JOC The Journal of Organic Chemistry

ARTICLE

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Chemistry of Heterocyclic Ketene Aminals: Construction of Imidazo(pyrido)[1,2-*a*]pyridines and Imidazo(pyrido)[3,2,1-*ij*][1,8]-naphthyridines via DABCO-Catalyzed Tandem Annulations

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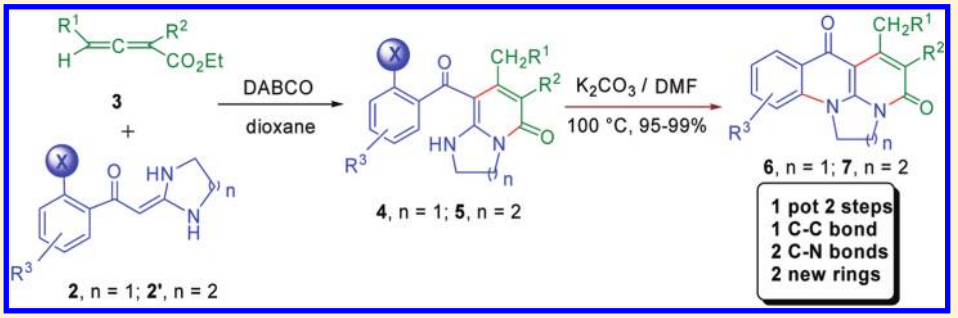
Supporting Information

ABSTRACT:



2-(2-Chloroaroyl)methyleneimidazolidines with four reactive sites show fascinating structural features and could be used as a new strategy for the synthesis of novel heterocycles. This paper presents our new findings in the reaction of 2-(2-chloroaroyl) methyleneimidazolidines with allenic esters affording functionalized imidazo(pyrido)[1,2-*a*]pyridines via DABCO-catalyzed tandem annulations. Of particular significance is the incorporation of an *o*-halo group into the aryl ring of 2-benzoylmethylene-imidazolidines to set up a convenient and general way for constructing unusual imidazo(pyrido)[3,2,1-*ij*][1,8]naphthyridines.

INTRODUCTION

Polarized *N*,*N*-acetals[1] **1** have been proven to be important synthons in the construction of heterocyclic systems. Reactions of cyclic ketene aminals of the general formula **1** with a variety of biselectrophilic reagents have so far been applied to make five- and six-membered and fused heterocycles during the past years (Figure 1).[2]

2-(2-Chloroaroyl)methyleneimidazolidines **2**, as novel heterocyclic ketene aminals (HKAs) with four reactive sites, show fascinating structural features of a highly polarized push−pull interaction C═C double bond and a Cl atom as leaving group (Figure 2). Since both α carbon and one secondary amino group can take part in the reaction with electrophiles and another *ortho* C−Cl would be subject to S_NAr reaction by attack of another nitrogen atom, the precursors **2** display a different reactivity profile in relation to that of **1** and could be applied to the construction of novel heterocycles.

Meanwhile, allenes, which are endowed with features by the presence of the cumulated diene structural unit, show unique reactivity in organic synthesis. Over the past decade, chemical transformations involving electron-deficient allenes have attracted much research interest, with a number of new allene-based reactions with high synthetic potentials having emerged.[3−6] Some of them have also been utilized in the syntheses of natural or biological important compounds.[7]

Bicyclic pyridone motifs **I** (Figure 3) are of general interest within medicinal chemistry with therapeutic properties, and a series of substituted variants of **I** ($n = 1, 2$) have been reported as a basis for analgesics and anti-inflammatory agents.[8] In an early study, Huang[2d] demonstrated a useful approach for bicyclic pyridones via aza−ene reaction of heterocyclic ketene aminals with ethyl propiolate. Recently, Lin[2i] reported a novel reaction involving HKAs with β-ketoester enol tosylates to synthesize bicyclic pyridones. These approaches represent an important advance toward the objective of a general method for the synthesis of motif **I**. Although much progress has been achieved in synthesis of motif **I**, the preparation of some specific substituted patterns remains difficult. It is of great importance to explore novel and efficient synthetic methods in order to meet the increasing scientific and practical demands.

So far, to the best of our knowledge, there have been no reports on the synthetic application of HKAs with allenic esters to synthesize imidazo(pyrido)[1,2-*a*]pyridines. On the basis of the above considerations and in the context of our efforts on developing strategies toward heterocycles,[9] herein we wish to present our new findings in the reactions of novel HKAs **2** with allenic esters **3** affording functionalized imidazo(pyrido)[1,2-*a*]pyridines via DABCO-catalyzed tandem annulations. Of particular significance is the

Received: October 31, 2010
Published: March 30, 2011

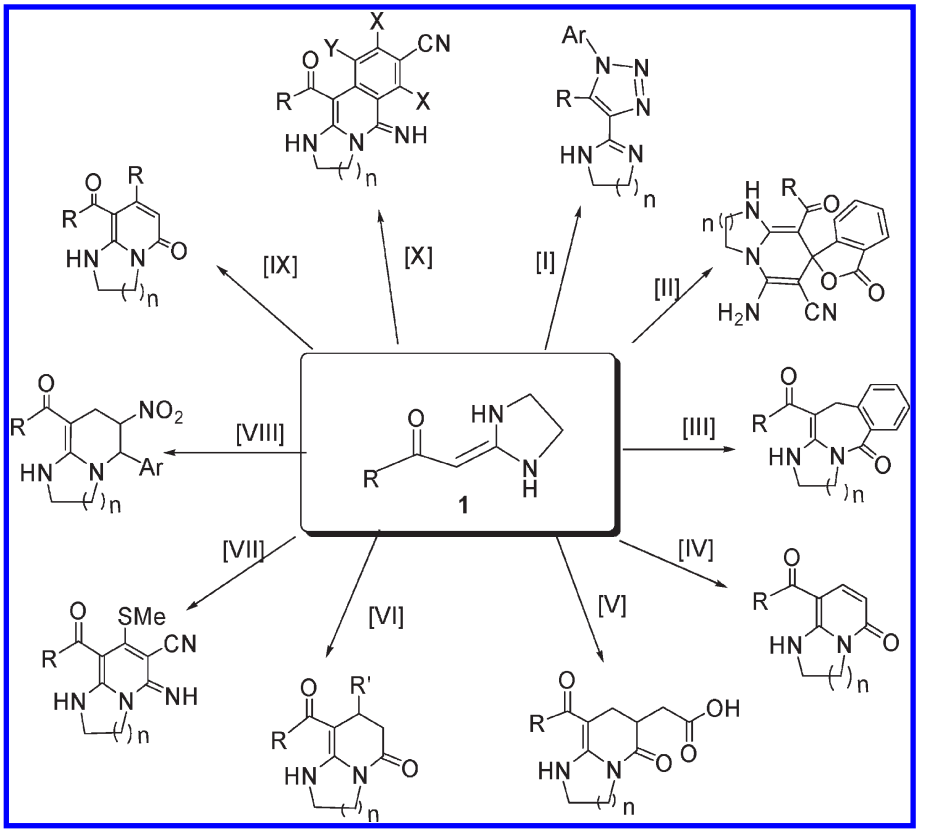


Figure 1. Reactions of HKAs with biselectrophilics. [I] aryl azides;[2a] [II] 2-[3-oxoisobenzofuran-1(3*H*)-ylidene]malononitrile;[2b] [III] ethyl 2-(bromomethyl)benzoate;[2c] [IV] propiolic acid ester;[2d] [V] itaconic anhydride;[2e] [VI] Meldrum's acid and aldehydes;[2f] [VII] bis-(methylthio)methylene malononitrile;[2g] [VIII] Baylis−Hillman acetates;[2h] [IX] polyhalo isophthalonitrile;[2i] [X] *β*-keto ester enol tosylates.[2j]

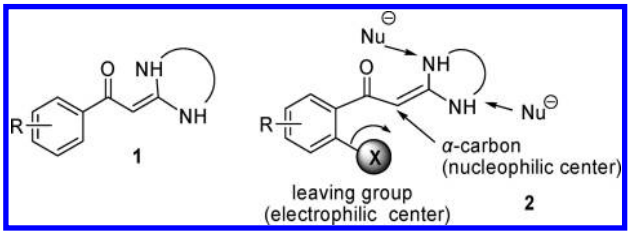


Figure 2. Functionalized heterocyclic ketene aminals (HKAs).

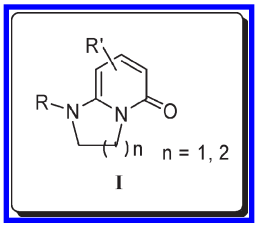


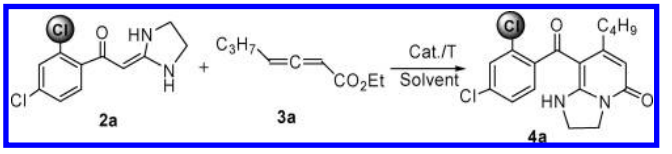
Figure 3. Bicyclic pyridone motifs **I**.

successful incorporation of an *o*-halo group into the aryl ring of HKAs **1** to construct unusual imidazo(pyrido)[3,2,1-*ij*][1,8]naphthyridines.

