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The Catalytic Friedel-Crafts Acylation Reaction Using a Catalyst Generated from $GaCl_3$ and a Silver Salt

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In the presence of a catalyst generated from $GaCl_3$ and a silver salt ($AgClO_4$ or $AgSbF_6$), the Friedel-Crafts acylation reaction of aromatic compounds such as anisole and veratrole with acid anhydrides smoothly proceeds to afford the corresponding aromatic ketones in high yields.

The Friedel-Crafts alkylation and acylation reactions are fundamental and important processes in organic synthesis including industrial chemistry.[1] While the alkylation reaction proceeds in the presence of a catalytic amount of Lewis acid such as $AlCl_3$ or BF_3, the acylation reaction requires a stoichiometric amount of Lewis acid due to the consumption by the coordination to the produced aromatic ketones, and rather drastic reaction conditions, tedious work up procedures, etc., remain as severe problems to overcome. Though some catalysts (which complete the reaction by the catalytic use) for the Friedel-Crafts acylation reaction such as activated iron sulfates,[2] iron oxides,[3] heteropoly acid,[4] trifluoromethanesulfonic acid,[5] or diphenylboryl hexachloroantimonate,[6] have been reported, development of more efficient and economical catalysts is still strongly required.

In the previous papers, we have shown that some combinations of Lewis acids, for example, tin(IV) chloride and zinc chloride,[7] antimony(V) chloride and tin(II) triflate,[8] tin(IV) chloride and tin(II) triflate;[9] etc.,[10] are effective catalysts for several carbon-carbon bond forming reactions. These catalysts are characterized as active cationic species which promote these reactions by using catalytic amounts, whereas the reactions are scarcely promoted when a Lewis acid is used alone. Quite recently, it was reported from our laboratory that highly α-selective glycosylation reaction is performed starting from O-benzyl protected 1-O-acetyl glucose and trimethylsilylalcoxides using a catalyst generated from $SnCl_4$ and silver perchlorate ($AgClO_4$).[11] In the course of our investigations based on this concept, we intended to develop a novel catalyst for the Friedel-Crafts acylation reaction by choosing a suitable combination of Lewis acids. In this communication, we would like to report a preliminary result on the catalytic Friedel-Crafts acylation reaction using $GaCl_3$ and a silver salt ($AgClO_4$ or $AgSbF_6$).

In the first place, the reaction of anisole with valeroyl anhydride was taking as a model, and several combinations of Lewis acids and $AgClO_4$ were examined (Table 1). It should be noted that the catalytic process can be attained in most cases by the suitable combination of the Lewis acid and $AgClO_4$, and the yields are improved when double the molar quantity of $AgClO_4$ is used. Among several Lewis acids, the best yield was obtained when $AgClO_4$ was combined with $GaCl_3$ (Table 1, entry 3). Next, effect of silver salts was examined and it was shown there that the reaction smoothly proceeded to produce the desired aromatic ketone in moderate to good yields when $GaCl_3$ was combined with $AgClO_4$, $AgSbF_6$, or AgOTf, while no desired product was obtained by the combination with $AgBF_4$ or $AgPF_6$ (Table 2).

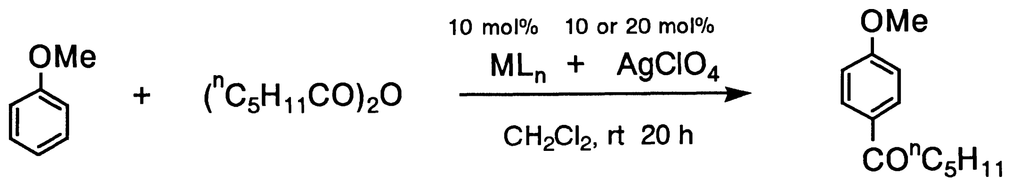

Table 1. Effect of Lewis Acids

Entry	ML_n	$AgClO_4$ 10 mol% Yield/%	$AgClO_4$ 20 mol% Yield/%
1	BCl_3	74	86
2	$AlCl_3$	62	89
3	$GaCl_3$	85	91
4	$InCl_3$	61	68
5	$SiCl_4$	74	84
6	$GeCl_4$	74	90
7	$SnCl_4$	73	86
8	$SbCl_5$	71	74
9	$TiCl_4$	32	56
10	$ZrCl_4$	45	70
11	$HfCl_4$	51	65

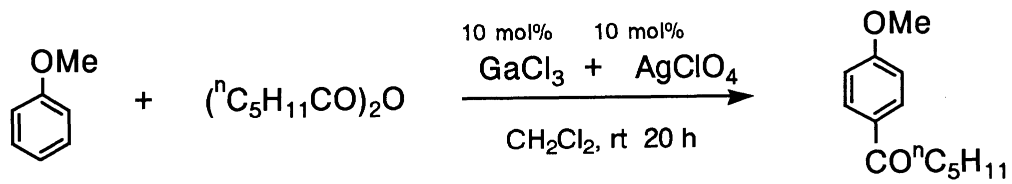

Table 2. Effect of Silver Salts

Entry	Silver Salt	Yield/%
1	$AgClO_4$	85
2	$AgSbF_6$	74
3	AgOTf	45
4	$AgBF_4$	0
5	$AgPF_6$	0

Several examples of this catalytic Friedel-Crafts acylation reaction are shown in Table 3. Anisole or veratrole smoothly reacts with acid anhydrides or benzoyl chloride to give the corresponding aromatic ketones in high yields. In these reactions, formation of other isomers (*o*- or *m*-) was not observed by ^1H and ^{13}C NMR.

