Lewis Acid-Mediated Carboxylation of Fused Aromatic Compounds with Carbon Dioxide

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(Received October 15, 2001; CL-011008)

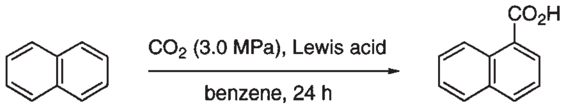
Direct and regioselective carboxylation of fused aromatic compounds with carbon dioxide is achieved with the aid of a Lewis acid. Thus, treatment of naphthalene, anthracene, and phenanthrene with carbon dioxide (3.0 MPa) in benzene at 40 °C in the presence of $AlBr_3$ gave 1-naphthoic acid, 9-anthracenecarboxylic acid, and 9-phenanthrenecarboxylic acid as the sole acid product in 43, 20, and 34% yields, respectively.

Regioselective functionalization of a fused aromatic compound, which has multiple reaction sites of similar reactivity, is a challenging subject. Although carboxy group is an important function in organic chemistry, aromatic carboxylic acids are generally prepared by indirect methods such as introduction of alkyl side chains, followed by the oxidation, or generation of arylmetal species to add to carbon dioxide, because it is quite hard to replace an aromatic hydrogen with a carboxy function. Among such direct carboxylation addressed in several papers are the Friedel-Crafts acylation with phosgene or its synthetic equivalents,[1] palladium(II)-catalyzed carboxylation with carbon monoxide or dioxide,[2] carboxylation of aromatic anion radicals generated by chemical or electrochemical reduction, or photoinduced electron transfer,[3] addition of dicarboxylmethyl radical generated from malonic acid and manganese(III) acetate and the following *in situ* transformations of the resulting dicarboxylic acid,[4] and cadmium(II)-catalyzed transcarboxylation with alkaline metal salts of aromatic carboxylic acids.[5] However, they suffer from low yield and/or insufficient regioselectivity.[6] In the course of our studies on the Lewis acid-catalyzed reaction of heterocumulenes,[7] we have found that fused aromatic compounds can be directly and regioselectively carboxylated with carbon dioxide in the presence of a Lewis acid. Close scrutiny of the literature revealed that Norris *et al.* reported the prototype as early as 1940.[8] They found that mesitylene reacted with carbon dioxide in the presence of $AlBr_3$ to give 2,4,6-trimethylbenzoic acid in 27% yield, accompanied by the Friedel-Crafts acylation of the substrate with the benzoic acid to give di-2,4,6-trimethylphenyl ketone in 45% yield. In spite of the potential importance of the Norris's reaction, it has only rarely appeared in scattered papers thereafter.[9] Here, we report our preliminary results of this apparent Friedel-Crafts-type carboxylation of fused aromatic compounds.[10]

The general procedure for the carboxylation is as follows: In a 50-cm^3 autoclave equipped with a glass inner tube and a magnetic stirring bar were charged a substrate (1.60 mmol), a Lewis acid and dry benzene (1.0 cm^3) under nitrogen and the apparatus was purged with carbon dioxide by the repeated pressurization and the subsequent expansion, the final pressure of carbon dioxide being adjusted to 3.0 MPa. The mixture was stirred at appropriate temperature for 24 h. After aqueous work-up, the crude product was purified by column chromatography on silica gel with diethyl ether–hexane (1 : 1) as the eluent.

First, the carboxylation of naphthalene was examined (Table 1). Benzene was employed as the solvent because it remained almost intact when treated with carbon dioxide in the presence of 1.0 equiv. of $AlCl_3$ even at elevated temperature. Naphthalene was carboxylated at room temperature in the presence of $AlCl_3$ to give 1-naphthoic acid as the sole acid product, the yield of which depended on the molar equivalence of the Lewis acid to the substrate (entries 1–3). Replacement of benzene by nitrobenzene or carbon disulfide as the solvent in the presence of 2.0 equiv. of $AlCl_3$ resulted in failure, giving no (in nitrobenzene) or considerably reduced amount (3%) of the naphthoic acid (in carbon disulfide). Reaction temperature also influenced the yield: While 1-naphthoic acid was obtained in 23% yield at 40 °C, no acid could be obtained at 60 °C, giving only neutral by-products (*vide infra*) (entries 4 and 5). As for the Lewis acid, $AlBr_3$, which combined the highest Lewis acidity and good solubility in benzene, showed the best performance among the Lewis acids examined (entries 6 and 7). On the other hand, $GaCl_3$[11] and $SnCl_4$, which were highly soluble in organic solvents but less strong in Lewis acidity than $AlCl_3$, showed quite less or no activity toward the reaction (entries 10 and 11). It should be noted, however, that $GaCl_3$ actually mediated the carboxylation of mesitylene at 40 °C, giving 2,4,6-trimethylbenzoic acid and di-2,4,6-trimethylphenyl ketone in 2 and 27% yields, respectively. As for the pressure of carbon dioxide, a pressure of 3.0 MPa seems to be sufficient for the carboxylation, while a decrease in pressure to 0.5 MPa slightly reduced the product yield (entries 8 and 9).[9c]

