Formation of Novel Phospha(P^V)azenes via a Redox Condensation Process between Phosphorus(III) Compounds and Azodicarbonamide

Shmuel Bittner,*[1a,b] Yonit Assaf,[1a] and Martin Pomerantz*[1c]

Department of Chemistry, Ben-Gurion University of the Negev, Beer Sheva 84120, Israel, and Department of Chemistry, The University of Texas at Arlington, Arlington, Texas 76019

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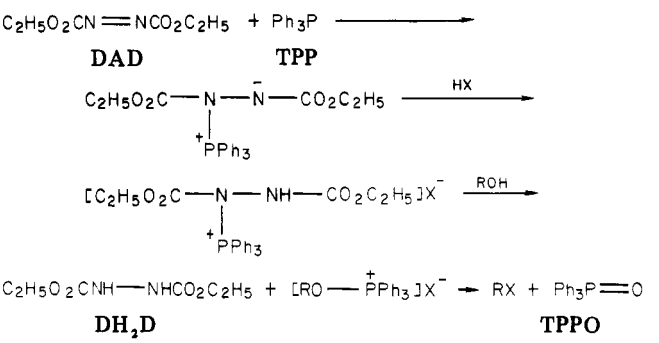
A new class of *N*-acylphospha(P^V)azenes (**3**, $R_3P{=}NCONHNHCONH_2$) was prepared by a rather novel redox condensation process using azodicarbonamide (**1**) and a variety of phosphines (**2**). The synthesis is simple and appears to be quite general. Structure proof rests on microanalysis as well as on IR, mass, and ^1H NMR spectroscopy. A possible mechanism is proposed.

The use of the redox system diethyl azodicarboxylate (DAD)–triphenylphosphine (TPP) in intermolecular and intramolecular dehydration reactions is well established.[2,3] Those reactions are said to proceed through formation of alkoxyphosphonium salts followed by S_N2-type displacement, in which triphenylphosphine oxide is the leaving group (Scheme I). As in many other phosphorus reactions,[4] here too, a phosphorus(III) compound is converted to a phosphorus(V) compound. Schematically, two hydrogens, one from the alcohol and one from the acidic component (HX), are transferred to the DAD to form diethyl hydrazinedicarboxylate (DH_2D). This dehydration reaction proceeds smoothly with most acidic compounds (carboxylic acids, phosphoric acids, phenols, imides, active methylene compounds), which are more acidic than the DH_2D.[5]

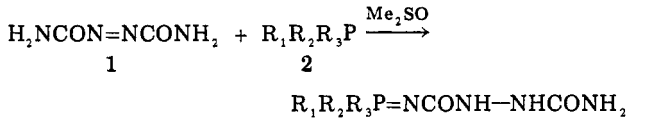
Scheme I



Results and Discussion

Azodicarbonamide (**1**) is the amide analogue of DAD, and it was of interest to compare its behavior with that of DAD in redox systems as described in Scheme I. Azodicarbonamide has a very low solubility in most of the common organic solvents; thus all of the reactions were performed in Me_2SO. When azodicarbonamide was allowed to react with TPP (**2a**) in the presence of either an acidic component or an alcohol or both, a precipitate formed almost spontaneously. After filtration and purification it was shown that dehydration did not occur, but rather a condensation product between the TPP and azodicarbonamide was formed, to which we have assigned structure **3a**. TPP and **1** in the absence of acids and alcohols also produced **3a** (Scheme II). This reaction is a rather novel one and provides an intramolecular variation of the reaction between phosphines, DAD, and amides which produces *N*-acylphospha(P^V)azenes.[6,7] As is the case with the TPP–DAD reactions, the present system is also a redox couple but one in which the azo moiety is reduced to the hydrazo functionality, while the phosphorus(III) compound is oxidized to the phosphorus(V) product, i.e., phospha(P^V)azene derivative **3**.

Scheme II[a]



[a] For **2** and **3**: a, $R_1 = R_2 = R_3 = Ph$; b, $R_1 = R_2 = Ph$, $R_3 = Me$; c, $R_1 = R_2 = Ph$, $R_3 = Et$; d, $R_1 = Ph$, $R_2 = R_3 = Me$; e, $R_1 = Ph$, $R_2 = R_3 = Et$; f, $R_1 = R_2 = R_3 = Et$; g, bis compound with $Ph_2P(CH_2)_2PPh_2$.

