Efficient Synthesis of 6-Amino-Substituted Pyridin-2(1*H*)-ones Using in situ Generated Propiolic Acid Chloride

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Abstract: A regioselective and highly efficient synthesis of 6-amino-substituted pyridin-2(1*H*)-ones is presented. In situ generated propiolic acid chloride was used for the cyclization of acyclic β-keto *N*,*S*-acetals to afford the heterocyclic core. Substitution by amines led to a flexible access of the target compounds.

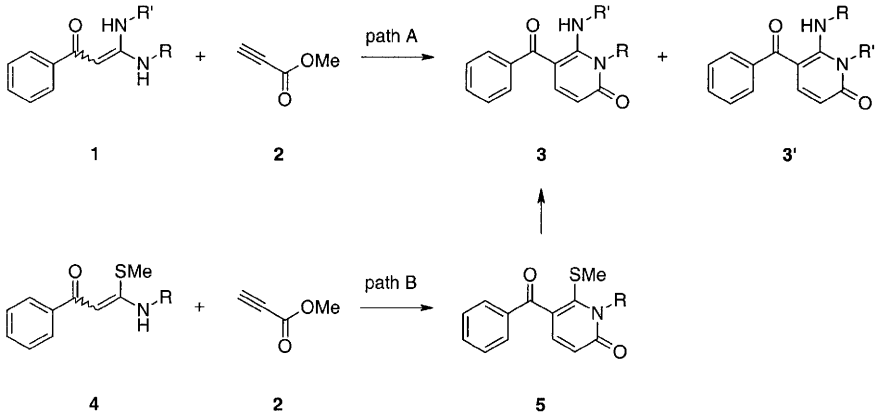
Key words: pyridin-2(1*H*)-ones, cyclizations, thioacetals, *N*,*S*-acetals, ring closure

The access to aminopyridinones from cyclic ketene aminals by cyclization with methyl propiolate is a well established method.[1] However, the regioselective synthesis of 6-amino-substituted pyridin-2(1*H*)-ones formally proceeding from non-symmetrical open-chain ketene aminals has not been reported so far. Mixed ketene aminals of the general structure **1** containing different amino residues R and R′ provide product mixtures of the two regioisomers **3** and **3′** (Scheme 1, path A).[2] Herein we report a selective and highly flexible synthesis leading to 6-amino-substituted pyridin-2(1*H*)-ones **3** according to path B (Scheme 1).

Since the substitution of methyl sulfide by amines has been reported on activated methylthiopyridinones,[3] we questioned whether an analogous reaction could be applicable for the selective synthesis of substituted pyridinones **3** from **5** (Scheme 1). We anticipated that the *N*,*S*-acetals **4** could be cyclized to **5** with propiolic acid ester following a procedure by Huang based on cyclic ketene *N*,*S*-acetals.[4]

The desired *N*,*S*-acetals **4** are readily available from acetophenone **6** via dithioacetals **7**[5] and subsequent substitution[6] or, alternatively, via β-keto thioamides **8** and alkylation (Scheme 2).[7,8]

Propiolic acid methyl ester **2** is the most general reagent described for the attempted cyclization (Scheme 1, **4** → **5**).[4] With the *N*,*S*-acetals **4** we observed that the reaction was very sensitive to the steric demands of the substrates and failed in the majority of the cases (Table 1, method A).[9] Compounds with phenylic or α-branched aliphatic residues did not react. Only α-linear derivatives comprising methyl- (entry 1), isobutyl-, phenethyl- and methoxyethylamine (entries 5–7) provided the desired products in low to moderate yields. The addition of a base like sodium hydroxide or potassium *tert*-butoxide[10] did not improve the results. Other reaction conditions like the activation of propiolic acid with carbonyldiimidazole[11] or with dicyclohexylcarbodiimide[12] failed. As reported in the literature, the more reactive acid chlorides have been used successfully in acylation/cyclization reactions of β-keto ketene *N*,*S*- and *N*,*N*-acetals. Amongst others, oxalyl[13] and malonyl dichloride,[14] 3-bromopropionyl chloride[15] and substituted acryloyl chlorides[16] have been applied.[17] However, the use of propiolic acid chloride is rare,[18] probably due to its instability and hazardous poten-



Scheme 1 Synthesis of 6-amino-substituted pyridin-2(1*H*)-ones **3**: cyclization of mixed aminals (path A) or regioselective approach (path B)

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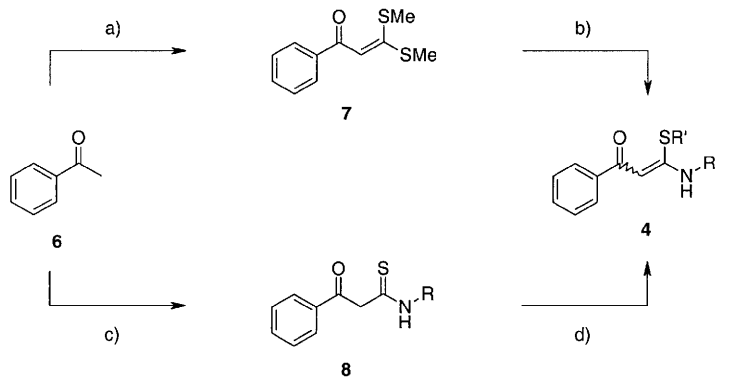


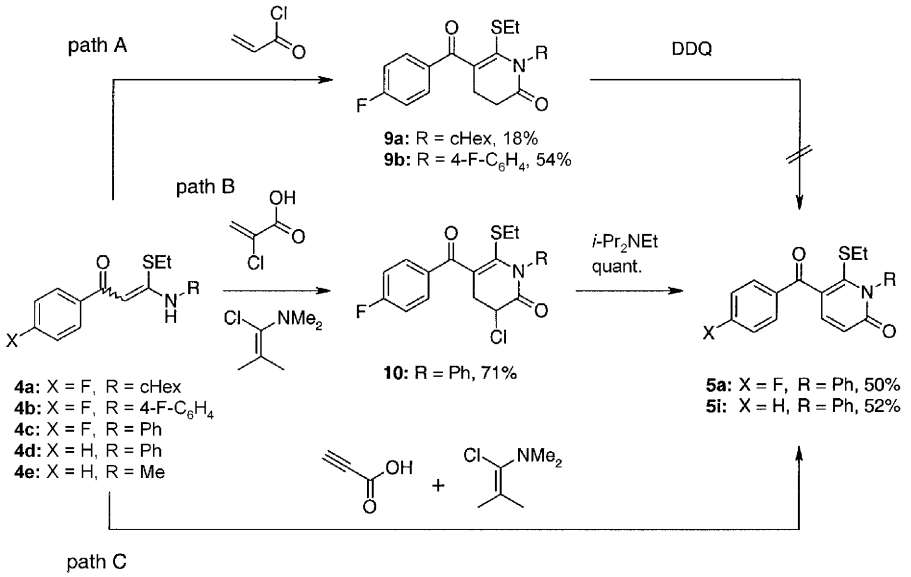
Scheme 2 Two alternative pathways leading to *N*,*S*-acetals **5**. *Reagents and conditions*: a) NaH, CS_2, MeI; b) RNH_2; c) NaH, RNCS; d) MeI or EtI

tial.[19] We therefore approached the formation of the pyridinone ring in two steps, a cyclization with acrylate followed by the oxidative aromatization of the ring system (Scheme 3, path A). The cyclization with acrylic acid chloride provided the cyclized compounds **9a** and **9b** in low to moderate yield, but an attempt to oxidize the dihydropyridinones **9** with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) to obtain the pyridinone system **5** failed.[20]

