

SHORT  
COMMUNICATIONS

## Staudinger Reaction in the Series of 4-Diazotetrahydrofuran-3-ones: Effect of Substituents in the Diazo and Phosphine Components

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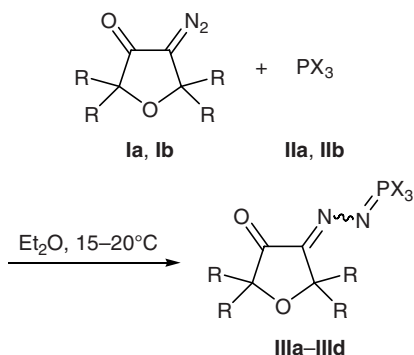
Compounds of the general formula  $R_2C=N-N=PX_3$  (phosphazines) are readily available through the Staudinger reaction [1]. They have long been used in organic synthesis for identification and purification of liquid and often unstable aliphatic diazo compounds as stable crystalline substances with sharp melting points [2]. In addition, these compounds attract increased interest as diaza analogs of alkylidenephosphoranes  $R_2C=PX_3$  that are used in the aza-Wittig reactions [3–5]. For example, some  $\alpha,\alpha$ -dioxo phosphazines ( $R = acyl$ ) were found to be effective aza-Wittig reagents in a new synthesis of substituted pyridazines [4, 5]. The present work was aimed at studying the Staudinger reaction in the series of 4-diazotetrahydrofuran-3-ones [6] with a view to obtain the corresponding  $\alpha$ -oxo phosphazines which could be used in the synthesis of nitrogen-containing and other heterocyclic systems via the aza-Wittig reaction.

As reactants we selected 4-diazo-2,2,5,5-tetraalkyltetrahydrofuran-3-ones **Ia** and **Ib** differing in the size of substituents in positions 2 and 5 of the heteroring and phosphines **IIa** and **IIb** differing in the nature of substituents on the phosphorus atom. The reactions were carried out at room temperature in diethyl ether or hexane. The reactions with more nucleophilic tris(dimethylamino)phosphine (**IIb**) were accompanied by appreciable heat evolution. Orange phosphazines **IIIa–IIIc** crystallized from the reaction mixtures on cooling to  $-5$  to  $-10^\circ\text{C}$  for a short time, and their yields ranged from 60 to 90% (Scheme 1). The structure of compounds **IIIa–IIIc** was confirmed by the  $^1\text{H}$  and  $^{13}\text{C}$  NMR, IR, and UV spectra and elemental analyses.

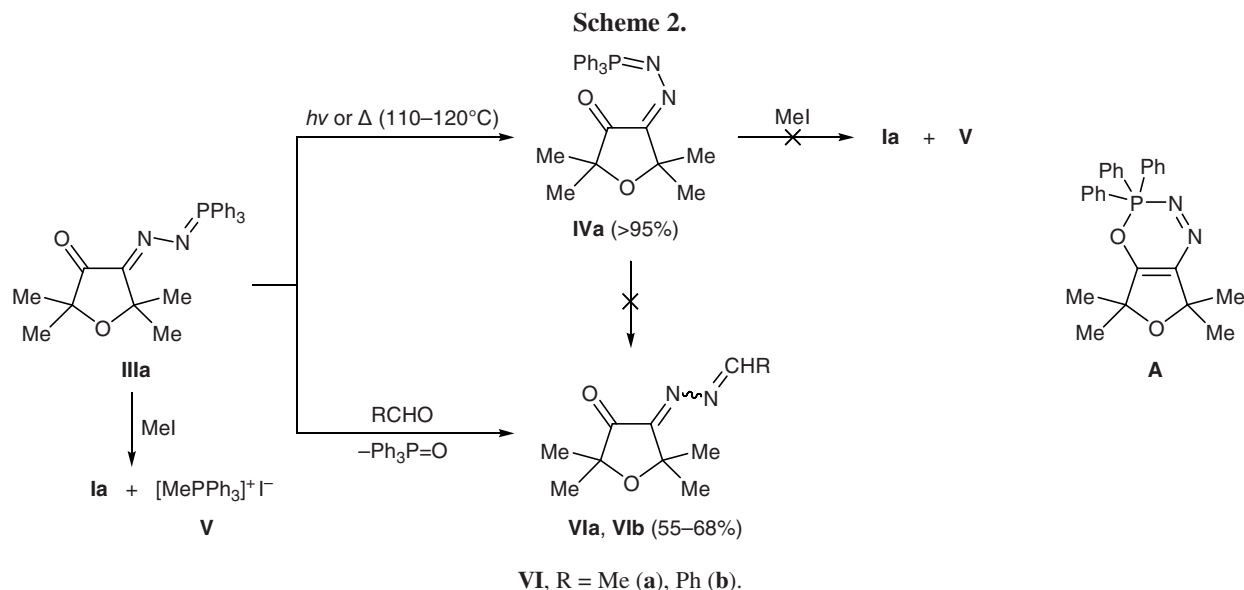
According to the  $^1\text{H}$  and  $^{13}\text{C}$  spectra, dissolution of **IIIa** and **IIIb** in chloroform- $d$  or acetone- $d_6$  is accompanied by their partial dissociation into initial diazofuranones **Ia** and **Ib** and triphenylphosphine. By contrast, tris(dimethylamino)phosphine derivatives **IIIc** and **IIId** turned out to be quite stable: no dissociation was observed under analogous conditions. Furthermore, unlike compounds **IIIc** and **IIId**, phosphazines **IIIa** and **IIIb** were partially hydrolyzed during chromatography on silica gel to give the corresponding hydrazones and triphenylphosphine oxide.

