The Acetylation of Toluene and Benzene with Acetyl Chloride and Bromide and Acetic Anhydride Catalyzed by Calcined Iron Sulfate Activated by Exposure to a Mixture of Benzyl Chloride and the Aromatics[1)]

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The acetylations of toluene and benzene with acetyl halides and acetic anhydride were studied over catalysts prepared by heat-treating $FeSO_4$ in air, followed by activation on exposure to benzyl chloride in toluene or benzene at 40—80 °C for 1 h, together with $FeCl_3$ and $AlCl_3$. The sulfates treated at 700 and 800 °C showed high activity. The former, activated at 60 °C, gave 68% methylacetophenones, and the latter, more than 90%, with an isomer distribution of 2% *ortho*-, 1% *meta*-, and 97% *para*-form in the reaction of toluene with acetyl halides at room temperature, while the maximum yield was 24% with $FeCl_3$ and 29% with $AlCl_3$. A high yield of acetophenone, 77%, was obtained over the $FeSO_4$ (700 °C) catalyst in the reaction of benzene with acetyl bromide at 60 °C for 1 h. The present catalysts were also highly active for the acetylation of toluene with acetic anhydride; *e.g.*, 55% methylacetophenones were obtained over the $FeSO_4$ (800 °C) catalyst at 100 °C for 5 h. $FeCl_3$ and $AlCl_3$ gave quite low yield compared with the present catalysts.

The Friedel-Crafts acylation of aromatics with acid anhydrides and acyl halides in the presence of acidic halide catalysts has been the subject of a great many investigations during the hundred years since the discovery of the reaction. Extensive reviews have discussed the reaction mechanism.[2-5)] Alkylation with alkyl halides requires only catalytic amounts of catalysts, whereas acylation affords ketones in yields which are proportional to the amount of catalysts. The reaction is complete when little more than a molecular proportion of catalyst is used. On the other hand, more than two moles of the Lewis catalyst are consumed in the case of acid anhydride as an acylating agent.

The acetylation of toluene and benzene with acetyl halides or acetic anhydride has also been performed with, at least, an equimolar amount of a catalyst for an acetylating agent by using such Lewis catalysts as anhydrous aluminum chloride, boron trifluoride, and iron(III) chloride.[6-11)] We have found that the acetylation of toluene and benzene with acetyl halides or acetic anhydride with a new catalyst at room temperature under the heterogeneous system gave methylacetophenones and acetophenone in good yields.

Experimental

The toluene and benzene, guaranteed reagents, were purified by distillation over sodium metal. The acetyl chloride, acetyl bromide, and acetic anhydride, all guaranteed reagents of the Wako Pure Chemical Co., were used without further purification. The acetyl chloride and bromide were stored in sealed ampoules until use in order to prevent hydrolysis. The catalysts were prepared as follows: $FeSO_4 \cdot 7H_2O$ (guaranteed grade of the Kanto Chemical Co.) was heated at 150 °C for 1 h, powdered below 100 mesh, and then calcined in a Pyrex or quartz glass tube at various temperatures in air for 3 h. The prepared catalyst was sealed in an ampoule until use. The activation of the catalyst was performed by heating a mixture of 50 ml of toluene or benzene, 1 g of the catalyst, and 1 ml of benzyl chloride at 60—100 °C. After the mixture has been cooled, an acetylating reagent (0.025 mol) was added, and the whole mixture was stirred at room temperature for 15—360 min. The catalyst was then removed by filtration, and the filtrate was washed with water several times and dried over anhydrous calcium chloride. The products were identified by means of a gas-chromatographic comparison with commercially available authentic samples and analyzed, using benzene (for the acetylation of toluene) or toluene (for the reaction of benzene) as the internal standard (a 1-m column of tritolyl phosphate on Celite 545, 110 °C, He: 1.0 kg/cm^2).

Results and Discussion

It was previously reported[12,13)] that the benzylation of toluene with benzyl chloride was markedly catalyzed by iron sulfates, which belong to the solid-acid type of catalysts, such as SiO–Al_2O_3 and $NiSO_4$. The iron sulfates also catalyzed the benzoylation of toluene with benzoyl chloride.[14)] The catalysts heat-treated at 700 °C showed the maximum activity in both reactions. The reaction rate in the benzoylation was, however, quite low. It took more than 50 min to complete the 30% conversion at 110 °C over the most active catalyst. Thus, the reaction rate of the acetylation of toluene with acetyl halides can be expected to be quite low because of the weak electrophilicity of the acetyl cation, CH_3CO^+. In fact, no product was detected in the gas-chromatographic analysis in the reaction of toluene with acetyl chloride at the reaction temperature of 50 °C, close to the boiling point of the chloride, over $FeSO_4$ heat-treated at 700 °C. However, the catalyst was found to be highly activated by exposure to benzyl chloride in toluene, and the acetylation proceeded at room temperature.

