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Access to Pyridyl-Substituted 1,3,5-Triazines from 4*H*-Pyrido[1,3]oxazin-4-ones via a Cyclocondensation Process

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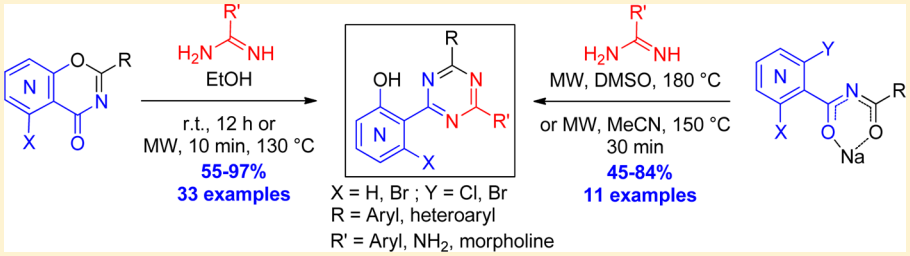
Supporting Information



ABSTRACT: Pyridyl-substituted 1,3,5-triazines were synthesized in good to excellent yields via an unprecedented one-step cyclocondensation of 4*H*-pyrido[1,3]oxazin-4-ones with amidines at room temperature or under microwave irradiations. The broad applicability was demonstrated by 33 examples with a variety of amidines and three different 4*H*-pyrido[1,3]oxazin-4-one chemical series. In addition, a one-pot process from 4*H*-pyrido[1,3]oxazin-4-one precursors (imide sodium salts) was developed and led to the desired triazines compounds, thus allowing a one-step economy in their global synthetic preparation. This approach provides rapid access to pyridyl (or pyridone)-substituted 1,3,5-triazines with high potential in various fields of application.

INTRODUCTION

In the past decades, 2,4,6-substituted 1,3,5-triazines have emerged as central building blocks for the elaboration of supramolecular structures,[1] dendrimers,[2] and ligands for transition-metal complexes.[3] Such chemical entities have found applications in many fields of materials science such as electroluminescence devices, liquid crystals, and organic light-emitting diodes (OLEDs), among others.[4] Besides, 2,4,6-substituted 1,3,5-triazine-based bioactive compounds have been also developed.[5]

Other interesting examples are the 2-(2′-hydroxyphenyl)-1,3,5-triazines reported as UV absorbers and possessing a crucial 2-hydroxyphenyl substituent.[6] Moreover, pyridyl-substituted 1,3,5-triazines have been reported as precursors of conducting or semiconducting polymers,[4a,7] ligands for transition-metal complexes exhibiting photophysical properties,[8] and promising medicinal compounds (e.g., adenosin receptor antagonists, protein kinases, and mTOR inhibitors) (Figure 1).[9]

There are well-established methods to form 2,4,6-substituted 1,3,5-triazines exhibiting two identical substituents. Cyclotrimerizations and cycloadditions with nitriles have been used extensively to prepare simple aryl-substituted triazines, but the yields remain low.[4a,d,7,8a,b,10] On the other hand, 2,4,6-substituted 1,3,5-triazines exhibiting three different substituents are often prepared by the sequential incorporation of each substituent onto cyanuric chloride.[2a,b,9b,c,11]

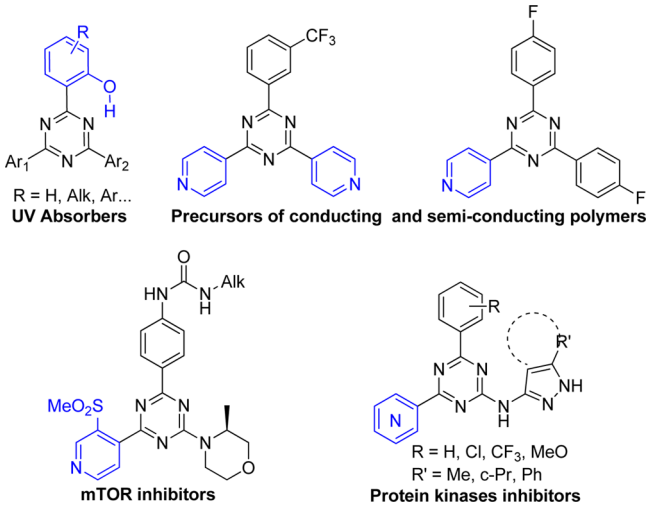


Figure 1. Selected examples of 2,4,6-substituted 1,3,5-triazines and their applications.

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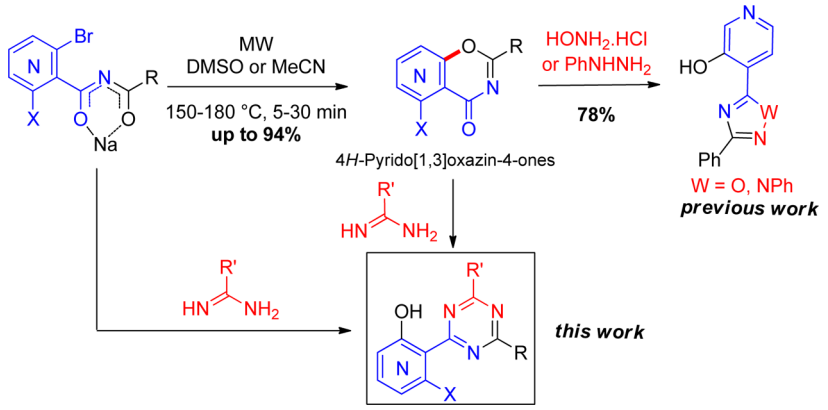
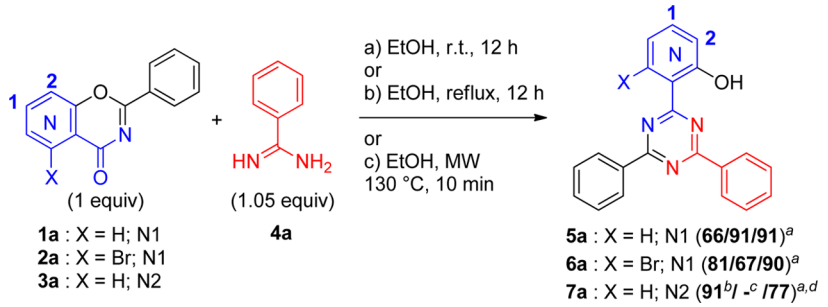


Figure 2. Accesses to pyridyl-substituted 1,2,4-oxadiazoles, 1,2,4-triazoles, and 1,3,5-triazines.

Scheme 1. Transformations of Pyrido-oxazinones 1a, 2a, and 3a into Triazines 5a, 6a, and 7a, Respectively



[a]Isolated yields using reaction conditions (a)/(b)/(c). [b]Total conversion after 30 min. [c]Not determined. [d]Obtained as its pyridone tautomer (solid state).

We wish here to report a complementary, alternative, efficient, and short access to 2,4,6-substituted 1,3,5-triazines bearing a pyridyl substituent. We recently disclosed an expeditive route to various 2-substituted 4*H*-pyrido[1,3]-oxazin-4-ones via an intramolecular O-arylation (Figure 2).[12] We were able to derivatize these compounds into pyridyl-substituted 1,2,4-triazoles and 1,2,4-oxadiazoles in one step, applying the procedures described for similar transformations of 4*H*-benzo[*e*][1,3]oxazin-4-ones.[13] Similarly, we envisioned the one-step conversion of these 2-substituted 4*H*-pyrido[1,3]-oxazin-4-ones into pyridyl-substituted 1,3,5-triazines. To the best of our knowledge, such a transformation to produce 2,4,6-substituted 1,3,5-triazines exhibiting a pyridyl substituent has not been reported to date. Our objective was also to reduce the number of synthetic steps to get to these structures by developing their direct preparation (two steps in one pot) from the 2-substituted 4*H*-pyrido[1,3]oxazin-4-one precursors (the imide sodium salts) (Figure 2)

Herein we disclose our study to determine the optimal reaction conditions for the cyclocondensation process and the extension of this methodology to a wide panel of 2-substituted 4*H*-pyrido[1,3]oxazin-4-ones[12] and amidines. Finally, a one-pot procedure from *N*-oxo-substituted bromo(iso)nicotinamides (pyrido-oxazinone precursors) is also described, thus providing a one-step economy in the global preparation of these compounds.

RESULTS AND DISCUSSION

With pyrido-oxazinones **1a**, **2a**, and **3a** as models, the transformation into triazines was realized using three different sets of reaction conditions [room temperature, reflux, or microwave (MW)-assisted] in the presence of 1.05 equiv of benzamidine (**4a**), applying a modified version of a procedure described for similar transformations of benzo-oxazinones[6a−e] (Scheme 1).

First, at room temperature, in the presence of **4a** in ethanol, the reaction proceeded in good to excellent yields, leading to the corresponding products (4,6-diphenyl-1,3,5-triazin-2-yl)-pyridinols **5a** (66%) and **6a** (81%) and 3-(4,6-diphenyl-1,3,5-triazin-2-yl)pyridin-2(1*H*)-one (**7a**) (91%). Under these conditions, we observed a faster conversion of **3a** (only 30 min) compared with the conversions of **1a** and **2a** (12 h). In refluxing ethanol, the same reaction furnished **5a** after 12 h in an improved yield of 91%, while **6a** was isolated in only 67% yield. Finally, **1a**, **2a**, and **3a** were submitted to microwave irradiation at 130 °C for 10 min, and **5a**, **6a**, and **7a** were obtained in good to excellent yields (91, 90, and 77%, respectively) with fewer byproducts in the reaction mixture. Because of its efficiency, the short time needed, and the excellent purity of the resulting compounds, this microwave-assisted protocol was chosen for further exemplification.

To further extend the synthetic scope of this reaction, we investigated the reactivity of several pyrido-oxazinones bearing an aryl or heteroaryl substituent (R) at C-2 (**1a−d**, **2a−g**, and **3a−e**) with six different amidine derivatives: **4a** (R′ = Ph), 4-fluorobenzamidine hydrochloride (**4b**) (R′ = 4-F-Ph), morpholinoformamidine hydrobromide (**4c**) (R′ = morpholinyl), guanidine hydrochloride (**4d**) (R′ = NH_2), *S*-methylisothiourea hemisulfate (**4e**) (R′ = SMe), and acetamide hydrochloride (**4f**) (R′ = Me) (Scheme 2). These amidines were chosen on the basis of their possible application for the synthesis of biologically active 1,3,5-triazines.

