Tetrahedron Vol. 50, No. 1, pp. 275-284, 1994
Printed in Great Britain

0040-4020/94 $6.00+.00

Stannylation in the Electrophilic 2- and 4/6-Pyrimidine Position and the Use of Stannylpyrimidines in Coupling and Tin-Lithium Exchange Reactions.

Jessie Sandosham and Kjell Undheim.*

Department of Chemistry, University of Oslo, N-0315 Oslo, Norway.

Abstract: 2-Stannylpyrimidines have been prepared by stannyl anion substitution in 2-chloropyrimidines. Stannylation in the 4-position was *via* the iodo-derivative or *via* the 4-lithio derivative and lithium-tin transmetallation. Tin-lithium exchange in the 2-position resulted in 2-lithiopyrimidine. Ketones were formed from the stannylpyrimidines and acid chlorides, aryl bromides required Pd-catalysis for coupling reaction.

Organostannyl reagents have become important intermediates in organic synthesis, e.g. in transition-metal catalyzed coupling reactions.[1] The stannanes, which are stable and easily handled compounds, are also useful for transmetallation reactions, e.g. for the generation of reactive organolithium species, especially when the latter may otherwise be difficult to prepare.[2] We have previously used transmetallation in the more usual opposite sense, from the lithio-derivative to the 5-stannyl-derivative.[3] Alternatively, the bromine in the pyrimidine 5-position can be replaced by a stannyl group from hexaalkylditin by a Pd-catalyzed coupling reaction in the presence of anhydrous fluoride ions.[4] Nucleophilic substitution of the 5-bromide by tri-n-butylstannyllithium could also be used.[4] The last two methods have been applied, to a limited extent, to the stannylation of the electrophilic 4/6 position of pyrimidine,[5] whereas stannylation of the electrophilic 2-position has not been reported so far. We hereby present work on stannylation in the electrophilic positions of pyrimidines, and the use of stannylpyrimidines in coupling reactions. The Pd-catalyzed coupling reaction is a useful method for introducing carbon substituents into pyrimidines.[6] 5-Stannylpyrimidines have previously been shown to bond readily with sp^2-hybridized carbon of organohalides, e.g. 5-acylpyrimidines are formed from the corresponding acyl chlorides.[7] We have now extended these studies to include the electrophilic pyrimidine positions.

Interest in the metallation of pyrimidines, especially the formation of organolithium derivatives of pyrimidines, is increasing judging by the number of recent reports.[8] We describe an efficient method of tin-lithium exchange resulting in the hitherto difficult-to-obtain 2-lithiopyrimidine.

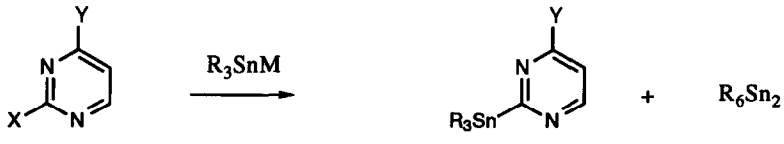
RESULTS AND DISCUSSION

Initially, tri-n-butylstannyllithium was used in stannylation (Scheme 1). This reagent was prepared from tri-n-butylstannane and LDA at 0 °C.[9] The reagent was then cooled to -78 °C and 2-chloropyrimidine added. Monitoring (TLC, GLC) showed that the reaction was completed after 3 h with the formation of the 2-stannylpyrimidine **3a** and hexabutylditin. Maximum yield (84 %) of the 2-stannylpyrimidine **3a** was obtained when the stannyl reagent was used within 30 min after formation; "ageing" of the anion with time resulted in the generation of hexabutylditin.[10] With 2,4-dichloropyrimidine as substrate there was little reaction at -78 °C, whereas higher temperatures led to extensive polymerization. Monosubstitution is possible, however, using tri-n-butylstannylsodium (*vide infra*).

In the second part of the metallation work trimethylstannyl derivatives were used. Trimethylstannyllithium

and -sodium were prepared from the respective metal and trimethylstannyl chloride.[11] The 2-stannylated product **3b** was obtained (46 %) from trimethylstannyllithium and 2-chloropyrimidine. The reaction of 2,4-dibromopyrimidine with trimethylstannylsodium ensured regioselective substitution in the 2-position, the product being 4-bromo-2-trimethylstannylpyrimidine (**3e**; 78 %), whereas the reaction with the corresponding stannyllithium resulted in extensive polymerization. The former reagent was also used in stannylating the 4-iodo derivatives in the less reactive pyridines.[11a]

In the third metallation approach, the triphenylstannyl group was introduced into 2-chloropyrimidine using the lithium reagent which was generated from lithium metal and triphenylstannyl chloride.[12] This resulted in 2-triphenylstannylpyrimidine (**3c**). The yield in this case was lower (35%) than for the trimethyl- or tri-n-butylstannylating agent.



