The Preparation and Rearrangements of 3,4-Disubstituted 1,2,4-Oxadiazoline-5-thiones †

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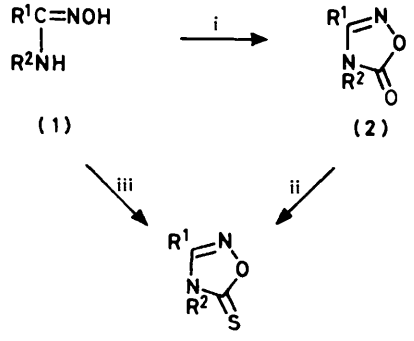
3,4-Disubstituted Δ^2-1,2,4-oxadiazoline-5-thiones are prepared by the reaction of *N*-substituted amidoximes with thiophosgene. Rearrangement, catalysed by either light or metallic copper, yields the corresponding 3,4-disubstituted Δ^2-1,2,4-thiadiazolin-5-ones.

Preparative Studies.—We have previously shown [1] that *N*-substituted amidoximes (1) react with ethyl chloroformate to give 3,4-disubstituted Δ^2-1,2,4-oxadiazolin-5-ones (2) (Scheme 1). We expected that the corresponding 5-thiones (3), which we wished to study, would be available by conversion from (2) using phosphorus pentasulphide, a reaction for which there are analogies.[2,3]

When (2a) [see Scheme for key to substituents on compounds (2), (3), and (4)] is refluxed in *o*-xylene with an excess of phosphorus pentasulphide for 3 h, it is mainly unchanged, only 5% of the thione (3a) being obtained. However, when it is heated at 150 °C for 30 min with an excess of phosphorus pentasulphide then (3a) is isolated in 52% yield.

Another method for the synthesis of compound (3) would be the interaction of (1) with thiophosgene.[4] Reaction of (1a) with thiophosgene ‡ (Scheme) in chloroform at *ca.* 22 °C gave compound (3a), but in only 26% yield. However, the mild conditions and the directness of the method, which obviates the need to make (2a) as an intermediate, recommended the process to us. It was therefore used for the preparation of compounds (3a—p), all of which were purified and fully characterised (see Experimental section).



	R^1	R^2 *		R^1	R^2
a;	Me	Me	i;	Pr^n	Me
b;	Me	Et	j;	Pr^n	Et
c;	Me	Pr^n	k;	Pr^n	Pr^n
d;	Me	Bu^n	l;	Pr^n	Bu^n
e;	Et	Me	m;	Bu^n	Me
f;	Et	Et	n;	Ph	Me
g;	Et	Pr^n	o;	Ph	Et
h;	Et	Bu^n	p;	Ph	Ph

* Throughout the paper, compounds designated as (2a—p), (3a—p), and (4a—p) have the substituents R^1 and R^2 as shown here.

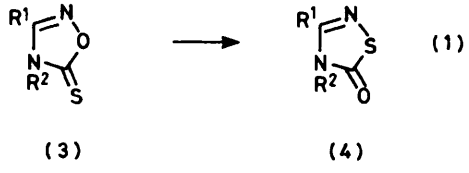
Scheme. *Reagents:* i, $ClCO_2Et$; ii, P_2S_5; iii, $Cl_2C{=}S$

Rearrangement Reactions.—We proposed to study the rearrangement shown in equation (1), which was unknown until our preliminary communication.[5]

Analogies to this hypothetical rearrangement can be found in the Schönberg rearrangement of diarylthionecarbonates to diarylthiocarbonates [6,7] and in the thermal rearrangement of aryldialkylthionecarbamates to aryldialkylthiocarbamates.[8,9] The kinetics of the Schönberg rearrangement are in accord with initial nucleophilic attack by sulphur, leading to a four-membered cyclic intermediate or transition state which collapses to the carbonyl rather than the thiocarbonyl product [7,10] (equation 2).

A similar two-step mechanism can be invoked for the rearrangement of *N*,*N*-dialkylthionecarbonates [9] and for the ready rearrangement of oxime thionecarbonates to thioxime carbamates.[11] However, free-radical mechanisms [12] as well as heterolysis of three-membered cyclic transition states [13] may also be involved.

It therefore seemed to us that heating compounds (3), with or without solvent, might lead to compounds (4). However, in great contrast to the open-chain analogues, compounds (3) are unchanged by 8—10 h reflux in acetone, benzene, toluene, or *o*-xylene. When diphenyl ether is used as solvent, the phenyl-substituted compounds (3n—p) rearranged in 8 h at 200 °C to their respective isomers (4n—p). All the other compounds (3a—m) decomposed in these conditions. Rapid analysis and characterisation of the products of the rearrangement were particularly simple as all compounds (4) have a C=O frequency (i.r.) at 1 673—1 683 cm^{-1}, whilst compounds (3) have three mixed C=S vibrations associated with a C=S group linked to at least one nitrogen [14] in the regions 1 460—1 478, 1 290—1 330, and 1 115—1 135 cm^{-1}.