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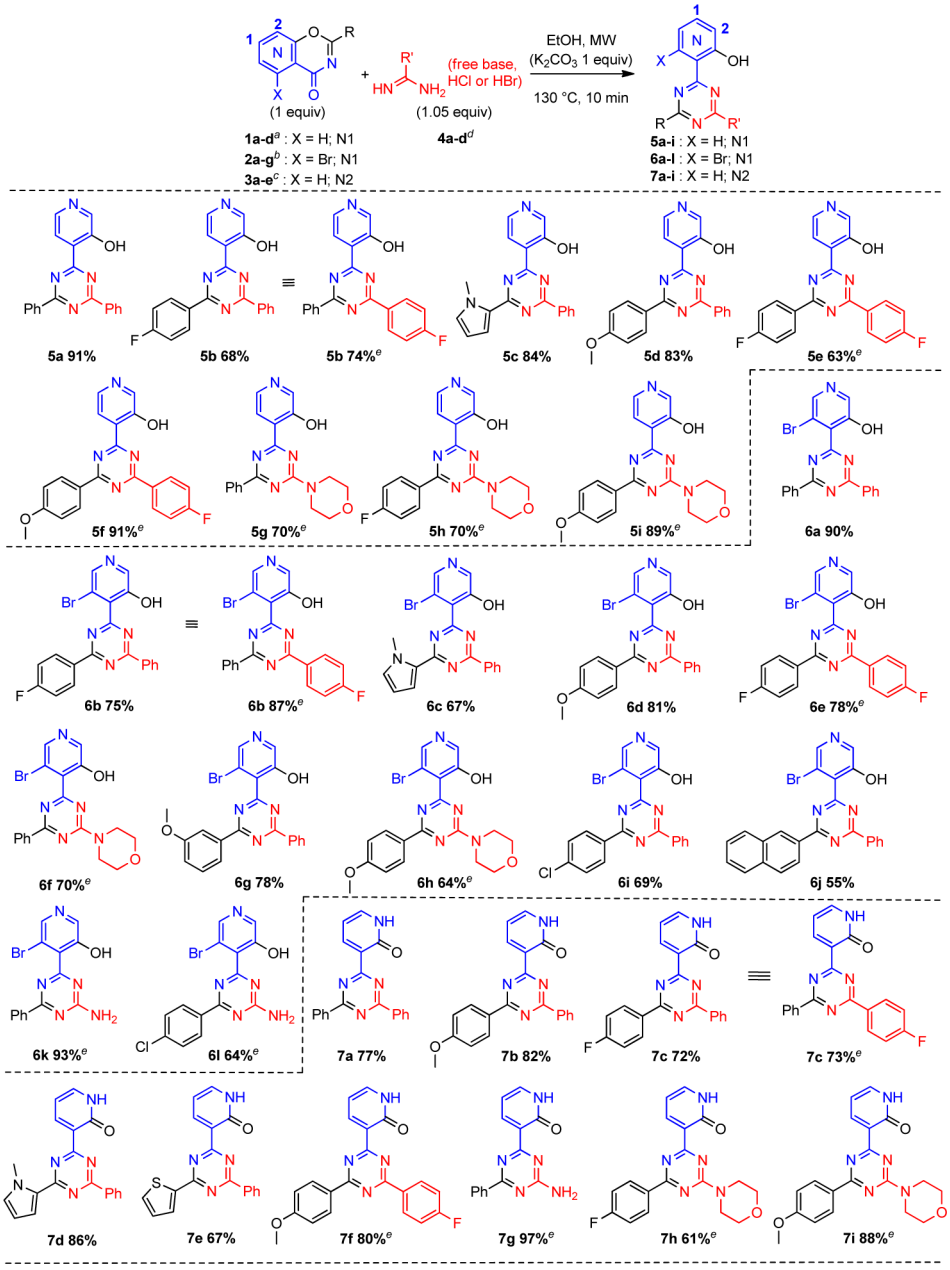
Scheme 2. Synthesis of Triazines 5a–i, 6a–l, and 7a–i from Pyrido-oxazinones 1a–d, 2a–g, and 3a–e under MW-Assisted Reaction Conditions



[a]**1a**, R = Ph; **1b**, R = 4-F-Ph; **1c**, R = *N*-Me-pyrrole; **1d**, R = 4-MeO-Ph. [b]**2a**, R = Ph; **2b**, R = 4-F-Ph; **2c**, R = *N*-Me-pyrrole; **2d**, R = 4-MeO-Ph; **2e**, R = 3-MeO-Ph; **2f**, R = 4-Cl-Ph; **2g**, R = 2-naphthyl. [c]**3a**, R = Ph; **3b**, R = 4-MeO-Ph; **3c**, R = 4-F-Ph; **3d**, R = *N*-Me-pyrrole; **3e**, R = 2-thiophenyl. [d]**4a** = benzamidine (R′ = Ph); **4b** = 4-fluorobenzamidine hydrochloride (R′ = 4-F-Ph); **4c** = morpholinoformamidine hydrobromide (R′ = morpholinyl); **4d** = guanidine hydrochloride (R′ = NH_2). [e]Reaction was run using 1 to 1.05 equiv of K_2CO_3.

In the presence of **4a**, this synthetic process occurred in good to excellent yields (from 55% for **6j** up to 91% for **5a**) with a wide compatibility regarding the substituent at the C-2 position over the three pyrido-oxazinone chemical series explored. Monosubstituted aryls exhibiting an electron-withdrawing group (**5b**, **6b**, **6i**, **7c**) or an electron-donating one (**5d**, **6d**, **7b**) were well-tolerated, as were a meta-substituted aryl group (**6g**), a naphthyl group (**6j**), and heteroaryl substituents such as *N*-methylpyrrole (**5c**, **6c**, **7d**) and thiophene (**7e**).

Other amidine derivatives were also employed, such as **4b–d**. These were obtained from commercial sources as hydrochloride or hydrobromide salts. Consequently, 1 equiv of potassium carbonate was added to the reaction mixture to generate the corresponding free bases and to allow the cyclocondensation to proceed (see Table S1 in the Supporting Information). Interestingly, the reaction of **4b** with the pyrido-oxazinones **1a**, **2a**, and **3a** (R = Ph) led to **5b** (74%), **6b** (87%), and **7c** (73%) respectively. These triazines were previously isolated from the cyclocondensation of **4a** (R′ = Ph) with pyrido-oxazinones **1b**, **2b**, and **3c** (R = 4-F-Ph) in 68, 75, and 72% yield, respectively. In both cases, these triazines were obtained in good and similar yields independent of the amidine used. In addition, the cyclocondensations of **4b** with pyrido-oxazinones **1b** and **2b** (R = 4-F-Ph) provided the

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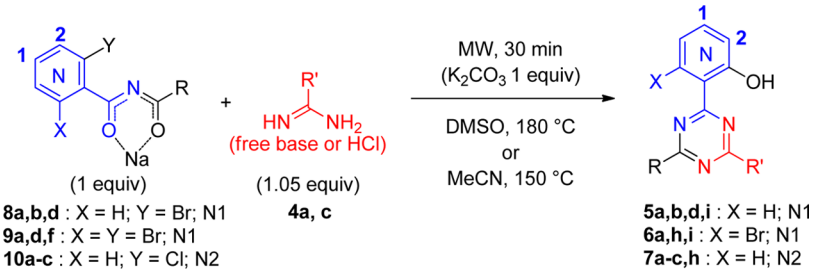
Table 1. One-Pot Process for the Preparation of Triazines 5, 6, and 7 from Imide Sodium Salts 8, 9, and 10



entry	SM	R	R′	product	one-pot yield (%)	sequential yield (%)
1	**8a**	Ph	Ph	**5a**	71[a]	62
2	**8d**	4-MeO-Ph	Ph	**5d**	75[a]	63
3	**8d**	4-MeO-Ph	morpholinyl	**5i**	74[b]	68
4	**8b**	4-F-Ph	Ph	**5b**	47[a]	34
5	**9a**	Ph	Ph	**6a**	45[a]	73
6	**9d**	4-MeO-Ph	morpholinyl	**6h**	56[b]	60
7	**9f**	4-Cl-Ph	Ph	**6i**	48[a]	51
8	**10a**	Ph	Ph	**7a**[d]	84[c]/58[e]	48
9	**10b**	4-MeO-Ph	Ph	**7b**[d]	75[c]/71[f]	71
10	**10c**	4-F-Ph	Ph	**7c**[d]	48[c]	58
11	**10c**	4-F-Ph	morpholinyl	**7h**[d]	55[b]	49

[a]Reaction was run in DMSO at 180 °C for 30 min. [b]Reaction was run in DMSO at 180 °C for 30 min with 1 equiv of K_2CO_3. [c]Reaction was run in MeCN at 150 °C for 30 min. [d]Obtained as its pyridone tautomer. [e]Multigram scale: Yield obtained using 2 g of **10a**. [f]Multigram scale: Yield obtained using 2 g of **10b**.

corresponding 4-(4,6-bis(4-fluorophenyl)-1,3,5-triazin-2-yl)-pyridinols **5e** and **6e** in good yields (63−78%). These could be considered as hydroxylated analogues of the conductive polymer precursor depicted in Figure 1,[4a] (synthesized in two steps in 21% overall yield). The yields were improved with pyrido-oxazinones exhibiting a *p*-methoxyphenyl substituent at C-2 (**1d** and **3b**), which furnished **5f** and **7f** in 80−91% yield. Finally, exposure to guanidine partners **4c** and **4d** gave morpholino-1,3,5-triazine (**5g−i**, **6f**, **6h**, **7h**, **7i**) and amino-1,3,5-triazine derivatives (**6k**, **6l**, **7g**) in good to excellent yields (61 up to 97%). This represents one of the most expeditive accesses to these structures, which may find useful applications in the field of medicinal chemistry.[9]

Unfortunately, when the above-mentioned procedure was used, the reaction of pyrido-oxazinone **2a** with **4e** (R′ = SMe) did not provide the corresponding triazine. A complex mixture of unidentified compounds was obtained in this case. The use of **4f** (R′ = Me) with **1a** and **2a** led to the corresponding triazines in only moderate yields (51−57%) and unsatisfactory purity (see Table S1 in the Supporting Information).

Although this synthetic process appears to be efficient, rapid, and compatible with a wide panel of substituents, pyridyl cores, and amidine partners, we were interested in developing a more expeditive protocol. From the optimal reaction conditions developed for the synthesis of the above-mentioned pyrido-oxazinones [MW-assisted intramolecular O-arylation of *N*-(hetero)aroyl(iso)nicotinamide sodium salts][12] and for the preparation of these pyridyl-substituted 1,3,5-triazines (MW, EtOH, 130 °C, 10 min), a one-pot procedure should be attainable: Starting from a mixture of the imide sodium salt **8**, **9**, or **10** (easily obtained in one step by benzoylation of commercial chloro- or bromonicotinamides) and the amidine partner (with 1 equiv of potassium carbonate if needed), the microwave-assisted one-pot experiment should be performed at 180 °C in DMSO or 150 °C in MeCN for 30 min (see Scheme S1 in Supporting Information). These are the adequate and unique conditions for the intramolecular O-arylation (the first of the two steps of the one-pot process) to proceed. Thereby, microwave irradiation of an equimolar mixture of imide **8a** and benzamidine **4a** in DMSO furnished the desired 1,3,5-triazine **5a** in 71% yield (Table 1, entry 1). Although a purification step was necessary to eliminate several polluting byproducts, the yield of this one-pot process was better than the overall yield of the two sequential steps (**8a** to **1a** = 68%[12] and **1a** to **5a** = 91%; overall yield = 62%).

Similarly, the one-pot transformation of **8b** and **8d** into **5b**, **5d**, and **5i** (Table 1, entries 2−4) occurred in better yields than in the sequential two-step chemical pathway (75% vs 63%; 74% vs 68%; and 47% vs 34%). Except for one example (Table 1, entry 10), the same trend was observed for the preparation of triazines **7a**, **7b**, and **7h** (Table 1, entries 8, 9 and 11). The best result was obtained with imide salt **10a** (chlorine atom at the C-2 position of the pyridine). The yield of the transformation of **10a** into **7a** was significantly improved via the one-pot process (84% vs 48% for the sequential pathway). This could be explained by the higher yield of the O-arylation step[12] (compared with the two above-mentioned chemical series) and by the less drastic reaction conditions (MeCN, 150 °C), reducing the degradation and undesired side reactions. In addition, the use of acetonitrile as the solvent allowed an easier workup (no aqueous workup). Moreover, on a multigram scale, **7a** and **7b** were isolated in significant yields of 58 and 71%, respectively, using 2 g of **10a** and **10b** (Table 1, entries 8 and 9).

Except for **6a**, the same one-pot transformation of precursors containing a 3,5-dibromo-pyridine motif (Table 1, entries 6 and 7) led to the corresponding triazines **6h** and **6i** in similar yields compared with their two-step synthesis.

