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# Aminations and arylations by direct $\mathrm{C}-\mathrm{O}$ activation for the design of 7,8-dihydro-6H-5,8-ethanopyrido [3,2-d] pyrimidines $\dagger$ 

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#### Abstract

The design of some novel disubstituted 7,8 -dihydro- $6 \mathrm{H}-5,8$-ethanopyrido[3,2- $d$ ] pyrimidine derivatives is reported. The series was developed from quinuclidinone, which afforded versatile platforms bearing one lactam function in position $\mathrm{C}-2$ that were then used to create $\mathrm{C}-\mathrm{N}$ or $\mathrm{C}-\mathrm{C}$ bonds for $\mathrm{S}_{N} \mathrm{Ar}$ or palladiumcatalyzed cross-coupling reactions by in situ $\mathrm{C}-\mathrm{O}$ 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-6H-5,8-ethanopyrido[3,2-d]pyrimidine derivative 49 were used to formally establish the structures of the products.


## 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 nitrogencontaining 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

[^0]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 $\left[1^{\prime}, 2^{\prime}: 1,5\right]$ pyrazolo $[3,4-d]$ pyrimidines or pyrido [ $\left.1^{\prime}, 2^{\prime}: 1,5\right]$ 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 crosscoupling 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.

Fig. 2 General scheme leading to 2,4 disubstituted quinuclidino pyrimidines under $\mathrm{C}-\mathrm{O}$ direct activation.


Scheme 1 Synthesis of 8-10.

7,8-dihydro-1 H -5,8-ethanopyrido[3,2- $d$ ]pyrimidin-2(6H)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 $\mathbf{8 - 1 0}$ 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 $\mathrm{C}-\mathrm{O}$ direct activation involving PyBroP and $\mathrm{Et}_{3} \mathrm{~N}^{35-37}$ 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 $80{ }^{\circ} \mathrm{C}$ and after 2 h the primary

Table 1 Optimization of amination conditions with 8

|  |  |  |  |
| :--- | :--- | :--- | :--- |
| Entry | Temp. $\left({ }^{\circ} \mathrm{C}\right)$ | $t_{1}$ | $t_{2}$ |
| 102 |  |  |  |

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 $100{ }^{\circ} \mathrm{C}$ 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 $100^{\circ} \mathrm{C}$. The nucleophilic attack of the amine on the activated heterocycle was the rate-limiting step. The second step was achieved during 17 h at $100^{\circ} \mathrm{C}$ and led to the desired compound 11 in $\mathbf{7 2 \%}$ of yield.

In order to explore the scope and limitations of this tandem sequence, we then condensed previously synthesized ethanopyrido $[3,2-d]$ pyrimidinones $\mathbf{A}$ 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 $\mathrm{S}_{N} \mathrm{Ar}$ 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 $\mathrm{S}_{N} \mathrm{Ar}$ method.

Table 2 Synthesis of 11-24


| Entry | $\mathrm{R}_{1}$ | $\mathrm{HNR}_{2} \mathrm{R}_{3}$ | Cpd, yield ${ }^{\text {a }}$ |
| :---: | :---: | :---: | :---: |
| 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 | $\mathrm{C}_{6} \mathrm{H}_{5} \mathrm{CH}_{2} \mathrm{NH}_{2}$ | 17, 51\% |
| 9 | H | $4-\mathrm{CH}_{3} \mathrm{O}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{CH}_{2} \mathrm{NH}_{2}$ | 18, 42\% |
| 10 | H | $4-\mathrm{CF}_{3}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{CH}_{2} \mathrm{NH}_{2}$ | 19, 39\% |
| 11 | H | Imidazole | 20, 22\% |
| 12 | H | $4-\mathrm{CH}_{3}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{NH}_{2}$ | 21, $\mathrm{ND}^{b}$ |
| 13 | H | $\delta$-Valerolactam | 22, $\mathrm{ND}^{b}$ |
| 15 | Me | Piperidine | 23, 86\% |
| 16 | F | Piperidine | 24, 79\% |

[^1]

| Entry | Catalyst (mol\%) | Ligand (mol\%) | Base | Temp. $\left({ }^{\circ} \mathrm{C}\right)$ | Yield ${ }^{\text {a }}$ (\%) |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 1 | $\mathrm{Pd}_{2} \mathrm{dba}_{3}(5 \%)$ | Xantphos (10\%) | $\mathrm{K}_{2} \mathrm{CO}_{3}$ | 130 | 19 |
| 2 | $\mathrm{Pd}(\mathrm{OAc})_{2}(5 \%)$ | Xantphos (10\%) | $\mathrm{K}_{2} \mathrm{CO}_{3}$ | 130 | 21 |
| 3 | $\mathrm{Pd}(\mathrm{OAc})_{2}(10 \%)$ | Xantphos (20\%) | $\mathrm{K}_{2} \mathrm{CO}_{3}$ | 130 | 40 |
| 4 | $\mathrm{Pd}(\mathrm{OAc})_{2}(10 \%)$ | Xantphos (20\%) | $\mathrm{K}_{2} \mathrm{CO}_{3}$ | 150 | 33 |
| 5 | $\mathrm{Pd}(\mathrm{OAc})_{2}(10 \%)$ | CyJohnPhos (20\%) | $\mathrm{K}_{2} \mathrm{CO}_{3}$ | 130 | 0 |
| 6 | $\mathrm{Pd}(\mathrm{OAc})_{2}(10 \%)$ | Ruphos (20\%) | $\mathrm{K}_{2} \mathrm{CO}_{3}$ | 130 | 0 |
| 7 | $\mathrm{Pd}(\mathrm{OAc})_{2}(10 \%)$ | Xantphos (20\%) | $\mathrm{Na}_{2} \mathrm{CO}_{3}$ | 130 | Traces |
| 8 | $\operatorname{Pd}(\mathrm{OAc})_{2}(10 \%)$ | Xantphos (20\%) | $\mathrm{Cs}_{2} \mathrm{CO}_{3}$ | 130 | 9 |

${ }^{a}$ Yield is indicated as isolated product.

First, we used $\delta$-valerolactam as amide to prevent any $\mathrm{S}_{N} \mathrm{Ar}$ competition, $\mathrm{Pd}_{2} \mathrm{dba}_{3}$ as the palladium source in the presence of Xantphos as bidentate ligand, $\mathrm{K}_{2} \mathrm{CO}_{3}$ 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 $\operatorname{Pd}(\mathrm{OAc})_{2}$, the same behaviour was observed and the desired compound 22 was obtained in a similar $21 \%$ yield. By increasing the catalytic charge to $10 \mathrm{~mol} \%$ the $O$-phosphonium species was consumed, affording 22 in $40 \%$ of yield accompanied with degradation. A fine adjustment of the temperature (to $150{ }^{\circ} \mathrm{C}$ ) drastically decreased the yield (entry 4) and the replacement of Xantphos with wellknown Buchwald ligands such as CyJohnPhos or Ruphos totally inhibited the reactivity. Changing the nature of the base indicated that the use of $\mathrm{Na}_{2} \mathrm{CO}_{3}$ and $\mathrm{Cs}_{2} \mathrm{CO}_{3}$ 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-fluo-rophenyl)-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 $\mathrm{C}-\mathrm{C}$ bond instead of a $\mathrm{C}-\mathrm{N}$ 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 $\mathrm{Pd}(\mathrm{OAc})_{2}$ at $110{ }^{\circ} \mathrm{C}$ in the presence of a bidentate phosphine proved to be a better catalytic system than with $\mathrm{PdCl}_{2}(\mathrm{dppf}) \cdot \mathrm{CH}_{2} \mathrm{Cl}_{2}$ or $\mathrm{Pd}\left(\mathrm{PPh}_{3}\right)_{4}$ (entries 1-3). Modulation of the base indicated an increase in the yield using $\mathrm{K}_{3} \mathrm{PO}_{4}$ 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 | $\mathrm{R}_{1}$ | $\mathrm{HNR}_{2} \mathrm{R}_{3}$ | Cpd, yield ${ }^{\text {a }}$ |
| 1 | H | 4-CH33-C6 $\mathrm{H}_{4} \mathrm{NH}_{2}$ | 21, 48\% |
| 2 | H | $\delta$-Valerolactam | 22, 40\% |
| 3 | H | 2-Pyrrolidinone | 25, 39\% |
| 4 | H | $\mathrm{C}_{6} \mathrm{H}_{5} \mathrm{NH}_{2}$ | 26, 56\% |
| 5 | H | $4-\mathrm{CH}_{3} \mathrm{O}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{NH}_{2}$ | 27, 48\% |
| 6 | H | $3-\mathrm{CH}_{3}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{NH}_{2}$ | 28, 31\% |
| 7 | H | $2-\mathrm{CH}_{3}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{NH}_{2}$ | 29, 15\% |
| 8 | H | $4-\mathrm{CF}_{3}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{NH}_{2}$ | 30, 56\% |
| 9 | H | $4-\mathrm{CN}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{NH}_{2}$ | 31, 35\% |
| 10 | H | $4-\mathrm{NO}_{2}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{NH}_{2}$ | 32, 39\% |
| 11 | H | 3-NH2-pyridine | 33, 34\% |
| 12 | H | 5- $\mathrm{NH}_{2}$-2-MeOpyridine | 34, 28\% |
| 13 | Me | $\mathrm{C}_{6} \mathrm{H}_{5} \mathrm{NH}_{2}$ | 35, 44\% |
| 14 | Me | $4-\mathrm{CF}_{3}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{NH}_{2}$ | 36, 49\% |
| 15 | F | $\mathrm{C}_{6} \mathrm{H}_{5} \mathrm{NH}_{2}$ | 37, traces |
| 16 | F | $4-\mathrm{CF}_{3}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{NH}_{2}$ | 38, $\mathrm{ND}^{b}$ |

${ }^{a}$ Cpd: compound number; yield is indicated as isolated product. ${ }^{b}$ Not detected.

Table 5 Optimization of the conditions for the formation of 39


| Entry | Catalyst/ligand | Base | Time step 2 | Temp step 2 | Yield ${ }^{\text {a }}$ (\%) |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 1 | $\mathrm{PdCl}_{2}(\mathrm{dppf}) \cdot \mathrm{CH}_{2} \mathrm{Cl}_{2}$ | $\mathrm{Na}_{2} \mathrm{CO}_{3}$ | 24 h | $110{ }^{\circ} \mathrm{C}$ | 50 |
| 2 | $\mathrm{Pd}\left(\mathrm{PPh}_{3}\right)_{4}$ | $\mathrm{Na}_{2} \mathrm{CO}_{3}$ | 24 h | $110{ }^{\circ} \mathrm{C}$ | 41 |
| 3 | $\mathrm{Pd}(\mathrm{OAc})_{2} /$ Xantphos | $\mathrm{Na}_{2} \mathrm{CO}_{3}$ | 24 h | $110{ }^{\circ} \mathrm{C}$ | 60 |
| 4 | $\mathrm{Pd}(\mathrm{OAc})_{2} /$ Xantphos | $\mathrm{Cs}_{2} \mathrm{CO}_{3}$ | 24 h | $110{ }^{\circ} \mathrm{C}$ | 50 |
| 5 | $\mathrm{Pd}(\mathrm{OAc})_{2} /$ Xantphos | $\mathrm{K}_{2} \mathrm{CO}_{3}$ | 24 h | $110{ }^{\circ} \mathrm{C}$ | 54 |
| 6 | $\mathrm{Pd}(\mathrm{OAc})_{2} /$ Xantphos | $\mathrm{K}_{3} \mathrm{PO}_{4}$ | 24 h | $110{ }^{\circ} \mathrm{C}$ | 68 |
| 7 | $\mathrm{Pd}(\mathrm{OAc})_{2} /$ Xphos | $\mathrm{K}_{3} \mathrm{PO}_{4}$ | 24 h | $110{ }^{\circ} \mathrm{C}$ | 62 |
| 8 | $\mathrm{Pd}(\mathrm{OAc})_{2} /$ Ruphos | $\mathrm{K}_{3} \mathrm{PO}_{4}$ | 24 h | $110{ }^{\circ} \mathrm{C}$ | 68 |
| 9 | $\mathrm{Pd}(\mathrm{OAc})_{2} /$ Ruphos | $\mathrm{K}_{3} \mathrm{PO}_{4}$ | 1 h | $150{ }^{\circ} \mathrm{C}$ | 70 |
|  |  |  |  | M.W. |  |

${ }^{a}$ 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 $150{ }^{\circ} \mathrm{C}$ 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

Table 6 Synthesis of 39-56


| Entry | $\mathrm{R}_{1}$ | $\mathrm{R}_{2} \mathrm{~B}(\mathrm{OH})_{2}$ | Cpd, yield ${ }^{\text {a }}$ |
| :---: | :---: | :---: | :---: |
| 1 | H | $4-\mathrm{CH}_{3}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{~B}(\mathrm{OH})_{2}$ | 39, $70 \%$ |
| 2 | H | $\mathrm{C}_{6} \mathrm{H}_{5} \mathrm{~B}(\mathrm{OH})_{2}$ | 40, 68\% |
| 3 | H | $3-\mathrm{CH}_{3}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{~B}(\mathrm{OH})_{2}$ | 41, 73\% |
| 4 | H | $2-\mathrm{CH}_{3}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{~B}(\mathrm{OH})_{2}$ | 42, 76\% |
| 5 | H | $4-\mathrm{CH}_{3} \mathrm{O}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{~B}(\mathrm{OH})_{2}$ | 43, 69\% |
| 6 | H | $4-\mathrm{OH}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{~B}(\mathrm{OH})_{2}$ | 44, 54\% |
| 7 | H | 4 -OTHP- $\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{~B}(\mathrm{OH})_{2}$ | 45, 69\% |
| 8 | H | 2 -NaphtylB $(\mathrm{OH})_{2}$ | 46, 67\% |
| 9 | H | 4 -F-C ${ }_{6} \mathrm{H}_{4} \mathrm{~B}(\mathrm{OH})_{2}$ | 47, 70\% |
| 10 | H | $4-\mathrm{CN}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{~B}(\mathrm{OH})_{2}$ | 48, $82 \%$ |
| 11 | H | $4-\mathrm{CF}_{3}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{~B}(\mathrm{OH})_{2}$ | 49, $72 \%$ |
| 12 | H | $4-\mathrm{NO}_{2}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{~B}(\mathrm{OH})_{2}$ | 50, 76\% |
| 13 | H | 3 -ThienylB(OH) ${ }_{2}$ | 51, 77\% |
| 14 | H | 3-PyridylB $(\mathrm{OH})_{2}$ | 52, 60\% |
| 15 | Me | $4-\mathrm{CH}_{3}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{~B}\left(\mathrm{OH}_{2}\right)$ | 53, 37\% |
| 16 | Me | $4-\mathrm{CN}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{~B}(\mathrm{OH})_{2}$ | 54, 52\% |
| 17 | F | $4-\mathrm{CH}_{3}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{~B}(\mathrm{OH})_{2}$ | 55, 45\% |
| 18 | F | $4-\mathrm{CN}-\mathrm{C}_{6} \mathrm{H}_{4} \mathrm{~B}(\mathrm{OH})_{2}$ | 56, 68\% |

[^2]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 $9 \mathbf{- 1 0}$ (entries 15-18) were less efficient than those conducted with 8 (entries 1 vs. 15 or $17,10 v s .16$ or 18).

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 $P 2_{1}$ 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 $\mathrm{CF}_{3}$ 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.
$=22.187(14) \AA, \beta=110.05(4)^{\circ}$ and $V=1890(3) \AA^{3}$. 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) A for the C-C bonds and from 1.332(6) to 1.356(5) for $\mathrm{N}-\mathrm{C}$ bonds within the aromatic rings, from $1.477(9)$ to $1.541(8) \AA, 1.430(6)$ to $1.488(7)$ and $1.309(9)$ to $1.336(10)$ for single $\mathrm{C}-\mathrm{C}, \mathrm{C}-\mathrm{N}$ and $\mathrm{C}-\mathrm{F}$ 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) ${ }^{\circ}$ 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) ${ }^{\circ}$ and $\left.26.9(2)^{\circ}\right)$ for both molecules. Fig. 3 shows one of the two independent molecules of $\mathbf{4 9}$ extracted from the crystal structure. The two molecules are very similar ( $\mathrm{RMSD}=0.452 \AA$ ) 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 $\mathrm{C}-\mathrm{O}$ activation sequence involving first PyBroP as activator and next a $\mathrm{S}_{N} \mathrm{Ar}$ or a palladium cross coupling reaction. Aminations were achieved under $\mathrm{S}_{N} \mathrm{Ar}$ reactions which were performed with a large variety of amines or using BuchwaldHartwig 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- $6 \mathrm{H}^{-}$ 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

${ }^{1} \mathrm{H}$ NMR and ${ }^{13} \mathrm{C}$ NMR spectra were recorded on a Bruker DPX 250 or 400 Mhz instrument using $\mathrm{CDCl}_{3}$ and DMSO- $d_{6}$. The chemical shifts are reported in parts per million ( $\delta$ 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 ( $0.063-0.200 \mathrm{~mm}$, 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-K $\alpha$ radiation. CCDC 2074887 contains the supplementary crystallographic data for this paper.

