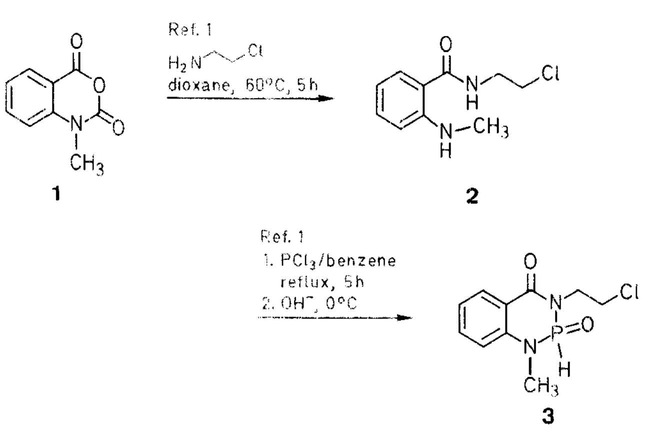
Studies on the Synthesis of Phosphorus Heterocycles I. [1,4,3]Thiazaphosphorino[3,4-*b*][1,3,2]benzodiazaphosphorine 12-Oxides

Ruyu Chen,* Rong Bao*

Institute of Elementoorganic Chemistry, Nankai University, Tianjin, People's Republic of China

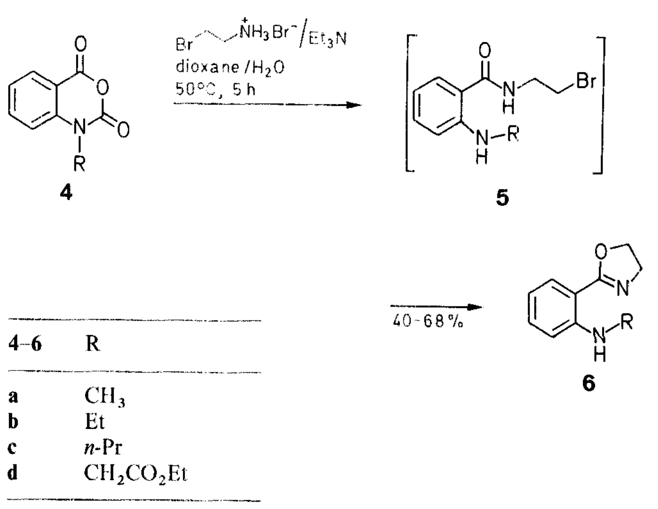
N-Substituted isatoic anhydrides **4** react with 2-bromoethylamino hydrobromide in the presence of triethylamine to form oxazolines **6**, which are treated with phosphorus trichloride to give a key intermediate **7**. Reaction of **7** with phenyl isothiocyanate yields fused phosphorus heterocycles **9**. Several methods for preparing compounds **9** and the mechanism of cyclization are discussed.

Coppola has reported[1] the synthesis of 1,3,2-benzodiazaphosphorine ring system **3** by the reaction of *N*-methylisatoic anhydride (**1**) with 2-chloroethylamine followed by treatment of the intermediate anthranilamide derivative **2** with phosphorus trichloride (Scheme **A**).



Scheme **A**

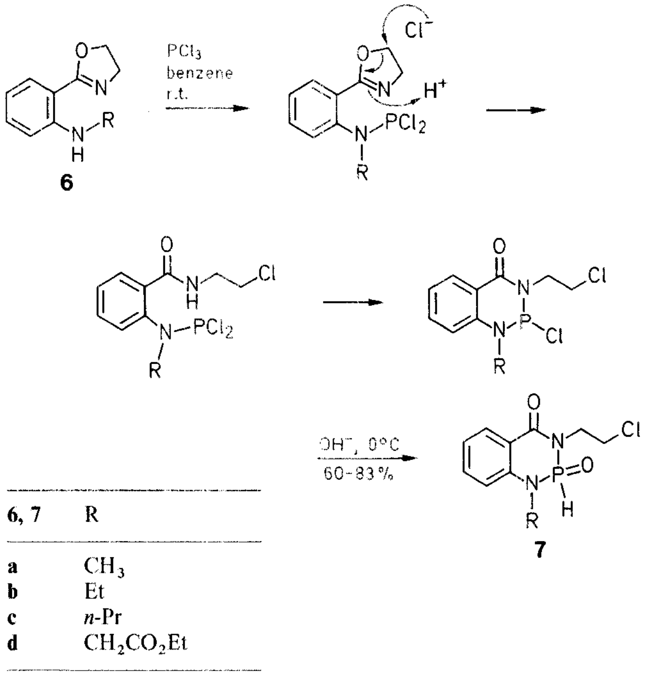
We attempted to synthesize several of such derivatives starting from *N*-substituted isatoic anhydrides **4** using 2-bromoethylamine (generated from its hydrobromide salt) in place of 2-chloroethylamine and obtained oxazolines **6** by cyclization of the expected intermediate anthranilamide derivatives **5** (Scheme **B**).