On the basis of the aforementioned results, we propose a plausible reaction mechanism for the one-pot transformation. The imide sodium salt first undergoes the intramolecular O-arylation process to give the corresponding pyrido-oxazinone

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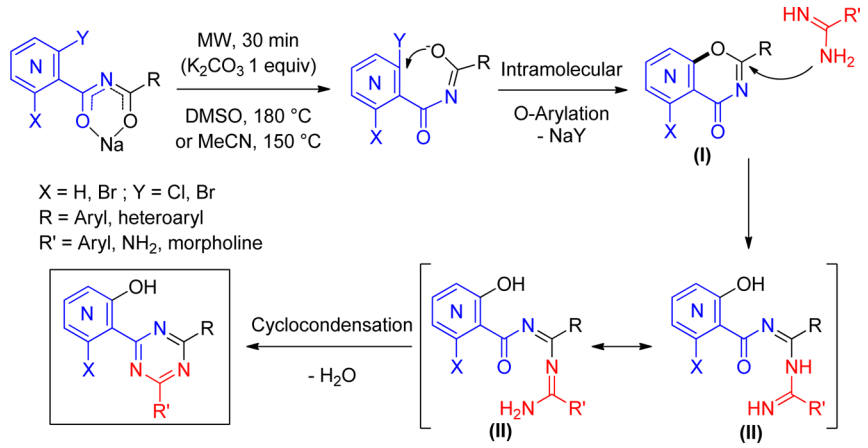
Scheme 3. Proposed Mechanism for the One-Pot Process



(**I**). Next, nucleophilic attack on nonisolated (**I**) by the corresponding amidine furnishes *N*-acylamidine intermediate (**II**), which gives the desired triazine after the cyclocondensation/dehydration sequence (Scheme 3).

Finally, starting from commercial halogenonicotinamides, these triazines were synthesized in two steps: (1) formation of the imide salt (with an average yield around 90%) followed by (2) a one-pot O-arylation/cyclocondensation process with yields of 45−84%. To our knowledge, this constitutes the most rapid and efficient access to trisubstituted 1,3,5-triazines possessing a pyridyl (or pyridone) substituent reported to date.

The hydroxy group on the pyridine of the 1,3,5-triazines prepared herein (**5** and **6**) may be useful for physical applications as a result of the intramolecular H-bond with one nitrogen atom of the triazine core.[14] Besides, valuable chemical transformations of this hydroxy group are currently under investigation. On the other hand, the resulting pyridone in compounds **7** may be of great interest for medicinal purposes.[15]

CONCLUSION

We have developed a rapid and efficient access to pyridyl-containing trisubstituted 1,3,5-triazines. Starting from previously described pyrido-oxazinones, we were able to generate the corresponding triazines in one step under microwave-assisted reaction conditions in good to excellent yields. This process was successfully applied to a wide panel of pyrido-oxazinones exhibiting aryl or heteroaryl substituents at C-2 and different types of pyridine cores in the presence of various amidine derivatives. Moreover, a one-pot process starting from the pyrido-oxazinone precursors (imide salts) allowed the access to these final compounds to be shortened. Importantly, this work provides a rapid and efficient way to prepare pyridyl-1,3,5-triazines with wide chemical diversity, leading to compounds of high interest in various fields of application.

EXPERIMENTAL SECTION

General Information. Unless otherwise indicated, all starting materials, reagents, and catalysts were obtained from commercial suppliers and used without further purification. Anhydrous tetrahydrofuran (THF), methanol (MeOH), ethanol (EtOH), dichloromethane (CH_2Cl_2), ethyl acetate (AcOEt), cyclohexane (Cy), and diethyl ether (Et_2O) were purchased with quality standards for analysis. Acetonitrile (MeCN) was purchased with quality standards for HPLC. Prior to use, THF was subsequently dried over activated molecular sieves (4 Å). Anhydrous dimethyl sulfoxide (DMSO) was purchased at a purity of >99.9%. Reactions involving air- or moisture-sensitive reagents or intermediates were carried out under an inert atmosphere of nitrogen or argon in glassware that had been oven-dried and then nitrogen-purged. Reaction temperatures are reported as the temperature of the bath surrounding the vessel, unless otherwise indicated. Flash chromatography was conducted according to the established Still protocol[16] using appropriately sized disposable columns of normal-phase silica with the indicated solvents. ^{1}H and ^{13}C (or J-MOD) NMR spectra were taken in deuterated chloroform ($CDCl_3$) or deuterated dimethyl sulfoxide (DMSO-d_6), unless otherwise noted. Chemical shifts (δ) are expressed in parts per million referenced to the residual solvent (i.e., ^{1}H 7.24 ppm, ^{13}C 77.1 ppm for chloroform; ^{1}H 2.50 ppm, ^{13}C 39.5 ppm for dimethyl sulfoxide). Splitting patterns are expressed as follows: s, singlet; d, doublet; t, triplet; q, quartet; p, pentet; m, multiplet; comp, overlapping multiplets of magnetically nonequivalent protons; br, broad; app, apparent. IR spectra were recorded on films or in solution with the indicated solvent. Microwave-assisted reactions were performed using a Biotage Initiator 2.0 apparatus in Biotage 2−5 or 10−20 mL microwave vials at the indicated temperature (detected by an IR sensor) in very high absorption mode for the indicated period of time. The spectral data and detailed procedures for the preparation of the following compounds have been already reported: **1a−d**, **2a−e**, **2g**, **3a**, **3c**, **3d**, **8a**, **8b**, **8d**, **9a**, and **9d**.[12]

General Procedure A: 4-(4,6-Diphenyl-1,3,5-triazin-2-yl)-pyridin-3-ol (5a). At room temperature under an argon atmosphere, to a solution of commercial benzamidine (**4a**) (56 mg, 0.47 mmol) in ethanol (10 mL) was added 2-phenyl-4*H*-pyrido[4,3-*e*][1,3]oxazin-4-one (**1a**) (100 mg, 0.45 mmol), and the resulting mixture was stirred at room temperature under argon for 12 h. Then the mixture was concentrated in vacuo, and the resulting residue was purified by flash chromatography eluting with CH_2Cl_2/AcOEt 100/0 to 50/50 to provide 96 mg (66% yield) of the desired product as a white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 12.60 (br s, 1H), 8.65 (d, J = 7.2 Hz, 4H), 8.54 (s, 1H), 8.48 (d, J = 5.1 Hz, 1H), 8.35 (d, J = 5.1 Hz, 1H), 7.78 (t, J = 7.3 Hz, 2H), 7.71 (t, J = 7.7 Hz, 4H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.5 (2C), 170.4, 155.3, 141.6, 140.5, 134.3 (2C), 133.8 (2C), 129.3 (4C), 128.8 (4C), 123.4, 0.121.6; IR (film, cm^{-1}) 3427, 3061, 1590, 1570, 1536, 1513, 1506, 1486, 1449, 1406, 1387, 1361, 1302, 1241, 1217, 1187, 1147, 1135, 1093, 1067, 1057, 1050, 1027, 1002, 927, 906, 870, 846, 825, 812, 784, 743, 690, 679, 650, 641, 611, 573, 549, 474; MS ESI+ m/z 327.1238 [$C_{20}H_{15}N_4O$ (M + 1) requires 327.1240]; mp 250−251 °C.

General Procedure B: 4-(4,6-Diphenyl-1,3,5-triazin-2-yl)-pyridin-3-ol (5a). Under an argon atmosphere, to a solution of commercial **4a** (54 mg, 0.45 mmol) in ethanol (10 mL) was added **1a** (100 mg, 0.45 mmol). The resulting mixture was refluxed for 12 h. Then the reaction mixture was cooled to room temperature and concentrated in vacuo, and the resulting residue was purified by flash chromatography eluting with CH_2Cl_2/ethyl acetate 100/0, 90/10, 80/

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20, 70/30, 60/40, 50/50 to provide 132 mg (91% yield) of the desired compound as a white solid.

General Procedure C: 4-(4,6-Diphenyl-1,3,5-triazin-2-yl)-pyridin-3-ol (5a). In a 10−20 mL microwave vial, to a solution of commercial **4a** (54 mg, 0.45 mmol) in ethanol (10 mL) was added **1a** (100 mg, 0.45 mmol). Then the microwave vial was sealed and submitted to microwave irradiation for 10 min at 130 °C using a Biotage Initiator 2.0 apparatus (in very high absorption mode). After 10 min, the vial was opened, and the reaction mixture was concentrated in vacuo. The resulting residue was then purified by flash chromatography eluting with CH_2Cl_2/ethyl acetate 100/0, 90/10, 80/20, 70/30, 60/40, 50/50 to provide 133 mg (91% yield) of the desired compound as a white solid.

*5-Bromo-4-(4,6-diphenyl-1,3,5-triazin-2-yl)pyridin-3-ol (**6a**).* The title compound was obtained in 81% yield (0.108 g) as a yellow powder from 5-bromo-2-phenyl-4*H*-pyrido[4,3-*e*][1,3]oxazin-4-one (**2a**) (100 mg) according to general procedure A, 67% yield (61 mg) from **2a** (68 mg) according to general procedure B, and 90% yield (120 mg) from **2a** (100 mg) according to general procedure C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.80 (br s, 1H), 8.62 (dt, J = 7.1, 1.5 Hz, 4H), 8.41 (s, 1H), 8.39 (s, 1H), 7.73 (tt, J = 7.3, 1.3 Hz, 2H), 7.65 (tt, J = 7.8, 1.6 Hz, 4H); J-MOD ^{13}C NMR (125 MHz, DMSO-d_6) δ 171.5, 171.3 (2C), 151.8, 141.6, 138.0, 134.6 (2C), 133.5 (2C), 132.4, 129.1 (4C), 128.7 (4C), 118.4; IR (film, cm^{-1}) 3432, 3069, 2747, 1599, 1588, 1544, 1504, 1466, 1446, 1395, 1349, 1330, 1314, 1303, 1196, 1179, 1156, 1134, 1067, 1053, 1028, 1006, 929, 895, 845, 814, 741, 699, 687, 678, 660, 648, 611, 565; MS ESI+ m/z 405.0346 [$C_{20}H_{14}BrN_4O$ (M + 1) requires 405.0346]; mp 218−220 °C.

*3-(4,6-Diphenyl-1,3,5-triazin-2-yl)pyridin-2(1H)-one (**7a**).* The title compound was obtained in 91% yield (0.133 g) as a white powder from 2-phenyl-4*H*-pyrido[3,2-*e*][1,3]oxazin-4-one (**3a**) (100 mg) according to general procedure A (in 30 min) and 77% yield (112 mg) from **2a** (100 mg) according to general procedure C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.19 (br s, 1H), 8.66 (d, J = 7.4 Hz, 4H), 8.57 (br d, J = 5.8 Hz, 1H), 7.78 (br s, 1H), 7.70 (t, J = 7.2 Hz, 2H), 7.64 (t, J = 7.6 Hz, 4H), 6.50 (br s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 171.5, 170.6 (2C), 160.2, 144.2, 141.3, 135.4 (2C), 132.9 (2C), 128.9 (4C), 128.6 (4C), 124.9, 105.4; IR (film, cm^{-1}) 3432, 3066, 1665, 1605, 1589, 1557, 1535, 1515, 1482, 1450, 1416, 1367, 1345, 1310, 1255, 1224, 1179, 1148, 1067, 1026, 1001, 888, 844, 813, 775, 755, 696, 681, 652, 643, 636, 601; MS ESI+ m/z 327.1241 [$C_{20}H_{15}N_4O$ (M + 1) requires 327.1240]; mp 249−251 °C.

*4-(4-(4-Fluorophenyl)-6-phenyl-1,3,5-triazin-2-yl)pyridin-3-ol (**5b**).* The title compound was obtained in 68% yield (0.096 g) as a white powder from 2-(4-fluorophenyl)-4*H*-pyrido[4,3-*e*][1,3]oxazin-4-one (**1b**) (100 mg) according to general procedure C or using general procedure D described below.

