Decarbonylative Diarylation of α-Methoxyacetic Acid Yielding Diarylmethanes Mediated by Lewis Acid and Trifluoroacetic Anhydride

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Reaction of α-methoxyacetic acid with aromatic compounds in the presence of trifluoroacetic anhydride and Lewis acid has been found to give diarylmethanes. Some of the intermediates in this transformation have been identified via direct observation by ^{1}H and ^{13}C NMR spectroscopy. The reaction route has been clarified as follows: a mixed acid anhydride is formed from α-methoxyacetic acid and trifluoroacetic anhydride, which gives a hemiacylal type intermediate via decarbonylation followed by successive double electrophilic aromatic substitutions yielding diarylmethanes.

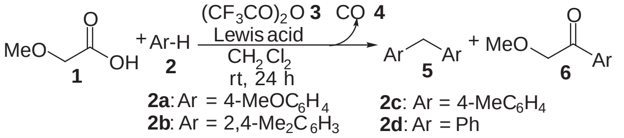
Electrophilic aromatic substitution of free carboxylic acid mediated by PPA (polyphosphoric acid),[1] the Eaton reagent (P_2O_5–MsOH; mixture of phosphorus pentoxide and methanesulfonic acid),[2] triflic acid,[3] and methanesulfonic acid[4] has been widely investigated. However, electrophilic aromatic substitution of α-keto- and α-alkoxycarboxylic acids has been scarcely reported.

Recently, we have found that decarbonylative α,α-diarylation reaction of α-alkoxycarboxylic acid proceeds instead of the Friedel–Crafts type acylation in the presence of phosphoric acid anhydride type mediators such as PPA or P_2O_5–MsOH.[5] About this arylation reaction, the scope and the limitation, the structural requirements, and the reaction mechanism have been elucidated. The plausible reaction pathway of this transformation is proposed to have following three stages: 1) formation of a reactive intermediate from an α-alkoxycarboxylic acid and phosphoric acid like mixed acid anhydride, 2) decarbonylative electrophilic attack of the intermediate to arenes yielding monoarylated intermediates, 3) electrophilic aromatic substitution of the monoarylated intermediates yielding decarbonylatively diarylated products.

During the course of the investigation on decarbonylative diarylation reaction, we have discriminated the two governing factors for the first and the second stages of this reaction. One is the forming ability for mixed acid anhydride type intermediate and the other is acidic mediation for decarbonylative diarylation. In this consequence, we have found that combination of other reagents taking the place of these two roles also induces decarbonylative diarylation. In this communication, we wish to discuss the reaction behavior, the governing factors, and the intermediates and the reaction pathway of the decarbonylative diarylation reaction of α-alkoxycarboxylic acid mediated by acid anhydride and Lewis acid.

The results of the reaction of α-methoxyacetic acid (**1**) with aromatic compounds **2** in the presence of trifluoroacetic anhydride (($(CF_3CO)_2O$) (**3**) and Lewis acids are shown in Table 1. In the reaction of α-methoxyacetic acid (**1**) with two equimolar amounts of anisole (**2a**) against acid **1**, diarylmethane **5** was obtained in a 55% yield with evolution of carbon monoxide (**4**) (Entry 1). The evolution of carbon monoxide (**4**) was confirmed by the aid of a gas indicator, Gas Indicator Tube No. 1H, GASTEC Corporation. On the other hand, neither carbon monoxide (**4**), diarylmethane **5**, nor α-methoxyacetophenone derivatives **6** were formed when the operation was carried out in the absence of $(CF_3CO)_2O$ (**3**) or Lewis acid (Entries 2 and 3). Therefore, combination of $(CF_3CO)_2O$ (**3**) and Lewis acids has been proved to promote this decarbonylative diarylation in the same manner as phosphoric acid anhydride type reagents. On the other hand, when an equimolar amount of anisole (**2a**) against acid **1** was allowed to react, diarylmethane **5** was also produced in a rather lower yield (38%, Entry 4). In contrast, when a large amount of anisole (**2a**) was treated, formation of

Table 1. Reaction of α-methoxyacetic acid (**1**) with aromatic compounds **2** in the presence of $(CF_3CO)_2O$ (**3**) and Lewis acids[a]



Entry	2	2/1 (mol/mol)	Lewis acid	3/1 (mol/mol)	Yield/%	
					5	6
1	**2a**	2	$AlCl_3$	1	55	0
2[b]	**2a**	2	—	1	0	0
3[b]	**2a**	2	$AlCl_3$	0	0	0
4	**2a**	1	$AlCl_3$	1	38	0
5	**2a**	10	$AlCl_3$	1	47	12
6[c]	**2a**	2	$AlCl_3$	1	38	0
7[d]	**2a**	40	P_2O_5–MsOH	0	49	0
8	**2a**	2	$SnCl_4$	1	31	0
9	**2a**	2	$ZnCl_2$	1	10	0
10	**2a**	2	$BF_3 \cdot OEt_2$	1	69	0
11	**2b**	2	$BF_3 \cdot OEt_2$	1	80	0
12	**2c**	2	$BF_3 \cdot OEt_2$	1	56	0
13	**2d**	2	$BF_3 \cdot OEt_2$	1	25	0

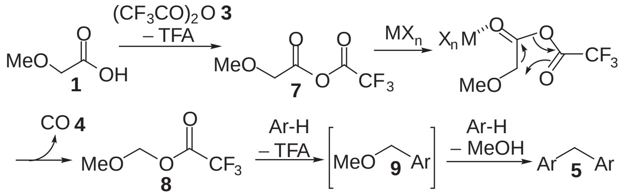
[a]Reaction conditions: α-methoxyacetic acid (**1**), 1 mmol; Lewis acid, 5 mmol; CH_2Cl_2, 5 mL. [b]Evolution of CO (**4**) was not confirmed. [c]Reflux, 4 h. [d]P_2O_5–MsOH (1 mL) was employed instead of Lewis acid and CH_2Cl_2.