RESULTS AND DISCUSSION

Initially, we focused our efforts on searching for potential catalysts and suitable reaction conditions by using the reaction of 1-(2,4-dichlorophenyl)-2-(imidazolidin-2-ylidene)ethanone **2a** with ethyl hepta-2,3-dienoate **3a** as a model. First, we examined the reaction in the presence of 20 mmol % of Et_3N, the compound 7-butyl-8-(2,4-dichlorobenzoyl)-2,3-dihydroimidazo[1,2-*a*]pyridin-5(1*H*)-one **4a** was obtained after stirring in refluxing CH_3CN (Table 1, entry 1).

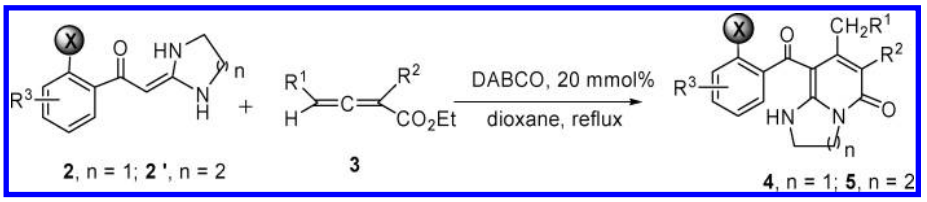
Table 1. Optimization of Reaction Conditions

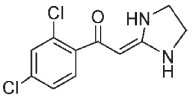
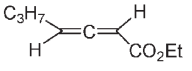
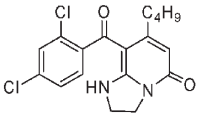
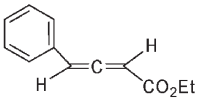
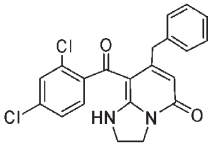
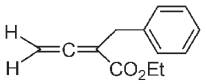
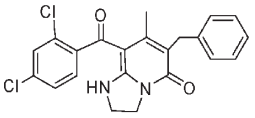
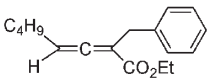
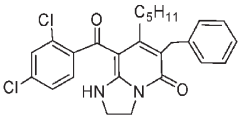
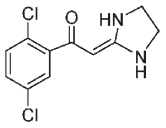
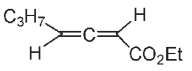
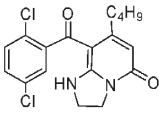
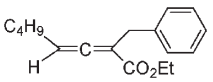
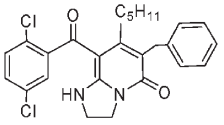
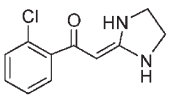
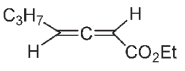
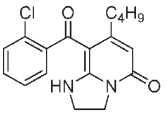
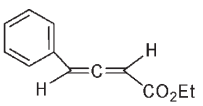
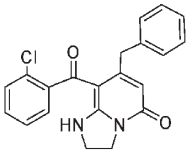
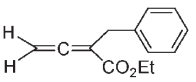
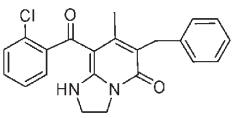


entry	catalyst (mmol %)	solvent	temp (°C)	isolated yield (%)
1	Et_3N (20)	CH_3CN	reflux	64
2	Et_3N (50)	CH_3CN	reflux	42
3	Et_3N (100)	CH_3CN	reflux	31
4		CH_3CN	reflux	15
5	NaH (100)	THF	reflux	21
6	NaH (100)	DMF	100	no reaction
7	DABCO (20)	CH_3CN	reflux	77
8	DMAP (20)	CH_3CN	reflux	70
9	Ph_3P (20)	CH_3CN	reflux	48
10	DABCO (20)	dioxane	reflux	88
11	DABCO (20)	C_2H_5OH	reflux	82
12	DABCO (50)	dioxane	reflux	83

dx.doi.org/10.1021/jo102167g |*J. Org. Chem.* 2011, 76, 3054–3063

Table 2. DABCO-Catalyzed Formation of Imidazo(pyrido)[1,2-*a*]pyridine Derivatives



Entry	Precursor **2/2′**	Precursor **3**	Product **4/5**	Yield (%)[a]
1	 **2a**	 **3a**	 **4a**	88
2	**2a**	 **3b**	 **4b**	78
3	**2a**	 **3c**	 **4c**	85
4	**2a**	 **3d**	 **4d**	65
5	 **2b**	 **3a**	 **4e**	84
6	**2b**	 **3d**	 **4f**	75
7	 **2c**	 **3a**	 **4g**	90
8	**2c**	 **3b**	 **4h**	71
9	**2c**	 **3c**	 **4i**	87

dx.doi.org/10.1021/jo102167g |*J. Org. Chem.* 2011, 76, 3054–3063

Table 2. Continued

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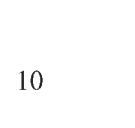
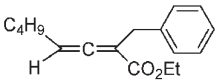
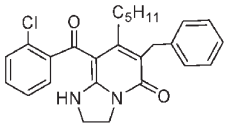
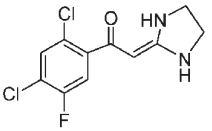
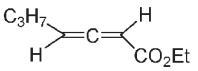
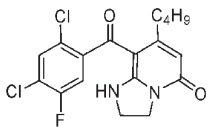
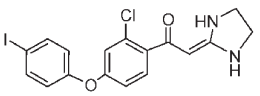
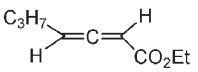
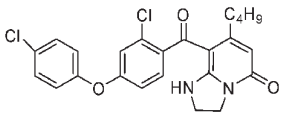
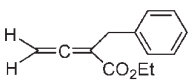
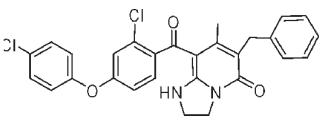
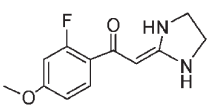
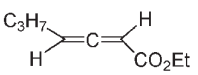
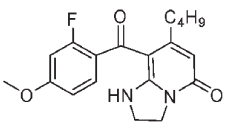
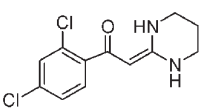
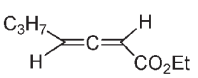
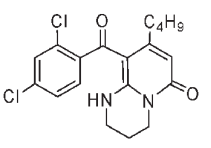
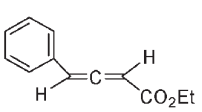
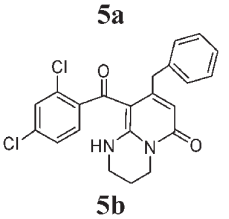
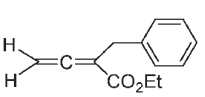
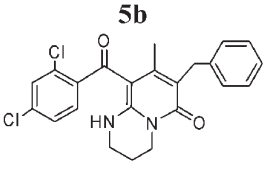
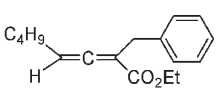
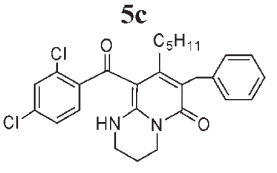
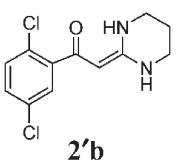
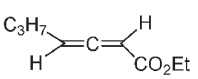
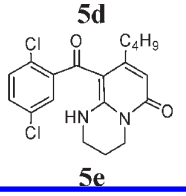
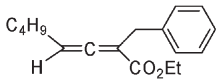
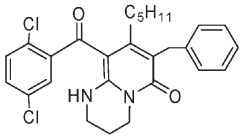
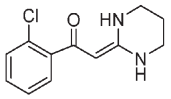
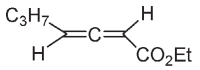
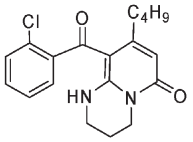
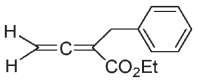
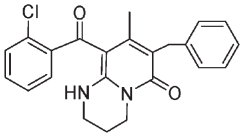
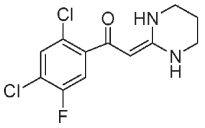
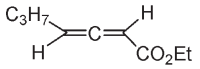
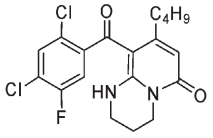
10	 **2c**	 **3d**	 **4j**	71
11	 **2d**	 **3a**	 **4k**	81
12	 **2e**	 **3a**	 **4l**	76
13	**2e**	 **3c**	 **4m**	82
14	 **2f**	 **3a**	 **4n**	69
15	 **2′a**	 **3a**	 **5a**	51
16	**2′a**	 **3b**	 **5b**	84
17	**2′a**	 **3c**	 **5c**	80
18	**2′a**	 **3d**	 **5d**	45
19	 **2′b**	 **3a**	 **5e**	49

dx.doi.org/10.1021/jo102167g |*J. Org. Chem.* 2011, 76, 3054–3063

Table 2. Continued

Entry	Precursor **2′/2′**	Precursor **3**	Product **4/5**	Yield (%)[a]
20	**2′b**	 **3d**	 **5f**	33
21	 **2′c**	 **3a**	 **5g**	70
22	**2′c**	 **3c**	 **5h**	79
23	 **2′d**	 **3a**	 **5i**	77

[a] Yield of isolated product.

