Heteroatom Rearrangements. Extension to Aliphatic Carboxylic Acids

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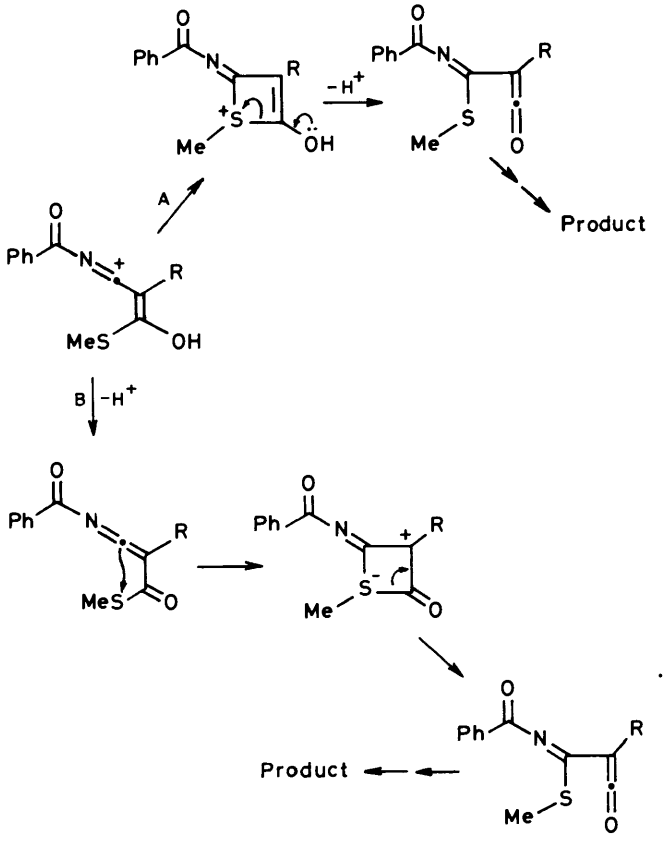
2-Cyano-3-mercapto-3-(methylthio)acrylamide condenses with aliphatic carboxylic acids in the presence of polyphosphoric acid trimethylsilyl ester to give the corresponding 1,3-thiazin-4-ones (S,N double unrearranged products); under the same conditions, 3-anilino-2-cyano-3-(methylthio)acrylamide gives 3-phenylpyrimidin-4-ones (N,N double rearranged products) together with 1-phenylpyrimidin-4-ones (N,N double unrearranged products). In the case of 2-cyano-3-hydroxy-3-(methylthio)acrylamide, O,N double rearranged cyclic and chain compounds are produced. Furthermore, such rearrangements are observed in the reaction with carboxylic acid anhydrides in the presence of toluene-*p*-sulphonic acid.

Heteroatom rearrangements such as S,N,O,N and N,N double rearrangements[1] have been observed when acrylonitriles substituted with two β-heteroatom groups (MeS or MeSe) and (SH, OH, or NHPh) are condensed with aromatic carboxylic acids in the presence of dehydrating agents bearing a phosphorus atom, such as polyphosphate ester (PPE),[2] polyphosphoric trimethylsilyl ester (PPSE),[3] phosphorus trichloride oxide, and propane-1-phosphoric acid cyclic anhydride (PPCA).[4]

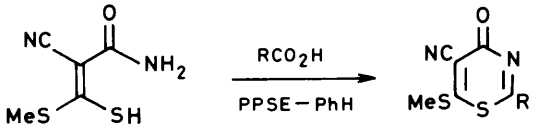
The mechanism of this rearrangement has been elucidated by ^{13}C labelling and crossover reactions,[4] and can be considered to proceed through path A or path B (Scheme 1).

The presence of a methylthiacyclobutenium compound proposed in path A has been reported in the recent literature,[6] and a similar mechanism has been used to explain the abnormal Beckmann rearrangement of α-(methylthio)isobutyrophenone *anti*-oxime toluene-*p*-sulphonate.[7] The path B shows a [1,3]thia-allylic rearrangement which has been investigated mainly by Kwart *et al.*[8]



Scheme 1.

Table 1. Preparation of compounds (2)



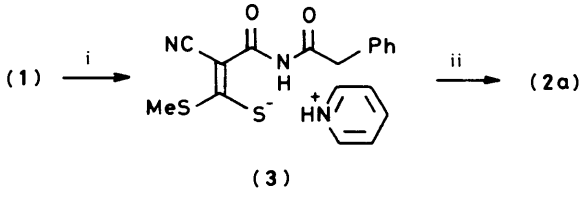
Product	R	Yield (%)
(2a)	$PhCH_2$	52
(2b)	Et	50
(2c)	Cyclohexyl	52

As an extension of the present reaction we employed aliphatic carboxylic acids in place of aromatic ones under the same conditions, and found several interesting results, including the fact that carboxylic acid anhydrides could acylate the cyano group of acrylonitrile derivatives in the presence of toluene-*p*-sulphonic acid (PTSA).

Results and Discussion

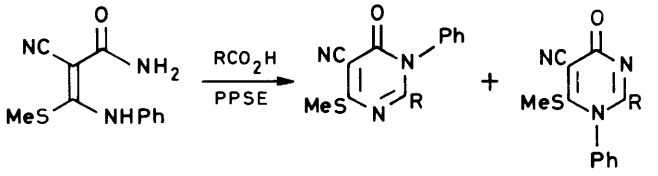
S,N *Double Rearrangement.*—A mixture of aliphatic carboxylic acids and 2-cyano-3-mercapto-3-(methylthio)acrylamide (1) was refluxed with PPSE–benzene solution for 10—20 min to give the corresponding cyclized products in moderate yields. Interestingly, they were unrearranged compounds (2), 2-substituted 5-cyano-6-methylthio-1,3-thiazin-4-ones. The results are summarized in Table 1.

