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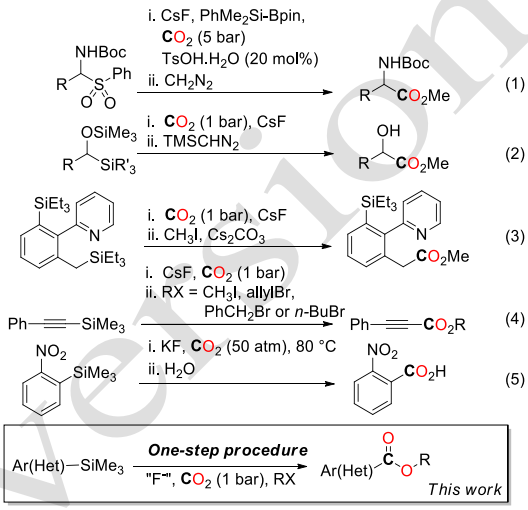
CO_2 Conversion to Esters by Fluoride-mediated Carboxylation of Organosilanes and Halide Derivatives

Xavier Frogneux,[†[a]] Niklas von Wolff, [†[a]] Pierre Thuéry,[[a]] Guillaume Lefèvre*[[a]] and Thibault Cantat*[[a]]

Abstract: The one-step conversion of CO_2 to hetero-aromatic esters is presented under metal-free conditions. Using fluoride anions as promoters for C–Si bond activation, pyridyl, furanyl and thiophenyl organosilanes are successfully carboxylated with CO_2, in the presence of an electrophile. The mechanism of this unprecedented reaction has been elucidated based on experimental and computational results, which show a unique catalytic influence of CO_2 in the C–Si bond activation of pyridylsilanes. The methodology is applied to 18 different esters and it has enabled the incorporation of CO_2 to a polyester material, for the first time.

The development of novel methodologies enabling the use of CO_2 is of high interest to benefit from this renewable and environmentally friendly carbon source in the production of chemicals. Recent efforts have targeted the formation of value-added products from CO_2.[1] For example, the reduction of CO_2 provides an entry to formate and methoxide derivatives and the reductive functionalization of CO_2 with amines has led to novel transformations over the last ten years.[2] Because C–C bonds are dominant in organic chemistry, the formation of C–C bonds with CO_2 will be of prominent utility. Transition-metal chemistry has played a substantial role in the development of such transformations, allowing for the coupling of CO_2 with alkynes, dienes, alkenes and aryl halides using on the one hand stoichiometric amounts of Ni or Fe, or on the other hand Pd, Cu, Ni, Fe, Rh, Au-based catalysts.[3] The formation of carboxylic acids with CO_2 has also been developed with various nucleophiles such as organoboranes,[4] organostannanes[5] and olefins[6] in transition metal-catalyzed systems. In this context, organosilanes are attractive nucleophiles, because they are less toxic and easier to prepare and handle than tin or boron reagents. Yet, organosilanes display a nucleophilicity 3 to 6 orders of magnitude lower than organoboranes and organostannanes[7] and their use in CO_2-based carboxylation reactions remains limited to a handful of examples (Scheme 1).

Because the C–Si bond features a low polarity, its activation with a fluoride source is necessary to generate a carbanion synthon, which can undergo a carboxylation with CO_2. Using CsF, the group of Sato recently reported the synthesis of α-amino acid derivatives (eq. 1)[8] and α-hydroxy acid derivatives (eq. 2)[9], and



Scheme 1. State of the art in fluoride-mediated carboxylation of C–Si bonds with CO_2.

