

A Novel S,N-Double Rearrangement; X-Ray Crystal Structure of 5-Carbamoyl-4-methylthio-2-phenyl-1,3-thiazin-6-one and Its 2,3-Dihydro-derivative

By MASATAKA YOKOYAMA,*^a MASAKI NAKAMURA,^a TSUNEO IMAMOTO,^a and KEI-ICHI YAMAGUCHI^b
^aDepartment of Chemistry, Faculty of Science, Chiba University, Yayoi-cho, Chiba City, Japan and
^bAnalytical Center of Chiba University, Yayoi-cho, Chiba City, Japan

Summary Condensation of 2-cyano-3-mercapto-3-(methylthio)acrylamide (**1**) with benzoic acid in the presence of polyphosphate ester gave 5-carbamoyl-4-methylthio-2-phenyl-1,3-thiazin-6-one (**5**); the structures of (**5**) and its 2,3-dihydro-derivative (**6**) were determined by single-crystal X-ray diffraction.

POLYPHOSPHATE ESTER (PPE)^{1,2} is a useful reagent for organic synthesis, especially for intramolecular cyclization and condensation reactions to form heterocycles.³ The reagent is different from the commonly used polyphosphoric acid (PPA) in that it is essentially aprotic and freely soluble in organic solvents such as chloroform so that the reaction with PPE can be carried out under mild conditions.

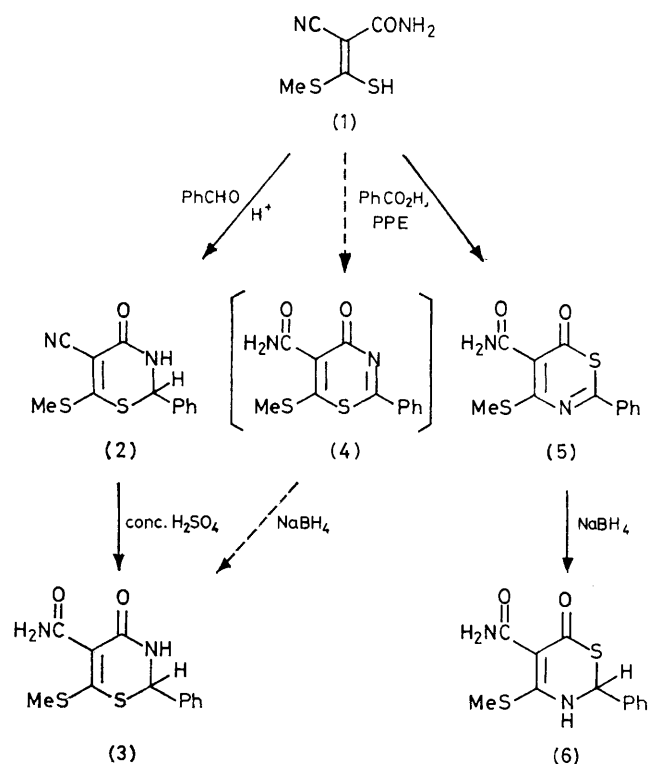
In this communication we report an unusual condensation reaction using PPE which involves a hitherto unknown S,N-double rearrangement.

In our continuing study on the chemistry of thiazines and related compounds,^{4,5} we intended to prepare the thiazinone (**3**) from the acrylamide (**1**) by two synthetic routes, as illustrated in the Scheme.

The first route consisted of the acid-catalysed condensation of (**1**) with benzaldehyde, followed by hydrolysis to give (**3**). The second route involved the reaction of (**1**) with benzoic acid using PPE as the condensation reagent which we expected to produce the 1,3-thiazin-4-one (**4**), which could then be reduced to (**3**).

The first route was accomplished easily; the intermediary dihydrothiazinone (**2**),^{4†} m.p. 225–226 °C (from AcOH–H₂O), was isolated quantitatively and was hydrolysed in concentrated sulphuric acid to yield (**3**),[†] m.p. 205–206 °C (from AcOH–H₂O), in 98% yield.