General Procedure D: 4-(4-(4-Fluorophenyl)-6-phenyl-1,3,5-triazin-2-yl)pyridin-3-ol (5b). In a 10−20 mL microwave vial, to a solution of commercial 4-fluorobenzamidine hydrochloride (**4b**) (82 mg, 0.47 mmol) and potassium carbonate (65 mg, 0.47 mmol) in ethanol (10 mL) was added **1a** (100 mg, 0.45 mmol). Then the microwave vial was sealed and submitted to microwave irradiation for 10 min at 130 °C using a Biotage Initiator 2.0 apparatus (in very high absorption mode). After 10 min, the vial was opened, and the reaction mixture was concentrated in vacuo. The resulting residue was then purified by flash chromatography eluting with CH_2Cl_2/ethyl acetate 100/0, 90/10, 80/20, 70/30, 60/40, 50/50 to provide 114 mg (74% yield) of the desired compound as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.66 (s, 1H), 8.59 (ddt, J = 8.9, 5.4, 2.1 Hz, 2H), 8.54 (d, J = 7.2 Hz, 1H), 8.52 (d, J = 4.4 Hz, 2H), 8.37 (d, J = 5.1 Hz, 1H), 8.27 (d, J = 5.1 Hz, 1H), 7.61 (tt, J = 7.3, 1.3 Hz, 1H), 7.53 (tt, J = 7.7, 1.6 Hz, 2H), 7.20 (tt, J = 8.6, 1.5 Hz, 2H); J-MOD ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 170.9, 170.3, 166.4 (d, J = 254 Hz, 1C), 156.2, 142.3, 140.5, 134.4, 133.7, 131.6 (d, J = 9.3 Hz, 2C), 130.8 (d, J = 2.9 Hz, 1C), 129.1 (4C), 123.1, 121.3, 116.2 (d, J = 21.8 Hz, 2C); ^{19}F NMR (188 MHz, $CDCl_3$) δ −104.6; IR (film, cm^{-1}) 3424, 3059, 2924, 2853, 1602, 1588, 1572, 1534, 1507, 1486, 1449, 1417, 1406, 1386, 1362, 1303, 1237, 1217, 1187, 1153, 1144, 1133, 1100, 1056, 1027, 1013, 1002, 855, 841, 822, 786, 765, 728, 693, 680, 591, 586, 571, 549, 504; MS ESI+ m/z 345.1145 [$C_{20}H_{14}FN_4O$ (M + 1) requires 345.1146]; mp 257−259 °C.

*4-(4-(1-Methyl-1H-pyrrol-2-yl)-6-phenyl-1,3,5-triazin-2-yl)pyridin-3-ol (**5c**).* The title compound was obtained in 84% yield (0.101 g) as a yellow powder from 2-(1-methyl-1*H*-pyrrol-2-yl)-4*H*-pyrido[4,3-*e*]-[1,3]oxazin-4-one (**1c**) (83 mg) according to general procedure C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.86 (br s, 1H), 8.48 (dt, J = 8.6, 3.2 Hz, 2H), 8.47 (s, 1H), 8.33 (d, J = 5.1 Hz, 1H), 8.29 (d, J = 5.1 Hz, 1H), 7.73 (tt, J = 7.2, 1.2 Hz, 1H), 7.66 (tt, J = 7.7, 1.6 Hz, 2H), 7.44 (dd, J = 4.1, 1.8 Hz, 1H), 7.35 (t, J = 2.1 Hz, 1H), 6.32 (dd, J = 4.1, 2.4 Hz, 1H), 4.23 (s, 3H); J-MOD ^{13}C NMR (100 MHz, DMSO-d_6) δ 169.5, 169.4, 164.4, 155.4, 141.4, 140.4, 134.5, 133.6, 133.4, 129.2 (2C), 128.5 (2C), 127.6, 123.2, 121.2, 119.6, 109.5, 38.6; IR (film, cm^{-1}) 3427, 3028, 2954, 1617, 1589, 1574, 1538, 1512, 1488, 1477, 1467, 1438, 1401, 1366, 1353, 1306, 1272, 1242, 1242, 1217, 1168, 1146, 1134, 1093, 1068, 1055, 1027, 1013, 991, 909, 870, 844, 824, 801, 788, 761, 735, 710, 691, 677, 663, 658, 647, 641, 616, 604, 570, 549; MS ESI+ m/z 330.1347 [$C_{19}H_{16}N_5O$ (M + 1) requires 330.1349]; mp 209−211 °C.

*4-(4-(4-Methoxyphenyl)-6-phenyl-1,3,5-triazin-2-yl)pyridin-3-ol (**5d**).* The title compound was obtained in 83% yield (0.116 g) as a white powder from 2-(4-methoxyphenyl)-4*H*-pyrido[4,3-*e*][1,3]-oxazin-4-one (**1d**) (100 mg) according to general procedure C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.89 (s, 1H), 8.58 (d, J = 8.6 Hz, 2H), 8.57 (s, 1H), 8.55 (d, J = 2.6 Hz, 2H), 8.41 (d, J = 5.2 Hz, 1H), 8.30 (d, J = 5.2 Hz, 1H), 7.62 (tt, J = 7.1, 1.2 Hz, 1H), 7.56 (t, J = 7.9 Hz, 2H), 7.04 (dt, J = 8.9, 2.7 Hz, 2H), 3.91 (s, 3H); J-MOD ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 170.6, 170.5, 164.2, 156.2, 142.1, 140.3, 134.8, 133.4, 131.1 (2C), 129.0 (2C), 128.9 (2C), 126.9, 123.4, 121.4, 114.4 (2C), 55.5; IR (film, cm^{-1}) 3432, 3012, 2932, 2839, 2040, 1913, 1607, 1587, 1570, 1533, 1507, 1488, 1448, 1423, 1408, 1390, 1362, 1341, 1305, 1262, 1219, 1175, 1145, 1134, 1114, 1067, 1058, 1050, 1025, 1002, 995, 914, 853, 840, 822, 788, 766, 732, 694, 675, 663, 651, 643, 634, 616, 611, 594, 572, 551, 512; MS ESI+ m/z 357.1342 [$C_{21}H_{17}N_4O_2$ (M + 1) requires 357.1346]; mp 182−184 °C.

*4-(4,6-Bis(4-fluorophenyl)-1,3,5-triazin-2-yl)pyridin-3-ol (**5e**).* The title compound was obtained in 63% yield (0.094 g) as a pale-yellow powder from **1b** (100 mg) in the presence of **4b** (76 mg, 0.43 mmol) and potassium carbonate (60 mg, 0.43 mmol) according to general procedure D. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.62 (s, 1H), 8.59 (ddt, J = 8.9, 5.4, 2.1 Hz, 4H), 8.53 (br s, 1H), 8.39 (d, J = 5.1 Hz, 1H), 8.28 (d, J = 5.0 Hz, 1H), 7.22 (tt, J = 8.6, 2.1 Hz, 4H); J-MOD ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 170.2 (2C), 166.5 (d, J = 254 Hz, 2C), 156.2, 142.3, 140.5, 131.6 (d, J = 9.3 Hz, 4C), 130.7 (d, J = 3.0 Hz, 2C), 123.1, 121.4, 116.3 (d, J = 21.9 Hz, 4C); ^{19}F NMR (188 MHz, $CDCl_3$) δ −104.3; IR (film, cm^{-1}) 3432, 3066, 2925, 1601, 1572, 1533, 1508, 1489, 1415, 1387, 1363, 1304, 1237, 1220, 1188, 1157, 1144, 1104, 1051, 1012, 860, 840, 817, 798, 768, 654, 636, 609, 591, 586, 571, 550, 508; MS ESI+ m/z 363.1061 [$C_{20}H_{13}F_2N_4O$ (M + 1) requires 363.1052]; mp 302−303 °C.

*4-(4-(4-Fluorophenyl)-6-(4-methoxyphenyl)-1,3,5-triazin-2-yl)-pyridin-3-ol (**5f**).* The title compound was obtained in 91% yield (0.134 g) as a white powder from **1d** (100 mg) in the presence of **4b** (72 mg, 0.41 mmol) and potassium carbonate (57 mg, 0.41 mmol) according to general procedure D. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.77 (s, 1H), 8.56 (ddt, J = 6.9, 5.4, 2.1 Hz, 2H), 8.48 (dt, J = 9.0, 2.0 Hz, 2H), 8.49 (s, 1H), 8.34 (d, J = 5.1 Hz, 1H), 8.25 (d, J = 5.1 Hz, 1H), 7.18 (tt, J = 8.9, 2.1 Hz, 2H), 7.00 (tt, J = 9.0, 2.1 Hz, 2H), 3.86 (s, 3H); J-MOD ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 170.4, 169.8, 166.3 (d, J = 254 Hz, 1C), 164.3, 156.2, 142.2, 140.4, 131.4 (d, J = 9.3 Hz, 2C), 131.1 (2C), 131.0 (d, J = 3.1 Hz, 1C), 126.7, 123.2, 121.3, 116.1 (d, J = 21.8 Hz, 2C), 114.4 (2C), 55.6; ^{19}F NMR (188 MHz, $CDCl_3$) δ −105.0; IR (film, cm^{-1}) 3432, 2938, 2841, 1601, 1585, 1571, 1535, 1506, 1464, 1417, 1388, 1363, 1308, 1261, 1235, 1219, 1174, 1145, 1114, 1100, 1057, 1029, 998, 859, 838, 815, 768, 653, 638, 610, 590, 571, 551, 513; MS ESI+ m/z 375.1259 [$C_{21}H_{16}FN_4O_2$ (M + 1) requires 375.1252]; mp 196−197 °C.

*4-(4-Morpholino-6-phenyl-1,3,5-triazin-2-yl)pyridin-3-ol (**5g**).* The title compound was obtained in 70% yield (0.105 g) as a white powder from **1a** (100 mg) in the presence of morpholinoformamidine

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hydrobromide (**4c**) (98 mg, 0.47 mmol) and potassium carbonate (65 mg, 0.47 mmol) according to general procedure D. ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.33 (s, 1H), 8.49 (s, 1H), 8.34 (dt, J = 7.2, 1.4 Hz, 2H), 8.22 (d, J = 5.1 Hz, 1H), 8.16 (d, J = 5.1 Hz, 1H), 7.59 (tt, J = 7.3, 1.2 Hz, 1H), 7.51 (t, J = 7.7 Hz, 2H), 4.10 (t, J = 5.2 Hz, 2H), 4.02 (t, J = 4.6 Hz, 2H), 3.83 (t, J = 5.1 Hz, 4H); J-MOD ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 169.8, 163.6, 156.4, 142.0, 140.0, 134.9, 132.8, 128.8 (2C), 128.5 (2C), 123.6, 121.1, 66.7, 66.6, 44.0, 43.9; IR (film, cm^{-1}) 3430, 3070, 2977, 2922, 2866, 1594, 1565, 1502, 1488, 1454, 1440, 1412, 1370, 1352, 1308, 1265, 1251, 1221, 1174, 1142, 1116, 1069, 1051, 1024, 1002, 974, 929, 908, 870, 856, 823, 787, 766, 710, 692, 679, 670, 642, 617, 579, 552, 544; MS ESI+ m/z 336.1448 [$C_{18}H_{18}N_5O_2$ (M + 1) requires 336.1455]; mp 257−258 °C.

*4-(4-(4-Fluorophenyl)-6-morpholino-1,3,5-triazin-2-yl)pyridin-3-ol (**5h**).* The title compound was obtained in 70% yield (0.102 g) as a pale-yellow powder from **1b** (100 mg) in the presence of **4c** (91 mg, 0.43 mmol) and potassium carbonate (60 mg, 0.43 mmol) according to general procedure D. ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.18 (s, 1H), 8.48 (s, 1H), 8.37 (ddt, J = 9.0, 5.4, 2.2 Hz, 2H), 8.22 (d, J = 5.1 Hz, 1H), 8.16 (d, J = 5.1 Hz, 1H), 7.18 (tt, J = 8.6, 2.1 Hz, 2H), 4.08 (t, J = 4.4 Hz, 2H), 4.01 (t, J = 4.4 Hz, 2H), 3.83 (t, J = 5.1 Hz, 4H); J-MOD ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 168.8, 165.9 (d, J = 253 Hz, 1C), 163.5, 156.3, 142.0, 140.1, 131.1, 130.9 (d, J = 9.1 Hz, 2C), 123.5, 121.1, 115.9 (d, J = 21.7 Hz, 2C), 66.6, 66.5, 44.0, 43.9; ^{19}F NMR (188 MHz, $CDCl_3$) δ −106.1; IR (film, cm^{-1}) 3430, 3043, 2974, 2924, 2876, 1603, 1575, 1561, 1497, 1489, 1454, 1441, 1422, 1403, 1372, 1304, 1272, 1264, 1250, 1227, 1174, 1156, 1142, 1114, 1103, 1072, 1057, 1002, 974, 930, 872, 858, 814, 771, 746, 702, 657, 636, 588, 577, 550, 542, 509; MS ESI+ m/z 354.1355 [$C_{18}H_{17}FN_5O_2$ (M + 1) requires 354.1360]; mp 251−253 °C.

