

Palladium Catalysis in the Synthesis of Hydroxymethylfuryl Pyrimidinyl Ketones

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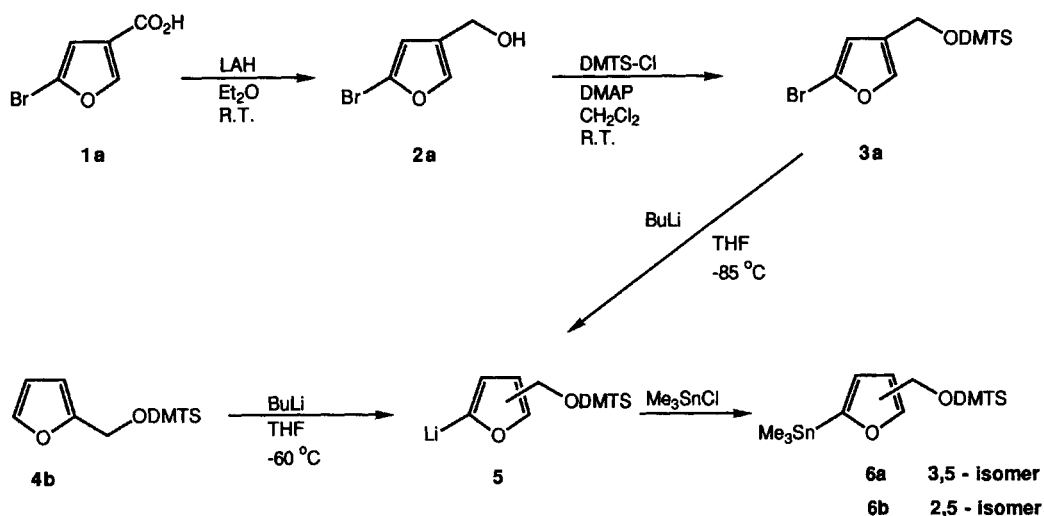
Furylmethyl silyl ethers have been stannylated by means of metal–metal exchange from the corresponding lithiofurans. Unsymmetrical heteroaryl ketones are formed in palladium-catalyzed coupling reactions between the stannylfurans and 2-methylthiopyrimidine-5-carbonyl chloride. Oxidation of the sulfenyl group and subsequent hydrolysis yield 5-furoyl-2(1*H*)-pyrimidinones.

5-Acylpyrimidines had received little attention up to the time when our study of methods for their preparation was started in order to make 5-acyl derivatives of pyrimidine systems available for biological evaluations.^{1–3} We are looking for compounds that will reversibly arrest the mitosis of cells in metaphase. Such compounds may be useful as growth-regulating adjuvants when used together with phase-specific antineoplastic drugs in treatment of diseases caused by uncontrolled, rapidly proliferating cells.⁴ Several N-1 substituted 5-halogeno-2(1*H*)-pyrimidinones are able to cause reversible arrest of cells in metaphase.^{4,5} Screening of 5-acylpyrimidinones has shown that certain 5-acyl derivatives of pyrimidinones have similar effects on the cell cycle.⁶ 5-Acyl derivatives are particularly attractive because of the possibility for fine manipulation of the electron-withdrawing effect from the acyl group by appropriate substitutions in the acyl moiety. In this report we describe

