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Bifunctional N-heterocyclic carbene ligands for Cu-catalyzed direct C–H carboxylation with CO_2†

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Diethylene glycol-functionalized imidazo[1,5-*a*]pyridin-3-ylidenes (DEG-ImPy) have been developed as bifunctional N-heterocyclic carbene ligands. The DEG-ImPy Cu(I) complexes efficiently catalyzed the direct C–H carboxylation of benzoxazole with CO_2, showing higher isolated yields than those with the *N*,*N'*-(2,6-diisopropylphenyl)imidazolylidene Cu catalyst.

Introduction

The use of N-heterocyclic carbenes (NHCs) as strong σ-donating ligands has become increasingly popular in homogeneous catalysis.[1] Numerous structural variations on the prototypical imidazolylidene skeleton have been used to modulate the electronic and steric properties of NHC ligands. Imidazo[1,5-*a*]pyridin-3-ylidene (ImPy) ligands, first developed by Glorius[2] and Lassaletta[3] in 2005, are a rigid bicyclic variant of NHCs. ImPy ligands are strong σ-donors[3,4] as the extended π-system can increase the electron density at the carbene center.[5] Substituents on the bicyclic ImPy can be projected into the metal coordination sphere, often resulting in bonding interactions with the metal.[3,6] Synthesis of ImPy precursors is concise and often allows late-stage incorporation of diverse functional substituents.[7] Owing to this feature, a number of ImPy-metal catalysts have been developed for various organic transformations (Fig. 1).[8] We envision that ImPy ligands could serve as a versatile framework for bifunctional NHC ligands.[9] Polyether units such as polyethylene glycol (PEG) are known as a CO_2-philic building block and have been utilized in ionic liquids for CO_2 capture[10] and as catalysts for CO_2 conversion.[11] Thus we were wondering whether introduction of diethylene glycol unit (DEG) into the ligand scaffold could render the ImPy bifunctional. Herein, we report the synthesis of diethylene glycol-functionalized imidazo[1,5-*a*]pyridin-3-ylidene (DEG-ImPy) copper complexes and their application in direct C–H carboxylation of benzoxazoles with CO_2. DEG-ImPy Cu exhibits higher catalytic activity than non-functionalized NHC–Cu catalysts.

Results and discussion

Synthesis of ligands and catalysts

Synthesis of imidazopyridinium salts (**4a–4g**) was accomplished following a modified procedure of the reported method (Scheme 1). 6-Mesitylpicolinaldehyde (**3**) was prepared by Bouveault aldehyde synthesis,[12] followed by Suzuki–Miyaura coupling.[13] ImPy precursors (**4a–4g**) were then synthesized from the functionalized anilines, formalin, and aldehyde **3** by Aron's method.[7] Among the synthesized ImPy ligands, imidazopyridinium salts (**4a–4c**, **4g**) were converted to the corresponding ImPy–copper(I) complexes (**5a–5c**, **5g**) by the reaction with copper chloride(I) in the presence of sodium *tert*-butoxide or through Ag transmetalation in reasonable isolated yields.

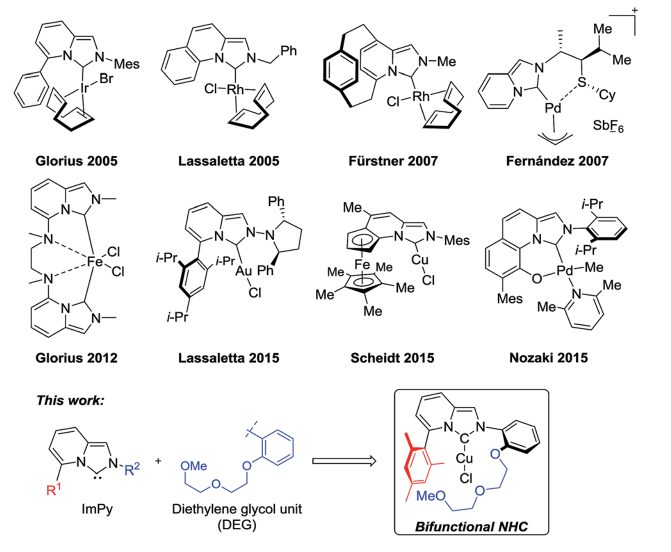

Fig. 1 Representative examples of metal complexes containing imidazo[1,5-*a*]pyridin-3-ylidene (ImPy) ligands.

