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Friedel–Crafts Benzoylation of Alkylbenzenes with Benzoic Anhydride Catalyzed by Solid Superacids

Hideo Nakamura* and Kazushi Arata*

Department of Science, Hokkaido University of Education, Hachiman-cho, Hakodate 040-8567

Received January 8, 2004; E-mail: karata@cc.hokkyodai.ac.jp

The liquid–solid phase benzoylation of mono-alkylbenzenes with methyl, ethyl, propyl, and butyl groups and xylenes was carried out with benzoic anhydride at 100–110 °C over solid superacids: SO_4/ZrO_2, WO_3/ZrO_2, and SO_4/HfO_2. The reactivity ratio obtained by the competitive method of reaction over WO_3/ZrO_2 was 1 to 4.6 for toluene to *p*-xylene and 1.1:10:1 among *o*-, *m*-, and *p*-xylenes, respectively. Although the SO_4/ZrO_2 catalyst gave high yields of 92 and 97% for toluene and ethylbenzene in a 3:7 distribution of *o*- and *p*-isomers, respectively, low yields were observed with propyl and butylbenzenes over the catalyst: that is, 5 and 2% for propylbenzene and isopropylbenzene, 14% for isobutylbenzene, and trace yields for butylbenzene, *s*-butylbenzene, and *t*-butylbenzene, respectively. The usual Friedel–Crafts benzoylation using $AlCl_3$ was examined in the present alkylbenzenes in order to confirm the low reactivity of both propyl and butylbenzenes. The results were similar to those with the SO_4/ZrO_2 catalyst; that is, the yields at 0 °C for 1 h were 37, 21, 6, 1, 0, 3, and 2% for toluene, ethylbenzene, propylbenzene, isopropylbenzene, butylbenzene, *s*-butylbenzene, and *t*-butylbenzene, respectively, showing an unexpected result where there was no distinction between homogeneous and heterogeneous conditions.

The catalytic acylation of aromatics via the Friedel–Crafts reaction for introducing functional substituents to the aromatic rings is an attractive challenge for clean technology as well as for organic synthesis. Thus, there have been several efforts to conduct the reaction using catalytic amounts of acidic promoters.[1–9] Yadav and Pujari synthesized 4-chlorobenzophenone, a pharmaceutical intermediate, via the acylation of benzene with 4-chlorobenzoyl chloride over sulfated zirconia, a solid superacid.[10]

Solid superacids of sulfated and supported metal oxides, such as sulfated zirconia (SO_4/ZrO_2) and tungstated zirconia (WO_3/ZrO_2), were synthesized by the addition of sulfate species to oxide surfaces of Fe, Ti, Zr, Hf, Sn, Al, and Si, or by supporting SnO_2, TiO_2, and Fe_2O_3 with WO_3 and ZrO_2 with MoO_3 and B_2O_3.[11,12] A previous paper reported a systematic study of those superacids for the benzoylation of toluene with benzoic anhydride and benzoyl chloride in the liquid–solid phase.[13] Most of the superacids showed satisfactory results, and several catalysts were also examined in a less reactive acylation: the acetylation of toluene; however, satisfactory results were not obtained. Thus, the acetylation of toluene with acetic anhydride was investigated in detail using catalysts selected from the above results, but it was demonstrated that the catalysts could not act efficiently to complete the reaction because of the most difficult acylation owing to a difficulty in the formation of an intermediate acetyl-cation ($MeCO^+$) from acetic anhydrides and acetyl halides. In this sense, the catalytic action was more effective for propionylation and butyrylation, more reactive acylations with longer hydrocarbon chains.[14] The acetylation, however, was quite effective on anisole, a more reactive substrate, over the SO_4/ZrO_2 catalyst.[14,15]

In a series of the Friedel–Crafts acylations catalyzed by superacids, the substrates have been limited mainly to toluene, and the development of wide substrates is in demand. This paper is concerned with a study of the catalytic benzoylation of alkylbenzenes, such as xylenes, ethylbenzene, propylbenzenes, and butylbenzenes, over superacid materials. The results were also compared with those by the usual reaction procedures using $AlCl_3$ as a catalyst.