Next, other attempts were also made. For example, we tried adding 50 mmol % Et_3N and adding 100 mmol % Et_3N and also tried without Et_3N (Table 1, entries 2−4). However, the yields of product **4a** were not satisfactory. Then, we used other various bases, including 100 mmol % NaH, 20 mmol % 1,4-diazabicyclo-(2.2.2)octane (DABCO), 20 mmol % DMAP, and 20 mmol % Lewis base Ph_3P, in a variety of solvents (Table 1, entries 5−11). To our delight, a break-through result was obtained when 20 mmol % DABCO was added to a solution of **3a** and **2a** in dioxane (Table 1, entry 10), in which **4a** was formed in good yield of 88%. Then we tried increasing the amount of DABCO to 50 mmol % but could not get a better yield of the desired product **4a** (Table 1, entry 12). So the optimum reaction conditions were dioxane as the solvent and 20 mmol % DABCO as the base (Table 1, entry 10). Compared to other bases, DABCO has been regarded as an unhindered and nucleophilic base and considered one of the best amine catalysts due to its unique properties.[10−13]

Next this methodology was also extended for the synthesis of pyrido[1,2-*a*]pyridines following a similar sequence by subjecting 1-(2,4-dichlorophenyl)-2-(tetrahydro pyrimidin-2(1*H*)-ylidene)-ethanone **2′a** to Michael addition/imine−enamine tautomerization with ethyl hepta-2,3-dienoate **3a** under identical conditions to give 8-butyl-9-(2,4-dichlorobenzoyl)-1,2,3,4-tetrahydropyrido-[1,2-*a*]pyrimidin-6-one **5a**.

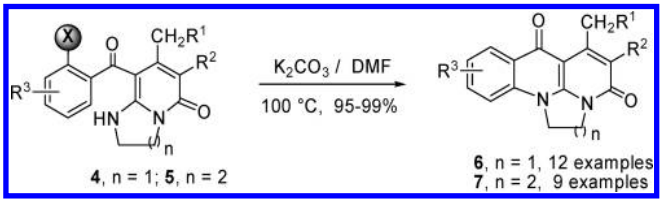
With the optimized conditions in hand, we explored the scope of this reaction, and these results are shown in Table 2. The reactions of **2/2′** with **3** proceeded smoothly to afford imidazo(pyrido)-[1,2-*a*]pyridine derivatives **4/5** in moderate to good yields. As can be seen from Table 2, there may be three factors influencing the yields of **4/5**: (1) the size of the substituents on allenic esters; the allenic esters with relatively smaller substituents often give higher yields, for example, **3a** or **3c** gave higher yields than **3b** or **3d**, respectively (Table 2, entries 1−4 and 7−10); (2) the size of heterocycles of heterocyclic ketene aminals; generally, five-membered HKAs often give higher yields than six-membered ones, for example, the reactions of **2a** or **2b** with **3d** gave 65% or 75%, respectively, whereas **2′a** or **2′b** produced yields of only 45% or 33% (Table 2, entries 4 and 18, entries 6 and 20); (3) the substituents on the aryl ring of HKA; the effects of various substituents on the aryl rings of HKAs used in our experiments on the reaction yields did not show obvious regularities.

The structural determination of all products was achieved by their ^1H NMR, ^{13}C NMR, IR ,and HRMS spectroscopic data, which are in agreement with the proposed structures, and unequivocally confirmed by X-ray diffraction analysis of product **4a** (see Supporting Information).

Functionalized naphthyridines represent an important class of organic molecules that attract the interest of both synthetic and medicinal chemists. More than 1000 patents were located claiming potential pharmaceutical applications.[11] Therefore, the synthesis of imidazo(pyrido)[3,2,1-*ij*][1,8]naphthyridines may be of great significance.

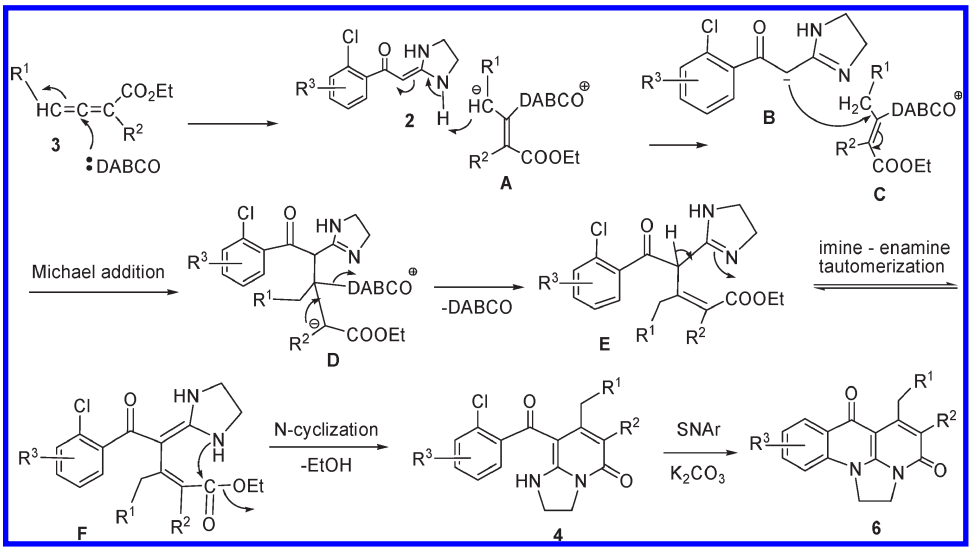
Our studies highlighted the concept of a substrate-design approach to the development of novel tandem reactions. As a result of incorporating an *o*-halo group into the aryl ring in the

Scheme 1. Synthesis of Imidazo(pyrido)[3,2,1-*ij*]-[1,8]naphthyridines 6/7 from 4/5



dx.doi.org/10.1021/jo102167g |*J. Org. Chem.* 2011, 76, 3054–3063

Scheme 2. Plausible Reaction Mechanism (e.g., Products 6)



HKA motif of **4**/**5**, we reasoned the subsequent intramolecular S_NAr reaction could occur *ortho*-selectively to form new fused imidazo(pyrido)[3,2,1-*ij*][1,8]naphthyridines **6**/**7**. So we directly explored the reactions of all of **4**/**5** in the presence of K_2CO_3 (1.0 equiv) in DMF at 100 °C for about 6 h monitored by TLC. To our surprise, except **4b** and **4c**, all other **4**/**5** gave the corresponding imidazo(pyrido)[3,2,1-*ij*][1,8]naphthyridines **6**/**7** in almost quantitative yields of 95−99% (Scheme 1). For that, we carefully examined the intramolecular S_NAr reactions of **4b** and **4c** in the presence of various other basic catalysts such as Na_2CO_3, NaOH, and NaH. However, we found that in all cases they could not react at all without any reasons for explanation.

The structures of all products **6**/**7** were characterized by IR, ^1H, ^{13}C NMR, HRMS spectroscopy and further confirmed by X-ray diffraction analysis of product **6g** (see the Supporting Information).

It is worthwhile to point out that the synthesis of imidazo(pyrido)[3,2,1-*ij*][1,8] naphthyridines has been scarcely reported with only two similar examples in the literatures.[1,14] Obviously, our novel strategy provides a more general and facile route to synthesize this type of compounds.

On the basis of the above results, a plausible mechanism for this reaction is proposed as shown in Scheme 2. Take products **6**, for example. Initially DABCO as a nucleophilic trigger reacts with allenic esters **3** to generate the zwitterionic intermediates **A**,[15] which abstracts a proton from **2** to produce **C**. Subsequent Michael addition of **B** to **C** gives another zwitterions **D**. The elimination of DABCO from **D** affords **E**. Then, the intermediates **E** undergo a rapid imine−enamine tautomerization to give **F**, and intramolecular cyclization of **F** leads to the formation of dihydroimidazo[1,2-*a*]pyridine(1*H*)-ones **4**. Finally, an intramolecular S_NAr of the *o*-chloro of aryl group by attack of NH group generates imidazo[3,2,1-*ij*][1,8]naphthyridine derivatives **6** with elimination of HCl.

CONCLUSION

In summary, this study highlighted the concept of a substrate-design approach to the development of novel tandem reactions by incorporating an *o*-halo group into the aryl ring of heterocyclic ketene aminals. A novel DABCO-catalyzed tandem annulation between 2-(2-chloroaroyl)methyleneimidazo(pyrido)lidines and allenic esters has been demonstrated, which opens the efficient and flexible way to synthesis of imidazo(pyrido)[1,2-*a*]pyridine and imidazo(pyrido)[3,2,1-*ij*][1,8]naphthyridine derivatives. On the basis of the experimental results in this domino reaction, nine reactive sites are involved; one C−C bond, two C−N bonds, and two new rings are constructed with all reactants efficiently utilized in the chemical transformation. A possible mechanism involving the ring-closure cascade reactions, including formation of zwitterion, Michael addition, intramolecular imine−enamine tautomerization, followed by cyclocondensation and intramolecular S_NAr, is represented. Further investigations to expand the scope of the diversity-oriented synthesis of 2-(2-chloroaroyl)methyleneimidazolidines as versatile building blocks are in progress and will be reported.