4-6	R
a	CH_3
b	Et
c	*n*-Pr
d	CH_2CO_2Et

Scheme **B**

The structure of new compounds **6** was confirmed by IR, ^{1}H-NMR, MS and elemental analyses (Table 1). Treatment of **6** with phosphorus trichloride produced the 1,3,2-benzodiazaphosphorines **7** in good yields (Table 2), for which we suggest the mechanism given in Scheme **C**.



6, 7	R
a	CH_3
b	Et
c	*n*-Pr
d	CH_2CO_2Et

Scheme **C**

Table 1. Compounds **6** Prepared

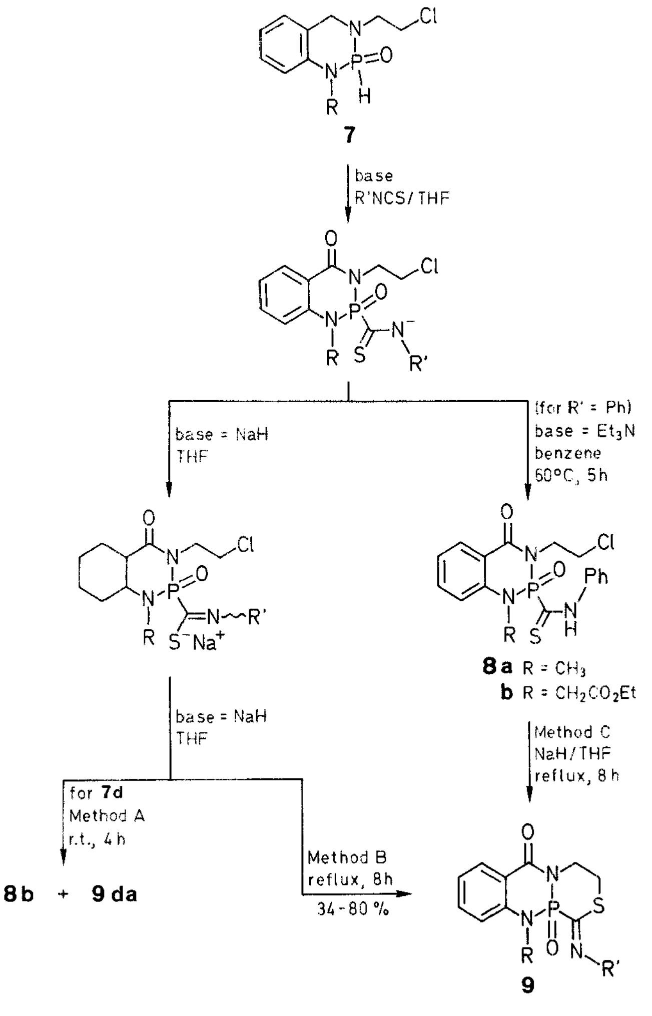
Product	Yield[a] (%)	mp (°C)[b]	Molecular Formula[c]
6a[d]	49	50–51	$C_{10}H_{12}N_2O$ (176.1)
6b	45	39–40	$C_{11}H_{14}N_2O$ (190.1)
6c	40	62–63	$C_{12}H_{16}N_2O$ (204.1)
6d	68	92–94	$C_{13}H_{16}N_2O_3$ (248.2)

[a] Yield of pure isolated product.

