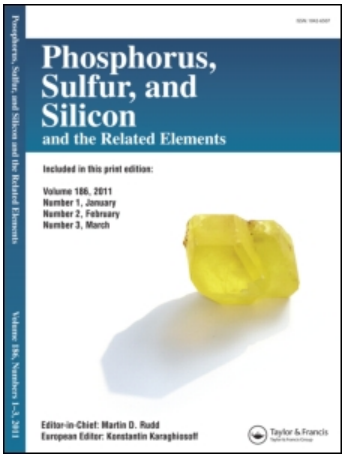

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1,3,2-DIAZAPHOSPHORINANES. IV. PREPARATION AND CONVERSIONS OF 4-OXO-1,3,2-DIAZAPHOSPHORINANES

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1,3,2-DIAZAPHOSPHORINANES. IV. PREPARATION AND CONVERSIONS OF 4-OXO-1,3,2-DIAZAPHOSPHORINANES

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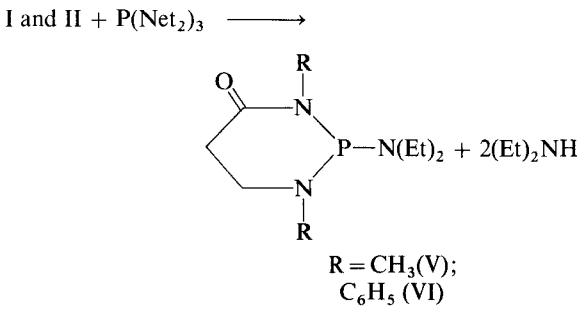
Novel 1,3,2-diazaphosphorinanes containing the carbonyl group in the ring have been obtained and their properties investigated. The structures of the products were identified by IR- and ^{31}P and ^{13}C NMR spectroscopy.

With respect to basicity and some other properties, 1,3,2-diazaphosphorinanes differ from the corresponding noncyclic phosphoric acid amides.[1–4] The favorable conditions that exist in such compounds for π-bonding of nitrogen and phosphorus atoms which are part of the six-member cyclic system are apparently responsible for the differences. In view of this, as well as the importance of such derivatives for the solution of the conformation and synthesis problems, the present work was directed at 4-oxo-1,3,2-diazaphosphorinanes.

4-Oxo-1,3,2-diazaphosphorinanes were synthesized from β-substituted propionic acid amides (I and II) which could be easily produced by reacting methyl acrylates with primary amines.[5,6] In conventional practice, diazaphosphorinanes are produced by reacting 1,3-diamines with phosphorus trichloride in the presence of a tertiary amine, which reaction yields 2-chloro-diazaphosphorinanes.[1–4,7–10] However, if aminoamides are to be used instead of diamines, phosphorylation with phosphorus trichloride fails to produce the desired compounds. It is interesting to note that alkyldichlorophosphines also poorly react with aminoamides (I and II). In this case the desired products are obtained, but in too small yields:

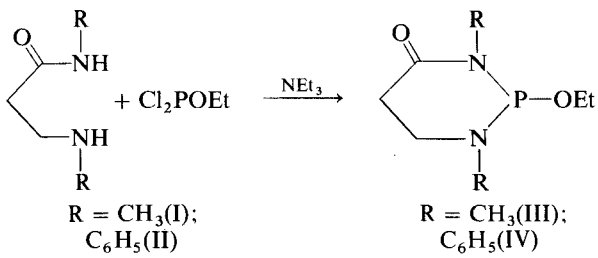
Phosphorylation of the aminoamides I and II with tri(diethylamino)phosphine:



was found to be a much more productive method for obtaining 4-oxo-1,3,2-diazaphosphorinanes.

