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Synthesis of 2-Arylpyridopyrimidinones, 6-Aryluracils, and Tri- and Tetrasubstituted Conjugated Alkenes via Pd-Catalyzed Enolic C−O Bond Activation−Arylation

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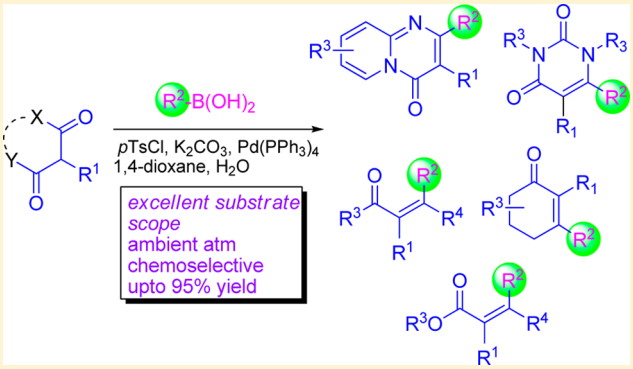
Supporting Information

ABSTRACT: A new and efficient approach for the synthesis of biologically important 2-aryl-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones and 6-aryluracils via previously unknown Pd-catalyzed enolic C−OH activation−arylation of pyridopyrimidin-2,4-diones and barbituric acids, respectively, with boronic acids is reported. The starting materials are readily available, and products are obtained in high yields. An efficient and chemo- and stereoselective access to various tri- and tetrasubstituted conjugated alkenones and alkenoates is also obtained in this arylation approach. Interestingly, the procedure for the construction of such diverse molecular frameworks is general and featured with excellent substrates scope, tolerance of a broad range of functionalities, the unusual viability of performing the reaction under open air and in aqueous cosolvent, and the amenability to a scale-up synthesis, which have been found to be common limitations in the conventional/classical routes. The application of the protocol in a simple one-step high-yield route to pharmaceutically important polyarylated pyridopyrimidinone demonstrates its further synthetic utility.



INTRODUCTION

The importance of nitrogen heterocycles in drug discovery processes has long been known. Major prescription drugs comprise these scaffolds. The pyrimidinone motif is one of the important N-heterocycles that occupy privileged positions in drug discovery. In particular, its pyridine-annulated analogues, pyrido[1,2-*a*]pyrimidin-4-ones, have been found to possess various biological activities.[1] Risperidone[2] and Paliperidone[3] are used as atypical oral antipsychotic drugs.[4] Recent studies have explored a particular derivative set of this structural motif, 2-aryl-substituted pyrido[1,2-*a*]pyrimidin-4-one, as being medicinally valuable. They have been ascribed a diverse range of bioactivities, such as selective aldose reductase inhibition,[5] hepatitis C virus NS3 protease inhibition,[6] improving the transcriptional functions of estrogen-related receptors,[7] quorum sensing inhibition,[8] and MexAB-OprM specific efflux pump inhibition.[9] 2-Arylpyridopyrimidinones (Figure 1) are prepared by a classical reaction of 2-aminopyridine with 3-aryl-3-oxopropanoate, but the method is nonflexible in incorporating versatile aryl moieties and poor to moderate yields in major cases.[5] Another approach involves the preparation of 2-chloropyridopyrimidinone by deoxychlorination of pyridopyrimidin-2,4-dione using excess $POCl_3$ or $SOCl_2$[10] and subsequently the Suzuki coupling with arylboronic acid. However, such a deoxychlorination process is notorious and hazardous, generating enormous waste materials, while on the other hand, as part of the current momentum of a minimizing global environmental concern, the research into the development of green synthesis has been realized as an essential practice by chemists in both industry and academia.[11,12] Moreover, the reaction in $POCl_3$/$SOCl_2$ solvent is detrimental for tolerating numerous functionalities and, thus, limits the potential in generating the substitution diversity in the product library.

One more well-known important motif of the pyrimidinone family is uracil. Its derivatives are present in uridine nucleosides and naturally occurring thymidine, are used as probes in indentifying the interactions between nucleosides/nucleotides and proteins,[13] and have shown a wide range of biological activities.[14,15] In recent years, C6-arylated uracil derivatives have received significant attention because of their various biological applications.

6-Aryluracils have been reported to be versatile pharmacologically active agents, e.g., GnRH antagonist,[16] anti-inflammatory agents,[17] dipeptidyl peptidase IV (DPP-4) inhibitors,[18] antiviral agents, and sirtuin inhibitors.[19−22] However, the synthetic methods for 6-aryluracils are limited. They include arylation of 6-iodouracils by photochemical reaction,[23] and Stille[24] or Suzuki−Miyaura[25] coupling. The limitations in the

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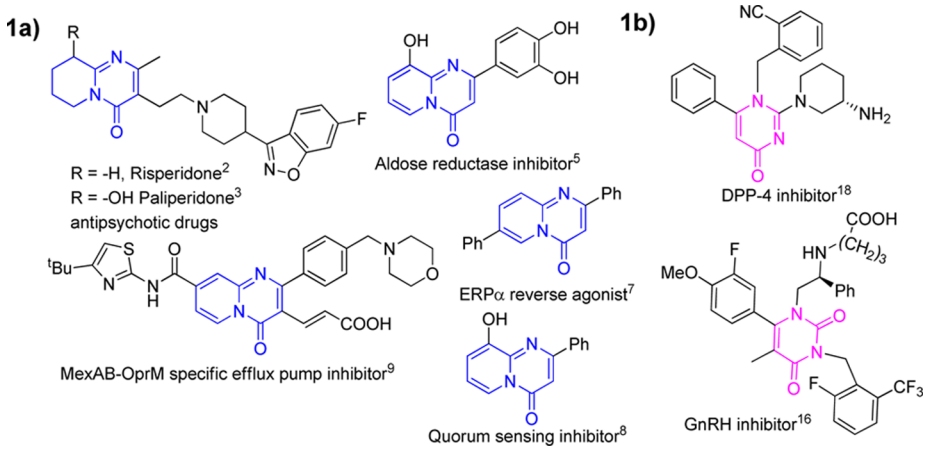

Figure 1. Representative bioactive (a) pyridopyrimidinones and (b) 6-aryluracils.

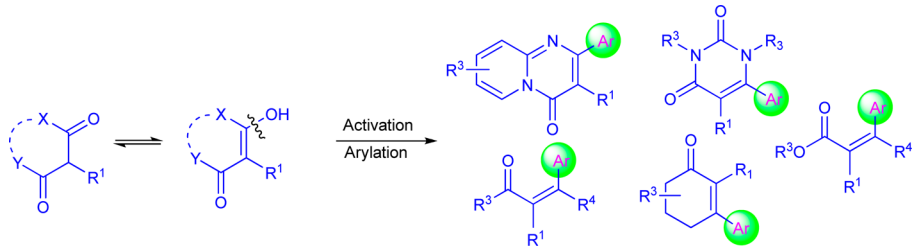

Figure 2. Access to 2-arylpyridopyrimidinones, 6-aryluracils, and tri- and tetrasubstituted conjugated alkenes.

