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One-pot synthesis of pyridines from 3-aza-1,5-enynes

Xiaoyi Xin, Dongping Wang, Xincheng Li, Boshun Wan *

Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian 116023, China

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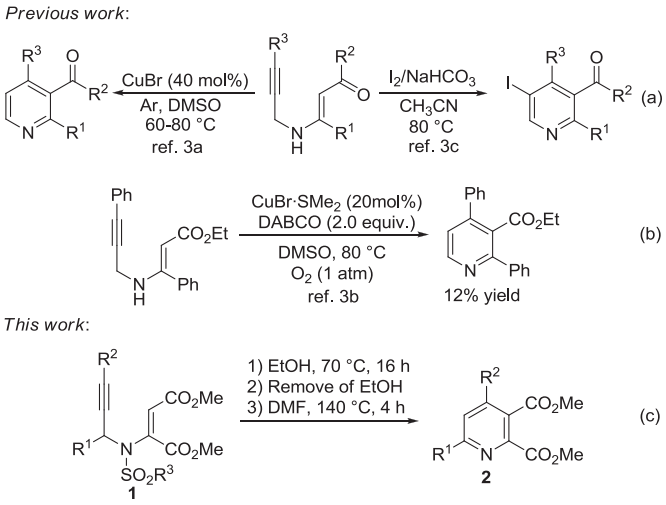
ABSTRACT

Efficient one-pot transformation of 3-aza-1,5-enynes to poly-substituted pyridines in good to excellent yields has been developed. This reaction involved cyclization of 3-aza-enynes and elimination of sulfinyl acids steps.

1. Introduction

Pyridine derivatives are an important class of heterocycle found in many natural products, active pharmaceuticals, and functional materials.[1] Although many methods are available for the synthesis of pyridines,[2] the development of new methods that benefit from readily available starting materials with operational simplicity continues to be a target of intense interest. The exploration of reaction diversity is an important goal of synthetic organic chemistry. 3-Aza-1,5-enynes was a versatile building block having diverse reaction patterns.[3] Cacchi and co-workers reported that *N*-propargylic β-enaminones could be selectively transformed into pyridines via 6-*endo-dig* cyclization (Scheme 1a, left) or pyrroles via 5-*exo-dig* cyclization.[3a] The pyridines were obtained using 40 mol % of CuBr, and an oxidation step was involved in the proposed mechanism, but the oxidant source was unclear.[3a] Chiba and co-workers also reported one example of *N*-propargylic-enaminone was transformed to pyridine in low yield in the presence of 20 mol % $CuBr{\cdot}SMe_2$ under 1 atm of oxygen atmosphere (Scheme 1b).[3b] Electrophilic iodocyclizations of *N*-propargylic β-enaminones with molecular iodine leading to iodo-substituted pyridines has been accomplished by Zora's research group (Scheme 1a, right).[3c] Saito and co-workers described that the similar structure, *N*-tosyl, *N*-propargylic β-enaminones, underwent Au(I)-catalyzed amino-Claisen rearrangement and heterocyclization to yield pyrroles and/or 1,2-dihydropyridines.[3d] Recently, we reported that 3-aza-1,5-enyne **1** (see Scheme 1c for structure) was selectively transformed into two kinds of functionalized pyrroles,[3e] 1,2-dihydropyridines and 3-iodo-1,2-dihydropyridines.[3f] In this paper, we report the transformation of 3-aza-1,5-enynes to pyridines in an efficient one-pot manner (Scheme 1c).



Scheme 1. Synthesis of pyridines from 3-aza-1,5-enyne frameworks.

2. Results and discussions

In the course of our investigation on the transformation of 3-aza-1,5-enyne **1** to *N*-heterocycles,[3e,f] we found that treatment of

* Corresponding author. Tel.: +86 411 84379260; fax: +86 411 84379223; e-mail address: bswan@dicp.ac.cn (B. Wan).

