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An Efficient Catalytic Friedel-Crafts Acylation Reaction of Equimolar Amounts of Aromatic Compounds and Free Carboxylic Acids or Their Trimethylsilylesters via Mixed Anhydrides

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In the presence of an active catalyst generated from $SiCl_4$ and $AgClO_4$, the Friedel-Crafts acylation reaction between equimolar amounts of aromatic compounds and mixed anhydrides, formed in situ from free carboxylic acids (or their trimethylsilylesters) and p-trifluoromethylbenzoic anhydride, smoothly proceeds at room temperature to afford the corresponding aromatic ketones in high yields.

While the Friedel-Crafts acylation reaction is a very useful tool for the synthesis of aromatic ketones even in industrial chemistry,1) the acylation reaction generally requires a stoichiometric amount of Lewis acid due to the consumption by the coordination to the produced aromatic ketones. Concerning the catalytic Friedel-Crafts acylation reaction of aromatic compounds with carboxylic acid anhydrides or acid chlorides, activated iron sulfates,2) iron oxides,3) heteropoly acid,4) trifluoromethanesulfonic acid,5) diphenylboryl hexachloroantimonate,6) or iron chloride,7) have been used as active promoters. Although aromatic ketones are also formed from free carboxylic acids by using methanesulfonic acid,8) zeolites,9) or trimethylsilyl polyphosphate10) as catalysts, rather drastic conditions are required. Therefore, further development of more efficient catalysts which promote the reaction under very mild conditions is still desired.

In the previous papers, it was shown that some active cationic species generated from Lewis acids and $AgClO_4$ were effective for the catalytic and highly stereoselective glycosylation of 1-O-acetyl-D-glucose with alkyl trimethylsilyl ethers.11) The above result led us to investigate the catalytic Friedel-Crafts acylation reaction of carboxylic acid anhydrides (2 mol) and aromatic compounds (1 mol) such as anisole (methoxybenzene) and veratrole (1,2-dimethoxybenzene) by using $GaCl_3$-$AgClO_4$ (or $AgSbF_6$)12) or $SbCl_5$-$LiClO_4$13) catalyst system, and it was found that the corresponding aromatic ketones were obtained in high yields. In addition, a new esterification method has been recently reported14) from our laboratory that the reaction of alkyl silyl ethers with mixed anhydrides, formed in situ from carboxylic acid trimethylsilylesters and p-trifluoromethylbenzoic anhydride, afforded the corresponding esters in high yields using an active Lewis acid catalyst. These results prompted us to study on the development of a convenient method for the Friedel-Crafts acylation reaction starting from equimolar amounts of carboxylic acids (or their trimethylsilylesters), aromatic compounds and p-trifluoromethylbenzoic anhydride by the promotion of $SiCl_4$-$AgClO_4$ catalyst system.

In the first place, several combinations of Lewis acids and $AgClO_4$ were examined by taking the reaction of anisole with acetic acid trimethylsilylester as a model (Table 1). Among several Lewis acids, it was shown that an active acidic species generated in situ from $SiCl_4$ and $AgClO_4$ gave good results. The best yield was obtained when the ratio of $SiCl_4 : AgClO_4$ was 1 : 3 (Table 1, entry 13).[15]

