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# STUDIES ON ORGANOPHOSPHORUS COMPOUNDS—XXVIII†

## SYNTHESES OF 3H-1,2-DITHIOLE-3-THIONES AND 4H-1,3,2,-OXAZAPHOSPHORINE DERIVATIVES FROM THE DIMER OF *p*-METHOXYPHENYLTHIONOPHOSPHINE SULFIDE AND DERIVATIVES OF 3-OXO CARBOXYLIC ACIDS

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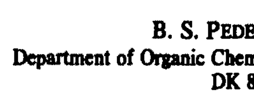
**Abstract**—Unsubstituted and 2-monosubstituted 3-oxo esters react with the dimer of *p*-methoxyphenylthionophosphine sulfide (1) and elemental sulfur in anhydrous toluene at 110° to give the corresponding 3H-1,2-dithiole-3-thiones (2) in nearly quantitative yields (90–95%). Ethyl 2,2-dimethyl 3-oxo-butanoate, failing to react in toluene at 110°, decomposes into a complex mixture at 140° in anhydrous xylene. Also secondary and tertiary 3-oxo-amides such as acetoacetanilide and N,N-dimethylacetoacetamide produce the corresponding 3H-1,2-dithiole-3-thiones (2) upon treatment with 1 and elemental sulfur. Primary 3-oxo-amides and 3-oxo-nitriles react with 1 in anhydrous toluene at 110° giving in all cases investigated, derivatives of 2,3-dihydro-2(4-methoxyphenyl)-4H-1,3,2-oxazaphosphorine-4-thiono-2-sulfide as main products (70–95%). $^1$H, $^{13}$C and $^{31}$P NMR data are tabulated and reaction mechanisms are suggested.

For some time we have been concerned with the thiation of different classes of carbonyl compounds using the dimer of *p*-methoxyphenylthionophosphine sulfide 1 as thiation reagent.

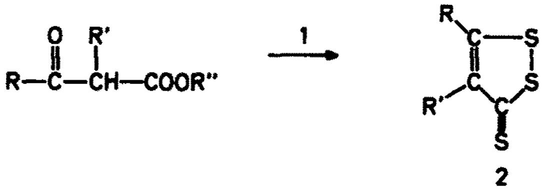


1

Thus we have found that 1 is a very efficient thiation reagent for ketones, amides, esters and S-substituted thioesters[1–4] as in most cases the corresponding thiocarbonyl compounds are produced in nearly quantitative yields.

In the study of the thiation of ketones[1] with 1 it was found that dibenzyl ketone produced the corresponding enthiole (1,3 - diphenyl - 2 - mercaptopropene) in fairly good yield. The isolation of 1,3 - diphenyl - 2 - mercaptopropene suggested a new method for the synthesis of enthioles and in attempts to prepare such enthioles we have investigated the reactions of 1 with 3-oxo-esters, 3-oxo-amides, and 3-oxo-nitriles.

*Reactions of 3-oxo-esters and* 1. Unsubstituted and 2-mono-substituted 3-oxo-esters react smoothly with 1 in anhydrous toluene at 110° producing the corresponding 3H-1,2-dithiole-3-thiones (2).



2

By use of 2 moles of 1 per mole of 3-oxo-ester the corresponding 3H-1,2-dithiole-3-thiones were isolated in yields of 65–70%. In attempts to optimize the yields of 3H-1,2-dithiole-3-thiones a great excess of 1 was used, but no improvements of the yields were found. However, a search of the literature revealed that the presence of elemental sulfur[5] in the reactions of 3-oxo-esters with $P_2S_5$ increased the yields of 3H-1,2-dithiole-3-thiones from about 20 to 40%. Therefore, a series of 3-oxo-esters were reacted with 1 and an excess of elemental sulfur (mole ratio 1:2:2), and as seen from Table 1, the corresponding 3H-1,2-dithiole-3-thiones were isolated in nearly quantitative yields. By isolating the excess of elemental sulfur it was shown that 1 mole of sulfur was consumed per mole of 3-oxo-ester. All the 3H-1,2-dithiole-3-thiones prepared (Table 1) are known and their $^1$H NMR,[6,7,18] IR,[8] UV,[9] and mass spectra[10] are in accordance with literature data. As only a few $^{13}$C NMR data of the 3H-1,2-dithiole-3-thiones are cited in the literature,[11] we have tabulated the chemical shifts of the carbons of the dithiole ring in Table 1. It is noted that the shifts of the C=S carbons are nearly unaffected by substituents. Also C-4 and C-5 are located within narrow limits and they are only slightly affected by substituents.