## Synthetic procedures

General procedure A: aldol condensation. To a solution of 3quinuclidinone 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 ( $3.99 \mathrm{~g}, 24.73 \mathrm{mmol}, 1.0 \mathrm{eq}$.) and sodium hydroxide ( $1.99 \mathrm{~g}, 49.7 \mathrm{mmol}, 2.0 \mathrm{eq}$.$) in a mixture of$ methanol/water (3/1, 75 mL ) and benzaldehyde ( 3.0 mL , $29.5 \mathrm{mmol}, 1.2 \mathrm{eq}$.$) . The reaction mixture was stirred 16 \mathrm{~h}$ at r.t. to afford $2(3.82 \mathrm{~g}, 72 \%)$ as a yellow solid. Rf (PE/EA: 90/10): 0.32. $M_{\mathrm{p}}$ : $141-143{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 2941,2873,1700,1621$, $1096,688 .{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 2.03(\mathrm{td}, J=3.1,7.9 \mathrm{~Hz}$, $4 \mathrm{H}, 2 \mathrm{xCH}_{2}$ ), $2.63(\mathrm{p}, J=3.0 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 3.00(\mathrm{dt}, J=7.6,12.5 \mathrm{~Hz}$, $2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}$ ), $3.16\left(\mathrm{dt}, J=7.8,13.4 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 7.02(\mathrm{~s}, 1 \mathrm{H}, \mathrm{C}=$ CH), 7.29-7.42 (m, 3H, 3xCHAr), 7.97-8.09 (m, 2H, 2xCHAr). ${ }^{13} \mathrm{C}$ NMR ( $\left.101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 26.3\left(2 \mathrm{xCH}_{2}\right), 40.7(\mathrm{CH}), 47.9\left(2 \mathrm{xN}^{2} \mathrm{CH}_{2}\right)$, $125.5(\mathrm{C}=\mathrm{CH}), 128.8(2 \mathrm{xCHAr}), 130.0\left(\mathrm{CH}_{\mathrm{Ar}}\right), 132.6\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 134.4$ $\left(\mathrm{C}_{\mathrm{Ar}}\right), 145.1(\mathrm{C}=\mathrm{CH}), 206.8(\mathrm{C}=\mathrm{O})$. HRMS $(\mathrm{EI} / \mathrm{MS}): ~ m / z$ calculated for $\mathrm{C}_{14} \mathrm{H}_{16} \mathrm{NO}: 214.1225[\mathrm{M}+\mathrm{H}]^{+}$; 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 $(4.00 \mathrm{~g}$, $24.79 \mathrm{mmol}, 1.0 \mathrm{eq}$. ) and sodium hydroxide ( $2.01 \mathrm{~g}, 50.27 \mathrm{mmol}$, 2.0 eq.) in a mixture of methanol/water ( $3 / 1,75 \mathrm{~mL}$ ) and $p$-tolualdehyde ( $3.5 \mathrm{~mL}, 29.68 \mathrm{mmol}, 1.2 \mathrm{eq}$.). The reaction mixture was stirred 16 h at r.t. to afford $3(3.05 \mathrm{~g}, 54 \%)$ as a yellow solid. Rf (EP/EA: 90/10): 0.48. $M_{\mathrm{p}}$ : 128-130 ${ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\left.\mathrm{cm}^{-1}\right) \nu: 2938,1700,1626,1507,1251,1092,810,517$. ${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 2.01(\mathrm{td}, J=7.9,2.9 \mathrm{~Hz}, 4 \mathrm{H}$, $2 \mathrm{xCH}_{2}$ ), $2.36\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{CH}_{3}\right), 2.62(\mathrm{p}, J=2.9 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 2.91-3.04$ (m, 2H, N-CH2), 3.09-3.22 (m, 2H, N-CH $), 7.00(\mathrm{~s}, 1 \mathrm{H}, \mathrm{C}=\mathrm{CH})$, $7.17\left(\mathrm{~d}, J=7.9 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.93\left(\mathrm{~d}, J=8.0 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right)$. ${ }^{13} \mathrm{C}$ NMR $\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 21.5\left(\mathrm{CH}_{3}\right), 25.9\left(2 \mathrm{xCH}_{2}\right), 40.3$ $(\mathrm{CH}), 47.5\left(2 \mathrm{xN}^{2} \mathrm{CH}_{2}\right), 125.2(=\mathrm{CH}), 129.1\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 131.2\left(\mathrm{C}_{\mathrm{q}}\right)$, $132.1\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 139.9\left(\mathrm{C}_{\mathrm{q}}\right), 144.0\left(\mathrm{C}_{\mathrm{q}}\right), 206.4(\mathrm{C}=\mathrm{O})$. HRMS (EI/ MS): $\mathrm{m} / \mathrm{z}$ calculated for $\mathrm{C}_{15} \mathrm{H}_{18} \mathrm{NO}$ : 228.1381; found 228.1383.
(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 $(4.00 \mathrm{~g}$, $24.76 \mathrm{mmol}, 1.0 \mathrm{eq}$.$) and sodium hydroxide ( 2.00 \mathrm{~g}, 50.00 \mathrm{mmol}$, 2.0 eq.) in a mixture of methanol/water (3/1, 75 mL ) and 4 -fluorobenzaldehyde ( $3.2 \mathrm{~mL}, 29.82 \mathrm{mmol}, 1.2 \mathrm{eq}$.$) . The reaction$ mixture was stirred 16 h at r.t. to afford 4 (4.33 g, 75\%) as a yellow solid. $\mathrm{Rf}(\mathrm{PE} / \mathrm{EA}: ~ 90 / 10): 0.30 . M_{\mathrm{p}}: 131-133{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 2943,1698,1619,1595,1502,1220,853 .{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 2.02\left(\mathrm{td}, J=7.9,3.0 \mathrm{~Hz}, 4 \mathrm{H}, 2 \mathrm{xCH}_{2}\right)$, 2.63 (p, $J=3.0 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 2.90-3.04\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.07-$ $3.21\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 6.97(\mathrm{~s}, 1 \mathrm{H},=\mathrm{CH}), 6.99-7.10(\mathrm{~m}, 2 \mathrm{H}$, $2 \mathrm{xCH}_{\mathrm{Ar}}$ ), $7.99-8.10\left(\mathrm{~m}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C} \mathrm{NMR}\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ $\delta: 26.0\left(2 \mathrm{xCH}_{2}\right), 40.3(\mathrm{CH}), 47.5\left(2 \mathrm{xN}-\mathrm{CH}_{2}\right), 115.5(\mathrm{~d}, J=21.5 \mathrm{~Hz}$, $\left.2 \mathrm{xCH}_{\mathrm{Ar}}\right), 123.9(=\mathrm{CH}), 130.3(\mathrm{~d}, J=3.4 \mathrm{~Hz}, \mathrm{C}=), 134.3(\mathrm{~d}, J=$ $\left.8.1 \mathrm{~Hz}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 144.3\left(\mathrm{~d}, J=2.6 \mathrm{~Hz}, \mathrm{C}_{\mathrm{Ar}}\right), 163.3(\mathrm{~d}, J=251.6 \mathrm{~Hz}$, $\left.\mathrm{C}_{\mathrm{Ar}}-\mathrm{F}\right)$, $206.3(\mathrm{C}=\mathrm{O}) .{ }^{19} \mathrm{~F}$ NMR ( $376 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta:-109.84$. HRMS (EI/MS): $m / z$ calculated for $\mathrm{C}_{14} \mathrm{H}_{15} \mathrm{FNO}: 232.1132[\mathrm{M}+$ $\mathrm{H}]^{+}$; found 232.1132.

4-Phenyl-3,4, 7, 8-tetrahydro-1H-5,8-ethanopyrido[3,2-d]pyr-imidin-2( $6 H$ )-one (5). $2(4.998 \mathrm{~g}, 23.43 \mathrm{mmol}, 1.0 \mathrm{eq}$.$) and urea$ ( $7.050 \mathrm{~g}, 117.38 \mathrm{mmol}, 5.0 \mathrm{eq}$. ) were ground in a mortar and put in a 100 mL -flask. The mixture was then heated at $220{ }^{\circ} \mathrm{C}$ in a pre-heated bath. After $30 \mathrm{~min}, 80 \mathrm{~mL}$ 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 $(80 \mathrm{~mL}), \mathrm{DCM}(80 \mathrm{~mL})$ and acetone $(2 \times 80 \mathrm{~mL})$ to afford 5 ( $3.505 \mathrm{~g}, 58 \%$ ) as a white solid. Rf (DCM/MeOH: 95/5): 0.44. $M_{\mathrm{p}}:>260^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 3295,2951,1681$, 1642, 1454, 1241, 752, 732, 691. ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{DMSO}-d_{6}$ ) $\delta$ : 1.30-1.43 (m, 1H, CH), 1.45-1.56 (m, 2H, 2xCH), 1.56-1.65 (m, $1 \mathrm{H}, \mathrm{CH}), 1.65-1.79(\mathrm{~m}, 1 \mathrm{H}, \mathrm{N}-\mathrm{CH}), 2.50-2.61(\mathrm{~m}, 3 \mathrm{H}, 2 \times \mathrm{N}-\mathrm{CH}$, $\mathrm{CH}), 2.76$ (ddd, $J=4.6,8.6,12.9 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{N}-\mathrm{CH}), 4.83(\mathrm{~d}, J=$ $2.1 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 6.98(\mathrm{~s}, 1 \mathrm{H}, \mathrm{NH}), 7.20-7.35\left(\mathrm{~m}, 5 \mathrm{H}, 5 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $8.35(\mathrm{~s}, 1 \mathrm{H}, \mathrm{NH}) .{ }^{13} \mathrm{C}$ NMR (101 MHz, DMSO-d $\left.{ }_{6}\right) \delta: 27.9(\mathrm{CH})$, $28.6\left(\mathrm{CH}_{2}\right), 28.7\left(\mathrm{CH}_{2}\right), 49.9\left(\mathrm{~N}-\mathrm{CH}_{2}\right), 50.0\left(\mathrm{~N}-\mathrm{CH}_{2}\right), 57.9(\mathrm{CH})$, $118.3\left(\mathrm{C}_{\mathrm{q}}\right), 126.7\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 127.1(\mathrm{CH}), 128.1\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 137.2$ $\left(\mathrm{C}_{\mathrm{q}}\right), 144.4\left(\mathrm{C}_{\mathrm{q}}\right), 152.5\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): $m / z$ calculated for $\mathrm{C}_{15} \mathrm{H}_{18} \mathrm{~N}_{3} \mathrm{O}: 256.1442[\mathrm{M}+\mathrm{H}]^{+}$; found: 256.1444 .

4-(p-Tolyl)-3,4,7,8-tetrahydro-1H-5,8-ethanopyrido[3,2-d]pyr-
imidin-2(6H)-one (6). 3 (3.97 g, $17.48 \mathrm{mmol}, 1.0 \mathrm{eq}$.$) and urea$ ( $5.25 \mathrm{~g}, 87.51 \mathrm{mmol}, 5.0$ eq.) were ground in a mortar and put in a 100 mL -flask. The mixture was then heated at $220^{\circ} \mathrm{C}$ in a preheated bath. After $30 \mathrm{~min}, 60 \mathrm{~mL}$ 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 $(60 \mathrm{~mL}), \mathrm{DCM}(60 \mathrm{~mL})$ and acetone $(2 \times 60 \mathrm{~mL})$ to afford 6 $(2.76 \mathrm{~g}, 58 \%)$ as a white solid. Rf (DCM/MeOH: 95/5): 0.22. $M_{\mathrm{p}}$ : $>260{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 3294,3091,2941,1644$, $1455,1340,1102,750 .{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{DMSO}-d_{6}$ ) $\delta: 1.31-$ $1.41(\mathrm{~m}, 1 \mathrm{H}, \mathrm{CH}), 1.43-1.56(\mathrm{~m}, 2 \mathrm{H}, 2 \mathrm{xCH}), 1.56-1.64(\mathrm{~m}, 1 \mathrm{H}$, $\mathrm{CH}), 1.70-1.81(\mathrm{~m}, 1 \mathrm{H}, \mathrm{N}-\mathrm{CH}), 2.27\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{CH}_{3}\right), 2.52-2.61(\mathrm{~m}$, $3 \mathrm{H}, 2 \mathrm{xN}-\mathrm{CH}, \mathrm{CH}), 2.69-2.80(\mathrm{~m}, 1 \mathrm{H}, \mathrm{N}-\mathrm{CH}), 4.78(\mathrm{~s}, 1 \mathrm{H}, \mathrm{NH}-$ $\mathrm{CH}), 6.91(\mathrm{~s}, 1 \mathrm{H}, \mathrm{NH}), 7.13\left(\mathrm{dd}, J=9.0,10.4 \mathrm{~Hz}, 4 \mathrm{H}, 4 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $8.31(\mathrm{~s}, 1 \mathrm{H}, \mathrm{NH}) .{ }^{13} \mathrm{C}$ NMR ( $\left.101 \mathrm{MHz}, \mathrm{DMSO}-d_{6}\right) \delta: 20.6\left(\mathrm{CH}_{3}\right)$, $27.8(\mathrm{CH}), 28.6\left(\mathrm{CH}_{2}\right), 28.7\left(\mathrm{CH}_{2}\right), 49.8\left(\mathrm{~N}-\mathrm{CH}_{2}\right), 50.0\left(\mathrm{~N}-\mathrm{CH}_{2}\right)$,
$57.6(\mathrm{CH}), 118.4\left(\mathrm{C}_{\mathrm{q}}\right), 126.6\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 128.6\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 136.0\left(\mathrm{C}_{\mathrm{q}}\right)$, $137.0\left(\mathrm{C}_{\mathrm{q}}\right), 141.5\left(\mathrm{C}_{\mathrm{q}}\right), 152.4\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): m/z calculated for $\mathrm{C}_{16} \mathrm{H}_{20} \mathrm{~N}_{3} \mathrm{O}: 270.1601[\mathrm{M}+\mathrm{H}]^{+}$; found: 270.1596 .

4-(4-Fluorophenyl)-3,4,7,8-tetrahydro-1H-5,8-ethanopyrido[3,2-d]pyrimidin-2( $6 H$ )-one (7). $4(2.0 \mathrm{~g}, 8 . \mathrm{mmol}, 1.0 \mathrm{eq}$.$) and urea$ ( $2.60 \mathrm{~g}, 43.42 \mathrm{mmol}, 5.0$ eq.) were ground in a mortar and put in a 50 mL -flask. The mixture was then heated at $220^{\circ} \mathrm{C}$ in a preheated bath. After $30 \mathrm{~min}, 30 \mathrm{~mL}$ 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 $(30 \mathrm{~mL})$, DCM $(30 \mathrm{~mL})$ and acetone $(2 \times 30 \mathrm{~mL})$ to afford 7 $(1.40 \mathrm{~g}, 59 \%)$ as a white solid. $\mathrm{Rf}(\mathrm{DCM} / \mathrm{MeOH}: 95 / 5): 0.19 . M_{\mathrm{p}}$ : 258-260 ${ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 3302,3093,2945,1638$, $1505,1221,1155,1098,748 .{ }^{1} \mathrm{H}$ NMR ( 400 MHz, DMSO- $d_{6}$ ) $\delta$ : $1.31-1.43(\mathrm{~m}, 1 \mathrm{H}, \mathrm{CH}), 1.44-1.53(\mathrm{~m}, 2 \mathrm{H}, 2 \mathrm{xCH}), 1.53-1.66(\mathrm{~m}$, $1 \mathrm{H}, \mathrm{CH}), 1.72(\mathrm{tt}, J=3.3,12.8 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{N}-\mathrm{CH}), 2.52-2.63(\mathrm{~m}, 3 \mathrm{H}$, $2 \mathrm{xN}-\mathrm{CH}, \mathrm{CH}), 2.70-2.81(\mathrm{~m}, 1 \mathrm{H}, \mathrm{N}-\mathrm{CH}), 4.85(\mathrm{~s}, 1 \mathrm{H}, \mathrm{NH}-\mathrm{CH})$, $7.00(\mathrm{~s}, 1 \mathrm{H}, \mathrm{NH}), 7.14\left(\mathrm{t}, J=8.7 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.29(\mathrm{dd}, J=$ $5.6,8.4 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}$ ) , $8.37(\mathrm{~s}, 1 \mathrm{H}, \mathrm{NH}) .{ }^{13} \mathrm{C}$ NMR ( 101 MHz , DMSO- $\left.d_{6}\right) \delta: 27.8(\mathrm{CH}), 28.6\left(2 \mathrm{xCH}_{2}\right), 49.8\left(\mathrm{~N}-\mathrm{CH}_{2}\right), 50.0(\mathrm{~N}-$ $\left.\mathrm{CH}_{2}\right), 57.1(\mathrm{CH}), 114.6\left(\mathrm{CH}_{\mathrm{Ar}}\right), 114.8\left(\mathrm{CH}_{\mathrm{Ar}}\right), 118.1\left(\mathrm{C}_{\mathrm{q}}\right), 128.5$ $\left(\mathrm{CH}_{\mathrm{Ar}}\right), 128.6\left(\mathrm{CH}_{\mathrm{Ar}}\right), 137.3\left(\mathrm{C}_{\mathrm{q}}\right), 140.6\left(\mathrm{~d}, J=2.9 \mathrm{~Hz}, \mathrm{C}_{\mathrm{q}}\right), 152.3$ $\left(\mathrm{C}_{\mathrm{q}}\right), 161.3\left(\mathrm{~d}, J=242.4 \mathrm{~Hz}, \mathrm{C}_{\mathrm{Ar}}-\mathrm{F}\right) .{ }^{19} \mathrm{~F}$ NMR (376 MHz, DMSO$\left.d_{6}\right) \delta:-115.92$. HRMS (EI/MS): $m / z$ calculated for $\mathrm{C}_{15} \mathrm{H}_{17} \mathrm{FN}_{3} \mathrm{O}$ : $274.1350[\mathrm{M}+\mathrm{H}]^{+}$; found: 274.1350 .

