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Aminations and arylations by direct C–O activation for the design of 7,8-dihydro-6*H*-5,8-ethanopyrido[3,2-*d*]pyrimidines†

Mazarine Laurent,[a] Stéphane Bostyn,[b] Mathieu Marchivie,[c] Yves Robin,[d] Sylvain Routier *[a] and Frédéric Buron *[a]

The design of some novel disubstituted 7,8-dihydro-6*H*-5,8-ethanopyrido[3,2-*d*]pyrimidine derivatives is reported. The series was developed from quinuclidinone, which afforded versatile platforms bearing one lactam function in position *C*-2 that were then used to create C–N or C–C bonds for S_NAr or palladium-catalyzed cross-coupling reactions by *in situ* C–O activation. The reaction conditions were optimized under microwave irradiation, and a wide range of amines or boronic acids were used to determine the scope and limitations of each method. To complete this study, the X-ray crystallographic data of 7,8-dihydro-6*H*-5,8-ethanopyrido[3,2-*d*]pyrimidine derivative **49** were used to formally establish the structures of the products.

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Introduction

Exploring chemical space is a major challenge to discover new biologically active small molecules.[1–3] This strategy has long been applied in heterocyclic chemistry, in particular through the design and the functionalization of fused polynitrogenated derivatives, which contain hetero-aromatic and aliphatic moieties.[4–8] The resulting original structures increase the molecular diversity and find applications in reagents, 3D fine chemical or novel pharmaceutical specialities.[9–11] Among those reported in the aliphatic series, quinuclidine holds an important place due to its presence in a number of natural products, such as *Cinchona officinalis* alkaloids or FDA-approved drugs (Fig. 1).[12–17] Moreover, this skeleton has also been used as a catalyst for the development of asymmetric aldolisation, Baylis–Hillman or Diels–Alder reactions.[18–23]

The fusion of quinuclidine to aromatic and nitrogen-containing heterocycle moieties has seldom been reported. Only a few references describe the synthesis and the reactivity of this skeleton with a pyridine group as an example.[24–26] This may be due to the strong Brønsted and Lewis basic character of the nitrogen atom, which is likely to inhibit a large panel of reactions.[27] For our own part, our group has developed efficient methodologies to functionalize and obtain biologically active molecules in the pyrimidine series such as pyrido[3-2,*d*]pyrimidines, pyrido[1′,2′:1,5]pyrazolo[3,4-*d*]pyrimidines or pyrido[1′,2′:1,5]pyrazolo[4,3-*d*]pyrimidine.[28–31] To escape from flatland and evaluate the replicability of our know-how in this poorly explored area, we propose in this paper the access to a 4-aryl-7,8-dihydro-1*H*-5,8-ethanopyrido[3,2-*d*]pyrimidin-2(6*H*)-one platform and its further substitution at the *C*-2 position.[32] This fused arylated skeleton **A** resulting from the fusion of a quinuclidine and a pyrimidine (quinuclidino-pyrimidinone) was functionalized by aminations or the Suzuki–Miyaura cross-coupling reaction using *in situ* C–O activation, an innovative and direct method that is particularly powerful to modulate heteroaromatic structures (Fig. 2).

Results and discussion

To perform the required *C*-2 amination or Suzuki–Miyaura cross-coupling reactions, some ethanopyrido[3,2-*d*]pyrimidinones of type **A** were prepared in two steps. First, 4-aryl-

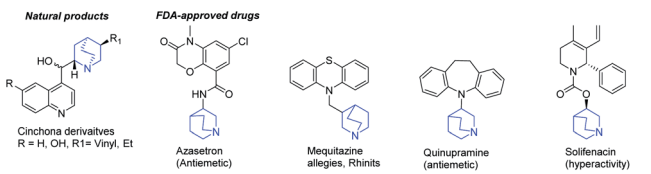

Fig. 1 Some examples of the compounds of interest with a quinuclidine moiety.

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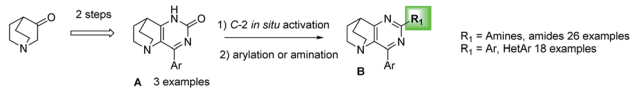
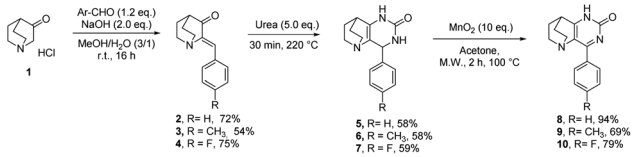


Fig. 2 General scheme leading to 2,4 disubstituted quinuclidino pyrimidines under C–O direct activation.



Scheme 1 Synthesis of **8–10**.

7,8-dihydro-1*H*-5,8-ethanopyrido[3,2-*d*]pyrimidin-2(6*H*)one **2–4** were obtained in satisfactory yields after aldol condensation between the commercially available 3-quinuclidinone hydrochloride **1** with three benzaldehydes in presence of sodium hydroxide. Next, a solvent-free condensation with urea was performed to generate bicyclic tetrahydropyrimidinones **5–7**.[33] Finally, an oxidative hetero aromatization was carried out using manganese dioxide[34] in acetone under microwave irradiation to access the desired platforms **8–10** in very good to excellent yields (Scheme 1).

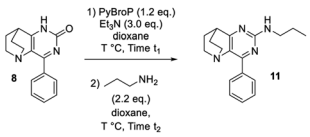
To take advantage of the lactam, we began our methodological study by a one-pot amination at the *C*-2 position using C–O direct activation involving PyBroP and Et_3N.[35–37] In this tandem reaction, the first *in situ* step generated the *O*-phosphonium leaving group, which was then displaced with the adequate nucleophile. In a first attempt, the reactivity was examined by treating 4-phenyl-pyrido[3,2-*d*]pyrimidinone **8** with *n*-propylamine and several reaction parameters (temperature, duration) were screened to reach an acceptable level of reaction efficiency (Table 1).[38,39]

The first step was also performed with **8** in the presence of PyBrOP at a temperature of 80 °C and after 2 h the primary amine (2.2 eq.) was added. After 3 additional hours, only a small proportion of the intermediate had been consumed and the desired product **11** was isolated in low yield whereas a large amount of starting material **8** was recovered. Increasing the temperature to 100 °C slightly enhanced the yield to 32%. A time reaction screening for each step (t_1 and t_2) led to interesting results. A full conversion of **8** to *O*-phosphonium was reached after 3 h at 100 °C. The nucleophilic attack of the amine on the activated heterocycle was the rate-limiting step. The second step was achieved during 17 h at 100 °C and led to the desired compound **11** in 72% of yield.

In order to explore the scope and limitations of this tandem sequence, we then condensed previously synthesized ethanopyrido[3,2-*d*]pyrimidinones **A** with various amines (Table 2). With 1-pentylamine and **8**, the yield decreased slightly (entry 2 *versus* 1). The same behaviour was observed when benzyl amines were used (entries 8–10). An attempted strengthening of nucleophilicity with secondary cyclic amines such as piperidine, morpholine or thiomorpholine increased the reactivity up to 82% (entries 3–7). Moreover, when piperidine was used as a secondary amine with ethanopyrido[3,2-*d*]pyrimidinones **9** and **10**, the two S_NAr reactions were efficiently achieved and compounds **23** and **24** were isolated in 86% and 79% of yield, respectively (entries 15–16).

During this investigation, we encountered two limitations when anilines or lactams, which are very weakly nucleophilic species, were used: the final compounds **21** and **22** (entries 12, 13) were never observed. To access these derivatives, it became necessary to develop a one-pot sequence involving *in situ* CO-activation followed by a Pd-catalyzed C–N bond forming sequence, an original alternative to the previously unsuccessful S_NAr method.

Table 1 Optimization of amination conditions with **8**



Entry	Temp. (°C)	t_1	t_2	Yield[a] (%)
1	80	2 h	3 h	23
2	100	2 h	3 h	32
3	100	3 h	3 h	48
4	100	4 h	3 h	47
5	100	3 h	6 h	58
6	100	3 h	17 h	72

[a] Yield is indicated as isolated product.

Table 2 Synthesis of **11–24**

Entry	R_1	HNR_2R_3	Cpd, yield[a]
1	H	Propylamine	**11**, 72%
2	H	Pentylamine	**12**, 59%
3	H	Piperidine	**13**, 77%
4	H	Morpholine	**14**, 82%
5	H	Thiomorpholine	**15**, 72%
7	H	4,4-Difluoropiperidine	**16**, 61%
8	H	$C_6H_5CH_2NH_2$	**17**, 51%
9	H	4-CH_3O-$C_6H_4CH_2NH_2$	**18**, 42%
10	H	4-CF_3-$C_6H_4CH_2NH_2$	**19**, 39%
11	H	Imidazole	**20**, 22%
12	H	4-CH_3-$C_6H_4NH_2$	**21**, ND[b]
13	H	δ-Valerolactam	**22**, ND[b]
15	Me	Piperidine	**23**, 86%
16	F	Piperidine	**24**, 79%

[a] Cpd: compound number; yield is indicated as isolated product. [b] Not detected.

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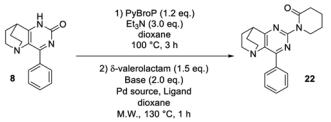
Table 3 Optimization of the conditions for the formation of **22**



Entry	Catalyst (mol%)	Ligand (mol%)	Base	Temp. (°C)	Yield[a] (%)
1	Pd_2dba_3 (5%)	Xantphos (10%)	K_2CO_3	130	19
2	$Pd(OAc)_2$ (5%)	Xantphos (10%)	K_2CO_3	130	21
3	$Pd(OAc)_2$ (10%)	Xantphos (20%)	K_2CO_3	130	40
4	$Pd(OAc)_2$ (10%)	Xantphos (20%)	K_2CO_3	150	33
5	$Pd(OAc)_2$ (10%)	CyJohnPhos (20%)	K_2CO_3	130	0
6	$Pd(OAc)_2$ (10%)	RuPhos (20%)	K_2CO_3	130	0
7	$Pd(OAc)_2$ (10%)	Xantphos (20%)	Na_2CO_3	130	Traces
8	$Pd(OAc)_2$ (10%)	Xantphos (20%)	Cs_2CO_3	130	9

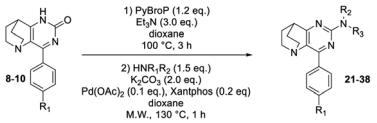
[a] Yield is indicated as isolated product.

First, we used δ-valerolactam as amide to prevent any S_NAr competition, Pd_2dba_3 as the palladium source in the presence of Xantphos as bidentate ligand, K_2CO_3 as base, and dioxane as solvent. With these conditions, the desired product **22** was isolated in low yield (19%, Table 3, entry 1) despite the total consumption of the starting material, indicating the low reactivity of the *O*-phosphonium intermediate. When the palladium catalyst was replaced by $Pd(OAc)_2$, the same behaviour was observed and the desired compound **22** was obtained in a similar 21% yield. By increasing the catalytic charge to 10 mol% the *O*-phosphonium species was consumed, affording **22** in 40% of yield accompanied with degradation. A fine adjustment of the temperature (to 150 °C) drastically decreased the yield (entry 4) and the replacement of Xantphos with well-known Buchwald ligands such as CyJohnPhos or Ruphos totally inhibited the reactivity. Changing the nature of the base indicated that the use of Na_2CO_3 and Cs_2CO_3 was not tolerated and showed the highest reaction sensitivity (entries 7, 8).

Next, the scope and generality of the Pd-coupling step were examined. The 2-pyrrolidinone reaction gave the desired product **25** with the same reactivity (Table 4, entry 2), whereas using aniline afforded product **26** in a good isolated yield of 56% (Table 4, entry 4). The reactions proceeded with the same efficiency regardless of the nature of the aniline used (*i.e.*, with electron-withdrawing or electron-donating substituents) and the compound **21** was finally synthesized with these conditions (entry 1). Steric hindrance symbolized by the presence of a methyl group on the aniline in *ortho vs. meta* or *para* position (entries 1, 6–7) induced a dramatic decrease in yield. With aminopyridines, reactivity was maintained and compounds **33** and **34** were isolated in 34% and 28% of yield, respectively. The sole limitation in this trend involved the use of 4-(4-fluorophenyl)-7,8-dihydro-1*H*-5,8-ethanopyrido[3,2-*d*]pyrimidinone **10** as starting material, which inhibited the reactivity whereas the tolyl derivative **9** restored the efficiency.

We next focused our attention on using this C–O activation strategy to create a C–C bond instead of a C–N bond under palladium catalysis.[28,40,41] In this tandem procedure, the PyBrop activation was achieved as previously described during 3 h and the reagents necessary to perform the cross coupling reaction were then added. Each parameter of the Suzuki–Miyaura reaction was modulated and the results are summarized in Table 5. 24 h of reaction with $Pd(OAc)_2$ at 110 °C in the presence of a bidentate phosphine proved to be a better catalytic system than with $PdCl_2(dppf)\cdot CH_2Cl_2$ or $Pd(PPh_3)_4$ (entries 1–3). Modulation of the base indicated an increase in the yield using K_3PO_4 instead of classical carbonates (entries 3–6) whereas optimization of the nature of the ligand clearly indicated that Xantphos and Ruphos

Table 4 Synthesis of **21–38**



Entry	R_1	HNR_2R_3	Cpd, yield[a]
1	H	4-CH_3-$C_6H_4NH_2$	**21**, 48%
2	H	δ-Valerolactam	**22**, 40%
3	H	2-Pyrrolidinone	**25**, 39%
4	H	$C_6H_5NH_2$	**26**, 56%
5	H	4-CH_3O-$C_6H_4NH_2$	**27**, 48%
6	H	3-CH_3-$C_6H_4NH_2$	**28**, 31%
7	H	2-CH_3-$C_6H_4NH_2$	**29**, 15%
8	H	4-CF_3-$C_6H_4NH_2$	**30**, 56%
9	H	4-CN-$C_6H_4NH_2$	**31**, 35%
10	H	4-NO_2-$C_6H_4NH_2$	**32**, 39%
11	H	3-NH_2-pyridine	**33**, 34%
12	H	5-NH_2-2-MeOpyridine	**34**, 28%
13	Me	$C_6H_5NH_2$	**35**, 44%
14	Me	4-CF_3-$C_6H_4NH_2$	**36**, 49%
15	F	$C_6H_5NH_2$	**37**, traces
16	F	4-CF_3-$C_6H_4NH_2$	**38**, ND[b]

[a] Cpd: compound number; yield is indicated as isolated product. [b] Not detected.

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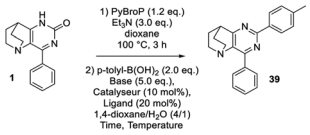
Table 5 Optimization of the conditions for the formation of **39**



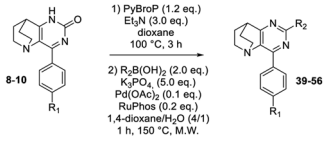
Entry	Catalyst/ligand	Base	Time step 2	Temp step 2	Yield[a] (%)
1	$PdCl_2(dppf)\cdot CH_2Cl_2$	Na_2CO_3	24 h	110 °C	50
2	$Pd(PPh_3)_4$	Na_2CO_3	24 h	110 °C	41
3	$Pd(OAc)_2$/Xantphos	Na_2CO_3	24 h	110 °C	60
4	$Pd(OAc)_2$/Xantphos	Cs_2CO_3	24 h	110 °C	50
5	$Pd(OAc)_2$/Xantphos	K_2CO_3	24 h	110 °C	54
6	$Pd(OAc)_2$/Xantphos	K_3PO_4	24 h	110 °C	68
7	$Pd(OAc)_2$/Xphos	K_3PO_4	24 h	110 °C	62
8	$Pd(OAc)_2$/Ruphos	K_3PO_4	24 h	110 °C	68
9	$Pd(OAc)_2$/Ruphos	K_3PO_4	1 h	150 °C M.W.	70

[a] Yield is indicated as isolated product.

gave the desired compound **39** in the best 68% yield under thermal conditions (entries 6–8). Finally, optimization under microwave irradiation (not shown) established that in the presence of Ruphos at 150 °C the reaction was achieved in only 1 h to furnish **39** in a 70% yield (entry 9).

