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First functionalization by metallation of the pyridine moiety of pyridopyrimidin-4(3*H*)-ones. Diazines. Part 36

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Abstract—Starting from *o*-aminopyridine carboxylic acids, a general synthetic route leading to various pyridopyrimidin-4(3*H*)-ones is described. The first metallation and functionalization of the pyridine moiety has been studied and a regioselective metallation at the *peri*-position C_5 of the pyridine ring has been highlighted.

1. Introduction

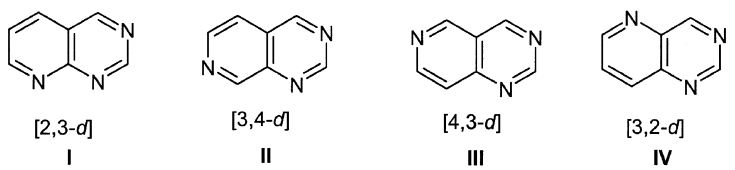
Among the pyridodiazines, the pyridopyrimidines have received much attention because of their potential biological activities as isosteres of quinazolines or pteridines. All four possible pyridopyrimidine systems, pyrido[2,3-*d*]pyrimidine **I**, pyrido[3,4-*d*]pyrimidine **II**, pyrido[4,3-*d*]pyrimidine **III** and pyrido[3,2-*d*]pyrimidine **IV** are known (Scheme 1). The pyrido[2,3-*d*]pyrimidine system has been more studied according to its medicinal applications such as inhibitor of the adenosine kinase[1] (AK) or dihydrofolate reductase[2] (DHFR) enzymes.

For the reason given above, the synthesis of pyridopyrimidine derivatives provides an interesting challenge. Construction of functionalized pyridopyrimidines involves cyclization of appropriately substituted pyrimidines or pyridines whose synthesis is not always easy. The functionalization via metallation of the pyridine moiety could provide a consistent strategy for the synthesis of new pyridopyrimidines.

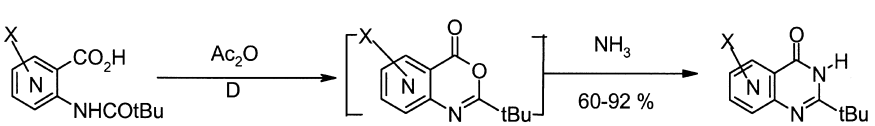
In previous papers, we have mentioned the lithiation of the benzene moiety of benzodiazines: cinnolines,[3] quinazolines,[4,5] quinoxalines and phtalazines.[5] As a continuation of our studies of metallation of *ortho*-condensed diazines, we report here the synthesis, the direct lithiation and functionalization of the pyridine moiety of pyridopyrimidin-4(3*H*)-ones.

Various syntheses of pyridopyrimidine systems have been previously described,[6] among them, a general synthetic route is the cyclization of *o*-acylaminopyridine carboxylic acids with acetic anhydride,[7] leading to pyrido[1,3]oxazin-4-ones intermediates which react with ammonia to give the expected pyridopyrimidin-4(3*H*)-ones (Scheme 2).

This synthetic route could be used with *o*-aminopyridine



Scheme 1.



Scheme 2.

Keywords: Metallation; Pyridopyrimidin-4(3*H*)-ones; Functionalization.
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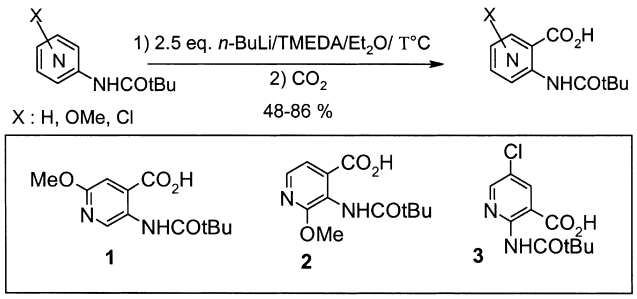
carboxylic acids as starting material which could be reacted with acid chlorides to give the expected *o*-acylaminopyridine carboxylic acids. The 2-aminonicotinic acid was the sole commercial material, the other *o*-acylaminopyridine carboxylic acids have been obtained from commercial aminopyridines which reacted with pivaloyl chloride to give the expected *N*-pivaloylaminopyridines. The pivaloylamino group, a very good *ortho*-directing group, allowed us to obtain *ortho* lithioderivatives which after reaction with carbon dioxide led to *o*-*N*-pivaloylaminopyridine carboxylic acids.[8] It could be noticed that, if most are known, three of them are new (**1**-**3**) ones (Scheme 3).



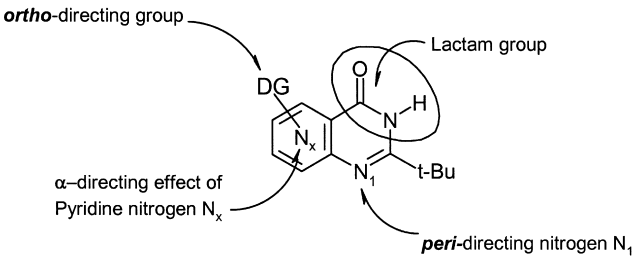
Scheme 3.

According to this general synthetic route, we have synthesized eight pyridopyrimidin-4(3*H*)-ones (**4**-**11**) among them compounds **6**-**11** are new ones. Compounds **4** and **5** were described as herbicides[9] (Scheme 4).

We have tested the direct lithiation and functionalization of the 2-*tert*-butylpyridopyrimidin-4(3*H*)-ones **4**-**11**.

During the lithiation of the benzene moiety of various benzodiazines,[3–5] it has been highlighted an exceptional regioselective metallation at the C_8 position, in *peri* to the ring nitrogen atom N_1. It has also been highlighted that the presence on the benzene moiety of a substituent inducing an *ortho*-directed metallation favored the lithiation reaction.

In the case of 2-*tert*-butylpyridopyrimidin-4(3*H*)-ones **4**-**11**, several parameters could be taken into account to direct the regioselectivity of the metallation (Scheme 5): the *peri* effect of the nitrogen atom N_1 of the pyrimidine moiety, the α effect of the nitrogen atom N_x of the pyridine moiety where the α position of the nitrogen atom was free and the *ortho*-effect of substituent such as a chlorine atom or a methoxy group for compounds **5**, **7**, **8**. For all these compounds except for **11**, it could be interesting to observe



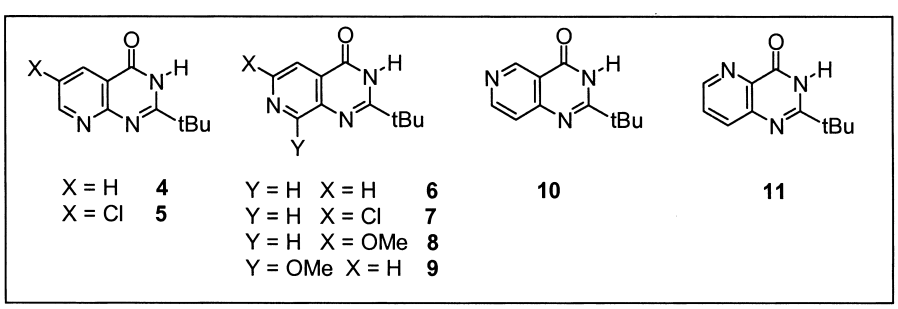
Scheme 5.

if the lactam group of the pyrimidinone moiety could have any influence on the *peri* position C_5 (Scheme 5).

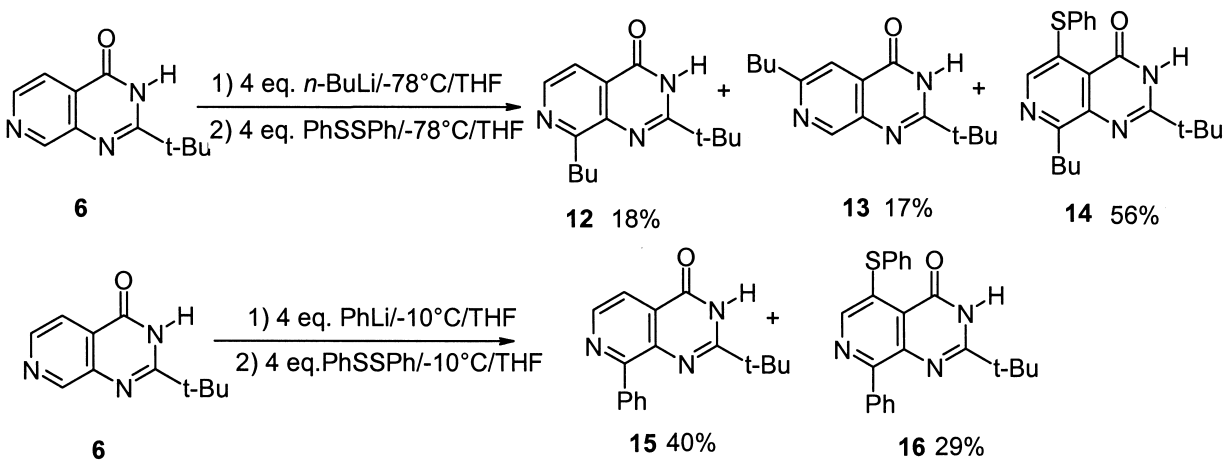
The lactam group has been previously used as *ortho*-directing group during the regioselective metallation at C_2 of the pyridine moiety of 5- or 6-methoxyquinolin-2(1*H*)-ones.[10] Otherwise, the lithiation of N_3-acylaminoquinazolin-4(3*H*)-ones has been described,[11] in this case, metallation occurred exclusively at C_2 which was influenced by the acylamino group on the ring nitrogen N_3. More recently, we have reported the metallation of quinazolones, these compounds underwent a regioselective metallation of the benzene moiety at the C_8 position, in *peri* to the ring nitrogen atom N_1, only when the benzene ring was substituted at C_7 position by a chlorine atom or a methoxy group.[5]

We have tested the metallation of 2-*tert*-butylpyridopyrimidin-4-(3*H*)-ones to appreciate if the presence of the pyridine nitrogen makes the deprotonation more easy than with quinazolones and could influence the regioselectivity. The presence of a *tert*-butyl group at the C_2 position has been chosen to avoid a nucleophilic attack of the metallating agent at this position[12,13] and to prevent the deprotonation on the carbon C_α of the lateral chain.[14–16]

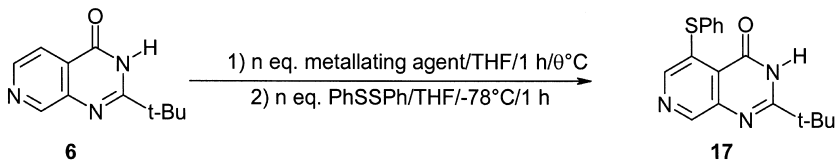
First, various attempts to metallate **6** with alkyllithiums have been performed. *n*-butyllithium and phenyllithium have been tested as metallating agent, followed by reaction with diphenyl disulfide as the electrophile. Treatment of **6** with 2 equiv. of *n*-butyllithium at −78 °C did not allow any reaction and 95% of starting material were recovered; use of 4 equiv. of butyllithium at this temperature afforded addition products (91%) besides a small amount of starting material (8%) (Scheme 6). Compounds **12** and **13** resulted from an addition at the α positions of the pyridine nitrogen (C_6 and C_8), whereas the main compound **14** resulted from an addition of *n*-butyllithium at C_8 followed by reaction



Scheme 4.



Scheme 6.



Scheme 7.

with electrophile at C_5, *peri* to the carbonyl of the lactam function.

When the reaction was performed with phenyllithium at −10 °C, two compounds **15** and **16** resulting from an addition reaction at C_8 were obtained in 69% total yield beside starting material (30%). For compound **14** as for compound **16**, we observed that the reaction with the electrophile has occurred at C_5 at the *peri* position of the lactam function.

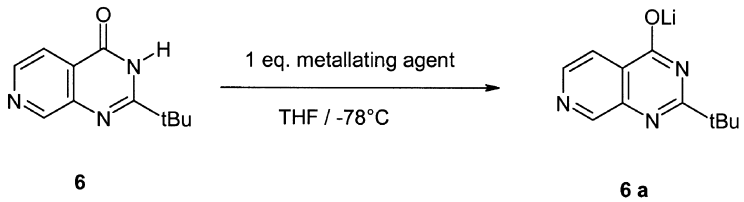
Reactions of addition observed with alkyllithiums as metallating agent urged us to use lithium alkylamides such as lithium 2,2,4,4-tetramethylpiperidide (LTMP) or lithium diisopropylamide (LDA) as metallating agent, which are known to be less nucleophilic than alkyllithiums. Later, the conditions of metallation have been established for compound **6**, with various amounts of lithium alkylamides as metallating agent, and diphenyl disulfide as the electrophile (Scheme 7, Table 1).

Table 1. Lithiation and functionalization of **6**

Entry	Metallating agent	*n* (equiv.)	Temperature *θ* (°C)	Compound **17** (%)
1	LTMP	2	−78	5
2	LTMP	4	−78	55
3	LTMP	4	0	45
4	LTMP	5	−78	75
5	LTMP	6	−78	90
6	LTMP	8	−78	97
7	LDA	8	−78	5

The results given in Table 1 revealed that a first attempt with 2 equiv. of LTMP at −78 °C afforded a small amount of **17** beside starting material (entry 1). With 4 equiv. of LTMP at −78 °C, the yield was improved to 55%, nevertheless, increasing the temperature to 0 °C gave a slightly lower yield (entries 2 and 3). A large excess of LTMP (6–8 equiv.) afforded **17** in very good yields (entries 5 and 6). When LDA, less basic than LTMP, was used even in large excess, only a few amount of **17** was obtained beside starting material (entry 7). The structure of compound **17** has been established thanks to its ^{1}H NMR spectrum which presented two singlets at 7.68 and 8.67 ppm assigned, to H_6 and H_8, highlighting a total regioselectivity at the C_5 position.

We have also tested if metallation could be performed by a mixture of bases. In the first step, the labile proton of the lactam function was trapped by 1 equiv. of base (*n*-BuLi or LTMP), leading to a lithium salt **6a** (Scheme 8) as this has been observed with its IR spectrum obtained with ReactIR™ spectrometer (Fig. 1). We could observe that the



Scheme 8.

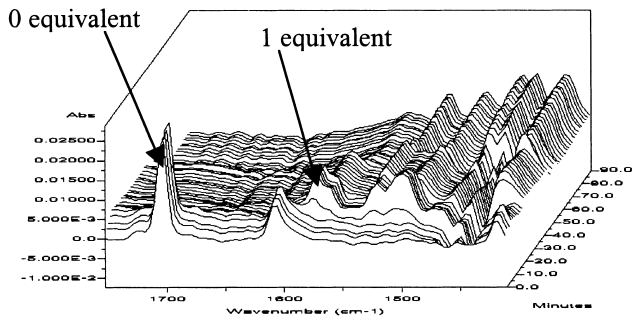


Figure 1. Spectroscopic analysis FTIR of **6** with *n* equivalent of *n*-butyllithium or LTMP.

introduction of 1 equiv. of metallating agent led to disappearance of peaks at 1700 and 1600 cm^{-1} assigned, respectively, to ν(C=O) and δ(N–H). The further equivalents of base could be used to induce either the metallation or additions.