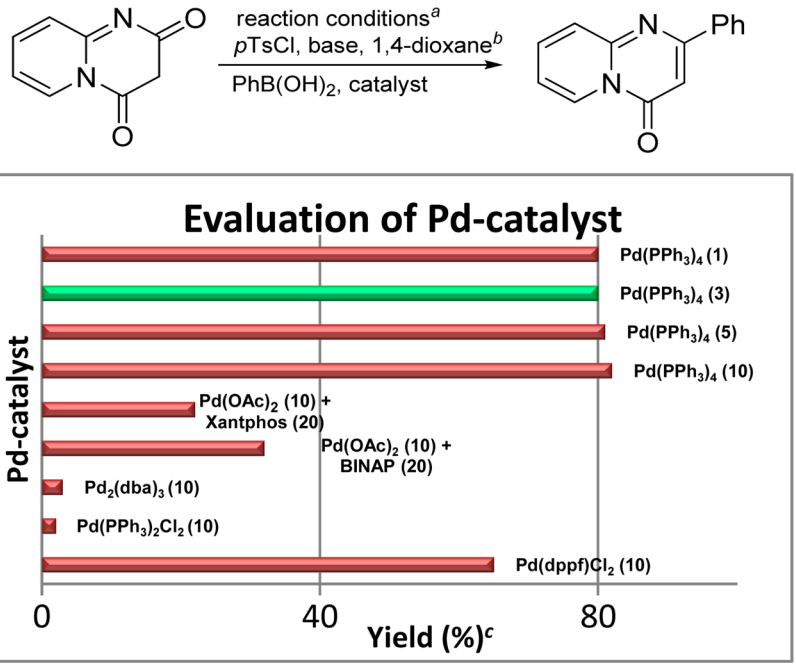

Figure 3. Evaluation of Pd catalysts. For footnote a, substrates, reagents, and conditions were as follows: pyridopyrimidine-2,4-dione (1 mmol), *p*-TsCl (1.3 equiv), K_2CO_3 (5 equiv), 1,4-dioxane (2 mL), H_2O (0.8 mL), then $ArB(OH)_2$ (2 equiv), catalyst, 100 °C. For footnote b, the solvent was used as received commercially without further distillation. For footnote c, the yield is the maximal conversion in the optimal time.

preparation of 6-iodouracils that are usually obtained by lithiation of uracils using LDA and iodination,[26] such as inflexibility, low yields, and the requirement of stringent anhydrous conditions,[27] make these photochemical/coupling methods impractical. Therefore, with an eye on the development of an alternative approach devoid of using 6-iodouracil as a precursor, recent efforts have been made for direct C6−H arylation of 1,3-dimethyluracil.[28−30] Nevertheless, the methodologies suffer from low reaction conversions and yields of products, the feasibility of reactions limited to electron-rich arylating substrates only, and the use of a strong base. Ricart et al. documented an interesting approach to the direct construction of C6-aryluracils, which involves formal [3+3]

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cycloaddition of metal carbene complexes with substituted ureas followed by oxidation.[31]

In transition metal-catalyzed cross-couplings, the recent attractive trend is, among others, the discovery of new variants[32,33] of reaction toward the convenient preparation of versatile molecular frameworks,[34] not limiting to biaryl only. Significant attention has been focused on the catalyzed arylation via C−O bond cleavage for the synthesis of biaryls,[35,36] but its conceptual variation in the direction of arylation via enolic C−O bond activation leading to the preparation of biologically important N-heterocyclic motifs has not yet been documented.[37,38] Herein, we report a new approach for the synthesis of 2-aryl-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones and 6-aryluracils from pyridopyrimidin-2,4-diones and barbituric acids, respectively, via Pd-catalyzed enolic C−O bond activation−arylation (Figure 2). Notably, pyridopyrimidin-2,4-diones are easily accessible, and barbituric acid is much more economical than uracil,[39] used as a synthetic precursor in previous methods. Moreover, this approach represents a one-step strategy of converting an N-heterocyclic scaffold to another. An efficient and chemo- and stereoselective route to various tri- and tetrasubstituted conjugated alkenone and alkenoate has also been identified.

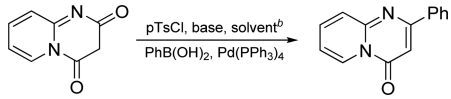
RESULTS AND DISCUSSION

At the outset of our studies of a model enolic activation−arylation reaction of pyridopyrimidin-2,4-dione with phenylboronic acid, we screened a number of Pd-catalytic conditions involving different solvents at varying temperatures with a few selected inexpensive activating agents, *p*-TsCl, $(EtO)_2P(O)Cl$, and *tert*-butoxycarbonyl anhydride. $Pd(PPh_3)_2Cl_2$ catalyst and *p*-TsCl in 1,4-dioxane provided the desired product, although in poor yield (maximally 11%), while other activating agents were found to be ineffective. Pd sources were then examined (Figure 3). Varied yields of the product were obtained with different Pd catalysts. $Pd(PPh_3)_4$ as a catalyst was proven to be the best, and its 3 mol % quantity was found to be optimal. The desired product did not form when the reaction was conducted in the absence of a Pd catalyst.

Among the bases tested, K_2CO_3 was most effective (Table 1). 1,4-Dioxane was found to be superior to other evaluated solvents ranging from weakly polar to polar aprotic. Remarkably, the reaction did not require any inert atmosphere and proceeded smoothly in the presence of water as a cosolvent (optimal quantity), which was plausibly proven to be essential for dissolving K_2CO_3 (entries 11−14).

To check the generality of the method, we investigated the reactions of various substituted pyridopyrimidinones with different arene boronic acids (Table 2). Pleasingly, the method was found to be flexible in accommodating the varied substrates. The successful synthesis of 2-arylpyridopyrimidin-4-one prompted us to consider an other enolizable motif-containing heterocyclic scaffold, barbituric acid, for the synthesis of biologically important 6-arylated uracils. Delightfully, barbituric acid underwent arylation smoothly with various arene boronic acids and afforded 6-aryluracils in high yields. Compared to the conventional/classical methods known for the synthesis of 2-arylpyridopyrimidin-4-one and 6-aryluracils, the enolic activation−arylation approach presented here is step-economical, convenient, and high-yielding, uses easily accessible or economical starting materials, and avoids hazardous reagents and stringent anhydrous conditions.