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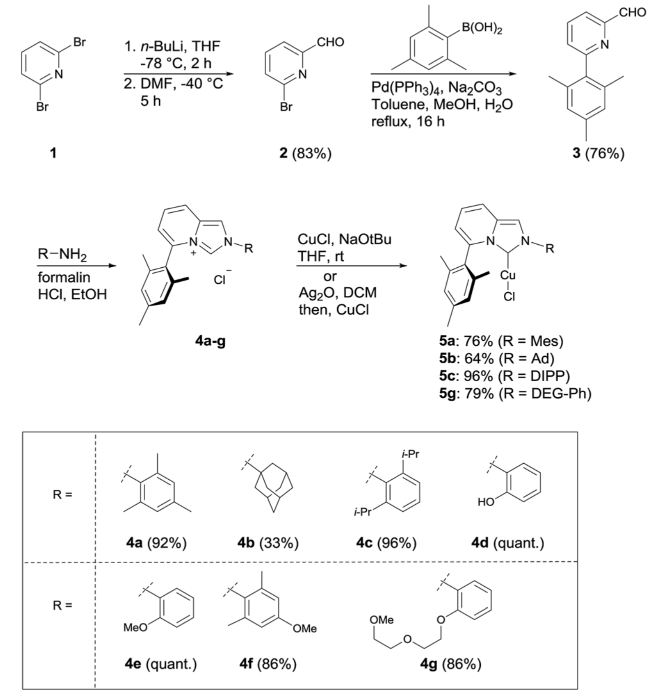


Scheme 1 Synthesis of DEG-ImPy ligands and ImPy–Cu(I) complexes.

X-ray crystallography

The structure of ImPy–Cu complex **5a** and **5g** were determined by X-ray diffraction analysis (Fig. 2). As with recently reported ImPy–copper complexes,[8j] geometry of both complexes is linear; C(1)–Cu(1)–Cl(1) 173.5(1)° (**5a**) and 173.7(4)° (**5g**). In case of **5g**, the mesityl group is in close proximity to the Cu metal center as the observed atom distance Cu(1)–C(8) is shorter (2.887 Å) than that of **5a** (2.957 Å). The aryl group on the nitrogen atom in **5a** is oriented nearly perpendicular to the NHC plane, resulting in a dihedral angle of 80.64° whereas the dihedral angle between the ImPy plane and the DEG-phenyl in **5g** is 50.84°.

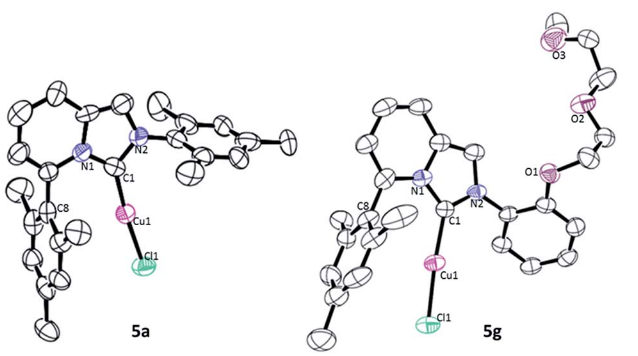


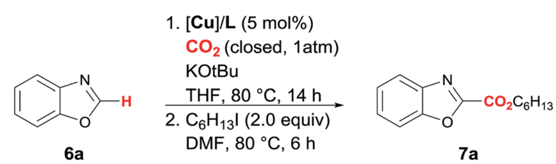
Fig. 2 ORTEP of molecular structure of ImPy–Cu complexes. Thermal ellipsoids are drawn at the 50% probability level. Hydrogen atoms have been omitted for clarity. Selected bond lengths (Å) and bond angles (°): **5a** Cu(1)–C(1) = 1.83(1), N(1)–C(1) = 1.38(1), C(1)–N(2) = 1.39(1), Cu(1)–Cl(1) = 2.135(5); N(1)–C(1)–N(2) = 102.4(8), C(1)–Cu(1)–Cl(1) = 173.7(4); **5g** Cu(1)–C(1) = 1.83(1), N(1)–C(1) = 1.38(1), C(1)–N(2) = 1.39(1), Cu(1)–Cl(1) = 2.135(5); N(1)–C(1)–N(2) = 103.5(3), C(1)–Cu(1)–Cl(1) = 173.5(1).

Catalytic properties of ImPy–Cu complexes

With the various ImPy ligands in hand, the catalytic activities of the ImPy–Cu complexes were evaluated in direct C–H carboxylation of benzoxazole using CO_2 (Table 1). Synthetic utilization of carbon dioxide (CO_2) as a sustainable C1 feedstock has attracted much attention recently.[14] Catalytic direct C–H carboxylation with CO_2 is an atom-economical transformation that affords carboxylic acid derivatives. Various C–H bonds of alkynes,[15] alkenes/arenes,[16,17] and alkanes,[18] can be substituted with CO_2H. Coinage–metal complexes with NHC ligands are efficient catalysts for direct C–H carboxylation. Following the procedure reported in the literature,[16c] initial studies were carried out using isolated NHC–Cu complexes (entries 1–4). ImPy–Cu complex with a 2,6-diisopropyl phenyl substituent (**5c**) showed higher catalytic activity in producing the corresponding ester than IPrCuCl under the same conditions (entry 4 *vs.* entry 1). It was examined whether the catalyst could be generated *in situ* from CuCl and NHC·HCl salt under the same reaction conditions. In most cases, *in situ*-formed catalysts from CuCl and NHC ligands showed better yields than the isolated Cu complexes (entries 5–7 *vs.* entries 1–3). Note that *in situ*-generated Cu catalysts from alkoxy-functionalized ImPy ligands exhibited very good yields (entries 10–12). While the hydroxy group (**4d**) was rather detrimental (entry 9), a methoxy group (**4e** and **4f**) resulted in increased yield (entries 10 and 11). ImPy ligand bearing a diethylene glycol moiety (**4g**, DEG-ImPy) exhibited excellent activity and afforded the desired product in quantitative yield (entry 12).