the carboxylation of benzylsilane derivatives featuring a directing group (eq. 3).[10] The group of Kondo developed the carboxylation of alkynylsilanes (eq. 4).[11] Early on, Effenberger and Spiegler reported the carboxylation of electron defficient arylsilanes using KF or CsF under high pressures of CO_2 (50 atm), presumably to avoid the formation of the free aryl anion (eq. 5).[12] These few examples highlight the small scope of reactive organosilanes, which is limited to the generation of stabilized carbanions having a corresponding pKa lower than 35. Additionally, the esterification step must be carried out in a second step to prevent a direct quenching of the carbon nucleophile by the electrophile ($RCHN_2$ or RX) in the formation of the ester product. Aromatic and heteroaromatic esters being key intermediates in the synthesis of polymers, pharmaceutical intermediates or final products,[13] we sought to enlarge the scope of ester derivatives available from CO_2 and organosilanes, under metal-free conditions. We show herein that a wide range of heteroaromatic silanes can be used in the direct synthesis of esters from CO_2, organohalides and a fluoride source; and the methodology has been transposed to the formation of a polyester material from CO_2. Mechanistic studies show that this reactivity can be enabled by a unique catalytic influence of CO_2 in the activation of the C–Si bond.

In the absence of any transition metal, the controlled activation of commercially available phenyltrimethylsilane (**1a**) and 2-(trimethylsilyl)pyridine (**2a**) with fluoride ions is challenging because the corresponding $C_6H_5^-$ and $C_5H_5N^-$ anions are unstabilized carbanions with a pKa of 45 and 44, respectively. Indeed, phenyltrimethylsilane (**1a**) exhibits no reactivity when subjected to an atmosphere of CO_2, in the presence of CH_3I and a variety of fluoride sources (CsF, TASF (tris(dimethylamino)sulfonium difluorotrimethylsilicate) and TBAT (tetrabutylammonium difluorotriphenylsilicate)). In contrast,

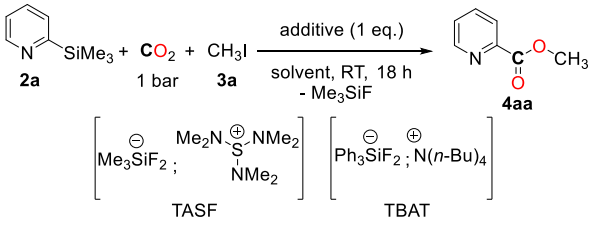
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traces of the methyl picolinate **4aa** are detected when **2a** is reacted with CO_2, CH_3I and CsF, TBAF.3H_2O or TMAF as a fluoride source (Table 1, entries 1-3). Whereas Brønsted bases such as Cs_2CO_3 or tBuOK are unable to promote the carboxylation of the substrate (Table 1, entries 4, 5), other anhydrous fluoride salts such as TASF and TBAT allowed for the formation of the methyl picolinate **4aa** in moderate to excellent yields (46% and 93% respectively) (Table 1, entries 6-7). It is worth noting that a procedure to recycle the Ph_3SiF by-product is possible by the addition of TBAF to re-form TBAT.[14] Carrying the reaction in THF or CH_2Cl_2 allowed for a nearly quantitative conversion to the ester.

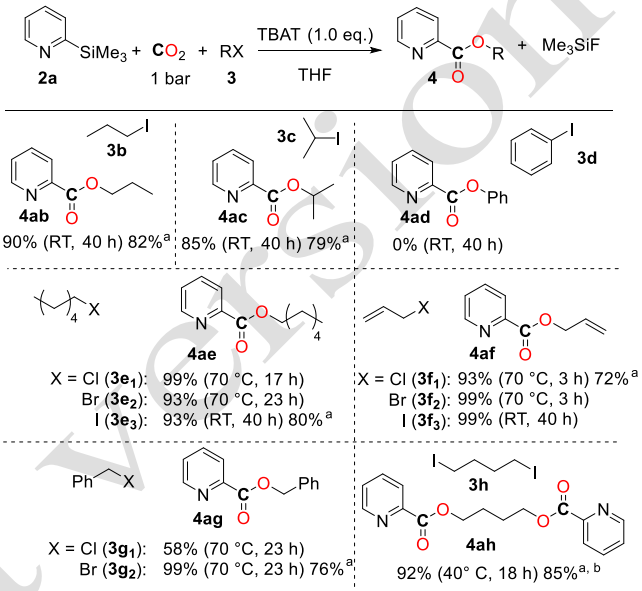
Table 1. Screening of the reaction conditions for the direct esterification of **2a** using CO_2 and CH_3I