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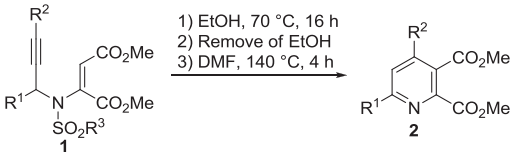
the model substrate **1a** (R^1=R^2=Ph, R^3=*p*-tolyl) in following three steps: 1) heated in ethanol at 70 °C for 16 h under argon atmosphere, 2) remove of the ethanol solvent under vacuum, 3) *N*,*N*-dimethylformamide (DMF) was added, the mixture was heated at 140 °C for 4 h under argon atmosphere, pyridine **2a**, was obtained in 99% isolated yield (Table 1, entry 1). The structure of the pyridine product was unambiguously confirmed by single-crystal X-ray diffraction analysis of its *o*-CF_3-substituted derivative **2e**.[4]

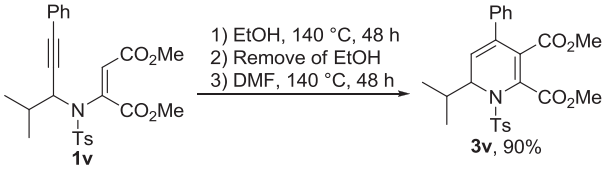
Next, we explored the scope and generality of this reaction, and the results are given in Table 1. Aryl R^1 groups bearing different substituents, including electron-neutral groups (entry 1), -donating groups (entries 2–4), -withdrawing groups (entry 5), and halogen groups (entries 6–8) were well tolerated, and the desired products were isolated with moderate to high yields (60–99%). For 2-CF_3 (entry 5, 69%) and 2-Br (entry 8, 60%) substituted substrate, the yields were lower even the reaction time was prolonged, this mainly reasoned from steric hindrance. A fused ring was also suitable for this process, although a relatively low yield was obtained (75%, entry 9). However, alkyl R^1 substituents were not tolerated (Eqs. 1 and 2), even at elevated temperature (140 °C) and prolonged time, the product were previously reported 1,2-dihydropyridines **3v** and **w**.[3f] These results indicated that an aryl R^1 is crucial in this system. Both aryl- and alkyl-substituted alkyne (R^2) units in the substrate were well tolerated (entries 10–18). We noted that alkyl-substituted alkyl substrates also reacted in good yields (entries 16–18). The electronic properties of the sulfonyl group (R^3) had a small impact on the yield (entries 1, 19, 20, the products of **1s** and **t** were same to **1a**). Moreover, the C=C bond is not limited to the (*E*)-geometry, substrate **1u** (entry 21) afforded the same product as **1a** (entry 1), although the yield was lower even after a longer reaction time.

Table 1
Scope of the synthesis of pyridines[a]