One 2,2-disubstituted 3-oxo-ester (ethyl 2,2-dimethyl acetoacetate) was reacted with 1 and sulfur as above, but no reaction occurred. Under more severe conditions (140° in xylene) a reaction took place giving a complex mixture of unidentified products.

*Reaction of 3-oxo-amides and 3-oxo-nitriles with* 1. Primary 3-oxo-amides react vigorously with 1 with evolution of $H_2S$. The main products were in all cases 4H-1,3,2-oxazaphosphorine derivatives, 3, in high yields (Table 2). Besides the main product small yields of the corresponding 3H-1,2-dithiole-3-thiones (2) were also isolated. The influence of elemental sulfur on the reaction was investigated and it was shown that the presence of elemental sulfur did not change the product dis-

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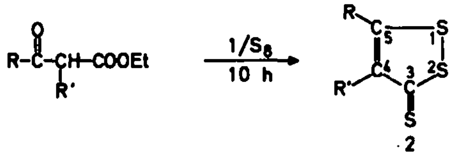
†Part XXVII. S. Scheibye, J. Kristensen and S.-O. Lawesson, *Tetrahedron* 35, 1339 (1979).

Table 1. Experimental and spectroscopic data for the reactions between 1 and 3-oxoesters



2

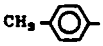
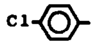
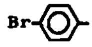
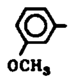
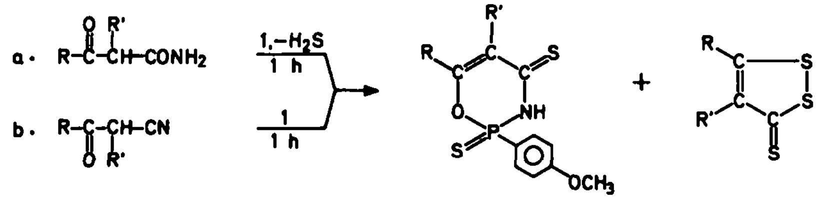
| R | R' | Yields of 2 | M.p.$^{Lit}$ | $^{13}$C NMR shifts (ppm) | | |
|---|---|---|---|---|---|---|
| | | | | C-3 | C-4 | C-5 |
| $-CH_3$ | H | 90 | $33^{12}$ | 216.7 | 139.4 | 172.1 |
| $-CH_3$ | $CH_3-\underset{\vert}{C}H-CH_3$ | 87 | $38^{13}$ | 215.6 | 149.5 | 168.1 |
| $-CH_2-CH_2-CH_2CH_2-$ | | 90 | $102^{12}$ | 215.3 | 143.4 | 169.2 |
|  | H | 95 | $126^{13}$ | 215.8 | 136.2 | 172.9 |
|  | H | 96 | $119^{14}$ | 215.0 | 135.1 | 173.0 |
|  | H | 90 | $116^{15}$ | 215.7 | 136.1 | 171.3 |
|  | H | 91 | $136^{16}$ | 215.4 | 136.1 | 171.1 |
|  | H | 92 | $129^{17}$ | 215.5 | 136.2 | 171.2 |
|  | H | 90 | $114^{18}$ | 216.6 | 136.2 | 172.8 |

Table 2. Experimental data for the reactions *a* and *b*



3 2

| Reaction | R | R' | Yield of 3 (%) | Yield of 2 (%) | M.p. of 3 (℃) |
|---|---|---|---|---|---|
| *a* | Ph | H | 94 | 3 | 56-60 |
| *a* | $Ph-CH_2$ | Ph | 85 | 2 | 167 |
| *a* | $CH_3-(CH_2)_3-CH_3$ | | 76 | 17 | 155 |
| *b* | Ph | H | 86 | - | 56-60 |
| *b* | $CH_3$ | Ph | 72 | - | 181 |

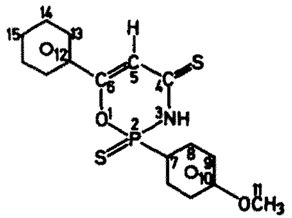
tribution. Two N-substituted 3-oxo-amides, acetoacetanilide and N,N-dimethylacetoacetamide, were reacted with 1 and elemental sulfur under experimental conditions as for the 3-oxo-esters. From both reactions 5-methyl-3H-1,2-dithiole-3-thione was isolated as the sole product in yields of 87 and 43%, respectively. Also reactions of 3-oxo-nitriles and 1 were studied and in all cases investigated 4H-1,3,2-oxazaphosphorine derivatives, 3, were isolated in good yields (Table 2).