Entry[a]	Additive [b]	Solvent	Yield (%)
1	CsF	THF	traces
2	TBAF.3H_2O	THF	7
3	TMAF	THF	traces
4	Cs_2CO_3	THF	0
5	tBuOK	THF	0
6	TASF	THF	46
7	TBAT	THF	93 (82)[c]
8	TBAT	CH_3CN	12
9	TBAT	CH_2Cl_2	95
10	TBAT	toluene	2
11	-	THF	0

[a] reaction conditions: NMR tube, **2a** (0.1 mmol), additive (0.1 mmol), **3a** (0.1 mmol), solvent (0.3 mL), CO_2 (1 bar). NMR yield determined with mesitylene as internal standard.. [b] TBAF=[*n*-Bu_4N][F]; TMAF=[Me_4N][F]. [c] Isolated yield.

The formation of **4aa** represents the first example of the direct carboxylation of a pyridylsilane reagent. Importantly, the organosilane is compatible with both CO_2 and the halogenoalkane and the reaction proceeds in one pot. In fact, changing the nature of the electrophile enables the formation of a large diversity of picolinic esters (Scheme 2). Primary and secondary alkyl and allyl iodides provided very good yields to the desired esters (**4ab** 90%, **4ac** 85%, **4ae** 93%, **4af** 99%) after 40 h at RT or 18 h at 40 °C (Scheme 2). Iodobenzene proved to be unreactive in this reaction indicating that the formation of the O–C bond occurs *via* a nucleophilic substitution. Importantly, the alkylation of the pyridine ring with the organic halide was not observed and the carbon nucleophile, released by C–Si bond activation, selectively reacts with CO_2. Bromoalkanes and chloroalkanes being less electrophilic, their utilization requires longer reaction times at RT (72 h) or mild heating (70 °C), as exemplified in the formation of **4ae**, **4af** and **4ag** in >93 %yield from various organic halides (Scheme 2). Interestingly, using a difunctional electrophilic species such as 1,4-diiodobutane, diester **4ah** is formed in 85% yield and crystals suitable for X-ray diffraction analysis could be isolated (see SI and Figure S6).

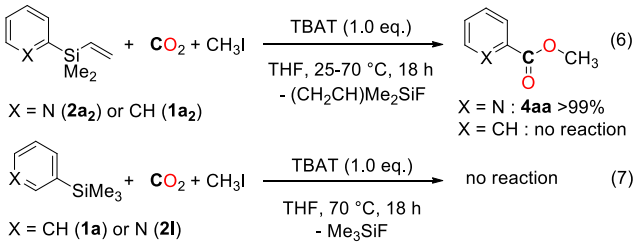


Scheme 2. Synthesis of picolinic esters by fluoride mediated carboxylation of 2-(trimethylsilyl)pyridine (**2a**) with various electrophiles. NMR yield. [a] Average isolated yield over two runs on 1 mmol scale. [b] 3h (0.5 eq.).

The substituents borne by the silicon center have a notable influence on the reactivity of the pyridylsilane reagent and different kinetic rates were measured when one methyl group in **2a** is replaced with a vinyl (**2a**$_2$), an allyl (**2a**$_3$) or a phenyl (**2a**$_4$) group. While the presence of an allyl group slows down the activation of the C–Si bond, introducing a phenyl or vinyl group at the silicon center enhances the kinetics of the carboxylation reaction (see SI).

