Heterogeneous gold(I)-catalysed annulation between 2-aminopyridines and propiolaldehydes leading to 3-acylimidazo[1,2-*a*]pyridines

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The heterogeneous annulation between 2-aminopyridines and propiolaldehydes was achieved in CH_2Cl_2 at 25 °C in the presence of 3 mol% of MCM-41-immobilised phosphine gold(I) complex (MCM-41-PPh_3-AuCl) and $AgSbF_6$ under air, yielding a variety of 3-acylimidazo[1,2-*a*]pyridines in good yields. This heterogeneous gold(I) catalyst can be easily prepared by a simple procedure, recovered by filtration of the reaction solution and recycled up to seven times without significant loss of activity.

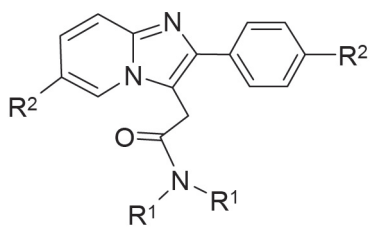
Keywords: gold, annulation, imidazo[1,2-*a*]pyridine, propiolaldehyde, heterogeneous catalysis

Imidazo[1,2-*a*]pyridine as a key core is found in numerous drugs and bioactive molecules, such as alpidem, saripidem, necopidem, minodronic acids and zolpidem (Fig. 1).[1] These drug molecules have been considered as attractive synthetic targets because of their excellent biological and pharmaceutical properties, including antibacterial, anxiolytic, antiulcer, antiviral, antiprotozoal, antiherpes and antiapoptotic activities.[2–4] As a result, many synthetic approaches have been developed for the construction of imidazo[1,2-*a*]pyridine scaffolds.[5] Traditional methods include the heterocyclisation of 2-aminopyridines with α-halocarbonyl compounds[6–8] and multicomponent coupling of 2-aminopyridines, aldehydes and ketones/alkynes/isonitriles.[9–11] Among a variety of new synthetic methods, transition metal-catalysed cyclisation reactions with various metals such as palladium,[12] copper,[13–16] silver[17,18] and iron[19] have proved to be a powerful and useful tool for the construction of imidazo[1,2-*a*]pyridines. Recently, Cao and co-workers reported copper(I)-catalysed synthesis of functionalised imidazo[1,2-*a*]pyridinealdehydes/ketones from propiolaldehydes and 2-aminopyridines by copper carbene oxidation using air as the sole oxidant [Scheme 1(a)].[20]

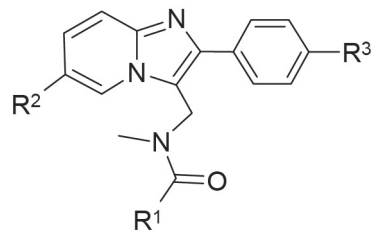
During the last few decades, homogeneous catalysis of organic transformations by gold complexes has become a powerful tool for the synthesis of valuable building blocks.[21] Gold-catalysed construction of heterocyclic compounds such as furans,[22] pyrroles,[23] indoles,[24] oxazoles[25] and butenolides[26] has attracted great interest due to their high efficiency and mild reaction conditions, which strongly enriched the synthetic methodologies of heterocycles. Recently, Cao *et al.* described gold(I)-catalysed synthesis of 3-acylimidazo[1,2-*a*]pyridines from propiolaldehydes and 2-aminopyridines by gold carbene oxidation using air as oxidant [Scheme 1(b)].[27]

Although these transition-metal-catalysed syntheses of imidazo[1,2-*a*]pyridines are highly efficient, in all cases homogeneous metal catalysts were used and the use of expensive palladium and gold as well as difficult recovery and non-recyclability of the metal catalysts make these methods of limited synthetic utility from environmental and economic points of view. In addition, homogeneous catalysis might result in heavy metal contamination of the desired isolated product, which is a particular drawback in the pharmaceutical industry. Recycling of homogeneous catalysts is a task of great economic and environmental importance, especially when expensive and/or toxic heavy metal complexes are used in chemical and pharmaceutical industries.[28] The heterogenisation of the existing homogeneous catalysts appears to be a logical solution to these problems.[29] There has been considerable interest in the development of heterogeneous catalytic systems that can be easily recycled whilst maintaining the inherent activity of the catalytic centre. However, to the best of our knowledge, no examples of heterogeneous transition metal-catalysed construction of imidazo[1,2-*a*]pyridines have been described until now, despite the practical benefits of heterogeneous catalysis.