Experimental

Catalyst Preparation. SO_4/ZrO_2 was prepared by calcining sulfated zirconia of Wako Pure Chemical Industries, Ltd., at 550 °C for 3 h. WO_3/ZrO_2 and SO_4/HfO_2 were prepared following the literature.[13,14]

Reaction Procedure. Benzoylation was carried out with a mixture of 140 mmol (15–22 mL) of alkylbenzene (purified by distillation before use), 2 mmol of benzoic anhydride (0.45 g), 0.5 g of catalyst, and 0.185 g (1 mmol) of tridecane as an internal standard with stirring under an argon atmosphere. A small amount of the sample was withdrawn periodically with a 1 mL syringe, diluted with ethyl acetate, separated from the catalyst by filtration, and analyzed by gas-liquid chromatography with an FID detector using a 25 m column of OV-1701 BONDED (120–220 °C). The yields were calculated based on the acylating reagents.

Reactions catalyzed by $AlCl_3$ (Wako Pure Chemical Industries, Ltd.) were performed at 0 °C in the same manner as the above procedures, the catalyst amount being three-times as much as the acylating agent, 6 mmol. After the reaction mixture was diluted with ethyl acetate, the organic phase was washed with water, saturated $NaHCO_3$, and brine followed by drying over $MgSO_4$. After the solvent was removed under reduced pressure, the products were analyzed.

Isolation and Identification of the Product. Silica-gel column chromatography was performed using Merck Kiesel 60 (70–230 mesh). The product isomers were identified by a comparison of their spectral data (^1H and ^{13}C NMR spectra on a JEOL

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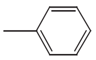
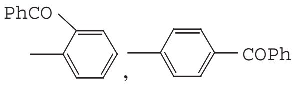
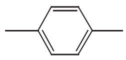
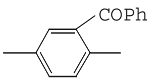
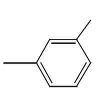
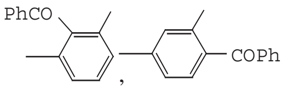
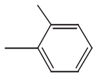
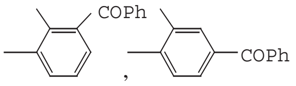
Table 1. Benzoylations of Toluene and Xylenes with Benzoic Anhydride at 100 °C for 2 h

Reactant	Catalyst	Yield/%	Products and isomer ratio
	SO_4/ZrO_2	82	 3:7
	WO_3/ZrO_2	41	
	SO_4/HfO_2	20	
	SO_4/ZrO_2	99	
	WO_3/ZrO_2	32	
	SO_4/HfO_2	14	
	SO_4/ZrO_2	98	 1:10
	WO_3/ZrO_2	92	
	SO_4/HfO_2	88	
	SO_4/ZrO_2	99	 1:3
	WO_3/ZrO_2	49	
	SO_4/HfO_2	19	

JNM-EX270) and retention times in GLC with those of authentic samples.

Results and Discussion

Benzoylations of Toluene and Xylenes. The benzoylation of toluene along with *o*-, *m*-, and *p*-xylenes with benzoic anhydride was carried out in the liquid phase at 100 °C over SO_4/ZrO_2, WO_3/ZrO_2, and SO_4/HfO_2, the former two of which showed the highest activity for the benzoylation of toluene among the solid superacids of sulfated and supported metal oxides, respectively, in the previous paper;[13] the results for 2 h are given in Table 1. As for the reaction of toluene, the previous results were reproduced, and the activity ratio was estimated to be 4:2:1 for SO_4/ZrO_2, WO_3/ZrO_2, and SO_4/HfO_2, respectively.

In the benzoylation of xylenes, 2,5-dimethylbenzophenone was formed from the reaction of *p*-xylene, 2,4- and 2,6-dimethylbenzophenones in the ratio 10:1 from *m*-xylene, and 2,3- and 3,4-dimethylbenzophenones in the ratio 1:3 from *o*-xylene. Although similar activities to those for toluene among the catalysts were observed with *o*- and *p*-xylenes, the yields obtained by the reaction of *m*-xylene were quite high in all cases, showing its high reactivity.