[b] Solvent for recrystallization: petroleum ether/EtOAc (5 : 1).

[c] Microanalyses obtained: C ±0.48, H ±0.64, N ±0.49. A better values were not obtained.

[d] See experimental for the spectral data.



9	R	R′	9	R	R′
aa	CH_3	Ph	**ca**	*n*-Pr	Ph
ab	CH_3	$4\text{-}CH_3C_6H_4$	**cb**	*n*-Pr	$4\text{-}CH_3C_6H_4$
ac	CH_3	$4\text{-}CH_3OC_6H_4$	**cc**	*n*-Pr	$4\text{-}CH_3OC_6H_4$
ad	CH_3	$4\text{-}ClC_6H_4$	**cd**	*n*-Pr	$4\text{-}ClC_6H_4$
ae	CH_3	$4\text{-}BrC_6H_4$	**ce**	*n*-Pr	$4\text{-}BrC_6H_4$
ba	Et	Ph	**da**	CH_2CO_2Et	Ph
bb	Et	$4\text{-}CH_3C_6H_4$	**db**	CH_2CO_2Et	$4\text{-}CH_3C_6H_4$
bc	Et	$4\text{-}CH_3OC_6H_4$	**dc**	CH_2CO_2Et	$4\text{-}CH_3OC_6H_4$
bd	Et	$4\text{-}ClC_6H_4$	**dd**	CH_2CO_2Et	$4\text{-}ClC_6H_4$
be	Et	$4\text{-}BrC_6H_4$	**de**	CH_2CO_2Et	$4\text{-}BrC_6H_4$

Scheme **D**

A series of condensed 1,3,2-benzodiazaphosphorines **9** were prepared by refluxing **7** with aryl isothiocyantes in the presence of sodium hydride in tetrahydrofuran (Scheme **D**). The new compounds were characterized by spectral data and elemental analyses (Table 3), and in the case of **9bd** the molecular structure was confirmed by X-ray analysis (Figure).

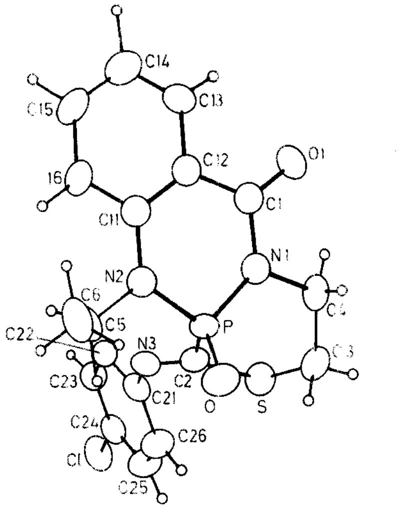


Figure: The molecular structure of **9bd**

From the Figure it can be seen that the ring carrying the sulfur atom has a boat conformation, and the P–C(2) and N(3)–C(21) bond are in *trans* postion. The bond lengths and angles of **9bd** are listed in Tables 4 and 5, respectively.

It was found that the use of different bases affected the direction of the reaction and yield of the products. When triethylamine was used as the base, the final product was **8** (Scheme **D**). Reaction of **7d** with phenyl isocyanate using sodium hydride as base at room temperature (Method **A**) afforded a mixture of **8b** and **9da**, while at the reflux temperature of THF (Method B) only **9** was obtained. We also attempted to synthesize **9** by cyclizing **8** (e.g. **8a**, Method C). Obviously Method C has more steps and gave lower yield than Method B (see experimental).

In summary, we have developed for the first time a one-pot synthesis of [1,4,3]thiazaphosphorino[3,4-*b*][1,3,2]benzodiazaphosphorine 12-oxides **9**. Results from preliminary bioassays indicate that **9aa** inhibits the growth of the coleptiles of wheat significantly.