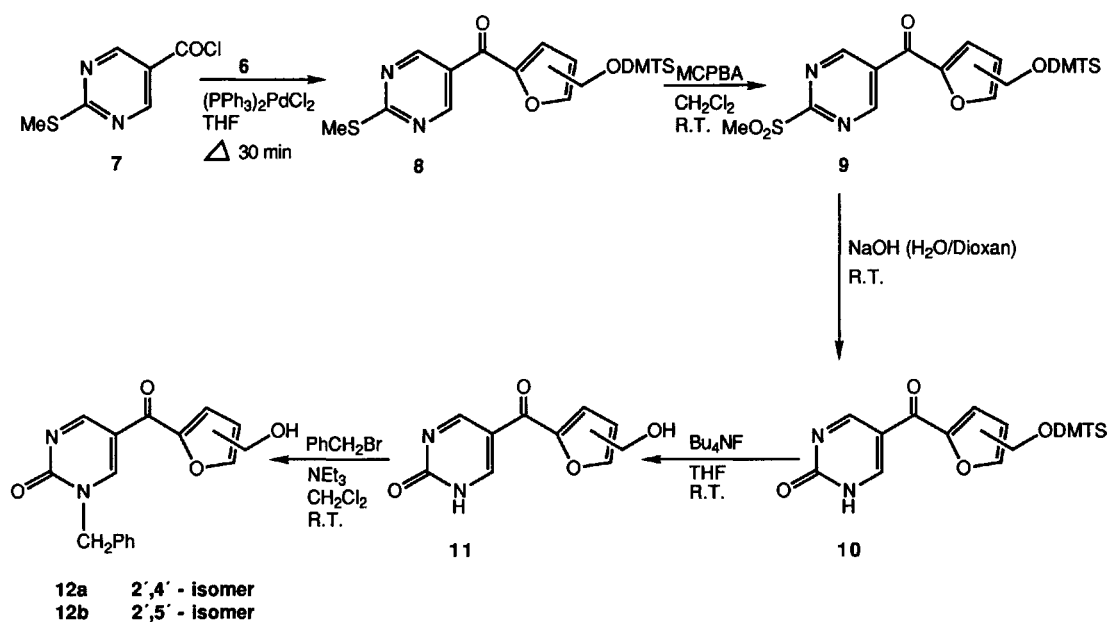
methods for introduction of hydroxyalkylfuranoyl substituents into the pyrimidine 5-position using palladium-mediated coupling reactions between stannylfurans and a pyrimidine-5-carbonyl chloride.

Scheme 1 shows the preparation of 5-trimethylstannyl derivatives of silyl protected 2- and 3-furylmethanol from the corresponding lithiofurans by metal–metal exchange. Since the hydrolytic stability of silyl ethers increases with the bulkiness of the silyl substituents,⁷ dimethylhexylsilyl (DMTS) ethers were used. These were prepared from the silyl chloride and the hydroxymethylfuran in pyridine solution in the presence of 4-*N,N*-dimethylaminopyridine (DMAP).

The silyl ether of 2-furylmethanol was lithiated in the 5-position with butyllithium at -60°C . Lithiation of 3-furylmethanol and silyl ethers is reported to yield a 2- and 5-lithiofuran isomer mixture.^{8,9} Selective lithiation of the



Scheme 1. DMTS = $\text{Me}_2\text{HexSi-}$



Scheme 2.

5-position in the 3-furylmethanol series was achieved by a halogen–metal exchange reaction between the bromo derivative **3a** and butyllithium at -85°C . The starting material in this series was 3-furylcarboxylic acid which was brominated in the 5-position. Literature methods failed to give both satisfactory yield and isomer purity of the desired product **1a**,¹⁰ which was best obtained by the treatment of 3-furancarboxylic acid with *N*-bromosuccinimide in acetic acid at ambient temperature. Reduction of the bromo acid **1a** with lithium aluminum hydride (LAH) gave the 3-furylmethanol **2a**.¹¹ Quenching of the lithiofuran **5** with trimethylstannyl chloride gave the 5-stannylfuran derivative **6**.