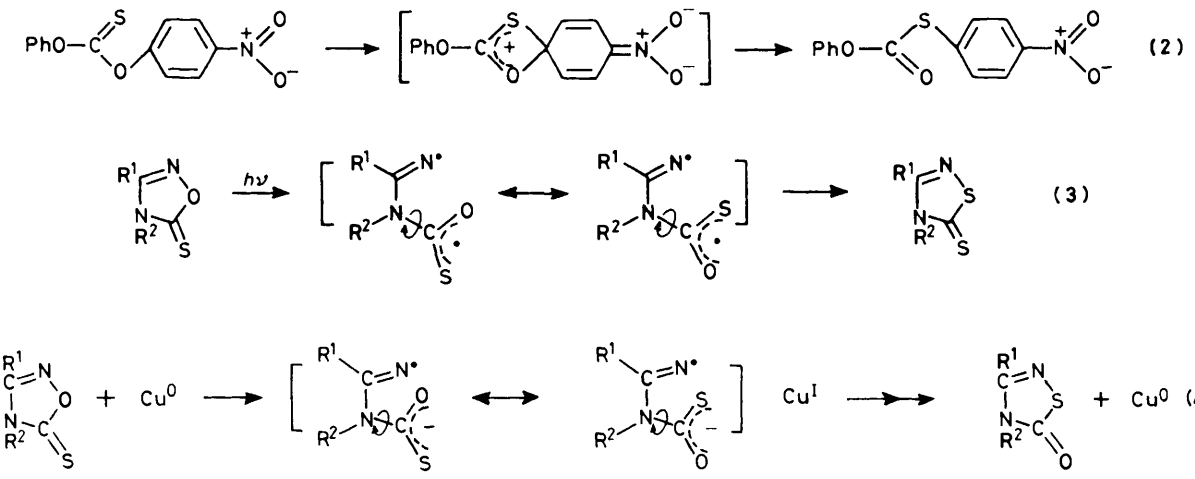


Irradiation of 3,4-diphenyl-Δ^2-1,2,4-oxadiazolin-5-one in dioxan induces rearrangement to 2-phenylimidazole.[15] We therefore subjected compounds (3a—p) to irradiation from a low-pressure mercury lamp and were pleased to observe smooth rearrangement in each case to compounds (4).

This new rearrangement may proceed through a four-membered transition state or intermediate, as postulated for

† Partly taken from the Docent thesis of D. Sümengen, Istanbul University, 1975.

‡ For the yields shown in Table 1, it is necessary that the thiophosgene be freshly purified by distillation at atmospheric pressure with protection from moisture.



the open-chain analogues (equation 1),[7,10] but an alternative, reasonable mechanism is shown in equation 3.

In order to test whether the thermal rearrangement of compounds (3) was sensitive to metal catalysis [based on the extreme similarity of the mass spectra of compounds (3) and (4) [5]] compound (3i) was heated for 4 h at 160 °C in diphenyl ether in the presence of a little iron powder. However, it remained unchanged. When the same compound was submitted to the same treatment but in the presence of a catalytic amount of copper powder it was converted into (4i). We find that this unique, copper-catalysed reaction is general (Table) and that reaction is normally complete in 4 h at 180 °C. In this way we were able to rearrange compounds (3a, b, f, i, h, n, o, and p). The reaction is efficient and is our recommended procedure for the production of 3,4-disubstituted Δ^2-1,2,4-thiadiazolin-5-ones (4). The mechanism of the copper-catalysed rearrangement is unknown, but one possibility is the redox sequence shown in equation (4).

Experimental

^{1}H N.m.r. spectra were taken on a Varian HA100 n.m.r. spectrometer, mass spectra on an A.E.I.MS9 mass spectrometer, and i.r. spectra on a Pye Unicam Model SP1050. Solvents used as reaction media or as eluants were dried and purified by standard methods prior to use.

Four of the experimental methods are described in detail. Their applications are shown in Tables 1 and 3 whilst microanalyses are given in Tables 2 and 4.