Various attempts have been performed with a total of 5 equiv. of bases at −78 °C in THF for 1 h as total reaction time and with diphenyl disulfide as the electrophile. We have tested a mixture of lithium alkylamide–alkyllithium in various ratios. When a mixture of bases was used, the first base was reacted for 30 min, then the second base was introduced and reacted again for 30 min. The experimental conditions and results are given in Table 2.

Table 2. Metallation of **6** with a mixture of bases

Entry	Bases	Compound **6** (%)	Compound **17** (%)
1	5 equiv. LTMP	25	75
2	(1) 1 equiv. *n*-BuLi (2) 4 equiv. LTMP	35	65
3	(1) 4 equiv. LTMP (2) 1 equiv. *n*-BuLi	5	90
4	(1) 3 equiv. LTMP (2) 2 equiv. *n*-BuLi	25	75
5	(1) 2 equiv. LTMP (2) 3 equiv. *n*-BuLi	66	33
6	(1) 4 equiv. LDA (2) 1 equiv. *n*-BuLi	90	10

Treatment of **6** with 5 equiv. of LTMP as sole base provided the five-substituted compound **17** in 75% yield (entry 1). With 1 equiv. of *n*-butyllithium followed by reaction of 4 equiv. of LTMP (entry 2), we observed the formation of **17** in slightly lower yield (65%). For the entries 3–5, we have first used (*n*) equivalents of LTMP followed by reaction with (5−*n*) equivalents of *n*-butyllithium, the results revealed that a large excess of LTMP improved the yield of compound **17**. The best results have been obtained with the experimental conditions of entry 3. When LDA was used as alkylamide under the conditions of the entry 3, only small amount of **17** was obtained beside starting material (entry 6).

These results require some comments: when *n* equivalents of lithium alkylamides were first introduced followed by addition of (5−*n*) equivalents of *n*-butyllithium, the metallation reaction was observed without addition, even if *n*-butyllithium was in excess. In this case, it could be assumed that the first equivalent of lithium alkylamide trapped the labile proton of the lactam function, the other equivalents were used to give aggregates which then could favor metallation by LTMP or *n*-BuLi without occurrence of competitive addition reaction. We have nevertheless used the conditions of metallation given in Table 1 (entry 6) to functionalize the 2-*tert*-butylpyridopyrimidin-4(3*H*)-ones **4**-**11**, because the work up of the reaction mixture was easier.

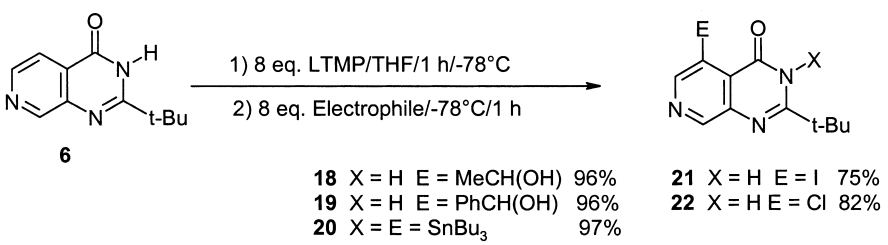
Treatment of **6** with 8 equiv. of LTMP at −78 °C followed by reaction with various electrophiles afforded five-substituted derivatives in very good yields (Scheme 9).

It must be noticed that when tributyltin chloride was used as the electrophile, a distannyl compound **20** was obtained, the presence of a lactam group was confirmed by its IR spectrum which exhibited a ν(CO) at 1688 cm^{-1}.

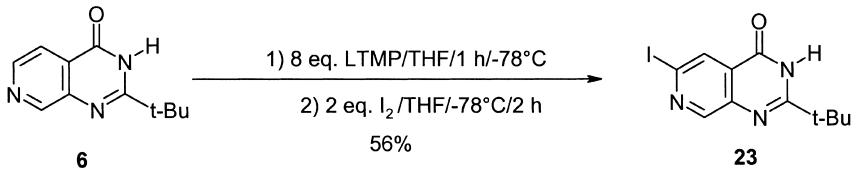
With iodine as the electrophile we have observed that the regioselectivity was dependent on the direct or inverse introduction of iodine. When iodine was introduced in the reaction mixture, two mono iodo derivatives at C_5 and C_6 were obtained, whereas compound **21** was the sole product isolated when the lithiated derivative was added to a solution of iodine in THF. The 6-iodo derivative **23** was obtained as sole product beside starting material (41%) by use of only 2 equiv. of iodine introduced in the reaction mixture after a 1 h reaction time (Scheme 10). Such a result could be explained by a 'halogen-dance' mechanism which has been previously described in the diazine series.[17]

It should be interesting to observe if the presence of a substituent such as a chlorine atom or a methoxy group could improve the reactivity towards lithiation and induce a particular regioselectivity. We have tested the metallation of substituted pyridopyrimidin-4(3*H*)-ones **7**-**9**.

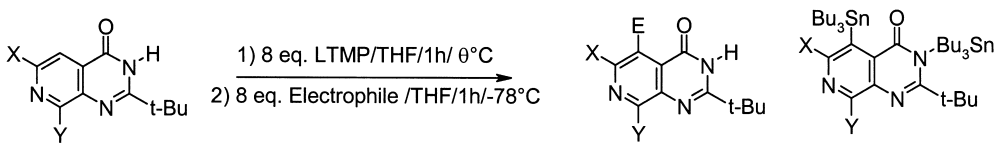
For all these compounds the C_5 position, *peri* to the



Scheme 9.



Scheme 10.



Scheme 11.

Table 3. Lithiation and functionalization of **7-9**

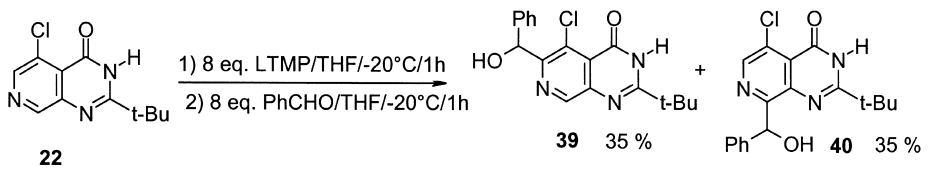
Starting material	X	Y	E	θ	Compounds (yield, %)
7	Cl	H	PhS	−78 °C	**24** (86)
			MeCH(OH)		**25** (97)
			PhCH(OH)		**26** (97)
			Bu_3Sn		**27** (84)
			I		**28** (87)
8	OMe	H	PhS	−78 to 0 °C	**29** (71)
			MeCH(OH)		**30** (92)
			PhCH(OH)		**31** (91)
			Bu_3Sn		**32** (75)
			I		**33** (88)
9	H	OMe	PhS	−78 to −20 °C	**34** (89)
			MeCH(OH)		**35** (90)
			PhCH(OH)		**36** (85)
			Bu_3Sn		**37** (75)
			I		**38** (85)

carbonyl group, was free as also one α position of the pyridine nitrogen atom. Various experimental conditions were tested and as before 8 equiv. of LTMP were necessary to obtain good yields (Scheme 11, Table 3).

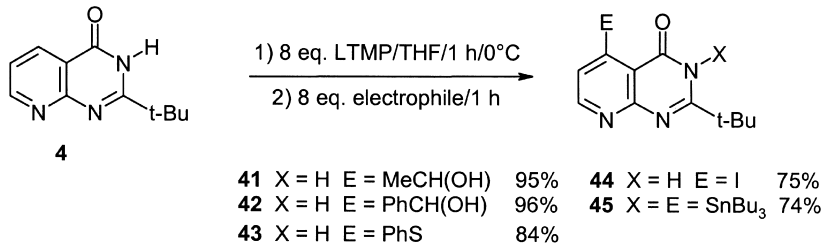
Under these experimental conditions, lithiation of **7-9** occurred exclusively at the C_5 position and reaction with various electrophiles led to 2-*tert*-butyl-5-substituted pyrido-[3,4-*d*]pyrimidin-4(3*H*)-ones **24-38** in good yields. As it has been previously mentioned, when tributyl tin chloride was used as the electrophile, the distannyl compounds **27**, **32** and **37** were obtained. It can be noticed that the presence of a methoxy group on the pyridine moiety required higher metallation temperature. For compounds **8** and **9** the metallating agent was introduced at −78 °C and the temperature was raised, respectively, to 0 °C and to −20 °C.

We have then tested the metallation of the 2-*tert*-butyl-5-chloropyrido [3,4-*d*]pyrimidin-4(3*H*)-one **22**, for this compound the C_5 position carried a chlorine atom and could not undergo lithiation, whereas positions C_6 and C_8 in α position to pyridine nitrogen atom were free. Treatment of **22** with 8 equiv. of LTMP at −20 °C for 1 h followed by reaction with benzaldehyde as electrophile afforded two compounds **39** and **40** in equal amounts with a global yield of 70% beside starting material (17%) (Scheme 12).

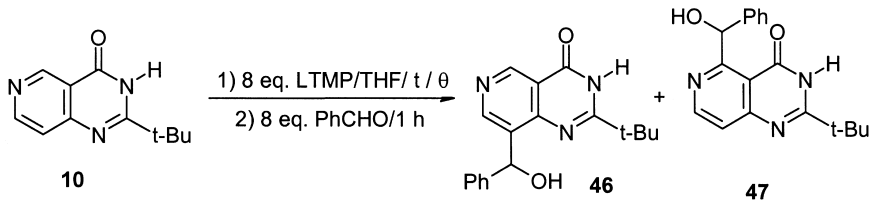
Despite the substitution of the C_5 position, this result indicated that metallation could occur at once at the C_6



Scheme 12.



Scheme 13.



Scheme 14.

Table 4. Metallation of compound **10**

Entry	Temperature , θ (°C)	Time, t (h)	Compound **46** (%)	Compound **47** (%)	Compound **10** (%)
1	−78	1	20	—	80
2	−20	1	92	3	5
3	0	1	75	18	7
4	20	1	62	29	9
5	20	2	9	74	16
6	20	3	7	76	17

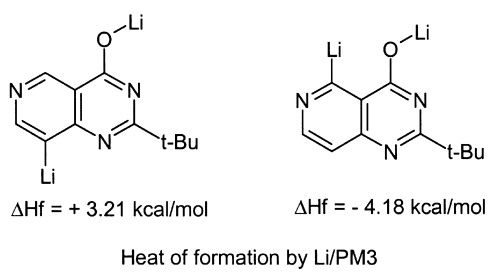
position influenced by the chlorine atom as *ortho*-directing group and the pyridine nitrogen atom, or at the C_8 position under influence of the two ring nitrogen atoms N_1 and N_7. It could be noticed that, if the single effect of the pyridine nitrogen N_7 was not sufficient to allow the metallation, the reaction became feasible when this effect was associated to an other effect such as an *ortho*-directing group or a *peri* ring nitrogen atom.

We have then tested the metallation of compounds **4** and **10** for which the C_5 position was kept free. Treatment of **4** with 8 equiv. of LTMP at 0 °C for 1 h, followed by reaction with various electrophiles led to five-substituted compounds **41**-**45** in good yields (Scheme 13).

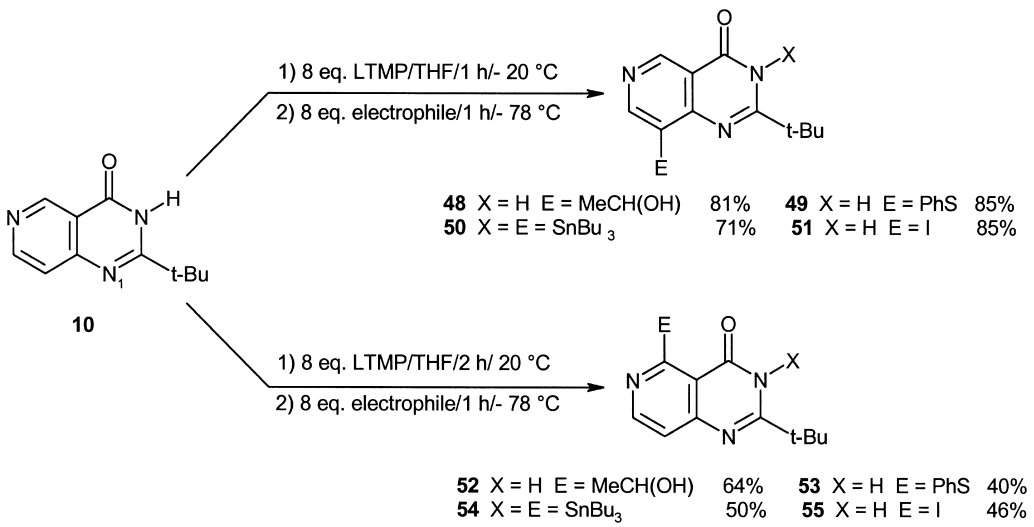
For compound **10**, the metallation reaction was performed with 8 equiv. of LTMP at various temperatures with benzaldehyde as the electrophile, under these conditions it has been observed that the regioselectivity was dependent on the temperature and the reaction time (Scheme 14, Table 4).

The results given in Table 4 revealed, that with a 1 h reaction time, only a few amount of **46** was obtained at −78 °C beside starting material (entry 1). When the temperature was raised to −20 °C, compound **46** was observed as the main product with a very good yield (entry 2). Then when temperature was increased from −20 °C to room temperature, we observed decreasing amounts of **46**, whereas the formation of **47** was growing up (entries 2–4). When the reaction was performed at 20 °C with rising reaction times, the compound **47** became the main product with 2 or 3 h for reaction time beside starting material (entries 4–6).

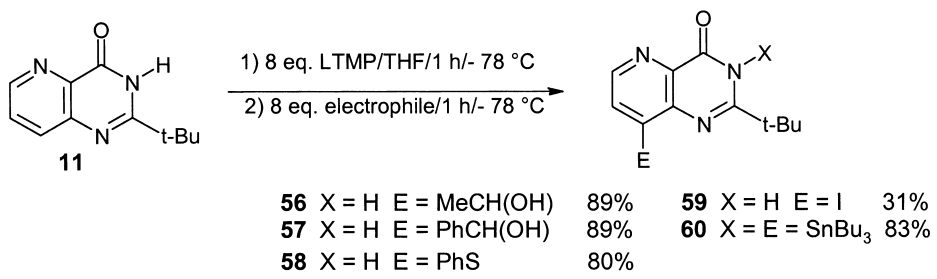
Regioselectivity of the lithiation could be discussed in terms of kinetic or thermodynamic control. Compound **47** which was obtained at higher temperatures and with a longer reaction time could be the thermodynamic compound while compound **46** obtained in softer conditions could be the kinetic compound. When deprotonation is thermodynamically controlled, heats of formation of the lithiated derivatives determined by semi-empirical Li/PM3 method could be examined as a simple approach to account for the regioselectivity. Heat of formation of the lithiated derivatives calculated by Li/PM3 method (Scheme 15) indicated that the C_5 lithiated intermediate is the more stable isomer, which is in agreement with the experimental results.



Scheme 15.



Scheme 16.



Scheme 17.

We have extended these results to other electrophiles and observed that at low temperature (−20 °C) with a reaction time of 1 h the eight-substituted compounds were obtained as main products in very good yields. When the reaction was performed at room temperature with a reaction time of 2 h, the C_5-substituted compounds were obtained in moderate yields (Scheme 16).

At last, we have tested the metallation of compound **11** for which the pyridine nitrogen atom is at the position 5, *peri* to the carbonyl group of the lactam function. It should be interesting to observe if the lithiation could be obtained and in the affirmative if a regioselectivity could de observed. Treatment of **11** with 8 equiv. of LTMP at −78 °C for 1 h followed by reaction with various electrophiles afforded the eight-substituted compounds **56-60** (Scheme 17).