In the last stage of this study, we investigated the modulation of the nature of the boron derivative to identify the potential limitations. In fact, whatever the substituent on the phenyl boronic acid (*i.e.*, electron-donating or withdrawing), or the steric hindrance induced by an *ortho* substitution, the C–C bond was efficiently generated and products were isolated in fairly good yields ranging from 54% to 82% (Table 6, products **39–50**). The only identified limit concerned the presence of an acidic proton which slightly altered the yield of the reaction but this constraint was easily removed by the use of a protective group such as THP (entries 6–7). The use of (Het)arylboronic acids such as thiophene or pyridine was well tolerated and compounds **51** and **52** were isolated in 77 and 60% of yield, respectively. Finally, proportionally, the reactions conducted with substituted ethanopyrido[3,2-*d*]pyrimidinones **9–10** (entries 15–18) were less efficient than those conducted with **8** (entries 1 *vs.* 15 or 17, 10 *vs.* 16 or 18).

Table 6 Synthesis of **39–56**



Entry	R_1	$R_2B(OH)_2$	Cpd, yield[a]
1	H	4-CH_3-$C_6H_4B(OH)_2$	**39**, 70%
2	H	$C_6H_5B(OH)_2$	**40**, 68%
3	H	3-CH_3-$C_6H_4B(OH)_2$	**41**, 73%
4	H	2-CH_3-$C_6H_4B(OH)_2$	**42**, 76%
5	H	4-CH_3O-$C_6H_4B(OH)_2$	**43**, 69%
6	H	4-OH-$C_6H_4B(OH)_2$	**44**, 54%
7	H	4-OTHP-$C_6H_4B(OH)_2$	**45**, 69%
8	H	2-NaphtylB$(OH)_2$	**46**, 67%
9	H	4-F-$C_6H_4B(OH)_2$	**47**, 70%
10	H	4-CN-$C_6H_4B(OH)_2$	**48**, 82%
11	H	4-CF_3-$C_6H_4B(OH)_2$	**49**, 72%
12	H	4-NO_2-$C_6H_4B(OH)_2$	**50**, 76%
13	H	3-ThienylB$(OH)_2$	**51**, 77%
14	H	3-PyridylB$(OH)_2$	**52**, 60%
15	Me	4-CH_3-$C_6H_4B(OH_2)$	**53**, 37%
16	Me	4-CN-$C_6H_4B(OH)_2$	**54**, 52%
17	F	4-CH_3-$C_6H_4B(OH)_2$	**55**, 45%
18	F	4-CN-$C_6H_4B(OH)_2$	**56**, 68%

[a] Cpd: compound number; yield is indicated as isolated product.

During our investigation, we were able to obtain single crystals of **49** suitable for X-ray diffraction analysis (Fig. 3). Compound **49** crystalizes in the monoclinic $P2_1$ space group with the following cell parameters: $a = 15.385(8)$, $b = 5.893(3)$, c

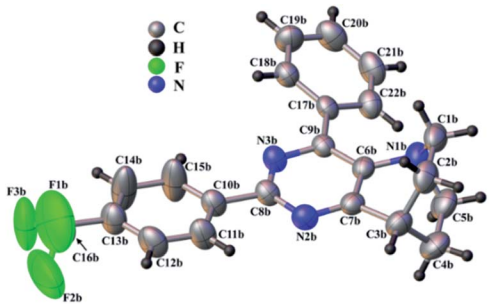


Fig. 3 View of the molecular structure of **49**. Only one of the two independent molecules of the asymmetric unit is shown (molecule B). The disorder on the CF_3 moiety is not represented for clarity. The labelling scheme of molecule A is the same but the suffix "b" has been replaced by suffix "a". The thermal atomic displacements are represented using ellipsoids at a 50% probability level.

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= 22.187(14) Å, β = 110.05(4) ° and V = 1890(3) Å^3. The asymmetric unit is composed of two independent molecules leading to four molecules in the unit cell.

Typical bond lengths are close to the expected values, ranging from 1.352(8) to 1.390(7) Å for the C–C bonds and from 1.332(6) to 1.356(5) for N–C bonds within the aromatic rings, from 1.477(9) to 1.541(8) Å, 1.430(6) to 1.488(7) and 1.309(9) to 1.336(10) for single C–C, C–N and C–F bonds respectively.

The pyrimidine and trifluoro-methyl-phenyl rings are almost coplanar with an angle between planes of 7.3(2) and 7.4(2)° for the two independent molecules. Nevertheless, this angle may be underestimated as the trifluoro-methyl-phenyl ring appears slightly disordered. The second phenyl ring, meanwhile, is significantly tilted from the pyrimidine ring plane (25.4(2)° and 26.9(2)°) for both molecules. Fig. 3 shows one of the two independent molecules of **49** extracted from the crystal structure. The two molecules are very similar (RMSD = 0.452 Å) except as regards the phenyl ring, which is reversely tilted in the two molecules.

Conclusions

In summary, the quick access to variously functionalized ethanopyrido[3,2-*d*]pyrimidines has been described herein. Aminated or arylated groups were introduced at the *C*-2 position of the ethanopyrido[3,2-*d*]pyrimidinones series using a tandem one-pot direct C–O activation sequence involving first PyBroP as activator and next a S_NAr or a palladium cross coupling reaction. Aminations were achieved under S_NAr reactions which were performed with a large variety of amines or using Buchwald–Hartwig cross-coupling reactions in combination with microwave irradiation. In addition, we have also reported the efficiency of the Suzuki–Miyaura reactions in *C*-2 position, which is compatible with all the boronylated starting material used. This work afforded a novel class of 1,4 disubstituted 7,8-dihydro-6*H*-5,8-ethanopyrido[3,2-*d*]pyrimidines which will undoubtedly have a major impact on the synthesis of new bioactive compounds that contain the rare ethanopyrido[3,2-*d*]pyrimidine scaffold as the central skeleton. Efforts to achieve these objectives are currently in progress.

Experimental section

Materials and methods

^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX 250 or 400 Mhz instrument using $CDCl_3$ and DMSO-d_6. The chemical shifts are reported in parts per million (δ scale), and all coupling constant (J) values are reported in hertz. The following abbreviations were used for the multiplicities: s (singlet), d (doublet), t (triplet), q (quartet), p (pentuplet), m (multiplet), sext (sextuplet), and dd (doublet of doublets). Melting points are uncorrected. IR absorption spectra were obtained on a PerkinElmer PARAGON 1000 PC, and the values are reported in inverse centimeters. HRMS spectra were acquired in positive mode with an ESI source on a Q-TOF mass by the "Fédération de Recherche" ICOA/CBM (FR2708) platform. Monitoring of the reactions was performed using silica gel TLC plates (silica Merck 60 F 254). Spots were visualized by UV light (254 nm and 356 nm). Column chromatography was performed using silica gel 60 (0.063–0.200 mm, Merck.). Microwave irradiation was carried out in sealed vessels placed in a Biotage Initiator or Biotage Initiator+ system (400 W maximum power). The temperatures were measured externally by IR. Pressure was measured by a non-invasive sensor integrated into the cavity lid. All reagents were purchased from commercial suppliers and were used without further purification. The crystal structure of **49** was solved by single crystal X-ray diffraction at room temperature using a Bruker Apex-II diffractometer with Mo-Kα radiation. CCDC 2074887 contains the supplementary crystallographic data for this paper.

Synthetic procedures

General procedure A: aldol condensation. To a solution of 3-quinuclidinone hydrochloride (1.0 eq.) and sodium hydroxide (2.0 eq.) in a mixture of methanol/water (3/1) was added the corresponding aldehyde (1.2 eq.). After stirring at room temperature for 16 h, the reaction mixture was concentrated under reduced pressure to evaporate the methanol. The obtained suspension was filtered, washed with water and dried under vacuum to afford the expected product as a solid.

*(Z)-2-Benzylidenequinuclidin-3-one (**2**).* The reaction was carried out as described in general procedure A using a solution of 3-quinuclidinone hydrochloride (3.99 g, 24.73 mmol, 1.0 eq.) and sodium hydroxide (1.99 g, 49.7 mmol, 2.0 eq.) in a mixture of methanol/water (3/1, 75 mL) and benzaldehyde (3.0 mL, 29.5 mmol, 1.2 eq.). The reaction mixture was stirred 16 h at r.t. to afford **2** (3.82 g, 72%) as a yellow solid. Rf (PE/EA: 90/10): 0.32. M_p: 141–143 °C. IR (ATR diamond, cm^{-1}) ν: 2941, 2873, 1700, 1621, 1096, 688. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.03 (td, J = 3.1, 7.9 Hz, 4H, 2xCH_2), 2.63 (p, J = 3.0 Hz, 1H, CH), 3.00 (dt, J = 7.6, 12.5 Hz, 2H, N–CH_2), 3.16 (dt, J = 7.8, 13.4 Hz, 2H, N–CH_2), 7.02 (s, 1H, C=CH), 7.29–7.42 (m, 3H, 3xCHAr), 7.97–8.09 (m, 2H, 2xCHAr). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 26.3 (2xCH_2), 40.7 (CH), 47.9 (2xN–CH_2), 125.5 (C=CH), 128.8 (2xCHAr), 130.0 (CH_{Ar}), 132.6 (2xCH_{Ar}), 134.4 (C_{Ar}), 145.1 (C=CH), 206.8 (C=O). HRMS (EI/MS): m/z calculated for $C_{14}H_{16}NO$: 214.1225 [M + H]$^+$; found 214.1226.

*(Z)-2-(4-Methylbenzylidene)quinuclidin-3-one (**3**).* The reaction was carried out as described in general procedure A using a solution of 3-quinuclidinone hydrochloride (4.00 g, 24.79 mmol, 1.0 eq.) and sodium hydroxide (2.01 g, 50.27 mmol, 2.0 eq.) in a mixture of methanol/water (3/1, 75 mL) and *p*-tolualdehyde (3.5 mL, 29.68 mmol, 1.2 eq.). The reaction mixture was stirred 16 h at r.t. to afford **3** (3.05 g, 54%) as a yellow solid. Rf (EP/EA: 90/10): 0.48. M_p: 128–130 °C. IR (ATR diamond, cm^{-1}) ν: 2938, 1700, 1626, 1507, 1251, 1092, 810, 517. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.01 (td, J = 7.9, 2.9 Hz, 4H, 2xCH_2), 2.36 (s, 3H, CH_3), 2.62 (p, J = 2.9 Hz, 1H, CH), 2.91–3.04 (m, 2H, N–CH_2), 3.09–3.22 (m, 2H, N–CH_2), 7.00 (s, 1H, C=CH), 7.17 (d, J = 7.9 Hz, 2H, 2xCH_{Ar}), 7.93 (d, J = 8.0 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 21.5 (CH_3), 25.9 (2xCH_2), 40.3 (CH), 47.5 (2xN-CH_2), 125.2 (=CH), 129.1 (2xCH_{Ar}), 131.2 (C_q), 132.1 (2xCH_{Ar}), 139.9 (C_q), 144.0 (C_q), 206.4 (C=O). HRMS (EI/MS): m/z calculated for $C_{15}H_{18}NO$: 228.1381; found 228.1383.

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*(Z)-2-(4-Fluorobenzylidene)quinuclidin-3-one (**4**).* The reaction was carried out as described in general procedure A using a solution of 3-quinuclidinone hydrochloride (4.00 g, 24.76 mmol, 1.0 eq.) and sodium hydroxide (2.00 g, 50.00 mmol, 2.0 eq.) in a mixture of methanol/water (3/1, 75 mL) and 4-fluorobenzaldehyde (3.2 mL, 29.82 mmol, 1.2 eq.). The reaction mixture was stirred 16 h at r.t. to afford **4** (4.33 g, 75%) as a yellow solid. Rf (PE/EA: 90/10): 0.30. M_p: 131–133 °C. IR (ATR diamond, cm^{-1}) ν: 2943, 1698, 1619, 1595, 1502, 1220, 853. ^1H NMR (400 MHz, $CDCl_3$) δ: 2.02 (td, $J = 7.9$, 3.0 Hz, 4H, 2xCH_2), 2.63 (p, $J = 3.0$ Hz, 1H, CH), 2.90–3.04 (m, 2H, N–CH_2), 3.07–3.21 (m, 2H, N–CH_2), 6.97 (s, 1H, =CH), 6.99–7.10 (m, 2H, 2xCH_{Ar}), 7.99–8.10 (m, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 26.0 (2xCH_2), 40.3 (CH), 47.5 (2xN-CH_2), 115.5 (d, $J = 21.5$ Hz, 2xCH_{Ar}), 123.9 (=CH), 130.3 (d, $J = 3.4$ Hz, C=), 134.3 (d, $J = 8.1$ Hz, 2xCH_{Ar}), 144.3 (d, $J = 2.6$ Hz, C_{Ar}), 163.3 (d, $J = 251.6$ Hz, C_{Ar}-F), 206.3 (C=O). ^{19}F NMR (376 MHz, $CDCl_3$) δ: −109.84. HRMS (EI/MS): m/z calculated for $C_{14}H_{15}FNO$: 232.1132 $[M + H]^+$; found 232.1132.

*4-Phenyl-3,4,7,8-tetrahydro-1H-5,8-ethanopyrido[3,2-d]pyrimidin-2(6H)-one (**5**).* **2** (4.998 g, 23.43 mmol, 1.0 eq.) and urea (7.050 g, 117.38 mmol, 5.0 eq.) were ground in a mortar and put in a 100 mL-flask. The mixture was then heated at 220 °C in a pre-heated bath. After 30 min, 80 mL of a solution of NaOH 2 N were added, and the resulting mixture was allowed to cool to room temperature. The precipitate formed was filtered, washed with water (80 mL), DCM (80 mL) and acetone (2 × 80 mL) to afford **5** (3.505 g, 58%) as a white solid. Rf (DCM/MeOH: 95/5): 0.44. M_p: >260 °C. IR (ATR diamond, cm^{-1}) ν: 3295, 2951, 1681, 1642, 1454, 1241, 752, 732, 691. ^1H NMR (400 MHz, DMSO-d_6) δ: 1.30–1.43 (m, 1H, CH), 1.45–1.56 (m, 2H, 2xCH), 1.56–1.65 (m, 1H, CH), 1.65–1.79 (m, 1H, N–CH), 2.50–2.61 (m, 3H, 2xN-CH, CH), 2.76 (ddd, $J = 4.6$, 8.6, 12.9 Hz, 1H, N–CH), 4.83 (d, $J = 2.1$ Hz, 1H, CH), 6.98 (s, 1H, NH), 7.20–7.35 (m, 5H, 5xCH_{Ar}), 8.35 (s, 1H, NH). ^{13}C NMR (101 MHz, DMSO-d_6) δ: 27.9 (CH), 28.6 (CH_2), 28.7 (CH_2), 49.9 (N–CH_2), 50.0 (N–CH_2), 57.9 (CH), 118.3 (C_q), 126.7 (2xCH_{Ar}), 127.1 (CH), 128.1 (2xCH_{Ar}), 137.2 (C_q), 144.4 (C_q), 152.5 (C_q). HRMS (EI/MS): m/z calculated for $C_{15}H_{18}N_3O$: 256.1442 $[M + H]^+$; found: 256.1444.

