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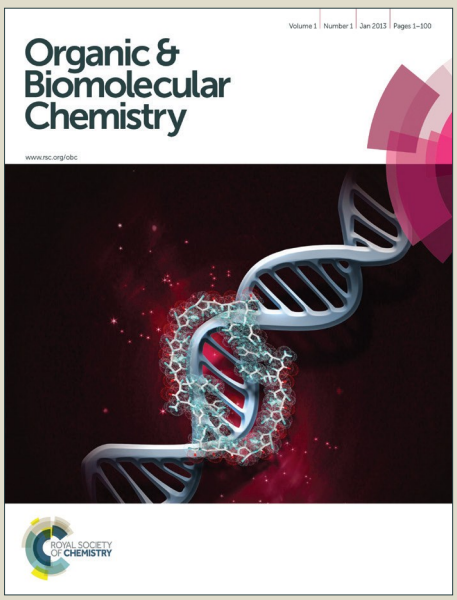

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Journal Name

ARTICLE

Synthesis of 6-substituted 2-phenacylpyridines from 2-(phenylethynyl)pyridine *via* isoxazolo[2,3-*a*]pyridinium salt

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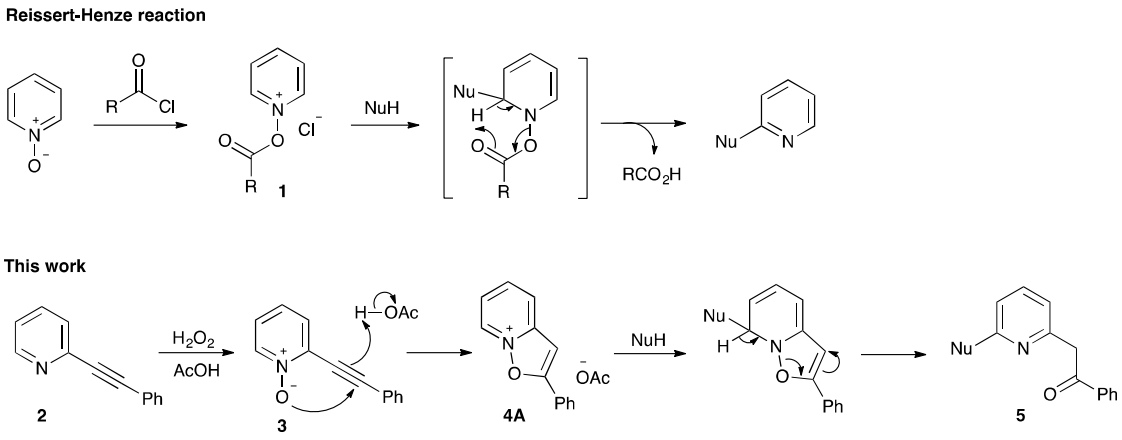
Abstract. When 2-(phenylethynyl)pyridine was oxidized, the formed *N*-oxide immediately cyclized at the ethynyl group to form isoxazolo[2,3-*a*]pyridinium salt. This salt underwent Reissert-Henze-type reactions with alcohol in the presence of a base to afford 6-substituted 2-phenacylpyridines, which are not easily synthesized through alternative procedures. When acetonitrile was used as a solvent, an amide functional group was introduced into the phenacylpyridine framework. Moreover, hetero-atom at the 6-position facilitated the oxidation of the phenacyl group to afford α-diketone upon simple exposure of the reaction mixture to air.

Introduction

Reissert-Henze reactions using *N*-acyloxypyridinium halides **1** (Reissert-Henze salts) are known as one of the most useful methods for the functionalization of pyridine rings, leading to 2-functionalized pyridines via nucleophilic addition and, rearomatization with the concomitant elimination of a carboxylic acid (Scheme 1).[1] Ethynylpyridines **2** have been widely used as synthetic intermediates for DNA-cleaving antitumor agents,[2] lobelane. Their transformation into various bicyclic pyrido compounds has also been reported.[3] Ethynylpyridine *N*-oxides can serve as key precursors for the construction of a larger compound library using Reissert-Henze reactions if they become easily available. While 4-ethynylpyridine *N*-oxides are readily obtained by the oxidation of 4-ethynylpyridine,[4] 2-ethynylpyridine *N*-oxides **3** are hitherto unknown. This fact prompted us to study the oxidation of 2-ethynylpyridine **2**.



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Electronic Supplementary Information (ESI) available: ^{1}H and ^{13}C NMR spectral data of compounds **7**, **9**, **11** and **14**. X-ray crystallographic data of **9a**. CCDC 1502083. For ESI and crystallographic data in CIF or other electronic format. See DOI: 10.1039/x0xx00000x

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Scheme 1 Reiisert-Henze reaction and similar type reaction using isoxazolopyridinium salt **4A**

It was found that the initially formed *N*-oxide **3** spontaneously converted to an isoxazolopyridinium salt **4A** by the intramolecular attack of the *N*-oxide onto an ethynyl group. This salt has both an electron-deficient pyridinium ring and a good enolate ion leaving group, similar to Reissert-Henze salt **1**. These structural features are considered to facilitate the synthesis of versatile 6-substituted 2-phenacylpyridines **3** upon treatment of salt **2a** with a nucleophile.

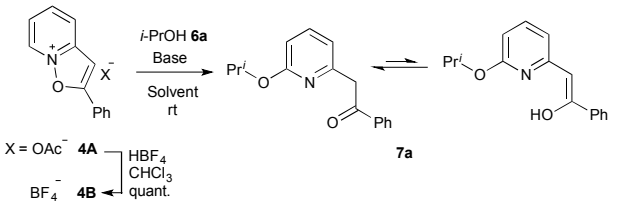
2-Phenacylpyridine derivatives **5** are widely used as antibacterial agents,[5] 11βHSD inhibitors,[6] and ligands.[7] In addition, 2-phenacylpyridines are important synthetic intermediates for the construction of the 4*H*-quinolizin-4-one scaffold, which has potential applications in the treatment of Alzheimer's disease,[8] Type 2 diabetes[9] and HIV,[10] and serves as precursors for some interesting alkaloids such as hydrangea,[11] lamellarins,[12] and sedamine.[13] Furthermore, 2-phenacylpyridine derivatives serve as precursors to indolizine derivatives for CRTH2 receptors,[14] bicyclic pyridines,[3] and bioactive natural products.[13]

2-Phenacylpyridine derivatives **5** are generally synthesized by hydration of the corresponding 2-(phenylethylnyl)pyridines (**2**) or by condensation of 2-picolyllithium with methyl benzoate.[15] However, these methods suffer from poor availability of the starting materials, require strong acidic conditions, and involve the use of toxic mercury salt as the catalysts. Transition-metal catalyzed carbonylative coupling reactions have recently been identified as possible routes to functionalized phenacylpyridines;[16] however, a purification step to avoid contamination of the products by metal species is necessary, which increases the cost of preparation of **5**. Other synthetic methods using a strong base such as BuLi, LDA, PhLi, or $NaNH_2$ sometimes suffer from low yields of the products and poor functional group tolerance.[17] Therefore, the development of efficient inexpensive, facile, and environmentally benign methods for synthesizing functionalized phenacylpyridines is highly desired. From this viewpoint, the development of a new synthetic method for 6-substituted 2-phenacylpyridines **5** was considered in this work. The obtained compounds were found to undergo oxidation, affording the corresponding α-diketones without any further treatment.