Preparation of 3,4-*Dimethyl*-Δ^2-1,2,4-*oxadiazoline*-5-*thione* (3a).—*Method A.* 3,4-Dimethyl-Δ^2-1,2,4-oxadiazolin-5-one (0.5 g, 4.38 mmol) [1] and phosphorus pentasulphide (0.4 g, 1.80 mmol) were mixed together in a 10-ml round-bottomed flask and heated at 150 °C for 30 min. Subsequent cooling gave a solid crude product which was powdered, extracted with hot ether, and filtered. The filtrate was evaporated under reduced pressure to give a crude solid, which was found by t.l.c. to contain some starting compound as impurity. The compound was purified by a silica-gel (200—300 mesh) column using ether–methanol–ethyl acetate mixture (1 : 1 : 1) as the mobile phase. The solvent was evaporated and the product crystallized from ether–light petroleum (40—60 °C) (1 : 1) and dried *in vacuo* to give compound (3a) (0.30 g, 53%); m.p. 67—68 °C; $\nu_{max.}$ (KBr) 1 610 (C=N), 1 472, 1 310, and 1 130 cm^{-1} (C=S); δ($CDCl_3$) 2.40 (s, 3 H, CCH_3), 3.47 (s, 3 H, NCH_3) (Found: C, 37.15; H, 4.8; N, 21.8; S, 24.3. Calc. for $C_4H_6N_2OS$: C, 36.91; H, 4.65; N, 21.52; S, 24.63%); *m/z* 130.

Method B. A solution of redistilled thiophosgene (0.96 g, 8.33 mmol) in chloroform (5 ml) was added dropwise to a stirred solution of *N*-methylacetamide oxime (2.20 g, 25 mmol) in chloroform (25 ml). An immediate precipitate of *N*-methylacetamide oxime hydrochloride [1] formed. The reaction mixture was stirred at room temperature for 10 h and filtered. The residue was washed with ether and the solution evaporated under reduced pressure at 20 °C to give a yellowish oily material (containing a trace of sulphur) which was dissolved in ether (10 ml) and filtered. The solution was then pumped down and the product crystallized from a mixture of ether–light petroleum (40—60 °C) (1 : 1) to give compound (3a) (0.28 g, 26%); m.p. 67—68 °C, identical in all respects with the sample obtained by method A.

Some of the 3,4-disubstituted Δ^2-1,2,4-oxadiazoline-5-thiones (3) were purified by preparative t.l.c. using 20 × 40-cm silica-gel GF_{254} coated plates. The band containing the substance was detected by short-wave (254 nm) u.v. light, and treated with chloroform, filtered and then evaporated at room temperature. Physical constants for the compounds are given below.

Compound (3b), crystallized from ether–light petroleum (40—60 °C) (1 : 1) in a freezer; m.p. 52—53 °C; $\nu_{max.}$ (KBr) 1 605 (C=N), 1 475, 1 320, and 1 132 cm^{-1} (C=S); δ($CDCl_3$) 1.37 (t, 3 H, CH_2CH_3), 2.42 (s, 3 H, CCH_3), and 3.96 (q, 2 H, CH_2CH_3); *m/z* 144.

Table 1. Preparation of 3,4-disubstituted-Δ^2-1,2,4-oxadiazoline-5-thiones (3) by method B [a]

Amidoxime	Reaction solvent	Reaction time (h)	% Yield (3) [b]
(1b)	C_6H_6	12	28
(1c)	CH_2Cl_2	10	29
(1d)	C_6H_6	16	35
(1e)	C_6H_6	15	38
(1f)	C_6H_6	10	37
(1g)	C_6H_6	10	28
(1h)	C_6H_6	12	25
(1i)	C_6H_6	10	41
(1j)	$CHCl_3$	15	30
(1k)	C_6H_6	16	34
(1l)	CH_2Cl_2	10	38
(1m)	C_6H_6	12	32
(1n)	CH_2Cl_2	8	62
(1o)	C_6H_6	8	66
(1p)	C_6H_6	6	71

[a] All reactions at *ca.* 22 °C. [b] In this and Table 3, yields are of solated, purified products.

Table 2. Analyses of 3,4-disubstituted Δ^2-1,2,4-oxadiazoline-5-thiones (3)

Compound	Found (%) C	H	N	S	Formula	Calculated (%) C	H	N	S
(3b)	41.69	5.38	19.22	22.35	$C_5H_8N_2OS$	41.65	5.59	19.43	22.24
(3c)	45.74	6.40	17.85	20.10	$C_6H_{10}N_2OS$	45.54	6.37	17.71	20.27
(3d)	49.02	7.15	16.11	18.75	$C_7H_{12}N_2OS$	48.81	7.02	16.26	18.61
(3d)	41.48	5.57	19.36	22.27	$C_5H_8N_2OS$	41.65	5.59	19.43	22.24
(3f)	45.78	6.32	17.73	19.90	$C_6H_{10}N_2OS$	45.54	6.37	17.71	20.27
(3g)	48.90	6.91	16.52	18.52	$C_7H_{12}N_2OS$	48.81	7.02	16.26	18.61
(3h)	51.30	7.61	14.89	17.20	$C_8H_{14}N_2OS$	51.58	7.58	15.04	17.21
(3i)	45.37	6.20	17.95	20.30	$C_6H_{10}N_2OS$	45.54	6.37	17.71	20.27
(3j)	48.57	7.33	16.19	18.46	$C_7H_{12}N_2OS$	48.81	7.02	16.26	18.61
(3k)	51.51	7.61	14.94	17.30	$C_8H_{14}N_2OS$	51.58	7.58	15.04	17.21
(3l)	53.94	7.90	13.87	16.15	$C_9H_{16}N_2OS$	53.97	8.05	13.99	16.01
(3m)	48.92	6.73	16.36	18.60	$C_7H_{12}N_2OS$	48.81	7.02	16.26	18.61
(3n)	56.36	4.23	14.66	16.40	$C_9H_8N_2OS$	56.23	4.19	14.57	16.68
(3o)	58.52	4.74	13.63	15.40	$C_{10}H_{10}N_2OS$	58.23	4.89	13.58	15.54
(3p)	65.84	3.91	11.04	12.50	$C_{14}H_{10}N_2OS$	66.12	3.96	11.02	12.61