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

4-(p-Tolyl)-7,8-dihydro-1H-5,8-ethanopyrido[3,2-d]pyrimidin$2(6 H)$-one (9). In a microwave vial of $10-20 \mathrm{~mL}, \mathrm{MnO}_{2}(1.11 \mathrm{~g}$, $12.8 \mathrm{mmol}, 10.0$ eq.) was added to a solution of $6(331 \mathrm{mg}$, $1.2 \mathrm{mmol}, 1.0$ eq.) in acetone ( 18 mL ). The reaction mixture was heated for 2 h at $100{ }^{\circ} \mathrm{C}$ under microwave irradiation. The reaction mixture was filtered through celite and washed with acetone $(20 \mathrm{~mL})$, DCM $(20 \mathrm{~mL})$ and $\mathrm{MeOH}(20 \mathrm{~mL})$. The solvents were evaporated to give $9(225 \mathrm{mg}, 69 \%)$ as a white solid without further purification. Rf (DCM/MeOH: 95/5): 0.27. $M_{\mathrm{p}}$ : $>260{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 2963,2942,2869,1710,1633,1449$, $1357,803,746 .{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{DMSO}-d_{6}$ ) $\delta: 1.68-1.80(\mathrm{~m}$, $\left.2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.02-2.13\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.41\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{CH}_{3}\right), 2.68-2.79$ $\left(\mathrm{m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.10-3.21\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.25(\mathrm{p}, J=2.6 \mathrm{~Hz}$, $1 \mathrm{H}, \mathrm{CH}), 7.40\left(\mathrm{~d}, J=8.0 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.72(\mathrm{~d}, J=8.2 \mathrm{~Hz}, 2 \mathrm{H}$,
$2 \mathrm{xCH}_{\mathrm{Ar}}$ ). ${ }^{13} \mathrm{C}$ NMR ( 101 MHz, DMSO- $d_{6}$ ) $\delta: 21.2\left(\mathrm{CH}_{3}\right), 25.3$ $\left(2 \mathrm{xCH}_{2}\right), 30.7(\mathrm{CH}), 48.8\left(2 \mathrm{xN}-\mathrm{CH}_{2}\right), 115.2(\mathrm{q}, J=288.7 \mathrm{~Hz}, \mathrm{TFA})$, $124.0\left(\mathrm{C}_{\mathrm{q}}\right), 124.6\left(\mathrm{C}_{\mathrm{q}}\right), 129.2\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.5\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 143.5\left(\mathrm{C}_{\mathrm{q}}\right)$, $149.5\left(\mathrm{C}_{\mathrm{q}}\right), 156.6\left(\mathrm{C}_{\mathrm{q}}\right), 158.5(\mathrm{q}, J=38.1 \mathrm{~Hz}, \mathrm{TFA}), 177.9(\mathrm{C}=\mathrm{O})$. HRMS (EI/MS): m/z calculated for $\mathrm{C}_{16} \mathrm{H}_{18} \mathrm{~N}_{3} \mathrm{O}: 268.1444$ [M + $\mathrm{H}]^{+}$; found: 268.1448.

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

General procedure B: $\mathbf{S}_{\boldsymbol{N}} \mathrm{Ar}$ via PyBroP activation. In a microwave vial, to a solution of $\mathbf{8}(200 \mathrm{mg}, 0.79 \mathrm{mmol}, 1.0 \mathrm{eq}$. and PyBroP ( $446 \mathrm{mg}, 0.96 \mathrm{mmol}, 1.2 \mathrm{eq}$.) in 1,4-dioxane ( 8 mL ) was added $\mathrm{Et}_{3} \mathrm{~N}$ ( $0.32 \mathrm{~mL}, 2.36 \mathrm{mmol}, 3.0 \mathrm{eq}$.). The mixture was then degassed by argon bubbling for 15 minutes. The sealed tube was heated at $100{ }^{\circ} \mathrm{C}$ for 3 h . After cooling, the corresponding amine ( 2.2 eq.) was added, and the reaction mixture was heated at $100{ }^{\circ} \mathrm{C}$ 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 $\mathbf{B}$ using propylamine $(0.14 \mathrm{~mL}$, $1.73 \mathrm{mmol}, 2.2$ eq.). After purification by silica gel flash chromatography ( $\mathrm{PE} / \mathrm{EA}, 70 / 30$ ), 11 ( $167 \mathrm{mg}, 72 \%$ ) was obtained as a white solid. $\mathrm{R} f(\mathrm{PE} / \mathrm{EA}: 70 / 30): 0.37 . M_{\mathrm{p}}: 149-151{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 3264,3115,2955,2869,1596,1360,1131$, $770,687,626 .{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 1.01(\mathrm{t}, J=7.4 \mathrm{~Hz}$, $\left.3 \mathrm{H}, \mathrm{CH}_{3}\right), 1.67\left(\mathrm{~h}, J=7.0 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 1.71-1.81\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right)$, $1.90-2.02\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.72\left(\mathrm{td}, J=4.7,11.2 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right)$, $3.04(\mathrm{p}, J=3.0 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 3.104-3.21\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.47(\mathrm{q}$, $\left.J=6.6 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 5.03(\mathrm{t}, J=5.8 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{NH}), 7.36-7.49(\mathrm{~m}$, $3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}$ ), $8.25\left(\mathrm{~d}, J=7.2 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C}$ NMR ( 101 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 11.7\left(\mathrm{CH}_{3}\right), 23.1\left(\mathrm{CH}_{2}\right), 27.8\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH})$, $43.7\left(\mathrm{CH}_{2}\right), 49.4\left(2 \mathrm{xN}-\mathrm{CH}_{2}\right), 128.1\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.5\left(\mathrm{CH}_{\mathrm{Ar}}\right), 129.8$ $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 131.4\left(\mathrm{C}_{\mathrm{q}}\right), 136.7\left(\mathrm{C}_{\mathrm{q}}\right), 155.6\left(\mathrm{C}_{\mathrm{q}}\right), 160.1\left(\mathrm{C}_{\mathrm{q}}\right), 175.6\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): $m / z$ calculated for $\mathrm{C}_{18} \mathrm{H}_{23} \mathrm{~N}_{4}: 295.1916[\mathrm{M}+\mathrm{H}]^{+}$; 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 $\mathbf{B}$ using amylamine $(0.20 \mathrm{~mL}$, $1.71 \mathrm{mmol}, 2.2$ eq.). After purification by silica gel flash chromatography (PE/EA, 70/30), 12 ( $150 \mathrm{mg}, 59 \%$ ) was obtained as a white solid. Rf (PE/AE: 70/30): 0.38. $M_{\mathrm{p}}: 138-140^{\circ} \mathrm{C}$. IR (ATR diamond, $\left.\mathrm{cm}^{-1}\right) \nu: 3256,2947,2867,1569,1359,1130,773,688$, 625. ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 0.92\left(\mathrm{t}, J=6.8 \mathrm{~Hz}, 3 \mathrm{H}, \mathrm{CH}_{3}\right)$, 1.31-1.47 (m, 4H, CH $)_{2}$, $1.66\left(\mathrm{q}, J=7.1 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{CH}_{2} \mathrm{CH}_{2} \mathrm{CH}_{2}{ }^{-}\right.$ $\left.\mathrm{CH}_{2} \mathrm{CH}_{3}\right), 1.69-1.81\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 1.90-2.02\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.72$ $\left(\operatorname{td}, J=5.0,11.4 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.04(\mathrm{p}, J=3.1 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH})$, $3.09-3.21\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.49\left(\mathrm{q}, J=6.6 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 5.02(\mathrm{t}, J$ $=5.7 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{NH}), 7.36-7.49\left(\mathrm{~m}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.25(\mathrm{~d}, J=$ $\left.7.1 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 14.2\left(\mathrm{CH}_{3}\right)$, $22.6\left(\mathrm{CH}_{2}\right), 27.8\left(2 \mathrm{XCH}_{2}\right), 29.3\left(\mathrm{CH}_{2}\right), 29.6\left(\mathrm{CH}_{2}\right), 33.7(\mathrm{CH}), 41.9$ $\left(\mathrm{CH}_{2}\right), 49.4\left(2 \mathrm{xN}^{2} \mathrm{CH}_{2}\right), 128.1\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.5\left(\mathrm{CH}_{\mathrm{Ar}}\right), 129.8$ $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 131.3\left(\mathrm{C}_{\mathrm{q}}\right), 136.7\left(\mathrm{C}_{\mathrm{q}}\right), 155.5\left(\mathrm{C}_{\mathrm{q}}\right), 160.0\left(\mathrm{C}_{\mathrm{q}}\right), 175.6\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): $m / z$ calculated for $\mathrm{C}_{20} \mathrm{H}_{27} \mathrm{~N}_{4}: 323.2230[\mathrm{M}+\mathrm{H}]^{+}$; 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 $(0.17 \mathrm{~mL}, 1.71 \mathrm{mmol}$, 2.2 eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), 13 ( $195 \mathrm{mg}, 77 \%$ ) was obtained as a white solid. Rf (PE/EA: 90/10): 0.41. $M_{\mathrm{p}}$ : 207-209 ${ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\left.\mathrm{cm}^{-1}\right) \nu: 2939,2863,1571,1503,1386,1290,776,694$, 624. ${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 1.60-1.69\left(\mathrm{~m}, 6 \mathrm{H}, 3 \mathrm{xCH}_{2}\right)$, 1.70-1.82 (m, 2H, CH 2 ), 1.89-2.01 (m, 2H, CH 2 ), $2.71(\mathrm{td}, J=4.8$, $\left.11.2 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.07(\mathrm{p}, J=3.1 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 3.10-3.21(\mathrm{~m}$, $\left.2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.87\left(\mathrm{t}, J=4.9 \mathrm{~Hz}, 4 \mathrm{H}, 2 \mathrm{xN}-\mathrm{CH}_{2}\right), 7.36-7.48(\mathrm{~m}, 3 \mathrm{H}$, $3 \mathrm{xCH}_{\mathrm{Ar}}$ ), $8.25-8.32\left(\mathrm{~m}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C}$ NMR $\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right)$ $\delta: 25.1\left(\mathrm{CH}_{2}\right), 26.0\left(2 \mathrm{xCH}_{2}\right), 27.7\left(2 \mathrm{xCH}_{2}\right), 33.9(\mathrm{CH}), 45.19$ $\left(2 \mathrm{xCH}_{2}\right), 49.5\left(2 \mathrm{xN}-\mathrm{CH}_{2}\right), 128.05\left(\mathrm{CH}_{\mathrm{Ar}}\right), 129.4\left(\mathrm{CH}_{\mathrm{Ar}}\right), 129.91$ $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.1\left(\mathrm{C}_{\mathrm{q}}\right), 137.1\left(\mathrm{C}_{\mathrm{q}}\right), 154.9\left(\mathrm{C}_{\mathrm{q}}\right), 159.6\left(\mathrm{C}_{\mathrm{q}}\right), 175.2\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): $m / z$ calculated for $\mathrm{C}_{20} \mathrm{H}_{25} \mathrm{~N}_{4}: 321.2074[\mathrm{M}+\mathrm{H}]^{+}$; found: 321.2070 .

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

4-(4-Phenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2yl)thiomorpholine (15). Compound 15 was obtained according to the general procedure $\mathbf{B}$ using thiomorpholine ( 0.17 mL ,
$1.68 \mathrm{mmol}, 2.2 \mathrm{eq}$.$) . After purification by silica gel flash chro-$ matography (PE/EA, 90/10), 15 ( $193 \mathrm{mg}, 72 \%$ ) was obtained as a white solid. Rf (PE/EA: 90/10): 0.36. $M_{\mathrm{p}}: 211-213{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu:$ 2951, 2926, 1555, 1481, 1387, 1258, 771, 696, $624 .{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 1.72-1.83\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 1.93-$ $2.05\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.68-2.80\left(\mathrm{~m}, 6 \mathrm{H}, 2 \mathrm{xS}^{2}-\mathrm{CH}_{2}, \mathrm{~N}-\mathrm{CH}_{2}\right), 3.09(\mathrm{p}, J$ $=3.0 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 3.13-3.24\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 4.24-4.30(\mathrm{~m}, 4 \mathrm{H}$, $\left.\mathrm{CH}_{2}-\mathrm{N}\right), 7.39-7.51\left(\mathrm{~m}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.27-8.36\left(\mathrm{~m}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right)$. ${ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 27.2\left(2 \mathrm{x} \mathrm{S}^{2}-\mathrm{CH}_{2}\right), 27.9\left(2 \mathrm{xCH}_{2}\right), 33.8$ $(\mathrm{CH}), 46.6\left(2 \mathrm{xCH}_{2}-\mathrm{N}\right), 49.4\left(2 \mathrm{xN}^{2}-\mathrm{CH}_{2}\right), 128.0\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.6$ $\left(\mathrm{CH}_{\mathrm{Ar}}\right), 129.8\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.9\left(\mathrm{C}_{\mathrm{q}}\right), 136.8\left(\mathrm{C}_{\mathrm{q}}\right), 155.0\left(\mathrm{C}_{\mathrm{q}}\right), 158.9$ $\left(\mathrm{C}_{\mathrm{q}}\right), 175.56\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): m/z calculated $\mathrm{C}_{19} \mathrm{H}_{23} \mathrm{~N}_{4} \mathrm{~S}$ : $339.1638[\mathrm{M}+\mathrm{H}]^{+}$; found: 339.1637.

2-(4,4-Difluoropiperidin-1-yl)-4-phenyl-7,8-dihydro-6H-5,8-etha-nopyrido[3,2-d]pyrimidine (16). Compound 16 was obtained according to the general procedure $\mathbf{B}$ using 4,4-difluoropiperidine hydrochloride ( $271 \mathrm{mg}, 1.72 \mathrm{mmol}, 2.2$ eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), 16 ( $172 \mathrm{mg}, 61 \%$ ) was obtained as a white solid. Rf (PE/EA: 90/10): $0.32 . M_{\mathrm{p}}: 212-214{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 2954,2871$, 1568, 1489, 1356, 1108, 1048, 777, 690, 624, 511. ${ }^{1} \mathrm{H}$ NMR (400 $\mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 1.61-1.85\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 1.83-2.23(\mathrm{~m}, 6 \mathrm{H}$, $3 \mathrm{xCH}_{2}$ ), $2.72\left(\mathrm{td}, J=5.1,11.5 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.09(\mathrm{p}, J=3.1 \mathrm{~Hz}$, $1 \mathrm{H}, \mathrm{CH}), 3.12-3.23\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 4.07(\mathrm{t}, J=5.8 \mathrm{~Hz}, 4 \mathrm{H}, 2 \mathrm{xN}-$ $\mathrm{CH}_{2}$ ), $7.27-7.57\left(\mathrm{~m}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.29(\mathrm{~d}, J=7.8 \mathrm{~Hz}, 2 \mathrm{H}$, $\left.2 \mathrm{xCH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C}$ NMR $\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 27.8\left(2 \mathrm{xCH}_{2}\right), 33.8(\mathrm{CH})$, $34.0\left(\mathrm{t}, J=22.6 \mathrm{~Hz}, 2 \mathrm{xCH}_{2}-\mathrm{CF}_{2}\right), 41.3\left(\mathrm{t}, J=5.2 \mathrm{~Hz}, 2 \mathrm{xN}^{2}-\mathrm{CH}_{2}\right)$, $49.3\left(2 \mathrm{xN}^{2}-\mathrm{CH}_{2}\right), 122.8\left(\mathrm{t}, J=241.7 \mathrm{~Hz}, \mathrm{CF}_{2}\right), 128.1\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $129.7\left(\mathrm{CH}_{\mathrm{Ar}}\right), 129.9\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 131.4\left(\mathrm{C}_{\mathrm{q}}\right), 136.7\left(\mathrm{C}_{\mathrm{q}}\right), 155.1\left(\mathrm{C}_{\mathrm{q}}\right)$, $158.8\left(\mathrm{C}_{\mathrm{q}}\right), 175.7\left(\mathrm{C}_{\mathrm{q}}\right) .{ }^{19} \mathrm{~F}$ NMR ( $376 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta:-96.89$. HRMS (EI/MS): m/z calculated $\mathrm{C}_{20} \mathrm{H}_{23} \mathrm{~F}_{2} \mathrm{~N}_{4}: 357.1885[\mathrm{M}+\mathrm{H}]^{+}$; found: 357.1886.
$N$-Benzyl-4-phenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d] pyrimidin-2-amine (17)