Table 2. Compound **7** Prepared

Product	Yield[a] (%)	mp (°C)	Molecular Formula[b] or Lit. mp (°C)	^1H-NMR ($CDCl_3$/TMS) δ, J(Hz)	MS (70 eV) m/z (%)
7a	83	135–137	137–139[1]	3.15 (d, 3H, $J = 8$, CH_3); 3.5–4.3 (m, 4.5H, $NCH_2CH_2 + PH/2$); 6.7–8.2 (m, $4H_{arom}$); 18.4 (s, 0.5H, PH/2)	–
7b	61	97–98	$C_{11}H_{14}ClN_2O_2P$ (272.6)	1.4 (t, 3H, $J = 5$, $CH_2C\underline{H}_3$); 4.6–5.4 (m, 6H, $C\underline{H}_2CH_3 + NCH_2CH_2$); 4.5, 11.2 (d, 1H, $^1J_{P,H} = 649$); 7.0–8.3 (m, $4H_{arom}$)	273 (M^+, 15); 275 ($M^+ + 2$,5)
7c	60	91–92	$C_{12}H_{16}ClN_2O_2P$ (286.6)	1.4 (t, 3H, $J = 5$, $CH_2CH_2C\underline{H}_3$); 1.7 (m, 2H, $CH_2C\underline{H}_2CH_3$); 4.5–5.1 (m, 6H, $C\underline{H}_2CH_2CH_3 + NCH_2CH_2$); 4.3, 11.5 (d, 1H, $^1J_{P,H} = 649$); 7.1–8.3 (m, $4H_{arom}$)	–
7d	65	110–112	$C_{13}H_{16}ClN_2O_4P$ (330.6)	1.2 (t, 3H, $CH_2C\underline{H}_3$); 3.5–5.0 (m, 8H, $NCH_2CH_2 + NC\underline{H}_2CO_2C\underline{H}_2CH_3$), 4.3, 11.5 (d, 1H, $^1J_{P,H} = 649$); 6.5–8.1 (m, $4H_{arom}$)	330 (M^+, 9); 332 ($M^+ + 2$,3)

[a] Yield of pure isolated product.

[b] Satisfactory microanalyses obtained: C ±0.42, H ±0.08, N ±0.38.

