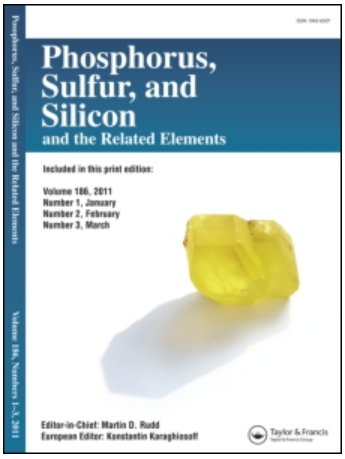

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THE PREPARATION AND REARRANGEMENT OF 3- PYRIDYL-4-ALKYL (OR ARYL)-1,2,4- OXADIAZOLE-5 (4H)-THIONES

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THE PREPARATION AND REARRANGEMENT OF 3-PYRIDYL-4-ALKYL (OR ARYL)-1,2,4-OXADIAZOLE-5(4H)-THIONES

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3-Pyridyl-4-alkyl (or aryl)-1,2,4-oxadiazole-5(4H)-thiones are prepared by the reaction of N-alkyl (or aryl) pyridine carboxamide oximes with thiophosgene. Rearrangement, catalysed by metallic copper, yields the corresponding 3,4-disubstituted-1,2,4-thiadiazole-5(4H)-ones.

Key words: 1,2,4-Oxadiazole-5(4H)-thiones; Copper-catalysed rearrangement; 1,2,4-thiadiazole-5(4H)-ones.

Derivatives of the 1,2,4-oxadiazole-5-thiones[1] and 1,2,4-thiadiazole-5-ones[2] have shown activity respectively as fungicides and as inhibitors of chronic convulsions. We have previously reported[3,4] the copper-catalysed rearrangement of alkyl and phenyl derivatives of 1,2,4-oxadiazole-5-thiones to the isomeric 1,2,4-thiadiazole-5-ones. The present investigation aims, in addition to preparing several new 1,2,4-oxadiazole-5-thiones and 1,2,4-thiadiazole-5-ones for evaluation of their biological activity, to generalize the copper-catalysed rearrangement of 1,2,4-oxadiazole-5-thiones to 1,2,4-thiadiazole-5-ones.

The compounds (**3**) were prepared either from the reaction of N-substituted pyridine carboxamide oximes (**1**) with thiophosgene or from the treatment of 3,4-disubstituted-1,2,4-oxadiazole-5(4H)-ones (**2**) with excess of phosphorus pentasulphide.

The thermal rearrangement of compounds (**3**) to compounds (**4**) was carried out with a catalytic amount of copper powder in diphenyl ether. The reaction was normally complete in 1–3 h at 200°C. Rapid analysis and characterization of the products of the rearrangement were particularly simple as all compounds (**4**) have a C=O frequency (i.r.) at 1673–1683 cm^{-1}, whilst compounds (**3**) have three mixed C=S vibrations associated with a C=S group linked to at least one nitrogen[5] in the regions 1460–1478, 1290–1330, and 1115–1135 cm^{-1}.

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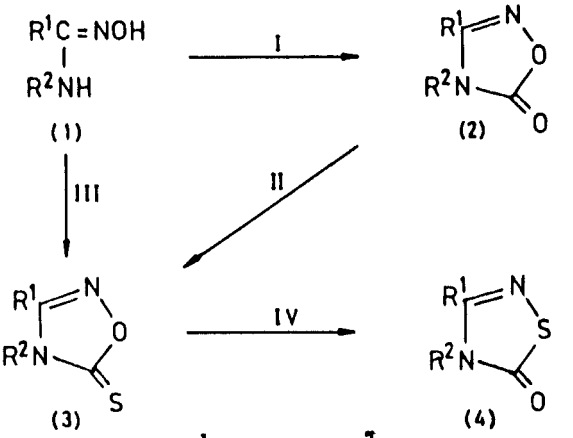
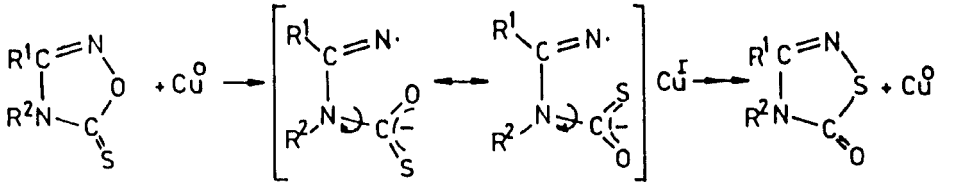