The strategy to use α-chloroacrylic acid chloride to generate a 'preformed' double bond was much more successful. In our hands, the in situ generation of the acid chloride proved to be superior to its isolation.[21] To achieve this, we used Ghosez' 1-chloro-*N*,*N*,2-trimethylprop-1-en-1-amine[22] (Scheme 3, path B). After preforming the acid chloride by treatment of the acid with one equivalent of the chlorination reagent in tetrahydrofuran at 0 °C, the reaction with the *N*,*S*-acetal **4c** yielded the desired product **10** in 71% yield. Subsequent treatment with Hünig's base in dichloromethane provided the desired pyridinone quantitatively.

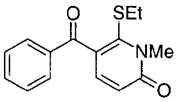
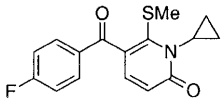
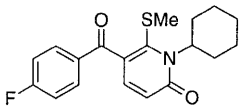
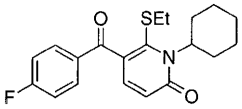
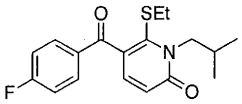
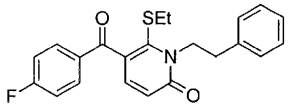
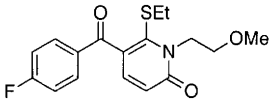
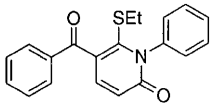
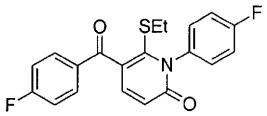
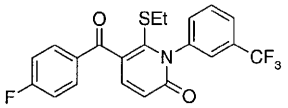
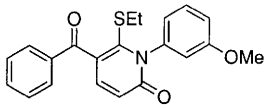
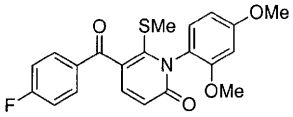
A more efficient method to prepare the pyridinone ring was the use of in situ generated propiolic acid chloride. We were pleased to find that Ghosez' reagent applied on propiolic acid allowed us to prepare pyridinones **5** from **4** in a single step (Scheme 3, path C). *N*,*S*-Acetals **4** containing an anilinic moiety were cyclized with yields of about 50% (Table 1, entries 8–12, method B). The isobutyl derivative **5f** was obtained in 73% yield compared to 17% with propiolic acid methyl ester (entry 5). Even with the sterically more demanding aliphatic α-branched amino moieties we obtained the desired heterocycles in moderate yields (entries 2–4, method B). The 6-ethylthio- and 6-methylthiopyridin-2(1*H*)-ones **5a**–**5m** were reasonably stable. After column chromatography on silica gel, the purity determined by HPLC was about 80% in most of the cases, which was sufficient for the subsequent transformation.

The final substitution of methyl- or ethylsulfide by amines led very cleanly to the target compounds **3**. The reactions are usually slow at room temperature, but in most cases they can be driven to completeness by adjusting the con-



Scheme 3 Cyclization of *N*,*S*-acetals with acrylic and propiolic acid derivatives

Table 1 6-Ethylthio- and 6-Methylthiopyridin-2(1*H*)-ones

Entry	Compd	Product	Yield Method A (%)[a]	Yield Method B (%)[b]
1	**5b**		45	–
2	**5c**		0	43
3	**5d**		0	34
4	**5e**		0	29
5	**5f**		17	73
6	**5g**		46	–
7	**5h**		29	–
8	**5i**		0	52
9	**5j**		–	51
10	**5k**		0	47
11	**5l**		–	53
12	**5m**		0	35

[a] Method A: propiolic acid methyl ester.
[b] Method B: propiolic acid, 1-chloro-*N*,*N*,2-trimethylprop-1-en-1-amine.

ditions (temperature, reaction time, equivalents of amine). With *N*-methyl pyridinone **5b** and a three-fold excess of an ethanolic solution of ethylamine the reaction yielded 92% of the desired amino product **3a** (Table 2, entry 1). Using less volatile amines, a slight excess was sufficient. Functionalized amines like 2-methoxyethylamine (entry 2) and benzylic amines (entry 3) reacted in good yields as did α-branched amines like cyclohexylamines (entry 4). However, the substitution with the sterically more hindered *tert*-butyl amine was much slower (entry 5). In this case, a 5-fold excess was used. After 20 hours the product was isolated in 36% yield (50% conversion). As expected, anilines proved to be much less reactive. Three equivalents of the aniline in refluxing toluene resulted in a con-

version of 50% and a 25% isolated yield after 24 hours (entry 6).

The reaction was also sensitive towards the steric demands of the substrate. With larger N-substituents on the pyridinone moiety, the reaction slowed down. For example, with the cyclopropylic substrate and cyclopropylmethylamine as nucleophile (Table 2, entry 7), heating to reflux was required to facilitate the substitution in 70% yield. The isobutyl derivative **5f** was more reactive: With benzylic amines, about 50% conversion was observed after 20 hours at room temperature, and reflux for further five hours completed the reaction (entry 9, 74% yield). Even with cyclohexylamine, product **3j** was isolated in high yield (entry 10).

The substrates with a phenyl residue incorporated, like **5a**, **5i**–**5m**, were much less reactive. At room temperature, only α-methylene amines reacted at sufficient speed (entries 13–16). α-Branched amines like cyclohexylamines (entry 17) needed three days at 70 °C with two equivalents of amine. With *t*-butyl amine no reaction could be observed even with three equivalents of amine after six days at 70 °C (entry 18).