Taken together, these data suggest that the formation of picolinic esters proceeds *via* a fluoride mediated activation of the C–Si bond, which releases a carbanion able to undergo carboxylation in the presence of CO_2 prior to the esterification step with the electrophile. Noticeably, no reaction occurred for arylsilanes that do not feature a nitrogen atom on the *ortho* position of the silyl group and both phenyldimethylvinylsilane (**1a**$_2$) and 3-(trimethylsilyl)pyridine (**2l**) are unreactive under the applied conditions (eq. 6 and 7). These results are puzzling given that the three anions $C_6H_5^-$, *o*-$C_5H_4N^-$ and *m*-$C_5H_4N^-$ have similar pK_as and hence similar stability. The mechanism of this novel transformation was thus investigated from stepwise reactions and DFT calculations so as to rationalize these findings.

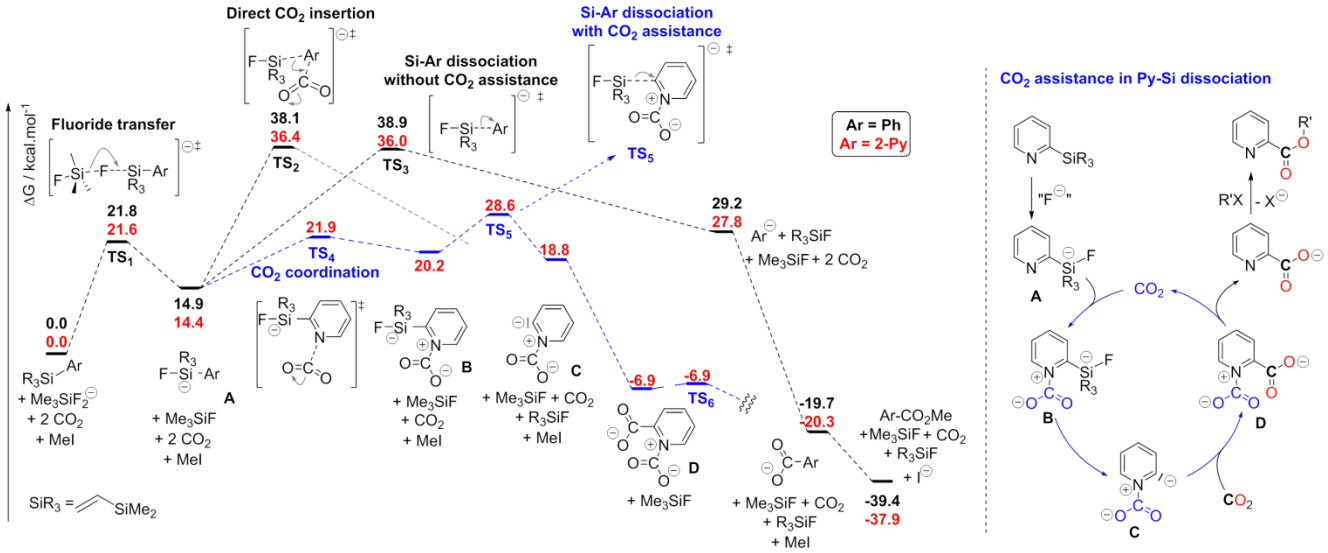
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Experimentally, under an argon atmosphere, silane **2a₂** is stable in the presence of TBAT and only a small amount of pyridine (6%) is detected by ^{1}H NMR after 22 h at 70 °C. However, in the presence of CO_2, the formation of a picolinate species 2-$PyCO_2^-$ is observed (68% yield), at room temperature (see SI). After addition of CH_3I, the ester **4aa** is obtained as the sole pyridine based product, along with NBu_4I. These results suggest that the pyridine anion $C_5H_4N^-$ does not form under the applied conditions and that CO_2 is required to facilitate the C–Si bond activation.