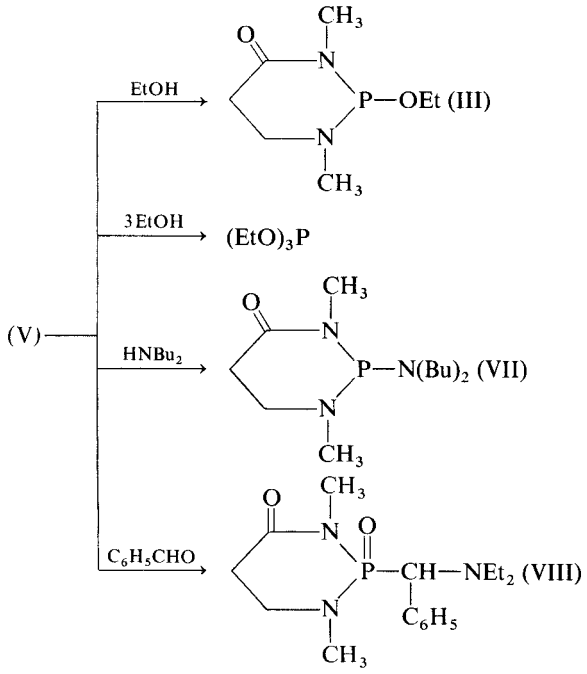
The reaction was carried out at 150°C, the product yields were almost 100%.

We believe that the difference in phosphonylation of compounds (I and II) with PCl_3 or $ROPCl_2$ and $P[N(C_2H_5)_2]_3$ are due to the tendency of the ambident carbamide group to become phosphonylated via two different paths (at O or P). In the case of reaction with tri(diethylamino)phosphine,



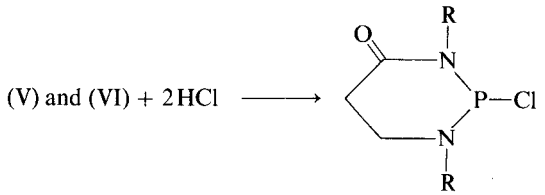
the phosphonylation involves nitrogen as already observed earlier in similar systems,[11,12]

The synthetic triamides V and VI reacted readily with various nucleophilic agents:



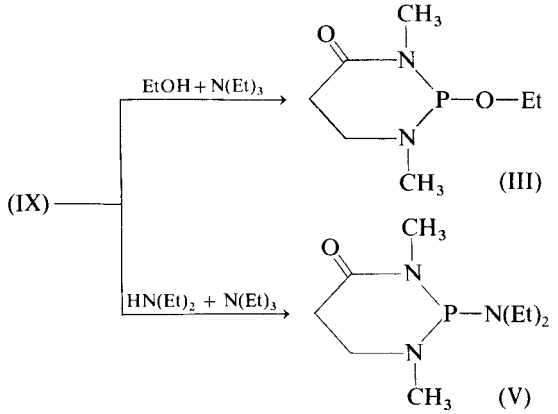
Both partial and complete alcoholysis experiments have shown that the exocyclic P—N bond easily breaks yielding the ester-amide (III); the conversion of an endocyclic P—N bond requires an excess of alcohol and longer heating.

It should be noted that the exocyclic P—N-bond easily reacts with hydrogen chloride producing cyclic compounds (IX and X):

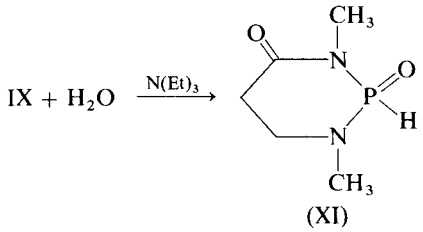


R = CH_3 (IX); C_6H_5 (X)

The reaction between the compound (IX) and ethyl alcohol delivers ester-amides (III) in good yield. Reaction between compound (IX) and diethylamine gives the cyclic triamide (V):



By hydrolysis in the presence of triethylamine 2-chloro-4-oxo-1,3,2-diazaphosphorinane (IX) was converted to compound (XI) in good yield:



It was difficult to isolate the partial cyclic phosphorous acid diamide (XI) because it contained triethylamine chlorohydrate. The crude product had therefore to be first passed through a silica gel column and then distilled under a high vacuum. In the ^{31}P NMR-spectra of this compound one doublet signal with a chemical shift of 6.5 ppm and a spin-spin interaction constant $^1J_{(P-H)}$ of 637 Hz can be observed.