EXPERIMENTAL SECTION

General Procedure for the Preparation of Products 4 or 5 (e.g., 4a). DABCO (0.092 g, 0.4 mmol) was added to a solution of ethyl hepta-2,3-dienoate **3a** (0.370 g, 2.4 mmol) and 1-(2,4-dichloro-phenyl)-2-(imidazolidin-2-ylidene)ethanone **2a** (0.514 g, 2.0 mmol) in 1,4-dioxene (30 mL). Then the mixture was heated at reflux for about 20 h. After the completion of the reaction as indicated by TLC (petroleum ether−EtOAc, 1:2, v/v) and cooling to room temperature, the solvent was removed in vacuum, and the residue was purified by the column chromatography to afford pure compound **4a.**

General Procedure for Synthesis of Products 6 or 7 (e.g., 6a). A mixture of corresponding **4a** (0.365 g, 1.0 mmol) and K_2CO_3 (0.138 g, 1.0 mmol) was heated to 100 °C in DMF (15 mL). After the completion of the reaction as indicated by TLC (petroleum ether−EtOAc, 1:4, v/v) at about 6 h, the mixture was cooled to room temperature. An amount of ice−water was added to precipitate the product, which was then filtered and washed with small amount of ethanol to give the pure product **6a**.

7-Butyl-8-(2,4-dichlorobenzoyl)-2,3-dihydroimidazo[1,2-a]pyridin-5(1H)-one (***4a***). Light yellow solid; mp 172−174 °C; IR (KBr, cm^{-1}) 1663, 1602, 1558, 825; ^1H NMR ($CDCl_3$) δ 9.01 (s,1H), 7.21−7.44 (m, 3H), 5.69 (s, 1H), 4.25 (t, J = 9.0 Hz, 2H), 3.98 (t, J = 9.0 Hz, 2H), 1.95 (s, w, 2H), 1.27 (s, w, 2H), 0.93−1.00 (m, 2H), 0.72 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 189.8, 160.8, 158.2, 156.2, 140.2, 135.8, 131.6, 129.9, 129.2, 127.2, 108.6, 98.4, 43.2, 42.7, 34.4, 32.1, 22.4, 13.5;

dx.doi.org/10.1021/jo102167g |*J. Org. Chem.* 2011, 76, 3054–3063

HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{18}H_{19}N_2O_2Cl_2$, 365.0824, found 365.0806.

*10-Chloro-benzo-1,2-dihydroimidazo[3,2,1-ij][1,8]naphthyridine-6-butyl-4,7-dione (**6a**).* White solid; mp 220−222 °C; IR (KBr, cm^{-1}) 1671, 1633, 1605, 1575, 1534, 949, 883, 833, 773; ^1H NMR ($CDCl_3$) δ 8.30 (d, J = 8.5 Hz, 1H), 7.11−7.31 (m, 2H), 6.05 (s, 1H), 4.48−4.55 (m, 4H), 3.11 (t, J = 7.5 Hz, 2H), 1.57−1.63 (m, 2H), 1.42−1.50 (m, 2H), 0.96 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 174.0, 160.1, 157.6, 149.0, 139.2, 136.9, 129.4, 124.0, 123.3, 113.6, 113.4, 100.8, 44.6, 43.1, 34.2, 31.7, 22.5, 13.9; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{18}H_{18}N_2O_2Cl$, 329.1057, found 329.1056.

*7-Benzyl-8-(2,4-dichlorobenzoyl)-2,3-dihydroimidazo[1,2-a]pyridin-5(1H)-one (**4b**).* Light yellow solid; mp 185−186 °C; IR (KBr, cm^{-1}) 1669, 1594, 1567, 978, 828, 782, 731; ^1H NMR ($CDCl_3$) δ 9.14 (s, 1H), 6.81−7.45 (m, 8H), 5.49 (s, 1H), 4.26 (t, J = 9.0 Hz, 2H), 3.99 (t, J = 9.0 Hz, 2H), 3.37 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 192.1, 163.0, 160.8, 155.9, 142.7, 140.1, 138.3, 133.8, 132.2, 131.6, 131.2, 130.9, 129.7, 129.1, 113.3, 101.2, 45.6, 45.2, 42.9; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{21}H_{17}N_2O_2Cl_2$, 365.0667, found 365. 0658.

*6-Benzyl-8-(2,4-dichlorobenzoyl)-7-methyl-2,3-dihydroimidazo[1,2-a]pyridin-(1H)-one (**4c**).* White solid; mp 173−175 °C; IR (KBr, cm^{-1}) 1714, 1649, 1584, 1560, 990, 826, 781, 699; ^1H NMR ($CDCl_3$) δ 8.90 (s, 1H), 7.12−7.41 (m, 8H), 4.28 (t, J = 8.5 Hz, 2H), 3.95 (t, J = 8.5 Hz, 2H), 3.88 (s, 2H), 1.68 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 190.0, 160.8, 156.4, 147.3, 141.0, 140.3, 135.6, 131.3, 129.9, 129.0, 128.2, 128.0, 127.4, 125.7, 118.5, 99.6, 43.7, 42.4, 31.6, 19.4; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{22}H_{19}N_2O_2Cl_2$, 413.0824, found 413.0834.

*6-Benzyl-8-(2,4-dichlorobenzoyl)-7-pentyl-2,3-dihydroimidazo[1,2-a]pyridin-5(1H)-one (**4d**).* White solid; mp 145−147 °C; IR (KBr, cm^{-1}) 1650, 1597, 1583, 1561, 826, 782, 728, 698; ^1H NMR ($CDCl_3$) δ 8.79 (s, 1H), 7.12−7.42 (m, 8H), 4.26 (t, J = 9.0 Hz, 2H), 3.90 (t, J = 9.0 Hz, 2H), 3.88 (s, 2H), 2.12 (s, w, 2H), 1.00−1.07 (m, 4H), 0.72−0.75 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 190.1, 161.2, 156.7, 152.3, 140.9, 140.1, 135.8, 131.7, 129.9, 129.4, 128.2, 128.0, 127.2, 125.7, 117.7, 98.3, 43.8, 42.4, 31.9, 31.5, 30.9, 30.1, 22.3, 13.9; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{26}H_{27}N_2O_2Cl_2$, 469.1450, found 469.1439.

*10-Chloro-benzo-1,2-dihydroimidazo[3,2,1-ij][1,8]naphthyridine-5-benzyl-6-pentyl-4,7-dione (**6d**).* White solid; mp 264−266 °C; IR (KBr, cm^{-1}) 1651, 1634, 1607, 1568, 1540, 840, 788, 741, 699; ^1H NMR ($CDCl_3$) δ 8.32 (d, J = 8.5 Hz, 1H), 7.09−7.28 (m, 7H), 4.54 (t, J = 8.5 Hz, 2H), 4.43 (t, J = 8.5 Hz, 2H), 4.01 (s, 2H), 3.26 (s, w, 2H), 1.42−1.45 (m, 4H), 1.28−1.35 (m, 2H), 0.88 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 174.1, 160.6, 153.7, 147.7, 140.4, 138.9, 136.8, 129.8, 128.3, 128.2, 125.9, 123.8, 123.5, 113.2, 100.8, 44.3, 43.6, 32.4, 31.2, 30.7, 29.7, 22.6, 14.1; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{26}H_{26}N_2O_2Cl$, 433.1683, found 433.1693.

*7-Butyl-8-(2,5-dichlorobenzoyl)-2,3-dihydroimidazo[1,2-a]pyridin-5(1H)-one (**4e**).* Light yellow solid; mp 139−141 °C; IR (KBr, cm^{-1}) 1668, 1602, 1545, 979, 809; ^1H NMR ($CDCl_3$) δ 9.08 (s, 1H), 7.33−7.43 (m, 3H), 5.75 (s, 1H), 4.26 (t, J = 8.5 Hz, 2H), 4.00 (t, J = 8.5 Hz, 2H), 1.95 (s, w, 2H), 1.29 (s, w, 2H), 0.95 (s, w, 2H), 0.73 (t, J = 4.5 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 188.9, 160.6, 158.3, 156.1, 143.0, 132.9, 131.1, 130.2, 128.8, 128.0, 108.5, 98.1, 43.1, 42.6, 34.2, 32.1, 22.4, 13.5; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{18}H_{19}N_2O_2Cl_2$, 365.0824, found 365.0833.

*9-Chloro-benzo-1,2-dihydroimidazo[3,2,1-ij][1,8]naphthyridine-6-butyl-4,7-dione (**6e**).* White solid; mp 237−239 °C; IR (KBr, cm^{-1}) 1663, 1635, 1578, 1542, 1509, 836; ^1H NMR ($CDCl_3$) δ 8.32 (s, 1H), 7.58 (d, J = 7.5 Hz, 1H), 7.07 (d, J = 7.5 Hz, 1H), 6.07 (s, 1H), 4.55 (s, 4H), 3.11 (t, J = 7.5 Hz, 2H), 1.57−1.63 (m, 2H), 1.46−1.49 (m, 2H), 0.97 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 173.5, 160.2, 157.8, 148.9, 134.6, 132.9, 129.6, 127.5, 125.9, 115.1, 113.6, 100.8, 44.8, 43.3, 34.3, 31.8, 22.5, 13.9; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{18}H_{18}N_2O_2Cl$, 329.1057, found 329.1042.

