JOC*Article*

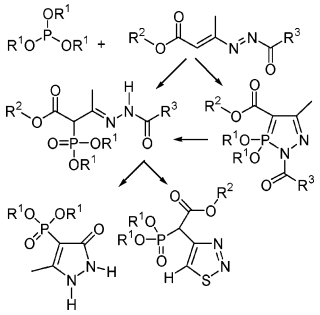
Solvent-Free Reaction of Some 1,2-Diaza-1,3-butadienes with Phosphites: Environmentally Friendly Access to New Diazaphospholes and *E*-Hydrazonophosphonates

Orazio A. Attanasi,[†] Graziano Baccolini,[‡] Carla Boga,[‡] Lucia De Crescentini,[†] Paolino Filippone,*[,†] and Fabio Mantellini*[,†]

Istituto di Chimica Organica, Università degli Studi di Urbino "Carlo Bo", Via Sasso 75, 61029 Urbino, Italy, and Dipartimento di Chimica Organica "A. Mangini", Università degli Studi di Bologna, Viale Risorgimento 4, 40136 Bologna, Italy

filippone@uniurb.it

Received February 7, 2005



The present article describes the reaction between 1,2-diaza-1,3-butadienes and trialkyl phosphites, under an atmosphere of nitrogen and under solvent-free conditions, to give alkyl 3,3-dialkoxy-2*H*-1,2,3λ^5-diazaphosphole-4-carboxylates that, in turn, are converted into corresponding *E*-hydrazonophosphonates by treatment with THF:water (95:5). These latter compounds are obtained directly by the reaction of 1,2-diaza-1,3-butadienes with trialkyl phosphites in the presence of air. These compounds are useful for the further preparation of dialkyl (5-methyl-3-oxo-2,3-dihydro-1*H*-4-pyrazolyl)phosphonates and 2-dialkoxyphosphoryl-1,2,3-thiadiazoles.

Introduction

Recently, 1,2-diaza-1,3-butadienes have been intensively studied by several authors and have been demonstrated to be interesting products and powerful intermediates in organic synthesis.[1,2] In our investigations, these compounds have manifested the aptitude to give rise to polyfunctionalized five-membered heterocycles, in particular, pyrazoles,[3] thiadiazoles,[4] and selenadiazoles[4] (Figure 1) by means of preliminary carbon−carbon or carbon−heteroatom bond formation and subsequent internal ring closure.

Previously, some of us used conjugated phenylazoalkenes to obtain 2*H*-1,2,3-diazaphosphole derivatives.[5]

FIGURE 1. Five-membered heterocycles obtained from 1,2-diaza-1,3-butadienes.

Generally, these compounds are prepared by the reaction of hydrazones with PCl_3. However, this procedure presents an important limitation: the large amount of HCl formed during the process may cause an easy P−N cleavage and consequent formation of related open-ring products[6] and may induce the acidic hydrolysis of the hydrazone bond, producing the parent carbonyl derivative.[7,8] The same behaviors have not been observed in the case of 1,2-diaza-1,3-butadienes. Considering these facts, we hypothesized that diazaphosphole derivatives could be useful intermediates for the ready formation of indoles,[9] pyrroles,[10] and other azaheterocycles.[11]

Some of us have preliminarily reported the reaction of phenylazostilbene (PAS) with some phosphites in hexane

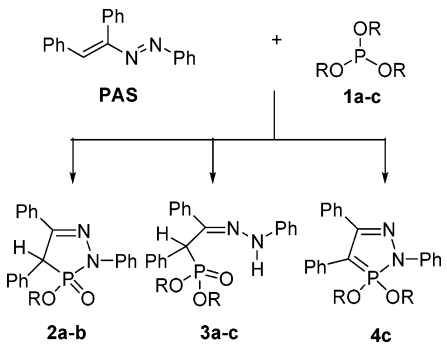
[†] Università degli Studi di Urbino.
[‡] Università degli Studi di Bologna.

(1) (a) Attanasi, O. A.; Caglioti, L. *Org. Prep. Proced. Int.* **1986**, *18*, 299. (b) Attanasi, O. A.; Filippone, P. *Synlett* **1997**, 1128. (c) Attanasi, O. A.; De Crescentini, L.; Filippone, P.; Mantellini, F.; Santeusanio, S. *Arkivoc* **2002**, *xi*, 274. (d) Attanasi, O. A.; De Crescentini, L.; Filippone, P.; Mantellini, F.; Santeusanio, S. *Synlett* **2003**, *8*, 1183. (e) Attanasi, O. A.; De Crescentini, L.; Favi, G.; Filippone, P.; Mantellini, F.; Santeusanio, S. *J. Org. Chem.* **2004**, *69*, 2686.