1 **2** **3**

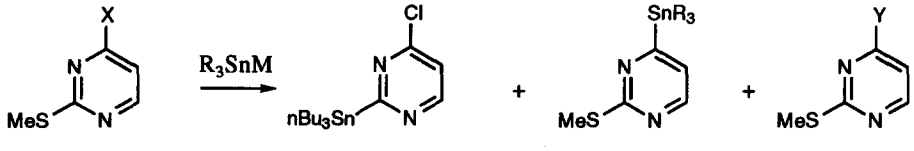
1a X = Cl, Y = H
b " = Cl, " = Cl
c " = Br, " = Br

2 R = nBu, M = Li, Na
" = Me, " = Li, Na
" = Ph, " = Li

3a R = nBu, Y = H
b " = Me, " = H
c " = Ph, " = H
d " = nBu, " = Cl
e " = Me, " = Br

Scheme 1

For the study of stannylation in the pyrimidine 4-position, unstable 4-chloropyrimidine[13] was stabilized by using the 2-methylthio analogue **4a** as substrate (Scheme 2). Previously, we have reported that stannyllithium and copper(I) reagents reacted sluggishly with this substrate.[5] Here, the reaction was initially performed at - 78 °C, allowed to reach ambient temperature and stirred for 48 h until all the starting pyrimidine was consumed. The chemoselectivity was low. Of the three products obtained, there were two monostannylated pyrimidines, *viz.* 4-chloro-2-tri-n-butylstannyl-pyrimidine (**3d**; 35 %) by substitution of the 2-methylthio group, and 2-methylthio-4-tri-n-butylstannyl-pyrimidine (**5a**; 20 %) by the expected substitution of the chlorine substituent. In addition, 2,4-dimethylthiopyrimidine (**6**) was isolated in 10 % yield. The formation of the latter is rationalized as a nucleophilic substitution of the chlorine in the 4-position by methanethiolate generated during the formation of **3d** by stannylation.



4 **2** **3d** **5** **6/7**

4a X = Cl
b " = I

2 R = nBu, Me

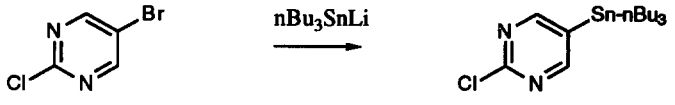
5a R = nBu
b " = Me

6 Y = SMe
7 " = H

Scheme 2

Selectivity for the 4-position, however, was achieved by replacing the chlorine with iodine (**4b**, Scheme 2). This resulted in the desired 4-stannylated derivative (**5a**; 52 %) and some dehalogenated compound (**7**; 40 %). Reaction between the 4-iodopyrimidine (**4b**) and trimethylstannylsodium gave the methyl analogue (**5b**, 67 %).

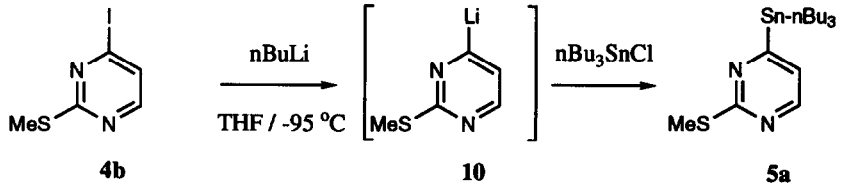
The findings (*vide supra*) show that the 2-position in pyrimidine is stannylated more readily than the 4/6-position. An attempt to stannylate 2,5-dichloropyrimidine was unsuccessful, whereas 5-bromo-2-chloro-pyrimidine (**8**) yielded the 5-stannyl derivative **9** (53 %, Scheme 3). Thus the bromine in the benzenoid 5-position is more readily replaced by the tin anion than the chlorine in the electrophilic 2-position.



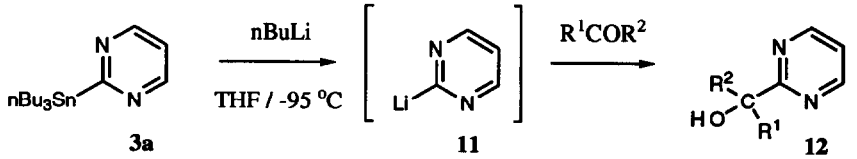
8 **9**

Scheme 3

Several mechanisms for this type of stannylation reactions have been proposed, one of which could involve a radical intermediate, thus accounting for the formation of hexaalkylditin in the reaction mixture.[14] Addition of galvinoxyl (3 mol %) as a free radical trap,[15] however, had only minor influence on the stannylation of 2-chloropyrimidine and no significant decrease in the amount of the ditin was observed.



4b **10** **5a**



3a **11** **12**

12a R^1 = Ph, R^2 = H

b " = Ph, " = Me

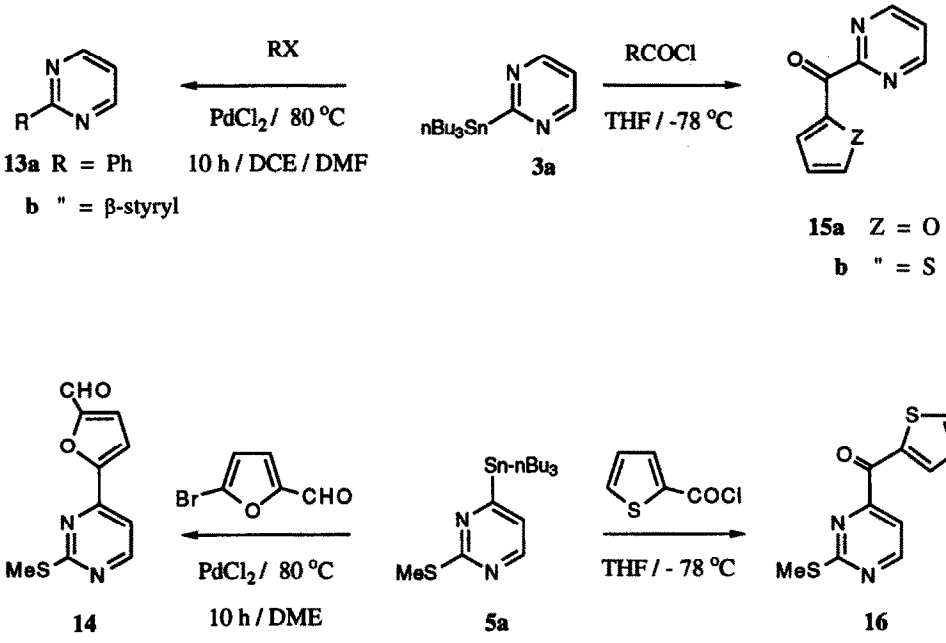
c " = β-styryl, " = H

Scheme 4

In the final approach to stannylation, metal-metal exchange reaction between an organostannyl halide and a metallated species, usually a lithiated species, was attempted (Scheme 4). Lithiation in electrophilic 4-position of

