[Regular Paper]

Friedel-Crafts Acylation of Anisole with Phthalic Anhydride
Catalyzed by Solid Superacid of Sulfated Zirconia

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Friedel-Crafts acylation of anisole with phthalic anhydride was performed over several types of sulfated zirconia catalysts prepared from zirconia gel, JRC-ZRO-2, JRO-ZRO-3, JRC-ZRO-4, and JRO-ZRO-5, which are reference catalysts supplied by the Reference Catalyst Committee of the Catalysis Society of Japan, by equilibrium adsorption method and the kneading method. The only product was the diacylated product $C_6H_4[CO(C_6H_4OCH_3)]_2$; no monoacylated product, $C_6H_4[CO(C_6H_4OCH_3)]COOH$, was observed. However, a large amount of monoacylated product was obtained when the acylation was catalyzed by the dissolved $AlCl_3$. Phthalic acid monoethyl ester was produced by posttreatment of the catalyst with ethanol. Reaction time and temperature had little effect on the yield of ethyl ester. The diacylated product is probably formed by the addition of two anisoles to one carbonyl group in phthalic anhydride with subsequent rearrangement of the anisole group to the carbon of the other carbonyl group, because the other carbonyl group on phthalic anhydride is likely to be activated on the surface of the superacid. Observations with various solid superacid catalysts indicated the superacid sites on the surface are required for the formation of diacylated product.

Keywords

Solid catalyst, Friedel-Crafts acylation, Anisole, Phthalic anhydride, Sulfated zirconia catalyst, Superacid

1. Introduction

The Friedel-Crafts reaction is one of the most important and fundamental reactions in organic chemistry and is used to prepare substituted aromatic compounds such as aromatic ketones. The Friedel-Crafts reaction is usually catalyzed by a Lewis acid such as aluminum trichloride in the homogeneous phase, usually using more than stoichiometric amounts of Lewis acid because the Lewis acids are deactivated by coordination with the aromatic ketones that are formed. However, the large amounts of $AlCl_3$ and other products generated by the hydrolysis of $AlCl_3$ after the reaction often cause serious environmental problems.

Heterogeneous catalysts are powerful tools for designing environmentally benign organic reactions, and solid acid catalysts are highly active for the Friedel-Crafts reaction^{1)–3)}. The solid superacids of the sulfated zirconia family are the most useful solid catalysts. Sulfated zirconia and related solid acids are synthesized by the addition of sulfate species to the oxide surfaces of Fe, Ti, Zr, Hf, Sn, Al, and Si^{3)–5)}. Tungstated metal oxides are prepared in a similar manner⁴⁾. These catalysts can be easily recovered from the reaction mixture

and reused after reactivation by heating.

A systematic study of these superacids for the benzylation of toluene with benzoic anhydride and benzoyl chloride in the liquid-solid phases showed a relationship between the highest acid strength of the catalysts and the yields of acylated products⁶⁾. Most superacids gave satisfactory yields of 2', 3', and 4'-methylbenzophenones using benzoyl chloride as the acylating agent. However, hydrogen chloride generation and consumption of benzoyl chloride during the formation of by-products presented problems. Therefore, the acylating agent was changed to an acid anhydride of phthalic acid to overcome these problems. Normally, a carboxylic acid anhydride forms the acylated product and carboxylic acid as the by-product. In the case of phthalic anhydride, the acylation results in no by-product. The resultant acylated benzoic acid includes the carboxylic acid functional group, and so can be converted into other derivatives.

Catalysis by solid acids, in particular solid superacids, must be investigated to apply acid anhydrides for acylation of aromatics. The present study describes the Friedel-Crafts acylation of anisole with phthalic anhydride on a solid superacid of sulfated zirconia, and proposes a reaction mechanism.

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Table 1 Acylation of Anisole with Phthalic Anhydride Catalyzed by S/Z-W and S/Z-5

Entry	Catalyst	Reaction temp. [°C]	mono-FC [%]	di-FC [%]	Ester [%]	Total [%]
1	S/Z-W	30	0	0	0	0
2	S/Z-W	80	0	2	34	36
3	S/Z-W	120	0	31	8	39
4	S/Z-5	30	0	0	0	0
5	S/Z-5	80	0	4	54	58
6	S/Z-5	120	0	15	33	48
7 ¹⁾	S/Z-W	120	0	10	3	13
8 ²⁾	S/Z-5	120	0	1	28	29

All reactions were carried out for 24 h.

