Lithiation and Thiylation of 5-Bromopyrimidines

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5-Thylated pyrimidines have been prepared by cyclization reactions, and by reactions involving lithiated pyrimidine intermediates. tert-Butyldimethylsilyl, trimethylsilyl, isopropyl and tert-butyl groups have been tried as O-protecting groups in the lithiation of 5-bromo-2(1H)-pyrimidinone. The trimethylsilyl group is cleaved during lithiation and the tert-butyldimethylsilyl group is cleaved by thiolates generated from disulfides during the thiylation. tert-Butyldimethylsilyl chloride together with a base in dichloromethane was used for O-silylation of pyrimidin-2-ones. tert-Butyldimethylsilyl 2-pyrimidinyl ethers are cleaved by acetic acid in chloroform.

Certain 2(1H)-pyrimidinones substituted at the 5-position are of interest for the studies of the reversible arrest of the cell cycle during mitosis. As a continuation of our studies of metaphase arrestors we describe herein work directed toward the preparation of 5-thylated 2(1H)-pyrimidinones.

The first route studied in the preparation of these compounds used as starting material, 2-chloro-3-(N,N-dimethylamino)acrylaldehyde (1) which was prepared from chloroacetic acid by a Vilsmeier formylation reaction followed by decarboxylation. Subsequent reactions of 1 with thiolates gave the 2-sulfenylacrylaldehydes (2), which were converted into 5-sulfenylpyrimidinones (3) by cyclization reactions with urea either in the presence of sodium ethoxide, or in the presence of an acid. The yields of the cyclization reactions were of the order 30%; 51% for the simple S-phenyl derivative (3a).

Alternative routes for the preparation of 3 were also studied. Direct substitution in a 5-halogenated pyrimidine is difficult to effect because the halogen is in a non-activated position. Substitution, however, can be facilitated by the presence of a 4-carboxy group. Thus the bromine substituent in 5-bromo-4-carboxy-2-methylthiopyrimidines can be displaced in reactions with thiophenolates under vigorous conditions. Recently we reported that the above compound can be lithiated and that the lithio species subsequently reacts readily with carbon electrophiles. In an attempt to find milder conditions we tried the analogous reaction using 5-bromo-2(1H)-pyrimidinone (4) for the synthesis of 5-thylated pyrimidinones (3). For the desired reaction, 4

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\text{Me}_2\text{NCH}=\text{CCHO} \xrightarrow{\text{RSH}} \text{Me}_2\text{NCH}=\text{CCHO} \xrightarrow{\text{SR}} \text{Me}_2\text{NCH}=\text{CCHO} \xrightarrow{\text{NH}_2\text{CONH}_2} \text{Me}_2\text{NCH}=\text{CCHO}
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Scheme 1.

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must be dilitiated. However this would lead to solubility problems in THF. Therefore the trimethylsilyloxy (TMS-O) derivatives (5) was prepared from 4 and hexamethyldisilazane (HMDS), and subsequently treated with two equivalents of butyllithium in the presence of 1,3-dimethyl-3,4,5,6-tetrahydro-2(1H)-pyrimidinone (DMPU). Two equivalents of metalling agent was used because cleavage of the O-Si bond in our phenolic ether was expected to take place. It is known that the silyloxy group is attacked by butyllithium although normally the stronger methyllithium or tert-butyllithium is used for this purpose. Migration of the silyl group from the oxygen to the lithiated carbon, as seen in many reactions, was not observed in these reactions which were carried out at low temperatures.

The dilitiated species from 5, in the form of a fine suspension, reacted readily with both benzaldehyde and furfural, to form the 5-hydroxymethyl derivatives (10) in ca. 70% yield.

Monolithiation of the pyrimidine 5-position was achieved using the 2-(tert-butyldimethylsilyloxy) (TBDMS-O) derivative (6). Several methods exist for making TBDMS ethers from alcohols, the most common being the use of tert-butyl(chloro)dimethylsilane in DMF in the presence of imidazole. The preparation of 6, however, from the acidic precursor (4) was best achieved in dichloromethane with the silyl chloride in the presence of triethylamine. Lithiation of 6 gave 7 which reacted with both benzaldehyde and furfural, to furnish the TBDMS 2-pyrimidinyl ether alcohols (8).

Fluorides under anhydrous conditions or aqueous hydrofluoric acid, have been recommended for the cleavage of TBDMS ethers. The TBDMS group in compound 8, however, was found to be readily removed simply by treatment of 8 with acetic acid in chloroform.