Results and Discussion

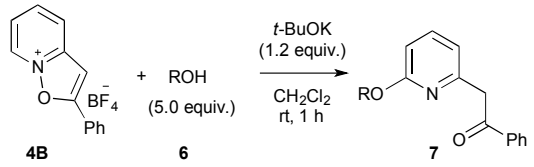
Initially, oxidation of ethynylpyridine **2** with H_2O_2-AcOH was carried out at 80 °C for 4 h. NMR examination of the reaction mixture indicated that isoxazolo[2,3-*a*]pyridinium acetate **4A**[18] was formed as an oily liquid, which was difficult to handle because of its instability and high viscosity. Thus, anion exchange was performed by the addition of HBF_4 to the reaction mixture affording salt **4B** as a yellow solid in quantitative yield; this salt was more stable and easily treatable than salt **4A**. The reaction of salt **4B** with *i*-PrOH **6a** in the presence of *t*-BuOK yielded alkoxylated phenacylpyridine **7a** and a mixture of keto-enol tautomers in 3:2 ratio. Optimization of the reaction conditions was performed using this reaction as the model reaction (Table 1). Among the several solvents tested, CH_2Cl_2 was found to be the most suitable for this reaction (entries 1–4). The reaction proceeded to completion within 1 h (entry 5). Although NEt_3 could also be used as a base, the efficiency in this case was lower than that observed when using *t*-BuOK. Consequently, the reaction conditions corresponding to entry 5 were determined to be the optimal conditions.

Table 1. Optimization of reaction conditions



entry	Solv.	Time/h	Base	Yield/%
1	DMSO	3	*t*-BuOK	0
2	THF	3	*t*-BuOK	0
3	$CHCl_3$	3	*t*-BuOK	60
4	CH_2Cl_2	3	*t*-BuOK	81
5	CH_2Cl_2	1	*t*-BuOK	79
6	CH_2Cl_2	20	NEt_3	45

Table 2. Synthesis of 6-alkoxylated phenacylpyridines **7**



entry	R		Yield/%
1	Me	**b**	98
2	Et	**c**	87
3	*t*-Bu	**d**	42
4	$PhCH_2$	**e**	25
5	$PhCh_2CH_2$	**f**	37
6	$HOCH_2CH_2$	**g**	58
7	$ClCH_2CH_2CH_2$	**h**	56
8	CH_2=$CHCH_2$	**i**	41
9	HC≡CCH_2	**j**	14
10[a]	H	**k**	48

[a] K_2CO_3 was used as a base.

With the optimized conditions in hand, we studied the substtrate scope of this method by conducting the reaction of salt **4B** with alcohols **6b–k** in the presence of *t*-BuOK (Table 2). In the reaction with MeOH **6b**, 6-methoxy-2-phenacylpyridine **7b** was obtained in excellent yield (entry 1). A bulky alkoxy

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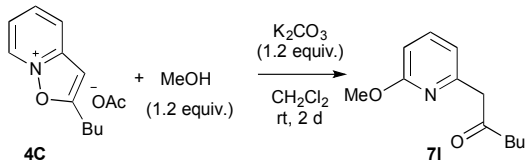
group could be introduced into the 6-position of the 2-phenacylpyridine framework, although the yields were reduced because of the competitive reaction of **4B** with water in the solvent (entries 2–5). This method was also applicable to alcohols **6g–j** having a functional group such as OH, Cl, CH=CH_2, and C≡CH and a series of 6-functionalized 2-phenacylpyridines **7g–j** were obtained (entries 6–9). Water reacted in a similar fashion, furnishing 6-hydroxy derivative **3k**. However, a complex mixture was obtained because **3k** is somewhat reactive, which results in further transformation to afford unidentified products (entry 10). It was also confirmed that alkyl substituted isoxazolopyridinium salt **4C** also underwent the reaction similarly to afford 2,6-disubstituted pyridine **7l** although the reaction conditions should be optimized (Scheme 2).



Scheme 2. Ring opening reaction of alkyl substituted isoxazolopyridinium salt **4C**

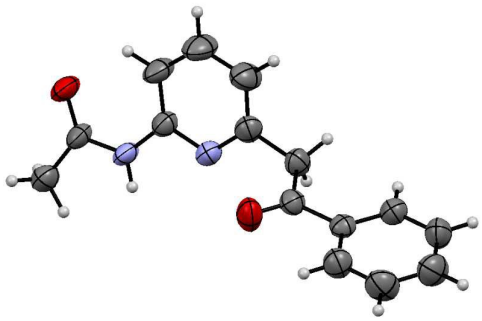
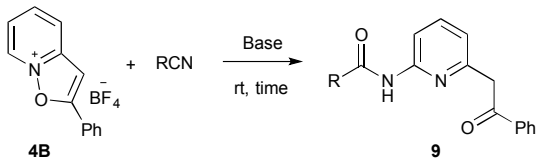


Figure 1. An ORTEP drawing of **9a**

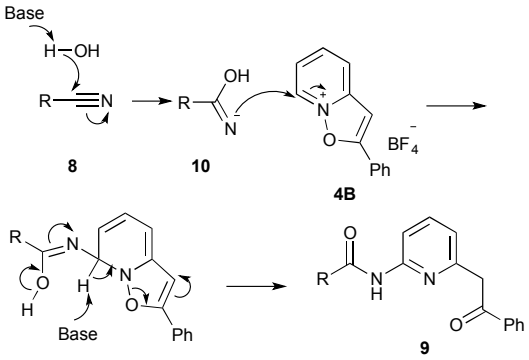
When the reaction of isoxazolopyridinium salt **4B** with *i*-PrOH **6a** was conducted in MeCN **8a**, a different reactivity was observed. Namely, an acetylamino group was introduced to the 6-position of 2-phenacylpyridine, affording **9a** without any detectable amount of alkoxylated 2-phenacylpyridine **7a**. The product **9a** also exists as a mixture of keto-enol tautomers in 6:1 ratio. The structure of **9a** was confirmed by both X-ray crystallography and spectral data (Figure 1). In this case, K_2CO_3 is the best choice, as it affords the highest yield of product **9a** (Table 3, entries 1–3). Furthermore, propanoylamino, isopropanoylamino, acryloylamino and phenylacetyl groups could be introduced to afford products **9b–e** in good yields (entries 4–7).Furthermore, this reaction was applicable to aromatic nitrile leading to aroylamino pyridine **9f**. This reaction is considered to proceed by the *N*-attack of intermediate **10** generated by the addition of hydroxide ion to nitrile (Scheme 3).

Table 3. Synthesis of 6-acylaminated 2-phenacylpyridines **9**



entry	R		Time/h	Base (equiv.)	Yield/%
1[a]	Me	**a**	3	*t*-BuOK (5)	24
2[a]	Me	**a**	20	Na_2CO_3 (1)	47
3[a]	Me	**a**	20	K_2CO_3 (1.2)	91
4[a]	Et	**b**	20	K_2CO_3 (1.2)	98
5[b]	*i*-Pr	**c**	20	K_2CO_3 (1.2)	64
6[b]	CH_2=CH	**d**	20	K_2CO_3 (1.2)	43
7[b]	$PhCH_2$	**e**	20	K_2CO_3 (1.2)	38
8[b]	*p*-ClC_6H_4	**f**	20	K_2CO_3 (1.2)	52

[a] Nitrile was used as the solvent. [b] 5 equivalents of nitrile were added to a solution of **4B** in CH_2Cl_2.