Table 1. Evaluation of Base, Additive, and Solvent[a]



	$PhB(OH)_2$ (equiv)	base (equiv)	solvent[b]	water (mL)	yield (%)[c]
1	2	K_3PO_4 (5)	1,4-dioxane	0.8	55
2	2	Et_3N (5)	1,4-dioxane	0.8	NR[d]
3	2	Na_2CO_3 (5)	1,4-dioxane	0.8	43
4	2	Cs_2CO_3 (5)	1,4-dioxane	0.8	35
5	2	K_2CO_3 (2.5)	1,4-dioxane	0.8	81
6	2	K_2CO_3 (1.5)	1,4-dioxane	0.8	65
7	2	K_2CO_3 (2.5)	toluene	0.8	NR[d]
8	2	K_2CO_3 (2.5)	DMF	0.8	22
9	2	K_2CO_3 (2.5)	MeCN	0.8	15
10[e]	2	K_2CO_3 (2.5)	THF	0.8	35
11	2	K_2CO_3 (2.5)	1,4-dioxane	0	25
12	2	K_2CO_3 (2.5)	1,4-dioxane	0.4	55
13	2	K_2CO_3 (2.5)	1,4-dioxane	1	88
14	2	K_2CO_3 (2.5)	1,4-dioxane	1.2	80
15	1.5	K_2CO_3 (2.5)	1,4-dioxane	1	89
16	1.2	K_2CO_3 (2.5)	1,4-dioxane	1	90

[a]Substrates, reagents, and condtions: pyridopyrimidine-2,4-dione (1 mmol), *p*-TsCl (1.3 equiv), base, solvent (2 mL), H_2O, then $ArB(OH)_2$, $Pd(PPh_3)_4$ (3 mol %), 100 °C. [b]Solvent used as received commercially without further distillation. [c]Yield for maximal conversion in the optimal time. [d]No reaction. [e]At 80 °C.

We were pleased to find that our developed approach provided also useful access to acyclic/cyclic and alkyl/aryl tri- and tetrasubstituted conjugated alkenes (carbonyl/ester) (Table 2, **9a−d**, **10a**, **10b**, **11a**, and **11b**).[40,41] Importantly, excellent stereoselectivity (90 to 100:5 to 0) for acyclic alkenes was obtained.

The stereoselectivity (*E*/*Z*) of tosyl intermediates in a representative example (**11a**) was found to be retained in the final arylated products. This as well as the requirement of a Pd catalyst indicates that the addition−elimination pathway is not involved in the reaction. These tri- and tetrasubstituted conjugated alkenones/oates have been, in general, prepared by the classical approach of addition of Grignard reagent to 1,3-dicarbonyl followed by dehydration,[42] and later by Heck coupling,[43] diarylation of α-oxo-ketene dithioacetal,[44] or Meyer−Schuster rearrangement of propargylic alcohol.[45] In comparison, this approach represents a simple and high-yield methodology, allows the incorporation of versatile aryl units into products, and is functionally compatible.

Next, we investigated the flexibility of the method for versatile boronic acids (Table 3). We found that a variety of aryl, heteroaryl, and arylalkenyl boronic acids containing both electron-donating and electron-withdrawing functionalities were feasible substrates in the arylation of pyridopyrimidin-2,4-dione. The reaction conversions were complete, and the

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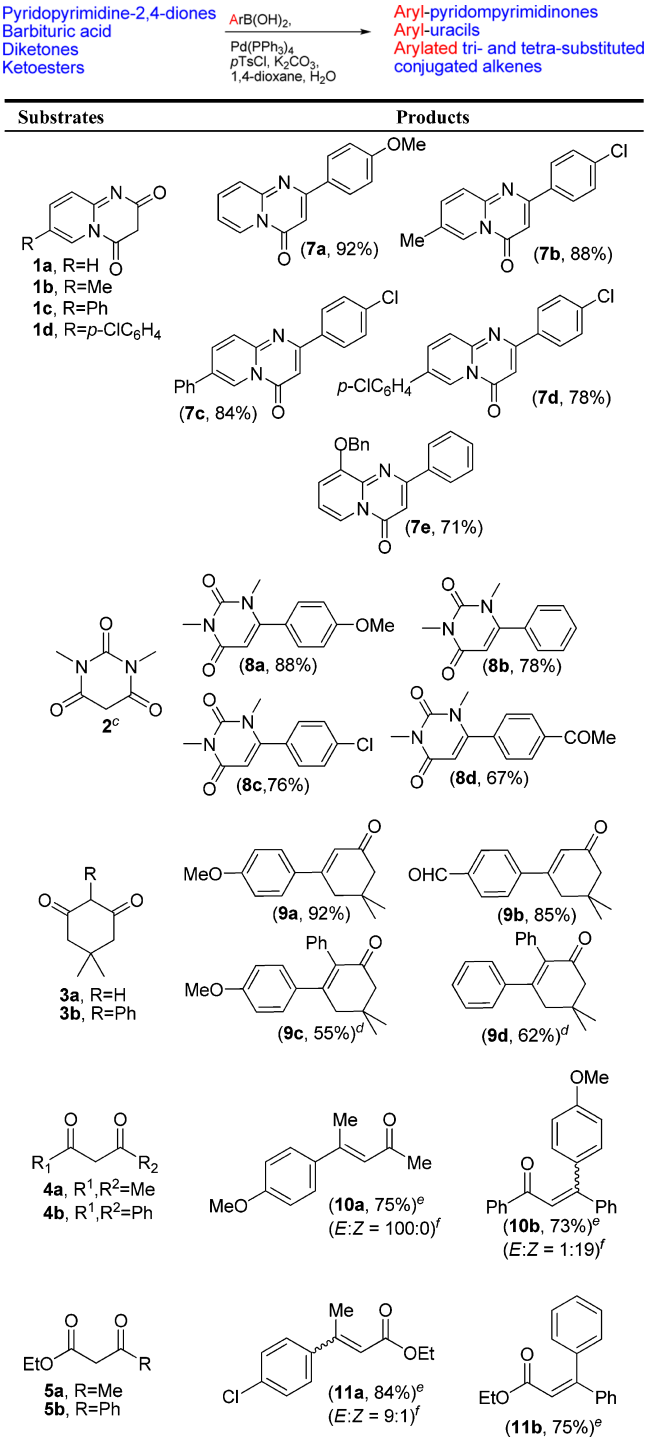
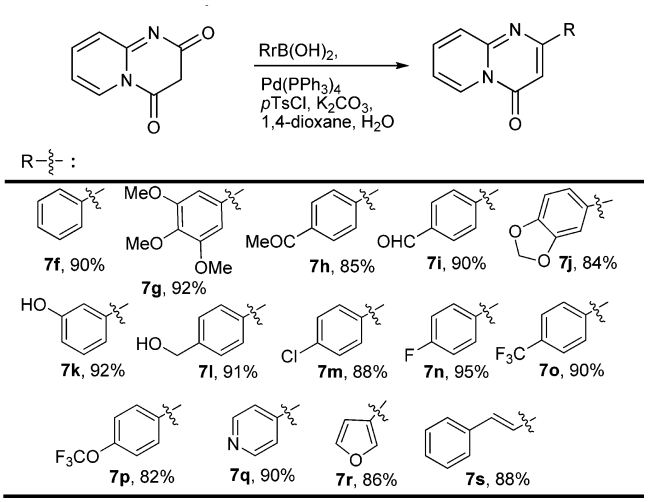
Table 2. Enolic−OH Bond Arylation of Versatile Motifs[a]