The lithiated species (7) reacts with disulfides at $-95^\circ$C with loss of the TBDMS group and formation of the 5-thiylated pyrimidinones (3). Since the tert-butyldimethylsilyloxy group is resistant towards lithiation and reaction with carbon electrophiles as in the formation of 8, it appears that it is the thiolate, generated from the disulfide in the thiylation reaction, which causes the cleavage of the Si-O bond. The dilitiated species from the TMS derivative (5) also reacted with disulfides to give the thylated pyrimidinones (3).

The cleavage of the TBDMS group in the thiyl-
ation reaction prompted us to search for more resistant hydroxy protecting groups. The isopropyl and tert-butyl groups were chosen. The protected compounds (14) were prepared from the 2-chloro precursor (12) by the reaction between the latter and sodium isopropoxide or potassium tert-butoxide. Both compounds were lithiated at −95 °C and reacted further with diphenyl disulfide to furnish the 5-thiolated pyrimidine ethers (16). Cleavage of the isoproxy function required heating with strong acid. The tert-butyl group in 16b, however, was removed at ambient temperature with dilute acid in methanol or in trifluoroacetic acid.

In the final route used for the preparation of the thiolated pyrimidinone (3a), 5-bromo-2-methylthiopyrimidine (13) was lithiated as above and treated further with diphenyl disulfide. The dithio derivative (18) was formed. When the latter is heated with strongly acidic methanolic solution, the 2-thio function is selectively hydrolyzed with the formation of 3a. Since 2-bromo-5-methylthiopyrimidine is a readily available starting material, this is a convenient route to 5-thiolated 2-pyrimidinones in those cases in which the desired product is not affected by the strongly acidic conditions of the final reaction step.

**Experimental**

The 1H NMR spectra were recorded at 60 MHz, the 13C spectra at 75 MHz. The MS spectra were recorded at 70 eV and are presented as m/z (% rel. int.). Isobutane was used for chemical ionization, [MS(Cl)]. THF for use in the organometallic reactions was dried by being refluxed and distilled over metallic sodium—benzenophenone.

**Preparation of 3-N,N-Dimethylamino-2-thioaryl-(benzyl)acrylaldehyde (2).** Compounds 2 were prepared essentially as described for 2a. 2-Chloro-3-(N,N-dimethylamino)acrylaldehyde was treated with the corresponding thiophenol in the presence of triethylamine. Literature procedures were used for the preparation of methyl 4-mercaptopentanoate and 3-chlorothiophenol, the other thiophenols were commercially available.

**2-Benzylthio-3-(N,N-Dimethylamino)acrylaldehyde (2b).** Compound 2b was obtained in 54% yield after flash chromatography on silica gel (CHCl3): m.p. 55–57 °C (Et2O–iPr2O). Anal. C13H15NOS: C, H. 1H NMR (CDCl3): δ 3.00 (NMe2), 3.75 (CH2), 7.30 (Ph), 7.40 (CH=C), 9.05 (CHO). MS: 221 (52, M), 130 (100), 102 (27), 101 (16), 100 (22), 91 (41), 87 (15).

**3-(N,N-Dimethylamino)-2-(4-methoxycarbonylphenylthio)acrylaldehyde (2c).** Compound 2e was obtained in 57% yield after flash chromatography on silica gel (EtOAc); m.p. 90–92 °C. Anal. C15H15NO2S: C, H. 1H NMR (CDCl3): δ 3.30 (NMe2), 3.90 (OME), 7.1–7.9 (C6H4), 7.62 (CH=C), 9.30 (CHO). MS: 265 (100, M), 236 (51), 192 (26), 100 (21), 98 (43), 91 (35), 81 (15).

**3-(N,N-Dimethylamino)-2-(2-methoxyphenylthio)acrylaldehyde (2d).** Compound 2d was obtained
in 47% yield after flash chromatography on silica gel (EtOAc); m.p. 124–126°C. Anal. C_{12}H_{15}NO_{3}S: C, H, \^1H NMR (CDCl$_3$): δ 3.25 (NMe$_2$), 3.85 (OMe), 6.6–7.4 (C$_6$H$_4$), 7.70 (CH=C), 9.18 (CHO). MS: 237 (100, M), 208 (51), 165 (19), 162 (29), 121 (26), 98 (51), 91 (17).