In the present work two chemical conversions of the cyclic diamide (XI) are reported:

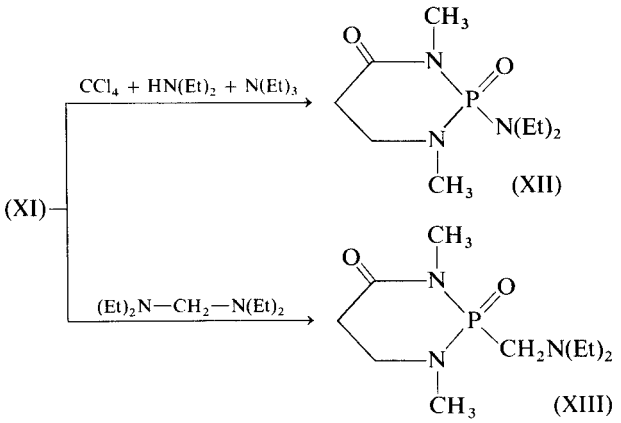
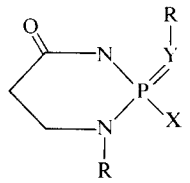


TABLE I

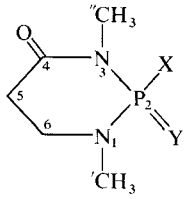
4-oxo-1,3,2-diazaphosphorinanes



N	R	X	Y	Yield (%)	B.p°C (mmHg)	d_4^{20}	n_D^{20}	MR_D found	MR_D calc.	Found % C	Found % H	Found % P	Calculated % C	Calculated % H	Calculated % P	$\delta^{31}P$ (ppm)
V	CH_3	$N(Et)_2$		85.0	110–111 (1)	1.0693	1.5085	60.66	61.53	49.23	8.98	14.55	49.76	9.22	14.28	107
III	CH_3	OEt		52.0	80–81 (1)	1.0878	1.4920	50.63	50.12	44.12	7.83	16.00	44.20	7.89	16.30	123
XII	CH_3	$N(Et)_2$	O	57.0	155–157 (10^{-4})	—	1.4898	—	—	45.91	8.82	13.02	46.35	8.59	13.30	12.75
VII	CH_3	$N(Bu)_2$		74.0	135–136 (1)	0.9370	1.4948	80.91	80.00	57.61	9.83	11.14	57.73	10.26	11.35	106.8
VIII	CH_3	CH-Ph | $N(Et)_2$	O	67.0	mp°C 175–176	—	—	—	—	60.53	7.73	9.52	59.44	8.05	9.59	23.0
IX	CH_3	Cl		72.0	96–97 (1)	1.3265	1.5410	42.74	42.71	33.20	5.03	16.78	33.24	5.54	17.17	145.2
X	C_6H_5	Cl		67.0	mp°C 161–162	—	—	—	—	58.71	4.72	10.44	59.11	4.58	10.14	131.25
XI	CH_3	H	O	63.5	Bath t° 135–140 (10^{-4})	—	1.5113	—	—	37.26	7.02	19.43	37.03	6.79	19.13	6.5 J_{P-H} 637 Hz
XIII	CH_3	$CH_2N(Et)_2$	O	79.5	Bath t° 135–140 (10^{-4})	1.0941	1.4958	65.92	65.59	48.81	9.12	12.20	48.58	8.90	12.55	24.7
XIV	CH_3	$N(Et)_2$	S	76.0	Bath t° 90–95 (10^{-4}) mp°C 43–44	—	—	—	—	43.52	8.21	12.00	43.38	8.03	12.40	70.5
XV	C_6H_5	$N(Et)_2$	S	64.0	mp°C 125–126	—	—	—	—	63.86	6.42	8.47	63.50	6.68	8.64	62.5
XVI	CH_3	OEt	S	72.0	108–109 (1,5)	—	1.5232	—	—	37.47	6.48	13.83	37.83	6.76	13.96	71.25

TABLE II

Chemical shifts, ppm, in the ^{13}C spectra and coupling constants $J_{(C-P)}$, Hz.