For the coupling reaction 2-methylthiopyrimidine-5-carboxylic acid was chosen because it is readily available from a cyclisation reaction from simple starting materials.² The pyrimidine-5-carboxylic acid as its carbonyl chloride **7** in tetrahydrofuran (THF), was coupled with the stannylfuran **6** using bis(triphenylphosphine)palladium(II) dichloride as a catalyst. The silyl ether function was not attacked by the stannyl chloride generated in the coupling reaction; for comparison, the *tert*-butyldimethylsilyl group on the pyrimidine-2-oxygen is cleaved under similar reaction conditions.³ For the chemoselective oxidation of the sulfide function to the sulfone **9** *m*-chloroperbenzoic acid (MCPBA) was used. Hydrolytic removal of the sulfonyl group proceeded readily under mild alkaline conditions; the hydrolysis is facilitated by the 5-acyl group (*para*-position). The 3-furylmethanol **11** was generated from its silyl protected precursor **10** by treatment of the latter with tetrabutylammonium fluoride in THF under anhydrous conditions. Finally the 5-furylpyrimidinone **12** was prepared by *N*-alkylation of **11** as its triethylamine salt with benzyl bromide.

Experimental

The ^1H and the ^{13}C NMR spectra were recorded in CDCl_3 at 60 and 75 MHz respectively, unless otherwise specified. The mass spectra were recorded under electron impact conditions at 70 eV ionization voltage. Isobutane or ammonia was used for chemical ionization (CI).

5-Bromo-3-furancarboxylic acid (1a). *N*-Bromosuccinimide (3.20 g, 18.0 mmol) was added with stirring to a solution of 3-furancarboxylic acid in acetic acid (10 ml) at ambient temperature. The reaction was weakly exothermic. The mixture was stirred at ambient temperature for 24 h and evaporated. The residual oil was extracted with diethyl ether, leaving behind the succinimide, and the ether solution evaporated. The residual reddish oil was triturated with water and the resultant solid crystallized from water; yield 1.40 g (41%), m.p. 136°C .^{9a} ^1H NMR: δ 6.70 (H-4), 8.10 (H-2).

5-Bromo-3-furylmethanol (2a). A solution of 5-bromo-3-furancarboxylic acid (1.58 g, 8.27 mmol) in dry diethyl ether (15 ml) was added dropwise with stirring to a solution of lithium aluminum hydride (0.34 g, 9.0 mmol) in dry diethyl ether (15 ml) at ambient temperature. The mixture was stirred for 15 min, after which 2 M NaOH (7 ml) was added. The two phases were separated and the ether solution was washed, dried (MgSO_4) and evaporated to give the product; yield 0.68 g (74%). ^1H NMR: δ 2.70 (OH), 4.50 (CH_2), 6.35 (H-4), 7.40 (H-2).¹⁰

5-Bromo-3-(dimethylhexylsilyloxymethyl)furan (3a). Dimethylhexylsilyl chloride (1.38 g, 7.40 mmol) was added dropwise with stirring to a solution of 5-bromo-3-furyl-

methanol (1.31 g, 7.40 mmol), triethylamine (0.91 g, 9.0 mmol) and DMAP (0.2 g) in dichloromethane (10 ml) at ambient temperature. The mixture was stirred at ambient temperature for 24 h when TLC monitoring showed the reaction to be complete. The mixture was filtered and the solid was washed with dichloromethane. The filtrate and washings were shaken with water (3×30 ml) and the organic solution was dried (MgSO₄) and evaporated. The residual oil was purified by flash chromatography on silica gel using light petroleum–EtOAc (7:3); the product was a colourless oil, 1.90 g (80%). Anal. C₁₃H₂₃BrO₂Si: C, H. ¹H NMR: δ 0.10 (SiMe₂), 0.9 and 1.10 (thx) 4.50 (CH₂), 6.30 (H-4), 7.30 (H-2). ¹³C NMR: δ (50 MHz): δ –3.26 (SiMe₂), 18.70, 20.49, 25.41, 34.39 (thx), 57.30 (CH₂O), 111.53 (C4), 122.75 (C3), 129.25 (C5), 141.20 (C2). MS: 320/318 (4/4, M), 235 (100), 233 (100), 207 (42), 205 (42), 161 (12), 159 (12), (84), 137 (75).