α-methoxyacetophenone derivative **6** (12%) along with diarylmethane **5** (47%) was observed (Entry 5). By this reaction system, α-methoxyacetic acid (**1**) and arene **2** are transformed into diarylmethane **5** more effectively in comparison to P_2O_5–MsOH mediated one (Entry 7).

From the point of dependence on the kind of Lewis acids, $BF_3 \cdot OEt_2$ is found to be the most effective Lewis acid among those we have been evaluated, as shown in Table 1 (Entries 1, 8–10). In contrast, employment of other Lewis acids for this reaction generally gave complex mixtures containing some unknown products (Entries 1, 8, and 9). Thus, choice of Lewis acid is significant to achieve high efficiency of decarbonylative diarylation of acid **1**. On the other hand, this reaction is proved to be applicable for other aromatic compounds, such as *m*-xylene (**2b**), toluene (**2c**), and benzene (**2d**), producing the corresponding diarylmethanes **5** (Entries 11–13).

For this transformation, some of the intermediates formed in situ were directly observed with the aid of ^1H and ^{13}C NMR spectroscopy. ^1H and ^{13}C NMR spectra of the reaction solution show that mixed-acid anhydride **7** and trifluoroacetic acid (TFA) are immediately formed after mixing of α-methoxyacetic acid (**1**) and $(CF_3CO)_2O$ (**3**) (Figure 1). Furthermore, when $BF_3 \cdot OEt_2$ was added to the solution of mixed-acid anhydride **7**, carbon monoxide (**4**) was evolved. The signals of hemiacylal equivalent to intermediate **8** is observed in the ^1H and ^{13}C NMR spectra of the solution (Figure 1).

Based on this observation, the reaction pathway is presumed as follows (Scheme 1): initially, α-methoxyacetic acid (**1**) reacts with $(CF_3CO)_2O$ (**3**) to form mixed-acid anhydride **7**. Trifluoroacetic anhydride (**3**) is known to give mixed-acid anhydride by the reaction with carboxylic acid[6] as well as *p*-trifluoromethylbenzoic anhydride[7] and diphenyl chlorophosphonate.[8] The acid anhydride **7** formed in situ is smoothly decarbonylated to generate hemiacylal intermediate **8**.



Scheme 1.

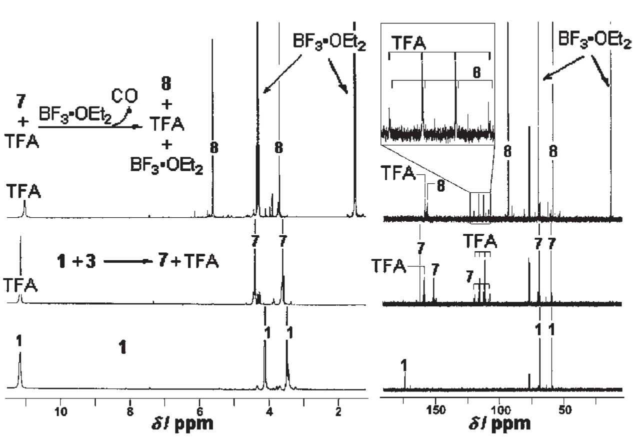


Figure 1. ^1H and ^{13}C NMR spectra of α-methoxyacetic acid (**1**) in $CDCl_3$ and the reaction mixtures obtained by addition of $(CF_3CO)_2O$ (**3**) and $BF_3 \cdot OEt_2$ in $CDCl_3$.

Furthermore, in this reaction system, electrophilic aromatic substitution of hemiacylal **8** should readily yield α-aryl-α-methoxymethane **9** in preference to the formation of diarylmethane **5**. However, the existence of α-aryl-α-methoxymethane **9** has not been observed under the reaction conditions examined. The transformation of the monoarylated compound **9** into diarylmethane **5** is supposed to be so fast that the formation of the intermediate **9** could not be observed.[5a] In this course of transformation, evolution of carbon monoxide (**4**) is evidently the driving force for the formation of the activated intermediate **8**, which readily gives the further arylated product of diarylmethane **5**.[9]

The preference of decarbonylative diarylation yielding diarylmethane **5** against electrophilic aromatic acylation giving acetophenone **6** is interpreted as follows: both of the two reaction pathways of mixed-acid anhydride **7**, decarbonylation and electrophilic aromatic acylation, have possibility to proceed via concerted process.[5c] However, decarbonylation of mixed-acid anhydride **7** proceeds far faster than concerted electrophilic aromatic acylation. Only when excess amount of aromatic compound is present, electrophilic aromatic acylation product **6** is generated in a low yield (Table 1, Entry 5). Generally, under the conditions described in this paper, electrophilic aromatic acylation scarcely proceeds in competition with decarbonylation of mixed-acid anhydride **7**.

In conclusion, we have found that combination of $(CF_3CO)_2O$ (**3**) and Lewis acid functions as a promoter of decarbonylative diarylation of α-methoxyacetic acid (**1**) in place of PPA and P_2O_5–MsOH. Furthermore, the intermediates in this transformation are experimentally identified as mixed-acid anhydride and hemiacylal compounds. Further work on clarification of scope and limitation of this transformation is currently being undertaken.

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