2. Conclusion

Starting from *o*-aminopyridine carboxylic acids, a general synthetic route leading to various pyridopyrimidin-4(3*H*)-ones has been described. The first metallation and functionalization of the pyridine moiety has been studied. An original regioselective metallation at the *peri* position C_5 of the pyridine ring has been observed when an excess of metallating agent was used, allowing access to a wide range of new substituted pyridopyrimidin-4(3*H*)-ones. In some cases, control of the experimental conditions allowed the formation of *peri* compounds either at C_5 or C_8 positions. This general synthetic route associated to palladium cross-coupling reactions is promising to access to new compounds.

3. Experimental

Melting points were determined on a Kofler hot-stage. The ^1H and ^{13}C NMR spectra were recorded in deuteriochloroform or deuteriodymethylsulfoxide on Bruker instrument (Avance 300). Microanalyses were performed on a Carlo Erba CHNOS 1160 apparatus. The IR spectra were obtained as potassium bromide pellets with a Perkin Elmer FTIR 1650 spectrophotometer.

All reagents were of commercial quality and were purchased from Aldrich Chemical Co. or Acros. 2-*tert*-Butylpyrido [3,2-*d*]pyrimidine-4(3*H*)-one **4** was synthesized according to the procedure described in the literature.[9]

3.1. Procedure A for the metallation of various *N*-pivaloylaminopyridines

An oven-dried three-necked round bottom flask was cooled in a dessicator and then equipped with a thermometer and a magnetic stirrer, and flushed with a nitrogen inlet. The flask was charged with *N*-pivaloylaminopyridine and stoppered with a rubber septum and anhydrous THF or diethylether

was introduced. After cooling to −78 °C, metallating agent and TMEDA were added dropwise via syringe. The mixture was stirred for 15 min and heated to *T* (°C). After 3 h of stirring at *T* (°C), a precipitate appeared and the suspension was cooled again to −78 °C and poured onto an excess of dry ice. After 1 h, the reaction mixture was hydrolyzed with 50 mL of water and was allowed to warm to room temperature, and the organic layer was removed under reduced pressure. The residue was partitioned between water and ethyl ether, and the aqueous phase separated and again washed with ethyl ether. The aqueous layer was acidified with 50% hydrochloric acid to give an off-white solid that was filtered, thoroughly washed with water. The solid was triturated with acetone and filtered to leave a white solid.

3.2. Procedure B for preparation of 2-*tert*-butylpyrido-pyrimidin-4(3*H*)-ones via 2-*tert*-butylpyrido[1,3]oxazin-4-ones

Acetic anhydride (20–100 mL) and *o*-(*N*-pivaloylamino)-pyridinecarboxylic acids (2–8 g) were refluxed together for 2 h. The excess of anhydride was removed by distillation under reduced pressure to give crude pyrido-oxazinone, then ammonia 15 N (30–150 mL) was added, and the mixture was stirred at room temperature for 24 h. Evaporation of the solution or suspension under reduced pressure yielded the pyridopyrimidinone by precipitation and filtration. To complete the conversion of pyrido-oxazinone into pyridopyrimidinone, the mixture could be heated with 5% aqueous sodium hydroxide for 15 min.

3.3. Procedure C for direct metallation of 2-*tert*-butyl-pyrido[3,4-*d*]pyrimidin-4(3*H*)-one by *n*-butyl-lithium or phenyllithium

A solution of 2-*tert*-butylpyridopyrimidin-4(3*H*)-one (50 mg, 0.24 mmol) in anhydrous THF (20 mL) was cooled to −78 °C, at this temperature a solution of *n*-butyllithium or phenyllithium (*n* equivalents) in hexane was introduced dropwise under an atmosphere of dry argon. The mixture was stirred for 15 min and warmed to the temperature *T* (°C). After 1 h of stirring at *T* (°C), the temperature was decreased again to −78 °C and the diphenyl disulfide (4 equiv., 215 mg) was introduced in solution with THF (5 mL). After 1 h, hydrolysis was carried out using a mixture of water and ethanol (1:1), the organic layer was removed under reduced pressure. The aqueous phase was extracted with ethyl acetate (3×20 mL), the combined organic extracts were then dried over magnesium sulfate and evaporated. The crude product was purified by column chromatography on silica gel.

3.4. Procedure D for metallation of 2-*tert*-butylpyrido-pyrimidin-4(3*H*)-ones by lithium 2,2,6,6-tetramethyl-piperidide

A solution of *n*-butyllithium (1.6 or 2.5 M in hexane) was added to cold (−78 °C), stirred and anhydrous mixture of THF (15 mL) and 2,2,6,6-tetramethylpiperidine (TMPH) under an atmosphere of dry nitrogen. The mixture was warmed to 0 °C and after 30 min, the mixture temperature was cooled to −78 °C and added to a cold (−78 °C) solution of the 2-*tert*-butylpyridopyrimidin-4(3*H*)-one in THF (10 mL). Then, the mixture was stirred for 5 min and heated to *T* (°C). After 1 h of stirring at *T* (°C), the temperature was decreased to −78 °C and the electrophile introduced and stirring was continued for *t* hour(s) at this temperature. Hydrolysis was then carried out at −78 °C using a solution of water and ethanol (1:1). When the electrophile was iodine, the solution was decolorized with sodium thiosulfate. At room temperature, water (10 mL) was added to the mixture and THF was removed under reduced pressure. The aqueous layer was extracted with dichloromethane or ethyl acetate (3×20 mL), the combined organic extracts were then dried over magnesium sulfate and evaporated. The crude product was purified by column chromatography on silica gel.

3.5. Procedure E for metallation of 2-*tert*-butylpyrido-pyrimidin-4(3*H*)-ones by lithium 2,2,6,6- tetramethyl-piperidide

The workup of the procedures D and E is similar but differs only by the order of introduction of the electrophile. For procedure E, the lithiated product was introduced into the electrophile solution.

3.5.1. 3-(*tert*-Butylcarbonylamino)-6-methoxy-isonicotinic acid (1). Metallation of *N*-(6-methoxy-3-pyridyl)-2,2-dimethylpropanamide (10 g, 48 mmol) according to the procedure A with *n*-BuLi 2.5 M (2.5 equiv., 48 mL), TMEDA (2.5 equiv., 18.13 mL) in anhydrous ethyl ether (300 mL) at *T*=−10 °C gave 7.43 g (61%) of **1** as a colorless solid, mp 240–241 °C; ^{1}H NMR ($CDCl_3$): δ 1.15 (s, 9H, *tert*-butyl); 3.78 (s, 3H, OMe); 7.12 (s, 1H, H_5); 9.00 (s, 1H, H_2); 10.49 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 27.5 (3 $Me_{tert\text{-butyl}}$); 49.0 (CMe_3); 53.9 (OMe); 110.5 (CH); 129.8 (C_{py}); 130.7 (C_{py}); 140.6 (CH); 159.8 (C_{py}); 167.9 (CO); 176.5 (CO). Anal. Calcd for $C_{12}H_{16}N_2O_4$ (252.27): C, 57.13; H, 6.39; N, 11.10. Found: C, 57.39; H, 6.76; N, 10.88.

3.5.2. 3-(*tert*-Butylcarbonylamino)-2-methoxy-isonicotinic acid (2). Metallation of *N*-(2-methoxy-3-pyridyl)-2,2-dimethylpropanamide (10 g, 48 mmol) according to the procedure A with *n*-BuLi 2.5 M (2.5 equiv., 48 mL), TMEDA (2.5 equiv., 18.13 mL) in anhydrous diethyl ether (300 mL) at *T*=−10 °C gave 8.41 g (69%) of **2** as a colorless solid, mp 39–40 °C; ^{1}H NMR ($CDCl_3$): δ 1.25 (s, 9H, *tert*-butyl); 3.96 (s, 3H, OMe); 7.19 (d, J_{5-6}=5.6 Hz, 1H, H_5); 7.98 (d, J=5.6 Hz, 1H, H_6); 7.89 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 27.5 (3 $Me_{tert\text{-butyl}}$); 39.8 (CMe_3); 54.8 (OMe); 116.7 (CH); 119.8 (C_{py}); 133.4 (C_{py}); 142.9 (CH); 157.4 (C_{py}); 167.5 (CO); 177.9 (CO). Anal. Calcd for $C_{12}H_{16}N_2O_4$ (252.27): C, 57.13; H, 6.39; N, 11.10. Found: C, 56.98; H, 6.09; N, 11.51.

3.5.3. 2-(*tert*-Butylcarbonylamino)-5-chloronicotinic acid (3). Metallation of *N*-(5-chloro-2-pyridyl)-2,2-dimethylpropanamide (10 g, 47 mmol) according to the procedure A with *tert*-BuLi 1.5 M (2.25 equiv., 48 mL) in anhydrous THF (150 mL) at *T*=−78 °C gave 11.35 g (94%) of **3** as a white solid mp 238–239 °C; ^{1}H NMR (DMSO): δ 1.52 (s, 9H, *tert*-butyl); 8.14 (d, J=2.8 Hz, 1H, H_4); 8.35 (d, J=2.8 Hz, 1H, H_6); 12.41 (s, 1H, NH); ^{13}C NMR (DMSO): δ 27.3 ($Me_{tert\text{-butyl}}$); 39.7 (CMe_3); 67.3 (CCl); 120.6 (C_{py});

124.7 (C_{py}); 138.8 (CH); 148.1 (CH); 150.8 (C_{py}); 166.8 (CO); 175.7 (CO). Anal. Calcd for $C_{11}H_{13}N_2O_3Cl$ (256.69): C, 51.47; H, 5.10; N, 10.91. Found: C, 51.38; H, 5.07; N, 11.03.

3.5.4. 2-*tert*-Butyl-6-chloropyrido[2,3-*d*]pyrimidin-4(3*H*)-one (5). Reaction of 2-(*tert*-butyl-carbonylamino)-5-chloronicotinic acid (3 g) with acetic anhydride (30 mL) according to the procedure B, followed by reaction with 15 N ammonia (100 mL) gave 2.286 g (82%) of **5** as a colorless solid, mp>250 °C; ^{1}H NMR (DMSO): δ 1.39 (s, 9H, *tert*-butyl); 8.47 (d, J_{5-7}=2.6 Hz, 1H, H_5); 8.94 (d, J=2.6 Hz, 1H, H_7); 12.38 (s, 1H, NH); ^{13}C NMR (DMSO): δ 27.9 ($3Me_{tert\text{-butyl}}$); 38.0 (CMe_3); 116.7 (C_{py}); 128.4 (C_{py}); 134.2 (CH_{py}); 154.6 (CH_{py}); 156.9 (C_{py}); 162.5 (C_{py}); 167.0 (C_{py}). Anal. Calcd for $C_{11}H_{12}N_3OCl$ (237.69): C, 55.59; H, 5.09; N, 17.68. Found: C, 55.71; H, 5.04; N, 17.73.

3.5.5. 2-*tert*-Butylpyrido[3,4-*d*]pyrimidin-4(3*H*)-one (6). Reaction of 3-(*tert*-butylcarbonyl-amino)isonicotinic acid (2.8 g) with acetic anhydride (30 mL) according to the procedure B, followed by reaction with 15 N ammonia (30 mL) gave 1.61 g (63%) of **6** as a colorless solid, mp 208–209 °C; ^{1}H NMR ($CDCl_3$): δ 1.43 (s, 9H, *tert*-butyl); 7.96 (dd, J_{6-5}=5.3 Hz, J_{6-8}=0.76 Hz, 1H, H_6); 8.61 (d, J=5.3 Hz, 1H, H_5); 9.10 (d, J=0.76 Hz, 1H, H_8); 11.10 (s, 1H, NH); ^{13}C NMIR ($CDCl_3$): δ 28.5 ($3Me_{tert\text{-butyl}}$); 38.1 (CMe_3); 118.3 (CH_{py}); 125.8 (C_{py}); 144.0 (C_{py}); 146.3 (CH_{py}); 152.0 (CH_{py}); 163.1 (C_{py}); 164.5 (C_{py}). Anal. Calcd for $C_{11}H_{13}N_3O$ (203.24): C, 65.01; H, 6.45; N, 20.67. Found: C, 64.98; H, 6.44; N, 20.20.

3.5.6. 2-*tert*-Butyl-6-chloropyrido[3,4-*d*]pyrimidin-4(3*H*)-one (7). Reaction of 3-(*tert*-butyl-carbonylamino)-6-chloro-isonicotinic acid (8 g) with acetic anhydride (80 mL) according to the procedure B, followed by reaction with 15 N ammonia (150 mL) gave 6.72 g (90%) of **7** as a brown solid, mp 237–238 °C; ^{1}H NMR ($CDCl_3$): δ 1.43 (s, 9H, *tert*-butyl); 7.98 (s, 1H, H_5); 8.87 (s, 1H, H_8); 11.19 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.5 ($3Me_{tert\text{-butyl}}$); 38.2 (CMe_3); 118.9 (CH_{py}); 128.2 (C_{py}); 143.0 (C_{py}); 147.8 (C_{py}); 152.0 (CH_{py}); 162.2 (C_{py}); 164.7 (C_{py}). Anal. Calcd for $C_{11}H_{12}N_3O_2Cl$ (237.68): C, 55.59; H, 5.09; N, 17.68. Found: C, 55.53; H, 5.37; N, 17.72.

3.5.7. 2-*tert*-Butyl-6-methoxypyrido[3,4-*d*]pyrimidin-4(3*H*)-one (8). Reaction of 3-(*tert*-butyl-carbonylamino)-6-methoxy-isonicotinic acid (2.42 g) with acetic anhydride (30 mL) according to the procedure B, followed by reaction with 15 N ammonia (30 mL) gave 1.43 g (65%) **8** as a colorless solid, mp 248–249 °C; ^{1}H NMR ($CDCl_3$): δ 1.39 (s, 9H, *tert*-butyl); 3.96 (s, 3H, OMe); 7.37 (s, 1H, H_5); 8.70 (s, 1H, H_8); 10.49 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.5 ($3Me_{tert\text{-butyl}}$); 37.7 (CMe_3); 54.7 (OMe); 103.3 (CH_{py}); 129.3 (C_{py}); 138.8 (C_{py}); 149.2 (CH_{py}); 160.7 (C_{py}); 162.6 (C_{py}); 162.8 (C_{py}). Anal. Calcd for $C_{12}H_{15}N_3O_2$ (233.27): C, 61.79; H, 6.48; N, 18.01. Found: C, 61.67; H, 6.72; N, 17.79.

3.5.8. 2-*tert*-Butyl-8-methoxypyrido[3,4-*d*]pyrimidin-4(3*H*)-one (9). Reaction of 3-(*tert*-butyl-carbonylamino)-2-methoxy-isonicotinic acid (6.8 g) with acetic anhydride (80 mL) according to the procedure B, followed by reaction with 15 N ammonia (150 mL) and 5% aqueous sodium hydroxyde (100 mL) gave 5.93 g (93%) of **9** as a colorless solid, mp>250 °C; ^{1}H NMR ($CDCl_3$): δ 1.44 (s, 9H, *tert*-butyl), 4.07 (s, 3H, OMe); 7.54 (d, J_{5-6}=5.3 Hz, 1H, H_5); 8.08 (d, J=5.3 Hz, 1H, H_6); 11.15 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.6 ($3Me_{tert\text{-butyl}}$); 38.2 (CMe_3); 55.0 (OMe); 111.7 (CH_{py}); 127.5 (C_{py}); 134.8 (C_{py}); 142.7 (CH_{py}); 160.4 (C_{py}); 162.8 (C_{py}); 163.8 (C_{py}). Anal. Calcd for $C_{12}H_{15}N_3O_2$ (233.27): C, 61.79; H, 6.48; N, 18.01. Found: C, 61.82; H, 6.65; N, 18.31.