Table 3. Rearrangements of compounds (2) to (4)

Substrate	Method C [a] Reaction time (h)	Yield (%)	Method D [b] Reaction time (h)	Temp. (°C)	Yield (%)
(3b)	10	50	4.5	180	66
(3c)	12	60			
(3d)	8	56			
(3e)	8	58			
(3f)	8	64	50	100	80
(3g)	7.5	55	5	200	71
(3h)	12	60			
(3i)	8	50	4	160	60
(3j)	8	59			
(3k)	10	40	24	*b*	67
(3l)	8	70			
(3m)	8.5	68			
(3n)	10	35	4	180	54
(3o)	11	41	3.5	180	75
(3p)	9	30	4	200	50

[a] All reactions on *ca.* 1-mmol scale in 100 ml dry MeOH except (3k) (100 ml, EtOH) and (3p) (THF, 80 ml). [b] All reactions on *ca.* 0.5-mmol scale in Ph_2O (0.5 ml) except (3k) which was refluxed in xylene.

Compound (3c) purified by preparative t.l.c. using chloroform (R_F 0.41), crystallized from light petroleum (40—60 °C) in a freezer; m.p. 26 °C; $\nu_{max.}$ (KBr) 1 605 (C=N), 1 475, 1 310, and 1 128 cm^{-1} (C=S); δ($CDCl_3$) 1.00 (t, 3 H, $CH_2CH_2CH_3$), 1.82 (q, 2 H, $CH_2CH_2CH_3$), 2.41 (s, 3 H, CCH_3), and 3.87 (t, 2 H, $CH_2CH_2CH_3$); *m/z* 158.

Compound (3d) purified by preparative t.l.c. using chloroform (R_F 0.41), crystallized from light petroleum (40—60 °C) in a freezer; m.p. 11 °C; n_D^{20} 1.5302; $\nu_{max.}$ (film) 1 603 (C=N), 1 475, 1 300, and 1 130 cm^{-1} (C=S); δ($CDCl_3$) 0.99 (t, 3 H, $CH_2CH_2CH_3$), 1.23—1.87 (m, 4 H, $CH_2CH_2CH_2CH_3$), 2.39 (s, 3 H, CCH_3), and 3.89 (t, 2 H, $CH_2CH_2CH_2CH_3$); *m/z* 172.

Compound (3e), recrystallized from ether–light petroleum (40—60 °C) (1 : 2); m.p. 58—59 °C; $\nu_{max.}$ (KBr) 1 600 (C=N), 1 475, 1 328, and 1 132 cm^{-1} (C=S); δ($CDCl_3$) 1.38 (t, 3 H, CH_2CH_3), 2.73 (q, 2 H, CH_2CH_3), and 3.48 (s, 3 H, NCH_3); *m/z* 144.

Compound (3f), recrystallized from light petroleum (40—60 °C); m.p. 63—64 °C; $\nu_{max.}$ (KBr) 1 592 (C=N), 1 470, 1 325, and 1 131 cm^{-1} (C=S); δ($CDCl_3$) 1.37 [dt, 6 H, $(CH_2CH_3)_2$], 2.74 (q, 2 H, CCH_2CH_3), and 3.97 (q, 2 H, NCH_2CH_3) *m/z* 158.

Compound (3g), recrystallized from light petroleum (40—60 °C) in a freezer; m.p. 37.5—38 °C; $\nu_{max.}$ (KBr) 1 592 (C=N), 1 472, 1 310, and 1 125 cm^{-1} (C=S); δ($CDCl_3$) 1.00 (t, 3 H, $CH_2CH_2CH_3$), 1.38 (t, 3 H, CH_2CH_3), 1.83 (q, 2 H, $CH_2CH_2CH_3$), 2.70 (q, 2 H, CH_2CH_3), and 3.84 (t, 2 H, $CH_2CH_2CH_3$); *m/z* 172.

