Preparation of 5-(Pyrrolylcarbonyl)- and 5-(Imidazolylcarbonyl)-pyrimidines

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2-Methylthio-5-(pyrrolylcarbonyl)-pyrimidines have been prepared from 1-methyl-2-tributylstannylpyrrole and 2-methylthiopyrimidine-5-carbonyl chloride by Pd-catalysis. Triphenylarsine was superior to triphenylphosphine as a ligand in the reaction. The reaction with phosphine ligands proceeded well when the polarization of the reactants was reversed as in the reaction between pyrrolecarbonyl chlorides and 2-methylthio-5-tributylstannylpyrimidine. 1-Methyl-5-tributylstannylimidazole has been prepared in a one-pot reaction from 1-methylimidazole in 91% yield.

For our continued studies on biologically active 2(1*H*)-pyrimidinones,[1] we were interested in the preparation of 5-(*N*-heteroaroyl)pyrimidinones. Herein we report on the synthesis of some 5-(pyrrolylcarbonyl)- and 5-(imidazolylcarbonyl)-pyrimidinones.

5-Acylpyrimidines can be prepared by reaction of an acid chloride with a 5-metallated pyrimidine,[2] by palladium-catalyzed cross-coupling reactions either between an acid chloride and a 5-stannylpyrimidine or a pyrimidine-5-carbonyl chloride and an organostannane,[3] or less conveniently by cyclisation reactions.[4]

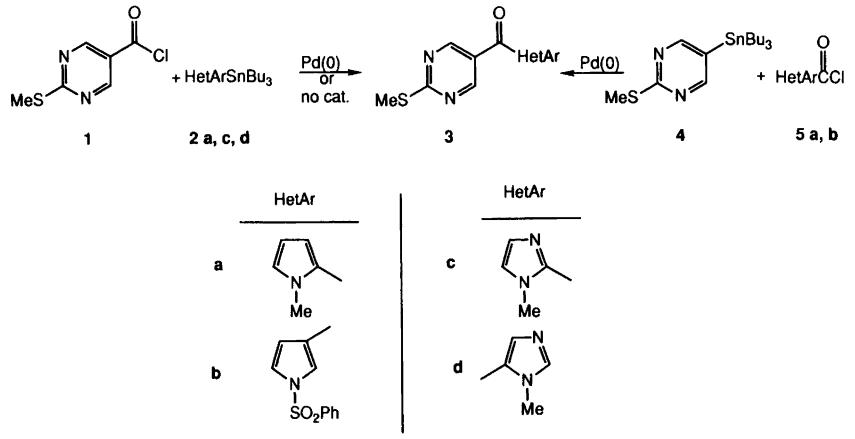
Palladium-catalyzed cross-coupling reactions proceed under mild conditions in high yields and with high selectivity.[5] In the present work attempts were made to react 1-methyl-2-tributylstannylpyrrole (**2a**), available from 1-methylpyrrole by lithiation followed by stannylation,[6] with the pyrimidine-5-carbonyl chloride **1**[2b] in the presence of a catalytic amount of bis(triphenylphosphine)-palladium(II) dichloride or tetrakis(triphenylphosphine)-palladium(0) to form **3a**. ^{1}H NMR spectroscopy of the crude product (i.e., after evaporation of the solvent) indicated that the stannylpyrrole **2a** had decomposed. The stannylpyrrole **2a**, however, does couple with benzoyl chloride or with iodobenzene to form 2-benzoyl-1-methylpyrrole[7] and 1-methyl-2-phenylpyrrole[8] in 56% and 70% yield, respectively.

Recently a large rate enhancement in palladium-catalyzed cross-coupling reactions between aryl halides and organostannanes has been observed by changing the ligands on palladium from triphenylphosphine to triphenylarsine.[9] We also observed a remarkable effect by changing the ligand to triphenylarsine from triphenylphosphine in the reaction between the acid chloride **1** and the stannylpyrrole **2a**. With the arsine ligand the cross-coupled product **3a** could be isolated in 72% yield after 7 h at ambient temperature, whereas the reaction failed with triphenylphosphine as the ligand (*vide supra*).

An alternative approach, which involves a change in polarities of the reactants in the coupling, is shown in the reaction between 1-methylpyrrole-2-carbonyl chloride (**5a**)[10] and 2-methylthio-5-tributylstannylpyrimidine (**4**):[11] the cross-coupled product **3a** was obtained in 72% yield using bis(triphenylphosphine)palladium(II) dichloride as the catalyst (Scheme 1). A minor product (10%) in this reaction was the homo-coupled bipyrimidine **10**[12] (Scheme 2).