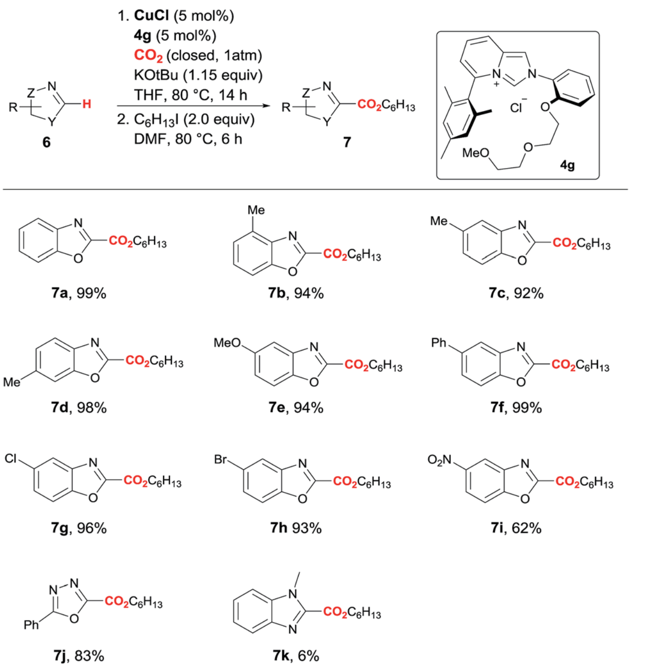
Using the optimal DEG-ImPy ligand (**4g**), the heteroarene substrate scope of the direct C–H carboxylation was examined

Table 1 Optimization of the C–H carboxylation conditions[a]



Entry	Metal salt	Ligand	Yield of **7a**[b] (%)
1	IPr-CuCl[c]	—	80
2	**5a**	—	52
3	**5b**	—	63
4	**5c**	—	95
5	CuCl	IPr·HCl	84
6	CuCl	**4a**	95
7	CuCl	**4b**	95
8	CuCl	**4c**	81
9	CuCl	**4d**	44
10	CuCl	**4e**	92
11	CuCl	**4f**	94
12	CuCl	**4g**	99

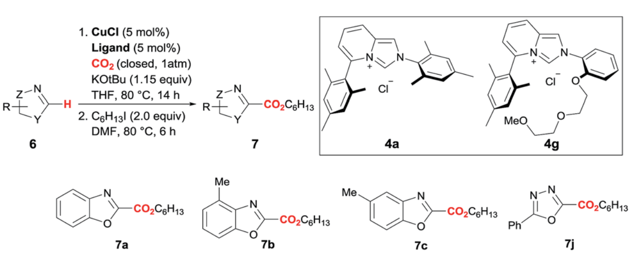
[a] Reaction conditions: benzoxazole (0.5 mmol), CuCl (5 mol%), ligand (5 mol%), KOtBu (1.15 equiv.), THF (2.5 mL), CO_2 (1 atm), 80 °C, 14 h, then evaporation of THF under vacuum, DMF (2.5 mL), $C_6H_{13}I$ (1.0 mmol), 80 °C, 6 h. [b] Yields of the isolated product (average of two runs). [c] [(IPr)CuCl] = 1,3-bis(2,6-di-isopropylphenyl) imidazolium copper(I) chloride.



Scheme 2 Substrate scopes of heteroarenes.

under the same conditions (Scheme 2). Overall, reactions with a variety of substituted benzoxazoles proceeded smoothly. Methyl-substituted benzoxazoles (**7b–7d**), regardless of the position of methyl group on the heterocyclic ring, gave high yields (92–98%). From the reactions with benzoxazoles containing electron donating (R = OMe, Ph) and withdrawing group such as halide (R = Cl, Br), the corresponding esters were obtained with yields of over 90%. The reaction also works for other heteroarene compounds, as the reaction with 2-phenyl-1,3,4-oxadizole afforded product **7j** with an 83% yield. However, *N*-methylbenzoimidazole afforded the product **7k** with a 6% yield.

As shown in Scheme 3, the Cu catalyst with DEG-ImPy·HCl (**4g**) exhibits superior catalytic activity than that with IPr·HCl as well as plain ImPy·HCl (**4a**). Use of ImPy ligand and introduction of a potential cation-binding DEG unit in the ligand framework resulted in improving the catalytic activity in the direct C–H carboxylation with CO_2.



	7a	7b	7c	7j
IPr•HCl	85	61	73	78
4a	95	82	92	79
4g	99	94	92	83

Scheme 3 Ligand comparison: isolated yields of the products from direct C–H carboxylation with CO_2.

