Beneficial Effect of TMSCl in the Lewis Acid-mediated Carboxylation of Aromatic Compounds with Carbon Dioxide

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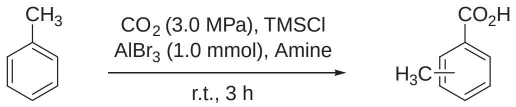
The Lewis acid-mediated carboxylation of aromatic compounds with CO$_2$ is significantly promoted by the addition of a large excess of chlorotrimethylsilane (TMSCl) to give arylcarboxylic acids in good to excellent yields.

Chemical fixation of CO$_2$ has been the subject of much interest in the field of organic synthesis.[1] Although many CO$_2$-fixation reactions have been developed to date, they are, in most cases, classified as "nucleophilic fixation," as represented by the Kolbe–Schmitt reaction, carbonation of Grignard reagents, and palladium-catalyzed cycloaddition of diene with CO$_2$,[2] in which an anionic species, as well as a catalytically-activated species, nucleophilically attacks to unactivated CO$_2$. On the other hand, few examples have been known for "electrophilic fixation," in which CO$_2$ is activated by coordination to a Lewis acid and electrophilically adds to a C=C bond, as is often the case with other carbonyl compounds.[3,4] It has been known that aromatic compounds are directly carboxylated with CO$_2$ with the aid of aluminum-based Lewis acids to give arylcarboxylic acids, though generally in poor yields.[5] The reaction is believed to involve the electrophilic attack of the Lewis acid-activated CO$_2$ to the aromatic ring to form an arenium intermediate, which eliminates a proton to give a carboxylic acid after aqueous workup (the S$_E$Ar mechanism). On the other hand, the S$_E$Ar reaction of arylsilanes occurs at the ipso position bearing the silyl moiety, owing to the stabilizing effect in the transition state by the $(p–\sigma)_\pi$ conjugation between the Si–C bond and the developing positive charge (the β-effect).[4] We have recently reported that aryltrimethylsilanes are efficiently carboxylated with CO$_2$ in the presence of AlBr$_3$.[6] In this reaction, trimethyl(*o*-tolyl)silane gave not only *o*-methylbenzoic acid (the ipso-substitution product) but also *p*-methylbenzoic acid. Formation of the latter was rationalized by the sequential reactions: initial protodesilylation[7] of the *o*-tolylsilane with incidental HBr in the reaction system, subsequent silylation of the resultant toluene at the para position to give *p*-tolylsilane, followed by the carboxylation at the ipso carbon of the silyl moiety. The silyl-transfer mechanism prompted us to examine the carboxylation of aromatic hydrocarbons in the presence of TMSCl in expectation of in-situ generation of arylsilanes under the Lewis acidic conditions. Herein, we wish to report that TMSCl significantly promotes the Friedel–Crafts-type carboxylation of aromatic hydrocarbons.

In our previous paper,[6] we reported that trimethyl(*p*-tolyl)silane (1.5 mmol), on treatment with 2.0 mol equiv. of AlBr$_3$ in benzene (1.0 cm^3) under CO$_2$ pressure (3.0 MPa) at room temperature, gave a 1:9 mixture of *o*- and *p*-methylbenzoic acid in 50% yield after chromatographic purification. We have found that a comparable crop (54%) of the acid mixture (*o*-:*p*- = 1:3) can be obtained by the reaction of toluene under the same conditions by addition of 1.2 mol equiv. of TMSCl, while the yield dropped to 10% (*o*-:*p*- = 3:97) in the absence of TMSCl. Electrophilic silylation of aromatic hydrocarbons with halosilanes in the presence of a Friedel–Crafts catalyst has yet to be realized, which is attributed to the great ease of protodesilylation of the resultant arylsilanes under the acidic conditions. However, Olah et al. found that a certain, albeit small amount ($\leq$1%) of arylsilane could be obtained in the reaction of benzene, as well as toluene, with TMSCl in the presence of AlCl$_3$ by addition of a hindered base, e.g. diisopropylethylamine (DIEA), to trap HCl eliminated in the silylation.[8] Thus, the carboxylation was examined in the presence of hindered bases. The substrate was used as a solvent instead of benzene to avoid formation of trimethylphenylsilane, which should lead to contamination of the desired carboxylic acids with benzoic acid.[6] Although introduction of several mol % of DIEA, as well as 2,6-di-*tert*-butyl-4-methylpyridine, against the Lewis acid actually promoted the reaction, addition exceeding a poor upper limit lowered the yield (Table 1, Entries 1–6), which would be attributed to the complexation of the amine with AlBr$_3$ to reduce the Lewis acidity. However, the yield could be improved by increasing the amount of TMSCl without the use of the amines (Entries 7–11).[9] The more TMSCl was added, the more the yield increased to reach 96% based on the amount of the AlBr$_3$. This suggests that 1 mol equiv. of AlBr$_3$ is consumed through the overall reaction.

