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N-heterocyclic carbene copper(i) catalysed
N-methylation of amines using CO₂†Orlando Santoro,^a Faïma Lazreg,^a Yury Minenkov,^b Luigi Cavallo^b and
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The *N*-methylation of amines using CO₂ and PhSiH₃ as source of CH₃ was efficiently performed using a *N*-heterocyclic carbene copper(i) complex. The methodology was found compatible with aromatic and aliphatic primary and secondary amines. Synthetic and computational studies have been carried out to support the proposed reaction mechanism for this transformation.

Introduction

The simple methylation of amines is a well-known transformation in organic chemistry leading to compounds having applications in the synthesis of dyes, natural products and fine chemicals.¹ Several synthetic protocols exist to achieve this transformation and include the nucleophilic substitution of electrophilic methylating reagents (*e.g.*, methyl iodide) and the methylation with formaldehyde in the presence of reducing reagents (*e.g.*, formic acid and metal hydride).² However, important drawbacks are associated with these procedures such as reagent toxicity or limitation in the substrate scope. Recently, alternative methodologies have been reported based on the use of CO₂ as a methylating reagent. CO₂ is an inexpensive, non-toxic and the most abundant carbon source. It is potentially the most attractive C₁ feedstock to introduce carbon into molecules.³ In 2013, Cantat and co-workers reported an interesting methodology based on zinc using [Zn(Cl)₂(IPr)] (IPr = *N,N'*-bis-[2,6-(di-*iso*-propyl)phenyl] imidazol-2-ylidene) as catalyst. Phenylsilane was used as the reducing reagent (Scheme 1).⁴ Almost concomitantly, Beller and co-workers disclosed a ruthenium-based methodology.⁵ For the latter, excess silane was required under 30 bar of carbon dioxide. Shortly after, the same group reported a variant of this transformation replacing the silane with hydrogen gas. However, high pressure of H₂ (60 bar) and CO₂ (20 bar) were

required as well as long reaction times (24 h to 48 h) and elevated temperature (140 °C). Independently, Leitner and co-workers reported that an alternative ruthenium based-system could enable this transformation.⁶ Recently, a nickel/phosphine system able to promote this transformation was investigated.⁷ Organocatalysts have also been shown as efficient promoters of this transformation.⁸ Finally, Beller and Cantat also showed that formic acid can be used as C₁ source or as both C₁ and hydrogen source.^{9,10} Despite their elegance, these protocols suffer from the use of relatively expensive metals and

R ₂ NH		→	R ₂ N-CH ₃	
C source (pressure)	H source (pressure)	Catalyst (loading)	Reaction conditions	Ref.
CO ₂ (1 bar)	PhSiH ₃	[Zn(Cl) ₂ (IPr)] (5 mol%)	THF, 100 °C, 20 h	4
CO ₂ (30 bar)	PhSiH ₃	[Ru(Cl) ₂ (dmsol) ₄] (2 mol%)	toluene, 100 °C, 10–36 h	5a
CO ₂ (20 bar)	H ₂ (60 bar)	[Ru(acac) ₃] (1 mol%)	THF, 140 °C, 24 h	5b
CO ₂ (20 bar)	H ₂ (60 bar)	[Ru(triphos)(tmm)] (2.5 mol%)	THF, 150 °C, 24 h	6
CO ₂ (1 bar)	9-BBN	proazaphosphatane superbase (1 mol%)	THF, 90 °C, 1 h	7a
CO ₂ (1 bar)	Ph ₂ SiH ₂	free NHC (5 mol%)	DMF, 50 °C, 24–48 h	7b
HCO ₂ H	PhSiH ₃	Karstedt's catalyst (1 mol%)	nBu ₂ O, rt, 18 h	8
HCO ₂ H		[Ru(COD)(methylallyl) ₂] (1 mol%)	THF, 150 °C, 24 h	9

Scheme 1 State-of-the-art for the methylation of amines with CO₂.^aEaStCHEM School of Chemistry, University of St Andrews, St Andrews, KY16 9ST, UK. E-mail: cc111@st-andrews.ac.uk^bPhysical Sciences and Engineering Division, King Abdullah University of Science and Technology (KAUST), Kaust Catalysis Center, Thuwal 23955-6900, Saudi Arabia

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ligands and, in some cases, high pressures and temperatures. In addition, mechanistic details for this reaction have not been explored yet. Recently, it has been shown that economical copper complexes can promote direct carboxylation of N–H and C–H bonds using CO₂.^{11,12} Indeed, [Cu(OH)(IPr)] (**1**) as catalyst allowed CO₂ insertion into a C–H and N–H bonds leading to the formation of carboxylic and carbamic acid derivatives, respectively.