10.1021/jo050242n CCC: $30.25
Published on Web 04/09/2005

at room temperature which required nearly 1 month for completion.[12] The reaction of PAS with trialkyl phosphites (**1a**−**b**) afforded a mixture of 3-alkoxy-2,4,5-triphenyl-3,4-dihydro-2*H*-1,2,3λ^5-diazaphosphol-3-ones (**2a**−**b**) and dialkyl {1,2-diphenyl-2-[(*Z*)-2-phenylhydrazono]-ethyl}-phosphonates (**3a**−**b**), derived by hydrolytic ring opening. The reaction of PAS with triphenyl phosphite (**1c**) produced 3,3-diphenoxy-2,4,5-triphenyl-3,4−2*H*-1,2,3λ^5-diazaphosphole (**4c**), together with the expected diphenyl {1,2-diphenyl-2-[(*Z*)-2-phenylhydrazono]ethyl}-phosphonate (**3c**) (Scheme 1). Product **4c** represents one of the rare examples in the literature[13−15] of such a compound with an ylide structure, which is likely favored by its aromatic character.

SCHEME 1[a]



[a] **a**: R = Me; **b**: R = Et; **c**: R = Ph.

By continuing our investigations of 1,2-diaza-1,3-butadienes as building blocks for the constructions of five-membered diazaheterorings, we decided to explore more extensively the reactions of dimethyl or diethyl phosphites with 1-alkoxycarbonyl or 1-aminocarbonyl-1,2-diaza-1,3-butadiene-4-carboxylates under solvent-free conditions, in an attempt to obtain faster reaction times by means of simple and environmentally friendly procedures.[4,16−18] We also planned to perform the reactions under a nitrogen atmosphere, to tentatively avoid the concomitant formation of hydrazonic derivatives **3**. Furthermore, we tried successfully to selectively obtain these hydrazonic derivatives in the presence of atmospheric moisture. In fact, these latter products have been shown to derive by the hydrolytic opening of diazaphospholes.

Results and Discussion

1-Aminocarbonyl-1,2-diaza-1,3-butadiene-4-carboxylates **5a**−**f** or 1-*tert*-butoxycarbonyl-1,2-diaza-1,3-butadiene-4-carboxylate **5g** reacted with four equivalents of trimethyl or triethyl phosphites **1a**−**b** under a nitrogen atmosphere in 4.0−7.5 h to give alkyl 3,3-dialkoxy-2*H*-1,2,3λ^5-diazaphosphole-4-carboxylates **6a**−**h** in nearly quantitative yields (Scheme 2, Route A; Table 1).

The reaction of 1,2-diaza-1,3-butadienes **5a**−**g** with four equivalents of trimethyl or triethyl phosphites **1a**−**b**, in the presence of atmospheric moisture, provided hydrazonophosphonates **7a**−**h** in *E* isomeric form within 2−4 days (Scheme 2, Route B; Table 1). The configuration of the C=N bond was determined by NOE experiments (DPFGSE-NOE sequence).[19] The irradiation of the meth-

(2) (a) Figuereido, J. O.; Kascheres C. *J. Org. Chem.* **1997**, *62*, 1164. (b) Caposcialli, N.; Novi, M.; Petrillo, G.; Tavani, C. *Tetrahedron* **1998**, *54*, 5315. (c) Schantl, J. R.; Nàdenik, P. *Synlett* **1998**, 786. (d) South, M. S. *J. Heterocycl. Chem.* **1999**, *36*, 301. (e) Banert, K. In *Targets in Heterocyclic Systems-Chemistry and Properties*; Attanasi, O. A., Spinelli, D., Eds.; Società Chimica Italiana: Rome, 2000; Vol. 3, p 1. (f) Polanc, S. In *Targets in Heterocyclic Systems-Chemistry and Properties*; Attanasi, O. A., Spinelli, D., Eds.; Società Chimica Italiana: Rome, 2000; Vol. 3, p 33. (g) Kuznetsov, M. A.; Kuznetsova L. M.; Schantl, J. *Russ. J. Org. Chem.* **2000**, *36*, 836. (h) Boeckman, R. K., Jr.; Reed, J. E.; Ge, P. *Org. Lett.* **2001**, *3*, 3651. (i) Boeckman, R. K., Jr.; Ge, P.; Reed, J. E. *Org. Lett.* **2001**, *3*, 3647. (j) Avalos, M.; Babiano, R.; Cintas, P.; Clemente, F. R.; Gordillo, R.; Hursthouse, M. B.; Jiménez, J. L.; Light, M. E.; Palacios, J. C. *Tetrahedron: Asymmetry* **2001**, *12*, 2261. (k) Alonso, C.; Palacios, F.; Rubiales, G.; Villegas, M. *Tetrahedron Lett.* **2004**, *45*, 4031.