Competitive Reaction among Toluene, *o*-, *m*-, and *p*-Xylenes. In order to confirm the intrinsic reactivities of the substrates, a competitive reaction method among the three xylenes along with toluene was tried. The competitive benzoylation between toluene and *p*-xylene was carried out over WO_3/ZrO_2 with the anhydride in equimolar amounts of toluene (7 mL) and *p*-xylene (8 mL); Fig. 1 shows the time variations of the total yields of isomers. Variations among the three isomers of xylene (5 mL each) were also conducted in the same manner as mentioned above. The reactions showed a continual increase of yield with time, close to first-order reaction kinetics with respect to the anhydride concentration. The reactions are thus judged to be heterogeneously catalytic.

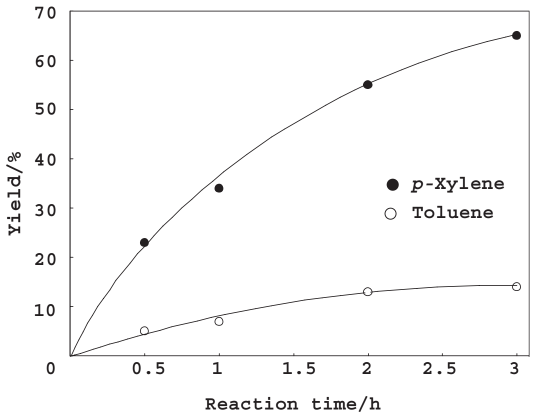


Fig. 1. Competitive reaction between *p*-xylene (●) and toluene (○) over WO_3/ZrO_2 at 90 °C.

Table 2. Competitive Reaction among Toluene and Xylenes over WO_3/ZrO_2 at 90 °C for 30 min

Reactant	Yield[a)]/%	Yield/%	Reactivity ratio	
o-Xylene		4		1.1
m-Xylene		30		10
p-Xylene	23	3	4.6	1
Toluene	5		1	

a) Reaction in Fig. 1.

The yields at 30 min of time are summarized in Table 2 together with their reactivity ratio, estimated by the yields. The ratio is 1 to 4.6 for toluene to *p*-xylene and 1.1 to 10 to 1 for *o*- to *m*- to *p*-xylenes, respectively. A large difference in the reactivities is reasonably based on the electron density on the benzene ring. The high reactivity of *p*-xylene against toluene is explained by the double electron-releasing effect of two methyl groups, and the extremely high value of *m*-xylene against *o*- and *p*-xylenes is interpreted by both *o*- and *p*-orientation effects of xylene brought by two methyl groups. The relative reactivity among *o*-, *m*-, and *p*-xylenes was determined to be 6:16:1, respectively, in the homogeneous reaction of benzoyl chloride with $AlCl_3$.[16]

Benzoylation of Isobutylbenzene. Since the benzoylation of methyl-activated benzenes was examined, the reaction of isobutylbenzene was accomplished in order to investigate how longer hydrocarbon chains work and how side chains act. Benzoylation following the method of toluene was performed over the SO_4/ZrO_2 catalyst at 110 °C for 4 h, but the yield was quite low, 14%. Supplementary examinations were attempted several times; the results were identical with the above. The time-variation of the reaction showed a failure of the catalyst to react further after 2–3 h, being different from the cases of toluene and xylenes, showing a continual increase of yield up to 100%. A question arose concerning the deactivation of the catalyst on account of an excess of the substrate. Thus, the reaction was carried out in solvents of cyclohexane, chlorobenzene, and nitrobenzene, frequently used in homogeneous Friedel–Crafts reactions. However, yields close to the above were just obtained by stirring a mixture of 2 mL of isobutylbenzene, 2 mmol of the anhydride, and 20 mL of solvent over the catalyst for 5 h.