Table I.[a] Yield, Physical Properties, and Elemental Analyses of Phospha(P^V)azenes **3**

compd	mol wt	formula	yield, %	mp, °C	recryst solv
3a	378.4	$C_{20}H_{19}N_4O_2P$	74	218–219	Me_2SO
3b	316.3	$C_{15}H_{17}N_4O_2P$	70	215–216	Me_2SO
3c	330.3	$C_{16}H_{19}N_4O_2P$	54	200–202	chloroform
3d	254.2	$C_{10}H_{15}N_4O_2P$	76	195–196	Me_2SO
3e	282.3	$C_{12}H_{19}N_4O_2P$	56	190–191	Me_2SO
3f	234.2	$C_8H_{19}N_4O_2P$	78	180–181	acetone
3g	630.6	$C_{30}H_{32}N_8O_4P_2$	66	226–227	Me_2SO

[a] Satisfactory analytical data (±0.4% for C, H, N, and P) were reported for all compounds listed in the table.

In order to probe the scope of this reaction, it was run with a variety of phosphines and with one diphosphine. The results are summarized in Table I. As can be seen, the yields were good, ranging from 54% for **3c** up to 78% isolated yield for **3f**, and no effort was made to optimize these yields. Tertiary phosphines containing 0–3 aliphatic groups (0–3 phenyl rings) all reacted essentially equally well. The structure proof for these compounds rests on elemental analysis (see footnote *a*, Table I) and on IR and ^1H NMR spectroscopy (Table II). It was possible to assign the NMR absorption of each of the two different NH

(1) (a) Ben-Gurion University of the Negev. (b) To whom correspondence concerning this paper should be sent at Ben-Gurion University; visiting professor at the University of Texas at Arlington, 1978–1979. (c) The University of Texas at Arlington, visiting professor at Ben-Gurion University, summer 1981.

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Table II. ^{1}H NMR and IR Spectral Data of Phospha(P^V)azenes 3

	^{1}H NMR, δ (mult, no. of H)					IR, cm^{-1}		
compd	ArH	NH	NH_2	CH_3	CH_2	$\bar{\nu}_{NH}$	$\bar{\nu}_{P=N}$	$\bar{\nu}_{C=O}$
3a	7.4-7.72 (m, 16)[h]	7.2 (br s, 1)[h]	5.65 (br s, 2)			3410, 3340, 3225	1315	1695, 1625
3b	7.32-7.88 (m, 11)[h]	7.2 (br s, 1)[h]	5.66 (br s, 2)	2.25 (d,[a] 3)		3395, 3300, 3200	1295	1650, 1620
3c	7.35-7.78 (m, 11)[h]	7.18 (br s, 1)[h]	5.64 (br s, 2)	1.1 (dt,[b] 3)	2.6 (m, 2)	3450, 3325, 3250	1290	1655, 1625
3d	7.4-7.75 (m, 6)[h]	7.1 (br s, 1)[h]	5.64 (br s, 2)	1.1 (d,[c] 6)		3395, 3300, 3200	1295	1675, 1620
3e	7.46-7.8 (m, 6)[h]	7.07 (br s, 1)[h]	5.61 (br s, 2)	0.93 (m,[d] 6)	2.28 (m,[e] 4)	3340, 3320, 3220	1295	1670, 1640
3f		7.18 (br s, 1), 7.48 (br s, 1)	5.63 (br s, 2)	1.0 (m,[f] 9)	1.9 (m,[g] 6)	3400, 3300, 3210	1305	1685, 1655
3g	7.4-7.8 (m, 21)[h]	7.15 (s, 1)[h]	5.8 (br s, 2)		2.81 (m, 4)	3425, 3375, 3225	1285	1660, 1625

[a] $^2J_{PH}$ = 14 Hz. [b] $^3J_{PH}$ = 19 Hz; $^3J_{HH}$ = 8 Hz. [c] $^2J_{PH}$ = 14 Hz. [d] $^3J_{PH}$ = 18 Hz; $^3J_{HH}$ = 6 Hz. [e] $^2J_{PH}$ = 14 Hz; $^3J_{HH}$ = 6 Hz. [f] $^3J_{PH}$ = 17 Hz; $^3J_{HH}$ = 7 Hz. [g] $^2J_{PH}$ = 18 Hz. [h] One NH hydrogen is buried under the aromatics.

groups and the NH_2 group. One broad singlet was found at ~δ 5.6 (2 H) which must be the NH_2 group. The other two absorptions were found at δ 7.2 (1 H) and at ca. δ 7.5 (1 H). The latter is buried under the aromatic protons (multiplet between δ 7.3 and 7.8), but careful integration of this area reveals the one extra hidden proton. Moreover, this hydrogen can be seen clearly in the NMR spectrum of **3f** (the phospha(P^V)azene formed from triethylphosphine) at δ 7.48. Since the NH hydrogen closer to the $Ph_3P{=}N$ group should be shielded compared to the other NH hydrogen, due to resonance form $Ph_3P^+{-}NR^-$, we attribute the δ 7.5 absorption to that hydrogen.