Table 3. The Catalytic Friedel-Crafts Acylation Reaction

R^1	R^2	R^3COX	Ag Salt	Conditions	Yield/%
OMe	H	$(^nC_5H_{11}CO)_2O$	$AgClO_4$	CH_2Cl_2, rt 20 h	91
OMe	H	$(^nC_5H_{11}CO)_2O$	$AgClO_4$	CH_2Cl_2, rt 20 h	85
OMe	H	Ac_2O	$AgClO_4$	CH_2Cl_2, rt 40 h	80
OMe	H	$(PhCO)_2O$	$AgSbF_6$	CH_2ClCH_2Cl, reflux 7 h	quant.
OMe	H	$(PhCO)_2O$	$AgSbF_6$	CH_2ClCH_2Cl, reflux 7 h	94
OMe	H	PhCOCl	$AgSbF_6$	CH_2ClCH_2Cl, reflux 7 h	96
OMe	H	$(^nC_4H_9CO)_2O$	$AgSbF_6$	CH_2ClCH_2Cl, reflux 7 h	89
OMe	OMe	$(^nC_5H_{11}CO)_2O$	$AgClO_4$	CH_2Cl_2, rt 21 h	quant.
OMe	OMe	$(^nC_4H_9CO)_2O$	$AgClO_4$	CH_2Cl_2, rt 6 h	93
OMe	Me	$(^nC_4H_9CO)_2O$	$AgClO_4$	CH_2Cl_2, rt 14 h	85

A typical experimental procedure is described for the reaction of anisole with vareloyl anhydride; $GaCl_3$ (0.04 mmol) and $AgClO_4$ (0.08 mmol) was stirred for 30 min in dichloromethane (0.5 ml) at rt, and then a mixture of anisole (0.4 mmol) and vareloyl anhydride (0.8 mmol) in dichloromethane (1.0 ml) was added. The reaction mixture was stirred for 20 h at rt, and then quenched with aq. sat. $NaHCO_3$. After usual work up, the crude product was purified by preparative TLC on silica gel to afford 1-(4-methoxyphenyl)-1-pentenone (91% yield).

At this stage, it is assumed that the active catalyst, $GaCl_2X$ or $GaClX_2$ (X=ClO_4 or SbF_6), would be generated by the combination of $GaCl_3$ and $AgClO_4$ or $AgSbF_6$,[12] and as shown in the catalytic cycle (Scheme 1), this novel catalyst reacts with an anhydride to afford the key intermediate 1 stabilized by ClO_4^- or SbF_6^-. Then 1 immediately reacts with the aromatic compound to give the desired ketone along with HX, which in turn reacts with $R_3CO_2GaCl_2$ to regenerate the catalyst.

Further investigations concerning the scope of the present reaction as well as the characterization of this novel catalyst are now in progress.

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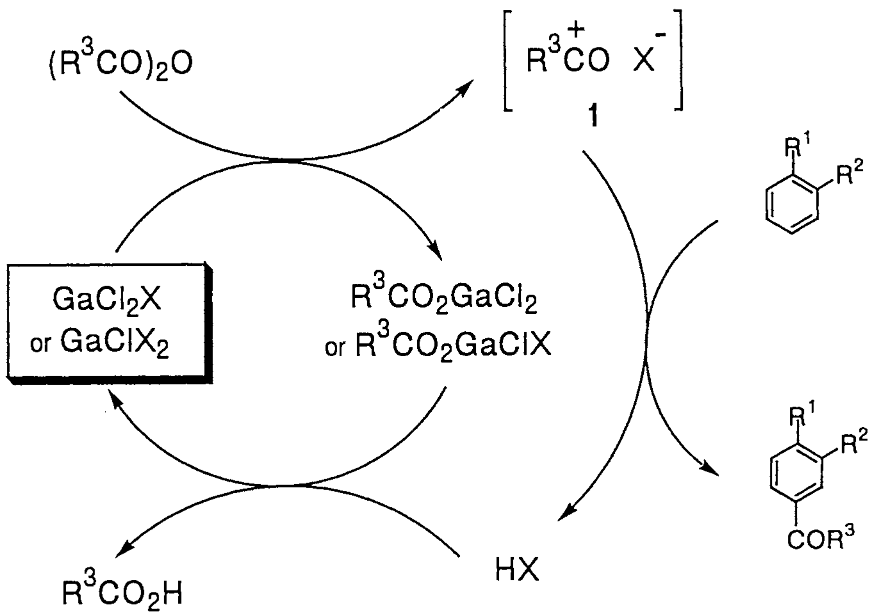

Scheme 1. The Catalytic Cycle

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