1) Catalyst weight was 150 mg. 2) Acylation with phthalic acid.

2. Experimental

2.1. Catalyst Preparation

Four types of zirconia, JRC-ZRO-2, JRO-ZRO-3, JRC-ZRO-4, and JRO-ZRO-5, which are reference catalysts supplied by the Reference Catalyst Committee of the Catalysis Society of Japan, were used as the precursor of sulfated zirconia⁷⁾. The zirconia gel was sulfated by the equilibrium adsorption method as follows. The zirconia was treated with sulfate ion by exposing 2 g of the dried and powdered zirconia in 30 ml of 1 N H₂SO₄ on a stem plugged glass filter for 1 h. The treated zirconia was filtered after removing the stem plug, dried on a glass filter at room temperature in a desiccator, and finally calcined in air at 873 K for 3 h in a glass ampoule. The ampoule was sealed while hot and the sample was kept in the ampoule until use. The solid superacids of sulfated zirconia obtained using JRC-ZRO-2, JRO-ZRO-3, JRC-ZRO-4, and JRO-ZRO-5 are named S/Z-2, S/Z-3, S/Z-4, and S/Z-5, respectively.

The catalysts were prepared by the kneading method as follows⁷⁾. The zirconia was dried at 373 K for 24 h, mixed with (NH₄)₂SO₄ powder in a weight ratio ZrO₂ : (NH₄)₂SO₄ = 1 : 0.2, and ground in an automatic mortar for 30 min, without solvent. The product was dried at 373 K for 24 h and then calcined at 873 K for 3 h in air.

Sulfated zirconia from Wako Pure Chemical Industries was calcined in air at 773 K for 3 h in a glass ampoule. The ampoule was sealed while hot. This catalyst is named S/Z-W. WO₃/ZrO₂⁸⁾, SO₄/SnO₂⁹⁾, SO₄/Fe₂O₃⁸⁾, and SO₄/Al₂O₃¹⁰⁾ were prepared according to the literatures.

2.2. Reaction Procedure

The acylation was carried out with a mixture of 9.2 mmol (1 ml) of distilled anisole, 0.68 mmol (0.1 g) of phthalic anhydride, and 0.3 g of catalyst. The mixture was stirred in a flask at 30, 80, and 120°C for 24 h under an argon atmosphere. After the reaction, the flask was cooled in flowing water, ethanol was added to the mixture, and the flask allowed to stand at room temperature for 10 min. The catalyst was removed by

suction filtration. The ethanol was evaporated under reduced pressure and the products were separated by thin layer chromatography (TLC). The products were weighed and the yield was determined based on the weight of product.

Reactions catalyzed by AlCl₃ were performed at 0°C as above, but with the catalyst amount triple that of the acylation reagent. After reaction, the mixture was diluted with diethyl ether. The organic phase was washed with water and dilute HCl followed by drying over Na₂SO₄. After removal of the diethyl ether under reduced pressure, the products were separated by TLC.

3. Results and Discussion

The acylation of anisole with phthalic anhydride was performed on S/Z-W and S/Z-5 catalysts at various temperatures as shown in **Table 1**. Diacylated product C₆H₄[CO(C₆H₄OCH₃)]₂, denoted as di-FC, and the monoethyl ester of phthalic acid shown in **Scheme 1** were obtained. The yields of di-FC and monoacylated product, C₆H₄[CO(C₆H₄OCH₃)]COOH, denoted as mono-FC, are also shown in **Table 1**.