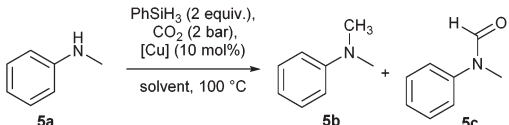
Moreover, copper-based complexes are well-established catalysts for the hydrosilylation of CO₂.^{13,14} Based on these observations, it was hypothesised that the reactivity of NHC–copper complexes could be extended to the methylation of N–H bonds. In particular, this could be performed in two steps: a carboxylation followed by a reduction. Herein, we reported the first Cu-catalysed methylation of amines with mechanistic insight into the fixation of CO₂ with amines.

Results and discussion

In the initial optimisation studies, *N*-methylaniline **5a** was chosen as the benchmark substrate (Table 1).

The hydroxide complex **1** (Fig. 1) showed interesting reactivity in solvents such as toluene or benzene. However, no activity was observed in alcohol solvents. By using its *tert*-butoxide congener, **2**, the conversion to the desired compound slightly increased (Table 1, entries 5 and 6). The nature of the NHC ligand was next examined. When the bulkier IPr* was used (**3**), only 22% conversion to the methylated product was observed. On the other hand, the IMes analogue complex [Cu(O^{*t*}Bu)(IMes)] **4** exhibits improved reactivity. Indeed, in the presence of **4**, full conversion into the desired product is observed in toluene after 20 h.

Table 1 Optimisation of the catalyst, solvent and reaction time^a

					
Entry	[Cu]	Solvent	Time (h)	5b ^b	5c ^b
1	1	Toluene	20	35%	65%
2	1	Benzene	20	40%	60%
3	1	Isopropanol	20	—	—
4	1	THF	20	24%	76%
5	2	Toluene	20	50%	50%
6	2	THF	20	48%	52%
7	3	THF	20	22%	78%
8	4	THF	20	96%	4%
9	4	Toluene	20	>99%	—
10	4	Toluene	2	40%	60%
11	4	Toluene	4	45%	55%
12	4	Toluene	6	57%	43%
13	4	Toluene	8	70%	30%

^a Reaction conditions: amine (0.25 mmol), [Cu] (10 mol%), PhSiH₃ (2 equiv.), solvent (2 mL), CO₂ (2 bar), 100 °C. ^b Conversion determined by GC, based on amine, minimum average of two reactions.

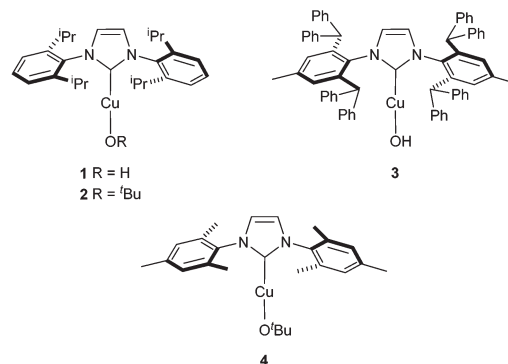
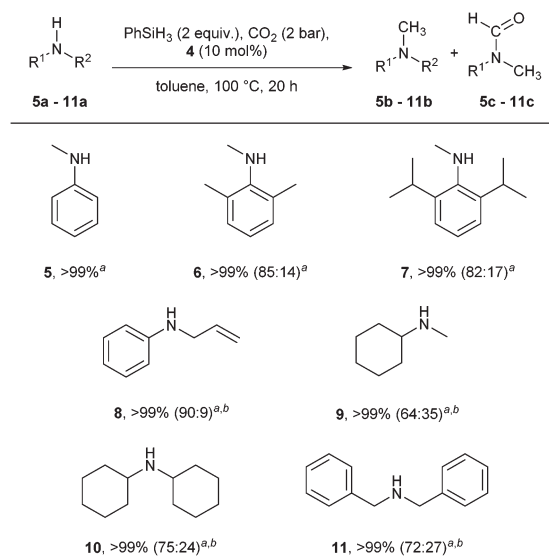


Fig. 1 Catalysts studied in the *N*-methylation.

Based on these promising results, the influence of the reaction time was examined. After 2 hours all starting material was converted into a mixture of amide (60%) and *N*-methylaniline (40%). This highlights that the CO₂ insertion occurs in less than 2 hours and that it is not the rate-limiting step in the transformation. As a function of time, the amount of *N*-methylation increased. After 8 hours, 70% of the desired compound was obtained. Finally, the optimal reaction conditions for the transformation were determined to be [Cu(O^{*t*}Bu)(IMes)] (10 mol%), phenylsilane at 100 °C under 2 bar of CO₂ for 20 h.

Using these conditions, the scope of the reaction was investigated, starting with secondary amines (Scheme 2).

N,N-Dimethylaniline **5b** was obtained quantitatively and selectively. Sterically congested *N*-methylanilines such as **6a** and **7a** were efficiently converted into the desired compounds,



Scheme 2 Cu-catalysed methylation of secondary amines using CO₂ as C₁ building block. Reaction conditions: amine (0.25 mmol), **4** (10 mol%), PhSiH₃ (2 equiv.), toluene (2 mL), CO₂ (2 bar), 100 °C, 20 h. Conversions determined by GC, based on amine, minimum average of two reactions. ^ab : c ratio. ^bKO^{*t*}Bu (10 mol%), PhSiH₃ (4 equiv.).

