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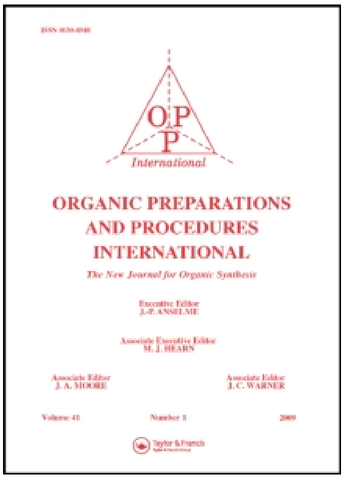

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ALKYL PHOSPHITES AND PHOSPHONATES AS ALKYLATING AGENTS FOR 1,3,4-THIADIAZOLIDINE-2,5-DITHIONES

M. M. Sidky[a]; M. R. Mahran[a]; M. F. Zayed[a]; W. M. Abdou[a]; T. S. Hafez[a]
[a] National Research Centre, Dokki-Cairo, EGYPT ARE

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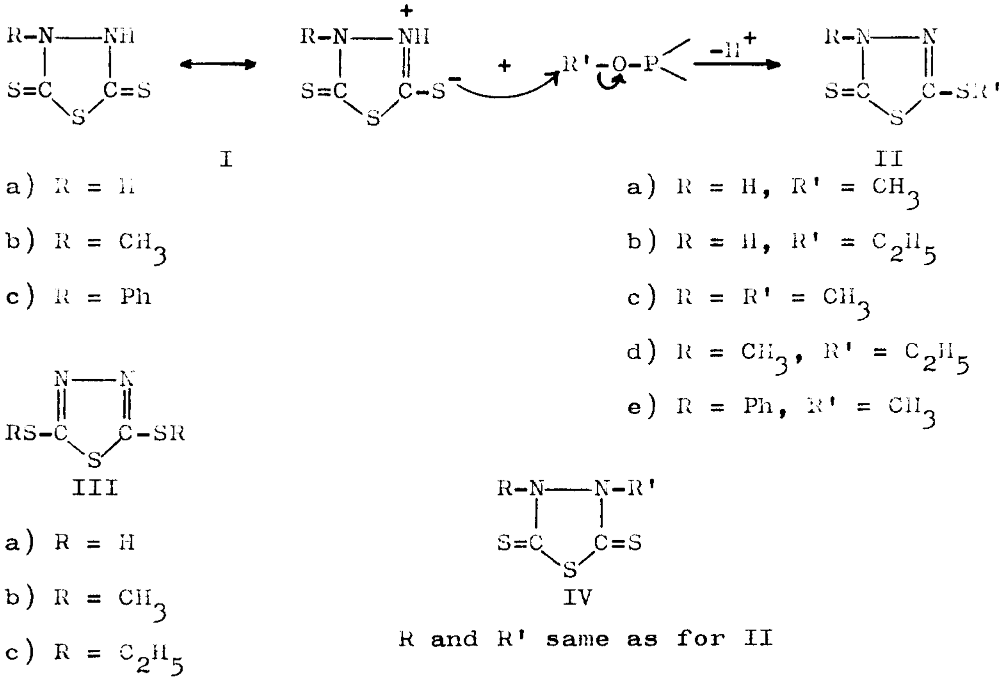
ALKYL PHOSPHITES AND PHOSPHONATES AS ALKYLATING AGENTS FOR 1,3,4-THIADIAZOLIDINE-2,5-DITHIONES

M. M. Sidky*, M. R. Mahran, M. F. Zayed, W. M. Abdou
and T. S. Hafez

National Research Centre, Dokki-Cairo, EGYPT, ARE

2-Alkylthio-1,3,4-thiadiazolidine-5-thiones of type II are useful intermediates in the synthesis of pesticides[1,2] and in a number of applications.[3-7] The methods described for the preparation of compounds II are either indirect and lengthy,[2,8,9] or produce differently alkylated compounds.[2,10-12]



Scheme 1

Alkyl phosphites and phosphonates have been known to convert acids to esters,[13] phenols and amines to the corresponding alkyl derivatives[13-15] and alcohols to ethers.[16] Since no information was found in the literature regarding the action of these reagents on thiols, it was therefore of interest to examine whether these reagents could alkylate compounds of type I to give II.

