bromine adduct.[4] We therefore applied our technique to a noncyclic phosphinic acid (diphenyl). Examination of the reaction product by ^{31}P NMR showed that the phosphinamide had not formed. Similarly, no phosphonamide was detected from methylphosphonic acid. However, the product mixture from the reaction with diethyl phosphate contained a component whose ^{31}P NMR signal (δ + 10.6) matched that (+11.1)[5] of the desired product, $Me_2NPO(OEt)_2$. Attempts to isolate this product from the mixture have not been successful. The yield was only about 30%; it was not improved on further experimentation. In its present form, therefore, the transamination seems to have a limited scope in phosphorus chemistry, and proceeds best when the special geometry and reactivity of the 5-membered ring is present.

p-Toluenesulfonic acid was also tried in the reaction with $(Me_2N)_3P$; a single product formed rapidly and was recognized as the salt $(Me_2N)_3\overset{+}{P}H$ p-$CH_3C_6H_4SO_3^-$ from its spectral properties, notably ^{31}P NMR (δ + 44.1, $^1J_{PH}$ = 639 Hz). The anion has very low nucleophilicity, and the salt proved to be quite stable; it was unchanged

TABLE I

Data for synthesis of 1-dialkylamino-3-phospholene-1-oxides

Compound	Molar ratio, acid to $(R_2N)_3P$	Yield, %	B.p. °C (mm)	Calcd, % C	Calcd, % H	Calcd, % P	Found, % C	Found, % H	Found, % P
1[a]	1 : 1[b]	93	98 (0.5)	—	—	—	—	—	—
2	2 : 1[c]	80	120 (0.5)	—	—	16.58	—	—	16.21
3	1 : 1[d]	95	103 (0.3)[e]	55.49	9.25	17.92	55.71	9.14	17.76
4	2 : 1[f]	75	120 (0.3)[g]	59.70	9.95	15.42	59.53	10.04	15.56

[a] Hygroscopic. Analysis not successful.
[b] At 2 : 1, yield = 90%; at 3 : 1, 65%.
[c] At 3 : 1, yield = 75%.
[d] At 2 : 1, yield = 91%; at 3 : 1, 68%.
[e] M.p. 39–40°.
[f] At 3 : 1, yield = 70%.
[g] M.p. 62–63° (pentane).

TABLE II

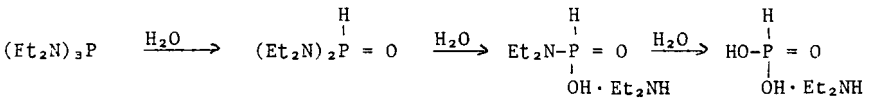
NMR spectral data for 1-dialkylamino-3-phospholene-1-oxides

Compound	δ ^{31}P		δ ^{13}C (J_{CP}, Hz) in $CDCl_3$						
	C_6D_6	$CDCl_3$	C-2	C-3	C-4	C-5	3-CH_3	N—C	N—C—CH_3
1	+63.5	+68.2	33.5(81.8)	136.9(14.7)	121.1(9.8)	30.3(80.6)	20.6(12.2)	35.8(0)	—
2	+60.9	+65.5	35.0(83.0)	137.1(15.6)	121.7(9.6)	32.6(80.1)	20.5(11.7)	38.0(3.9)	14.3(2.0)
3	+56.9	+61.5	34.7(83.5)	127.5(11.0)	127.5(11.0)	34.7(83.5)	16.0(14.3)	35.3(2.0)	—
4	+53.5	+58.4	37.4(82.0)	128.9(11.0)	128.9(11.0)	37.4(82.0)	16.3(13.9)	38.4(3.0)	14.4(2.9)

on refluxing in benzene for 48 h. No evidence for the formation of such a salt from the phosphorus-based acids was obtained. Sulfonic acids are also not prone to undergo dehydration to anhydrides, which may be a complicating factor with the phosphorus acids.