The structure of the products of (2) can be supported by the presence of the following fragment ions in the mass spectra; *m/z* 43 $(CONH)^+$ and 91 $(CH_3SCS)^+$. Furthermore, 2-benzyl-5-cyano-6-methylthio-1,3-thiazin-4-one (2a) was



Reagents: i, $PhCH_2COCl$, pyridine; ii, PPSE

Table 2. Preparation of compounds (6) and (7)

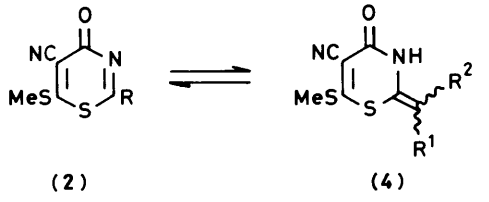


(5) (6) (7)

Products	R	Yield (%) (6)	(7)	Total
(6a), (7a)	Me	12	26	38
(6b), (7b)	Et	46	12	58
(6c), (7c)	$PhCH_2$	42	4	46
(6d), (7d)	Cyclohexyl	21	10	31

prepared from the pyridinium salt of 2-cyano-3-mercapto-3-methylthio-*N*-(phenylacetyl)acrylamide (**3**), on treatment with PPSE. These results support the assignment of unrearranged structure (**2**) for the products.

The n.m.r. data of (**2**) show that they exist as a mixture of tautomer (**2**) and *E,Z*-isomers of the exocyclic methylene tautomers (**4**).

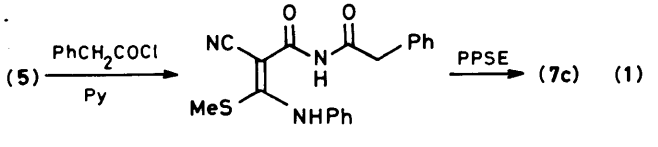


(2) (4)

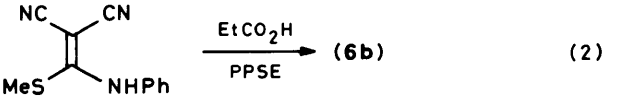
The hard and soft acids and bases (HSAB) rule[9] can explain why the aliphatic carboxylic acids do not undergo the S,N double rearrangement. That is, an acyl cation which is 'harder' than benzoyl attacks exclusively on the 'hard' nucleophilic site of (**1**), resulting in the formation of products (**2**).

N,N *Double Rearrangement.*—This reaction was carried out under the same conditions as described in the case of aromatic carboxylic acids.[1] Table 2 shows the results obtained from the reaction of 3-anilino-2-cyano-3-(methylthio)acrylamide (**5**) with some aliphatic carboxylic acids.

In this reaction the product was found to be a mixture of rearranged compound (**6**), a 2-substituted 5-cyano-6-methylthio-3-phenylpyrimidin-4(3*H*)-one, and unrearranged compound (**7**), the corresponding 2-substituted 5-cyano-6-methylthio-1-phenylpyrimidin-4(1*H*)-one. This result is the same as that obtained in the case of aromatic carboxylic acids.[1]



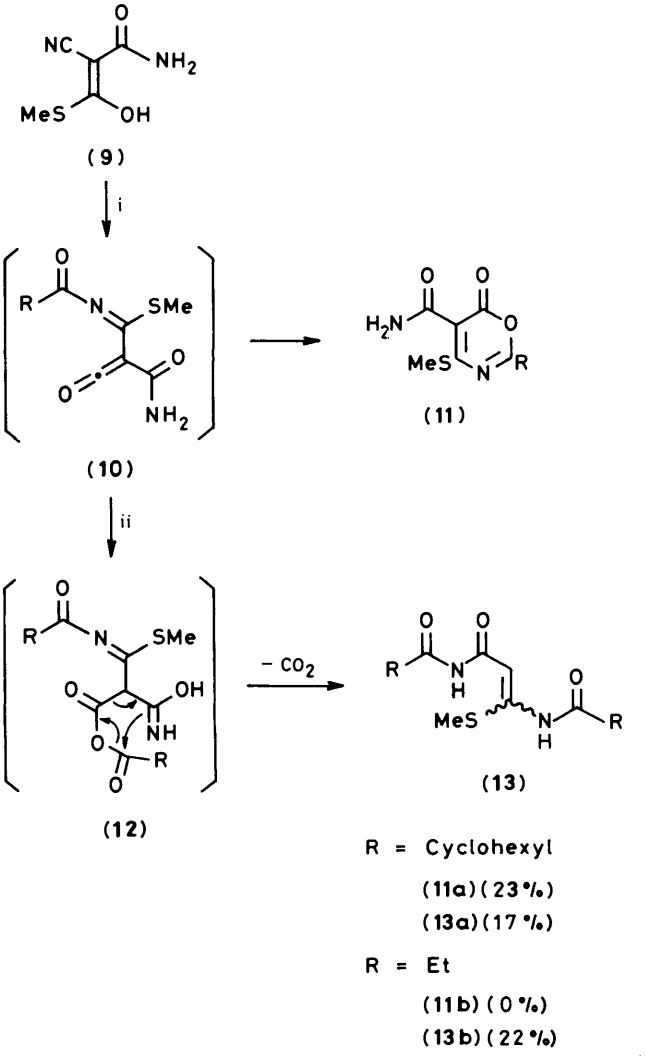
(8) (1)



(2)

The structure of products (**7**) was determined by the facts that (i) compound (**8**), which was obtained by the acylation of compound (**5**), cyclized the product (**7c**) in the presence of PPSE [equation (1)], and (ii) compound (**6b**) was also obtained from the reaction of 3-anilino-2-cyano-3-(methylthio)acrylonitrile with propionic acid in the presence of PPSE [equation (2)].