Table 3. Compounds **9** Prepared

Product	Yield[a] (%)	mp (°C)	Molecular Formula[b]	^{1}H-NMR ($CDCl_3$/TMS) δ, J(Hz)	MS (70 eV) m/z (M^+, %)
9aa	70	134–136	$C_{17}H_{16}N_3O_2PS$ (357.2)	3.2 (dt, 1H, $J = 4$, 14.4, SCH_a); 3.3 (d, 3H, $J = 7.2$, CH_3); 3.9–4.5 (m, 3H, SCH_eCH_2); 6.9–8.2 (m, 9H_{arom})	357 (34)
9ab	78	130–131	$C_{18}H_{18}N_3O_2PS$ (371.2)	2.3 (s, 3H, $ArC\underline{H}_3$); 3.1 (dt, 1H, $J = 3.6$, 14.4, SCH_a); 3.3 (d, 3H, $J = 7.2$, NCH_3); 3.9–4.6 (m, 3H, SCH_eCH_2); 6.7–7.3 (m, 8H_{arom})	371 (9)
9ac	58	150–151	$C_{18}H_{18}N_3O_3PS$ (387.2)	3.15 (dt, 1H, $J = 3.6$, 14.4, SCH_a); 3.5 (d, 3H, $J = 7.2$, NCH_3); 3.8 (d, 3H, OCH_3); 3.9–4.6 (m, 3H, SCH_eCH_2); 6.7–8.3 (m, 8H_{arom})	–
9ad	48	161–162	$C_{17}H_{15}ClN_3O_2PS$ (391.7)	3.14 (dm, 1H, $J = 14.4$, SCH_a); 3.44 (d, 3H, $J = 7.2$, CH_3); 3.7–4.6 (m, 3H, SCH_eCH_2); 6.7–7.3 (m, 8H_{arom})	391 (33)
9ae	61	146–148	$C_{17}H_{15}BrN_3O_2PS$ (436.2)	3.15 (dm, 1H, $J = 3.6$, 14.4, SCH_a); 3.9–4.6 (3H, SCH_eCH_2); 6.7–8.3 (m, 8H_{arom})[c]	437 (16)
9ba	80	168–169	$C_{18}H_{18}N_3O_2PS$ (371.2)	1.4 (t, 3H, $CH_2C\underline{H}_3$); 3.13 (dt, 1H, $J = 3.6$, 14.4, SCH_a); 3.8–4.7 (m, 5H, $SCH_eCH_2 + C\underline{H}_2CH_3$); 6.8–7.3 (m, 9$H_{arom}$)	371 (50)
9bb	70	137–138	$C_{19}H_{20}N_3O_2PS$ (385.3)	1.4 (t, 3H, $CH_2C\underline{H}_3$); 2.3 (s, 3H, $ArC\underline{H}_3$); 3.1 (dt, 1H, $J = 3.6$, 14.4, SCH_a); 3.7–4.7 (m, 5H, $SCH_eCH_2 + C\underline{H}_2CH_3$); 6.7–8.3 (m, 8$H_{arom}$)	385 (80)
9bc	70	125–126	$C_{19}H_{20}N_3O_3PS$ (401.3)	1.4 (t, 3H, $CH_2C\underline{H}_3$); 3.1 (d, 1H, $J = 14.4$, SCH_a); 3.75 (s, 3H, OCH_3); 3.8–4.6 (m, 5H, $SCH_eCH_2 + C\underline{H}_2CH_3$); 6.7–8.3 (m, 8$H_{arom}$)	401 (100)
9bd	70	81–82	$C_{18}H_{17}ClN_3O_2PS$ (405.7)	1.44 (t, 3H, CH_2CH_3); 3.14 (dt, 1H, $J = 3.6$, 14.4, SCH_a); 3.8–4.6 (m, 5H, $SCH_eCH_2 + C\underline{H}_2CH_3$); 6.7–8.3 (m, 8$H_{arom}$)	–
9ca	53	154–155	$C_{19}H_{20}N_3O_2PS$ (385.1)	1.0 (t, 3H, CH_3); 1.8 (m, 2H, $NCH_2C\underline{H}_2CH_3$); 3.15 (d, 1H, $J = 14.4$, SCH_a); 3.6–4.6 (m, 5H, $SCH_eCH_2 + NC\underline{H}_2CH_2CH_3$); 6.8–7.3 (m, 9$H_{arom}$)	385 (17)
9cb	60	110–112	$C_{20}H_{22}N_3O_2PS$ (399.3)	1.0 (t, 3H, CH_3); 1.84 (m, 2H, $NCH_2C\underline{H}_2CH_3$); 3.12 (dt, 1H, $J = 3.6$, 14.4, SCH_a); 3.7–4.6 (m, 5H, $SCH_eCH_2 + NC\underline{H}_2CH_2CH_3$); 6.7–8.3 (m, 8$H_{arom}$)[c]	399 (30)
9cc	59	142–143	$C_{20}H_{22}N_3O_3PS$ (415.3)	1.0 (t, 3H, CH_3); 1.84 (m, 2H, $NCH_2C\underline{H}_2CH_3$); 3.13 (dt, 1H, $J = 3.6$, 14.4, SCH_a); 3.75 (s, 3H, OCH_3); 3.8–4.7 (m, 5H, SCH_eCH_2); $NCH_2CH_2CH_3$); 6.8–8.3 (m, 8H_{arom})	465 (14)
9cd	71	105–106	$C_{19}H_{19}ClN_3O_2PS$ (419.7)	1.0 (t, 3H, CH_3); 1.8 (m, 2H, $NCH_2C\underline{H}_2CH_3$); 3.2 (dm, 1H, $J = 14.4$, SCH_a); 3.7–4.6 (m, 5H, $SCH_eCH_2 + NC\underline{H}_2CH_2CH_3$); 6.75–8.3 (m, 8$H_{arom}$)	–
9ce	61	68–69	$C_{19}H_{19}BrN_3O_2PS$ (464.3)	1.0 (t, 3H, CH_3); 1.84 (m, 2H, $NCH_2C\underline{H}_2CH_3$); 3.13 (dm, 1H, $J = 14.4$, SCH_a); 3.7–4.6 (m, 5H, $SCH_eCH_2 + NC\underline{H}_2CH_2CH_3$); 6.6–8.3 (m, 8$H_{arom}$)	–
9da	13	161–162	$C_{20}H_{20}N_3O_4PS$ (429.3)	1.12 (t, 3H, CH_3); 3.2 (dt, 1H, $J = 4$, 14.4, SCH_a); 3.3–4.6 (m, 5H, $C\underline{H}_2CH_3 + SCH_eCH_2$); 4.79 (q, 2H, $J = 7.6$, 9, NCH_2CO); 7.6–8.3 (m, 9H_{arom})	429 (25)
9db	50	123–124	$C_{21}H_{22}N_3O_4PS$ (443.3)	1.16 (t, 3H, CH_3); 2.32 (s, 3H, $ArC\underline{H}_3$); 3.1 (dt, 1H, $J = 14.4$, SCH_a); 3.7–4.6 (m, 3H, SCH_eCH_2); 4.8 (q, 2H, $J = 7.6$, NCH_2CO); 6.7–7.3 (m, 8H_{arom})	443 (25)
9dc	54	78–79	$C_{21}H_{22}N_3O_5PS$ (459.3)	1.13 (t, 3H, CH_3); 3.2 (dt, 1H, $J = 4.7$, 14.4, SCH_a); 3.78 (s, 3H, OCH_3); 3.9–4.7 (m, 5H, $SCH_eCH_2 + C\underline{H}_2CH_3$); 4.78 (q, 2H, $J = 7.6$, 9, NCH_2CO); 6.7–8.3 (m, 8H_{arom})	459 (5)
9dd	63	128–130	$C_{20}H_{19}ClN_3O_4PS$ (463.7)	1.12 (t, 3H, CH_3); 3.2 (dt, 1H, $J = 3.6$, 14.4, SCH_a); 3.8–4.6 (m, 3H, SCH_eCH_2); 4.76 (q, 2H, $J = 7.6$, 9, CH_2CO); 6.78–8.3 (m, 8H_{arom})	463 (10)
9de	34	124–125	$C_{20}H_{19}BrN_3O_4PS$ (508.3)	1.12 (t, 3H, CH_3); 3.2 (dt, 1H, $J = 4$, 14.4, SCH_a); 3.7–4.6 (m, 5H, $SCH_eCH_2 + C\underline{H}_2CH_3$); 4.76 (q, 2H, $J = 7.6$, 9, CH_2CO); 6.6–8.3 (m, 8H_{arom})	509 (16)