The different reactivities of **1a₂**, **2a₂** and **2l** were further investigated using DFT calculations (Scheme 3). For both the phenyl (**1a₂**) and pyridine (**2a₂**) derivatives, the formation of the carboxylate anion Ar–CO_2^- is favored thermodynamically (ΔG < -19.7 kcal.mol^{-1}) and the esterification step is also mildly exergonic. Using $Me_3SiF_2^-$ as a fluoride source model, the formation of the pentavalent anionic species $PhSiMe_2(CHCH_2)F^-$ (**A$_{Ph}$**) from **1a₂** is endothermic yet accessible at RT (ΔG = 21.8 kcal.mol^{-1}). Nevertheless, the direct carboxylation of **A$_{Ph}$** to Ph–CO_2^- (**TS₂**) or the generation of the free $C_6H_5^-$ anion (**TS₃**) is incompatible with the reaction conditions, with high-energy transition states (TSs) lying at 38.1 and 38.9 kcal.mol^{-1}, respectively. Replacing the phenyl group with a pyridine core only stabilizes these two TSs by 2.9 kcal.mol^{-1}, revealing that the C–Si bond activation follows a different pathway for **2a₂**. Formation of anion **A$_{2\text{-Py}}$** is accompanied with an increase of negative charge on the nitrogen atom of the pyridine core, from 0.48 in **2a₂** to 0.52 in **A$_{2\text{-Py}}$**, thereby enabling fixation of CO_2 to the N atom. The formation of the resulting CO_2-adduct **B** involves an energy barrier of 7.5 kcal.mol^{-1} (TS_4). We found that introducing an electron withdrawing group (EWG), namely CO_2, significantly facilitates the C–Si bond cleavage and the release of a stabilized anion (**C**), *via* an accessible **TS₅** at 28.6 kcal.mol^{-1}. **C** readily undergoes carboxylation at the carbanionic position to yield **D**, prior to a decarboxylation of the N–CO_2^- moiety to 2-$PyCO_2^-$. Overall, this mechanism requires a low energy demand of 28.6 kcal.mol^{-1} and it highlights the unique role of CO_2 in this transformation, which acts both as a reactant and a catalyst able to facilitate the C–Si bond cleavage. In fact, whereas carboxylation of electron defficient arylsilanes is possible,[12] the method reported herein uses reversible CO_2-coordination as a mean of traceless heteroarene activation. The driving force for the fluoride-mediated carboxylation of **2a₂** derives from the stabilization of anion **C**, which is reflected in the decreased pKa of the pyridine-CO_2 adduct at the 2 position (30.2 vs 43.4 in pyridine, Scheme 3). In contrast, a carbanion at the 3 position of the pyridine-CO_2 adduct is characterized by a pKa of 32.0 and its formation from **2l** is 3.9 kcal.mol^{-1} higher in energy than for **2a₂**, in line with their different reactivities.

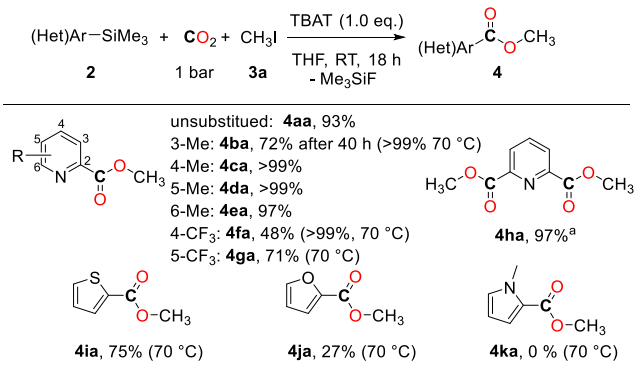
Based on these findings, the esterification of a variety of heteroaromatic silanes was carried out, with CO_2, CH_3I and TBAT (Scheme 4). Introducing a trifluoromethyl EWG on the 4 or 5 positions of the pyridine ring somewhat deactivates the reaction at RT and heating at 70 °C is desirable to reach good conversions into **4fa** and **4ga** (>99% and 71%, respectively). This behavior results from a destabilization of the pyridine-CO_2 adduct (**B**). In contrast, the presence of a methyl group on positions 4, 5 and 6 is beneficial and excellent conversions (72-99%) to the desired methyl picolinates were obtained. Diester **4ha** could be obtained from 2,6-(di-trimethylsilyl)pyridine with an excellent 97% yield. The carboxylation of other heterocycles is also feasible: 2-(thienyl)trimethylsilane affords **4ia** in a good 75% yield while the furyl derivative **4ja** is obtained under the same conditions in a low 27% yield. For these substrates, it is likely that activation of the heteroaryl-silane with CO_2 is unnecessary as the aromatic anions are stable enough (pKa < 35).[16] Nonetheless, the pyrrole derivative *N*-methyl-(2-triethylsilyl)pyrrole remained unreacted, even after 40 h at 70 °C. The corresponding *N*-methyl-pyrrole