Table 3. Benzoylations of Alkylbenzenes with Benzoic Anhydride at 110 °C for 4 h

Reactant	Catalyst	Yield/%	Isomers/%	
			o-	*p*-
Isobutylbenzene	SO_4/ZrO_2	14	9	91
	SO_4/SnO_2	7	8	92
	SO_4/HfO_2	4	8	92
	WO_3/ZrO_2	4	7	93
Butylbenzene	SO_4/ZrO_2	Trace		
s-Butylbenzene	SO_4/ZrO_2	Trace		
t-Butylbenzene	SO_4/ZrO_2	Trace		
Tetralin	SO_4/ZrO_2	Trace		
Propylbenzene	SO_4/ZrO_2	5	28	72
Isopropylbenzene	SO_4/ZrO_2	2	15	85
Ethylbenzene	SO_4/ZrO_2	97	30	70
Toluene	SO_4/ZrO_2	92	27	71

The benzoylation of isobutylbenzene was performed over other catalysts, WO_3/ZrO_2 and SO_4/HfO_2, together with SO_4/SnO_2, where the SnO_2 catalyst was recently reported to be a solid superacid with its acid strength higher than that of SO_4/ZrO_2, and was prepared by following the literature.[17,18] The results are given in Table 3. Although yields higher than 14% were expected, SO_4/SnO_2 gave just 7% yield.

The product distribution was 7–9% 2- and 91–93% 4-isobutylbenzophenones, and the meta isomer was not detected. The low ortho-substitution compared with the case of toluene is based on the steric hindrance of a large isobutyl group.

Benzoylations of Benzenes with Methyl, Ethyl, Propyl, and Butyl Groups. Since the results in the benzoylation of isobutylbenzene were unexpected, the reactivities of other alkylated benzenes were compared. Table 3 summarizes the results in the benzoylation of toluene, ethylbenzene, propylbenzene, isopropylbenzene, butylbenzene, *s*-butylbenzene, and *t*-butylbenzene over SO_4/ZrO_2 under the same conditions as those of isobutylbenzene. Toluene and ethylbenzene showed reasonable conversions of 92 and 97% in the distribution 3:7 of *o*- and *p*-isomers, respectively. On the other hand, the conversions of propyl- and butyl-activated benzenes were surprisingly low, far from the results that we expected when considering the reactivity of the organic compounds, the highest yield being 5% for propylbenzene. Their inactivity is independent of the interaction of the hydrocarbon chains with the catalyst surface, because tetralin, equivalent to cyclic butylbenzene, is also inactive.

Homogeneous Benzoylations of Benzenes with Methyl, Ethyl, Propyl, and Butyl Groups. The present low conversions of various propyl and butylbenzenes lead to a question regarding whether active species on the solid surface are poisoned, that is, whether there is a distinction between homogeneous and heterogeneous conditions. Therefore, the present benzoylation was carried out under the usual, homogeneous, Friedel–Crafts conditions using $AlCl_3$ as a catalyst. The results are shown in Fig. 2 as the time-variations of conversion. It can be seen that all of the reactions progress continuously with time at 0 °C, but the process of the reaction shows S-shaped curves without following the first-order kinetics with respect to the anhydride, particularly in the cases of propyl and butylbenzenes. The reaction homogeneously proceeded based on the coordination of $AlCl_3$ with the acylating reagent, followed by forming complexes with both the carbonyl product and produced benzoic acid.

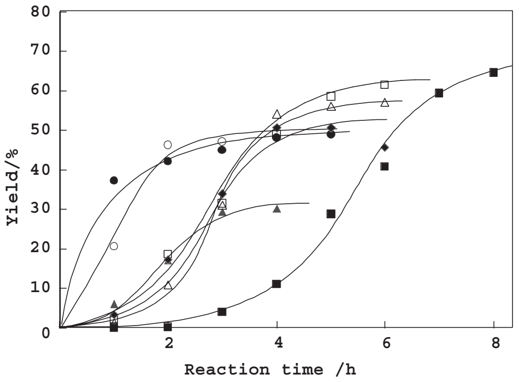


Fig. 2. Benzoylations of toluene (●), ethylbenzene (○), propylbenzene (▲), isopropylbenzene (△), butylbenzene (■), isobutylbenzene (□), and *s*-butylbenzene (◆) with benzoic anhydride catalyzed by $AlCl_3$ at 0 °C.