*6-Benzyl-8-(2,5-dichlorobenzoyl)-7-pentyl-2,3-dihydroimidazo[1,2-a]pyridin-5(1H)-one (**4f**).* Yellow solid; mp 139−141 °C; IR (KBr, cm^{-1}) 1646, 1594, 1558, 814, 784, 696; ^1H NMR ($CDCl_3$) δ 8.86 (s, 1H), 7.12−7.31 (m, 8H), 4.28 (t, J = 8.0 Hz, 2H), 3.95 (t, J = 8.0 Hz, 2H), 3.89 (s, 2H), 2.12 (s, w, 2H), 1.01−1.09 (s, w, 4H), 0.72−0.75 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 189.4, 161.1, 156.8, 152.2, 142.9, 140.7, 132.9, 131.0, 130.2, 128.9, 128.2, 128.2, 127.9, 125.7, 117.6, 98.1, 43.8, 42.4, 31.9, 31.4, 30.8, 30.2, 22.3, 13.8; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{26}H_{27}N_2O_2Cl_2$, 469.1450, found 469.1434.

*9-Chloro-benzo-1,2-dihydroimidazo[3,2,1-ij][1,8]naphthyridine-5-benzyl-6-pentyl-4,7-dione (**6f**).* White solid; mp 177−179 °C; IR (KBr, cm^{-1}) 1652, 1630, 1594, 1569, 1542, 1509, 806, 748, 696; ^1H NMR ($CDCl_3$) δ 8.37 (d, J = 14.0 Hz, 1H), 7.04−7.56 (m, 7H), 4.47−4.56 (m, 4H), 4.02 (s, 2H), 3.27 (s, w, 2H), 1.44 (s, w, 4H), 1.31−1.34 (m, 2H), 0.88 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 173.8, 161.0, 153.9, 147.9, 140.8, 134.7, 133.0, 129.6, 128.6, 128.5, 127.9, 126.4, 126.3, 123.8, 115.2, 101.0, 44.8, 44.0, 32.7, 31.5, 31.0, 30.0, 22.9, 14.4; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{26}H_{26}N_2O_2Cl$, 433.1683, found 433.1680.

*7-Butyl-8-(2-chlorobenzoyl)-2,3-dihydroimidazo[1,2-a]pyridin-5(1H)-one (**4g**).* Light yellow solid; mp 138−140 °C; IR (KBr, cm^{-1}) 1663, 1602, 1561, 1550, 762; ^1H NMR ($CDCl_3$) δ 9.07 (s, 1H), 7.25−7.41 (m, 4H), 5.67 (s, 1H), 4.23 (t, J = 8.5 Hz, 2H), 3.96 (t, J = 8.5 Hz, 2H), 1.91 (s, w, 2H), 1.25 (s, w, 2H), 0.86−0.93 (m, 2H), 0.68 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 191.0, 160.8, 158.2, 156.6, 141.8, 130.5, 130.0, 128.2, 126.8, 108.3, 98.5, 43.1, 42.6, 34.3, 32.1, 22.4, 13.5; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{18}H_{20}N_2O_2Cl$, 331.1213, found 331.1220.

*Benzo-1,2-dihydroimidazo[3,2,1-ij][1,8]naphthyridine-6-butyl-4,7-dione (**6g**).* White solid; mp 224−226 °C; IR (KBr, cm^{-1}) 1668, 1622, 1575, 1545, 1509, 754; ^1H NMR ($CDCl_3$) δ 8.36 (dd, J_1 = 7.0 Hz, J_2 = 1.0 Hz, 1H), 7.07−7.64 (m, 3H), 6.00 (s, 1H), 4.49 (s, 4H), 3.11 (t, J = 7.5 Hz, 2H), 1.57−1.63 (m, 2H), 1.42−1.49 (m, 2H), 0.95 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 174.8, 160.3, 157.8, 148.8, 136.1, 132.8, 127.6, 124.8, 123.4, 113.5, 113.2, 100.7, 44.5, 43.1, 34.3, 31.8, 22.5, 14.0; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{18}H_{19}N_2O_2$, 295.1447, found 295.1454.

*7-Benzyl-8-(2-chlorobenzoyl)-2,3-dihydroimidazo[1,2-a]pyridin-5-(1H)-one (**4h**).* Yellow solid; mp 181−183 °C; IR (KBr, cm^{-1}) 1670, 1592, 1563, 979, 767, 744; ^1H NMR ($CDCl_3$) δ 9.16 (s, 1H), 6.81−7.38 (m, 9H), 5.45 (s, 1H), 4.25 (t, J = 9.0 Hz, 2H), 4.00 (t, J = 9.0 Hz, 2H), 3.32 (s, 2H); ^{13}C NMR ($CDCl_3$) δ 190.8, 160.6, 158.2, 154.2, 141.8, 137.8, 130.5, 130.3, 129.9, 129.0, 128.4, 128.1, 126.9, 126.5, 110.4, 98.9, 43.2, 42.7, 40.2; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{21}H_{18}N_2O_2Cl$, 365.1057, found 365.1068.

*Benzo-1,2-dihydroimidazo[3,2,1-ij][1,8]naphthyridine-6-benzyl-47-dione (**6h**).* White solid; mp 289−291 °C; IR (KBr, cm^{-1}) 1668, 1627, 1608, 1577, 1549, 760, 720; ^1H NMR ($CDCl_3$) δ 8.41 (d, J = 7.5 Hz, 1H), 7.09−7.68 (m, 8H), 5.93 (s, 1H), 4.61 (s, 2H), 4.51 (s, 4H); ^{13}C NMR ($CDCl_3$) δ 175.1, 160.2, 156.2, 148.8, 138.6, 136.2, 133.0, 129.5, 128.5, 128.0, 126.5, 124.9, 123.6, 114.4, 113.5, 100.6, 44.6, 43.2, 39.6; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{21}H_{17}N_2O_2$, 329.1290, found 329.1278.

*6-Benzyl-8-(2-chlorobenzoyl)-7-methyl-2,3-dihydromidazo[1,2-a]pyridin-5(1H)-one (**4i**).* Yellow solid; mp 190−192 °C; IR (KBr, cm^{-1}) 1647, 1597, 1567, 1544, 777, 749, 695; ^1H NMR ($CDCl_3$) δ 8.94 (s, 1H), 7.11−7.39 (m, 9H), 4.26 (t, J = 9.0 Hz, 2H), 3.92 (t, J = 9.0 Hz, 2H), 3.87 (s, 2H), 1.66 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 193.8, 163.4, 158.9, 150.3, 145.1, 142.9, 132.8, 132.5, 130.7, 130.5, 129.5, 128.2, 120.7, 102.3, 46.2, 44.9, 34.2, 21.7; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{22}H_{20}N_2O_2Cl$, 379.1213, found 379.1214.

*Benzo-1,2-dihydroimidazo[3,2,1-ij][1,8]naphthyridine-5-benzyl-6-methyl-4,7-dione (**6i**).* White solid; mp >300 °C; IR (KBr, cm^{-1}) 1652, 1629, 1609, 1574, 1551, 884, 764, 704; ^1H NMR ($CDCl_3$) δ 8.39 (d, J = 8.0 Hz, 1H), 7.10−7.62 (m, 8H), 4.48−4.58 (m, 4H), 4.03 (s, 2H), 1.61

(s, 3H); ^{13}C NMR ($CDCl_3$) δ 178.1, 162.9, 151.8, 149.7, 142.5, 138.6, 135.2, 130.8, 130.5, 128.4, 127.7, 126.2, 125.8, 115.7, 103.7, 46.8, 46.1, 33.9, 20.6; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{22}H_{19}N_2O_2$, 343.1447, found 343.1453.

*6-Benzyl-8-(2-chlorobenzoyl)-7-pentyl-2,3-dihydroimidazo[1,2-a]pyridin-5(1H)-one (**4j**).* White solid; mp 120−122 °C; IR (KBr, cm^{-1}) 1645, 1590, 1557, 761, 699; ^{1}H NMR ($CDCl_3$) δ 8.83 (s, 1H), 7.12−7.40 (m, 9H), 4.29 (t, J = 9.0 Hz, 2H), 3.95 (t, J = 9.0 Hz, 2H), 3.88 (s, 2H), 2.11 (s, w, 2H), 0.98−1.05 (m, 4H), 0.70−0.73 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 191.5, 161.2, 156.7, 152.8, 141.6, 140.9, 130.7, 130.4, 130.0, 128.4, 128.2, 128.0, 126.8, 125.7, 117.4, 98.5, 43.8, 42.4, 31.9, 31.5, 30.8, 30.1, 22.2, 13.9; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{26}H_{28}N_2O_2Cl$, 435.1839, found 435.1837.

*Benzo-1,2-dihydroimidazo[3,2,1-ij][1,8]naphthyridine-5-benzyl-6-pentyl-4,7-dione (**6j**).* White solid; mp 237−239 °C; IR (KBr, cm^{-1}) 1648, 1609, 1572, 1549, 758, 701; ^{1}H NMR ($CDCl_3$) δ 8.39 (d, J = 8.0 Hz, 1H), 7.05−7.55 (m, 8H), 4.42−4.53 (m, 4H), 4.02 (s, 2H), 3.29 (s, w, 2H), 1.46 (s, w, 4H), 1.29−1.37 (m, 2H), 0.89 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 174.9, 160.8, 153.9, 147.5, 140.6, 136.0, 132.6, 128.3, 128.2, 128.0, 125.9, 125.1, 123.2, 123.0, 113.2, 100.6, 44.2, 43.6, 32.4, 31.1, 30.7, 29.7, 22.6, 14.1; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{26}H_{27}N_2O_2$, 399.2073, found 399.2066.

