Chemistry of Phosphorus Ylides, 13[1] Reactions with Phosphacumulenes. VII:[1] Novel Synthesis of Pyridazinones and Pyridazinethiones from the Reaction of Cumulated Phosphorus Ylides with Monohydrazones of α-Diketones, Acenaphthenequinone, and Indantrione#

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The behavior of the reactive phosphacumulenes **2a,b**, towards different α-diketone monohydrazones **1**, **5**, **11**, and **13**, acenaphthenequinone monohydrazone **8** and indantrione monohydrazone **16** has been studied. In some cases the resulted phosphoranes directly cyclize by an intramolecular Wittig reaction with the formation of pyridazinones **4a**, **6**, **9**, **12**, and **17** and pyridazinethione **4b**. Structure of the new products were assigned according to consistent analytical and spectroscopic data.

The intramolecular Wittig reaction has been proved by Bestmann[2] to be an excellent method for the synthesis of cyclic compounds. In this connection the reactive phosphacumulenes **2a,b** are of special interest, since they react with H-acidic compounds containing carbonyl group, to yield phosphoranes, which subsequently undergo an intramolecular Wittig reaction, in some cases, to give the cyclic component. As a part of our continuous interest in the chemistry of these phosphacumulenes, we describe here, the synthesis of pyridazinones **4a**, **6**, **9**, **12**, and **17** and pyridazinethione **4b** from the reaction of (2-oxovinylidene)-**2a** and (2-thioxovinylidene)triphenylphosphorane **2b** with some α-diketone monohydrazones **1**, **5**, **11**, and **13**, acenaphthenequinone monohydrazone **8** and indantrione monohydrazone **16**. Pyridazinethiones are known as central nervous depressants.[3]

Results and Discussion

We have now examined the reaction of naphtho[2,1-*b*]furan-1,2-dione 2-phenylhydrazone (**1**) with (2-oxovinylidene)triphenylphosphorane (**2a**). Compounds **1** and **2a** react in molar ratio 1 : 1 at 25 °C in tetrahydrofuran (THF) for 6h to give the pyridazinone **4a** together with triphenylphosphine oxide. The IR, ^{1}H NMR and MS spectra as well as the elemental analysis were consistent with structure **4a**. Its IR spectrum shows the absorption band of the pyridazinone C=O at 1700 cm^{-1} and no absorption for the lactone C=O.[4] The ^{1}H NMR of **4a** exhibits absorption at δ=6.83—7.82 (m, 12H, CH= and aromatics), its elemental analysis and molecular weight determination agree with formula $C_{20}H_{12}N_2O_2$ (*m/z* 312, M$^+$).

As a point of interest to prepare heterocylic compounds with thioxo group, the behavior of naphtho-[2,1-*b*]furan-1,2-dione 2-phenylhydrazone (**1**) towards (2-thioxovinylidene) triphenylphosphorane (**2b**) was investigated, too. Thus, compound **1** was reacted with **2b** in boiling toluene for 8 h, yielding the pyridazinethione **4b**. Its IR spectrum shows absorption band at 1240 cm^{-1} attributable to C=S group.[5] The ^{1}H NMR shift recorded for the product **4b** was δ=7.22—8.00 (m, 12H, CH= and aromatics). In the MS of **4b** the peak at *m/z*=328 (M$^+$) was observed.

The reaction of 3,3-diphenyl-1,2-indandione 1-phenylhydrazone (**5**) and phosphorane **2a** was performed in THF at room temperature for 6 h, to give the corresponding pyridazinone **6** and tiphenylphosphine oxide. The IR of compound **6** showed absorption band at 1650 cm^{-1} (C=O). The ^{1}H NMR spectrum of this pyridazinone **6** had signals at δ=7.11—7.73 (m, 20H, CH= and aromatics) and in the MS the signal *m/z*=412 (M$^+$) was observed. However, only the phosphorane adduct **7** was isolated when the previously mentioned monohydrazone **5** was allowed to react with phosphorane **2b** in boiling toluene for 8 h. The IR spectrum of the phosphorane **7** confirms the proposed structure showing absorption bands at 1690 cm^{-1} (C=O), 1460 (P-aryl)[5] and 1250 (C=S). Its ^{1}H NMR displayed the following signals at δ=4.5 (d, 1H *J*=7 Hz, CH=P), 7.33—7.90 (m, 34H, aromatics). The ^{31}P NMR shift recorded for the product **7** was δ=+40.02 and its MS showed the peak at *m/z* 706 (M$^+$).