*4-(4-(4-Methoxyphenyl)-6-morpholino-1,3,5-triazin-2-yl)pyridin-3-ol (**5i**).* The title compound was obtained in 89% yield (0.128 g) as a white powder from **1d** (100 mg) in the presence of **4c** (87 mg, 0.41 mmol) and potassium carbonate (57 mg, 0.41 mmol) according to general procedure D. ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.47 (s, 1H), 8.48 (s, 1H), 8.31 (dt, J = 9.0, 2.0 Hz, 2H), 8.21 (d, J = 5.1 Hz, 1H), 8.16 (d, J = 5.1 Hz, 1H), 7.00 (dt, J = 9.0, 2.0 Hz, 2H), 4.08 (t, J = 4.4 Hz, 2H), 4.00 (d, J = 4.4 Hz, 2H), 3.89 (s, 3H), 3.82 (t, J = 5.1 Hz, 4H); J-MOD ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 169.2, 163.6, 163.5, 156.4, 141.9, 139.9, 130.5 (2C), 127.2, 123.7, 121.1, 114.1 (2C), 66.6 (2C), 55.5, 44.0, 43.9; IR (film, cm^{-1}) 3432, 2972, 2932, 2874, 1594, 1573, 1561, 1496, 1447, 1424, 1409, 1373, 1308, 1268, 1259, 1222, 1170, 1140, 1119, 1053, 1030, 1002, 973, 871, 862, 855, 844, 812, 770, 706, 657, 637, 595, 579, 544, 512; MS ESI+ m/z 366.1566 [$C_{19}H_{20}N_5O_3$ (M + 1) requires 366.1561]; mp 211−213 °C.

*5-Bromo-4-(4-(4-fluorophenyl)-6-phenyl-1,3,5-triazin-2-yl)-pyridin-3-ol (**6b**).* The title compound was obtained in 75% yield (0.099 g) as a yellow powder from 5-bromo-2-(4-fluorophenyl)-4*H*-pyrido[4,3-*e*][1,3]oxazin-4-one (**2b**) (100 mg) according to general procedure C and 87% yield (0.122 g) as a yellow powder from **2a** (100 mg) in the presence of **4b** (60 mg, 0.35 mmol) and potassium carbonate (48 mg, 0.35 mmol) according to general procedure D. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.80 (br s, 1H), 8.68 (ddt, J = 9.0, 5.6, 2.0 Hz, 2H), 8.61 (dt, J = 7.1, 1.4 Hz, 2H), 8.41 (s, 1H), 8.39 (s, 1H), 7.73 (tt, J = 7.3, 1.3 Hz, 1H), 7.64 (t, J = 7.7 Hz, 2H), 7.46 (tt, J = 8.8, 2.0 Hz, 2H); J-MOD ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.0, 171.8, 170.8, 165.9 (d, J = 251 Hz, 1C), 152.2, 142.1, 138.4, 134.9, 133.9, 132.7, 132.0 (d, J = 9.4 Hz, 2C), 131.5 (d, J = 2.8 Hz, 1C), 129.5 (2C), 129.2 (2C), 118.9, 116.6 (d, J = 21.9 Hz, 2C); ^{19}F NMR (188 MHz, DMSO-d_6) δ −105.9; IR (film, cm^{-1}) 3427, 3063, 2924, 2852, 1600, 1587, 1541, 1503, 1467, 1448, 1418, 1402, 1389, 1350, 1328, 1304, 1238, 1194, 1151, 1134, 1102, 1068, 1052, 1027, 1003, 896, 857, 834, 788, 763, 745, 727, 693, 678, 658, 653, 617, 593, 587, 564, 518; MS ESI+ m/z 423.0243 [$C_{20}H_{13}BrFN_4O$ (M + 1) requires 423.0251]; mp 201−203 °C.

*5-Bromo-4-(4-(1-methyl-1H-pyrrol-2-yl)-6-phenyl-1,3,5-triazin-2-yl)pyridin-3-ol (**6c**).* The title compound was obtained in 67% yield (0.089 g) as a white powder from 5-bromo-2-(1-methyl-1*H*-pyrrol-2-yl)-4*H*-pyrido[4,3-*e*][1,3]oxazin-4-one (**2c**) (100 mg) according to general procedure C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.78 (br s, 1H), 8.48 (dt, J = 7.1, 1.5 Hz, 2H), 8.36 (s, 1H), 8.34 (s, 1H), 7.68 (tt, J = 7.4, 1.3 Hz, 1H), 7.60 (tt, J = 7.2, 1.6 Hz, 2H), 7.40 (dd, J = 4.0, 1.8 Hz, 1H), 7.28 (t, J = 2.1 Hz, 1H), 6.26 (dd, J = 4.0, 2.5 Hz, 1H), 4.18 (s, 3H); J-MOD ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.6, 170.4, 165.7, 152.0, 141.5, 138.0, 135.1, 133.1, 132.9, 132.7, 129.0 (2C), 128.5 (2C), 128.0, 119.3, 118.6, 109.1, 38.4; IR (film, cm^{-1}) 3428, 3066, 2954, 2862, 1586, 1557, 1537, 1508, 1479, 1458, 1446, 1433, 1391, 1365, 1342, 1308, 1268, 1194, 1178, 1155, 1141, 1094, 1065, 1054, 1027, 1013, 1003, 995, 895, 861, 844, 819, 786, 760, 735, 708, 689, 681, 657, 650, 616, 603, 565, 506; MS ESI+ m/z 408.0453 [$C_{19}H_{15}BrN_5O$ (M + 1) requires 408.0454]; mp 167−169 °C.

*5-Bromo-4-(4-(4-methoxyphenyl)-6-phenyl-1,3,5-triazin-2-yl)-pyridin-3-ol (**6d**).* The title compound was obtained in 81% yield (0.106 g) as a yellow powder from 5-bromo-2-(4-methoxyphenyl)-4*H*-pyrido[4,3-*e*][1,3]oxazin-4-one (**2d**) (100 mg) according to general procedure C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.99 (br s, 1H), 8.64 (d, J = 7.3 Hz, 2H), 8.63 (d, J = 7.1 Hz, 2H), 8.52 (s, 1H), 8.46 (s, 1H), 7.65 (tt, J = 7.2, 1.4 Hz, 1H), 7.58 (tt, J = 7.6, 1.6 Hz, 2H), 7.08 (dt, J = 9.0, 2.0 Hz, 2H), 3.93 (s, 3H); J-MOD ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 171.0, 170.2, 164.7, 157.1, 145.4, 141.2, 135.1, 134.0, 131.9 (2C), 129.6 (2C), 129.4 (2C), 127.4, 123.8, 119.5, 114.9 (2C), 56.0; IR (film, cm^{-1}) 3428, 3065, 2935, 2840, 1605, 1585, 1541, 1499, 1466, 1448, 1424, 1402, 1393, 1352, 1306, 1260, 1196, 1176, 1155, 1137, 1115, 1069, 1054, 1028, 1003, 894, 854, 834, 787, 765, 731, 693, 676, 659, 653, 635, 618, 595, 566, 522; MS ESI+ m/z 435.0459 [$C_{21}H_{16}BrN_4O_2$ (M + 1) requires 435.0451]; mp 168−170 °C.

*4-(4,6-Bis(4-fluorophenyl)-1,3,5-triazin-2-yl)-5-bromopyridin-3-ol (**6e**).* The title compound was obtained in 78% yield (0.107 g) as a yellow powder from **2b** (100 mg) in the presence of **4b** (57 mg, 0.33 mmol) and potassium carbonate (43 mg, 0.31 mmol) according to general procedure D. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.58 (br s, 1H), 8.69 (ddt, J = 9.3, 5.4, 2.2 Hz, 4H), 8.55 (s, 1H), 8.49 (s, 1H), 7.29 (tt, J = 8.8, 2.0 Hz, 4H); J-MOD ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.0, 170.8 (2C), 165.9 (d, J = 251 Hz, 2C), 152.2, 142.0, 138.4, 132.7, 132.0 (d, J = 9.4 Hz, 4C), 131.5 (d, J = 2.2 Hz, 2C), 118.8, 116.6 (d, J = 21.9 Hz, 4C); ^{19}F NMR (188 MHz, $CDCl_3$) δ −105.8; IR (film, cm^{-1}) 3431, 3077, 1599, 1541, 1504, 1456, 1417, 1403, 1385, 1349, 1300, 1238, 1194, 1152, 1135, 1103, 1013, 897, 862, 853, 827, 770, 689, 587, 561, 523, 511; MS ESI+ m/z 441.0156 [$C_{20}H_{12}BrF_2N_4O$ (M + 1) requires 441.0157]; mp 168−171 °C.

*5-Bromo-4-(4-morpholino-6-phenyl-1,3,5-triazin-2-yl)pyridin-3-ol (**6f**).* The title compound was obtained in 70% yield (0.096 g) as a yellow powder from **2a** (100 mg) in the presence of **4c** (73 mg, 0.35 mmol) and potassium carbonate (48 mg, 0.35 mmol) according to general procedure D. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.73 (br s, 1H), 8.38 (dt, J = 7.2, 1.3 Hz, 2H), 8.32 (s, 1H), 8.30 (s, 1H), 7.62 (t, J = 7.3 Hz, 1H), 7.53 (t, J = 7.3 Hz, 2H), 4.02 (br s, 2H), 3.81 (br s, 2H), 3.75 (br s, 2H), 3.68 (br s, 2H); J-MOD ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.8, 170.7, 164.3, 152.3, 142.0, 138.2, 135.8, 133.2, 132.9, 129.1 (2C), 128.7 (2C), 118.9, 66.2 (2C), 43.9, 43.8; IR (film, cm^{-1}) 3429, 2969, 2918, 2857, 1594, 1562, 1493, 1466, 1447, 1409, 1386, 1358, 1307, 1268, 1232, 1211, 1179, 1159, 1115, 1069, 1052, 1025, 1008, 973, 895, 865, 834, 824, 786, 764, 706, 696, 678, 653, 573, 548, 511; MS ESI+ m/z 414.0552 [$C_{18}H_{17}BrN_5O_2$ (M + 1) requires 414.0560]; mp 169−170 °C.

*5-Bromo-4-(4-(3-methoxyphenyl)-6-phenyl-1,3,5-triazin-2-yl)-pyridin-3-ol (**6g**).* The title compound was obtained in 78% yield (0.102 g) as a yellow powder from 5-bromo-2-(3-methoxyphenyl)-4*H*-pyrido[4,3-*e*][1,3]oxazin-4-one (**2e**) (100 mg) according to general procedure C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.90 (br s, 1H), 8.61 (dt, J = 7.2, 1.2 Hz, 2H), 8.38 (d, J = 7.0 Hz, 2H), 8.20 (d, J = 7.8 Hz, 1H), 8.09 (t, J = 2.2 Hz, 1H), 7.73 (t, J = 7.3 Hz, 1H), 7.64 (t, J = 7.7 Hz, 2H), 7.56 (t, J = 7.9 Hz, 1H), 7.30 (dd, J = 8.0, 2.1 Hz, 1H), 3.89 (s, 3H); J-MOD ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4 (2C), 170.4, 160.6, 157.0, 145.6, 141.3, 136.3, 134.9, 134.2, 130.5, 129.7 (2C), 129.5 (2C), 123.6, 122.2, 120.4, 119.5, 114.4, 55.9; IR (film, cm^{-1}) 3428, 3065, 2925, 2853, 1601, 1587, 1546, 1506, 1468, 1448, 1425, 1398, 1350, 1303, 1284, 1254, 1212, 1194, 1176, 1155, 1127, 1080, 1056, 1030, 1005, 994, 918, 894, 871, 839, 788, 756, 714, 689, 677,

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660, 647, 616, 572, 502; MS ESI+ m/z 435.0456 [$C_{21}H_{16}BrN_4O_2$ (M + 1) requires 435.0451]; mp 147−149 °C.