Table 2 Synthesis of 6-Amino-Substituted Pyridin-2(1*H*)-ones

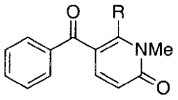
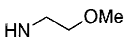
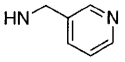
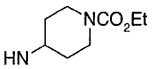
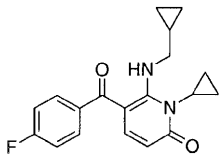
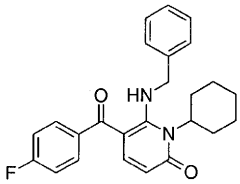
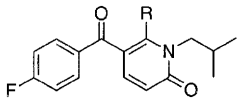
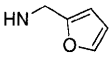
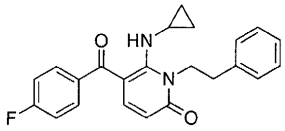
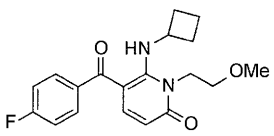
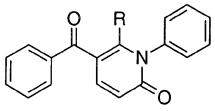
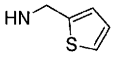
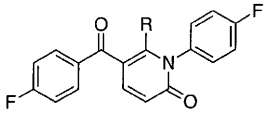
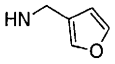
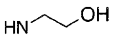
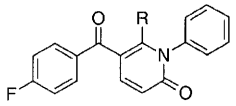
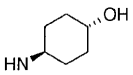
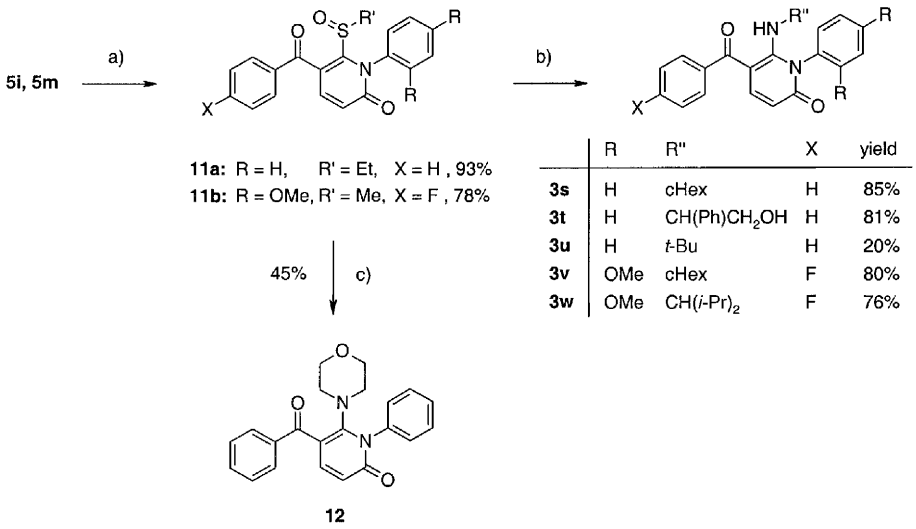
Entry	Sulfide	Product	R	Compd	Yield (%)
1	**5b**			**3a**	92
2				**3b**	79
3				**3c**	76
4				**3d**	90
5				**3e**	36
6				**3f**	25
7	**5c**			**3g**	70
8	**5d**			**3h**	71
9	**5f**			**3i**	74
10				**3j**	74
11	**5g**			**3k**	45
12	**5h**			**3l**	59

Table 2 Synthesis of 6-Amino-Substituted Pyridin-2(1*H*)-ones (continued)

Entry	Sulfide	Product	R	Compd	Yield (%)
13	**5i**			**3m**	77
14				**3n**	86
15	**5j**			**3o**	58
16				**3p**	43
17	**5a**			**3q**	57
18				**3r**	0

To overcome the restrictions attributed to the steric demands of substrate and reagent, we aimed at a further activation of the substrate by oxidation of sulfides **5i** and **5m**, which was achieved with MCPBA (Scheme 4). Sulfoxides **11a** and **11b** were much more reactive toward nucleophilic substitution than the corresponding sulfides. For example, **5i** did not react with cyclohexylamine at room temperature and needed to be heated to reflux overnight to yield 59% of product **3s**. With sulfoxide **11a**, the reaction was complete after two hours under similar conditions with an isolated yield of 85% (Scheme 4). Phenylalaninol reacted in 81% yield to the desired product **3t**, the otherwise unreactive *tert*-butylamine in 20% yield. One example of a secondary amine reacting with the sulfoxide was provided with morpholine and **11a**, which gave substitution product **12** in 45% yield. With **11b** and cyclohexylamine, 80% of the desired product **3v** were obtained. Even the sterically very demanding 2,4-dimethylpentan-3-amine reacted within 48 hours with an isolated yield of 76% (**3w**).

In summary, we have developed a regioselective and highly flexible synthesis of 6-amino-substituted pyridine-2(1*H*)-ones. The two different substituents may independently be of aliphatic or aromatic nature. We have demonstrated that in situ generated propiolic acid chloride, which has not been used with ketene *N*,*S*-acetals so far, allows the cyclization yielding 6-methylthio or 6-ethylthio pyridinones. The final transformation gives rapid access to unsymmetrically N,N-bissubstituted aminopyridinones. Given the broad substrate tolerance of the sequence, especially with respect to the substitution of sulfides or sulfoxides by amines, the synthesis shown allows a combinatorial access to the target compounds.



	R	R''	X	yield
3s	H	cHex	H	85%
3t	H	$CH(Ph)CH_2OH$	H	81%
3u	H	*t*-Bu	H	20%
3v	OMe	cHex	F	80%
3w	OMe	$CH(i\text{-}Pr)_2$	F	76%

Scheme 4 Substitution of sulfoxides. *Reagents and conditions*: a) MCPBA (1.05 equiv), CH_2Cl_2, r.t.; b) $R'NH_2$ (1.2–2.0 equiv), toluene, reflux; c) Morpholine (2.0 equiv), toluene, reflux

^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance spectrometers operating at 400 MHz and 500 MHz for ^{1}H and 125 MHz for ^{13}C in DMSO-d_6. ^{1}H NMR data are reported in the following order: chemical shifts, multiplicities (br: broadened; s: singlet; d: doublet; t: triplet), coupling constants. Integration is provided. Flash column chromatography was performed with silica gel 60 (0.063–0.200 mm) from Merck KGaA, Darmstadt, Germany. Solvents for extraction and chromatography were reagent grade and used as received. THF, EtOH and toluene used as reaction media were purchased in absolute grade and used as received. Commercial reagents were used without purification.

Synthesis of β-Keto *N*,*S*-Acetals 4; General Procedure

β-Keto thioamides **8** were synthesized from the corresponding acetophenones and isothiocyanates following a known procedure.[7] They were isolated as yellow solids and characterized by LC-MS and ^{1}H NMR spectroscopy and showed the keto-enol tautomerism described in the literature.[8] The thioamides **8** were dissolved in acetone (to give a 0.13 M solution) and treated with K_2CO_3 (1.1 equiv) and iodoethane (1.1 equiv) at r.t. After 2 h the mixture was concentrated in vacuo, treated with H_2O (10 mL/mmol) and then extracted twice with EtOAc (2 × 100 mL). The organic layers were dried (Na_2SO_4) and evaporated to yield the β-keto *N*,*S*-acetals as yellow solids, which were occasionally purified by column chromatography on silica gel (CH_2Cl_2). Representative examples are:

3-(Cyclohexylamino)-3-(ethylthio)-1-(4-fluorophenyl)prop-2-en-1-one (4a)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.22–1.41 (m, 5 H), 1.33 (t, *J* = 7.3 Hz, 3 H), 1.50–1.57 (m, 1 H), 1.64–1.73 (m, 2 H), 1.87–1.95 (m, 2 H), 3.13 (q, *J* = 7.3 Hz, 2 H), 3.56–3.66 (m, 1 H), 5.75 (s, 1 H), 7.24 (dd, *J* = 9.1, 8.5 Hz, 2 H), 7.93 (dd, *J* = 8.5, 5.8 Hz, 2 H), 12.0 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.5, 23.6, 24.71, 24.73, 32.5, 52.0, 85.7, 115.0 (d, $^2J_{C,F}$ = 21.4 Hz), 129.1 (d, $^3J_{C,F}$ = 8.8 Hz), 136.4 (d, $^4J_{C,F}$ = 2.9 Hz), 163.5 (d, $^1J_{C,F}$ = 248 Hz), 166.9, 181.9.