3.5.9. 2-*tert*-Butylpyrido[4,3-*d*]pyrimidin-4(3*H*)-one (10). Reaction of 4-(*tert*-butylcarbonyl-amino)nicotinic acid (6.44 g) with acetic anhydride (100 mL) according to the procedure B, followed by reaction with 15 N ammonia (100 mL) gave 5.155 g (87%) of **10** as a colorless solid, mp 248–249 °C; ^{1}H NMR (DMSO): δ 1.13 (s, 9H, *tert*-butyl); 7.30 (d, J_{7-8}=5.65 Hz, 1H, H_8); 8.56 (d, J=5.65 Hz, 1H, H_7); 9.02 (s, 1H, H_5); 12.03 (s, 1H, NH); ^{13}C NMR (DMSO): δ 27.9 ($3Me_{tert\text{-butyl}}$); 38.0 (CMe_3); 116.7 (C_{py}); 120.9 (CH_{py}); 149.6 (CH_{py}); 153.6 (CH_{py}); 161.9 (C_{py}); 168.2 (C_{py}). Anal. Calcd for $C_{11}H_{13}N_3O$ (203.24): C, 65.01; H, 6.45; N, 20.67. Found: C, 65.11; H, 6.43; N, 20.64.

3.5.10. 2-*tert*-Butylpyrido[3,2-*d*]pyrimidin-4(3*H*)-one (11). A solution of 3-aminopicolinic acid (1.50 g) and pivaloyl chloride (3.27 mL, 2.5 equiv.) in pyridine (10 mL) was refluxed for 30 min. The mixture was cooled to 10 °C, diluted with water and extracted with dichloromethane (3×25 mL). The combined organic extracts were then dried over magnesium sulfate and evaporated under reduced pressure to give crude pyrido-oxazinone. Then, 15 N ammonia (50 mL) was added and the mixture was stirred at room temperature for 24 h. Evaporation of the solution or suspension under reduced pressure yielded 1.71 g (78%) of **11** as a brown solid, mp 250–251 °C; ^{1}H NMR (DMSO): δ 1.42 (s, 9H, *tert*-butyl); 7.83 (dd, J_{6-7}=4.5 Hz, J_{7-8}=8.3 Hz, 1H, H_7); 8.09 (dd, J_{8-6}=1.5 Hz, J=8.3 Hz, 1H, H_8); 8.81 (dd, J=4.5, 1.5 Hz, 1H, H_6); 12.24 (s, 1H, NH); ^{13}C NMR (DMSO): δ 28.1 ($3Me_{tert\text{-butyl}}$); 37.6 (CMe_3); 129.0 (CH_{py}); 135.9 (CH_{py}); 137.9 (C_{py}); 145.3 (C_{py}); 149.1 (CH_{py}); 161.1 (C_{py}); 163.8 (C_{py}). Anal. Calcd for $C_{11}H_{13}N_3O$ (203.24): C, 65.01; H, 6.45; N, 20.67. Found: C, 64.87; H, 6.44; N, 20.82.

3.6. Metallation of 2-*tert*-butylpyrido[3,4-*d*]pyrimidin-4(3*H*)-one (6)

According to the procedure C with *n*-BuLi 1.6 M (4 equiv., 0.63 mL), T=−78 °C followed by reaction with diphenyldisulfide (4 equiv., 215 mg) gave after purification by column chromatography (silicagel, eluent: (1) dichloromethane, (2) diethyl ether) 11 mg (18%) of 8-*n*-butyl-2-*tert*-butylpyrido[3,4-*d*]pyrimidin-4(3*H*)-one (**12**), 10 mg (17%) of 6-*n*-butyl-2-*tert*-butylpyrido[3,4-*d*]pyrimidin-4(3*H*)-one (**13**) and 51 mg (56%) of 8-*n*-butyl-2-*tert*-butyl-5-phenylthiopyrido[3,4-*d*]pyrimidin-4(3*H*)-one (**14**).

3.6.1. 8-*n*-Butyl-2-*tert*-butylpyrido[3,4-*d*]pyrimidin-4(3*H*)-one (12). Light brown solid, mp 120–121 °C; ^{1}H NMR ($CDCl_3$): δ 0.90 (t, J=7.3 Hz, 3H, Me); 1.37 (m, 2H, CH_2); 1.40 (s, 9H, *tert*-butyl); 1.68 (m, 2H, CH_2); 3.23 (t, J=7.6 Hz, 2H, CH_2); 7.80 (d, J_{5-6}=5.5 Hz, 1H, H_5); 8.48 (d, J=5.5 Hz, 1H, H_6); 10.53 (s, 1H, NH); ^{13}C NMR

($CDCl_3$): δ 14.3 (Me); 23.1 (CH_2); 28.5 ($3Me_{tert\text{-}butyl}$); 31.9 (CH_2); 33.7 (CH_2); 38.2 (*C*Me_3); 116.3 (CH_{py}); 125.6 (C_{py}); 134.1 (C_{py}); 145.0 (CH_{py}); 162.7 (C_{py}); 163.6 (C_{py}); 163.9 (C_{py}). Anal. Calcd for $C_{15}H_{21}N_3O$ (259.35): C, 69.47; H, 8.16; N, 16.20. Found: C, 69.53; H, 8.11; N, 16.28.

3.6.2. 6-*n*-Butyl-2-*tert*-butylpyrido[3,4-*d*]pyrimidin-4(3*H*)-one (13). Light brown solid, mp 114–115 °C; ^1H NMR ($CDCl_3$): δ 0.88 (t, *J*=7.3 Hz, 3H, Me); 1.33 (m, 2H, CH_2); 1.39 (s, 9H, *tert*-butyl); 1.64 (m, 2H, CH_2); 3.08 (t, *J*=7.7 Hz, 2H, CH_2); 8.18 (s, 1H, H_5); 10.12 (s, 1H, NH); 10.22 (s, 1H, H_6); ^{13}C NMR ($CDCl_3$): δ 14.3 (Me); 23.0 (CH_2); 28.5 ($3Me_{tert\text{-}butyl}$); 30.0 (CH_2); 32.0 (CH_2); 32.9 (CH_2); 38.2 (*C*Me_3); 111.6 (C_{py}); 113.2 (C_{py}); 133.2 (CH_{py}); 136.3 (CH_{py}); 151.7 (CH_{py}); 152.9 (C_{py}); 162.2 (C_{py}); 167.4 (C_{py}). Anal. Calcd for $C_{15}H_{21}N_3O$ (259.35): C, 69.47; H, 8.16; N, 16.20. Found: C, 69.36; H, 8.09; N, 15.98.

3.6.3. 8-*n*-Butyl-2-*tert*-butyl-5-phenylthiopyrido[3,4-*d*]-pyrimidin-4(3*H*)-one (14). Colorless solid, mp 160–161 °C; ^1H NMR ($CDCl_3$): δ 0.86 (t, *J*=7.3 Hz, 3H, Me); 1.32 (m, 2H, CH_2); 1.45 (s, 9H, *tert*-butyl); 1.64 (m, 2H, CH_2); 3.08 (t, *J*=7.6 Hz, 2H, CH_2); 7.40 (m, 3H, Ph); 7.58 (m, 2H, Ph); 7.59 (s, 1H, H_6); 11.84 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 14.3 (Me); 23.0 (CH_2); 28.5 ($3Me_{tert\text{-}butyl}$); 31.6 (CH_2); 33.2 (CH_2); 38.3 (*C*Me_3); 121.3 (C_{py}); 130.0 (CH_{Ph}); 130.4 ($2CH_{Ph}$); 131.1 (C_{Ph}); 134.1 (C_{py}); 136.4 ($2CH_{Ph}$); 141.3 (CH_{py}); 142.6 (C_{py}); 158.2 (C_{py}); 163.3 (C_{py}); 164.5 (C_{py}). Anal. Calcd for $C_{21}H_{25}N_3OS$ (367.51): C, 68.63; H, 6.86; N, 11.43; S, 8.73. Found: C, 68.67; H, 6.79; N, 12.01; S, 8.82.

3.7. Metallation of 2-*tert*-butylpyrido[3,4-*d*]pyrimidin-4(3*H*)-one (6)

According to the procedure C with PhLi 1.8 M (4.2 equiv., 0.57 mL), *T*=0 °C, followed by reaction with diphenyl disulfide (4 equiv., 215 mg) gave after purification by column chromatography (silica, eluent: dichloromethane/diethylether, 7:3)) 27 mg (40%) of 2-*tert*-butyl-8-phenyl-pyrido[3,4-*d*]pyrimidin-4(3*H*)-one (**15**) and 28 mg (29%) of 2-*tert*-butyl-8-phenyl-5-phenylthio-pyrido[3,4-*d*]pyrimidin-4(3*H*)-one (**16**).

3.7.1. 2-*tert*-Butyl-8-phenylpyrido[3,4-*d*]pyrimidin-4(3*H*)-one (15). Light brown solid, mp 218–219 °C; ^1H NMR ($CDCl_3$): δ 1.39 (s, 9H, *tert*-butyl); 7.39 (m, 3H, Ph); 7.96 (d, J_{5-6}=4.9 Hz, 1H, H_5); 8.13 (m, 2H, Ph); 8.68 (d, *J*=4.9 Hz, 1H, H_6); 11.29 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.5 ($3Me_{tert\text{-}butyl}$); 38.5 (*C*Me_3); 117.6 (CH_{py}); 127.0 (C_{py}); 128.0 ($2CH_{Ph}$); 129.2 (CH_{Ph}); 131.4 ($2CH_{Ph}$); 138.0 (C_{Ph}); 141.6 (C_{py}); 145.7 (CH_{py}); 157.9 (C_{py}); 163.1 (C_{py}); 163.6 (C_{py}). Anal. Calcd for $C_{16}H_{16}N_3O$ (266.33): C, 72.16; H, 6.06; N, 15.78. Found: C, 72.19; H, 6.11; N, 15.81.

3.7.2. 2-*tert*-Butyl-8-phenyl-5-phenylthiopyrido[3,4-*d*]-pyrimidin-4(3*H*)-one (16). Colorless solid, mp>250 °C; ^1H NMR ($CDCl_3$): δ 1.44 (s, 9H, *tert*-butyl); 7.38 (m, 6H, Ph); 7.63 (m, 2H, Ph); 7.80 (s, 1H, H_6); 8.05 (m, 2H, Ph); 11.63 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.6 ($3Me_{tert\text{-}butyl}$); 38.6 (*C*Me_3); 122.4 (C_{py}); 127.9 ($2CH_{Ph}$); 128.8 (CH_{Ph}); 130.2 (CH_{Ph}); 130.6 ($2CH_{Ph}$); 130.8 (C_{Ph}); 131.0 ($2CH_{Ph}$); 136.2 (C_{py}); 136.4 ($2CH_{Ph}$); 138.0 (C_{Ph}); 142.0 (CH_{py}); 142.1 (C_{py}); 152.1 (C_{py}); 163.4 (C_{py}); 164.3 (C_{py}). Anal. Calcd for $C_{23}H_{21}N_3OS$ (387.51): C, 71.29; H, 5.46; N, 10.84; S, 8.27. Found: C, 71.34; H, 5.51; N, 10.90; S, 8.21.

3.7.3. 2-*tert*-Butyl-5-phenylthiopyrido[3,4-*d*]pyrimidin-4(3*H*)-one (17). Metallation of **6** (100 mg, 0.48 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 2.46 mL), TMPH (8 equiv., 0.67 mL), *T*=−78 °C, followed by reaction with diphenyl disulfide (8 equiv., 860 mg) in solution with anhydrous THF (5 mL), *t*=1 h, gave after purification by column chromatography (silicagel, eluent: petroleum ether/di ethyl ether , 1:1)) 159 mg (97%) of **12** as a yellow solid, mp>250 °C; ^1H NMR ($CDCl_3$): δ 1.46 (s, 9H, *tert*-butyl); 7.43 (m, 3H, Ph); 7.60 (m, 2H, Ph); 7.68 (s, 1H, H_6); 8.67 (s, 1H, H_8); 11.87 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.5 ($3Me_{tert\text{-}butyl}$); 38.2 (*C*Me_3); 121.4 (C_{py}); 130.3 (CH_{Ph}); 130.5 (C_{Ph}); 130.6 ($2CH_{Ph}$); 136.4 ($2CH_{Ph}$); 137.3 (C_{py}); 142.5 (CH_{py}); 144.7 (C_{py}); 146.5 (CH_{py}); 164.0 (C_{py}); 165.0 (C_{py}). Anal. Calcd for $C_{17}H_{17}N_3OS$ (311.40): C, 65.57; H, 5.50; N, 13.49; S, 10.30. Found: C, 65.33; H, 5.51; N, 13.26; S, 9.98.

3.7.4. 2-*tert*-Butyl-5-(1-hydroxyethyl)pyrido[3,4-*d*]pyrimidin-4(3*H*)-one (18). Metallation of **6** (100 mg, 0.48 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 2.46 mL), TMPH (8 equiv., 0.67 mL), *T*=−78 °C, followed by reaction with acetaldehyde (10 equiv., 0.27 mL), *t*=1 h, gave after purification by column chromatography (silicagel, eluent: petroleum ether/ethyl acetate, 1:1)) 116 mg (96%) of **18** as a white solid, mp 244–245 °C; ^1H NMR (DMSO): δ 1.24 (s, 9H, *tert*-butyl); 1.26 (d, *J*=6.4 Hz, 3H, Me); 5.32 (d, *J*=4.5 Hz, 1H, OH); 5.83 (dq, *J*=5.8, 4.5 Hz, 1H, C*H*OH); 8.70 (s, 1H, H_6); 8.74 (s, 1H, H_8); 12.02 (s, 1H, NH); ^{13}C NMR (DMSO): δ 26.3 (Me); 27.9 ($3Me_{tert\text{-}butyl}$); 37.5 (*C*Me_3); 64.3 (CHOH); 121.7 (C_{py}); 141.5 (C_{py}); 143.3 (CH_{py}); 143.6 (C_{py}); 149.5 (CH_{py}); 162.2 (C_{py}); 164.9 (C_{py}). Anal. Calcd for $C_{13}H_{17}N_3O$ (247.29): C, 63.14; H, 6.93; N, 16.96. Found: C, 62.98; H, 7.07; N, 16.53.