Table 2 Influence of additives on the composition of the reaction mixture

Entry	Substrate	Reaction conditions			
		I	II	III	IV
1	8a	b : 49% c : 50%	b : 53% c : 46%	b : 44% c : 55%	b : 90% c : 9%
2	9a	b : 14% c : 85%	b : 40% c : 59%	b : 33% c : 66%	b : 64% c : 35%
3	10a	b : 45% c : 54%	b : 62% c : 37%	b : 70% c : 29%	b : 75% c : 24%
4	11a	b : 15% c : 84%	b : 59% c : 40%	b : 46% c : 53%	b : 72% c : 27%

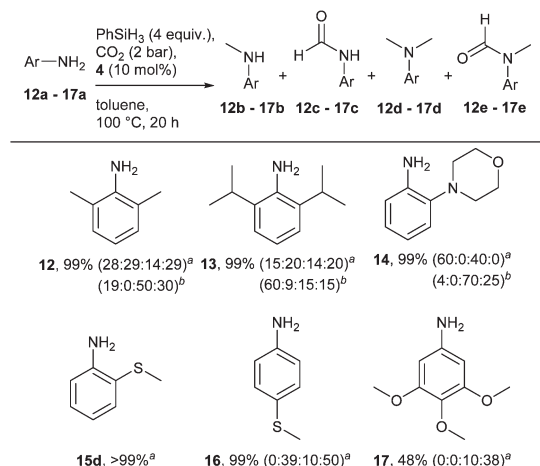
Reaction conditions: amine (0.25 mmol), **4** (10 mol%), toluene (2 mL), CO₂ (2 bar), 100 °C, 20 h. Conversions determined by GC, based on amine, minimum average of two reactions. **I**: 2 equiv. PhSiH₃, no base. **II**: 2 equiv. PhSiH₃, 10 mol% KO^tBu. **III**: 4 equiv. PhSiH₃, no base. **IV**: 4 equiv. PhSiH₃, 10 mol% KO^tBu.

the major product being the methylated compound (85% and 82%, respectively). In contrast, while full consumption of starting materials was also observed with compounds **8–11**, the major product under these reaction conditions (2 equiv. PhSiH₃, no base) was the amide intermediate. In order to overcome this issue, the reaction conditions were further optimised, and the addition of additives was investigated (Table 2).

By adding a catalytic amount of KO^tBu (10 mol% – **II**), an important increase in the formation of the methylated compound was observed for substrates **9a–11a** while only a slight improvement was observed for **8a**. The same trend was observed by doubling the amount of silane. Finally, by combining the two variations (4 equiv. of silane and 10 mol% KO^tBu), the conversion of all substrates towards the desired compounds was drastically improved. Although KO^tBu may be required to promote catalyst regeneration, by doubling its amount no further improvement was observed.

It is interesting to note that, under our standard reaction conditions, *i.e.* without adding 10 mol% of KO^tBu, substrate **9a** leads to a 14% conversion of the methylated compound while the more hindered *N,N*-dicyclohexylamine (**10a**) is converted in 45%.

Primary amines were next considered (Scheme 3). All substrates investigated were completely converted into a mixture of mono- and di-methylated compounds and their corresponding amide derivatives. Interestingly, the bulkiness of the *ortho* substituents of substrates **12a** and **13a** did not affect the outcome of the reaction; both led to the dimethylated product. No amide intermediate was observed with substrate **14a**. In the case of methylthio-anilines, the position of the (S–CH₃) substituent proved to be crucial. While 2-(methylthio)-aniline (**15a**) was fully converted into the dimethylated product, only 10% of