*7-Butyl-8-(2,4-dichloro-5-fluorobenzoyl)-2,3-dihydroimidazo[1,2-a]pyridin-5(1H)-one (**4k**).* Light yellow solid; mp 169−171 °C; IR (KBr, cm^{-1}) 1663, 1594, 1561, 883; ^{1}H NMR ($CDCl_3$) δ 9.02 (s, 1H), 7.48 (d, J = 7.5 Hz, 1H), 7.09 (d, J = 7.5 Hz, 1H), 5.70 (s, 1H), 4.25 (t, J = 9.0 Hz, 2H), 3.99 (t, J = 9.0 Hz, 2H), 1.97 (s, w, 2H), 1.29 (s, w, 2H), 0.95−1.03 (m, 2H), 0.73 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 188.0, 160.6, 158.3, 155.8, 141.6, 131.6, 126.1, 123.0, 116.2, 116.1, 108.7, 98.0, 43.1, 42.7, 34.2, 32.0, 22.4, 13.5; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{18}H_{18}N_2O_2Cl_2F$, 383.0729, found 383.0712.

*9-Fluoro-10-chloro-benzo-1,2-dihydroimidazo[3,2,1-ij][1,8]naphthyridine-6-butyl-4,7-dione (**6k**).* White solid; mp 242−244 °C; IR (KBr, cm^{-1}) 1667, 1641, 1611, 1599, 1575, 1548, 1509, 846; ^{1}H NMR ($CDCl_3$) δ 8.10 (d, J = 7.5 Hz, 1H), 7.19 (d, J = 7.5 Hz, 1H), 6.06 (s, 1H), 4.48−4.56 (m, 4H), 3.09 (t, J = 7.5 Hz, 2H), 1.55−1.61 (m, 2H), 1.41−1.49 (m, 2H), 0.95 (t, J = 6.5 Hz, 3H) ; ^{13}C NMR ($CDCl_3$) δ 173.2, 160.1, 157.6, 155.6, 153.6, 149.1, 132.8, 127.1, 127.0, 124.8, 115.6, 114.8, 114.6, 113.8, 100.4, 44.9, 43.1, 34.2, 31.8, 22.5, 13.9; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{18}H_{17}N_2O_2ClF$, 347.0963, found 347.0967.

*7-Butyl-8-(2-chloro-4-(4-chlorophenoxy)benzoyl)-2,3-dihydroimidazo-[1,2-a]pyridin-5(1H)-one (**4l**).* Light yellow solid; mp 156−158 °C; IR (KBr, cm^{-1}) 1663, 1588, 1565, 1484, 830; ^{1}H NMR ($CDCl_3$) δ 8.94 (s, 1H), 6.89−7.36 (m, 7H), 5.69 (s, 1H), 4.24 (t, J = 8.5 Hz, 2H), 3.97 (t, J = 8.5 Hz, 2H), 1.99 (s, w, 2H), 1.28 (s, w, 2H), 0.96−1.03 (m, 2H), 0.73 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 190.4, 158.7, 158.2, 156.5, 154.4, 136.8, 132.2, 130.2, 129.8, 121.0, 119.5, 116.5, 108.5, 98.6, 43.3, 42.7, 34.5, 32.1, 22.6, 13.6; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{24}H_{23}N_2O_3Cl_2$, 457.1086, found 457.1096.

*10-(4-Chlorophenoxy)-benzo-1,2-dihydroimidazo[3,2,1-ij][1,8]naphthyridine-6-butyl-4,7-dione (**6l**).* White solid; mp 227−229 °C; IR (KBr, cm^{-1}) 1667, 1633, 1611, 1576, 1546, 1477, 839, 787; ^{1}H NMR ($CDCl_3$) δ 8.32 (d, J = 9.0 Hz, 1H), 6.60−7.40 (m, 6H), 6.03 (s, 1H), 4.39−4.50 (m, 4H), 3.13(t, J = 7.5 Hz, 2H), 1.58−1.64 (m, 2H), 1.42−1.50 (m, 2H), 0.95 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 174.4, 161.6, 160.3, 158.0, 153.8, 149.1, 137.9, 130.3, 121.6, 120.5, 113.5, 113.4, 101.4, 100.6, 44.7, 43.1, 34.4, 31.9, 22.6, 14.1; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{24}H_{22}N_2O_3Cl$, 421.1319, found 421.1316.

*6-Benzyl-8-(2-chloro-4-(4-chlorophenoxy)benzoyl)-7-methyl-2,3-dihydroimidazo [1,2-a]pyridin-5(1H)-one (**4m**).* Light yellow solid; mp 157−159 °C; IR (KBr, cm^{-1}) 1644, 1601, 1584, 1484, 689; ^{1}H NMR ($CDCl_3$) δ 8.81 (s, 1H), 6.87−7.35 (m, 12H), 4.29 (t, J = 9.0 Hz, 2H), 3.96 (t, J = 9.5 Hz, 2H), 3.89 (s, 2H), 1.72 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 190.8, 160.9, 158.7, 156.4, 154.3, 147.5, 140.4, 137.5, 131.9, 130.2, 129.8, 129.6, 128.3, 128.0, 125.8, 121.1, 119.5, 118.4, 116.7, 99.9, 43.9, 42.5, 31.8, 19.4; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{28}H_{23}N_3O_2Cl_2$, 505.1086, found 505.1096.

*10-(4-Chlorophenoxy)-benzo-1,2-dihydroimidazo[3,2,1-ij][1,8]naphthyridine-5- benzyl-6-methyl-4,7-dione (**6m**).* White solid; mp 270−272 °C; IR (KBr, cm^{-1}) 1652, 1636, 1613, 1572, 1548, 1478, 824, 781, 739, 699; ^{1}H NMR ($CDCl_3$) δ 8.31 (d, J = 9.0 Hz, 1H), 6.58−7.40 (m, 11H), 4.53 (t, J = 8.5 Hz, 2H), 4.36 (t, J = 8.5 Hz, 2H), 4.02 (s, 2H), 2.83 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 175.1, 161.4, 160.4, 153.9, 149.3, 147.4, 140.0 137.7, 130.4, 130.3, 128.4, 128.3, 126.0, 123.8, 121.6, 120.6, 113.4, 101.2, 44.4, 43.6, 31.5, 18.2; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{28}H_{22}N_2O_2Cl$, 469.1319, found 469.1325.

*7-Butyl-8-(2-fluoro-4-methoxybenzoyl)-2,3-dihydroimidazo[1,2-a]pyridin-5(1H)-one (**4n**).* Light yellow solid; mp 122−124 °C; IR (KBr, cm^{-1}) 1664, 1621, 1597, 1575, 1554, 849, 802; ^{1}H NMR ($CDCl_3$) δ 8.40 (s, 1H), 7.34 (t, J = 8.5 Hz, 1H), 6.74 (dd, J_1 = 8.5 Hz, J_2 = 2.5 Hz, 1H), 6.62 (dd, J_1 = 6.5 Hz, J_2 = 2.0 Hz, 1H), 5.71 (s, 1H), 4.24 (t, J = 9.0 Hz, 2H), 3.93 (t, J = 9.0 Hz, 2H), 2.12 (t, J = 7.5 Hz, 2H), 1.22−1.28 (m, 2H), 0.94−1.02 (m, 2H), 0.70 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 189.1, 163.0, 161.4, 160.9, 159.4, 157.3, 156.9, 130.6, 123.0, 110.2, 108.3, 101.9, 101.7, 99.2, 55.8, 43.4, 42.6, 34.4, 32.4, 22.3, 13.6; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{19}H_{22}N_2O_3F$, 345.1614, found 345.1625.

*10-Methoxy-benzo-1,2-dihydroimidazo[3,2,1-ij][1,8]naphthyridine-6-butyl-4,7-dione (**6n**).* White solid; mp 234−236 °C; IR (KBr, cm^{-1}) 1672, 1615, 1577, 1548, 1489, 866, 813, 779; ^{1}H NMR ($CDCl_3$) δ 8.24 (d, J = 8.5 Hz, 1H), 6.85 (dd, J_1 = 8.5 Hz, J_2 = 2.0 Hz, 1H), 6.38 (d, J = 2.0 Hz, 1H), 5.97 (s, 1H), 4.39−4.49 (m, 4H), 3.10 (t, J = 7.5 Hz, 2H), 1.56−1.62 (m, 2H), 1.42−1.49 (m, 2H), 0.95 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 174.5, 163.4, 160.2, 157.9, 148.9, 137.9, 129.6 118.7, 113.0, 110.5, 100.3, 97.6, 55.7, 44.5, 43.1, 34.3, 31.8, 22.6, 14.0; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{19}H_{21}N_2O_3$, 325.1552, found 325.1562.

*8-Butyl-9-(2,4-dichlorobenzoyl)-1,2,3,4-tetrahydropyrido[1,2-a]pyrimidin-6-one (**5a**).* Light yellow solid; mp 148−150 °C; IR (KBr, cm^{-1}) 1660, 1564, 861, 839, 811, 789; ^{1}H NMR ($CDCl_3$) δ 11.42 (s, 1H), 7.21−7.45 (m, 3H), 5.78 (s, 1H), 4.09 (t, J = 6.0 Hz, 2H), 3.54 (t, J = 6.0 Hz, 2H), 2.09−2.14 (m, 2H), 1.89 (t, J = 7.0 Hz, 2H), 1.28 (s, w, 2H), 0.95−1.03 (m, 2H), 0.73 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 190.2, 161.6, 156.4, 155.4, 141.0, 136.1, 132.3, 130.4, 130.0, 127.4, 107.0, 99.4, 39.7, 39.1, 35.8, 32.4, 22.7, 19.4, 13.8; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{19}H_{21}N_2O_2Cl_2$, 379.0980, found 379.0966.