[a]Substrate (1 mmol), *p*-TsCl (1.3 equiv), K_2CO_3 (2.5 equiv), 1,4-dioxane (2 mL), H_2O (1 mL), then $RB(OH)_2$ (1.2−1.5 equiv), $Pd(PPh_3)_4$ (3 mol %), 100 °C, 1−1.5 h (24 h for **9c** and **9d**). [b]KOH (1.5 equiv) replacing K_2CO_3 was added. [c]$Pd(PPh_3)_4$ (10 mol %). [d]DABCO (1.5 equiv) replacing K_2CO_3 was added. [e]Determined by ^1H NMR.

products were obtained in high to excellent yields. The tolerance of several functional groups on both aryl boronic acids and pyridopyrimidin-2,4-diones, including aldehyde, acetyl, and phenolic and alcoholic hydroxyl groups, in the reaction is remarkable (Tables 2 and 3). In the previously

Table 3. Arylation with Various Boronic Acids[a]

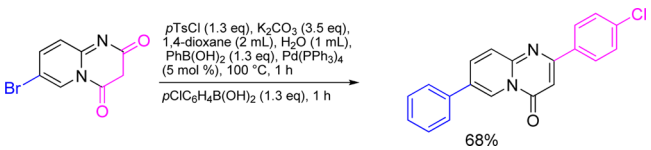


[a]Substrates, reagents, and condtions: pyridopyrimidine-2,4-dione (1 mmol), *p*-TsCl (1.3 equiv), K_2CO_3 (2.5 equiv), 1,4-dioxane (2 mL), H_2O (1 mL), then $RB(OH)_2$ (1.2−1.5 equiv), $Pd(PPh_3)_4$ (3 mol %), 100 °C, 1−1.5 h.

known methods, the preparation of 2-arylpyridopyrimidinones with numerous substitutions/functionalities on the fused pyridine ring[46] (e.g., methyl and benzyloxy) or 2-aryl moieties[47] have been found to be poor-yielding. In contrast, our developed approach has comfortably accommodated these variations in the scaffold, affording high yields. The protocol has shown excellent substrate scope, tolerance of a broad range of functionalities, and high-yield access of products. The reaction conditions proved also to be amenable to a scale-up synthesis (investigated up to 20 mmol).

Polyarylated pyridopyrimidinones are known to enhance the transcriptional functions of nuclear estrogen-related receptor α (ERRα).[7] These compounds have been prepared before via multireaction steps[7] but, interestingly, can now be readily accessible in high yields using the approach presented here via one-pot chemoselective polyarylation. The reaction of 7-bromo-pyridopyrimidin-2,4-dione with two similarly reactive arylboronic acids preceded chemoselective arylations and provided 2,7-diaryl-substituted pyrido[1,2-*a*]pyrimidin-4-one in high yields (Scheme 1). This demonstrates the further

Scheme 1. One-Pot Synthesis of a Multiarylated Heterocycle



synthetic utility of our developed method. The arylation takes place chemoselectively first at C7-Br and subsequently at C2-OH. The only intermediate formed was isolated from the resultant mixture obtained by stopping the reaction at an intermediate time (after 40 min). It was found to be 7-phenyl-2-(4-methylbenzenesulfonyloxy)-4*H*-pyrido[1,2-*a*]pyrimidin-4-one (**7c1**).

In conclusion, a new and efficient method for the synthesis of biologically important 2-aryl-4*H*-pyrido[1,2-*a*]pyrimidin-4-ones and 6-aryluracils from pyridopyrimidin-2,4-diones and barbituric acids, respectively, via Pd-catalyzed enolic C−OH

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activation−arylation with boronic acids has been established. This method opens up a practical strategy of generating a valuable N-heterocyclic unit in high yield from a readily available scaffold of a completely different class of N-heterocycle that contains an enolizable moiety. In this approach, versatile cyclic/acyclic aryl/alkyl tri- and tetrasubstituted conjugated carbonyls/esters are accessible in high yields with chemo- and stereoselectivities. The method has also been successfully applied to a simple high-yield synthesis of pharmaceutically important polyarylated pyridopyrimidinone. This protocol is quite resourceful in broad applications to the synthesis of biologically and synthetically important motifs.

EXPERIMENTAL SECTION

General Information. Infrared (IR) spectra were recorded on a FTIR instrument with an ATR and IR microscope spectrometer. ^{1}H NMR spectra were recorded on a 400 MHz spectrometer. Data are reported as follows: chemical shifts in parts per million from tetramethylsilane as an internal standard in $CDCl_3$/CD_3OD/DMSO-d_6 integration, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; td, triplet of doublets; dt, doublet of triplets; ddd, doublet of doublets of doublets; br, broad), and coupling constants (hertz). ^{13}C NMR spectra were recorded on a 100 MHz spectrometer with complete proton decoupling. Chemical shifts are reported in parts per million from the residual solvent as an internal standard. High-resolution mass spectra (HRMS) were recorded on a high-resolution LC−MS/MS instrument with a "Q-TOF" mass analyzer. For thin layer chromatography (TLC) analysis throughout this work, Merck precoated TLC plates (silica gel 60 GF254, 0.25 mm) were used. The products were purified by column chromatography silica gel 60-120 (Merck, silica gel 60−120 mesh, neutral, spherical) or neutral alumina column chromatography.

The starting materials and solvents were used as received from commercial suppliers without further purification.

Typical Experimental Procedure for Direct C−OH Bond Arylation of Enolizable and/or Tautomerizable Motifs. *p*-TsCl (1.3 equiv, 124 mg, 0.65 mmol) was added to a mixture of the substrate (0.5 mmol) and K_2CO_3 (2.5 equiv, 173 mg, 1.25 mmol) in 1,4-dioxane (2 mL) and H_2O (1 mL) in a round-bottom flask. The mixture was stirred under open air for 1 h at rt (25−28 °C). The boronic acid (1.2 equiv, 0.6 mmol) and $Pd(PPh_3)_4$ (3 mol %, 17 mg, 0.015 mmol) were subsequently added, and the mixture was heated at 100 °C under open air. For compounds **8a−d** KOH (1.5 equiv, 42 mg, 0.65 mmol) and for compounds **10a−11b** DABCO (1.5 equiv, 84 mg, 0.65 mmol) in place of K_2CO_3 (2.5 equiv) was added after substrate, and K_2CO_3 (1 equiv, 69 mg, 0.5 mmol) was added after Pd catalyst. Upon completion of the reaction as indicated by TLC (1−1.5 h), the resultant mixture was cooled to rt and extracted with EtOAc (2 × 25 mL). The combined organic solution was washed with water (2 × 5 mL) and brine (1 × 5 mL), dried with anhydrous Na_2SO_4, and concentrated under reduced pressure. The column chromatographic purification of the crude mass was performed on neutral alumina (for compounds **7a−s** and **8a−d**) using EtOAc/hexane (30−40%) as the eluting solvent and on silica gel (for compounds **9a−11b**) eluting with EtOAc/hexane (2−10%) to afford the arylated products.