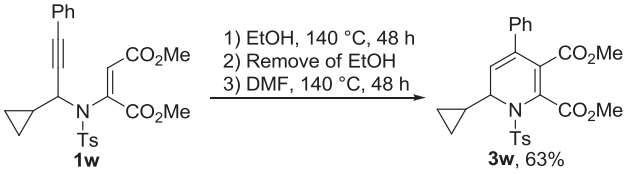


Entry	1	R^1	R^2	R^3	Yield (%)[b]
1	**1a**	Ph	Ph	4-MeC_6H_4	99 (**2a**)
2	**1b**	2-MeC_6H_4	Ph	4-MeC_6H_4	96 (**2b**)
3	**1c**	3-MeC_6H_4	Ph	4-MeC_6H_4	99 (**2c**)
4	**1d**	4-MeC_6H_4	Ph	4-MeC_6H_4	91 (**2d**)
5[c]	**1e**	2-$CF_3C_6H_4$	Ph	4-MeC_6H_4	69 (**2e**)
6	**1f**	4-FC_6H_4	Ph	4-MeC_6H_4	95 (**2f**)
7	**1g**	2-ClC_6H_4	Ph	4-MeC_6H_4	88 (**2g**)
8[c]	**1h**	2-BrC_6H_4	Ph	4-MeC_6H_4	60 (**2h**)
9[c]	**1i**	1-Naphthyl	Ph	4-MeC_6H_4	75 (**2i**)
10	**1j**	Ph	2-MeC_6H_4	4-MeC_6H_4	95 (**2j**)
11	**1k**	Ph	3-MeC_6H_4	4-MeC_6H_4	95 (**2k**)
12	**1l**	Ph	4-MeC_6H_4	4-MeC_6H_4	92 (**2l**)
13	**1m**	Ph	4-$MeOC_6H_4$	4-MeC_6H_4	86 (**2m**)
14	**1n**	Ph	4-FC_6H_4	4-MeC_6H_4	96 (**2n**)
15	**1o**	Ph	4-ClC_6H_4	4-MeC_6H_4	83 (**2o**)
16[c,d]	**1p**	Ph	^{n}Pr	4-MeC_6H_4	90 (**2p**)
17[c,d]	**1q**	Ph	^{n}Bu	4-MeC_6H_4	87 (**2q**)
18[d,e]	**1r**	Ph	Cy	4-MeC_6H_4	90 (**2r**)
19	**1s**	Ph	Ph	Ph	93 (**2a**)
20	**1t**	Ph	Ph	2-ClC_6H_4	91 (**2a**)
21[d]	**1u**[f]	Ph	Ph	4-MeC_6H_4	44 (**2a**)

[a] Reaction conditions: **1** (0.2 mmol) of in ethanol (2.0 mL) was heated at 70 °C for 16 h under argon atmosphere, then ethanol was removed under vacuum and DMF was added, the mixture was heated at 140 °C for 4 h under argon atmosphere unless otherwise noted.
[b] Isolated yields.
[c] Step 3: 24 h.
[d] Step 1: 100 °C.
[e] Step 3: 36 h.
[f] The double bond configuration of the reactant is (*Z*).

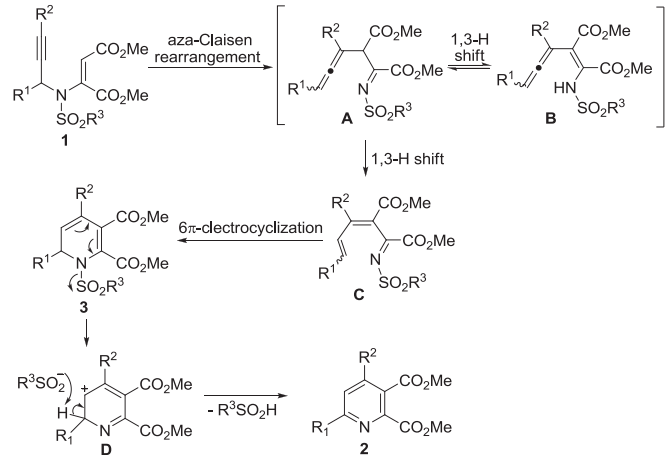


(1)



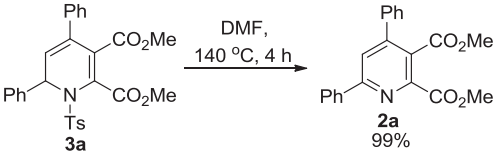
(2)

A plausible reaction mechanism is depicted in Scheme 2. In step 1, aza-Claisen rearrangement of **1** followed by 6π-electrocyclization leads to 1,2-dihydropyridines **3**.[3f] Then elimination of sulfinic acids[5] from **3** followed a proposed E_1-like mechanism: dissociation of aryl sulfinic anion generates a carbon cation **D**, aryl sulfinic anion abstracts a proton furnishes pyridine product **2**.



Scheme 2. Proposed mechanism.

To verify the process from 1,2-dihydropyridines **3** to pyridines **2**, we treated the isolated 1,2-dihydropyridines **3a**[3f] as the starting material with the same conditions as used for **1a** in step 3 (Eq. 3). As expected, the same product, pyridine **2a**, was obtained in the same yield (99%) as the standard conditions (Table 1, entry 1).



(3)

3. Conclusion

In summary, we have developed an efficient one-pot method for the synthesis of pyridines from 3-aza-1,5-enynes with high yields. The mechanism of containing an aza-Claisen rearrangement, 6π-electrocyclization, and elimination of aryl sulfinic acid was proposed. This work provides an alternate access to construct pyridines directly from available building blocks.