O,N *Double Rearrangement.*—When 2-cyano-3-hydroxy-3-(methylthio)acrylamide (**9**) was treated with cyclohexanecarboxylic acid in the presence of PPSE–chloroform solution, a rearranged compound, 2-cyclohexyl-4-methylthio-6-oxo-1,3-oxazine-5-carboxamide (**11a**), was obtained together with an unexpected compound, 3-cyclohexanecarboxamido-*N*-cyclohexylcarbonyl)-3-(methylthio)acrylamide (**13a**). In the case of propionic acid, only 3-methylthio-3-propionamido-*N*-propionylacrylamide (**13b**) was isolated, and the oxazinecarboxamide (**11b**) was not observed. The formation of products (**13**) is believed to occur as shown in Scheme 2; an intermediate (**10**) is produced by the acylation of the cyano group, and then (**10**) adds to a second molecule of carboxylic acid to give the anhydride (**12**), which then decarboxylates to give product (**13**).



R = Cyclohexyl
(11a) (23%)
(13a) (17%)
R = Et
(11b) (0%)
(13b) (22%)

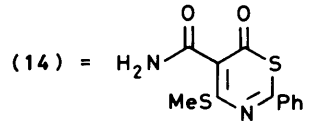
Scheme 2. *Reagents:* i, RCO_2H, PPSE; ii, RCO_2H

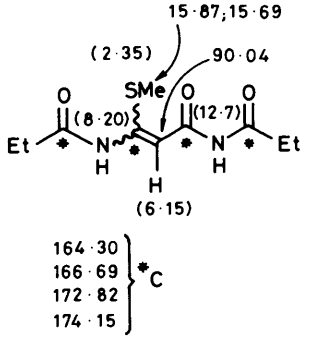
The structure of products (**13**) was determined tentatively on the basis of elemental analysis and spectral evidence: the mass spectrum shows a characteristic fragment ion $(M - RCONH)^+$ and $(M - RCO)^+$; ^1H and ^{13}C n.m.r. data support the

Table 3. Products obtained from compounds (**1**), (**5**), and (**9**), with yields in parentheses

Starting material	Carboxylic acid anhydrides	
	$(PhCO)_2O$	$(RCO)_2O$
(**1**)	(**14**)[a] (8%)	(**2b**) (32%) (**2c**) (28%)
(**5**)	(**7e**) (R = Ph) (13%)	(**7a**) (66%) (**7b**) (80%) (**7d**) (14%)
(**9**)	(**11c**) (R = Ph) (81%)	(**13a**) (21%) (**13b**) (30%) (**13c** (R = Me) (21%)

(**14**) =





The chemical shifts from the ^1H n.m.r. spectrum are shown in parentheses

structure (**13**). Furthermore, the ^{13}C n.m.r. data for compound (**13b**) show that it exists as a mixture of 2*E* and 2*Z* isomers.

*Heteroatom Rearrangement using a Carboxylic Acid Anhydride and Toluene-*p*-sulphonic Acid.*—We found that compounds (**1**), (**5**), and (**9**) reacted with carboxylic acid anhydrides in the presence of PTSA to give the corresponding rearranged or unrearranged products (Table 3).

This reaction may occur according to the following process: A mixed acid anhydride generated from reaction of an acid anhydride with PTSA attacks the nitrogen atom of the cyano group. Then, a 1,3-transfer of the methylthio group takes place to afford rearranged products (**11c**), (**13**), and (**14**). When the amide (**5**) was used as a starting compound, unrearranged products (**7a**—**e**) were the only products isolated, perhaps because an immonium intermediate generated in the acidic medium inhibited the acylation of the cyano group. In the reaction of compound (**1**) with an aliphatic carboxylic acid anhydride, an acyl cation which is 'harder' than aroyl attacks exclusively at the amide group to give unrearranged compounds (**2b** and **c**).

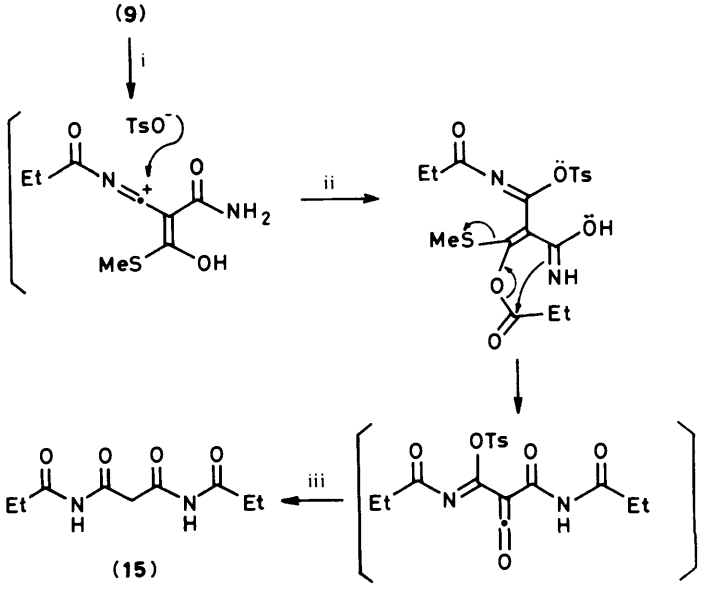
Furthermore, when compound (**9**) reacted with propionic anhydride in the presence of PTSA it gave *N*,*N*′-bis(propionyl)-malonamide (**15**) in 13% yield, in addition to compound (**13b**). Compound (**15**) is believed to be formed as shown in Scheme 3.