(3) (a) Attanasi, O. A.; Filippone, P.; Mei, A. *Tetrahedron* **1992**, *48*, 1707. (b) Attanasi, O. A., Filippone, P.; Fiorucci, C.; Mantellini, F. *Tetrahedron Lett.* **1999**, *40*, 3891.

(4) (a) Attanasi, O. A.; De Crescentini, L.; Filippone, P.; Mantellini, F. *Synlett* **2001**, *4*, 557. (b) Attanasi, O. A.; De Crescentini, L.; Favi, G.; Filippone, P.; Giorgi, G.; Mantellini, F.; Santeusanio, S. *J. Org. Chem.* **2003**, *68*, 1947.

(5) Baccolini, G.; Todesco, P. E. *J. Org. Chem.* **1974**, *39*, 2650.

(6) For reviews about diazaphospholes see (a) Schmidpeter, A.; Karaghiosoff, K. Azaphospholes. In *Rings, Clusters and Polymers in Main Group and Transition Element*; Roesky, H. W., Ed.; Elsevier: Amsterdam, 1989; p 308. (b) Schmidpeter, A.; Karaghiosoff, K. Heterophospholes. In *Multiple Bonds and Low Coordination in Phosphorus Chemistry*; Regitz, M., Scherer, O. J., Eds.; Thieme G.: Stuttgart, Germany, 1990; p 258. (c) Majoral, J. P. *Synthesis* **1978**, 557. (d) Schmidpeter, A. In *Comprehensive Heterocyclic Chemistry-II*; Katrizky, A. R., Rees, C. W., Scriven, E. F. V., Eds.; Pergamon: Oxford, U.K.; 1996; Vol. 4, p 771.

(7) (a) Attanasi, O. A.; Gasperoni, S. *Gazz. Chim. Ital.* **1978**, *108*, 137. (b) Attanasi, O. A.; Gasperoni, S.; Carletti, C. *J. Prakt. Chem.* **1980**, *322*, 1063. (c) Attanasi, O. A.; Grossi, M.; Serra-Zanetti, F. *J. Chem. Res. (S)* **1983**, 322.

(8) (a) McOmie, J. F. W. *Protective Groups in Organic Chemistry*; Plenum Press: London, 1973. (b) Kocienski, P. J. *Protecting Groups*; Thieme G.: Stuttgart, Germany; 1994. (c) Schelhaas, M.; Waldmann, H. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2056. (d) Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*; John Wiley & Sons: New York, 1999. (e) Hanson, J. R. *Protecting Groups in Organic Synthesis*; Sheffield Academic Press: Sheffield, U.K.; 1999.

(9) Baccolini, G.; Todesco, P. E. *J. Chem. Soc., Chem. Commun.* **1981**, 563.

(10) Baccolini, G.; Sandali. C. *J. Chem. Soc., Chem. Commun.* **1987**, 788.

(11) Baccolini, G. In *Topics in Heterocyclic Systems-Synthesis, Reactions and Properties*; Attanasi, O. A., Spinelli, D., Eds.; Research Signpost: Trivandrum, India; 1996; Vol. 1, p 103.

(12) (a) Baccolini, G.; Todesco, P. E. *Tetrahedron Lett.* **1978**, *26*, 2313. (b) Baccolini, G.; Todesco, P. E.; Bartoli, G. *Phosphorus Sulfur* **1980**, *9*, 203.

(13) (a) Baccolini, G.; Dalpozzo, R.; Mele, V.; Mezzina, E. *Phosphorus Sulfur* **1988**, *39*, 179. (b) Baccolini, G.; Orsolan, G.; Mezzina, E. *Tetrahedron Lett.* **1995**, *36*, 447.