4. Experimental section

4.1. General method

All reactions were carried out under an atmosphere of argon using standard Schlenk techniques. Solvents were treated prior to use according to the standard methods. Column chromatography was carried out on silica gel (300–400 mesh) using a forced flow of eluent at 0.3–0.5 bar pressure. For TLC, silica gel GF_{254} was used and visualized by fluorescence quenching under UV light. NMR spectra were recorded at room temperature in $CDCl_3$ on 400 MHz Bruker DRX-400 or 500 MHz Bruker DRX-500 NMR spectrometers. The chemical shifts for ^1H NMR were recorded in parts per million downfield from tetramethylsilane (TMS) with the solvent resonance as the internal standard (7.26 ppm for $CDCl_3$). The chemical shifts for ^{13}C NMR were recorded in ppm downfield using the central peak of $CDCl_3$ (77.16 ppm) as the internal standard. Coupling constants (*J*) are reported in Hertz and refer to apparent peak multiplications. The abbreviations s, d, t, q, and m stand for singlet, doublet, triplet, quartet, and multiplet in that order. HRMS data were obtained with Micromass HPLC–Q-TOF mass spectrometer.

4.2. General procedure for the syntheses of pyridines 2

In a Schlenk tube equipped with a magnetic stirrer bar, starting material **1** (0.2 mmol) and ethanol (2 mL) were added. The resulting mixture was stirred at 70 °C under argon protection for 16 h. The solvent ethanol was removed under vacuum and then DMF (1 mL) was added, the mixture was heated at 140 °C for 4 h under argon atmosphere. The solvent was removed under vacuum. The residue was directly purified by flash chromatography (eluent: 50:1–10:1 petroleum ether/ethyl acetate) to give the desired pyridine **2**.

*4.2.1. Dimethyl 4,6-diphenylpyridine-2,3-dicarboxylate (**2a**).* Unknown compound, colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ 8.10–8.04 (m, 2H), 7.87 (s, 1H), 7.52–7.42 (m, 8H), 4.02 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.9, 165.8, 158.0, 150.1, 146.5, 137.8, 137.5, 130.1, 129.2, 129.1, 128.8, 128.7, 128.2, 127.5, 123.8, 53.3, 52.7; HRMS Calculated for $C_{21}H_{17}NO_4Na$ $[M+Na]^+$ 370.1055, found 370.1057.

*4.2.2. Dimethyl 4-phenyl-6-(o-tolyl)pyridine-2,3-dicarboxylate (**2b**).* Unknown compound, colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.43 (s, 6H), 7.33–7.22 (m, 3H), 3.97 (s, 3H), 3.74 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 164.7, 159.7, 148.44, 144.6, 137.7, 136.2, 135.3, 130.2, 128.9, 128.2, 127.8, 127.6, 127.2, 126.8, 126.5, 125.2, 52.3, 51.8, 19.5; HRMS Calculated for $C_{22}H_{19}NO_4Na$ $[M+Na]^+$ 384.1212, found 384.1216.

*4.2.3. Dimethyl 4-phenyl-6-(m-tolyl)pyridine-2,3-dicarboxylate (**2c**).* Unknown compound, colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.84 (s, 1H), 7.82 (d, *J*=7.8 Hz, 1H), 7.49–7.39 (m, 5H), 7.35 (t, *J*=7.6 Hz, 1H), 7.24 (d, *J*=8.7 Hz, 1H), 4.00 (s, 3H), 3.71 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 165.8, 158.2, 150.0, 146.3, 138.8, 137.7, 137.5, 130.9, 129.1, 128.9, 128.8, 128.7, 128.2, 128.1, 124.6, 123.9, 53.3, 52.7, 21.6; HRMS Calculated for $C_{22}H_{19}NO_4Na$ $[M+Na]^+$ 384.1212, found 384.1211.