The second sequence was carried out as follows: a mixture of (**1**) (20 mmol), benzoic acid (20 mmol), PPE (12 g), and chloroform (80 ml) was refluxed for 1 h. The solvent was removed under reduced pressure and the residual red oil was triturated with ethanol to give ca. 5 g of an orange powder. This material was heated in refluxing ethanol for 1 h, followed by chromatography on silica gel using benzene–ethyl acetate as eluant to yield yellow needles,^{5†} m.p. 222–223 °C (from AcOH–H₂O) in 61% yield. This compound was converted, on treatment with NaBH₄ in ethanol, into colourless prisms,[†] m.p. 177–178 °C (from AcOH–H₂O) in 97% yield.



SCHEME

† Compound (**2**) ν_{\max} (KBr) 3290 (NH), 2950 (aliph. CH), 2200 (CN), 1660 (CO), and 1608 (NH) cm⁻¹; δ (CD₃SOCD₃) 9.1 (d, *J* 4 Hz, 1H, NH), 7.45 (s, 5H, Ph), 6.3 (d, *J* 4 Hz, 1H, CH), and 2.65 (s, 3H, SMe); λ_{\max} (95% EtOH) 235 (sh), 280 (ϵ 13,000), and 336 (15,000) nm; (**3**) ν_{\max} (KBr) 3350, 3150 (NH), 3000 (arom. CH), 2850 (aliph. CH), and 1640 (CO) cm⁻¹; δ (CD₃SOCD₃) 8.9 (d, *J* 4 Hz, 1H, NH), 8.2 (br. s, 1H, NH₂), 7.5 (m, 5H, Ph), 7.3 (br. s, 1H, NH₂), 6.1 (d, *J* 4 Hz, 1H, CH), and 2.3 (s, 3H, SMe); λ_{\max} (99% EtOH) 238 (sh), 278 (ϵ 5600), and 332 (7000) nm; *m/e* 280 (*M*⁺) (10%) and 105 (100%); (**5**) ν_{\max} (KBr) 3380, 3160 (NH₂), and 1640 (CO) cm⁻¹; δ (CD₃SOCD₃) 8.1 (m, 2H, Ph), 7.8 (m, 3H, Ph), and 2.7 (s, 3H, SMe); λ_{\max} (99% EtOH) 235 (sh), 227 (ϵ 16,000), and 340 (7500) nm; (**6**) ν_{\max} (KBr) 3380, 3280, 3150 (NH), and 1645 (CO) cm⁻¹; δ (CD₃SOCD₃) 8.8 (d, *J* 5 Hz, 1H, NH), 7.9 (br. s, 1H, NH₂), 7.4 (s, 5H, Ph), 6.9 (br. s, 1H, NH₂), 6.3 (d, *J* 5 Hz, 1H, CH), and 2.4 (s, 3H, SMe); λ_{\max} (99% EtOH) 243 (ϵ 11,000), 270 (sh), and 331 (8400) nm; *m/e* 280 (*M*⁺) (2%) and 173 (100%). Satisfactory elemental analyses were obtained.

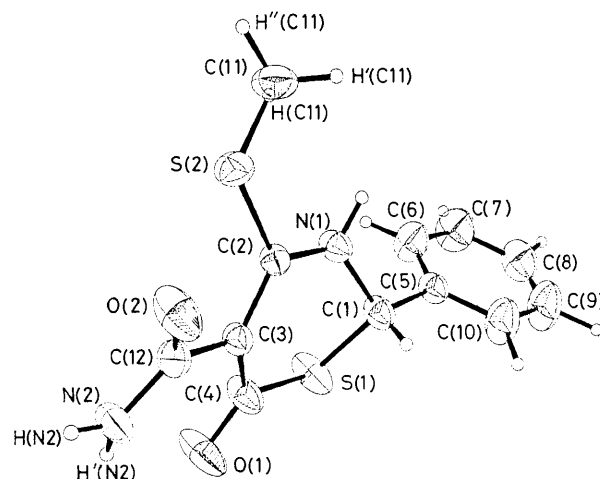


FIGURE 1. ORTEP drawing of (**6**). All non-hydrogen atoms are represented by 50% thermal ellipsoids; hydrogen atoms are represented by arbitrarily small spheres.