It was interesting that compound **IIIa** underwent isomerization into **IVa** on heating above melting point or irradiation in the visible region ( $\lambda > 310\text{ nm}$ ). The structure of **IVa** was determined on the basis of spectral ( $^1\text{H}$  and  $^{13}\text{C}$  NMR) and analytical data. The  $^{13}\text{C}$  NMR spectra of **IIIa** and **IVa** each contained a set of 10 carbon signals whose positions differed insignificantly; therefore, we ruled out furo[3,4- $e$ ][1,3,4,2 $\lambda^5$ ]-

Scheme 1.



**I**, R = Me (**a**), RR = (CH<sub>2</sub>)<sub>5</sub> (**b**); **II**, X = Ph (**a**), Me<sub>2</sub>N (**b**);  
**III**, R = Me, X = Ph (**a**), Me<sub>2</sub>N (**c**); RR = (CH<sub>2</sub>)<sub>5</sub>, X = Ph (**b**),  
Me<sub>2</sub>N (**d**).



oxadiazaphosphinine structure **A** assumed initially for the product of photochemical reaction. The isomeric configurations of compounds **IIIa** and **IVa** were determined by X-ray analysis of their single crystals. It should be noted that phosphazines **IIIb–III d** failed to undergo analogous thermal (200°C) or photochemical isomerization.

Stereoisomeric *syn*- and *anti*-phosphazines **IIIa** and **IVa** showed essentially different reactivities. Compound **IIIa**, like other compounds of this type [2, 7], reacted with methyl iodide to produce methyl(triphenyl)phosphonium iodide (**V**) and diazo ketone **Ia**.<sup>\*</sup> Stereoisomeric phosphazine **IVa** remained unchanged even after prolonged heating with methyl iodide in benzene. Compounds **IIIa** and **IVa** behaved differently in the aza-Wittig reaction. Phosphazine **IIIa** reacted with acetaldehyde and benzaldehyde even at room temperature to give the corresponding azines **VIa** and **VIb** and triphenylphosphine oxide, whereas isomer **IVa** almost did not change on heating with the same aldehydes in boiling benzene for several hours (Scheme 2).

We can conclude that the reactivity of phosphazines derived from 4-diazo-2,2,5,5-tetraalkyltetrahydrofuran-3-ones is largely determined by the substituent in the diazo ketone and that their stability depends primarily upon the phosphine nature.

<sup>\*</sup> According to the TLC data, diazo ketone **Ia** isolated in such a way was contaminated with hydrolysis products of phosphazine **IIIa** (the corresponding hydrazone and triphenylphosphine oxide); therefore, the "phosphazine" procedure described in [2, 7] cannot be regarded as an effective method for purification of diazo ketones **I**.

### Phosphazines **IIIa–III d** (general procedure).

A solution of diazo ketone **Ia** or **Ib** in a minimal amount of anhydrous diethyl ether or hexane was added in small portions over a period of 5–10 min to a solution of phosphine **IIa** or **IIb** (as a rule, 1.05–1.10 equiv with respect to **I**) in a minimal amount of anhydrous diethyl ether or hexane (in the reaction with **IIb**). The light yellow solution almost instantaneously turned dark red (the reaction with **IIb** was accompanied by slight heat evolution). The mixture was kept for 10–12 h in a refrigerator, and the precipitate was filtered off through a glass filter, washed with cold diethyl ether or hexane, and dried in a vacuum desiccator at a residual pressure of 1–2 mm.