The structure of compound (**15**) was determined by comparison with the i.r. spectrum of an authentic specimen which described the preparation of *N*,*N*′-diacetylmalonamide.[10]

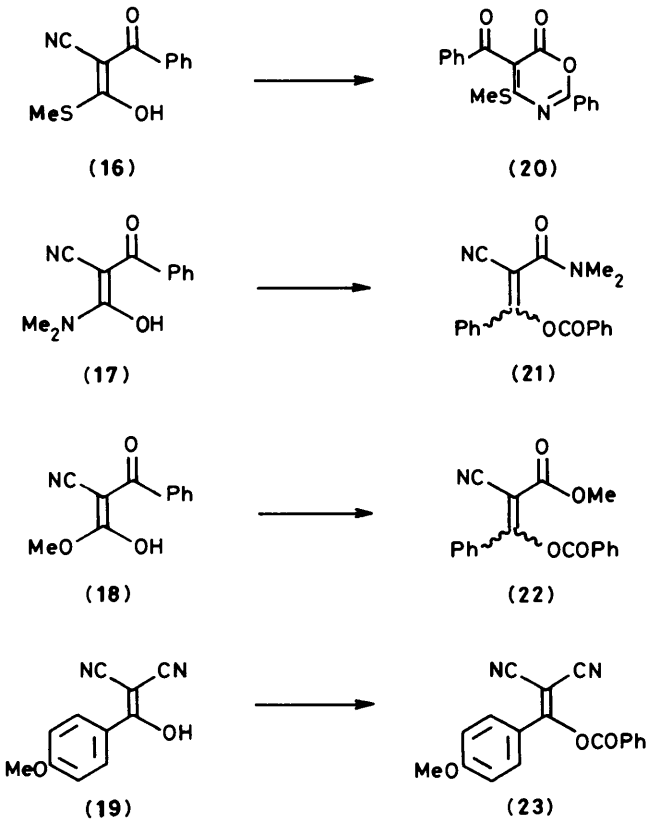
Limitation of this Reaction.—Judging from the reaction mechanism this reaction is ultimately a 1,3-rearrangement of the methylthio group. In order to probe whether dimethylamino, methoxy, and phenyl groups undergo such rearrangement under the same conditions as described above, 2-benzoyl-3-hydroxy-3-(methylthio)acrylonitrile (**16**), 2-benzoyl-3-dimethylamino-3-hydroxyacrylonitrile (**17**), 2-benzoyl-3-hydroxy-3-methoxyacrylonitrile (**18**), and α-cyano-β-hydroxy-*p*-methoxycinnamonitrile (**19**) were prepared and allowed to react with benzoic acid. The results are shown in Scheme 4.

Compound (**16**) was converted into the rearranged product (**20**), 5-benzoyl-4-methylthio-2-phenyl-1,3-oxazin-6-one, while the products from compounds (**17**)—(**19**) were the corresponding *O*-acylated compounds (**21**)—(**23**) respectively instead of the expected rearranged products.

These results show that heteroatoms of second-period elements do not undergo this rearrangement. Thus, the



Scheme 3. *Reagents:* i, $(EtCO)_2O$, PTSA; ii, $EtCO_2H$; iii, water ($-CO_2$)



Scheme 4. *Reagents:* $PhCO_2H$, PPSE

rearrangement seems to require large *p*-orbitals (3*p* or 4*p*) or *d*-orbitals.

Experimental

Microanalyses were performed with a Perkin-Elmer 240 elemental analyser at the Analytical Center of Chiba University. I.r. spectra were recorded on a Hitachi 215 spectrometer. ^1H N.m.r. spectra were determined with Japan Electron Optics Lab. (JEOL) JNM-FX-270, MH-100, and C-60HL instruments. ^{13}C N.m.r. spectra were recorded with a JEOL JNM-FX-270 machine. Chemical shifts are given relative to $SiMe_4$ as internal standard. Mass spectra were measured on a Hitachi M-60 spectrometer at an ionizing energy at 70 eV.

Silica gel used in column chromatography was Wakogel C-200, and silica gel used for t.l.c. was Wakogel B-5F. Special grade phosphorus pentaoxide was purchased from Wako Pure Chemical Industries, Ltd. Benzene and chloroform were purified by standard procedures and tetrahydrofuran (THF) was distilled from sodium diphenylketyl. Compound (**1**) was prepared by our method.[5]

Preparation of 2-*Benzyl*-5-*cyano*-6-*methylthio*-1,3-*thiazin*-4-*one* (**2a**).—A mixture of phosphorus pentaoxide (1 g, 3.5 mmol), hexamethyldisiloxane (HMDSO) (2 ml, 10 mmol), and dry benzene (10 ml) was heated at reflux for 0.5 h under argon. To the PPSE–benzene solution thus obtained were added successively the amide (**1**) (0.5 g, 2.9 mmol) and phenylacetic acid (0.4 g, 2.9 mmol). The resultant mixture was refluxed for 10—20 min. The orange crystals produced were collected and recrystallized from ethanol to give the *title compound* (**2a**) as orange needles (0.4 g, 52%), m.p. 177—178 °C (Found: C, 56.7; H, 3.75; N, 10.1. $C_{13}H_{10}N_2OS_2$ requires C, 56.91; H, 3.67; N, 10.21%); $\nu_{max.}$(KBr) 3 120w, 3 010s, 2 860s, 2 200s, and 1 660 cm^{-1}; δ_H (60 MHz; [$^2H_5$]pyridine) 7—8 (br, $\frac{12}{13}$ H, NH), 7.4 (m, 5 H, Ph), 6.56 (s, $\frac{9}{13}$ H, CH), 6.05 (s, $\frac{3}{13}$ H, CH), 4.24 (s, $\frac{1}{13}$ H, 2-CH_2), 2.72 (s, $\frac{3}{13}$ H × 3, SMe), and 2.48 (s, $\frac{9}{13}$ H × 3, SMe); n.m.r. data show that the product consists of compound (**2a**), plus the *E* isomer of (**4a**)* and the *Z* isomer of (**4a**) in the ratio 1:3:9; *m/z* 274 (M^+), 91 (CH_3SCS^+), and 43 ($CONH^+$).

Compounds (**2b**) and (**2c**) were prepared from the corresponding acids by the same method as described above. Their n.m.r. measurements did not give satisfactory results because of decomposition in the n.m.r. solvent.

5-*Cyano*-2-*ethyl*-6-*methylthio*-1,3-*thiazin*-4-*one* (**2b**): orange needles (from AcOH), m.p. 158—161 °C (Found: C, 45.3; H, 3.8; N, 13.25. $C_8H_8N_2OS_2$ requires C, 45.26; H, 3.80; N, 13.20%); $\nu_{max.}$(KBr) 3 380w, 3 140w, 2 900w, 2 200s, 1 650vs, and 1 570s cm^{-1}.