For the preparation of the 5-(pyrrolylcarbonyl)-pyrimidines with the carbonyl group in the pyrrole 3-position, the acidic proton on pyrrole has to be removed either by alkylation or acylation. We chose to protect the pyrrole nitrogen by *N*-sulfonylation.[13] The required 1-phenylsulfonylpyrrole-3-carboxylic acid (**8**) was made by a modified literature procedure,[14] and the acid chloride **5b** by a standard procedure (Scheme 2). In the subsequent Pd-catalyzed cross-coupling of the pyrrole-3-carbonyl chloride **5b** with 2-methylthio-5-tributylstannylpyrimidine (**4**) the product **3b** was isolated in 61% yield. Other products in the reaction were the decarbonylated pyrimidine **9** (7%) and the homocoupled bipyrimidine **10**[12] (18%).

In the imidazole series coupling of a stannylimidazole with a pyrimidine-5-carbonyl chloride was expected to be the better Pd-catalyzed route (*vide supra*) to products like **3**, since imidazolecarbonyl chlorides are known to be unstable.[15] 1-Methyl-2-tributylstannylimidazole (**2c**),[16] which was prepared from 1-methylimidazole by lithiation followed by stannylation, was reacted with 2-methylthiopyrimidine-5-carbonyl chloride (**1**) at −78°C to give **3c** in 81% yield. In this reaction, as well as in the reaction of benzoyl chloride with the stannylimidazole **2c**, no catalyst was necessary. In the latter case 2-benzoyl-1-methylimidazole[17a] was isolated in 59% yield. *ipso*-Substitution in other aryltin compounds with aryl halides has been reported.[18] Since no catalyst was necessary

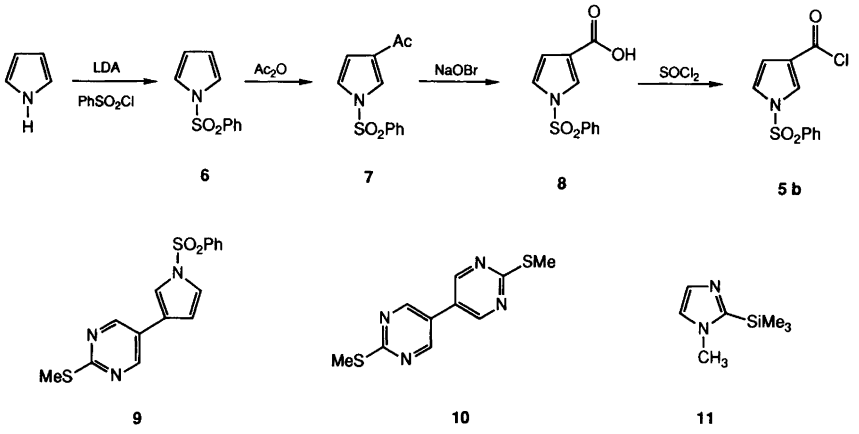


Scheme 1.

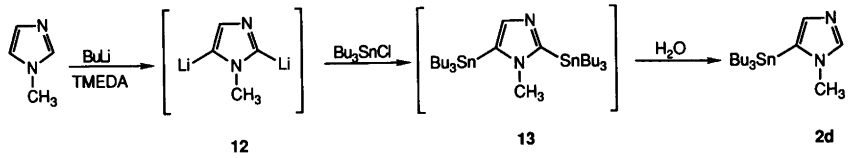
to effect the coupling between the stannylimidazole **2c** and the pyrimidine-5-carbonyl chloride **1**, we expected that 1-methyl-2-trimethylsilylimidazole (**11**)[17] would also react easily with the pyrimidine-5-carbonyl chloride **1** to give the coupled product **3c**, since a number of electrophiles have been reacted with 1-methyl-2-trimethylsilylimidazole (**11**) to give 2-substituted imidazoles in good yields.[17] The reaction between the trimethylsilylimidazole **11** and the pyrimidine-5-carbonyl chloride **1**, however, gave low yields (0–10%) of the pyrimidine **3c**.

The positional reactivity order for lithiation of 1,3-azoles is $2 > 5 \gg 4$.[19] Thus some 2-triorganostannylimidazoles have been synthesized by reaction of 2-lithioimidazoles with triorganostannyl chlorides.[16] For the preparation of 5-stannylimidazoles by the lithiation with subsequent metal–metal exchange, the 2-position had to be blocked. 5-Stannylimidazoles with a 2-methyl substituent are known,[20] but the methyl group is not readily replaceable. A stannyl group in the 2-position in 1-methylimidazole, however, is labile towards hydrolysis,[16] more so than a stannyl group in the 4- or 5-position. Similar variations in reactivity have been reported for trimethylsilyl substituted imidazoles.[21] Dilithiation of 1-methylimidazole is possible with an excess of butyllithium. The product is the imidazole (**12**)[21] which is reacted with two equivalents of tributylstannyl chloride presumably to give the distannylated imidazole **13**. The latter was hydrolyzed *in situ* to give 1-methyl-5-tributylstannylimidazole (**2d**) in 91% yield (Scheme 3).