pyrimidine has previously been achieved by proton abstraction using a strong base such as LDA,[16] or by the treatment of 4-bromide with nBuLi.[17] Lithiation of 4-chloropyrimidine, however, is complicated by competitive reactions such as addition to the unsubstituted azomethine (C=N) bond.[18] The 4-iodopyrimidine **4b**, however, could be lithiated selectively in the 4-position using nBuLi at - 95 °C (Scheme 4). The lithiated species was trapped with tri-n-butylstannyl chloride to give the 4-stannylated derivative **5a** in good yield (76 %).

Attempts to lithiate 2-chloro-, 2-bromo- or 2-iodopyrimidine met with little success; adduct formation by addition of the lithiating species to the other electrophilic pyrimidine position is a major side-reaction.[19] Quenching the reaction mixture after the attempt to lithiate 2-iodopyrimidine resulted in a low yield (10 % by GLC) of the stannylated product **3a**. 2-Lithiopyrimidine (**11**) was formed selectively and in a satisfactory yield by reversing the order of metal exchange (Scheme 4). Thus treatment of the 2-stannylpyrimidine **3a** with nBuLi at - 78 °C led to exclusive metal-metal exchange whereby 2-lithiopyrimidine (**11**) was generated as verified by its subsequent reactions. Addition of the carbonyl compounds benzaldehyde, acetophenone and cinnamaldehyde to the reaction mixture gave the corresponding alcohols **12a** (78 %), **12b** (61 %) and **12c** (53 %) .



Scheme 5

In the same manner as in the benzenoid 5-position,[3,4,6] the stannyl group in the electrophilic pyrimidine position can be replaced by carbon substituents using Pd-catalyzed coupling reactions with organohalides, and presumably triflates. Bis(triphenylphosphine)palladium(II) chloride, [$(PPh_3)_2PdCl_2$] was the catalyst added to the reaction mixture.

The choice of solvent varied with the substrate (Scheme 5). 2-Phenylpyrimidine (**13a**; 43 %) was formed from iodobenzene, and 2-(β-styryl)pyrimidine (**13b**; 58 %) from β-bromostyrene. 5-Bromofurfural failed to couple with the 2-stannylpyrimidine **3a** but it readily reacted with 2-methylthio-4-tri-n-butylstannylpyrimidine (**5a**) in the 4-position to give product **14** (82 %). We have previously shown that in the pyrimidine 5-position

the analogous reaction took place in close to quantitative yield.[4]

Unlike the reaction with 5-stannylpyrimidines where catalysis is required,[7] acid chlorides reacted with the 2-stannylpyrimidine to give the corresponding ketones (**15**) in the absence of any catalyst (Scheme 5). The addition of a catalyst led to polymerization. The reaction between the 2-stannylpyrimidine **3a** and furoyl chloride was almost instantaneous at - 78 °C in THF, and the ketone **15a** was isolated in 52 % yield. Similarly, 2-thiophenecarbonyl chloride gave in the ketone **15b** in 62 % yield. The catalyst was also excluded for the reaction in the 4-position. With thiophene-2-carbonyl chloride, the ketone **16** was obtained in 64 % yield from 2-methylthio-4-tri-n-butylstannylpyrimidine (**5a**) at - 78 °C. Few examples of such uncatalyzed *ipso*-substitution of stannylazines by acyl halides have previously been reported.[20]

We have shown that pyrimidines can be stannylated in the 2- and 4/6- electrophilic positions by different methods. 2-Stannylpyrimidines are obtained in good yields by nucleophilic substitution of the chloropyrimidine using stannyl anions while access to 4-stannylpyrimidine is best gained *via* the iodo-lithio-stannyl exchange reaction at low temperatures.

2-Stannylpyrimidine undergoes tin-lithium exchange and the anion formed can be trapped by carbonyl compounds.

These stannyl derivatives participate in the Stille-type palladium-catalyzed coupling reaction and formed ketones without catalysis.

EXPERIMENTAL

^{1}H NMR spectra were recorded at 300 MHz, ^{13}C NMR spectra at 75 MHz. Mass spectra were recorded at 70 eV ionizing voltage. Ammonia was used for chemical ionization (CI). MS spectra are presented as *m/z* (% rel. int.). THF used in the reactions was dried by distillation over metallic sodium and benzophenone, dichloromethane distilled over calcium hydride and 1,2-dichloroethane (DCE) over phosphorus pentoxide. DMF was first shaken with NaOH pellets, then distilled over BaO. DME was distilled over sodium. Tri-n-butylstannane and trimethylstannyl chloride, were obtained from Fluka and were used without further purification.