2-(Dimethylhexylsilyloxymethyl)furan (4b). Dimethylhexylsilyl chloride (17.88 g, 100 mmol) was added dropwise with stirring at –60°C to a solution of freshly distilled 2-furylmethanol (10.00 g, 100 mmol), triethylamine (15.15 g, 150 mmol) and DMAP (0.2 g) in dichloromethane (50 ml). The mixture was stirred at –60°C for 2 h, allowed to reach ambient temperature and stirred for 20 h when TLC showed the reaction to be complete. The mixture was filtered and the solid washed with dichloromethane. The filtrate and washings were shaken with water (3×100 ml) and the organic solution was dried (MgSO₄), evaporated. The residual oil was distilled to yield a colourless liquid, b.p. 76–78°C/0.03 mmHg, yield 20.00 g (83%). Anal. C₁₃H₂₄O₂Si: C, H. ¹H NMR: δ 0.20 (SiMe₂), 1.0 (thx), 4.70 (CH₂), 6.3 (H-3,4), 7.5 (H-5). ¹³C NMR: δ –3.42 (SiMe₂), 18.39, 20.22, 25.21, 34.14 (thx), 57.87 (CH₂O), 106.85 (C3), 110.02 (C4), 141.73 (C5), 154.47 (C2). MS(Cl): 241 (0.7, M+H), 172 (7), 159 (3), 156 (5), 155 (38), 123 (8), 98 (17), 76 (100).

3-Dimethylhexylsilyloxymethyl-5-(trimethylstannyl)furan (6a). Butyllithium in hexane (1.6 M; 4.40 ml, 7.04 mmol) was added dropwise, by means of a syringe, to a stirred solution of 5-bromo-3-dimethylhexylsilyloxymethylfuran (1.77 g, 5.55 mmol) in dry THF (25 ml) under argon at –85°C. The mixture was stirred at –70°C for 60 min, after which the temperature was lowered to –85°C and a solution of trimethylstannyl chloride (1.40 g, 7.04 mmol) in dry THF (5 ml) added dropwise with stirring. The mixture was stirred at –85°C for 10 min before the mixture was allowed to reach ambient temperature and the stirring was continued for 3 h. The mixture was then poured into 10% aqueous NH₄Cl (10 ml) and the resultant mixture was stirred vigorously for 5 min. The two phases were separated, the aqueous phase extracted with diethyl ether (3×20 ml), and the combined organic phases were washed with water (3×20 ml), dried (MgSO₄) and filtered. The filtrate was evaporated and the product was purified by distillation (Kugelrohr); yield 1.80 g (80%), b.p.

170°C/0.03 mmHg. Anal. C₁₆H₃₂O₂SiSn: C, H. ¹H NMR: δ 0.20 (SiMe₂), 0.32 (SnMe₃), 1.0 and 1.70 (thx), 4.70 (CH₂), 6.70 (H-4), 7.70 (H-2). MS: 403 (11, M), 336 (10), 334 (5), 319 (4), 262 (7), 260 (5), 258 (6), 256 (18), 254 (11), 186 (8), 184 (10), 182 (100), 181 (29), 180 (37), 179 (28), 178 (29).