Scheme 3. A plausible mechanism for forming **9**

Unexpectedly, the obtained 6-alkoxy-2-phenacylpyridines **7a** and **7b** underwent oxidation to yield the corresponding α-diketones **11a** and **11b** when allowed to stand at room temperature in air or oxygen atmosphere under light (Table 4, entries 1–3).[19] Unsubstituted phenacylpyridine **12** showed no change under the same conditions (entry 4). When oxidation of **7b** was performed using oxidants such as *m*CPBA, diketone **11b** was efficiently obtained (entry 5). Although 6-methoxy-2-phenacylpyridine **7b** was readily oxidized, it could be stored without any problem under nitrogen atmosphere under dark (entry 6). Similar oxidations were also observed for **7a** and **9a**, yielding the corresponding α-diketones **11a** and **14**, respectively, although the yield was lower (entries 7–10). On the other hand, no conversion of **7b** was observed upon treatment with TEMPO resulting in the quantitative recovery of **7b** (entry 11). These results indicate that a hetero-atom at

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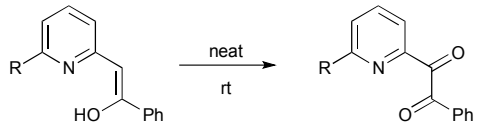
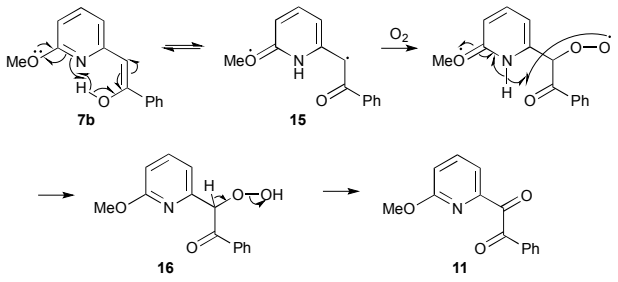
the 6-position is crucial for oxidation of the phenacyl group, and this oxidation proceeds via the radical mechanism, as illustrated in Scheme 4. The hetero-atom is considered to serve as a single electron donor to form diradical **15**, which traps molecular oxygen to give hydroperoxide **16**. The subsequent dehydration furnishes α-diketones **11** and **14**. A detailed study of the reaction mechanism is now in progress, and the results will be reported in due course.

Table 4. Oxidation of the phenacyl group leading to α-diketone



entry	Substrate R		Time/d	Atmosphere	Product	Yield/%
1	MeO	**7b**	3	air	**11b**	17
2	MeO	**7b**	12	air	**11b**	52
3	MeO	**7b**	5	O_2	**11b**	36
4[a]	H	**12**	5	O_2	**13**	0
5[b]	MeO	**7b**	1	Ar	**11b**	86
6	MeO	**7b**	5	N_2	**11b**	0
7	*i*-PrO	**7a**	5	air	**11a**	27
8[b]	*i*-PrO	**7a**	1	Ar	**11a**	40
9	AcNH	**9a**	3	air	**14**	trace
10[b]	AcNH	**9a**	4	Ar	**14**	49
11[c]	MeO	**7b**	12	air	**11b**	0

[a] Heated at 60 °C. [b] *m*CPBA (2equiv.) was added. [c] TEMPO (5 equiv.) was added.



Scheme 4. A plausible mechanism for the oxidation of phenacylpyridine **7b**

Recently, hetaryl α-diketones have attracted much attention because of their interesting physiological and biological activities.[20] These compounds are useful synthetic intermediates for pharmaceuticals exhibiting antiinflammatory,[21] antinociceptive,[21a] antipyretic[21a] and antirheumatiod activities.[22] However, the synthetic methods for α-diketones suffer from several disadvantages.[23] Fortunately, our synthetic method proceeds under mild conditions, gives good product yields, and has operational simplicity. Thus, we believe that this new approach will find broad utility in the design and synthesis of aforementioned α-diketones.

Conclusions

In summary, we present a facile and efficient synthetic route to 6-functionalized 2-phenacylpyridines starting from the cheap and readily available 2-(phenylethynyl)pyridine. The oxidation of these products was also investigated, which furnished the corresponding α-diketones in good yields without any further treatment. This method requires only simple manipulations under mild conditions, and is transition-metal free. Thus, this method would be advantageous for the construction of a vast library of functionalized phenacylpyridines.

Experimental Section

General information

All the reagents and solvents were commercially available and used as received. The ^{1}H NMR spectra were measured on a Bruker Ascend-400 at 400 MHz with TMS as an internal standard. The ^{13}C NMR spectra were measured on a Bruker Ascend-400 at 100 MHz, and assignments were performed by DEPT experiments. The IR spectra were recorded on a JASCO FT/IR-4200 spectrometer. The melting points were determined on a Yanaco micro-melting-points apparatus, and were uncorrected. The high resolution mass spectra were measured on a AB SCIEX Triple TOF 4600. X-ray diffraction was made on a Rigaku AFC7R diffractometer with graphite monochromatized Mo-Kα radiation.

General procedure for the formation of salt 4

To a solution of 2-(phenylethynyl)pyridine **1** (360 mg, 2 mmol), were added H_2O_2 (412 μl, 4 mmol) and AcOH (1.8 ml, 4 mmol), and the resultant mixture was heated at 80 °C for 4 h. The reaction mixture was then concentrated in vacuo to afford salt **4A** as oily liquid. Then, a solution of HBF_4 (134 μl, 4 mmol) in CH_2Cl_2 (100 μl) was added to salt **4A**; and the mixture was washed with ethyl acetate (1 × 10 mL). After removal of solvent, the yellow solid **4B** was obtained (549.0 mg, 1.94 mmol, 97%).

2-Phenylisoxazolo[2,3-*a*]pyridinium tetrafluoroborate (4B)

Yellow solid; mp = 162–163 °C

^{1}H NMR (DMSO-d_6, 400 MHz): 9.86 (d, *J* = 7.1 Hz, 1H), 8.44 (dd, *J* = 8.4, 8.4 Hz, 1H), 8.41 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.16 (s, 1H), 8.11–8.08 (m, 2H), 7.94 (ddd, *J* = 8.4, 7.1, 1.6 Hz, 1H), 7.76–7.70 (m, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz): 194.0 (C), 145.4 (C), 139.7 (CH), 133.2 (CH), 131.1 (CH), 129.8 (CH), 126.8 (CH), 123.4 (C), 121.6 (CH), 121.1 (C), 98.9 (CH); ^{11}B NMR (DMSO-d_6, 128 MHz): –1.29; ^{19}F NMR (DMSO-d_6, 376 MHz): –148.4;HRMS Calcd for ($M–BF_4^-$) $C_{13}H_9NO$: 196.0749, found: 196.0757.

General experimental procedure for the formation of 2-benzoylmethyl-6-(2-propoxy)pyridine (7a)

To a solution of salt **4B** (57 mg, 0.2 mmol) in $CHCl_3$ (5 mL), *i*-PrOH (**6a**, 0.8 ml, 1 mmol) and *t*-BuOK (27 mg, 0.24 mmol) were added, and the resultant mixture was stirred at room temperature for 1 h. The insoluble materials were removed by filtration and the filtrate was concentrated. Extraction of

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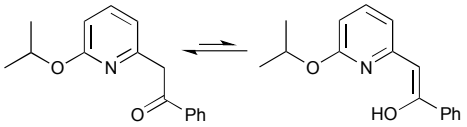
the residue with acetonitrile (1 × 10 mL) afforded almost pure phenacylpyridine **7a** as yellow oil (31 mg, 0.12 mmol, 60%).

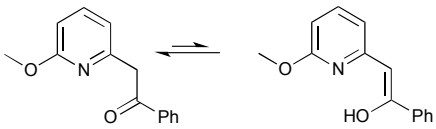
The reactions of the salt **4B** with other alcohols **6** were performed in a similar manner.



