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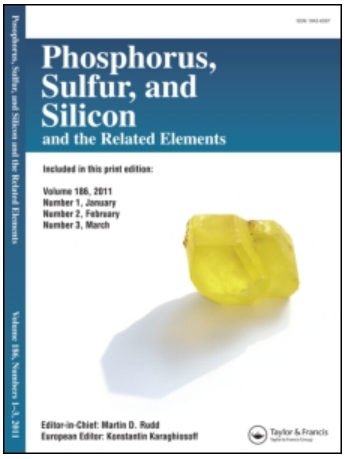

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
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AN EFFICIENT SYNTHESIS OF 4-DIMETHOXYPHOSPHONYL SUBSTITUTED PYRAZOLES AND PYRAZOLINE-5-ONES

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To cite this Article Khotinen, Alexander V. and Polozov, Alexander M.(1993) 'AN EFFICIENT SYNTHESIS OF 4-DIMETHOXYPHOSPHONYL SUBSTITUTED PYRAZOLES AND PYRAZOLINE-5-ONES', Phosphorus, Sulfur, and Silicon and the Related Elements, 83: 1, 53 — 58
To link to this Article: DOI: 10.1080/10426509308034347
URL: http://dx.doi.org/10.1080/10426509308034347

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Phosphorus, Sulfur, and Silicon, 1993, Vol. 83, pp. 53–58
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AN EFFICIENT SYNTHESIS OF 4-DIMETHOXYPHOSPHONYL SUBSTITUTED PYRAZOLES AND PYRAZOLINE-5-ONES

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(Received July 6, 1993; in final form August 3, 1993)

2-Dimethoxyphosphonyl-1,3-dicarbonyl compounds (**1a–c**) were used for the synthesis of 4-dimethoxyphosphonyl substituted pyrazoles (**2a–e**) and pyrazoline-5-ones (**5a–c**). Intermediate hydrazones (**3b, c**) were also isolated. **5a** exists in the OH tautomeric form, whereas **5c**—in the NH form. Tautomeric transition from the OH into the NH form was found for **5b** at the melting point.

Key words: ^{13}C-NMR-spectra; hydrazine; pyrazole; pyrazoline-5-one; tautomer.

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INTRODUCTION

The derivatives of pyrazole have been used in medicine,[1] dye chemistry,[1] as pesticides[2] and in the liquid-liquid extraction of heavy metals.[3,4] Taking into account a successful application of phosphonates as biologically active compounds,[2] and extractants of metals,[5] the general and practical synthesis of alkoxyphosphonyl substituted pyrazoles and pyrazoline-5-ones would be very useful.

Three main methods have been described for these compounds: displacement reaction by phosphorus nucleophiles,[6–8] cyclocondensation of phosphorus substituted hydrazones of vinylcarbonyl compounds,[9–13] and addition of hydrazines to β-dicarbonyl functionalized phosphonates.[14,15] Nevertheless, all of these methods were rather limited: polyaryl substituted pyrazoles were not available. The more potentially useful β-dicarbonyl approach[14,15] was restricted by absence of appropriate phosphorus precursors.

We have reported a method, based on the standard reaction of β-dicarbonyl compounds with hydrazines,[1] using previously described 2-dialkoxyphosphonyl substituted 1,3-dicarbonyl compounds (**1a–c**)[16,17] which give high yields of the title compounds. Unusual tautomeric behavior of pyrazoline-5-ones is observed.