5-*Cyano*-2-*cyclohexyl*-6-*methylthio*-1,3-*thiazin*-4-*one* (**2c**): orange needles (from AcOH), m.p. 163—165 °C (Found: C, 54.2; H, 5.35; N, 10.6. $C_{12}H_{14}N_2OS_2$ requires C, 54.10; H, 5.30; N, 10.52%); $\nu_{max.}$(KBr) 3 110s, 3 010s, 2 900s, 2 800s, and 2 200s cm^{-1}; *m/z* 266 (M^+), 91 (CH_3SCS^+), and 43 ($CONH^+$).

Preparation of Pyridinium Salt of 2-*Cyano*-3-*mercapto*-3-*methylthio*-N-(*phenylacetyl*)*acrylamide*, (**3**), *and its Sodium Analogue*.—To a mixture of compound (**1**) (1 g, 5.8 mmol), pyridine (1 ml), and chloroform (7 ml) was added phenylacetyl chloride (1 ml, 7.6 mmol). The resulting mixture was stirred overnight. The white crystals of the salt (**3**) (0.78 g, 37%) were collected, washed with ethanol, and then stirred with saturated aqueous $NaHCO_3$ solution for several hours to afford the corresponding sodium salt as white crystals in quantitative yield. Recrystallization from ethanol gave white needles, m.p. 165—167 °C (Found: C, 49.7; H, 3.6; N, 8.7. $C_{13}H_{11}N_2NaO_2S_2$ requires C, 49.67; H, 3.84; N, 8.91%); $\nu_{max.}$(KBr) 3 550s, 3 070w, 2 880s, 2 200vs, 1 700vs, and 1 620vs cm^{-1}; δ_H [60 MHz; $(CD_3)_2SO$] 13.5 (br, 1 H, OH), 7.3 (s, 5 H, Ph), 3.4 (s, 2 H, CH_2), and 2.5 (s, 3 H, SMe).

Compound (**2a**) was also obtained from the salt (**3**) in the usual way by using PPSE, in 80% yield.

Preparation of 5-*Cyano*-2-*methyl*-6-*methylthio*-3-*phenylpyrimidin*-4(3H)-*one* (**6a**).—To PPSE prepared from the reaction of phosphorus pentaoxide (2.5 g, 8.8 mmol), dry chloroform (4 ml), and HMDSO (8 ml, 40 mmol) were added compound (**5**)[1] (466 mg, 2 mmol) and acetic acid (120 mg, 2 mmol). The mixture was stirred and heated at 120 °C for 3 h and was then quenched with water, and extracted with chloroform. The extract was rotary evaporated to give a yellow oil, which was triturated with ethyl acetate to afford white crystals of the *title compound* (**6a**) (134 mg, 26%). The above ethyl acetate filtrate was purified in the usual way by t.l.c. with acetic acid–benzene (1:4) as eluant to give white crystals of the 1H-*isomer* (**7a**) (60 mg, 12%).

Compound (**6a**): white needles (from EtOH), m.p. 216—217 °C (Found: C, 60.4; H, 4.65; N, 16.2. $C_{13}H_{11}N_3OS$ requires C, 60.45; H, 4.68; N, 16.27%); $\nu_{max.}$(KBr) 3 020s, 2 950w, 2 200s, 1 640vs, 1 600vs, and 1 580vs cm^{-1}; δ_H (100 MHz; $CDCl_3$) 7.6 (m, 3 H, Ph), 7.4 (m, 2 H, Ph), 2.8 (s, 3 H, SMe), and 2.2 (s, 3 H, Me); *m/z* 257 (M^+).

5-*Cyano*-2-*methyl*-6-*methylthio*-1-*phenylpyrimidin*-4(1H)-*one* (**7a**): white needles (from EtOH), m.p. 192—193 °C (Found: C, 60.4; H, 4.4; N, 16.2%); $\nu_{max.}$(KBr) 3 030m, 2 980w, 2 200s, 1 680vs, and 1 535vs cm^{-1}; δ_H (100 MHz; $CDCl_3$) 7.5 (m, 3 H, Ph), 7.2 (m, 2 H, Ph), 2.6 (s, 3 H, SMe), and 2.2 (s, 3 H, Me); *m/z* 257 (M^+).

Compounds (**6b**) and (**7b—d**) were obtained in a similar fashion to that mentioned above.

* (**4a**) = (**4**; R^1,R^2 = H, Ph).

5-Cyano-2-ethyl-6-methylthio-3-phenylpyrimidin-4(3H)-one (**6b**): white needles (from EtOH), m.p. 230—232 °C (Found: C, 61.9; H, 4.75; N, 15.5. $C_{14}H_{13}N_3OS$ requires C, 61.97; H, 4.83; N, 15.49%); $\nu_{max.}$(KBr) 3 020s, 2 960s, 2 900s, 2 200s, 1 640vs, 1 600vs, and 1 580vs cm^{-1}; δ_H [100 MHz; $(CD_3)_2SO$] 7.65 (s, 5 H, Ph), 2.7 (s, 3 H, SMe), 2.3 (q, 2 H, *J* 7 Hz, CH_2), and 1.1 (t, 3 H, *J* 7 Hz, Me); *m/z* 271 (M^+).

Reaction of 3-Anilino-2-cyano-3-(methylthio)acrylonitrile with Propionic Acid.—A mixture of PPSE [prepared by the same method as mentioned in the preparation of compound (**6a**)], 3-anilino-2-cyano-3-(methylthio)acrylonitrile (430 mg, 2 mmol), and propionic acid (148 mg, 2 mmol) was stirred and heated at 120 °C for 3 h and was then quenched with water. Standard work-up afforded compound (**6b**) (481 mg, 88%).