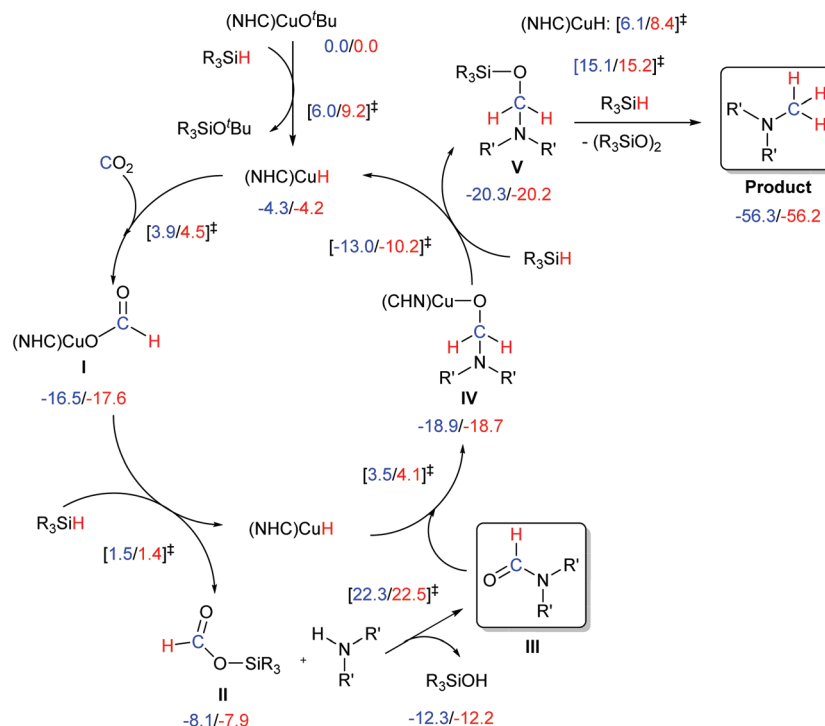
Scheme 3 Cu-catalysed methylation of anilines. Reaction conditions: amine (0.25 mmol), **4** (10 mol%), PhSiH₃ (2 equiv.), toluene (2 mL), CO₂ (2 bar), 100 °C, 20 h. Conversions determined by GC, based on amine, minimum average of two reactions. ^a**b** : **c** : **d** : **e** ratio. ^bKO^tBu (10 mol%).

the corresponding *para*-substituted product was isolated. Also in this case, the addition of a catalytic amount of KO^tBu proved to have a positive effect on the reaction. In fact, the formation of the monomethylated compound **13b** was improved while an increase in dimethylated product was observed for substrates **12a** and **14a**.

Mechanistic studies

The proposed mechanism for the methylation of amines with CO₂ and silane is depicted in Scheme 4. The first steps of this pathway involve the formation of a hydride species followed by the insertion of CO₂ into the Cu–H bond affording a Cu-formato species (**I**). The latter complex undergoes meta-thesis with the silane to afford the copper hydride species and the siloxane **II**. The siloxane then reacts with the amine to form the amide derivative (**III**). The amide would further react with the [Cu(H)(NHC)] to form species **IV**. This intermediate, in the presence of silane, would regenerate the hydrido complex and release the desired compound.

In order to obtain a more detailed understanding of the pathway described, we carried out DFT calculations with both IMes- and IPr-based catalysts. The energetics of the transformation are reported in Scheme 4. Calculations indicate that activation of the initial pre-catalyst to the [Cu(H)(NHC)] species, as well as the CO₂ activation step by its insertion into the Cu–H bond of [Cu(H)(NHC)], leading to the formato species **I**, are relatively easy steps, with free energy barriers less than 10 kcal mol^{−1}. The reactivity of **I** with the silane has a relatively low energy barrier of 18–19 kcal mol^{−1}. This step regenerates [Cu(H)(NHC)], and liberates HC(O)OSiR₃ (**II**), which can react with the amine to generate the amide intermediate **III**. Although this organic transformation is energetically quite expensive, *ca.* 30 kcal mol^{−1}, it is consistent with



Scheme 4 Pathways for methylation *via* CO₂ insertion. DFT calculated ΔG (kcal mol⁻¹) are reported for NHC = IMes and IPr.

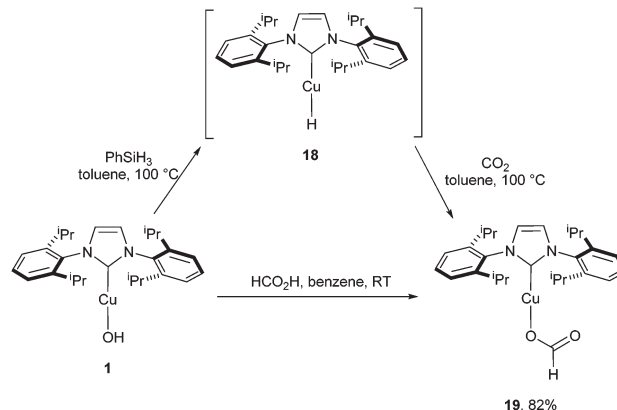
the harsh experimental conditions and previous computational work.^{15,16} Once formed, the amide can easily react with [Cu(H)(NHC)] to generate [Cu(OCH₂NR'₂)(NHC)] (**IV**), which can liberate R₃Si–O–CH₂–NR'₂ (**V**) through reaction with R₃SiH *via* fairly small activation barrier of 10–13 kcal mol⁻¹. The next step, reduction of **V** with hydrosilane, despite being highly favorable thermodynamically, occurs *via* fairly high activation barriers of ~35.0 kcal mol⁻¹ when the transformation is not catalysed.¹⁵

On the other hand, when catalysed by [Cu(H)(NHC)] the barrier of this transformation is reduced to 26–28 kcal mol⁻¹.¹⁵

To support these computational findings, synthetic studies were carried out. Phenylsilane was added to a solution of [Cu(OH)(IPr)] and the reaction was monitored by ¹H NMR.