*4-(p-Tolyl)-3,4,7,8-tetrahydro-1H-5,8-ethanopyrido[3,2-d]pyrimidin-2(6H)-one (**6**).* **3** (3.97 g, 17.48 mmol, 1.0 eq.) and urea (5.25 g, 87.51 mmol, 5.0 eq.) were ground in a mortar and put in a 100 mL-flask. The mixture was then heated at 220 °C in a pre-heated bath. After 30 min, 60 mL of a solution of NaOH 2 N were added, and the resulting mixture was allowed to cool to room temperature. The precipitate formed was filtered, washed with water (60 mL), DCM (60 mL) and acetone (2 × 60 mL) to afford **6** (2.76 g, 58%) as a white solid. Rf (DCM/MeOH: 95/5): 0.22. M_p: >260 °C. IR (ATR diamond, cm^{-1}) ν: 3294, 3091, 2941, 1644, 1455, 1340, 1102, 750. ^1H NMR (400 MHz, DMSO-d_6) δ: 1.31–1.41 (m, 1H, CH), 1.43–1.56 (m, 2H, 2xCH), 1.56–1.64 (m, 1H, CH), 1.70–1.81 (m, 1H, N–CH), 2.27 (s, 3H, CH_3), 2.52–2.61 (m, 3H, 2xN-CH, CH), 2.69–2.80 (m, 1H, N–CH), 4.78 (s, 1H, NH–CH), 6.91 (s, 1H, NH), 7.13 (dd, $J = 9.0$, 10.4 Hz, 4H, 4xCH_{Ar}), 8.31 (s, 1H, NH). ^{13}C NMR (101 MHz, DMSO-d_6) δ: 20.6 (CH_3), 27.8 (CH), 28.6 (CH_2), 28.7 (CH_2), 49.8 (N–CH_2), 50.0 (N–CH_2), 57.6 (CH), 118.4 (C_q), 126.6 (2xCH_{Ar}), 128.6 (2xCH_{Ar}), 136.0 (C_q), 137.0 (C_q), 141.5 (C_q), 152.4 (C_q). HRMS (EI/MS): m/z calculated for $C_{16}H_{20}N_3O$: 270.1601 $[M + H]^+$; found: 270.1596.

*4-(4-Fluorophenyl)-3,4,7,8-tetrahydro-1H-5,8-ethanopyrido[3,2-d]pyrimidin-2(6H)-one (**7**).* **4** (2.0 g, 8. mmol, 1.0 eq.) and urea (2.60 g, 43.42 mmol, 5.0 eq.) were ground in a mortar and put in a 50 mL-flask. The mixture was then heated at 220 °C in a pre-heated bath. After 30 min, 30 mL of a solution of NaOH 2 N were added, and the resulting mixture was allowed to cool to room temperature. The precipitate formed was filtered, washed with water (30 mL), DCM (30 mL) and acetone (2 × 30 mL) to afford **7** (1.40 g, 59%) as a white solid. Rf (DCM/MeOH: 95/5): 0.19. M_p: 258–260 °C. IR (ATR diamond, cm^{-1}) ν: 3302, 3093, 2945, 1638, 1505, 1221, 1155, 1098, 748. ^1H NMR (400 MHz, DMSO-d_6) δ: 1.31–1.43 (m, 1H, CH), 1.44–1.53 (m, 2H, 2xCH), 1.53–1.66 (m, 1H, CH), 1.72 (tt, $J = 3.3$, 12.8 Hz, 1H, N–CH), 2.52–2.63 (m, 3H, 2xN-CH, CH), 2.70–2.81 (m, 1H, N–CH), 4.85 (s, 1H, NH–CH), 7.00 (s, 1H, NH), 7.14 (t, $J = 8.7$ Hz, 2H, 2xCH_{Ar}), 7.29 (dd, $J = 5.6$, 8.4 Hz, 2H, 2xCH_{Ar}), 8.37 (s, 1H, NH). ^{13}C NMR (101 MHz, DMSO-d_6) δ: 27.8 (CH), 28.6 (2xCH_2), 49.8 (N–CH_2), 50.0 (N–CH_2), 57.1 (CH), 114.6 (CH_{Ar}), 114.8 (CH_{Ar}), 118.1 (C_q), 128.5 (CH_{Ar}), 128.6 (CH_{Ar}), 137.3 (C_q), 140.6 (d, $J = 2.9$ Hz, C_q), 152.3 (C_q), 161.3 (d, $J = 242.4$ Hz, C_{Ar}-F). ^{19}F NMR (376 MHz, DMSO-d_6) δ: −115.92. HRMS (EI/MS): m/z calculated for $C_{15}H_{17}FN_3O$: 274.1350 $[M + H]^+$; found: 274.1350.

*4-Phenyl-7,8-dihydro-1H-5,8-ethanopyrido[3,2-d]pyrimidin-2(6H)-one (**8**).* In a microwave vial of 10–20 mL, MnO_2 (873 mg, 10.0 mmol, 10.0 eq.) was added to a solution of **5** (259 mg, 1.0 mmol, 1.0 eq.) in acetone (12 mL). The reaction mixture was heated for 2 h at 100 °C under microwave irradiation. The reaction mixture was filtered through celite and washed with acetone (20 mL), DCM (20 mL) and MeOH (20 mL). The solvents were evaporated to give **8** (237 mg, 94%) as a white solid without further purification. Rf (DCM/MeOH: 95/5): 0.38. M_p: >260 °C. IR (ATR diamond, cm^{-1}) ν: 2967, 2928, 1626, 1551, 1442, 1390, 1324, 1128, 776, 747, 685. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.74–1.86 (m, 2H, CH_2), 1.94–2.06 (m, 2H, CH_2), 2.72 (td, $J = 4.7$, 11.3, 11.7 Hz, 2H, N–CH_2), 3.08–3.19 (m, 3H, N–CH_2, CH), 7.44–7.56 (m, 3H, 3xCH_{Ar}), 8.02 (d, $J = 7.0$ Hz, 2H, 2xCH_{Ar}), 13.00 (s, 1H, NH). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.0 (2xCH_2), 33.9 (CH), 49.3 (2xN-CH_2), 126.1 (C_q), 128.6 (2xCH_{Ar}), 129.8 (2xCH_{Ar}), 131.2 (CH_{Ar}), 158.8 (C_q). HRMS (EI/MS): m/z calculated for $C_{15}H_{16}N_3O$: 254.1286 $[M + H]^+$; found: 254.1288.

*4-(p-Tolyl)-7,8-dihydro-1H-5,8-ethanopyrido[3,2-d]pyrimidin-2(6H)-one (**9**).* In a microwave vial of 10–20 mL, MnO_2 (1.11 g, 12.8 mmol, 10.0 eq.) was added to a solution of **6** (331 mg, 1.2 mmol, 1.0 eq.) in acetone (18 mL). The reaction mixture was heated for 2 h at 100 °C under microwave irradiation. The reaction mixture was filtered through celite and washed with acetone (20 mL), DCM (20 mL) and MeOH (20 mL). The solvents were evaporated to give **9** (225 mg, 69%) as a white solid without further purification. Rf (DCM/MeOH: 95/5): 0.27. M_p: >260 °C. IR (ATR diamond, cm^{-1}) ν: 2963, 2942, 2869, 1710, 1633, 1449, 1357, 803, 746. ^1H NMR (400 MHz, DMSO-d_6) δ: 1.68–1.80 (m, 2H, CH_2), 2.02–2.13 (m, 2H, CH_2), 2.41 (s, 3H, CH_3), 2.68–2.79 (m, 2H, N–CH_2), 3.10–3.21 (m, 2H, N–CH_2), 3.25 (p, $J = 2.6$ Hz, 1H, CH), 7.40 (d, $J = 8.0$ Hz, 2H, 2xCH_{Ar}), 7.72 (d, $J = 8.2$ Hz, 2H,

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2xCH_{Ar}). ^{13}C NMR (101 MHz, DMSO-d_6) δ: 21.2 (CH_3), 25.3 (2xCH_2), 30.7 (CH), 48.8 (2xN-CH_2), 115.2 (q, J = 288.7 Hz, TFA), 124.0 (C_q), 124.6 (C_q), 129.2 (2xCH_{Ar}), 130.5 (2xCH_{Ar}), 143.5 (C_q), 149.5 (C_q), 156.6 (C_q), 158.5 (q, J = 38.1 Hz, TFA), 177.9 (C=O). HRMS (EI/MS): m/z calculated for $C_{16}H_{18}N_3O$: 268.1444 [M + H]$^+$; found: 268.1448.

*4-(4-Fluorophenyl)-7,8-dihydro-1H-5,8-ethanopyrido[3,2-d]pyrimidin-2(6H)-one (**10**).* In a microwave vial of 10–20 mL, MnO_2 (1.30 g, 15.0 mmol, 10.0 eq.) was added to a solution of **7** (413 mg, 1.5 mmol, 1.0 eq.) in acetone (18 mL). The reaction mixture was heated for 2 h at 100 °C under microwave irradiation. The reaction mixture was filtered through celite and washed with acetone (20 mL), DCM (20 mL) and MeOH (20 mL). The solvents were evaporated to give **10** (321 mg, 79%) as a white solid without further purification. Rf (DCM/MeOH, 95/5): 0.30. M_p: >260 °C. IR (ATR diamond, cm^{-1}) ν: 2944, 1651, 1590, 1556, 1450, 1359, 1230, 1157, 800, 658. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.68–1.80 (m, 2H, CH_2), 2.02–2.14 (m, 2H, CH_2), 2.70–2.81 (m, 2H, N–CH_2), 3.12–3.22 (m, 2H, N–CH_2), 3.25 (p, J = 3.0 Hz, 1H, CH), 7.43 (t, J = 8.7 Hz, 2H, 2xCH_{Ar}), 7.88 (dd, J = 8.7, 5.3 Hz, 2H, 2xCH_{Ar}), 14.00 (s, TFA). ^{13}C NMR (101 MHz, DMSO-d_6) δ: 25.20 (2xCH_2), 30.84 (CH), 48.92 (2xN-CH_2), 115.34 (q, J = 290.4 Hz, TFA), 115.66 (CH_{Ar}), 115.88 (CH_{Ar}), 124.01 (C_q), 124.40 (d, J = 2.7 Hz, C_q), 133.24 (CH_{Ar}), 133.33 (CH_{Ar}), 150.35 (C_q), 155.47 (C_q), 158.54 (m, TFA), 164.64 (d, J = 251.8 Hz, C_{Ar}-F), 177.85 (C_q). ^{19}F NMR (376 MHz, $CDCl_3$) δ: −75.86 (TFA), −100.94. HRMS (EI/MS): m/z calculated for $C_{15}H_{15}FN_3O$: 272.1194 [M + H]$^+$; found: 272.1194.

General procedure B: S_NAr *via* PyBroP activation. In a microwave vial, to a solution of **8** (200 mg, 0.79 mmol, 1.0 eq.) and PyBroP (446 mg, 0.96 mmol, 1.2 eq.) in 1,4-dioxane (8 mL) was added Et_3N (0.32 mL, 2.36 mmol, 3.0 eq.). The mixture was then degassed by argon bubbling for 15 minutes. The sealed tube was heated at 100 °C for 3 h. After cooling, the corresponding amine (2.2 eq.) was added, and the reaction mixture was heated at 100 °C for 17 h. After cooling to room temperature, the solven was evaporated under reduced atmosphere. The crude material was purified by flash chromatography on silica gel to give the desired compound.

*4-Phenyl-N-propyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-amine (**11**).* Compound **11** was obtained according to the general procedure **B** using propylamine (0.14 mL, 1.73 mmol, 2.2 eq.). After purification by silica gel flash chromatography (PE/EA, 70/30), **11** (167 mg, 72%) was obtained as a white solid. R*f* (PE/EA: 70/30): 0.37. M_p: 149–151 °C. IR (ATR diamond, cm^{-1}) ν: 3264, 3115, 2955, 2869, 1596, 1360, 1131, 770, 687, 626. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.01 (t, J = 7.4 Hz, 3H, CH_3), 1.67 (h, J = 7.0 Hz, 2H, CH_2), 1.71–1.81 (m, 2H, CH_2), 1.90–2.02 (m, 2H, CH_2), 2.72 (td, J = 4.7, 11.2 Hz, 2H, N–CH_2), 3.04 (p, J = 3.0 Hz, 1H, CH), 3.104–3.21 (m, 2H, N–CH_2), 3.47 (q, J = 6.6 Hz, 2H, CH_2), 5.03 (t, J = 5.8 Hz, 1H, NH), 7.36–7.49 (m, 3H, 3xCH_{Ar}), 8.25 (d, J = 7.2 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 11.7 (CH_3), 23.1 (CH_2), 27.8 (2xCH_2), 33.7 (CH), 43.7 (CH_2), 49.4 (2xN-CH_2), 128.1 (2xCH_{Ar}), 129.5 (CH_{Ar}), 129.8 (2xCH_{Ar}), 131.4 (C_q), 136.7 (C_q), 155.6 (C_q), 160.1 (C_q), 175.6 (C_q). HRMS (EI/MS): m/z calculated for $C_{18}H_{23}N_4$: 295.1916 [M + H]$^+$; found: 295.1917.

*N-Pentyl-4-phenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-amine (**12**).* Compound **12** was obtained according to the general procedure **B** using amylamine (0.20 mL, 1.71 mmol, 2.2 eq.). After purification by silica gel flash chromatography (PE/EA, 70/30), **12** (150 mg, 59%) was obtained as a white solid. Rf (PE/AE: 70/30): 0.38. M_p: 138–140 °C. IR (ATR diamond, cm^{-1}) ν: 3256, 2947, 2867, 1569, 1359, 1130, 773, 688, 625. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.92 (t, J = 6.8 Hz, 3H, CH_3), 1.31–1.47 (m, 4H, CH_2), 1.66 (q, J = 7.1 Hz, 2H, $CH_2CH_2CH_2$-CH_2CH_3), 1.69–1.81 (m, 2H, CH_2), 1.90–2.02 (m, 2H, CH_2), 2.72 (td, J = 5.0, 11.4 Hz, 2H, N–CH_2), 3.04 (p, J = 3.1 Hz, 1H, CH), 3.09–3.21 (m, 2H, N–CH_2), 3.49 (q, J = 6.6 Hz, 2H, CH_2), 5.02 (t, J = 5.7 Hz, 1H, NH), 7.36–7.49 (m, 3H, 3xCH_{Ar}), 8.25 (d, J = 7.1 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 14.2 (CH_3), 22.6 (CH_2), 27.8 (2xCH_2), 29.3 (CH_2), 29.6 (CH_2), 33.7 (CH), 41.9 (CH_2), 49.4 (2xN-CH_2), 128.1 (2xCH_{Ar}), 129.5 (CH_{Ar}), 129.8 (2xCH_{Ar}), 131.3 (C_q), 136.7 (C_q), 155.5 (C_q), 160.0 (C_q), 175.6 (C_q). HRMS (EI/MS): m/z calculated for $C_{20}H_{27}N_4$: 323.2230 [M + H]$^+$; found: 323.2230.

*4-Phenyl-2-(piperidin-1-yl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidine (**13**).* Compound **13** was obtained according to the general procedure **B** using piperidine (0.17 mL, 1.71 mmol, 2.2 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), **13** (195 mg, 77%) was obtained as a white solid. Rf (PE/EA: 90/10): 0.41. M_p: 207–209 °C. IR (ATR diamond, cm^{-1}) ν: 2939, 2863, 1571, 1503, 1386, 1290, 776, 694, 624. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.60–1.69 (m, 6H, 3xCH_2), 1.70–1.82 (m, 2H, CH_2), 1.89–2.01 (m, 2H, CH_2), 2.71 (td, J = 4.8, 11.2 Hz, 2H, N–CH_2), 3.07 (p, J = 3.1 Hz, 1H, CH), 3.10–3.21 (m, 2H, N–CH_2), 3.87 (t, J = 4.9 Hz, 4H, 2xN-CH_2), 7.36–7.48 (m, 3H, 3xCH_{Ar}), 8.25–8.32 (m, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 25.1 (CH_2), 26.0 (2xCH_2), 27.7 (2xCH_2), 33.9 (CH), 45.19 (2xCH_2), 49.5 (2xN-CH_2), 128.05 (CH_{Ar}), 129.4 (CH_{Ar}), 129.91 (2xCH_{Ar}), 130.1 (C_q), 137.1 (C_q), 154.9 (C_q), 159.6 (C_q), 175.2 (C_q). HRMS (EI/MS): m/z calculated for $C_{20}H_{25}N_4$: 321.2074 [M + H]$^+$; found: 321.2070.