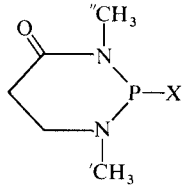


Cpd. No.	X	Y	Parameter	C^4	C^5	C^6	N-$'CH_3$	N-$''CH_3$	C^7	C^8
III	OCH_2CH_3	—	δ	169.2	33.2	44.8	31.1	37.3	59.8	16.9
			J	6.1	0	7.3	31.1	39.6	15.9	3.1
V	$N(CH_2CH_3)_2$	—	δ	170.0	34.6	39.6	30.36	37.9	45.5	14.73
			J	6.1	0	20.7	28.1	35.4	4.3	2.4
XVI	OCH_2CH_3	S	δ	169.6	32.6	44.0	28.8	36.6	63.1	16.05
			J	0	0	0	4.7	6.1	5.4	2.5
†	OCH_2CH_3	—	δ	45.5	26.3	45.5	39.9	39.9	60.4	18.1
			J	6.4	0.6	6.4	31.4	31.4	19.3	4.9
†	$N(CH_2CH_3)_2$	—	δ	47.6	27.3	47.6	39.9	39.9	41.3	15.7
			J	3.0	0.5	3.0	31.9	31.9	19.5	2.5

† The data for unsubstituted 1,3,2-diazaphosphorinanes taken from [4] are reported here for comparison.

TABLE III

Effect of carbonyl substitution of chemical shifts of ^{13}C

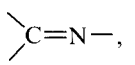


Compound	X	$\alpha(C^4)$	$\beta(C^5)$	$\gamma(C^6)$	N'-CH_3	N''-CH_3
III	OCH_2CH_3	123.7	6.9	−0.7	−8.8	−2.6
V	$N(CH_2CH_3)_2$	122.4	7.3	−8.0	−9.54	−2.4

The compounds (III, V, IV) were easily oxidized and combined with sulfur yielding the corresponding phosphates and thiophosphates (XII, XIV, XV, XVI). The yields and characteristic constants of the reaction products are shown in Table I.

The structures of the synthesized compounds were identified by IR- and ^{31}P and ^{13}C NMR-spectroscopy. The IR spectra of (XIV and XV) show strong absorption around 1690 cm^{-1} (XIV) and 1715 cm^{-1} (XV) which indicates the presence of the

group in the cycle. The spectra did not contain the characteristic absorption bands of the group



demonstrating that by the phosphonylation reaction only the diazaphosphorinane cycle was obtained. It should be noted that the HV- and IR-absorption of the carbonyl group in 4-oxo-1,3,2-diazaphosphorinanes and in the starting amino-amides (I, II) were very similar, which means that the original p, π-bonding is preserved in the synthesized systems.

The ^{31}P NMR spectra obtained in this work show that all the compounds having the carbonyl group in the 4-position exist as one geometrical isomer. The chemical shifts of ^{31}P are listed in Table 1, the ^{13}C NMR spectra in Table II)†

It was found, for instance, that the carbonyl group could selectively affect the N-methyl group position within the ring skeleton. This effect manifested itself as inequality of the respective P—N—C geminate coupling constants. The effect was found to be different for P(III) and P(V) compounds.

The carbonyl group may also be detected by its magnetic screening of the neighbouring carbon atoms. By comparing these results with the data on the magnetic screening of symmetrical diazaphosphorinanes[4] we were able to detect carbonyl substitution in 1,3,2-diazaphosphorinanes (see Table III).

EXPERIMENTAL

All the reactions were carried out in a dry nitrogen atmosphere. The reagents were chromatographed on a Brockman II alumina layer in systems: benzene-dioxane (3:1; A) and methanol-benzene-chloroform (1:3:4; B). The chromatograms were developed with iodine vapor.

The ^{13}C and ^{31}P NMR spectra were taken with the aid of Bruker-HX-90E and C-60 HL instruments. The ^{13}C chemical shifts were measured relative to TMS. The chemical shifts of ^{31}P were related to 85% phosphoric acid.

2-Ethoxy-4-oxo-1,3-dimethyl-1,3,2-diazaphosphorinane (III).