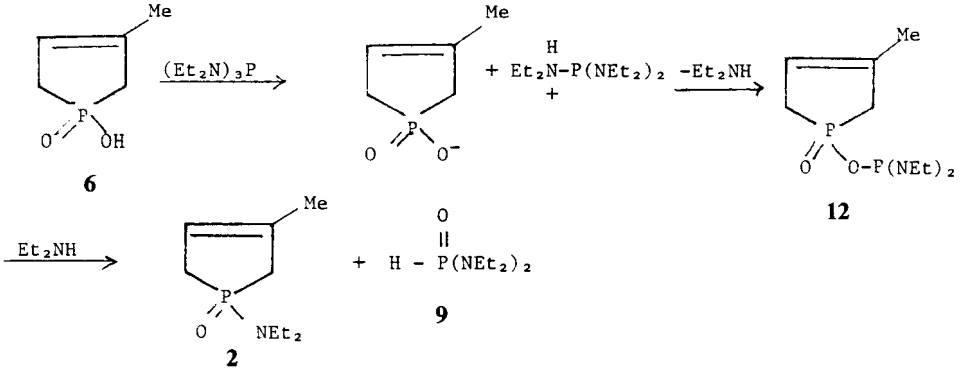
Mechanism of Amide Formation

^{31}P NMR spectroscopy has been employed to probe the mechanism of phosphinamide formation. The reaction of 3-phospholene **6** with $(Et_2N)_3P$ had a rate suitable for this study. The products from the successive replacement of Et_2N by HO— from the trisaminophosphine were first prepared and characterized. These products were made by partial hydrolysis, with the first to form being the bisamino derivative **9** (δ ^{31}P ($CDCl_3$) + 17.9, $^1J_{PH}$ = 564 Hz) followed by the monoamino derivative **10** (δ ^{31}P ($CDCl_3$) = +2.0, $^1J_{PH}$ = 584 Hz). Phosphorous acid (probably as salt **11**), δ ^{31}P (D_2O) + 2.8, $^1J_{PH}$ = 569 Hz was the product of complete hydrolysis.

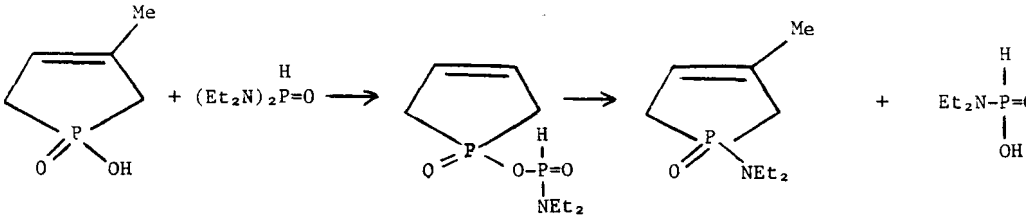


9 **10** **11**

In the 1 : 1 reaction of **6** and $(Et_2N)_3P$ the final products were the phosphinamides **2** and **9**. The reaction proceeded too rapidly to observe intermediate products, but from later observations (*vide infra*) the presence of anhydride **12** can be inferred.

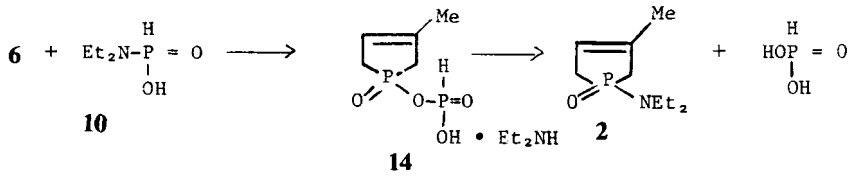


The bisamino derivative **9** is slower in its reaction with acid **6** than is the trisamino compound. However, when **6** is present initially in a 2 : 1 ratio with respect to the trisamino phosphine, **9** can then function as a donor of Et_2N to form anhydride **13**. In this case, the anhydride is stable enough to permit detection by NMR before its decay. It gave weak doublet of doublet signals at δ ^{31}P +62.3 and −0.8 ($^3J_{PP}$ = 29.3 Hz) with the upfield doublet splitting further ($^1J_{PH}$ = 560 Hz) when proton coupling was restored.



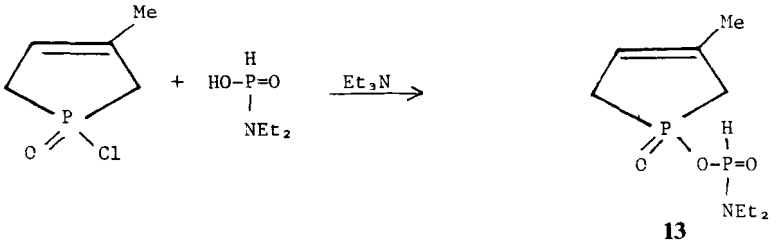
6 **13** **2**

Compound **10** can also function as a Et_2N donor when the reactant ratio (3 : 1) demands it, and the anhydride can then be detected by a weak doublet of doublets (δ ^{31}P + 62.4 and −8.5, $^3J_{PP}$ = 26.9 Hz; proton coupling gave $^1J_{PH}$ = 654 for the upfield signal) probably as the Et_2NH salt (**14**).



10 **14** **2**

To insure the correctness of the anhydride structures **13** and **14**, they were generated in solution by the independent reactions shown below. Anhydride **13** had the same ^{31}P NMR spectral parameters as given above. The anhydride from phosphorous acid was obtained as the triethylamine salt (**15**), but its ^{31}P spectrum was nearly identical to the diethylamine salt **14**.