(14) (a) Arbuzov, B. A.; Dianova, E. N.; Zabotina, E. Ya. *Izv. Akad. Nauk, Ser. Khim.* **1981**, 2635. (b) Diallo, O.; Boisdon, M. T.; Lopez, L.; Malavaud, C.; Barrans, J. *Tetrahedron Lett.* **1986**, *27*, 2971. (c) Arbuzov, B. A.; Dianova, E. N. *Dokl. Akad. Nauk SSSR* **1980**, *255*, 1117. (d) Arbuzov, B. A.; Dianova, E. N.; Sharipova, S. M. *Izv. Akad. Nauk, Ser. Khim.* **1981**, 1600. (e) Litvinov, I. A.; Struchkov, Yu. T.; Arbuzov, B. A.; Dianova, E. N.; Galeeva, I. Z. *Izv. Akad. Nauk, Ser. Khim.* **1983**, 2280.

(15) SciFinder Scholar, CAS, American Chemical Society: Columbus, Ohio; 2004.

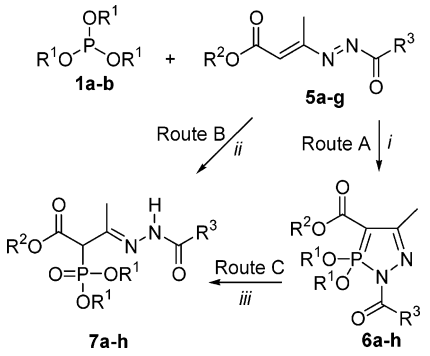
(16) (a) Varma, R. S. *Green Chem.* **1999**, 43. (b) Metzger, J. O. *Angew. Chem., Int. Ed.* **1998**, *37*, 2975. (c) Tanaka, K.; Toda, F. *Chem. Rev.* **2000**, *100*, 1025. (d) Varma, R. S. *Pure Appl. Chem.* **2001**, *73*, 193. (e) Cave, G. W. V.; Raston, C. L.; Scott, J. L. *Chem. Commun.* **2001**, 2159. (f) Tanaka, K.; Toda, F. In *Solvent-free Organic Synthesis*; Wiley-VCH: Weinheim, Germany; 2003.

(17) (a) Loh, T.-P.; Huang, J.-M.; Goh, S.-H.; Vittal, J. *Org. Lett.* **2000**, *2*, 1291. (b) Hajipour, A. R.; Arbabian, M.; Ruoho, A. E. *J. Org. Chem.* **2002**, *67*, 8622. (c) Xu, Z.-B.; Lu, Y.; Guo, Z.-R. *Synlett* **2003**, *4*, 564. (d) Lee, J. C.; Bae, Y. H. *Synlett* **2003**, *4*, 507. (e) Yadav, L. D. S.; Singh, S. *Synthesis* **2003**, *1*, 63.

(18) Attanasi, O. A.; De Crescentini, L.; Favi, G.; Filippone, P.; Mantellini, F.; Santeusanio, S. *Synlett* **2004**, *3*, 549.

(19) (a) Stonehouse, J.; Adell, P.; Keeler, J.; Shaka, A. J. *J. Am. Chem. Soc.* **1994**, *116*, 6037. (b) Stott, K.; Stonehouse, J.; Keeler, J.; Hwang, T. L.; Shaka, A. J. *J. Am. Chem. Soc.* **1995**, *117*, 4199. (c) Stott, K.; Keeler, J.; Van, Q. N.; Shaka, A. J. *J. Magn. Reson.* **1997**, *125*, 302. (d) Van, Q. N.; Smith, E. M.; Shaka, A. J. *J. Magn. Reson.* **1999**, *141*, 191.

SCHEME 2[a]



[a] Reagents and conditions: *i*, rt, nitrogen atmosphere; *ii*, rt; *iii*, rt, THF + H_2O.

yl signal at about 1.9 ppm enhances the NH signal at ~9 ppm and vice versa: this evidence suggests the proximity of these two groups, which is in good agreement with the *E* configuration of the C=N center. Yields and reaction times of compounds **6a**−**h** and **7a**−**h** are shown in Table 1.

The formation of alkyl 3,3-dialkoxy-2*H*-1,2,3λ^5-diazaphosphole-4-carboxylates **6** likely occurs because of the preliminary nucleophilic attack of the phosphorus at the terminal carbon atom of the azo-ene system with the formation of a zwitterionic intermediate (**I**). The subsequent intramolecular attack of the negative nitrogen at the positive phosphorus atom gives rise to dihydrodiazaphosphole intermediate **II**. The conversion of **II** into the corresponding diazaphospholes **6** by the loss of an alcohol molecule is favored by the aromatic character of these latter compounds (Scheme 3).