2-Dimethylhexylsilyloxymethyl-5-trimethylstannylfuran (6b). Butyllithium in hexane (1.6 M; 15.62 ml, 25.0 mmol) was added dropwise with stirring by means of a syringe, to a solution of 2-(dimethylhexylsilyloxymethyl)furan (5.0 g, 20.80 mmol) in dry THF (50 ml) under argon at –60°C. The mixture was stirred at this temperature for 10 min, after which the temperature was allowed to rise to 20°C over 20 min, then lowered to –60°C and a solution of trimethylstannyl chloride (5.0 g, 25.0 mmol) in dry THF (10 ml) was added dropwise with stirring. The mixture was stirred at –60°C for 10 min and the mixture allowed to reach ambient temperature. The stirring was continued for 3 h, after which the mixture was poured into 10% aqueous NH₄Cl (30 ml). The two phases were separated, and the aqueous phase was extracted with diethyl ether (3×50 ml). The combined organic phases were washed with water (4×50 ml), dried (MgSO₄) and filtered, and the filtrate evaporated. The product was purified by distillation; yield 6.20 g (74%), b.p. 92–96°C/0.005 mmHg. Anal. C₁₆H₃₂O₂SiSn: C, H. ¹H NMR: δ 0.20 (SiMe₂), 0.40 (SnMe₃), 1.0–1.7 (thx), 4.80 (CH₂), 6.40 and 6.66 (H-3,4). ¹³C NMR (50 MHz): δ –9.11 (SnMe₃), –3.13 (SiMe₂), 18.71, 20.52, 25.46, 34.41 (thx), 58.45 (CH₂O), 107.46 (C4), 122.03 (C-3), 159.65 (C5), 160.65 (C2). MS: 408/407/406/405/404/403/402/401 (3/6/11/15/13/15/12/15, M), 387 (15), 383 (16), 336 (46), 335 (42), 334 (30), 332 (21), 329 (20), 326 (33), 325 (72), 324 (42), 323 (58), 322 (28), 321 (45), 255 (31), 245 (100), 243 (74), 242 (30), 241 (52), 182 (81), 180 (55), 178 (34).

2-Methylthio-5-(4-dimethylhexylsilyloxymethyl-2-furoyl)pyrimidine (8a). A mixture of bis(triphenylphosphine)palladium(II) dichloride (0.80 g, 1.1 mmol), 2-methylthiopyrimidine-5-carbonyl chloride (2.82 g, 15.0 mmol) and 3-(dimethylhexylsilyloxymethyl-5-trimethylstannyl)furan (5.83 g, 14.4 mmol), in dry THF (120 ml) was heated under reflux for 30 min when TLC monitoring showed that the reaction had gone to completion. The reaction mixture was concentrated to a quarter of its volume and diethyl ether added to the cold mixture. The washed (aqueous NaCl; 3×20 ml) and dried (MgSO₄) solution was evaporated and the product purified by flash chromatography on silica gel using light petroleum–EtOAc (4:1). The product was an oil; yield 4.34 g (73%). Anal. C₁₉H₂₈N₂O₃SSi: C, H. ¹H NMR: δ 0.10 (SiMe₂), 1.8 and 1.40 (thx), 2.60 (SMe), 4.55 (CH₂), 7.20 (H-5'), 7.55 (H-2'), 9.05 (H-4,6). ¹³C NMR: δ –3.62 (SiMe₂), 14.07 (SMe), 18.30, 20.10, 25.03, 33.98 (thx), 56.55 (CH₂O), 113.32 (C4'), 119.25 (C3'), 129.19 (C5), 143.88 (C5'), 157.59 (C4,6), 152.30 (C2'), 176.64 (C2), 177.58 (C=O, ketone). MS(Cl): 393 (100, M+H), 379 (3), 324 (4), 313 (3), 309 (6), 307 (7), 279 (2), 251 (10).

2-Methylthio-5-(5-dimethylhexylsilyloxymethyl-2-furoyl)-pyrimidine (8b). Compound **8b** was prepared as above from 2-methylthiopyrimidine-5-carbonyl chloride (15 mmol), 2-(dimethylhexylsilyloxymethyl-5-trimethylstannyl)furan (14.4 mmol) in the presence of bis(triphenylphosphine)palladium(II) dichloride (1.1 mmol) in THF (120 ml). The mixture was heated under reflux for 30 min and the product was purified as described above. The product was a pale yellow oil; yield 77 %. Anal. $C_{19}H_{28}N_2O_3SSi$: C, H. 1H NMR: δ 0.10 (SiMe₂), 1.8 and 1.40 (thx), 2.60 (SMe), 4.55 (CH₂), 7.20 (H-5'), 7.55 (H-3'), 9.05 (H-4,6). ^{13}C NMR: δ -3.62 (SiMe₂), 14.07 (SMe), 18.30, 20.10, 25.03, 33.98 (thx), 56.55 (CH₂O), 113.32 (C4'), 119.25 (C3'), 129.19 (C5), 148.88 (C5'), 157.59 (C4,6), 152.30 (C2'), 176.64 (C2), 177.58 (C=O, ketone). MS(Cl): 393 (100, M+H), 379 (3), 324 (4), 313 (3), 309 (6), 307 (7), 279 (2), 251 (10).