HRMS: *m*/*z* [M$^+$] calcd for $C_{17}H_{22}FNOS$: 307.1406; found: 307.1409.

3-(Ethylthio)-1-(4-fluorophenyl)-3-[(4-fluorophenyl)amino]prop-2-en-1-one (4b)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.28 (t, *J* = 7.3 Hz, 3 H), 3.12 (q, *J* = 7.3 Hz, 2 H), 6.05 (s, 1 H), 7.24–7.33 (m, 4 H), 7.38 (dd, *J* = 8.6, 4.9 Hz, 2 H), 8.03 (dd, *J* = 8.3, 5.9 Hz, 2 H), 13.40 (s, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.2, 25.1, 88.5, 115.2 (d, $^2J_{C,F}$ = 21.5 Hz), 115.9 (d, $^2J_{C,F}$ = 22.7 Hz), 127.5 (d, $^3J_{C,F}$ = 8.7 Hz), 129.6 (d, $^3J_{C,F}$ = 9.0 Hz), 133.9 (d, $^4J_{C,F}$ = 2.8 Hz), 135.7 (d, $^4J_{C,F}$ = 2.8 Hz), 160.3 (d, $^1J_{C,F}$ = 244 Hz), 163.8 (d, $^1J_{C,F}$ = 249 Hz), 166.8, 183.2.

HRMS: *m*/*z* [M$^+$] calcd for $C_{17}H_{15}F_2NOS$: 319.0842; found: 319.0836.

3-Anilino-3-(ethylthio)-1-(4-fluorophenyl)prop-2-en-1-one (4c)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.29 (t, *J* = 7.3 Hz, 3 H), 3.13 (q, *J* = 7.3 Hz, 2 H), 6.06 (s, 1 H), 7.27–7.36 (m, 5 H), 7.44 (t, *J* = 7.7 Hz, 2 H), 8.04 (dd, *J* = 8.4, 5.8 Hz, 2 H), 13.58 (s, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.1, 25.2, 88.6, 115.2 (d, $^2J_{C,F}$ = 21.5 Hz), 124.8, 126.3, 129.2, 129.5 (d, $^3J_{C,F}$ = 9.0 Hz), 135.8 (d, $^4J_{C,F}$ = 2.8 Hz), 137.6, 163.8 (d, $^1J_{C,F}$ = 249 Hz), 166.4, 183.2.

HRMS: *m*/*z* [M$^+$] calcd for $C_{17}H_{16}FNOS$: 301.0937; found: 301.0940.

3-Anilino-3-(ethylthio)-1-phenylprop-2-en-1-one (4d)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.29 (t, *J* = 7.3 Hz, 3 H), 3.12 (q, *J* = 7.3 Hz, 2 H), 6.08 (s, 1 H), 7.29 (t, *J* = 7.3 Hz, 1 H), 7.34 (d, *J* = 7.7 Hz, 2 H), 7.41–7.56 (m, 5 H), 7.96 (d, *J* = 7.3 Hz, 2 H), 13.65 (s, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.2, 25.2, 88.8, 124.7, 126.3, 126.9, 128.4, 129.2, 131.1, 137.7, 139.3, 166.1, 184.5.

HRMS: *m*/*z* [M$^+$] calcd for $C_{17}H_{17}NOS$: 283.1031; found: 283.1028.

3-(Ethylthio)-3-(methylamino)-1-phenylprop-2-en-1-one (4e)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.34 (t, *J* = 7.3 Hz, 3 H), 3.00 (d, *J* = 5.0 Hz, 3 H), 3.12 (q, *J* = 7.3 Hz, 2 H), 5.78 (s, 1 H), 7.40–7.48 (m, 3 H), 7.85 (d, *J* = 7.1 Hz, 2 H), 11.65 (br s, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.5, 24.6, 29.9, 85.8, 126.6, 128.1, 130.3, 140.0, 169.1, 183.1.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{12}H_{16}NOS$: 222.0948; found, 222.0940.

Cyclization with in situ Generated Propilic Acid Chloride; General Procedure

Propiolic acid (12 mmol) was dissolved in THF (20 mL) and cooled to 0 °C. 1-Chloro-*N*,*N*,2-trimethylprop-1-en-1-amine (12 mmol) was added and the mixture was stirred at 0 °C for 2 h. Subsequently, a solution of the β-keto *N*,*S*-acetal **4** (10 mmol) in THF (15 mL) was added and the reaction was stirred at r.t. for 24 h. The mixture was evaporated, and the crude product was purified by column chromatography on silica gel (CH_2Cl_2–MeOH, 50:1) yielding 6-(ethylthio)pyridin-2(1*H*)-ones **5** as reddish oils in about 80% purity, which crystallized after storage in the refrigerator. As unstable compounds, 6-(ethylthio)pyridin-2(1*H*)-ones **5** were used without further purification.

5-Benzoyl-6-(ethylthio)-1-phenylpyridin-2(1*H*)-one (5i)

As a representative example, the compound was purified by preparative HPLC and isolated as a light yellow solid.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.69 (t, *J* = 7.4 Hz, 3 H), 2.27 (q, *J* = 7.4 Hz, 2 H), 6.65 (d, *J* = 9.4 Hz, 1 H), 7.40 (d, *J* = 7.6 Hz, 2 H), 7.46 (t, *J* = 7.2 Hz, 1 H), 7.49–7.58 (m, 5 H), 7.67 (t, *J* = 7.3 Hz, 1 H), 7.90 (d, *J* = 7.5 Hz, 2 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.7, 30.6, 120.6, 124.5, 128.6, 128.8, 128.9, 129.1, 129.5, 133.5, 137.2, 138.4, 138.9, 143.0, 162.2, 193.4.

HRMS: *m*/*z* [M$^+$] calcd for $C_{20}H_{17}NO_2S$: 335.0980; found: 335.0977.

Substitution Reaction; General Procedure

The 6-methylthio or 6-ethylthio pyridinone (0.3 mmol) was dissolved in EtOH (2 mL) or toluene (2 mL). The amine (1.1 equiv) was added and the reaction was stirred at r.t. overnight. Less reactive substrates required elevated temperatures. After the completion of the reaction volatile components were removed and the crude product was purified by preparative HPLC. All new compounds gave satisfactory spectroscopic data.

