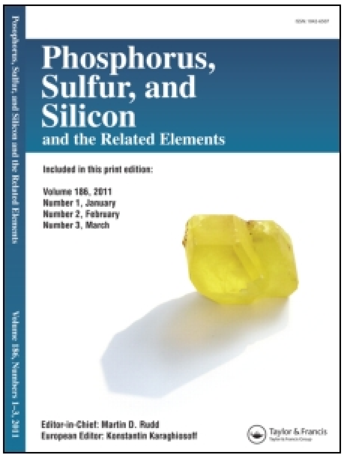

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

SYNTHESIS AND METHYLATION OF SOME 1,2,4-THIADIAZOLE-5-THIONES

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To cite this Article Agirbaş, Hikmet , Dürüst, Yaşar and Sumengen, Dogan(1992) 'SYNTHESIS AND METHYLATION OF SOME 1,2,4-THIADIAZOLE-5-THIONES', Phosphorus, Sulfur, and Silicon and the Related Elements, 66: 1, 321 — 324
To link to this Article: DOI: 10.1080/10426509208038363
URL: http://dx.doi.org/10.1080/10426509208038363

Phosphorus, Sulfur, and Silicon, 1992, Vol. 66, pp. 321–324
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Communication

SYNTHESIS AND METHYLATION OF SOME 1,2,4-THIADIAZOLE-5-THIONES

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(Received June 6, 1991; Revised August 20, 1991)

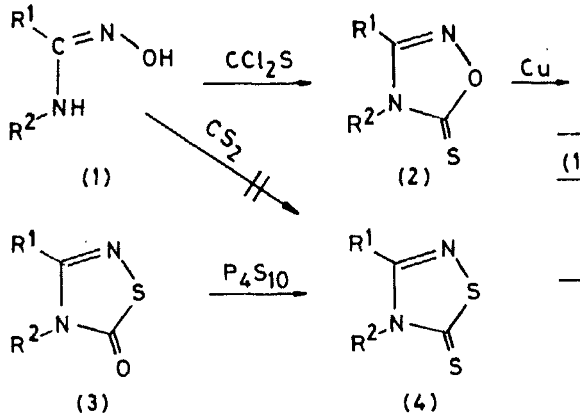
3,4-Disubstituted-1,2,4-thiadiazole-5(4H)-thiones (**4**) have been prepared by the treatment of 3,4-disubstituted-1,2,4-thiadiazole-5(4H)-ones (**3**) with P_4S_{10}. S-Methyl derivatives were obtained from the methylation of 3-substituted-1,2,4-thiadiazole-5(4H)-thiones with CH_2N_2.

Key words: 1,2,4-Thiadiazole-5(4H)-ones/thionation; 1,2,4-thiadiazole-5(4H)-thiones; 1,2,4-thiadiazoles.

We previously reported[1,2] that some 3,4-disubstituted-1,2,4-oxadiazole-5(4H)-thiones (**2**) rearrange thermally to 3,4-disubstituted-1,2,4-thiadiazole-5(4H)-ones (**3**) in the presence of a copper catalyst. We expected that thionation of the rearrangement products would give 3,4-disubstituted-1,2,4-thiadiazole-5(4H)-thiones (**4**). Therefore, we prepared (**2a**) from the reaction of N-p-tolylbenzamide oxime (**1a**) with thiophosgene. The thermal rearrangement of (**2a**) gave (**3a**). This compound was refluxed in xylene with an excess of P_4S_{10} for 6.5 h and 36% of (**4a**) was obtained (Scheme I). Similarly, thionation of (**3b**) with P_4S_{10} was carried out in xylene and (**4b**) (26%) was obtained.

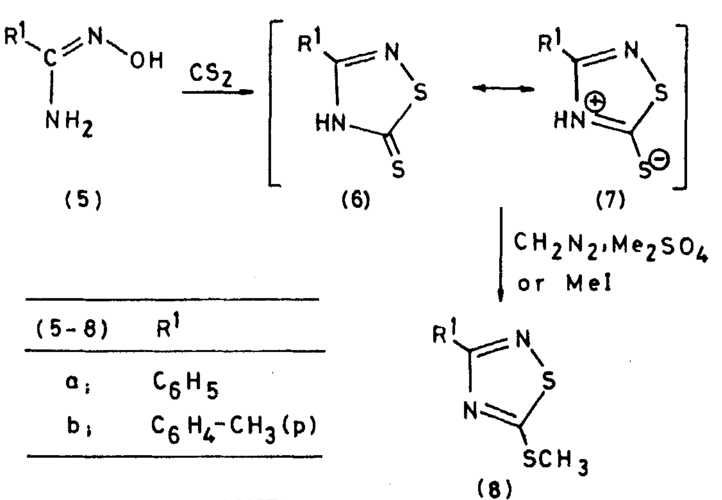
In order to obtain 3,4-disubstituted-1,2,4-thiadiazole-5(4H)-thiones (**4**) directly, we reacted N-methyl (or p-tolyl) benzamide oximes with CS_2 without success, and in each case starting materials were recovered. However, when we reacted amide oximes with CS_2, we obtained 3-substituted-1,2,4-thiadiazole-5(4H)-thiones (**6**) (Scheme II).