2-(3-Chlorophenylthio)-3-(N,N-dimethylamino)-acrylaldehyde (2e). Compound 2e was obtained in 41% yield after flash chromatography on silica gel (EtOAc); m.p. 88–90°C (Et$_2$O–iPr$_2$O). Anal. C$_{11}$H$_9$ClNO$_5$: C, H, \^1H NMR (CDCl$_3$): δ 3.30 (NMe$_2$), 7.0–7.2 (C$_6$H$_4$), 7.60 (CH=C), 9.20 (CHO). MS: 243/241 (42/100, M), 214 (16), 212 (49), 170 (12), 168 (32), 100 (29), 98 (53), 81 (15).

General procedure for the preparation of 5-aryl (benzyl)thio-2(H)-pyrimidinone (3) by cyclcondensation of 2. Compounds 3a–e were prepared by minor modification of the method described for 3a. The acrylaldehyde (2) (1.0 mmol), urea (2.0 mmol) and sodium ethoxide (2.0 mmol) in ethanol (100 ml) were heated together under reflux, overnight. The sodium salt of the pyrimidinone crystallized from the reaction mixture on being cooled and was isolated by filtration. The sodium salt was dissolved in the minimum amount of water at 80°C and the solution acidified with acetic acid whereupon the pyrimidinone precipitated.

5-Benzylthio-2(H)-pyrimidinone (3b). Compound 3b was obtained in 35% yield, m.p. 160–161°C. Anal. C$_{11}$H$_{10}$NS$_2$: C, H. \^1H NMR ([H$_2$]Me$_2$SO): δ 4.00 (CH$_2$), 7.30 (Ph), 8.10 (2 H, H-4,6). MS: 218 (7, M), 92 (8), 91 (100), 65 (12).


5-(3-Chlorophenylthio)-2(H)-pyrimidinone (3e). Compound 3e was obtained in 33% yield, m.p. 184°C (EtOH). Anal. C$_{11}$H$_9$ClNO$_3$: C, H. \^1H NMR ([H$_2$]Me$_2$SO): δ 6.9–7.6 (C$_6$H$_4$), 8.50 (2 H, H-4,6). MS: 240/238 (36/100, M), 203 (16), 148 (20), 138 (16), 111 (13), 108 (10).

5-(4-Methoxycarbonylphenylthio)-2(H)-pyrimidinone (3e). A solution of 3-(N,N-dimethylamino)-2-(4-methoxycarbonylphenylthio)acrylaldehyde (5.00 g, 19 mmol), urea (1.24 g, 21 mmol) and 37% HCl (6 ml) in methanol (100 ml) was stirred at 45°C for 2 days. The cold solution was diluted and neutralized with aqueous NaOH, and the mixture was left to stand in the cold (4°C) before the precipitated product was filtered off; yield 35%, m.p. 260°C. Anal. C$_{12}$H$_{10}$N$_2$O$_3$: C, H. \^1H NMR ([H$_2$]Me$_2$SO): δ 3.85 (OMe), 7.2–8.0 (C$_6$H$_4$), 8.50 (2 H, H-4,6). MS: 262 (100, M), 261 (7), 233 (4), 231 (28), 220 (111), 218 (5), 203 (24).

5-Bromo-2-trimethylsilylopyrimidine (5) was prepared from 4 by reaction with HMDS as previously described.5

5-Bromo-2-tert-butyldimethylsilylopyrimidine (6). Triethylamine (6.68 g, 66 mmol) was added to a solution of 5-bromo-2(1H)-pyrimidinone (11.55 g, 66 mmol) in dry dichloromethane (250 ml), and the mixture was stirred at ambient temperature for 30 min. tert-Butyl(chloro)dimethylsilane (10.0 g, 66 mmol) was then added and the mixture stirred at ambient temperature for 2 h. The dichloromethane was removed by distillation, the residue extracted with diethyl ether (2×100 ml), the ether distilled off, and the residue distilled; yield 17.2 g (90%), b.p. 72°C/0.01 mmHg. \^1H NMR (CDCl$_3$): δ 0.35 (Me$_2$Si), 1.10 (tBuSi), 8.50 (2 H, H-4,6). MS (CI): 291/289 (100/100, M+H), 253 (3), 234 (2), 233 (22), 231 (27), 212 (7), 211 (42), 153 (9).