Next, we have studied the behavior of acenaphthenequinone monophenylhydrazone **8** towards phosphorane **2a**. When compound **8** was heated with **2a** in toluene for 8 h, the pyridazinone **9** was obtained along with triphenylphosphine oxide. Structural assignment for **9** was supported by the MS, IR and ^{1}H NMR spectral data. In the MS of **9** the molecular ion peak was observed at *m/z* 296. The IR spectrum showed the C=O at 1730 cm^{-1} and the ^{1}H NMR spectrum revealed the presence of the aromatic protons and the =CH at δ=7.22—7.82. On the other hand, phosphorane **2b** reacted with the monohydrazone **8**, in boiling toluene for 8 h to give only the phosphorane **10**. Absorption bands shown by the IR spectrum of compound **10**, at 1720 cm^{-1}, 1440, 1250, are attributed to the C=O, P-aryl and C=S, respectively. The ^{1}H NMR spectrum of

#Dedicated to Professor Dr. Hans Jürgen Bestmann on the ocassion of his 68th birthday.

10 disclosed the presence of signals at $\delta=4.52$ (d, 1H, $J=6.5$ Hz, CH=P) and 7.41—7.82 (m, 26H, aromatics). The ^{31}P NMR shift recorded for the product **10** was $\delta=+40.6$ ppm and its MS showed the peak at m/z 590 (M^+).

In addition, the 3(2*H*)-pyridazinone **12** could be obtained by reacting benzil monophenylhydrazone (**11**) with the cumulated phosphorus ylide **2a** in boiling toluene for 8 h. The IR spectrum of compound **12** revealed characteristic band at 1760 cm^{-1}(C=O), and the ^{1}H NMR showed the singnals at $\delta=7.42$—7.92 (m, 16H, CH= and aromatics). The mass spectrum of compound **12** showed the molecular ion peak (M^+) at m/z 324. No reaction was observed between **11** and **2b**, even when the reactants were practically unchanged.

We have also found that *N*-methylisatin 3-phenylhydrazone (**13**) reacts with **2a** or **2b** in boiling toluene for 8 h to give only the crystalline phosphoranes **14** or **15** respectively. In the IR spectrum of compound **14**, the C=O bands appear at 1750 and 1690 cm^{-1}, and the ^{1}H NMR signals appear at $\delta=3.32$ (s, 3H, CH_3), 4.23 (d, 1H, $J=6$ Hz, CH=P) and 7.11—7.74 (m, 24H, aromatics). The ^{31}P NMR signal of compound **14** appears at $\delta=+40.05$ and $m/z=553$ (M^+) was observed in its MS. On the other hand, the IR spectrum of the phosphorane **15** shows strong absorption bands at 1720 (C=O) and 1260 cm^{-1} (C=S) and its ^{1}H NMR disclosed the presence of signals at $\delta=3.33$ (s, 3H, CH_3), 4.23 (d, 1H, $J=7.5$ Hz, CH=P), and 6.92—7.73 (m, 24H, aromatics). Moreover, a signal at +41.32 was observed in its ^{31}P NMR and its MS showed the molecular ion peak at m/z 569.