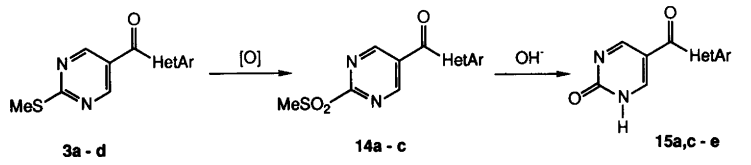
The coupling of 1-methyl-5-tributylstannylimidazole (**2d**) with 2-methylthiopyrimidine-5-carbonyl chloride (**1**) was run without catalyst to give **3d** in 62% yield. A small amount of **3c** (<3%, from ^{1}H NMR) was also observed due to coupling in the 2-position of imidazole. We believe that the coupled product in the 2-position of imidazole must come from an *in situ* rearrangement of the starting material, intermediates or products since careful analysis of the 5-tributylstannylimidazole **2d** did not reveal the presence of any 2-tributylstannylimidazole **2c**. When the coupling was run in the presence of a catalytic amount of palladium, lower yields of the product **3d** (25–31%) than in the uncatalyzed reaction were obtained. In addition the amount of the product coupled in the 2-position of the imidazole (**3c**) increased (4–8%, from ^{1}H NMR spectroscopy). Change of solvent to toluene, change of catalyst from bis(triphenylphosphine)-



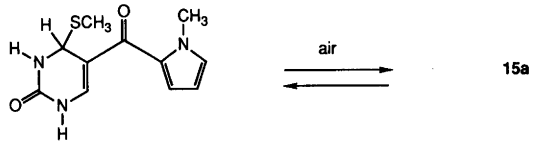
Scheme 2.



Scheme 3.



a HetAr = 1-Methylpyrrol-2-ylcarbonyl
b HetAr = 1-Phenylsulfonylpyrrol-3-ylcarbonyl
c HetAr = 1-Methylimidazol-2-ylcarbonyl
d HetAr = 1-Methylimidazol-5-ylcarbonyl
e HetAr = Pyrrol-3-ylcarbonyl



Scheme 4.

palladium(II) dichloride to tetrakis(triphenylphosphine)-palladium(0) and variation in the reaction temperature, did not significantly increase the yield of **3d**.

The decreased yield of coupling product when Pd-catalysis was attempted, was unexpected. In separate experiments it was found that the 5-stannylimidazole **2d** was not affected by the palladium catalyst after a period of 3 days. When methanol was added to a solution of **2d** in $CDCl_3$ the ^1H NMR spectrum remained unchanged for 6 h. Also, benzoyl chloride reacted with the 5-stannylimidazole **2d** in the presence of a palladium catalyst to give a low yield of 5-coupled product ($\approx$10%).

In order to convert the 2-methylthiopyrimidines **3** into 2-pyrimidinones **15**,[1] the sulfides **3a**, **3b** and **3c** were oxidized to the sulfones **14** followed by alkaline hydrolysis. In the case of **3d** direct hydrolysis of the sulfide to the corresponding 2-pyrimidinone **15d** was feasible. Attempts to hydrolyze the methyl sulfide **3a** directly to the 2-pyrimidinone **15a** with 2 M NaOH gave, however, a mixture of the methylthio adduct **16** and the free 2-pyrimidinone **15a** in a ratio of 4:1; the former is formed by thiol addition to **15a** which is reversible. The equilibrium could be shifted towards the free 2-pyrimidinone **15a** by treatment of the adduct with air (see the Experimental and Scheme 4).

Experimental

The mass spectra under electron impact conditions were recorded at 70 eV. Isobutane was used for chemical ionization (CI). The spectra are presented as *m/z* (% rel. int.). The ^1H NMR spectra were recorded at 200 MHz or 300 MHz and the ^{13}C NMR spectra at 50 MHz or 75 MHz. Dichloromethane was distilled from CaH_2.

Compounds available by literature methods: 2-Methylthiopyrimidine-5-carbonyl chloride (**1**).[2b] 1-Methyl-2-tributylstannylpyrrole (**2a**).[6] 1-Methyl-2-tributylstannylimidazole (**2c**).[16] 2-Methylthio-5-tributylstannylpyrimidine (**4**).[11] 1-Methylpyrrole-2-carbonyl chloride (**5a**).[10]

