

O,N and *N,N* Double Rearrangement

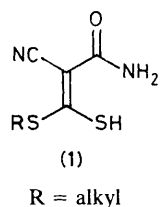
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2-Cyano-3-hydroxy-3-(methylthio)acrylamide and 2-cyano-3-methylthio-3-(phenylamino)acrylamide condense with benzoic acid in the presence of polyphosphoric acid trimethylsilyl ester to give 5-cyano-4-methylthio-2-phenyl-1,3-oxazin-6-one (*O,N* double rearranged product) and 5-cyano-6-methylthio-2,3-diphenyl-1,3-diazin-4-one (*N,N* double rearranged product), respectively.

From the mechanistic interpretation of the *S,N* double rearrangement¹ which is observed on the condensation of 3-alkylthio-2-cyano-3-(mercapto)acrylamide (1) with aryl carboxylic acids in the presence of polyphosphate ester (PPE), the use of the *O*-analogue and *N*-analogue of (1) under the same conditions could give rise to hitherto unknown *O,N* and *N,N* double rearrangements, respectively. As expected, these condensation reactions, involving the simultaneous interchange of heteroatoms, were observed when 2-cyano-3-hydroxy-3-(methylthio)acrylamide (2)[†] and 2-cyano-3-methylthio-3-(phenylamino)acrylamide (3)[†] were treated with benzoic acid in the presence of polyphosphoric acid trimethylsilyl ester (PPSE).² We report here the first examples of these novel heteroatom rearrangements which we have called *O,N* double rearrangement and *N,N* double rearrangement.

These condensation reactions required high temperatures (140–160 °C). Therefore the use of PPSE gave better results than PPE because PPSE is more stable to heating than PPE. Hexamethyldisiloxane (4 ml), phosphorus pentoxide (2 g),



[†] Compound (2) was prepared from the reaction of cyanoacetamide with *S,S*-dimethyl dithiocarbonate in the presence of sodium hydride and copper(I) iodide in 78% yield; white prisms; m.p. >340 °C; i.r. (KBr) 3310, 3160 (vs), 2200 (s), and 1680 cm⁻¹ (vs); n.m.r. (CDCl₃-CD₃COCD₃) δ 7.5 (br, 3H, NH₂, OH) and 2.4 (s, 3H, SMe). Compound (3) was prepared from the reaction of 2-cyano-3,3-bis(methylthio)acrylamide with aniline in 99% yield; white needles; m.p. 147–149 °C; *m/z* 233 (*M*⁺); i.r. (KBr) 3450 (s), 3390 (vs), 3300 (s), 3240 (s), 3170 (vs), 2200 (vs), and 1650 cm⁻¹ (vs); n.m.r. (CDCl₃-CD₃COCD₃) δ 12.6 (br, 1H, NH) 7.4 (s, 5H, Ph), 6.42 (br, 2H, NH₂), and 2.2 (s, 3H, SMe).

and chloroform (10 ml) were refluxed for 30 min. The solvent was removed *in vacuo* to afford a colourless viscous solution of PPSE, to which benzoic acid was added. The mixture was stirred for 10 min at 120 °C and then (2) (2 mmol) was added. The resulting mixture was stirred for 2 h at 120 °C and then worked up in the usual way to give 5-cyano-4-methylthio-2-phenyl-1,3-oxazin-6-one (4) (equation 1) as yellow plates. The results are summarized in Table 1.

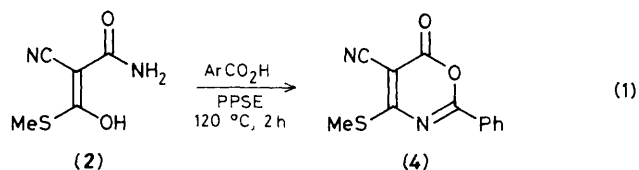


Table 1. The formation of (4) from (2) [equation (1)].