Mesoporous MCM-41 materials have recently been shown to be powerful supports for immobilisation of homogeneous metal catalysts such as palladium, rhodium, molybdenum, gold and copper complexes.[30–33] We have reported the synthesis of an MCM-41-immobilised phosphine gold(I) complex (MCM-41-PPh_3-AuCl) and its successful application to direct C_{sp^2}–C_{sp} bond functionalisation of arylalkynes through a nitrogenation process to form amides.[34] In order to expand further our Au(I)-MCM-41 chemistry toolbox,[32,34] we report here the first heterogeneous gold(I)-catalysed annulation between 2-aminopyridines and



Alpidem (R^1 = *n*-propyl, R^2 = Cl)
Zolpidem (R^1 = Me, R^2 = Me)



Saripidem (R^1 = *n*-propyl, R^2 = H, R^3 = Cl)
Necopidem (R^1 = *i*-Bu, R^2 = Me R^3 = Et)

Fig. 1 Clinical medicines containing the imidazo[1,2-*a*]pyridine core structure.

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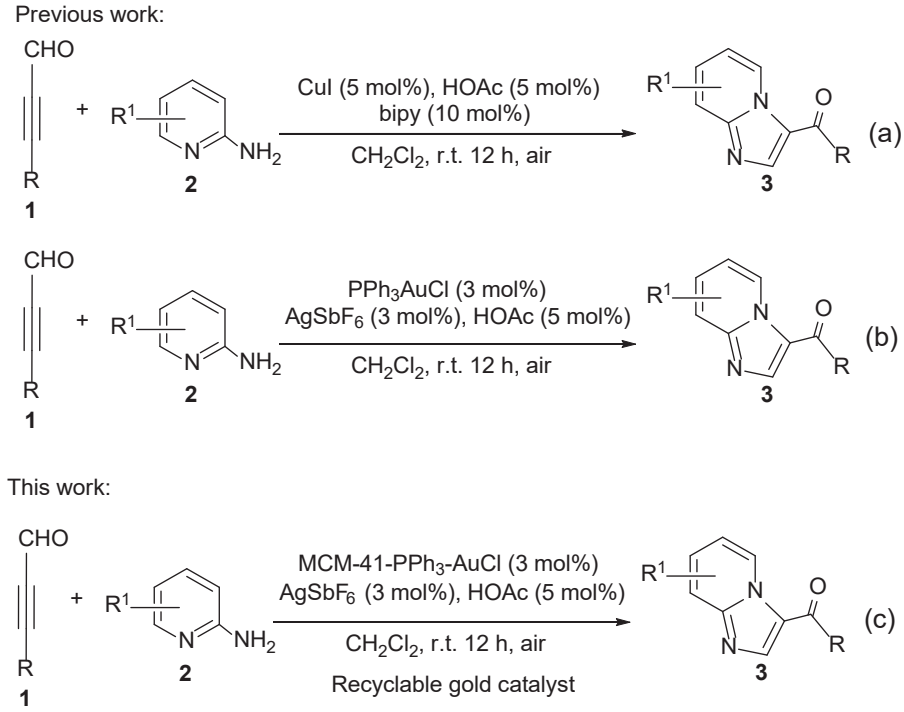
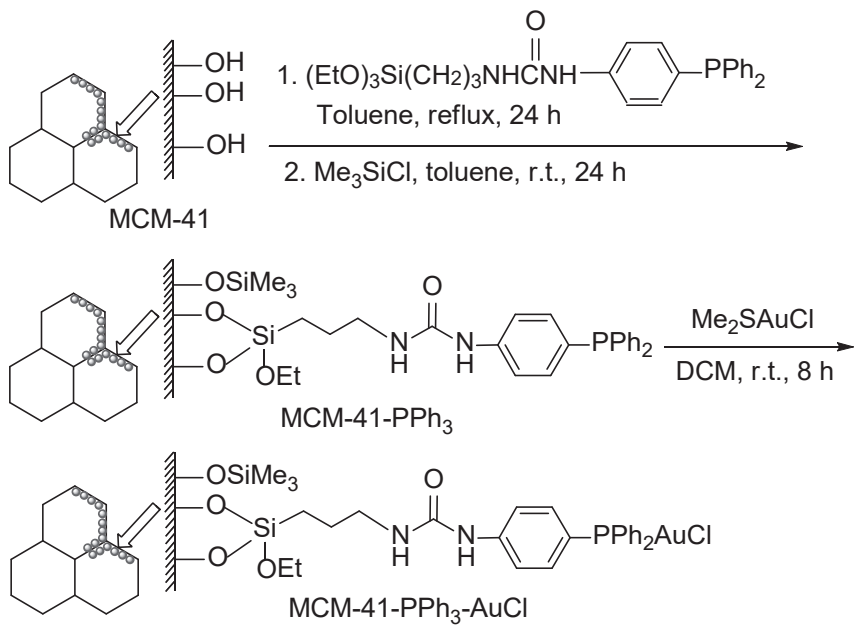


Scheme 1



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propiolaldehydes leading to 3-acylimidazo[1,2-*a*]pyridines in good yields under mild conditions [Scheme 1(c)].