Compound 17 was obtained according to the general procedure B using benzylamine ( $0.19 \mathrm{~mL}, 1.73 \mathrm{mmol}, 2.2 \mathrm{eq}$.). After purification by silica gel flash chromatography (PE/EA, 60/ 40), 17 ( $141 \mathrm{mg}, 51 \%$ ) was obtained as a white solid. Rf (PE/EA: $70 / 30$ ): $0.45 . M_{\mathrm{p}}: 182-184^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 3252$, 3084, 2940, 2869, 1570, 1543, 1347, 1133, 774, 689, 626. ${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 1.69-1.82(\mathrm{~m}, 2 \mathrm{H}), 1.92-2.03(\mathrm{~m}, 2 \mathrm{H}), 2.73$ $(\mathrm{td}, J=5.1,11.4 \mathrm{~Hz}, 2 \mathrm{H}), 3.06(\mathrm{p}, J=3.1 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 3.11-3.22$ $(\mathrm{m}, 2 \mathrm{H}), 4.73\left(\mathrm{~d}, J=5.8 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{NH}-\mathrm{CH}_{2}\right), 5.35(\mathrm{t}, J=5.7 \mathrm{~Hz}, 1 \mathrm{H}$, NH ), $7.27\left(\mathrm{t}, J=7.3 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right), 7.34(\mathrm{t}, J=7.4 \mathrm{~Hz}, 2 \mathrm{H}$, $2 \mathrm{xCH}_{\mathrm{Ar}}$ ), $7.39-7.48\left(\mathrm{~m}, 5 \mathrm{H}, 5 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.26(\mathrm{~d}, J=8.1 \mathrm{~Hz}, 2 \mathrm{H}$, $\left.2 \mathrm{xCH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C}$ NMR $\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 27.8\left(2 \mathrm{XCH}_{2}\right), 33.7(\mathrm{CH})$, $46.0\left(\mathrm{NH}-\mathrm{CH}_{2}\right), 49.4\left(2 \mathrm{xN}^{2}-\mathrm{CH}_{2}\right), 127.2\left(\mathrm{CH}_{\mathrm{Ar}}\right), 127.8\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $128.1\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 128.6\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.6\left(\mathrm{CH}_{\mathrm{Ar}}\right), 129.9\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $131.9\left(\mathrm{C}_{\mathrm{q}}\right), 136.6\left(\mathrm{C}_{\mathrm{q}}\right), 139.9\left(\mathrm{C}_{\mathrm{q}}\right), 159.7\left(\mathrm{C}_{\mathrm{q}}\right), 175.9\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): m/z calculated $\mathrm{C}_{22} \mathrm{H}_{23} \mathrm{~N}_{4}$ : $343.1917[\mathrm{M}+\mathrm{H}]^{+}$; 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 $\mathbf{B}$ using 4-methoxybenzylamine ( $0.23 \mathrm{~mL}, 1.75 \mathrm{mmol}, 2.2 \mathrm{eq}$.). 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): $0.26 . M_{\mathrm{p}}$ :
$204-206{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 3252,2945,1595,1569$, 1544, 1509, 1242, 1172, 1031, 808, 690. ${ }^{1} \mathrm{H}$ NMR ( 400 MHz , $\left.\mathrm{CDCl}_{3}\right) \delta: 1.68-1.81\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 1.91-2.03\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.66-$ $2.79\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.06(\mathrm{p}, J=2.9 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 3.11-3.22(\mathrm{~m}$, $\left.2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.80\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{OCH}_{3}\right), 4.65(\mathrm{~d}, J=5.7 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{NH}-$ $\left.\mathrm{CH}_{2}\right), 5.32\left(\mathrm{t}, J=5.8 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{NH}-\mathrm{CH}_{2}\right), 6.88(\mathrm{dt}, J=3.0,8.8 \mathrm{~Hz}$, $\left.2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.35\left(\mathrm{dt}, J=2.6,8.8 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.39-7.48(\mathrm{~m}$, $3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}$ ), 8.27 (dd, $J=1.7,7.8 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}$ ). ${ }^{13} \mathrm{C}$ NMR $\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 27.8\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH}), 45.5\left(\mathrm{NH}-\mathrm{CH}_{2}\right)$, $49.4\left(2 \mathrm{xN}^{2} \mathrm{CH}_{2}\right), 55.4\left(\mathrm{CH}_{3}\right), 114.0\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 128.1\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.1$ $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.6\left(\mathrm{CH}_{\mathrm{Ar}}\right), 129.9\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 131.8\left(\mathrm{C}_{\mathrm{q}}\right), 131.9\left(\mathrm{C}_{\mathrm{q}}\right)$, $136.6\left(\mathrm{C}_{\mathrm{q}}\right), 158.9\left(\mathrm{C}_{\mathrm{q}}\right), 159.7\left(\mathrm{C}_{\mathrm{q}}\right), 175.8\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): m/z calculated for $\mathrm{C}_{23} \mathrm{H}_{25} \mathrm{~N}_{4} \mathrm{O}$ : $373.2023[\mathrm{M}+\mathrm{H}]^{+}$; found: 373.2020.

4-Phenyl-N-(4-(trifluoromethyl)benzyl)-7,8-dihydro-6H-5,8-etha-nopyrido[3,2-d]pyrimidin-2-amine (19). Compound 19 was obtained according to the general procedure $\mathbf{B}$ using 4(trifluoromethyl)benzylamine ( $0.25 \mathrm{~mL}, 1.75 \mathrm{mmol}, 2.2 \mathrm{eq}$.$) .$ After purification by silica gel flash chromatography (PE/EA, 80/ 20 to 70/30), 19 ( $129 \mathrm{mg}, 39 \%$ ) was obtained as a white solid. Rf (PE/EA: 70/30): 0.25. $M_{\mathrm{p}}$ : 180-182 ${ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu$ : 3255, 2948, 1566, 1326, 1112, 1061, 691. ${ }^{1} \mathrm{H}$ NMR ( 400 MHz , $\left.\mathrm{CDCl}_{3}\right) \delta: 1.67-1.81\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 1.92-2.04\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.66-$ $2.79\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.05(\mathrm{p}, J=3.0 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 3.11-3.22(\mathrm{~m}$, $\left.2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 4.79\left(\mathrm{~d}, J=6.1 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{NH}-\mathrm{CH}_{2}\right), 5.52(\mathrm{t}, J=6.1 \mathrm{~Hz}$, $1 \mathrm{H}, \mathrm{NH}), 7.37-7.47\left(\mathrm{~m}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.53(\mathrm{~d}, J=8.1 \mathrm{~Hz}, 2 \mathrm{H}$, $2 \mathrm{xCH}_{\mathrm{Ar}}$ ), $7.59\left(\mathrm{~d}, J=8.2 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.19-8.26(\mathrm{~m}, 2 \mathrm{H}$, $2 \mathrm{xCH}_{\mathrm{Ar}}$ ). ${ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 27.8\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH})$, $45.5\left(\mathrm{NH}-\mathrm{CH}_{2}\right), 49.3\left(2 \mathrm{xN}-\mathrm{CH}_{2}\right), 124.3\left(\mathrm{~d}, J=271.9 \mathrm{~Hz}, \mathrm{C}_{\mathrm{q}}-\mathrm{CF}_{3}\right)$, $125.5\left(\mathrm{q}, J=3.7 \mathrm{~Hz}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 127.8\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 128.1\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $129.4\left(\mathrm{~d}, J=32.2 \mathrm{~Hz}, \mathrm{CF}_{3}\right), 129.7\left(\mathrm{CH}_{\mathrm{Ar}}\right), 129.8\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 132.2$ $\left(\mathrm{C}_{\mathrm{q}}\right), 136.4\left(\mathrm{C}_{\mathrm{q}}\right), 144.3\left(\mathrm{C}_{\mathrm{q}}\right), 155.5\left(\mathrm{C}_{\mathrm{q}}\right), 159.5\left(\mathrm{C}_{\mathrm{q}}\right), 176.1\left(\mathrm{C}_{\mathrm{q}}\right) .{ }^{19} \mathrm{~F}$ NMR ( $376 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta:-62.37$. HRMS (EI/MS): $m / z$ calculated for $\mathrm{C}_{23} \mathrm{H}_{22} \mathrm{~F}_{3} \mathrm{~N}_{4}$ : $411.1791[\mathrm{M}+\mathrm{H}]^{+}$; 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 ( $123 \mathrm{mg}, 1.80 \mathrm{mmol}$, 2.2 eq.). After purification by silica gel flash chromatography (PE/EA, 70/30), 20 ( $55 \mathrm{mg}, 22 \%$ ) was obtained as a white solid. Rf (PE/EA: 70/30): $0.10 . M_{\mathrm{p}}: 198-200^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu$ : 2963, 2926, 2868, 1561, 1468, 1435, 1387, 1050, 691. ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 1.73-1.85\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.02-2.15(\mathrm{~m}, 2 \mathrm{H}$, $\left.\mathrm{CH}_{2}\right), 2.75\left(\mathrm{td}, J=5.1,11.6 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.21-3.32(\mathrm{~m}, 2 \mathrm{H}$, $\left.\mathrm{N}-\mathrm{CH}_{2}\right), 3.34(\mathrm{p}, J=3.1 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 7.18\left(\mathrm{~s}, 1 \mathrm{H}, \mathrm{CH}_{\text {imidazole }}\right)$, $7.51\left(\mathrm{dd}, J=2.5,4.5 \mathrm{~Hz}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.00\left(\mathrm{~s}, 1 \mathrm{H}, \mathrm{CH}_{\text {imidazole }}\right)$, 8.41-8.49 (m, 2H, $2 \mathrm{xCH}_{\mathrm{Ar}}$ ), $8.70\left(\mathrm{~s}, 1 \mathrm{H}, \mathrm{CH}_{\text {imidazole }}\right) .{ }^{13} \mathrm{C}$ NMR $\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 27.7\left(2 \mathrm{xCH}_{2}\right), 33.6(\mathrm{CH}), 48.8\left(2 \mathrm{xN}^{2}-\mathrm{CH}_{2}\right)$, $116.9\left(\mathrm{CH}_{\text {imidazole }}\right), 128.4\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.2\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.4$ $\left(\mathrm{CH}_{\text {imidazole }}\right), 130.8\left(\mathrm{CH}_{\text {Ar }}\right), 135.0\left(\mathrm{C}_{\mathrm{q}}\right), 136.4\left(\mathrm{CH}_{\text {imidazole }}\right), 138.9$ $\left(\mathrm{C}_{\mathrm{q}}\right), 151.3\left(\mathrm{C}_{\mathrm{q}}\right), 156.2\left(\mathrm{C}_{\mathrm{q}}\right), 177.7\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): m/z calculated for $\mathrm{C}_{18} \mathrm{H}_{18} \mathrm{~N}_{5}$ : $304.1557[\mathrm{M}+\mathrm{H}]^{+}$; 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 ( $214 \mathrm{mg}, 0.80 \mathrm{mmol}, 1.0 \mathrm{eq}$.) and piperidine ( $0.17 \mathrm{~mL}, 1.71 \mathrm{mmol}, 2.2 \mathrm{eq}$.). After purification by silica gel flash chromatography (PE/EA, 100/0 to 90/10), 23 ( $230 \mathrm{mg}, 86 \%$ ) was obtained as a light yellow solid. Rf ( $\mathrm{PE} / \mathrm{EA}$ : 90/10): 0.51. $M_{\mathrm{p}}: 186-188{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 2929$,

2848, 1589, 1564, 1549, 1496, 1385, 1291, 810. ${ }^{1} \mathrm{H}$ NMR (400 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 1.60-1.69\left(\mathrm{~m}, 6 \mathrm{H}, 3 \mathrm{xCH}_{2}\right), 1.69-1.79(\mathrm{~m}, 2 \mathrm{H}$, $\mathrm{CH}_{2}$ ), 1.90-1.99 (m, 2H, CH2), $2.39\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{CH}_{3}\right), 2.65-2.77(\mathrm{~m}$, $\left.2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.06(\mathrm{p}, J=3.0 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 3.09-3.20(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-$ $\mathrm{CH}_{2}$ ), 3.83-3.90 (m, $\left.4 \mathrm{H}, 2 \mathrm{xN}-\mathrm{CH}_{2}\right), 7.24(\mathrm{~d}, J=8.0 \mathrm{~Hz}, 2 \mathrm{H}$, $2 \mathrm{xCH}_{\mathrm{Ar}}$ ), $8.20\left(\mathrm{~d}, J=8.2 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C}$ NMR ( 101 MHz , $\left.\mathrm{CDCl}_{3}\right) \delta: 21.6\left(\mathrm{CH}_{3}\right), 25.1\left(\mathrm{CH}_{2}\right), 26.0\left(2 \mathrm{xCH}_{2}\right), 28.0\left(2 \mathrm{xCH}_{2}\right), 33.9$ (CH), $45.1\left(2 \mathrm{xN}^{2} \mathrm{CH}_{2}\right), 49.5\left(2 \mathrm{xN}^{2} \mathrm{CH}_{2}\right), 128.8\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.8$ $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.2\left(\mathrm{C}_{\mathrm{q}}\right), 134.4\left(\mathrm{C}_{\mathrm{q}}\right), 139.5\left(\mathrm{C}_{\mathrm{q}}\right), 154.9\left(\mathrm{C}_{\mathrm{q}}\right), 159.6\left(\mathrm{C}_{\mathrm{q}}\right)$, $175.0\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): $m / z$ calculated for $\mathrm{C}_{21} \mathrm{H}_{27} \mathrm{~N}_{4}$ : $335.2230[\mathrm{M}+\mathrm{H}]^{+}$; found: 355.2229.