*4.2.4. Dimethyl 4-phenyl-6-(p-tolyl)pyridine-2,3-dicarboxylate (**2d**).* Unknown compound, colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J*=7.9 Hz, 2H), 7.85 (s, 1H), 7.44 (s, 5H), 7.29 (d, *J*=7.8 Hz, 2H), 4.02 (s, 3H), 3.73 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 164.8, 156.9, 148.9, 145.3, 139.3, 136.5, 133.9, 128.7, 128.1, 127.8, 127.4, 127.1, 126.3, 122.3, 52.2, 51.7, 20.4; HRMS Calculated for $C_{22}H_{19}NO_4Na$ $[M+Na]^+$ 384.1212, found 384.1205.

*4.2.5. Dimethyl 4-phenyl-6-(2-(trifluoromethyl)phenyl)pyridine-2,3-dicarboxylate (**2e**).* Unknown compound, white solid, mp 154–155 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J*=7.8 Hz, 1H), 7.67–7.62 (m, 2H), 7.59–7.53 (m, 2H), 7.45 (s, 5H), 4.00 (s, 3H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 165.4, 158.3, 149.3, 145.6, 138.4, 136.9, 132.0, 131.9, 129.7, 129.4, 129.3, 128.9, 128.3, 127.7, 127.6, 126.7 (q, *J*=5.2 Hz), 124.1 (d, *J*=273.9 Hz), 53.5, 52.9; ^{19}F NMR (377 MHz, $CDCl_3$) δ −56.91; HRMS Calculated for $C_{22}H_{16}NO_4F_3Na$ $[M+Na]^+$ 438.0929, found 438.0950.

*4.2.6. Dimethyl 6-(4-fluorophenyl)-4-phenylpyridine-2,3-dicarboxylate (**2f**).* Unknown compound, colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J*=8.5, 5.5 Hz, 2H), 7.82 (s, 1H), 7.44 (m, 5H), 7.17 (t, *J*=8.6 Hz, 2H), 4.01 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 165.7, 164.2 (d, *J*=250.3 Hz), 156.9, 150.2, 146.4, 137.3, 133.9, 133.8, 129.4 (d, *J*=8.6 Hz), 129.2, 128.8, 128.1, 123.4, 116.0 (d, *J*=21.8 Hz), 53.3, 52.8; ^{19}F NMR (377 MHz, $CDCl_3$) δ −111.63; HRMS Calculated for $C_{21}H_{16}NO_4FNa$ $[M+Na]^+$ 388.0961, found 388.0965.

*4.2.7. Dimethyl 6-(2-chlorophenyl)-4-phenylpyridine-2,3-dicarboxylate (**2g**).* Unknown compound, white solid, mp 97–98 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.68 (d, *J*=7.0 Hz, 1H), 7.47 (m, 6H), 7.42–7.33 (m, 2H), 4.01 (s, 3H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 165.5, 157.3, 149.1, 137.7, 137.0, 132.4, 132.0, 131.9, 130.5, 130.3, 129.4, 129.3, 128.9, 128.5, 128.3, 127.4, 53.5, 52.9; HRMS Calculated for $C_{21}H_{16}NO_4NaCl$ $[M+Na]^+$ 404.0666, found 404.0654.

*4.2.8. Dimethyl 6-(2-bromophenyl)-4-phenylpyridine-2,3-dicarboxylate (**2h**).* Unknown compound, white solid, mp 108–109 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.65 (d, *J*=8.0 Hz, 1H), 7.60 (d, *J*=7.6 Hz, 1H), 7.51–7.35 (m, 6H), 7.26 (t, *J*=8.5 Hz, 1H), 3.98 (s, 3H), 3.74 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 165.5, 158.7, 149.0, 145.8, 139.8, 137.0, 133.6, 131.9, 130.7, 129.5, 129.3, 128.9, 128.5, 128.3, 128.0, 121.9, 53.5, 52.9; HRMS Calculated for $C_{21}H_{16}NO_4NaBr$ $[M+Na]^+$ 448.0160, found 448.0150.