Results and discussion

The MCM-41-immobilised phosphine gold(I) complex (MCM-41-PPh_3-AuCl) was prepared by a simple two-step procedure as shown in Scheme 2.[34] First, mesoporous MCM-41 was condensed with 1-[4-(diphenylphosphino)phenyl]-3-[3-(triethoxysilyl)-propyl]urea in toluene at 110 ºC, followed by silylation with Me_3SiCl to give Ph_3P-functionalised MCM-41 (MCM-41-PPh_3). Then the latter was reacted with Me_2SAuCl in dichloromethane (DCM) to afford the MCM-41-immobilised phosphine gold(I) complex (MCM-41-PPh_3-AuCl) as a grey powder. The gold content of the complex was found to be 0.38 mmol g^{-1} according to inductively coupled plasma atomic emission spectroscopy (ICP-AES) measurements.

In our initial screening experiments, the reaction of 3-phenylpropiolaldehyde (**1a**) with 2-aminopyridine (**2a**) was investigated to optimise the reaction conditions and the results are summarised in Table 1. First, various supported gold(I) catalysts were examined in CH_2Cl_2 at 25 ºC (Table 1, entries 1–5). When MCM-41-PPh_3-AuCl was used as catalyst, the desired product **3a** was isolated in moderate yield (Table 1, entry 1). Then various silver salts such as AgOTf, $AgSbF_6$, $AgBF_4$ and AgOAc were tested as co-catalysts. It was found that $AgSbF_6$ as co-catalyst was the most efficient and gave **3a** in 81% yield (Table 1, entry 3). When $AgSbF_6$ alone was used as catalyst the reaction did not take place, indicating that

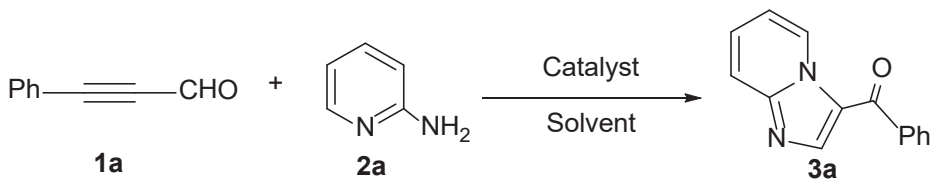
the gold(I) catalyst plays a key role in the annulation reaction (Table 1, entry 6). We next examined the effect of solvents on the model reaction (Table 1, entries 7–13). When DMF, DMAc, DMSO, MeCN, THF and dioxane were used as solvents, the reaction afforded the desired **3a** in 61–75% yields and toluene as solvent gave a lower yield. So, CH_2Cl_2 as solvent was the best choice (Table 1, entry 3). We attempted to improve the yield by raising the reaction temperature. Unfortunately, the yield decreased gradually on increasing the temperature from 25 to 60 ºC (Table 1, entries 14 and 15). Finally, the amount of the catalyst was also screened. Reducing the amount of the catalyst to 1.5 mol% resulted in a lower yield and a long reaction time was required (Table 1, entry 16). Increasing the amount of the catalyst could shorten the reaction time, but did not improve the yield significantly (Table 1, entry 17). Thus, the optimised reaction conditions for this transformation are MCM-41-PPh_3-AuCl/$AgSbF_6$ (3 mol%) in CH_2Cl_2 at 25 ºC under air for 12 h (Table 1, entry 3).

With the optimised conditions in hand, we next investigated the scope and limitation of this heterogeneous gold(I)-catalysed annulation reaction using a range of propiolaldehydes **1a–d** and 2-aminopyridines **2a–h** as the reactants; the results are summarised in Table 2. Firstly, 3-phenylpropiolaldehyde (**1a**) was used to explore the scope of the 2-aminopyridines. As shown in Table 2, the annulation reactions of substituted 2-aminopyridines **2b–h** with **1a** proceeded smoothly under the optimised conditions to afford the corresponding 3-benzoylimidazo[1,2-*a*]pyridines **3b–h** in 66–89% yields (Table 2, entries 2–8). The results indicated that the reaction was compatible with a range of substituents in all positions on the pyridine ring of the 2-aminopyridine. The halo groups (chloro or bromo) on the pyridine ring remained intact under the optimised conditions. We next examined the scope of propiolaldehydes **1**. The alkyl-substituted propiolaldehyde oct-2-ynal (**1b**) proved to be also a suitable reactant and the reactions with different 2-aminopyridines gave the desired imidazo-[1,2-*a*]pyridine derivatives **3i–k** in 63–72% yields (Table 2, entries 9–11). Interestingly, the reaction was found to be perhaps quite general as using 3-(trimethylsilyl)propiolaldehyde (**1c**) as a reactant, the corresponding products **3l–p** were produced in 60–68% yields (Table 2, entries 12–16). It is noteworthy that when propiolaldehyde (**1d**) was used, the expected products **3q–s** could be formed in 58–69% yields (Table 2, entries 17–19). These results indicate that the heterogeneous gold(I) catalytic system is applicable to aryl-, alkyl- and silyl-substituted as well as terminal propiolaldehydes.