	R^1	R^2
a;	2-Pyr	Me
b;	2-Pyr	Et
c;	2-Pyr	Pr
d;	2-Pyr	Ph
e;	3-Pyr	p-MeC_6H_4
f;	4-Pyr	Me
g;	4-Pyr	p-MeC_6H_4

Reagents: I, $ClCO_2Et$; II, P_2S_5; III, $Cl_2C{=}S$; IV, Cu powder

Analogies to this rearrangement can be found in the Schönberg rearrangement of diarylthione carbonates to diarylthiocarbonates[6,7] and in the thermal rearrangement of aryldialkylthionecarbamates to aryldialkylthiocarbamates.[8,9] The mechanism of the copper-catalysed rearrangement is unknown, but one possibility is the redox sequence as shown below.



In order to test whether the rearrangement occurs without catalysis, compounds (**3a–c**) were heated for 10 h at 200°C in diphenyl ether, but they remained unchanged. However, when the same compounds were submitted to the same treatment for 5–11 h (Table II) at 250°C, they were converted into compounds (**4a–f**). Only compound (**3g**) was decomposed at this temperature. An alternative reasonable mechanism for the thermal rearrangement is shown below.

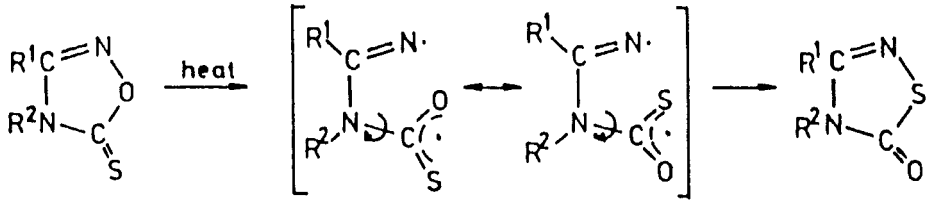


TABLE I

Analytical data for compounds (3) and (4)

Comp.	Yield (%)	M.P. (°C)	Molecular formula	Found (calculated) (%) C	H	N
(3b)	40	95–96	$C_9H_9N_3OS$ (207.2)	52.42 (52.15)	4.40 (4.37)	20.11 (20.27)
(3c)	54	64–65	$C_{10}H_{11}N_3OS$ (221.2)	54.44 (54.28)	5.07 (5.01)	19.12 (18.98)
(3d)	64	136–137	$C_{13}H_9N_3OS$ (255.3)	61.25 (61.16)	3.75 (3.55)	16.52 (16.45)
(3e)	55	159–160	$C_{14}H_{11}N_3OS$ (269.3)	62.35 (62.43)	4.23 (4.11)	15.49 (15.60)
(3f)	43	158–159	$C_8H_7N_3OS$ (193.2)	49.40 (49.72)	3.65 (3.70)	21.74 (21.70)
(3g)	62	162–163	$C_{14}H_{11}N_3OS$ (269.3)	61.90 (62.43)	4.11 (4.11)	15.42 (15.60)
(4b)	33	67–68	$C_9H_9N_3OS$ (207.2)	52.50 (52.15)	4.60 (4.37)	20.30 (20.27)
(4c)	54	oil	$C_{10}H_{11}N_3OS$[a] (221.2)			
(4d)	53	111–112	$C_{13}H_9N_3OS$ (255.3)	61.66 (61.16)	3.50 (3.55)	16.46 (16.45)
(4e)	65	140–141	$C_{14}H_{11}N_3OS$ (269.3)	62.14 (62.43)	3.96 (4.11)	15.45 (15.60)
(4f)	33	106–107	$C_8H_7N_3OS$ (193.2)	49.97 (49.72)	3.68 (3.65)	21.70 (21.74)
(4g)	40	110–111	$C_{14}H_{11}N_3OS$ (269.3)	62.25 (62.43)	4.21 (4.44)	15.58 (15.60)

[a] Exact mass of **(4c)**; Calcd: 221.0623; Found: 221.0616.