*11-Chloro-benzo-1,2,3-trihydropyrido[3,2,1-ij][1,8]naphthyridine-7-butyl-5,8-dione (**7a**).* White solid; mp 239−241 °C; IR (KBr, cm^{-1}) 1660, 1622, 1589, 1569, 1506, 943, 924, 875, 844, 776; ^{1}H NMR ($CDCl_3$) δ 8.34 (d, J = 8.5 Hz, 1H), 7.47 (s, 1H), 7.33 (d, J = 8.5 Hz, 1H), 6.20 (s, 1H), 4.30 (s, w, 2H), 4.21 (s, w, 2H), 3.17 (t, J = 7.5 Hz, 2H), 2.36 (s, w, 2H), 1.56−1.62 (m, 2H), 1.43−1.50 (m, 2H), 0.95 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 174.6, 160.8, 156.9, 147.1, 140.0, 139.1, 128.8, 124.3, 123.2, 114.4, 113.2, 104.3, 46.3, 38.8, 35.8, 32.1, 22.7, 19.6, 14.0; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{19}H_{20}N_2O_2Cl$, 343.1213, found 343.1223.

*8-Benzyl-9-(2,4-dichlorobenzoyl)-1,2,3,4-tetrahydropyrido[1,2-a]pyrimidin-6-one (**5b**).* Yellow solid; mp 164−166 °C; IR (KBr, cm^{-1}) 1664, 1557, 815, 785, 716; ^{1}H NMR ($CDCl_3$) δ 11.64 (s, 1H), 6.84−7.39 (m, 8H), 5.51 (s, 1H), 4.08 (t, J = 5.5 Hz, 2H), 3.55 (s, 2H), 3.22−3.40 (m, 2H), 2.11−2.14 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 192.2, 163.7, 157.9, 155.6, 143.4, 140.3, 138.2, 134.2, 132.4, 132.1, 131.4, 130 9, 129.5, 129.0, 111.6, 101.8, 43.8, 41.9, 41.3, 21.6; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{22}H_{19}N_2O_2Cl_2$, 413.0824, found 413.0843.

*11-Chloro-benzo-1,2,3-trihydropyrido[3,2,1-ij][1,8]naphthyridine-7-benzyl-5,8-dione (**7b**).* White solid; mp 268−269 °C; IR (KBr, cm^{-1}) 1668, 1621, 1596, 1576, 1509, 846, 786, 710; ^{1}H NMR($CDCl_3$) δ: 8.33 (d, J = 8.5 Hz, 1H), 7.20−7.47 (m, 7H), 6.08 (s, 1H), 4.64 (s, 2H), 4.28

(t, J = 6.0 Hz, 2H), 4.18 (t, J = 6.0 Hz, 2H), 2.33−2.38 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 177.3, 163.3, 157.5, 149.6, 142.6, 141.7, 141.5, 132.0, 131.4, 130.9, 128.8, 126.9, 125.7, 117.0, 116.8, 106.7, 48.7, 43.6, 41.4, 22.1; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{22}H_{18}N_2O_2Cl$, 377.1057, found 377.1047.

7-Benzyl-9-(2,4-dichlorobenzoyl)-8-methyl-1,2,3,4-tetra-hydropyrido[1,2-a]pyrimidin-6-one (**5c**). Light yellow solid; mp 143−145 °C; IR (KBr, cm^{-1}) 1644, 1571, 832, 812, 786, 727, 697; ^{1}H NMR ($CDCl_3$) δ 11.34 (s, 1H), 7.12−7.42 (m, 8H), 4.12 (s, w, 2H), 3.87 (s, 2H), 3.52 (s, w, 2H), 2.12 (s, w, 2H), 1.63 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 192.4, 164.0, 156.3, 150.1, 144.1, 142.9, 138.1, 134.4, 132.6, 132.1, 130.8, 130.5, 129.7, 128.2, 119.3, 102.7, 42.4, 41.1, 34.8, 23.2, 21.9; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{23}H_{21}N_2O_2Cl_2$, 427.0980, found 427.0974.

11-Chloro-benzo-1,2,3-trihydropyrido[3,2,1-ij][1,8]naphthyridine-6-benzyl-7-methyl-5,8-dione (**7c**). White solid; mp 261−263 °C; IR (KBr, cm^{-1}) 1624, 1594, 1574, 1511, 783, 749, 702; ^{1}H NMR ($CDCl_3$) δ 8.34 (d, J = 8.5 Hz, 1H), 7.13−7.47 (m, 7H), 4.33 (t, J = 6.0 Hz, 2H), 4.19 (t, J = 6.0 Hz, 2H), 4.09 (s, 2H), 2.34−2.38 (m, 2H), 1.61 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 177.9, 163.6, 151.6, 148.0, 142.5, 142.4, 141.5, 131.4, 130.8, 130.7, 128.4, 126.7, 126.0, 125.5, 116.8, 107.3, 48.5, 42.1, 34.8, 22.3, 22.2; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{23}H_{20}N_2O_2Cl$, 391.1213, found 391.1216.

7-Benzyl-9-(2,4-dichlorobenzoyl)-8-pentyl-1,2,3,4-tetrahydropyrido[1,2-a]pyrimidin-6-one (**5d**). Yellow solid; mp 129−131 °C; IR (KBr, cm^{-1}) 1635, 1575, 1567, 1538, 913, 822, 811, 784, 693; ^{1}H NMR ($CDCl_3$) δ 11.06 (s, 1H), 7.12−7.43 (m, 8H), 4.11 (t, J = 5.5 Hz, 2H), 3.89 (s, 2H), 3.50 (s, w, 2H), 2.07−2.14 (m, 2H), 1.62 (s, w, 2H), 1.03−1.09 (m, 4H), 0.84 (s, w, 2H), 0.75 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 190.2, 162.1, 153.8, 152.7, 141.1, 140.8, 135.9, 132.3, 130.2, 128.3, 128.0, 127.2, 125.8, 115.9, 98.8, 40.1, 38.8, 32.3, 32.0, 30.5, 22.4, 19.5, 13.9; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{27}H_{29}N_2O_2Cl_2$, 483.1606, found 483.1590.

11-Chloro-benzo-1,2,3-trihydropyrido[3,2,1-ij][1,8]naphthyridine-6-benzyl-7-pentyl-5,8-dione (**7d**). White solid; mp 185−187 °C; IR (KBr, cm^{-1}) 1624, 1594, 1569, 1506, 836, 784, 726; ^{1}H NMR ($CDCl_3$) δ 8.39 (d, J = 8.5 Hz, 1H), 7.15−7.48 (m, 7H), 4.33 (t, J = 6.0 Hz, 2H), 4.20 (t, J = 6.0 Hz, 2H), 4.08 (s, 2H), 3.32 (s, w, 2H), 2.34−2.38 (m, 2H), 1.42−1.52 (m, 4H), 1.32−1.38 (m, 2H), 0.89 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 175.0, 161.5, 153.5, 146.1, 140.5, 139.9, 139.0, 129.2, 128.4, 128.2, 126.0, 124.2, 123.6, 122.5, 114.3, 104.3, 46.3, 39.8, 32.6, 32.0, 31.5, 30.0, 22.7, 19.9, 14.2; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{27}H_{28}N_2O_2Cl$, 447.1839, found 447.1829.

8-Butyl-9-(2,5-dichlorobenzoyl)-1,2,3,4-tetrahydropyrido[1,2-a]-pyrimidin-6-one (**5e**). Yellow solid; mp 148−150 °C; IR (KBr, cm^{-1}) 1668, 1569, 864, 825; ^{1}H NMR ($CDCl_3$) δ 11.56 (s, 1H), 7.25−7.36 (m, 3H), 5.74 (s, 1H), 4.08 (s, 2H), 3.54 (s, 2H), 2.09−2.13 (m, 2H), 1.88 (s, w, 2H), 1.28 (s, w, 2H), 0.97 (s, w, 2H), 0.73 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 189.1, 161.4, 155.9, 155.5, 143.7, 132.9, 131.4, 130.2, 129.3, 128.6, 107.1, 98.8, 39.4, 38.9, 35.4, 32.2, 22.6, 19.2, 13.6; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{19}H_{21}N_2O_2Cl_2$, 379.0980, found 379.0978.

10-Chloro-benzo-1,2,3-trihydropyrido[3,2,1-ij][1,8]naphthyridine-7-butyl-5,8-dione (**7e**). White solid; mp 217−219 °C; IR (KBr, cm^{-1}) 1663, 1624, 1580, 844, 803; ^{1}H NMR ($CDCl_3$) δ 8.38 (s, 1H), 7.59 (d, J = 9.0 Hz, 1H), 7.42 (d, J = 9.0 Hz, 1H), 6.22 (s, 1H), 4.29 (t, J = 6.0 Hz, 2H), 4.23 (t, J = 6.0 Hz, 2H), 3.17 (t, J = 7.5 Hz, 2H), 2.34−2.39 (m, 2H), 1.56−1.62 (m, 2H), 1.43−1.51 (m, 2H), 0.96 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 174.2, 161.0, 157.1, 147.2, 137.9, 132.8, 130.1, 126.7, 126.1, 116.2, 113.3, 104.3, 46.4, 39.0, 36.0, 32.3, 22.8, 19.8, 14.1; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{19}H_{20}N_2O_2Cl$, 343.1213, found 343.1214.