To determine whether the observed catalysis was due to the heterogeneous catalyst MCM-41-PPh_3-AuCl or to a leached gold species in solution, we focused on the annulation reaction of 3-phenylpropiolaldehyde (**1a**) with 2-aminopyridine (**2a**). We filtered off the catalyst at 25 ºC after 5 h of reaction time and allowed the filtrate to react further. We found that, after removal of the catalyst, no further reaction was observed, indicating that leached gold species from the catalyst (if any) are not responsible for the observed activity. It was also confirmed by ICP-AES analysis that no gold species could be detected in the filtrate. These results suggest that the gold(I) complex was stable during the reaction and the observed catalysis was intrinsically heterogeneous.

A possible mechanism for this heterogeneous gold(I)-catalysed annulation reaction of propiolaldehydes **1** with 2-aminopyridines **2** is outlined in Scheme 3. Firstly, HOAc-promoted condensation of **1a** and **2a** takes place to form intermediate **A**. Then coordination of the MCM-41-PPh_3-

Table 1 Optimisation of the reaction conditions[a]



1a **2a** **3a**

Entry	Catalyst	Solvent	Temp. (°C)	Yield (%)[b]
1	MCM-41-PPh_3-AuCl	CH_2Cl_2	25	49
2	MCM-41-PPh_3-AuCl/AgOTf	CH_2Cl_2	25	63
3	MCM-41-PPh_3-AuCl/$AgSbF_6$	CH_2Cl_2	25	81
4	MCM-41-PPh_3-AuCl/$AgBF_4$	CH_2Cl_2	25	58
5	MCM-41-PPh_3-AuCl/AgOAc	CH_2Cl_2	25	50
6	$AgSbF_6$	CH_2Cl_2	25	0
7	MCM-41-PPh_3-AuCl/$AgSbF_6$	DMF	25	69
8	MCM-41-PPh_3-AuCl/$AgSbF_6$	DMAc	25	61
9	MCM-41-PPh_3-AuCl/$AgSbF_6$	DMSO	25	65
10	MCM-41-PPh_3-AuCl/$AgSbF_6$	MeCN	25	68
11	MCM-41-PPh_3-AuCl/$AgSbF_6$	THF	25	71
12	MCM-41-PPh_3-AuCl/$AgSbF_6$	Toluene	25	51
13	MCM-41-PPh_3-AuCl/$AgSbF_6$	Dioxane	25	75
14	MCM-41-PPh_3-AuCl/$AgSbF_6$	CH_2Cl_2	40	66
15	MCM-41-PPh_3-AuCl/$AgSbF_6$	CH_2Cl_2	60	38
16[c]	MCM-41-PPh_3-AuCl/$AgSbF_6$	CH_2Cl_2	25	63
17[d]	MCM-41-PPh_3-AuCl/$AgSbF_6$	CH_2Cl_2	25	82

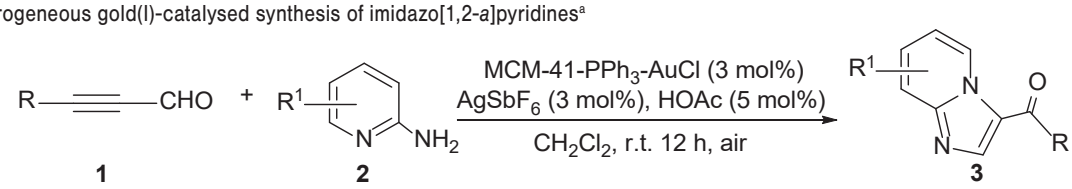
[a]All reactions were performed using **1a** (0.5 mmol), **2a** (0.7 mmol), catalyst (3 mol%), HOAc (5 mol%), in solvent (3 mL) under air for 12 h.

[b]Isolated yield.

[c]1.5 mol% catalyst was used for 24 h.

[d]5 mol% catalyst was used for 8 h.