TABLE II

Complete conversion of compounds (3) into compounds (4)

Comp.	R_F	Eluant	Comp.	R_F	Reaction Temp. (°C)	Catalyst	Reaction Time (h)
(3b)	0.54	Benzene	**(4b)**	0.25	200	Cu	1
					200	Ag	3
					250	—	5
(3c)	0.55	Benzene: $CHCl_3$ (1:2)	**(4c)**	0.18	200	Cu	1.5
					200	Ag	5
					250	—	6
(3d)	0.52	MeOH: $CHCl_3$: Light petroleum (40–60°C) (1:2:5)	**(4d)**	0.26	200	Cu	2
					200	Ag	8
					250	—	7
(3e)	0.51	Benzene: Ethyl acetate: Light petroleum (40–60°C) (1:3:1)	**(4e)**	0.43	200	Cu	3
					200	Ag	6
					250	—	5
(3f)	0.45	Ethylacetate	**(4f)**	0.31	200	Cu	2
					200	Ag	4
					250	—	6
(3g)	0.57	Ethylacetate: Light petroleum (40–60°C) (3:1)	**(4g)**	0.44	200	Cu	2
					200	Ag	5
					250	—	6 (dec.)

Although the reaction took longer time, the rearrangement was found sensitive to silver catalysis. When compounds (**3a–g**) were heated for 3–8 h (Table II) at 200°C in diphenyl ether in the presence of a few pieces of silver shavings they were converted into compounds (**4a–g**).

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).

Preparation of 3-(2-pyridyl)-4-methyl-1,2,4-oxadiazole-5(4H)-thione (**3a**)*-Method A.* 3-(2-Pyridyl)-4-methyl-1,2,4-oxadiazole-5(4H)-one (0.27 g, 1.52 mmol) and phosphorus pentasulphide (0.100 g, 0.45 mmol) were refluxed in xylene (25 ml) for 12 h. Hot solution was filtered and xylene was evaporated under reduced pressure to give a crude solid. The crude product was recrystallized from ether and dried in vacuo to give compound (**3a**) (0.21 g, 71%); m.p. 129–130°C; —IR(KBr): 1580, 1570 and 1550 (C=N), 1450, 1287 and 1110 cm^{-1} (C=S); —^{1}H-NMR ($CDCl_3$): δ 3.92 (*s*, 3H, CH_3), 7.57 (*m*, 1 aromatic H), 7.92 (*m*, 2 aromatic H) and 8.77 (*d*, 1 aromatic H) (Found: C, 49.63; H, 3.84; N, 22.00. Calcd. for $C_8H_7N_3OS$: C, 49.72; H, 3.65; N, 21.74%).

Method B. A solution of redistilled thiophosgene (1.15 g, 10 mmol) in chloroform (5 ml) was added dropwise to an ice-cooled solution of N-methylpyridine-2-carboxamidoxime (1.51 g, 10 mmol) and pyridine (1.58 g, 20 mmol) in $CHCl_3$ (250 ml). Reaction mixture was stirred at room temperature for 3 days. The solvent was evaporated under reduced pressure at 20°C and the product was recrystallized from benzene-light petroleum (40–60°C) (1:1) to give compound (**3a**) (1.10 g, 57%); m.p. 129–130°C, identical in all respects with the sample obtained by method A.

Preparation of 3-(2-pyridyl)-4-methyl-1,2,4-thiadiazole-5(4H)-one (**4a**). Compound (**3a**) (0.193 g, 1 mmol) was heated in diphenyl ether (0.5 ml) in a tube for 1 h at 200°C in the presence of a catalytic quantity of copper powder. Reaction mixture was extracted with acetone (3 × 15 ml) and filtered. The solvent was evaporated under reduced pressure, and remaining solid was recrystallized from *n*-pentane to give compound (**4a**) (0.097 g, 50%); m.p. 94–95°C; —IR(KBr): 1680 (C=O) and 1580 cm^{-1} (C=N); —^{1}H-NMR ($CDCl_3$): δ 3.72 (*s*, 3, CH_3), 7.45 (*m*, 1 aromatic H), 7.95 (*m*, 2 aromatic H) and 8.67 (*d*, 1 aromatic H) (Found: C, 49.53; H, 3.59; N, 21.77. Calcd. for $C_8H_7N_3OS$: C, 49.72; H, 3.65; N, 21.74%).