Compound (3h), purified by preparative t.l.c. using chloroform (R_F 0.59) crystallized from pentane in a freezer; m.p. 29—29.5 °C; $\nu_{max.}$ (KBr) 1 595 (C=N), 1 470, 1 300, and 1 130 cm^{-1} (C=S); δ($CDCl_3$) 0.99 (t, 3 H, $CH_2CH_2CH_2CH_3$), 1.39 (t, 3 H, CH_2CH_3), 1.44—1.95 (m, 4 H, $CH_2CH_2CH_2CH_3$), 2.71 (q, 2 H, CH_2CH_3), and 3.88 (t, 2 H, $CH_2CH_2CH_2CH_3$); *m/z* 186.

Compound (3i), recrystallized from ether–n-heptane (1 : 1) in a freezer; m.p. 47.5—48.5 °C; $\nu_{max.}$ (KBr) 1 602 (C=N), 1 478, 1 300, and 1 128 cm^{-1} (C=S); δ($CDCl_3$) 1.08 (t, 3 H, $CH_2CH_2CH_3$), 1.82 (q, 2 H, $CH_2CH_2CH_3$), 2.67 (t, 2 H, $CH_2CH_2CH_3$), and 3.46 (s, 3 H, NCH_3); *m/z* 158.

Compound (3j), purified by preparative t.l.c. using methanol–chloroform–light petroleum (50—70 °C) (1 : 2 : 5) (R_F 0.65). Crystallized from light petroleum (40—60 °C) in a freezer; m.p. 27—27.5 °C; $\nu_{max.}$ (KBr) 1 592 (C=N), 1 470, 1 330, and 1 130 or 1 090 cm^{-1} (C=S); δ($CDCl_3$) 1.08 (t, 3 H, $CH_2CH_2CH_3$), 1.37 (t, 3 H, CH_2CH_3), 1.85 (q, 2 H, $CH_2CH_2CH_3$), 2.66 (t, 2 H, $CH_2CH_2CH_3$), and 3.97 (q, 2 H, CH_2CH_3); *m/z* 172.

Compound (3k), purified by preparative t.l.c. using chloroform (R_F 0.53), crystallized from pentane in a freezer; m.p. 28.5—29 °C; $\nu_{max.}$ (KBr) 1 592 (C=N), 1 475, 1 310, and 1 128 cm^{-1} (C=S); δ($CDCl_3$) 1.07 [dt, 6 H, $(CH_2CH_2CH_3)_2$], 1.62—2.02 [m, 4 H, $(CH_2CH_2CH_3)_2$], 2.63 (t 2 H, $CCH_2CH_2CH_3$), and 3.84 (t, 2 H, $NCH_2CH_2CH_3$); *m/z* 186.

Compound (3l), recrystallized from light petroleum (40—60 °C) in a freezer; m.p. 33—33.5 °C; $\nu_{max.}$ (KBr) 1 593 (C=N), 1 475, 1 300, and 1 130 cm^{-1} (C=S); δ($CDCl_3$) 1.07 (t, 6 H, $CH_2CH_2CH_3$ and $CH_2CH_2CH_2CH_3$), 1.26—2.03 (m, 6 H, $CH_2CH_2CH_3$ and $CH_2CH_2CH_2CH_3$), 2.62 (t, 2 H, $CH_2CH_2CH_3$), and 3.86 (t, 2 H, $CH_2CH_2CH_2CH_3$); *m/z* 200.

Compound (3m), purified by preparative t.l.c. using methanol–chloroform–light petroleum (40—60 °C) (1 : 2 : 5) (R_F 0.50), crystallized from light petroleum (40—60 °C) in a freezer; m.p. 21—22 °C; n_D^{22} 1.5350; $\nu_{max.}$ (film) 1 595 (C=N), 1 475, 1 310, and 1 120 cm^{-1} (C=S), δ($CDCl_3$) 1.00 (t, 3 H, $CH_2CH_2CH_2CH_3$), 1.32—1.93 (m, 4 H, $CH_2CH_2CH_2CH_3$), 2.70 (t, 2 H, $CH_2CH_2CH_2CH_3$), and 3.47 (3 H, NCH_3); *m/z* 172.