*4-(4-Phenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-yl)morpholine (**14**).* Compound **14** was obtained according to the general procedure **B** using morpholine (0.15 mL, 1.73 mmol, 2.2 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), **14** (210 mg, 82%) was obtained as a white solid. Rf (PE/EA: 90/10): 0.20. M_p: 212–214 °C. IR (ATR diamond, cm^{-1}) ν: 2949, 2858, 1552, 1483, 1385, 1263, 1115, 774, 688, 624. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.69–1.81 (m, 2H, CH_2), 1.91–2.03 (m, 2H, CH_2), 2.72 (td, J = 4.7, 11.1 Hz, 2H, N–CH_2), 3.09 (p, J = 3.1 Hz, 1H, CH), 3.17 (ddd, J = 4.8, 9.6, 13.8 Hz, 2H, N–CH_2), 3.81 (q, J = 3.9, 4.4 Hz, 4H, 2xCH_2-O), 3.88 (q, J = 3.4, 4.0 Hz, 4H, 2xN-CH_2), 7.37–7.49 (m, 3H, 3xCH_{Ar}), 8.26–8.35 (m, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.9 (2xCH_2), 33.8 (CH), 44.8 (2xN-CH_2), 49.4 (2xN-CH_2), 67.17 (2xCH_2-O), 128.1 (2xCH_{Ar}), 129.7 (CH_{Ar}), 129.92 (2xCH_{Ar}), 131.5 (C_q), 136.8 (C_q), 155.0 (C_q), 159.5 (C_q), 175.5 (C_q). HRMS (EI/MS): m/z calculated for $C_{19}H_{23}N_4O$: 323.1866 [M + H]$^+$; found: 323.1868.

*4-(4-Phenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-yl)thiomorpholine (**15**).* Compound **15** was obtained according to the general procedure **B** using thiomorpholine (0.17 mL,

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1.68 mmol, 2.2 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), **15** (193 mg, 72%) was obtained as a white solid. Rf (PE/EA: 90/10): 0.36. M_p: 211–213 °C. IR (ATR diamond, cm^{-1}) ν: 2951, 2926, 1555, 1481, 1387, 1258, 771, 696, 624. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.72–1.83 (m, 2H, CH_2), 1.93–2.05 (m, 2H, CH_2), 2.68–2.80 (m, 6H, 2xS-CH_2, N–CH_2), 3.09 (p, J = 3.0 Hz, 1H, CH), 3.13–3.24 (m, 2H, N–CH_2), 4.24–4.30 (m, 4H, CH_2–N), 7.39–7.51 (m, 3H, 3xCH_{Ar}), 8.27–8.36 (m, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.2 (2x S–CH_2), 27.9 (2xCH_2), 33.8 (CH), 46.6 (2xCH_2-N), 49.4 (2xN-CH_2), 128.0 (2xCH_{Ar}), 129.6 (CH_{Ar}), 129.8 (2xCH_{Ar}), 130.9 (C_q), 136.8 (C_q), 155.0 (C_q), 158.9 (C_q), 175.56 (C_q). HRMS (EI/MS): m/z calculated $C_{19}H_{23}N_4S$: 339.1638 [M + H]$^+$; found: 339.1637.

*2-(4,4-Difluoropiperidin-1-yl)-4-phenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidine (**16**).* Compound **16** was obtained according to the general procedure **B** using 4,4-difluoropiperidine hydrochloride (271 mg, 1.72 mmol, 2.2 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), **16** (172 mg, 61%) was obtained as a white solid. Rf (PE/EA: 90/10): 0.32. M_p: 212–214 °C. IR (ATR diamond, cm^{-1}) ν: 2954, 2871, 1568, 1489, 1356, 1108, 1048, 777, 690, 624, 511. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.61–1.85 (m, 2H, CH_2), 1.83–2.23 (m, 6H, 3xCH_2), 2.72 (td, J = 5.1, 11.5 Hz, 2H, N–CH_2), 3.09 (p, J = 3.1 Hz, 1H, CH), 3.12–3.23 (m, 2H, N–CH_2), 4.07 (t, J = 5.8 Hz, 4H, 2xN-CH_2), 7.27–7.57 (m, 3H, 3xCH_{Ar}), 8.29 (d, J = 7.8 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.8 (2xCH_2), 33.8 (CH), 34.0 (t, J = 22.6 Hz, 2xCH_2-CF_2), 41.3 (t, J = 5.2 Hz, 2xN-CH_2), 49.3 (2xN-CH_2), 122.8 (t, J = 241.7 Hz, CF_2), 128.1 (2xCH_{Ar}), 129.7 (CH_{Ar}), 129.9 (2xCH_{Ar}), 131.4 (C_q), 136.7 (C_q), 155.1 (C_q), 158.8 (C_q), 175.7 (C_q). ^{19}F NMR (376 MHz, $CDCl_3$) δ: −96.89. HRMS (EI/MS): m/z calculated $C_{20}H_{23}F_2N_4$: 357.1885 [M + H]$^+$; found: 357.1886.

N-Benzyl-4-phenyl-7,8-dihydro-6*H*-5,8-ethanopyrido[3,2-*d*]pyrimidin-2-amine (**17**)

Compound **17** was obtained according to the general procedure **B** using benzylamine (0.19 mL, 1.73 mmol, 2.2 eq.). After purification by silica gel flash chromatography (PE/EA, 60/40), **17** (141 mg, 51%) was obtained as a white solid. Rf (PE/EA: 70/30): 0.45. M_p: 182–184 °C. IR (ATR diamond, cm^{-1}) ν: 3252, 3084, 2940, 2869, 1570, 1543, 1347, 1133, 774, 689, 626. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.69–1.82 (m, 2H), 1.92–2.03 (m, 2H), 2.73 (td, J = 5.1, 11.4 Hz, 2H), 3.06 (p, J = 3.1 Hz, 1H, CH), 3.11–3.22 (m, 2H), 4.73 (d, J = 5.8 Hz, 2H, NH–CH_2), 5.35 (t, J = 5.7 Hz, 1H, NH), 7.27 (t, J = 7.3 Hz, 1H, CH_{Ar}), 7.34 (t, J = 7.4 Hz, 2H, 2xCH_{Ar}), 7.39–7.48 (m, 5H, 5xCH_{Ar}), 8.26 (d, J = 8.1 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.8 (2xCH_2), 33.7 (CH), 46.0 (NH–CH_2), 49.4 (2xN-CH_2), 127.2 (CH_{Ar}), 127.8 (2xCH_{Ar}), 128.1 (2xCH_{Ar}), 128.6 (2xCH_{Ar}), 129.6 (CH_{Ar}), 129.9 (2xCH_{Ar}), 131.9 (C_q), 136.6 (C_q), 139.9 (C_q), 159.7 (C_q), 175.9 (C_q). HRMS (EI/MS): m/z calculated $C_{22}H_{23}N_4$: 343.1917 [M + H]$^+$; found: 343.1919.

*N-(4-Methoxybenzyl)-4-phenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-amine (**18**).* Compound **18** was obtained according to the general procedure **B** using 4-methoxybenzylamine (0.23 mL, 1.75 mmol, 2.2 eq.). After purification by silica gel flash chromatography (PE/EA, 80/20 to 70/30), **18** (126 mg, 42%) was obtained as a white solid. **Rf** (PE/EA: 70/30): 0.26. M_p: 204–206 °C. IR (ATR diamond, cm^{-1}) ν: 3252, 2945, 1595, 1569, 1544, 1509, 1242, 1172, 1031, 808, 690. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.68–1.81 (m, 2H, CH_2), 1.91–2.03 (m, 2H, CH_2), 2.66–2.79 (m, 2H, N–CH_2), 3.06 (p, J = 2.9 Hz, 1H, CH), 3.11–3.22 (m, 2H, N–CH_2), 3.80 (s, 3H, OCH_3), 4.65 (d, J = 5.7 Hz, 2H, NH–CH_2), 5.32 (t, J = 5.8 Hz, 1H, NH–CH_2), 6.88 (dt, J = 3.0, 8.8 Hz, 2H, 2xCH_{Ar}), 7.35 (dt, J = 2.6, 8.8 Hz, 2H, 2xCH_{Ar}), 7.39–7.48 (m, 3H, 3xCH_{Ar}), 8.27 (dd, J = 1.7, 7.8 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.8 (2xCH_2), 33.7 (CH), 45.5 (NH–CH_2), 49.4 (2xN-CH_2), 55.4 (CH_3), 114.0 (2xCH_{Ar}), 128.1 (2xCH_{Ar}), 129.1 (2xCH_{Ar}), 129.6 (CH_{Ar}), 129.9 (2xCH_{Ar}), 131.8 (C_q), 131.9 (C_q), 136.6 (C_q), 158.9 (C_q), 159.7 (C_q), 175.8 (C_q). HRMS (EI/MS): m/z calculated for $C_{23}H_{25}N_4O$: 373.2023 [M + H]$^+$; found: 373.2020.

*4-Phenyl-N-(4-(trifluoromethyl)benzyl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-amine (**19**).* Compound **19** was obtained according to the general procedure **B** using 4-(trifluoromethyl)benzylamine (0.25 mL, 1.75 mmol, 2.2 eq.). After purification by silica gel flash chromatography (PE/EA, 80/20 to 70/30), **19** (129 mg, 39%) was obtained as a white solid. Rf (PE/EA: 70/30): 0.25. M_p: 180–182 °C. IR (ATR diamond, cm^{-1}) ν: 3255, 2948, 1566, 1326, 1112, 1061, 691. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.67–1.81 (m, 2H, CH_2), 1.92–2.04 (m, 2H, CH_2), 2.66–2.79 (m, 2H, N–CH_2), 3.05 (p, J = 3.0 Hz, 1H, CH), 3.11–3.22 (m, 2H, N–CH_2), 4.79 (d, J = 6.1 Hz, 2H, NH–CH_2), 5.52 (t, J = 6.1 Hz, 1H, NH), 7.37–7.47 (m, 3H, 3xCH_{Ar}), 7.53 (d, J = 8.1 Hz, 2H, 2xCH_{Ar}), 7.59 (d, J = 8.2 Hz, 2H, 2xCH_{Ar}), 8.19–8.26 (m, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.8 (2xCH_2), 33.7 (CH), 45.5 (NH–CH_2), 49.3 (2xN-CH_2), 124.3 (d, J = 271.9 Hz, C_q-CF_3), 125.5 (q, J = 3.7 Hz, 2xCH_{Ar}), 127.8 (2xCH_{Ar}), 128.1 (2xCH_{Ar}), 129.4 (d, J = 32.2 Hz, CF_3), 129.7 (CH_{Ar}), 129.8 (2xCH_{Ar}), 132.2 (C_q), 136.4 (C_q), 144.3 (C_q), 155.5 (C_q), 159.5 (C_q), 176.1 (C_q). ^{19}F NMR (376 MHz, $CDCl_3$) δ: −62.37. HRMS (EI/MS): m/z calculated for $C_{23}H_{22}F_3N_4$: 411.1791 [M + H]$^+$; found: 411.1792.

*2-(1H-Imidazol-1-yl)-4-phenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidine (**20**).* Compound **20** was obtained according to the general procedure **B** using imidazole (123 mg, 1.80 mmol, 2.2 eq.). After purification by silica gel flash chromatography (PE/EA, 70/30), **20** (55 mg, 22%) was obtained as a white solid. Rf (PE/EA: 70/30): 0.10. M_p: 198–200 °C. IR (ATR diamond, cm^{-1}) ν: 2963, 2926, 2868, 1561, 1468, 1435, 1387, 1050, 691. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.73–1.85 (m, 2H, CH_2), 2.02–2.15 (m, 2H, CH_2), 2.75 (td, J = 5.1, 11.6 Hz, 2H, N–CH_2), 3.21–3.32 (m, 2H, N–CH_2), 3.34 (p, J = 3.1 Hz, 1H, CH), 7.18 (s, 1H, $CH_{imidazole}$), 7.51 (dd, J = 2.5, 4.5 Hz, 3H, 3xCH_{Ar}), 8.00 (s, 1H, $CH_{imidazole}$), 8.41–8.49 (m, 2H, 2xCH_{Ar}), 8.70 (s, 1H, $CH_{imidazole}$). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.7 (2xCH_2), 33.6 (CH), 48.8 (2xN-CH_2), 116.9 ($CH_{imidazole}$), 128.4 (2xCH_{Ar}), 130.2 (2xCH_{Ar}), 130.4 ($CH_{imidazole}$), 130.8 (CH_{Ar}), 135.0 (C_q), 136.4 ($CH_{imidazole}$), 138.9 (C_q), 151.3 (C_q), 156.2 (C_q), 177.7 (C_q). HRMS (EI/MS): m/z calculated for $C_{18}H_{18}N_5$: 304.1557 [M + H]$^+$; found: 304.1557.

*2-(Piperidin-1-yl)-4-(p-tolyl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidine (**23**).* Compound **23** was obtained according to the general procedure **B** using **9** (214 mg, 0.80 mmol, 1.0 eq.) and piperidine (0.17 mL, 1.71 mmol, 2.2 eq.). After purification by silica gel flash chromatography (PE/EA, 100/0 to 90/10), **23** (230 mg, 86%) was obtained as a light yellow solid. Rf (PE/EA: 90/10): 0.51. M_p: 186–188 °C. IR (ATR diamond, cm^{-1}) ν: 2929,

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2848, 1589, 1564, 1549, 1496, 1385, 1291, 810. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.60–1.69 (m, 6H, 3xCH_2), 1.69–1.79 (m, 2H, CH_2), 1.90–1.99 (m, 2H, CH_2), 2.39 (s, 3H, CH_3), 2.65–2.77 (m, 2H, N–CH_2), 3.06 (p, J = 3.0 Hz, 1H, CH), 3.09–3.20 (m, 2H, N–CH_2), 3.83–3.90 (m, 4H, 2xN-CH_2), 7.24 (d, J = 8.0 Hz, 2H, 2xCH_{Ar}), 8.20 (d, J = 8.2 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 21.6 (CH_3), 25.1 (CH_2), 26.0 (2xCH_2), 28.0 (2xCH_2), 33.9 (CH), 45.1 (2xN-CH_2), 49.5 (2xN-CH_2), 128.8 (2xCH_{Ar}), 129.8 (2xCH_{Ar}), 130.2 (C_q), 134.4 (C_q), 139.5 (C_q), 154.9 (C_q), 159.6 (C_q), 175.0 (C_q). HRMS (EI/MS): m/z calculated for $C_{21}H_{27}N_4$: 335.2230 [M + H]$^+$; found: 355.2229.