This reduced compound (m.p. 177–178 °C) was compared with (3) (m.p. 205–206 °C) prepared by the first route. Both compounds showed similar n.m.r. and u.v. spectra, but their i.r. and mass spectra were different. All the spectroscopic data suggested that the reduced compound had the structure (6) rather than (3). In order to confirm this structure, we carried out a single-crystal *X*-ray diffraction study. Figure 1 shows an ORTEP drawing,[‡] and the results showed unequivocally that the reduced product had the structure (6). It is interesting that the positions of the sulphur and nitrogen atoms in the isomeric heterocycles (3) and (6) are interchanged.

We then investigated the structure of the precursor (m.p. 222–223 °C) of (6). We had believed that its structure was (4) on the basis of spectroscopic data, but the *X*-ray diffraction study on compound (6) suggested the possibility of an alternative structure (5). A single-crystal *X*-ray diffraction study (Figure 2) confirmed that structure (5) was correct.[‡]

These results indicate that an S,N-double rearrangement

[‡] *Crystal data*: large, well shaped orthorhombic crystals of (6) were obtained by slow evaporation of an acetone–methanol solution; C₁₂H₁₂N₂O₂S₂: space group *Pbcn* (*D*_{2h}¹⁴, No. 60); *a* = 13.218(3), *b* = 9.562(3), *c* = 20.220(10) Å; *Z* = 8. Lattice constants and intensity data for (6) were measured using graphite-monochromated Mo-*K*_α radiation on a Rigaku AFC-5 diffractometer. A total of 2598 unique reflections with *F*₀ > 2σ(*F*₀) were obtained using the ω–2θ scanning method with a 2θ scan speed of 2°/min to 2θ = 60°. The structure was solved by the RASA-II system (Rigaku Corp.) based on the direct method, and refined to a final *R* value of 0.062. Monoclinic single crystals of (5) were obtained by slow evaporation of a CHCl₃–EtOH solution; C₁₂H₁₀N₂O₂S₂: space group *P*2₁/*c* (*C*_{2h}⁵); *a* = 7.6920(4), *b* = 5.1635(4), *c* = 31.4901(15) Å, β = 105.515(7)°; *Z* = 4. A total of 2060 unique reflections with *F*₀ > 2σ(*F*₀) were collected and the structure was solved and refined as for compound (6) to a final *R* value of 0.0672. The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Rd., Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

¹ W. Pollmann and G. Schramm, *Biochim. Biophys. Acta*, 1964, **80**, 1.

² M. P. Cava, M. V. Lakshmikantham, and M. J. Mitchell, *J. Org. Chem.*, 1969, **34**, 2655.

³ L. F. Fieser and M. Fieser, 'Reagents for Organic Synthesis,' I, P. 892; II, P. 333; III, P. 229; IV, P. 394; V, P. 539; VI, P. 474 and references cited therein.

⁴ M. Yokoyama, *Bull. Chem. Soc. Jpn.*, 1971, **44**, 1610.

⁵ M. Yokoyama, Y. Sawachi, and T. Issu, *J. Org. Chem.*, 1973, **38**, 802.

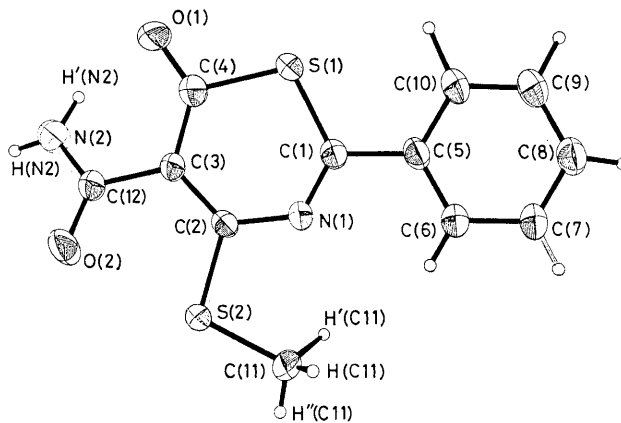


FIGURE 2. ORTEP drawing of (5).

took place in the condensation step of (1) with benzoic acid in the presence of PPE.

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