1-Methyl-(5-tributylstannyl)imidazole **2d**. 1-Methylimidazole (1.60 ml, 20.1 mmol) was added slowly to a mixture of BuLi (1.6 M in hexane; 30.2 ml, 48.3 mmol) and TMEDA (7.16 ml, 47.7 mmol) in dry hexane (20 ml) under N_2 at $-20°C$. The reaction mixture was stirred for 30 min at $-20°C$ and at ambient temperature for 1 h, cooled to $-20°C$ again and tributylstannyl chloride (13.4 ml, 49.6 mmol) in hexane (10 ml) was added dropwise. The mixture was stirred for 15 min at $-20°C$ and at ambient temperature for 18 h, before ethyl acetate (10 ml) and water (10 ml) were added. The organic phase was separated and the aqueous phase extracted with ethyl acetate (10 ml). The combined organic phases were dried ($MgSO_4$), evaporated and the crude product was purified by chromatography on silica gel (EtOAc–MeOH 96:4); yield 6.78 g (91%). Anal. $C_{16}H_{32}N_2Sn$: C,H. ^1H NMR ($CDCl_3$): δ 0.83–1.65 ($SnBu_3$), 3.61 (CH_3N), 6.96 (H-4, s), 7.55 (H-2, s). ^{13}C NMR ($CDCl_3$): δ 9.9, 13,4, 27.0, 28.9 ($SnBu_3$), 34.7 (CH_3N), 129.5 (C-5), 138.8 and 140.8 (C-2,4). MS: 315 (100), 314 (38), 313 (75), 312 (30), 311 (44), 259 (50), 257 (40), 203 (56), 201 (84), 200 (30), 199 (58), 197 (23), 121 (28), 83 (30).

5-(1-Methylpyrrol-2-ylcarbonyl)-2-methylthiopyrimidine **3a**. *Method A.* A solution of 1-methylpyrrole-2-carbonyl chloride (2.90 g, 20.2 mmol) in dry THF was added to a mixture of 2-methylthio-5-tributylstannylpyrimidine (6.00 g, 14.4 mmol) and bis(triphenylphosphine)palladium(II) dichloride (0.406 g, 0.58 mmol) in dry THF. The mixture was refluxed under N_2 for 6 h before the cooled reaction mixture was evaporated and the crude product purified by chromatography on silica gel (light petroleum–EtOAc 3:1); yield 2.43 g (72%), m.p. 81–82°C. Anal. $C_{11}H_{11}N_3OS$: H. Calc. C, 56.63. Found 57.13. Found: *M*, 233.0620. Calc. for $C_{11}H_{11}N_3OS$: 233.0623. ^{1}H NMR ($CDCl_3$): δ 2.61 (CH_3S), 4.01 (CH_3N), 6.19 (H-4′, dd), 6.74 (H-3′, dd, $J_{3',4'}$ 4.5 Hz, $J_{3',5'}$ 1.6 Hz), 6.96 (H-5′, dd, $J_{3',5'}$ 1.6 Hz, $J_{4',5'}$ 2.6 Hz), 8.88 (H-4,6, s). ^{13}C NMR ($CDCl_3$): δ 15.0 (CH_3S), 37.8 (CH_3N), 108.6 (C-4′), 122.2 (C-3′), 127.5 (C-5), 129.3 (C-2′), 131.9 (C-5′), 156.3 (C-4,6), 174.5 (C-2), 179.7 (C=O). MS: 233 (100, *M*), 232 (30), 218 (11), 186 (7), 158 (16), 137 (23), 133 (11), 108 (45), 80 (17), 78 (12).

Method B. A mixture of 2-methylthiopyrimidine-5-carbonyl chloride (0.100 g, 0.53 mmol), $Pd_2(dba)_3(CHCl_3)$ (0.022 g, 0.02 mmol) and triphenylarsine (0.052 g, 0.17 mmol) in dry THF (5 ml) was stirred under N_2 for 10 min before a solution of 1-methyl-2-tributylstannylpyrrole (0.216 g, 0.58 mmol) in dry THF was added. The mixture was stirred under N_2 at ambient temperature for 7 h and evaporated and the crude product was purified by chromatography on silica gel (light petroleum–EtOAc 3:1); yield 0.089 g (72%).

2-Methylthio-5-(1-phenylsulfonylpyrrol-3-ylcarbonyl)-pyrimidine **3b**. The title compound was prepared as for **3a** (Method A) above, yield 61%, m.p. 137–138°C. Anal. $C_{16}H_{13}N_3O_3S_2$: C, H. ^{1}H NMR ($CDCl_3$): δ 2.60 (CH_3S), 6.76 (H-4′, dd), 7.23 (H-5′, dd, $J_{2',5'}$ 2.1 Hz, $J_{4',5'}$ 3.3 Hz), 7.51–7.62 (3H, Ph, m), 7.67 (H-2′, dd, $J_{2',4'}$ 1.7 Hz, $J_{2',5'}$ 2.1 Hz), 7.91 (2H, Ph, m), 8.88 (H-4,6, s). ^{13}C NMR ($CDCl_3$) δ 14.3 (CH_3S), 113.5 (C-4′), 122.1 (C-5′), 125.7 (C-2′), 126.6 (C-5 or C-3′), 127.2 (C-2″,6″), 129.8 (C-3″,5″), 134.8 (C-4″), 137.8 (C-1″), 157.2 (C-4,6), 176.8 (C-2), 185.3 (C=O). MS: 359 (65, *M*), 234 (6), 218 (19), 190 (5), 153 (2), 141 (16), 125 (6), 94 (12), 78 (24), 77 (100). In addition *2-methylthio-5-(1-phenylsulfonylpyrrol-3-yl)-pyrimidine* **9** (7%; *vide infra*) and 2,2′-bis(methylthio)-5,5′-bipyrimidine **10**[12] (18%) were isolated.