The monoacylated product is the expected product in this reaction¹¹⁾. The carboxylic acid formed by monoacylation has lower reactivity than the acid anhydride or the acyl chloride as a reagent for acylation. Consequently, further acylation is expected to be difficult. To confirm this prediction, acylation with phthalic acid was examined (Entry 8). The amount of di-FC was small as expected. mono-FC was not obtained and the compound produced by further acylation was obtained at elevated temperatures (**Table 1**). In addition, ethyl monoester was also obtained. Presumably the monoester was generated when ethyl alcohol was added for the posttreatment of this reaction. This ester was not obtained from the mixture of phthalic anhydride and ethyl alcohol without catalyst. The catalysts used in this study did not show any activity for acylation or ester formation at 30°C. The ester yield was dependent on the catalyst amount, and the yield was less than half using 150 mg of S/Z-W (Entry 7) compared to using

Scheme 1 Friedel-Crafts Acylation of Anisole with Phthalic Anhydride

Scheme 2 Acylation of Anisole with Phthalic Anhydride Catalyzed by Aluminum Chloride

Table 2 Acylation of Anisole with Phthalic Anhydride Catalyzed by Aluminum Chloride

Condition	Reaction temp. [°C]	Reaction time [h]	Yield (mono : di) [%]
Homogeneous	0	24	30 : 1
Heterogeneous	0	24	46 : 7

300 mg of S/Z-W (Entry 3). The findings at elevated reaction temperatures suggest that phthalic anhydride forms a complex with an active site on the catalyst surface. The surface complex then reacts with ethanol and is desorbed from the surface as the monoester. The obtained products were quite different from those of the well known obtained in homogeneous reaction, and are characteristic of the reaction over the solid superacid.

To confirm the typical product of Friedel-Crafts acylation in a homogeneous system, the acylation of anisole with phthalic anhydride was performed in the presence of AlCl_3 (Scheme 2). The reaction was carried out at 0°C because of the higher activity of AlCl_3 . Products were mono-FC and di-FC, which was produced by further acylation of the carboxylic acid (Table 2). The *ortho*-isomer of mono-FC was not observed by nuclear magnetic resonance (NMR) analysis. The reaction conditions and yields of each product are shown in Table 2. In the homogeneous condition, AlCl_3 was dissolved in anisole and phthalic anhydride was added to the anisole solution. A small portion of AlCl_3 was suspended in the solvent. In the heterogeneous condition, solid AlCl_3 was added to the anisole solution of phthalic anhydride, so a large portion of the AlCl_3 was present in the solid phase during the reaction. A large amount of mono-FC was obtained for both reaction

conditions, quite different for the solid superacid of sulfated zirconia, on which no mono-FC was produced.

The relative amount of di-FC produced was larger in the heterogeneous condition than in the homogeneous condition. The reaction would be catalyzed by both the dissolved and solid AlCl_3 in the heterogeneous condition. The dissolved AlCl_3 can catalyze the formation of mono-FC as shown in the homogeneous condition. However, the dissolved AlCl_3 cannot produce the di-FC. Therefore, di-FC is formed under the heterogeneous condition on the catalyst surface. Presumably the difference in structures between the complex of dissolved AlCl_3 and phthalic anhydride, and the surface intermediate of the complex on Al^{3+} would affect the product selectivity.

The reaction forming di-FC is specific to the heterogeneous condition as shown in Tables 1 and 2. To confirm the reactivity of mono-FC, acylation with mono-FC was carried out on AlCl_3 in the homogeneous condition and on S/Z-5 (Scheme 3). AlCl_3 showed no activity for the acylation with mono-FC (Table 3). A small amount of di-FC was obtained from the acylation with phthalic anhydride as shown in Table 2. The activity of AlCl_3 in the homogeneous phase for acylation of anisole with mono-FC is estimated to be very low, which indicates that phthalic anhydride is converted directly into di-FC on solid AlCl_3 , not by successive

Scheme 3 Acylation of Anisole with mono-FC

Table 3 Acylation of Anisole with mono-FC on AlCl_3 and S/Z-5

Catalyst	Condition	Reaction temp. [$^{\circ}\text{C}$]	Reaction time [h]	Yield (di-FC : di-FC* ^{a)}) [%]
AlCl_3	Homogeneous	0	24	0 : 0
S/Z-5	Heterogeneous	120	4	73 : 6

a) See Scheme 3.