Compound (3n), recrystallized from ether–light petroleum

Table 4. Analysis of 3,4-disubstituted Δ^2-1,2,4-thiadiazolin-5-ones (4)

Compound	Found (%) C	H	N	S	Formula	Calculated (%) C	H	N	S
(4b)	41.60	5.61	19.72	22.40	$C_5H_8N_2OS$	41.65	5.59	19.43	22.24
(4c)	45.72	6.40	17.43	20.42	$C_6H_{10}N_2OS$	45.54	6.37	17.71	20.27
(4d)	48.55	6.92	16.22	18.92	$C_7H_{12}N_2OS$	48.81	7.02	16.26	18.61
(4e)	41.82	5.76	19.13	22.50	$C_5H_8N_2OS$	41.65	5.59	19.43	22.24
(4f)	45.75	6.33	17.51	19.95	$C_6H_{10}N_2OS$	45.54	6.37	17.71	20.27
(4g)	48.68	7.05	15.97	19.00	$C_7H_{12}N_2OS$	48.81	7.02	16.26	18.61
(4h)	51.79	7.40	15.20	17.00	$C_8H_{14}N_2OS$	51.58	7.58	15.04	17.21
(4i)	45.74	6.44	17.60	20.60	$C_6H_{10}N_2OS$	45.54	6.37	17.71	20.27
(4j)	48.77	6.85	16.27	18.80	$C_7H_{12}N_2OS$	48.81	7.02	16.26	18.61
(4k)	51.36	7.28	15.07	16.90	$C_8H_{14}N_2OS$	51.58	7.58	15.04	17.21
(4l)	54.21	8.40	13.81	16.30	$C_9H_{16}N_2OS$	53.97	8.05	13.99	16.01
(4m)	48.63	6.73	16.07	18.77	$C_7H_{12}N_2OS$	48.81	7.02	16.26	18.61
(4n)	56.18	4.00	14.54	16.90	$C_9H_8N_2OS$	56.23	4.19	14.57	16.68
(4o)	58.55	4.62	13.73	15.80	$C_{10}H_{10}N_2OS$	58.23	4.89	13.58	15.54
(4p)	66.10	3.72	11.30	12.20	$C_{14}H_{10}N_2OS$	66.12	3.96	11.02	12.61

(40—60 °C) (1 : 1); m.p. 119—120 °C; $\nu_{max.}$ (KBr) 1 612 (C=N), 1 475, 1 290, and 1 130 cm^{-1} (C=S); δ($CDCl_3$) 3.55 (s, 3 H, NCH_3), and 7.62 (s, 5 H, aromatic H); *m/z* 192.

Compound (3o), recrystallized from ether–light petroleum (40—60 °C) (1 : 3) in a freezer; m.p. 56—57 °C; $\nu_{max.}$ (KBr) 1 613 (C=N), 1 470, 1 320, and 1 135 cm^{-1} (C=S); δ($CDCl_3$) 1.31 (t, 3 H, CH_2CH_3), 4.00 (q, 2 H, CH_2CH_3), and 7.59 (s, 5 H, aromatic H); *m/z* 206.

Compound (3p), recrystallized from ethanol, m.p. 168—169 °C; $\nu_{max.}$ (KBr) 1 610 (C=N), 1 460, 1 310, and 1 115 cm^{-1} (C=S); δ($CDCl_3$) 7.34 (m, 10 H, aromatic H); *m/z* 254.

Method C. The preparation of 3,4-*dimethyl*-Δ^2-1,2,4-*thiadiazolin*-5-*one* (4a). Compound (3a) (0.15 g, 1.15 mmol) dissolved in dry methanol (100 ml) in a 12SW low-pressure Hanovia Photochemical Reactor, was irradiated for 12 h with stirring and under a slow stream of dry nitrogen gas.

At the end of the irradiation the yellow solution was evaporated at room temperature under reduced pressure to give a yellow liquid containing a trace amount of sulphur. An ether solution of the residue was applied to a silica-gel plate (GF_{254}) and purified by preparative t.l.c. using methanol–chloroform–light petroleum (40—60 °C) (1 : 2 : 5) as eluant (R_F 0.65). The band containing the product was detected by short-wave (254 nm) u.v. light, extracted with chloroform, and filtered. The solution was then evaporated at room temperature under reduced pressure, and crystallized from light petroleum (40—60 °C) in a freezer. The crystals were dried *in vacuo* to give compound (4a) (0.05 g, 33%); m.p. 35—36 °C; $\nu_{max.}$ (KBr) 1 680 (C=O), 1 583 cm^{-1} (C=N); δ($CDCl_3$) 2.35 (s, 3 H, CCH_3), and 3.32 (s, 3 H, NCH_3) (Found: C, 36.6; H, 4.40; N, 21.3; S, 24.35. Calc. for $C_4H_6N_2OS$: C, 36.91; H, 4.65; N, 21.52; S, 24.63%); *m/z* 130.

All of the 3,4-disubstituted Δ^2-1,2,4-thiodiazolin-5-ones (4) were purified by preparative t.l.c. using 20 × 40-cm silica-gel GF_{254} coated plates, as described in method C unless otherwise stated. Physical constants and other details for the compounds are given below.