2-tert-Butyldimethylsiloxy-5-(α-hydroxybenzyl)pyrimidine (8a). Butyllithium (1.6 M) in hexane (8.75 ml, 14 mmol) was added dropwise from a syringe to a stirred solution of 5-bromo-2-tert-butyldimethylsiloxy pyrimidine (2.0 g, 7.0 mmol) and DMPU (0.90 g, 7.0 mmol) in dry THF (80 ml) under N$_2$ at –90°C. The pale yellow mixture was stirred at –90 to –85°C for 90 min, when a solution of benzaldehyde (1.49 g, 14 mmol) in dry THF (7 ml) was added. The mixture was stirred at –85°C for 30 min, then allowed to reach 0°C at which it was allowed to stand for 20 h. The mixture was poured into 10%
aqueous NH₄Cl (30 ml) and stirred vigorously for 5 min. The phases were separated; the aqueous phase was extracted with chloroform (2×40 ml) and the combined organic phases were washed (2×50 ml), dried (MgSO₄) and the solvent distilled off. The residue was distilled (Kugelrohr), b.p. 220–230°C/0.01 mmHg, yield 1.50 g (68%). Anal. C₉H₁₉N₄O₆Si: C, H. ¹H NMR (CDCl₃): δ 0.24 (Me₃Si), 0.92 (tBuSi), 3.77 (OH), 5.67 (CH), 7.25 (Ph), 8.25 (2 H, H-4,6). MS (Cl): 317 (M+H), 299 (8), 260 (8), 259 (38), 148 (12), 147 (100), 143 (44), 142 (12), 133 (13), 107 (99).

2-tert-Butyldimethylsilyloxy-5-(a-hydroxy-2-fur-furyl)pyrimidinone (8b). Compound 8b was obtained from furfural and 6 as above in 61 % yield, b.p. 200–205°C/0.05 mmHg (Kugelrohr). Anal. C₁₃H₂₆N₄O₄Si: C, H. ¹H NMR (CDCl₃): δ 0.30 (Me₃Si), 0.96 (tBuSi), 4.59 (OH), 5.75 (CH), 6.15/6.26/7.31 (3 H, Fur.), 8.42 (2 H, H-4,6). MS (Cl): 307 (100, M+H), 291 (11), 289 (22), 250 (16), 249 (89), 221 (8), 143 (17), 133 (27), 81 (18).

5-(α-Hydroxybenzyl)-2(1H)-pyrimidinone (10a). 2-tert-Butyldimethylsilyloxy-5-(α-hydroxybenzyl)pyrimidinone (0.60 g, 1.96 mmol) was added to a solution of chloroform (5 ml) and acetic acid (5 ml) and the mixture was stirred at ambient temperature for 3 h after which time diethyl ether (20 ml) was added. The precipitate that formed was the pure product; yield 0.37 g (97 %), m.p. 173°C. Anal. C₁₁H₁₈N₂O₂: C, H. ¹H NMR (DMSO-d₆): δ 5.72 (CH), 6.12 (OH), 7.3–7.5 (Ph), 8.24 (2 H, H-4,6). MS: 202 (91, M), 201 (31), 186 (16), 185 (13), 173 (11), 158 (9), 145 (17), 130 (19), 123 (47), 105 (64), 97 (85), 79 (100), 78 (98), 77 (99).

5-(α-Hydroxy-2-fur-furyl)-2(1H)-pyrimidinone (10b). Compound 10b was obtained by hydrolysis of 8b as described above in 77 % yield, m.p. 190°C. Anal. C₁₃H₂₆N₄O₄: C, H. ¹H NMR (DMSO-d₆): δ 5.71 (CH), 6.18 (OH), 7.72/6.52 (3 H, Fur.), 8.28 (2 H, H-4,6). MS: 192 (100, M), 176 (27), 175 (67), 164 (55), 163 (27), 147 (30), 136 (22), 135 (13), 123 (63).

Preparation of 5-(α-hydroxybenzyl)-2(1H)-pyrimidinone (10a) from compound 5. Butyllithium (1.6 M) in hexane (10 ml, 16.2 mmol) was added dropwise from a syringe to a stirred solution of 5-bromo-2-trimethylsilyloxypyrimidine (2.0 g, 8.1 mmol) and DMPU (1.04 g, 8.1 mmol) in dry THF (80 ml) at −95°C under N₂. The pale yellow mixture was stirred at −85°C for 90 min, whereupon a solution of benzaldehyde (1.72 g, 16.2 mmol) in dry THF (7 ml) was added dropwise. The mixture was allowed to reach 0°C and stirred for a further 20 h, after which time it was poured into 10 % aqueous NH₄Cl (30 ml). The mixture was stirred for a few min before being extracted with chloroform (2×50 ml). The aqueous solution was concentrated under reduced pressure until the product started to precipitate; yield 1.30 g (57 %).