[a] Yield of pure isolated product.

[b] Microanalyses showed the following derivations: C ±0.45, H ±0.30, N ±0.46.

[c] Selected data.

Melting points are uncorrected. IR spectra were recorded on a Nicolet 5 DX spectrophotometer. ^{1}H-NMR spectra were obtained using a JEOL FX-90 Q spectrometer. The X-ray analysis of compound **9bd** was done on a ENRAF-NONIUS CAD4 diffractometer. Microanalyses were obtained using a CHN CORDERD MT-3 element analyzer.

Benzene and THF were dried with NaH. PCl_3 was distilled freshly before use. Petroleum ether used has the boiling range 60–90 °C.

2-(2-Ethoxycarbonylmethylphenylamino)-4,5-dihydrooxazole (6d); Typical Procedure:

To a solution of **4d**[3] (42 mmol) in dioxane (160 mL) and water (40 mL) is added 2-bromoethylamino hydrobromide (8.6 g, 42 mmol) at 40 °C. The mixture is warmed to 50 °C and Et_3N is added. After stirring for 3 h at 50 °C, the mixture is cooled and extracted with EtOAc (2 × 50 mL). The organic phase is separated, dried (Na_2CO_3) and the solvent is evaporated at reduced pressure. The residual brown oil is purified by chromatography on a silica gel column (100 cm × 4 cm, 250–300 mesh) using petroleum ether/EtOAc (5:1, 1500 mL) as eluent. Evaporation of the solvent affords a colorless solid; yield: 7 g (68 %); mp 92–94 °C (petroleum ether/EtOAc) (Table 1).