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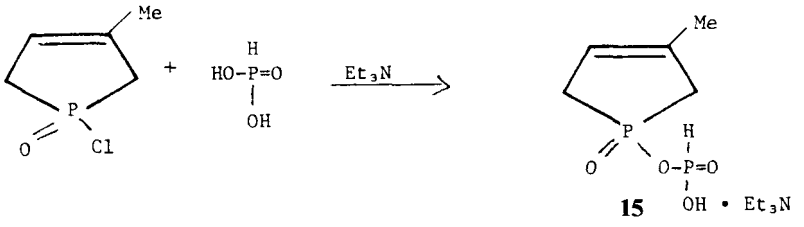

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EXPERIMENTAL SECTION

General. Proton NMR spectra were obtained on an IBM NR-80 spectrometer at 80 MHz, using tetramethylsilane (TMS) as an internal standard. Phosphorus-31 spectra (FT) were obtained on a JEOL-FX 90Q spectrometer at 36.2 MHz, using 85% H_3PO_4 as an external standard with an internal deuterium lock. Negative shifts are upfield and positive shifts downfield of the reference. Carbon-13 spectra (FT) were obtained on a JEOL FX-90Q spectrometer at 22.5 MHz, using TMS as an internal standard. Broadband proton noise-decoupling was employed on all carbon-13 and phosphorus-31 NMR spectra. Melting points were taken on a Mel-Temp apparatus and are corrected; boiling points are uncorrected. Combustion analyses were performed by MHW Laboratories, Phoenix, AZ.

Transaminations of 1-hydroxy-3-phospholene-1-oxides with a molar equivalent of tris(N,N-dialkylamino)phosphines. A solution of 0.010 mol of the phospholene and 0.010 mol of the aminophosphine was prepared in 20 ml of benzene and allowed to stand for 24 h. Benzene was removed under reduced pressure, and the residue taken up in 3% methanol in chloroform. The solution was mixed with 5 g of silica gel, creating an exotherm, and the mixture was stirred for 1 h. The mixture was filtered and further purified by chromatography on silica gel with the same solvent. Final purification was accomplished by distillation. Data from the syntheses of amides **1**, **2**, **3**, and **4** are provided in Table I; spectral data appear in Table II.

Transamination with one-half or one-third of a molar equivalent of aminophosphine. A solution of 0.010 mol of the aminophosphine in 30 ml of benzene was treated with either 0.020 mol or 0.030 mol of the 1-hydroxyphospholene-1-oxide. The solution was refluxed for 6 h under nitrogen. The product was isolated as in the preceding procedure, with omission of the batch silica gel treatment.

2-(N,N-Dimethylamino)-1,3,4,7-tetrahydroisophosphindole-2-oxide (**5**). 2-Hydroxy-1,3,4,7-tetrahydroisophosphindole-2-oxide[2a] (1.2 g, 7.0 mmol) was suspended in 50 ml of benzene and treated with 1.2 g (7.4 mmol) of tris(*N,N*-dimethylamino) phosphine. The mixture was stirred for 1 h and then washed with 50 ml of saturated sodium bicarbonate. The aqueous layer was washed with three 50-ml portions of chloroform, and the organic extracts dried over magnesium sulfate. Solvent was removed and the residue was chromatographed on silica gel with 3% methanol in chloroform as eluant. The amide (**5**) was obtained as a white solid (1.0 g, 66%); it was extremely hygroscopic and was not analyzed; ^{31}P NMR ($CDCl_3$) δ +62.2; ^{13}C NMR δ 28.9 ($^3J_{PC}$ = 15.3 Hz, C-4,7), 33.1 ($^1J_{PC}$ = 83.5 Hz, C-1,3), 35.6(CH_3), 123.5 ($^4J_{PC}$ = 2.5 Hz, C-5,6), 128.3 ($^2J_{PC}$ = 12.1 Hz, C-3a,7a).

Reaction of p-toluenesulfonic acid with tris(N,N-dimethylamino)phosphine. Anhydrous *p*-toluenesulfonic acid (0.86 g, 5.0 mmol) in 20 ml of benzene was treated with 0.815 g (5.0 mmol) of tris(*N,N*-dimethylamino)phosphine. Some oil separated rapidly. The mixture was refluxed for 48 h. The oil and the liquid gave the same ^{31}P NMR signal and were combined: ^{31}P δ + 44.1 with $^1J_{PH}$ = 639 Hz; ^{13}C NMR δ 19.4 CH_3—C, 33.8 (d, J = 5.5 Hz, CH_3—N), 124.0, 126.6, 137.1, 142.6 (all Ar carbons); ^{1}H NMR δ 2.65 (d, $^3J_{PH}$ = 11 Hz, CH_3—N).

Reaction of diethyl phosphate with tris(N,N-dimethylamino)phosphine. A solution of 1.34 g (10 mmol) of diethyl phosphate and 1.63 g (10 mmol) of tris(*N,N*-dimethylamino)phosphine in 25 ml of benzene was refluxed for 30 h. Benzene was removed on a rotary evaporator and the liquid residue Kugelrohr-distilled. ^{31}P NMR showed the presence of several compounds; signals were recognized for $(Me_2N)_2PHO$ (**9**) at δ +23.3 and $(EtO)_2PO(OH)$ at +0.2, with reaction products at +10.6 (presumably $(Me_2N)P(O)(OEt)_2$, lit.[5] + 11.1), and −1.2 (unidentified; $^1J_{PH}$ = 0). The desired $(Me_2N)P(O)(OEt)_2$ was formed in 30% yield from the starting $(EtO)_2PO(OH)$, as approximated by integration of the ^{31}P signals. Attempts to isolate the product by chromatography were not successful.

ACKNOWLEDGMENTS

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