The solid state IR spectrum of 3-methyl-1,2,4-thiadiazole-5(4H)-thione was taken by Lacasse and Muchowski[3] and no SH stretching absorption was observed. Additionally, 3-phenyl-1,2,4-oxadiazole-5(4H)-thione was examined by Sèlim and Sèlim[4] and the authors ascribed to the compound the thione structure from IR measurements. However, they asserted the predominance of the SH tautomer in solution. Elguero and co-authors[5a] criticized Sèlim and Sèlim, and taking into account the results on 1,2,4-oxadiazole-5(4H)-ones[5b,6] they suggested[5c] an NH structure to be more likely for the 1,2,4-oxadiazole-5(4H)-thiones in solution as well as the solid state. A thione structure for 1,2,4-thiadiazole-5(4H)-thiones was also suggested to be more likely taking into consideration the known structures of the 1,3-thiazole-2-thiones[5d] and 1,2,4-triazole-5-thiones.[5e]



(1-4)	R^1	R^2
a;	C_6H_5	C_6H_4-CH_3(p)
b;	C_6H_5	CH_3

SCHEME I



(5-8)	R^1
a;	C_6H_5
b;	C_6H_4-CH_3(p)

SCHEME II

Our solid state IR spectrum of 3-phenyl-1,2,4-thiadiazole-5(4H)-thione (**6a**) gave NH absorptions at 3025 and 3010 cm^{-1} and C=S absorptions at 1470, 1335 and 1100 cm^{-1}, but no SH absorption was observed in the region of 2600–2500 cm^{-1}. We hoped that methylation of this compound would possibly give N-methyl derivative. Therefore, we methylated this compound with CH_2N_2 and TLC (silica gel, ethanol-chloroform-n-hexane, 1:2:5, eluant) of the crude product gave only one spot (R_F:0.61), which was not (**4b**) (R_F:0.51). The ^{1}H NMR spectrum of the compound showed a SCH_3 peak at 2.70 ppm (lit[7]: at 2.80 ppm for 5-methylthio-1,2,4-oxadiazole). We didn't observe a NCH_3 peak at 3.65 ppm, which was present in the ^{1}H NMR spectrum of (**4b**). So, the methylation took place at sulfur atom and (**8a**) was obtained. Methylation of the same compound was also carried out with Me_2SO_4 or MeI, and again (**8a**) was obtained. Methylation of (**6b**) with CH_2N_2 also gave only (**8b**) (Scheme II).

EXPERIMENTAL

IR spectra: Perkin-Elmer Model 177. ^{1}H-NMR spectra:Bruker Spectrospin (200 and 360 MHz), EM 390 (90 MHz) and Varian T 60 A (60 MHz). Elemental analyses were performed at the Analytische Laboratorien (Elbach, Germany).

3-Phenyl-4-(p-tolyl)-1,2,4-oxadiazole-5(4H)-thione (**2a**). A solution of thiophosgene (1.69 g, 14 mmol) in chloroform (5 ml) was added dropwise to an ice-cooled solution of compound (**1a**) (3.33 g, 14 mmol) in pyridine (8.5 ml). The reaction mixture was stirred at room temperature for 20 h. Then the mixture was poured into cold water (50 ml). The resulting precipitate was filtered, washed with water, and dried in vacuo. After crystallization from ethanol, the IR spectrum of the product gave a C=O absorption at ~ 1770 cm^{-1}. Therefore, the impure solid was refluxed with an excess of P_4S_{10} in xylene for 10 h. The reaction mixture was filtered, and the solvent was evaporated under reduced pressure. The crude product was recrystallized from ethanol, yielding compound (**2a**) (3.01 g, 76%); m.p. 163–165°C; IR(KBr) 1600, 1588 (C=N), 1480, 1287, and 1108 cm^{-1} (C=S); NMR(CDCl$_3$) δ 2.47 (s, 3, CH$_3$) and 7.25 (m, 9 aromatic H). (Found: C, 66.90; H, 4.60; N, 10.44; S, 11.88. Calcd. for $C_{15}H_{12}N_2OS$: C, 67.14; H, 4.50; N, 10.43; S, 11.94%.)