*5-Bromo-4-(4-(4-methoxyphenyl)-6-morpholino-1,3,5-triazin-2-yl)pyridin-3-ol (**6h**).* The title compound was obtained in 64% yield (0.085 g) as a yellow powder from **2d** (100 mg) in the presence of **4c** (66 mg, 0.31 mmol) and potassium carbonate (41 mg, 0.30 mmol) according to general procedure D. ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.81 (br s, 1H), 8.40 (br s, 1H), 8.37 (br s, 1H), 8.30 (dt, J = 8.9, 2.0 Hz, 2H), 6.99 (dt, J = 9.0, 1.9 Hz, 2H), 4.08 (t, J = 4.7 Hz, 4H), 3.89 (s, 3H), 3.81 (q, J = 4.4 Hz, 4H); J-MOD ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 169.2, 164.1, 163.7, 157.7, 144.7, 140.9, 130.9 (2C), 127.4, 123.9, 119.2, 114.6 (2C), 67.2, 67.1, 55.9, 45.0, 44.4; IR (film, cm^{-1}) 3424, 3007, 2972, 2919, 2867, 2840, 1593, 1556, 1495, 1466, 1448, 1418, 1365, 1305, 1269, 1236, 1212, 1182, 1171, 1156, 1117, 1073, 1052, 1027, 1009, 973, 891, 857, 850, 818, 785, 770, 691, 638, 597, 570, 549, 518; MS ESI+ m/z 444.0653 [$C_{19}H_{19}BrN_5O_3$ (M + 1) requires 444.0665]; mp 181−183 °C.

General Procedure E: Sodium (3,5-Dibromoisonicotinoyl)(4-chlorobenzoyl)amide (9f). At 0 °C under an argon atmosphere, to a solution of commercial 3,5-dibromoisonicotinamide (0.486 g, 1.74 mmol) in THF (50 mL) was added NaH (60% dispersion in oil, 139 mg, 3.47 mmol), and the reaction mixture was then stirred at 0 °C for 1 h. Next, at −78 °C, pure 4-chlorobenzoyl chloride (303 mg, 1.74 mmol) was added, and the reaction mixture was slowly warmed to room temperature. After one night, the mixture was filtered and concentrated in vacuo, and the resulting residue was triturated in Et_2O to provide, after filtration, 750 mg (98% yield) of the crude desired compound as a yellow powder. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.57 (s, 2H), 8.02 (d, J = 8.4 Hz, 2H), 7.40 (d, J = 8.4 Hz, 2H); J-MOD ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.0, 171.8, 153.1, 149.3 (2C), 138.0, 135.1, 130.6 (2C), 127.5 (2C), 116.9 (2C); IR (neat, cm^{-1}) 2924, 1622, 1589, 1569, 1543, 1403, 1275, 1089, 1012, 897, 758; MS (only the free-imide NH can be detected) ESI+ m/z 416.8633 [$C_{13}H_8Br_2ClN_2O_2$ (M − Na + 2) requires 416.8635]; mp 267−269 °C.

General Procedure F: 5-Bromo-2-(4-chlorophenyl)-4*H*-pyrido[4,3-*e*][1,3]oxazin-4-one (2f). In each of two 10−20 mL microwave vials was placed 500 mg of crude sodium (3,5-dibromoisonicotinoyl)(4-chlorobenzoyl)amide (**9f**). Then 20 mL of anhydrous DMSO was added to each vial, and the vials were sealed. The resulting mixtures were then submitted to microwave irradiation under stirring for 20 min at 180 °C using a Biotage Initiator 2.0 apparatus (in very high absorption mode). After 20 min, the reaction mixtures were gathered, diluted with 150 mL of AcOEt, and washed with brine (3 × 150 mL). The organic layer was then dried over sodium sulfate, filtered, and concentrated in vacuo. The resulting residue was triturated in Et_2O, filtered, and dried under vacuum for 2 h at 80 °C to yield to 562 mg (74% yield) of the corresponding final compound as a pale-yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (2s, 2H), 8.35 (ddd, J = 8.8, 4.4, 2.4 Hz, 2H), 7.58 (ddd, J = 8.4, 4.4, 2.8 Hz, 2H); J-MOD ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 161.8, 151.2, 150.8, 141.7, 139.3, 130.8 (2C), 129.4 (2C), 127.0, 121.9, 118.0; IR (neat, cm^{-1}) 3044, 1693, 1592, 1566, 1321, 1241, 1091, 931, 846, 739, 695, 609; MS ESI+ m/z 336.9375 [$C_{13}H_7BrClN_2O_2$ (M + H) requires 336.9373]; mp 217−219 °C.

*5-Bromo-4-(4-(4-chlorophenyl)-6-phenyl-1,3,5-triazin-2-yl)-pyridin-3-ol (**6i**).* The title compound was obtained in 69% yield (0.091 g) as a white powder from 5-bromo-2-(4-chlorophenyl)-4*H*-pyrido[4,3-*e*][1,3]oxazin-4-one (**2f**) (0.101 g) according to general procedure C in 3 mL of EtOH. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.66 (br s, 1H), 8.47−8.50 (m, 4H), 8.43 (s, 1H), 8.36 (s, 1H), 7.57 (m, 1H), 7.43−7.51 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 170.2, 169.9, 156.6, 144.8, 140.7, 140.3, 134.0, 133.9, 132.9, 130.6 (2C), 129.3 (2C), 129.2 (2C), 129.0 (2C), 123.1, 119.1; IR (neat, cm^{-1}) 3069, 1675, 1589, 1538, 1422, 1340, 1285, 921, 845, 795, 739, 700, 609, 482; MS ESI+ m/z 438.9951 [$C_{20}H_{13}BrClN_4O$ (M + H) requires 438.9955]; mp 201−203 °C.

*5-Bromo-4-(4-naphthalen-2-yl-6-phenyl-1,3,5-triazin-2-yl)-pyridin-3-ol (**6j**).* The title compound was obtained in 55% yield (0.075 g) as a white powder from 5-bromo-2-(naphthalen-2-yl)-4*H*-pyrido[4,3-*e*][1,3]oxazin-4-one (**2g**) (0.106 g) according to general procedure C in 3 mL of EtOH. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.96 (br s, 1H), 9.12 (s, 1H), 8.64 (d, J = 6.9 Hz, 2H), 8.57 (dd, J = 8.7, 1.7 Hz, 1H), 8.52 (s, 1H), 8.46 (s, 1H), 8.02 (d, J = 8.4 Hz, 1H), 7.94 (d, J = 8.7 Hz, 1H), 7.87 (d, J = 7.6 Hz, 1H), 7.55−7.66 (m, 5H); J-MOD ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 170.8, 169.8, 156.6, 145.1, 140.9, 136.0, 134.4, 133.7, 132.8, 131.6, 131.0, 129.6, 129.3 (2C), 129.0 (2C), 128.8, 128.6, 127.8, 126.8, 124.6, 123.0, 119.0; IR (neat, cm^{-1}) 3054, 2690, 2873, 1537, 1495, 1461, 1390, 1151, 1115, 952, 837; 784, 756, 469; MS ESI+ m/z 455.0501 [$C_{24}H_{16}BrN_4O$ (M + H) requires 455.0502]; mp 195−197 °C.

*4-(4-Amino-6-phenyl-1,3,5-triazin-2-yl)-5-bromopyridin-3-ol (**6k**).* The title compound was obtained in 93% yield (0.106 g) as a yellow powder from **2a** (100 mg) in the presence of guanidine hydrochloride (**4d**) (33 mg, 0.35 mmol) and potassium carbonate (48 mg, 0.35 mmol) according to general procedure D. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.76 (s, 1H), 8.33 (br s, 2H), 8.33 (br s, 2H), 7.85 (br s, 2H), 7.60 (t, J = 7.2 Hz, 1H), 7.52 (t, J = 7.6 Hz, 2H); J-MOD ^{13}C NMR (100 MHz, DMSO-d_6) δ 171.1, 171.0, 167.3, 152.3, 141.9, 138.0, 136.1, 133.3, 132.6, 129.0 (2C), 128.5 (2C), 118.9; IR (film, cm^{-1}) 3383, 3332, 3138, 3074, 2732, 1675, 1640, 1558, 1517, 1492, 1457, 1412, 1393, 1312, 1217, 1169, 1147, 1110, 1069, 1029, 1005, 968, 900, 868, 847, 825, 788, 766, 709, 685, 660, 622, 603, 570, 513; MS ESI+ m/z 344.0142 [$C_{14}H_{11}BrN_5O$ (M + 1) requires 344.0141]; mp 311−313 °C.

*4-(4-Amino-6-(4-chlorophenyl)-1,3,5-triazin-2-yl)-5-bromopyridin-3-ol (**6l**).* The title compound was obtained in 64% yield (0.073 g) as a white powder from **2f** (0.100 g) in the presence of **4d** (1 equiv) and potassium carbonate (1 equiv) according to general procedure D in 3 mL of EtOH. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.74 (br s, 1H), 8.32 (d, J = 8.7 Hz, 2H), 8.30 (s, 1H), 8.28 (s, 1H), 7.92 (br s, 2H), 7.61 (d, J = 8.7 Hz, 2H); J-MOD ^{13}C NMR (100 MHz, DMSO-d_6) δ 175.9, 175.0, 172.1, 157.0, 146.7, 142.8, 142.3, 139.7, 138.0, 135.0 (2C), 134.0 (2C), 123.6; IR (neat, cm^{-1}) 3371, 3092, 1675, 1582, 1555, 1519, 1506, 1380, 1308, 1217, 1089, 965, 900, 867, 698; MS ESI + m/z 377.9750 [$C_{14}H_{10}BrClN_5O$ (M + H) requires 377.9751]; mp 306−308 °C.

*Sodium (2-Chloronicotinoyl)(4-methoxybenzoyl)amide (**10b**).* The crude title compound was obtained in 100% yield (2 g) as a white powder from commercial 2-chloronicotinamide (1 g, 6.39 mmol) in THF (120 mL) according to general procedure E. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.27 (dd, J = 4.7, 2.0 Hz, 1H), 8.02 (dt, J = 8.9, 2.0 Hz, 2H), 7.87 (dd, J = 7.5, 2.0 Hz, 1H), 7.35 (dd, J = 7.5, 4.7 Hz, 1H), 6.87 (dt, J = 8.9, 2.0 Hz, 2H), 3.78 (s, 3H); J-MOD ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.6, 173.4, 161.3, 148.0, 147.0, 139.1, 138.2, 132.9, 131.0 (2C), 112.9, 113.0 (2C), 55.5; IR (film, cm^{-1}) 3418, 3073, 3002, 2934, 2837, 1734, 1602, 1574, 1511, 1496, 1448, 1394, 1318, 1303, 1253, 1181, 1159, 1105, 1060, 1030, 905, 848, 826, 781, 761, 714, 693, 649, 634, 603, 572; MS (only the free-imide NH can be detected) ESI+ m/z 291.0529 [$C_{14}H_{12}ClN_2O_3$ (M − Na + 2) requires 291.0531]; mp 287−289 °C.

*2-(4-Methoxyphenyl)-4H-pyrido[3,2-e][1,3]oxazin-4-one (**3b**).* The title compound was obtained in 87% yield (213 mg) as a white solid from crude sodium (2-chloronicotinoyl)(4-methoxybenzoyl)-amide (**10b**) (300 mg, 0.96 mmol) according to general procedure F in 20 mL of anhydrous acetonitrile at 150 °C with 15 min of MW irradiation in very high absorption mode. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.79 (dd, J = 4.8, 2.0 Hz, 1H), 8.48 (dd, J = 7.6, 2.0 Hz, 1H), 8.28 (dt, J = 9.0, 2.0 Hz, 2H), 7.67 (dd, J = 7.7, 4.7 Hz, 1H), 7.20 (dt, J = 9.0, 2.0 Hz, 2H), 3.91 (s, 3H); J-MOD ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 165.5, 165.0, 160.3, 154.6, 138.5, 132.6 (2C), 124.1, 121.5, 114.9 (2C), 114.0, 56.1; IR (CH_2Cl_2, cm^{-1}) 3059, 3016, 2975, 2935, 2843, 1692, 1653, 1615, 1608, 1594, 1555, 1512, 1472, 1443, 1425, 1340, 1307, 1283, 1236, 1206, 1171, 1143, 1119, 1101, 1032, 880, 846, 788, 651, 634, 575, 535, 514; MS ESI+ m/z 255.0763 [$C_{14}H_{11}N_2O_3$ (M + 1) requires 255.0764]; mp 201−203 °C.