Yellow oil (keto form : enol form = 3 : 2)

^{1}H NMR ($CDCl_3$, 400 MHz): keto form: 8.08 (dd, *J* = 7.2, 2.0 Hz, 2H), 7.53–7.38 (m, 4H), 6.81 (d, *J* = 7.2 Hz, 1H), 6.51 (d, *J* = 7.6 Hz, 1H), 5.19 (sep, *J* = 6.0 Hz, 1H), 4.33 (s, 2H), 1.24 (d, *J* = 6.0 Hz, 6H); enol form: 14.03 (s, 1H), 7.80 (dd, *J* = 8.0, 2.0 Hz, 2H), 7.53–7.38 (m, 4H), 6.65 (d, *J* = 7.6 Hz, 1H), 6.46 (dd, *J* = 8.4, 0.8 Hz, 1H), 6.05 (s, 1H), 5.19 (sep, *J* = 6.4 Hz, 1H), 1.38 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): keto form: 197.2 (C), 163.1 (C), 152.8 (C), 139.0 (CH), 136.8 (C), 133.0 (CH), 129.0 (CH), 128.4 (CH), 116.0 (CH), 109.3 (CH), 67.9 (CH), 48.2 (CH_2), 21.9 (CH_3); enol form: 161.0 (C), 160.4 (C), 155.9 (C), 139.7 (CH), 136.0 (C), 129.1 (CH), 128.3 (CH), 125.3 (CH), 113.8 (CH), 107.4 (CH), 95.8 (CH), 69.0 (CH), 22.9 (CH_3); IR (neat): 1683, 1275 cm^{-1}; HRMS Calcd for (M+H) $C_{16}H_{18}NO_2$: 256.1332, found: 256.1337.

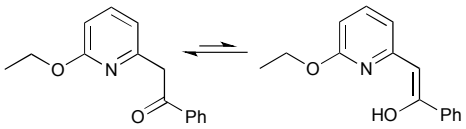
2- Benzoylmethyl-6-methoxypyridine (7b)



Yellow oil (keto form : enol form = 2 : 1)

^{1}H NMR ($CDCl_3$, 400 MHz): keto form: 8.08 (dd, *J* = 8.0, 1.2 Hz, 2H), 7.55–7.35 (m, 4H), 6.84 (d, *J* = 7.2 Hz, 1H), 6.57 (d, *J* = 8.4 Hz, 1H), 4.35 (s, 2H), 3.83 (s, 3H); enol form: 14.05 (s, 1H), 7.80 (dd, *J* = 8.4, 2.0 Hz, 2H), 7.55–7.35 (m, 4H), 6.66 (dd, *J* = 7.2, 0.4 Hz, 1H), 6.50 (dd, *J* = 8.0, 0.4 Hz, 1H), 6.05 (s, 1H), 3.99 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): keto form: 197.1 (C), 163.8 (C), 152.8 (C), 139.0 (CH), 136.8 (C), 132.9 (CH), 128.9 (CH), 128.5 (CH), 116.6 (CH), 108.7 (CH), 53.3 (CH_3), 48.2 (CH_2); enol form: 161.9 (C), 160.5 (C), 156.0 (C), 139.7 (CH), 135.9 (C), 129.2 (CH), 128.4 (CH), 125.3 (CH), 114.1 (CH), 106.5 (CH), 95.8 (CH), 53.4 (CH_3); IR (neat): 1685, 1268 cm^{-1}; HRMS Calcd for (M+H) $C_{14}H_{14}NO_2$: 228.1019, found: 228.1016.

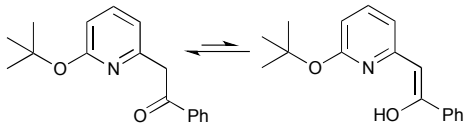
2- Benzoylmethyl-6-ethoxypyridine (7c)



Yellow oil (keto form : enol form = 1 : 1)

^{1}H NMR ($CDCl_3$, 400 MHz): keto form: 8.09 (dd, *J* = 7.6, 0.8 Hz, 2H), 7.55–7.36 (m, 4H), 6.84 (d, *J* = 7.2 Hz, 1H), 6.49 (d, *J* = 8.4 Hz, 1H), 4.41 (q, *J* = 7.2 Hz, 2H), 4.36 (s, 2H), 1.47 (t, *J* = 7.2 Hz, 3H); enol form: 14.10 (s, 1H), 7.82 (dd, *J* = 6.8, 2.4 Hz, 2H), 7.55–7.36 (m, 4H), 6.67 (d, *J* = 7.6 Hz, 1H), 6.55 (d, *J* = 8.0 Hz, 1H), 6.05 (s, 1H), 4.27 (q, *J* = 6.8 Hz, 2H), 1.31 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): keto form: 197.1 (C), 163.5 (C), 152.8 (C), 139.0 (CH), 138.7 (C), 133.0 (CH), 129.0 (CH), 128.5 (CH), 116.4 (CH), 108.7 (CH), 62.2 (CH_2), 62.6 (CH_2), 29.1 (CH_3); enol form: 161.5 (C), 160.5 (C), 156.0 (C), 139.6 (CH), 136.8 (C), 129.2 (CH), 128.3 (CH), 125.2 (CH), 113.9 (CH), 106.7 (CH), 95.8 (CH), 48.2 (CH_2), 14.6 (CH_3); IR (neat): 1684, 1265 cm^{-1}; HRMS Calcd for (M+H) $C_{15}H_{16}NO_2$: 242.1176, found: 242.1177.

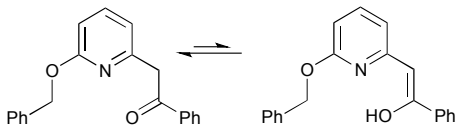
2-Benzoylmethyl-(6-tert-butoxy)pyridine (7d)



Yellow oil (keto form : enol form = 7 : 1)

^{1}H NMR ($CDCl_3$, 400 MHz): keto form: 8.08 (dd, *J* = 8.8, 1.2 Hz, 2H), 7.54–7.37 (m, 4H), 6.80 (d, *J* = 7.2 Hz, 1H), 6.48 (d, *J* = 8.0 Hz, 1H), 4.32 (s, 2H), 1.46 (s, 9H); enol form: 14.02 (s, 1H), 7.82 (dd, *J* = 8.4, 2.0 Hz, 2H), 7.54–7.37 (m, 4H), 6.79 (d, *J* = 7.6 Hz, 1H), 6.49 (d, *J* = 8.0 Hz, 1H), 6.03 (s, 1H), 1.60 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): keto form: 197.3 (C), 163.5 (C), 152.6 (C), 138.7 (CH), 136.8 (C), 132.9 (CH), 129.0 (CH), 128.7 (CH), 115.8 (CH), 111.2 (CH), 79.5 (C), 48.1 (CH_2), 28.6 (CH_3); enol form: 161.3 (C), 155.9 (C), 139.4 (CH), 135.9 (C), 129.1 (CH), 128.9 (C), 128.5 (CH), 125.3 (CH), 114.8 (CH), 110.5 (CH), 95.9 (CH), 79.5 (C), 29.1 (CH_3); IR (neat): 1643, 1262 cm^{-1}; HRMS Calcd for (M+H) $C_{17}H_{20}NO_2$: 270.1488, found: 270.1478.

2-Benzoylmethyl-6-benzyloxypyridine (7e)



Yellow oil (keto form : enol form = 3 : 1)

^{1}H NMR ($CDCl_3$, 400 MHz): keto form: 8.07 (dd, *J* = 8.0, 0.8 Hz, 2H), 7.58–7.28 (m, 9H), 6.87 (d, *J* = 7.2 Hz, 1H), 6.64 (d, *J* = 8.0 Hz, 1H), 5.29 (s, 2H), 4.36 (s, 2H); enol form: 13.90 (s, 1H), 7.82 (dd, *J* = 8.0, 0.8 Hz, 2H), 7.58–7.28 (m, 9H), 6.71 (d, *J* = 7.6 Hz, 1H), 6.58 (d, *J* = 8.0 Hz, 1H), 6.09 (s, 1H), 5.39 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): keto form: 197.0 (C), 163.2 (C), 152.8 (C), 139.2 (CH), 137.5 (C), 136.8 (C), 133.1 (CH), 129.0 (CH), 128.5 (CH), 128.4 (CH), 128.1 (CH), 127.1 (CH), 116.8 (CH), 109.2 (CH), 67.5 (CH_2), 48.2 (CH_2); enol form: 161.4 (C), 160.5 (C), 156.0 (C), 139.8 (CH), 136.3 (C), 135.9 (C), 129.2 (CH), 128.6 (CH), 128.4 (CH), 128.2 (CH), 128.0 (CH), 125.3 (CH), 114.4 (CH), 106.9 (CH), 95.8 (CH), 68.3 (CH_2); IR (neat): 1684, 1305 cm^{-1}; HRMS Calcd for (M+H) $C_{20}H_{18}NO_2$: 304.1132, found: 304.1135.