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

General procedure C: Buchwald-Hartwig cross coupling via PyBroP activation. In a microwave vial, to an argon-degassed solution of 8 ( $253 \mathrm{mg}, 1.00 \mathrm{mmol}, 1.0$ eq.) and PyBroP ( $559 \mathrm{mg}, 1.20 \mathrm{mmol}, 1.2 \mathrm{eq}$. ) in 1,4-dioxane ( 10 mL ), was added $\mathrm{Et}_{3} \mathrm{~N}(0.40 \mathrm{~mL}, 2.96 \mathrm{mmol}, 3.0 \mathrm{eq}$.$) . The reaction was heated for$ 3 h at $100^{\circ} \mathrm{C}$. After cooling, $\mathrm{K}_{2} \mathrm{CO}_{3}(276 \mathrm{mg}, 2.00 \mathrm{mmol}, 2.0$ eq.), the required amine (1.5.0 eq.), $\operatorname{Pd}(\mathrm{OAc})_{2}(22 \mathrm{mg}, 0.10 \mathrm{mmol}, 0.1$ eq.) and Xantphos ( $116 \mathrm{mg}, 0.20 \mathrm{mmol}, 0.2 \mathrm{eq}$.) were added to the reaction mixture. The sealed tube was heated at $130{ }^{\circ} \mathrm{C}$ 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 $(2 \times 20 \mathrm{~mL})$, dried over $\mathrm{MgSO}_{4}$, 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 $\mathbf{C}$ using 2-piperidone ( 0.14 mL , $1.51 \mathrm{mmol}, 1.5 \mathrm{eq}$.$) . After purification by silica gel flash chro-$ matography (DCM/MeOH, 95-5), 22 ( $133 \mathrm{mg}, 40 \%$ ) was obtained as a light yellow solid. Rf (DCM/MeOH: 95/5): 0.43. $M_{\mathrm{p}}$ : $216-218{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 2943,1670,1562,1377$, $1153,838,776,696,624 .{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 1.79(\mathrm{~m}$, $\left.2 \mathrm{H}, \mathrm{CH}_{2}\right), 1.91-2.10\left(\mathrm{~m}, 6 \mathrm{H}, \mathrm{CH}_{2}, 2 \mathrm{xCH}_{2, \text { lactame }}\right), 2.63(\mathrm{t}, J=$ $\left.6.4 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{C}(\mathrm{O})-\mathrm{CH}_{2}\right), 2.73\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.17-3.28(\mathrm{~m}, 2 \mathrm{H}$, $\left.\mathrm{N}-\mathrm{CH}_{2}\right), 3.34(\mathrm{p}, J=2.9 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 3.97(\mathrm{t}, J=5.6 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{N}-$
$\mathrm{CH}_{2}$ ), $7.39-7.51\left(\mathrm{~m}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.25-8.39\left(\mathrm{~m}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C}$ NMR ( $\left.101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 21.4\left(\mathrm{CH}_{2}\right), 23.3\left(\mathrm{CH}_{2}\right), 27.7\left(2 \mathrm{xCH}_{2}\right)$, $33.5(\mathrm{CH}), 33.6(\mathrm{C}(\mathrm{O})-\mathrm{CH}), 48.8\left(2 \mathrm{xN}^{2} \mathrm{CH}_{2}\right), 49.2\left(\mathrm{~N}-\mathrm{CH}_{2}\right), 128.2$ $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.2\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.2\left(\mathrm{CH}_{\mathrm{Ar}}\right), 135.5\left(\mathrm{C}_{\mathrm{q}}\right), 138.3\left(\mathrm{C}_{\mathrm{q}}\right)$, $156.3\left(\mathrm{C}_{\mathrm{q}}\right), 157.7\left(\mathrm{C}_{\mathrm{q}}\right), 170.9(\mathrm{C}=\mathrm{O}), 176.5\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): $\mathrm{m} / \mathrm{z}$ calculated for $\mathrm{C}_{20} \mathrm{H}_{23} \mathrm{~N}_{4} \mathrm{O}$ : $335.1866[\mathrm{M}+\mathrm{H}]^{+}$; 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 ( $134 \mathrm{mg}, 1.57 \mathrm{mmol}$, 1.5 eq.). After purification by silica gel flash chromatography (EA/PE, 80/20 to 90/10), 25 ( $125 \mathrm{mg}, 39 \%$ ) was obtained as a light yellow solid. Rf (EA/PE: 90/10): 0.18. $M_{\mathrm{p}}$ : 211-213 ${ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\left.\mathrm{cm}^{-1}\right) \nu: 2942,1727,1557,1384,1350,1131,775,693$, 622. ${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 1.72-1.85\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 1.96-$ $2.08\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.14\left(\mathrm{p}, J=7.7 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.65-2.77(\mathrm{~m}$, $\left.4 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}, \mathrm{C}(\mathrm{O})-\mathrm{CH}_{2}\right), 3.16-3.27\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.36(\mathrm{p}, J=$ $2.9 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 4.18\left(\mathrm{t}, J=7.1 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 7.40-7.51(\mathrm{~m}$, $3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}$ ), 8.37-8.46 (m, 2H, $2 \mathrm{xCH}_{\mathrm{Ar}}$ ). ${ }^{13} \mathrm{C}$ NMR ( 101 MHz , $\left.\mathrm{CDCl}_{3}\right) \delta: 17.9\left(\mathrm{CH}_{2}\right), 27.7\left(2 \mathrm{xCH}_{2}\right), 33.6(\mathrm{CH}), 33.8\left(\mathrm{C}(\mathrm{O})-\mathrm{CH}_{2}\right)$, $48.6\left(\mathrm{~N}-\mathrm{CH}_{2}\right), 48.9\left(2 \mathrm{xN}^{2}-\mathrm{CH}_{2}\right), 128.3\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.2\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $130.3\left(\mathrm{CH}_{\text {Ar }}\right), 135.8\left(\mathrm{C}_{\mathrm{q}}\right), 136.9\left(\mathrm{C}_{\mathrm{q}}\right), 154.5\left(\mathrm{C}_{\mathrm{q}}\right), 155.2\left(\mathrm{C}_{\mathrm{q}}\right), 174.7$ $(\mathrm{C}=\mathrm{O}), 176.5\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): $\mathrm{m} / \mathrm{z}$ calculated for $\mathrm{C}_{19} \mathrm{H}_{21} \mathrm{~N}_{4}$ : $321.1711[\mathrm{M}+\mathrm{H}]^{+}$; 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 $(0.14 \mathrm{~mL}, 143 \mathrm{mg}, 1.53 \mathrm{mmol}, 1.5$ eq.). After purification by silica gel flash chromatography (PE/ EA, $90 / 10$ to $80 / 20$ ), 26 ( $186 \mathrm{mg}, 56 \%$ ) was obtained as a white solid. Rf (PE/EA: 80/20): 0.27. $M_{\mathrm{p}}$ : 191-193 ${ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\left.\mathrm{cm}^{-1}\right) \nu: 2956,1563,1529,1446,1424,1364,768,743$, 685. ${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 1.72-1.85\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 1.96-$ $2.08\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.69-2.82\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.12-3.26(\mathrm{~m}, 3 \mathrm{H}$, $\left.\mathrm{N}-\mathrm{CH}_{2}, \mathrm{CH}\right), 7.02(\mathrm{t}, J=7.4 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 7.20(\mathrm{~s}, 1 \mathrm{H}, \mathrm{NH}), 7.35$ $(\mathrm{t}, J=7.8 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}), 7.40-7.53\left(\mathrm{~m}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.74(\mathrm{~d}, J=$ $7.7 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}$ ), $8.33\left(\mathrm{dd}, J=1.8,8.0 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 27.8\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH}), 49.3(2 \mathrm{xN}-$ $\left.\mathrm{CH}_{2}\right), 118.8\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 122.0\left(\mathrm{CH}_{\mathrm{Ar}}\right), 128.2\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.0$ $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.9\left(\mathrm{CH}_{\mathrm{Ar}}\right), 130.0\left(2 \mathrm{XCH}_{\mathrm{Ar}}\right), 133.3\left(\mathrm{C}_{\mathrm{q}}\right), 136.3\left(\mathrm{C}_{\mathrm{q}}\right)$, $140.3\left(\mathrm{C}_{\mathrm{q}}\right), 155.6\left(\mathrm{C}_{\mathrm{q}}\right), 157.2\left(\mathrm{C}_{\mathrm{q}}\right), 176.0\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): m/z calculated for $\mathrm{C}_{21} \mathrm{H}_{21} \mathrm{~N}_{4}$ : $329.1761[\mathrm{M}+\mathrm{H}]^{+}$; 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 $(187 \mathrm{mg}$, $1.51 \mathrm{mmol}, 1.5 \mathrm{eq}$.$) . After purification by silica gel flash chro-$ matography (PE/EA, 90/10 to 80/20), 27 ( $173 \mathrm{mg}, 48 \%$ ) was obtained as a dark red solid. Rf (PE/EA: 80/20): 0.19. $M_{\mathrm{p}}$ : 223$225{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 3242,2920,1566,1508,1357$, $12369,1038,822,696,625 .{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 1.71-$ $1.83\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 1.94-2.07\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.68-2.81(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-$ $\mathrm{CH}_{2}$ ), 3.13 (p, $\left.J=2.9 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}\right), 3.15-3.25\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right)$, $3.81\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{CH}_{3}\right), 6.91\left(\mathrm{~d}, J=9.2 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.04(\mathrm{~s}, 1 \mathrm{H}$, $\mathrm{NH}), 7.39-7.51\left(\mathrm{~m}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.61\left(\mathrm{~d}, J=9.0 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right)$, 8.31 (dd, $J=1.6,7.9 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}$ ). ${ }^{13} \mathrm{C}$ NMR ( 101 MHz , $\left.\mathrm{CDCl}_{3}\right) \delta: 27.8\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH}), 49.3\left(2 \mathrm{xN}^{2} \mathrm{CH}_{2}\right), 55.7\left(\mathrm{CH}_{3}\right)$, $114.3\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 120.9\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 128.2\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.8\left(\mathrm{CH}_{\mathrm{Ar}}\right)$, $129.9\left(2 \mathrm{xCH}_{\text {ar }}\right), 132.9\left(\mathrm{C}_{\mathrm{q}}\right), 133.6\left(\mathrm{C}_{\mathrm{q}}\right), 136.6\left(\mathrm{C}_{\mathrm{q}}\right), 155.1\left(\mathrm{C}_{\mathrm{q}}\right)$,
$155.6\left(\mathrm{C}_{\mathrm{q}}\right), 157.5\left(\mathrm{C}_{\mathrm{q}}\right), 176.0\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): m/z calculated for $\mathrm{C}_{22} \mathrm{H}_{23} \mathrm{~N}_{4} \mathrm{O}: 359.1866[\mathrm{M}+\mathrm{H}]^{+}$; 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 $\mathbf{C}$ using $p$-toluidine ( $165 \mathrm{mg}, 1.54 \mathrm{mmol}$, 1.5 eq.). After purification by silica gel flash chromatography (PE/EA, 100/0 to 80/20), 21 ( $165 \mathrm{mg}, 48 \%$ ) was obtained as a light orange solid. Rf (PE/EA: 80/20): 0.20. $M_{\mathrm{p}}$ : 222-224 ${ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu$ : 3294, 2943, 2867, 1589, 1519, 1425, 1355, $780,698,624 .{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 1.72-1.83(\mathrm{~m}, 2 \mathrm{H}$, $\mathrm{CH}_{2}$ ), 1.95-2.07 (m, 2H, CH 2 ), $2.34\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{CH}_{3}\right), 2.69-2.81(\mathrm{~m}$, $\left.2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.11-3.25\left(\mathrm{~m}, 3 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}, \mathrm{CH}\right), 7.13(\mathrm{~s}, 1 \mathrm{H}, \mathrm{NH})$, $7.15\left(\mathrm{~d}, J=8.2 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.40-7.52\left(\mathrm{~m}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.61$ (d, $J=8.4 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}$ ), $8.32\left(\mathrm{dd}, J=1.7,8.0 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right.$ ). ${ }^{13} \mathrm{C}$ NMR ( $\left.101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 20.9\left(\mathrm{CH}_{3}\right), 27.8\left(2 \mathrm{XCH}_{2}\right), 33.7$
 $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.8\left(\mathrm{CH}_{\mathrm{Ar}}\right), 129.9\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 131.5\left(\mathrm{C}_{\mathrm{q}}\right), 133.1\left(\mathrm{C}_{\mathrm{q}}\right)$, $136.4\left(\mathrm{C}_{\mathrm{q}}\right), 137.7\left(\mathrm{C}_{\mathrm{q}}\right), 155.6\left(\mathrm{C}_{\mathrm{q}}\right), 157.3\left(\mathrm{C}_{\mathrm{q}}\right), 175.9\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): $m / z$ calculated for $\mathrm{C}_{22} \mathrm{H}_{23} \mathrm{~N}_{4}: 343.1917[\mathrm{M}+\mathrm{H}]^{+}$; 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 $\mathbf{C}$ using $m$-toluidine $(0.16 \mathrm{~mL}$, $1.47 \mathrm{mmol}, 1.5 \mathrm{eq}$.$) . After purification by silica gel flash chro-$ matography (DCM/PE, 80/20), 28 ( $106 \mathrm{mg}, 31 \%$ ) was obtained as a light yellow solid. Rf (DCM/PE: 80/20): $0.14 . M_{\mathrm{p}}: 230-232^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 3226,2940,1562,1531,1488,1422$, $1357,1165,770,690,625 .{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 1.73-$ $1.85\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 1.96-2.08\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.38\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{CH}_{3}\right)$, 2.69-2.82 (m, 2H, N-CH2), 3.13-3.26 (m, 3H, N-CH, CH$), 6.84$ $\left(\mathrm{d}, J=7.4 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right), 7.12(\mathrm{~s}, 1 \mathrm{H}, \mathrm{NH}), 7.23(\mathrm{t}, J=7.8 \mathrm{~Hz}, 1 \mathrm{H}$, $\mathrm{CH}_{\mathrm{Ar}}$ ), $7.40-7.51\left(\mathrm{~m}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.54\left(\mathrm{~s}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right), 7.58(\mathrm{dd}, J$ $\left.=8.1,2.2 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right), 8.31-8.38\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C}$ NMR ( 101 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 21.8\left(\mathrm{CH}_{3}\right), 27.8\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH}), 49.3(2 \mathrm{xN}-$ $\left.\mathrm{CH}_{2}\right), 115.9\left(\mathrm{CH}_{\mathrm{Ar}}\right), 119.5\left(\mathrm{CH}_{\mathrm{Ar}}\right), 122.9\left(\mathrm{CH}_{\mathrm{Ar}}\right), 128.2\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $128.8\left(\mathrm{CH}_{\mathrm{Ar}}\right), 129.9\left(\mathrm{CH}_{\mathrm{Ar}}\right), 130.0\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 133.2\left(\mathrm{C}_{\mathrm{q}}\right), 136.4\left(\mathrm{C}_{\mathrm{q}}\right)$, $138.7\left(\mathrm{C}_{\mathrm{q}}\right), 140.2\left(\mathrm{C}_{\mathrm{q}}\right), 155.5\left(\mathrm{C}_{\mathrm{q}}\right), 157.2\left(\mathrm{C}_{\mathrm{q}}\right), 176.0\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): $m / z$ calculated for $\mathrm{C}_{22} \mathrm{H}_{23} \mathrm{~N}_{4}: 343.1917[\mathrm{M}+\mathrm{H}]^{+}$; 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 $\mathbf{C}$ using o-toluidine $(0.10 \mathrm{~mL}$, $1.46 \mathrm{mmol}, 1.5$ eq.). After purification by silica gel flash chromatography (DCM/PE, 70/30 to 80/20), 29 ( $54 \mathrm{mg}, 15 \%$ ) was obtained as a beige solid. Rf (DCM/PE: 70/30): 0.16. $M_{\mathrm{p}}$ : 208$210^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 3212,2946,1564,1529,1361$, $744,684,625 .{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 1.72-1.85(\mathrm{~m}, 2 \mathrm{H}$, $\mathrm{CH}_{2}$ ), 1.96-2.07 (m, 2H, CH 2 ), $2.37\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{CH}_{3}\right), 2.70-2.82(\mathrm{~m}$, $\left.2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.11-3.26\left(\mathrm{~m}, 3 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}, \mathrm{CH}\right), 6.88(\mathrm{~s}, 1 \mathrm{H}, \mathrm{NH})$, $6.99\left(\mathrm{td}, J=7.4,1.3 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right), 7.21\left(\mathrm{~d}, J=7.3 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right)$, $7.27\left(\mathrm{td}, J=7.8,1.6 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right), 7.39-7.51\left(\mathrm{~m}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right)$, 8.29-8.36 (m, 3H, $2 \mathrm{xCH}_{\mathrm{Ar}}, \mathrm{CH}_{\mathrm{Ar}}$ ). ${ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta$ : $18.3\left(\mathrm{CH}_{3}\right), 27.8\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH}), 49.3\left(2 \mathrm{xN}^{2}-\mathrm{CH}_{2} \mathrm{~N}-\mathrm{CH}_{2}\right), 120.4$ $\left(\mathrm{CH}_{\mathrm{Ar}}\right), 122.6\left(\mathrm{CH}_{\mathrm{Ar}}\right), 126.7\left(\mathrm{CH}_{\mathrm{Ar}}\right), 127.2\left(\mathrm{C}_{\mathrm{q}}\right), 128.2\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $129.8\left(\mathrm{CH}_{\mathrm{Ar}}\right), 130.0\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.4\left(\mathrm{CH}_{\mathrm{Ar}}\right), 133.2\left(\mathrm{C}_{\mathrm{q}}\right), 136.3\left(\mathrm{C}_{\mathrm{q}}\right)$, $138.3\left(\mathrm{C}_{\mathrm{q}}\right), 155.6\left(\mathrm{C}_{\mathrm{q}}\right), 157.5\left(\mathrm{C}_{\mathrm{q}}\right), 176.0\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): m/z calculated for $\mathrm{C}_{22} \mathrm{H}_{23} \mathrm{~N}_{4}$ : $343.1917[\mathrm{M}+\mathrm{H}]^{+}$; found: 343.1916.

4-Phenyl-N-(4-(trifluoromethyl)phenyl)-7,8-dihydro-6H-5,8-etha-nopyrido[3,2-d]pyrimidin-2-amine (30). Compound 30 was obtained according to general procedure $\mathbf{C}$ using 4(trifluoromethyl)aniline ( $0.19 \mathrm{~mL}, 243 \mathrm{mg}, 1.50 \mathrm{mmol}, 1.5 \mathrm{eq}$.$) .$ After purification by silica gel flash chromatography (DCM/PE, 80/20), 30 ( $212 \mathrm{mg}, 56 \%$ ) was obtained as a beige solid. Rf (DCM/PE: 80/20): $0.20 . M_{\mathrm{p}}: 182-184^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 3280,2957,1534,1415,1321,1109,1066,836,625 .{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 1.73-1.84\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 1.98-2.09(\mathrm{~m}, 2 \mathrm{H}$, $\mathrm{CH}_{2}$ ), 2.69-2.82 (m, 2H, N-CH2), 3.14-3.28 (m, 3H, N-CH2, CH), $7.36(\mathrm{~s}, 1 \mathrm{H}, \mathrm{NH}), 7.44-7.55\left(\mathrm{~m}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.59(\mathrm{~d}, J=8.6 \mathrm{~Hz}$, $\left.2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.85\left(\mathrm{~d}, J=8.5 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.29-8.36(\mathrm{~m}, 2 \mathrm{H}$, $2 \mathrm{xCH}_{\mathrm{Ar}}$ ). ${ }^{13} \mathrm{C}$ NMR ( $\left.101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 27.8\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH})$, $49.2\left(2 \mathrm{xN}^{\left.-\mathrm{CH}_{2}\right), 117.9\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 123.3\left(\mathrm{C}_{\mathrm{q}}\right), 124.8(\mathrm{~d}, J=}\right.$ $\left.241.0 \mathrm{~Hz}, \mathrm{C}_{\mathrm{q}}-\mathrm{CF}_{3}\right), 126.3\left(\mathrm{q}, J=3.9 \mathrm{~Hz}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 128.3\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $130.0\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.1\left(\mathrm{CH}_{\mathrm{Ar}}\right), 134.1\left(\mathrm{C}_{\mathrm{q}}\right), 136.0\left(\mathrm{C}_{\mathrm{q}}\right), 143.4(\mathrm{~d}, J=$ $0.9 \mathrm{~Hz}, \mathrm{CF}_{3}$ ), $155.8\left(\mathrm{C}_{\mathrm{q}}\right), 156.6\left(\mathrm{C}_{\mathrm{q}}\right), 176.3\left(\mathrm{C}_{\mathrm{q}}\right) .{ }^{19} \mathrm{~F}$ NMR (376 $\mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta:-61.65$. HRMS ( $\mathrm{EI} / \mathrm{MS}$ ): $\mathrm{m} / \mathrm{z}$ calculated for $\mathrm{C}_{22} \mathrm{H}_{20} \mathrm{~F}_{3} \mathrm{~N}_{4}: 397.1635[\mathrm{M}+\mathrm{H}]^{+}$; 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 $\mathbf{C}$ using 4 -aminobenzonitrile ( $177 \mathrm{mg}, 1.50 \mathrm{mmol}, 1.5 \mathrm{eq}$.). After purification by silica gel flash chromatography (PE/EA, 90/10 to 70/30), 31 ( $124 \mathrm{mg}, 35 \%$ ) was obtained as a light yellow solid. Rf (DCM/PE: 80/20): 0.16. $M_{\mathrm{p}}: 234-236{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu$ : 3399, 2923, 2214, 1566, 1517, 1413, 1357, 1171, 834, 687, 535. ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 1.71-1.84\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 1.98-2.11(\mathrm{~m}, 2 \mathrm{H}$, $\left.\mathrm{CH}_{2}\right), 2.68-2.81\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.15-3.28\left(\mathrm{~m}, 3 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}, \mathrm{CH}\right)$, $7.43-7.55\left(\mathrm{~m}, 4 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}, \mathrm{NH}\right), 7.60\left(\mathrm{~d}, J=8.8 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $7.85\left(\mathrm{~d}, J=8.8 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.25-8.35\left(\mathrm{~m}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 27.8\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH}), 49.1(2 \mathrm{xN}-$ $\left.\mathrm{CH}_{2} 2 \mathrm{xN}-\mathrm{CH}_{2}\right), 104.0\left(\mathrm{C}_{\mathrm{q}}\right), 118.0\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 119.7\left(\mathrm{C}_{\mathrm{q}}\right), 128.3$ $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.9\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.2\left(\mathrm{CH}_{\mathrm{Ar}}\right), 133.3\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 134.5$ $\left(\mathrm{C}_{\mathrm{q}}\right), 135.8\left(\mathrm{C}_{\mathrm{q}}\right), 144.3\left(\mathrm{C}_{\mathrm{q}}\right), 155.9\left(\mathrm{C}_{\mathrm{q}}\right), 156.2\left(\mathrm{C}_{\mathrm{q}}\right), 176.5\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): m/z calculated for $\mathrm{C}_{22} \mathrm{H}_{20} \mathrm{~N}_{5}: 354.1713[\mathrm{M}+\mathrm{H}]^{+}$; 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 $\mathbf{C}$ using 4-nitroaniline ( 208 mg , $1.50 \mathrm{mmol}, 1.5 \mathrm{eq}$.$) . The obtained solid was washed with DCM$ and dried under vacuo to afford $32(148 \mathrm{mg}, 39 \%)$ as a yellow solid. Rf (PE/EA: 80/20): 0.17. $M_{\mathrm{p}}$ : >260 ${ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\left.\mathrm{cm}^{-1}\right) \nu: 3386,2940,1530,1488,1416,1324,1111$, 840, 686, 584. ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 1.74-1.85(\mathrm{~m}, 2 \mathrm{H}$, $\left.\mathrm{CH}_{2}\right), 2.01-2.12\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.70-2.81\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.13-$ $3.29\left(\mathrm{~m}, 3 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}, \mathrm{CH}\right), 7.45-7.54\left(\mathrm{~m}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.56(\mathrm{~s}, 1 \mathrm{H}$, $\mathrm{NH}), 7.89\left(\mathrm{~d}, J=9.2 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.24(\mathrm{~d}, J=9.2 \mathrm{~Hz}, 2 \mathrm{H}$, $2 \mathrm{xCH}_{\mathrm{Ar}}$ ), $8.32\left(\mathrm{dd}, J=2.3,7.3 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C}$ NMR (101 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 27.8\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH}), 49.1\left(2 \mathrm{xN}^{2} \mathrm{CH}_{2}\right), 117.3$ $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 125.5\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 128.4\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.0\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.3$ $\left(\mathrm{CH}_{\mathrm{Ar}}\right), 134.9\left(\mathrm{C}_{\mathrm{q}}\right), 135.7\left(\mathrm{C}_{\mathrm{q}}\right), 141.6\left(\mathrm{C}_{\mathrm{q}}\right), 146.3\left(\mathrm{C}_{\mathrm{q}}\right), 156.0\left(\mathrm{C}_{\mathrm{q}}\right)$, $156.0\left(\mathrm{C}_{\mathrm{q}}\right), 176.6\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): $\mathrm{m} / \mathrm{z}$ calculated for $\mathrm{C}_{21} \mathrm{H}_{20} \mathrm{~N}_{5} \mathrm{O}_{2}: 374.1612[\mathrm{M}+\mathrm{H}]^{+}$; 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
to the general procedure $\mathbf{C}$ using 3 -aminopyridine ( 142 mg , $1.5 \mathrm{mmol}, 1.5 \mathrm{eq}$.$) . After purification by silica gel flash chro-$ matography (EA/PE, $70 / 30$ ), 33 ( $115 \mathrm{mg}, 34 \%$ ) was obtained as a light yellow solid. Rf (EA/PE: 70/30): 0.30. $M_{\mathrm{p}}: 211-213{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 2954,1531,1428,1386,1353,692,623$. ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 1.71-1.83\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 1.97-2.10$ ( $\mathrm{m}, 2 \mathrm{H}, \mathrm{CH}_{2}$ ), 2.68-2.81 (m, 2H, N-CH $), 3.12-3.26(\mathrm{~m}, 3 \mathrm{H} ; \mathrm{N}-$ $\mathrm{CH}_{2}, \mathrm{CH}$ ), 7.27 (dd, $J=8.3,4.8 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}$ ), $7.36(\mathrm{~s}, 1 \mathrm{H}, \mathrm{NH})$, 7.40-7.54 (m, $3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}$ ), $8.20-8.37\left(\mathrm{~m}, 4 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $8.83\left(\mathrm{~d}, J=2.2 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C} \operatorname{NMR}\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 27.8$ $\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH}), 49.2\left(2 \mathrm{xN}^{2} \mathrm{CH}_{2}\right), 123.5\left(\mathrm{CH}_{\mathrm{Ar}}\right), 125.4\left(\mathrm{CH}_{\mathrm{Ar}}\right)$, $128.3\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.0\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.1\left(\mathrm{CH}_{\mathrm{Ar}}\right), 133.9\left(\mathrm{C}_{\mathrm{q}}\right), 136.0$ $\left(\mathrm{C}_{\mathrm{q}}\right), 137.0\left(\mathrm{C}_{\mathrm{q}}\right), 140.7\left(\mathrm{CH}_{\mathrm{Ar}}\right), 143.0\left(\mathrm{CH}_{\mathrm{Ar}}\right), 155.8\left(\mathrm{C}_{\mathrm{q}}\right), 156.8$ $\left(\mathrm{C}_{\mathrm{q}}\right), 176.3\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): m/z calculated for $\mathrm{C}_{20} \mathrm{H}_{20} \mathrm{~N}_{5}$ : $330.1713[\mathrm{M}+\mathrm{H}]^{+}$; found: 330.1714.