Characterization Data for Arylated Products (7a−11b). *2-(4-Methoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one*[5] ***(7a)***. Light yellow solid: 116 mg, 92%; mp 148−150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (d, J = 7.1 Hz, 1H), 8.09 (d, J = 8.7 Hz, 2H), 7.76−7.70 (m, 2H), 7.11 (dd, J = 6.8 Hz, J = 5.8 Hz, 1H), 7.02 (d, J = 8.7 Hz, 2H), 6.87 (s, 1H), 3.89 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.8, 161.5, 158.6, 150.9, 136.0, 129.5, 128.9, 127.2, 126.6, 114.9, 114.1, 98.7, 55.4; IR ν_{max} 3037, 1667, 1637, 1253, 1027 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{13}N_2O_2$ [M + H]$^+$ m/z 253.0977, found m/z 253.0979.

2-(4-Chlorophenyl)-7-methyl-4H-pyrido[1,2-a]pyrimidin-4-one ***(7b)***. Light yellow solid: 119 mg, 88%; mp 210−212 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.00 (d, J = 8.5 Hz, 2H), 7.64−7.58 (m, 2H), 7.43 (d, J = 8.5 Hz, 2H), 6.83 (s, 1H), 2.43 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.2, 158.4, 149.9, 139.3, 136.7, 135.7, 128.9, 128.6, 126.1, 125.7, 124.7, 99.5, 18.4; IR ν_{max} 2924, 1686, 1645, 823 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{12}ClN_2O$ [M(^{35}Cl) + H]$^+$ m/z 271.0638, found m/z 271.0639.

2-(4-Chlorophenyl)-7-phenyl-4H-pyrido[1,2-a]pyrimidin-4-one ***(7c)***. Greenish-yellow solid: 139 mg, 84%; mp 195−197 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.26 (d, J = 1.9 Hz, 1H), 8.06−8.02 (m, 3H), 7.77 (d, J = 9.2 Hz, 1H), 7.68−7.64 (m, 2H), 7.53−7.49 (m, 2H), 7.48−7.44 (m, 3H), 6.88 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.4, 158.6, 150.1, 136.9, 136.3, 135.6, 135.4, 129.40, 129.36, 129.0, 128.9, 128.7, 126.88, 126.79, 124.2, 99.8; IR ν_{max} 3071, 2922, 1682, 1633, 822 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{13}ClN_2ONa$ [M(^{35}Cl) + Na]$^+$ m/z 355.0614, found m/z 355.0609.

2,7-Bis(4-chlorophenyl)-4H-pyrido[1,2-a]pyrimidin-4-one ***(7d)***. Greenish-yellow solid: 143 mg, 78%; mp 208−210 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.22 (d, J = 1.9 Hz, 1H), 8.02 (d, J = 8.6 Hz, 2H), 7.97 (dd, J = 9.3 Hz, J = 2.2 Hz, 1H), 7.77 (dd, J = 9.2 Hz, J = 0.4 Hz, 1H), 7.59 (d, J = 8.6 Hz, 2H), 7.50−7.43 (m, 4H), 6.88 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.5, 158.4, 149.9, 137.0, 135.9, 135.5, 135.2, 133.8, 129.6, 129.0, 128.7, 128.13, 128.09, 127.0, 124.2, 99.9; IR ν_{max} 3089, 1690, 1634, 813 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{13}Cl_2N_2O$ [M(^{35}Cl^{35}Cl) + H]$^+$ m/z 367.0405, found m/z 367.0399.

9-(Benzyloxy)-2-phenyl-4H-pyrido[1,2-a]pyrimidin-4-one ***(7e)***. White solid: 116 mg, 71%; mp 180−184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (dd, J = 7.1 Hz, J = 1.3 Hz, 1H), 8.18−8.14 (m, 2H), 7.54−7.34 (m, 8H), 7.05 (dd, J = 7.6 Hz, J = 1.2 Hz, 1H), 6.98−6.95 (m, 2H), 5.38 (s, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.7, 158.9, 151.5, 145.8, 137.3, 135.7, 130.6, 128.80, 128.78, 128.3, 127.5, 127.1, 119.6, 114.3, 114.1, 100.6, 71.7; IR ν_{max} 1687, 1376, 1275, 1171 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{17}N_2O_2$ [M + H]$^+$ m/z 329.1280, found m/z 329.1282.

6-(4-Methoxyphenyl)-1,3-dimethylpyrimidine-2,4(1H,3H)-dione[28] ***(8a)***. Light yellow solid: 108 mg, 88%; mp 107−109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, J = 8.7 Hz, 2H), 6.98 (d, J = 8.7 Hz, 2H), 5.68 (s, 1H), 3.87 (s, 3H), 3.40 (s, 3H), 3.25 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.5, 160.9, 154.6, 152.8, 129.3, 125.6, 114.3, 102.4, 55.4, 34.6, 28.0; IR ν_{max} 2956, 1697, 1645, 1249, 1177 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{14}N_2O_3Na$ [M + Na]$^+$ m/z 269.0902, found m/z 269.0906.

1,3-Dimethyl-6-phenylpyrimidine-2,4(1H,3H)-dione[28] ***(8b)***. White solid: 84 mg, 78%; mp 142−145 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50−7.46 (m, 3H), 7.34−7.32 (m, 2H), 5.70 (s, 1H), 3.41 (s, 3H), 3.22 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.5, 154.6, 152.7, 133.4, 130.2, 129.0, 127.8, 102.5, 34.6, 28.0; IR ν_{max} 3057, 1689, 1637 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{12}N_2O_2Na$ [M + Na]$^+$ m/z 239.0797, found m/z 239.0791.

6-(4-Chlorophenyl)-1,3-dimethylpyrimidine-2,4(1H,3H)-dione[30] ***(8c)***. White solid: 96 mg, 76%; mp 122−124 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.4 Hz, 2H), 5.68 (s, 1H), 3.40 (s, 3H), 3.22 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.2, 153.4, 152.6, 136.6, 131.7, 129.4, 129.2, 102.7, 34.6, 28.1; IR ν_{max} 3084, 1697, 1651, 838 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{11}ClN_2O_2Na$ [M + Na]$^+$ m/z 273.0407, found m/z 273.0400.

6-(4-Acetylphenyl)-1,3-dimethylpyrimidine-2,4(1H,3H)-dione ***(8d)***. Off-white solid: 86 mg, 67%; mp 126−128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J = 8.4 Hz, 2H), 7.45 (d, J = 8.4 Hz, 2H), 5.69 (s, 1H), 3.39 (s, 3H), 3.20 (s, 3H), 2.64 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 192.2, 157.4, 148.7, 147.7, 133.5, 132.8, 124.1, 123.4, 97.9, 29.8, 23.3, 21.9; IR ν_{max} 3060, 2959, 1697, 1682, 1650 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{15}N_2O_3$ [M + H]$^+$ m/z 259.1082, found m/z 259.1079.