5-Cyano-2-ethyl-6-methylthio-1-phenylpyrimidin-4(1H)-one (**7b**): brown needles (from EtOH), m.p. 207—208 °C (Found: C, 62.0; H, 4.9; N, 15.55%); $\nu_{max.}$(KBr) 3 040m, 2 970s, 2 920m, 2 220s, 1 690vs, and 1 540vs cm^{-1}; δ_H (100 MHz; $CDCl_3$) 7.3 (m, 3 H, Ph), 7.0 (m, 2 H, Ph), 2.6 (s, 3 H, SMe), 2.4 (q, 2 H, *J* 7 Hz, CH_2), and 1.2 (t, 3 H, *J* 7 Hz, Me); *m/z* 271 (M^+).

2-Benzyl-5-cyano-6-methylthio-3-phenylpyrimidin-4(3H)-one (**6c**): white needles (from EtOH), m.p. 197—198 °C (Found: C, 68.55; H, 4.55; N, 12.7. $C_{19}H_{15}N_3OS$ requires C, 68.45; H, 4.53; N, 12.60%); $\nu_{max.}$(KBr) 3 020w, 2 900w, 2 220s, 1 640vs, 1 600vs, and 1 580vs cm^{-1}; δ_H [100 MHz; $(CD_3)_2SO$] 7.5 (s, 5 H, Ph), *ca.* 7.0 (m, 5 H, Ph), 3.7 (s, 2 H, CH_2), and 2.6 (s, 3 H, SMe); *m/z* 333 (M^+).

2-Benzyl-5-cyano-6-methylthio-1-phenylpyrimidin-4(1H)-one (**7c**): white needles (from EtOH), m.p. 207—209 °C (Found: C, 68.3; H, 4.65; N, 12.5%); $\nu_{max.}$(KBr) 3 042m, 3 010m, 2 890w, 2 200s, 1 690vs, and 1 535 vs cm^{-1}; δ_H (100 MHz; $CDCl_3$) 7.4 (m, 3 H, Ph), 7.2 (m, 2 H, Ph), 6.9 (m, 5 H, Ph), 3.8 (s, 2 H, CH_2), and 2.6 (s, 3 H, SMe); *m/z* 333 (M^+).

5-Cyano-2-cyclohexyl-6-methylthio-3-phenylpyrimidin-4(3H)-one (**6d**): white needles (from EtOH), m.p. 156—158 °C (Found: C, 66.5; H, 5.9; N, 13.0. $C_{18}H_{19}N_3OS$ requires C, 66.46; H, 5.84; N, 12.92%); $\nu_{max.}$(KBr) 3 040w, 2 900s, 2 820m, 2 200m, 1 660vs, 1 600vs, and 1 585vs cm^{-1}; δ_H [100 MHz; $(CD_3)_2SO$] 7.6 (s, 5 H, Ph), 3.3 (s, 1 H, CH), 2.7 (s, 3 H, Me), and *ca.* 1.5 (br, 10 H, cyclohexyl H); *m/z* 325 (M^+).

5-Cyano-2-cyclohexyl-6-methylthio-1-phenylpyrimidin-4(1H)-one (**7d**): brown needles (from EtOH), m.p. 255—256 °C (Found: C, 66.6; H, 5.5; N, 12.9%); $\nu_{max.}$(KBr) 3 040w, 2 930, 2 900, 2 840s, 2 200s, 1 675vs, and 1 530vs cm^{-1}; δ_H (100 MHz; $CDCl_3$) 7.4 (m, 3 H, Ph), 7.1 (m, 2 H, Ph), 2.6 (s, 3 H, SMe), and 1.0—1.9 (m, 11 H, cyclohexyl H); *m/z* 325 (M^+).

Preparation of 3-Anilino-2-cyano-3-methylthio-N-(phenylacetyl)acrylamide (**8**).—To a mixture of primary amide (**5**) (0.6 g, 2.6 mmol), pyridine (1 ml), and chloroform (20 ml) was added phenylacetyl chloride (1 ml, 7.6 mmol). The mixture was refluxed for 4 h and then evaporated under reduced pressure to give a red oil. The oil was added to water and the mixture was extracted with ethyl acetate. The extract was evaporated to give white crystals of the title compound (**8**) (0.78 g, 85%); $\nu_{max.}$(KBr) 3 350w, 3 200m, 3 140m, 3 050w, 2 900w, 2 200s, and 1 710vs cm^{-1}; δ_H [100 MHz; $(CD_3)_2SO$] 11.4 (br, 0.5 H, NHCO), 10.6 (br, 0.5 H, NHCO), 7.5 (m, 10 H, 2 × Ph), 5.6 (br, 1 H, N*H*Ph), 3.9 (d, 2 H, *J* 6 Hz, CH_2), and 2.45 (s, 3 H, SMe); *m/z* 351 (M^+).

Conversion of Secondary Amide (**8**) *into Pyrimidinone* (**7c**).—Compound (**8**) (0.5 g, 1.4 mmol) was added to a PPSE–benzene solution which was prepared from phosphorus pentaoxide (1 g), HMDSO (2 ml), and dry benzene (5 ml) in the same way as described for the preparation of compound (**2a**). The mixture was refluxed for 3 h and then quenched with water. The crystals obtained were worked up in the usual way to give compound (**7c**) (0.28 g, 60%).

Preparation of 2-Cyclohexyl-4-methylthio-6-oxo-6H-1,3-oxazine-5-carboxamide (**11a**) *and 3-Cyclohexanecarboxamido-N-cyclohexylcarbonyl-3-(methylthio)acrylamide* (**13a**).—To a PPSE–chloroform solution prepared from the reaction of phosphorus pentaoxide (1 g, 3.5 mmol), HMDSO (4 ml, 20 mmol), and dry chloroform were added the amide (**9**) [1] (158 mg, 1 mmol) and cyclohexanecarboxylic acid (128 mg, 1 mmol). The mixture was stirred under reflux for 3 h, quenched with water, and extracted with ethyl acetate. The extract was rotary evaporated to give a yellow oil, which was purified in the usual way by t.l.c. (eluant: ethyl acetate–hexane 2:1); the *oxazinone* (**11a**) was obtained from the lower part of the t.l.c. plate, and the *imide* (**13a**) from the upper part.