Some of the 3,4-disubstituted-1,2,4-thiadiazole-5(4H)-ones (4) were purified by preparative t.l.c. using 20 × 20 cm-silica gel HF_{254} coated plates. The band containing the substance was detected by shortwave (254 nm) u.v. light and treated with chloroform, filtered and then evaporated at room temperature.

Analytical data for compounds (**3**) and (**4**) are given in Table I. The spectroscopic data of these compounds are given below.

Compound (**3b**), recrystallized from benzene-light petroleum (40–60°C) (1:1), —IR(KBr): 1593, 1582, 1560 (C=N), 1460, 1297 and 1120 cm^{-1} (C=S); —^{1}H-NMR ($CDCl_3$): δ 1.37 (*t*, 3H, CH_3), 4.57 (*q*, 2H, $\underline{CH_2}CH_3$), 7.55 (*m*, 1 aromatic H), 7.95 (*m*, 2 aromatic H) and 8.80 (*d*, 1 aromatic H).

Compound (**3c**), recrystallized from *n*-pentane; —IR(KBr): 1575, 1545 (C=N), 1465, 1270 and 1110 cm^{-1} (C=S); —^{1}H-NMR ($CDCl_3$): δ 0.93 (*t*, 3H, CH_3), 1.86 (sext, 2H, $CH_2\underline{CH_2}CH_3$), 4.60 (*t*, 2H, $\underline{CH_2}CH_2CH_3$), 7.73 (*m*, 1 aromatic H), 8.20 (*m*, 2 aromatic H) and 9.00 (*m*, 1 aromatic H).

Compound (**3d**), recrystallized from ether; —IR(KBr): 1580, 1555 (C=N), 1465, 1288 and 1140 cm^{-1} (C=S); —^{1}H-NMR ($CDCl_3$): δ 7.25–7.51 (*m*, 6 aromatic H), 7.76–7.85 (*m*, 2 aromatic H), and 8.39–8.44 (*m*, 1 aromatic H).

Compound (**3e**), recrystallized from ethanol; —IR(KBr): 1590, 1560 (C=N), 1475, 1278 and 1120 cm^{-1} (C=S), —^{1}H-NMR (DMSO-d_6): δ 2.34 (*s*, 3H, CH_3), 7.36 (*m*, 4 aromatic H), 7.50 (*m*, 1 aromatic H), 7.77 (*m*, 1 aromatic H) and 8.67 (*m*, 2 aromatic H).

Compound (**3f**), recrystallized from chloroform-*n*-hexane (1:1); —IR(KBr): 1605, 1572 (C=N), 1465, 1282 and 1115 cm^{-1} (C=S); —^{1}H-NMR (DMSO-d_6): δ 3.50 (*s*, 3H, CH_3), 7.70 (*d*, 2 aromatic H) and 8.80 (*d*, 2 aromatic H).

Compound (**3g**), recrystallized from ethanol; —IR(KBr): 1600, 1575 (C=N), 1475, 1278 and 1110 cm^{-1} (C=S); —^{1}H-NMR ($CDCl_3$): δ 2.46 (*s*, 3H, CH_3), 7.33 (*m*, 6 aromatic H) and 8.73 (*m*, 2 aromatic H).

Compound (**4b**), purified by preparative t.l.c. using methanol-chloroform-light petroleum (40–60°C) (1:2:5) (R_F 0.66), recrystallized from *n*-pentane; —IR(KBr): 1660 (C=O) and 1580 cm^{-1} (C=N); —^{1}H-NMR ($CDCl_3$): δ 1.23 (*t*, 3H, $CH_2\underline{CH_3}$), 4.30 (*q*, 2H, $\underline{CH_2}CH_3$), 7.30 (*m*, 1 aromatic H), 7.80 (*m*, 2 aromatic H) and 8.60 (*d*, 1 aromatic H).

Compound (**4c**), purified by preparative t.l.c. using methanol-chloroform-light petroleum (40–60°C) (1:2:5) (R_F 0.50); —IR (liquid film): 1670 (C=O) and 1578 cm^{-1} (C=N); —^{1}H-NMR ($CDCl_3$): δ 0.86 (*t*, 3H, $CH_2CH_2\underline{CH_3}$), 1.64 (sext, 2H, $CH_2\underline{CH_2}CH_3$), 4.27 (*t*, 2H, $\underline{CH_2}CH_2CH_3$), 7.44 (*m*, 1 aromatic H), 7.86 (*m*, 1 aromatic H), 8.02 (*m*, 1 aromatic H) and 8.66 (*d*, 1 aromatic H).