The data are in accordance with the *in situ* formation of [Cu(H)(IPr)] (**18**) (Scheme 5).¹⁷ The subsequent reaction of this species with CO₂ (2 bar) led to the formation of [Cu{OC(O)H}-(IPr)] (**19**).^{13,18} The same outcome was obtained by reacting [Cu(OH)(IPr)] with formic acid in benzene.

In order to corroborate the other steps of the proposed mechanism, stoichiometric NMR experiments were carried out (Scheme 6). By reacting **19** with *N*-methylaniline **5a** in the presence of PhSiH₃, 50% conversion towards *N*-methylformanilide **5c** was observed. Noteworthy, the formation of the dimethylated compound was not observed. This is probably due to the short reaction time (7 hours rather than 20 hours).¹⁵ As highlighted in Scheme 6, the presence of silane is crucial for the formylation of *N*-methylaniline. In fact, the reaction solely promoted by **19** was unsuccessful in the presence or absence of KO^tBu.¹⁵

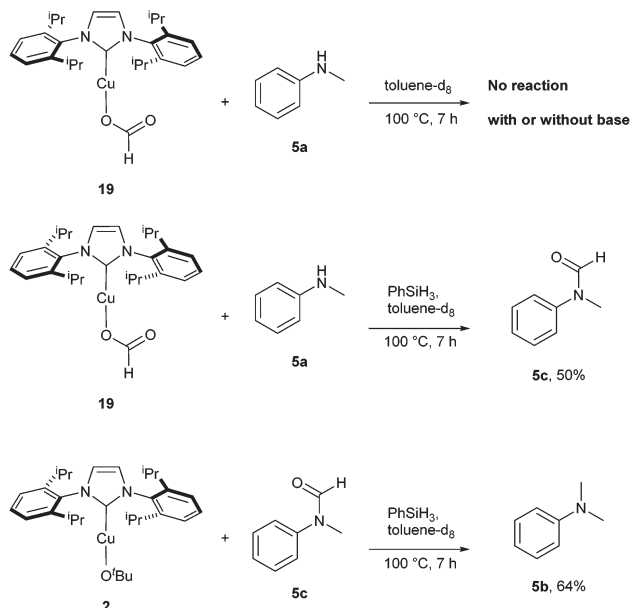


Scheme 5 Formation of [Cu{OC(O)H}-(IPr)].

Finally, the reduction of **5c** promoted by PhSiH₃ in the presence of the copper catalyst was carried out. After 7 hours, the reaction led to 64% conversion of the amide into the methylated product **5b** confirming the methylation proceeds *via* *N*-formylamine intermediates.¹⁵

Conclusions

In conclusion, the first NHC-copper-catalysed methylation of N–H bonds using CO₂ and silane as reagents was reported. The scope of this transformation showed that secondary amines are converted under relatively mild conditions into the



Scheme 6 NMR experiments.

desired methylated products while primary amines provide a distribution of products depending on the nature of the substrate. DFT calculations supported by experimental work were carried out in order to elucidate the mechanism of this transformation.

Experimental

General information

All reactions were carried out under argon atmosphere using standard Schlenk and glovebox techniques. Chemicals were used as received unless otherwise noted. Dry toluene was obtained from a PureSolv SPS-400-5 solvent purification system. ^1H , and $^{13}\text{C}\{-^1\text{H}\}$ Nuclear Magnetic Resonance (NMR) spectra were recorded on a Bruker-400 MHz or 300 MHz spectrometers using the residual solvent peak as reference (CDCl_3 : $\delta_{\text{H}} = 7.26$ ppm, $\delta_{\text{C}} = 77.16$ ppm, CD_2Cl_2 : $\delta_{\text{H}} = 5.32$ ppm, $\delta_{\text{C}} = 53.84$ ppm, C_7D_8 : $\delta_{\text{H}} = 2.08$ ppm, $\delta_{\text{C}} = 20.4$ ppm) at 298 K. Elemental analyses were performed at London Metropolitan University. HMRS analyses were carried out by the EPSRC National Mass Spectrometry Service Centre at Swansea University.

Synthesis of $[\text{Cu}(\text{OH})(\text{IPr}^*)]$ (3)

In a glovebox, a round bottom flask was charged with $[\text{Cu}(\text{Cl})(\text{IPr}^*)]$ (250 mg, 0.25 mmol), CsOH (74 mg, 2 equiv.) and THF (12.5 mL). The reaction mixture was stirred at room temperature during 15 hours. The suspension was filtered through a plug of celite. The solution was concentrated and pentane (10 mL) was added. The colourless precipitate was collected by filtration and washed with pentane (3×5 mL). The product was obtained as a colourless solid in 89% yield (215 mg, 0.22 mmol). ^1H NMR (300 MHz, C_7D_8 , 298 K): $\delta = 1.74$ (s, 6H,