We have now examined the reaction of 1,2,3-indantrione 2-phenylhydrazone (**16**) with the cumulated phosphorus ylides **2a,b**. Compound **16** and **2a** react in molar ratio 1:1 in THF at room temperature for 6 h to give the pyridazinone **17**, together with triphenylphosphine oxide. Evidence for participation of pyridazinone structure **17** is provided by the frequences of the C=O bands in the IR spectrum, at 1740 cm^{-1} (indenone) and 1690 cm^{-1} (pyridazinone). The ^{1}H NMR spectrum of **17** showed signals at $\delta=7.82$ (m, 10H, CH= and aromatics), and in the MS the peak at $m/z=274$ (M^+) was observed. The reaction of the indantrione phenylhydrazone **16** with **2b** was conducted in boiling toluene for 8 h to give the phosphorane adduct **18**. The IR spectrum of **18** revealed the presence of strong absorption bands at 1740 cm^{-1} (C=O, indene) and 1250 cm^{-1} (C=S). The ^{1}H NMR spectrum of the phosphorane **18** showed signals at $\delta=4.33$ (d, $J=4$ Hz, 1H, CH=P) and $\delta=7.32$—7.78 (m, 24H, aromatics). The ^{31}P NMR shift recorded for compound **18** was $\delta=+40.03$.

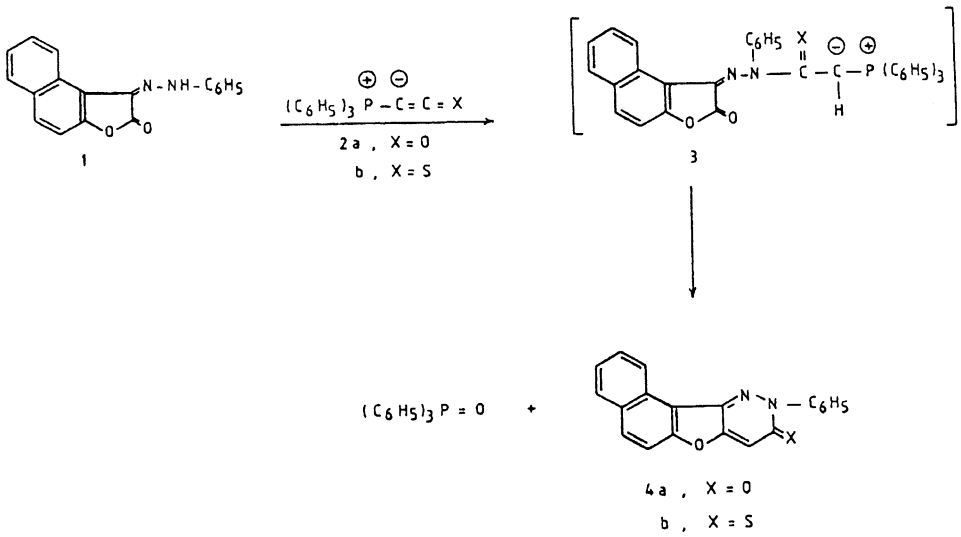
Conclusion

The results of the present investigation clearly show that the reaction of monophenylhydrazones of α-diketones, *o*-quinone and vicinal triketone, with phosphacumulenes **2a,b** offers a novel and direct route for the synthesis of nitrogen heterocycles. For example, addition of naphtho[2,1-*b*]furan-1,2-dione 2-phenylhydrazone (**1**) to (2-oxovinylidene)-**2a** or (2-thioxovinylidene)triphenylphosphorane **2b**, affords, firstly, the corresponding phosphoranes **3**, which cyclize according to an intramolecular Wittig reaction yielding the respective pyridazinone **4a** or pyridazinethione **4b**, (Scheme 1).

The well-established difference in the reactivity of phosphacumulenes (**2a**>**2b**)[6] is also demonstrated in the present study. Thus, (2-oxovinyldene)triphenylphosphorane (**2a**) reacts smoothly with the phenylhydrazones (e.g. **5**, **8**, and **16**) to give phosphoranes, which readily cyclize to the respective pyridazinones **6**, **9**, and **17**. On the other hand, (2-thioxovinylidene)-phosphorane (**2b**) reacts less rapidly to yield the corresponding resonance-stabilized phosphoranes **7**, **10**, and **18**. No reaction was observed between benzil monophenylhydrazone (**11**) and the thioxo compound **2b** (Table 1). Therefore, it is safe to state that the reaction course between phosphacumulenes and monophophenylhydrazones is rather dependent on a number of parameters. These include the nature of the reactants, the type of the solvent or the reaction temperature. In the case of the 1:1 adducts **14** and **15**, the carbonyl group is deactivated by virtue of its amidic nature. This does not allow the reaction to proceed more to give the respective ring structure via elimination of triphenylphosphine oxide. The relatively more reactive lactone-carbonyl (in **1**), alkylcarbonyl (in **5**), and arylcarbonyl (in **8**, **11**, and **16**) facilitates ring closure to yield the cyclic structures even at ambient temp. (cf. **1**→**4**). In the case of the 1:1 adducts **7**, **10**, **14**, **15**, and **18**, these adducts were recovered practically unchanged upon heating in toluene for 8 h, or thermolysis (200 °C) for 30 min under reduced pressure (0.5 mmHg, 1 mmHg=133.322 Pa).