*4-(4-Fluorophenyl)-2-(piperidin-1-yl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidine (**24**).* Compound **24** was obtained according to the general procedure **B** using **10** (214 mg, 0.79 mmol, 1.0 eq.) and piperidine (0.17 mL, 1.71 mmol, 2.2 eq.). After purification by silica gel flash chromatography (PE/EA, 100/0 to 90/10), **24** (212 mg, 79%) was obtained as a beige solid. Rf (PE/EA: 90/10): 0.43. M_p: 196–198 °C. IR (ATR diamond, cm^{-1}) ν: 2936, 2863, 1578, 1503, 1384, 1225, 817, 796. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.61–1.69 (m, 6H, 3xCH_2), 1.70–1.81 (m, 2H, CH_2), 1.89–2.01 (m, 2H, CH_2), 2.63–2.76 (m, 2H, N–CH_2), 3.06 (p, J = 2.9 Hz, 1H, CH), 3.10–3.20 (m, 2H, N–CH_2), 3.83–3.90 (m, 4H, 2xN-CH_2), 7.10 (t, J = 8.8 Hz, 2H, 2xCH_{Ar}), 8.39 (dd, J = 8.9, 5.8 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 25.0 (CH_2), 26.0 (2xCH_2), 27.9 (2xCH_2), 33.8 (CH), 45.1 (2xN-CH_2), 49.4 (2xN-CH_2), 114.8 (CH_{Ar}), 115.0 (CH_{Ar}), 130.1 (C_q), 131.9 (CH_{Ar}), 132.0 (CH_{Ar}), 133.3 (C_q), 153.5 (C_q), 159.5 (C_q), 163.7 (d, J = 249.1 Hz, C_q-F), 175.3 (C_q). ^{19}F NMR (376 MHz, $CDCl_3$) δ: −111.9. HRMS (EI/MS): m/z calculated for $C_{20}H_{24}FN_4$: 339.1980 [M + H]$^+$; found: 339.1976.

General procedure C: Buchwald–Hartwig cross coupling *via* PyBroP activation. In a microwave vial, to an argon-degassed solution of **8** (253 mg, 1.00 mmol, 1.0 eq.) and PyBroP (559 mg, 1.20 mmol, 1.2 eq.) in 1,4-dioxane (10 mL), was added Et_3N (0.40 mL, 2.96 mmol, 3.0 eq.). The reaction was heated for 3 h at 100 °C. After cooling, K_2CO_3 (276 mg, 2.00 mmol, 2.0 eq.), the required amine (1.5.0 eq.), $Pd(OAc)_2$ (22 mg, 0.10 mmol, 0.1 eq.) and Xantphos (116 mg, 0.20 mmol, 0.2 eq.) were added to the reaction mixture. The sealed tube was heated at 130 °C for 1 h under microwave irradiation. After cooling to room temperature, the solvent was evaporated under reduced pressure and the crude material was diluted in DCM (20 mL). The organic layer was washed with water (2 × 20 mL), dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude mixture was purified by flash chromatography on silica gel to obtain the desired compound.

*1-(4-Phenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-yl)piperidin-2-one (**22**).* Compound **22** was obtained according to the general procedure **C** using 2-piperidone (0.14 mL, 1.51 mmol, 1.5 eq.). After purification by silica gel flash chromatography (DCM/MeOH, 95–5), **22** (133 mg, 40%) was obtained as a light yellow solid. Rf (DCM/MeOH: 95/5): 0.43. M_p: 216–218 °C. IR (ATR diamond, cm^{-1}) ν: 2943, 1670, 1562, 1377, 1153, 838, 776, 696, 624. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.79 (m, 2H, CH_2), 1.91–2.10 (m, 6H, CH_2, 2x$CH_{2,lactame}$), 2.63 (t, J = 6.4 Hz, 2H, C(O)–CH_2), 2.73 (m, 2H, N–CH_2), 3.17–3.28 (m, 2H, N–CH_2), 3.34 (p, J = 2.9 Hz, 1H, CH), 3.97 (t, J = 5.6 Hz, 2H, N–CH_2), 7.39–7.51 (m, 3H, 3xCH_{Ar}), 8.25–8.39 (m, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 21.4 (CH_2), 23.3 (CH_2), 27.7 (2xCH_2), 33.5 (CH), 33.6 (C(O)–CH), 48.8 (2xN-CH_2), 49.2 (N–CH_2), 128.2 (2xCH_{Ar}), 130.2 (2xCH_{Ar}), 130.2 (CH_{Ar}), 135.5 (C_q), 138.3 (C_q), 156.3 (C_q), 157.7 (C_q), 170.9 (C=O), 176.5 (C_q). HRMS (EI/MS): m/z calculated for $C_{20}H_{23}N_4O$: 335.1866 [M + H]$^+$; found: 335.1865.

*1-(4-Phenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-yl)pyrrolidin-2-one (**25**).* Compound **23** was obtained according to general procedure **C** using 2-pyrrolidone (134 mg, 1.57 mmol, 1.5 eq.). After purification by silica gel flash chromatography (EA/PE, 80/20 to 90/10), **25** (125 mg, 39%) was obtained as a light yellow solid. Rf (EA/PE: 90/10): 0.18. M_p: 211–213 °C. IR (ATR diamond, cm^{-1}) ν: 2942, 1727, 1557, 1384, 1350, 1131, 775, 693, 622. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.72–1.85 (m, 2H, CH_2), 1.96–2.08 (m, 2H, CH_2), 2.14 (p, J = 7.7 Hz, 2H, CH_2), 2.65–2.77 (m, 4H, N–CH_2, C(O)–CH_2), 3.16–3.27 (m, 2H, N–CH_2), 3.36 (p, J = 2.9 Hz, 1H, CH), 4.18 (t, J = 7.1 Hz, 2H, N–CH_2), 7.40–7.51 (m, 3H, 3xCH_{Ar}), 8.37–8.46 (m, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 17.9 (CH_2), 27.7 (2xCH_2), 33.6 (CH), 33.8 (C(O)–CH_2), 48.6 (N–CH_2), 48.9 (2xN-CH_2), 128.3 (2xCH_{Ar}), 130.2 (2xCH_{Ar}), 130.3 (CH_{Ar}), 135.8 (C_q), 136.9 (C_q), 154.5 (C_q), 155.2 (C_q), 174.7 (C=O), 176.5 (C_q). HRMS (EI/MS): m/z calculated for $C_{19}H_{21}N_4$: 321.1711 [M + H]$^+$; found: 321.1710.

*N,4-Diphenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-amine (**26**).* Compound **26** was obtained according to general procedure **C** using aniline (0.14 mL, 143 mg, 1.53 mmol, 1.5 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10 to 80/20), **26** (186 mg, 56%) was obtained as a white solid. Rf (PE/EA: 80/20): 0.27. M_p: 191–193 °C. IR (ATR diamond, cm^{-1}) ν: 2956, 1563, 1529, 1446, 1424, 1364, 768, 743, 685. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.72–1.85 (m, 2H, CH_2), 1.96–2.08 (m, 2H, CH_2), 2.69–2.82 (m, 2H, N–CH_2), 3.12–3.26 (m, 3H, N–CH_2, CH), 7.02 (t, J = 7.4 Hz, 1H, CH), 7.20 (s, 1H, NH), 7.35 (t, J = 7.8 Hz, 2H, 2xCH), 7.40–7.53 (m, 3H, 3xCH_{Ar}), 7.74 (d, J = 7.7 Hz, 2H, 2xCH_{Ar}), 8.33 (dd, J = 1.8, 8.0 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.8 (2xCH_2), 33.7 (CH), 49.3 (2xN-CH_2), 118.8 (2xCH_{Ar}), 122.0 (CH_{Ar}), 128.2 (2xCH_{Ar}), 129.0 (2xCH_{Ar}), 129.9 (CH_{Ar}), 130.0 (2xCH_{Ar}), 133.3 (C_q), 136.3 (C_q), 140.3 (C_q), 155.6 (C_q), 157.2 (C_q), 176.0 (C_q). HRMS (EI/MS): m/z calculated for $C_{21}H_{21}N_4$: 329.1761 [M + H]$^+$; found: 329.1758.

*N-(4-Methoxyphenyl)-4-phenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-amine (**27**).* Compound **27** was obtained according to general procedure **C** using *p*-anisidine (187 mg, 1.51 mmol, 1.5 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10 to 80/20), **27** (173 mg, 48%) was obtained as a dark red solid. Rf (PE/EA: 80/20): 0.19. M_p: 223–225 °C. IR (ATR diamond, cm^{-1}) ν: 3242, 2920, 1566, 1508, 1357, 12 369, 1038, 822, 696, 625. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.71–1.83 (m, 2H, CH_2), 1.94–2.07 (m, 2H, CH_2), 2.68–2.81 (m, 2H, N–CH_2), 3.13 (p, J = 2.9 Hz, 1H, CH), 3.15–3.25 (m, 2H, N–CH_2), 3.81 (s, 3H, CH_3), 6.91 (d, J = 9.2 Hz, 2H, 2xCH_{Ar}), 7.04 (s, 1H, NH), 7.39–7.51 (m, 3H, 3xCH_{Ar}), 7.61 (d, J = 9.0 Hz, 2H, 2xCH_{Ar}), 8.31 (dd, J = 1.6, 7.9 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.8 (2xCH_2), 33.7 (CH), 49.3 (2xN-CH_2), 55.7 (CH_3), 114.3 (2xCH_{Ar}), 120.9 (2xCH_{Ar}), 128.2 (2xCH_{Ar}), 129.8 (CH_{Ar}), 129.9 (2xCH_{Ar}), 132.9 (C_q), 133.6 (C_q), 136.6 (C_q), 155.1 (C_q),

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155.6 (C_q), 157.5 (C_q), 176.0 (C_q). HRMS (EI/MS): *m/z* calculated for $C_{22}H_{23}N_4O$: 359.1866 $[M + H]^+$; found: 359.1863.

*4-Phenyl-N-(p-tolyl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-amine (**21**).* Compound **21** was obtained according to general procedure **C** using *p*-toluidine (165 mg, 1.54 mmol, 1.5 eq.). After purification by silica gel flash chromatography (PE/EA, 100/0 to 80/20), **21** (165 mg, 48%) was obtained as a light orange solid. Rf (PE/EA: 80/20): 0.20. M_p: 222–224 °C. IR (ATR diamond, cm^{-1}) ν: 3294, 2943, 2867, 1589, 1519, 1425, 1355, 780, 698, 624. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.72–1.83 (m, 2H, CH_2), 1.95–2.07 (m, 2H, CH_2), 2.34 (s, 3H, CH_3), 2.69–2.81 (m, 2H, N–CH_2), 3.11–3.25 (m, 3H, N–CH_2, CH), 7.13 (s, 1H, NH), 7.15 (d, J = 8.2 Hz, 2H, 2xCH_{Ar}), 7.40–7.52 (m, 3H, 3xCH_{Ar}), 7.61 (d, J = 8.4 Hz, 2H, 2xCH_{Ar}), 8.32 (dd, J = 1.7, 8.0 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 20.9 (CH_3), 27.8 (2xCH_2), 33.7 (CH), 49.3 (2xN-CH_2), 119.0 (2xCH_{Ar}), 128.2 (2xCH_{Ar}), 129.4 (2xCH_{Ar}), 129.8 (CH_{Ar}), 129.9 (2xCH_{Ar}), 131.5 (C_q), 133.1 (C_q), 136.4 (C_q), 137.7 (C_q), 155.6 (C_q), 157.3 (C_q), 175.9 (C_q). HRMS (EI/MS): *m/z* calculated for $C_{22}H_{23}N_4$: 343.1917 $[M + H]^+$; found: 343.1917.

*4-Phenyl-N-(m-tolyl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-amine (**28**).* Compound **28** was obtained according to the general procedure **C** using *m*-toluidine (0.16 mL, 1.47 mmol, 1.5 eq.). After purification by silica gel flash chromatography (DCM/PE, 80/20), **28** (106 mg, 31%) was obtained as a light yellow solid. Rf (DCM/PE: 80/20): 0.14. M_p: 230–232 °C. IR (ATR diamond, cm^{-1}) ν: 3226, 2940, 1562, 1531, 1488, 1422, 1357, 1165, 770, 690, 625. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.73–1.85 (m, 2H, CH_2), 1.96–2.08 (m, 2H, CH_2), 2.38 (s, 3H, CH_3), 2.69–2.82 (m, 2H, N–CH_2), 3.13–3.26 (m, 3H, N–CH_2, CH), 6.84 (d, J = 7.4 Hz, 1H, CH_{Ar}), 7.12 (s, 1H, NH), 7.23 (t, J = 7.8 Hz, 1H, CH_{Ar}), 7.40–7.51 (m, 3H, 3xCH_{Ar}), 7.54 (s, 1H, CH_{Ar}), 7.58 (dd, J = 8.1, 2.2 Hz, 1H, CH_{Ar}), 8.31–8.38 (m, 2H, CH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 21.8 (CH_3), 27.8 (2xCH_2), 33.7 (CH), 49.3 (2xN-CH_2), 115.9 (CH_{Ar}), 119.5 (CH_{Ar}), 122.9 (CH_{Ar}), 128.2 (2xCH_{Ar}), 128.8 (CH_{Ar}), 129.9 (CH_{Ar}), 130.0 (2xCH_{Ar}), 133.2 (C_q), 136.4 (C_q), 138.7 (C_q), 140.2 (C_q), 155.5 (C_q), 157.2 (C_q), 176.0 (C_q). HRMS (EI/MS): *m/z* calculated for $C_{22}H_{23}N_4$: 343.1917 $[M + H]^+$; found: 343.1914.

*4-Phenyl-N-(o-tolyl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-amine (**29**).* Compound **29** was obtained according to the general procedure **C** using *o*-toluidine (0.10 mL, 1.46 mmol, 1.5 eq.). After purification by silica gel flash chromatography (DCM/PE, 70/30 to 80/20), **29** (54 mg, 15%) was obtained as a beige solid. Rf (DCM/PE: 70/30): 0.16. M_p: 208–210 °C. IR (ATR diamond, cm^{-1}) ν: 3212, 2946, 1564, 1529, 1361, 744, 684, 625. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.72–1.85 (m, 2H, CH_2), 1.96–2.07 (m, 2H, CH_2), 2.37 (s, 3H, CH_3), 2.70–2.82 (m, 2H, N–CH_2), 3.11–3.26 (m, 3H, N–CH_2, CH), 6.88 (s, 1H, NH), 6.99 (td, J = 7.4, 1.3 Hz, 1H, CH_{Ar}), 7.21 (d, J = 7.3 Hz, 1H, CH_{Ar}), 7.27 (td, J = 7.8, 1.6 Hz, 1H, CH_{Ar}), 7.39–7.51 (m, 3H, 3xCH_{Ar}), 8.29–8.36 (m, 3H, 2xCH_{Ar}, CH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 18.3 (CH_3), 27.8 (2xCH_2), 33.7 (CH), 49.3 (2xN-CH_2N-CH_2), 120.4 (CH_{Ar}), 122.6 (CH_{Ar}), 126.7 (CH_{Ar}), 127.2 (C_q), 128.2 (2xCH_{Ar}), 129.8 (CH_{Ar}), 130.0 (2xCH_{Ar}), 130.4 (CH_{Ar}), 133.2 (C_q), 136.3 (C_q), 138.3 (C_q), 155.6 (C_q), 157.5 (C_q), 176.0 (C_q). HRMS (EI/MS): *m/z* calculated for $C_{22}H_{23}N_4$: 343.1917 $[M + H]^+$; found: 343.1916.