Starting materials prepared by literature methods. 2,4-Dibromopyrimidine,[21] 2-bromopyrimidine,[22] 2-iodopyrimidine,[23] 4-chloro-2-methylthiopyrimidine,[24] 4-iodo-2-methylthiopyrimidine,[5] 2,5-dichloropyrimidine,[25] and 5-bromo-2-chloropyrimidine.[26]

General procedure for stannylation using stannyl(IV) anions Tri-n-butylstannyllithium was generated by the treatment of tri-n-butylstannane (5 mmol) with a THF solution (10 ml) of LDA (5 mmol) at 0 °C. Trimethylstannyllithium and -sodium were formed by the reaction of the metal (10 mmol) with trimethylstannyl chloride (5 mmol) in THF (10 ml) at 0 °C for 3-10 h. The reaction mixture was then filtered through a plug of dried glass wool under N_2 to remove unreacted metal. Similar treatment of the respective metal and stannyl chloride resulted in tri-n-butylstannylsodium and triphenylstannyllithium. A solution of the halopyrimidine (4.5 mmol) in THF (10 ml) was added dropwise, with vigorous stirring, to a solution of the trialkylstannyl anion (5 mmol) in THF (10 ml) maintained at -78 °C under N_2. The reaction was monitored by TLC and GLC. When no further changes were observed, the reaction mixture was allowed to warm up to 0 °C, quenched with saturated NH_4Cl solution and extracted with EtOAc, washed (H_2O), dried ($MgSO_4$) and purified by flash chromatography on a silica column using hexane/EtOAc (4:1) as eluent, and finally by distillation or recrystallization.

2-Tri-n-butylstannylpyrimidine (***3a***). 1.36 g of compound ***3a*** was obtained (84 %) from tri-n-butylstannyllithium which was generated from tri-n-butylstannane and LDA. After 1 h at -78 °C the cold bath was removed and the reaction mixture allowed to warm to 0 °C, then worked up as described above; b.p.120 °C/

0.005 mmHg. (Found: C, 52.22; H, 8.13. Calc. for $C_{16}H_{30}N_2Sn$: C, 52.06; H, 8.19%). ^1H NMR ($CDCl_3$): δ 0.88 (m, 9H, 3xCH_3), 1.19 (m, 6H, 3xCH_2), 1.35 (m, 6H, 3xCH_2), 1.60 (m, 6H, 3xCH_2), 7.11 (t, 1H, H-5, $J_{5,4/6}$ 5 Hz), 8.68 (d, 2H, H-4,6, $J_{4/6,5}$ 5 Hz). ^{13}C NMR ($CDCl_3$): δ 10.03 (CH_2), 13.48 (CH_3), 27.09 (CH_2), 28.80 (CH_2), 119.09 (C-5), 154.48 (C-4,6), 188.94 (C-2). MS (CI): 371 (100, M^++1), 370 (40, M^+), 369 (72), 368 (43), 330 (10), 328 (7), 326 (5), 313 (4), 311 (3).

2-Trimethylstannylpyrimidine (***3b***) Compound ***3b*** was obtained from trimethylstannyllithium in 0.68 g (62 %) yield, and from trimethylstannylsodium in 0.81 g (74 %) yield; b.p. 50 °C / 0.005 mmHg (Kugelrohr oven). (Found: C, 34.79; H, 5.13. Calc. for $C_7H_{12}N_2Sn$: C, 34.62; H, 4.98 %). ^1H NMR ($CDCl_3$): δ -0.001 (s, 9H, 3xCH_3, $J_{Sn,H}$ 27 Hz), 6.75 (t, 1H, H-5, $J_{5,4/6}$ 5 Hz), 8.29 (d, 2H, H-4,6, $J_{4/6,5}$ 5 Hz). ^{13}C NMR ($CDCl_3$): δ -9.39 (Sn$\underline{C}H_3$), 119.38 (C-5), 154.70 (C-4/6), 188.70 (C-2). MS (EI): 244 (13 , M^+), 242 (14), 232 (17), 231 (14), 229 (100), 228 (38), 227 (78), 226 (37), 225 (47), 164 (25), 135 (58), 120 (15).

2-Triphenylstannylpyrimidine (***3c***). Compound ***3c*** was generated from triphenylstannyllithium in 0.68 g (35 %) yield; m.p. 148 °C. (Found: C, 61.69; H, 4.28. Calc. for $C_{22}H_{18}N_2Sn$: C, 61.58; H, 4.23 %). ^1H NMR ($CDCl_3$): δ 7.17 (t, 1H, H-5, $J_{5,4/6}$ 4.98 Hz), 7.35-7.76 (m, 15H, 3xPh), 8.75 (d, 2H, H-4/6, $J_{4/6,5}$ 4.98 Hz). ^{13}C NMR ($CDCl_3$): δ 120.20 (C-5), 128.16 (C-2′/6′), 129.14 (C-4′), 137.21 (C-3′/5′), 137.73 (C-1′), 155.48 (C-4/6), 186.63 (C-2). MS (EI): 429 (100, M^+), 427 (75), 426 (33), 425 (41), 353 (21), 351 (43), 349 (30), 197 (91), 195 (66), 193 (39), 120 (51), 118 (38), 77 (23).