3-Phenyl-4-methyl-1,2,4-oxadiazole-5(4H)-thione (**2b**). *m.p. 119–120°C (lit.*[2] *119–120°C).* 3-Phenyl-4-(*p*-tolyl)-1,2,4-thiadiazole-5(4H)-one (**3a**). Compound (**2a**) (1.350 g, 5 mmol) was heated in xylene (50 ml) with catalytic amount of Cu powder for 10 h. The hot solution was filtered and xylene was evaporated under reduced pressure. The remaining solid was recrystallized from ethanol, yielding (**3a**) (0.715 g, 53%); m.p. 119–120°C; IR(KBr) 1675 (C=O) and 1600 cm^{-1} (C=N); NMR(CDCl$_3$) δ 2.35 (s, 3, CH$_3$), 7.25 (m, 9 aromatic H). (Found: C, 67.11; H, 4.61; N, 10.03; S, 11.69. Calcd. for $C_{15}H_{12}N_2OS$: C, 67.14; H, 4.50; N, 10.43; S, 11.94%.)

3-Phenyl-4-methyl-1,2,4-thiadiazole-5(4H)-one (**3b**). *m.p. 77–78°C (lit.*[2] *77–78°C).* 3-Phenyl-4-(*p*-tolyl)-1,2,4-thiadiazole-5(4H)-thione (**4a**). Compound (**3a**) (0.580 g, 2.1 mmol) was heated with an excess of P_4S_{10} (0.186 g, 0.42 mmol) in xylene for 6.5 h. The hot reaction mixture was filtered and xylene was evaporated under reduced pressure. The remaining crude product was chromatographed on Silica Gel HF$_{254}$ layer with chloroform-n-hexane (1:10), (R$_F$: 0.61), and crystallized from ethanol, yielding (**4a**) (0.221 g, 36%); m.p. 152–153°C; IR(KBr) 1600, 1585 (C=N), 1485, 1305 and 1106 cm^{-1} (C=S); NMR(CDCl$_3$) δ 2.38(s, 3, CH$_3$), 7.25 (m, 9 aromatic H). (Found: C, 63.13; H, 4.09; N, 9.77; S, 22.23. Calcd. for $C_{15}H_{12}N_2S_2$: C, 63.34; H, 4.25; N, 9.85; S, 22.54%.)

3-Phenyl-4-methyl-1,2,4-thiadiazole-5(4H)-thione (**4b**). Compound (**3b**) (0.100 g, 0.52 mmol) was heated with an excess of P_4S_{10} (0.034 g, 0.075 mmol) in toluene (20 ml) for 4 h. The hot reaction mixture was filtered and the filtrate was evaporated under reduced pressure. The remaining crude product was chromatographed on Silica Gel HF$_{254}$ layer with ethanol-chloroform-n-hexane (1:2:5) (R$_F$: 0.51), crystallized from n-pentane, yielding (**4b**) (0.040 g, 26%); m.p. 131–132°C; IR(KBr) 1590 (C=N), 1478, 1295 and 1120 cm^{-1} (C=S); NMR(CDCl$_3$) δ 3.65 (s, 3, NCH$_3$), 7.56 (s, 5, aromatic H). (Found: C, 51.61; H, 3.64; N, 13.19 Calcd. for $C_9H_8N_2S_2$: C, 51.89; H, 3.87; N, 13.44%.)

3-Phenyl-1,2,4-thiadiazole-5(4H)-thione (**6a**). m.p. 161–162°C (lit.[8] 162°C); IR(KBr) 3025, 3010 (NH), 1585, 1570 (C=N), 1470, 1335 and 1080 cm^{-1} (C=S); NMR (DMSO-d$_6$) δ 7.40 (m, 3, aromatic H) and 7.90 (m, 2, aromatic H).

3-(p-Tolyl)-1,2,4-thiadiazole-5(4H)-thione (**6b**). m.p. 165–166°C (lit.[9] 165°C); IR(KBr) 3025, 3000, (NH), 1593, 1570 (C=N), 1482, 1327 and 1102 cm^{-1} (C=S); NMR(DMSO-d$_6$) δ 2.00 (s, 3, CH$_3$), 7.30 (d, 2, aromatic H) and 7.93 (d, 2, aromatic H).