*4-Phenyl-N-(4-(trifluoromethyl)phenyl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-amine (**30**).* Compound **30** was obtained according to general procedure **C** using 4-(trifluoromethyl)aniline (0.19 mL, 243 mg, 1.50 mmol, 1.5 eq.). After purification by silica gel flash chromatography (DCM/PE, 80/20), **30** (212 mg, 56%) was obtained as a beige solid. Rf (DCM/PE: 80/20): 0.20. M_p: 182–184 °C. IR (ATR diamond, cm^{-1}) ν: 3280, 2957, 1534, 1415, 1321, 1109, 1066, 836, 625. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.73–1.84 (m, 2H, CH_2), 1.98–2.09 (m, 2H, CH_2), 2.69–2.82 (m, 2H, N–CH_2), 3.14–3.28 (m, 3H, N–CH_2, CH), 7.36 (s, 1H, NH), 7.44–7.55 (m, 3H, 3xCH_{Ar}), 7.59 (d, J = 8.6 Hz, 2H, 2xCH_{Ar}), 7.85 (d, J = 8.5 Hz, 2H, 2xCH_{Ar}), 8.29–8.36 (m, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.8 (2xCH_2), 33.7 (CH), 49.2 (2xN-CH_2), 117.9 (2xCH_{Ar}), 123.3 (C_q), 124.8 (d, J = 241.0 Hz, C_q-CF_3), 126.3 (q, J = 3.9 Hz, 2xCH_{Ar}), 128.3 (2xCH_{Ar}), 130.0 (2xCH_{Ar}), 130.1 (CH_{Ar}), 134.1 (C_q), 136.0 (C_q), 143.4 (d, J = 0.9 Hz, CF_3), 155.8 (C_q), 156.6 (C_q), 176.3 (C_q). ^{19}F NMR (376 MHz, $CDCl_3$) δ: −61.65. HRMS (EI/MS): *m/z* calculated for $C_{22}H_{20}F_3N_4$: 397.1635 $[M + H]^+$; found: 397.1633.

*4-((4-Phenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-yl)amino)benzonitrile (**31**).* Compound **31** was obtained according to the general procedure **C** using 4-aminobenzonitrile (177 mg, 1.50 mmol, 1.5 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10 to 70/30), **31** (124 mg, 35%) was obtained as a light yellow solid. Rf (DCM/PE: 80/20): 0.16. M_p: 234–236 °C. IR (ATR diamond, cm^{-1}) ν: 3399, 2923, 2214, 1566, 1517, 1413, 1357, 1171, 834, 687, 535. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.71–1.84 (m, 2H, CH_2), 1.98–2.11 (m, 2H, CH_2), 2.68–2.81 (m, 2H, N–CH_2), 3.15–3.28 (m, 3H, N–CH_2, CH), 7.43–7.55 (m, 4H, 3xCH_{Ar}, NH), 7.60 (d, J = 8.8 Hz, 2H, 2xCH_{Ar}), 7.85 (d, J = 8.8 Hz, 2H, 2xCH_{Ar}), 8.25–8.35 (m, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.8 (2xCH_2), 33.7 (CH), 49.1 (2xN-$CH_2$2xN-CH_2), 104.0 (C_q), 118.0 (2xCH_{Ar}), 119.7 (C_q), 128.3 (2xCH_{Ar}), 129.9 (2xCH_{Ar}), 130.2 (CH_{Ar}), 133.3 (2xCH_{Ar}), 134.5 (C_q), 135.8 (C_q), 144.3 (C_q), 155.9 (C_q), 156.2 (C_q), 176.5 (C_q). HRMS (EI/MS): *m/z* calculated for $C_{22}H_{20}N_5$: 354.1713 $[M + H]^+$; found: 354.1710.

*N-(4-Nitrophenyl)-4-phenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-amine (**32**).* Compound **32** was obtained according to general procedure **C** using 4-nitroaniline (208 mg, 1.50 mmol, 1.5 eq.). The obtained solid was washed with DCM and dried under *vacuo* to afford **32** (148 mg, 39%) as a yellow solid. Rf (PE/EA: 80/20): 0.17. M_p: >260 °C. IR (ATR diamond, cm^{-1}) ν: 3386, 2940, 1530, 1488, 1416, 1324, 1111, 840, 686, 584. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.74–1.85 (m, 2H, CH_2), 2.01–2.12 (m, 2H, CH_2), 2.70–2.81 (m, 2H, N–CH_2), 3.13–3.29 (m, 3H, N–CH_2, CH), 7.45–7.54 (m, 3H, 3xCH_{Ar}), 7.56 (s, 1H, NH), 7.89 (d, J = 9.2 Hz, 2H, 2xCH_{Ar}), 8.24 (d, J = 9.2 Hz, 2H, 2xCH_{Ar}), 8.32 (dd, J = 2.3, 7.3 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.8 (2xCH_2), 33.7 (CH), 49.1 (2xN-CH_2), 117.3 (2xCH_{Ar}), 125.5 (2xCH_{Ar}), 128.4 (2xCH_{Ar}), 130.0 (2xCH_{Ar}), 130.3 (CH_{Ar}), 134.9 (C_q), 135.7 (C_q), 141.6 (C_q), 146.3 (C_q), 156.0 (C_q), 156.0 (C_q), 176.6 (C_q). HRMS (EI/MS): *m/z* calculated for $C_{21}H_{20}N_5O_2$: 374.1612 $[M + H]^+$; found: 374.1607.

*4-Phenyl-N-(pyridin-3-yl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-amine (**33**).* Compound **33** was obtained according

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to the general procedure **C** using 3-aminopyridine (142 mg, 1.5 mmol, 1.5 eq.). After purification by silica gel flash chromatography (EA/PE, 70/30), **33** (115 mg, 34%) was obtained as a light yellow solid. Rf (EA/PE: 70/30): 0.30. M_p: 211–213 °C. IR (ATR diamond, cm^{-1}) ν: 2954, 1531, 1428, 1386, 1353, 692, 623. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.71–1.83 (m, 2H, CH_2), 1.97–2.10 (m, 2H, CH_2), 2.68–2.81 (m, 2H, N–CH_2), 3.12–3.26 (m, 3H; N–CH_2, CH), 7.27 (dd, J = 8.3, 4.8 Hz, 1H, CH_{Ar}), 7.36 (s, 1H, NH), 7.40–7.54 (m, 3H, 3xCH_{Ar}), 8.20–8.37 (m, 4H, 2xCH_{Ar}, 2xCH_{Ar}), 8.83 (d, J = 2.2 Hz, 1H, CH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.8 (2xCH_2), 33.7 (CH), 49.2 (2xN-CH_2), 123.5 (CH_{Ar}), 125.4 (CH_{Ar}), 128.3 (2xCH_{Ar}), 130.0 (2xCH_{Ar}), 130.1 (CH_{Ar}), 133.9 (C_q), 136.0 (C_q), 137.0 (C_q), 140.7 (CH_{Ar}), 143.0 (CH_{Ar}), 155.8 (C_q), 156.8 (C_q), 176.3 (C_q). HRMS (EI/MS): m/z calculated for $C_{20}H_{20}N_5$: 330.1713 $[M + H]^+$; found: 330.1714.

*N-(6-Methoxypyridin-3-yl)-4-phenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-amine (**34**).* Compound **34** was obtained according to the general procedure **C** using 5-amino-2-methoxypyridine (0.12 mL, 189 mg, 1.52 mmol, 1.5 eq.). After purification by silica gel flash chromatography (PE/EA, 50/50), **34** (102 mg, 28%) was obtained as a light orange solid. Rf (PE/EA: 50/50): 0.52. M_p: 183–185 °C. IR (ATR diamond, cm^{-1}) ν: 1942, 1537, 1490, 1348, 1278, 1035, 831, 691, 624. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.73–1.81 (m, 2H, CH_2), 1.95–2.07 (m, 2H, CH_2), 2.68–2.80 (m, 2H, N–CH_2), 3.13 (p, J = 2.9 Hz, 1H, CH), 3.15–3.25 (m, 2H, N–CH_2), 3.94 (s, 3H, O–CH_3), 6.77 (d, J = 8.9 Hz, 1H, CH_{Ar}), 6.95 (s, 1H, NH), 7.39–7.51 (m, 3H, 3xCH_{Ar}), 8.04 (dd, J = 8.9, 2.8 Hz, 1H, CH_{Ar}), 8.22–8.31 (m, 2H, 2xCH_{Ar}), 8.42 (d, J = 2.7 Hz, 1H, CH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.8 (2xCH_2), 33.7 (CH), 49.3 (2xN-CH_2), 53.6 (O–CH_3), 110.5 (CH_{Ar}), 128.2 (2xCH_{Ar}), 129.9 (2xCH_{Ar}), 129.9 (CH_{Ar}), 131.0 (C_q), 131.7 (CH_{Ar}), 133.4 (C_q), 136.1 (C_q), 137.8 (CH_{Ar}), 155.8 (C_q), 157.3 (C_q), 160.0 (C_q), 176.2 (C_q). HRMS (EI/MS): m/z calculated for $C_{21}H_{22}N_5O$: 360.1819 $[M + H]^+$; found: 360.1819.

N-Phenyl-4-(*p*-tolyl)-7,8-dihydro-6*H*-5,8-ethanopyrido[3,2-*d*]pyrimidin-2-amine (**35**)

Compound **35** was obtained according to general procedure **C** using **9** (274 mg, 1.02 mmol, 1.0 eq.) and aniline (0.14 mL, 1.53 mmol, 1.5 eq.). After purification by silica gel flash chromatography (PE/EA: 90/10 to 80/20), **35** (156 mg, 44%) was obtained as a beige solid. Rf (PE/EA: 80/20): 0.50. M_p: 195–197 °C. IR (ATR diamond, cm^{-1}) ν: 3229, 2960, 1574, 1531, 1429, 1362, 1171, 812, 742, 688. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.71–1.84 (m, 2H, CH_2), 1.95–2.07 (m, 2H, CH_2), 2.42 (s, 3H, CH_3), 2.68–2.81 (m, 2H, N–CH_2), 3.12–3.25 (m, 3H, N–CH_2, CH), 7.01 (tt, J = 7.3, 1.2 Hz, 1H, CH_{Ar}), 7.15 (s, 1H, NH), 7.29 (d, J = 7.9 Hz, 2H, 2xCH_{Ar}), 7.30–7.38 (m, 2H, 2xCH_{Ar}), 7.70–7.77 (m, 2H, 2xCH_{Ar}), 8.24 (d, J = 8.3 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 21.6 (CH_3), 27.8 (2xCH_2), 33.7 (CH), 49.3 (2xN-CH_2), 118.7 (2xCH_{Ar}), 121.9 (CH_{Ar}), 129.0 (2xCH_{Ar}), 129.0 (2xCH_{Ar}), 129.9 (2xCH_{Ar}), 133.1 (C_q), 133.5 (C_q), 140.0 (C_q), 140.4 (C_q), 155.7 (C_q), 157.1 (C_q), 175.8 (C_q). HRMS (EI/MS): m/z calculated for $C_{22}H_{23}N_4$: 343.1917 $[M + H]^+$; found: 343.1916.

*4-(p-Tolyl)-N-(4-(trifluoromethyl)phenyl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-amine (**36**).* Compound **36** was obtained according to general procedure **C** using **9** (264 mg, 0.98 mmol, 1.0 eq.) and 4-(trifluoromethyl)aniline (0.19 mL, 1.50 mmol, 1.5 eq.). After purification by silica gel flash chromatography (PE/EA: 90/10 to 80/20), **36** (200 mg, 49%) was obtained as a beige solid. Rf (PE/EA: 80/20): 0.20. M_p: 195–197 °C. IR (ATR diamond, cm^{-1}) ν: 3270, 2962, 1576, 1536, 1318, 1100, 1064, 838. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.71–1.84 (m, 2H, CH_2), 1.97–2.09 (m, 2H, CH_2), 2.43 (s, 3H, CH_3), 2.68–2.81 (m, 2H, N–CH_2), 3.13–3.27 (m, 3H, N–CH_2, CH), 7.30 (d, J = 8.0 Hz, 2H, 2xCH_{Ar}), 7.37 (s, 1H, NH), 7.58 (d, J = 8.4 Hz, 2H, 2xCH_{Ar}), 7.85 (d, J = 8.5 Hz, 2H, 2xCH_{Ar}), 8.24 (d, J = 8.3 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 21.5 (CH_3), 27.7 (2xCH_2), 33.6 (CH), 49.0 (2xN-CH_2), 117.7 (2xCH_{Ar}), 124.6 (d, J = 252.1 Hz, C_q-CF_3), 126.1 (q, J = 3.8 Hz, 2xCH_{Ar}), 128.9 (2xCH_{Ar}), 129.8 (2xCH_{Ar}), 133.1 (C_q), 133.8 (C_q), 140.2 (C_q), 143.3 (d, J = 0.6 Hz, CF_3), 155.7 (C_q), 156.4 (C_q), 176.0 (C_q). ^{19}F NMR (376 MHz, $CDCl_3$) δ: −61.63. HRMS (EI/MS): m/z calculated for $C_{23}H_{22}F_3N_4$: 411.1791 $[M + H]^+$; found: 411.1791.

General procedure D: Suzuki–Miyaura cross-coupling. In a microwave vial, to an argon-degassed solution of **8** (200 mg, 0.79 mmol, 1.0 eq.) and PyBroP (446 mg, 0.96 mmol, 1.2 eq.) in 1,4-dioxane (8 mL), was added Et_3N (0.32 mL, 239 mg, 2.36 mmol, 3.0 eq.) and the reaction was heated for 3 h at 100 °C. After cooling, a solution of K_3PO_4 (849 mg, 4.00 mmol, 5.0 eq.) in H_2O (2 mL), the required arylboronic acid (2.0 eq.), $Pd(OAc)_2$ (18 mg, 0.08 mmol, 0.1.0 eq.) and RuPhos (74 mg, 0.16 mmol, 0.2 eq.) were added to the reaction mixture. The sealed tube was heated at 150 °C for 1 h under microwave irradiation. After cooling to room temperature, the solvent was evaporated under reduced pressure and the crude material was diluted in DCM (20 mL). The organic layer was washed with water (2 × 20 mL), dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude mixture was purified by flash chromatography on silica gel to obtain the desired compound.

*4-Phenyl-2-(p-tolyl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidine (**39**).* Compound **39** was obtained according to the general procedure **D** using *p*-tolylboronic acid (239 mg, 1.60 mmol, 2.0 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), **39** (182 mg, 70%) was obtained as a white solid. Rf (PE/EA: 90/10): 0.40. M_p: 192–194 °C. IR (ATR diamond, cm^{-1}) ν: 2963, 2924, 2871, 1550, 1387, 1170, 772, 689, 623. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.76–1.87 (m, 2H, CH_2), 2.01–2.13 (m, 2H, CH_2), 2.43 (s, 3H, CH_3), 2.77 (td, J = 4.9, 11.5 Hz, 2H, N–CH_2), 3.20–3.32 (m, 2H, N–CH_2), 3.38 (p, J = 2.8, 3.2 Hz, 1H, CH), 7.30 (d, J = 7.8 Hz, 2H, 2xCH_{Ar}), 7.43–7.56 (m, 3H, 3xCH_{Ar}), 8.47 (dd, J = 8.1, 12.2 Hz, 4H, 4xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 21.6 (CH_3), 27.9 (2xCH_2), 33.7 (CH), 48.9 (2xN-CH_2), 128.2 (2xCH_{Ar}), 128.3 (2xCH_{Ar}), 129.3 (2xCH_{Ar}), 130.0 (CH_{Ar}), 130.2 (2xCH_{Ar}), 135.7 (C_q), 136.4 (C_q), 139.0 (C_q), 140.3 (C_q), 154.7 (C_q), 161.2 (C_q), 175.1 (C_q). HRMS (EI/MS): m/z calculated for $C_{22}H_{22}N_3$: 328.1808 $[M + H]^+$; found: 328.1808.