Compound (4b), eluant, chloroform (R_F 0.44); crystallized from pentane in a freezer; m.p. 27 °C; $\nu_{max.}$ (KBr) 1 676 (C=O) and 1 580 cm^{-1} (C=N); δ($CDCl_3$) 1.30 (t, 3 H, CH_2CH_3), 2.38 (s, 3 H, CCH_3), and 3.82 (q, 2 H, CH_2CH_3); *m/z* 144.

Compound (4c), eluant, methanol–chloroform–light petroleum (40—60 °C) (1 : 2 : 5) (R_F 0.65), crystallized from pentane in a freezer; m.p. 30—31 °C; $\nu_{max.}$ (KBr) 1 680 (C=O) and 1 580 cm^{-1} (C=N); δ($CDCl_3$) 0.97 (t, 3 H, $CH_2CH_2CH_3$), 1.71 (q, 2 H, $CH_2CH_2CH_3$), 2.36 (s, 3 H, CCH_3), and 3.70 (t, 2 H, $CH_2CH_2CH_3$); *m/z* 158.

Compound (4d), eluant, methanol–chloroform–light petroleum (40—60 °C) (1 : 2 : 5) (R_F 0.53); chloroform as eluant (R_F 0.30); n_D^{20} 1.5163; $\nu_{max.}$ (film) 1 685 (C=O) and 1 583 cm^{-1} (C=N); δ($CDCl_3$) 0.97 (t, 3 H, $CH_2CH_2CH_2CH_3$), 1.24—1.84 (m, 4 H, $CH_2CH_2CH_2CH_3$), 2.36 (s, 3 H, CCH_3), and 3.75 (t, 2 H, $CH_2CH_2CH_2CH_3$); *m/z* 172.

Compound (4e), eluant, chloroform (R_F 0.38), n_D^{20} 1.5283; $\nu_{max.}$ (film) 1 685 (C=O) and 1 595 cm^{-1} (C=N); δ($CDCl_3$) 1.33 (t, 3 H, CH_2CH_3), 2.65 (q, 2 H, CH_2CH_3) and 3.32 (s, 3 H, NCH_3); *m/z* 144.

Compound (4f), eluant, chloroform (R_F 0.38), crystallized from light petroleum (40—60 °C); m.p. 40—41 °C; $\nu_{max.}$ (KBr) 1 683 (C=O) and 1 565 cm^{-1} (C=N); δ($CDCl_3$) 1.33 [dt, 6 H, $(CH_2CH_3)_2$], 2.64 (q, 2 H, CCH_2CH_3) and 3.80 (q, 2 H, NCH_2CH_3); *m/z* 158.

Compound (4g), eluant, chloroform (R_F 0.44); methanol–chloroform–light petroleum (40—60 °C) (1 : 2 : 5) as eluant (R_F 0.62); n_D^{20} 1.5152; $\nu_{max.}$ (film) 1 682 (C=O) and 1 597 cm^{-1} (C=N); δ($CDCl_3$) 0.97 (t, 3 H, $CH_2CH_2CH_3$), 1.34 (t, 3 H, CH_2CH_3), 1.72 (q, 2 H, $CH_2CH_2CH_3$), 2.63 (q, 2 H, CH_2CH_3), and 3.70 (t, 2 H, $CH_2CH_2CH_3$); *m/z* 172.

Compound (4h), eluant, chloroform (R_F 0.41); methanol–chloroform–light petroleum (40—60 °C) (1 : 2 : 5) as eluant (R_F 0.70); n_D^{20} 1.5090; $\nu_{max.}$ (film) 1 682 (C=O) and 1 560 cm^{-1} (C=N); δ($CDCl_3$) 0.97 (t, 3 H, $CH_2CH_2CH_2CH_3$), 1.34 (t, 3 H, CH_2CH_3), 1.38—1.85 (m, 4 H, $CH_2CH_2CH_2CH_3$), 2.63 (q, 2 H, CH_2CH_3), and 3.72 (t, 2 H, $CH_2CH_2CH_2CH_3$); *m/z* 186.

Compound (4i), eluant, chloroform (R_F 0.38); methanol–chloroform–light petroleum (40—60 °C) (1 : 2 : 5) as eluant (R_F 0.65); n_D^{20} 1.5220; $\nu_{max.}$ (film) 1 682 (C=O) and 1 568 cm^{-1} (C=N); δ($CDCl_3$) 1.05 (t, 3 H, $CH_2CH_2CH_3$), 1.82 (q, 2 H, $CH_2CH_2CH_3$), 2.60 (t, 2 H, $CH_2CH_2CH_3$), and 3.33 (s, 3 H, NCH_3); *m/z* 158.