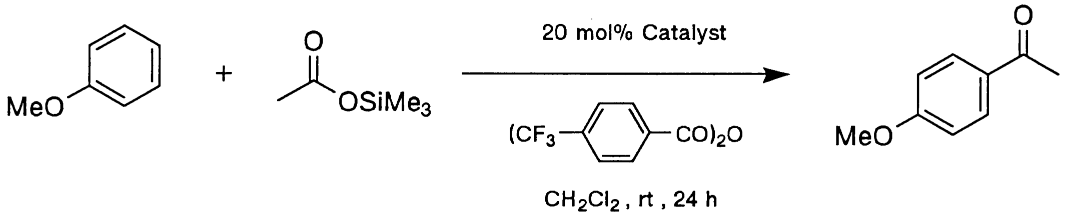


Table 1. Effect of Lewis Acids

Entry	Catalyst	Yield / %[a]	Entry	Catalyst	Yield / %[a]
1	$TiCl_4 + 2AgClO_4$	28	8	$HfCl_4 + 2AgClO_4$	53
2	$SbCl_5 + 2AgClO_4$	48	9	$Me_2SiCl_2 + 2AgClO_4$	44
3	$GaCl_3 + 2AgClO_4$	40	10	$MeSiCl_3 + 2AgClO_4$	60
4	$AlCl_3 + 2AgClO_4$	59	11	$MeSiCl_3 + 3AgClO_4$	61
5	$GeCl_4 + 2AgClO_4$	58	12	$SiCl_4 + 2AgClO_4$	60
6	$ZrCl_4 + 2AgClO_4$	56	13	$SiCl_4 + 3AgClO_4$	68
7	$BiCl_3 + 2AgClO_4$	54	14	$SiCl_4 + 4AgClO_4$	67

a) 4-Methoxy-4'-trifluoromethylbenzophenone was not obtained.

Several examples of the present catalytic Friedel-Crafts acylation reaction are shown in Table 2. Anisole, veratrole and 1-methoxy-2-methylbenzene smoothly reacted with equimolar amounts of carboxylic acid trimethylsilylesters at room temperature to give the corresponding Friedel-Crafts products in high yields. In these reactions, formation of other isomers (*o*- or *m*-) was not observed by ^1H and ^{13}C NMR. Furthermore, it was found that several free carboxylic acids were successfully employed in the present reaction (Table 2). It was also found that the intramolecular Friedel-Crafts acylation reaction of free 4-phenylbutyric acid proceeded at room temperature to give 3,4-dihydro-1(2*H*)-naphthalenone in quantitative yield (Table 2, entry 15).

A typical experimental procedure is described for the reaction of 1-methoxy-2-methylbenzene with hexanoic acid trimethylsilylester; $SiCl_4$ (0.08 mmol) and $AgClO_4$ (0.24 mmol) were stirred for 1 h in dichloromethane (2.0 ml) at rt, and then a mixture of hexanoic acid trimethylsilylester (0.4 mmol) and p-trifluoromethylbenzoic anhydride (0.4 mmol) in dichloromethane (3.0 ml) and a solution of 1-methoxy-2-methylbenzene (0.4 mmol) in dichloromethane (1.0 ml) were successively added. The reaction mixture was stirred for 23 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-(3-methoxy-4-methylphenyl)-1-hexanone in quantitative yield.