Compound (**11a**): white needles (from $CHCl_3$), m.p. 198—199 °C (Found: C, 53.5; H, 6.2; N, 10.3. $C_{12}H_{16}N_2O_3S$ requires C, 53.71; H, 6.01; N, 10.44%); $\nu_{max.}$(KBr) 3 350s, 3 130s, 2 920s, 2 840m, 1 720vs, and 1 660vs cm^{-1}; δ_H (100 MHz; $CDCl_3$) 8.1 and 7.7 (br, 2 H, NH_2), 2.4 (s, 3 H, SMe), and 2.1—1.2 (m, 11 H, cyclohexyl H); *m/z* 268 (M^+).

Compound (**13a**): white needles (from benzene), m.p. 204—205 °C (Found: C, 61.3; H, 8.0; N, 8.0. $C_{18}H_{28}N_2O_3S$ requires C, 61.33; H, 8.01; N, 7.95%); $\nu_{max.}$(KBr) 3 220, 3100m, 2 900, 2 830, 1 700vs, and 1 680vs cm^{-1}; δ_H (100 MHz; $CDCl_3$) 12.5 (br, 1 H, CONHCO), 8.0 (br, 1 H, NH), 6.3 (s, 1 H, 2-H), 2.3 (s, 3 H, SMe), and 1.3—2.0 (m, 22 H, 2 × cyclohexyl H); *m/z* 352 (M^+).

3-Methylthio-3-propionamido-*N*-propionylacrylamide (**13b**) was prepared using the same procedure as that described for compounds (**11a**) and (**13a**).

Compound (**13b**): white needles (from benzene), m.p. 199—200 °C (Found: C, 49.5; H, 6.6; N, 11.6. $C_{10}H_{16}N_2O_3S$ requires C, 49.16; H, 6.60; N, 11.47%); $\nu_{max.}$(KBr) 3 240, 3 150, 3 080s, 2 975, 2 925, 2 900s, and 1 720vs cm^{-1}; δ_H (100 MHz; $CDCl_3$) 12.7 (br, 1 H, CONHCO), 8.2 (br, 1 H, NH), 6.1 (s, 1 H, 2-H), 2.5 (m, 4 H, 2 × CH_2), 2.3 (s, 3 H, SMe), and 1.2 (m, 6 H, 2 × Me); *m/z* 244 (M^+).

Preparation of 4-Methylthio-6-oxo-2-phenyl-6H-1,3-thiazine-5-carboxamide (**14**).—A mixture of compound (**1**) (174 mg, 1 mmol), PTSA monohydrate (190 mg, 1 mmol), and benzoic acid anhydride (2.26 g, 10 mmol) was stirred and heated at 45—55 °C for 7 min. To the cooled mixture was added an excess of ethanol to give white crystals of the title product (**14**) (22 mg, 8%).

Compounds (**11c**), (**2b**), (**2c**), (**7a**), (**7b**), (**7d**), (**13a**—**c**), and (**15**) were prepared in the same way as described above. In the case of compound (**7e**) the reaction was carried in toluene.

Compound (**11c**): yellow needles (from EtOH–AcOH), m.p. 257—258 °C (Found: C, 54.95; H, 4.0; N, 10.6. $C_{12}H_{10}N_2O_3S$ requires C, 54.95; H, 3.84; N, 10.68%); $\nu_{max.}$(KBr) 3 360, 3 140s, 2 980, 2 900w, 1 720vs, and 1 670s cm^{-1}; δ_H (100 MHz; $CDCl_3$) 8.35 (br, 1 H, NH), 8.3 (m, 2 H, Ph), 7.6 (m, 3 H, Ph), 5.6 (br, 1 H, NH), and 2.6 (s, 3 H, SMe); *m/z* 262 (M^+).

Compound (**13c**): pale yellow needles (from benzene), m.p. 165—167 °C (Found: C, 44.4; H, 5.6; N, 12.9. $C_8H_{12}N_2O_3S$ requires C, 44.43; H, 5.59; N, 12.95%); $\nu_{max.}$(KBr) 3 250, 3 150s, 2 940, 2 920m, and 1 740vs cm^{-1}; δ_H [100 MHz; $CDCl_3$–$(CD_3)_2SO$] 12.5 (br, 1 H, CONHCO), 10.0 (br, 1 H, NH), 5.7 (s, 1 H, 2-H), 2.25 (m, 6 H, 2 × Me), and 2.15 (m, 3 H, SMe); *m/z* 216 (M^+).

Compound (**15**): white plates (from EtOH), m.p. 164—165 °C (Found: C, 50.3; H, 6.5; N, 12.9. Calc. for $C_9H_{14}N_2O_4$: C, 50.46; H, 6.59; N, 13.08%); $\nu_{max.}$(KBr) 3 250, 3 140s, 3 010, 2 970, 2 940m, 1 740, 1 720vs, and 1 690vs cm^{-1}; δ_H (100 MHz; $CDCl_3$) 8.4 (br, 2 H, 2 NH), 4.1 (s, 2 H, CH_2), 2.55 (q, 4 H, *J* 7 Hz,

2 × CH_2Me), and 1.2 (t, 6 H, *J* 7 Hz, 2 × CH_2Me); *m/z* 215 $(M + 1)^+$.

Preparation of 2-benzoyl-3-hydroxy-3-(methylthio)acrylonitrile (**16**).—To an ice-cooled mixture of sodium hydride (400 mg, 10 mmol) and THF (30 ml) was added dropwise a mixture of *S*-methyl 2-(cyano)thioacetate (295 mg, 2.6 mmol), benzoyl chloride (0.35 ml, 3 mmol), and THF (30 ml). The resultant mixture was stirred at room temperature for 1.5 h and then quenched with water. The reaction mixture was washed with ethyl acetate, acidified with dilute HCl, and extracted with ethyl acetate. The extract was rotary evaporated to give the *title compound* (**16**) as white needles (from hexane) in 43% yield, m.p. 118—119 °C (Found: C, 60.25; H, 4.2; N, 6.3. $C_{11}H_9NO_2S$ requires C, 60.26; H, 4.14; N, 6.39%); $\nu_{max.}$(KBr) 2 200s, 1 580vs, and 1 560vs, cm^{-1}; δ_H (100 MHz; $CDCl_3$) 14.80 (br, 1 H, OH), 7.85 (m, 2 H, Ph), 7.40 (m, 3 H, Ph), and 2.40 (s, 3 H, SMe); *m/z* 219 (M^+).