3-(4-Methoxyphenyl)-5,5-dimethylcyclohex-2-enone[48] ***(9a)***. Yellow oil: 106 mg, 92%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, J = 8.9 Hz, 2H), 6.93 (d, J = 8.9 Hz, 2H), 6.39 (t, J = 1.3 Hz, 1H), 3.85 (s, 3H), 2.62 (d, J = 1.2 Hz, 2H), 2.32 (s, 2H), 1.13 (s, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 200.1, 161.2, 156.9, 135.0, 131.1, 128.1, 126.8, 122.6, 114.1, 55.4, 50.9, 42.1, 33.7, 28.5; IR ν_{max} 2956, 1653,

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1596, 1239, 1179 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{19}O_2$ $[M + H]^+$ m/z 231.1385, found m/z 231.1389.

3-(4-Formylphenyl)-5,5-dimethylcyclohex-2-enone (**9b**). Light yellow solid: 97 mg, 85%; mp 111−113 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 10.05 (s, 1H), 7.93 (d, J = 8.1 Hz, 2H), 6.68 (d, J = 8.3 Hz, 2H), 6.46 (s, 1H), 2.67 (d, J = 1.2 Hz, 2H), 2.37 (s, 2H), 1.15 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 199.7, 191.5, 155.9, 144.9, 136.9, 130.0, 126.8, 126.2, 50.9, 42.3, 33.8, 28.4; IR ν_{max} 3103, 1689, 1637 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{17}O_2$ $[M + H]^+$ m/z 229.1228, found m/z 229.1221.

3-(4-Methoxyphenyl)-5,5-(dimethyl)-2-phenylcyclohex-2-enone (**9c**). White solid: 84 mg, 55%; mp 120−122 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.19−7.12 (m, 3H), 6.96−6.93 (m, 4H), 6.66 (d, J = 8.9 Hz, 2H), 3.72 (s, 3H), 2.71 (s, 2H), 2.51 (s, 2H), 1.19 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 198.5, 159.1, 155.0, 136.1, 135.8, 133.1, 131.0, 130.0, 129.8, 127.7, 126.6, 113.3, 55.2, 51.7, 47.0, 33.0, 28.2; IR ν_{max} 3010, 2958, 1655, 1605, 1252, 1175 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{23}O_2$ $[M + H]^+$ m/z 307.1698, found m/z 307.1698.

2,3-(Diphenyl)-5,5-(dimethyl)cyclohex-2-enone (**9d**). White solid: 86 mg, 62%; mp 150−152 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.16−7.11 (m, 6H), 7.01−6.99 (m, 2H), 6.93−6.91 (m, 2H), 2.72 (s, 2H), 2.53 (s, 2H), 1.20 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 198.5, 155.5, 141.0, 136.7, 135.4, 130.9, 128.0, 127.9, 127.7, 127.6, 126.8, 51.7, 47.1, 33.2, 28.22; IR ν_{max} 3031, 2949, 1658 cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{21}O$ $[M + H]^+$ m/z 277.1592, found m/z 277.1592.

(E)-4-(4-Methoxyphenyl)pent-3-en-2-one[49] (**10a**). White solid: 71 mg, 75%; mp 69−71 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 8.9 Hz, 2H), 6.90 (d, J = 8.9 Hz, 2H), 6.49 (d, J = 0.6 Hz, 1H), 3.83 (s, 3H), 2.52 (d, J = 1.1 Hz, 1H), 2.27 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 198.8, 160.6, 153.3, 134.5, 127.9, 122.9, 113.9, 55.3, 32.2, 18.0; IR ν_{max} 2925, 1673, 1584, 1246, 1172 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{14}O_2Na$ $[M+ Na]^+$ m/z 213.0892, found m/z 213.0891.

(Z)-3-(4-Methoxyphenyl)-1,3-diphenylprop-2-en-1-one[50] (**10b**). Fluorescent yellow oil: 114 mg, 73%; ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 7.1 Hz, 2H), 7.47 (tt, J = 7.4 Hz, J = 1.3 Hz, 1H), 7.41−7.34 (m, 7H), 7.11 (d, J = 8.8 Hz, 2H), 7.00 (s, 1H), 6.77 (d, J = 8.8 Hz, 2H), 3.77 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 192.9, 159.9, 154.8, 141.9, 138.4, 132.6, 131.5, 131.2, 129.7, 128.84, 128.76, 128.40, 128.36, 123.4, 113.5, 55.2; IR ν_{max} 3057, 1655, 1598, 1579, 1246, 1174 cm^{-1}; HRMS (ESI) calcd for $C_{22}H_{18}O_2Na$ $[M + Na]^+$ m/z 337.1205, found m/z 337.1205.

(E)-Ethyl 3-(4-Chlorophenyl)but-2-enoate[51] (**11a**). Clear oil: 94 mg, 84%; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 8.7 Hz, 2H), 7.33 (d, J = 8.7 Hz, 2H), 6.11 (q, J = 1.2 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 2.54 (d, J = 1.2 Hz, 3H), 1.31 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.7, 154.0, 140.6, 134.9, 128.7, 127.6, 117.5, 59.9, 17.8, 14.3; IR ν_{max} 2929, 1712, 1629, 827 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{14}ClO_2$ $[M + H]^+$ m/z 225.0682, found m/z 225.0673.

Ethyl 3,3-Diphenylacrylate[52] (**11b**). Clear oil: 94 mg, 75%; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.36 (m, 3H), 7.35−7.27 (m, 5H), 7.23−7.19 (m, 2H), 6.36 (s, 1H), 4.04 (q, J = 7.1 Hz, 2H), 1.10 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.2, 156.5, 140.8, 139.0, 129.4, 129.1, 128.4, 128.3, 128.1, 127.9, 117.5, 60.1, 14.0; IR ν_{max} 3028, 2979, 1720, 1700, 1262, 1149 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{17}O_2$ $[M + H]^+$ m/z 253.1228, found m/z 253.1225.

2-Phenyl-4H-pyrido[1,2-a]pyrimidin-4-one[5] (**7f**). Light yellow solid: 100 mg, 90%; mp 141−143 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.07 (d, J = 7.1 Hz, 1H), 8.10−8.08 (m, 2H), 7.74−7.73 (m, 2H), 7.53−7.49 (m, 3H), 7.14−7.11 (m, 1H), 6.92 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.0, 158.6, 151.0, 137.3, 136.1, 130.6, 128.8, 127.4, 127.3, 126.8, 115.2, 100.1; IR ν_{max} 3131, 1678, 1634 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{10}N_2ONa$ $[M + Na]^+$ m/z 245.0691, found m/z 245.0687.

2-(3,4,5-Trimethoxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one (**7g**). Light yellow solid: 144 mg, 92%; mp 188−200 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.07 (dt, J = 7.1 Hz, J = 1.1 Hz, 1H), 7.76−7.75 (m, 2H), 7.35 (s, 2H), 7.16−7.12 (m, 1H), 6.87 (s, 1H), 3.98 (s, 6H), 3.92 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.6, 158.6, 153.4, 150.9, 140.4, 136.2, 132.6, 127.3, 126.7, 115.2, 104.7, 99.7, 60.9, 56.3; IR ν_{max} 2917, 2849, 1674, 1629, 1230, 1119 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{17}N_2O_4$ $[M + H]^+$ m/z 313.1188, found m/z 313.1189.