*4.2.9. Dimethyl 6-(naphthalen-1-yl)-4-phenylpyridine-2,3-dicarboxylate (**2i**).* Unknown compound, white solid, mp 136–137 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.11 (dd, *J*=5.5, 4.2 Hz, 1H), 7.95 (d, *J*=8.2 Hz, 1H), 7.93–7.90 (m, 1H), 7.78 (s, 1H), 7.67 (dd, *J*=7.1, 1.2 Hz, 1H), 7.56 (dd, *J*=8.2, 7.1 Hz, 1H), 7.54–7.50 (m, 2H), 7.50–7.45 (m, 5H), 4.01 (s, 3H), 3.79 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.0, 165.8, 160.0, 149.7, 146.2, 137.2, 136.9, 134.1, 131.2, 130.0, 129.3, 129.1, 128.9, 128.6, 128.5, 128.3, 128.2, 127.1, 126.3, 125.4, 125.3, 53.5 52.9; HRMS Calculated for $C_{25}H_{19}NO_4Na$ $[M+Na]^+$ 420.1212, found 420.1213.

*4.2.10. Dimethyl 6-phenyl-4-(o-tolyl)pyridine-2,3-dicarboxylate (**2j**).* Unknown compound, colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J*=7.9, 1.6 Hz, 2H), 7.78 (s, 1H), 7.53–7.43 (m, 3H), 7.36–7.21 (m, 3H), 7.15 (d, *J*=7.4 Hz, 1H), 4.02 (s, 3H), 3.61 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.3, 165.9, 157.7, 150.5, 146.5, 137.7, 136.7, 135.6, 130.3, 130.1, 129.3, 129.1, 128.9, 128.6, 127.5,

125.6, 123.9, 53.3, 52.5, 20.1; HRMS Calculated for $C_{22}H_{19}NO_4Na$ $[M+Na]^+$ 384.1212, found 384.1207.

*4.2.11. Dimethyl 6-phenyl-4-(m-tolyl)pyridine-2,3-dicarboxylate (**2k**).* Unknown compound, colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J=6.9 Hz, 2H), 7.87 (s, 1H), 7.53–7.41 (m, 3H), 7.34 (t, J=6.9 Hz, 1H), 7.24 (m, 3H), 4.02 (s, 3H), 3.75 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 165.8, 157.9, 150.2, 146.3, 138.6, 137.8, 137.4, 130.0, 129.9, 129.0, 128.8, 128.7, 128.6, 127.5, 125.2, 123.8, 53.2, 52.7, 21.5; HRMS Calculated for $C_{22}H_{19}NO_4Na$ $[M+Na]^+$ 384.1212, found 384.1202.

*4.2.12. Dimethyl 6-phenyl-4-(p-tolyl)pyridine-2,3-dicarboxylate (**2l**).* Unknown compound, colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, J=6.9 Hz, 2H), 7.86 (s, 1H), 7.52–7.41 (m, 3H), 7.34 (d, J=8.0 Hz, 2H), 7.26 (d, J=8.1 Hz, 2H), 4.01 (s, 3H), 3.76 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 165.8, 157.9, 150.1, 146.3, 139.3, 137.8, 134.5, 130.0, 129.6, 129.0, 128.1, 127.5, 123.8, 110.1, 53.3, 52.7, 21.4; HRMS Calculated for $C_{22}H_{19}NO_4Na$ $[M+Na]^+$ 384.1212, found 384.1221.

*4.2.13. Dimethyl 4-(4-methoxyphenyl)-6-phenylpyridine-2,3-dicarboxylate (**2m**).* Unknown compound, white solid, mp 96–97 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J=6.9 Hz, 2H), 7.86 (s, 1H), 7.53–7.43 (m, 3H), 7.40 (d, J=8.7 Hz, 2H), 6.99 (d, J=8.7 Hz, 2H), 4.02 (s, 3H), 3.86 (s, 3H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 165.9, 160.5, 158.0, 149.7, 137.9, 130.0, 129.7, 129.6, 129.1, 128.8, 127.5, 123.8, 114.4, 110.1, 55.5, 53.3, 52.8; HRMS Calculated for $C_{22}H_{19}NO_5Na$ $[M+Na]^+$ 400.1161, found 400.1143.