3.7.5. 2-*tert*-Butyl-5-(hydroxyphenylmethyl)pyrido[3,4-*d*]-pyrimidin-4(3*H*)-one (19). Metallation of **6** (50 mg, 0.24 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.33 mL), *T*=−78 °C, followed by reaction with benzaldehyde (8 equiv., 0.27 mL), *t*=1 h, gave after purification by column chromatography (silicagel, eluent: petroleum ether/ethyl acetate, 1:1)) 73 mg (96%) of **19** as a colorless solid, mp 194–195 °C; ^1H NMR ($CDCl_3$): δ 1.33 (s, 9H, *tert*-butyl); 5.49 (d, *J*=7.5 Hz, 1H, OH); 6.36 (d, *J*=7.5 Hz, 1H, C*H*OH); 7.22 (m, 5H, Ph); 8.42 (s, 1H, H_6); 9.05 (s, 1H, H_8); 10.70 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.5 ($3Me_{tert\text{-}butyl}$); 37.8 (*C*Me_3); 72.9 (CHOH); 123.2 (C_{py}); 127.0 ($2CH_{Ph}$); 127.8 (CH_{Ph}); 128.6 ($2CH_{Ph}$); 136.5 (C_{Ph}); 142.5 (C_{py}); 145.5 (C_{py}); 146.7 (CH_{py}); 152.5 (CH_{py}); 164.1 (C_{py}); 164.3 (C_{py}). Anal. Calcd for $C_{18}H_{19}N_3O_2$ (309.36): C, 69.88; H, 6.19; N, 13.58. Found: C, 69.79; H, 6.18; N, 13.68.

3.7.6. 2-*tert*-Butyl-5,N_3-bis(tributylstannyl)pyrido[3,4-*d*]-pyrimidin-4(3*H*)-one (20). Metallation of **6** (100 mg, 0.48 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 2.46 mL), TMPH (8 equiv., 0.67 mL), *T*=−78 °C, followed by reaction with tri-*n*-butylstannyl

chloride (8 equiv., 1.08 mL), t=1 h, gave after purification by column chromatography (silicagel, eluent: ethyl acetate) 372 mg (97%) of **20** as a colorless solid, mp 108–109 °C; ^{1}H NMR ($CDCl_3$): δ 0.80 (m, 18H, 6Me); 1.19 (m, 24H, 12CH_2); 1.37 (s, 9H, *tert*-butyl); 1.69 (m, 12H, 6CH_2); 8.62 (t, J_{H6-Sn}=10.7 Hz, 1H, H_6); 8.97 (t, J_{H8-Sn}=3.7 Hz, 1H, H_8); ^{13}C NMR ($CDCl_3$): δ 11.5 (CH_2); 13.9 (Me); 14.0 (Me); 17.3 (CH_2); 27.3 (CH_2); 27.7 (CH_2); 28.2 (CH_2); 28.6 (3Me$_{tert\text{-butyl}}$); 29.5 (CH_2); 37.8 (*C*Me$_3$); 131.0 (C_{py}); 135.1 (C_{py}); 144.1 (C_{py}); 151.3 (CH_{py}); 153.1 (CH_{py}); 162.9 (C_{py}); 163.6 (C_{py}). Anal. Calcd for $C_{35}H_{65}N_3OSn_2$ (781.34): C, 53.80; H, 8.39; N, 5.38. Found: C, 53.72; H, 8.31; N, 5.59.

3.7.7. 2-*tert*-Butyl-5-iodopyrido[34-*d*]pyrimidin-4(3*H*)-one (21). Metallation of **6** (50 mg, 0.24 mmol) according to the procedure E with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.33 mL), T=−78 °C, followed by reaction with iodine (8 equiv., 500 mg) in solution with anhydrous THF (5 mL), t=1 h, gave after purification by column chromatography (silicagel, eluent: dichloromethane/diethyl ether, 7:3)) 61 mg (75%) of **21** as a colorless solid, mp>250 °C; ^{1}H NMR (DMSO): δ 1.20 (s, 9H, *tert*-butyl), 8.71 (s, 1H, H_6), 8.78 (s, 1H, H_8), 12.12 (s, 1H, NH); ^{13}C NMR (DMSO): δ 27.8 (3Me$_{tert\text{-butyl}}$), 37.8 (*C*Me$_3$), 90.1 (C_{py}), 125.7 (C_{py}), 144.9 (C_{py}), 150.7 (CH_{py}), 155.2 (CH_{py}), 160.3 (C_{py}), 165.2 (C_{py}). Anal. Calcd for $C_{11}H_{12}N_3OI$ (329.14): C, 40.14; H, 3.67; N, 12.77. Found: C, 40.07; H, 3.59; N, 12.85.

3.7.8. 2-*tert*-Butyl-5-chloropyrido[3,4-*d*]pyrimidin-4(3*H*)-one (22). Metallation of **6** (500 mg, 2.46 mmol) according to the procedure E with *n*-BuLi 1.6 M (9 equiv., 13.85 mL), TMPH (9 equiv., 3.74 mL), T=−78 °C, followed by reaction with hexachloroethane (9 equiv., 5.25 g) in solution with anhydrous THF (15 mL), t=1 h, gave after filtration 476 mg (82%) of **22** as a colorless solid, mp>250 °C; ^{1}H NMR (DMSO): δ 1.45 (s, 9H, *tert*-butyl); 8.67 (s, 1H, H_6); 8.98 (s, 1H, H_8); 12.40 (s, 1H, NH); ^{13}C NMR (DMSO): δ 27.9 (3Me$_{tert\text{-butyl}}$); 37.7 (*C*Me$_3$); 122.8 (C_{py}); 128.0 (C_{py}); 145.3 (C_{py}); 145.9 (CH_{py}); 149.7 (CH_{py}); 160.0 (C_{py}); 166.3 (C_{py}). Anal. Calcd for $C_{11}H_{12}N_3OCl$ (237.68): C, 55.59; H, 5.09; N, 17.68. Found: C, 55.41; H, 5.18; N, 17.71.

3.7.9. 2-*tert*-Butyl-6-iodopyrido[3,4-*d*]pyrimidin-4(3*H*)-one (23). Metallation of **6** (50 mg, 0.24 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.33 mL), T=−78 °C, followed by reaction with iodine (2 equiv., 125 mg) in solution with anhydrous THF (5 mL), t=2 h, gave after purification by column chromatography (silicagel, eluent: dichloromethane/ethyl ether, 5:5)) 45 mg of **23** as a colorless solid (56%), mp 210–211 °C; ^{1}H NMR ($CDCl_3$): δ 1.42 (s, 9H, *tert*-butyl); 8.34 (s, 1H, H_6); 8.83 (s, 1H, H_8); 11.27 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.5 (3Me$_{tert\text{-butyl}}$); 38.3 (*C*Me$_3$); 111.6 (C_{py}); 127.4 (C_{py}); 129.4 (CH_{py}); 143.5 (C_{py}); 152.7 (CH_{py}); 161.8 (C_{py}); 165.2 (C_{py}). Anal. Calcd for $C_{11}H_{12}N_3OI$ (329.14): C, 40.14; H, 3.67; N, 12.77. Found: C, 40.26; H, 3.82; N, 12.13.

3.7.10. 2-*tert*-Buyl-6-chloro-5-phenylthiopyrido[3,4-*d*]-pyrimidin-4(3*H*)-one (24). Metallation of **7** (50 mg, 0.21 mmol) according to the procedure E with *n*-BuLi 1.6 M (8 equiv., 1.05 mL), TMPH (8 equiv., 0.29 mL), T=−78 °C, followed by reaction with diphenyl disulfide (8 equiv., 367 mg) in solution with anhydrous THF (5 mL), t=1 h, gave after purification by column chromatography (silicagel, eluent: dichloromethane/ethyl acetate, 9:1)) 62 mg (86%) of **24** as a yellow solid, mp 211–212 °C; ^{1}H NMR ($CDCl_3$): δ 1.34 (s, 9H, *tert*-butyl); 7.10 (m, 5H, Pb); 8.82 (s, 1H, H_8); 11.41 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.3 (3Me$_{tert\text{-butyl}}$); 38.1 (*C*Me$_3$); 126.6 (CH_{Ph}); 127.7 (C_{py}); 128.4 (2CH_{Ph}); 129.3 (C_{Ph}); 129.4 (2CH_{Ph}); 136.5 (C_{py}); 144.8 (C_{py}); 151.4 (CH_{py}); 153.5 (C_{py}); 161.6 (C_{py}); 165.6 (C_{py}). Anal. Calcd for $C_{17}H_{16}N_3OSCl$ (345.85): C, 59.04; H, 4.66; N, 12.15; S, 9.27. Found: C, 59.07; H, 4.67; N, 11.97; S, 9.22.

3.7.11. 2-*tert*-Butyl-6-chloro-5-(1-hydroxyethyl)pyrido-[3,4-*d*]pyrimidin-4(3*H*)-one (25). Metallation of **7** (50 mg, 0.21 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.05 mL), TMPH (8 equiv., 0.29 mL), T=−78 °C, followed by reaction with acetaldehyde (9 equiv., 0.11 mL), t=1 h, gave after purification by column chromatography (silicagel, eluent: dichloromethane/ethyl acetate, 8:2)) 51 mg (87%) of **25** as a colorless solid, mp 202–203 °C; ^{1}H NMR ($CDCl_3$): δ 1.42 (s, 9H, *tert*-butyl); 1.59 (d, J=6.8 Hz, 3H, Me); 5.58 (dq, J=6.2 Hz, 1H, C*H*OH); 6.13 (d, J=12.0 Hz, 1H, OH); 8.83 (s, 1H, H_8); 10.50 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 22.4 (Me); 28.5 (3Me$_{tert\text{-butyl}}$); 37.8 (*C*Me$_3$); 68.7 (CHOH); 125.4 (C_{py}); 137.8 (C_{py}); 145.5 (C_{py}); 146.9 (C_{py}); 151.2 (CH_{py}); 163.9 (C_{py}); 164.0 (C_{py}). Anal. Calcd for $C_{13}H_{16}N_3O_2Cl$ (281.74): C, 55.42; H, 5.72; N, 14.91. Found: C, 55.41; H, 5.95; N, 14.77.

3.7.12. 2-*tert*-Butyl-6-chloro-5-(hydroxyphenylmethyl)-pyrido[3,4-*d*]pyrimidin-4(3*H*)-one (26). Metallation of **7** (50 mg, 0.21 mmol) according the to procedure D with *n*-BuLi 1.6 M (8 equiv., 1.05 mL), TMPH (8 equiv., 0.29 mL), T=−78 °C, followed by reaction with benzaldehyde (8 equiv., 0.17 mL), t=1 h, gave after purification by column chromatography (silicagel, eluent: petroleum ether/ethyl acetate, 5:5)) 70 mg (97%) of **26** as a colorless solid, mp 227–228 °C; ^{1}H NMR ($CDCl_3$): δ 1.28 (s, 9H, *tert*-butyl); 6.34 (d, J=12.0 Hz, 1H, C*H*OH); 6.64 (d, J=12.0 Hz, 1H, OH); 7.19 (m, 5H, Ph); 8.91 (s, 1H, H_8); 9.71 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.4 (3Me$_{tert\text{-butyl}}$); 37.7 (*C*Me$_3$); 72.9 (CHOH); 125.9 (C_{py}); 126.2 (2CH_{Ph}); 127.6 (CH_{Ph}); 128.6 (2CH_{Ph}); 135.5 (C_{py}); 142.1 (CH_{Ph}); 145.6 (C_{py}); 148.6 (C_{py}); 151.9 (CH_{py}); 162.8 (C_{py}); 164.1 (C_{py}). Anal. Calcd for $C_{18}H_{18}N_3O_2Cl$ (343.81): C, 62.88; H, 5.28; N, 12.22. Found: C, 62.68; H, 5.36; N, 11.92.

3.7.13. 2-*tert*-Butyl-5,N$_3$-bis(tributylstannyl)-6-chloro-pyrido[3,4-*d*]pyrimidin-4(3*H*)-one (27). Metallation of **7** (50 mg, 0.21 mmol) according to the procedure E with *n*-BuLi 1.6 M (8 equiv., 1.05 mL), TMPH (8 equiv., 0.29 mL), T=−78 °C, followed by reaction with tri-*n*-butylstannyl chloride (8 equiv., 0.47 mL), t=1 h, gave after purification by column chromatography (silicagel, eluent: dichloromethane) 92 mg (84%) of **27** as an oil; ^{1}H NMR ($CDCl_3$): δ 0.79 (t, J=7.1 Hz, 9H, Me); 1.18 (m, 12H, CH_2); 1.35 (s, 9H, *tert*-butyl); 1.44 (m, 6H, CH_2); 8.72 (t, J_{H8-Sn}= 3.0 Hz, 1H, H_8); 8.89 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 14.1 (Me); 15.2 (CH_2); 27.7 (CH_2); 28.6 (3Me$_{tert\text{-butyl}}$); 29.5

(CH_2); 37.6 (CMe_3); 134.3 (C_{py}); 138.3 (C_{py}); 143.1 (C_{py}); 151.3 (CH_{py}); 156.6 (C_{py}); 162.3 (C_{py}); 162.6 (C_{py}). Anal. Calcd for $C_{23}H_{38}N_3OClSn$ (526.73): C, 52.45; H, 7.27; N, 7.98. Found: C, 52.41; H, 7.26; N, 7.79.

3.7.14. 2-*tert*-Butyl-6-chloro-5-iodopyrido[3,4-*d*]pyrimidin-4(3*H*)-one (28). Metallation of **7** (50 mg, 0.21 mmol) according to the procedure E with *n*-BuLi 1.6 M (8 equiv., 1.05 mL), TMPH (8 equiv., 0.29 mL), $T=-78$ °C, followed by reaction with iodine (8 equiv., 427 mg) in solution with anhydrous THF (5 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: ethyl acetate/dichloromethane, 1:9)) 66 mg (87%) of **28** as a yellow solid, mp 238–239 °C; ^{1}H NMR ($CDCl_3$): δ 1.45 (s, 9H, *tert*-butyl); 8.74 (s, 1H, H_8); 11.52 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.5 ($3Me_{tert\text{-butyl}}$); 38.3 (CMe_3); 90.9 (C_{py}); 128.9 (C_{py}); 143.8 (C_{py}); 151.1 (C_{py}); 154.2 (C_{py}); 161.3 (C_{py}); 165.0 (C_{py}). Anal. Calcd for $C_{11}H_{11}N_3OClI$ (363.58): C, 36.34; H, 3.05; N, 11.56. Found: C, 36.42; H, 2.89; N, 11.05.

3.7.15. 2-*tert*-Butyl-6-methoxy-5-phenylthiopyrido[3,4-*d*]-pyrimidin-4(3*H*)-one (29). Metallation of **8** (50 mg, 0.21 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.07 mL), TMPH (8 equiv., 0.29 mL), $T=0$ °C, followed by reaction with dipheny disulfide (8 equiv., 380 mg) in solution with anhydrous THF (5 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: dichloromethane) 52 mg (71%) of **29** as a yellow solid, mp 210–211 °C; ^{1}H NMR ($CDCl_3$): δ 1.35 (s, 9H, *tert*-butyl); 3.72 (s, 3H, OMe); 7.10 (m, 5H, Ph); 8.61 (s, 1H, H_8); 10.50 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.4 ($3Me_{tert\text{-butyl}}$); 37.6 (CMe_3); 54.8 (OMe); 114.4 (C_{py}); 126.3 (CH_{Ph}); 128.8 (C_{Ph}); 128.9 ($2CH_{Ph}$); 128.9 ($2CH_{Ph}$); 137.5 (C_{py}); 140.4 (C_{py}); 148.0 (CH_{py}); 161.1 (C_{py}); 161.5 (C_{py}); 162.2 (C_{py}). Anal. Calcd for $C_{18}H_{19}N_3O_2S$ (341.43): C, 63.32; H, 5.61; N, 12.31; S, 9.39. Found: C, 63.21; H, 5.84; N, 12.35; S, 9.47.