Xylenes and mesitylene could also be effectively carboxylated by employing 5.0 mol equiv. of TMSCl (Table 2). In the case of *o*- and *p*-xylene, 2,4-dimethylbenzoic acid was obtained

Table 1. Carboxylation of toluene in the presence of TMSC1 and amine



Entry	TMSCl/ AlBr$_3$[a]	Amine	Amine/ AlBr$_3$[a]	Yield[b]/% (*o*-:*p*- ratio)
1	1.0	—	—	21 (1:3)
2	1.0	DIEA	0.010	29 (1:3)
3	1.0		0.050	32 (1:3)
4	1.0		0.10	26 (1:3)
5	1.0		0.50	19 (1:3)
6	1.0		1.0	9 (1:3)
7	2.0	—	—	45 (1:4)
8	3.0	—	—	63 (1:4)
9	4.0	—	—	73 (1:5)
10	5.0	—	—	80 (1:5)
11	10.0	—	—	96 (1:6)

[a]Molar ratio. [b]Based on the quantity of AlBr$_3$.

Table 2. Carboxylation of aromatic hydrocarbons in the presence of TMSCl

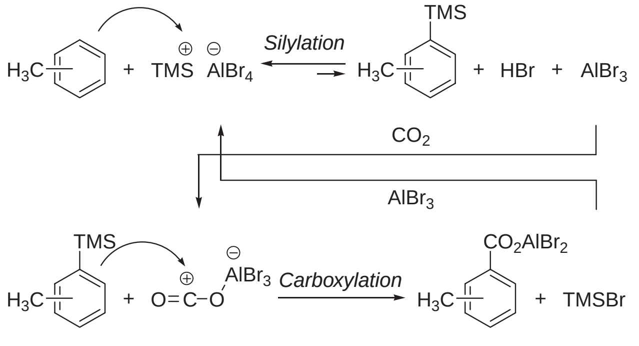
Entry	Substrate	Product (Distribution)	Yield /%
1[a]	*o*-xylene	Dimethylbenzoic acid (3,4-:2,3-:2,4- = 15:1:1)	51[b]
2[a]	*m*-xylene	Dimethylbenzoic acid (2,4-:2,6- = 1:trace)	50[b]
3[a]	*p*-xylene	Dimethylbenzoic acid (2,5-:2,4- = 5:1)	53[b]
4[a]	mesitylene	2,4,6-Trimethylbenzoic acid 2,2′,4,4′,6,6′-Hexamethylbenzophenone	87[b] 6[b]
5[c]	naphthalene	naphthoic acid (1-:2- = 8:1)	40[d]

[a]Reaction conditions were the same as those for Entry 10 in Table 1. [b]Based on the quantity of $AlBr_3$. [c]Reaction conditions: CO_2 (3.0 MPa), substrate (1.0 mmol), TMSCl (3.0 mmol), $AlBr_3$ (3.0 mmol), benzene (2.0 cm^3), rt, 3 h. [d]Based on the quantity of the substrate.

as a minor product (Entries 1 and 3), suggesting that a part of the substrate isomerized to thermodynamically more stable *m*-xylene prior the silylation under the Lewis acidic conditions.

In order to shed light on the reaction mechanism, mass balance of the silylating reagent was examined. The reaction was conducted by using TMSBr (5.3 mmol) instead of TMSCl. After the reaction, volatile materials were collected in vacuo in two liquid-nitrogen-cooled tandem traps and analyzed by GC, indicating that 5.1 mmol of TMSBr was recovered. On the other hand, 0.32 mmol of the carboxylic acid was isolated from the residue after aqueous workup. The difference of 0.2 mmol between the amount of TMSBr employed and that recovered, which is less than the crop of the carboxylic acid, should be attributed to an inevitable loss during the recovery, considering the fact that TMSBr is highly volatile and that any silylated compounds were detected by ^{1}H NMR analysis of the residue, as well as the distillate. Based on these observations, a feasible reaction mechanism was depicted in Scheme 1.[10] The silylation of toluene with TMSBr with the aid of $AlBr_3$ affords the arylsilane, which undergoes the carboxylation with the Lewis acid-activated CO_2 to give an aluminum carboxylate at the expense of an equimolar amount of $AlBr_3$, while recovering TMSBr. The first step is an equilibrium reaction, the position of the equilibrium lying far to the left. The addition of a large excess of the silylating reagent shifts the equilibrium to the right to promote the second reaction, giving the aluminum carboxylate in higher yield.

In conclusion, we have shown here that halotrimethylsilanes promote the Friedel–Crafts-type carboxylation of aromatic hydrocarbons. It is suggested that the aromatic substrates are silylated in situ by an electrophilic aromatic substitution with the aid of the Lewis acid. Further studies on the reaction mechanism are in progress.



Scheme 1.

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9 Typical procedure for the carboxylation (Tabel 1, Entry 10): In a 50 cm^3 autoclave equipped with a glass inner tube and a magnetic stirring bar were charged toluene (2.0 cm^3), $AlBr_3$ (270 mg, 1.0 mmol), and TMSCl (540 mg, 5.0 mmol) under N_2 and the apparatus was purged with CO_2 by repeated pressurization and subsequent expansion, the final pressure being adjusted to 3.0 MPa. After stirred at room temperature for 3 h, the mixture was worked up and purified by column chromatography on silica gel with diethyl ether–hexane (1:1) as the eluent to give a mixture of *o*- and *p*-methylbenzoic acid (110 mg, 80%). The ratio of ortho- and para-isomers was determined to be 1:5 by ^{1}H NMR analysis ($CDCl_3$, 500 MHz).

10 Another plausible mechanism is that a species generated from CO_2, TMSCl, and the Lewis acid directly attacks to the aromatic hydrocarbon.