The S-alkyl derivatives IIa-e were obtained in a variety of ways. For example, IIa was generated in 85% yield by reaction of Ia with dimethyl phosphite (DMP) in boiling benzene for 2 hrs., in the presence of trace amounts of p-toluenesulfonic acid. Compound IIa was also obtained in a better yield (>95%) by treatment of Ia with trimethyl phosphite (TMP), in absence of solvent, at room temperature and in 80% yield by reaction of Ia with dimethyl methyl phosphonate (DMMP) in absence of solvent at 100° for 3 hrs. Under all conditions, less than 5% of 2,5-bis(methylthio)-1,3,4-thiadiazole IIIb was isolated. It is worthy to mention that whereas the reaction of dialkyl phosphites (DAP) with Ia proceeds only in presence of p-TsOH, its presence was unnecessary in the cases with thiadiazolidines Ib and Ic.

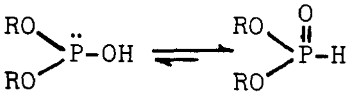
The reaction may be viewed as occurring <u>via</u> attack of the sulfur on the alkyl group of the phosphorus reagent as depicted in Scheme 1. The results obtained in the present study has shown that alkyl phosphites and phosphonates can alkylate compounds of type I to give II which are thus obtained in better yield than the previously reported. It is also interesting that only S-alkyl and not N-alkyl IV derivatives are

TABLE. Yields and ^1H NMR data of Thioethers II

Cmpd	DMP^b	DEP^b	TMP^b	TEP^b	DMMP^b	^1H NMR data^a
IIa	85^c	---	>95	---	80	2.64 (SCH_3, s), 11.24 (SH or NH, bs)^d
b	---	80^c	---	>95	---	3.15 (S-ethyl-CH_2, q), 1.40 (S-ethyl-CH_3, t), 12.17 (SH or NH, bs)^d
c	90	---	95	---	80	2.68 (S-CH_3, s), 3.90 (N-CH_3, s)
d	---	90	---	95	---	3.20 (S-ethyl-CH_2, q), 1.45 (S-ethyl-CH_3, t), 3.85 (N-CH_3, s)
e	75	---	80	---	70	2.60 (S-CH_3, s), 7.06 (N-C_6H_5, m)

a) Chemical shifts are in δ-scale. b) DMP = dimethyl phosphite; DEP = diethyl phosphite; TMP = trimethyl phosphite; TEP = triethyl phosphite; DMMP = dimethyl methyl phosphonate.
c) Reaction carried out in presence of traces of p-TsOH.
d) Exchangeable with D_2O; s = singlet; bs = broad singlet; q = quintet; t = triplet; m = multiplet.

isolated. The alkylating power of the phosphorus compounds studied increases in the order $(RO)_2P(O)R$ < $(RO)_2P$-OH < $(RO)_3P$. This is apparently related to the valency of the phosphorus atom as trivalent phosphorus compounds appear to be more effective than derivatives of pentavalent phosphorus. The fact that dialkyl phosphites (DAP) are intermediate in alkylating power might be explained in terms of the presence of these compounds as tautomeric mixtures[17] of the trivalent and pentavalent states.



R = alkyl

EXPERIMENTAL

Dialkyl phosphites,[18,19] trialkyl phosphites[20,21] and dimethyl methyl phosphonate[22] were freshly distilled. The 1,3,4-thiadiazolidines Ia, Ib, Ic were prepared according to established procedures[10,11] and freshly recrystallized. Authentic specimens of thioethers IIa, IIb, IIc and IIe were prepared by known procedures[2,9,10,12] for direct comparisons (mp., mixed mp. as well as comparative TLC, IR and ^{1}H NMR spectra). Solvent systems of benzene-ethyl acetate 9:1 and 8:2 (v/v) were used for TLC and iodine vapour was the visualizing agent. The IR spectra were recorded in KBr with a Beckmann 4220 Infracord and the ^{1}H NMR spectra were measured (in $CDCl_3$ or DMSO-d_6) at 60 MHz on a Varian EM 360L NMR Spectrometer, using TMS as an internal standard. The mass spectra were taken at 70 eV on MAT 112 Mass Spectrometer using the direct inlet technique.