*2,4-Diphenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidine (**40**).* Compound **40** was obtained according to general procedure **D** using phenylboronic acid (195 mg, 1.60 mmol, 2.0 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), **40** (171 mg, 68%) was obtained as a white solid. Rf (PE/EA: 90/10): 0.30. M_p: 195–197 °C. IR (ATR diamond, cm^{-1}) ν: 2945, 2921, 1553, 1389, 768, 692, 624. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.75–1.89 (m, 2H, CH_2), 2.02–2.14 (m, 2H, CH_2), 2.72–2.84 (m,

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2H, N–CH_2), 3.21–3.32 (m, 2H, N–CH_2), 3.40 (p, J = 2.9 Hz, 1H, CH), 7.42–7.56 (m, 6H, 6xCH_{Ar}), 8.50 (dd, J = 1.7, 8.1 Hz, 2H, 2xCH_{Ar}), 8.57 (dd, J = 1.8, 8.0 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.8 (2xCH_2), 33.7 (CH), 48.9 (2xN-CH_2), 128.2 (2xCH_{Ar}), 128.3 (2xCH_{Ar}), 128.5 (2xCH_{Ar}), 130.0 (CH_{Ar}), 130.2 (2xCH_{Ar}), 136. (C_q), 138.4 (C_q), 139.3 (C_q), 154.8 (C_q), 161.1 (C_q), 175.2 (C_q). HRMS (EI/MS): m/z calculated for $C_{21}H_{20}N_3$: 314.1652 [M + H]$^+$; found: 314.1655.

*4-Phenyl-2-(m-tolyl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d] pyrimidine (**41**).* Compound **41** was obtained according to general procedure **D** using *m*-tolylboronic acid (215 mg, 1.58 mmol, 2.0 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), **41** (189 mg, 73%) was obtained as a white solid. Rf (PE/EA: 90/10): 0.27. M_p: 191–193 °C. IR (ATR diamond, cm^{-1}) ν: 2961, 2946, 2869, 1553, 1385, 1376, 771, 733, 690, 624. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.75–1.88 (m, 2H, CH_2), 2.02–2.14 (m, 2H, CH_2), 2.47 (s, 3H, CH_3), 2.71–2.84 (m, 2H, N–CH_2), 3.21–3.32 (m, 2H, N–CH_2), 3.39 (p, J = 3.0 Hz, 1H, CH), 7.28 (d, J = 7.5 Hz, 1H, CH_{Ar}), 7.39 (t, J = 7.9 Hz, 1H, CH_{Ar}), 7.43–7.56 (m, 3H, 3xCH_{Ar}), 8.36 (d, J = 6.9 Hz, 2H, 2xCH_{Ar}), 8.48 (dt, J = 1.5, 2.3, 6.4 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 21.7 (CH_3), 27.9 (2xCH_2), 33.7 (CH), 48.9 (2xN-CH_2), 125.6 (CH_{Ar}), 128.3 (2xCH_{Ar}), 128.5 (CH_{Ar}), 128.8 (CH_{Ar}), 130.0 (CH_{Ar}), 130.2 (2xCH_{Ar}), 131.1 (CH_{Ar}), 136.3 (C_q), 138.1 (C_q), 138.3 (C_q), 139.2 (C_q), 154.9 (C_q), 161.3 (C_q), 175.1 (C_q). HRMS (EI/MS): m/z calculated for $C_{22}H_{22}N_3$: 328.1808 [M + H]$^+$; found: 328.1813.

*4-Phenyl-2-(o-tolyl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d] pyrimidine (**42**).* Compound **42** was obtained according to general procedure **D** using *o*-tolylboronic acid (215 mg, 1.58 mmol, 2.0 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), **42** (196 mg, 76%) was obtained as a white solid. Rf (PE/EA: 90/10): 0.22. M_p: 228–230 °C. IR (ATR diamond, cm^{-1}) ν: 2944, 2869, 1552, 1387, 1131, 844, 767, 736, 695, 623. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.79–1.88 (m, 2H, CH_2), 2.03–2.14 (m, 2H, CH_2), 2.66 (s, 3H, CH_3), 2.75–2.87 (m, 2H, N–CH_2), 3.22–3.34 (m, 2H, N–CH_2), 3.38 (p, J = 2.9 Hz, 1H, CH), 7.27–7.38 (m, 3H, 3xCH_{Ar}), 7.38–7.55 (m, 3H, 2xCH_{Ar}, CH_{Ar}), 7.87–7.94 (m, 1H, CH_{Ar}), 8.44 (dd, J = 1.8, 8.0 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 21.5 (CH_3), 27.9 (2xCH_2), 33.6 (CH), 48.9 (2xN-CH_2), 126.0 (CH_{Ar}), 128.3 (2xCH_{Ar}), 129.1 (CH_{Ar}), 130.0 (CH_{Ar}), 130.2 (2xCH_{Ar}), 130.6 (CH_{Ar}), 131.3 (CH_{Ar}), 136.2 (C_q), 137.3 (C_q), 138.5 (C_q), 138.9 (C_q), 154.6 (C_q), 164.1 (C_q), 174.9 (C_q). HRMS (EI/MS): m/z calculated for $C_{22}H_{22}N_3$: 328.1808 [M + H]$^+$; found: 328.1813.

*2-(4-Methoxyphenyl)-4-phenyl-7,8-dihydro-6H-5,8-ethanopyrido [3,2-d]pyrimidine (**43**).* Compound **43** was obtained according to general procedure **D** using 4-methoxyphenylboronic acid (244 mg, 1.60 mmol, 2.0 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), **43** (188 mg, 69%) was obtained as a white solid. Rf (PE/EA: 90/10): 0.24. M_p: 204–206 °C. IR (ATR diamond, cm^{-1}) ν: 2960, 2935, 1549, 1387, 1247, 1031, 772, 694. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.75–1.87 (m, 2H, CH_2), 2.01–2.12 (m, 2H, CH_2), 2.77 (td, J = 5.0, 11.4 Hz, 2H, N–CH_2), 3.20–3.31 (m, 2H, N–CH_2), 3.36 (p, J = 3.0 Hz, 1H, CH), 3.89 (s, 3H, O–CH_3), 7.01 (d, J = 8.5 Hz, 2H, 2xCH_{Ar}), 7.42–7.55 (m, 3H, 3xCH_{Ar}), 8.47 (d, J = 7.7 Hz, 2H, 2xCH_{Ar}), 8.52 (d, J = 8.4 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.9 (2xCH_2), 33.7 (CH), 49.0 (2xN-CH_2), 55.4 (O–CH_3), 113.9 (2xCH_{Ar}), 128.2 (2xCH_{Ar}), 129.9 (2xCH_{Ar}), 129.9 (CH_{Ar}), 130.2 (2xCH_{Ar}), 131.1 (C_q), 136.4 (C_q), 138.6 (C_q), 154.7 (C_q), 160.9 (C_q), 161.5 (C_q), 175.0 (C_q). HRMS (EI/MS): m/z calculated for $C_{22}H_{22}N_3O$: 344.1757 [M + H]$^+$; found: 344.1759.

*4-(4-Phenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-yl)phenol (**44**).* Compound **44** was obtained according to general procedure **D** using 4-hydroxyphenylboronic acid (219 mg, 1.59 mmol, 2.0 eq.). After purification by silica gel flash chromatography (PE/EA, 80/20), **44** (141 mg, 54%) was obtained as a white solid. Rf (PE/EA: 80/20): 0.17. M_p: 254–256 °C. IR (ATR diamond, cm^{-1}) ν: 3059, 2942, 2675, 1610, 1552, 1400, 1238, 1166, 774, 688, 625. ^{1}H NMR (400 MHz, DMSO-d_6) δ: 1.61–1.75 (m, 2H, CH_2), 1.97–2.11 (m, 2H, CH_2), 2.58–2.71 (m, 2H, N–CH_2), 3.14–3.21 (m, 2H, N–CH_2), 3.23 (p, J = 2.3 Hz, 1H, CH), 6.89 (td, J = 1.7, 8.7 Hz, 2H, 2xCH_{Ar}), 7.45–7.57 (m, 3H, 3xCH_{Ar}), 8.34 (td, J = 2.0, 8.7 Hz, 2H, 2xCH_{Ar}), 8.39 (dd, J = 1.9, 7.8 Hz, 2H, 2xCH_{Ar}), 9.88 (s, 1H, OH). ^{13}C NMR (101 MHz, DMSO-d_6) δ: 27.0 (2xCH_2), 33.0 (CH), 48.2 (2xN-CH_2), 115.3 (2xCH_{Ar}), 128.0 (2xCH_{Ar}), 128.6 (C_q), 129.5 (2xCH_{Ar}), 129.8 (CH_{Ar}), 129.8 (CH_{Ar}), 135.7 (C_q), 138.2 (C_q), 153.5 (C_q), 159.6 (C_q), 159.8 (C_q), 175.1 (C_q). HRMS (EI/MS): m/z calculated for $C_{21}H_{20}N_3O$: 330.1601 [M + H]$^+$; found: 330.1602.

*4-Phenyl-2-(4-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidine (**45**).* Compound **45** was obtained according to general procedure **D** using 4-(tetrahydro-2*H*-pyran-2-yloxy)phenylboronic acid (358 mg, 1.61 mmol, 2.0 eq.). After purification by silica gel flash chromatography (PE/EA, 80/20), **45** (230 mg, 69%) was obtained as a white solid. Rf (PE/EA: 80/20): 0.34. M_p: 210–212 °C. IR (ATR diamond, cm^{-1}) ν: 2940, 2872, 1551, 1386, 1236, 1163, 1113, 958, 920, 768, 693. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.57–1.75 (m, 3H, 3xCH_{THP}), 1.76–1.85 (m, 2H, CH_2), 1.86–1.95 (m, 2H, 2xCH_{THP}), 1.97–2.12 (m, 3H, CH_2, CH_{THP}), 2.70–2.83 (m, 2H, N–CH_2), 3.19–3.31 (m, 2H, N–CH_2), 3.36 (p, J = 2.9 Hz, 1H, CH), 3.59–3.68 (m, 1H, CH_{THP}), 3.89–3.99 (m, 1H, CH_{THP}), 5.52 (t, J = 3.3 Hz, 1H, O–CH–O), 7.15 (d, J = 8.8 Hz, 2H, 2xCH_{Ar}), 7.44–7.55 (m, 3H, 3xCH_{Ar}), 8.43–8.53 (m, 4H, 2xCH_{Ar}, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 18.9 ($CH_{2,THP}$), 25.3 ($CH_{2,THP}$), 27.9 (2xCH_2), 30.4 ($CH_{2,THP}$), 33.7 (CH), 48.9 (2xN-CH_2), 62.2($CH_{2,THP}$), 96.3 (O–CH–O), 116.3 (2xCH_{Ar}), 128.2 (2xCH_{Ar}), 129.8 (2xCH_{Ar}), 129.9 (CH_{Ar}), 130.2 (2xCH_{Ar}), 131.9 (C_q), 136.4 (C_q), 138.7 (C_q), 154.7 (C_q), 159.0 (C_q), 160.9 (C_q), 175.0 (C_q). HRMS (EI/MS): m/z calculated for $C_{26}H_{28}N_3O_2$: 414.2176 [M + H]$^+$; found: 414.2174.

*2-(2-Naphthalen-2-yl)-4-phenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidine (**46**).* Compound **46** was obtained according to general procedure **D** using 2-naphthylboronic acid (275 mg, 1.60 mmol, 2.0 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), **46** (196 mg, 67%) was obtained as a white solid. Rf (PE/EA: 90/10): 0.35. M_p: 210–212 °C. IR (ATR diamond, cm^{-1}) ν: 2949, 2868, 1552, 1391, 1380, 773, 755, 700, 625. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.80–1.92 (m, 2H, CH_2), 2.05–2.16 (m, 2H, CH_2), 2.74–2.87 (m, 2H, N–CH_2), 3.23–3.34 (m, 2H, N–CH_2), 3.45 (p, J = 2.9 Hz, 1H, CH), 7.46–7.60 (m, 5H, 3xCH_{Ar}, 2xCH_{Ar}), 7.86–7.93 (m, 1H, CH_{Ar}), 7.97 (d, J = 8.7 Hz, 1H, CH_{Ar}), 8.01–8.09 (m, 1H, CH_{Ar}), 8.50–8.57 (m, 2H, 2xCH_{Ar}), 8.71 (dd, J = 1.7, 8.6 Hz, 1H, CH_{Ar}), 9.10 (s, 1H, CH_{Ar}). ^{13}C NMR (101 MHz,

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$CDCl_3$) δ: 27.9 (2xCH_2), 33.7 (CH), 48.9 (2xN-CH_2), 125.6 (CH_{Ar}), 126.2 (CH_{Ar}), 126.9 (CH_{Ar}), 127.8 (CH_{Ar}), 128.1 (CH_{Ar}), 128.3 (2xCH_{Ar}), 128.3 (CH_{Ar}), 129.3 (CH_{Ar}), 130.1 (CH_{Ar}), 130.3 (CH_{Ar}), 133.5 (C_q), 134.6 (C_q), 135.7 (C_q), 136.3 (C_q), 139.3 (C_q), 155.0 (C_q), 161.0 (C_q), 175.3 (C_q). HRMS (EI/MS): *m/z* calculated for $C_{25}H_{22}N_3$: 364.1808 $[M + H]^+$; found: 364.1812.

*2-(4-Fluorophenyl)-4-phenyl-7,8-dihydro-6H-5,8-ethanopyrido [3,2-d]pyrimidine (**47**).* Compound **47** was obtained according to general procedure **D** using 4-fluorophenylboronic acid (224 mg, 1.60 mmol, 2.0 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), **47** (186 mg, 70%) was obtained as a white solid. Rf (PE/EA: 90/10): 0.42. M_p: 178–180 °C. IR (ATR diamond, cm^{-1}) ν: 2922, 2864, 1601, 1555, 1389, 1151, 832, 768, 688, 622. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.75–1.87 (m, 2H, CH_2), 2.02–2.14 (m, 2H, CH_2), 2.71–2.83 (m, 2H, N–CH_2), 3.21–3.32 (m, 2H, N–CH_2), 3.37 (p, $J = 2.9$ Hz, 1H, CH), 7.12–7.22 (m, 2H, 2xCH_{Ar}), 7.45–7.56 (m, 3H, 3xCH_{Ar}), 8.47 (dd, $J = 1.7$, 8.0 Hz, 2H, 2xCH_{Ar}), 8.57 (dd, $J = 5.9$, 9.3 Hz, 2H,2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.8 (2xCH_2), 33.7 (CH), 48.9 (2xN-CH_2), 115.3 (CH_{Ar}), 115.5 (CH_{Ar}), 128.3 (2xCH_{Ar}), 130.1 (CH_{Ar}), 130.2 (2xCH_{Ar}), 130.3 (CH_{Ar}), 130.4 (CH_{Ar}), 134.6 (d, $J = 2.9$ Hz, C_q), 136.1 (C_q), 139.2 (C_q), 154.9 (C_q), 160.19 (C_q), 164.5 (d, $J = 249.5$ Hz, C_{Ar}-F), 175.3 (C_q). ^{19}F NMR (376 MHz, $CDCl_3$) δ: −111.46. HRMS (EI/MS): *m/z* calculated for $C_{21}H_{19}FN_3$: 332.1558 $[M + H]^+$; found: 332.1563.

*4-(4-Phenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-yl)benzonitrile (**48**).* Compound **48** was obtained according to general procedure **D** using 4-cyanophenylboronic acid (236 mg, 1.60 mmol, 2.0 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), **48** (224 mg, 82%) was obtained as a white solid. Rf (PE/EA: 90/10): 0.22. M_p: 202–204 °C. IR (ATR diamond, cm^{-1}) ν: 2956, 2922, 2227, 1549, 1389, 771, 693, 622, 541. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.74–1.87 (m, 2H, CH_2), 2.05–2.16 (m, 2H, CH_2), 2.71–2.83 (m, 2H, N–CH_2), 3.23–3.34 (m, 2H, N–CH_2), 3.40 (p, $J = 2.9$ Hz, 1H, CH), 7.47–7.57 (m, 3H, 3xCH_{Ar}), 7.79 (d, $J = 8.5$ Hz, 2H, 2xCH_{Ar}), 8.43–8.54 (m, 2H, 2xCH_{Ar}), 8.69 (d, $J = 8.5$ Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.8 (2xCH_2), 33.7 (CH), 48.8 (2xN-CH_2), 113.5 (C_q), 119.1 (C_q), 128.4 (2xCH_{Ar}), 128.8 (2xCH_{Ar}), 130.2 (2xCH_{Ar}), 130.4 (2xCH_{Ar}), 132.4 (2xCH_{Ar}), 135.8 (C_q), 140.3 (C_q), 142.5 (C_q), 155.1 (C_q), 159.1 (C_q), 175.7 (C_q). HRMS (EI/MS): *m/z* calculated for $C_{22}H_{19}N_4$: 339.1604 $[M + H]^+$; found: 339.1608.