RESULTS AND DISCUSSION

4-Dimethoxyphosphonyl substituted pyrazoles (**2a–e**) were obtained in a one-pot reaction; the intermediate hydrazones were not identified (Scheme I). 3-Dimethoxyphosphonyl-2,4-pentanedione (**1a**) reacts with hydrazines under neutral

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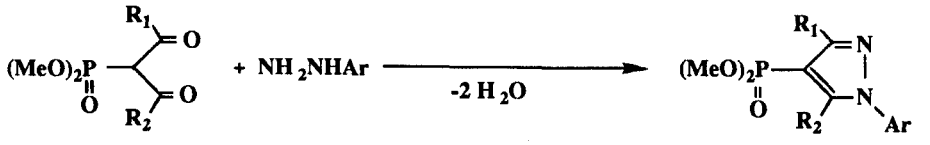
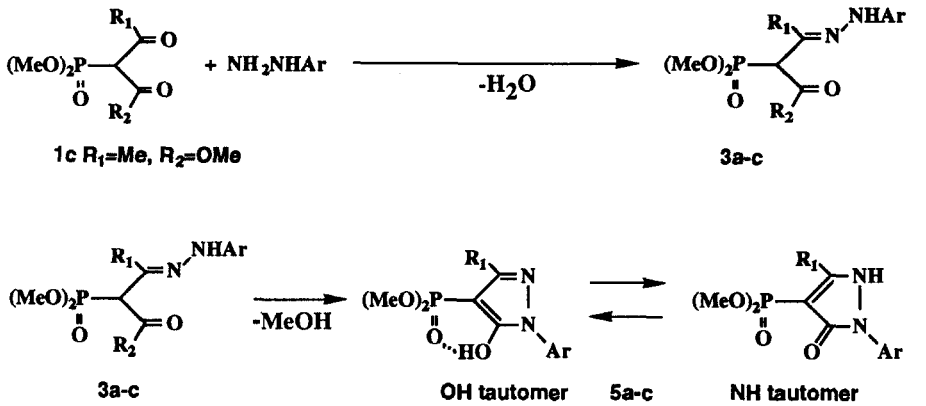


1a,b 2a-e

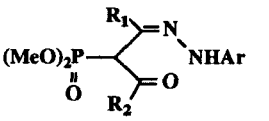
1	2	R_1=R_2	Ar
a	a	Me	Ph
a	b	Me	C_6H_4-4-NO_2
a	c	Me	C_6H_3-2,4-$(NO_2)_2$
b	d	Ph	Ph
b	e	Ph	C_6H_4-4-NO_2

SCHEME I



1c R_1=Me, R_2=OMe 3a-c 3a-c OH tautomer 5a-c NH tautomer

3	5	Ar
a[a]	a	Ph
b	b	C_6H_4-4-NO_2
c	c	C_6H_3-2,4-$(NO_2)_2$



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[a] 3a was not isolated.

SCHEME II

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TABLE I

Dimethoxyphosphonylpyrazoles (**2a–e**)

Product[a]	Yield[b] %	mp (C°)	Molecular formula[c]	IR (nujol) ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS) δ (ppm), J (Hz)	^{13}C-NMR ($CDCl_3$/TMS)[d] δ (ppm), J (Hz)
2a	65	oil	$C_{13}H_{17}N_2O_3P$	1536, 1247	2.33 (s, 3H); 2.38 (d, 3H, J = 2); 3.67 (d, 6H, J = 11); 7.1 (m, 5H)	12.1 (s); 12.4 (s); 52.3 (d, J = 5.2); 104.0 (d, J = 216.1); 147.2 (d, J = 25.7); 152.6 (d, J = 13.2)
2b	78	146–148 (MeOH)	$C_{13}H_{16}N_3O_5P$	1538, 1245	2.25 (s, 3H); 2.51 (d, 3H, J = 2); 3.58 (d, 6H, J = 11); 7.1–8.2 (m, 4H)	12.3 (s); 13.4 (s); 52.3 (d, J = 5.9); 106.0 (d, J = 204.4); 148.0 (d, J = 25.5); 153.7 (d, J = 13.2)
2c	90	154–156 (MeOH)	$C_{13}H_{15}N_4O_7P$	1540, 1245	2.23 (s, 3H); 2.37 (d, 3H, J = 2); 3.61 (d, 6H, J = 11); 8.1–8.7 (m, 3H)	11.4 (s); 13.2 (s); 52.4 (d, J = 5.9); 105.5 (d, J = 216.2); 149.5 (d, J = 26.5); 154.7 (d, J = 13.2)
2d	76	165–167 (MeOH)	$C_{23}H_{21}N_2O_3P$	1537, 1250	3.63 (d, 6H, J = 11); 6.8–7.8 (m, 14H)	
2e	78	190–192 (MeOH)	$C_{23}H_{20}N_3O_5P$	1535, 1248	3.61 (d, 6H, J = 11); 6.8–8.3 (m, 13H)	

