METALLIC BROMIDES AS CATALYSTS FOR THE FRIEDEL-CRAFTS KETONE SYNTHESIS

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Previous studies in these laboratories (Dermer, Wilson, Johnson, and Dermer 1941; Dermer and Billmeier 1942) have involved quantitative comparisons of the abilities of metallic chlorides to catalyze formation of p-methylacetophenone from acetyl chloride and excess toluene. The same reaction and analytical methods have now been used to obtain corresponding data for a number of metallic bromides .Thus the experimental procedure consisted of preparing catalysts, effecting the reaction with measured amounts of reagents, steam-distilling the ketone and excess toluene, and determining the amount of ketone present by means of hydroxylamine hydrochloride and standard alcoholic alkali.

Excepting aluminum bromide, the metallic bromides have scarcely been tried as catalysts in the ketone synthesis. Menshutkin (1914) found antimony tribromide better than antimony trichloride for increasing the rate of reaction of benzene and its derivatives with benzoyl chloride. Pajeau (1937) reported beryllium bromide inactive as a catalyst for the ketone synthesis.

EXPERIMENTAL

Anhydrous aluminum bromide was prepared from heated aluminum and bromine as directed by Winter and Cramer (1940); the center fraction boiled at 267-269°, whereas the literature, reviewed by Winter and Cramer, gives several values in this vicinity as the boiling point. Antimony tribromide was similarly made; the observed boiling point was 280-281°, the literature values being about 280° (Mellor 1929). Stannic bromide similarly prepared had the boiling point 202-203°, comparable to the accepted values of 201-205° (Mellor 1927b).

Ferric bromide was prepared by passing bromine vapor over heated iron powder in a silica combustion tube, Pyrex glass being too low-melting. Great difficulty was experienced in obtaining this product free from ferrous bromide, which may have remained as a contaminant. Essentially the same procedure as for ferric bromide was used to make tellurium tetrabromide, molybdenum tetrabromide, and tungsten pentabromide. Here again determinations of metal/bromine ratios would have been desirable checks of purity, but time did not permit their use.

Anhydrous titanium tetrabromide was made from the tetrachloride by extended treatment with excess dry hydrogen bromide at 50-60° (Bond and Crone 1934); b. p. 230-231°, literature b. p. 229-230° (Mellor 1927a).

Mercuric bromide and anhydrous aluminum chloride were obtained as C. P. chemicals and used without purification. Cadmium bromide hydrate was fused merely long enough to expel the water. Zinc bromide was dehydrated and purified by distilling it from one one leg of a Faraday tube to the other under reduced pressure.

Precautions were taken to preserve and use these catalysts with a minimum excess of moisture.

All other reagents (acetyl bromide, acetyl chloride, toluene, hydroxylamine hydrochloride, etc.) were C,. P. quality, used without further purification.

In the earlier experiments (by S.) six ml of toluene and 0.014 mole of catalyst were placed in a dry 200-ml flask bearing half a 19/38 ground-glass joint, treated with exactly 1 ml (1.06 g) of acetyl chloride, and heated for one hour under reflux at about 95° by means of a boiling water bath. Later the Perrier (1900) procedure was used at room temperatures in stoppered agitated 50 ml flasks (experiments by M.). One ml of acetyl bromide previously chilled to 10-15° was pipetted into the dry flask, the catalyst (in varying amounts) added with external cooling, and then 10 ml of cooled toluene introduced. The flask was immediately stoppered and mechanically shaken for two or four hours.

At the end of a synthesis run of either type, water was introduced, and then enough alkali to render the mixture basic to phenolphthalein. Distillation of the flask contents in a current of steam gave a mixture of *P*-methylacetophenone, toluene, and water, of which about 75 ml was collected. The distillate was treated with C. P. sodium nitrate or sodium chloride for its salting-out effect, the toluene layer separated, and the aqueous layer extracted with two 5 ml portions of benzene to remove all ketone. The extracts were treated with 20 ml of about 0.5 N hydroxylamine hydrochloride in methanol, previously neutralized to bromphenol blue or preferably butter-yellow. Titration of the liberated hydrochloric acid with 0.1 or 0.5 N standard sodium methoxide in methanol was done sometimes after two hours of heating under pressure at 120°, but more often after 24 hours at room temperatures. In the latter method the endpoint usually faded and titration had to be renewed at about 24-hour intervals until the color was permanent. Blanks were found indispensable.