5-(1-Methylimidazol-2-ylcarbonyl)-2-methylthiopyrimidine **3c**. 2-Methylthiopyrimidine-5-carbonyl chloride (2.38 g, 12.62 mmol) in dry THF (60 ml) was added dropwise to a solution of 1-methyl-2-tributylstannylimidazole (5.70 g, 15.36 mmol) in dry THF (60 ml) at −78°C. The reaction mixture was stirred under N_2 in the cooling bath which was allowed to reach ambient temperature. After 24 h the solvent was evaporated off and the crude product triturated with light petroleum (3 × 20 ml) to give an analytically pure product; yield 2.38 g (81%), m.p. 111°C. Anal. $C_{10}H_{10}N_4OS$: C, H. ^{1}H NMR ($CDCl_3$): δ 2.63 (CH_3S), 4.10 (CH_3N), 7.17 and 7.25 (H-4′,5′, s), 9.44 (H-4,6, s). ^{13}C NMR ($CDCl_3$): δ 14.3 (CH_3S), 36.4 (CH_3N), 125.8 (C-5), 127.6 and 129.9 (C-4′,5′), 142.3 (C-2′), 159.1 (C-4,6), 176.4 (C-2), 179.8 (C=O). IR (KBr): 1635 cm^{-1} (CO). MS: 234 (14, *M*), 233 (20), 219 (18), 161 (28), 160 (12), 110 (11), 109 (93), 106 (12), 83 (17), 82 (31), 81 (25), 53 (100).

5-(1-Methylimidazol-5-ylcarbonyl)-2-methylthiopyrimidine **3d**. A solution of 1-methyl-5-tributylstannylimidazole (1.34 g, 3.61 mmol) in dry THF (25 ml) was added dropwise to a solution of 2-methylthiopyrimidine-5-carbonyl chloride (0.62 g, 3.29 mmol) in dry THF (25 ml) at ambient temperature. The reaction mixture was stirred under N_2 for 24 h at ambient temperature, the solvent was evaporated off and the crude product was purified by chromatography on silica gel (EtOAc–MeOH 96:4); yield 0.475 g (62%), m.p. 156–158°C. Anal. $C_{10}H_{10}N_4OS$: C,H. ^{1}H NMR ($CDCl_3$): δ 2.62 (CH_3S), 4.03 (CH_3N), 7.66 and 7.80 (H-2′,4′, s), 8.92 (H-4,6, s). ^{13}C NMR ($CDCl_3$): δ 14.4 (CH_3S), 34.7 (CH_3N), 126.7 and 129.6 (C-5,5′), 140.7 and 144.3 (C-2′,4′), 156.9 (C-4,6), 176.7 (C-2), 180.5 (C=O). IR (KBr): 1618 cm^{-1} (CO). MS: 235 (13), 234 (100, *M*), 219 (5), 153 (6), 133 (14), 109 (30), 83 (12), 81 (15), 69 (29).

1-Phenylsulfonylpyrrole-3-carbonyl chloride **5b**. 1-Phenylsulfonylpyrrole-3-carboxylic acid (1.00 g, 3.98 mmol) in thionyl chloride (25 ml) was stirred under N_2 at ambient temperature for 2 h before the thionyl chloride was evaporated off. The crude product was purified by chromatography on silica gel (light petroleum–EtOAc 3:1); yield 0.634 g (59%), m.p. 90–92°C. Found: *M* 268.9917. Calc. for $C_{11}H_8ClNO_3S$: 268.9913. ^{1}H NMR ($CDCl_3$): δ 6.69 (H-4, dd), 7.16 (H-5, dd, $J_{2,5}$ 2.3 Hz, $J_{4,5}$ 3.4 Hz), 7.5–7.7 (3 H, Ph, m), 7.92 (H-2, dd, $J_{2,4}$ 1.6 Hz, $J_{2,5}$ 2.3 Hz), 7.95 (2 H, Ph, m). ^{13}C NMR ($CDCl_3$): δ 113.6 (C-4), 122.1 (C-5), 124.6 (C-3), 127.3 (C-2′,6′), 128.7 (C-2), 129.9 (C-3′,5′), 135.0 (C-4′), 137.4 (C-1′), 160.7 (C=O). MS: 271/269 (2/5, *M*), 235 (31), 234 (100), 141 (59), 125 (12), 115 (8), 94 (14), 93 (45), 78 (23), 77 (100).