Compound (4j), layer, silica gel HF_{254}; eluant, chloroform (R_F 0.53); n_D^{20} 1.5155; $\nu_{max.}$ (film) 1 680 (C=O) and 1 562 cm^{-1} (C=N); δ($CDCl_3$) 1.05 (t, 3 H, $CH_2CH_2CH_3$), 1.29 (t, 3 H, CH_2CH_3), 1.83 (q, 2 H, $CH_2CH_2CH_3$), 2.58 (t, 2 H, $CH_2CH_2CH_3$), and 3.80 (q, 2 H, CH_2CH_3); *m/z* 172.

Compound (4k); layer, silica gel HF_{254}; eluant, chloroform (R_F 0.38); methanol–chloroform–light petroleum (40—60 °C) (1 : 2 : 5) as eluant (R_F 0.79); n_D^{20} 1.5102; $\nu_{max.}$ (film) 1 685 (C=O) and 1 562 cm^{-1} (C=N); δ($CDCl_3$) 1.04 [dt, 6 H, $(CH_2CH_2CH_3)_2$], 1.54—2.00 [m, 4 H, $(CH_2CH_2CH_3)_2$], 2.56 (t, 2 H, $CCH_2CH_2CH_3$) and 3.69 (t, 2 H, $NCH_2CH_2CH_3$); *m/z* 186.

Compound (4l), layer, silica gel HF_{254}; eluant, chloroform

(R_F 0.50); methanol–chloroform–light petroleum (40—60 °C) (1 : 2 : 5) as eluant (R_F 0.63); n_D^{20} 1.5044; $\nu_{max.}$ (film) 1 685 (C=O) and 1 562 (C=N); δ($CDCl_3$) 1.04 (t, 6 H, $CH_2CH_2CH_3$ and $CH_2CH_2CH_2CH_3$), 1.24—2.00 (m, 6 H, $CH_2CH_2CH_3$ and $CH_2CH_2CH_2CH_3$), 2.58 (t, 2 H, $CH_2CH_2CH_3$), and 3.74 (t, 2 H, $CH_2CH_2CH_2CH_3$); *m/z* 200.

Compound (4m), eluant, chloroform (R_F 0.38); methanol–chloroform–light petroleum (40—60 °C) (1 : 2 : 5) as eluant (R_F 0.77; n_D^{20} 1.5153; $\nu_{max.}$ (film) 1 680 (C=O) and 1 565 cm^{-1} (C=N); δ($CDCl_3$) 0.95 (t, 3 H, $CH_2CH_2CH_2CH_3$), 1.25—1.92 (m, 4 H, $CH_2CH_2CH_2CH_3$), 2.60 (t, 2 H, $CH_2CH_2CH_2CH_3$), and 3.32 (s, 3 H, NCH_3); *m/z* 172.

Compound (4n), eluant, chloroform (R_F 0.47); crystallized from pentane; m.p. 77—78 °C; $\nu_{max.}$ (KBr) 1 680 (C=O) and 1 585 cm^{-1} (C=N); δ($CDCl_3$) 3.37 (s, 3 H, NCH_3) and 7.53 (s, 5 H, aromatic H); *m/z* 192.

Compound (4o), eluant, chloroform (R_F 0.53); crystallized from light petroleum (40—60 °C); m.p. 51—52 °C; $\nu_{max.}$ (KBr) 1 675 (C=O) and 1 580 cm^{-1} (C=N); δ($CDCl_3$) 1.21 (t, 3 H, CH_2CH_3), 3.83 (q, 2 H, CH_2CH_3), and 7.50 (s, 5 H, aromatic H); *m/z* 206.

Compound (4p), eluant, methanol–chloroform–light petroleum (40—60 °C) (1 : 3 : 10) (R_F 0.74); crystallized from ether–light petroleum (40—60 °C) (1 : 2); m.p. 126—127 °C; $\nu_{max.}$ (KBr) 1 673 (C=O) and 1 595 cm^{-1} (C=N); δ($CDCl_3$) 7.28 (m, 10 H, aromatic H); *m/z* 254.

Method D. Compound (3a) (0.08 g, 0.56 mmol) was heated in diphenyl ether (0.5 ml) in a tube for 3.5 h at 180 °C in the presence of a catalytic quantity of copper powder. A pink colour dominated the solution. The product was isolated and purified by preparative t.l.c. as described in method C, to give compound (4a) (0.035 g, 44%), identical in all respects with the sample obtained by method C. The representative details for some of the compounds (4) are given in Table 3. Diphenyl ether was used as solvent, unless otherwise stated, and the products were isolated as described in method C.

Miscellaneous Experiments.—(i) Compound (3i) was heated in diphenyl ether for 4 h at 160 °C in the presence of a little iron powder. The compound was recovered unchanged.

(ii) Compound (4i) was heated in diphenyl ether for 3 h at 180 °C in the presence of a catalytic quantity of iron powder. The compound was recovered unchanged.

(iii) Compound (4g) was heated in diphenyl ether for 4 h at 200 °C. The compound was recovered unchanged.

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