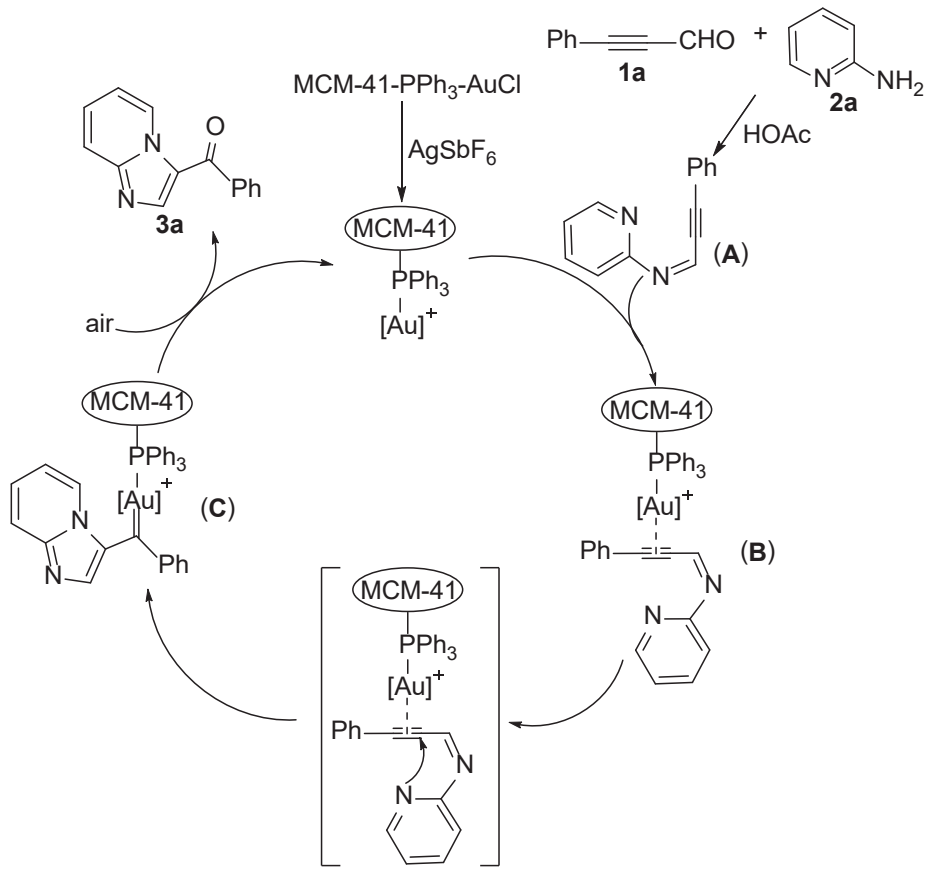
Table 2 Heterogeneous gold(I)-catalysed synthesis of imidazo[1,2-*a*]pyridines[a]



1 2 3

Entry	R	R^1	Product	Yield (%)[b]
1	Ph	H	**3a**	81
2	Ph	5-Me	**3b**	72
3	Ph	4-Me	**3c**	70
4	Ph	3-Me	**3d**	66
5	Ph	4-Cl	**3e**	67
6	Ph	4-Br	**3f**	73
7	Ph	4-EtOCO	**3g**	89
8	Ph	4-F_3C	**3h**	84
9	*n*-C_5H_{11}	3-Me	**3i**	63
10	*n*-C_5H_{11}	4-EtOCO	**3j**	65
11	*n*-C_5H_{11}	5-Me	**3k**	72
12	Me_3Si	H	**3l**	64
13	Me_3Si	3-Me	**3m**	68
14	Me_3Si	4-Me	**3n**	60
15	Me_3Si	5-Me	**3o**	67
16	Me_3Si	4-Br	**3p**	63
17	H	4-Me	**3q**	58
18	H	4-Cl	**3r**	62
19	H	5-Me	**3s**	69

[a]All reactions were performed using **1** (0.5 mmol), **2** (0.7 mmol), MCM-41-PPh_3-AuCl/$AgSbF_6$ (3 mol%), HOAc (5 mol%), in CH_2Cl_2 (3 mL) at 25 °C under air for 12 h.
[b]Isolated yield.



Scheme 3

$AuSbF_6$ complex generated *in situ* from MCM-41- PPh_3-AuCl and $AgSbF_6$ to the alkyne moiety in intermediate **A** affords an MCM-41- bound phosphine-Au(I) alkyne complex **B**, which is followed by an intramolecular 5-*exo-dig* cyclisation to give an MCM-41-bound phosphine-Au(I) carbene complex **C**. Finally, intermediate **C** undergoes carbene oxidation with oxygen metathesis to afford the desired product **3a** and regenerate the MCM-41-PPh_3-Au(I) complex.

The MCM-41-PPh_3-AuCl complex can be easily separated and recovered by simple filtration of the reaction solution. We next examined the recycling of the catalyst by using the annulation reaction of 3-phenylpropiolaldehyde (**1a**) with 2-amino-4-ethoxycarbonylpyridine (**2g**). After completion of the reaction, the catalyst was recovered by simple filtration and washed with 25–28 wt% $NH_3{\cdot}H_2O$ (2 × 5 mL), distilled water (2 × 5 mL) and acetone (2 × 5 mL). After being air-dried, it was reused directly without further purification. The recovered gold catalyst was used in the next run and almost the same yield of **3g** was observed for eight consecutive cycles (89, 88, 87, 87, 86, 85, 86 and 86% respectively). It is noteworthy that the reaction catalysed by the recovered catalyst did not need the addition of $AgSbF_6$ because the MCM-41-PPh_3-AuCl had been converted into MCM-41-PPh_3-$AuSbF_6$ after the first cycle.

In conclusion, we have developed a novel and practical method for the synthesis of 3-carbonyl-substituted imidazo[1,2-*a*] pyridines through the annulation reaction of propiolaldehydes with 2-aminopyridines by using an MCM-41-immobilised phosphine gold(I) complex (MCM-41-PPh_3-AuCl) and $AgSbF_6$ as catalysts. The reactions generated a variety of imidazo[1,2-*a*] pyridine derivatives in moderate to good yields under mild conditions. Importantly, this heterogeneous gold(I) catalyst can be easily recovered by simple filtration and recycled at least seven times without significant loss of catalytic activity, thus making this procedure economically and environmentally more acceptable.