Compounds (**17**) and (**18**) were prepared in a similar manner to that described above.

Compound (**17**): white needles (from $CHCl_3$–hexane), m.p. 85—86 °C (yield 60%) (Found: C, 66.7; H, 5.6; N, 12.9. $C_{12}H_{12}N_2O_2$ requires C, 66.65; H, 5.59; N, 12.95%); $\nu_{max.}$(KBr) 2 200s, 1 585vs, and 1 550vs cm^{-1}; δ_H (100 MHz; $CDCl_3$) 16.80 (br, 1 H, OH), 7.80 (m, 2 H, Ph), 7.40 (m, 3 H, Ph), and 3.20 (s, 6 H, 2 × Me); *m/z* 216 (M^+).

Compound (**18**): white needles (from EtOH), m.p. 74—75 °C (yield 66%) (Found: C, 65.0; H, 4.5; N, 6.9. $C_{11}H_9NO_3$ requires C, 65.02; H, 4.46; N, 6.89%); $\nu_{max.}$(KBr) 2 200s and 1 640s cm^{-1}; δ_H (100 MHz; $CDCl_3$–CCl_4) 13.95 (br, 1 H, OH), 7.90 (m, 2 H, Ph), 7.45 (m, 3 H, Ph), and 3.95 (s, 3 H, OMe); *m/z* 203 (M^+).

*Preparation of α-Cyano-β-hydroxy-*p*-methoxycinnamonitrile* (**19**).—To a solution of sodium ethoxide (10 mmol) in ethanol (10 ml) was added malononitrile (330 mg, 5 mmol) followed by *p*-anisoyl chloride (1.02 g, 6 mmol) and the mixture was stirred for 2 h at room temperature. The reaction mixture was acidified with dilute HCl, washed with benzene, and evaporated to give white crystals. Recrystallization from chloroform gave the *title compound* (**19**) (36% yield) as white plates, m.p. 187—188 °C (Found: C, 65.8; H, 4.0; N, 14.0. $C_{11}H_8N_2O_2$ requires C, 66.00; H, 4.03; N, 13.99%); $\nu_{max.}$(KBr) *ca.* 3 030br, 2 230, 2 220vs, and 1 600vs cm^{-1}; δ_H (100 MHz; $CDCl_3$–[$^2H_5$]pyridine) 11.3 (br, 1 H, OH), 7.8 and 6.8 (ABq, 4 H, J_{AB} 9 Hz, 4-$MeOC_6H_4$), and 3.7 (s, 3 H, Me); *m/z* 200 (M^+).

Preparation of Compounds (**20**)—(**23**).—Compounds (**16**)—(**19**) were allowed to react with benzoic acid in the presence of PPSE in the same manner as described for the preparation of compound (**6a**). Standard work-up gave compounds (**20**)—(**23**) in 73, 18, 13, and 35% yield, respectively.

5-Benzoyl-4-methylthio-2-phenyl-1,3-oxazin-6-one (**20**): yellow needles (from $CHCl_3$–hexane), m.p. 149—150 °C (Found: C, 66.9; H, 4.1; N, 4.2. $C_{18}H_{13}NO_3S$ requires C, 66.86; H, 4.05; N, 4.33%); $\nu_{max.}$(KBr) 1 740s and 1 620s cm^{-1}; δ_H [100 MHz; $CDCl_3$–$(CD_3)_2SO$] 8.15 (m, 2 H, Ph), 7.75 (m, 2 H, Ph), 7.45 (m, 6 H, Ph), and 2.60 (s, 3 H, SMe); *m/z* 323 (M^+).

β-Benzoyloxy-α-cyano-NN-dimethylcinnamide (**21**): yellow needles (from $CHCl_3$), m.p. 119—120 °C; $\nu_{max.}$(KBr) 2 200m, 1 750vs, and 1 650vs cm^{-1}; δ_H (100 MHz; $CDCl_3$) 8.10 (m, 2 H, Ph), 7.20 (m, 8 H, 2 × Ph), 2.98 (s, 3 H, Me), and 2.93 (s, 3 H, Me) [Found: M^+, 320.1160 (±0.005). $C_{19}H_{16}N_2O_3$ requires *M*, 320.1160].

Methyl β-Benzoyloxy-α-cyanocinnamate (**22**): viscid oil (Found: C, 70.3; H, 4.2; N, 4.55. $C_{18}H_{13}NO_4$ requires C, 70.35; H, 4.26; N, 4.56%); $\nu_{max.}$(KBr) 2 220m, 1 750vs, and 1 740vs cm^{-1}; δ_H (100 MHz; $CDCl_3$) 7.95 (m, 2 H, Ph), 7.75 (m, 2 H, Ph), 7.40 (m, 6 H, 2 × Ph), and 3.70 (s, 3 H, OMe); *m/z* 307 (M^+).

*β-Benzoyloxy-α-cyano-*p*-methoxycinnamonitrile* (**23**): white needles (from $CHCl_3$), m.p. 92—93 °C; $\nu_{max.}$(KBr) 3 030w, 2 950, 2 910, 2 820w, 2 210s, 1 760vs, and 1 600vs cm^{-1}; δ_H (100 MHz; $CDCl_3$), 8.2 (m, 2 H, Ph), 7.9 and 7.0 (ABq, 4 H, *J* 9 Hz, 4-$MeOC_6H_4$), 7.6 (m, 3 H, Ph), and 3.9 (s, 3 H, Me) [Found: M^+, 304.0848 (± 0.005). $C_{18}H_{12}O_3N_2$ requires *M*, 304.0847].

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Received 2nd *April* 1986; *Paper* 6/651