Ar	Yield/%	M.p./°C
Ph	77	195–196
2-Naphthyl	68	263–264
<i>p</i> -Anisyl	79	201–203
<i>p</i> -Chlorophenyl	74	201–203
<i>p</i> -Nitrophenyl	56	213–214
2-Furyl	49	190–191

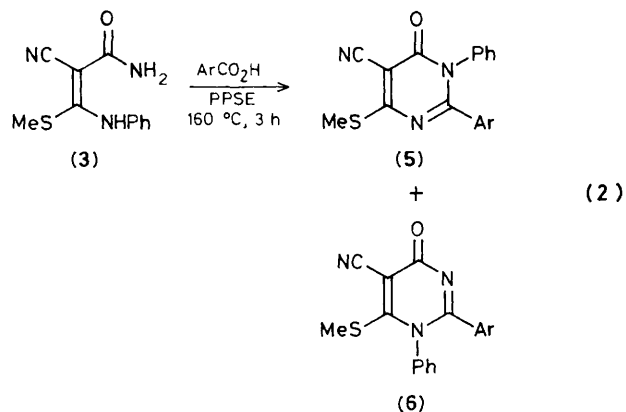


Table 2. The formation of (5) and (6) from (3) [equation (2)].

Ar	Yield/%		M.p./°C	
	(5)	(6)	(5)	(6)
Ph	49	11	236—237	244—245
<i>p</i> -Nitrophenyl	54	24	268—269	213—214

The *N,N* double rearrangement was carried out using the same procedure as described for the *O,N* double rearrangement, equation (2). Table 2 shows the results.

It is noticeable that unrearranged products (6) are isolated as byproducts in the case of the *N,N* double rearrangement. However, (3) reacts with aroyl chloride in the presence of pyridine to form only (6) possibly because it is a charge-controlled reaction.‡

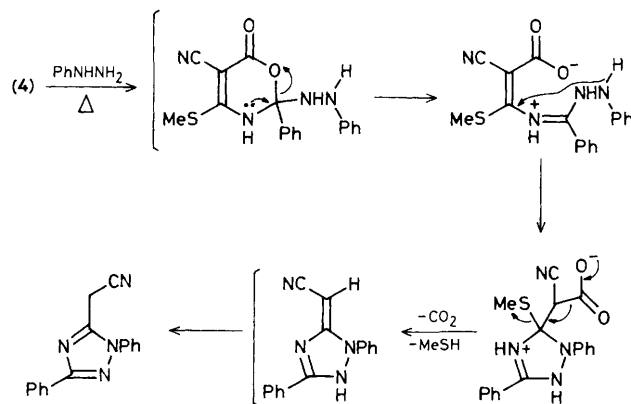
The structure of (4) was confirmed by spectroscopic evidence§ and the formation of 5-cyanomethyl-1,3-diphenyl-1,2,4-triazole³ from the reaction of (4) with phenylhydrazine, as shown in Scheme 1. The following support the structure of (5). (i) Alkali hydrolysis of (5) afforded *N*-phenyl-2-cyano-3-benzoylamino-3-(methylthio)acrylamide¶ and (ii) intramolecular condensation of *N*-benzoyl-2-cyano-3-methylthio-3-(phenylamino)acrylamide†† in the presence of PPSE gave 5-cyano-6-methylthio-1,2-diphenyl-1,3-diazin-4-one (6), a positional isomer of (5).

‡ It can be postulated that an aroyl-like cation generated from an aroyl carboxylic acid using a condensation reagent containing phosphorus attacks the nitrogen atom of the cyano group [a soft nucleophilic site on (2) or (3)] to form the heteroatom double rearranged product (an orbital-controlled reaction).

§ The stretching vibration of the carbonyl group of (4) is at 1740 cm⁻¹ which is characteristic of a lactone.

¶ Yellow powder; m.p. 209—210 °C; *m/z* 251 (*M*⁺).

†† This compound was prepared by benzoylation of (3) in the usual way; yellow powder; m.p. 123—124 °C.

**Scheme 1**

In conclusion, the mechanism of these heteroatom rearrangements are analogous to that of the *S,N* double rearrangement. However, it is not clear at present why the *N,N* double rearrangement is accompanied by a side reaction forming the unrearranged product.

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References

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