Indeed, hydrazonophosphonates **7** were derived by hydrolytic ring opening of diazaphosphole **6** through the intermediate **III** and the subsequent cleavage of the P−N bond.

This pathway was confirmed by the treatment of diazaphospholes **6a**−**h** with THF:water (95:5) (Scheme 2, Route C; Table 1), which produced the corresponding hydrazonophosphonates **7a**−**h** in 24−36 h in quantitative yields. This behavior was checked by monitoring the reaction between trimethyl phosphite (**1a**) and 1,2-diaza-1,3-butadiene **5a** directly in an NMR tube by ^{31}P NMR spectroscopy. The spectra (in $CDCl_3$) showed a gradual disappearance of the signal at 57.13 ppm that was ascribable to compound **6a** and the concomitant appearance of that at 20.25 ppm related to **7a**.

In turn, the compounds **7a** and **e** can be conveniently used for the construction of dimethyl or diethyl (5-methyl-3-oxo-2,3-dihydro-1*H*-4-pyrazolyl)phosphonates **8a**−**b** by treatment with sodium hydride in THF at room temperature. The closure to the pyrazolone ring is due to the intramolecular nucleophilic attack of the NH hydrazonic nitrogen atom at the ester group with loss of an alcohol molecule. The concomitant base-promoted hydrolytic cleavage of the aminocarbonyl group linked to the nitrogen in position 1 of the pyrazolone also takes place (Scheme 4).[3]

Moreover, the compounds **7a**, **b**, and **f** readily produced 2-dialkoxyphosphoryl-1,2,3-thiadiazoles **9a**−**c** by treatment with thionyl chloride under solvent-free conditions, according to a typical Hurd−Mori reaction.[4] Yields and reaction times of compounds **8a**−**b** and **9a**−**c** are shown in Table 2.

Conclusion

The present article describes the general protocol for the selective preparation of alkyl 3,3-dialkoxy-2*H*-1,2,3λ^5-diazaphosphole-4-carboxylates in high yields under a nitrogen atmosphere. To the best of our knowledge, this represents one of the rare examples reported in the literature for the synthesis of such products.[13−15] Because the procedure does not require the use of solvent or additional catalyst, this process is economical, environmentally friendly, and particularly adequate for large-scale production.[16−18]

In addition, a similar procedure in the presence of atmospheric moisture permits the selective production of hydrazonophosphonate derivatives that can be conveniently used for the preparation of interesting dimethyl or diethyl (5-methyl-3-oxo-2,3-dihydro-1*H*-4-pyrazolyl)-phosphonates[20] and 2-dialkoxyphosphoryl-1,2,3-thiadiazoles.[4]

Experimental Section

General Methods. Reagents and solvents, workup procedures, and analyses were performed in general as described in the Supporting Information.

General Procedure for the Synthesis of Alkyl 3,3-Dialkoxy-2*H*-1,2,3λ^5-diazaphosphole-4-carboxylates 6a−h (Route A). 1,2-Diaza-1,3-butadienes **5a**−**g** (1 mmol) as a mixture of *E*/*Z* isomers[21] and dialkyl phosphites **1a**−**b** (4 mmol) were magnetically stirred for 4.0−7.5 h under nitrogen atmosphere. The residual trialkyl phosphite was removed under reduced pressure to give the crude alkyl 3,3-dialkoxy-2*H*-1,2,3λ^5-diazaphosphole-4-carboxylates **6a**−**h** in good purity. Further purification can be obtained by crystallization from ethyl acetate-cyclohexane.