N-(6-Methoxypyridin-3-yl)-4-phenyl-7,8-dihydro-6H-5,8-ethano-pyrido[3,2-d]pyrimidin-2-amine (34). Compound 34 was obtained according to the general procedure $\mathbf{C}$ using 5-amino-2methoxypyridine ( $0.12 \mathrm{~mL}, 189 \mathrm{mg}, 1.52 \mathrm{mmol}, 1.5 \mathrm{eq}$.). After purification by silica gel flash chromatography (PE/EA, 50/50), $34(102 \mathrm{mg}, 28 \%)$ was obtained as a light orange solid. Rf (PE/ EA: 50/50): $0.52 . M_{\mathrm{p}}$ : $183-185{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu$ : 1942, 1537, 1490, 1348, 1278, 1035, 831, 691, 624. ${ }^{1}$ H NMR (400 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 1.73-1.81\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 1.95-2.07\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right)$, $2.68-2.80\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.13(\mathrm{p}, J=2.9 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 3.15-$ $3.25\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.94\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{O}-\mathrm{CH}_{3}\right), 6.77(\mathrm{~d}, J=8.9 \mathrm{~Hz}, 1 \mathrm{H}$, $\left.\mathrm{CH}_{\mathrm{Ar}}\right), 6.95(\mathrm{~s}, 1 \mathrm{H}, \mathrm{NH}), 7.39-7.51\left(\mathrm{~m}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.04(\mathrm{dd}, J=$ $\left.8.9,2.8 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right), 8.22-8.31\left(\mathrm{~m}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.42(\mathrm{~d}, J=$ $\left.2.7 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 27.8\left(2 \mathrm{xCH}_{2}\right)$, $33.7(\mathrm{CH}), 49.3\left(2 \mathrm{xN}^{2} \mathrm{CH}_{2}\right), 53.6\left(\mathrm{O}-\mathrm{CH}_{3}\right), 110.5\left(\mathrm{CH}_{\mathrm{Ar}}\right), 128.2$ $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.9\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.9\left(\mathrm{CH}_{\mathrm{Ar}}\right), 131.0\left(\mathrm{C}_{\mathrm{q}}\right), 131.7\left(\mathrm{CH}_{\mathrm{Ar}}\right)$, $133.4\left(\mathrm{C}_{\mathrm{q}}\right), 136.1\left(\mathrm{C}_{\mathrm{q}}\right), 137.8\left(\mathrm{CH}_{\mathrm{Ar}}\right), 155.8\left(\mathrm{C}_{\mathrm{q}}\right), 157.3\left(\mathrm{C}_{\mathrm{q}}\right), 160.0$ $\left(\mathrm{C}_{\mathrm{q}}\right), 176.2\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): m/z calculated for $\mathrm{C}_{21} \mathrm{H}_{22} \mathrm{~N}_{5} \mathrm{O}$ : $360.1819[\mathrm{M}+\mathrm{H}]^{+}$; found: 360.1819.
$N$-Phenyl-4-( $p$-tolyl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d] pyrimidin-2-amine (35)

Compound 35 was obtained according to general procedure C using 9 ( $274 \mathrm{mg}, 1.02 \mathrm{mmol}, 1.0 \mathrm{eq}$.) and aniline ( 0.14 mL , $1.53 \mathrm{mmol}, 1.5 \mathrm{eq}$.$) . After purification by silica gel flash chro-$ matography (PE/EA: 90/10 to 80/20), 35 ( $156 \mathrm{mg}, 44 \%$ ) was obtained as a beige solid. Rf (PE/EA: 80/20): 0.50. $M_{\mathrm{p}}: 195-197^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 3229,2960,1574,1531,1429,1362$, $1171,812,742,688 .{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 1.71-1.84(\mathrm{~m}$, $2 \mathrm{H}, \mathrm{CH}_{2}$ ), 1.95-2.07 (m, 2H, CH ${ }_{2}$ ), $2.42\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{CH}_{3}\right), 2.68-2.81$ $\left(\mathrm{m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.12-3.25\left(\mathrm{~m}, 3 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}, \mathrm{CH}\right), 7.01(\mathrm{tt}, J=7.3$, $\left.1.2 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right), 7.15(\mathrm{~s}, 1 \mathrm{H}, \mathrm{NH}), 7.29(\mathrm{~d}, J=7.9 \mathrm{~Hz}, 2 \mathrm{H}$, $2 \mathrm{xCH}_{\mathrm{Ar}}$ ), $7.30-7.38\left(\mathrm{~m}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.70-7.77\left(\mathrm{~m}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $8.24\left(\mathrm{~d}, J=8.3 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta$ : $21.6\left(\mathrm{CH}_{3}\right), 27.8\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH}), 49.3\left(2 \mathrm{xN}^{2} \mathrm{CH}_{2}\right), 118.7$ $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 121.9\left(\mathrm{CH}_{\mathrm{Ar}}\right), 129.0\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.0\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.9$ $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 133.1\left(\mathrm{C}_{\mathrm{q}}\right), 133.5\left(\mathrm{C}_{\mathrm{q}}\right), 140.0\left(\mathrm{C}_{\mathrm{q}}\right), 140.4\left(\mathrm{C}_{\mathrm{q}}\right), 155.7\left(\mathrm{C}_{\mathrm{q}}\right)$, $157.1\left(\mathrm{C}_{\mathrm{q}}\right), 175.8\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): $\mathrm{m} / \mathrm{z}$ calculated for $\mathrm{C}_{22} \mathrm{H}_{23} \mathrm{~N}_{4}$ : $343.1917[\mathrm{M}+\mathrm{H}]^{+}$; 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 , $0.98 \mathrm{mmol}, 1.0 \mathrm{eq}$. ) and 4 -(trifluoromethyl)aniline ( 0.19 mL ,
$1.50 \mathrm{mmol}, 1.5 \mathrm{eq}$.$) . After purification by silica gel flash chro-$ matography (PE/EA: 90/10 to 80/20), 36 ( $200 \mathrm{mg}, 49 \%$ ) was obtained as a beige solid. Rf (PE/EA: 80/20): 0.20. $M_{\mathrm{p}}: 195-197^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 3270,2962,1576,1536,1318,1100$, 1064, 838. ${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 1.71-1.84\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right)$, 1.97-2.09 (m, 2H, CH 2 ), $2.43\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{CH}_{3}\right), 2.68-2.81(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-$ $\mathrm{CH}_{2}$ ), 3.13-3.27 (m, 3H, N-CH2, CH), $7.30(\mathrm{~d}, J=8.0 \mathrm{~Hz}, 2 \mathrm{H}$, $2 \mathrm{XCH}_{\mathrm{Ar}}$ ), $7.37(\mathrm{~s}, 1 \mathrm{H}, \mathrm{NH}), 7.58\left(\mathrm{~d}, J=8.4 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.85$ $\left(\mathrm{d}, J=8.5 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.24\left(\mathrm{~d}, J=8.3 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C}$ NMR ( $\left.101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 21.5\left(\mathrm{CH}_{3}\right), 27.7\left(2 \mathrm{xCH}_{2}\right), 33.6(\mathrm{CH})$, $49.0\left(2 \mathrm{xN}^{2} \mathrm{CH}_{2}\right), 117.7\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 124.6\left(\mathrm{~d}, J=252.1 \mathrm{~Hz}, \mathrm{C}_{\mathrm{q}}-\mathrm{CF}_{3}\right)$, $126.1\left(\mathrm{q}, J=3.8 \mathrm{~Hz}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 128.9\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.8\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $133.1\left(\mathrm{C}_{\mathrm{q}}\right), 133.8\left(\mathrm{C}_{\mathrm{q}}\right), 140.2\left(\mathrm{C}_{\mathrm{q}}\right), 143.3\left(\mathrm{~d}, J=0.6 \mathrm{~Hz}, \mathrm{CF}_{3}\right), 155.7$ $\left(\mathrm{C}_{\mathrm{q}}\right), 156.4\left(\mathrm{C}_{\mathrm{q}}\right), 176.0\left(\mathrm{C}_{\mathrm{q}}\right) .{ }^{19} \mathrm{~F}$ NMR ( $376 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta$ : -61.63. HRMS (EI/MS): $m / z$ calculated for $\mathrm{C}_{23} \mathrm{H}_{22} \mathrm{~F}_{3} \mathrm{~N}_{4}: 411.1791$ $[\mathrm{M}+\mathrm{H}]^{+}$; found: 411.1791.