Preparation of 5-(α-hydroxyfurfuryl)-2(1H)-pyrimidinone (10b) from compound 5. Compound 10b was prepared as above using furfural instead of benzaldehyde; yield 71 %.

2-tert-Butyldimethylsilyloxy-5-phenylthiopyrimidine (11a). tert-Butyl(chloro)dimethylsilanes (43 mg, 0.28 mmol) was added to a mixture of 5-phenylthio-2(1H)-pyrimidinone (58.1 mg, 0.28 mmol) and triethylamine (0.30 mg, 0.28 mmol) in acetonitrile (3.0 ml). The mixture was stirred at ambient temperature for 2 h, the solvent was distilled off, and the residue was extracted with diethyl ether. The ether solution was washed, dried (MgSO₄), and purified by chromatography on silica gel (EtOAc); yield 57 mg (63 %), m.p. ca. 25°C (wax). Anal. C₁₉H₂₃N₄O₂S: C, H. ¹H NMR (CDCl₃): δ 0.30 (SiMe₃), 0.95 (tBuSi), 7.25 (Ph), 8.50 (2 H, H-4,6).

Thiolation of 5-bromopyrimidines in the preparation of 3. 5-Bromo-2-trimethylsilyloxypyrimidine or 5-bromo-2-tert-butyldimethylsilyloxypyrimidine (7.0 mmol) was lithiated as described above and treated with a disulfide (14 mmol) at −85°C. The mixture was stirred at −85°C for 30 min and kept at 0°C for 20 h, before being poured into 10 % aqueous NH₄Cl (30 ml). The mixture was stirred vigorously for 5 min and extracted with chloroform (4×50 ml), and the washed and dried (MgSO₄) solution was evaporated to yield the product.

The disulfide substrates used in the reaction which were not commercially available, bis(4-methoxy carbonylphenyl) disulfide,¹⁴ bis(2-methylphenyl) disulfide¹⁵ and bis(3-chlorophenyl) disulfide¹⁶ were made by a general literature procedure.¹⁷
5-Phenylthio-2(1H)-pyrimidinone (3a) was obtained as an oily material which crystallized on being triturated with diethyl ether; yield 51%, m.p. 217–219°C (EtOH). Anal. C₉H₇N₂O₂S: C, H. ¹H NMR (CDCl₃): δ 7.30 (Ph), 8.45 (2 H, H-4,6). MS: 204 (100, M), 203 (19), 162 (16), 104 (18), 95 (4), 77 (22).

5-Benzylthio-2(1H)-pyrimidinone (3b) was obtained in 26% yield.

5-(4-Methoxybenzyl)thio-2(1H)-pyrimidinone (3c) was obtained in 30% yield.

5-(2-Methoxyphenylthio)-2(1H)-pyrimidinone (3d) was obtained in 42% yield.

5-(3-Chlorophenylthio)-2(1H)-pyrimidinone (3e) was obtained in 5% yield.

5-Bromo-2-isopropoxypyrimidine (14a). Sodium (2.15 g, 0.093 mol) was added in portions to 2-propanol (500 ml). When all the sodium had reacted, 5-bromo-2-chloropyrimidine (16.4 g, 8.5 mmol) was added, and the mixture was stirred at ambient temperature overnight before most of the solvent was distilled off under reduced pressure. The residue was poured into water and the mixture was extracted with diethyl ether (3×200 ml). The dried (MgSO₄) solution was evaporated and the residue was distilled; b.p. 44–46°C/0.08 mmHg, yield 1.3 g (76%). Anal. C₉H₇BrN₂O₃: C, H. ¹H NMR (CDCl₃): 1.40/5.25 (iPr), 8.50 (2 H, H-4,6). MS: 218/216 (28/28, M), 203/201 (4/4), 177 (30), 176 (80), 175 (32), 174 (80), 95 (100).

5-Bromo-2-tert-butoxyacrylpyrimidine (14b). Compound 14b was prepared as above from potassium tert-butoxide (23.3 mmol) in tert-butyl alcohol (250 ml) and 5-bromo-2-chloropyrimidine (15.5 mmol). The crude product was purified either by recrystallisation from light petroleum or by sublimation at 30°C/0.001 mmHg; yield 71%, m.p. 64–65°C. Anal. C₉H₇BrN₂O₂: C, H. ¹H NMR (CDCl₃): δ 1.60 (tBu), 8.40 (2 H, H-4,6). MS(CI): 217 (10), 177 (100), 175 (100), 97 (31), 85 (24).