Methyl 2-(Aminocarbonyl)-3,3-dimethoxy-5-methyl-2*H*-1,2,3λ^5-diazaphosphole-4-carboxylate (6a). White solid; mp 118−120 °C; IR (Nujol) ν_{max} 3382, 3241, 3195, 1710, 1671 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.26 (d, 3H, $^4J_{HP}$ = 0.8 Hz), 3.68 (s, 3H), 3.84 (d, 6H, $^3J_{HP}$ = 13.6 Hz), 5.58 and 6.53 (2 br s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 18.1 (q, $^3J_{CP}$ = 6.1 Hz), 50.4 (q), 56.2 (q, $^2J_{CP}$ = 6.8 Hz), 59.7 (s, $^1J_{CP}$ = 206.7 Hz), 154.3 (s, $^3J_{CP}$ = 8.4 Hz), 156.5 (s, $^2J_{CP}$ = 34.9 Hz), 164.9 (s, $^2J_{CP}$ = 19.0 Hz); ^{31}P NMR (162 MHz, DMSO-d_6) δ 57.13; MS (ESI+) *m*/*z* 264 (M+H), 286 (M+Na), 304 (M+K). Anal. Calcd for $C_8H_{14}N_3O_5P$: C, 36.51; H, 5.36; N, 15.97. Found: C, 36.39; H, 5.47; N, 16.09.

General Procedure for the Synthesis of *E*-Hydrazonophosphonates 7a−h (Route B). 1,2-Diaza-1,3-butadienes **5a**−**g** (1 mmol) as a mixture of *E*/*Z* isomers[21] and dialkyl phosphites **1a**−**b** (4 mmol) were magnetically stirred for 24.0−96.0 h in the presence of air moisture. The residual trialkyl phosphite was removed under reduced pressure to give *E*-hydrazonophosphonates **7a**−**h** in good purity. Further purification can be obtained by crystallization from ethyl acetate-cyclohexane.

General Procedure for the Synthesis of *E*-Hydrazonophosphonates 7a−h (Route C). A solution of alkyl 3,3-dialkoxy-2*H*-1,2,3λ^5-diazaphosphole-4-carboxylates **6a**−**h** (1 mmol) in tetrahydrofuran:water (9.5:0.5 mL) was magnetically

(20) Khotinen, A. V.; Polozov, A. M.; Alexander, M. *Phosphorus, Sulfur Silicon Relat. Elem.* **1993**, *83*, 53.

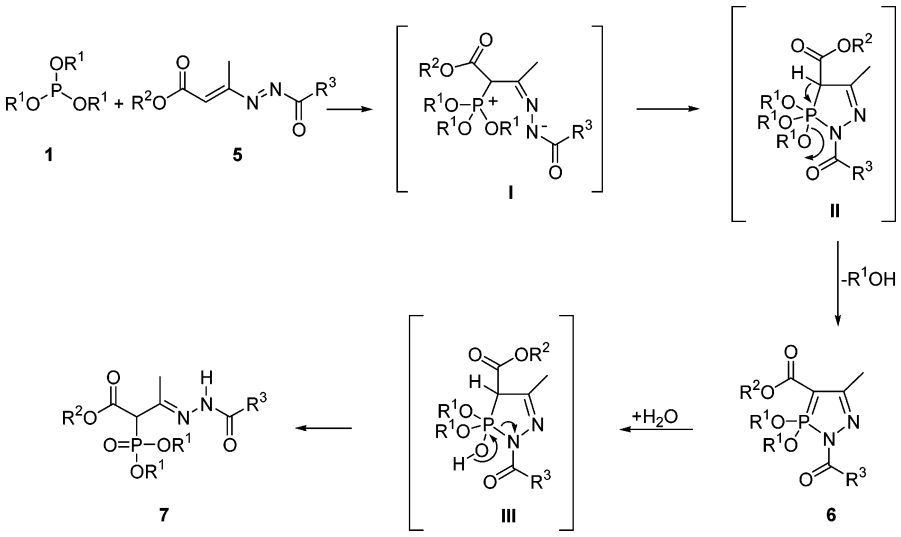
(21) (a) Attanasi, O. A.; Filippone, P.; Mei, A.; Santeusanio, S. *Synthesis* **1984**, 671. (b) Attanasi, O. A.; Filippone, P.; Mei, A.; Santeusanio, S. *Synthesis* **1984**, 873.