*3-(4-(4-Methoxyphenyl)-6-phenyl-1,3,5-triazin-2-yl)pyridin-2(1H)-one (**7b**).* The title compound was obtained in 82% yield (0.115 g) as a yellow powder from 2-(4-methoxyphenyl)-4*H*-pyrido[3,2-*e*][1,3]oxazin-4-one (**3b**) (100 mg) according to general procedure C.

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^{1}H NMR (500 MHz, DMSO-d_6) δ 12.19 (br s, 1H), 8.63 (d, J = 7.1 Hz, 2H), 8.61 (dt, J = 9.0, 2.0 Hz, 2H), 8.54 (br s, 1H), 7.78 (br s, 1H), 7.69 (tt, J = 7.2, 2.3 Hz, 1H), 7.63 (t, J = 7.7 Hz, 2H), 7.17 (dt, J = 8.9, 2.8 Hz, 2H), 6.51 (br s, 1H), 3.90 (s, 3H); J-MOD ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 170.2, 170.0, 165.7, 164.1, 153.1, 139.6, 134.9, 133.2, 131.1 (2C), 129.0 (2C), 128.9 (2C), 127.1, 116.2, 114.3 (2C), 113.8, 55.5; IR (film, cm^{-1}) 3426, 3070, 2935, 2836, 1657, 1608, 1590, 1559, 1535, 1511, 1485, 1449, 1412, 1370, 1347, 1308, 1265, 1238, 1173, 1145, 1104, 1067, 1041, 1030, 994, 897, 888, 833, 805, 775, 695, 644, 592, 510; MS ESI+ m/z 357.1345 [$C_{21}H_{17}N_4O_2$ (M + 1) requires 357.1346]; mp 194−195 °C.

*3-(4-(4-Fluorophenyl)-6-phenyl-1,3,5-triazin-2-yl)pyridin-2(1H)-one (**7c**).* The title compound was obtained in 72% yield (0.102 g) as a white powder from 2-(4-fluorophenyl)-4*H*-pyrido[3,2-*e*][1,3]oxazin-4-one (**3c**) (100 mg) according to general procedure C and 73% yield (112 mg) as a white powder from **3a** (100 mg) in the presence of **4b** (82 mg, 0.47 mmol) and potassium carbonate (62 mg, 0.45 mmol) according to general procedure D. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.07 (br s, 1H), 8.71 (ddt, J = 8.9, 5.7, 2.1 Hz, 2H), 8.65 (dt, J = 7.0, 1.5 Hz, 2H), 8.57 (d, J = 6.0 Hz, 1H), 7.77 (br s, 1H), 7.70 (tt, J = 7.2, 1.4 Hz, 1H), 7.63 (tt, J = 7.0, 1.6 Hz, 2H), 7.46 (tt, J = 8.8, 2.0 Hz, 2H), 6.49 (br s, 1H); J-MOD ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 171.1, 170.7, 170.4, 166.7 (d, J = 253 Hz, 1C), 165.9, 153.2, 140.3, 135.0, 134.0, 132.0 (d, J = 9.4 Hz, 2C), 131.4 (d, J = 3.0 Hz, 1C), 129.5 (2C), 129.4 (2C), 116.5 (d, J = 21.9 Hz, 2C), 116.4; ^{19}F NMR (188 MHz, $CDCl_3$) δ −107.1; IR (film, cm^{-1}) 3429, 3072, 1666, 1603, 1589, 1559, 1511, 1448, 1411, 1366, 1310, 1227, 1176, 1144, 1094, 1059, 1026, 1015, 898, 888, 855, 834, 818, 772, 695, 658, 643, 637, 600, 587, 538, 515, 501; MS ESI+ m/z 345.1144 [$C_{20}H_{14}FN_4O$ (M + 1) requires 345.1146]; mp 256−258 °C.

*3-(4-(1-Methyl-1H-pyrrol-2-yl)-6-phenyl-1,3,5-triazin-2-yl)pyridin-2(1H)-one (**7d**).* The title compound was obtained in 86% yield (0.125 g) as a white powder from 2-(1-methyl-1*H*-pyrrol-2-yl)-4*H*-pyrido-[3,2-*e*][1,3]oxazin-4-one (**3d**) (100 mg) according to general procedure C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 13.95 (br s, 1H), 8.91 (dd, J = 7.6, 1.9 Hz, 1H), 8.50 (dt, J = 7.3, 1.2 Hz, 2H), 8.41 (br d, J = 2.1 Hz, 1H), 7.61 (tt, J = 7.3, 1.2 Hz, 1H), 7.54 (m, 3H), 7.01 (dd, J = 7.6, 4.8 Hz, 1H), 6.96 (t, J = 2.0 Hz, 1H), 6.29 (dd, J = 4.1, 2.4 Hz, 1H), 4.27 (s, 3H); J-MOD ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 169.6 (2C), 165.8, 164.8, 139.3 (2C), 135.2, 133.0, 132.3, 128.9 (2C), 128.8 (2C), 128.4, 120.1, 116.3, 109.6, 38.9; IR (film, cm^{-1}) 3428, 3110, 3067, 3002, 2955, 1660, 1591, 1536, 1516, 1477, 1438, 1396, 1373, 1343, 1309, 1271, 1254, 1227, 1177, 1144, 1108, 1093, 1069, 1058, 1027, 1010, 992, 887, 829, 844, 801, 776, 738, 695, 659, 650, 642, 634, 604, 578, 517; MS ESI+ m/z 330.1348 [$C_{19}H_{16}N_5O$ (M + 1) requires 330.1349]; mp 197−199 °C.

*Sodium (2-Chloronicotinoyl)(thiophene-2-carbonyl)amide (**10e**).* The title compound was obtained in 97% yield (0.896 g) as a yellow powder from commercial 2-chloronicotinamide (500 mg, 3.19 mmol) and commercial thiophene-2-carbonyl chloride (515 mg, 3.51 mmol) according to general procedure E. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.29 (dd, J = 4.7, 2.0 Hz, 1H), 7.86 (dd, J = 7.5, 2.0 Hz, 1H), 7.52 (ddd, J = 5.4, 3.8, 1.1 Hz, 2H), 7.36 (dd, J = 7.5, 4.7 Hz, 1H), 7.02 (dd, J = 5.0, 3.7 Hz, 1H); J-MOD ^{13}C NMR (125 MHz, DMSO-d_6) δ 173.3, 169.7, 147.9, 146.8, 146.7, 138.3, 137.8, 129.6, 128.9, 127.2, 122.5; IR (film, cm^{-1}) 3432, 3075, 2926, 1734, 1605, 1575, 1555, 1501, 1417, 1398, 1361, 1290, 1251, 1221, 1118, 1097, 1076, 1059, 1042, 1021, 985, 915, 860, 828, 801, 779, 757, 712, 707, 650, 629, 609, 550; MS (only the free-imide NH can be detected) ESI+ m/z 266.9984 [$C_{11}H_8ClN_2O_2S$ (M − Na + 2) requires 266.9989]; mp 190−192 °C.

*2-(Thiophen-2-yl)-4H-pyrido[3,2-e][1,3]oxazin-4-one (**3e**).* The title compound was obtained in 71% yield (0.169 g) as a white powder from sodium (2-chloronicotinoyl)(thiophene-2-carbonyl)-amide (**10e**) (300 mg) according to general procedure F in 20 mL of anhydrous acetonitrile at 150 °C with 15 min of MW irradiation in very high absorption mode. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.78 (dd, J = 4.7, 2.0 Hz, 1H), 8.46 (dd, J = 7.7, 2.0 Hz, 1H), 8.18 (d, J = 4.4 Hz, 2H), 7.67 (dd, J = 7.6, 4.7 Hz, 1H), 7.38 (t, J = 4.4 Hz, 1H); J-MOD ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.8, 160.5, 159.6, 154.6, 137.9, 137.2, 135.0, 133.5, 129.9, 124.5, 113.9; IR (film, cm^{-1}) 3055, 2984, 1734, 1695, 1614, 1588, 1563, 1513, 1470, 1415, 1367, 1338, 1240, 1226, 1205, 1142, 1130, 1099, 1059, 1049, 1011, 896, 869, 859, 787, 618, 534; MS ESI+ m/z 231.0225 [$C_{11}H_7N_2O_2S$ (M + 1) requires 231.0223]; mp 180−182 °C.

*3-(4-Phenyl-6-(thiophen-2-yl)-1,3,5-triazin-2-yl)pyridin-2(1H)-one (**7e**).* The title compound was obtained in 67% yield (0.097 g) as a white powder from 2-(thiophen-2-yl)-4*H*-pyrido[3,2-*e*][1,3]oxazin-4-one (**3e**) (100 mg) according to general procedure C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.61 (br s, 1H), 8.98 (dd, J = 7.7, 2.0 Hz, 1H), 8.57 (dt, J = 7.1, 1.8 Hz, 2H), 8.43 (br s, 1H), 8.31 (dd, J = 3.8, 1.2 Hz, 1H), 7.70 (dd, J = 5.0, 1.2 Hz, 1H), 7.64 (tt, J = 7.3, 1.4 Hz, 1H), 7.56 (tt, J = 7.1, 1.6 Hz, 2H), 7.25 (dd, J = 4.9, 3.8 Hz, 1H), 7.03 (dd, J = 7.3, 5.0 Hz, 1H); J-MOD ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 170.1, 167.1, 165.6, 153.0, 140.6, 140.1, 134.5, 133.8, 133.6, 132.8, 129.1 (5C), 116.4, 113.7; IR (film, cm^{-1}) 3428, 3069, 1659, 1589, 1559, 1532, 1511, 1482, 1448, 1437, 1412, 1396, 1372, 1308, 1230, 1175, 1137, 1068, 1048, 1029, 1016, 886, 860, 838, 819, 773, 720, 696, 663, 652, 641, 630, 583, 508; MS ESI+ m/z 333.0809 [$C_{18}H_{13}N_4OS$ (M + 1) requires 333.0804]; mp 235−237 °C.

*3-(4-(4-Fluorophenyl)-6-(4-methoxyphenyl)-1,3,5-triazin-2-yl)-pyridin-2(1H)-one (**7f**).* The title compound was obtained in 80% yield (0.118 g) as a yellow powder from **3b** (100 mg) in the presence of **4b** (72 mg, 0.41 mmol) and potassium carbonate (57 mg, 0.41 mmol) according to general procedure D. ^{1}H NMR (400 MHz, $CDCl_3$) (NH does not appear) δ 9.03 (dd, J = 7.7, 2.0 Hz, 1H), 8.67 (dd, J = 8.8, 5.4 Hz, 2H), 8.59 (d, J = 8.9 Hz, 2H), 8.47 (dd, J = 2.8, 2.0 Hz, 1H), 7.27 (tt, J = 8.6, 1.9 Hz, 2H), 7.08 (m, 3H), 3.96 (s, 3H); J-MOD ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 170.0, 169.6, 166.2 (d, J = 253 Hz, 1C), 165.6, 164.2, 153.0, 139.7, 131.4 (d, J = 7.8 Hz, 2C), 131.2, 131.1 (2C), 126.9, 116.1, 116.0 (d, J = 23.3 Hz, 2C), 114.4 (2C), 113.8, 55.5; ^{19}F NMR (188 MHz, $CDCl_3$) δ −105.4; IR (film, cm^{-1}) 3436, 3075, 3006, 2933, 2837, 1666, 1601, 1587, 1533, 1508, 1411, 1370, 1348, 1306, 1257, 1227, 1173, 1145, 1103, 1029, 888, 859, 828, 799, 772, 730, 689, 656, 637, 592, 588, 511; MS ESI+ m/z 375.1258 [$C_{21}H_{16}FN_4O_2$ (M + 1) requires 375.1251]; mp 191−192 °C.