**2,2,5,5-Tetramethyl-4-[(triphenyl- $\lambda^5$ -phosphanylidene)hydrazono]tetrahydrofuran-3-one (**IIIa**)** (low-melting isomer) was obtained from 3.65 g (0.014 mol) of triphenylphosphine (**IIa**) and 2.34 g (0.014 mol) of diazo ketone **Ia** in diethyl ether. Yield 4.7 g (78%), orange crystals, mp 107–109°C (from Et<sub>2</sub>O), *R*<sub>f</sub> 0.13 (benzene). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.35 s (6H, CH<sub>3</sub>), 1.37 s (6H, CH<sub>3</sub>). Found, %: C 72.43; H 6.57; N 6.39. C<sub>26</sub>H<sub>27</sub>N<sub>2</sub>O<sub>2</sub>P. Calculated, %: C 72.53; H 6.33; N 6.51.

**2,2:5,5-Bis(pentamethylene)-4-[(triphenyl- $\lambda^5$ -phosphanylidene)hydrazono]tetrahydrofuran-3-one (**IIIb**)** was obtained from 2.03 g (7.7 mmol) of triphenylphosphine (**IIa**) and 1.9 g (7.7 mmol) of diazo ketone **Ib** in anhydrous diethyl ether. Yield 2.3 g (59%), orange crystals, mp 82–84°C (from Et<sub>2</sub>O). Found, %: C 75.17; H 6.99; N 5.66. C<sub>32</sub>H<sub>35</sub>N<sub>2</sub>O<sub>2</sub>P. Calculated, %: C 75.26; H 6.92; N 5.49.

**2,2,5,5-Tetramethyl-4-[[tris(dimethylamino)- $\lambda^5$ -phosphanylidene]hydrazono]tetrahydrofuran-3-one (IIIc)** was synthesized from 2.06 g (0.013 mol) of hexamethylphosphorous triamide (IIb) and 2.19 g (0.013 mol) of diazo ketone Ia in anhydrous diethyl ether. Yield 3.4 g (80%), orange crystals, mp 105–107°C (from Et<sub>2</sub>O). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.32 s (6H, CH<sub>3</sub>), 1.42 s (6H, CH<sub>3</sub>), 2.74 d (18H, CH<sub>3</sub>N, <sup>3</sup>J<sub>PH</sub> = 10 Hz). Found, %: C 50.83; H 9.02; N 21.10. C<sub>14</sub>H<sub>30</sub>N<sub>5</sub>O<sub>2</sub>P. Calculated, %: C 50.73; H 9.14; N 21.13.

**2,2:5,5-Bis(pentamethylene)-4-[[tris(dimethylamino)- $\lambda^5$ -phosphanylidene]hydrazono]tetrahydrofuran-3-one (IIIId)** was obtained from 1.3 g (8.0 mmol) of phosphine IIb and 1.9 g (7.7 mmol) of diazo ketone Ib. Yield 2.9 g (92%), orange crystals, mp 113–115°C (from hexane). Found, %: C 58.33; H 9.22; N 16.70. C<sub>20</sub>H<sub>38</sub>N<sub>5</sub>O<sub>2</sub>P. Calculated, %: C 58.36; H 9.32; N 17.02.

**Thermal isomerization of phosphazine IIIa.** Compound IIIa, (1.0 g, 2.3 mmol), was placed in a test tube equipped with a reflux condenser and was heated for 8–10 min at 140°C on an oil bath. The material melted at 105–110°C, solidified, and melted again on heating to 169–173°C.

**2,2,5,5-Tetramethyl-4-[(triphenyl- $\lambda^5$ -phosphanylidene)hydrazono]tetrahydrofuran-3-one (IVa)** (high-melting isomer). Yield 1.0 g (100%), yellow crystals, mp 174–175°C (decomp.; from anhydrous methanol), *R*<sub>f</sub> 0.29 (petroleum ether–diethyl ether, 10:1). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.46 s (6H, CH<sub>3</sub>), 1.84 s (6H, CH<sub>3</sub>). Found, %: C 72.50; H 6.20; N 6.43. C<sub>26</sub>H<sub>27</sub>N<sub>2</sub>O<sub>2</sub>P. Calculated, %: C 72.55; H 6.28; N 6.51.