TABLE I

Yields of p-Methylacetophenone Produced by Metallic Bromides Tested

CATALYST	CONDITIONS OF RUN [a]	MOLES CATALYST/ MOLE CH_3COX	TIME (HRS)	YIELDS OF KETONE %
$AlCl_3$	M	1.6[b]	0.25	77.3, 77.3
	M	1.6[b]	2	75.9, 77.7
	M	1.6[b]	3	77.3, 76.5
$AlBr_3$	S	1.1	1	70.7, 70.4
	M	1.0	2	82.4
	M	1.5	2	83.9
	M	2.0	2	81.6
	M	3.0	4	79.3
$FeBr_3$	S	1.1	1	5.6, 5.3
	M	1.0	2	37.3
	M	1.5	2	41.3
	M	2.0	2	47.5, 48.5
	M	3.0	4	59.0, 63.2
$SbBr_3$	S	1.1	1	6.7, 6.3
	M	1.0	2	0.6
	M	1.5	2	2.8
	M	2.0	2	9.2, 9.8
	M	3.0	4	26.8, 26.5, 27.0
	M	4.0	4	1.5, 2.1, 1.9
$ZnBr_2$	S	1.1	1	4.1, 3.9
	M	1.0	2	2.6
	M	1.5	2	3.9
	M	2.0	2	4.1, 7.1, 7.0
	M	3.0	4	15.2, 17.6, 17.7
	M	4.0	4	14.2, 17.8, 17.5
$TlBr_3$	S	1.1	1	10.4, 11.3
	M	1.0	2	3.6, 3.3

TABLE I, (Cont'd)

CATALYST	CONDITIONS OF RUN [a]	MOLES CATALYST/ MOLE CH_3COX	TIME (HRS)	YIELDS OF KETONE %
$TiBr_4$	M	1.5	2	4.6, 4.8
	M	2.0	2	11.8, 12.1
	M	3.0	4	7.3, 7.7, 8.1
$TeBr_4$	S	1.1	1	1.6, 1.4
	M	1.0	2	1.5, 1.0
	M	1.5	2	1.1, 0.8
	M	2.0	2	0.9, 1.0
	M	3.0	4	2.6
	M	4.0	4	3.8
$MoBr_4$	M	1.0	2	1.8
	M	1.5	2	3.4
	M	2.0	2	2.8
	M	3.0	4	0.0, 0.0
WBr_5	M	1.0	2	0.8
	M	1.5	2	0.8
	M	2.0	2	1.5
	M	3.0	4	0.8
$CdBr_2$	M	1.0	2	0.9
	M	1.5	2	1.0
	M	2.0	2	0.8
	M	3.0	4	0.6
	M	4.0	4	0.7
$HgBr_2$	M	1.0	2	0.4
	M	1.5	2	0.3
	M	2.0	2	0.2, 0.1
	M	3.0	4	0.7, 0.8
	M	4.0	4	0.3, 0.3
$SnBr_4$	S	1.1	1	0.9, 0.9
	M	1.0	2	0.4, 0.4
	M	1.5	2	0.3, 0.5
	M	2.0	2	0.3, 0.2
	M	3.0	4	0.3, 0.2

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[a] Synthesis runs of the type done by S. are marked S; others are marked M.

[b] Acetyl chloride was used by M. for the runs with $AlCl_3$ only; in all other M runs CH_3COBr was employed.

It is first of interest to compare yields with those in the literature, insofar as that is possible. The 77-84% maximum yields of *P*-methylacetophenone obtained with aluminum chloride and aluminum bromide are as good as reported anywhere for this particular compound. An elaborate study of optimum conditions for the synthesis of acetophenone (Salmi and Vaihkonen 1946) reported yields as high as 90.5%, but for *P*-methylacetophenone the best records have been 70% (Sorge 1902), 71% (Dermer, Wilson, Johnson, and Dermer 1941), 74% (Dermer and Billmeier 1942), and 80% (Verley 1897). In contrast to these yields, 96-98% of the theoretical amount of benzophenone can be made by the Friedel-Crafts reaction. We conclude that such semiquantitative yields cannot be expected for alkyl aryl ketones because of their tendency to undergo aldol condensations in the presence of acids.