Table 4 Acylation of Anisole with Phthalic Anhydride Catalyzed by Sulfated Zirconia Catalysts at 120°C for 24 h

Entry	Catalyst	di-FC [%]	Ester [%]	di-FC + Ester [%]
1	S/Z-2 ^{a)}	7	35	42
2	S/Z-3 ^{a)}	10	43	53
3	S/Z-4 ^{a)}	5	43	48
4	S/Z-5 ^{a)}	15	33	48
5	S/Z-2 ^{b)}	1	47	48
6	S/Z-3 ^{b)}	8	32	40
7	S/Z-4 ^{b)}	2	38	40
8	S/Z-5 ^{b)}	5	40	45

a) Equilibrium adsorption method. b) Kneading method.

reactions *via* mono-FC.

In contrast, S/Z-5 showed activity for this reaction at 120°C . mono-FC was converted into di-FC and a related compound, di-FC* (Scheme 3) in the short time of 4 h. The reaction of phthalic anhydride can convert mono-FC into di-FC because of the high catalytic activity of S/Z-5. However, mono-FC was not observed in the acylation of anisole with phthalic anhydride, as shown in Table 1. In addition, di-FC* was not obtained with phthalic anhydride as the acylation reagent. Therefore, a new mechanism for direct formation of di-FC from phthalic anhydride should be considered.

The effects of the preparation method of sulfated zirconia are shown in Table 4. S/Z-5 prepared by the equilibrium adsorption method was the most active for di-FC formation. S/Z-3 also showed relatively high activity. The equilibrium adsorption method is more effective to prepare sulfated zirconia for acylation than the kneading method.

Catalysts prepared by the equilibrium adsorption method also provided higher total yields of di-FC and

ester. However, the total yields were in the range of 40-57%, so the differences were relatively small in comparison to those of di-FC yields.

Acylation was investigated over various solid superacids as summarized in Table 5. mono-FC was not obtained on all catalysts in the same way as on sulfated zirconia. The monoester was also produced on all catalysts. di-FC production was observed over WO_3/ZrO_2 and SO_4/SnO_2 . The acylated product was not obtained over $\text{SO}_4/\text{Fe}_2\text{O}_3$ and $\text{SO}_4/\text{Al}_2\text{O}_3$. The acid strengths of WO_3/ZrO_2 and SO_4/SnO_2 were higher than those of $\text{SO}_4/\text{Fe}_2\text{O}_3$ and $\text{SO}_4/\text{Al}_2\text{O}_3$. The heat of Ar adsorption, which is related to the acid strength, is shown in Table 5, and indicates that the acylation of anisole with phthalic anhydride occurs on superacid sites, and monoester is formed on weaker acid sites.

The total yields of di-FC and ester were almost the same as shown in Table 1, even though the reaction temperature was increased. Figure 1 shows the time course of di-FC and ester yields. The yield of di-FC was increased with increasing reaction time. The ester yield in the initial period was high. However, the yield increase in the later period was very small in comparison with the high yield in the initial period. Therefore, the ester yield was almost constant during the reaction in the later period, according to the possible reaction mechanism shown in Schemes 4 and 5.

Phthalic anhydride is activated by a homogeneous Lewis acid such as AlCl_3 , resulting in formation of the complex of phthalic anhydride and AlCl_3 . This complex is converted into the acylated product of mono-FC. In this case, the addition of the second anisole does not occur because the formed carboxyl group has a lower reactivity for acylation of anisole in the presence of

Table 5 Acylation of Anisole with Phthalic Anhydride over Various Solid Catalysts at 120°C for 24 h

Entry	Catalyst	mono-FC [%]	di-FC [%]	Ester [%]	Heat of Ar ads. [kJ·mol ⁻¹]
1	WO ₃ /ZrO ₂	0	23	20	21.6 ⁽¹²⁾
2	SO ₄ /SnO ₂	0	12	10	23.5 ⁽¹²⁾
3	SO ₄ /Fe ₂ O ₃	0	0	29	18.9 ⁽¹²⁾
4	SO ₄ /Al ₂ O ₃	0	0	27	18.9 ⁽¹⁰⁾

Scheme 4 Formation of mono-FC by AlCl₃ and Adsorbed Species on Sulfated Zirconia

□: di-FC, ○: ester.