Compound (**4d**), recrystallized from ether; —IR(KBr): 1675 (C=O) and 1585 cm^{-1} (C=N); —^{1}H-NMR ($CDCl_3$): δ 7.25 (*m*, 6 aromatic H), 7.70 (*m*, 2 aromatic H) and 8.33 (*m*, 1 aromatic H).

Compound (**4e**), recrystallized from ether; —IR(KBr): 1670 (C=O), 1580 and 1560 cm^{-1} (C=N); —^{1}H-NMR ($CDCl_3$): δ 2.38 (*s*, 3H, CH_3), 7.15 (*m*, 5 aromatic H), 7.63 (*m*, 1 aromatic H) and 8.58 (*m*, 2 aromatic H).

Compound (**4f**), recrystallized from light petroleum (40–60°C); —IR(KBr): 1675 (C=O) and 1600 cm^{-1} (C=N); —^{1}H-NMR ($CDCl_3$): δ 3.42 (*s*, 3H, CH_3), 7.50 (*d*, 2 aromatic H) and 8.84 (*d*, 2 aromatic H).

Compound (**4g**), recrystallized from light petroleum (40–60°C); —IR(KBr): 1670 (C=O), 1620 and 1580 cm^{-1} (C=N); —^{1}H-NMR ($CDCl_3$): δ 2.41 (*s*, 3H, CH_3), 7.05 (*m*, 2 aromatic H), 7.20 (*m*, 2 aromatic H), 7.26 (*m*, 2 aromatic H) and 8.58 (*m*, 2 aromatic H).

Miscellaneous Experiments. (i) Compounds (**3a–g**) were heated for 10 h at 200°C in diphenyl ether. T.l.c. (silica gel) indicated only one spot for each experiment under u.v. light, confirmed by their R_F values (Table II) as the initial compounds.

(ii) Compound (**3a**), (0.040 g, 0.2 mmol) were heated for 11 h at 250°C in diphenyl ether (0.5 ml). T.l.c. (silica gel) indicated only one spot corresponding to the rearrangement product (**4a**) (R_F 0.43) (MeOH: CH_2Cl_2: Light petroleum, 40–60°C) (1:2:5).

(iii) Compound (**3a**) (0.040 g, 0.2 mmol) were heated for 5 h at 200°C in diphenyl ether (0.5 ml) in the presence of a few pieces of silver shavings. T.l.c. (silica gel) gave one spot, corresponding to the rearrangement product (**4a**), confirmed by its R_F value of 0.43.

Reaction times and the temperatures for the conversion of compounds (**3b–g**) into compounds (**4b–g**) with or without catalyst are given in Table II.

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REFERENCES

1. Y. Uchiyama and Y. Hashimoto, Japan. Kobai 74 13, 177 (CI. 16E391-2), 05 February 1974, Appl. 72 55, 593 6 June 1972 (C. A., 80: 133442).
2. E. Takeuchi and S. Suga, JP 61, 106, 575/86, 106, 575/. (CI.CO7D417/06) 24th May 1986. (C. A., 105: 226587).
3. A. Pelter and D. Sümengen, *Tetrahedron Lett.*, **22,** 1945 (1977).
4. D. Sümengen and A. Pelter, *J. Chem. Soc. Perkin Trans. I*, 687 (1983).
5. C. N. R. Rao, R. Venkataraghavan and T. R. Kasturi, *Can. J. Chem.*, **42,** 36 (1964).
6. A. Schönberg and L. Vargha, *Chem. Ber.*, **63,** 178 (1930); A. Schönberg, L. Vargha and W. Paul, *Ann. Chem.*, **483,** 107 (1930).
7. H. R. Al-Kazimi, D. S. Tarbell and D. Plant, *J. Am. Chem. Soc.*, **77,** 2479 (1955).
8. K. Miyazaki, *Tetrahedron Lett.*, 2793 (1968).
9. M. S. Newman and H. A. Karnes, *J. Org. Chem.*, **31,** 3980 (1966).