Conclusions

Diethylene glycol-functionalized imidazo[1,5,*a*] pyridin-3-ylidenes (DEG-ImPy) ligands have been developed as a bifunctional NHC ligand. Cu catalyst generated *in situ* with the DEG-ImPy·HCl salts efficiently catalyzed the direct C–H carboxylation of various heterocyclic compounds with CO_2, resulting in higher yields than those with the imidazolylidene carbene ligand (IPr). Further studies of DEG-ImPy ligands relating to cation-binding capabilities as well as application in other catalysis are currently under way in our laboratory.

Experimental sections

General remarks

All reactions were carried out under an inert argon atmosphere using the Schlenk technique or a glovebox. All reactions using CO_2 were conducted in a 30 mL Schlenk flask equipped with Teflon-valve. Nuclear magnetic resonance (NMR) spectra were recorded on a JEOL spectrometer, operating at 400 MHz or 300 MHz for ^1H NMR and at 100 MHz or 75 MHz for ^{13}C NMR. All chemical shifts for ^1H and ^{13}C NMR spectroscopy were assigned to residual signals from $CDCl_3$ (^1H) at 7.26 ppm and (^{13}C) at 77.16 ppm, CD_2Cl_2 (^1H) at 5.32 ppm and (^{13}C) at 53.84 ppm, or DMSO-d_6 (^1H) at 2.50 ppm and (^{13}C) at 39.52 ppm. High resolution GC mass spectra were recorded using a JEOL JMS-700 MStation mass spectrometer. Infrared spectra were obtained on a Nicolet iS10 FT-IR spectrometer with an ATR unit and recorded in wave numbers (cm^{-1}).

Materials

Tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), *N*,*N*-dimethylformamide (DMF) and diethyl ether (Et_2O) were dried under a positive pressure of dry nitrogen using a J. C. Meyer Solvent Purification System prior to use. Toluene and *n*-hexane were distilled from calcium hydride and ethanol was dried over 4 Å molecular sieves. Unless specified, all the other chemicals were purchased from Sigma-Aldrich Co., Acros Organics, TCI, Alfa Aesar, and Strem Chemicals Inc. and were used as received without further purification. Commercial carbon dioxide (99.99%) was purchased by Sinil Gas Co. and used without further purification. Benzoxazole, 5-methylbenzoxazole, and 5-chlorobenzoxazole were purchased and purified by flash column chromatography. Other benzoxazole derivatives[19] and oxadiazole[20] were synthesized as reported previously. 6-Bromopicolinaldehyde (**2**),[12] 6-mesitylpicolinaldehyde (**3**),[13] 4-Methoxy-2,6-dimethylaminine,[21] IPr·HCl,[22] and (IPr)CuCl[23] were prepared according to the literature.

Catalyst preparation

2,5-Dimesityl imidazo[1,5-*a*]pyridinium chloride (4a). The procedure was modified from a report by Aron *et al.*[7] 2,4,6-Trimethylaniline (84.8 μL, 0.604 mmol), 6-mesitylpicolinaldehyde **3** (136 mg, 0.604 mmol), formalin (65.0 μL, 0.900 mmol) and 1.25 M HCl in EtOH (546 μL, 0.660 mmol) were added to dry

EtOH (1.20 mL) and stirred at room temperature for 12 hours. The crude product was purified by flash column chromatography (CH_2Cl_2 : MeOH 10 : 1). The product was collected by re-precipitation using Et_2O and CH_2Cl_2 to obtain a product **4a** (216 mg, 92%) as an ivory powder. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.30 (s, 1H), 8.87 (d, J = 9.4 Hz, 1H), 7.93 (s, 1H), 7.46 (dd, J = 9.4, 6.9 Hz, 1H), 7.05 (m, 3H), 6.98 (s, 2H), 2.34 (s, 3H), 2.32 (s, 3H), 2.02 (s, 6H), 1.97 (s, 6H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.7, 141.6, 136.8, 133.7, 133.3, 132.2, 130.9, 129.7, 129.6, 126.3, 125.6, 121.3, 120.4, 120.3, 118.8, 21.2, 21.0, 19.1, 17.2 ppm; IR (ATR): ν = 3058, 2919, 1652, 1610, 1553, 1154, 1034, 844, 829, 731, 679 cm^{-1}; HR-MS (EI): calcd for $C_{25}H_{27}N_2$ [M]$^+$ 355.2174 found 355.2170.

2-((1*S*,3*R*)-Adamantanyl)-5-mesityl-imidazo[1,5-*a*]pyridinium chloride (4b). With the same method used in the synthesis of **4a**, **4b** (33%) was obtained as a white powder from 1-adamantylamine and 6-mesitylpicolinaldehyde **3**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.65 (s, 1H), 8.32 (d, J = 9.3 Hz, 1H), 7.94 (s, 1H), 7.29 (dd, J = 9.4, 6.8 Hz, 1H), 7.07 (s, 2H), 6.89 (d, J = 6.8 Hz, 1H), 2.38 (s, 3H), 2.29 (s, 9H), 1.99 (s, 6H), 1.77 (m, 6H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.4, 137.2, 133.5, 131.6, 129.7, 126.6, 124.6, 119.7, 119.5, 117.8, 115.6, 62.5, 43.1, 35.2, 29.6, 21.4, 19.5 ppm; IR (ATR): ν = 3065, 2999, 2915, 2855, 1651, 1612, 1550, 1454, 1308, 1143, 1103, 854, 814, 714, 663 cm^{-1}; HR-MS (EI): calcd for $C_{26}H_{31}N_2$ [M]$^+$ 371.2487 found 371.2488.