General procedure D: Suzuki-Miyaura cross-coupling. In a microwave vial, to an argon-degassed solution of $8(200 \mathrm{mg}$, $0.79 \mathrm{mmol}, 1.0$ eq.) and PyBroP ( $446 \mathrm{mg}, 0.96 \mathrm{mmol}, 1.2$ eq.) in 1,4-dioxane ( 8 mL ), was added $\mathrm{Et}_{3} \mathrm{~N}(0.32 \mathrm{~mL}, 239 \mathrm{mg}$, $2.36 \mathrm{mmol}, 3.0$ eq.) and the reaction was heated for 3 h at $100{ }^{\circ} \mathrm{C}$. After cooling, a solution of $\mathrm{K}_{3} \mathrm{PO}_{4}(849 \mathrm{mg}, 4.00 \mathrm{mmol}$, 5.0 eq.) in $\mathrm{H}_{2} \mathrm{O}(2 \mathrm{~mL})$, the required arylboronic acid ( 2.0 eq .), $\operatorname{Pd}(\mathrm{OAc})_{2}(18 \mathrm{mg}, 0.08 \mathrm{mmol}, 0.1 .0$ eq.) and RuPhos $(74 \mathrm{mg}$, $0.16 \mathrm{mmol}, 0.2$ eq.) were added to the reaction mixture. The sealed tube was heated at $150{ }^{\circ} \mathrm{C}$ 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 $(2 \times 20 \mathrm{~mL})$, dried over $\mathrm{MgSO}_{4}$, 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 $\mathbf{D}$ using $p$-tolylboronic acid ( 239 mg , $1.60 \mathrm{mmol}, 2.0 \mathrm{eq}$.$) . After purification by silica gel flash chro-$ matography (PE/EA, 90/10), 39 ( $182 \mathrm{mg}, 70 \%$ ) was obtained as a white solid. Rf (PE/EA: 90/10): 0.40. $M_{\mathrm{p}}: 192-194{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\left.\mathrm{cm}^{-1}\right) \nu: 2963,2924,2871,1550,1387,1170,772,689$, 623. ${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 1.76-1.87\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.01-$ $2.13\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.43\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{CH}_{3}\right), 2.77(\mathrm{td}, J=4.9,11.5 \mathrm{~Hz}$, $\left.2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.20-3.32\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.38(\mathrm{p}, J=2.8,3.2 \mathrm{~Hz}$, $1 \mathrm{H}, \mathrm{CH}), 7.30\left(\mathrm{~d}, J=7.8 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.43-7.56(\mathrm{~m}, 3 \mathrm{H}$, $3 \mathrm{xCH}_{\mathrm{Ar}}$ ), $8.47\left(\mathrm{dd}, J=8.1,12.2 \mathrm{~Hz}, 4 \mathrm{H}, 4 \mathrm{xCH}_{\mathrm{Ar}}\right.$ ). ${ }^{13} \mathrm{C}$ NMR ( 101 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 21.6\left(\mathrm{CH}_{3}\right), 27.9\left(2 \mathrm{XCH}_{2}\right), 33.7(\mathrm{CH}), 48.9(2 \mathrm{xN}-$ $\left.\mathrm{CH}_{2}\right), 128.2\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 128.3\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.3\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.0$ $\left(\mathrm{CH}_{\text {Ar }}\right), 130.2\left(2 \mathrm{xCH}_{\text {Ar }}\right), 135.7\left(\mathrm{C}_{\mathrm{q}}\right), 136.4\left(\mathrm{C}_{\mathrm{q}}\right), 139.0\left(\mathrm{C}_{\mathrm{q}}\right), 140.3$ $\left(\mathrm{C}_{\mathrm{q}}\right), 154.7\left(\mathrm{C}_{\mathrm{q}}\right), 161.2\left(\mathrm{C}_{\mathrm{q}}\right), 175.1\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): m/z calculated for $\mathrm{C}_{22} \mathrm{H}_{22} \mathrm{~N}_{3}$ : $328.1808[\mathrm{M}+\mathrm{H}]^{+}$; 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 $\mathbf{D}$ using phenylboronic acid ( $195 \mathrm{mg}, 1.60 \mathrm{mmol}, 2.0 \mathrm{eq}$.$) .$ After purification by silica gel flash chromatography (PE/EA, 90/ 10), 40 ( $171 \mathrm{mg}, 68 \%$ ) was obtained as a white solid. Rf (PE/EA: 90/10): 0.30. $M_{\mathrm{p}}$ : 195-197 ${ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu$ : 2945, 2921, 1553, 1389, 768, 692, 624. ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta$ : 1.75-1.89 (m, 2H, CH 2 ), 2.02-2.14 (m, 2H, CH 2 ), 2.72-2.84 (m,
$2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}$ ), $3.21-3.32\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.40(\mathrm{p}, J=2.9 \mathrm{~Hz}, 1 \mathrm{H}$, $\mathrm{CH}), 7.42-7.56\left(\mathrm{~m}, 6 \mathrm{H}, 6 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.50(\mathrm{dd}, J=1.7,8.1 \mathrm{~Hz}, 2 \mathrm{H}$, $2 \mathrm{xCH}_{\mathrm{Ar}}$ ), $8.57\left(\mathrm{dd}, J=1.8,8.0 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right) \cdot{ }^{13} \mathrm{C}$ NMR ( 101 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 27.8\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH}), 48.9\left(2 \mathrm{xN}^{2}-\mathrm{CH}_{2}\right), 128.2$ $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 128.3\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 128.5\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.0\left(\mathrm{CH}_{\mathrm{Ar}}\right), 130.2$ $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right)$, 136. $\left(\mathrm{C}_{\mathrm{q}}\right), 138.4\left(\mathrm{C}_{\mathrm{q}}\right), 139.3\left(\mathrm{C}_{\mathrm{q}}\right), 154.8\left(\mathrm{C}_{\mathrm{q}}\right), 161.1\left(\mathrm{C}_{\mathrm{q}}\right)$, $175.2\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): $\mathrm{m} / \mathrm{z}$ calculated for $\mathrm{C}_{21} \mathrm{H}_{20} \mathrm{~N}_{3}$ : $314.1652[\mathrm{M}+\mathrm{H}]^{+}$; 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 $\mathbf{D}$ using $m$-tolylboronic acid ( 215 mg , $1.58 \mathrm{mmol}, 2.0 \mathrm{eq}$.$) . After purification by silica gel flash chro-$ matography (PE/EA, 90/10), 41 ( $189 \mathrm{mg}, 73 \%$ ) was obtained as a white solid. Rf (PE/EA: 90/10): 0.27. $M_{\mathrm{p}}: 191-193{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\left.\mathrm{cm}^{-1}\right) \nu:$ 2961, 2946, 2869, 1553, 1385, 1376, 771, 733, $690,624 .{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 1.75-1.88\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right)$, 2.02-2.14 (m, 2H, CH $)_{2}$, $2.47\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{CH}_{3}\right), 2.71-2.84(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-$ $\left.\mathrm{CH}_{2}\right), 3.21-3.32\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.39(\mathrm{p}, J=3.0 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH})$, $7.28\left(\mathrm{~d}, J=7.5 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right), 7.39\left(\mathrm{t}, J=7.9 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right), 7.43-$ $7.56\left(\mathrm{~m}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.36\left(\mathrm{~d}, J=6.9 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.48(\mathrm{dt}, J$ $\left.=1.5,2.3,6.4 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta$ : $21.7\left(\mathrm{CH}_{3}\right), 27.9\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH}), 48.9\left(2 \mathrm{xN}-\mathrm{CH}_{2}\right), 125.6$ $\left(\mathrm{CH}_{\mathrm{Ar}}\right), 128.3\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 128.5\left(\mathrm{CH}_{\mathrm{Ar}}\right), 128.8\left(\mathrm{CH}_{\mathrm{Ar}}\right), 130.0\left(\mathrm{CH}_{\mathrm{Ar}}\right)$, $130.2\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 131.1\left(\mathrm{CH}_{\mathrm{Ar}}\right), 136.3\left(\mathrm{C}_{\mathrm{q}}\right), 138.1\left(\mathrm{C}_{\mathrm{q}}\right), 138.3\left(\mathrm{C}_{\mathrm{q}}\right)$, $139.2\left(\mathrm{C}_{\mathrm{q}}\right), 154.9\left(\mathrm{C}_{\mathrm{q}}\right), 161.3\left(\mathrm{C}_{\mathrm{q}}\right), 175.1\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): m/z calculated for $\mathrm{C}_{22} \mathrm{H}_{22} \mathrm{~N}_{3}$ : $328.1808[\mathrm{M}+\mathrm{H}]^{+}$; 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, $1.58 \mathrm{mmol}, 2.0 \mathrm{eq}$.$) . After purification by silica gel flash chro-$ matography (PE/EA, 90/10), 42 ( $196 \mathrm{mg}, 76 \%$ ) was obtained as a white solid. Rf (PE/EA: 90/10): 0.22. $M_{\mathrm{p}}: 228-230{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\left.\mathrm{cm}^{-1}\right) \nu$ : 2944, 2869, 1552, 1387, 1131, 844, 767, 736, $695,623 .{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 1.79-1.88\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right)$, 2.03-2.14 (m, 2H, CH 2 ), $2.66\left(\mathrm{~s}, 3 \mathrm{H}, \mathrm{CH}_{3}\right), 2.75-2.87(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-$ $\left.\mathrm{CH}_{2}\right), 3.22-3.34\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.38(\mathrm{p}, J=2.9 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH})$, 7.27-7.38 (m, $\left.3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.38-7.55\left(\mathrm{~m}, 3 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}, \mathrm{CH}_{\mathrm{Ar}}\right)$, $7.87-7.94\left(\mathrm{~m}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right), 8.44\left(\mathrm{dd}, J=1.8,8.0 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right)$. ${ }^{13} \mathrm{C}$ NMR $\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 21.5\left(\mathrm{CH}_{3}\right), 27.9\left(2 \mathrm{XCH}_{2}\right), 33.6$ $(\mathrm{CH}), 48.9\left(2 \mathrm{xN}^{2} \mathrm{CH}_{2}\right), 126.0\left(\mathrm{CH}_{\mathrm{Ar}}\right), 128.3\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.1\left(\mathrm{CH}_{\mathrm{Ar}}\right)$, $130.0\left(\mathrm{CH}_{\mathrm{Ar}}\right), 130.2\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.6\left(\mathrm{CH}_{\mathrm{Ar}}\right), 131.3\left(\mathrm{CH}_{\mathrm{Ar}}\right), 136.2$ $\left(\mathrm{C}_{\mathrm{q}}\right), 137.3\left(\mathrm{C}_{\mathrm{q}}\right), 138.5\left(\mathrm{C}_{\mathrm{q}}\right), 138.9\left(\mathrm{C}_{\mathrm{q}}\right), 154.6\left(\mathrm{C}_{\mathrm{q}}\right), 164.1\left(\mathrm{C}_{\mathrm{q}}\right)$, $174.9\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): $\mathrm{m} / \mathrm{z}$ calculated for $\mathrm{C}_{22} \mathrm{H}_{22} \mathrm{~N}_{3}$ : $328.1808[\mathrm{M}+\mathrm{H}]^{+}$; 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 $\mathbf{D}$ using 4-methoxyphenylboronic acid ( $244 \mathrm{mg}, 1.60 \mathrm{mmol}, 2.0 \mathrm{eq}$.). After purification by silica gel flash chromatography (PE/EA, 90/10), 43 ( $188 \mathrm{mg}, 69 \%$ ) was obtained as a white solid. Rf (PE/EA: 90/10): 0.24. $M_{\mathrm{p}}$ : 204-206 ${ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 2960,2935,1549,1387,1247,1031,772,694$. ${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 1.75-1.87\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.01-2.12$ ( $\mathrm{m}, 2 \mathrm{H}, \mathrm{CH}_{2}$ ), $2.77\left(\mathrm{td}, J=5.0,11.4 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.20-3.31$ (m, 2H, N-CH2), $3.36(\mathrm{p}, J=3.0 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 3.89(\mathrm{~s}, 3 \mathrm{H}, \mathrm{O}-$ $\left.\mathrm{CH}_{3}\right), 7.01\left(\mathrm{~d}, J=8.5 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.42-7.55(\mathrm{~m}, 3 \mathrm{H}$, $3 \mathrm{xCH}_{\mathrm{Ar}}$ ), $8.47\left(\mathrm{~d}, J=7.7 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.52(\mathrm{~d}, J=8.4 \mathrm{~Hz}, 2 \mathrm{H}$, $\left.2 \mathrm{xCH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C}$ NMR $\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 27.9\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH})$,
$49.0\left(2 \mathrm{xN}^{2}-\mathrm{CH}_{2}\right), 55.4\left(\mathrm{O}-\mathrm{CH}_{3}\right), 113.9\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 128.2\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $129.9\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.9\left(\mathrm{CH}_{\mathrm{Ar}}\right), 130.2\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 131.1\left(\mathrm{C}_{\mathrm{q}}\right), 136.4$ $\left(\mathrm{C}_{\mathrm{q}}\right), 138.6\left(\mathrm{C}_{\mathrm{q}}\right), 154.7\left(\mathrm{C}_{\mathrm{q}}\right), 160.9\left(\mathrm{C}_{\mathrm{q}}\right), 161.5\left(\mathrm{C}_{\mathrm{q}}\right), 175.0\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): m/z calculated for $\mathrm{C}_{22} \mathrm{H}_{22} \mathrm{~N}_{3} \mathrm{O}: 344.1757$ [M + $\mathrm{H}]^{+}$; found: 344.1759.

4-(4-Phenyl-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-2$y l) p h e n o l(44)$. Compound 44 was obtained according to general procedure D using 4-hydroxyphenylboronic acid (219 mg, $1.59 \mathrm{mmol}, 2.0 \mathrm{eq}$.$) . After purification by silica gel flash chro-$ matography (PE/EA, 80/20), 44 ( $141 \mathrm{mg}, 54 \%$ ) was obtained as a white solid. Rf (PE/EA: 80/20): 0.17. $M_{\mathrm{p}}: 254-256{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 3059,2942,2675,1610,1552,1400,1238$, 1166, 774, 688, 625. ${ }^{1} \mathrm{H}$ NMR ( 400 MHz , DMSO- $d_{6}$ ) $\delta: 1.61-1.75$ $\left(\mathrm{m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 1.97-2.11\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.58-2.71(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-$ $\mathrm{CH}_{2}$ ), 3.14-3.21 (m, 2H, N-CH2), $3.23(\mathrm{p}, J=2.3 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH})$, $6.89\left(\mathrm{td}, J=1.7,8.7 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.45-7.57\left(\mathrm{~m}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $8.34\left(\mathrm{td}, J=2.0,8.7 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.39(\mathrm{dd}, J=1.9,7.8 \mathrm{~Hz}$, $2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}$ ), $9.88(\mathrm{~s}, 1 \mathrm{H}, \mathrm{OH}) .{ }^{13} \mathrm{C}$ NMR ( 101 MHz, DMSO- $d_{6}$ ) $\delta$ : $27.0\left(2 \mathrm{xCH}_{2}\right), 33.0(\mathrm{CH}), 48.2\left(2 \mathrm{xN}^{2}-\mathrm{CH}_{2}\right), 115.3\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 128.0$ $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 128.6\left(\mathrm{C}_{\mathrm{q}}\right), 129.5\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.8\left(\mathrm{CH}_{\mathrm{Ar}}\right), 129.8\left(\mathrm{CH}_{\mathrm{Ar}}\right)$, $135.7\left(\mathrm{C}_{\mathrm{q}}\right), 138.2\left(\mathrm{C}_{\mathrm{q}}\right), 153.5\left(\mathrm{C}_{\mathrm{q}}\right), 159.6\left(\mathrm{C}_{\mathrm{q}}\right), 159.8\left(\mathrm{C}_{\mathrm{q}}\right), 175.1$ $\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): $m / z$ calculated for $\mathrm{C}_{21} \mathrm{H}_{20} \mathrm{~N}_{3} \mathrm{O}: 330.1601$ [M $+\mathrm{H}]^{+}$; found: 330.1602.

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

2-(2-Naphthalen-2-yl)-4-phenyl-7,8-dihydro-6H-5,8-ethanopyr-ido[3,2-d]pyrimidine (46). Compound 46 was obtained according to general procedure D using 2-naphthylboronic acid ( 275 mg , $1.60 \mathrm{mmol}, 2.0 \mathrm{eq}$.$) . After purification by silica gel flash chro-$ matography (PE/EA, 90/10), 46 ( $196 \mathrm{mg}, 67 \%$ ) was obtained as a white solid. Rf (PE/EA: 90/10): 0.35. $M_{\mathrm{p}}: 210-212{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\left.\mathrm{cm}^{-1}\right) \nu: 2949,2868,1552,1391,1380,773,755,700$, 625. ${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 1.80-1.92\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.05-$ $2.16\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.74-2.87\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.23-3.34(\mathrm{~m}, 2 \mathrm{H}$, $\left.\mathrm{N}-\mathrm{CH}_{2}\right), 3.45(\mathrm{p}, J=2.9 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 7.46-7.60\left(\mathrm{~m}, 5 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right.$, $2 \mathrm{xCH}_{\mathrm{Ar}}$ ), $7.86-7.93\left(\mathrm{~m}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right), 7.97\left(\mathrm{~d}, J=8.7 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right)$, $8.01-8.09\left(\mathrm{~m}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right), 8.50-8.57\left(\mathrm{~m}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.71(\mathrm{dd}, J=$ $\left.1.7,8.6 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right), 9.10\left(\mathrm{~s}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C}$ NMR ( 101 MHz ,
$\left.\mathrm{CDCl}_{3}\right) \delta: 27.9\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH}), 48.9\left(2 \mathrm{xN}^{2}-\mathrm{CH}_{2}\right), 125.6\left(\mathrm{CH}_{\mathrm{Ar}}\right)$, $126.2\left(\mathrm{CH}_{\mathrm{Ar}}\right), 126.9\left(\mathrm{CH}_{\mathrm{Ar}}\right), 127.8\left(\mathrm{CH}_{\mathrm{Ar}}\right), 128.1\left(\mathrm{CH}_{\mathrm{Ar}}\right), 128.3$ $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 128.3\left(\mathrm{CH}_{\mathrm{Ar}}\right), 129.3\left(\mathrm{CH}_{\mathrm{Ar}}\right), 130.1\left(\mathrm{CH}_{\mathrm{Ar}}\right), 130.3\left(\mathrm{CH}_{\mathrm{Ar}}\right)$, $133.5\left(\mathrm{C}_{\mathrm{q}}\right), 134.6\left(\mathrm{C}_{\mathrm{q}}\right), 135.7\left(\mathrm{C}_{\mathrm{q}}\right), 136.3\left(\mathrm{C}_{\mathrm{q}}\right), 139.3\left(\mathrm{C}_{\mathrm{q}}\right), 155.0$ $\left(\mathrm{C}_{\mathrm{q}}\right), 161.0\left(\mathrm{C}_{\mathrm{q}}\right), 175.3\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): m/z calculated for $\mathrm{C}_{25} \mathrm{H}_{22} \mathrm{~N}_{3}: 364.1808[\mathrm{M}+\mathrm{H}]^{+}$; 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 , $1.60 \mathrm{mmol}, 2.0 \mathrm{eq}$.$) . After purification by silica gel flash chro-$ matography (PE/EA, $90 / 10), 47(186 \mathrm{mg}, 70 \%)$ was obtained as a white solid. Rf (PE/EA: 90/10): 0.42. $M_{\mathrm{p}}$ : 178-180 ${ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu:$ 2922, 2864, 1601, 1555, 1389, 1151, 832, 768, 688, 622. ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 1.75-1.87\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right)$, $2.02-2.14\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.71-2.83\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.21-3.32$ ( $\mathrm{m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}$ ), $3.37(\mathrm{p}, J=2.9 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 7.12-7.22(\mathrm{~m}, 2 \mathrm{H}$, $2 \mathrm{xCH}_{\mathrm{Ar}}$ ), $7.45-7.56\left(\mathrm{~m}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.47(\mathrm{dd}, J=1.7,8.0 \mathrm{~Hz}, 2 \mathrm{H}$, $2 \mathrm{xCH}_{\mathrm{Ar}}$ ), 8.57 (dd, $J=5.9,9.3 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}$ ). ${ }^{13} \mathrm{C}$ NMR ( 101 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 27.8\left(2 \mathrm{XCH}_{2}\right), 33.7(\mathrm{CH}), 48.9\left(2 \mathrm{xN}^{2}-\mathrm{CH}_{2}\right), 115.3$ $\left(\mathrm{CH}_{\mathrm{Ar}}\right), 115.5\left(\mathrm{CH}_{\mathrm{Ar}}\right), 128.3\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.1\left(\mathrm{CH}_{\mathrm{Ar}}\right), 130.2$ $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.3\left(\mathrm{CH}_{\mathrm{Ar}}\right), 130.4\left(\mathrm{CH}_{\mathrm{Ar}}\right), 134.6\left(\mathrm{~d}, J=2.9 \mathrm{~Hz}, \mathrm{C}_{\mathrm{q}}\right)$, $136.1\left(\mathrm{C}_{\mathrm{q}}\right), 139.2\left(\mathrm{C}_{\mathrm{q}}\right), 154.9\left(\mathrm{C}_{\mathrm{q}}\right), 160.19\left(\mathrm{C}_{\mathrm{q}}\right), 164.5(\mathrm{~d}, J=$ $\left.249.5 \mathrm{~Hz}, \mathrm{C}_{\mathrm{Ar}}-\mathrm{F}\right), 175.3\left(\mathrm{C}_{\mathrm{q}}\right) .{ }^{19} \mathrm{~F}$ NMR ( $376 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta$ : -111.46. HRMS (EI/MS): $m / z$ calculated for $\mathrm{C}_{21} \mathrm{H}_{19} \mathrm{FN}_{3}: 332.1558$ [ $\mathrm{M}+\mathrm{H}]^{+}$; found: 332.1563.