5-Benzoyl-6-(ethylamino)-1-methylpyridin-2(1*H*)-one (3a)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.22 (t, *J* = 7.2 Hz, 3 H), 3.42–3.48 (m, 2 H), 3.49 (s, 3 H), 5.73 (d, *J* = 9.6 Hz, 1 H), 7.33 (d, *J* = 9.6 Hz, 1 H), 7.47–7.56 (m, 5 H), 9.82 (br. s, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 15.6, 33.0, 41.8, 100.4, 104.7, 128.2, 128.3, 130.7, 139.6, 142.7, 159.1, 162.3, 192.7.

HRMS: *m*/*z* [M$^+$] calcd for $C_{15}H_{16}N_2O_2$: 256.1212; found: 256.1208.

5-Benzoyl-6-[(2-methoxyethyl)amino]-1-methylpyridin-2(1*H*)-one (3b)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 3.27 (s, 3 H), 3.48 (s, 3 H), 3.50 (t, *J* = 4.7 Hz, 2 H), 3.59 (dt, *J* = 4.7, 4.7 Hz, 2 H), 5.74 (d, *J* = 9.5 Hz, 1 H), 7.34 (d, *J* = 9.5 Hz, 1 H), 7.47–7.57 (m, 5 H), 10.00 (t, *J* = 4.7 Hz, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 33.5, 46.4, 58.2, 71.0, 100.7, 105.0, 128.2, 128.3, 130.6, 139.6, 142.6, 159.8, 162.3, 192.7.

HRMS: *m/z* [M$^+$] calcd for $C_{16}H_{18}N_2O_3$: 286.1317; found: 286.1311.

5-Benzoyl-1-methyl-6-[(pyridin-3-ylmethyl)amino]pyridin-2(1*H*)-one (3c)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 3.57 (s, 3 H), 4.65 (d, *J* = 4.9 Hz, 2 H), 5.78 (d, *J* = 9.5 Hz, 1 H), 7.29 (d, *J* = 9.5 Hz, 1 H), 7.32–7.39 (m, 3 H), 7.46 (t, *J* = 7.4 Hz, 2 H), 7.51–7.56 (m, 1 H), 7.71 (d, *J* = 7.7 Hz, 1 H), 8.46–8.50 (m, 2 H), 9.71 (t, *J* = 4.9 Hz, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 32.6, 47.1, 101.5, 105.3, 123.6, 128.2, 128.3, 130.8, 133.2, 135.4, 139.1, 142.3, 148.7, 148.9, 158.1, 162.0, 192.5.

HRMS: *m/z* [M$^+$] calcd for $C_{19}H_{17}N_3O_2$: 319.1321; found: 319.1319.

Ethyl 4-[(3-Benzoyl-1-methyl-6-oxo-1,6-dihydropyridin-2-yl)amino]piperidine-1-carboxylate (3d)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.16 (t, *J* = 7.1 Hz, 3 H), 1.31–1.41 (m, 2 H), 1.90 (d, *J* = 10.9 Hz, 2 H), 2.99 (br s, 2 H), 3.50 (s, 3 H), 3.80–3.90 (m, 3 H), 4.01 (q, *J* = 7.1 Hz, 2 H), 5.86 (d, *J* = 9.6 Hz, 1 H), 7.37 (d, *J* = 9.6 Hz, 1 H), 9.49–9.52 (m, 4 H), 7.54–7.59 (m, 1 H), 9.63 (d, *J* = 9.1 Hz, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 14.5, 32.5, 33.5, 41.8, 52.8, 60.7, 102.4, 106.7, 128.30, 128.34, 130.9, 139.4, 142.4, 154.5, 159.0, 162.3, 193.9.

HRMS: *m/z* [M$^+$] calcd for $C_{21}H_{25}N_3O_4$: 383.1845; found: 383.1844.

5-Benzoyl-6-(*tert*-butylamino)-1-methylpyridin-2(1*H*)-one (3e)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.24 (s, 9 H), 3.52 (s, 3 H), 6.05 (d, *J* = 9.5 Hz, 1 H), 7.38 (d, *J* = 9.5 Hz, 1 H), 7.51–7.55 (m, 3 H), 7.59–7.63 (m, 2 H), 7.85 (s, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 30.1, 35.6, 58.6, 108.8, 109.8, 128.5, 128.9, 131.8, 138.8, 141.5, 158.7, 162.6, 195.1.

HRMS: *m/z* [M$^+$] calcd for $C_{17}H_{20}N_2O_2$: 284.1525; found: 284.1524.

6-Anilino-5-benzoyl-1-methylpyridin-2(1*H*)-one (3f)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 3.22 (s, 3 H), 6.11 (d, *J* = 9.5 Hz, 1 H), 6.88 (d, *J* = 7.7 Hz, 2 H), 7.02 (t, *J* = 7.5 Hz, 1 H), 7.23 (t, *J* = 7.5 Hz, 2 H), 7.40–7.55 (m, 6 H), 10.34 (s, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 32.5, 104.8, 109.4, 120.0, 123.2, 128.1, 128.3, 129.2, 131.4, 138.4, 140.8, 141.7, 152.7, 162.3, 193.4.

HRMS: *m/z* [M$^+$] calcd for $C_{19}H_{16}N_2O_2$: 304.1212; found: 304.1210.

1-Cyclopropyl-6-[(cyclopropylmethyl)amino]-5-(4-fluorobenzoyl)pyridin-2(1*H*)-one (3g)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.31–0.35 (m, 2 H), 0.54–0.58 (m, 2 H), 0.67–0.71 (m, 2 H), 1.08–1.17 (m, 1 H), 1.17–1.22 (m, 2 H), 3.13–3.18 (m, 1 H), 3.57 (dd, *J* = 6.9, 4.7 Hz, 2 H), 5.59 (d, *J* = 9.6 Hz, 1 H), 7.25–7.33 (m, 3 H), 7.52 (dd, *J* = 8.3, 5.7 Hz, 2 H), 10.87 (br s, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 3.48, 11.6, 12.0, 30.1, 51.1, 99.2, 105.0, 115.2 (d, $^2J_{C,F}$ = 21.7 Hz), 130.5 (d, $^3J_{C,F}$ = 8.7 Hz), 136.4 (d, $^4J_{C,F}$ = 3.1 Hz), 142.4, 160.5, 162.9 (d, $^1J_{C,F}$ = 248 Hz), 163.6, 191.0.

HRMS: *m/z* [M$^+$] calcd for $C_{19}H_{19}FN_2O_2$: 326.1431; found: 326.1423.