2-Benzoylmethyl-6-(2-phenylethoxy)pyridine (7f)

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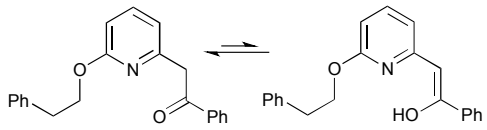
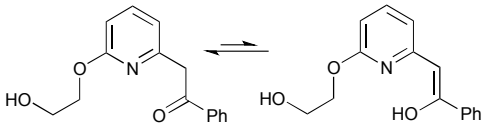
DOI: 10.1039/C6OB01942K



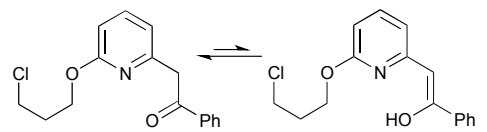
Yellow oil (keto form : enol form = 3 : 1)
^{1}H NMR ($CDCl_3$, 400 MHz): keto form: 8.06 (dd, *J* = 8.4, 0.8 Hz, 2H), 7.53–7.28 (m, 9H), 6.84 (d, *J* = 7.2 Hz, 1H), 6.55 (d, *J* = 8.4 Hz, 1H), 4.43 (t, *J* = 7.2 Hz, 2H), 4.33 (s, 2H), 2.99 (t, *J* = 7.2 Hz, 2H); enol form: 13.99 (s, 1H), 7.80 (dd, *J* = 8.0, 0.8 Hz, 2H), 7.53 –7.28 (m, 9H), 6.67 (d, *J* = 7.6 Hz, 1H), 6.49 (d, *J* = 8.4 Hz, 1H), 6.04 (s, 1H), 4.55 (t, *J* = 6.8 Hz, 2H), 3.15 (t, *J* = 6.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): keto form: 197.1 (C), 163.3 (C), 152.8 (C), 139.1 (CH), 138.6 (C), 136.8 (C), 133.1 (CH), 129.0 (three CH signals overlapped), 128.4 (CH), 126.3 (CH), 116.5 (CH), 108.9 (CH), 66.4 (CH_2), 48.1 (CH_2), 35.4 (CH_2); enol form: 161.4 (C), 160.5 (C), 156.0 (C), 139.7 (CH), 138.1 (C), 135.9 (C), 129.2 (CH), 129.1 (CH), 128.3 (two CH signals overlapped), 126.5 (CH), 125.3 (CH), 114.1 (CH), 106.8 (CH), 95.8 (CH), 66.9 (CH_2), 35.5 (CH_2); IR (neat): 1695, 1266 cm^{-1}; HRMS Calcd for (M+H) $C_{21}H_{20}NO_2$: 318.1488, found: 318.1473.

2-Benzoylmethyl-6-(2-hydroxyethoxy)pyridine (7g)



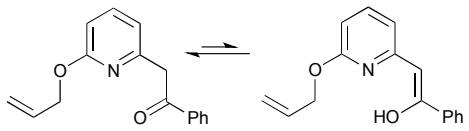
Yellow oil (keto form : enol form = 6 : 1)
^{1}H NMR ($CDCl_3$, 400 MHz): keto form: 8.07–8.03 (m, 2H), 7.58 –7.38 (m, 4H), 6.90 (d, *J* = 7.2 Hz, 1H), 6.66 (d, *J* = 8.0 Hz, 1H), 4.40 (t, *J* = 6.4 Hz, 2H), 4.36 (s, 2H), 3.88 (t, *J* = 6.4 Hz, 2H), 1.58 (br s, 1H); enol form: 13.90 (s, 1H), 7.80 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.58–7.38 (m, 4H), 6.72 (dd, *J* = 7.6, 0.8 Hz, 1H), 6.55 (dd, *J* = 8.4, 0.8 Hz, 1H), 6.10 (s, 1H), 4.01 (t, *J* = 9.2 Hz, 2H), 3.95 (t, *J* = 9.2 Hz, 2H), 2.17 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): keto form: 196.6 (C), 163.5 (C), 152.5 (C), 139.6 (CH), 136.6 (C), 133.2 (CH), 128.6 (CH), 128.4 (CH), 117.2 (CH), 109.3 (CH), 68.4 (CH_2), 62.6 (CH_2), 47.7 (CH_2); enol form: 160.1 (C), 156.5 (C), 139.9 (CH), 135.9 (C), 133.1(C), 129.7 (CH), 128.4 (CH), 125.3 (CH), 114.5 (CH), 106.6 (CH), 95.7 (CH), 67.7 (CH_2), 61.2 (CH_2); IR (neat): 1682, 1265, 1207 cm^{-1}; HRMS Calcd for (M+H) $C_{15}H_{16}NO_3$: 258.1125, found: 258.1123.

2-Benzoylmethyl-6-(3-chloro-1-propoxy)pyridine (7h)



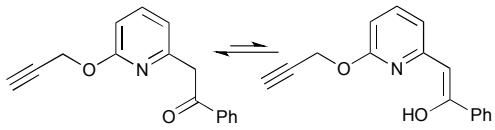
Yellow oil (keto form : enol form = 3 : 2)
^{1}H NMR ($CDCl_3$, 400 MHz): keto form: 8.07 (dd, *J* = 7.2, 1.2 Hz, 2H), 7.57–7.37 (m, 4H), 6.87 (d, *J* = 7.2 Hz, 1H), 6.58 (d, *J* = 8.4 Hz, 1H), 4.36 (t, *J* = 6.4 Hz, 2H), 4.34 (s, 2H), 3.65 (t, *J* = 6.4 Hz, 2H), 2.13 (tt, *J* = 6.4, 6.4 Hz, 2H); enol form: 13.90 (s, 1H), 7.81 (dd, *J* = 8.4, 1.6 Hz, 2H), 7.57–7.37 (m, 4H), 6.69 (d, *J* = 7.6 Hz, 1H), 6.50 (d, *J* = 8.0 Hz, 1H), 6.06 (s, 1H), 4.48 (t, *J* = 6.4 Hz, 2H), 3.76 (t, *J* = 6.4 Hz, 2H), 2.29 (tt, *J* = 6.4, 6.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): keto form: 197.0 (C), 163.2 (C), 152.9 (C), 139.2 (CH), 136.8 (C), 133.1 (CH), 128.9 (CH), 128.5 (CH), 116.7 (CH), 108.8 (CH), 62.4 (CH_2),48.1 (CH_2), 41.7 (CH_2), 32.1 (CH_2); enol form: 161.3 (C), 160.6 (C), 156.1 (C), 139.8 (CH), 135.8 (C), 129.2 (CH), 128.3 (CH), 125.2 (CH), 114.3 (CH), 106.5 (CH), 95.7 (CH), 62.8 (CH_2), 41.3 (CH_2), 31.9 (CH_2); IR (neat): 1681, 1154 cm^{-1}; HRMS Calcd for (M+H) $C_{16}H_{17}ClNO_2$: 290.0942, found: 290.0949.