Fig. 1 Time Course of Yields of di-FC and Ester over S/Z-5 Prepared by the Equilibrium Adsorption Method

AlCl₃.

Phthalic anhydride molecules are adsorbed on active acid sites on the surface of sulfated zirconia, and several types of surface complexes are expected to form. The

carbonyl group must be activated by acid for the formation of di-FC. Therefore, an intermediate of type A in **Scheme 4** is expected.

Phthalic anhydride also forms another structure on the surface of sulfated zirconia that seems to be similar to the complex with AlCl₃. This type of intermediate, type C in **Scheme 4**, might be more stable. This intermediate can interact with the catalyst surface in two ways, the carboxyl group with negative charge and positive charge on the carbonyl group. Intermediate type C must be desorbed after the reaction with ethanol in the posttreatment procedure, but might be stable under the reaction conditions. The amount of intermediate type C is estimated to be constant during the reaction because the number of active sites for intermediate type C formation is limited. Intermediate type C would be desorbed after the reaction with ethanol used in the posttreatment. As discussed above, the weaker acid sites are suitable for the formation of type C intermediate.

Reactions similar to the present acylation are well known. Fluorescein and phenolphthalein can be synthesized from phthalic anhydride with resorcinol or phenol by acid catalyzed Friedel-Crafts acylations¹³⁾. In these reactions, the addition of resorcinol or phenol occurs at one carbonyl group of phthalic anhydride. The same reaction would take place in the acylation of present study, as shown in **Scheme 5**. The two ani-

Scheme 5 Reaction Mechanism for di-FC Formation

sole molecules are bonded to one carbonyl group of phthalic anhydride. The other carbonyl group might be also activated on the surface of the superacid. As a result, one anisole would be transferred to the carbon at the carbonyl group and the furan ring opened. Finally, di-FC is formed and desorbed from the catalyst surface. Reaction temperatures above 80°C are probably required for this rearrangement and desorption of product.

4. Conclusion

Friedel-Crafts acylation of anisole with phthalic anhydride was performed over several types of sulfated zirconia catalysts and related solid superacids. The products were $C_6H_4[CO(C_6H_4OCH_3)]_2$, the diacylated product, and the monoacylated product, whereas $C_6H_4[CO(C_6H_4OCH_3)]COOH$, was not observed. Phthalic acid monoethyl ester was produced by post-treatment of the catalyst with ethanol.

di-FC is expected to be formed by the addition of two anisole molecules to phthalic anhydride with a subsequent rearrangement of the anisole group to the carbon of the other carbonyl group. This reaction was catalyzed by superacid sites, and the ester was formed

on the weaker acid sites.

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要 旨

**硫酸化ジルコニア固体超強酸触媒を使用した
無水フタル酸によるアニソールのフリーデル・クラフツ型アシル化反応**

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無水フタル酸によるアニソールのフリーデル・クラフツ型アシル化反応を, 触媒学会提供のジルコニアゲル (JRC-ZRO-2, JRO-ZRO-3, JRC-ZRO-4, JRO-ZRO-5) を用いて, 平衡吸着法と混練法で調製した硫酸化ジルコニアで行った。生成物は2カ所のアシル化が起こった $\text{C}_6\text{H}_4[\text{CO}(\text{C}_6\text{H}_4\text{OCH}_3)]_2$ だけで, 片方だけのアシル化で生成する $\text{C}_6\text{H}_4[\text{CO}(\text{C}_6\text{H}_4\text{OCH}_3)]\text{COOH}$ は見られなかった。溶媒に溶解した AlCl_3 では, 片方だけのアシル化生成物が大量に得られた。フタル酸の一方だけにエステル化

された生成物がエタノールによる後処理で生成した。反応温度や時間は, エステルの収量にあまり影響しなかった。2カ所のアシル化された生成物は, 無水フタル酸の一方のカルボニル基への2個のアニソールの付加と, それに続く超強酸性により活性化されたもう一方のカルボニル基へのアニソールの転移反応により生成したと推定した。種々の固体超強酸での反応結果より, 2カ所でのアシル化には表面の超強酸点が必要であることが示された。

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