3-Phenyl-5-methylthio-1,2,4-thiadiazole (**8a**). Method A. The ethereal solution of diazomethane (45 ml) was added dropwise to an ice-cooled solution of compound (**6a**) (0.226 g, 1.1 mmol). The reaction mixture was stirred for 1 h. The solvent was evaporated under reduced pressure and the residual solid was recrystallized from light petroleum (50–70°C), yielding (**8a**) (0.150 g, 80%); m.p. 81–82°C; IR(KBr) 1570 cm^{-1} (C=N); NMR(CDCl$_3$) δ 2.70 (s, 3, SCH$_3$), 7.33 (m, 3, aromatic H), 8.13 (m, 2, aromatic H). (Found: C, 51.78; H, 3.73; N, 13.36; S, 30.62. Calcd. for $C_9H_8N_2S_2$: C, 51.89; H, 3.87; N, 13.44; S, 30.78%.)

Method B. Compound (**6a**) (0.060 g, 0.30 mmol) was dissolved in water (0.1 ml) containing NaOH (0.016 g). To this solution a solution of dimethyl sulfate (0.056 g, 0.44 mmol) in methanol (0.1 ml) was added dropwise. The reaction mixture was stirred overnight and the resulting solid matter was dried in vacuo. The solid was extracted with light petroleum (40–60°C) (2 × 20 ml) and the solvent was evaporated under reduced pressure. The crude product was recrystallized from light petroleum (40–

60°C), yielding (**8a**) (0.030 g, 47%), identical in all respects with the compound obtained by method A.

Method C. Compound (**6a**) (1.00 g 5 mmol) was dissolved in water (50 ml) containing NaOH (0.2 g, 5 mmol). To this solution methyl iodide (0.75 g, 5 mmol) was added dropwise. An immediate precipitation was observed. The reaction mixture was stirred for 6 h. The precipitate was filtered, dried in vacuo and recrystallized from light petroleum (40–60°C), yielding (**8a**) (0.080 g, 75%), identical in all respects with the compound obtained by method A.

3-(p-Tolyl)-5-methylthio-1,2,4-thiadiazole (**8b**). The ethereal solution of diazomethane (50 ml) was added dropwise to an ice-cooled solution of compound (**6b**) (0.230 g, 1.3 mmol) in acetone (5 ml). The reaction mixture was stirred for 30 min. The solvent was evaporated under reduced pressure, the remaining solid was recrystallized from light petroleum (40–60°C), yielding (**8b**) (0.20 g, 82%); m.p. 77–78°C; IR(KBr) 1600 cm^{-1} (C=N); NMR($CDCl_3$) δ 2.10 (s, 3, CH_3), 2.50 (s, 3, SCH_3), 7.13 (m, 2, aromatic H), 8.10 (m, 2, aromatic H). (Found: C, 54.02; H, 4.40; N, 12.50; S, 28.76. Calcd. for $C_{10}H_{10}N_2S_2$: C, 54.02; H, 4.53; N, 12.60; S, 28.84%.)

ACKNOWLEDGEMENTS

The financial assistance of Karadeniz Technical University Research Fund is gratefully acknowledged.

REFERENCES

1. A. Pelter and D. Sümengen, *Tetrahedron Lett.*, **22,** 1945 (1977).
2. D. Sümengen and A. Pelter, *J. Chem. Soc. Perkin Trans I*, 687 (1983).
3. G. Lacasse and J. M. Muchowski, *Can. J. Chem.*, **51,** 2353 (1973).
4. M. Sèlim and M. Sèlim, *Bull. Soc. Chim.*, 823 (1969).
5. a) J. Elguero, C. Marzin, A. R. Katritzky and P. Linda, 'The Tautomerism of Heterocycles' in Advances in Heterocyclic Chemistry, Sup. 1, p. 15, Academic Press. New York (1976); b) Ibid., p. 378; c) ibid., p. 404; d) ibid., p. 398; e) ibid., p. 405.
6. A. R. Katritzky, B. Wallis, R. T. C. Brownlee and R. D. Topsom, *Tetrahedron*, **21,** 1681 (1965).
7. K. Kaji, H. Nagashima, Y. Ohhata, K. Tabashi and H. Oda, *J. Heterocyclic Chem.*, **22,** 161 (1985).
8. G. Crayen, *Chem. Ber.*, **24,** 385 (1891).
9. L. H. Schubart, *Chem. Ber.*, **22,** 2441 (1889).