2-(2,6-Diisopropylphenyl)-5-mesityl imidazo[1,5-*a*]pyridinium chloride (4c). With the same method used in the synthesis of **4a**, **4c** (96%) was obtained as an ivory powder from 2,6-diisopropylaniline and 6-mesitylpicolinaldehyde **3**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.35 (s, 1H), 9.02 (m, 1H), 7.91 (s, 1H), 7.57–7.53 (m, 2H), 7.31 (m, 2H), 7.13 (d, J = 6.9 Hz, 1H), 7.07 (s, 2H), 2.35 (s, 3H), 2.09 (m, 2H), 2.03 (s, 6H), 1.25 (d, J = 6.8 Hz, 6H), 1.04 (d, J = 6.9 Hz, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.9, 141.8, 137.0, 133.0, 132.9, 132.5, 132.2, 130.7, 129.7, 126.5, 125.9, 124.7, 121.5, 120.8, 120.6, 28.8, 24.7, 23.9, 21.3, 19.1 ppm; IR (ATR): ν = 3073, 3041, 2958, 2924, 2867, 1652, 1551, 1449, 1300, 1172, 1109, 853, 799, 754, 681 cm^{-1}; HR-MS (EI): calcd for $C_{28}H_{33}N_2$ [M]$^+$ 397.2643 found 397.2648.

2-(2-Hydroxyphenyl)-5-mesityl-2*H*-imidazo[1,5-*a*]pyridinium chloride (4d). Compound **4d** was prepared analogously to **4a**. **4d** was synthesized from 2-aminophenol and 6-mesitylpicolinaldehyde **3**. The crude product was purified by recrystallization using Et_2O and CH_2Cl_2 to obtain a product **4d** (quant.) as an ivory powder. ^{1}H NMR (400 MHz, DMSO-d_6): δ 11.46 (br s, 1H), 9.38 (s, 1H), 8.70 (s, 1H), 8.01 (d, J = 9.3 Hz, 1H), 7.59 (d, J = 7.9 Hz, 1H), 7.47 (dd, J = 9.3, 7.0 Hz, 1H), 7.39 (m, 2H), 7.18 (d, J = 6.8 Hz, 1H), 7.10 (s, 2H), 6.98 (m, 1H), 2.33 (s, 3H), 2.03 (s, 6H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6): δ 151.1, 139.8, 137.1, 133.1, 131.4, 129.7, 128.9, 127.0, 126.6, 125.8, 125.1, 122.5, 119.3, 119.1, 117.4, 117.3, 115.9, 20.8, 18.9 ppm; IR (ATR): ν = 3179, 3166, 3179, 2914, 2688, 2571, 1654, 1607, 1551, 1518, 1464, 1350, 1227, 1173, 805, 752, 654 cm^{-1}; HR-MS (FAB): calcd for $C_{22}H_{21}N_2O$ [M]$^+$ 329.1654 found 329.1656.

5-Mesityl-2-(2-methoxyphenyl)-2*H*-imidazo[1,5-*a*]pyridinium chloride (4e). With the same method used in the synthesis of **4d**, **4e** (quant.) was obtained as a white powder from 2-methoxyaniline and 6-mesitylpicolinaldehyde **3**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.46 (d, J = 6.0 Hz, 1H), 8.58 (dd, J = 9.3, 3.8 Hz, 1H), 8.27 (s, 1H), 7.90 (m, 1H), 7.50 (t, J = 8.4 Hz, 1H), 7.35 (t, J = 9.3 Hz, 1H), 7.18 (t, J = 9.2 Hz, 1H), 7.08 (m, 3H), 6.97 (d, J = 6.8 Hz, 1H), 3.82 (s, 3H), 2.37 (s, 3H), 2.07 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.5, 141.4, 137.1, 133.1, 132.4, 131.1, 129.5, 126.6, 126.4, 124.9, 123.4, 122.3, 122.1, 119.9, 119.8, 118.0, 112.6, 56.4, 21.2, 19.3 ppm; IR (ATR): ν = 3187, 2995, 2918, 2858, 1654, 1604, 1556, 1518, 1455, 1261, 1130, 1022, 850, 760, 654 cm^{-1}; HR-MS (FAB): calcd for $C_{23}H_{23}N_2O$ [M]$^+$ 343.1810 found 343.1802.