2-Benzoylmethyl-6-(2-propen-1-oxy)pyridine (7i)



Yellow oil (keto form : enol form = 3 : 1)
^{1}H NMR ($CDCl_3$, 400 MHz): keto form: 8.06 (dd, *J* = 8.0, 1.2 Hz, 2H), 7.57–7.38 (m, 4H), 6.85 (d, *J* = 7.2 Hz, 1H), 6.60 (d, *J* = 8.0 Hz, 1H), 6.02 - 5.98 (m, 1H), 5.35 (dd, *J* = 17.2, 1.6 Hz, 1H), 5.18 (dd, *J* = 11.2, 1.2 Hz, 1H), 4.75 (dd, *J* = 6.4, 1.2 Hz, 2H), 4.34 (s, 2H); enol form: 13.85 (s, 1H), 7.80 (dd, *J* = 8.0, 1.6 Hz, 2H), 7.57 –7.38 (m, 4H), 6.69 (d, *J* = 7.6 Hz, 1H), 6.56 (d, *J* = 8.4 Hz, 1H), 6.17 - 6.06 (m, 1H), 6.05 (s, 1H), 5.48 (dd, *J* = 17.2, 1.6 Hz, 1H), 5.34 (dd, *J* = 10.4, 1.6 Hz, 1H), 4.87 (dd, *J* = 5.2, 1.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): keto form: 197.0 (C), 163.0 (C), 152.8 (C), 139.1 (CH), 136.8 (C), 133.1 (CH), 132.6 (CH), 129.0 (CH), 128.5 (CH), 117.4 (CH_2), 116.7 (CH), 108.9 (CH), 66.5(CH_2), 48.2 (CH_2); enol form: 161.6 (C), 160.4 (C), 155.9 (C), 139.8 (CH), 135.9 (C), 133.7 (CH), 129.2 (CH), 128.4 (CH), 125.3 (CH), 118.2 (CH_2), 114.3 (CH), 106.8 (CH), 95.8 (CH), 67.1 (CH_2); IR (neat): 1682, 1263 cm^{-1}; HRMS Calcd for (M+H) $C_{16}H_{16}NO_2$: 254.1176, found: 254.1165.

2-Benzoylmethyl-6-(2-propynyloxy)pyridine (7j)



Yellow oil (keto form : enol form = 5 : 1)
^{1}H NMR ($CDCl_3$, 400 MHz): keto form: 8.08 (dd, *J* = 7.2, 1.2 Hz, 2H), 7.58–7.37 (m, 4H), 6.91 (d, *J* = 7.6 Hz, 1H), 6.66 (d, *J* = 8.4 Hz, 1H), 4.88 (d, *J* = 2.4 Hz, 2H), 4.37 (s, 2H), 2.40 (t, *J* = 2.4 Hz, 1H); enol form: 13.35 (s, 1H), 7.81 (dd, *J* = 8.4, 2.0 Hz, 2H), 7.58 –7.37 (m, 4H), 6.75 (d, *J* = 7.6 Hz, 1H), 6.58 (d, *J* = 8.0 Hz, 1H), 6.06 (s, 1H), 4.98 (d, *J* = 2.4 Hz, 2H), 2.55 (t, *J* = 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): keto form: 196.9 (C), 161.9 (C), 152.7 (C), 139.4 (CH), 136.8 (C), 133.1 (CH), 129.0 (CH), 128.5 (CH), 117.4 (CH), 109.1 (CH), 79.3 (C), 74.0 (CH), 53.3 (CH_2), 48.0 (CH_2); enol form: 161.5 (C),160.4 (C), 155.9 (C), 139.9 (CH), 135.8 (C), 129.3 (CH), 128.3 (CH), 125.3 (CH), 115.1 (CH), 106.8 (CH), 95.8 (CH), 77.2 (C), 75.4 (CH), 53.9 (CH_2); IR (neat): 1685, 1173 cm^{-1}; HRMS Calcd for (M+H) $C_{16}H_{14}NO_2$: 252.1019, found: 252.1011.

2-Benzoylmethyl-6-hydroxypyridine (7k)

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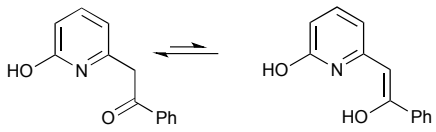
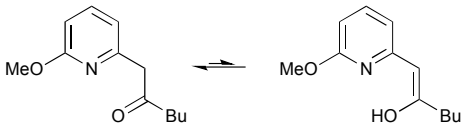
DOI: 10.1039/C6OB01942K



Yellow solid (keto form : enol form = 1 : 1); mp = 168–169 °C
^{1}H NMR ($CDCl_3$, 400 MHz): keto form: 12.29–12.20 (br, 1H), 8.03 (d, *J* = 7.6 Hz, 2H), 7.61 (t, *J* = 9.2 Hz, 1H), 7.50 (dd, *J* = 9.2, 7.6 Hz, 2H), 7.37 (dd, *J* = 9.2, 6.8 Hz, 1H), 6.42 (d, *J* = 9.2 Hz, 1H), 6.13 (d, *J* = 6.8 Hz, 1H), 4.25 (s, 2H); enol form: 14.40 (s, 1H), 7.72 (d, *J* = 7.2 Hz, 2H), 7.29–7.21 (m, 3H), 7.02 (dd, *J* = 8.4, 8.4 Hz, 1H), 5.75 (s, 1H), 5.42 (d, *J* = 8.4 Hz, 2H), 5.40 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): keto form: 194.6 (C), 165.1 (C), 149.9 (C), 141.4 (CH), 136.0 (C), 133.9 (CH), 128.9 (CH), 128.6 (CH), 118.5 (CH), 107.1 (CH), 41.9 (CH_2); enol form: 174.1 (C), 161.9 (C), 153.9 (C), 143.4 (C), 140.0 (CH), 127.4 (CH), 125.6 (CH), 104.2 (CH), 96.2 (CH), 83.5 (CH), 79.1 (CH); IR (neat): 1680 cm^{-1}; HRMS Calcd for (M+H) $C_{13}H_{12}NO_2$: 214.0863, found: 214.0855.

2-Methoxy-6-(2-oxo-1-hexyl)pyridine (7l)

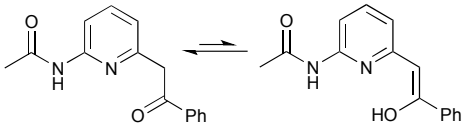


Yellow oil (keto form : enol form = 8 : 1)
^{1}H NMR ($CDCl_3$, 400 MHz): keto form: 7.50 (dd, *J* = 8.3, 7.2 Hz, 1H), 6.76 (d, *J* = 7.2 Hz, 1H), 6.61 (d, *J* = 8.3 Hz, 1H), 3.90 (s, 3H), 3.76 (s, 2H), 2.53 (t, *J* = 7.4 Hz, 2H), 1.60–1.53 (m, 2H), 1.34–1.24 (m, 2H), 0.87 (t, *J* = 7.3 Hz, 3H); enol form: 13.54 (s, 1H), 7.47 (dd, *J* = 8.2, 7.5 Hz, 1H), 6.49 (d, *J* = 7.5 Hz, 1H), 6.44 (d, *J* = 8.3 Hz, 1H), 5.29 (s, 1H), 3.94 (s, 3H), 2.25 (t, *J* = 7.6 Hz, 2H), 1.76–1.68 (m, 2H), 1.46–1.36 (m, 2H), 0.94 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): keto form: 208.0 (C), 163.8 (C), 152.6 (C), 139.0 (CH), 116.5 (CH), 108.2 (CH), 53.3 (CH_3), 52.1 (CH_2), 42.3 (CH_2), 25.8 (CH_2), 22.3 (CH_2), 13.8 (CH_3); enol form: signals of enol form were too small to be assigned; IR (ATR): 1712, 1265 cm^{-1}; HMRS Calcd for (M+H) $C_{12}H_{17}NO_2$: 208.1332, found: 208.1325.