2-Methylsulfonyl-5-(4-dimethylhexylsilyloxymethyl-2-furoyl)pyrimidine (9a). A solution of 2-methylthio-5-(4-dimethylhexylsilyloxymethyl-2-furoyl)pyrimidine (1.20 g, 3.06 mmol) and MCPBA (1.55 g, 9.0 mmol) in dichloromethane (80 ml) was stirred at ambient temperature for 3 h when TLC monitoring showed the reaction to be complete. The mixture was then shaken with saturated aqueous sodium hydrogen sulfite (3×40 ml), and then with saturated aqueous sodium hydrogen carbonate (3×40 ml) and the solution dried (MgSO₄) and evaporated. The residual product was purified by flash chromatography on silica gel using light petroleum–EtOAc (1:1); yield 1.20 g (81 %) of an oily material. 1H NMR: δ 0.10 (SiMe₂) and 1.5 (thx), 3.30 (SO₂Me), 4.70 (CH₂), 7.40 (H-3'), 7.70 (H-5'), 9.50 (H-4,6). ^{13}C NMR: δ -3.65 (SiMe₂), 18.28, 20.09, 25.04, 33.94 (thx), 39.02 (SO₂Me), 56.42 (CH₂O), 113.88 (C4'), 120.71 (C3'), 129.96 (C5), 145.09 (C5'), 151.64 (C2'), 159.01 (C4,6), 167.23 (C2), 179.98 (C=O, ketone). MS(Cl): 442 (100, M+H), 427 (6), 426 (14), 425 (46), 395 (8), 393 (29), 363 (5), 362 (11), 356 (7).

2-Methylsulfonyl-5-(5-dimethylhexylsilyloxymethyl-2-furoyl)pyrimidine (9b). Compound **9b** was prepared from 2-methylthio-5-(5-dimethylhexylsilyloxymethyl-2-furoyl)pyrimidine by oxidation with MCPBA as described above; yield 92 %, non-crystalline solid. Anal. $C_{19}H_{28}N_2O_5SSi$: C, H. 1H NMR: δ 0.13 (SiMe₂), 0.9 and 1.50 (thx), 3.40 (SO₂Me), 4.80 (CH₂), 6.60 (H-4', d, *J* 4.0 Hz), 7.50 (H-3', d), 9.40 (H-4,6). ^{13}C NMR: δ -3.32 (SiMe₂), 18.67, 20.41, 25.45, 34.33 (thx), 39.48 (SO₂Me), 58.72 (CH₂O), 110.82 (C4'), 123.78 (C3'), 132.79 (C5), 151.27 (C5'), 159.65 (C4,6), 163.03 (C2'), 167.93 (C2), 176.52 (C=O, ketone). MS (Cl): 425 (100, M+H), 409 (4), 356 (7), 341 (10), 340 (15), 339 (72), 265 (6), 233 (3).