**Reaction of phosphazine IIIa with methyl iodide.** A solution of 0.85 g (6 mmol) of freshly distilled methyl iodide in 3 ml of benzene was added to a solution of 1.27 g (3 mmol) of isomer IIIa in 10 ml of anhydrous benzene, and the mixture was heated to the boiling point. After several minutes, the precipitate was filtered off, washed with anhydrous benzene, and dried in a vacuum desiccator. Yield of methyl(triphenyl)phosphonium iodide (V) 1.05 g (87%), mp 184–185°C [7]. The solvent was distilled off from the filtrate under reduced pressure (1–2 mm) to isolate 0.53 g of compound Ia. According to the TLC data, the latter contained impurities of the corresponding hydrazone and triphenylphosphine oxide.

**Reaction of phosphazine IVa with methyl iodide.** High-melting isomer IVa, 0.5 g (1.2 mmol), was dissolved in 15 ml of benzene on heating, a solution of 0.34 g (2.4 mmol) of methyl iodide in 3 ml of benzene

was added, and the mixture was heated for 7 h under reflux. The mixture was cooled, and the precipitate was filtered off and washed with benzene. Yield of phosphonium iodide V 17 mg (3.5%), mp 178–184°C [7]. The solvent was distilled off from the filtrate to obtain initial phosphazine IVa. Yield 0.41 g (79%), mp 170–173°C (decomp.), *R*<sub>f</sub> 0.29 (petroleum ether–diethyl ether, 10:1).

**Reaction of phosphazines IIIa and IVa with aldehydes (general procedure).** A 15-ml flask was thoroughly dried and charged with 0.215 g (0.5 mmol) of phosphazine IIIa or its solution in 1.5–2 ml of benzene (in the reaction with benzaldehyde), 1.5–2 ml of freshly distilled acetaldehyde or 0.053 g (0.5 mmol) of benzaldehyde was added (acetaldehyde was added until the mixture turned homogeneous), and the mixture was left to stand for 24 h at 18–20°C, the progress of the reaction being monitored by TLC and <sup>1</sup>H NMR spectroscopy. Unreacted aldehyde and the solvent were distilled off under reduced pressure, the residue was treated with benzene–petroleum ether (~10:1; 3 × 10 ml) to separate triphenylphosphine oxide, and the solvent was removed to isolate azine VIa or VIb.

In the reactions of phosphazine IVa with acetaldehyde and benzaldehyde under analogous conditions, as well as in the reaction of IVa with benzaldehyde on heating in boiling benzene for 24 h, no azine VIa or IVb was formed, and only the initial reactants were detected in the reaction mixture by <sup>1</sup>H NMR spectroscopy.

**4-Ethylidenehydrazono-2,2,5,5-tetramethyltetrahydrofuran-3-one (VIa).** Yield 55% (according to the <sup>1</sup>H NMR data), *R*<sub>f</sub> 0.46 (petroleum ether–diethyl ether, 1:1). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.35 s (6H, CH<sub>3</sub>), 1.55 s (6H, CH<sub>3</sub>), 2.13 d (3H, CH<sub>3</sub>, *J* = 5.6 Hz), 7.92 q (1H, CH=N, *J* = 5.6 Hz).

**4-Benzylidenehydrazono-2,2,5,5-tetramethyltetrahydrofuran-3-one (VIb).** Yield 68% (according to the <sup>1</sup>H NMR data), mp 94–96°C (from benzene), *R*<sub>f</sub> 0.64 (petroleum ether–diethyl ether, 1:1). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 1.41 s (6H, CH<sub>3</sub>), 1.67 s (6H, CH<sub>3</sub>), 7.49 m (3H, *m*-H, *p*-H), 7.83 d (2H, *o*-H, *J* = 6.5 Hz), 8.54 s (1H, CH=N).

The <sup>1</sup>H and <sup>13</sup>C NMR spectra were recorded on a Bruker AM-300 spectrometer at 300 and 75.5 MHz, respectively, using CDCl<sub>3</sub> as solvent and TMS as internal reference. The progress of reactions was monitored by TLC on Silufol UV-254 plates. The elemental compositions were determined on a Heraeus CHNO Rapid

Analyses. Diazo ketones **Ia** and **Ib** were synthesized according to the procedures described in [6].

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