TABLE 1. Yields and Reaction Times of Alkyl 3,3-Dialkoxy-2*H*-1,2,3λ^5-diazaphosphole-4-carboxylates 6a−h and *E*-Hydrazonophosphonates 7a−h

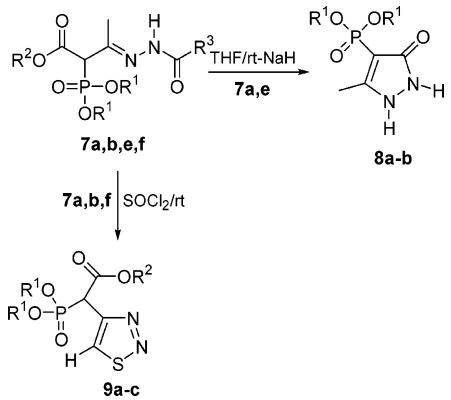
1	R^1	5	R^2	R^3	6	yield (%)	7	yield (%)		time (h)		
1a	Me	**5a**	Me	NH_2	**6a**	98[a,b]	**7a**	95[c]	98[d]	4.0[b]	24.0[c]	24.0[d]
1a	Me	**5b**	Et	NH_2	**6b**	97[a,b]	**7b**	94[a,c]	97[d]	6.5[b]	28.0[c]	32.0[d]
1a	Me	**5c**	$C(CH_3)_3$	NH_2	**6c**	96[a,b]	**7c**	95[a,c]	97[d]	5.5[b]	72.0[c]	34.0[d]
1a	Me	**5d**	$CH_2CH{=}CH_2$	NH_2	**6d**	96[a,b]	**7d**	93[a,c]	95[d]	7.5[b]	58.0[c]	28.0[d]
1b	Et	**5b**	Et	NH_2	**6e**	91[a,b]	**7e**	89[a,c]	97[d]	6.0[b]	96.0[c]	36.0[d]
1b	Et	**5e**	Bn	NH_2	**6f**	87[a,b]	**7f**	89[a,c]	95[d]	5.5[b]	60.0[c]	24.0[d]
1b	Et	**5f**	Et	NHPh	**6g**	88[a,b]	**7g**	91[a,c]	94[d]	4.5[b]	30.0[c]	26.0[d]
1b	Et	**5g**	Me	$OC(CH_3)_3$	**6h**	91[a,b]	**7h**	88[a,c]	98[d]	7.0[b]	28.0[c]	30.0[d]

[a] Yields of pure isolated products are based on reagents **5a**−**g**. [b] Route A (Scheme 2). [c] Route B (Scheme 2). [d] Route C (Scheme 2); yields of pure isolated products are based on reagents **6a**−**h**.

SCHEME 3



SCHEME 4



stirred for 24−36 h. The mixture was dried over anhydrous sodium sulfate and then the solvent was evaporated under reduced pressure to give crude hydrazonophosphonates **7a**−**h** in good purity. Further purification can be obtained by crystallization from ethyl acetate-cyclohexane.

Methyl 3-[(*E*)-2-(Aminocarbonyl)hydrazono]-2-(dimethoxyphosphoryl)butanoate (7a). White solid; mp 101−105 °C; IR (Nujol) ν_{max} 3460, 3205, 1744, 1719 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.04 (d, 3H, $^4J_{HP}$ = 1.6 Hz), 3.73−3.85 (m, 9H), 4.06 (d, 1H, $^2J_{HP}$ = 24.4 Hz), 5.47 and 6.09 (2 br s, 2H), 8.91 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.0 (q), 53.0 (q), 53.6 (q, $^2J_{CP}$ = 7.8 Hz), 54.4 (d, $^1J_{CP}$ = 144.2 Hz), 141.3 (s, $^2J_{CP}$ = 7.6 Hz), 157.7 (s), 166.5 (s, $^2J_{CP}$ = 4.2 Hz); ^{31}P NMR (162 MHz, $CDCl_3$) δ 20.25; MS (ESI+) *m/z* 282 (M+H), 304 (M+Na), 322 (M+K). Anal. Calcd for $C_8H_{16}N_3O_6P$: C, 34.17; H, 5.74; N, 14.94. Found: C, 33.94; H, 6.02; N, 15.07.

TABLE 2. Yields and Reaction Times of Dialkyl (5-Methyl-3-oxo-2,3-dihydro-1*H*-4-pyrazolyl)phosphonates 8a−b and 2-Dialkoxyphosphoryl-1,2,3-thiadiazoles 9a−c

7	R^1	R^2	R^3	8	yield (%)[a]	time (h)	9	yield (%)[a]	time (h)
7a	Me	Me	NH_2	**8a**	89	1.5	**9a**	72	0.8
7b	Me	Et	NH_2				**9b**	77	1.2
7e	Et	Et	NH_2	**8b**	95	2.5			
7f	Et	Bn	NH_2				**9c**	71	1.0

[a] Yields of pure isolated products.