4-Chloro-2-tributylstannylpyrimidine (***3d***). Compound ***3d*** was obtained in 0.84 g (46 %) yield by reacting 2,4-dichloropyrimidine with tri-n-butylstannylsodium. It was also formed from 4-chloro-2-methylthiopyrimidine ***4a*** with tri-n-butylstannyllithium in 0.64 g (35 %) yield; b.p. 200 °C /0.03 mmHg (Kugelrohr oven). (Found: C, 47.67; H 7.24. Calc. for $C_{16}H_{29}ClN_2Sn$: C, 47.62; H, 7.24 %). ^1H NMR ($CDCl_3$): δ 0.89 (m, 9H, 3xCH_3), 1.19 (m, 6H, 3xCH_2), 1.31 (m, 6H, 3xCH_2), 1.55 (m, 6H, 3xCH_2), 7.14 (d, 1H, H-5, $J_{5,6}$ 5.44 Hz), 8.51 (d, 1H, H-6, $J_{6,5}$ 5.44 Hz). ^{13}C NMR ($CDCl_3$): δ 10.37 (CH_2), 13.74 (CH_3), 27.10 (CH_2), 28.75 (CH_2), 119.61 (C-5), 155.46 (C-6), 159.43 (C-4), 190.82 (C-2). MS (CI): 407/405 (38/100, M^++2), 406 (24), 404 (39), 405/403 (25/73, M^+), 401 (36), 385 (5), 381 (4), 366 (13), 362 (10).

4-Bromo-2-trimethylstannylpyrimidine (***3e***). Compound ***3e*** was obtained in 1.02 g (72 %) yield by reacting trimethylstannylsodium with 2,4-dibromopyrimidine; b.p. 85 °C / 0.05mmHg (Kugelrohr oven). (Found: C, 26.34; H, 3.57. Calc. for $C_7H_{11}BrN_2Sn$: C, 26.13; H 3.45 %). ^1H NMR ($CDCl_3$): δ 0.377 (s, 9H, Sn($C\underline{H}_3$)$_3$), 7.42 (d, 1H, H-5, $J_{5,6}$ 4.6 Hz), 8.29 (d, 1H, H-6, $J_{6,5}$ 4.6 Hz). ^{13}C NMR ($CDCl_3$): δ -9.33 (Sn($\underline{C}H_3$)$_3$), 128.09 (C-5), 153.69 (C-4), 155.73 (C-6), 190.16 (C-2). MS (EI): 322 (21, M^+), 321 (13), 320 (16), 311 (19), 307 (100), 305 (68), 303 (30), 277 (16), 275 (11), 243 (19), 241 (14), 231 (59), 229 (98), 227 (67), 225 (28), 164 (94), 163 (70), 162 (77), 135 (52).

2-Methylthio-4-tributylstannylpyrimidine (***5a***). Compound ***5a*** was isolated in 0.37 g (20 %) yield from the reaction of 4-chloro-2-methylthiopyrimidine with tri-n-butylstannyllithium and was shown to be identical (b.p.110-111 °C / 0.01 mmHg; reported 112 °C / 0.01 mmHg) with authentic material.[5] A yield of 0.97 g (52 %) resulted when the 4-chloro derivative ***4a*** was replaced by the 4-iodopyrimidine ***4b*** in the above reaction. It was also prepared in 1.42 g (76 %) yield by treating a THF solution of compound ***4b*** (5 mmol) with equimolar amount of nBuLi (5 mmol) while maintaining -95 °C temperature and an inert atmosphere. An 1.1 equivalent THF solution of tri-n-butylstannyl chloride (5.5 mmol) was added after 1 h, allowed to warm up gradually overnight, quenched with saturated NH_4Cl solution and worked up as above.

2-Methylthio-4-trimethystannylpyrimidine (***5b***). Treatment of 4-iodo-2-methylthiopyrimidine with trimethylstannyllithium gave compound ***5b*** in 0.88 g (67 %) yield and was found to be identical with the known compound.[5]

2,4-Dimethylthiopyrimidine (***6***). Compound ***6*** was isolated in 10 % yield from the reaction of 4-chloro-2-methylthiopyrimidine and tri-n-butylstannyllithium and was found to be identical with authentic material (b.p. reported 139-140 °C / 6 mmHg; found 141 °C / 8 mmHg).[27]

2-Methylthiopyrimidine (***7***). Compound ***7*** was formed in 41 % on treating 4-iodo-2-methylthiopyrimidine with tri-n-butylstannyllithium and was found to be identical with authentic material b.p. reported 109 °C / 28 mmHg; found 87 °C / 8 mmHg).[28]

2-Chloro-5-tributylstannylpyrimidine (***9***). Compound ***9*** was obtained in 0.97 g (53 %) yield by reacting 5-bromo-2-chloropyrimidine with tri-n-butylstannyllithium; b.p. 150 °C / 0.02 mmHg (Kugelrohr oven). (Found: C, 47.81; H, 7.38. Calc. for $C_{16}H_{29}ClN_2Sn$: C, 47.62; H, 7.24 %). ^{1}H NMR ($CDCl_3$): δ 0.81 (m, 9H, 3xCH_3), 1.10 (m, 6H, 3xCH_2), 1.26 (m, 6H, 3xCH_2), 1.45 (m, 6H, 3xCH_2), 8.49 (s, 2H, H-4,6, $J_{Sn,H-4,6}$ 8.2 Hz). ^{13}C NMR ($CDCl_3$): δ 9.56 (CH_2), 13.28 (CH_3), 26.94 (CH_2), 28.63 (CH_2), 131.93 (C-5), 165.22 (C-4,6), 170.71 (C-2). MS (CI): 407/405 (38/100, M^++2), 404 (38), 405/403 (21/71, M^+), 402 (25), 401 (35), 366 (3), 364 (8), 363 (3), 362 (5), 360 (3), 308 (2).