Experimental

All melting points are uncorrected. Solvents were dried by standard technique. All reactions were carried out under N_2 atmosphere. The α-diketone, *o*-quinone and triketone monophenylhydrazones, naphtho[2,1-*b*]furan-1,2-dione 2-phenylhydrazone (**1**),[7] 3,3-diphenyl-1,2-indandione 1-phenylhydrazone (**5**),[8] acenaphthenequinone monophenylhydrazone (**8**),[9] benzil monophenylhydrazone (**11**),[10] *N*-methylisatin 3-phenylhydrazone (**13**),[11] and 1,2,3-indantrione 2-phenylhydrazone (**16**),[12] were prepared according to established procedures. The IR spectra were measured in KBr, on a Carl Zeiss Infracord Spectrometer Model UR 10. The ^{1}H NMR spectra were run in $CDCl_3$ at 90 MHz on a Varian Spectrometer using tetramethylsilane as an internal reference. ^{31}P NMR spectra were run on Spectrometer JNM-PS 100 JEOL, in $CDCl_3$, using H_3PO_4 as external standard. MS, spectrometry were carried at 70 eV on Karatos Equipment provided with data system. Analytical data were obtained from the Microanalysis Laboratory, National Research Centre, Cairo.



Scheme 1.

Table 1. Pyridazinones (**6**, **9**, **12**, and **17**) and Phosphoranes (**7**, **10**, **14**, **15**, and **18**) Resulted from the Reaction of Monophenylhydrazones (**5**, **8**, **11**, **13**, and **16**) with Phosphacumulene Ylides (**2a**,**b**)

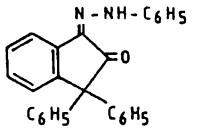
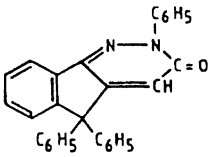
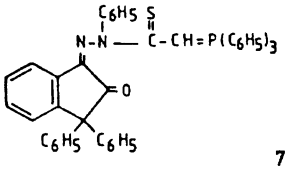
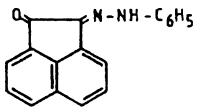
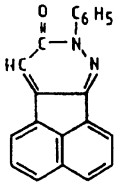
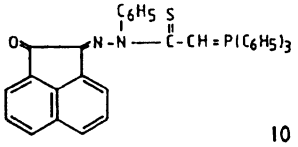
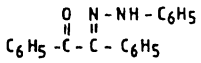
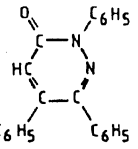
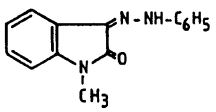
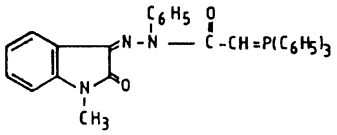
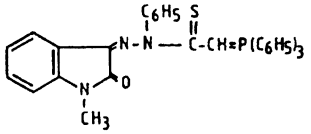
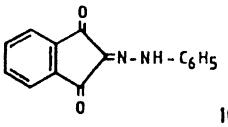
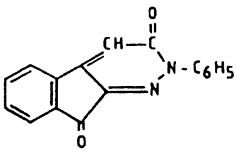
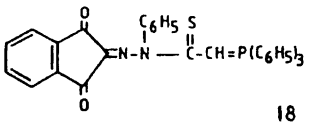
α-Diketone Monophenylhydrazone	$^{\oplus}_{\ominus}$ $+(C_6H_5)_3P-C=C=O$ **2a**	$^{\oplus}_{\ominus}$ $+(C_6H_5)_3P-C=C=S$ **2b**
 **5**	 **6**	 **7**
 **8**	 **9**	 **10**
 **11**	 **12**	no reaction
 **13**	 **14**	 **15**
 **16**	 **17**	 **18**