General method for amidation of 4B

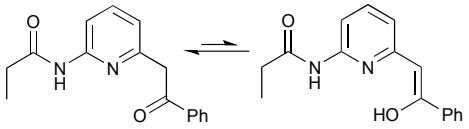
To a solution of salt **4B** (85 mg, 0.3 mmol) in acetonitrile (5 mL), potassium carbonate (50 mg, 0.36 mmol) was added, and the resultant mixture was stirred at room temperature for 20 h. The insoluble materials were removed by filtration and the filtrate was concentrated to afford amidated phenacylpyridine **9a** as yellow oil (70 mg, 0.273 mmol, 91%).
In the case of **9b**, propionitrile was used as a solvent instead of acetonitrile. In the case of **9c**, 5 equivalents of acrylonitrile were added in dichloromethane solution of **4B**.

6-Benzoylmethyl-2-ethanoylaminopyridine (9a)



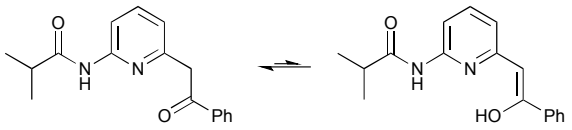
Yellow plates (keto form : enol form = 6 : 1)
Mp = 155–156 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): keto form: 8.06 (d, *J* = 8.0 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 2H), 7.84 (br s, 1H), 7.66 (dd, *J* = 8.0, 7.6 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.45 (dd, *J* = 8.0, 7.6 Hz, 2H), 7.02 (d, *J* = 7.6 Hz, 1H), 4.36 (s, 2H), 2.17 (s, 3H); enol form: 13.79 (s, 1H), 7.85 (br s, 1H), 7.82 (d, *J* = 8.0 Hz, 2H), 7.66 (t, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 7.6 Hz, 1H), 7.40 (dd, *J* = 8.0, 7.6 Hz, 1H), 7.39 (dd, *J* = 8.0, 8.0 Hz, 2H), 6.86 (d, *J* = 8.0 Hz, 1H), 6.05 (s, 1H), 2.24 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): keto form: 196.6 (C), (one signal for quaternary carbon lacked), 153.6 (C), 151.0 (C), 139.0 (CH), 136.6 (C), 133.3 (CH), 128.7 (two CH groups overlapped), 119.9 (CH), 111.8 (CH), 47.8 (CH_2), 24.7 (CH_3); enol form: 168.5 (C), 161.1 (C), 156.9 (C), (two signals for quaternary carbon lacked), 139.4 (CH), 128.6 (CH), 128.4 (CH), 125.3 (CH), 117.7 (CH), 109.5 (CH), 95.4 (CH), 24.8 (CH_3); IR (neat): 3430, 1642, 1455 cm^{-1}; HRMS Calcd for (M+H) $C_{15}H_{15}N_2O_2$: 255.1128, found: 255.1132.

2-Benzoylmethyl-6-propanolaminopyridine (9b)



Yellow oil (keto form : enol form = 6 : 1)
^{1}H NMR ($CDCl_3$, 400 MHz): keto form: 8.09 (d, *J* = 8.0 Hz, 1H), 8.01 (d, *J* = 7.6 Hz, 2H), 7.89 (br s, 1H), 7.66 (dd, *J* = 8.0, 7.6 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.46 (dd, *J* = 7.6, 7.6 Hz, 2H), 6.99 (d, *J* = 7.6 Hz, 1H), 4.35 (s, 2H), 2.39 (q, *J* = 7.6 Hz, 2H), 1.23 (t, *J* = 7.6 Hz, 3H); enol form: 13.04 (s, 1H), 7.92 (d, *J* = 8.0 Hz, 2H), 7.80 (br s, 1H), 7.78 (dd, *J* = 8.0, 6.8 Hz, 1H), 7.66 (t, *J* = 8.0 Hz, 1H), 7.40–7.37 (m, 3H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.04 (s, 1H), 2.45 (q, *J* = 7.6 Hz, 2H), 1.27 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): keto form: 196.6 (C), 172.3 (C), 153.5 (C), 151.1 (C), 138.9 (CH), 136.6 (C), 133.3 (CH), 128.9 (CH), 128.7 (CH), 119.8 (CH), 111.9 (CH), 47.8 (CH_2), 30.8 (CH_2), 9.3 (CH_3); enol form: 172.2 (C), 161.1 (C), 156.8 (C), 148.1 (C), 139.3 (CH), 135.7 (C), 129.4 (CH), 128.4 (CH), 125.3 (CH), 117.6 (CH), 109.5 (CH), 95.4 (CH), 30.9 (CH_2), 9.3 (CH_3); IR (neat): 3433, 1677, 1630 cm^{-1}; HRMS Calcd for (M+H) $C_{16}H_{17}N_2O_2$: 269.1286, found: 269.1289.

2-Benzoylmethyl-6-(2-methylpropanoyl)aminopyridine (9c)



Yellow oil (keto form : enol form = 3 : 2)
^{1}H NMR ($CDCl_3$, 400 MHz): keto form: 8.10 (d, *J* = 8.3 Hz, 1H), 8.03–8.01 (m, 2H), 7.85 (br, 1H), 7.64 (t, *J* = 7.9 Hz, 1H), 7.55 (tt, *J* = 7.4, 1.3 Hz, 1H), 7.48–7.36 (m, 2H), 7.00 (d, *J* = 7.1 Hz, 1H), 4.36 (s, 2H), 2.55–2.46 (m, 1H) 1.23 (d, *J* = 6.9 Hz, 6H); enol form: 13.83 (s, 1H), 7.93 (dd, *J* = 8.3, 0.7 Hz, 1H), 7.85 (br, 1H), 7.80–7.78 (m, 2H), 7.64 (t, *J* = 7.9 Hz, 1H), 7.48–7.36 (m, 3H), 6.84 (dd, *J* = 7.7, 0.7 Hz, 1H), 6.04 (s, 1H), 2.62–2.53 (m, 1H), 1.25 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): keto form: 196.6 (C), 175.5 (C), 153.5 (C), 151.2 (C), 138.9

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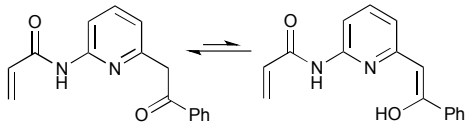
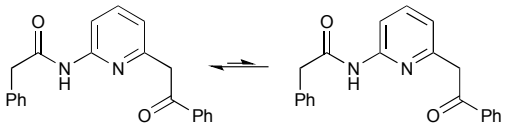
(CH), 136.6 (C), 133.3 (CH), 128.7 (CH), 128.6 (CH), 119.9 (CH), 111.9 (CH), 47.9 (CH_2), 36.8 (CH), 19.4 (CH_3); enol form: 161.0 (C), 156.8 (C), 148.3 (C), 139.3 (CH), 135.7 (C), 129.4 (CH), 128.4 (CH), 125.3 (CH), 117.6 (CH), 109.6 (CH), 95.4 (CH), 36.8 (CH), 19.4 (CH_3); IR (ATR): 1693, 1681 cm^{-1}; HMRS Calcd for (M+H) $C_{17}H_{18}N_2O_2$: 283.1441, found: 283.1443.