These new phosphor heterocycles were characterized by means of $^1$H NMR, $^{13}$C NMR, MS and elemental analyses. The $^{13}$C NMR spectra were compeltely assigned for all the phosphor heterocycles, but this complete assignment is only tabulated for 6-phenyl-2,3-dihydro-2(4-methoxy-phenyl)-4H-1,3,2-oxazaphosphorine-4-thione-2-sulfide as an illustrative example (Table 3). The chemical shift at 192.7 is characteristic for the C=S carbon of 4H-1,3,2-oxazaphosphorine derivatives and a $J_{^{31}P-^{13}C(7)}$ coupling constant of 144 Hz is only compatible with a P=S bond.[4]

Table 4 shows $^{13}$C and $^{31}$P NMR data of the 4H-1,3,2-oxazaphosphorine derivatives. Only $^{13}$C NMR data of the skeleton carbons are tabulated and it is seen that the chemical shifts and the $J_{^{31}P-^{13}C}$ coupling constants of these are only slightly affected by substituents.

The $^{31}$P NMR chemical shifts agree very well with those found for the 4H-1,3,2-benzoxazaphosphorine derivatives.[4]

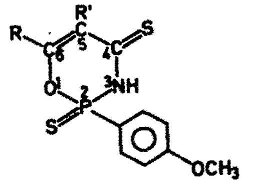
Table 3. $^{13}$C NMR data for 6-phenyl-2,3-dihydro-2(4-methoxyphenyl)-4H-1,3,2-oxazaphosphorine-4-thione-2-sulfide



| Carbon No. | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $^{13}$C shift (ppm)$^{a)}$ | 192.7 | 108.8 | 152.7 | 122.6 | 133.8 | 114.4 | 164.2 | 55.6 | 131.0 | 126.7 | 129.0 | 132.1 |
| $J_{^{31}P-^{13}C}$ (Hz) | 5.1 | 7.2 | 10.0 | 144.0 | 15.5 | 17.0 | 2.6 | - | 6.2 | - | - | - |

a) The spectra were run in CDCl$_3$ with TMS as internal ref·rence.

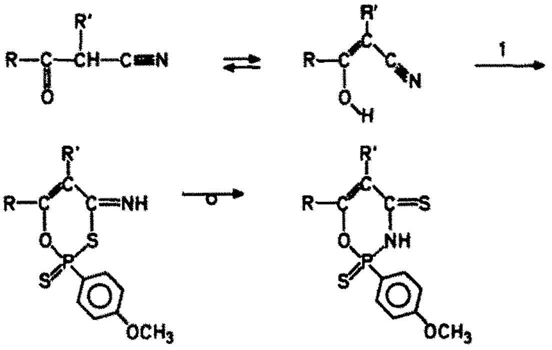
Table 4. $^{13}$C and $^{31}$P NMR data of the ring carbons in the 4H-1,3,2-oxazaphosphorine-4-thione-2-sulfide derivatives



| R | R' | $\delta_{C4}$ (ppm) | $J_{^{31}P-^{13}C(4)}$ (Hz) | $\delta_{C5}$ (ppm) | $J_{^{31}P-^{13}C(5)}$ (Hz) | $\delta_{C6}$ (ppm) | $J_{^{31}P-^{13}C(6)}$ (Hz) | $\delta_{^{31}P}$ (ppm) |
|---|---|---|---|---|---|---|---|---|
| Ph- | H- | 192.7 | 5.1 | 108.8 | 7.2 | 152.7 | 10.0 | 67.7 |
| CH$_3$- | Ph- | 194.0 | 5.4 | 123.0 | 7.7 | 154.6 | 11.4 | 65.3 |
| -CH$_2$-(CH$_2$)$_2$-CH$_2$- | | 194.3 | 4.8 | 116.5 | 7.5 | 155.4 | 11.4 | 71.0 |

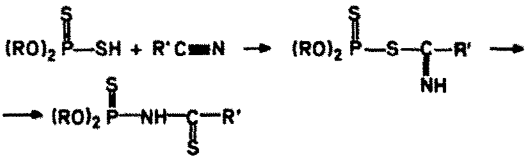
(Solvent: CDCl$_3$; $^{13}$C chemical shifts relative to TMS; $^{31}$P chemical shifts relative to 85% H$_3$PO$_4$).