2-(4-Acetylphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one (**7h**). Off-white solid: 112 mg, 85%; mp 205−207 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.08 (d, J = 7.1 Hz, 1H), 8.18 (d, J = 8.0 Hz, 2H), 8.08 (d, J = 8.0 Hz, 2H), 7.81−7.75 (m, 2H), 7.17 (dd, J = 6.8 Hz, J = 5.8 Hz, 1H), 6.95 (s, 1H), 2.66 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 197.6, 160.6, 158.5, 151.1, 141.5, 138.3, 136.5, 128.7, 127.6, 127.3, 126.8, 115.6, 100.8, 26.8; IR ν_{max} 3124, 1685, 1669, 1634 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{12}N_2O_2Na$ $[M + Na]^+$ m/z 287.0797, found m/z 287.0799.

2-(4-Formylphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one (**7i**). Off-white solid: 112 mg, 90%; mp >200 °C; ^1H NMR (400 MHz, $CDCl_3$/DMSO-d_6) δ 10.1 (s, 1H), 9.09 (d, J = 7.0 Hz, 1H), 8.26 (d, J = 8.0 Hz, 2H), 8.03 (d, J = 8.0 Hz, 2H), 7.86−7.79 (m, 2H), 7.23 (dd, J = 6.3 Hz, J = 6.2 Hz, 1H), 6.97 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/DMSO-d_6) δ 192.1, 160.7, 158.7, 151.1, 142.8, 137.5, 136.8, 130.1, 128.1, 127.3, 126.8, 115.9, 101.0; IR ν_{max} 3118, 2852, 2755, 1699, 1685, 1632, 1605 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{10}N_2O_2Na$ $[M + Na]^+$ m/z 273.0640, found m/z 273.0642.

2-(Benzo[d][1,3]dioxol-5-yl)-4H-pyrido[1,2-a]pyrimidin-4-one (**7j**). Off-white solid: 112 mg, 84%; mp 213−215 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.05 (d, J = 7.1 Hz, 1H), 7.74 (ddd, J = 9.0 Hz, J = 6.2 Hz, J = 1.6 Hz, 1H), 7.69 (ddd, J = 9.0 Hz, J = 1.7 Hz, J = 0.9 Hz, 1H), 7.66 (dd, J = 8.2 Hz, J = 1.8 Hz, 1H), 7.61 (d, J = 1.8 Hz, 1H), 7.12 (ddd, J = 6.3 Hz, J = 1.7 Hz, J = 0.9 Hz, 1H), 6.92 (d, J = 8.1 Hz, 1H), 6.81 (s, 1H), 6.05 (s, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 161.4, 158.6, 150.9, 149.9, 148.3, 136.2, 131.5, 127.3, 126.6, 122.2, 115.0, 108.5, 107.6, 101.6, 99.1; IR ν_{max} 2912, 1682, 1629, 1478, 1249, 1036 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{11}N_2O_3$ $[M + H]^+$ m/z 267.0769, found m/z 267.0763.

2-(3-Hydroxyphenyl)-4H-pyrido[1,2-a]pyrimidin-4-one (**7k**). Off-white solid: 109 mg, 92%; mp 242−244 °C; ^1H NMR (400 MHz, DMSO-d_6) δ 8.98 (d, J = 6.8 Hz, 1H), 7.98 (dt, J = 6.8 Hz, J = 1.4 Hz, 1H), 7.76 (d, J = 8.8 Hz, 1H), 7.64−7.60 (m, 2H), 7.38−7.34 (m, 1H), 7.32 (d, J = 7.9 Hz, 1H), 6.94 (dd, J = 7.9 Hz, J = 1.9 Hz, 1H), 6.91 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 160.9, 158.15, 158.13, 151.0, 138.5, 138.1, 130.3, 127.4, 126.6, 118.5, 118.2, 116.6, 114.4, 99.0; IR ν_{max} 3296, 1673, 1633, 1454, 1280 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{11}N_2O_2$ $[M + H]^+$ m/z 239.0820, found m/z 239.0818.

2-[4-(Hydroxymethyl)phenyl]-4H-pyrido[1,2-a]pyrimidin-4-one (**7l**). White solid: 115 mg, 91%; mp 190−192 °C; ^1H NMR (400 MHz, $CDCl_3$/DMSO-d_6) δ 9.01 (d, J = 6.9 Hz, 1H), 8.10 (d, J = 7.7 Hz, 2H), 7.87 (dd, J = 8.0 Hz, J = 7.3 Hz, 1H), 7.73 (d, J = 8.8 Hz, 1H), 7.48 (d, J = 7.7 Hz, 2H), 7.25 (dd, J = 6.8 Hz, J = 6.7 Hz, 1H), 6.86 (s, 1H), 5.18 (t, J = 5.6 Hz, OH), 4.65 (d, J = 5.6 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/DMSO-d_6) δ 161.9, 158.7, 151.6, 146.1, 137.6, 136.2, 127.9, 127.8, 127.5, 127.3, 116.4, 99.6, 64.0; IR ν_{max} 3315, 3115, 1652, 1629, 1471, 1444 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{12}N_2O_2Na$ $[M + Na]^+$ m/z 275.0803, found m/z 275.0803.

2-(4-Chlorophenyl)-4H-pyrido[1,2-a]pyrimidin-4-one[53] (**7m**). White solid: 113 mg, 88%; mp 195−197 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.07 (d, J = 7.1 Hz, 1H), 8.05 (d, J = 8.6 Hz, 2H), 7.79−7.71 (m, 2H), 7.48 (d, J = 8.6 Hz, 2H), 7.15 (ddd, J = 6.0 Hz, J = 5.8 Hz, J = 1.4 Hz, 1H), 6.88 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.7, 158.5, 151.0, 136.9, 136.4, 135.6, 129.0, 128.7, 127.3, 126.7, 115.3, 99.8; IR ν_{max} 2916, 1679, 1625, 819 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_9ClN_2ONa$ $[M(^{35}Cl) + Na]^+$ m/z 279.0301, found m/z 279.0300.

2-(4-Fluorophenyl)-4H-pyrido[1,2-a]pyrimidin-4-one[53] (**7n**). White solid: 114 mg, 95%; mp 185−187 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 9.06 (d, J = 7.1 Hz, 1H), 8.09 (dd, J = 8.8 Hz, J = 5.4 Hz, 2H), 7.75 (dt, J = 8.8 Hz, J = 1.4 Hz, 1H), 7.71 (d, J = 8.7 Hz, 1H), 7.17 (t, J = 8.8 Hz, 2H), 7.12 (d, J = 6.2 Hz, 1H), 6.85 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.5 (d, J_{C-F} = 249 Hz), 160.9, 158.5, 151.0, 136.3, 133.3 (d, $J_{C-C-C-C-F}$ = 3 Hz), 129.5 (d, $J_{C-C-C-F}$ = 9 Hz), 127.3, 126.7, 115.8 (d, J_{C-C-F} = 21 Hz), 115.3, 99.6; IR ν_{max} 3042, 1681, 1633, 1233 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_9FN_2ONa$ $[M + Na]^+$ m/z 263.0597, found m/z 263.0601.