1-Phenylsulfonylpyrrole **6**. Lithium diisopropylamide (2 M solution in cyclohexane, ethylbenzene and THF, 60 ml, 120 mmol) was added to a solution of pyrrole (6.76 g, 101 mmol) in THF (70 ml) under N_2 at −78°C. The reaction mixture was stirred at ambient temperature for 2 h, cooled to −78°C and benzenesulfonyl chloride (19.3 g, 109 mmol) in dry THF (70 ml) added dropwise. The mixture was stirred for 2 h at −78°C, water (10 ml) was carefully added, the THF evaporated off and the residue extracted into dichloromethane. The organic phase was washed with a solution of 0.1 M HCl (350 ml) and NH_4Cl (50 g). The aqueous phase was separated and extracted with dichloromethane (3 × 70 ml). The com-

bined organic phases were washed with a solution of 0.1 M HCl (350 ml) and NH_4Cl (50 g), before it was dried ($MgSO_4$) and evaporated. The crude product was recrystallized from methanol (charcoal); yield 20.0 g (96%), m.p. 90–91°C, lit. 89–89.5°C.[13]

1-Phenylsulfonylpyrrole-3-carboxylic acid **8**. Compound **8** was made from 3-acetyl-1-phenylsulfonylpyrrole **7** by analogy with a literature procedure;[14] yield (86%), m.p. 155–157°C. Anal. $C_{11}H_9NO_4S$: H. Calc. C, 52.58. Found C, 51.97. Found: *M* 251.0251. Calc. for $C_{11}H_9NO_4S$: 251.0252. ^1H NMR ($CDCl_3$): δ 6.68 (H-4, dd) 7.13 (H-5, dd, $J_{2,5}$ 2.4 Hz, $J_{4,5}$ 3.3 Hz), 7.50–7.65 (3H, Ph, m), 7.84 (H-2, dd, $J_{2,4}$ 1.5 Hz, $J_{2,5}$ 2.4 H2), 7.91 (2 H,. Ph, m). ^{13}C NMR ($CDCl_3$): δ 113.6 (C-4), 119.8 (C-3), 121.3 (C-5), 126.2 (C-2), 127.1 (C-2',6'), 129.6 (C-3',5'), 134.4 (C-4'), 138.0 (C-1'), 168.2 (C=O). MS: 251 (23, *M*), 234 (1), 142 (2), 141 (20), 125 (2), 115 (2), 94 (5), 93 (32), 78 (7), 77 (100).

2-Methylthio-5-(1-phenylsulfonylpyrrol-3-yl)-pyrimidine **9**. M.p. 134–136°C. Found: *M* 331.0443. Calc. for $C_{15}H_{13}N_3O_2S_2$: 331.0449. ^1H NMR ($CDCl_3$): δ 2.56 (CH_3S), 6.55 (H-4', dd), 7.25 (H-5', dd, $J_{2',5'}$ 2.2 Hz, $J_{4',5'}$ 3.3 Hz), 7.43 (H-2', dd, $J_{2',4'}$ 1.7 Hz, $J_{2',5'}$ 2.2 Hz), 7.52–7.63 (3 H, Ph, m), 7.91 (2 H, Ph, m), 8.60 (H-4,6, s). ^{13}C NMR ($CDCl_3$): δ 14.0 (CH_3S), 111.2 (C-4'), 116.3 (C-2'), 122.2 (C-5'), 122.4 (C-5 or C-3'), 122.6 (C-5 or C-3'), 126.8 (C-2",6"), 129.4 (C-3",5"), 134.1 (C-4"), 138.3 (C-1"), 153.7 (C-4,6), 170.5 (C-2). MS: 331 (84, *M*), 298 (2), 191 (14), 190 (100), 163 (10), 141 (5), 90 (11), 78 (13), 77 (48).

5-(1-Methylpyrrol-2-ylcarbonyl)-2-methylsulfonylpyrimidine **14a**. MCPBA (0.444 g, 2.57 mmol) was added to a solution of 5-(1-methylpyrrol-2-ylcarbonyl)-2-methylthiopyrimidine (0.200 g, 0.86 mmol) in dichloromethane (5 ml) under N_2. The reaction mixture was stirred at ambient temperature for 18 h, triturated with saturated aqueous sodium hydrogen sulfite (3 × 10 ml) and with saturated $NaHCO_3$ (3 × 10 ml) and the dried ($MgSO_4$) solution was evaporated. The crude product was recrystallized from EtOAc–hexane; yield 0.186 g (82%), m.p. 157°C (EtOAc–hexane). Anal. $C_{11}H_{11}N_3O_3S$: C, H. ^1H NMR ($CDCl_3$): δ 3.39 (CH_3SO_2), 4.04 (CH_3N), 6.24 (H-4', dd), 6.70 (H-3', dd, $J_{3',4'}$ 4.3 Hz, $J_{3',5'}$ 1.6 Hz), 7.05 (H-5', dd, $J_{3',5'}$ 1.6 Hz, $J_{4',5'}$ 2.4 Hz), 9.19 (H-4,6, s). ^{13}C NMR ($CDCl_3$): δ 37.7 (CH_3N), 39.5 (CH_3SO_2), 109.6 (C-4'), 123.9 (C-3'), 129.1 (C-2'), 133.7 (C-5'), 134.8 (C-5), 157.8 (C-4,6), 166.3 (C-2), 178.0 (C=O). MS: 265 (43, *M*), 264 (10), 186 (66), 172 (10), 159 (16), 158 (10), 108 (100), 94 (16), 80 (20), 79 (5).