*3-(4-Amino-6-phenyl-1,3,5-triazin-2-yl)pyridin-2(1H)-one (**7g**).* The title compound was obtained in 97% yield (0.172 g) as a yellow powder from **3a** (150 mg) in the presence of **4d** (67 mg, 0.70 mmol) and potassium carbonate (92 mg, 0.67 mmol) according to general procedure D. ^{1}H NMR (400 MHz, DMSO-d_6) (NH does not appear) δ 8.39 (d, J = 7.0 Hz, 2H), 8.30 (d, J = 6.0 Hz, 1H), 7.97 (d, J = 2.9 Hz, 1H), 7.57 (m, 3H), 6.50 (t, J = 5.7 Hz, 1H); J-MOD ^{13}C NMR (100 MHz, DMSO-d_6) δ 170.9, 170.5, 166.5, 164.3, 148.3, 140.3, 136.3, 132.5, 129.0 (2C), 128.5 (2C), 118.8, 111.9; IR (film, cm^{-1}) 3346, 3209, 1661, 1638, 1602, 1561, 1521, 1466, 1436, 1384, 1312, 1301, 1235, 1159, 1135, 1084, 1058, 1030, 996, 898, 878, 832, 812, 781, 767, 720, 698, 668, 635, 623, 601, 582, 536, 516; MS ESI+ m/z 266.1031 [$C_{14}H_{12}N_5O$ (M + 1) requires 266.1036]; mp >315 °C.

*3-(4-(4-Fluorophenyl)-6-morpholino-1,3,5-triazin-2-yl)pyridin-2(1H)-one (**7h**).* The title compound was obtained in 61% yield (0.089 g) as a white powder from **3c** (100 mg) in the presence of **4c** (91 mg, 0.43 mmol) and potassium carbonate (57 mg, 0.41 mmol) according to general procedure D. ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.1 (br s, 1H), 8.75 (dd, J = 7.6, 2.0 Hz, 1H), 8.38 (m, 3H), 7.18 (tt, J = 9.6, 2.1 Hz, 2H), 6.95 (dd, J = 7.7, 4.8 Hz, 1H), 4.07 (br s, 2H), 3.99 (br s, 2H), 3.82 (t, J = 5.1 Hz, 4H); J-MOD ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 169.0, 166.2 (d, J = 252 Hz, 1C), 166.1, 163.8, 153.2, 139.5, 131.6 (d, J = 2.1 Hz, 1C), 131.3 (d, J = 9.1 Hz, 2C), 116.3, 116.2 (d, J = 21.7 Hz, 2C), 114.1, 67.1, 67.0, 44.4, 44.3; ^{19}F NMR (188 MHz, $CDCl_3$) δ −108.2; IR (film, cm^{-1}) 3432, 3070, 2962, 2861, 1659, 1606, 1590, 1561, 1503, 1485, 1447, 1425, 1407, 1379, 1370, 1305, 1275, 1235, 1202, 1147, 1117, 1071, 1042, 1001, 973, 886, 849, 822, 795, 772, 745, 715, 678, 660, 633, 616, 588, 545, 516, 504; MS ESI+ m/z 354.1365 [$C_{18}H_{17}FN_5O_2$ (M + 1) requires 354.1360]; mp 228−230 °C.

*3-(4-(4-Methoxyphenyl)-6-morpholino-1,3,5-triazin-2-yl)pyridin-2(1H)-one (**7i**).* The title compound was obtained in 88% yield (0.127 g) as a white powder from **3b** (100 mg) in the presence of **4c** (87 mg, 0.41 mmol) and potassium carbonate (57 mg, 0.41 mmol) according

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to general procedure D. ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.5 (br s, 1H), 8.74 (dd, J = 7.6, 2.0 Hz, 1H), 8.37 (dd, J = 4.8, 2.1 Hz, 1H), 8.33 (d, J = 8.9 Hz, 2H), 7.00 (dt, J = 8.9, 2.7 Hz, 2H), 6.93 (dd, J = 7.6, 4.8 Hz, 1H), 4.07 (br s, 2H), 4.00 (br s, 2H), 3.88 (s, 3H), 3.82 (t, J = 5.1 Hz, 4H); J-MOD ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 168.9, 165.9, 163.5, 163.4, 152.7, 138.9, 130.5 (2C), 127.3, 115.8, 114.1 (2C), 113.7, 66.6 (2C), 55.5, 44.0, 43.9; IR (film, cm^{-1}) 3431, 3066, 3003, 2962, 2917, 2863, 2840, 1660, 1596, 1583, 1557, 1502, 1465, 1455, 1444, 1419, 1383, 1370, 1307, 1273, 1255, 1202, 1187, 1173, 1152, 1142, 1112, 1071, 1043, 1022, 1002, 972, 927, 885, 861, 848, 821, 797, 777, 749, 714, 685, 662, 648, 634, 616, 595, 546, 517; MS ESI+ m/z 366.1552 [$C_{19}H_{20}N_5O_3$ (M + 1) requires 366.1560]; mp 236−238 °C.

*Sodium Benzoyl(2-chloronicotinoyl)amide (**10a**).* The crude title compound was obtained in 95% yield (1.81 g) as a white powder from commercial 2-chloronicotinamide (1 g, 6.39 mmol) in THF (120 mL) and commercial benzoyl chloride (0.78 mL, 6.71 mmol) according to general procedure E. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.26 (dd, J = 4.7, 2.0 Hz, 1H), 8.04 (dt, J = 6.7, 1.3 Hz, 2H), 7.85 (dd, J = 7.5, 2.0 Hz, 1H), 7.31−7.40 (m, 4H); J-MOD ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.6, 173.9, 148.0, 147.0, 140.4, 139.1, 138.2, 130.3, 129.1 (2C), 127.8 (2C), 122.9; IR (film, cm^{-1}) 3422, 3055, 1740, 1613, 1577, 1502, 1486, 1449, 1394, 1315, 1295, 1252, 1165, 1125, 1102, 1061, 1043, 1023, 901, 822, 765, 734, 703, 687, 662, 626, 578; MS (only the free-imide NH can be detected) ESI+ m/z 261.0418 [$C_{13}H_{10}ClN_2O_2$ (M − Na + 2) requires 261.0425]; mp 186−188 °C.

*Sodium (2-Chloronicotinoyl)(4-fluorobenzoyl)amide (**10c**).* The crude title compound was obtained in 100% yield (1.92 g) as a white powder from commercial 2-chloronicotinamide (1 g, 6.39 mmol) in THF (120 mL) and commercial 4-fluorobenzoyl chloride (0.79 mL, 6.71 mmol) according to general procedure E. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.28 (dd, J = 4.7, 2.0 Hz, 1H), 8.10 (ddt, J = 8.8, 6.0, 2.0 Hz, 2H), 7.88 (dd, J = 7.5, 2.0 Hz, 1H), 7.35 (dd, J = 7.4, 4.7 Hz, 1H), 7.13 (tt, J = 9.0, 2.1 Hz, 2H); J-MOD ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.0, 173.5, 163.9 (d, J = 245 Hz, 1C), 148.2, 147.0, 138.9, 138.3, 136.9, 131.5 (d, J = 8.7 Hz, 2C), 122.9, 114.5 (d, J = 21.1 Hz, 2C); ^{19}F NMR (188 MHz, $CDCl_3$) δ −111.8; IR (film, cm^{-1}) 3417, 3071, 1622, 1599, 1589, 1558, 1510, 1444, 1387, 1310, 1292, 1226, 1175, 1148, 1099, 1061, 1014, 854, 843, 829, 794, 780, 761, 726, 710, 684, 645, 592, 557; MS (only the free-imide NH can be detected) ESI + m/z 279.0332 [$C_{13}H_9ClFN_2O_2$ (M − Na + 2) requires 279.0331]; mp 278−280 °C.

General Procedure G: "One-Pot Process" for the Preparation of 4-(4,6-Diphenyl-1,3,5-triazin-2-yl)pyridin-3-ol (5a). In a 10−20 mL MW vial, to a solution of sodium benzoyl(3-bromoisonicotinoyl)amide (**8a**) (200 mg, 0.61 mmol) in DMSO (12 mL) was added **4a** (73 mg, 0.61 mmol). Then the microwave vial was sealed and submitted to microwave irradiation for 30 min at 180 °C using a Biotage Initiator 2.0 apparatus (in very high absorption mode). After 30 min, the whole mixture was transferred to a separatory funnel containing 100 mL of an aqueous solution of NaCl and extracted with CH_2Cl_2 (2 × 100 mL). Then the combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The resulting residue was purified on silica gel to provide 142 mg (71%) of the desired product **5a** as a yellow-brown powder.

Similarly, compounds **5b**, **5d**, **6a**, and **6i** were obtained in yields of 47% (94 mg), 75% (150 mg), 45% (89 mg), and 48% (104 mg) from sodium (3-bromoisonicotinoyl)(4-fluorobenzoyl)amide (**8b**) (200 mg), sodium (3-bromoisonicotinoyl)(4-methoxybenzoyl)amide (**8d**) (200 mg), sodium benzoyl(3,5-dibromoisonicotinoyl)amide (**9a**) (200 mg), and **9f** (220 mg), respectively, according to general procedure G.

General Procedure H: "One-Pot Process" for the Preparation of 4-(4-(4-Methoxyphenyl)-6-morpholino-1,3,5-triazin-2-yl)-pyridin-3-ol (5i). In a MW vial, a solution of **4c** (96 mg, 0.46 mmol) and potassium carbonate (60 mg, 0.43 mmol) in DMSO (5 mL) was stirred for 15 min, and then **8d** (155 mg, 0.43 mmol) was added. The microwave vial was sealed and submitted to microwave irradiation for 30 min at 180 °C using a Biotage Initiator 2.0 apparatus (in very high absorption mode). After 30 min, the whole mixture was transferred to a separatory funnel containing 10 mL of an aqueous solution of NaCl and extracted with CH_2Cl_2 (2 × 10 mL). Then the combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The resulting residue was purified on silica gel to provide 117 mg (74% yield) of the desired product **5i** as a pale-yellow powder.

Similarly, **6h** and **7h** were obtained in 56% yield (125 mg) and 55% yield (98 mg) from sodium (3,5-dibromoisonicotinoyl)(4-methoxybenzoy)amide (**9d**) (218 mg) and sodium (2-chloronicotinoyl)(4-fluorobenzoyl)amide (**10c**) (150 mg) respectively, according to general procedure H.

Compounds **7a**, **7b**, and **7c** were obtained in 84% (195 mg), 75% (171 mg) and 48% (109 mg) from sodium benzoyl(2-chloronicotinoyl)amide (**10a**) (200 mg), **10b** (200 mg), and **10c** (200 mg), respectively, according to general procedure G, but the MW-assisted reactions were performed in acetonitrile at 150 °C for 20 min.

Multigram-Scale Procedure: "One-Pot Process" for the Preparation of 3-(4,6-Diphenyl-1,3,5-triazin-2-yl)pyridin-2(1*H*)-one (7a). Compound **10a** (2 g, 7.08 mmol) was equally distributed into four MW vials (4 × 500 mg) and then diluted with 20 mL of acetonitrile in each vial. Benzamidine **4a** (213 g, 1.77 mmol) was added to each of the four reaction mixtures, and then the microwave vials were sealed and submitted to microwave irradiation for 20 min at 150 °C using a Biotage Initiator 2.0 apparatus (in very high absorption mode). Then the reaction mixtures were gathered, diluted with CH_2Cl_2, and concentrated in vacuo. The resulting residue was purified on silica gel to provide 1.345 g (58% yield) of the desired product **7a** as a white powder.

Similarly, compound **7b** was obtained in 71% yield (1.623 g) as a yellow powder from 2 g of **10b** according to the multigram-scale procedure.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Scope and limitations of the transformation of pyrido-oxazinones into trisubstituted 1,3,5-triazines (Table S1); one-pot process for the preparation of **6a** from **9a** in EtOH (Scheme S1); copies of ^{1}H and ^{13}C NMR spectra of compounds **2f**, **3b**, **3e**, **5a−i**, **6a−l**, **7a−i**, **9f**, **10a−c**, and **10e**; and mass spectra of compounds **6a**, **6h**, and **6i**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

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