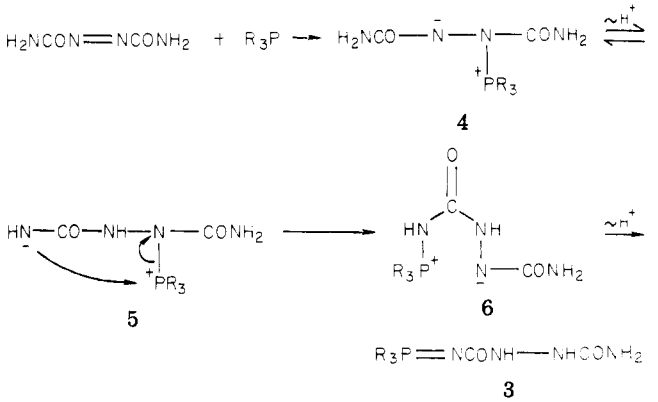
The chemical shifts of the methyl and ethyl hydrogens in **3** agree with literature data as do the $^2J_{PH}$ (13–14 Hz)[8] and the $^3J_{PH}$ (17–19 Hz) coupling constants.

As can be seen from Table II, all compounds show a strong absorption in the IR region around 1300 cm^{-1}. This absorption is attributed to the P=N stretching vibration and occurs at the expected frequency.[9,10] The narrow range of frequencies found is consistent with the findings of Weigraebe and Bock[11] that the influence of the substituents on the phosphorus atom on $\bar{\nu}$(P=N) is relatively small, being no more than 50 cm^{-1}. Two carbonyl absorptions are obvious in the range 1625–1695 cm^{-1}, and three NH vibration frequencies are observed in the range of 3200–3450 cm^{-1}. In addition, the mass spectrum of **3a** was totally consistent with the assigned structure. The most abundant peaks were at m/e 360 ($M^+ - H_2O$), 301 ($M^+ - C_6H_5$), 277 ($M^+ - Ph_3PN$), 183, and 77.

This reaction which we have discovered is quite unique in the sense that during the process, two hydrogens are transferred internally from the amide function of the molecule to the azo function of the same molecule. A possible mechanism for this reaction involves formation of a quaternary phosphonium salt (**4**) in equilibrium with structure **5**. In an internal displacement reaction, this intermediate can produce the phosphonium amide structure **6** which can then collapse to the product **3** by proton transfer (Scheme III).

These steps are exactly analogous to the accepted mechanisms for intermolecular reactions of this type,[2,3] although the detailed mechanism for the amide reactions

Scheme III



to form phospha(P^V)azenes has not been established.[6,7]

In summary, we have discovered a rather novel synthesis of a new class of phospha(P^V)azenes (**3**) by an intramolecular oxidation–reduction–condensation reaction involving a phosphine and azodicarbonamide. Furthermore, the synthesis is very simple and appears to be quite general.

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are not corrected. Infrared spectra were recorded on a Perkin-Elmer Model 377 spectrophotometer. Proton magnetic resonance spectra were run by using either a Varian XL-100 or a T-60 spectrophotometer, as solutions in Me_2SO-d_6 with tetramethylsilane as an internal standard. Mass spectra were recorded on a Varian MAT CH-7 spectrometer. Elemental analyses were performed by the Microanalytical Laboratories at the Hebrew University in Jerusalem.

General Procedure for the Reaction between Phosphines and Azodicarbonamide. To a stirred solution of phosphine (0.01 mol) in 20 mL of dimethyl sulfoxide was added 1.16 g of azodicarbonamide (0.01 mol) in 20 mL of dimethyl sulfoxide. The yellow azo solution turned almost immediately to a pale orange or colorless. In some cases (**3a, e–g**), the crude product started to precipitate within a few minutes, and precipitation was completed by cooling to 5 °C for 1 h. The phospha(P^V)azenes were filtered, washed with ether, and recrystallized (see Table I). With some of the phosphines (**3b, d**), precipitation occurred only upon prolonged cooling. In the case of diphenylethylphosphine, no precipitation took place even after prolonged cooling, and the product was obtained after solvent removal in vacuo and column separation (from hydrazinedicarbonamide; silica gel). Physical data of the products are given in Table I and IR and NMR data

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in Table II.

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Registry No. 1, 123-77-3; **2a**, 603-35-0; **2b**, 1486-28-8; **2c**, 607-01-2; **2d**, 672-66-2; **2e**, 1605-53-4; **2f**, 554-70-1; **2g**, 1663-45-2; **3a**, 79731-18-3; **3b**, 79731-19-4; **3c**, 79731-20-7; **3d**, 79731-21-8; **3e**, 79731-22-9; **3f**, 79731-23-0; **3g**, 79731-24-1.