3.7.16. 2-*tert*-Butyl-5-(1-hydroxyethyl)-6-methoxypyrido-[3,4-*d*]pyrimidin-4(3*H*)-one (30). Metallation of **8** (50 mg, 0.21 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.07 mL), TMPH (8 equiv., 0.29 mL), $T=0$ °C, followed by reaction with acetaldehyde (10 equiv., 0.10 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: petroleum ether/diethyl ether, 3:7)) 54 mg (92%) of **30** as a colorless solid, mp 227–228 °C; ^{1}H NMR ($CDCl_3$): δ 1.41 (s, 9H, *tert*-butyl); 1.53 (d, $J=6.4$ Hz, 3H, Me); 4.00 (s, 3H, OMe); 5.63 (d, $J=12.4$ Hz, 1H, OH); 5.77 (dq, $J=5.9$ Hz, 1H, *CH*OH); 8.66 (s, 1H, H_8); 11.14 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 23.4 (Me); 28.5 ($3Me_{tert\text{-butyl}}$); 37.5 (CMe_3); 54.8 (OMe); 64.5 (CHOH); 125.1 (C_{py}); 125.3 (C_{py}); 140.4 (C_{py}); 148.1 (CH_{py}); 159.0 (C_{py}); 160.3 (C_{py}); 165.3 (C_{py}). Anal. Calcd for $C_{14}H_{19}N_3O_3$ (277.32): C, 60.63; H, 6.91; N, 15.15. Found: C, 60.59; H, 7.12; N, 14.98.

3.7.17. 2-*tert*-Butyl-5-(hydroxyphenylmethyl)-6-methoxy-pyrido[3,4-*d*]pyrimidin-4(3*H*)-one (31). Metallation of **8** (50 mg, 0.21 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.07 mL), TMPH (8 equiv., 0.29 mL), $T=0$ °C, followed by reaction with benzaldehyde (8 equiv., 0.18 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: dichloromethane/ethyl acetate, 7:3)) 67 mg (91%) of **31** as a colorless solid, mp>250 °C; ^{1}H NMR ($CDCl_3$): δ 1.41 (s, 9H, *tert*-butyl); 3.95 (s, 3H, OMe); 5.97 (d, $J=12.4$ Hz, 1H, *CH*OH); 6.84 (d, $J=12.4$ Hz, 1H, OH); 7.18 (m, 5H, Ph); 8.72 (s, 1H, H_8); 10.49 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.3 ($3Me_{tert\text{-butyl}}$); 37.3 (CMe_3); 55.0 (OMe); 68.8 (CHOH); 122.6 (C_{Ph}); 125.9 (C_{py}); 126.4 ($2CH_{Ph}$); 127.2 (CH_{Ph}); 128.3 ($2CH_{Ph}$); 140.5 (C_{py}); 143.6 (C_{py}); 148.9 (CH_{py}); 159.8 (C_{py}); 160.5 (C_{py}); 164.5 (C_{py}). Anal. Calcd for $C_{19}H_{21}N_3O_3$ (339.39): C, 67.24; H, 6.24; N, 12.38. Found: C, 67.28; H, 6.34; N, 12.16.

3.7.18. 2-*tert*-Butyl-5,N_3-bis(tributylstannyl)-6-methoxy-pyrido[3,4-*d*]pyrimidin-4(3*H*)-one (32). Metallation of **8** (50 mg, 0.21 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.07 mL), TMPH (8 equiv., 0.29 mL), $T=0$ °C, followed by reaction with tri-*n*-butylstannyl chloride (8 equiv., 0.48 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: diethyl ether/petroleum ether, 5:5)) 130 mg (75%) of **32** as an oil; ^{1}H NMR ($CDCl_3$): δ 0.79 (m, 18H, Me); 1.13 (m, 24H, CH_2); 1.32 (s, 9H, *tert*-butyl); 1.42 (m, 12H, CH_2); 3.87 (s, 3H, OMe); 8.56 (t, $J_{H8-Sn}=3.03-3.39$ Hz, 1H, H_8); ^{13}C NMR ($CDCl_3$): δ 13.6 (CH_2); 14.2 (Me); 27.8 (CH_2); 28.7 ($3Me_{tert\text{-butyl}}$); 29.7 (CH_2); 37.3 (CMe_3); 54.2 (OMe); 121.4 (C_{py}); 135.0 (C_{py}); 139.4 (C_{py}); 148.9 (CH_{py}); 158.7 (C_{py}); 163.3 (C_{py}); 167.6 (C_{py}). Anal. Calcd for $C_{44}H_{67}N_3O_2Sn_2$ (811.36): C, 53.29; H, 8.32; N, 5.18. Found: C, 53.61; H, 8.04; N, 5.46.

3.7.19. 2-*tert*-Butyl-5-iodo-6-methoxypyrido[3,4-*d*]pyrimidin-4(3*H*)-one (33). Metallation of **8** (50 mg, 0.21 mmol) according to the procedure E with *n*-BuLi 1.6 M (8 equiv., 1.07 mL), TMPH (8 equiv., 0.29 mL), $T=0$ °C, followed by reaction with iodine (8 equiv., 432 mg) in solution with anhydrous THF (5 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: dichloromethane/diethyl ether, 9:1)) 67 mg (88%) of **33** as a yellow solid, mp>250 °C; ^{1}H NMR (DMSO): δ 1.39 (s, 9H, *tert*-butyl); 4.02 (s, 3H, OMe); 8.86 (s, 1H, H_8); 12.06 (s, 1H, NH); ^{13}C NMR (DMSO): δ 27.8 ($3Me_{tert\text{-butyl}}$); 37.4 (CMe_3); 55.7 (OMe); 75.6 (C_{py}); 129.1 (C_{py}); 139.6 (C_{py}); 147.5 (CH_{py}); 160.5 (C_{py}); 160.6 (C_{py}); 161.7 (C_{py}). Anal. Calcd for $C_{12}H_{14}N_3O_2I$ (359.16): C, 40.13; H, 3.93; N, 11.70. Found: C, 40.10; H, 4.02; N, 11.52.

3.7.20. 2-*tert*-Butyl-8-methoxy-5-phenylthiopyrido[3,4-*d*]-pyrimidin-4(3*H*)-one (34). Metallation of **9** (50 mg, 0.21 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.07 mL), TMPH (8 equiv., 0.29 mL), $T=-20$ °C, followed by reaction with diphenyl disulfide (8 equiv., 380 mg) in solution with anhydrous THF (5 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: ethyl acetate/petroleum ether, 5:5)) 65 mg (89%) of **34** as a yellow solid, mp 249–250 °C; ^{1}H NMR ($CDCl_3$): δ 1.47 (s, 9H, *tert*-butyl); 3.95 (s, 3H, OMe); 7.25 (s, 1H, H_6); 7.38 (m, 3H, Ph); 7.53 (m, 2H, Ph); 11.98 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.5 ($3Me_{tert\text{-butyl}}$); 38.3 (CMe_3); 54.9 (OMe); 123.8 (C_{py}); 127.1 (C_{Ph}); 129.5 (CH_{Ph}); 128.9 ($2CH_{Ph}$); 132.1 (C_{py}); 135.4 (C_{py}); 135.6 ($2CH_{Ph}$); 139.4 (CH_{py}); 157.8 (C_{py}); 163.7 (C_{py}); 164.7 (C_{py}). Anal. Calcd

for $C_{18}H_{19}N_3O_2S$ (341.43): C, 63.32; H, 5.61; N, 12.31; S, 9.39. Found: C, 62.99; H, 5.68; N, 12.61; S, 9.46.

3.7.21. 2-*tert*-Butyl-5-(1-hydroxyethyl)-8-methoxypyrido-[3,4-*d*]pyrimidin-4(3*H*)-one (35). Metallation of **9** (50 mg, 0.21 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.07 mL), TMPH (8 equiv., 0.29 mL), $T=-20$ °C, followed by reaction with acetaldehyde (10 equiv., 0.10 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: ethyl acetate) 53 mg (90%) of **35** as a colorless solid, mp>250 °C; ^{1}H NMR ($CDCl_3$): δ 1.44 (s, 9H, *tert*-butyl); 1.57 (d, $J=6.4$ Hz, 3H, Me); 4.06 (s, 3H, OMe); 4.91 (d, $J=7.9$ Hz, 1H, OH); 5.22 (dq, $J=6.9$ Hz, 1H, C*H*OH); 8.09 (s, 1H, H_6); 10.52 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 23.4 (Me); 28.6 ($3Me_{tert\text{-butyl}}$); 37.9 (CMe_3); 55.1 (OMe); 67.6 (CHOH); 124.8 (C_{py}); 130.9 (C_{py}); 136.3 (C_{py}); 141.1 (CH_{py}); 160.3 (C_{py}); 163.2 (C_{py}); 163.5 (C_{py}). Anal. Calcd for $C_{14}H_{19}N_3O_3$ (277.32): C, 60.63; H, 6.91; N, 15.15. Found: C, 60.32; H, 7.03; N, 14.96.

3.7.22. 2-*tert*-Butyl-5-(hydroxyphenylmethyl)-8-methoxy-pyrido[3,4-*d*]pyrimidin-4(3*H*)-one (36). Metallation of **9** (50 mg, 0.21 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.07 mL), TMPH (8 equiv., 0.29 mL), $T=-20$ °C, followed by reaction with benzaldehyde (8 equiv., 0.18 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: ethyl acetate) 61 mg (85%) of **36** as a colorless solid, mp>250 °C; ^{1}H NMR ($CDCl_3$): δ 1.36 (s, 9H, *tert*-butyl); 4.05 (s, 3H, OMe); 5.44 (d, $J=8.7$ Hz, 1H, C*H*OH); 6.13 (d, $J=8.6$ Hz, 1H, OH); 7.26 (m, 5H, Ph); 7.84 (s, 1H, H_6); 9.82 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.6 ($3Me_{tert\text{-butyl}}$); 37.9 (CMe_3); 55.1 (OMe); 73.1 (CHOH); 122.6 (C_{py}); 125.9 (C_{py}); 126.8 ($2CH_{Ph}$); 127.5 (CH_{Ph}); 128.5 ($2CH_{Ph}$); 129.2 (C_{Ph}); 140.5 (C_{py}); 143.0 (C_{py}); 143.4 (CH_{py}); 163.4 (C_{py}); 167.7 (C_{py}). Anal. Calcd for $C_{19}H_{21}N_3O_3$ (339.39): C, 67.24; H, 6.24; N, 12.38. Found: C, 67.19; H, 6.39; N, 12.45.

3.7.23. 2-*tert*-Butyl-5,N$_3$-bis(tributylstannyl)-8-mehoxy-pyrido[3,4-*d*]pyrimidin-4(3*H*)-one (37). Metallation of **9** (50 mg, 0.21 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.07 mL), TMPH (8 equiv., 0.29 mL), $T=-20$ °C, followed by reaction with tri-*n*-butylstannyl chloride (8 equiv., 0.48 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: diethyl ether) 130 mg (75%) of **37** as an oil; ^{1}H NMR ($CDCl_3$): δ 0.80 (m, 18H, Me); 1.07 (m, 24H, CH_2); 1.29 (s, 9H, *tert*-butyl); 1.48 (m, 12H, CH_2); 4.04 (s, 3H, OMe); 8.09 (t, $J_{H6-Sn}=11.7$ Hz, 1H, H_6); ^{13}C NMR ($CDCl_3$): δ 11.5 (CH_2); 13.9 (Me); 14.1 (Me); 17.8 (CH_2); 27.2 (CH2); 27.7 (CH2); 28.2 (CH2); 28.7 ($3Me_{tert\text{-butyl}}$); 29.6 (CH_2); 37.8 (CMe_3); 54.8 (OMe); 125.0 (C_{py}); 132.2 (C_{py}); 135.1 (C_{py}); 149.8 (CH_{py}); 160.8 (C_{py}); 161.8 (C_{py}); 163.1 (C_{py}). Anal. Calcd for $C_{44}H_{67}N_3O_2Sn_2$ (811.36): C, 53.29; H, 8.32; N, 5.18. Found: C, 53.55; H, 8.43; N, 5.20.

3.7.24. 2-*tert*-Butyl-5-iodo-8-methoxypyrido[3,4-*d*]pyri-midin-4(3*H*)-one (38). Metallation of **9** (50 mg, 0.21 mmol) according to the procedure E with *n*-BuLi 1.6 M (8 equiv., 1.07 mL), TMPH (8 equiv., 0.29 mL), $T=-20$ °C, followed by reaction with iodine (8 equiv., 432 mg) in solution with anhydrous THF (5 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: dichloromethane/ethyl acetate, 5:5)) 62 mg (80%) of **38** as a colorless solid, mp>250 °C; ^{1}H NMR (DMSO): δ 1.47 (s, 9H, *tert*-butyl); 4.03 (s, 3H, OMe); 8.44 (s, 1H, H_8); 11.78 (s, 1H, NH); ^{13}C NMR (DMSO): δ 28.6 ($3Me_{tert\text{-butyl}}$); 38.5 (CMe_3); 55.3 (OMe); 76.2 (C_{py}); 125.7 (C_{py}); 136.7 (C_{py}); 152.0 (CH_{py}); 161.1 (C_{py}); 161.8 (C_{py}); 164.3 (C_{py}). Anal. Calcd for $C_{12}H_{14}N_3O_2I$ (359.16): C, 40.13; H, 3.93; N, 11.70. Found: C, 40.09; H, 4.09; N, 11.64.

3.8. Metallation of 2-*tert*-Butyl-5-chloropyrido[3,4-*d*]-pyrimidin-4(3*H*)-one (22)

The titled compound (50 mg, 0.21 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.05 mL), TMPH (8 equiv., 0.29 mL), $T=-20$ °C, followed by reaction with benzaldehyde (8 equiv., 0.17 mL), $t=1$ h, gave after purification by preparative chromatography (C_{18} column (5 μm, 10×250 mm), eluent (4 mL/min): MeOH/water (55:45), UV detection (245 nm)), 25 mg (35%) of 2-*tert*-butyl-5-chloro-6-(hydroxyphenylmethyl)pyrido[3,4-*d*]pyrimidin-4(3*H*)-one **39** and 25 mg (35%) of 2-*tert*-butyl-5-chloro-8-(hydroxyphenylmethyl)pyrido[3,4-*d*]pyrimidin-4(3*H*)-one **40**.

3.8.1. 2-*tert*-Butyl-5-chloro-6-(hydroxyphenylmethyl)-pyrido[3,4-*d*]pyrimidin-4(3*H*)-one (39). A colorless solid, mp 227–228 °C; ^{1}H NMR ($CDCl_3$): δ 1.39 (s, 9H, *tert*-butyl); 4.99 (d, $J=7.1$ Hz, 1H, OH); 6.15 (d, $J=7.1$ Hz, 1H, *CH*OH); 7.24 (m, 5H, Ph); 8.97 (s, 1H, H_8); 11.13 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.4 ($3Me_{tert\text{-butyl}}$); 38.1 (CMe_3); 72.2 (CHOH); 123.6 (C_{py}); 127.0 (C_{Ph}); 127.7 ($2CH_{Ph}$); 128.2 (CH_{Ph}); 128.8 ($2CH_{Ph}$); 142.0 (C_{py}); 145.5 (C_{py}); 148.5 (CH_{py}); 155.0 (C_{py}); 161.5 (C_{py}); 165.5 (C_{py}). Anal. Calcd for $C_{18}H_{18}N_3O_2Cl$ (343.81): C, 62.88; H, 5.28; N, 12.22. Found: C, 62.83; H, 5.44; N, 12.36.