To a mixture of 0.06 mol of N-methyl-amide of β-methylamino-propionic acid (I) and 0.12 mol of triethylamine dissolved in 150 ml of abs. benzene are added at 0–5°C 0.06 mols of ethyl dichlorophosphite. The reaction mixture is kept for two hours at room temperature, triethylamine chlorohydrate is filtered off, the solvent is removed, and the residue is distilled *in vacuo*. Yield 5.9 g (52%), b.p. 80–81°C (1 mm), n_D^{20} 1.4920; d_4^{20} 1.0878; MR_D 50.63; calc. 50.12; R_f in system A is 0.91; NMR $\delta^{31}P$ 123 ppm.

2-Ethoxy-4-oxo-1,3-diphenyl-1,3,2-diazaphosphorinane (IV)

By the above-described procedure, 3.1 g (34%) of compound (IV) is obtained from 0.03 mol of β-anilinopropionic acid anilide (II), 0.06 mol of triethylamine and 0.03 mol of ethyl-dichlorophosphite, b.p. 202–207°C (10^{-4} mm); n_D^{20} 1.5561; R_f in the system A is 0.75; NMR δ ^{31}P 115 ppm.

† The signals in the ^{13}C spectra were assigned on the basis of the chemical shifts as well as against the results of partial double resonance experiments.[13]

2-Diethylamido-4-oxo-1,3-dimethyl-1,3,2-diazaphosphorinane (V)

0.09 Mol of aminoamide (1), 0.09 mol of tri(diethylamino)phosphine are heated in a Claisen flask at 140–150°C simultaneously with nitrogen until diethylamine is developed. The residue is distilled *in vacuo*. Yield 5.5 g (85%); b.p. 110–111°C (1 mm); n_D^{20} 1.5085; d_4^{20} 1.0693; MR_D60.66; calc. 61.53; R_f in system A is 0.85; MNR δ ^{31}P qp7 ppm.

2 - Diethylamido - 4 - oxo - 1,3 - diphenyl - 1,3,2 - diazaphosphorinane (VI)

By the above-described procedure, 11.9 g (81%) of compound (VI) are obtained from 0.04 mol of anilinoanilide (II) and 0.04 mol of tri(diethylamino)phosphine. NMR δ ^{31}P 98 ppm; R_f in system A is 0.56.

Alcoholysis of 2 - diethylamido - 4 - oxo - 1,3 - dimethyl - 1,3,2 - diazaphosphorinane

a) 0.01 Mol of triamide (V) and 0.01 mol of ethyl-alcohol are heated for one hour at 70°C and then distilled *in vacuo*. The yield of 2-ethoxy-4-oxo-1,3-dimethyl-1,3,2-diazaphosphorinane (III) is 1.9 g (86.5%); b.p. 80°C (1 mm Hg); NMR δ ^{31}P 122.5 ppm; R_f in system A is 0.91.

b) 0.01 mol of triamide and 0.05 mol of ethylalcohol are stirred for three hours at 70°C, the excess of alcohol is removed and the residue is distilled *in vacuo*. The yield of triethylphosphite is 1.6 g (81%). B.p. 62–64°C (25 mm); n_D^{20} 1.4105; R_f in system A is 0.95; NMR δ ^{31}P 138 ppm.

2 - Dibutylamido - 4 - oxo - 1,3 - dimethyl - 1,3,2 - diazaphosphorinane (VII)

0.02 Mol of the cyclic triamide (III) and 0.02 mol of dibutylamine are heated at a temperature 135–140°C until diethylamine development stops. The residue is distilled *in vacuo*. Yield 4 g (74%); b.p. 135–136°C (1 mm); n_D^{20} 1.4948; d_4^{20} 0.9370; MR_D 80.91; calc. 80.00; R_f in system B 0.83; NMR δ ^{31}P 106.8 ppm.

Reaction between 2 - diethylamido - 4 - oxo - 1,3 - dimethyl - 1,3,2 - diazaphosphorinane and benzaldehyde

The mixture of 0.018 mol of triamide (III) and 0.018 mol of benzaldehyde is heated for three hours at 70°C. Yield of (VIII) is 3.95 g (67%); m.p. 175–176°C; R_f in system B is 0.75; NMR δ ^{31}P 23 ppm.