Reaction of 2-tri-n-butylstannylpyrimidine with nBuLi. 2-Tri-n-butylstannylpyrimidine (0.93 g, 2.5 mmol) was dissolved in THF (5 ml), cooled to -78 °C and nBuLi (1.67ml of a 1.5M sol., 2.5 mmol) added under N_2 atmosphere. When TLC monitoring showed that there was no more starting stannane, the generated 2-lithiopyrimidine was trapped by the addition of carbonyl compounds (3 mmol) while vigorous stirring and a temperature of - 78 °C were maintained. The reaction mixture was warmed to ambient temperature overnight, quenched with saturated NH_4Cl sol., extracted with EtOAc, dried ($MgSO_4$), and purified on a silica flash column using $CHCl_3$ as eluent.

1-Phenyl-1-(2-pyrimidinyl)methanol (***12a***). Compound ***12a*** was obtained in 0.36 g (78 %) yield by trapping the 2-lithiopyrimidine with PhCHO (0.3 ml, 3 mmol). (Found: C, 71.17; H 5.56. Calc. for $C_{11}H_{10}N_2O$: C, 70.95; H 5.41 %). ^{1}H NMR ($CDCl_3$): δ 5.86 (s, 1H, CH), 7.15 (t, 1H, H-5, $J_{5,4/6}$ 4.94 Hz), 7.23-7.50 (m, 5H, Ph), 8.63 (d, 2H, H-4/6, $J_{4/6,5}$ 4.94 Hz). ^{13}C NMR ($CDCl_3$): δ 75.78 (CH), 119.96 (C-5), 127.17 (C-3´, 5´), 128.90 (C-1´), 128.97 (C-2´, 6´), 142.66 (C-4´), 157.64 (C-4,6), 170.57 (C-2). MS (CI): 187 (100, M^++1), 170 (5), 169 (17), 153 (1), 139 (2), 105 (3), 81(2).

1-Phenyl-1-(2-pyrimidinyl)ethanol (***12b***). Compound ***12b*** was formed by trapping the 2-lithiopyrimidine with acetophenone (0.3 ml, 3 mmol) in 0.31 g (61 %) yield. (Found: C, 72.19; H, 6.18. Calc. for $C_{12}H_{12}N_2O$: C, 71.98; H 6.04 %). ^{1}H NMR ($CDCl_3$): δ 2.01 (s, 3H, CH_3), 5.49 (s, 1H, OH), 7.10 (t, 1H, H-5, $J_{5,4/6}$ 4.8 Hz), 7.18-7.66 (m, 5H, Ph), 8.66 (d, 2H, H-4,6, $J_{4/6,5}$ 4.8 Hz). ^{13} C NMR ($CDCl_3$): δ 29.06 (CH_3), 119.62 (C-5), 125.93 (COH), 126.10 (C-3´, 5´), 127.50 (C-4´), 128.59 (C-2´,6´), 128.97 (C-1´), 157.43 (C-4,6), 173.63 (C-2). MS (EI): 200 (55.9, M^+), 186 (11), 185 (77), 157 (15), 123 (27), 121 (33), 107 (51), 105 (44), 81 (23), 80 (47), 79 (28), 78 (13), 77 (50).

1-β-Styryl-1-(2-pyrimidinyl)methanol (***12c***). Compound ***12c*** was isolated in 0.28 g (53 %) yield by treating 2-lithiopyrimidine with cinnamaldehyde (0.38 ml, 3 mmol). (Found: C, 73.71; H, 5.82. Calc. for $C_{13}H_{12}N_2O$: C, 73.57; H 5.70 %). ^{1}H NMR ($CDCl_3$): δ 5.52 (d, 1H, CHOH, $J_{\alpha,\beta}$ 5.5 Hz), 6.49 (dd, 1H, H-β, $J_{\beta,\alpha}$ 5.5 Hz, $J_{\beta,\gamma}$ 15.6 Hz), 6.87 (d,1H, H-γ, $J_{\gamma,\beta}$ 15.6 Hz), 7.17 (t, 1H, H-5, $J_{5,4/6}$ 4.95 Hz), 7.22-7.40 (m, 5H, Ph), 8.71 (d, 2H, H-4/6, $J_{4/6,5}$ 4.95 Hz). ^{13}C NMR ($CDCl_3$): δ 74.55 (CHOH), 120.19

(C-5), 127.17 (C-3,5′), 128.17 (C-γ), 128.99 (C-2′,6′), 130.24 (C-β), 131.56 (C-4′), 137.10 (C-1′), 157.74 (C-4,6), 170.15 (C-2). MS(EI): 212 (43, M^+), 210 (48), 194 (9), 181 (35), 148 (18), 131 (55), 105(43), 103 (66), 91 (49), 87 (19), 80 (100).

Palladium-catalyzed coupling of stannylpyrimidines with organohalides. The stannylpyrimidine (2.0-2.5 mmol), the organohalide (2.5-3.0 mmol) and bis(triphenylphosphine)palladium(II) chloride (3-5 mol %) and solvent were heated together until TLC showed no more starting pyrimidine. The reaction mixture was diluted with light petroleum, saturated KF solution added and the precipitated stannyl fluoride filtered off through a plug of celite and the filtrate extracted with EtOAc, washed (H_2O), dried ($MgSO_4$) and purified on a silica flash column with light petroleum / EtOAc (2:1) as eluent.