*4-Phenyl-2-(4-(trifluoromethyl)phenyl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidine (**49**).* Compound **49** was obtained according to general procedure **D** using 4-(trifluoromethyl) phenylboronic acid (303 mg, 1.60 mmol, 2.0 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), **49** (222 mg, 72%) was obtained as a white solid. Rf (PE/EA: 90/10): 0.40 M_p: 166–168 °C. IR (ATR diamond, cm^{-1}) ν: 2953, 1552, 1389, 1320, 1116, 1061, 774, 690. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.76–1.89 (m, 2H, CH_2), 2.04–2.16 (m, 2H, CH_2), 2.78 (td, $J = 5.1$, 11.7 Hz, 2H, N–CH_2), 3.23–3.34 (m, 2H, N–CH_2), 3.41 (p, $J = 3.2$ Hz, 1H, CH), 7.45–7.58 (m, 3H, 3xCH_{Ar}), 7.75 (d, $J = 8.1$ Hz, 2H, 2xCH_{Ar}), 8.50 (dt, $J = 1.6$, 7.5 Hz, 2H, 2xCH_{Ar}), 8.69 (d, $J = 8.0$ Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.8 (2xCH_2), 33.7 (CH), 48.8 (2xN-CH_2), 124.4 (d, $J = 272.2$ Hz, C_q-CF_3), 125.5 (q, $J = 3.8$ Hz, 2xCH_{Ar}), 128.3 (2xCH_{Ar}), 128.6 (2xCH_{Ar}), 130.2 (2xCH_{Ar}), 130.3 (CH_{Ar}), 131.8 (d, $J = 32.2$ Hz, CF_3), 135.9 (C_q), 140.0 (C_q), 141.7 (d, $J = 1.7$ Hz, C_q), 155.0 (C_q), 159.6 (C_q), 175.6 (C_q). ^{19}F NMR (376 MHz, $CDCl_3$) δ: −62.59. HRMS (EI/MS): *m/z* calculated for $C_{22}H_{19}F_3N_3$: 382.1526 $[M + H]^+$; found: 382.1525.

*2-(4-Nitrophenyl)-4-phenyl-7,8-dihydro-6H-5,8-ethanopyrido [3,2-d]pyrimidine (**50**).* Compound **50** was obtained according to general procedure **D** using 4-nitrophenylboronic acid (268 mg, 1.60 mmol, 2.0 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), **50** (206 mg, 76%) was obtained as an orange solid. Rf (PE/EA: 90/10): 0.40. M_p: 191–193 °C. IR (ATR diamond, cm^{-1}) ν: 2925, 2872, 1555, 1519, 1388, 1350, 839, 688. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.75–1.88 (m, 2H, CH_2), 2.06–2.18 (m, 2H, CH_2), 2.72–2.84 (m, 2H, N–CH_2), 3.24–3.35 (m, 2H, N–CH_2), 3.41 (p, $J = 2.8$ Hz, 1H, CH), 7.47–7.58 (m, 3H, 3xCH_{Ar}), 8.34 (dt, $J = 2.0$, 9.0 Hz, 2H, 2xCH_{Ar}), 8.44–8.54 (m, 2H, 2xCH_{Ar}), 8.75 (dt, $J = 2.3$, 9.0 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.8 (2xCH_2), 33.7 (CH), 48.8 (2xN-CH_2), 123.8 (2xCH_{Ar}), 128.4 (2xCH_{Ar}), 129.2 (2xCH_{Ar}), 130.2 (2xCH_{Ar}), 130.4 (CH_{Ar}), 135.7 (C_q), 140.4 (C_q), 144.2 (C_q), 149.1 (C_q), 155.2 (C_q), 158.8 (C_q), 175.8 (C_q). HRMS (EI/MS): *m/z* calculated for $C_{21}H_{19}N_4O_2$: 359.1503 $[M + H]^+$; found: 359.1506.

*4-Phenyl-2-(thiophen-3-yl)-7,8-dihydro-6H-5,8-ethanopyrido [3,2-d]pyrimidine (**51**).* Compound **51** was obtained according to general procedure **D** using 3-thienylboronic acid (208 mg, 1.62 mmol, 2.0 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), **51** (195 mg, 77%) was obtained as a white solid. Rf (PE/EA: 90/10): 0.19. M_p: 189–191 °C. IR (ATR diamond, cm^{-1}) ν: 2956, 2867, 1553, 1386, 1342, 819, 689, 623. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.75–1.86 (m, 2H, CH_2), 2.00–2.13 (m, 2H, CH_2), 2.76 (td, $J = 5.5$, 12.2 Hz, 2H, N–CH_2), 3.19–3.31 (m, 2H, N–CH_2), 3.35 (p, $J = 3.3$ Hz, 1H, CH), 7.38 (t, $J = 3.7$ Hz, 1H, CH_{Ar}), 7.42–7.55 (m, 3H, 3xCH_{Ar}), 8.00 (d, $J = 5.0$ Hz, 1H, CH_{Ar}), 8.31–8.36 (m, 1H, CH_{Ar}), 8.45 (d, $J = 7.9$ Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.8 (2xCH_2), 33.6 (CH), 48.9 (2xN-CH_2), 125.8 (CH_{Ar}), 127.3 (CH_{Ar}), 127.8 (CH_{Ar}), 128.2 (2xCH_{Ar}), 130.0 (CH_{Ar}), 130.2 (2xCH_{Ar}), 136.1 (C_q), 138.8 (C_q), 142.3 (C_q), 154.9 (C_q), 158.5 (C_q), 175.2 (C_q). HRMS (EI/MS): *m/z* calculated for$C_{19}H_{18}N_3S$: 320.1216 $[M + H]^+$; found: 320.1223.

*4-Phenyl-2-(pyridin-3-yl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidine (**52**).* Compound **52** was obtained according to general procedure **D** using 3-pyridinylboronic acid (200 mg, 1.63 mmol, 2.0 eq.). After purification by silica gel flash chromatography (PE/EA, 50/50), **52** (152 mg, 60%) was obtained as a white solid. Rf (PE/EA: 50/50): 0.25. M_p: 231–233 °C. IR (ATR diamond, cm^{-1}) ν: 2926, 2864, 1552, 1387, 1371, 1023, 843, 692, 620. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.75–1.87 (m, 2H, CH_2), 2.02–2.15 (m, 2H, CH_2), 2.77 (td, $J = 5.1$, 11.6 Hz, 2H, N–CH_2), 3.22–3.33 (m, 2H, N–CH_2), 3.40 (p, $J = 3.1$ Hz, 1H, CH), 7.42 (dd, $J = 4.8$, 8.0 Hz, 1H, CH_{Ar}), 7.45–7.56 (m, 3H, 3xCH_{Ar}), 8.50 (d, $J = 7.6$ Hz, 2H, 2xCH_{Ar}), 8.70 (d, $J = 4.8$ Hz, 1H, CH_{Ar}), 8.80 (d, $J = 7.8$ Hz, 1H, CH_{Ar}), 9.76 (s, 1H, CH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.8 (2xCH_2), 33.6 (CH), 48.8 (2xN-CH_2), 123.3 (CH_{Ar}), 128.3 (2xCH_{Ar}), 130.2 (2xCH_{Ar}), 130.3 (CH_{Ar}), 133.8 (C_q), 135.5 (CH_{Ar}), 135.9 (C_q), 139.9 (C_q), 150.1 (CH_{Ar}), 151.0 (CH_{Ar}), 155.0 (C_q), 159.2 (C_q), 175.6 (C_q). HRMS (EI/MS): *m/z* calculated for $C_{20}H_{19}N_4$: 315.1604 $[M + H]^+$; found: 315.1602.

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*2,4-Di-p-tolyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidine (**53**).* Compound **53** was obtained according to general procedure **D** using **9** (215 mg, 0.80 mmol, 1.0 eq.) and *p*-tolylboronic acid (215 mg, 1.58 mmol, 2.0 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), **53** (101 mg, 37%) was obtained as a beige solid. Rf (PE/EA: 90/10): 0.34. M_p: 193–195 °C. IR (ATR diamond, cm^{-1}) ν: 2965, 2934, 2869, 1547, 1387, 1179, 812, 803, 744. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.74–1.87 (m, 2H, CH_2), 2.00–2.12 (m, 2H, CH_2), 2.43 (s, 6H, 2xCH_3), 2.70–2.83 (m, 2H, N–CH_2), 3.19–3.31 (m, 2H, N–CH_2), 3.37 (p, J = 2.9 Hz, 1H, CH), 7.31 (dd, J = 5.9, 8.0 Hz, 4H, 4xCH_{Ar}), 8.36–8.42 (m, 2H, 2xCH_{Ar}), 8.42–8.48 (m, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 21.6 (CH_3), 21.6 (CH_3), 27.9 (2xCH_2), 33.7 (CH), 48.9 (2xN-CH_2), 128.3 (2xCH_{Ar}), 129.0 (2xCH_{Ar}), 129.3 (2xCH_{Ar}), 130.1 (2xCH_{Ar}), 133.6 (C_q), 135.7 (C_q), 138.8 (C_q), 140.1 (C_q), 140.2 (C_q), 154.8 (C_q), 161.1 (C_q), 174.8 (C_q). HRMS (EI/MS): m/z calculated for $C_{23}H_{24}N_3$: 342.1965 $[M + H]^+$; found: 342.1962.

*4-(4-(p-Tolyl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-yl)benzonitrile (**54**).* Compound **54** was obtained according to general procedure **D** using **9** (215 mg, 0.80 mmol, 1.0 eq.) and 4-cyanophenylboronic acid (238 mg, 1.62 mmol, 2.0 eq.). After purification by silica gel flash chromatography (DCM/PE, 60/40 to 80/20), **54** (148 mg, 52%) was obtained as a beige solid. Rf (DCM/PE: 80/20): 0.55. M_p: 236–238 °C. IR (ATR diamond, cm^{-1}) ν: 2940, 2227, 1548, 1387, 1167, 816, 612. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.73–1.86 (m, 2H, CH_2), 2.03–2.15 (m, 2H, CH_2), 2.44 (s, 3H, CH_3), 2.70–2.82 (m, 2H, N–CH_2), 3.22–3.33 (m, 2H, N–CH_2), 3.38 (p, J = 2.8 Hz, 1H, CH), 7.33 (d, J = 8.0 Hz, 2H, 2xCH_{Ar}), 7.78 (d, J = 8.6 Hz, 2H, 2xCH_{Ar}), 8.39 (d, J = 8.3 Hz, 2H, 2xCH_{Ar}), 8.68 (d, J = 8.5 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 21.6 (CH_3), 27.8 (2xCH_2), 33.7 (CH), 48.8 (2xN-CH_2), 113.4 (C_q), 119.1 (C_q), 128.8 (2xCH_{Ar}), 129.1 (2xCH_{Ar}), 130.2 (2xCH_{Ar}), 132.4 (2xCH_{Ar}), 133.0 (C_q), 140.0 (C_q), 140.7 (C_q), 142.6 (C_q), 155.2 (C_q), 159.0 (C_q), 175.5 (C_q). HRMS (EI/MS): m/z calculated for $C_{23}H_{21}N_4$: 353.1761 $[M + H]^+$; found: 353.1759.

*4-(4-Fluorophenyl)-2-(p-tolyl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidine (**55**).* Compound **55** was obtained according to general procedure **D** using **10** (110 mg, 0.40 mmol, 1.0 eq.) and *p*-tolylboronic acid (109 mg, 0.80 mmol, 2.0 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), **55** (63 mg, 45%) was obtained as a white solid. Rf (PE/EA: 90/10): 0.49. M_p: 164–166 °C. IR (ATR diamond, cm^{-1}) ν: 2926, 2869, 1550, 1505, 1386, 1220, 1155, 819. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.74–1.87 (m, 2H, CH_2), 2.01–2.13 (m, 2H, CH_2), 2.43 (s, 3H, CH_3), 2.70–2.82 (m, 2H, N–CH_2), 3.19–3.31 (m, 2H, N–CH_2), 3.37 (p, J = 2.9 Hz, 1H, CH), 7.18 (t, J = 8.8 Hz, 2H, 2xCH_{Ar}), 7.30 (d, J = 8.0 Hz, 2H, 2xCH_{Ar}), 8.44 (d, J = 8.2 Hz, 2H, 2xCH_{Ar}), 8.59 (dd, J = 5.8, 8.8 Hz, 2H, 2xCH_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 21.6 (CH_3), 27.8 (2xCH_2), 33.6 (CH), 48.8 (2xN-CH_2), 115.1 (CH_{Ar}), 115.3 (CH_{Ar}), 128.2 (2xCH_{Ar}), 129.3 (2xCH_{Ar}), 132.3 (CH_{Ar}), 132.4 (CH_{Ar}), 132.5 (d, J = 3.2 Hz, C_q), 135.5 (C_q), 138.7 (C_q), 140.4 (C_q), 153.4 (C_q), 161.1 (C_q), 164.1 (d, J = 250.5 Hz, C_q-F), 175.2 (C_q). ^{19}F NMR (376 MHz, $CDCl_3$) δ: −110.90. HRMS (EI/MS): m/z calculated for $C_{22}H_{21}FN_3$: 346.1714 $[M + H]^+$; found: 346.1710.

*4-(4-(4-Fluorophenyl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2-yl)benzonitrile (**56**).* Compound **56** was obtained according to general procedure **D** using **10** (109 mg, 0.40 mmol, 1.0 eq.) and 4-cyanophenylboronic acid (118 mg, 0.80 mmol, 2.0 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), **56** (97 mg, 68%) was obtained as a white solid. Rf (PE/EA: 90/10): 0.20. M_p: 237–239 °C. IR (ATR diamond, cm^{-1}) ν: 2950, 2917, 2221, 1602, 1544, 1504, 1382, 1157, 824, 568. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.74–1.86 (m, 2H, CH_2), 2.05–2.17 (m, 2H, CH_2), 2.70–2.81 (m, 2H, N–CH_2), 3.22–3.34 (m, 2H, N–CH_2), 3.39 (p, J = 2.8 Hz, 1H, CH), 7.19 (t, J = 8.7 Hz, 2H, 2xCH_{Ar-F}), 7.79 (d, J = 8.5 Hz, 2H, 2xCH_{Ar-CN}), 8.60 (dd, J = 5.6, 8.9 Hz, 2H, 2xCH_{Ar-F}), 8.67 (d, J = 8.5 Hz, 2H, 2xCH_{Ar-CN}). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 27.7 (2xCH_2), 33.7 (CH), 48.7 (2xN-CH_2), 113.6 (C_q), 115.3 (CH_{Ar-F}), 115.5 (CH_{Ar-F}), 119.1 (C_q), 128.8 (2xCH_{Ar-CN}), 131.9 (d, J = 3.1 Hz, C_q), 132.4 (2xCH_{Ar-CN}), 132.4 (CH_{Ar-F}), 132.5 (CH_{Ar-F}), 139.9 (C_q), 142.4 (C_q), 153.8 (C_q), 159.1 (C_q), 164.3 (d, J = 251.4 Hz, C_q-F), 175.8 (C_q). ^{19}F NMR (376 MHz, $CDCl_3$) δ: −110.06. HRMS (EI/MS): m/z calculated for $C_{22}H_{18}FN_4$: 357.1510 $[M + H]^+$; found: 357.1505.

Conflicts of interest

The authors declare no conflict of interest.

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