5-Mesityl-2-(4-methoxy-2,6-dimethylphenyl)-2*H*-imidazo[1,5-*a*]pyridinium chloride (4f). With the same method used in the synthesis of **4a**, **4f** (86%) was obtained a white powder from 4-methoxy-2,6-dimethylaniline and 6-mesitylpicolinaldehyde **3**. ^{1}H NMR (400 MHz, CD_2Cl_2): δ 9.00 (s, 1H), 8.54 (d, J = 9.4 Hz, 1H), 8.15 (s, 1H), 7.49 (dd, J = 9.4, 6.9 Hz, 1H), 7.10 (d, J = 6.8 Hz, 1H), 7.06 (s, 2H), 6.71 (s, 2H), 3.78 (s, 3H), 2.32 (s, 3H), 2.02 (s, 6H), 1.97 (s, 6H) ppm; ^{13}C NMR (100 MHz, CD_2Cl_2): δ 161.2, 141.7, 137.3, 136.0, 133.8, 132.3, 129.7, 126.7, 126.6, 126.0, 122.6, 120.6, 119.7, 118.9, 114.3, 55.9, 21.2, 19.3, 17.8 ppm; IR (ATR): ν = 3126, 3021, 2955, 2914, 2871, 1651, 1596, 1548, 1494, 1457, 1321, 1295, 1215, 1195, 1178, 1081, 1059, 1034, 868, 849, 818, 686 cm^{-1}; HR-MS (FAB): calcd for $C_{25}H_{27}N_2$ O [M]$^+$ 371.2123 found 371.2144.

5-Mesityl-2-(2-(2-(2-methoxyethoxy)ethoxy)phenyl)-2*H*-imidazo[1,5-*a*]pyridinium chloride (4g). With the same method used in the synthesis of **4a**, **4g** (86%) was obtained as a white powder from 2-(2-(2-methoxyethoxy)ethoxy)aniline **9** and 6-mesitylpicolinaldehyde **3**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.44 (s, 1H), 8.55 (s, 1H), 8.48 (d, J = 9.4 Hz, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.46 (t, J = 7.6 Hz, 1H), 7.35 (dd, J = 9.3, 6.8, Hz, 1H), 7.17 (t, J = 7.7 Hz, 1H), 7.10 (d, J = 8.5 Hz, 1H), 7.05 (s, 2H), 6.94 (d, J = 6.8 Hz, 1H), 4.22 (t, J = 4.5 Hz, 2H), 3.64 (t, J = 5.3 Hz, 2H), 3.41 (m, 2H), 3.30 (m, 2H), 3.17 (s, 3H), 2.35 (s, 3H), 2.05 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.4, 141.1, 137.1, 133.2, 132.0, 130.8, 129.3, 126.4, 126.3, 124.9, 123.8, 122.7, 122.2, 119.8, 119.2, 117.4, 114.3, 71.3, 69.7, 68.3, 68.1, 58.6, 21.1, 19.3 ppm; IR (ATR): ν = 3371, 3182, 2975, 2914, 1654, 1603, 1556, 1516, 1459, 1312, 1295, 1261, 1209, 1131, 1110, 851, 754, 654 cm^{-1}; HR-MS (FAB): calcd for $C_{27}H_{31}N_2O_3$ [M]$^+$ 431.2335 found 431.2330.

(2,5-Dimesityl imidazo[1,5-*a*]pyridinyl)copper(I) chloride (5a). 2,5-Dimesityl imidazo[1,5-*a*]pyridinium chloride **4a** (39.1 mg, 0.100 mmol), copper chloride(I) (9.90 mg, 0.100 mmol), and sodium *tert*-butoxide (10.6 mg, 0.110 mmol) were dissolved in THF (2.50 mL). The reaction mixture was stirred at room temperature overnight. The crude product was purified by flash column chromatography (*n*-hexane : ethyl acetate 3 : 1) and concentrated under reduced pressure to obtain a product **5a** as a green powder with 76% yield. Single crystals suitable for crystallography were obtained by liquid diffusion of *n*-hexane into a saturated ethyl acetate solution at room temperature. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 (d, J = 9.2 Hz, 1H), 7.25 (s, 1H), 7.04 (m, 3H), 6.92 (s, 2H), 6.53 (d, J = 6.6 Hz, 1H), 2.40 (s, 3H), 2.30 (s, 3H), 2.08 (s, 6H), 1.94 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.0, 139.5, 139.0, 136.3, 136.2, 134.0, 131.5, 130.2, 129.6, 129.4, 123.5, 116.5, 115.1, 112.6, 21.5, 21.2, 19.73, 17.7 ppm (signal from the carbon bonded metal was not detected); IR (ATR): ν = 3136, 2953, 2915, 2855, 1651, 1491, 1441, 1359, 1315, 1196, 1155, 1032, 851, 792, 784, 736, 682 cm^{-1}; HR-MS (EI): calcd for $C_{25}H_{26}N_2CuCl$ [M] 452.1081 found 452.1081.

(2-Adamantyl-5-mesityl imidazo[1,5-*a*]pyridinyl) copper(I) chloride (5b). With the same method used in the synthesis of **5a**, compound **5b** was obtained as a white powder with 64% yield from **4b**. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (s, 1H), 7.34 (d, *J* = 9.2 Hz, 1H), 7.05 (s, 2H), 6.92 (dd, *J* = 9.2, 6.6 Hz, 1H), 6.42 (d, *J* = 6.5 Hz, 1H), 2.46 (s, 6H), 2.42 (s, 3H), 2.24 (s, 3H), 2.01 (s, 6H), 1.75 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.9, 138.8, 136.3, 130.1, 129.9, 129.7, 122.5, 116.6, 114.8, 108.2, 59.6, 45.0, 35.8, 30.0, 21.6, 19.7 ppm (signal from the carbon bonded metal was not detected); IR (ATR): ν = 3181, 3045, 2911, 2850, 1650, 1452, 1304, 1156, 1081, 866, 780, 737, 705, 669 cm^{-1}; HR-MS (EI): calcd for $C_{26}H_{30}N_2CuCl$ [M] 468.1394 found 468.1398.