CH_3), 5.58 (s, 2H, H^4 and H^5), 5.60 (s, 4H, CHPh_2), 6.97–7.01 (m, 28H, CHAr), 7.17 (m, 8H, CHAr), 7.41 (m, 8H, CHAr). $^{13}\text{C}\{-^1\text{H}\}$ NMR (75 MHz, C_7D_8 , 298 K): $\delta = 21.1$ (s, CH_3), 51.7 (s, CHPh_2), 123.2 (s, C^4 and C^5), 126.8 (s, CH Ar), 127.0 (s, CH Ar), 128.3 (s, CH Ar), 128.6 (s, CH Ar), 128.7 (s, CH Ar), 129.1 (s, CH Ar), 129.9 (s, CH Ar), 130.3 (s, $\text{C}^{\text{IV}}\text{Ar}$), 130.6 (s, $\text{C}^{\text{IV}}\text{Ar}$), 141.7 (s, $\text{C}^{\text{IV}}\text{Ar}$), 143.5 (s, $\text{C}^{\text{IV}}\text{Ar}$), 143.7 (s, $\text{C}^{\text{IV}}\text{Ar}$). C^2 has not been observed. Elem. Anal.: Calcd for $\text{C}_{25}\text{H}_{33}\text{CuN}_2\text{O}$: C, 83.40; H, 5.78, N, 2.82. Found: C, 83.46, H, 5.65, N, 2.74.

General procedure for the methylation

Under an argon atmosphere, a 3 mL vial was charged with $[\text{Cu}(\text{O}^t\text{Bu})(\text{IMes})]$ (4) (11 mg, 10 mol%), KO^tBu (2.8 mg, 10 mol %) and toluene (2 mL). The amine substrate (0.25 mmol, 1 equiv.) and PhSiH_3 (123 μL , 1.0 mol, 4 equiv.) were added and the vial was sealed with a septum cap. The septum cap was pierced with a syringe needle and placed into a six-slot steal autoclave. The autoclave was sealed, purged twice with CO_2 and heated at 100 $^\circ\text{C}$ (oil bath) under CO_2 atmosphere (2 bar) for 20 hours. The reaction mixture was then allowed to cool and the gas was carefully released. The reaction mixture was analysed by gas chromatography (GC). In the case of isolated products, dichloromethane (5 mL) was added to the crude and the mixture was extracted with HCl 1 M (3×10 mL). The aqueous layer was neutralised by addition of K_2CO_3 (pH = 12) and extracted with diethyl ether (3×10 mL). The ether layer was dried over Na_2SO_4 . Removal of the solvent afforded the desired compounds.

3,4,5-Trimethoxy-N,N-dimethylaniline, 17b. ^1H NMR (400 MHz, CDCl_3 , 298 K): $\delta = 2.93$ (s, 6H, N- CH_3), 3.78 (s, 3H, O- CH_3), 3.86 (s, 6H, O- CH_3), 5.95 (s, 2H, CH phenyl) $^{13}\text{C}\{-^1\text{H}\}$ NMR (75 MHz, CDCl_3 , 298 K): $\delta = 41.3$ (s, N- CH_3), 56.13 (s, O- CH_3), 61.2 (s, O- CH_3), 91.0 (s, CH Ar), 130.0 (s, $\text{C}^{\text{IV}}\text{Ar}$), 147.9 (s, $\text{C}^{\text{IV}}\text{Ar}$), 153.8 (s, $\text{C}^{\text{IV}}\text{Ar}$). HMRS (APCI) m/z Calcd for $[\text{C}_{11}\text{H}_{17}\text{O}_3\text{N} + \text{H}]^+$ 212.1281. Found 212.1279.

Synthesis of $[\text{Cu}\{\text{OC}(\text{O})\text{H}\}(\text{IPr})]$, (19)

Under an argon atmosphere, a vial was charged with $[\text{Cu}(\text{OH})(\text{IPr})]$ (1) (200 mg, 0.21 mmol, 1 equiv.), formic acid (16 μL , 0.21 mmol, 1 equiv.) and benzene (2 mL). The mixture was stirred at room temperature for 1 hour, the solution was then concentrated under reduced pressure. The addition of pentane (10 mL) afforded a colourless solid collected by filtration (Yield = 82%). ^1H NMR (400 MHz, CDCl_3 , 298 K): $\delta = 1.22$ (d, $^3J_{\text{H-H}} = 6.8$ Hz, 12H, CH- CH_3), 1.29 (d, $^3J_{\text{H-H}} = 6.8$ Hz, 12H, CH- CH_3), 2.56 (sept, $^3J_{\text{H-H}} = 7.0$ Hz, 4H, CH- CH_3 isopropyl), 7.15 (s, 2H, H^4 and H^5), 7.29 (d, $^3J_{\text{H-H}} = 7.8$ Hz, 4H, CH phenyl), 7.48 (t, $^3J_{\text{H-H}} = 7.9$ Hz, 2H, CH phenyl), 8.11 (s, 1H, C(O)H formyl) $^{13}\text{C}\{-^1\text{H}\}$ NMR (75 MHz, CDCl_3 , 298 K): $\delta = 24.0$ (s, CH- CH_3), 24.8 (s, CH- CH_3), 28.8 (s, CH- CH_3), 123.3 (s, $\text{C}^{\text{IV}}\text{Ar}$), 124.3 (s, CH Ar), 130.6 (s, C^4 and C^5), 134.5 (s, $\text{C}^{\text{IV}}\text{Ar}$), 145.7 (s, CH Ar), 167.9 (s, OC(O)H), 180.4 (s, C^2).