5-(4-Dimethylhexylsilyloxymethyl-2-furoyl)-2(1H)-pyrimidinone (10a). 2 M NaOH (12 ml) was added to a mixture of 2-methylsulfonyl-5-(4-dimethylhexylsilyloxymethyl-2-fur-

oyl)pyrimidine (3.26 g, 7.7 mmol) in dioxane–water (1:1; 40 ml), and the mixture stirred at ambient temperature for 15 min when all the solid had dissolved. The pH of the solution was adjusted to ca. 6 by gradual addition of acetic acid whereupon the product precipitated; yield 1.95 g (70 %), m.p. 160 °C. Anal. $C_{18}H_{26}N_2O_4Si$: C, H. 1H NMR: δ 0.10 (SiMe₂), 0.8 and 1.7 (thx), 4.60 (CH₂), 7.30 (H-5'), 7.60 (H-3'), 9.20 (H-4,6). ^{13}C NMR: δ -3.40 (SiMe₂), 18.52, 20.31, 25.23, 34.16, (thx), 56.77 (CH₂O), 115.60 (C4'), 119.22 (C3'), 129.51 (C5), 143.74 (C5'), 152.39 (C2'), 158.09 (C4,6), 159.37 (C2), 174.75 (C=O, ketone). MS (Cl): 363 (100, M+H), 361 (3), 295 (2), 294 (4), 279 (7), 278 (4), 277 (12), 222 (2), 221 (2).

5-(5-Dimethylhexylsilyloxymethyl-2-furoyl)-2(1H)-pyrimidinone (10b). Compound **10b** was prepared from 2-methylsulfonyl-5-(5-dimethylhexylsilyloxymethyl-2-furoyl)pyrimidine by hydrolysis with 2 M NaOH as described above; yield 82 %, m.p. 178–180 °C. Anal. $C_{18}H_{26}N_2O_4Si$: C, H. 1H NMR: δ 0.13 (SiMe₂), 0.9 and 1.6 (thx), 4.80 (CH₂), 6.50 (H-4', d, *J* 4.0 Hz), 7.40 (H-3', d), 9.20 (H-4,6). ^{13}C NMR (50 MHz): δ -3.29 (SiMe₂), 18.69, 20.45, 25.47, 34.36 (thx), 58.86 (CH₂O), 110.19 (C4'), 116.34 (C5), 121.84 (C3'), 151.73 (C5'), 158.92 (C2'), 160 (C2), 161.36 (C4,6), 171.11 (C=O, ketone). MS(Cl): 363 (100, M+H), 294 (5), 279 (4), 278 (9), 277 (44), 249 (5).

5-(4-Hydroxymethyl-2-furoyl)-2(1H)-pyrimidinone (11a). Tetrabutylammonium fluoride (0.5 M solution in THF; 13.6 ml, 6.79 mmol) was added dropwise by means of a syringe to a solution of 5-(4-dimethylhexylsilyloxymethyl-2-furoyl)-2(1H)-pyrimidinone (0.82 g, 2.20 mmol) in THF (10 ml) at 0 °C under argon. The mixture was stirred at ambient temperature for 2 h, cooled to ca. 5 °C and acetic acid added slowly until precipitation of the product was complete; yield 0.38 g (78 %), m.p. 273 °C. Anal. $C_{10}H_8N_2O_4$: C, H. 1H NMR (DMSO-*d*₆): δ 5.12 (CH₂O), 8.14 (H-3'), 8.66 (H-5'), 9.57 (H-4,6). ^{13}C NMR (DMSO-*d*₆): δ 54.42 (CH₂O), 113.71 (C4'), 119.56 (C3'), 129.35 (C5), 144.50 (C5'), 151.26 (C2'), 155.73 (C2), 158.61 (C4,6), 175.35 (C=O, ketone). MS: 220 (100, M), 219 (11), 218 (52), 202 (49), 192 (11), 191 (31), 190 (11), 174 (30), 173 (15), 163 (18), 162 (20).