Table 1. Effects of reaction variables on the carboxylation of napthalene



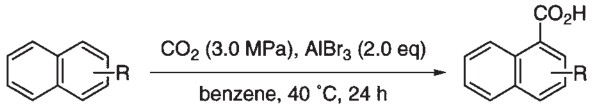
Entry	Lewis acid (eq)	Temp. / °C	Yield / %
1	$AlCl_3$ (1.0)	r.t.	9
2	$AlCl_3$ (2.0)	r.t.	16
3	$AlCl_3$ (3.0)	r.t.	15
4	$AlCl_3$ (2.0)	40	23
5	$AlCl_3$ (2.0)	60	0
6	$AlBr_3$ (2.0)	40	38
7[a]	$AlBr_3$ (2.0)	40	43
8[b]	$AlBr_3$ (2.0)	40	33
9[c]	$AlBr_3$ (2.0)	40	37
10	$GaCl_3$ (2.0)	40	trace
11	$SnCl_4$ (2.0)	40	0

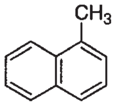
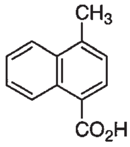
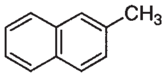
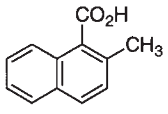
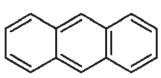
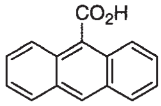
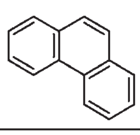
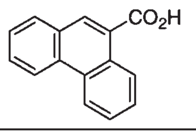
[a] The amount of the solvent was reduced to 0.5 cm^3. [b] The pressure of CO_2 was decreased to 0.5 MPa. [c] The pressure of CO_2 was increased to 5.0 MPa.

Next, several other aromatic compounds were subjected to the carboxylation under the optimized conditions (Table 2). While 1-bromonaphthalene, which had an electron withdrawing group, gave no acid product, 1-methylnaphthalene, as well as the 2-methyl isomer, gave the corresponding 1-naphthoic acid (entries 1 and 2). This tendency coincides with that in the electrophilic aromatic substitution. Anthracene and phenanthrene were also carboxylated regioselectively, giving 9-anthracene- and 9-phenanthrene-carboxylic acid, respectively (entries 3, 4).

Fused aromatic compounds are known to have a marked tendency for dehydrocoupling to form polyaryls under the conditions of the Friedel-Crafts reaction (the Scholl reaction).[12] It should be mentioned that the present reaction gave many neutral by-products, consuming all the substrate. The IR analysis of the neutral extract from the reaction mixture in the carboxylation of naphthalene revealed that it contained no carbonyl compound. Distillation of the extract by use of a Kugelrohr, followed by careful chromatography of the distillate on a silica gel or alumina column isolated 2-phenylnaphthalene and 3,4-dihydro-1,2′-binaphthalene as the products identified. Therefore, it is obvious that the Scholl-type reaction competes with the carboxylation. Interestingly, 1-methoxynaphthalene gave 4-phenyl-1-tetralone in 59% yield under the optimized conditions without formation of any carboxylic acid.[13] The mechanism of the carboxylation is not clear at present but it may involve attack of a carbon dioxide which is activated by the Lewis acid to the aromatic ring to form an arenium ion, which eliminates a proton to give a carboxylic acid after the aqueous workup. Another plausible mechanism involves scavenging the aromatic cation radical intermediate in the Scholl reaction by carbon dioxide. It is known that the Scholl reaction is accelerated by the addition of a metal salt such as $CuCl_2$ or $FeCl_3$, which oxidizes the substrate to the cation radical species.[12] However, treatment of naphthalene with 0.5 equiv. of $AlCl_3$-$CuCl_2$ (1 : 1) in 1,2-dichlorobenzene under carbon dioxide (3.0 MPa) at room temperature gave only polymerized materials.[14] Therefore, although further studies must be done to elucidate the mechanism, carbon dioxide seems to be activated by the Lewis acid to the extent that it can add to aromatic nuclei, which may create a new possibility to use carbon dioxide as an electrophile.

Table 2. Carboxylation of arenes



Entry	Substance	Product	Yield / %
1			33
2			28
3			20
4			34

In conclusion, we have shown here that fused aromatic compounds can be carboxylated with carbon dioxide with the aid of a Lewis acid. The high regioselectivity and the relatively good product yields are characteristic of this reaction, which will compete well with the conventional multistep syntheses of these carboxylic acids.[15]

We are grateful to the referees for their useful suggestions. This work was supported in part by grants from the Ministry of Education, Culture, Sports, Science, and Technology, Japan (Grant-in-Aid for Scientific Research No. 13650908) and the Center of Interdisciplinary Research (Tohoku University).

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