2-Phenylpyrimidine (***13a***). 2-Tri-n-butylstannylpyrimidine (0.93 g, 2.5 mmol), iodobenzene (0.62 g, 3 mmol) and bis(triphenylphosphine)palladium(II) chloride (0.52 g, 3 mol %) in 1, 2-dichloroethane (5 ml) were heated under reflux overnight to give compound ***13a*** in 0.134 g (43 %) yield. It was found to be identical (m.p. reported 37-38 °C; found 36-37 °C) with the known compound.[29]

2-(β-Styryl)pyrimidine (***13b***). 2-Tri-n-butylstannylpyrimidine (0.93 g, 2.5 mmol), β-bromostyrene (0.52 g, 3 mmol) and bis(triphenylphosphine)palladium(II) chloride (0.52 g, 3 mol %) were heated at 80 °C in DMF (5 ml) overnight and the reaction worked up as described above to give 0.26 g (58 %) of compound ***13b*** which was identical spectroscopically with the authentic material.[30]

4-(5-Formyl-2-furyl)-2-methylthiopyrimidine (***14***). 2-Methylthio-4-tri-n-butylstannylpyrimidine (0.83 g, 2 mmol), 5-bromofurfural (0.44 g, 2.5 mmol) and bis(triphenylphosphine)palladium(II) chloride (0.7 g, 5 mol %) in DMF were heated at 80 °C for 3 h. at which time TLC showed that no more starting pyrimidine was present. After purification, ***14*** was obtained in 0.36 g (82 %) yield; m.p. 121 °C. (Found: C, 54.72; H, 3.74. Calc. for $C_{10}H_8N_2O_2S$: C, 54.53; H 3.66 %). ^{1}H NMR ($CDCl_3$): δ 2.6 (s, 3H, SCH_3), 7.36 (d, 1H, H-4′, $J_{4',3'}$ 3.71 Hz), 7.42 (d, 1H, H-3′, $J_{3',4'}$ 3.71 Hz), 7.47 (d, 1H, H-5, $J_{5,6}$ 5.12 Hz), 8.63 (d, 1H, H-6, $J_{6,5}$ 5.12 Hz), 9.76 (s, 1H, CHO). ^{13} C NMR ($CDCl_3$): δ 110.00 (C-3′), 113.82 (C-4′), 121.8 (C-5), 153.67 (C-4), 154.25 (C-2), 155.78 (C-2′), 158.31 (C-6), 173.37 (C-5′), 177.82 (CHO). MS (EI): 220 (100, M^+), 218.9 (16), 174.0 (23), 145 (30), 117 (12), 110 (22), 90 (6), 63 (12).

Coupling of stannylpyrimidine with acid chloride. The stannylpyrimidine (2.5 mmol) was dissolved in THF (5 ml) and cooled to -78 °C under N_2, then the acyl chloride (3.0 mmol) added slowly. The reaction was monitored by TLC. On completion, the solution was diluted with light petroleum, spun for 1-2 h, then filtered and finally purified on a silica flash column with $CHCl_3$ as eluent.

2-(2-Furoyl)pyrimidine (***15a***). Compound ***15a*** was formed at once in 0.23 g (52 %) yield on adding 2-furoyl chloride (0.4 g, 3 mmol) to 2-tri-n-butylstannylpyrimidine (0.93 g, 2.5 mmol). The product was identical spectroscopically with an authentic sample.[31]

2-(2-Thiophenecarbonyl)pyrimidine (***15b***). Compound ***15b*** was formed in 0.29 g (62 %) yield within 5 min of mixing 2-tributylstannylpyrimidine (0.93g, 2.5 mmol) with 2-thiophenecarbonyl chloride (0.44 g, 3 mmol). (Found: C, 57.03; H, 3.29. Calc. for $C_9H_6N_2OS$: C, 56.83; H, 3.18 %). ^{1}H NMR ($CDCl_3$): δ 7.32 (m, 1H, H-4′), 7.65 (t, 1H, H-5, $J_{5,4/6}$ 4.85 Hz), 7.92 (m, 1H, H-3′), 8.43 (m,1H, H-5′), 9.12 (d, 2H, H-4,6, $J_{4/6,5}$ 4.85 Hz). ^{13}C NMR ($CDCl_3$): δ 122.98 (C-5), 128.27(C-3′), 136.86 (C-5′), 137.47 (C-4′), 140.63 (C-2′), 157.76 (C-4,6), 161.18 (C-2), 182 (CO). MS (EI): 190 (17, M^+), 162 (23), 111 (100), 83 (19), 82 (6), 79 (6), 53 (24).

2-Methylthio-4-(2-thiophenecarbonyl)pyrimidine **(*16*).** Compound ***16*** was formed in 0.38 g (64 %) yield on adding 2-thiophenecarbonyl chloride (0.44 g, 3 mmol) to 2-methylthio-4-tri-n-butylstannyl-pyrimidine (1.04 g, 2.5 mmol). (Found: C, 51.02; H 3.57. Calc. for $C_{10}H_8N_2OS_2$: C, 50.83; H, 3.41 %). ^{1}H NMR ($CDCl_3$): δ 2.67 (s, 3H, SCH_3), 7.18 (dd, 1H, H-4′, $J_{4',5'}$ 4.9 Hz, $J_{4',3'}$ 3.9 Hz), 7.65 (d, 1H, H-5, $J_{5,6}$ 4.98 Hz), 7.78 (dd, 1H, H-5′, $J_{5',3'}$ 1.2 Hz, $J_{5,'4'}$ 4.9 Hz), 8.36 (dd, 1H, H-3′, $J_{3,'4'}$ 3.9 Hz, $J_{3,'5'}$ 1.2 Hz), 8.75 (d, 1H, H-6, $J_{6,5}$ 4.98 Hz). ^{13}C NMR ($CDCl_3$): δ 14.66 (SCH_3), 114.84 (C-4′), 128.52 (C-5), 137.66 (C-3′), 137.76 (C-5′), 139.33 (C-2′), 159.77 (C-6), 160.71 (C-4), 173.71 (C-2), 182.86 (CO). MS (EI): 236 (45, M^+), 221 (17), 208 (13), 189 (11), 157 (100), 129 (16).