(2-(2,6-Diisopropylphenyl)-5-mesityl imidazo[1,5-*a*]pyridinyl)-copper(I) chloride (5c). With the same method used in the synthesis of **5a**, compound **5c** was obtained as a pale yellow powder with 96% yield from **4c**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.46 (m, 2H), 7.30 (s, 1H), 7.22 (d, *J* = 7.8 Hz, 2H), 7.08 (m, 3H), 6.56 (d, *J* = 6.6 Hz, 1H), 2.40 (s, 3H), 2.18 (m, 2H), 2.09 (s, 6H), 1.18 (d, *J* = 6.8 Hz, 6H), 1.12 (d, *J* = 6.8 Hz, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.1, 141.2, 139.0, 136.2, 135.5, 131.2, 130.6, 130.1, 129.7, 124.0, 123.8, 116.5, 115.3, 113.8, 28.5, 24.9, 24.2, 21.5, 19.6 ppm (signal from the carbon bonded metal was not detected); IR (ATR): ν = 3144, 2960, 2922, 2864, 1739, 1651, 1468, 1366, 1313, 1178, 846, 808, 797, 787, 767, 731, 684 cm^{-1}; HR-MS (EI): calcd for $C_{28}H_{32}N_2CuCl$ [M] 494.1550 found 494.1552.

(5-Mesityl-2-(2-(2-(2-methoxyethoxy)ethoxy)phenyl)-2,3-dihydroimidazo[1,5-*a*]pyridin-3-yl)copper(I) chloride (5g). 5-Mesityl-2-(2-(2-(2-methoxyethoxy)ethoxy)phenyl)-2H-imidazo[1,5-*a*]pyridinium chloride **4g** (149 mg, 0.320 mmol) and silver(II)oxide (74 mg, 0.320 mmol) were dissolved in CH_2Cl_2 (7.40 mL). The reaction mixture was stirred at room temperature overnight in the dark. The mixture was then filtered through a Celite pad and washed with CH_2Cl_2. The crude product was dissolved in CH_2Cl_2 (14 mL) and copper chloride(I) (63 mg, 0.640 mmol) was added in one portion. The reaction was stirred at room temperature overnight. The mixture was then filtered through a Celite pad and washed with CH_2Cl_2. The crude product was purified by flash column chromatography (*n*-hexane : ethyl acetate 1 : 6) and concentrated under reduced pressure to obtain a product **5g** as an ivory powder with 79% yield. Single crystals suitable for crystallography were obtained by liquid diffusion of *n*-hexane into a saturated benzene or THF solution at room temperature. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (s, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.41 (d, *J* = 9.3 Hz, 1H), 7.33 (t, *J* = 7.1 Hz, 1H), 7.04 (s, 2H), 6.98 (m, 3H), 6.46 (d, *J* = 6.5 Hz, 1H), 4.18 (t, *J* = 4.4 Hz, 2H), 3.74 (t, *J* = 4.8 Hz, 2H), 3.56 (m, 2H), 3.48 (m, 2H), 3.34 (s, 3H), 2.40 (s, 3H), 2.08 (s, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.6, 152.1, 140.8, 138.5, 136.3, 130.7, 130.4, 130.1, 129.5, 129.4, 128.1, 122.9, 121.3, 116.7, 115.0, 114.4, 113.6, 71.9, 70.6, 69.3, 68.3, 59.0, 21.5, 19.7 ppm; IR (ATR): ν = 3146, 2882, 2226, 1651, 1601, 1505, 1452, 1359, 1291, 1104, 911, 847, 788, 729 cm^{-1}; HR-MS (FAB): calcd for $C_{27}H_{30}N_2CuClO_3$ [M] 528.1241 found 528.1221.

2-(2-Methoxyethoxy)ethyl 4-methylbenzenesulfonate (8). Diethylene glycol monomethyl ether (6.01 g, 50 mmol), *p*-toluene sulfonyl chloride (11.4 g, 60 mmol), and pyridine (8.09 mL, 100 mmol) were combined at 0 °C, then stirred for 6 h at the same temperature. The reaction mixture was extracted with Et_2O and water, and washed with 1 N HCl. The organic phase was dried over anhydrous $MgSO_4$, filtered, and concentrated in a vacuum. The crude product was purified by flash column chromatography (*n*-hexane : ethyl acetate 3 : 1) to give a product **8** (90%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J* = 8.2 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 4.15 (m, 2H), 3.67 (m, 2H), 3.56 (m, 2H), 3.46 (m, 2H), 3.33 (s, 3H), 2.43 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) 144.8, 132.8, 129.8, 127.9, 71.7, 70.6, 69.2, 68.6, 59.0, 21.6 ppm.