6-(Benzylamino)-1-cyclohexyl-5-(4-fluorobenzoyl)pyridin-2(1*H*)-one (3h)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.06–1.14 (m, 3 H), 1.51–1.56 (m, 1 H), 1.73 (d, *J* = 9.0 Hz, 4 H), 2.55–2.65 (m, 2 H), 4.14 (t, *J* = 11.4 Hz, 1 H), 4.54 (d, *J* = 5.8 Hz, 2 H), 5.73 (d, *J* = 9.5 Hz, 1 H), 7.25–7.32 (m, 4 H), 7.35–7.38 (m, 4 H), 7.49 (dd, *J* = 8.4, 5.7 Hz, 2 H), 10.11 (t, *J* = 5.8 Hz, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 24.9, 25.6, 29.5, 51.2, 60.8, 102.4, 108.7, 115.3 (d, $^2J_{C,F}$ = 21.8 Hz), 127.2, 127.7, 128.7, 131.0 (d, $^3J_{C,F}$ = 8.9 Hz), 136.0 (d, $^4J_{C,F}$ = 3.0 Hz), 137.8, 142.1, 160.9, 163.4 (d, $^1J_{C,F}$ = 249 Hz), 163.5, 192.1.

HRMS: *m/z* [M$^+$] calcd for $C_{25}H_{25}FN_2O_2$: 404.1900; found: 404.1893.

5-(4-Fluorobenzoyl)-6-[(2-furylmethyl)amino]-1-isobutylpyridin-2(1*H*)-one (3i)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.82 (d, *J* = 6.5 Hz, 6 H), 2.17 (sept, *J* = 6.5 Hz, 1 H), 4.08 (br s, 2 H), 4.43 (d, *J* = 4.6 Hz, 2 H), 5.75 (d, *J* = 9.7 Hz, 1 H), 6.16 (s, 1 H), 6.34 (s, 1 H), 7.25–7.33 (m, 3 H), 7.50–7.56 (m, 3 H), 8.66 (t, *J* = 4.6 Hz, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 19.4, 25.6, 42.6, 48.1, 101.4, 105.4, 108.5, 110.4, 115.1 (d, $^2J_{C,F}$ = 21.8 Hz), 131.5 (d, $^3J_{C,F}$ = 9.1 Hz), 135.4 (d, $^4J_{C,F}$ = 2.9 Hz), 142.3, 142.9, 150.0, 155.7, 161.9, 163.6 (d, $^1J_{C,F}$ = 249 Hz), 190.4.

HRMS: *m/z* [M$^+$] calcd for $C_{21}H_{21}FN_2O_3$: 368.1536; found: 368.1526.

6-(Cyclohexylamino)-5-(4-fluorobenzoyl)-1-isobutylpyridin-2(1*H*)-one (3j)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.81 (d, *J* = 6.6 Hz, 6 H), 1.12–1.23 (m, 1 H), 1.24–1.35 (m, 4 H), 1.50 (d, *J* = 12.1 Hz, 1 H), 1.60–1.69 (m, 2 H), 1.79–1.86 (m, 2 H), 2.13 (sept, *J* = 6.6 Hz, 1 H), 3.37–3.45 (m, 1 H), 3.90–4.10 (m, 2 H), 5.81 (d, *J* = 9.5 Hz, 1 H), 7.30–7.37 (m, 3 H), 7.60 (dd, *J* = 8.3, 5.7 Hz, 2 H), 9.47 (d, *J* = 7.7 Hz, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 19.5, 23.9, 24.8, 25.6, 32.9, 49.9, 55.8, 101.8, 106.4, 115.3 (d, $^2J_{C,F}$ = 21.8 Hz), 131.1 ($^3J_{C,F}$ = 8.9 Hz), 135.9 (d, $^4J_{C,F}$ = 3.0 Hz), 142.5, 157.8, 162.4, 163.5 (d, $^1J_{C,F}$ = 249 Hz), 192.4.

HRMS: *m/z* [M$^+$] calcd for $C_{22}H_{27}FN_2O_2$: 370.2057; found: 370.2058.

6-(Cyclopropylamino)-5-(4-fluorobenzoyl)-1-(2-phenylethyl)pyridin-2(1*H*)-one (3k)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.53–0.66 (m, 4 H), 2.62–2.68 (m, 1 H), 2.87 (t, *J* = 7.7 Hz, 2 H), 4.44 (t, *J* = 7.7 Hz, 2 H), 5.70 (d, *J* = 9.3 Hz, 1 H), 7.21–7.36 (m, 8 H), 7.70 (dd, *J* = 8.0, 5.7 Hz, 2 H), 9.12 (s, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 9.49, 28.5, 32.9, 42.8, 100.5, 104.2, 115.3 (d, $^2J_{C,F}$ = 21.8 Hz), 126.3, 128.2, 128.7, 131.5 (d, $^3J_{C,F}$ = 9.0 Hz), 135.4 (d, $^4J_{C,F}$ = 3.0 Hz), 138.1, 142.2, 155.8, 161.5, 163.6 (d, $^1J_{C,F}$ = 249 Hz), 190.4.

HRMS *m/z* [M + H$^+$] calcd for $C_{23}H_{22}FN_2O_2$: 377.1660; found: 377.1670.

6-(Cyclobutylamino)-5-(4-fluorobenzoyl)-1-(2-methoxyethyl)pyridin-2(1*H*)-one (3l)

^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.50–1.61 (m, 1 H), 1.62–1.70 (m, 1 H), 1.92–2.02 (m, 2 H), 2.15–2.23 (m, 2 H), 3.28 (s, 3 H), 3.62 (t, *J* = 5.0 Hz, 2 H), 3.99 (m, 1 H), 4.23 (t, *J* = 5.0 Hz, 2 H), 5.71 (d, *J* = 9.5 Hz, 1 H), 7.29–7.35 (m, 3 H), 7.64 (dd, *J* = 7.4, 6.0 Hz, 2 H), 9.19 (d, *J* = 5.0 Hz, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 13.9, 31.0, 42.8, 51.0, 58.4, 69.3, 100.3, 104.8, 115.4 (d, $^2J_{C,F}$ = 21.8 Hz), 131.4 (d, $^3J_{C,F}$ = 8.9 Hz), 135.5 (d, $^4J_{C,F}$ = 3.0 Hz), 142.9, 155.6, 162.0, 163.6 (d, $^1J_{C,F}$ = 249 Hz), 190.5.

HRMS: *m*/*z* [M$^+$] calcd for $C_{19}H_{21}FN_2O_3$: 344.1536; found: 344.1533.

5-Benzoyl-6-(isobutylamino)-1-phenylpyridin-2(1*H*)-one (3m)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.71 (d, *J* = 6.6 Hz, 6 H), 1.57 (tsept, *J* = 6.6, 6.2 Hz, 1 H), 2.16 (dd, *J* = 6.2, 5.5 Hz, 2 H), 5.71 (d, *J* = 9.6 Hz, 1 H), 7.42–7.57 (m, 11 H), 11.29 (t, *J* = 5.5 Hz, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 19.5, 28.3, 52.0, 98.8, 104.1, 127.9, 128.3, 129.0, 129.1, 129.6, 130.2, 137.5, 139.9, 144.3, 157.8, 161.7, 192.8.