[a] The ^{31}P chemical shifts ($CHCl_3$, 18–21 ppm) are in a good accord with the proposed structure.
[b] Yield of isolated product.
[c] Satisfactory microanalyses: C ± 0.31, H ± 0.18, N ± 0.4, P ± 0.11.
[d] The spectra of **2d, e** were not recorded because of low solubility.

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TABLE II

Hydrazonodimethoxyphosphonyl oxobutyrates (**3b, c**) and dimethoxyphosphonylpyrazolinones (**5a–c**)

Product[a]	Yield[b] %	mp (C°)	Molecular formula[c]	IR (nujol) ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS) δ (ppm), J (Hz)	^{13}C-NMR ($CDCl_3$/TMS)[f] δ (ppm), J (Hz)
3b	75	148–150	$C_{13}H_{17}N_3O_7P$	1725, 1228	2.05 (s, 1.5H); 2.09 (s, 1.5H); 3.62 (s, 3H); 3.62 (d, 3H, J = 11); 3.65 (d, 3H, J = 11); 4.12 (d, 1H, J = 23); 6.8–7.8 (m, 4H); 9.08 (s, 1H)	15.1 (s); 53.7 (d, J = 7.0); 54.1 (s); 55.5 (d, J = 134.2); 142.3 (d, J = 8.2); 167.7 (J = 3.1)
3c	80	150[e] (MeOH)	$C_{13}H_{16}N_4O_9P$	1728, 1230	1.92 (s, 1.5H); 1.95 (s, 1.5H); 3.58 (s, 3H); 3.59 (d, 3H, J = 11); 3.62 (d, 3H, J = 11); 4.07 (d, 1H, J = 23); 7.2–8.3 (m, 3H); 10.40 (s, 1H)	16.1 (s); 54.0 (s); 54.9 (d, J = 7.0); 55.6 (d, J = 134.4); 150.3 (d, J = 6.5); 167.6 (J = 2.8)
5a	72	100–101 (CH_3CN)	$C_{12}H_{15}N_2O_4P$	1550, 1195	2.15 (s, 3H); 3.61 (d, 6H, J = 11); 7.1 (m, 5H), 9.85 (s, 1H)	15.2 (s); 55.2 (d, J = 7.9); 96.3 (d, J = 217.3); 149.2 (d, J = 9.9); 163.7 (d, J = 16.8)
5b	65	130–135 (CH_3CN) 168–170[d]	$C_{12}H_{14}N_3O_6P$	1546, 1202 1673, 1240[d]	2.16 (s, 3H); 3.62 (d, 6H, J = 11); 7.1–8.0 (m, 4H), 8.36 (s, 1H)	14.8 (s); 54.8 (d, J = 7.9); 95.9 (d, J = 215.4); 151.9 (d, J = 10.0); 161.8 (d, J = 20.8)
5c	51	171–173 (CH_3CN)	$C_{12}H_{13}N_4O_8P$	1667, 1243	2.15 (s, 3H); 3.58 (d, 6H, J = 11); 7.30 (s, 1H); 7.4–8.3 (m, 3H)	

[a] The ^{31}P chemical shift ($CHCl_3$, 18–20 ppm for **3** and 18–21 ppm for **5** are in a good accord with the proposed structure.
[b] Yield of isolated product.
[c] Beginning of the cyclisation reaction.
[d] NH tautomer.
[e] Satisfactory microanalysis: C ± 0.26, H ± 0.14, N ± 0.4, P ± 0.11.
[f] The spectrum of **5c** was not recorded because of low solubility.

conditions, whereas 2-dimethoxyphosphonyl-1,3-diphenyl-1,3-propanedione (**1b**) only reacts in the presence of $HClO_4$ as a catalyst. Pyrazoles (**2a–e**) were isolated after drying with $MgSO_4$ their acetonitryl solutions and were purified by recrystallization (Table I).