An example of the reaction by the activated catalyst is as follows. A mixture of toluene (50 ml), benzyl chloride (0.5 ml), and 1 g of $FeSO_4$ calcined at 700 °C was heated at 60 °C for 1 h; after cooling, acetyl chloride (0.025 mol) was added to the mixture, after which the whole mixture was stirred at room temperature. Thus, the aromatic compound for the acetylation is the toluene used in the activation of the catalyst. A

TABLE 1. YIELD(%) FOR ACETYLATION OF TOLUENE WITH ACETYL CHLORIDE AND BROMIDE AT ROOM TEMPERATURE[a)]

Catalyst	Temp of calcn./°C	Acetylating reagent	Yield/%							Isomer distribution/%		
			15 min	30 min	60 min	90 min	120 min	150 min	180 min	*o*-,	*m*-,	*p*-
$FeSO_4$	500	CH_3COCl	12	13								
	600	CH_3COCl	17		16							
	700	CH_3COCl	52		68		68			2	1	97
	700	CH_3COBr	61	65	67					2	1	97
	700[b)]	CH_3COBr							0			
	700[c)]	CH_3COBr		70	78							
	750	CH_3COCl		53	77		82					
	800	CH_3COCl			31	54	88	90	90	2	1	97
	800	CH_3COBr	13	34	87		92			2	1	97
	900	CH_3COCl			1		8					
$FeCl_3$		CH_3COCl	23	22	22					3	1	96
$FeCl_3$		CH_3COBr	24									
$AlCl_3$		CH_3COCl	26		29					2	2	96
$AlCl_3$		CH_3COBr	22									

a) Activated at 60 °C by the addition of 1 ml of benzyl chloride; catalyst amount: 1 g. b) Without treatment with benzyl chloride, 0% for 300 min. c) Reacted at 60 °C.

mixture of *o*-, *m*-, and *p*-methylacetophenone was obtained in a 21% yield after 60 min. The longer the period of reaction the more products were given: 31% for 120 min and 34% for 180 min. The reaction with acetyl bromide under the same conditions gave a 40% yield in 30 min and a 42% yield in 60 min.

The catalytic activity was dependent on the temperature of activation; *i.e.*, mixtures of methylacetophenones were obtained in 11, 21, 29, and 30% yields for 3 h when activated at 40, 50, 70, and 80 °C respectively, 60 °C thus being the most activating temperature (34% for 3 h). The acetylation with the chloride was performed over $AlCl_3$ and $FeCl_3$, but the product amount was only 9% for 3 h with both catalysts and 11% for even a period of 11 h with $FeCl_3$ under the same reaction conditions.

Table 1 shows the yields of the products for the acetylation of toluene with acetyl chloride and bromide at room temperature catalyzed by iron sulfates calcined at various temperatures, followed by activation with benzyl chloride at 60 °C; the yields obtained with $FeCl_3$ and $AlCl_3$ are also shown for comparison. As has already been mentioned, iron sulfate calcined at any temperature was completely inactive for the acetylation at room temperature unless otherwise activated. The catalytic activity of activated $FeSO_4$ changed remarkably with the calcination temperature. The sulfates calcined at 500, 600, and 900 °C showed low activity. However, a considerable amount, 68%, of methylacetophenones was obtained over the catalyst prepared by calcining at 700 °C with both acetyl chloride and bromide, and the sulfate calcined at 800 °C gave methylacetophenones in more than a 90% yield, though its reaction rate was slower than that when using the catalyst calcined at 700 °C. $FeSO_4$(750 °C)** falls into the intermediate range between the above two catalysts. The catalysts treated at 500 and 600 °C were found to be dissolved in the reaction mixture, and $FeSO_4$(700 °C) was slightly dissolved, while the materials calcined at 800 °C and 900 °C were insoluble.

When $FeCl_3$ and $AlCl_3$ were used instead of the present catalysts under similar conditions, the maximum yields were 24% and 29% respectively, quite close to the expected maximum yields estimated from the molar amounts of these catalysts and the acetylating reagent.

The acetylations was carried out with acetic anhydride as the acetylating agent over the sulfates treated at 700 °C and 800 °C, as is shown in Table 2. The reaction was performed over 60 °C because of the slow rate of the reaction. Whereas $FeCl_3$ and $AlCl_3$ produced less than 15% of methylacetophenones in 3 h at 80 °C, $FeSO_4$(700 °C) gave a 38% yield under the same conditions and even 44% in 5 h. It should be noted that 55% methylacetophenones were obtained over $FeSO_4$(800 °C) at 100 °C in 5 h. The selectivity was lower than that in the case of acetyl halides, whose isomer distribution was 2% *ortho*-, 1% *meta*-, and 97% *para*-methylacetophenone (Table 1).