2-Isopropoxy-5-phenylthiopyrimidine (16a). A solution of 5-bromo-2-isopropoxyacrylpyrimidine (2.0 g, 9.2 mmol) in dry THF (100 ml) was cooled to −100°C and butyllithium in hexane (1.5 M; 6.1 ml; 9.2 mmol) was added slowly via a syringe. The reaction mixture was allowed to reach −80°C (80 min) before diphenyl disulfide (2.4 g, 11 mmol) in dry THF (10 ml) was added slowly (10 min). The reaction mixture was allowed to reach ambient temperature (ca. 2 h), poured into water, neutralized, and extracted into diethyl ether. The ether solution was dried (MgSO₄) and evaporated and the residual product was purified by flash chromatography on silica gel (toluene); yield 1.3 g (57%), b.p. 124–128°C/0.08 mmHg. Anal. C₁₆H₁₄N₂O₂S: C, H. ¹H NMR (CDCl₃): 1.40/5.28 (iPr), 7.21 (Ph), 8.55 (2 H, H-4,6). MS: 246 (40, M), 204 (14), 204 (100), 203 (26), 162 (15), 134 (5), 132 (8).

2-tert-Butoxy-5-phenylthiopyrimidine (16b). Compound 16b was prepared as above from 5-bromo-2-tert-butoxyacrylpyrimidine and diphenyl disulfide. The crude product was purified by flash chromatography (CH₂Cl₂); m.p. 87°C, yield 63%. Anal. C₁₇H₁₆N₂O₂S: C, H. ¹H NMR (CDCl₃): δ 1.65 (tBu), 7.25 (Ph), 8.50 (2 H, H-4,6). MS: 260 (5, M), 205 (16), 204 (100), 203 (14), 162 (8), 77 (12).

Preparation of 5-phenylthio-2-(1H)-pyrimidinone (3a) by dealkylation of 16. (a) 2-Isopropoxy-5-phenylthiopyrimidine (1.0 g, 4.1 mmol) was heated with 2 ml conc. HCl in 10 ml MeOH for 48 h. The mixture was then evaporated to dryness to furnish the hydrochloric salt of 3a in quantitative yield.

(b) (i) 2-tert-Butoxy-5-phenylthiopyrimidine (1.0 g, 3.8 mmol) was added to a solution of 2 M HCl (10 ml) and methanol (10 ml) and the mixture was stirred at ambient temperature for 30 min before being evaporated to dryness to furnish the hydrochloride salt of 3a in quantitative yield. (ii) 2-tert-Butoxy-5-phenylthiopyrimidine (0.11 g, 0.4 mmol) in trifluoroacetic acid (3 ml) was stirred at ambient temperature for 2 h before the acid was removed under reduced pressure. The product (3a) was obtained in almost quantitative yield.

2-Methylthio-5-phenylthiopyrimidine (18). Butyllithium (1.6 M) in hexane (3.5 ml, 5.5 mmol) was added dropwise via a syringe to a stirred solution of 5-bromo-2-methylthiopyrimidine (1.0 g, 4.9 mmol) and DMFU (0.64 g, 5.0 mmol) in dry
THF (60 ml) under N₂ at −95°C. The pale yellow mixture was stirred at −85°C for 90 min, whereupon a solution of diphenyl disulfide (1.20 g, 5.5 mmol) in dry THF (8 ml) was added dropwise. The mixture was stirred at −85°C for 30 min and at 0°C for 20 h, before being poured into 1 M HCl (30 ml). The mixture was stirred, the phases were separated. The aqueous phase was extracted with chloroform (3×50 ml) and the combined organic phases were washed and dried (MgSO₄), the solvent was evaporated and the residue was chromatographed on neutral alumina using light petroleum−diethyl ether (7:3), yield 0.56 g (49%), m.p. 59°C (EtOH). Anal. C₁₁H₁₀N₂S₂: C, H. ¹H NMR (CDCl₃) δ 2.60 (SMe), 7.25 (Ph), 8.45 (2 H, H-4,6).

Preparation of 5-phenylthio-2(1H)-pyrimidinone (3a) by hydrolysis of 18. Conc. HCl (10 ml) was added to a solution of 2-methylthio-5-phenylthio pyrimidine (0.23 g, 0.98 mmol) in methanol (20 ml). The mixture was heated at 60°C for 96 h, after which time diethyl ether was added to the cold reaction mixture. The oily precipitate was triturated with diethyl ether to give a crystalline material which was recrystallized from ethanol; yield 0.19 g (95%).

References

Received February 17, 1988.