Pyrazoline-5-one (**5a**) was obtained in a similar manner from methyl 3-dimethoxyphosphonyl-4-oxobutyrate (**1c**) and phenylhydrazine at ambient temperature (Scheme II). Less nucleophilic 4-nitro and 2,4-dinitrophenyl substituted hydrazines lead under the same conditions to intermediate hydrazones (**3b, c**). Their ^1H n.m.r. spectra confirmed the hydrazonic form (Table II). Their *trans* structure follows from the ^{13}C n.m.r. spectra: $\delta(CH_3)$ 15.0 ppm in **3b** and 16.0 ppm in **3c**, while for methyl 2-(phenylhydrazono)-4-oxobutyrate the $\delta(CH_3)$ signal is at 16.1 ppm in the *trans* and at 24.7 ppm in the *cis* isomer.[18] Obviously heating at 120°C was necessary for the isomerisation of the *trans* isomer (**3**) into the *cis* isomer (**4**), in which cyclization may occur. After drying, the title compounds (**5a–c**) were purified by recrystallisation. We failed to improve yields of **5b, c** using a one-pot reaction.

Unlike in 1-phenyl-3-methylpyrazoline-5-one[1,19,20] only OH tautomers (**5a–c**) are observed in $CDCl_3$ solution, which is evident from IR and ^1H n.m.r. spectroscopic data. The low-frequency shift of the P=O group absorption in the IR spectra ($CDCl_3$, 0.1–0.01 M) is attributed to the strong intramolecular hydrogen bonding. **5a, b** crystallise from solutions as OH tautomers, **5c** as NH tautomer. Heating of the OH tautomer **5b** at the melting point (135°C) causes a tautomeric transition into the NH tautomer with a higher melting point (168–170°C). A subsequent fusion of latter followed by cooling gives again the OH tautomer of **5b**.

In summary 2-dimethoxyphosphonyl-1,3-dicarbonyl compounds are key building blocks for the synthesis of dialkoxyphosphonyl substituted pyrazoles (**2a–e**) and pyrazoline-5-ones (**5a–c**).

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EXPERIMENTAL

IR spectra were recorded on a Specord-75 spectrometer. ^1H n.m.r. spectra were obtained on a Tesla-BS 467A (60 MHz), and ^{31}P n.m.r. spectra recorded on a 8 MHz spectrometer. Melting points were determined on a Kofler melting point apparatus and are uncorrected.

2-Dimethoxyphosphonyl-1,3-dicarbonyl compounds (**1a–c**) were prepared by the method described by us earlier.[16,17] Hydrazines were commercial reagents. Acetonitrile was distilled from phosphorus pentoxide. Diglyme was distilled under reduced pressure.

1-Aryl-4-(dimethoxyphosphonyl)-3,5-dimethylpyrazoles (**2a–c**), *methyl 2-(arylhydrazono)-3-(dimethoxyphosphonyl)-4-oxobutyrates* (**3b, c**) *and 1-phenyl-3-methyl-4-(dimethoxyphosphonyl)-pyrazoline-5-one* (**5a**). A solution (or suspension) of the hydrazine (1 mmol) in CH_3CN (5 ml) was added at once to a solution of the 2-(dimethoxyphosphonyl)-1,3-dicarbonyl compound (**1a–c**) (1 mmol) and the mixture was stirred at room temperature for 0.5 h. After drying over $MgSO_4$ the mixture was filtered, washed with CH_3CN (3 ml) and the solvent was then evaporated. The crude product (**2a**) was chromatographed on silica gel (100–160 um, column 15 1 cm, ethylacetate); **2b, c** and **3b, c** were purified by suction and recrystallized from MeOH, **5a** from CH_3CN.