2-Methylsulfonyl-5-(1-phenylsulfonylpyrrol-3-ylcarbonyl)-pyrimidine **14b**. MCPBA (55%, 2.18 g, 6.95 mmol) in dry dichloromethane (55 ml) was added to a solution of 2-methylthio-5-(1-phenylsulfonylpyrrol-3-ylcarbonyl)pyrimidine (0.500 g, 1.39 mmol) in dichloromethane (17 ml) under N_2. The reaction mixture was stirred at ambient temperature for 2 h, triturated with saturated aqueous sodium hydrogen sulfite (3 × 40 ml) and with sodium hydrogen carbonate (3 × 40 ml) and the dried ($MgSO_4$) solution was evaporated; yield 0.518 g (95%), m.p. 213–215°C. Anal. $C_{16}H_{13}N_3O_5S_2$: C, H. ^1H NMR (DMSO-d_6): δ 3.48 (CH_3SO_2), 6.87 (H-4', dd), 7.62 (H-5', dd, $J_{2',5'}$ 2.2 Hz, $J_{4',5'}$ 3.3 Hz), 7.65–7.81 (3 H, Ph, m), 8.12 (2 H, Ph, m), 8.29 (H-2', dd, $J_{2',4'}$ 1.7 Hz, $J_{2',5'}$ 2.2 Hz), 9.35 (H-4,6, s). ^{13}C NMR (DMSO-d_6): δ 38.5 (CH_3SO_2), 112.9 (C-4'), 123.0 (C-5'), 126.8 (C-3'), 127.4 (C-2",6"), 128.9 (C-2'), 130.1 (C-3",5"), 133.7 (C-5), 135.4 (C-4"), 137.0 (C-1"), 158.5 (C-4,6), 166.5 (C-2), 184.7 (C=O). MS: 391 (15, *M*), 363 (1), 250 (1), 234 (2), 142 (4), 141 (46), 93 (7), 78 (8), 77 (100).

5-(1-Methylpyrrol-2-ylcarbonyl)-2(1H)-pyrimidinone **15a**. 2 M Sodium hydroxide (2.4 ml, 4.8 mmol) was added to a suspension of 5-(1-methylpyrrol-2-ylcarbonyl)-2-methylsulfonylpyrimidine (0.639, 2.41 mmol) in dioxane (10 ml) and water (10 ml). The reaction mixture was stirred at ambient temperature for 30 min, acidified with 1 M HCl and the precipitate collected and dried; yield 0.436 g (89%), m.p. 202–204°C. Anal. $C_{10}H_9N_3O_2$: C, H. ^1H NMR (DMSO-d_6): δ 3.86 (CH_3N), 6.17 (H-4', dd), 6.86 (H-3', dd, $J_{3',4'}$ 4.0 Hz, $J_{3',5'}$ 1.5 Hz), 7.25 (H-5', dd, $J_{3',5'}$ 1.5 Hz, $J_{4',5'}$ 2.5 Hz), 8.60 (H-4,6, s). ^{13}C NMR (DMSO-d_6): δ 36.4 (CH_3N), 107.6 (C-4'), 115.2 (C-5), 120.3 (C-3'), 128.0 (C-2'), 131.5 (C-5'), 154.5 (C-2), 156.4 (C-4,6), 177.5 (C≡O). MS: 203 (100, *M*), 202 (79), 188 (6), 174 (16), 133 (19), 123 (4), 120 (15), 108 (50), 95 (16), 80 (28).

5-(1-Methylimidazol-2-ylcarbonyl)-2(1H)-pyrimidinone **15c**. 1 M Sodium hydroxide (6 ml) was added to a solution of 5-(1-methylimidazol-2-ylcarbonyl)-2-methylsulfonylpyrimidine[22] (0.728 g, 2.73 mmol) in dioxane (26 ml) and water (26 ml) at 0°C. The reaction mixture was stirred at ambient temperature for 15 min, concentrated to ca. 10 ml on a rotary evaporator and acidified with acetic acid. The solution was left in the refrigerator for 12 h before the precipitate was collected and dried; yield 0.453 g (81%), m.p. 255°C. Anal. $C_9H_8N_4O_2$: C, H. ^1H NMR (DMSO-d_6): δ 3.97 (CH_3N), 7.21 and 7.60 (H-4',5', s), 9.24 (H-4,6, s). ^{13}C NMR (DMSO-d_6): δ 36.0 (CH_3N), 114.1 (C-5), 128.6 and 129.1 (C-4',5'), 141.9 (C-2'), 155.5 (C-2), 160.2 (C-4,6), 176.9 (C≡O). IR(KBr): 1610, 1680 cm^{-1} (CO). MS: 204 (51, *M*), 203 (100), 176 (33), 175 (44), 148 (28), 123 (13), 121 (37), 109 (24), 96 (31), 95 (26).