2-Chloro-4-oxo-1,3,2-diazaphosphorinanes (X,XI)

To a solution of 0.08 mol of hydrogen chloride in dry dioxane 0.04 mol of triamides (V or VI) are added at a temperature between −10 and −15°C. The reaction mixture is kept for three hours at room temperature, diethylamine chlorohydrate is filtered off and the residue is distilled *in vacuo*. The yields and constants are given in Table I.

Reaction between 2 - (H) - 2,4 - dioxo - 1 - 1,3 - dimethyl - 1,3,2 - diazaphosphorinane (XI) and tetraethyl diaminomethylane

The mixture of 0.02 mol of compound (XI) and 0.02 mol of tetraethyl diaminomethylene is heated for an hour at 120–125°C. The diethylamine product is condensed and the residue is

distilled *in vacuo*. Yield of compound (XIII) 4.1 g (79.5%); bath temp. 135–140°C (10^{-4} mm); n_D^{20} 1.4958; d_4^{20} 1.0941; MR_D 65.92, calc. 65.59; NMR δ ^{31}P 24.7 ppm; R_f in system A is 0.37.

2-Diethylamido-2-thio-4-oxo-1,3,2-diazaphosphorinane (XIV and XV)

The mixture of 0.01 mol of the triamide (V or VI) and 0.01 mol of sulphur in 15 ml of abs. benzene is stirred over three hours at room temperature. The solvent is removed and the residue is distilled *in vacuo*. The yield and constants of XIV and XV are given in Table I.

2 - Ethoxy - 2 - thio - 4 - oxo - 1,3 - dimethyl - 1,3,2 - diazaphos - phorinane (XVI)

Using the preceding procedure 5.9 g (72%) of compound (XVI) are obtained from 0.04 mol of ester-amide (III) and 0.04 mol of sulfur. b.p. 108–109°C (1.5 mm); R_f in system A is 0.94; NMR δ ^{31}P 71.25 ppm.

2 - (H) - 2,4 - dioxo - 1,3 - dimethyl - 1,3,2-diazaphosphorinane (XI)

A mixture of 0.045 mol of water, 0.045 mol triethylamine and 5 ml of tetrahydrofuran is added at a temperature of 0 to 5°C to 0.045 mol of compound (IX) in 80 ml abs. benzene. The reaction mixture is stirred for 5 hours at room temperature, the triethylamine hydrochloride precipitate is filtered off, the solvent is removed and the residue is distilled *in vacuo*. Yield 4.6 g (63.5%); b.p. 135–140° (10^{-4}); R_f in system A on silica gel is 0.18; n_D^{20} 1.5113; d_4^{20} 1.1631; MR_D 41.74, calc. 41.33; NMR δ ^{31}P 6.5 ppm; $^1J_{(P-H)}$ 637 Hz.

2 - Diethylamido - 2,4 - dioxo - 1,3 - dimethyl - 1,3,2 - diazaphos - phorinane (XII)

a) A stream of nitrogen oxides is passed through a solution of 0.02 mol of compound (V) in 15 ml of abs. benzene for a period of 3 hours. The solvent is removed, the residue distilled *in vacuo*. Yield 2.8 g (57%); b.p. 155–157°C (10^{-4} mm); n_D^{20} 1.4898; NMR ^{31}P 12.75 ppm.

b) 0.02 mol of 2-(H)-2,4-dioxo-1,3-dimethyl-1,3,2-diazaphosphorinane (XI) are added to a mixture of 0.04 mol of diethylamine and 0.02 mol of CCl_4 in 40 ml of abs. benzene at 0° to 5°C. The reaction mixture is stirred for 5 hours at room temperature, the diethylamine hydrochloride residue is filtered off, the solvent is removed and the residue is distilled *in vacuo*. Yield 3.8 g (41%); b.p. 150–155°C (10^{-4} mm); n_D^{20} 1.4895; R_f in system A is 0.43; NMR ^{31}P 12.5 ppm.

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