HRMS: *m*/*z* [M$^+$] calcd for $C_{22}H_{22}N_2O_2$: 346.1681; found: 346.1676.

5-Benzoyl-1-phenyl-6-[(2-thienylmethyl)amino]pyridin-2(1*H*)-one (3n)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 3.77 (d, *J* = 4.6 Hz, 2 H), 5.78 (d, *J* = 9.7 Hz, 1 H), 6.84 (br s, 1 H), 6.93 (t, *J* = 3.5 Hz, 1 H), 7.44–7.61 (m, 12 H), 10.59 (t, *J* = 4.6 Hz, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 43.1, 99.6, 105.0, 126.4, 126.7, 127.1, 128.1, 128.4, 129.4, 129.5, 129.6, 130.6, 137.1, 139.3, 139.7, 144.2, 156.9, 161.7, 193.0.

HRMS: *m*/*z* [M$^+$] calcd for $C_{23}H_{18}N_2O_2S$: 386.1089; found: 386.1087.

5-(4-Fluorobenzoyl)-1-(4-fluorophenyl)-6-[(3-furylmethyl)amino]pyridin-2(1*H*)-one (3o)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 3.51 (d, *J* = 4.4 Hz, 2 H), 5.76 (d, *J* = 9.6 Hz, 1 H), 6.35 (s, 1 H), 7.33 (t, *J* = 8.7 Hz, 2 H), 7.40 (t, *J* = 8.6 Hz, 2 H), 7.47 (d, *J* = 9.6 Hz, 1 H), 7.50–7.56 (m, 5 H), 7.61 (s, 1 H), 10.76 (t, *J* = 4.4 Hz, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 39.8, 99.1, 104.4, 109.8, 115.2 (d, $^2J_{C,F}$ = 21.7 Hz), 116.1 (d, $^2J_{C,F}$ = 22.9 Hz), 120.9, 130.6 (d, $^3J_{C,F}$ = 8.8 Hz), 131.8 (d, $^3J_{C,F}$ = 8.9 Hz), 133.1 (d, $^4J_{C,F}$ = 3.0 Hz), 136.0 (d, $^4J_{C,F}$ = 3.1 Hz), 140.5, 143.96, 144.02, 156.9, 161.5 (d, $^1J_{C,F}$ = 152 Hz), 161.6, 163.5 (d, $^1J_{C,F}$ = 153 Hz), 191.2.

HRMS: *m*/*z* [M$^+$] calcd for $C_{23}H_{16}F_2N_2O_3$: 406.1129; found: 406.1120.

5-(4-Fluorobenzoyl)-1-(4-fluorophenyl)-6-[(2-hydroxyethyl)amino]pyridin-2(1*H*)-one (3p)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.47 (dt, *J* = 7.0, 4.9 Hz, 2 H), 3.33 (2 H, under water peak), 4.88 (t, *J* = 4.7 Hz, 1 H), 5.70 (d, *J* = 9.6 Hz, 1 H), 7.34 (t, *J* = 8.8 Hz, 2 H), 7.38 (t, *J* = 8.5 Hz, 2 H), 7.46 (d, *J* = 9.6 Hz, 1 H), 7.49 (dd, *J* = 8.7, 4.9 Hz, 2 H), 7.57 (dd, *J* = 8.2, 5.7 Hz, 2 H), 11.04 (br s, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 47.5, 59.2, 98.7, 103.6, 115.2 (d, $^2J_{C,F}$ = 21.7 Hz), 116.0 (d, $^2J_{C,F}$ = 22.8 Hz), 130.5 (d, $^3J_{C,F}$ = 8.8 Hz), 131.8 (d, $^3J_{C,F}$ = 8.8 Hz), 133.5 (d, $^4J_{C,F}$ = 3.1 Hz), 136.3 (d, $^4J_{C,F}$ = 3.1 Hz), 144.2, 157.5, 161.4 (d, $^1J_{C,F}$ = 154 Hz), 161.7, 163.3 (d, $^1J_{C,F}$ = 155 Hz), 191.0.

HRMS: *m*/*z* [M$^+$] calcd for $C_{20}H_{16}F_2N_2O_3$: 370.1129; found: 370.1124.

5-(4-Fluorobenzoyl)-6-[(*trans*-4-hydroxycyclohexyl)amino]-1-phenylpyridin-2(1*H*)-one (3q)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.57–0.64 (m, 2 H), 1.05–1.12 (m, 2 H), 1.55–1.63 (m, 4 H), 1.86–1.96 (m, 1 H), 3.21–3.28 (m, 1 H), 4.48 (d, *J* = 3.9 Hz, 1 H), 5.75 (d, *J* = 9.7 Hz, 1 H), 7.34 (t, *J* = 8.7 Hz, 2 H), 7.43–7.48 (m, 3 H), 7.54–7.61 (m, 5 H), 11.16 (d, *J* = 8.8 Hz, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 31.1, 33.2, 52.5, 67.1, 99.1, 104.6, 115.4 (d, $^2J_{C,F}$ = 21.7 Hz), 128.8, 129.1, 129.5, 130.6 (d, $^3J_{C,F}$ = 8.7 Hz), 136.4 (d, $^4J_{C,F}$ = 3.1 Hz), 137.8, 144.3, 157.2, 161.7, 163.1 (d, $^1J_{C,F}$ = 248 Hz), 191.6.

HRMS: *m*/*z* [M$^+$] calcd for $C_{24}H_{23}FN_2O_3$: 406.1693; found: 406.1704.

5-Benzoyl-6-(ethylsulfinyl)-1-phenylpyridin-2(1*H*)-one (11a)

5-Benzoyl-6-(ethylthio)-1-phenylpyridin-2(1*H*)-one **5i** (600 mg, 1.79 mmol) was dissolved in CH_2Cl_2 (8 mL) and cooled to 0 °C. MCPBA (77%, 420 mg, 1.88 mmol) was added and the mixture was warmed to r.t. After stirring for 3 h the reaction was cooled to 0 °C and filtered. The filtrate was extracted twice with a sat. solution of $NaHCO_3$ (2 × 10 mL) and brine (10 mL). The organic layer was dried (Na_2SO_4) and the solvent was evaporated. The crude product was purified by column chromatography on silica gel (EtOAc–petroleum ether, 2:1) to yield 614 mg (93%) of a slightly yellow solid.

^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.95 (t, *J* = 7.5 Hz, 3 H), 2.90–3.05 (m, 2 H), 6.67 (d, *J* = 9.4 Hz, 1 H), 7.47 (d, *J* = 9.4 Hz, 1 H), 7.49–7.61 (m, 6 H), 7.62–7.68 (m, 2 H), 7.84–7.87 (m, 2 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 7.6, 47.7, 119.1, 121.1, 128.4, 128.8, 129.2, 129.4, 129.5, 129.6, 129.8, 133.2, 135.7, 137.0, 139.0, 151.9, 160.8, 192.5.