Reaction of Thiadiazolidines I with DAP. *General procedure*.- A mixture of compound Ia (6.0 g, 0.04 mole), DMP (9.5 g, 0.08 mole) and few crystals of *p*-TsOH were refluxed in dry benzene (30 ml) for 2 hrs. After removing the volatile materials, *in vacuo*, the residual substance was treated with 10% NaOH aq., and the alkali-insoluble, oily material was extracted with ether. After evaporation of ether, the residual oil was distilled under pressure to give IIIb[23,24] (0.3 g, 5%), bp. 133°/3mmHg.

MW: Calcd 178, Found (ms): 178

The alkaline solution was neutralized with HCl aq. (10%) and the precipitated material was collected (ca. 85%) and recrystallized from methanol to give colourless crystals of

IIa, mp. and mixed mp. 136°.[2,10]

Under similar conditions, the reaction of Ia with DEP in presence of *p*-TsOH afforded a mixture of 2,5-bis(ethylthio)-1,3,4-thiadiazole (IIIc)(0.4 g, 5%) and 2-ethylthio-1,3,4-thiadiazolidine-5-thione (IIb) (5.7 g, 80%). Compound IIIc was obtained from petroleum ether bp. 40-60° as colourless crystals, mp. and mixed mp.[9] The colourless crystals of IIb were obtained from chloroform-cyclohexane, mp. and mixed mp. 125-127°.[2,9] MS: m/e 178 (M^+, base peak).

Under similar reaction conditions, the following S-alkyl ethers were prepared by the action of DAP on compound Ib and Ic both in absence and presence of *p*-TsOH:

a) *2-Methylthio-4-methyl-1,3,4-thiadiazolidine-5-thione* (IIc) (6.0 g, 90%), mp. and mixed mp. 88°[10-12]

b) *2-Ethylthio-4-methyl-1,3,4-thiadiazolidine-5-thione* (IId) (6.5 g, 90%), mp. 45-46° (from ethanol aq.).

Anal. Calcd for $C_5H_8N_2S_3$: C, 31.25; H, 4.17; N, 14.58; S, 50.00

Found: C, 31.20; H, 4.32; N, 14.78; S, 49.83

IR: bands at 1470 cm^{-1} $(-\overset{|}{N}-\overset{|}{C}=S)$[11] and at 1425 cm^{-1} $(-N=\overset{|}{C}-S-)$[11]

c) 2-Methylthio-4-phenyl-1,3,4-thiadiazolidine-5-thione (IIe) (6.8 g, 75%), mp. and mixed mp. 108-109°.[12]

Reaction of Thiadiazolidines I with TAP. *General procedure*.- Trimethyl phosphite (TMP, 9.9 g, 0.08 mole) was added dropwise with efficient stirring to compound Ia (6.0 g, 0.04 mole) at 0-5° then left at room temperature for 24 hrs. After removing the volatile materials *in vacuo*, 10% NaOH aq. (25 ml) was added and then, the alkali-insoluble oily material was extracted twice with ether. After evaporation of the solvent (ether), the residual oil was distilled under reduced pressure to give IIIb (0.3 g, 5%), bp. 133° at 3 mmHg.[24] The alkaline solution was neutralized with aq. HCl (10%) and the precipitated material was collected (6.3 g, >95%) and recrystallized from methanol to give colourless crystals which proved to be IIa, mp. and mixed mp. 136°.[2,10]

Under similar conditions, the reaction of Ia with triethyl phosphite (TEP) afforded a mixture of 2,5-bis(ethylthio)-1,3,4-thiadiazole (IIIc), (0.4 g, 5%) mp. and mixed 21-22°[9] together with 2-ethylthio-1,3,4-thiadiazolidine-5-thione (IIb)(6.8 g, 95%) mp. and mixed mp. 125-127°.[2,9]

Similarly, the reaction of compound Ib or Ic with TAP afforded the respective S-alkyl ether. Table 1 should be consulted for yields of thioethers IIc-e.

Reaction of Thiadiazolidines I with DMMP. General procedure.- A mixture of Ia (6.0 g, 0.04 mole) and DMMP (9.9 g, 0.08 mole) in dry benzene (30 ml) was refluxed for 3 hrs. After evaporation of the volatile materials *in vacuo*, 10% NaOH aq. (25 ml) was added and the alkali-insoluble oil was extracted with ether. After evaporating the solvent *in vacuo*, the residual oil was distilled under reduced pressure to give IIIb (0.3g, 5%), bp. 133°/3 mmHg[24]; its IR spectrum was superimposable with that of an authentic sample.[24] The alkaline solution was neutralized with aq. HCl (10%) and the precipitated material collected (5.2 g, 80%) was recrystallized from methanol to give colourless crystals of IIa, mp. and mixed mp. 136°.[2,10]

Under the similar conditions, DMMP reacted with Ib and Ic to give the respective S-methyl ethers IIc and IIe.