5-(5-Hydroxymethyl-2-furoyl)-2(1H)-pyrimidinone (11b). Compound **11b** was prepared from 5-(5-dimethylhexylsilyloxymethyl-2-furoyl)-2(1H)-pyrimidinone by cleavage of the dimethylhexylsilyl group with tetrabutylammonium fluoride as described above; yield 82 %, m.p. 278–280 °C (H₂O). Anal. $C_{10}H_8N_2O_4$: C, H. 1H NMR (DMSO-*d*₆): δ 4.65 (CH₂), 5.5 (OH), 6.71 (H-4', d, *J* 3.4 Hz), 7.55 (H-3', d), 9.00 (H-4,6). ^{13}C NMR (DMSO-*d*₆): δ 56.02 (CH₂O), 109.89 (C4'), 113.84 (C5), 121.09 (C3'), 150.32 (C5'), 155.41 (C2'), 160.00 (C2), 161.11 (C4,6), 175.15 (C=O, ketone). MS: 220 (100, M), 219 (1), 218 (2), 203 (6), 191 (10), 189 (73), 163 (10), 161 (17).

1-Benzyl-5-(4-hydroxymethyl-2-furoyl)-2(1H)-pyrimidinone (12a). A mixture of triethylamine (0.07 ml, 0.04 mmol) and 5-(4-hydroxymethyl-2-furoyl)-2(1H)-pyrimidinone (61 mg, 0.28 mmol) in dichloromethane (3 ml) was stirred for 15 min after which time all the solid had dissolved. Benzyl bromide (84 mg, 0.49 mmol) was added and the mixture was stirred at ambient temperature for 2 h when TLC showed the reaction to be complete. The mixture was evaporated and the residue purified by flash chromatography on silica gel using CHCl_3 -diethyl ether-ethanol (5:4:1) to give a white product; yield 71 mg (82%), m.p. 167°C. Anal. $\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}_4$: C, H. ^1H NMR ($\text{DMSO}-d_6$): δ 4.54 (CH_2 , d, J 5.7 Hz), 5.57 (OH, t, J 5.7 Hz), 5.20 (NCH_2), 6.46 (H-4', d, J 3.3 Hz), 7.46 (H-3', d), 7.3–7.4 (Ph), 9.09 (H-6, d, J 3.3 Hz), 9.13 (H-4, d). ^{13}C NMR ($\text{DMSO}-d_6$): δ 53.93 (CH_2OH), 54.29 (NCH_2), 114.37 (C4'), 119.98 (C3'), 129.30 (C5), 128.03, 128.54, 128.64, 135.43 (Ph), 144.71 (C5'), 150.80 (C6), 153.43 (C2'), 154.38 (C2), 165.30 (C4), 175.06 (C=O, ketone). MS: 310 (66, M), 409 (7), 308 (20), 221 (9), 219 (23), 201 (20), 125 (14), 92 (17), 91 (100).

1-Benzyl-5-(5-hydroxymethyl-2-furoyl)-2(1H)-pyrimidinone (12b). Compound **12b** was prepared from triethylamine and 5-(5-hydroxymethyl-2-furoyl)-2(1H)-pyrimidinone by alkylation with benzyl bromide as described above; yield 82%, m.p. 167°C. Anal. $\text{C}_{17}\text{H}_{14}\text{N}_2\text{O}_4$: C, H. ^1H NMR ($\text{DMSO}-d_6$): δ 4.54 (CH_2 , d, J 5.7 Hz), 5.57 (OH, t, J 5.7 Hz), 5.20 (NCH_2), 6.46 (H-4', d, J 3.3 Hz), 7.46 (H-3', d),

7.3–7.4 (Ph), 9.09 (H-6, d, J 3.3 Hz), 9.13 (H-4, d). ^{13}C NMR ($\text{DMSO}-d_6$): δ 53.93 (CH_2OH), 55.86 (NCH_2), 109.52 (C4'), 114.48 (C5), 121.35 (C3'), 127.94, 128.14, 128.56, 135.47 (Ph), 149.84 (C6), 153.31 (C5'), 154.42 (C2'), 161.24 (C2), 165.29 (C4), 174.85 (C=O, ketone). MS: 310 (4, M), 308 (34), 279 (7), 251 (4), 217 (5), 123 (7), 92 (11), 91 (100).

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