2-Benzoylmethyl-6-propenoylaminopyridine (9d)



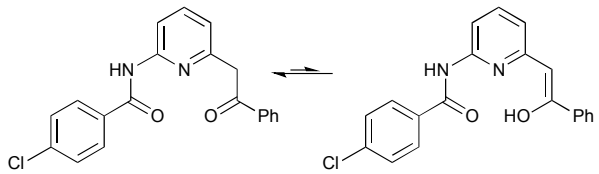
Yellow oil (keto form : enol form = 6 : 1)
^{1}H NMR ($CDCl_3$, 400 MHz): keto form: 8.21 (br s, 1H), 8.20 (d, *J* = 8.4 Hz, 1H), 8.02 (d, *J* = 8.4 Hz, 2H), 7.69 (t, *J* = 8.0 Hz, 1H), 7.59 (dd, *J* = 8.4, 7.6 Hz, 1H), 7.48 (dd, *J* = 8.4, 8.0 Hz, 2H), 7.04 (d, *J* = 7.6 Hz, 1H), 6.46 (dd, *J* = 16.8, 0.8 Hz, 1H), 6.28 (dd, *J* = 16.8, 6.4 Hz, 1H), 5.80 (dd, *J* = 6.4, 0.8 Hz, 1H), 4.38 (s, 2H); enol form: 9.93 (s, 1H), 7.96–7.92 (m, 6H), 7.80 (dd, *J* = 8.0, 2.0 Hz, 2H), 7.70 (t, *J* = 8.0 Hz, 1H), 6.48 (dd, *J* = 17.6, 0.8 Hz, 1H), 6.34 (dd, *J* = 7.6, 0.8 Hz, 1H), 6.06 (s, 1H), 5.87 (dd, *J* = 17.6, 7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): keto form: 196.5 (C), 163.6 (C), 153.6 (C), 151.1 (C), 132.9 (CH), 136.5 (C), 133.4 (CH), 128.7 (two CH groups overlapped), 128.5 (CH_2), 125.3 (CH), 120.3 (CH), 112.4 (CH), 27.6 (CH_2); enol form: signals of enol form were too small to be assigned; IR (neat): 3418, 1676, 1634 cm^{-1}; HRMS Calcd for (M+H) $C_{16}H_{15}N_2O_2$: 267.1128, found: 267.1138.

2-Benzoylmethyl-6-phenylethanoylaminopyridine (9e)



Dark brown oil (keto form : enol form = 2 : 1)
^{1}H NMR ($CDCl_3$, 400 MHz): keto form: 8.08 (d, *J* = 8.2 Hz, 1H), 8.00–7.98 (m, 2H), 7.75 (br, 1H), 7.65 (t, *J* = 7.9 Hz, 1H), 7.55 (tt, *J* = 7.4, 1.2 Hz, 1H), 7.46–7.31 (m, 7H), 6.99 (d, *J* = 7.4 Hz, 1H), 4.31 (s, 2H), 3.72 (s, 2H); enol form: 13.16 (s, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.80–7.76 (m, 2H), 7.69 (s, 1H), 7.46–7.31 (m, 8H), 6.83 (d, *J* = 7.7 Hz, 1H), 6.01 (s, 1H), 3.77 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): keto form: 196.6 (C), 169.3 (C), 153.5 (C), 150.8 (C), 138.9 (CH), 136.5 (C), 134.0 (C), 133.3 (CH) 129.4 (CH), 129.1 (CH), 128.7 (CH), 128.6 (CH), 127.6 (CH), 120.2 (CH), 111.9 (CH), 47.8 (CH_2), 45.0 (CH_2); enol form: signals of enol form were too small to be assigned; IR (ATR): 1693, 1687 cm^{-1}; HMRS Calcd for (M+H) $C_{21}H_{18}N_2O_2$: 331.1441, found: 331.1449.

2-Benzoylmethyl-6-(4-chlorobenzoylamino)pyridine (9f)



Yellow oil (keto form : enol form = 6 : 5)
^{1}H NMR ($CDCl_3$, 400 MHz): keto form: 8.42 (br, 1H), 8.21 (d, *J* = 8.2 Hz, 1H), 8.05–8.01 (m, 3H), 7.87–7.82 (m, 2H), 7.70 (t, *J* = 7.9 Hz, 1H), 7.56 (tt, *J* = 7.4, 1.3 Hz, 1H), 7.48–7.38 (m, 2H), 7.06 (d, *J* = 7.4 Hz, 1H), 4.38 (s, 2H); enol form: 13.73 (s, 1H), 8.36 (br, 1H), 7.87–7.82 (m, 2H), 7.80–7.78 (m, 2H), 7.48–7.38 (m, 7H), 6.90 (d, *J* = 7.7 Hz, 1H), 6.07 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): keto form: 196.6 (C), 164.5 (C), 153.8 (C), 151.0 (C), 139.1 (CH), 138.6 (C), 136.6 (C), 133.4 (CH), 132.6 (C), 129.1 (CH), 128.7 (CH), 128.7 (CH), 128.6 (CH), 120.5 (CH), 112.2 (CH), 47.8 (CH_2); enol form: 164.6 (C), 161.2 (C), 157.1 (C), 148.1 (C), 139.4 (CH), 138.8 (C), 138.6 (C), 135.6 (C), 132.5 (C), 129.5 (CH), 129.2 (CH), 129.1 (CH), 128.7 (CH), 128.4 (CH), 118.2 (CH), 109.9 (CH), 95.4 (CH); IR (ATR): 1687, 1680 cm^{-1}; HMRS Calcd for (M+H) $C_{20}H_{15}ClN_2O_2$: 351.0895, found: 351.0911.

6-Isopropoxy-2-(1,2-dioxo-2-phenylethyl)pyridine (11a)

Yellow oil
^{1}H NMR ($CDCl_3$, 400 MHz): 7.90 (dd, *J* = 8.4, 1.2 Hz, 2H), 7.78 - 7.74 (m, 2H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.51–7.47 (m, 2H), 6.89 (dd, *J* = 7.6, 2.8 Hz, 1H), 4.84 (sep, *J* = 6.4 Hz, 1H), 1.05 (d, *J* = 6.4 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): 197.2 (C), 195.4 (C), 162.9 (C), 148.8 (C), 139.3 (CH), 134.2 (CH), 133.7 (C), 129.1 (CH), 128.8 (CH), 117.5 (CH), 115.8 (CH), 62.9 (CH), 21.4 (CH_3); IR (neat): 1680, 1673, 1274 cm^{-1}; HRMS Calcd for (M+H) $C_{16}H_{16}NO_3$: 270.1125, found: 270.1123.

6-Methoxy-2-(1,2-dioxo-2-phenylethyl)pyridine (11b)

Yellow oil
^{1}H NMR ($CDCl_3$, 400 MHz): 7.91 (dd, *J* = 6.8, 6.8 Hz, 2H), 7.79 (d, *J* = 6.8 Hz, 2H), 7.63 (dd, *J* = 6.8, 2.0 Hz, 1H), 7.50 (dd, *J* = 6.8, 6.8 Hz, 1H), 7.49 (t, *J* = 6.8 Hz, 1H), 6.98 (dd, *J* = 6.8, 2.0 Hz, 1H), 3.64 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 196.7 (C), 195.1 (C), 163.6 (C), 148.8 (C), 139.3 (CH), 134.3 (CH), 133.6 (C), 129.2 (CH), 128.8 (CH), 116.9 (CH), 116.5 (CH), 53.5 (CH_3); IR (neat): 1791, 1680, 1275 cm^{-1}; HRMS Calcd for (M+H) $C_{14}H_{12}NO_3$: 242.0812, found: 242.0813.

6-Ethanoylamino-2-(1,2-dioxo-2-phenylethyl)pyridine (14)

Yellow oil
^{1}H NMR ($CDCl_3$, 400 MHz): 8.47 (br s, 1H), 8.09–7.91 (m, 5H), 7.68 (t, *J* = 6.0 Hz, 1H), 7.50 (dd, *J* = 8.0, 8.0 Hz, 2H), 2.16 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): 195.6 (C), 194.2 (C), 152.2 (C), 149.4 (C), 139.6 (CH), 134.7 (CH), 133.6 (C), 133.2 (C), 129.6 (CH), 128.9 (CH), 119.2 (CH), 118.8 (CH), 24.6 (CH_3); HRMS Calcd for (M+H) $C_{15}H_{13}N_2O_2$: 269.0921, found: 269.0920.

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