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2-[4-(Trifluoromethyl)phenyl]-4H-pyrido[1,2-a]pyrimidin-4-one[10] ***(7o)***. Crystal white solid: 131 mg, 90%; mp 196−198 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (dd, J = 6.1 Hz, J = 0.9 Hz, 1H), 8.20 (d, J = 8.1 Hz, 2H), 7.81−7.74 (m, 4H), 7.18 (ddd, J = 6.4 Hz, J = 1.8 Hz, J = 0.8 Hz, 1H), 6.93 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.3, 158.4, 151.1, 140.6, 136.5, 132.1 (q, J_{C-C-F} = 32 Hz), 127.7, 127.3, 126.8, 125.6 (q, $J_{C-C-C-F}$ = 4 Hz), 123.9 (q, J_{C-F} = 271 Hz), 115.6, 100.6; IR ν_{max} 3055, 1692, 1637, 1107 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_9F_3N_2ONa$ $[M + Na]^+$ m/z 313.0565, found m/z 313.0561.

2-[4-(Trifluoromethoxy)phenyl]-4H-pyrido[1,2-a]pyrimidin-4-one ***(7p)***. Crystal white solid: 125 mg, 82%; mp 152−154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (d, J = 7.1 Hz, 1H), 8.14 (d, J = 8.8 Hz, 2H), 7.80−7.72 (m, 2H), 7.34 (d, J = 8.8 Hz, 2H), 7.16 (dt, J = 7.1 Hz, J = 1.7 Hz, 1H), 6.88 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.6, 158.5, 151.0 (dd, $J_{C-O-C-F}$ = 8 Hz, $J_{C-O-C-F}$ = 2 Hz), 136.4, 135.8, 129.1, 127.3, 126.8, 120.9, 120.2 (q, J_{C-F} = 270 Hz), 115.4, 100.0; IR ν_{max} 3081, 1683, 1633, 1250, 1209, 1144 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_9F_3N_2O_2Na$ $[M + Na]^+$ m/z 329.0514, found m/z 329.0520.

2-(Pyridin-4-yl)-4H-pyrido[1,2-a]pyrimidin-4-one[10] ***(7q)***. Off-white solid: 100 mg, 90%; mp 212−214 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.10 (d, J = 7.1 Hz, 1H), 8.78 (d, J = 5.7 Hz, 2H), 7.95 (dd, J = 4.6 Hz, J = 1.5 Hz, 2H), 7.84−7.80 (m, 1H), 7.78 (d, J = 8.1 Hz, 1H), 7.21 (dt, J = 7.2 Hz, J = 1.6 Hz, 1H), 6.96 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.4, 158.5, 151.3, 150.6, 144.6, 136.7, 127.4, 126.9, 121.3, 115.9, 100.9; IR ν_{max} 3119, 1697, 1630 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{10}N_3O$ $[M + H]^+$ m/z 224.0824, found m/z 224.0821.

2-(Furan-3-yl)-4H-pyrido[1,2-a]pyrimidin-4-one ***(7r)***. Cream solid: 91 mg, 86%; mp 130−132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (dd, J = 6.6 Hz, J = 0.4 Hz, 1H), 8.16 (dd, J = 1.4 Hz, J = 0.8 Hz, 1H), 7.74−7.70 (m, 1H), 7.63 (td, J = 8.9 Hz, J = 0.9 Hz, 1H), 7.52 (t, J = 1.7 Hz, 1H), 7.10 (dt, J = 7 Hz, J = 1.4 Hz, 1H), 6.87 (dd, J = 1.8 Hz, J = 0.8 Hz, 1H), 6.61 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.4, 156.7, 151.3, 144.3, 143.8, 136.2, 127.3, 126.3, 125.7, 114.9, 108.5, 99.4; IR ν_{max} 2916, 1676, 1628, 1442, 1115 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_8N_2O_2Na$ $[M + Na]^+$ m/z 235.0484, found m/z 235.0470.

(E)-2-Styryl-4H-pyrido[1,2-a]pyrimidin-4-one ***(7s)***. Light yellow solid: 109 mg, 88%; mp 139−141 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (d, J = 7.0 Hz, 1H), 7.88 (d, J = 15.8 Hz, 1H), 7.71 (dt, J = 6.6 Hz, J = 1.4 Hz, 1H), 7.66−7.61 (m, 3H), 7.42−7.33 (m, 3H), 7.07 (dt, J = 7.2 Hz, J = 1.4 Hz, 1H), 7.02 (d, J = 15.8 Hz, 2H), 6.49 (s, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.1, 158.5, 150.9, 137.3, 136.2, 135.8, 129.3, 128.8, 127.7, 127.3, 126.33, 126.28, 114.7, 102.4; IR ν_{max} 3081, 1683, 1633, 1607 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{12}N_2ONa$ $[M + Na]^+$ m/z 271.0848, found m/z 271.0852.

Spectral Data for Intermediates 7c1 and 11a1. *7-Phenyl-2-(4-methylbenzenesulfonyloxy)-4H-pyrido[1,2-a]pyrimidin-4-one* ***(7c1)***. Yellow solid: 161 mg, 82%; mp >200 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.24 (d, J = 2.0 Hz, 1H), 8.10 (dd, J = 9.1 Hz, J = 2.2 Hz, 1H), 7.99 (d, J = 8.4 Hz, 2H), 7.66−7.62 (m, 3H), 7.54−7.47 (m, 3H), 7.38 (d, J = 8.2 Hz, 2H), 6.13 (s, 1H), 2.47 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.8, 159.2, 149.3, 145.8, 138.0, 134.9, 133.6, 130.5, 129.8, 129.5, 129.2, 128.8, 126.9, 125.9, 124.8, 91.6, 21.8; IR ν_{max} 1704, 1637, 1371, 1165 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{17}N_2O_4S$ $[M + H]^+$ m/z 393.0909, found m/z 393.0902.

(E)-Ethyl 3-(Tosyloxy)but-2-enoate[54] ***(11a1)***. Colorless oil: 122 mg, 86%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.4 Hz, 2H), 7.37 (d, J = 8.0 Hz, 2H), 5.71 (q, J = 0.9 Hz, 1H), 4.14 (q, J = 9.1 Hz, 2H), 2.47 (s, 3H), 2.27 (d, J = 0.9 Hz, 3H), 1.26 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.4, 162.3, 145.7, 132.9, 130.0, 128.2, 111.0, 60.5, 21.7, 18.6, 14.1; IR ν_{max} 2926, 1717, 1657, 1367, 1177 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{16}O_5SNa$ $[M + Na]^+$ m/z 307.0616, found m/z 307.0615.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Scanned ^{1}H and ^{13}C NMR spectra for products **7a−11b**. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00771.

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Notes

The authors declare no competing financial interest.

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