*4.2.14. Dimethyl 4-(4-fluorophenyl)-6-phenylpyridine-2,3-dicarboxylate (**2n**).* Unknown compound, colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J=6.9 Hz, 2H), 7.84 (s, 1H), 7.45 (m, 5H), 7.16 (t, J=8.5 Hz, 2H), 4.02 (s, 3H), 3.75 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 165.7, 163.3 (d, J=249.4 Hz), 158.1, 149.0, 146.4, 137.6, 133.4, 130.2, 130.1, 129.1, 128.7, 127.5, 123.7, 115.9 (d, J=21.8 Hz), 53.3, 52.8; ^{19}F NMR (377 MHz, $CDCl_3$) δ −112.58; HRMS Calculated for $C_{21}H_{16}NO_4FNa$ $[M+Na]^+$ 388.0961, found 388.0967.

*4.2.15. Dimethyl 4-(4-chlorophenyl)-6-phenylpyridine-2,3-dicarboxylate (**2o**).* Unknown compound, white solid, mp 120–121 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J=6.7 Hz, 2H), 7.83 (s, 1H), 7.53–7.42 (m, 5H), 7.38 (d, J=8.5 Hz, 2H), 4.02 (s, 3H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 165.7, 158.2, 148.9, 146.5, 137.6, 135.9, 135.6, 130.3, 129.6, 129.2, 129.1, 128.6, 127.5, 123.6, 53.4, 52.9; HRMS Calculated for $C_{21}H_{16}NO_4NaCl$ $[M+Na]^+$ 404.0666, found 404.0649.

*4.2.16. Dimethyl 6-phenyl-4-propylpyridine-2,3-dicarboxylate (**2p**).* Unknown compound, colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J=7.0 Hz, 2H), 7.73 (s, 1H), 7.51–7.40 (m, 3H), 3.98 (s, 3H), 3.96 (s, 3H), 2.79–2.65 (m, 2H), 1.76–1.64 (m, 2H), 0.99 (t, J=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 166.0, 157.9, 151.5, 138.0, 129.9, 129.2, 129.0, 127.4, 123.6, 110.1, 53.2, 52.8, 35.2, 23.7, 14.0; HRMS Calculated for $C_{18}H_{19}NO_4Na$ $[M+Na]^+$ 336.1212, found 336.1206.

*4.2.17. Dimethyl 4-butyl-6-phenylpyridine-2,3-dicarboxylate (**2q**).* Unknown compound, colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ 8.05–7.98 (m, 2H), 7.73 (s, 1H), 7.50–7.41 (m, 3H), 3.98 (s, 3H), 3.95 (s, 3H), 2.76–2.72 (m, 2H), 1.70–1.60 (m, 2H), 1.44–1.36 (m, 2H), 0.94 (t, J=7.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.1, 166.0, 157.9, 151.8, 146.4, 138.0, 129.9, 129.2, 129.0, 127.4, 123.6, 53.1, 52.8, 33.0, 32.6, 22.6, 13.9; HRMS Calculated for $C_{19}H_{21}NO_4Na$ $[M+Na]^+$ 350.1368, found 350.1374.

*4.2.18. Dimethyl 4-cyclohexyl-6-phenylpyridine-2,3-dicarboxyla-te (**2r**).* Unknown compound, colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, J=6.7 Hz, 2H), 7.80 (s, 1H), 7.47 (m, 3H), 3.98 (s, 6H ($2CH_3$)), 2.69 (t, J=10.4 Hz, 1H), 1.90 (dd, J=25.2, 12.1 Hz, 4H), 1.79 (d, J=12.3 Hz, 1H), 1.54–1.24 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 166.0, 158.2, 156.1, 145.7, 138.3, 129.8, 129.3, 129.0, 127.5, 120.9, 53.2, 52.9, 41.5, 33.7, 26.6, 26.0; HRMS Calculated for $C_{21}H_{23}NO_4Na$ $[M+Na]^+$ 376.1525, found 376.1512.

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Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.10.038.

References and notes

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