General Procedure for the Synthesis of Dialkyl (5-Methyl-3-oxo-2,3-dihydro-1*H*-4-pyrazolyl)phosphonates 8a−b. To a magnetically stirred solution of hydrazonophosphonates **7a** and **e** (1 mmol) in tetrahydrofuran (10 mL), a stoichiometric amount of sodium hydride (1 mmol) was added. The conversion into pertinent dialkyl (5-methyl-3-oxo-2,3-dihydro-1*H*-4-pyrazolyl)phosphonates **8a**−**b** occurred in 1.5−2.5 h. The reaction mixture was neutralized with Amberlyst 15H (2.5 mmol) and left under magnetic stirring for about 1.0 h. After filtration of the resin and evaporation of the reaction solvent, products **8a**−**b** were purified by flash chromatography on a silica gel column and crystallized from ethyl acetate-cyclohexane.

Dimethyl (5-Methyl-3-oxo-2,3-dihydro-1*H*-4-pyrazolyl)-phosphonate (8a). White solid; mp 200−203 °C; IR (Nujol) ν_{max} 3292, 3165, 1730, 1683, 1642 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.99 (d, 3H, $^4J_{HP}$ = 0.4 Hz), 3.48 (d, 6H, $^3J_{HP}$ = 11.2 Hz), 6.78 (br s, 1H), 8.99 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 15.8 (q), 51.8 (q, $^2J_{CP}$ = 4.6 Hz), 152.6 (s, $^2J_{CP}$ = 15.2 Hz), 153.7 (s), 168.5 (s, $^2J_{CP}$ = 22.7 Hz); MS (ESI+) *m/z* 207 (M+H), 229 (M+Na), 247 (M+K). Anal. Calcd for $C_6H_{11}N_2O_4P$: C, 34.96; H, 5.38; N, 13.59. Found: C, 34.84; H, 5.45; N, 13.43.

General Procedure for the Synthesis of Alkyl 2-(Dialkoxyphosphoryl)-2-(1,2,3-thiadiazol-4-yl)acetates 9a–c. Hydrazonophosphonates **7a**, **b**, and **f** (1 mmol) were magnetically stirred in thionyl chloride (10 mL) at room temperature for 0.8−1.2 h. The crude was neutralized with a saturated aqueous solution of sodium hydrogen carbonate until pH ∼ 7 and then was extracted with ethyl acetate. The organic layer was washed with water and dried with sodium sulfate. 2-Dialkoxyphosphoryl-1,2,3-thiadiazoles **9a–c** were crystallized from diethyl ether-light petroleum ether (40−60 °C).

Methyl 2-(Dimethoxyphosphoryl)-2-(1,2,3-thiadiazol-4-yl)acetate (9a). Yellow solid; mp 101−103 °C; IR (Nujol) ν_{max} 3108, 1745, 1720 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.67 (d, 3H, $^3J_{HP}$ = 11.2 Hz), 3.80 (s, 3H), 3.81 (d, 3H, $^3J_{HP}$ = 11.2 Hz), 5.32 (d, 1H, $^2J_{HP}$ = 24.4 Hz), 8.93 (d, 1H, $^4J_{HP}$ = 2.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 45.1 (d, $^1J_{CP}$ = 132.0 Hz), 53.4 (q), 54.0 (q, $^2J_{CP}$ = 6.8 Hz), 136.3 (d, $^3J_{CP}$ = 3.8 Hz), 153.2 (s, $^2J_{CP}$ = 6.9 Hz), 166.3 (s, $^2J_{CP}$ = 4.5 Hz); MS (EI) *m/z* 266 (1) [M$^+$], 252 (60), 206 (47), 192 (67), 179 (100). Anal. Calcd for $C_7H_{11}N_2O_5PS$: C, 31.58; H, 4.16; N, 10.52. Found: C, 31.61; H, 4.25; N, 10.23.

Acknowledgment. This work was supported by the financial assistance from the Ministero dell'Università, dell'Istruzione e della Ricerca (MIUR)-Roma and Università degli Studi di Urbino.

Supporting Information Available: General procedures for the preparation of compounds **6a–h**, **7a–h**, **8a–b**, and **9a–c**; product characterization data and ^{1}H, ^{13}C, and ^{31}P peak listing for **6a–h**, **7a–h**, **8a–b**, and **9a–c**; ^{31}P spectra from the reaction between **5a** and **1b** directly done in NMR tube. This material is available free of charge via the Internet at http://pubs.acs.org.

JO050242N