A defense of the technique, used in this work, of performing the Friedel-Crafts reaction in sealed containers is desirable, since Verley (1897), Groggins (1947:766), and doubtless others have thought the removal of hydrogen halide desirable or even essential to maximum yield. Groggins has in fact supplied experimental data to show a 3-4% improvement in yield of 4′-chloro-2-benzoylbenzoic acid when hydrogen chloride was swept out as produced. This procedure is based on conceiving the Friedel-Crafts reaction as reversible, so that removal of hydrogen chloride would "shift the equilibrium" in favor of ketone. Removal of the acid would also reduce its aldol-condensation effect on the ketone, but since the metallic halides are also condensing agents, this factor is probably unimportant.

Against removal of hydrogen chloride three arguments may be advanced. First, it complicates the experimental procedure, especially when a volatile acid chloride is being used. Second, benzophenone is not cleaved by hydrogen chloride in presence of aluminum chloride to yield benzoyl chloride and benzene (Olivier 1918). In other words, this Friedel-Crafts reaction is not reversible. Reversibility is well known for the hydrocarbon synthesis, but probably is not appreciable in the ordinary ketone synthesis. Third, hydogen chloride is known to activate aluminum chloride acting as a catalyst and thus to favor the reaction; indeed, Thomas (1941: 72-76) suggests that the real catalyst is not aluminum chloride, but hydrogen tetrachloroaluminate.

The lower yields and other divergencies of results of the S method from those obtained by M are attributed to the use of the Perrier procedure, lower temperatures, unmixed catalysts, and more nearly optimum amount of catalysts by M. "Unmixed catalysts" designates those in which no exchange of halogen can occur, as when acetyl bromide is used with aluminum bromide. Using acetyl chloride with metallic bromide catalysts makes it even more uncertain than usual just what the true catalyst is; it probably has the same effect as employing a mixed chloride-bromide catalyst (Norris and Wood 1940).

Like Norris and Wood (1940) and Oliver (1918), we have found aluminum bromide to be a slightly better catalyst in the ketone synthesis than aluminum chloride. Antimony tribromide showed an abrupt and surprising decrease in yield with increased amount of catalyst, but this behavior agrees with the observations of Menshutkin (1914), who found increasing amount of antimony tribromide to make resinification and decomposition very evident. Similar but smaller decreases were shown by titanium tetrabromide and molybdenum tetrabromide; earlier results obtained at room temperatures for the chlorides of the same elements (Dermer and Billmeier 1942) show a similar tendency of these catalysts to destroy product.

Qualitatively, the order of activity for the bromide catalysts is $AlBr_3$ > $FeBr_3$ > $SbBr_3$ > $ZnBr_2$ > $TiBr_4$ > $TeBr_4$ > $MoBr_4$ > WBr_5 > $CdBr_2$ > $HgBr_2$> $SnBr_4$. It cannot be correlated with the solubilities of the bromides in the organic mixture. For the chlorides Dermer and Billmeier found the order $AlCl_3$ > $FeCl_3$ > $CbCl_5$ > $SbCl_5$ > $TiCl_4$ > $MoCl_5$ > $TeCl_4$ > $SnCl_4$ > $TeCl_2$ > $BeCl_2$> $ZnCl_2$ > $BiCl_3$. It is evident that the positions of the halides of zinc, tin, and antimony are different in the two series. Antimony trichloride has been reported as a noncatalyst (Dermer, Wilson, Johnson, and Dermer 1941) but it was tested only in boiling toluene, where any small yield it may have produced would have been destroyed again.

Altogether it must be admitted that except for aluminum bromide and zinc bromide, the metallic chlorides are both cheaper and better catalysts for this Friedel-Crafts ketone synthesis. It would be interesting to study Lewis acids in general for such catalytic power and find out how well acidity correlates with catalytic ability. Luder and Zuffanti (1946: 108) suggest this, but clearly it would be advisable to choose a reaction not complicated, as the acetophenone synthesis is, by consecutive reactions.

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