$C_{13}H_{16}N_2O_3$	calc.	C 62.90	H 6.45	N 11.29
(248.2)	found	63.38	6.64	11.09

IR (KBr): ν = 1740 (C=O), 1635 cm^{-1} (C=N).

^{1}H-NMR ($CDCl_3$/TMS): δ = 1.3 (t, 3H, CH_3); 4.0 (s, 2H, $PhNC\underline{H}_2$); 4.1–4.2 (m, 6H, $OCH_2 + OCH_2CH_2N$); 6.4–6.8 (m, 4H_{arom}); 8.6 (br, 1H, NH).

MS (70 eV): m/z (%) = 248 (M^+, 17).

Table 4. Selected Bond Lengths (Å) of **9bd**

P	O	1.468(2)	C3	C4	1.532(5)
P	N1	1.668(3)	C5	C6	1.512(5)
P	N2	1.639(2)	C11	C12	1.404(5)
P	C2	1.829(3)	C11	C16	1.392(4)
S	C2	1.771(4)	C12	C13	1.396(4)
S	C3	1.815(4)	C13	C14	1.376(5)
C1	C24	1.747(3)	C14	C15	1.383(6)
O1	C1	1.212(4)	C15	C16	1.386(4)
N1	C1	1.395(4)	C21	C22	1.381(4)
N1	C4	1.483(4)	C21	C26	1.396(4)
N2	C5	1.487(5)	C22	C23	1.389(5)
N2	C11	1.408(3)	C23	C24	1.375(5)
N3	C2	1.267(4)	C24	C25	1.378(5)
N3	C21	1.426(4)	C25	C26	1.381(5)
C1	C12	1.469(4)			

Table 5. Selected Bond Angles (deg.) of **9bd**

O	P	N1	116.7(1)	N2	C5	C6	111.7(3)
O	P	N2	115.4(1)	N2	C11	C12	120.9(2)
O	P	C2	110.4(1)	N2	C11	C16	120.4(3)
N1	P	N2	104.1(1)	C12	C11	C16	118.9(3)
N1	P	C2	100.5(1)	C1	C12	C11	124.4(2)
N2	P	C2	108.6(1)	C1	C12	C13	116.6(3)
C2	S	C3	100.4(2)	C11	C12	C13	119.0(3)
P	N1	C1	127.4(3)	C12	C13	C14	122.1(4)
P	N1	C4	117.3(3)	C13	C14	C15	118.4(3)
C1	N1	C4	115.3(2)	C14	C15	C16	121.0(4)
P	N2	C5	113.5(2)	C11	C16	C15	120.6(3)
P	N2	C11	125.4(3)	N3	C21	C22	118.0(3)
C5	N2	C11	121.1(2)	N3	C21	C26	122.0(3)
C2	N3	C21	122.9(3)	C22	C21	C26	119.8(4)
O1	C1	N1	119.3(3)	C21	C22	C23	120.5(3)
O1	C1	C12	123.5(3)	C22	C23	C24	118.7(3)
N1	C1	C12	117.3(3)	C1	C24	C23	119.3(2)
P	C2	S	114.7(2)	C1	C24	C25	118.9(2)
P	C2	N3	118.6(2)	C23	C24	C25	121.7(4)
S	C2	N3	126.6(2)	C24	C25	C26	119.4(4)
S	C3	C4	112.9(2)	C21	C26	C25	119.8(3)
N1	C4	C3	112.8(3)				

1-Alkyl-3-(2-chloroethyl)-4-oxo-1,2,3,4-tetrahydro-1,3,2-benzodiazaphosphorine 2-Oxides (7); General Procedure:

To a solution of **6** (2 mmol) in dry benzene (40 mL) is added dropwise PCl_3 (3.1 g, 2.3 mmol). A large amount of yellow solid precipitates immediately, which disappears on heating with evolution of copious amount of gaseous HCl. The mixture is refluxed for 5 h, cooled to room temperature and diluted with EtOAc (50 mL). The mixture is washed with cold 5% $NaHCO_3$ solution (3 × 30 mL) at 0 °C and the organic phase is separated. The organic phase is dried (Na_2SO_4) and concentrated under reduced pressure to give the product **7** as a colorless solid, which is recrystallized from benzene (Table 2).