Preparation of 2-Ethylthio-4-methyl-1,3,4-thiadiazolidine-5-thione.- A mixture of 4-methyl-1,3,4-thiadiazolidine-2,5-dithione (Ib) (1 g, 0.006 mole), ethyl iodide (6 ml, 0.03 mole) and anhydrous K_2CO_3 (5 g) in dry acetone (100 ml) was refluxed for 8 hrs. then filtered while hot. After evaporation of the volatile materials *in vacuo*, the residue was triturated with petroleum ether bp. 40-60° and then allowed to cool in an ice-chest. The solid obtained was recrystallized from aqueous ethanol to give colourless needles (0.8 g, 75%) of IId, mp. and mixed mp. 45-46°, the IR and ^{1}H NMR spectra were identical to those of an authentic sample.

REFERENCES

1. E. Somers, Can. J. Botany, 36, 997 (1958); CA., 53, 4446 (1959).
2. A. Rüfenacht, Helv. Chim. Acta, 55, 1178 (1972).
3. F. H. Wells and D. M. Lyde, Brit. Pat., 939,997 (1963); CA. 60, 1339 (1964).
4. Celanese Corp. of America, Neth. Appl. Pat., 6,412,402 (1965); CA. 64, 5264 (1966).
5. O. Abraham, U. S. Pat., 3,980,573 (1976); CA. 86, 109039 (1977).
6. H. Krzikalla, H. Pohlemann and K. E. Kling, Ger. Pat., 959,402 (1957); CA. 54, 6048 (1960).
7. S. Tsuchida, R. Ohio, H. Shibaoka, T. Asai, T. Ichikawa and S. Ogawa, Ger. Pat., 1,963,295 (1970); CA. 73, 72091 (1970).
8. J. Sandström, Acta Chem. Scand., 14, 1939 (1960).
9. J. Sandström, Arkiv Kemi, 4, 297 (1952); *ibid*, 8, 487 (1955).
10. L. L. Bambas, "The Chemistry of Heterocyclic Compounds", Edited by A. Weissberger, Interscience Ltd., London, 1952, p.177.
11. G. D. Thorn, Can. J. Chem., 38, 1439 (1960).

12. M.Busch, Ber., 27, 2507, 2513 (1894).
13. P. Sutter and C. D. Weis, Phosphorus & Sulfur, 6, 335 (1978).
14. M. Fieser and L. F. Fieser, "Reagents for Organic Synthesis", Vol. 4, p. 542, John Wiley & Sons, New York, N. Y., 1974.
15. M. Fieser and L. F. Fieser, ibid, Vol. 5, p. 716; T. Tanabe, K. Yamauchi and M. Kinoshita, Bull. Chem. Soc. Japan, 49, 3224 (1976).
16. Y. Kashman, J. Org. Chem., 37, 912 (1972).
17. L. W. Daasch, J. Am. Chem. Soc., 80, 5301 (1958).
18. P. W. Gann and R. L. Heider, U. S. Pat., 2,692,890 (1954); CA. 49, 12529 (1955).
19. H. McCombie, B. C. Saunders and G. J. Stacey, J. Chem. Soc., 380 (1945).
20. T. Milobendzki and A. Sachnowski, Chem. Polski, 15, 34 (1917); CA. 13, 2865 (1919).
21. A. H. Ford-Moore and B. J. Perry, Organic Syntheses, 31, 111 (1951).
22. S. R. Landauer and H. N. Rydon, J. Chem. Soc., 2224 (1953); CA. 48, 9904 (1954).
23. G. A. Pnevmaticakis, E. C. Stathis and E. R. Fields, J. Inorg. Nucl. Chem., 28 (9) 2059 (1966); CA. 65, 18142 (1966).
24. L. Gandino and A. Baldassarri, Ital. Pat., 786,488 (1967); CA. 70, 38912 (1969).

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