Table 2. Analytical and Physical Data for Pyridazinones (**4a**, **6**, **9**, **12**,**17**), Pyridazinethione (**4b**), and Phosphoranes (**7**, **10**, **14**, **15**, **18**)

Compound (color)	Solvent of cryst.	Mp °C	Yield %	Molecular formula	Analysis C %	H %	N %	Calcd/Found P %	S %
4a[a] Yellow	Chloroform/ hexane	193	88	$C_{20}H_{12}N_2O_2$	76.92 77.00	3.85 3.80	8.97 9.00	— —	— —
4b[b] Orange	Chloroform/ hexane	205	75	$C_{20}H_{12}N_2OS$	73.17 73.20	3.66 3.70	8.54 8.50	— —	— —
6[a] Deep orange	THF/ pet.ether 40—60	277	90	$C_{29}H_{20}N_2O$	84.47 84.40	4.85 4.90	6.97 6.80	— —	— —
7[c] Red	Benzene/pet. ether 60—80	128	73	$C_{47}H_{35}N_2OPS$	79.89 79.90	4.96 5.00	3.96 4.00	4.39 4.42	4.53 4.60
9[b] Reddish brown	Benzene/pet. ether 60—80	190	80	$C_{20}H_{12}N_2O$	81.08 81.10	4.05 4.10	9.46 9.52	— —	— —
10[c] Brown	Benzene/pet. ether 60—80	167	77	$C_{37}H_{27}N_2OPS$	76.82 76.90	4.67 4.72	4.84 4.88	5.36 5.40	5.54 5.60
12[b] Yellow	Chloroform/ hexane	247	85	$C_{22}H_{16}N_2O$	81.48 81.51	4.94 5.10	8.64 8.70	— —	— —
14[c] Orange	Chloroform/ hexane	121	76	$C_{35}H_{28}N_3O_2P$	75.95 75.81	5.06 5.10	7.59 7.70	5.60 5.75	— —
15[c] Dark yellow	Benzene/pet. ether 60—80	191	70	$C_{35}H_{28}N_3OPS$	73.81 73.75	4.92 5.00	7.38 7.45	5.45 5.60	5.62 5.70
17[a] Golden yellow	Benzene	195	85	$C_{17}H_{10}N_2O_2$	74.45 74.40	3.65 3.72	10.22 10.20	— —	— —
18[c] Orange	Benzene	162	78	$C_{35}H_{25}N_2O_2PS$	73.94 74.00	4.40 4.45	4.93 5.10	5.45 5.56	5.63 5.75

a) Prepared according to procedure (A). b) Prepared according to procedure (B). c) Prepared according to procedure (C).

Reaction of Phosphacumulenes 2a, b with α-Diketone Monohydrazones 1, 5, 11, and 13, Acenaphthenequinone Monohydrazone 8 and Indantrione Monophenylhydrazone 16. Preparation of the New Pyridazinones 4a, 6, 9, 12, and 17, Pyridazinethione 4b and Phosphoranes 7, 10, 14, 15 and 18. Procedure A : To a solution of (2-oxovinylidene)-triphenylphosphorane (**2a**)[13] (0.01 mol) in 20 ml tetrahydrofuran, was added drop by drop with stirring at room temperature, a solution of the α-diketone **1**,**5** or indantrione monophenylhydrazone **16** (0.01 mol) in 20 ml THF. The reaction mixture was left for 6 h during which the color was changed from yellow to red. After THF was distilled under reduced pressure, the residue that left behind was dissolved in 20 ml chloroform, followed by 20 ml hexane and left overnight in the refrigerator. The pydrazinone **4a**, **6** or **17** that formed was filtered off and crystallized from the appropriate solvent (Table 2). The chloroform/hexane filtrate, was chromatographed on alumina, affording colorless crystals of triphenylphosphine oxide, mp and mixed mp 151 °C.