The acetylation of benzene was performed with highly active catalysts, $FeSO_4$(700 °C) and $FeSO_4$(800 °C). The results are shown in Table 3. Since the reaction rate was quite low, the reaction temperature taken was 50 °C and 60 °C in the cases of the chloride and bromide respectively, both temperatures close to their boiling points. The catalysts were almost inactive for this reaction with acetic anhydride at 80 °C. The activity of $FeSO_3$(700 °C) was higher than that of $FeSO_4$(800 °C) in contrast with the observations of the reaction of toluene. Although the reaction with acetyl chloride showed a slower rate than that with the bromide, as was seen also in the case of toluene, the $FeSO_4$(700 °C) catalyst gave a 49% conversion to acetophenone in 6 h. A high yield, 77%, was obtained over this catalyst with acetyl bromide over a period of 1 h. $FeCl_3$ and $AlCl_3$ afforded 20% and 16% yield respectively when reacted with the bromide for 1 h.

On the exposure of the catalysts to a mixture of

** Numbers in parentheses here and elsewhere indicate the calcination temperatures.

TABLE 2. YIELD (%) FOR ACETYLATION OF TOLUENE WITH ACETIC ANHYDRIDE[a)]

Catalyst	Temp of calcn./°C	Reaction temp/°C	Yield/% 1.0 h	3.0 h	5.0 h	Isomer distribution/% *o*-,	*m*-,	*p*-
$FeSO_4$	700	room temp[b)]			4			
	700[c)]	60		17				
	700	80	15	38	44			
	700	100		39		15	3	82
	800	80			33			
	800	100		48	55	14	2	84
$FeCl_3$		80		15		8	2	90
$AlCl_3$		80		11		4	6	90

a) Activated at the reaction temperature by the addition of 1 ml of benzyl chloride; catalyst amount: 1 g.
b) Activated at 60 °C. c) 22% for 22 h.

TABLE 3. YIELD (%) OF ACETOPHENONE FOR ACETYLATION OF BENZENE WITH ACETYL CHLORIDE, ACETYL BROMIDE, AND ACETIC ANHYDRIDE[a)]

Catalyst	Temp of calcn./°C	Acetylating reagent	Reaction temp/°C	Yield/% 1.0 h	1.5 h	2.0 h	6.0 h
$FeSO_4$	700	CH_3COCl	50			27	49
	700	CH_3COBr	room temp		21		
	700	CH_3COBr	60	77			
	700[b)]	$(CH_3CO)_2O$	80				0.3
	800	CH_3COCl	50			13	26
	800	CH_3COBr	60	45			

a) Activated at 60 °C by the addition of 1 ml of benzyl chloride; catalyst amount: 1 g. b) Activated at 80 °C.

benzyl chloride and toluene or benzene, it appears likely that iron chloride was newly formed on the catalyst surface because of the HCl evolved by the benzylation of toluene or benzene with benzyl chloride, the iron chloride thus acting as a catalyst. After the activation of the catalysts, gas-chromatographic (GC) analysis showed the benzylation of toluene and benzene to be 100% complete. The $FeSO_4$(700 °C) catalyst was separated from the mixture of benzyl chloride and toluene after the activation, washed with toluene, and dried, and finally its IR spectrum was taken, together with that of commercial $FeCl_3$ for reference.*** The spectra showed an absorption band at 1600 cm^{-1} which is assigned to water molecule coordinated to $FeCl_3$. However, this separated catalyst produced only 10% of methylacetophenones in a reaction of 2 h with acetyl chloride. The differently prepared HCl-treated catalyst, which had been prepared by exposing $FeSO_4$(700 °C) to a stream of the mixed gas of N_2 (20 ml/min) and HCl (26 ml/min) for 20 min and then to N_2 gas for 30 min,[15] gave a 28% conversion at the highest in the acetylation of toluene with acetyl chloride. It may, therefore, be considered that the catalyst surface was activated by complicated interactions with benzyl chloride and HCl evolved by the benzylation. As for alkyl halides other than benzyl chloride, *t*-butyl and isopropyl chlorides were examined, but these halides did not activate the catalysts. GC analysis revealed that the catalysts are not active at all for the *t*-butylation and isopropylation of toluene or benzene.

The Friedel-Crafts acylation of aromatic hydrocarbons such as toluene and benzene is characterized by a generally high selectivity of the reactions reflected in high substrate-rate ratios (usually $k_{toluene}/k_{benzene} > 100$) and related predominant *para*-substitution. The competitive acetylation of toluene and benzene was studied over the present catalysts. The obtained values of k_T/k_B, the relative rate between toluene and benzene, were 99.2 with $FeSO_4$(700 °C) and CH_3COCl, 98.6 with $FeSO_4$(800 °C) and CH_3COCl, 33.6 with $FeSO_4$(800 °C) and CH_3COBr, and 65.2 with $FeSO_4$-(800 °C) and $(CH_3CO)_2O$.[16] Several workers have determined the k_T/k_B value to be 121—141 over Lewis catalysts with a high para positional selectivity (95.5—98.3% *para* isomer).[6,17,18] These high values reflect the week electrophilic nature of the acetyl cation. The present values are relatively small in comparison with those literature values, especially that in the $FeSO_4$-(800 °C) and the CH_3COBr system, in spite of the high para selectivity. This suggests that the present acetylation was not just catalyzed by iron chlorides on the catalyst surface.

*** The infrared spectra were obtained using Nujol and KBr tablets.

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