2-(2-(2-Methoxyethoxy)ethoxy)aniline (9). To a solution of 2-nitrophenol (139 mg, 1.00 mmol) and potassium carbonate (138 mg, 1.00 mmol) in DMF (3.50 mL) was added a solution of 2-(2-methoxyethoxy)ethyl 4-methylbenzenesulfonate **8** (274 mg, 1.00 mmol) in DMF (2.00 mL) and allowed to reflux overnight. Afterward, the mixture was cooled to room temperature. The solvent was evaporated and the residue was dissolved in ethyl acetate. The organic phase was washed with water, dried over anhydrous $MgSO_4$, then filtered and concentrated in a vacuum. The crude mixture was subjected to hydrogenation over Pd/C in MeOH (8.00 mL) at room temperature under H_2 atmosphere for 24 h. Pd/C was filtered through a Celite pad and the filtrate was concentrated under reduced pressure. The crude product was purified by flash column chromatography (*n*-hexane : ethyl acetate 2 : 1) to give a product **9** (84%, 2 steps) as a dark orange oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.82–6.78 (m, 2H), 6.73–6.67 (m, 2H), 4.16 (m, 2H), 3.86 (m, 2H), 3.71 (m, 2H), 3.57 (m, 2H), 3.39 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 146.1, 136.8, 121.5, 118.0, 115.0, 112.5, 71.7, 70.4, 69.6, 68.0, 58.9 ppm.; IR (ATR): ν = 3458, 3358, 3058, 2924, 2876, 2822, 1616, 1505, 1458, 1277, 1218, 1105, 1053, 927, 848, 738 cm^{-1}; HR-MS (EI): calcd for $C_{11}H_{17}NO_3$ $[M]^+$ 211.12 found 211.1209.

General procedure for catalytic direct C–H carboxylation with CO_2

General procedures for ImPy Cu-catalyst generated *in situ* for direct C–H carboxylation of heterocyclic compound. General procedures were adapted from those used by Hou *et al.*[16c] Ligand (5 mol%), copper chloride(I) (2.50 mg, 5 mol%), and potassium *tert*-butoxide (65.1 mg, 0.580 mmol) were added to a 30 mL Schlenk flask equipped with Teflon-valve in a glove box. THF (2.50 mL) was added to the reaction flask and stirred at room temperature for 4 hours. Under an Ar atmosphere, a heterocyclic compound (59.6 mg, 0.500 mmol) was added to the reaction mixture. The mixture was degassed through three freeze–pump–thaw cycles and CO_2 (1 atm) was charged into the reaction flask. The sealed Schlenk flask was stirred at 80 °C for 14 hours. After the reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure. DMF (2.50 mL) and 1-iodohexane (0.150 mL, 1.00 mmol) were added to the mixture under an Ar atmosphere and stirred at 80 °C for 6 hours. The reaction mixture was dissolved in ethyl acetate and washed with water. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated in a vacuum. The crude product was purified by flash column chromatography (*n*-hexane : ethyl acetate 8 : 1) to give the product.

General procedures for ImPy Cu-catalyzed carboxylation of benzoxazole with CO_2. ImPy–Cu complexes (5 mol%) and potassium *tert*-butoxide (61.7 mg, 0.550 mmol) were added to a 30 mL Schlenk flask equipped with Teflon-valve in a glove box and THF (2.50 mL) was charged into the reaction flask. Benzoxazole (59.6 mg, 0.500 mmol) was added and the mixture was degassed through three freeze–pump–thaw cycles. CO_2 (1 atm) was charged into the reaction flask. The reaction mixture was stirred at 80 °C for 14 hours. After the reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure. DMF (2.50 mL) and 1-iodohexane (0.150 mL, 1.00 mmol) were added to the mixture under an Ar atmosphere and stirred at 80 °C for 6 hours. Subsequent procedures remained the same as described above.

All compounds were reported materials[16c] except for 5-methoxy-benzoxazole-2-carboxylic acid hexyl ester (**7e**).

5-Methoxy-benzoxazole-2-carboxylic acid hexyl ester (7e). Yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (dd, $J = 9.0$, 2.3 Hz, 1H), 7.25 (t, $J = 2.4$ Hz, 1H), 7.08 (dt, $J = 9.1$, 2.5 Hz, 1H), 4.43 (td, $J = 6.8$, 2.0 Hz, 2H), 3.82 (d, $J = 2.3$ Hz, 3H), 1.85–1.77 (m, 2H), 1.43–1.28 (m, 6H), 0.85 (m, 3H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.2, 156.6, 153.4, 145.6, 141.5, 118.0, 112.0, 103.5, 67.3, 56.0, 31.4, 28.5, 25.5, 22.5, 14.0 ppm; IR (ATR): $\nu = 2932$, 2856, 1732, 1609, 1544, 1484, 1438, 1325, 1260, 1205, 1152, 1025, 853, 815 cm^{-1}; HR-MS (EI): calcd for $C_{15}H_{19}NO_4$ [M] 277.1314 found 277.1312.

Conflicts of interest

There are no conflicts to declare.

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