Scheme 3 Fluoride-mediated Computed pathway for the carboxylation of **1a₂** and **2a₂** (PBE0-GD3**,** PCM THF)

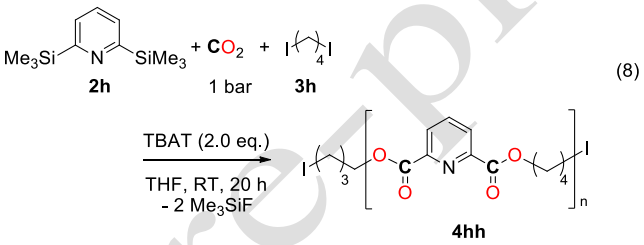
anion presents a high pKa of 39.6.[16] This lack of reactivity can thus be explained by the steric hindrance on the nitrogen center and its absence of nucleophilic character for the coordination of CO_2.

From a practical perspective, heteroaromatic esters **4** are usually prepared by carboxylation of the corresponding *ortho*-lithiated aromatics (e.g. 2-lithiopyridine) with the subsequent addition of an electrophile or *via* oxidation of methylated heteroaromatics to the carboxylate derivative, followed by condensation of an alcohol.[15] Given that novel catalytic methods recently appeared to form



Scheme 4. Fluoride-mediated esterification of aromatic silanes with CO_2 and CH_3I

heteroaromatic silanes by C-H bond functionalization, without the need for a lithiation step,[17] the carboxylation strategy presented herein offers an attractive pathway to the synthesis of esters **4**. Furthermore, the carboxylation of pyridylsilane derivatives proceeds using CO_2 as a traceless activator (*via* the formation of stabilized carbanion **C**). This enables the carboxylation of pyridylsilanes at RT but also the use of an electrophile in an one-step procedure, for the first time. To further highlight these findings, the polymerization version of the present transformation was attempted (eq. 8).



(8)

Under an atmosphere of CO_2, disilane **2h** reacts at RT with **3h** to afford a polyester material (**4hh**). GPC and NMR data reveal that **4hh** is characterized by a succession of picolinate and butyl moieties. The polymerization degree exceeds 4 resulting from the incorporation of ca. 8 CO_2 molecules (see SI). While many efforts are currently devoted to promoting the incorporation of CO_2 in polycarbonate materials, the formation of oligomer **4hh** represents the first example of CO_2 conversion to a polyester chain and it offers a novel venue for the utilization of CO_2 in polymer chemistry.[18] Current efforts are devoted to expand this proof-of-concept.

Acknowledgements

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Keywords: CO_2 • organosilicon compounds • mechanism • DFT calculations

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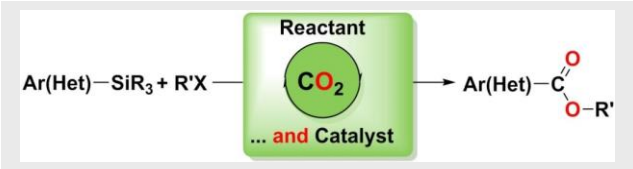
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CO_2 Conversion to Esters by Fluoride-mediated Carboxylation of Organosilanes and Halide Derivatives

A novel methodology is described to convert CO_2 to hetero-aromatic esters in the presence of organosilanes and organic halides, using fluoride anions as promoters for C–Si bond activation. CO_2 exhibits a unique catalytic influence of CO_2 in the C–Si bond cleavage of pyridylsilanes, serving as a traceless activator.

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