5-(1-Methylimidazol-5-ylcarbonyl)-2(1H)-pyrimidinone **15d**. 2 M Sodium hydroxide (8.8 ml) was added to a suspension of 5-(1-methylimidazol-5-ylcarbonyl)-2-methylthiopyrimidine (0.394 g, 1.68 mmol) in dioxane (5 ml) and water (5 ml) at 0°C. The reaction mixture was stirred at 65°C for 14 h before it was acidified with acetic acid to pH ca. 5. The solution was concentrated to ca. 5 ml

at reduced pressure and left in the refrigerator for 6 h before the precipitate was collected and dried; yield 0.163 g (47%), m.p. 272°C (decomp.). Found: *M* 204.0644. Calc. for $C_9H_8N_4O_2$: 204.0647. ^{1}H NMR (DMSO-d_6): δ 3.85 (CH_3N), 7.75 and 8.01 (H-2',4', s). 8.68 (H-4,6, s). ^{13}C NMR (DMSO-d_6): δ 33.4 (CH_3N), 114.8 (C-5), 128.6 (C-5'), 138.8 and 144.1 (C-2',4'), 155.2 (C-2), 157.7 (C-4,6), 178.2 (C=O). IR(KBr): 1615, 1670 cm^{-1} (CO). MS: 205 (12), 204 (100, *M*), 203 (70), 176 (13), 149 (17), 123 (15), 121 (18), 109 (54), 96 (29), 95 (17), 81 (37).

5-(Pyrrol-3-ylcarbonyl)-2-(1H)-pyrimidinone **15e**. 5 M Sodium hydroxide (10 ml, 50 mmol) was added to a suspension of 2-methylsulfonyl-5-(1-phenylsulfonyl-pyrrol-5-ylcarbonyl)pyrimidine (0.494 g, 1.26 mmol) in dioxane (10 ml). The reaction mixture was stirred at ambient temperature for 4 h, extracted with EtOAc (2 × 8 ml) and the aqueous phase was acidified to pH ca. 5 with conc. HCl. The solution was left in the refrigerator overnight and the precipitate collected and dried; yield 0.182 g (76%), m.p. 280–300°C (decomp.). Anal. $C_9H_7N_3O_2$: C, H. ^{1}H NMR (DMSO-d_6): δ 6.53 (H-4', dd), 6.91 (H-5', dd, $J_{2',5'}$ 2.3 Hz, $J_{4',5'}$ 4.2 Hz), 7.57 (H-2', dd, $J_{2',4'}$ 2.4 Hz, $J_{2',5'}$ 2.3 Hz), 8.64 (H-4,6, s). ^{13}C NMR (DMSO-d_6): δ 108.9 (C-4'), 116.2 (C-5), 120.2 (C-5'), 122.7 (C-3'), 125.5 (C-2'), 155.8 (C-2), 157.8 (C-4,6), 183.1 (C=O). MS: 189 (59, *M*), 188 (4), 161 (5), 160 (7), 133 (6), 123 (1), 119 (5), 95 (7), 94 (100).

3,4-Dihydro-5-(1-methylpyrrol-2-ylcarbonyl)-4-methylthio-2(1H)-pyrimidinone **16**. 2 M Sodium hydroxide (2.1 ml, 4.2 mmol) was added to a suspension of 5-(1-methylpyrrol-2-ylcarbonyl)-2-methylthiopyrimidine (0.100, 0.43 mmol) in dioxane (2 ml) and water (2 ml) at 0°C. The reaction mixture was stirred at 65°C for 2.5 h, acidified with 1 M HCl to pH 3.5 and left in the refrigerator for 24 h before the precipitate was collected; yield 0.069 g. The ^{1}H NMR spectrum of the product showed that it was a mixture of the title compound and the 2-pyrimidinone **15a** in the ratio 4:1. ^{1}H NMR (DMSO-d_6): δ 2.06 (CH_3S), 3.75 (CH_3N), 5.52 (H-4, d), 6.08 (H-4', dd), 6.66 (H-3', dd, $J_{3',4'}$ 3.9 Hz, $J_{3',5'}$ 1.7 Hz), 7.09 (H-5', dd, $J_{3',5'}$ 1.7 Hz, $J_{4',5'}$ 2.5 Hz), 7.18 (H-6, d), 8.05 (H-3, d, $J_{3,4}$ 3.3 Hz), 9.29 (H-1, d, $J_{1,6}$ 5.3 Hz). MS: 203 (M − MeSH, 100), 202 (70), 188 (5), 174 (14), 147 (10), 146 (11), 133 (15), 120 (11), 108 (40), 80 (22).

When air was bubbled through the solution of the dihydro isomer for 90 min, the adduct formation was in part reversed, the products in the solution by NMR analysis were **16** and **15a** in the ratio 2:3.

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