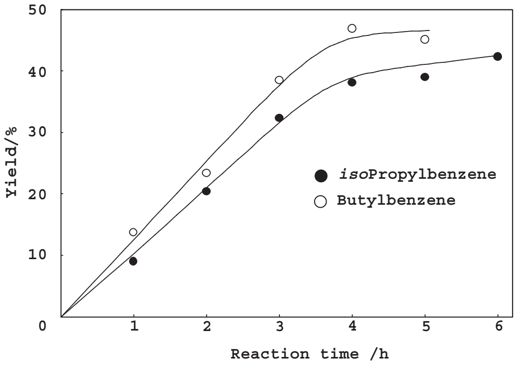


Fig. 3. Benzoylations of isopropylbenzene (●) and butylbenzene (○) with benzoic anhydride and $AlCl_3$ by the addition of H_2O (10 µL) at 0 °C.

The results given in Fig. 2 lead to a question whether the active species are created during the reaction, for instance HCl derived from the reaction of $AlCl_3$ with contaminated H_2O. Thus, the benzoylations of isopropyl and butylbenzenes, showing wide S-curves in Fig. 2, were performed with the addition of H_2O (10 µL); the results are shown in Fig. 3. Both of the reactions show a continual increase of yield with time in striking contrast with those in Fig. 2, indicating the catalytic effect of the produced HCl. However, benzoylation did not occur with HCl only without $AlCl_3$; that is, the reaction of toluene with benzoyl chloride and H_2O, where HCl was supposed to be produced, did not take place, but subsequently proceeded by the addition of $AlCl_3$.

In consideration of the above results, it is proposed that the reaction is performed with benzoyl chloride as the acylating agent, derived from the reaction of benzoic anhydride with HCl, produced by the hydrolysis of $AlCl_3$. Thus, the possibility of benzoyl chloride being formed was examined, and the chloride was detected by the analysis of TLC after 30 min of reaction in the reaction of toluene with benzoic anhydride and $AlCl_3$ at 0 °C, and not detected after 2 h because of probable completion of the reaction. Therefore, it would be advisable

Table 4. Benzoylations of Alkylbenzenes with Benzoic Anhydride Catalyzed by $AlCl_3$ at 0 °C for 1 h

Reactant	Yield/%	Isomers/%	
		o-	*p*-
Toluene	37	10	90
Ethylbenzene	21	0	100
Propylbenzene	6	0	100
Isopropylbenzene	1	0	100
Butylbenzene	0		
s-Butylbenzene	3	0	100
t-Butylbenzene	2	0	100

that the reaction is a benzoylation with the produced benzoyl chloride when the system consists of benzoic anhydride and $AlCl_3$.

The yields of the corresponding benzophenones together with the isomer distribution in the early period, where genuine benzoylation with the anhydride is probable, are summarized in Table 4. The results are in harmony with those with the SO_4/ZrO_2 catalyst. The observations show a surprising reactivity of the substrates, and are probably against a well-known fact in organic chemistry as well as the Friedel–Crafts reaction.[19,20] The inactivity of propyl and butyl substrates is, of course, not based on the steric hindrance of propyl and butyl groups because of high selectivity to the para position. High conversions in the benzoylation of propyl and butylbenzenes have been reported, for instance, 72 and 75% in yield for propylbenzene and butylbenzene with $AlCl_3$ and benzoyl chloride as the acylating agent.[21,22] However, those results were based on an individual reaction to obtain a high yield under the optimum conditions, not on a comparative method following reaction kinetics. Regarding this point, the present procedure over solid superacids seems to be reasonable, judging from the competitive reaction of xylenes.

Conclusion

The Friedel–Crafts benzoylation of alkyl-activated benzenes with benzoic anhydride shows that propyl and butylbenzenes, including their isomers, are exceedingly inactive in spite of the high reactivities of toluene and ethylbenzene, whether the reaction condition is homogeneous or heterogeneous using $AlCl_3$ or sulfated zirconia as a catalyst, disabling the result from interpreting the activity of the benzene ring by the electron-releasing effect of the alkyl groups.

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