1-Aryl-4-(dimethoxyphosphonyl)-3,5-diphenylpyrazoles (**2d, e**). A few drops of 70% $HClO_4$ were added to a mixture of the hydrazine (1 mmol) and the diketone (**1b**) (3.32 g, 1 mmol) and the mixture was stirred at room temperature for 10 min. Then $NaHCO_3$ (0.1 g) was added. After drying over $MgSO_4$ the mixture was filtered, washed with CH_3CN (3 ml) and solvent was then evaporated. The crude products (**2d, e**) were purified by suction and recrystallized from MeOH.

1-Aryl-3-methyl-4-(dimethoxyphosphonyl)-pyrazoline-5-ones (**5b, c**). A suspension of the hydrazine (1 mmol) in diglime (10 ml) was added at once to a solution of the methyl 3-(dimethoxyphosphonyl)-2-oxobutyrate (**1c**) in diglime (5 ml) and the mixture was stirred at room temperature for 0.5 h. After drying over $MgSO_4$ for 0.5 h the mixture was filtered, washed with CH_3CN (3 ml) and heated at 120°C under nitrogen bubbling for 0.5 h. After drying over $MgSO_4$, the solvent was evaporated under reduced pressure. The crude products (**5b, c**) were purified by suction and recrystallized from CH_3CN.

REFERENCES

1. J. Elguero, "Comprehensive Heterocyclic Chemistry," ed. A. R. Katritzky, C. V. Rees and K. T. Rotts, Pergamon Press, Oxford, **5,** 167 (1984).
2. N. N. Melnikov, "Pesticides," Nauka, Moskow (1987).
3. A. Roy and K. Nag, *J. Inorg. Nucl. Chem.*, **40,** 331 (1978).
4. B. Kuznic and D. M. Crakis-Sulikowska, *Monatsh. Chem.*, **119,** 89 (1988).
5. G. Sturtz, J. C. Clement, A. Daniel, J. Moliner and M. Lenxi, *Bull. Soc. Chim. Fr.*, 167 (1981).
6. D. Redmore, *Chem. Rev.*, **71,** 315 (1971).
7. I. I. Grandberg and A. N. Kost, *Zh. Obshch. Khim.*, **31,** 129 (1961).
8. A. A. Tolmachev, A. I. Sviridone, A. N. Kostyuk and E. S. Kozlov, *Zh. Obshch. Khim.*, **62,** 2395 (1992).
9. E. E. Aboujaoude, N. Collignon and Ph. Savignac, *Tetrahedron.*, **41,** 427 (1985).
10. B. C. Saunders and P. Simpson, *J. Chem. Soc.*, 3351 (1963).
11. E. Oheer and E. Zbiral, *Monatsh. Chem.*, **115,** 493 (1984).
12. H. G. Henning, G. Petzold and G. Busse, *Zeit. Chem.*, **8,** 302 (1968).
13. O. Guenther and K. Hartke, *Arch. Pharm.*, **308,** 693 (1975).
14. M. H. Maguire, R. K. Ralph and G. Shaw, *J. Chem. Soc.*, 2299 (1958).
15. E. E. Nifant'ev, S. I. Patlina and E. I. Matrosov, *Khim. Geterot. Soed.*, 513 (1977).
16. A. M. Polozov, N. A. Polezhaeva, A. H. Mustaphin, A. B. Khotinen and B. A. Arbuzov, *Synthesis*, 515 (1990).
17. A. M. Polozov, A. H. Mustaphin and A. V. Khotinen, *Phosphorus, Sulphur and Silicon*, **73,** 153 (1992).
18. A. R. Katritzky, P. Boorczynski and D. L. Ostercamp, *J. Chem. Soc., Perkin. Trans. II.*, 969 (1987).
19. V. G. Vinokurov, V. S. Troutskay, N. I. Grandberg and Yu. A. Pentin, *Zh. Obshch. Khim.*, 2597 (1963).
20. D. Zeigan, E. Kleinpeter, H. Wilde and G. Mann, *J. Pract. Chem.*, **323,** 188 (1981).

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