As to the mechanisms of the above reactions our understanding is not complete. To account for the formation of P-heterocycles with a P–O moiety, it is suggested that the reaction of the enole-form of the substrate with 1 gives a thiophosphoric acid intermediate in the first step. A subsequent P–SH addition to the nitrile, followed by a rearrangement gives the final product 3.



3

It is well-known that alcohols react with 1 with formation of a P–O bond[19] and the reaction between nitriles and 0,0-dialkylthiophosphoric acids has recently been elucidated:[20]



$$(RO)_2\overset{S}{\overset{\|}{P}}-SH + R'C\equiv N \rightarrow (RO)_2\overset{S}{\overset{\|}{P}}-S-\underset{NH}{\underset{\|}{C}}-R' \rightarrow (RO)_2\overset{S}{\overset{\|}{P}}-NH-\underset{S}{\underset{\|}{C}}-R'$$

The formation of 3 from 3-oxocarboxylic amide and 1 can also be accounted for in a similar way, but the reaction of 3-oxocarboxylic esters and 1 awaits further work for mechanistic clarifications.

Finally, it should be mentioned that trimeric *p*-methoxyphenylthionophosphine oxide (*6*) was isolated from the reactions of $\beta$-keto-esters and $\beta$-keto-amides with 1.

6

This compound has earlier been characterized by elementary analyses, MS, IR and $^1$H NMR[2] and now we have recorded and analyzed its $^{31}$P NMR spectrum. The $^{31}$P NMR spectrum is a $AB_2$ spectrum the analysis[21] of which gives $\delta_A = 73.3$ and $\delta_B = 71.1$, relative to 85% $H_3PO_4$. The coupling constant $J_{AB}$ is found to be 49.3 Hz.

## EXPERIMENTAL

$^1$H NMR spectra were recorded at 60 MHz on a Varian A-60 spectrometer. $^{13}$C NMR spectra and $^{31}$P NMR spectra were recorded at 20 MHz and 32 MHz, respectively, on a Varian CFT-20 spectrometer. TMS was used as internal standard and chemical shifts are expressed in $\delta$-values. $CDCl_3$ was used as solvent. IR spectra were recorded on a Beckman IR-18 spectrometer. Mass spectra were recorded on a Micromass 7070 F Mass spectrometer operating at 70 eV using direct inlet. Elementary analyses were carried out by Novo Microanalytic Laboratory, Novo Industry A/S, Novo Allé, DK-2880 Bagsvaerd, supervised by Dr. R. Amsler. Silica gel 60 (Merck) was used for chromatography. M.ps and b.ps are uncorrected.

*Compound* 1 was prepared as described earlier.[1]

*General procedure for the reactions of 3-oxo-esters with* 1. 0.005 moles of 3-oxo-ester, 0.012 moles of 1 and 0.01 moles of elemental sulfur in 10 ml anhyd toluene were kept at 110° for 10 hr. After cooling to room temp. the mixture was placed on a silica gel column and the toluene was eluated with ether/light petroleum (5:95). On a renewed eluation with ether/light petroleum (30:70) the 3H-1,2-dithiole-3-thiones were isolated. The 3H-1,2-dithiole-3-thiones are known and they were identified by m.p., UV, IR, NMR spectroscopy, MS and elementary analyses. Some data are collected in Table 1.

*General procedure for the reaction of 3-oxo-nitriles and primary $\beta$-keto-amides with* 1. 0.005 moles of 3-oxo compound and 0.006 moles of 1 in 10 ml anhyd toluene were kept at 110° for 1 hr. After cooling to room temp. the mixture was separated on a silica gel column with $CH_2Cl_2$/light petroleum (60:40). The isolated 4H-1,3,2-oxzazphosphorine derivatives were identified by $^1$H, $^{13}$C and $^{31}$P NMR spectroscopy, MS and elementary analyses.