HRMS: *m*/*z* [M$^+$] calcd for $C_{20}H_{17}NO_3S$: 351.0929; found: 351.0930.

5-Benzoyl-6-(cyclohexylamino)-1-phenylpyridin-2(1*H*)-one (3s)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.65–0.77 (m, 2 H), 0.97–1.11 (m, 3 H), 1.29–1.36 (m, 1 H), 1.46–1.57 (m, 4 H), 1.93–2.03 (m, 1 H), 5.73 (d, *J* = 9.7 Hz, 1 H), 7.44–7.61 (m, 11 H), 11.26 (d, *J* = 9.0 Hz, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 23.8, 24.3, 33.1, 52.5, 99.0, 104.3, 127.8, 128.2, 128.7, 129.0, 129.3, 130.1, 137.7, 139.8, 144.2, 156.9, 161.6, 192.8.

HRMS: *m*/*z* [M$^+$] calcd for $C_{24}H_{24}N_2O_2$: 372.1838; found: 372.1827.

5-Benzoyl-6-[(2-hydroxy-1-phenylethyl)amino]-1-phenylpyridin-2(1*H*)-one (3t)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 3.23–3.30 (m, 1 H), 3.39–3.46 (m, 1 H), 3.53–3.60 (m, 1 H), 5.13 (t, *J* = 5.0 Hz, 1 H), 5.74 (d, *J* = 9.7 Hz, 1 H), 6.82 (dd, *J* = 7.8, 1.8 Hz, 2 H), 6.89 (d, *J* = 7.8 Hz, 1 H), 7.20–7.28 (m, 3 H), 7.36 (t, *J* = 7.6 Hz, 1 H), 7.47 (d, *J* = 9.7 Hz, 1 H), 7.46–7.63 (m, 8 H), 11.25 (br s, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 59.9, 65.6, 100.1, 104.7, 126.4, 127.3, 128.0, 128.2, 128.3, 128.7, 128.9, 129.0, 129.2, 129.5, 130.4, 136.9, 138.8, 139.7, 144.2, 157.5, 161.5, 193.1.

HRMS: *m*/*z* [M$^+$] calcd for $C_{26}H_{22}N_2O_3$: 410.1630; found: 410.1633.

5-Benzoyl-6-(*tert*-butylamino)-1-phenylpyridin-2(1*H*)-one (3u)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.80 (s, 9 H), 5.99 (d, *J* = 9.6 Hz, 1 H), 7.43–7.48 (m, 4 H), 7.50–7.56 (m, 4 H), 7.58–7.64 (m, 3 H), 8.46 (s, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 29.8, 57.5, 105.7, 108.7, 128.3, 128.6, 128.7, 128.8, 130.2, 131.3, 138.4, 139.0, 143.1, 158.3, 161.8, 194.4.

HRMS: *m/z* [M$^+$] calcd for $C_{22}H_{22}N_2O_2$: 346.1681; found: 346.1692.

6-(Cyclohexylamino)-1-(2,4-dimethoxyphenyl)-5-(4-fluorobenzoyl)pyridin-2(1*H*)-one (3v)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.27–0.87 (m, 2 H), 0.99–1.13 (m, 3 H), 1.38–1.41 (m, 1 H), 1.47–1.60 (m, 4 H), 2.39–2.48 (m, 1 H), 3.77 (s, 3 H), 3.85 (s, 3 H), 5.67 (d, *J* = 9.7 Hz, 1 H), 6.68 (d, *J* = 8.5 Hz, 1 H), 6.79 (s, 1 H), 7.25 (d, *J* = 8.5 Hz, 1 H), 7.33 (t, *J* = 8.7 Hz, 2 H), 7.42 (d, *J* = 9.7 Hz, 1 H), 7.57 (dd, *J* = 8.7, 4.9 Hz, 2 H), 11.26 (d, *J* = 8.9 Hz, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 24.0, 24.1, 24.4, 33.3, 33.6, 52.6, 55.7, 55.8, 98.5, 104.1, 105.3, 115.2 (d, $^2J_{C,F}$ = 21.7 Hz), 118.8, 130.1, 130.5 (d, $^3J_{C,F}$ = 8.7 Hz), 136.4 (d, $^4J_{C,F}$ = 3.1 Hz), 144.0, 155.8, 157.0, 161.3, 162.9 (d, $^1J_{C,F}$ = 247.7 Hz), 191.3.

HRMS: *m/z* [M$^+$] calcd for $C_{26}H_{27}FN_2O_4$: 450.1955; found: 450.1943.

1-(2,4-Dimethoxyphenyl)-5-(4-fluorobenzoyl)-6-[(1-isopropyl-2-methylpropyl)amino]pyridin-2(1*H*)-one (3w)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.64 (d, *J* = 6.6 Hz, 3 H), 0.69 (d, *J* = 6.6 Hz, 3 H), 0.76 (d, *J* = 6.7 Hz, 6 H), 1.58–1.70 (m, 2 H), 2.60–2.66 (m, 1 H), 3.73 (s, 3 H), 3.84 (s, 3 H), 5.67 (d, *J* = 9.6 Hz, 1 H), 6.68 (d, *J* = 8.5 Hz, 1 H), 6.76 (s, 1 H), 7.19 (d, *J* = 8.5 Hz, 1 H), 7.33 (t, *J* = 8.7 Hz, 2 H), 7.44 (d, *J* = 9.6 Hz, 1 H), 7.57 (dd, *J* = 8.7, 4.9 Hz, 2 H), 11.17 (br s, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 17.8, 18.0, 19.7, 29.8, 30.4, 55.4, 55.6, 63.5, 98.9, 99.2, 104.1, 105.1, 115.2 (d, $^2J_{C,F}$ = 21.7 Hz), 118.6, 130.6 (d, $^3J_{C,F}$ = 8.8 Hz), 131.4, 136.4 (d, $^4J_{C,F}$ = 3.0 Hz), 144.2, 155.3, 159.7, 161.2, 161.6, 162.9 (d, $^1J_{C,F}$ = 248 Hz), 191.4.

HRMS: *m/z* [M$^+$] calcd for $C_{27}H_{31}FN_2O_4$: 466.2268; found: 466.2264.

5-Benzoyl-6-morpholin-4-yl-1-phenylpyridin-2(1*H*)-one (12)

^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.62–2.85 (m, 8 H), 6.26 (d, *J* = 9.4 Hz, 1 H), 7.42–7.47 (m, 4 H), 7.52–7.59 (m, 4 H), 7.68 (t, *J* = 7.4 Hz, 1 H), 7.83–7.86 (m, 2 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 50.4, 64.4, 111.4, 113.7, 128.0, 128.6, 128.7, 129.4, 129.5, 133.1, 137.8, 138.3, 141.5, 155.6, 162.7, 193.1.

HRMS: *m/z* [M$^+$] calcd for $C_{22}H_{20}N_2O_3$: 360.1474; found: 360.1471.

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