Experimental

All reagents were used as received without further purification. The MCM-41-PPh_3-AuCl complex was prepared according to our previous procedure.[34] The gold content was determined to be 0.38 mmol g^{-1} by ICP-AES. DCM was dried over P_2O_5 and distilled before use. All reactions were carried out under air in oven-dried glassware with magnetic stirring. ^{1}H NMR spectra were recorded on a Bruker Avance 400 spectrometer (at 400 MHz) with TMS as an internal standard using $CDCl_3$ as the solvent. ^{13}C NMR spectra were recorded on the Bruker Avance 400 spectrometer (at 100 MHz) using $CDCl_3$ as the solvent. FTIR spectra were recorded using a PerkinElmer 782 Fourier transform spectrophotometer. HRMS spectra were recorded on a Bruker MicroTOF-Q II spectrometer with micromass MS software using electrospray ionisation. Gold content was determined using ICP-AES on an Atomscan16 (TJA Corporation) instrument.

Synthesis of 3-benzoylimidazo[1,2-a]pyridine (**3a**)*; typical procedure*

A mixture of 3-phenylpropiolaldehyde (**1a**) (0.5 mmol), 2-aminopyridine (**2a**) (0.7 mmol) and HOAc (5 mol%) was stirred in dry CH_2Cl_2 (3 mL) for 30 min at 25 ºC. Then MCM-41-PPh_3-AuCl (39.5 mg, 0.015 mmol) and $AgSbF_6$ (5.2 mg, 0.015 mmol) were added and this mixture was stirred at 25 ºC for 12 h under air. After completion of the reaction, the mixture was diluted with ethyl acetate (15 mL) and filtered. The gold catalyst was washed with 25–28 wt% $NH_3{\cdot}H_2O$ (2 × 5 mL), distilled water (2 × 5 mL) and acetone (2×5 mL) and air-dried if to be reused. The filtrate was quenched with water (10 mL) and the aqueous phase was extracted with ethyl acetate (2 × 10 mL). The combined extract was dried over anhydrous $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography using petroleum ether (60–90 °C)/ethyl acetate (6:1) as eluent to afford the desired product **3a**.

*3-Benzoylimidazo[1,2-*a*]pyridine* (**3a**): White solid; m.p. 104–105 ºC (lit.[27] 103–104 ºC); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.76 (d, *J* = 6.8 Hz, 1H), 8.21 (s, 1H), 7.88 (d, *J* = 7.2 Hz, 2H), 7.81 (d, *J* = 8.8 Hz, 1H), 7.63–7.52 (m, 4H), 7.16 (t, *J* = 7.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.8, 149.1, 145.7, 139.3, 132.0, 129.4, 128.9, 128.8, 128.6, 123.6, 117.8, 115.1.

*3-Benzoyl-6-methylimidazo[1,2-*a*]pyridine* (**3b**): White solid; m.p. 125–126 ºC (lit.[27] 126–127 ºC); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.58 (s, 1H), 8.16 (s, 1H), 7.90–7.85 (m, 2H), 7.71 (d, *J* = 8.8 Hz, 1H), 7.63–7.58 (m, 1H), 7.53 (t, *J* = 7.4 Hz, 2H), 7.41 (dd, *J* = 8.8, 1.6 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.8, 148.1, 145.7, 139.5, 132.3, 131.9, 128.8, 128.6, 126.9, 126.8, 125.2, 117.0, 18.4.

*3-Benzoyl-7-methylimidazo[1,2-*a*]pyridine* (**3c**):[27] Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.62 (d, *J* = 6.8 Hz, 1H), 8.15 (s, 1H), 7.90–7.84 (m, 2H), 7.61–7.49 (m, 4H), 6.99 (dd, *J* = 7.0, 1.4 Hz, 1H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.6, 149.6, 146.0, 141.1, 139.4, 131.9, 128.8, 128.5, 128.1, 124.6, 117.6, 116.4, 21.6.

*3-Benzoyl-8-methylimidazo[1,2-*a*]pyridine* (**3d**): White solid; m.p. 123–124 ºC (lit.[27] 125–126 ºC); ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.61 (d, *J* = 6.8 Hz, 1H), 8.18 (s, 1H), 7.90–7.85 (m, 2H), 7.63–7.58 (m, 1H), 7.53 (t, *J* = 7.4 Hz, 2H), 7.35 (d, *J* = 7.0 Hz, 1H), 7.06 (t, *J* = 7.0 Hz, 1H), 2.70 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.9, 149.2, 145.0, 139.4, 132.0, 128.9, 128.6, 128.5, 127.6, 126.6, 124.0, 115.2, 16.9.