Procedure B : A mixture of phosphacumulene **2a** or **2b** (0.01 mol), α-diketone monophenylhydrazone **1** and **11**, acenaphthenquinone monophenylhydrazone **8** or indantrione monophenylhydrazone **16** (0.01 mol) and toluene (40 ml) was refluxed for 8 h. Toluene was distilled off and the residue that left behind was crystallized from benzene to give the pyridazinethione **4b** or the pyridazinones **9**, **12**, and **17** respectively (Table 2). The benzene filtrate, afforded upon concentration and addition of hexane, a colorless precipitate, which upon recrystallization gave triphenylphosphine oxide, mp and mixed mp 151 °C.

Procedure C : A mixture of the phosphacumulene **2a** or **2b** (0.01 mol) and **5**, **13**, **8** or **16** (0.01 mol) was boiled in toluene (40 ml) for 8 h. Toluene was removed under vacuum and the residue was crystallized to give the phosphoranes **7**, **10**, **14**, **15** or **18**, respectively (Table 2).

The starting materials were recovered unchanged when the reactions were done in THF.

Attempted Cyclization of the Phosphoranes 7, 10, 14, 15, and 18. When the phosphorane adducts **7**, **10**, **14**, **15** or **18**, were heated in boiling toluene for 8 h or heated in a cold finger sublimator at 200 °C (bath temperature) for 30 min under reduced pressure (0.5 mmHg), these adducts were recovered unchanged.

Attempted Reaction of (2-Thioxovinylidene)triphenylphosphorane (2b) and Benzil Monophenylhydrazone 11. When compounds **2b** (0.11 mol) and **11** (0.1 mol) were boiled in toluene (50 ml) for 12 h, no reaction was observed, and the reactants were recovered practically un-

changed.

References

1) For Part 12 : cf. F. M. Soliman and M. M. Said, *Sulfur Lett.*, **13**, 213 (1991); Part 11 : F. M. Soliman and M. M. Said, *Z. Naturforsch., B*, **46B**, 1105 (1991).

2) H. J. Bestmann and R. Schobert, *Synthesis*, **1989**, 419 ; R. W. Saalfrank, W. Hafner, J. Markmann, and H. J. Bestmann, *Tetrahedron*, **44**, 5095 (1988).

3) S. Umio, K. Kariyone, and T. Kishimoto, Japan Patent (Kokai) 69-02993, (1969); *Chem. Abstr.*, **70**, 78008 Y (1969).

4) K. Heusler, J. Kebrle, C. Meystre, H. Ueberwasser, P. Wieland, G. Anner, and A. Wettstein, *Helv. Chim. Acta*, **42**, 2043 (1959).

5) D. H. Williams and I. Fleming, "Spectroscopic Methods in Organic Chemistry," McGraw-Hill Book Company, Maidenhead, UK (1987), pp. 55—56.

6) H. J. Bestmann, *Angew. Chem.*, **89**, 361 (1977).

7) For the preparation of compound **1** cf. : M. Giua and V. De Franciscis, *Gazz. Chim. Ital.*, **54**, 509 (1924).

8) For the preparation of compound **5** cf.: P. E. Gagnon, R. Hudon, I. Cantin, and J. Ganas, *Trans. R. Soc. Can., Sect. 3*, **33**, 47 (1939).

9) For the preparation of compound **8** cf.: C. Graebe and E. Gfeller, *Justus Liebigs Ann. Chem.*, **276**, 1 (1893).

10) For the preparation of compound **11** cf.: C. Bulow, *Justus Liebigs Ann.Chem.*, **236**, 184 (1886).

11) For the preparation of compound **13** cf.: H. G. Colman, *Justus Liebigs Ann.Chem.*, **248**, 114 (1888).

12) For the preparation of compound **16** cf.: J. Scheiber and G. Hopfer, *Ber.*, **53**, 697 (1920).

13) For the preparation of compound **2a**,**b**, cf.: H. J. Bestmann and D. Sandmeier, *Angew. Chem., Int. Ed. Engl.*, **14**, 634 (1975).