7-Benzyl-9-(2,5-dichlorobenzoyl)-8-pentyl-1,2,3,4-tetrahydropyrido-[1,2-a]pyrimidin-6-one (**5f**). Yellow solid; mp 124−126 °C; IR (KBr, cm^{-1}) 1646, 1576, 886, 789, 702; ^{1}H NMR ($CDCl_3$) δ 11.16 (s, 1H), 7.12−7.34 (m, 8H), 4.11 (t, J = 5.5 Hz, 2H), 3.90 (s, 2H), 3.51 (s, w, 2H), 2.08−2.13 (m, 2H), 1.61 (s, w, 2H), 1.04−1.10 (m, 4H), 0.83 (s, 2H), 0.76 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 189.5, 162.0, 154.0, 152.6, 143.6, 141.0, 132.9, 131.5, 130.4, 129.6, 129.1, 128.3, 128.0, 125.8, 116.0, 98.6, 40.1, 38.8, 32.3, 32.1, 30.6, 22.4, 19.5, 14.0; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{27}H_{29}N_2O_2Cl_2$, 483.1606, found 483.1615.

10-Chloro-benzo-1,2,3-trihydropyrido[3,2,1-ij][1,8]naphthyridine-6-benzyl-7-pentyl-5,8-dione (**7f**). White solid; mp 169−171 °C; IR (KBr, cm^{-1}) 1624, 1575, 806, 743, 699; ^{1}H NMR ($CDCl_3$) δ 8.40 (d, J = 2.0 Hz, 1H), 7.13−7.58 (m, 7H), 4.32 (t, J = 6.0 Hz, 2H), 4.21 (t, J = 6.0 Hz, 2H), 4.07 (s, 2H), 3.32 (s, w, 2H), 2.33−2.37 (m, 2H), 1.44−1.52 (m, 4H), 1.31−1.38 (m, 2H), 0.90 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 174.4, 161.5, 153.5, 146.0, 140.6, 137.6, 132.6, 129.9, 128.4, 128.2, 126.8, 126.2, 126.0, 122.5, 116.0, 104.2, 46.3, 39.7, 32.6, 32.0, 31.5, 30.0, 22.7, 19.9, 14.2; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{27}H_{28}N_2O_2Cl$, 447.1839, found 447.1818.

8-Butyl-9-(2-chlorobenzoyl)-1,2,3,4-tetrahydropyrido[1,2-a]pyrimidin-6-one (**5g**). Yellow solid; mp 139−141 °C; IR (KBr, cm^{-1}) 1665, 1571, 854, 773; ^{1}H NMR ($CDCl_3$) δ 11.54 (s, 1H), 7.24−7.41 (m, 4H), 5.71 (s, 1H), 4.07 (t, J = 5.0 Hz, 2H), 3.51 (t, J = 5.0 Hz, 2H), 2.07−2.11 (m, 2H), 1.84 (s, w, 2H), 1.23−1.27 (m, 2H), 0.89−0.96 (m, 2H), 0.68 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 191.1, 161.4, 156.3, 155.2, 142.4, 131.0, 130.4, 130.2, 128.7, 126.7, 106.6, 99.0, 39.3, 38.8, 35.3, 32.0, 22.4, 19.1, 13.5; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{19}H_{22}N_2O_2Cl$, 345.1370, found 345.1374.

Benzo-1,2,3-trihydropyrido[3,2,1-ij][1,8]naphthyridine-7-butyl-5,8-dione (**7g**). White solid; mp 149−151 °C; IR (KBr, cm^{-1}) 1668, 1619, 1602, 1575, 1521, 840, 755; ^{1}H NMR ($CDCl_3$) δ 8.41 (dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz, 1H), 7.35−7.67 (m, 3H), 6.19 (s, 1H), 4.27 (t, J = 5.5 Hz, 2H), 4.23 (t, J = 5.5 Hz, 2H), 3.19 (t, J = 7.5 Hz, 2H), 2.32−2.36 (m, 2H), 1.58−1.64 (m, 2H), 1.43−1.50 (m, 2H), 0.95 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 175.4, 161.0, 157.2, 147.0, 139.4, 132.8, 127.1, 124.8, 123.8, 114.3, 112.8, 104.2, 46.0, 38.9, 35.9, 32.2, 22.7, 19.7, 14.0; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{19}H_{21}N_2O_2$, 309.1603, found 309.1595.

7-Benzyl-9-(2-chlorobenzoyl)-8-methyl-1,2,3,4-tetrahydropyrido-[1,2-a]pyrimidin-6-one (**5h**). Light yellow solid; mp 131−133 °C; IR (KBr, cm^{-1}) 1647, 1578, 770, 754, 731, 697; ^{1}H NMR ($CDCl_3$) δ 11.39 (s, 1H), 7.11−7.40 (m, 9H), 4.12 (t, J = 5.5 Hz, 2H), 3.87 (s, 2H), 3.52 (s, w, 2H), 2.09−2.14 (m, 2H), 1.61 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 193.8, 164.0, 156.3, 150.5, 145.7, 143.0, 133.4, 132.7, 131.2, 130.7, 130.5, 129.3, 128.1, 119.0, 102.7, 42.4, 41.1, 34.8, 22.9, 22.0; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{23}H_{22}N_2O_2Cl$, 393.1370, found 393.1385.

Benzo-1,2,3-trihydropyrido[3,2,1-ij][1,8]naphthyridine-6-benzyl-7-methyl-5,8-dione (**7h**). White solid; mp 273−275 °C; IR (KBr, cm^{-1}) 1634, 1625, 1602, 1575, 1517, 758, 703; ^{1}H NMR ($CDCl_3$) δ 8.41 (dd, J_1 = 8.0 Hz, J_2 = 1.5 Hz, 1H), 7.14−7.67 (m, 8H), 4.33 (t, J = 6.0 Hz, 2H), 4.24 (t, J = 6.0 Hz, 2H), 4.09 (s, 2H), 2.33−2.37 (m, 2H), 1.64 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 178.7, 163.8, 151.8, 147.9, 142.7, 141.7, 135.1, 130.8, 130.7, 129.6, 128.3, 127.6, 126.1, 125.0, 116.6, 107.2, 48.3, 42.1, 34.8, 22.4, 22.2; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{23}H_{21}N_2O_2$, 357.1603, found 357.1607.

8-Butyl-9-(2,4-dichloro-5-fluorobenzoyl)-1,2,3,4-tetrahydropyrido-[1,2-a]pyrimidin-6-one (**5i**). Light yellow solid; mp 167−169 °C; IR (KBr, cm^{-1}) 1672, 1563, 878, 870, 791, 726; ^{1}H NMR ($CDCl_3$) δ 11.45 (s, 1H), 7.48 (d, J = 7.0 Hz, 1H), 7.08 (d, J = 7.0 Hz, 1H), 5.74 (s, 1H), 4.07 (s, w, 2H), 3.53 (s, w, 2H), 2.10 (t, J = 5.0 Hz, 2H), 1.90 (s, w, 2H), 1.30 (s, w, 2H), 0.97−1.05 (m, 2H), 0.74 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 187.9, 161.2, 157.6, 155.4, 142.1, 131.7, 126.5, 122.7, 116.7, 116.5, 107.1, 98.5, 39.3, 38.8, 35.3, 32.0, 22.4, 19.0, 13.5; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{19}H_{20}N_2O_2Cl_2F$, 397.0886, found 397.0879.

10-Fluoro-11-chloro-benzo-1,2,3-trihydropyrido[3,2,1-ij][1,8]naphthyridine-7-butyl-5,8-dione (**7i**). White solid; mp 225−227 °C; IR (KBr, cm^{-1}) 1661, 1632, 1607, 1581, 833, 786; ^{1}H NMR ($CDCl_3$) δ 8.11 (d, J = 7.0 Hz, 1H), 7.54 (d, J = 7.0 Hz, 1H), 6.21 (s, 1H), 4.28 (t, J = 5.5 Hz, 2H), 4.20 (t, J = 5.5 Hz, 2H), 3.14 (t, J = 7.5 Hz, 2H), 2.34−2.39

(m, 2H), 1.54−1.60 (m, 2H), 1.43−1.49 (m, 2H), 0.94 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 176.1, 163.2, 159.3, 158.2, 156.2, 149.7, 138.4, 130.2, 129.3, 129.1, 127.4, 119.5, 116.1, 115.8, 106.3, 49.1, 41.3, 38.3, 34.6, 25.2, 22.1, 16.5; HRMS (ESI-TOF, $[M + H]^+$) calcd for $C_{19}H_{19}N_2O_2ClF$, 361.1119, found 361.1120.

■ ASSOCIATED CONTENT

Supporting Information. Experimental procedures; copies of ^{1}H NMR, ^{13}C NMR, and HRMS spectra of all new compounds; and X-ray data for compounds **4a** and **6g** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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■ ACKNOWLEDGMENT

This work was financially supported by the National Natural Science Foundation of China (Nos. 20872074 and 21072110) and the Natural Science Foundation of Shandong Province (Nos. Z2008B03 and ZR2010BM007).

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