*3-Benzoyl-7-chloroimidazo[1,2-*a*]pyridine* (**3e**):[27] Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.68 (d, *J* = 7.2 Hz, 1H), 8.20 (s, 1H), 7.87 (d, *J* = 7.2 Hz, 2H), 7.82 (s, 1H), 7.63 (t, *J* = 7.2 Hz, 1H), 7.56–7.51 (m, 2H), 7.14 (dd, *J* = 7.4, 2.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.8, 149.1, 146.0, 138.9, 136.1, 132.3, 129.1, 128.8, 128.7, 128.2, 116.9, 116.6.

*3-Benzoyl-7-bromoimidazo[1,2-*a*]pyridine* (**3f**):[27] Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.61 (d, *J* = 7.2 Hz, 1H), 8.18 (s, 1H), 8.01 (d, *J* = 1.6 Hz, 1H), 7.87 (d, *J* = 7.2 Hz, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.57–7.50 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.8, 149.1, 145.8, 138.9, 132.3, 132.0, 129.3, 128.8, 128.7, 123.8, 119.0, 109.6.

*3-Benzoyl-7-ethoxycarbonylimidazo[1,2-*a*]pyridine* (**3g**): Yellow oil; IR (neat): 3069, 2982, 1689, 1608, 1385, 1276, 1109 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.76 (d, *J* = 7.2 Hz, 1H), 8.51 (s, 1H), 8.31 (s, 1H), 7.90 (d, *J* = 7.2 Hz, 2H), 7.74–7.69 (m, 1H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.58–7.54 (m, 2H), 4.47 (q, *J* = 7.2 Hz, 2H), 1.46 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.1, 167.7, 148.2, 146.3, 138.9, 132.4, 130.9, 128.9, 128.7, 128.5, 124.2, 119.8, 114.3, 62.1, 14.3; HRMS calcd for $C_{17}H_{14}N_2O_3^+$: [M^+]: 294.1004; found: 294.1011.

*3-Benzoyl-7-trifluoromethylimidazo[1,2-*a*]pyridine* (**3h**):[20] Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.85 (d, *J* = 7.2 Hz, 1H), 8.32 (s, 1H), 8.11 (s, 1H), 7.90 (d, *J* = 7.2 Hz, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.56 (t, *J* = 7.6 Hz, 2H), 7.34–7.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 185.1, 147.4, 146.1, 138.6, 132.6, 132.5, 130.8 (q, $^2J_{C-F}$ = 34.3 Hz), 129.6, 128.8, 128.7, 122.8 (q, $^1J_{C-F}$ = 271.0 Hz), 115.6 (q, $^3J_{C-F}$ = 4.7 Hz), 110.8 (q, $^3J_{C-F}$ = 2.8 Hz).

*1-(8-Methylimidazo[1,2-*a*]pyridin-3-yl)hexan-1-one* (**3i**):[27] Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.54 (d, *J* = 6.8 Hz, 1H), 8.34 (s, 1H), 7.29 (d, *J* = 7.2 Hz, 1H), 7.00 (t, *J* = 6.8 Hz, 1H), 2.92 (t, *J* = 7.6 Hz, 2H), 2.67 (s, 3H), 1.75–1.67 (m, 2H), 1.47–1.39 (m, 4H), 0.96 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.8, 142.1, 127.9, 127.5, 126.6, 124.2, 115.0, 39.6, 31.6, 25.1, 22.5, 16.9, 13.7.

*Ethyl 3-hexanoylimidazo[1,2-*a*]pyridine-7-carboxylate* (**3j**): Yellow oil; IR (neat): 2979, 2926, 2870, 1685, 1662, 1386, 1218, 1106 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.70 (d, *J* = 7.2 Hz, 1H), 8.46 (s, 1H), 8.45 (s, 1H), 7.66 (dd, *J* = 7.2, 0.8 Hz, 1H), 4.45 (q, *J* = 7.2 Hz, 2H), 2.95 (t, *J* = 7.6 Hz, 2H), 1.81–1.71 (m, 2H), 1.47–1.37 (m, 7H), 0.94 (t, *J* = 7.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.1, 164.5, 147.8, 143.7, 130.9, 128.3, 119.8, 114.1, 62.0, 39.8, 31.5, 24.8, 22.5, 14.2, 13.9; HRMS calcd for $C_{16}H_{20}N_2O_3^+$: [M^+]: 288.1474; found: 288.1469.

*1-(6-Methylimidazo[1,2-*a*]pyridin-3-yl)hexan-1-one* (**3k**):[27] Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.51 (s, 1H), 8.31 (s, 1H), 7.66 (d, *J* = 9.2 Hz, 1H), 7.35 (d, *J* = 9.2 Hz, 1H), 2.90 (t, *J* = 7.4 Hz, 2H), 2.42 (s, 3H), 1.75–1.69 (m, 2H), 1.46–1.40 (m, 4H), 0.96 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.7, 149.2, 142.7, 139.0, 131.8, 126.7, 125.0, 116.8, 39.5, 31.6, 25.1, 22.5, 18.4, 13.7.