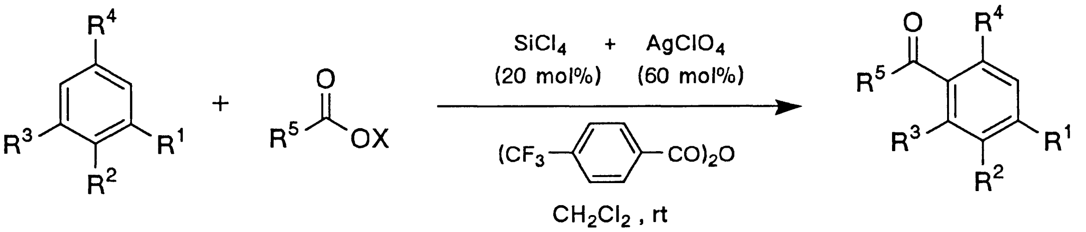


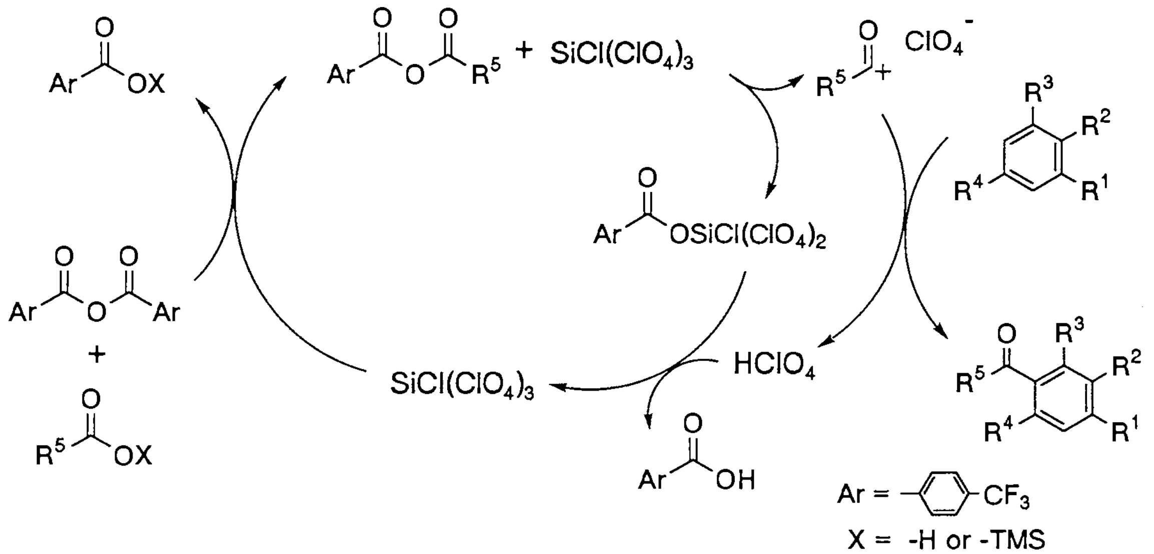
Table 2. The Friedel-Crafts Acylation Reaction via Mixed Anhydrides

Entry	R^1	R^2	R^3	R^4	R^5	X	Time / h	Yield / %
1	MeO	H	H	H	Me	TMS	24	68
2	MeO	H	H	H	n-C_4H_9	TMS	22	68
3	MeO	Me	H	H	n-C_4H_9	TMS	19	quant.
4	MeO	MeO	H	H	n-C_4H_9	TMS	20	quant.
5	MeO	H	H	H	n-C_5H_{11}	TMS	76	84
6	MeO	H	H	H	n-C_5H_{11}	H	76	84
7	MeO	Me	H	H	n-C_5H_{11}	TMS	23	quant.
8	MeO	Me	H	H	n-C_5H_{11}	H	24	quant.
9	MeO	MeO	H	H	n-C_5H_{11}	TMS	19	89
10	MeO	MeO	H	H	n-C_5H_{11}	H	19	86
11	MeO	H	H	H	c-Hex	TMS	25	quant.
12	MeO	Me	H	H	c-Hex	TMS	25	quant.
13	Me	H	Me	Me	Me	TMS	24	95
14[a]	—	—	—	—	$Ph(CH_2)_3$	TMS	12	86
15[a]	—	—	—	—	$Ph(CH_2)_3$	H	24	quant.

a) Intramolecular Friedel-Crafts acylation reaction gave 3,4-dihydro-1(2*H*)-naphtalenone.

At this stage, it is assumed that a carboxylic acid or its trimethylsilylester, RCOOX (X=H or $SiMe_3$), reacts with p-trifluoromethylbenzoic anhydride to afford the mixed anhydride as shown in the catalytic cycle (Scheme 1). Then the initially formed mixed anhydride reacts with an aromatic compound to give the corresponding ketone. The above two sequential reactions are effectively promoted by the active catalyst, $SiCl(ClO_4)_3$, generated from $SiCl_4$ and $AgClO_4$.

Further investigations concerning the scope of the present reaction are now in progress.



Scheme 1. The catalytic cycle.

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