Computational details

Geometry optimisations and calculations of thermochemical corrections. All geometry optimisations were performed using

the PBE GGA¹⁹ functional as implemented in PRIRODA 13 DFT code.²⁰ All electron basis sets (L1)²¹ comparable in quality to the correlation consistent valence double- ζ plus polarisation (cc-PVDZ) basis sets of Dunning were used. All stationary geometries were characterised by analytically calculated Hessian matrix. Possible relativistic effects (for copper) were taken into account *via* the Dyall Hamiltonian.²²

The default, adaptively generated PRIRODA grid, corresponding to an accuracy of the exchange–correlation energy per atom (1×10^{-8} hartree) was decreased by a factor of 100 for more accurate evaluation of the exchange–correlation energy. Default values were used for the Self-Consistent-Field (SCF) convergence and the maximum gradient for geometry optimisation criterion (1×10^{-4} au), whereas the maximum displacement geometry convergence criterion was decreased to 0.0018 au.

Translational, rotational, and vibrational partition functions for thermal corrections to arrive at total Gibbs free energies were computed within the ideal-gas, rigid-rotor, and harmonic oscillator approximations. The temperature used in the calculations of thermochemical corrections was set to 298.15 K in all the cases.

Single-point (SP) energy evaluations. The energies were re-evaluated at optimised geometries by means PBE GGA functional as implemented in Gaussian 09 code.²³ The effects from dispersion were included *via* DFT-D3(BJ)²⁴ correction term. All electron def2-tzvp basis sets of Ahlrichs groups were used with corresponding density-fitting basis sets.²⁵ The default value for the SP SCF convergence was adopted. The “Integral (grid = ultrafine)” option was used for evaluation of the exchange–correlation term.

Solvent effects. Electrostatic and non-electrostatic solvent effects were estimated by means of SMD²⁶ solvation model as implemented in Gaussian 09 code. The internal program values for toluene (dielectric constant, *etc.*) were adopted. A standard state corresponding to 1 M ideal dilute solution was used.