Synthesis with α-Heterosubstituted Phosphonate Carbanions. 12.[1] X-ray Structure Determination of (*R*,*S*)-Diphenyl 1-(4-Bromoanilino)-1-(4,5-methylenedioxy-2-nitrophenyl)methanephosphonate

Michael D. Crenshaw, S. J. Schmolka, Hans Zimmer,* Robert Whittle, and R. C. Elder*

Department of Chemistry, University of Cincinnati, Cincinnati, Ohio 45221

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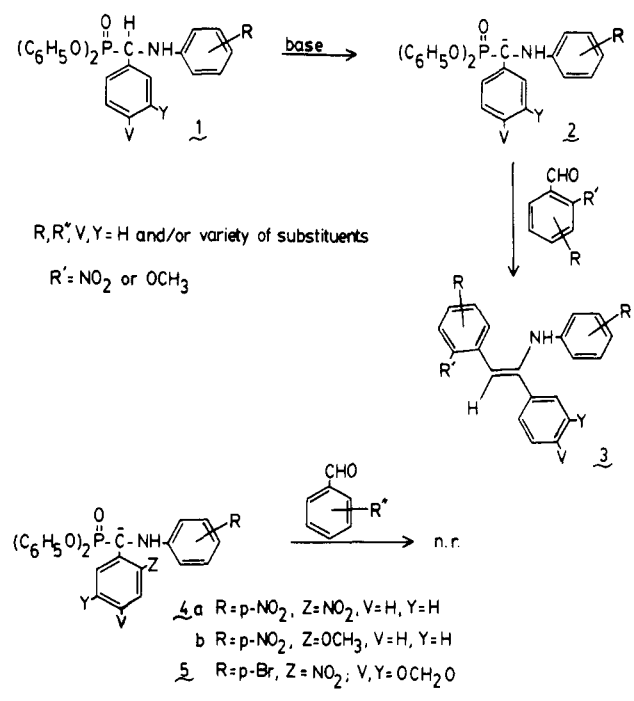
The reaction of (*R*,*S*)-diphenyl 1-(4-nitroanilino)-1-(2-methoxyphenyl)methanephosphonate with KOH in methanol followed by addition of an aldehyde is expected to yield rapidly in an aldol-type condensation the corresponding enamine. However, transesterification of the phosphonate occurs instead to yield (*R*,*S*)-dimethyl 1-(4-nitroanilino)-1-(2-methoxyphenyl)methanephosphonate at a somewhat slower rate. If the ortho substituent is either NO_2 or OCH_3, the desired enamine is not produced under a variety of conditions. An X-ray structure determination of an analogous, unreactive phosphonate, (*R*,*S*)-diphenyl 1-(4-bromoanilino)-1-(4,5-methylenedioxy-2-nitrophenyl)methanephosphonate, $P2_1/n$, a = 10.779 (4) Å, b = 20.694 (7) Å, c = 13.336 (3) Å, β = 109.470 (1)°, U = 2803.4 Å^3, Z = 4 (with two solvent molecules per unit cell when recrystallized from benzene), d_{measd} = 1.48 (2), d_{calcd} = 1.467 g cm^{-3}, R_1 = 0.054, R_2 = 0.033, indicates that steric hindrance may explain the failure of the resulting carbanion to react with the aldehyde. The structure results are compared to those for the reactive compound, diethyl 1-anilino-1-phenylmethanephosphonate.

Introduction

Phosphonates of the general form, diphenyl 1-(4-nitroanilino)-1-arylmethanephosphonate (**1**) are useful in the syntheses of ketones, indoles,[2a] benzo[*b*]furans,[2b] and quinolines.[2c] They are readily deprotonated by base to give the carbanions (**2**) which subsequently react with a wide variety of aldehydes to yield the corresponding enamines (**3**; Scheme I). If an ortho substituent (as in **4**) is present on the phenyl ring bound to the carbanion carbon atom, enamines are not obtained. However, the color change asociated with the carbanion formation is observed. For example, with the ortho substituents NO_2 or OCH_3 and the reactant aldehydes *trans*-cinnamaldehyde or benzaldehyde, no aldol-type condensation product is formed. Carbanions of 1-anilino-1-phenylmethanephosphonates which lack an ortho substituent[2a,b] do react with ortho-substituted benzaldehydes.

Since it apeared likely that carbanion formation takes place for all of these compounds but that the carbanion formed in nonreactive cases might be too sterically hindered for subsequent, successful nucleophilic attack on the aldehyde,[3] we have determined the single-crystal structure of one of the nonreactive phosphonate starting materials by X-ray methods and report it here.

Scheme I



Results and Discussion

The structure of the title compound, **5**, is shown in Figure 1. The structure of another phosphonate, (*R*,*S*)-diethyl 1-anilino-1-phenylmethane phosphonate, **6** (Figure 2), which will react under similar conditions to yield an enamine, has been published.[4] Pertinent bond lengths and angles from the structures of the two phosphonates are included in Table I for comparison. The O–C bond lengths of the esters differ as expected due to the difference in hybridization between phenyl carbon (sp^2)

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