REFERENCE

1 Stille, J. K. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 508-524.

2 Pereyre, M.; Quinard, J.-P.; Rahm, A. *Tin in Organic Synthesis* Butterworths; London; 1987; Ch. 9.

3 Sandosham, J.; Benneche, T.; Møller, B.S.; Undheim, K. *Acta Chem. Scand.* **1988**, *Ser.B42*, 455-461.

4 Sandosham, J; Undheim, K. *Acta Chem. Scand.* **1989**, *43*, 684-689.

5 Majeed, A. J.; Anthonsen, Ø.; Benneche, T.; Undheim, K. *Tetrahedron* **1989**, *45*, 993-1006.

6 a) Undheim, K.; Benneche, T. *Acta Chem. Scand.* **1993**, *47*, 102-121; b) Kalinin, V. N. *Synthesis* **1992**, 413-532; c) Undheim, K.; Benneche, T. *Heterocycles* **1990**, *30*, 1155-1193.

7 Arukwe, J.; Undheim, K. *Acta Chem. Scand.* **1991**, *45*, 914-918.

8 a) Ple, N.; Turck, A.; Martin, P.; Barbey, S.; Queguiner. G. *Tetrahedron lett* . **1993**, *34*, 1605-1608; b) Whale, R. F.; Coe, P. L.; Walker. R. T. *Nucleosides and Nucleotides* **1992**, *11*, 425-442; c) Ple, N.; Turck, A.; Bardin, F.; Queguiner. G. *J. Heterocycl. Chem* **1992**, *29*, 467-70; d) Radinov, R.; Chanev, Kh.; Khaimova, M. *J. Org. Chem.* **1991**, *56*, 4793-4796.

9 Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481-1487.

10 Reimann, W.; Kuivila, H. G.; Farah, D.; Apoussidis, T. *Organometallics* **1987**, *6*, 557-565.

11 a) Yamamoto, Y; Yanagi, A. *Chem. Pharm. Bull. Jpn.* **1982**, *30*, 1731-1737; b) Tamborski, C.; Ford, F. E.; Soloski, E. J. *J. Org. Chem.* **1963**, *28*, 237-239; c) Kuivila, H. G.; Considine, J. L.; Kennedy, J. D. *J.Am. Chem. Soc.* **1972**, *94*, 7206-7208.

12 Tamborski, C.; Ford, F. E. *J. Org. Chem.* **1963**, *28*, 181-184.

13 Boarland, M. P. V.; McOmie, J. F. W. *J. Chem. Soc.* **1951**, 1218-1221.

14 Rossi, R. A; de Rossi, R. H. *Aromatic Substitution by the SRN1 Mechanism* Am. Chem. Soc. Washington. D. C. 1983.

15 Chong, J. M.; Mar, E. K. *Tetrahedron* **1989**, *45*, 7709-7716.

16 Kress, T. J. *J. Org. Chem.*. **1979**, *44*, 2981-2982.

17 Langley, B. W. *J. Am. Chem. Soc.* **1956**, *78*, 2136-2141.

18 Harden, D. B.; Mokrosz, M. J.; Strekowski, L. *J. Org. Chem.*. **1988**, *53*, 4137-4140.

19 Stekowski, L.; Harden, D. B.; Grubb III, W. B.; Patterson, S. E.; Czarny, A.; Mokrosz, M. J.; Cegla, M. T.; Wydra. R. L. *J. Heterocyclic Chem.* **1990**, *27*, 1393-1400.

20 a) Gaare, K.; Repstad, T.; Benneche, T.; Undheim, K. *Acta Chem. Scand.* **1993**, *47*, 57-62; b) see ref.2 p 203.

21 Bly, D. D.; Mellom, M. G. *J. Org. Chem.* **1962**, *27*, 2945-2946.

22 Caton, M.P.L.; Hurst, D. T.; McOmie, J.F.W.; Hunt, R. R. *J. Chem. Soc (C).* **1967**, 1204-1209.

23 Brown, D. J.; Waring, P. *Aust. J. Chem.* **1973**, *26*, 443-447.

24 Matsukawa, T.; Ohta, B. *J. Pharm. Soc. Jpn.* **1949**, *69*, 489-491; *Chem. Abs.* **1950**, *44*, 3456d.

25 English, J. P.; Clark, J. H.; Sheperd, R. G.; Marson, H. W.; Krapcho, J.; Roblin Jr, R. O. *J. Am. Chem. Soc.* **1946**, *68*, 1039-1049.
26 Brown, D. J.; Lyall, J. M. *Aust. J. Chem.* **1964**, *17*, 794-802.
27 Shadbolt, R. S.; Ulbricht, T. L. V. *Chem. Ind. (london).* **1966**(11), 459-460; *Chem. Abs.* **1966**, *64*, 15877a.
28 Boarland, M.P. V.; McOmie, J. F. W. *J. Chem. Soc.* **1952**, 3716-3722.
29 Lythgoe, B.; Rayner, C. S.; *J. Chem. Soc.* **1951**, 2323-2329.
30 Erb, H. S.; Bluhm,T. *Org. Mag. Reson.* **1980**, *14*, 285-289.
31 Siemanowski, W.; Witzel, H. *Liebigs Ann. Chem.* **1984**, 1731-1739.

(*Received in UK* 18 *August* 1993; *revised* 21 *September* 1993; *accepted* 8 *October* 1993)