*Imidazo[1,2-*a*]pyridin-3-yl(trimethylsilyl)methanone* (**3l**): Yellow oil; IR (neat): 2925, 2823, 1661, 1515, 1487, 1322, 1253, 1164 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.77 (d, *J* = 6.8 Hz, 1H), 8.42 (s, 1H), 7.83–7.76 (m, 1H), 7.55–7.49 (m, 1H), 7.08 (t, *J* = 7.0 Hz, 1H), 0.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 147.8, 145.0, 129.7, 129.0, 128.8, 117.5, 115.3, –1.6; HRMS calcd for $C_{11}H_{14}N_2OSi^+$: [M^+]: 218.0875; found: 218.0863.

*(8-Methylimidazo[1,2-*a*]pyridin-3-yl)(trimethylsilyl)methanone* (**3m**): Yellow oil; IR (neat): 2927, 2821, 1659, 1513, 1489, 1325, 1250, 1157 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.62 (d, *J* = 6.8 Hz, 1H), 8.40 (s, 1H), 7.31 (d, *J* = 7.2 Hz, 1H), 6.98 (t, *J* = 6.8 Hz, 1H), 2.68 (s, 3H), 0.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.2, 147.9, 144.5, 129.7, 128.7, 127.3, 126.7, 115.3, 16.9, –1.6; HRMS calcd for $C_{12}H_{16}N_2OSi^+$: [M^+]: 232.1032; found: 232.1037.

*(7-Methylimidazo[1,2-*a*]pyridin-3-yl)(trimethylsilyl)methanone* (**3n**): Yellow oil; IR (neat): 2919, 2825, 1662, 1511, 1485, 1328, 1249, 1161 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.62 (d, *J* = 7.2 Hz, 1H), 8.37 (s, 1H), 7.58 (s, 1H), 6.92 (d, *J* = 7.2 Hz, 1H), 2.48 (s, 3H), 0.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 148.4, 145.0, 141.7, 128.2, 125.2, 117.9, 116.1, 21.6, –1.6; HRMS calcd for $C_{12}H_{16}N_2OSi^+$: [M^+]: 232.1032; found: 232.1033.

*(6-Methylimidazo[1,2-*a*]pyridin-3-yl)(trimethylsilyl)methanone* (**3o**): Yellow oil; IR (neat): 2926, 2820, 1662, 1518, 1484, 1321, 1254, 1165 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.62 (s, 1H), 8.37 (s, 1H), 7.68 (d, *J* = 9.0 Hz, 1H), 7.37 (d, *J* = 9.0 Hz, 1H), 2.40 (s, 3H), 0.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 145.0, 132.4, 130.9, 128.9, 127.0, 125.4, 116.7, 18.3, –1.6; HRMS calcd for $C_{12}H_{16}N_2OSi^+$: [M^+]: 232.1032; found: 232.1027.

*(7-Bromoimidazo[1,2-*a*]pyridin-3-yl)(trimethylsilyl)methanone* (**3p**): Yellow oil; IR (neat): 2919, 2823, 1658, 1515, 1490, 1327, 1249, 1158 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.63 (d, *J* = 7.2 Hz, 1H), 8.37 (s, 1H), 7.95 (d, *J* = 1.2 Hz, 1H), 7.17 (dd, *J* = 7.2, 2.0 Hz, 1H), 0.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 148.0, 145.3, 130.9, 129.0, 128.9, 123.8, 119.1, –1.7; HRMS calcd for $C_{11}H_{13}BrN_2OSi^+$: [M^+]: 295.9981; found: 295.9984.

*7-Methylimidazo[1,2-*a*]pyridine-3-carbaldehyde* (**3q**):[20] Yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 9.89 (s, 1H), 9.35 (d, *J* = 6.8 Hz, 1H), 8.26 (s, 1H), 7.56 (s, 1H), 6.97 (d, *J* = 6.8 Hz, 1H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.4, 149.9, 147.1, 141.9, 127.8, 124.8, 117.9, 116.5, 21.7.

*7-Chloroimidazo[1,2-*a*]pyridine-3-carbaldehyde* (**3r**): Yellow oil; IR (neat): 1638, 1519, 1487, 1325, 1281, 1226 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 9.94 (s, 1H), 9.43 (d, *J* = 7.2 Hz, 1H), 8.32 (s, 1H), 7.81 (d, *J* = 2.0 Hz, 1H), 7.13 (d, *J* = 5.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.9, 149.3, 147.2, 141.8, 128.8, 125.8, 117.0, 114.7; HRMS calcd for $C_8H_5ClN_2O^+$: [M^+]: 180.0090; found: 180.0082.

*6-Methylimidazo[1,2-*a*]pyridine-3-carbaldehyde* (**3s**):[20] Yellow oil; ^1H NMR (400 MHz, $CDCl_3$): δ 9.98 (s, 1H), 9.39 (s, 1H), 8.34 (s, 1H), 7.76 (d, *J* = 3.2 Hz, 1H), 7.49 (dd, *J* = 9.2, 1.2 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.7, 148.3, 146.7, 133.0, 126.7, 125.7, 124.8, 117.0, 18.2.

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