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Notes and references

- (a) J. M. Adams and S. Cory, *Nature*, 1975, **255**, 28; (b) D. Dominissini, S. Moshitch-Moshkovitz, S. Schwartz, M. Salmon-Divon, L. Ungar, S. Osenberg, K. Cesarkas, J. Jacob-Hirsch, N. Amariglio, M. Kupiec, R. Sorek and G. Rechavi, *Nature*, 2012, **485**, 201; (c) E. L. Greer and Y. Shi, *Nat. Rev. Genet.*, 2012, **13**, 343; (d) K. D. Meyer, Y. Saletore, P. Zumbo, O. Elemento, C. E. Mason and S. R. Jaffrey, *Cell*, 2012, **149**, 1635; (e) *Kirk-Othmer Encyclopedia of Chemical Technology*, Wiley, New York, 4th edn, 1992, p. 438.
- (a) H. T. Clarke, H. B. Gillespie and S. Z. Weisshaus, *J. Am. Chem. Soc.*, 1933, **55**, 4571; (b) E. Farkas and C. J. Sunman, *J. Org. Chem.*, 1985, **50**, 1110; (c) J. R. Harding, J. R. Jones, S. Y. Lu and R. Wood, *Tetrahedron Lett.*, 2002, **43**, 9487; (d) S. Kim, C. H. Oh, J. S. Ko, K. H. Ahn and Y. J. Kim, *J. Org. Chem.*, 1985, **50**, 1927; (e) H. Alinezhad, M. Tajbakhsh and R. Zamani, *Synth. Commun.*, 2006, **36**, 3609; (f) H. Alinezhad, M. Tajbakhsh, F. Salehian and K. Fazli, *Synth. Commun.*, 2010, **40**, 2415; (g) M. Tanis and G. Rauniyar, *US Pat*, 5105013, 1992; (h) M. Selva, P. Tundo and A. Perosa, *J. Org. Chem.*, 2002, **67**, 9238; (i) P. Tundo and M. Selva, *Acc. Chem. Res.*, 2002, **35**, 706; (j) M. Selva, P. Tundo and A. Perosa, *J. Org. Chem.*, 2003, **68**, 7374; (k) M. Selva, P. Tundo and T. J. Foccardi, *Org. Chem.*, 2005, **70**, 2476; (l) M. Selva, A. Perosa, P. Tundo and D. Brunelli, *J. Org. Chem.*, 2006, **71**, 5770; (m) M. Selva and A. Perosa, *Green Chem.*, 2008, **10**, 457; (n) T. Oku, Y. Arita, H. Tsuneki and T. Ikariya, *J. Am. Chem. Soc.*, 2004, **126**, 7368; (o) Y. Zhao, S. W. Foo and S. Saito, *Angew. Chem., Int. Ed.*, 2011, **50**, 3006.
- (a) *Carbon Dioxide as Chemical Feedstock*, ed. M. Aresta, Wiley-VCH, Weinheim, 2010; (b) M. Aresta, in *Activation of Small Molecules*, ed. W. B. Tolman, Wiley-VCH, Weinheim, 2006, ch. 1; (c) D. H. Gibson, in *Comprehensive Coordination Chemistry-II*, ed. J. A. McCleverty and T. J. Meyer, Elsevier Ltd., Amsterdam, 2003, vol. 1, section 1.30, p. 595.
- O. Jacquet, X. Frogneux, C. D. N. Gomes and T. Cantat, *Chem. Sci.*, 2013, **4**, 2127.
- (a) Y. Li, X. Fang, K. Junge and M. Beller, *Angew. Chem., Int. Ed.*, 2013, **52**, 9568; (b) Y. Li, I. Sorribes, T. Yan, K. Junge and M. Beller, *Angew. Chem., Int. Ed.*, 2013, **52**, 12156.
- K. Beydoun, T. vom Stein, J. Klankermayer and W. Leitner, *Angew. Chem., Int. Ed.*, 2013, **52**, 9554.
- L. González-Sebastián, M. Flores-Alamo and J. J. García, *Organometallics*, 2015, **34**, 763.
- (a) E. Blondiaux, J. Pouessel and T. Cantat, *Angew. Chem., Int. Ed.*, 2014, **53**, 12186; (b) S. Das, F. D. Bobbink, G. Laurenczy and P. J. Dyson, *Angew. Chem., Int. Ed.*, 2014, **53**, 12876.
- I. Sorribes, K. Junge and M. Beller, *Chem. – Eur. J.*, 2014, **20**, 7878.
- S. Savourey, G. Lefèvre, J. Berthet and T. Cantat, *Chem. Commun.*, 2014, **50**, 14033.
- I. I. F. Boogaerts, G. C. Fortman, M. R. L. Furst, C. S. J. Cazin and S. P. Nolan, *Angew. Chem., Int. Ed.*, 2010, **49**, 8674.
- G. C. Fortman, A. M. Z. Slawin and S. P. Nolan, *Organometallics*, 2010, **29**, 3966.
- L. Zhang, J. Cheng and Z. Hou, *Chem. Commun.*, 2013, **49**, 4782.

- 14 K. Motokura, D. Kashiwame, N. Takahashi, A. Miyaji and T. Baba, *Chem. – Eur. J.*, 2013, **19**, 10030.
- 15 See ESI† for further information.
- 16 S. Ilieva, B. Galabov, D. G. Musaev, K. Morokuma and H. F. Schaefer, *J. Org. Chem.*, 2003, **68**, 1496.
- 17 (a) N. P. Mankad, D. S. Laitar and J. P. Sadighi, *Organometallics*, 2004, **23**, 3369; (b) M. R. Uehling, R. P. Rucker and G. Lalic, *J. Am. Chem. Soc.*, 2014, **136**, 8799; (c) A. M. Whittaker and G. Lalic, *Org. Lett.*, 2013, **15**, 1112.
- 18 C. M. Wyss, B. K. Tate, J. Bacsá, T. G. Gray and J. P. Sadighi, *Angew. Chem., Int. Ed.*, 2013, **52**, 12920.
- 19 J. P. Perdew, K. Burke and M. Ernzerhof, *Phys. Rev. Lett.*, 1997, **78**, 1396; J. P. Perdew, K. Burke and M. Ernzerhof, *Phys. Rev. Lett.*, 1996, **77**, 3865.
- 20 D. N. Laikov and Y. A. Ustynyuk, *Russ. Chem. Bull.*, 2005, **54**, 820.
- 21 D. N. Laikov, *Chem. Phys. Lett.*, 2005, **416**, 116.
- 22 K. G. Dyall, *J. Chem. Phys.*, 1994, **100**, 2118.
- 23 M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski and D. J. Fox, *GAUSSIAN 09 (Revision D.01)*, Gaussian, Inc., Wallingford CT, 2009.
- 24 S. Grimme, J. Antony, S. Ehrlich and H. Krieg, *J. Chem. Phys.*, 2010, **132**, 224306.
- 25 (a) F. Weigend and R. Ahlrichs, *PCCP*, 2005, **7**, 3297; (b) F. Weigend, *PCCP*, 2006, **8**, 1057.
- 26 A. V. Marenich, C. J. Cramer and D. G. Truhlar, *J. Phys. Chem. B*, 2009, **113**, 6378.