6 - *Phenyl - 2,3 - dihydro - 2(4 - methoxyphenyl) - 4H* - 1,3,2 - *oxazaphosphorine - 4 - thione - 2 - sulfide*. Yields, m.ps, $^{13}$C and $^{31}$P NMR data are recorded in Tables 2, 3 and 4. $^1$H NMR: 3.85 (3H, s); 6.8–8.2 (11H, m). MS: M$^+$ *m/e* 347. (Found: C, 55.48; H, 4.07; N, 3.91; P, 8.68. Calc.: C, 55.32, H, 4.06; N, 4.03; P, 8.9%).

5,6 - *Tetramethylene - 2,3 - dihydro - 2(4 - methoxyphenyl) - 4H - 1,3,2 - oxazaphosphorine - 4 - thione - 2 - sulfide*. Yields, m.ps, $^{13}$C and $^{31}$P NMR spectral data are recorded in Tables 2 and 4. $^1$H NMR: 1.5–1.9 (4H, m); 2.3 (2H, m); 2.63 (2H, m), 3.88 (3H, s); 6.8–8.2 (4H, m); 8.5 (1H, d). MS: M$^+$ *m/e* 325. (Found: C, 51.68; H, 4.96; N, 4.31; P, 9.52. Calc.: C, 51.40; H, 4.91; N, 4.26; P, 9.74%).

6 - *Methyl - 5 - phenyl - 2,3 - dihydro - 2(4 - methoxyphenyl) - 4H - 1,3,2 - oxazaphosphorine - 4 - thione - 2 - sulfide*. Yields, m.ps, $^{13}$C and $^{31}$P NMR spectral data are recorded in Tables 2 and 4. $^1$H NMR: 1.86 (3H, s); 3.88 (3H, s); 6.9–8.3 (9H, m). MS: M$^+$ *m/e* 361. (Found: C, 56.49; H, 4.46; N, 3.87; P, 8.57. Calc.: C, 56.49; H, 4.41; N, 3.88; P, 8.87%).

## REFERENCES

[1] B. S. Pedersen, S. Scheibye, N. H. Nilsson and S.-O. Lawesson, *Bull. Soc. Chim. Belg.* 87, 223 (1978).
[2] S. Scheibye, B. S. Pedersen and S.-O. Lawesson, *Ibid.* 87, 229 (1978).
[3] B. S. Pedersen, S. Scheibye, K. Clausen and S.-O. Lawesson, *Ibid.* 87, 293 (1978).
[4] S. Scheibye, B. S. Pedersen and S.-O. Lawesson, *Ibid.* 87, 299 (1978).
[5] U. Schmidt, A. Lüttringhaus and H. Trefzger, *Liebigs Ann.* 631, 129 (1960).
[6] M. Saquet and A. Thuillier, *Bull. Soc. Chim. Fr.* 1582 (1966).
[7] R. F. C. Brown, I. D. Rau and S. Sternhell, *Austral. J. Chem.* 18, 1211 (1965).
[8] D. Gentric and P. Saumagne, *Internat. J. Sulphur Chem.* A2, 15 (1972).
[9] P. S. Landis, *Chem. Rev.* 65, 237 (1965).
[10] C. Th. Pedersen and J. Møller, *Acta Chem. Scand.* 26, 250 (1972).
[11] N. Plavac, I. W. J. Still, M. S. Chauhan and D. M. McKinnon, *Can. J. Chem.* 53, 836 (1975).
[12] N. Lozach and L. Legrand, *C. R. Acad Sci., Paris* 234, 1291 (1952).
[13] A. Thuillier and J. Vialle, *Bull. Soc. Chim. Fr.* 2182 (1962).
[14] L. Legrand, *Ibid.* 1599 (1959).
[15] B. J. Lindberg, R. Pinel and Y. Mollier, *Tetrahedron* 30, 2537 (1974).
[16] L. Legrand and N. Lozach, *Bull. Soc. Chim. Fr.* 1686 (1959).
[17] N. Lozach, M. Denis, Y. Mollier and J. Teste, *Ibid.* 1016 (1953).

[18] A. Dorange, F. Tonnard and F. Venien, *C. R. Acad. Sci., Ser. C* **276**, 1057 (1973).
[19] P. E. Newallis, J. P. Chupp and L. C. D. Groenweghe, *J. Org. Chem.* **27**, 3829 (1962).
[20] H. J. Meyer, I. Thomsen and S.-O. Lawesson, (to be published).
[21] R. J. Abraham, *The Analysis of High Resolution NMR Spectra*. Elsevier, Amsterdam (1971).