1-Substituted 3-(2-Chloroethyl)-2-(*N*-phenylthiocarbamoyl)-4-oxo-1,2,3,4-tetrahydro-1,3,2-benzodiazaphosphorine 2-Oxides 8a and 8b; General Procedure:

To a solution of **3a** or **3d** (3.8 mmol) in a mixture of dry benzene (40 mL) and Et_3N (0.38 g, 3.8 mmol), is added phenylisothiocyanate (0.52 g, 3.8 mmol). After stirring at 60 °C for 5 h, the solvent is evaporated under reduced pressure and the residue is chromatographed on a silica gel column (50 cm × 3.5 cm, 250–300 mesh) using petroleum ether/EtOAc (2:1, 1000 mL) as eluent. Evaporation of the solvent under reduced pressure affords the product.

8a; yield: 61%; mp 182–184 °C.

$C_{17}H_{17}ClN_3O_2PS$	calc.	C 51.84	H 4.32	N 10.67
(393.7)	found	52.34	4.43	10.67

^{1}H-NMR ($CDCl_3$/TMS): δ = 3.16 (d, 3 H, J = 9 Hz, CH_3); 3.6–4.5 (m, 4 H, NCH_2CH_2); 6.9–8.3 (m, 9 H_{arom}).

MS (70 eV): m/z (%) = 393 (M^+, 39); 395 (M^+ + 2, 13).

8b; yield: 65%; mp 117–119 °C.

$C_{20}H_{21}ClN_3O_4PS$	calc.	C 51.67	H 4.25	N 9.04
(465.7)	found	52.03	4.81	8.63

^{1}H-NMR ($CDCl_3$/NMR): δ = 1.2 (t, 3 H, $CH_2C\underline{H}_3$); 3.5–5.0 (m, 8 H, $NCH_2CO + C\underline{H}_2CH_3 + NCH_2CH_2Cl$); 6.3–8.5 (m, 9 H_{arom}).

MS (70 eV): m/z (%) = 465 (M^+, 36); 467 (M^+ + 2, 12).

11-Substituted 1-Arylimino-6-oxo-3,4,6,11-tetrahydro[1,4,3]thiazaphosphorino[3,4-*b*][1,3,2]benzodiazaphosphorine 12-Oxides 9; General Procedure:

Method A (*for* **9da**): To a solution of **7d** (1 g, 3 mmol) in dry THF (40 mL) at 0 °C is added NaH (80% suspension in oil, 90 mg, 3 mmol) followed by phenylisothiocyanate (0.4 g, 3 mmol). After stirring at room temperature for 4 h, the mixture is poured into ice/water (50 mL) and extracted with EtOAc (40 mL). The organic layer is dried (Na_2SO_4) and evaporated under reduced pressure to obtain a yellowish oil, which is chromatographed on a silica gel column (50 cm × 3.5 cm, 250–300 mesh) using petroleum ether/EtOAc (2:1, 1000 mL) as eluent to separate **8b** and **9da**.

8b; yield: 0.6 g (43%); mp 117–119 °C.

9da; yield: 0.17 g (13%); mp 161–162 °C (Table 3).

Method B (for **9aa**–**9de**): To a solution of **7** (2.4 mmol) in dry THF (40 mL) at 0 °C is added NaH (80% suspension in oil, 70 mg, 2.4 mmol). After stirring at 0 °C for 30 min, the appropriate arylisothiocyanate (2.4 mmol) is added. The mixture is refluxed for 8 h, poured onto ice/water (40 mL) and worked up as described in Method A (Table 3).

Method C (*for* **9da**): To a solution of **8b** (0.6 g, 1.3 mmol) in dry THF (20 mL) at 0 °C is added NaH (80% suspension in oil, 20 mg, 1.3 mmol). After stirring for 1 h, the mixture is refluxed for 8 h, cooled and added to EtOAc (20 mL) at 0 °C. Ice/water (20 mL) is then added and the mixture is worked up as given in Method A to afford **9da**; yield: 0.25 g (45%); mp 161–162 °C.

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