3.8.2. 2-*tert*-Butyl-5-chloro-8-(hydroxyphenylmethyl)-pyrido[3,4-*d*]pyrimidin-4(3*H*)-one (40). A colorless solid, mp 250–251 °C; ^{1}H NMR (DMSO): δ 1.42 (s, 9H, *tert*-butyl); 6.17 (s, 1H, OH); 6.66 (d, $J=6.0$ Hz, 1H, *CH*OH); 7.37 (2m, 5H, Ph); 8.57 (s, 1H, H_6); 12.39 (s, 1H, NH); ^{13}C NMR (DMSO): δ 28.1 ($3Me_{tert\text{-butyl}}$); 38.0 (CMe_3); 70.9 (CHOH); 122.6 (C_{py}); 126.7 (C_{Ph}); 126.8 ($2CH_{Ph}$); 127.0 (CH_{py}); 127.1 (CH_{Ph}); 128.2 ($2CH_{Ph}$); 142.2 (C_{py}); 143.2 (C_{py}); 144.0 (C_{py}); 155.7 (C_{py}); 159.9 (C_{py}). Anal. Calcd for $C_{18}H_{18}N_3O_2Cl$ (343.81): C, 62.88; H, 5.28; N, 12.22. Found: C, 62.95; H, 5.43; N, 12.35.

3.8.3. 2-*tert*-Butyl-5-(1-hydroxyethyl)pyrido[2,3-*d*]pyri-midin-4(3*H*)-one (41). Metallation of **4** (50 mg, 0.24 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), $T=0$ °C, followed by reaction with acetaldehyde (8 equiv., 0.11 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: ethyl acetate) 57 mg (95%) of **41** as a colorless solid, mp>250 °C; ^{1}H NMR ($CDCl_3$): δ 1.46 (s, 9H, *tert*-butyl); 1.55 (d, $J=6.6$ Hz, 3H, Me); 4.39 (s, 1H, OH); 5.83 (dq, $J=6.6$ Hz, 1H, C*H*OH); 7.49 (d, $J_{6-7}=4.9$ Hz, 1H, H_6); 8.87 (d, $J=4.9$ Hz, 1H, H_7); 11.17 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 23.7 (Me), 28.5 ($3Me_{tert\text{-butyl}}$); 38.0 (CMe_3); 68.3 (CHOH); 113.0 (C_{py}); 120.1 (CH_{py}); 156.8 (CH_{py}); 158.6 (C_{py}); 161.0 (C_{py}); 165.4 (C_{py}), 165.8

(C_{py}). Anal. Calcd for $C_{13}H_{17}N_3O$ (247.29): C, 63.14; H, 6.93; N, 16.96. Found: C, 62.98; H, 7.07; N, 16.53.

3.8.4. 2-*tert*-Butyl-5-(hydroxyphenylmethyl)pyrido[2,3-*d*]-pyrimidin-4(3*H*)-one (42). Metallation of **4** (50 mg, 0.24 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), T=0 °C, followed by reaction with benzaldehyde (8 equiv., 0.27 mL), t=1 h, gave after purification by column chromatography (silicagel, eluent: diethyl ether/ethyl acetate, 1:1)) 73 mg (96%) of **42** as a colorless solid, mp 147–148 °C; ^{1}H NMR ($CDCl_3$): δ 1.38 (s, 9H, *tert*-butyl); 5.18 (d, J=6.8 Hz, 1H, OH); 6.50 (d, J=6.8 Hz, 1H, C*H*OH); 7.20 (d, J_{6-7}=4.9 Hz, 1H, H_6); 7.25 (m, 5H, Ph); 8.82 (d, J=4.9 Hz, 1H, H_7); 10.56 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.5 ($3Me_{tert\text{-butyl}}$); 37.9 (CMe_3); 73.6 (CHOH); 113.6 (C_{py}); 122.4 (CH_{py}); 127.3 ($2CH_{Ph}$); 128.2 (CH_{Ph}); 128.8 ($2CH_{Ph}$); 141.4 (C_{Ph}); 156.0 (C_{py}); 156.7 (CH_{py}); 161.1 (C_{py}); 165.1 (C_{py}); 165.7 (C_{py}). Anal. Calcd for $C_{18}H_{19}N_3O_2$ (309.36): C, 69.88; H, 6.19; N, 13.58. Found: C, 69.72; H, 6.26; N, 13.45.

3.8.5. 2-*tert*-Butyl-5-phenylthiopyridol[2,3-*d*]pyrimidin-4(3*H*)-one (43). Metallation of **4** (50 mg, 0.24 mmol) according to the procedure E with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), T=0 °C, followed by reaction with diphenyl disulfide (8 equiv., 430 mg) in solution with anhydrous THF (5 mL), t=1 h, gave after purification by column chromatography (silicagel, eluent: (1) dichloromethane, (2) diethyl ether/dichloromethane (3:7)) 64 mg (84%) of **43** as a yellow solid, mp 249–250 °C; ^{1}H NMR ($CDCl_3$): δ 1.50 (s, 9H, *tert*-butyl); 6.43 (d, J_{6-7}=5.65 Hz, 1H, H_6); 7.48 (m, 3H, Ph); 7.55 (m, 2H, Ph); 8.36 (d, J=5.65 Hz, 1H, H_7); 11.83 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.6 ($3Me_{tert\text{-butyl}}$); 38.3 (CMe_3); 112.2 (C_{py}); 118.3 (CH_{py}); 130.4 (C_{Ph}); 130.7 (CH_{Ph}); 130.7 ($2CH_{Ph}$); 136.4 ($2CH_{Ph}$); 154.1 (CH_{py}); 157.5 (C_{py}); 160.5 (C_{py}); 165.1 (C_{py}); 166.6 (C_{py}). Anal. Calcd for $C_{17}H_{17}N_3OS$ (311.40): C, 65.57; H, 5.50; N, 13.49; S, 10.30. Found: C, 65.48; H, 5.72; N, 13.21; S, 10.46.

3.8.6. 2-*tert*-Butyl-5-iodopyrido[2,3-*d*]pyrimidin-4(3*H*)-one (44). Metallation of **4** (50 mg, 0.24 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), T=0 °C, followed by reaction with iodine (8 equiv., 500 mg) in solution with anhydrous THF (5 mL), t=1 h, gave after purification by column chromatography (silicagel, eluent: (1) diethyl ether, (2) ethyl acetate/diethyl ether (1:1)) 60 mg (75%) of **44** as a colorless solid, mp 200–201 °C; ^{1}H NMR ($CDCl_3$): δ 1.49 (s, 9H, *tert*-butyl); 7.95 (d, J_{6-7}=4.9 Hz, 1H, H_6); 8.35 (d, J=4.9 Hz, 1H, H_7); 11.65 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 27.1 ($3Me_{tert\text{-butyl}}$); 37.1 (CMe_3); 104.4 (C_{py}); 114.9 (C_{py}); 134.9 (CH_{py});153.7 (CH_{py}); 158.2 (C_{py}); 161.8 (C_{py}); 165.1 (C_{py}). Anal. Calcd for $C_{11}H_{12}N_3OI$, (329.14): C, 40.14; H, 3.67; N, 12.77. Found: C, 40.23; H, 3.63; N, 12.26.

3.8.7. 2-*tert*-Buty1-5,N_3-bis(tributylstannyl)pyrido[2,3-*d*]-pyrimidin-4(3*H*)-one (45). Metallation of **4** (50 mg, 0.24 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), T=0 °C, followed by reaction with tri-*n*-butylstannyl chloride (8 equiv., 0.54 mL), t=1 h, gave after purification by column chromatography (silicagel, eluent: diethyl ether) 142 mg (74%) of **45** as an oil; ^{1}H NMR ($CDCl_3$): δ 0.82 (m, 18H, 6Me); 1.17 (m, 24H, $12CH_2$); 1.40 (s, 9H, *tert*-butyl); 1.54 (m, 12H, $6CH_2$); 7.51 (td, J_{6-7}=4.5 Hz, J_{H6-Sn}= 8.5 Hz, IH, H_6); 8.74 (q, J=4.1 Hz, J_{H7-Sn}=10.5 Hz, 1H, H_7); ^{13}C NMR ($CDCl_3$): δ 9.10 (CH_2); 14.0 (Me); 14.1 (Me); 17.9 (CH_2); 27.2 (CH_2); 27.7 (CH_2); 28.2 (CH_2); 28.6 ($3Me_{tert\text{-butyl}}$); 29.5 (CH_2); 37.9 (CMe_3); 121.2 (C_{py}); 131.3 (CH_{py}); 154.2 (CH_{py}); 158.7 (C_{py}); 159.3 (C_{py}); 164.6 (C_{py}); 164.6 (C_{py}). Anal. Calcd for $C_{35}H_{65}N_3OSn_2$ (781.34): C, 53.80; H, 8.39; N, 5.38. Found: C, 53.67; H, 8.24; N, 5.09.

3.8.8. 2-*tert*-Butyl-8-(hydroxyphenylmethyl)pyrido[4,3-*d*]-pyrimidin-4(3*H*)-one (46). Metallation of **10** (50 mg, 0.24 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), T= −20 °C, followed by reaction with benzaldehyde (8 equiv., 0.27 mL), t=1 h, gave after purification by column chromatography (silicagel, eluent: (1) dichioromethane/ethyl acetate (5:5), (2) ethyl acetate) 73 mg (96%) of **46** as a colorless solid, mp 186–187 °C; ^{1}H NMR ($CDCl_3$): δ 1.40 (s, 9H, *tert*-butyl); 5.65 (d, J=6.8 Hz, 1H, OH); 6.19 (d, J=6.8 Hz, 1H, C*H*OH); 7.21 (m, 3H, Ph); 7.37 (m, 2H, Ph); 8.67 (s, 1H, H_7); 9.31 (s, 1H, H_5); 11.81 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.4 ($3Me_{tert\text{-butyl}}$); 38.7 (CMe_3); 73.5 (CHOH); 116.3 (C_{py}); 126.7 ($2CH_{Ph}$); 127.9 (CH_{Ph}); 128.7 ($2CH_{Ph}$); 133.6 (C_{Ph}); 143.1 (C_{py}); 149.8 (CH_{py}); 151.9 (C_{py}); 152.1 (CH_{py}); 163.5 (C_{py}); 167.6 (C_{py}). Anal. Calcd for $C_{18}H_{19}N_3O_2$ (309.36): C, 69.88; H, 6.19; N, 13.58. Found: C, 69.48; H, 6.33; N, 13.49.

3.8.9. 2-*tert*-Butyl-5-(hydroxyphenylmethyl)pyrido[4,3-*d*]-pyrimidin-4(3*H*)-one (47). Metallation of **10** (50 mg, 0.24 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), T=20 °C, followed by reaction with benzaldehyde (8 equiv., 0.27 mL), t=1 h, gave after purification by column chromatography (silicagel, eluent: dichloromethane/ethyl acetate (1:1)) 51 mg (67%) of **47** as a colorless solid, mp 183–184 °C; ^{1}H NMR ($CDCl_3$): δ 1.32 (s, 9H, *tert*-butyl); 5.62 (d, J=8.7 Hz, 1H, OH); 6.84 (d, J=8.7 Hz, 1H, C*H*OH); 7.18 (m, 5H, Ph); 7.45 (d, J_{7-8}= 5.65 Hz, 1H, H_8); 8.70 (d, J=5.65 Hz, 1H, H_7); 10.86 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.4 ($3Me_{tert\text{-butyl}}$); 38.1 (CMe_3); 73.4 (CHOH); 113.8 (C_{py}); 121.6 (CH_{py}); 127.7 ($2CH_{Ph}$); 127.7 (CH_{Ph}); 128.5 ($2CH_{Ph}$); 143.5 (C_{Ph}); 151.4 (CH_{py}); 156.8 (C_{py}); 162.9 (C_{py}); 164.2 (C_{py}); 167.5 (C_{py}). Anal. Calcd for $C_{18}H_{19}N_3O_2$ (309.36): C, 69.88; H, 6.19; N, 13.58. Found: C, 69.67; H, 6.24; N, 13.34.

3.8.10. 2-*tert*-Butyl-8-(1-hydroxyethyl)pyrido[4,3-*d*]pyrimidin-4(3*H*)-one (48). Metallation of **10** (50 mg, 0.24 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), T= −20 °C, followed by reaction with acetaldehyde (8 equiv., 0.11 mL), t=1 h, gave after purification by preparative chromatography (C_{18} column (10 μm, 4.6×250 mm), eluent (1 mL/min): MeOH/water (7:3), UV detection (220 nm)), 49 mg (81%) of **48** as a colorless solid, mp 174–175 °C; ^{1}H NMR ($CDCl_3$): δ 1.45 (s, 9H, *tert*-butyl); 1.62 (d, J=6.4 Hz, 3H, Me); 5.03 (d, J=7.53 Hz, 1H, OH); 5.20 (m, 1H, C*H*OH); 8.69 (s, 1H, H_7); 9.35 (s, 1H, H_5); 11.58 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 24.6 (Me); 28.4 ($3Me_{tert\text{-burtyl}}$),

38.6 (CMe_3); 68.3 (CHOH); 116.3 (C_{py}); 134.6 (C_{py}); 149.7 (CH_{py}); 151.1 (CH_{py}); 152.1 (C_{py}); 163.4 (C_{py}); 167.9 (C_{py}). Anal. Calcd for $C_{13}H_{17}N_3O$ (247.9): C, 63.14; H, 6.93; N, 16.96. Found: C, 63.02; H, 7.08; N, 16.78.

3.8.11. 2-*tert*-Butyl-8-phenylthiopyrido[4,3-*d*]pyrimidin-4(3*H*)-one (49). Metallation of **10** (50 mg, 0.24 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), $T=-20$ °C, followed by reaction with diphenyl disulfide (8 equiv., 430 mg) in solution with anhydrous THF (5 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: ethyl acetate/dichloromethane (1:1)) 65 mg (85%) of **49** as a colorless solid, mp 223–224 °C; ^{1}H NMR ($CDCl_3$): δ 1.42 (s, 9H, *tert*-butyl); 7.36 (m, 3H, Ph); 7.51 (m, 2H, Ph); 8.12 (s, 1H, H_7); 9.15 (s, 1H, H_5); 11.46 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.4 ($3Me_{tert\text{-butyl}}$); 38.7 (CMe_3); 115.8 (C_{py}); 129.5 (CH_{Ph}); 130.2 ($2CH_{Ph}$); 130.9 (C_{Ph}); 133.7 (C_{py}); 135.0 ($2CH_{Ph}$); 146.9 (CH_{py}); 150.5 (CH_{py}); 150.8 (C_{py}); 163.5 (C_{py}); 167.4 (C_{py}). Anal. Calcd for $C_{17}H_{17}N_3OS$ (311.40): C, 65.57; H, 5.50; N, 13.49; S, 10.30. Found: C, 65.38; H, 5.61; N, 13.12; S, 10.39.