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

4-Phenyl-2-(4-(trifluoromethyl)phenyl)-7,8-dihydro-6H-5,8-etha-nopyrido[3,2-d]pyrimidine (49). Compound 49 was obtained according to general procedure D using 4-(trifluoromethyl) phenylboronic acid ( $303 \mathrm{mg}, 1.60 \mathrm{mmol}, 2.0$ eq.). After purification by silica gel flash chromatography (PE/EA, 90/10), 49 ( $222 \mathrm{mg}, 72 \%$ ) was obtained as a white solid. Rf (PE/EA: 90/10): $0.40 M_{\mathrm{p}}: 166-168{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 2953,1552$, $1389,1320,1116,1061,774,690 .{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta$ : 1.76-1.89 (m, 2H, CH $)_{2}$, $2.04-2.16\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.78(\mathrm{td}, J=5.1$, $11.7 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}$ ), $3.23-3.34\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.41(\mathrm{p}, J=$ $3.2 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 7.45-7.58\left(\mathrm{~m}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.75(\mathrm{~d}, J=8.1 \mathrm{~Hz}$, $\left.2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.50\left(\mathrm{dt}, J=1.6,7.5 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.69(\mathrm{~d}, J=$ $8.0 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}$ ). ${ }^{13} \mathrm{C}$ NMR ( $\left.101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 27.8\left(2 \mathrm{xCH}_{2}\right)$, 33.7 (CH), $48.8\left(2 \mathrm{xN}^{2}-\mathrm{CH}_{2}\right), 124.4\left(\mathrm{~d}, J=272.2 \mathrm{~Hz}, \mathrm{C}_{\mathrm{q}}-\mathrm{CF}_{3}\right), 125.5$ $\left(\mathrm{q}, J=3.8 \mathrm{~Hz}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 128.3\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 128.6\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.2$
$\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.3\left(\mathrm{CH}_{\mathrm{Ar}}\right), 131.8\left(\mathrm{~d}, J=32.2 \mathrm{~Hz}, \mathrm{CF}_{3}\right), 135.9\left(\mathrm{C}_{\mathrm{q}}\right)$, $140.0\left(\mathrm{C}_{\mathrm{q}}\right), 141.7\left(\mathrm{~d}, J=1.7 \mathrm{~Hz}, \mathrm{C}_{\mathrm{q}}\right), 155.0\left(\mathrm{C}_{\mathrm{q}}\right), 159.6\left(\mathrm{C}_{\mathrm{q}}\right), 175.6$ $\left(\mathrm{C}_{\mathrm{q}}\right) .{ }^{19} \mathrm{~F}$ NMR ( $376 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta:-62.59$. HRMS (EI/MS): $\mathrm{m} / \mathrm{z}$ calculated for $\mathrm{C}_{22} \mathrm{H}_{19} \mathrm{~F}_{3} \mathrm{~N}_{3}: 382.1526[\mathrm{M}+\mathrm{H}]^{+}$; 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 $\mathbf{D}$ using 4-nitrophenylboronic acid ( 268 mg , $1.60 \mathrm{mmol}, 2.0 \mathrm{eq}$.$) . After purification by silica gel flash chro-$ matography (PE/EA, 90/10), 50 ( $206 \mathrm{mg}, 76 \%$ ) was obtained as an orange solid. Rf (PE/EA: 90/10): 0.40. $M_{\mathrm{p}}: 191-193{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\left.\mathrm{cm}^{-1}\right) \nu: 2925,2872,1555,1519,1388,1350,839,688$. ${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 1.75-1.88\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.06-2.18$ $\left(\mathrm{m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.72-2.84\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.24-3.35(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-$ $\left.\mathrm{CH}_{2}\right), 3.41(\mathrm{p}, J=2.8 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 7.47-7.58\left(\mathrm{~m}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $8.34\left(\mathrm{dt}, J=2.0,9.0 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.44-8.54\left(\mathrm{~m}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $8.75\left(\mathrm{dt}, J=2.3,9.0 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C}$ NMR ( $101 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 27.8\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH}), 48.8\left(2 \mathrm{xN}^{2}-\mathrm{CH}_{2}\right), 123.8\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 128.4$ $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.2\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.2\left(2 \mathrm{XCH}_{\mathrm{Ar}}\right), 130.4\left(\mathrm{CH}_{\mathrm{Ar}}\right), 135.7$ $\left(\mathrm{C}_{\mathrm{q}}\right), 140.4\left(\mathrm{C}_{\mathrm{q}}\right), 144.2\left(\mathrm{C}_{\mathrm{q}}\right), 149.1\left(\mathrm{C}_{\mathrm{q}}\right), 155.2\left(\mathrm{C}_{\mathrm{q}}\right), 158.8\left(\mathrm{C}_{\mathrm{q}}\right)$, $175.8\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): $\mathrm{m} / \mathrm{z}$ calculated for $\mathrm{C}_{21} \mathrm{H}_{19} \mathrm{~N}_{4} \mathrm{O}_{2}$ : $359.1503[\mathrm{M}+\mathrm{H}]^{+}$; 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, $1.62 \mathrm{mmol}, 2.0 \mathrm{eq}$.$) . After purification by silica gel flash chro-$ matography (PE/EA, 90/10), 51 ( $195 \mathrm{mg}, 77 \%$ ) was obtained as a white solid. Rf (PE/EA: 90/10): 0.19. $M_{\mathrm{p}}$ : 189-191 ${ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\left.\mathrm{cm}^{-1}\right) \nu: 2956,2867,1553,1386,1342,819,689,623$. ${ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 1.75-1.86\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.00-2.13$ $\left(\mathrm{m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.76\left(\mathrm{td}, J=5.5,12.2 \mathrm{~Hz}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.19-3.31$ $\left(\mathrm{m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.35(\mathrm{p}, J=3.3 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 7.38(\mathrm{t}, J=3.7 \mathrm{~Hz}$, $\left.1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right), 7.42-7.55\left(\mathrm{~m}, 3 \mathrm{H}, 3 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.00(\mathrm{~d}, J=5.0 \mathrm{~Hz}, 1 \mathrm{H}$, $\left.\mathrm{CH}_{\mathrm{Ar}}\right), 8.31-8.36\left(\mathrm{~m}, 1 \mathrm{H}, \mathrm{CH}_{\mathrm{Ar}}\right), 8.45\left(\mathrm{~d}, J=7.9 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right)$. ${ }^{13} \mathrm{C}$ NMR $\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 27.8\left(2 \mathrm{xCH}_{2}\right), 33.6(\mathrm{CH}), 48.9(2 \mathrm{xN}-$ $\left.\mathrm{CH}_{2}\right), 125.8\left(\mathrm{CH}_{\mathrm{Ar}}\right), 127.3\left(\mathrm{CH}_{\mathrm{Ar}}\right), 127.8\left(\mathrm{CH}_{\mathrm{Ar}}\right), 128.2\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $130.0\left(\mathrm{CH}_{\mathrm{Ar}}\right), 130.2\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 136.1\left(\mathrm{C}_{\mathrm{q}}\right), 138.8\left(\mathrm{C}_{\mathrm{q}}\right), 142.3\left(\mathrm{C}_{\mathrm{q}}\right)$, $154.9\left(\mathrm{C}_{\mathrm{q}}\right), 158.5\left(\mathrm{C}_{\mathrm{q}}\right), 175.2\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): m/z calculated for $\mathrm{C}_{19} \mathrm{H}_{18} \mathrm{~N}_{3} \mathrm{~S}: 320.1216[\mathrm{M}+\mathrm{H}]^{+}$; found: 320.1223 .

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

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 $9(215 \mathrm{mg}, 0.80 \mathrm{mmol}, 1.0 \mathrm{eq}$.) and p-tolylboronic acid ( $215 \mathrm{mg}, 1.58 \mathrm{mmol}, 2.0 \mathrm{eq}$.). 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. $M_{\mathrm{p}}$ : $193-195{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 2965,2934,2869,1547$, $1387,1179,812,803,744 .{ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 1.74-$ $1.87\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.00-2.12\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.43\left(\mathrm{~s}, 6 \mathrm{H}, 2 \mathrm{xCH}_{3}\right)$, 2.70-2.83 (m, 2H, N-CH $), 3.19-3.31\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.37$ (p, $J$ $=2.9 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}$ ), 7.31 (dd, $J=5.9,8.0 \mathrm{~Hz}, 4 \mathrm{H}, 4 \mathrm{xCH}_{\mathrm{Ar}}$ ), $8.36-$ $8.42\left(\mathrm{~m}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.42-8.48\left(\mathrm{~m}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C}$ NMR (101 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 21.6\left(\mathrm{CH}_{3}\right), 21.6\left(\mathrm{CH}_{3}\right), 27.9\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH})$, $48.9\left(2 \mathrm{xN}^{\left.-\mathrm{CH}_{2}\right)}\right.$, $128.3\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.0\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.3\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right)$, $130.1\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 133.6\left(\mathrm{C}_{\mathrm{q}}\right), 135.7\left(\mathrm{C}_{\mathrm{q}}\right), 138.8\left(\mathrm{C}_{\mathrm{q}}\right), 140.1\left(\mathrm{C}_{\mathrm{q}}\right)$, $140.2\left(\mathrm{C}_{\mathrm{q}}\right), 154.8\left(\mathrm{C}_{\mathrm{q}}\right), 161.1\left(\mathrm{C}_{\mathrm{q}}\right), 174.8\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): $m / z$ calculated for $\mathrm{C}_{23} \mathrm{H}_{24} \mathrm{~N}_{3}: 342.1965[\mathrm{M}+\mathrm{H}]^{+}$; found: 342.1962.

4-(4-(p-Tolyl)-7,8-dihydro-6H-5,8-ethanopyrido[3,2-d]pyrimidin-$2-y l$ )benzonitrile (54). Compound 54 was obtained according to general procedure $\mathbf{D}$ using $9(215 \mathrm{mg}, 0.80 \mathrm{mmol}, 1.0 \mathrm{eq}$.$) and 4-$ cyanophenylboronic acid ( $238 \mathrm{mg}, 1.62 \mathrm{mmol}, 2.0 \mathrm{eq}$.). After purification by silica gel flash chromatography (DCM/PE, 60/40 to $80 / 20$ ), 54 ( $148 \mathrm{mg}, 52 \%$ ) was obtained as a beige solid. Rf (DCM/PE: 80/20): 0.55. $M_{\mathrm{p}}$ : $236-238{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 2940,2227,1548,1387,1167,816,612 .{ }^{1} \mathrm{H}$ NMR ( 400 MHz , $\left.\mathrm{CDCl}_{3}\right) \delta: 1.73-1.86\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.03-2.15\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.44$ $\left(\mathrm{s}, 3 \mathrm{H}, \mathrm{CH}_{3}\right), 2.70-2.82\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.22-3.33(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-$ $\mathrm{CH}_{2}$ ), $3.38(\mathrm{p}, J=2.8 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 7.33(\mathrm{~d}, J=8.0 \mathrm{~Hz}, 2 \mathrm{H}$, $\left.2 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.78\left(\mathrm{~d}, J=8.6 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.39(\mathrm{~d}, J=8.3 \mathrm{~Hz}, 2 \mathrm{H}$, $2 \mathrm{xCH}_{\mathrm{Ar}}$ ), $8.68\left(\mathrm{~d}, J=8.5 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C} \mathrm{NMR}(101 \mathrm{MHz}$, $\left.\mathrm{CDCl}_{3}\right) \delta: 21.6\left(\mathrm{CH}_{3}\right), 27.8\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH}), 48.8\left(2 \mathrm{xN}-\mathrm{CH}_{2}\right)$, $113.4\left(\mathrm{C}_{\mathrm{q}}\right), 119.1\left(\mathrm{C}_{\mathrm{q}}\right), 128.8\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.1\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 130.2$ $\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 132.4\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 133.0\left(\mathrm{C}_{\mathrm{q}}\right), 140.0\left(\mathrm{C}_{\mathrm{q}}\right), 140.7\left(\mathrm{C}_{\mathrm{q}}\right), 142.6$ $\left(\mathrm{C}_{\mathrm{q}}\right), 155.2\left(\mathrm{C}_{\mathrm{q}}\right), 159.0\left(\mathrm{C}_{\mathrm{q}}\right), 175.5\left(\mathrm{C}_{\mathrm{q}}\right)$. HRMS (EI/MS): m/z calculated for $\mathrm{C}_{23} \mathrm{H}_{21} \mathrm{~N}_{4}$ : $353.1761[\mathrm{M}+\mathrm{H}]^{+}$; 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 $\mathbf{D}$ using $10(110 \mathrm{mg}, 0.40 \mathrm{mmol}, 1.0 \mathrm{eq}$.$) and$ p-tolylboronic acid ( $109 \mathrm{mg}, 0.80 \mathrm{mmol}, 2.0 \mathrm{eq}$.$) . After purifi-$ cation by silica gel flash chromatography (PE/EA, 90/10), 55 ( $63 \mathrm{mg}, 45 \%$ ) was obtained as a white solid. Rf (PE/EA: 90/10): 0.49. $M_{\mathrm{p}}: 164-166{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu: 2926,2869$, $1550,1505,1386,1220,1155,819 .{ }^{1} \mathrm{H} \operatorname{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta$ : 1.74-1.87 (m, 2H, $\mathrm{CH}_{2}$ ), 2.01-2.13 (m, 2H, $\mathrm{CH}_{2}$ ), $2.43(\mathrm{~s}, 3 \mathrm{H}$, $\left.\mathrm{CH}_{3}\right), 2.70-2.82\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.19-3.31\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.37$ $(\mathrm{p}, J=2.9 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 7.18\left(\mathrm{t}, J=8.8 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 7.30(\mathrm{~d}, J$ $=8.0 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}$ ), $8.44\left(\mathrm{~d}, J=8.2 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right), 8.59$ (dd, $\left.J=5.8,8.8 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}}\right) .{ }^{13} \mathrm{C} \operatorname{NMR}\left(101 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 21.6$ $\left(\mathrm{CH}_{3}\right), 27.8\left(2 \mathrm{xCH}_{2}\right), 33.6(\mathrm{CH}), 48.8\left(2 \mathrm{xN}^{2} \mathrm{CH}_{2}\right), 115.1\left(\mathrm{CH}_{\mathrm{Ar}}\right)$, $115.3\left(\mathrm{CH}_{\mathrm{Ar}}\right), 128.2\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 129.3\left(2 \mathrm{xCH}_{\mathrm{Ar}}\right), 132.3\left(\mathrm{CH}_{\mathrm{Ar}}\right), 132.4$ $\left(\mathrm{CH}_{\mathrm{Ar}}\right), 132.5\left(\mathrm{~d}, J=3.2 \mathrm{~Hz}, \mathrm{C}_{\mathrm{q}}\right), 135.5\left(\mathrm{C}_{\mathrm{q}}\right), 138.7\left(\mathrm{C}_{\mathrm{q}}\right), 140.4\left(\mathrm{C}_{\mathrm{q}}\right)$, $153.4\left(\mathrm{C}_{\mathrm{q}}\right), 161.1\left(\mathrm{C}_{\mathrm{q}}\right), 164.1\left(\mathrm{~d}, J=250.5 \mathrm{~Hz}, \mathrm{C}_{\mathrm{q}}-\mathrm{F}\right), 175.2\left(\mathrm{C}_{\mathrm{q}}\right)$. ${ }^{19} \mathrm{~F}$ NMR ( $376 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta:-110.90$. HRMS (EI/MS): $\mathrm{m} / \mathrm{z}$ calculated for $\mathrm{C}_{22} \mathrm{H}_{21} \mathrm{FN}_{3}: 346.1714[\mathrm{M}+\mathrm{H}]^{+}$; 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 $\mathbf{D}$ using $10(109 \mathrm{mg}, 0.40 \mathrm{mmol}$, 1.0 eq. ) and 4-cyanophenylboronic acid ( $118 \mathrm{mg}, 0.80 \mathrm{mmol}, 2.0$ eq.). After purification by silica gel flash chromatography (PE/ EA, $90 / 10$ ), 56 ( $97 \mathrm{mg}, 68 \%$ ) was obtained as a white solid. Rf (PE/EA: 90/10): 0.20. $M_{\mathrm{p}}$ : $237-239{ }^{\circ} \mathrm{C}$. IR (ATR diamond, $\mathrm{cm}^{-1}$ ) $\nu$ : 2950, 2917, 2221, 1602, 1544, 1504, 1382, 1157, 824, 568. ${ }^{1} \mathrm{H}$ NMR ( $400 \mathrm{MHz}, \mathrm{CDCl}_{3}$ ) $\delta: 1.74-1.86\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.05-2.17(\mathrm{~m}$, $\left.2 \mathrm{H}, \mathrm{CH}_{2}\right), 2.70-2.81\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right), 3.22-3.34\left(\mathrm{~m}, 2 \mathrm{H}, \mathrm{N}-\mathrm{CH}_{2}\right)$, 3.39 (p, $J=2.8 \mathrm{~Hz}, 1 \mathrm{H}, \mathrm{CH}), 7.19\left(\mathrm{t}, J=8.7 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}-\mathrm{F}}\right)$, $7.79\left(\mathrm{~d}, J=8.5 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}-\mathrm{CN}}\right), 8.60(\mathrm{dd}, J=5.6,8.9 \mathrm{~Hz}, 2 \mathrm{H}$, $2 \mathrm{xCH}_{\mathrm{Ar}-\mathrm{F}}$ ), $8.67\left(\mathrm{~d}, J=8.5 \mathrm{~Hz}, 2 \mathrm{H}, 2 \mathrm{xCH}_{\mathrm{Ar}-\mathrm{CN}}\right) .{ }^{13} \mathrm{C}$ NMR (101 $\left.\mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta: 27.7\left(2 \mathrm{xCH}_{2}\right), 33.7(\mathrm{CH}), 48.7\left(2 \mathrm{xN}^{2}-\mathrm{CH}_{2}\right), 113.6$ $\left(\mathrm{C}_{\mathrm{q}}\right), 115.3\left(\mathrm{CH}_{\mathrm{Ar}-\mathrm{F}}\right), 115.5\left(\mathrm{CH}_{\mathrm{Ar}-\mathrm{F}}\right), 119.1\left(\mathrm{C}_{\mathrm{q}}\right), 128.8\left(2 \mathrm{xCH}_{\mathrm{Ar}-\mathrm{CN}}\right)$, $131.9\left(\mathrm{~d}, J=3.1 \mathrm{~Hz}, \mathrm{C}_{\mathrm{q}}\right), 132.4\left(2 \mathrm{xCH}_{\mathrm{Ar}-\mathrm{CN}}\right), 132.4\left(\mathrm{CH}_{\mathrm{Ar}-\mathrm{F}}\right), 132.5$ $\left(\mathrm{CH}_{\text {Ar-F }}\right), 139.9\left(\mathrm{C}_{\mathrm{q}}\right), 142.4\left(\mathrm{C}_{\mathrm{q}}\right), 153.8\left(\mathrm{C}_{\mathrm{q}}\right), 159.1\left(\mathrm{C}_{\mathrm{q}}\right), 164.3(\mathrm{~d}, J$ $\left.=251.4 \mathrm{~Hz}, \mathrm{C}_{\mathrm{q}}-\mathrm{F}\right), 175.8\left(\mathrm{C}_{\mathrm{q}}\right) .{ }^{19} \mathrm{~F}$ NMR $\left(376 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta$ : -110.06. HRMS (EI/MS): $\mathrm{m} / \mathrm{z}$ calculated for $\mathrm{C}_{22} \mathrm{H}_{18} \mathrm{FN}_{4}: 357.1510$ $[\mathrm{M}+\mathrm{H}]^{+}$; found: 357.1505.

## Conflicts of interest

The authors declare no conflict of interest.

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[^1]:    ${ }^{a}$ Cpd: compound number; yield is indicated as isolated product. ${ }^{b}$ Not detected.

[^2]:    ${ }^{a}$ Cpd: compound number; yield is indicated as isolated product.