3.8.12. 2-*tert*-Butyl-8,N$_3$-bis(tributylstannyl)pyrido[4,3-*d*]-pyrimidin-4(3*H*)-one (50). Metallation of **10** (50 mg, 0.24 mmol) according the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), $T=-20$ °C, followed by reaction with tri-*n*-butylstannyl chloride (8 equiv., 0.54 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: diethyl ether) 137 mg (71%) of **50** as a colorless solid, mp 125–126 °C; ^{1}H NMR ($CDCl_3$): δ 0.80 (m, 18H, 6Me); 1.19 (m, 24H, $12CH_2$); 1.43 (s, 9H, *tert*-butyl); 1.52 (m, 12H, $6CH_2$); 8.76 (t, $J_{H7-Sn}=11.4$ Hz, 1H, H_7); 9.35 (s, 1H, H_5); ^{13}C NMR ($CDCl_3$): δ 10.7 (CH_2), 14.0 (2Me); 18.1 (CH_2); 27.2 (CH_2); 27.9 (CH_2); 28.2 (CH_2); 28.6 ($3Me_{tert\text{-butyl}}$); 29.5 (CH_2); 38.4 (CMe_3); 115.9 (C_{py}); 136.4 (C_{py}); 150.3 (CH_{py}); 159.6 (C_{py}); 160.1 (CH_{py}); 164.5 (C_{py}); 166.7 (C_{py}). Anal. Calcd for $C_{35}H_{65}N_3OSn_2$ (781.34): C, 53.80; H, 8.39; N, 5.38. Found: C, 53.71; H, 8.13; N, 5.51.

3.8.13. 2-*tert*-Butyl-8-iodopyrido[4,3-*d*]pyrimidin-4(3*H*)-one (51). Metallation of **10** (50 mg, 0.24 mmol) according to the procedure E with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), $T=-20$ °C, followed by reaction with iodine (8 equiv., 500 mg) in solution with anhydrous THF (5 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: diethyl ether/dichloromethane (1:1)) 69 mg (85%) of **51** as a colorless solid, mp>250 °C; ^{1}H NMR ($CDCl_3$): δ 1.45 (s, 9H, *tert*-butyl); 9.16 (s, 1H, H_7): 9.27 (s, lH, H_5); 11.19 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.5 ($3Me_{tert\text{-butyl}}$); 38.8 (CMe_3); 98.1 (C_{py}); 117.3 (C_{py}); 150.1 (CH_{py}); 154.3 (C_{py}); 161.4 (CH_{py}); 163.1 (C_{py}); 168.5 (C_{py}). Anal. Calcd for $C_{11}H_{12}N_3OI$ (329.14): C, 40.14; H, 3.67; N, 12.77. Found: C, 40.56; H, 3.83; N, 12.61.

3.8.14. 2-*tert*-Butyl-5-(1-hydroxyethyl)pyrido[4,3-*d*]pyrimidin-4(3*H*)-one (52). Metallation of **10** (50 mg, 0.24 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), $T=20$ °C, followed by reaction with acetaldehyde (8 equiv., 0.11 mL), $t=1$ h, gave after purification by preparative chromatography (C_{18} column (5 μm, 10×250 mm), eluent (4 mL/min): MeOH/water (45:55), UV detection (245 nm)), 39 mg (64%) of **52** as a colorless solid, mp 203–204 °C; ^{1}H NMR ($CDCl_3$): δ 1.44 (s, 9H, *tert*-butyl); 1.46 (d, $J=6.25$ Hz, 3H, Me); 5.11 (m, 1H, OH); 5.80 (m, 1H, C*H*OH); 7.44 (d, $J_{7-8}=5.7$ Hz, 1H, H_8); 8.64 (d, $J=5.7$ Hz, 1H, H_7); 11.76 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 25.1 (Me); 28.4 ($3Me_{tert\text{-butyl}}$); 38.2 (CMe_3); 68.5 (CHOH); 112.9 (C_{py}); 121.3 (CH_{py}); 151.3 (CH_{py}); 156.8 (C_{py}); 163.7 (C_{py}); 166.8 (C_{py}); 167.6 (C_{py}). Anal. Calcd for $C_{13}H_{17}N_3O$ (247.29): C, 63.14; H, 6.93; N, 16.96. Found: C, 62.95; H, 7.23; N, 16.94.

3.8.15. 2-*tert*-Butyl-5-phenylthiopyrido[4,3-*d*]pyrimidin-4(3*H*)-one (53). Metallation of **10** (50 mg, 0.24 mmol) according the procedure D **A** with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), $T=20$ °C, followed by reaction with diphenyl disulfide (8 equiv., 430 mg) in solution with anhydrous THF (5 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: ethyl acetate/dichloromethane (1:9)) 30 mg (40%) of **53** as a colorless solid, mp>250 °C; ^{1}H NMR ($CDCl_3$): δ 1.46 (s, 9H, *tert*-butyl); 7.10 (d, $J=5.65$ Hz, 1H, H_8); 7.25 (m, 3H, Ph); 7.53 (m, 2H, Ph); 8.29 (s, 1H, H_7); 11.88 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.5 ($3Me_{tert\text{-butyl}}$); 38.3 (CMe_3); 113.4 (C_{py}); 117.4 (CH_{py}); 129.4 ($2CH_{Ph}$); 129.4 (CH_{Ph}); 131.1 (C_{Ph}); 136.2 ($2CH_{Ph}$); 152.6 (CH_{py}); 156.6 (C_{py}); 163.6 (C_{py}); 164.0 (C_{py}); 167.5 (C_{py}). Anal. Calcd for $C_{17}H_{17}N_3OS$ (311.40): C, 65.57; H, 5.50; N, 13.49; S, 10.30. Found: C, 65.35; H, 5.74; N, 13.45; S, 10.37.

3.8.16. 2-*tert*-Butyl-5,N$_3$-bis(tributylstannyl)pyrido[4,3-*d*]-pyrimidin-4(3*H*)-one (54). Metallation of **10** (50 mg, 0.24 mmol) according to the procedure D **A** with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), $T=20$ °C, followed by reaction with tri-*n*-butylstannyl chloride (8 equiv., 0.54 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: ethyl acetate/petroleum ether (1:9)) 96 mg (50%) of **54** as a glassy solid, mp<50 °C; ^{1}H NMR ($CDCl_3$): δ 0.82 (m, 18H, 6Me); 1.18 (m, 24H, $12CH_2$); 1.34 (s, 9H, *tert*-butyl); 1.47 (m, 12H, $6CH_2$); 7.28 (d, $J_{7-8}=5.65$ Hz, lH, H_8); 8.87 (d, $J=5.65$ Hz, 1H, H_7); ^{13}C NMR ($CDCl_3$): δ 11.6 (CH_2); 14.0 (Me); 14.1 (Me); 17.9 (CH_2); 27.2 (CH_2); 27.8 (CH_2); 28.2 (CH_2); 28.6 ($3Me_{tert\text{-butyl}}$); 29.6 (CH_2); 37.9 (CMe_3); 119.3 (CH_{py}); 121.8 (C_{py}); 152.7 (C_{py}); 154.0 (CH_{py}); 163.4 (C_{py}); 165.4 (C_{py}); 181.0 (C_{py}). Anal. Calcd for $C_{33}H_{65}N_3OSn_2$ (781.34): C, 53.80; H, 8.39; N, 5.38. Found: C, 54.07; H, 8.46; N, 5.26.

3.8.17. 2-*tert*-Butyl-5-iodopyrido[4,3-*d*]pyrimidin-4(3*H*)-one (55). Metallation of **10** (50 mg, 0.24 mmol) according to the procedure E with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), $T=20$ °C, followed by reaction with iodine (8 equiv., 500 mg) in solution with anhydrous THF (5 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: diethyl ether/dichloromethane (2.5:7.5)) 37 mg (46%) of **55** as a brown solid, mp 213–214 °C; ^{1}H NMR ($CDCl_3$): δ 1.45 (s, 9H, *tert*-butyl); 7.41 (d, $J_{7-8}=5.3$ Hz, 1H, H_8); 8.39 (d, $J=5.3$ Hz, 1H, H_7); 11.63 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.5 ($3Me_{tert\text{-butyl}}$); 38.6 (CMe_3); 117.4 (C_{py}); 117.9 (C_{py}); 122.0 (CH_{py}); 153.2 (CH_{py}); 155.9 (C_{py}); 162.0 (C_{py}); 167.7 (C_{py}). Anal. Calcd

for $C_{11}H_{12}N_3OI$ (329.14): C, 40.14; H, 3.67; N, 12.77. Found: C, 40.26; H, 3.87; N, 12.64.

3.8.18. 2-*tert*-Butyl-8-(1-hydroxyethyl)pyrido[3,2-*d*]pyrimidin-4(3*H*)-one (56). Metallation of **11** (50 mg, 0.24 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), $T=-78$ °C, followed by reaction with acetaldehyde (8 equiv., 0.11 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: ethyl acetate) 54 mg (89%) of **56** as a colorless solid, mp>250 °C; ^{1}H NMR ($CDCl_3$): δ 1.43 (s, 9H, *tert*-butyl); 1.58 (d, $J=6.4$ Hz, 3H, Me); 5.23 (q, $J=6.4$ Hz, 1H, C*H*OH); 7.50 (d, $J_{6-7}=4.15$ Hz, 1H, H_7); 8.73 (d, $J=4.15$ Hz, 1H, H_6); 10.82 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 24.0 (Me); 28.7 ($3Me_{tert\text{-butyl}}$); 38.1 (*C*Me_3); 69.1 (CHOH); 125.5 (CH_{py}); 137.7 (C_{py}); 143.9 (C_{py}); 150.0 (CH_{py}); 150.6 (C_{py}); 162.2 (C_{py}); 163.0 (C_{py}). Anal. Calcd for $C_{13}H_{17}N_3O$ (247.29): C, 63.14; H, 6.93; N, 16.96. Found: C, 63.06; H, 7.09; N, 16.52.

3.8.19. 2-*tert*-Butyl-8-(hydroxyphenylmethyl)pyrido-[3,2-*d*]pyrimidin-4(3*H*)-one (57). Metallation of **11** (50 mg, 0.24 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), $T=-78$ °C, followed by reaction with benzaldehyde (8 equiv., 0.27 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: ethyl acetate) 68 mg (89%) of **57** as a white solid, mp 216–217 °C; ^{1}H NMR (DMSO): δ 1.35 (s, 9H, *tert*-butyl); 6.31 (m, 1H, OH); 6.54 (m, 1H, C*H*OH); 7.22 (m, 3H, Ph); 7.49 (m, 2H, Ph); 7.94 (d, $J_{6-7}=4.9$ Hz, 1H, H_7); 8.72 (d, $J=4.9$ Hz, 1H, H_6); 11.07 (s, 1H, NH); ^{13}C NMR (DMSO): δ 28.6 ($3Me_{tert\text{-butyl}}$); 38.3 (*C*Me_3); 69.2 (CHOH); 124.2 (CH_{py}); 126.9 ($2CH_{Ph}$); 127.3 (CH_{Ph}); 128.3 ($2CH_{Ph}$); 137.1 (C_{Ph}); 142.2 (C_{py}); 144.4 (C_{py}); 148.3 (CH_{py}); 151.2 (C_{py}); 162.4 (C_{py}); 163.1 (C_{py}). Anal. Calcd for $C_{18}H_{19}N_3O_2$ (309.36): C, 69.88; H, 6.19; N, 13.58. Found: C, 69.92; H, 5.82; N, 12.96.

3.8.20. 2-*tert*-Butyl-8-phenylthiopyrido[3,2-*d*]pyrimidin-4(3*H*)-one (58). Metallation of **11** (50 mg, 0.24 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), $T=-78$ °C, followed by reaction with diphenyl disulfide (8 equiv., 430 mg) in solution with anhydrous THF (5 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: ethyl acetate/dichloromethane (1:1)) 60 mg (80%) of **58** as a colorless solid, mp>250 °C; ^{1}H NMR ($CDCl_3$): δ 1.47 (s, 9H, *tert*-butyl); 6.71 (d, $J=4.9$ Hz, 1H, H_7); 7.44 (m, 3H, Ph); 7.55 (m, 2H, Ph); 8.36 (d, $J_{6-7}=4.9$ Hz, 1H, H_6); 11.24 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.7 ($3Me_{tert\text{-butyl}}$); 38.3 (*C*Me_3); 123.1 (CH_{py}); 129.4 (C_{Ph}); 130.5 (CH_{Ph}); 130.6 ($2CH_{Ph}$); 136.3 ($2CH_{Ph}$); 142.3 (C_{py}); 144.6 (C_{py}); 148.9 (CH_{py}); 152.3 (C_{py}); 162.7 (C_{py}); 163.1 (C_{py}). Anal. Calcd for $C_{17}H_{17}N_3OS$ (311.40): C, 65.57; H, 5.50; N, 13.49; S, 10.30. Found: C, 65.28; H, 5.64; N, 12.94; S, 9.92.

3.8.21. 2-*tert*-Butyl-8-iodopyrido[3,2-*d*]pyrimidin-4(3*H*)-one (59). Metallation of **11** (50 mg, 0.24 mmol) according to the procedure E with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), T=−78 °C, followed by reaction with iodine (8 equiv., 500 mg) in solution with anhydrous THF (5 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: ethyl acetate) 25 mg (31%) of **59** as a colorless solid, mp 236–237 °C; ^{1}H NMR ($CDCl_3$): δ 1.45 (s, 9H, *tert*-butyl); 8.15 (d, $J_{6-7}=4.9$ Hz, 1H, H_7); 8.31 (d, $J=4.9$ Hz, 1H, H_6); 10.93 (s, 1H, NH); ^{13}C NMR ($CDCl_3$): δ 28.7 ($3Me_{tert\text{-butyl}}$); 38.4 (*C*Me_3); 114.0 (C_{py}); 137.3 (C_{py}); 139.5 (CH_{py}); 146.6 (C_{py}); 149.4 (CH_{py}); 162.1 (C_{py}); 164.1 (C_{py}). Anal. Calcd for $C_{11}H_{12}N_3OI$ (329.14): C, 40.14; H, 3.67; N, 12.77. Found: C, 40.45; H, 4.12; N, 12.57.

3.8.22. 2-*tert*-Butyl-8,N$_3$-bis(tributylstannyl)pyrido[3,2-*d*]-pyrimidin-4(3*H*)-one (60). Metallation of **11** (50 mg, 0.24 mmol) according to the procedure D with *n*-BuLi 1.6 M (8 equiv., 1.23 mL), TMPH (8 equiv., 0.34 mL), T=−78 °C, followed by reaction with tri-*n*-butylstannyl chloride (8 equiv., 0.54 mL), $t=1$ h, gave after purification by column chromatography (silicagel, eluent: ethyl acetate/dichloromethane, 1:1) 159 mg (83%) of **60** as a glassy solid, mp<50 °C; ^{1}H NMR ($CDCl_3$): δ 0.82 (m, 18H, 6Me); 1.18 (m, 24H, $12CH_2$); 1.41 (s, 9H, *tert*-butyl); 1.50 (m, 12H, $6CH_2$); 7.51 (td, $J_{6-7}=4.15$ Hz, $J_{H6-Sn}=18.84$ Hz, 1H, H_7); 8.65 (d, $J=4.15$ Hz, 1H, H_6); ^{13}C NMR ($CDCl_3$): δ 10.8 (CH_2); 13.9 (Me); 14.0 (Me); 17.9 (CH_2); 27.2 (CH_2); 27.7 (CH_2); 28.2 (CH_2); 28.9 ($3Me_{tert\text{-butyl}}$); 29.4 (CH_2); 37.9 (*C*Me_3); 136.1 (C_{py}); 137.2 (CH_{py}); 148.4 (CH_{py}); 151.3 (C_{py}); 157.0 (C_{py}); 162.0 (C_{py}); 163.2 (C_{py}). Anal. Calcd for $C_{35}H_{65}N_3OSn_2$ (781.34): C, 53.80; H, 8.39; N, 5.38. Found: C, 53.62; H, 8.76; N, 5.23.

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