

Antimony(V) Chloride-Benzyltriethylammonium Chloride Complex as an Efficient Catalyst for Friedel–Crafts Acylation Reactions

An-ping Huang,^a Xue-yuan Liu,^a Lian-hua Li,^a Xiao-li Wu,^a Wei-min Liu,^b Yong-min Liang^{a,b,*}

^a National Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, P. R. China

^b Laboratory of Solid Lubrication, Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, Lanzhou 730000, P. R. China

Phone: (+86)-931-8912593, fax: (+86)-931-8912582, e-mail: liangym1@hotmail.com

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Abstract: A novel catalytic system, the complex of antimony(V) chloride (SbCl_5) and benzyltriethylammonium chloride (TEBA), $\text{C}_6\text{H}_5\text{CH}_2\text{NEt}_3(\text{SbCl}_5)_2\text{Cl}$ complex, is described for Friedel–Crafts acylation reactions of aromatics with acyl and sulfonyl chlorides. The catalyst has a number of useful characteristics, such as ready access, minimal toxicity, reusability, insensitivity to atmosphere and moisture, rapid acylation with high yield, and ease of operation.

Keywords: antimony(V) chloride; benzyltriethylammonium chloride; catalysis; Friedel–Crafts acylation reactions; Lewis acids

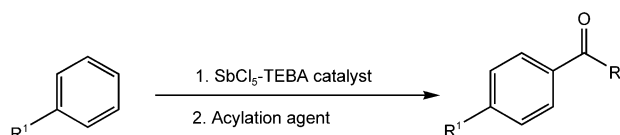
The Friedel–Crafts acylation reaction is a useful procedure for forming carbon–carbon bonds on aryl rings, and is a common procedure in organic synthesis as well as in the chemical industry.^[1] The basic operation of the Friedel–Crafts acylation and related reactions requires the addition of a Lewis acid as catalyst, such as metal chloride^[2] (AlCl_3 , SbCl_5 , BF_3 , FeCl_3 , BiCl_3 , TiCl_4 and SnCl_4), which is often strongly oxyphilic. Additionally, some other systems containing triflic acid^[3] and lithium perchlorate^[4] have been also reported for such reactions.^[5] Various acylation operating conditions using transition metals (In ,^[6] Hf ,^[3a,5c,7] Ag ,^[8] and Ga ^[9]) as catalysts have been reported recently. But these catalysts are generally expensive and require long reaction times to complete the transformation, although the yield of product is satisfactory. Since the Friedel–Crafts acylation has unlimited potential for generating novel aryl derivatives, alternative catalysts for this type of reactions are desirable, which can be chosen for specific goals in terms of reaction time, yield, substrate scope, catalyst turnover, and operational practicability.

In the present work, we report a novel Lewis acid catalytic system, the antimony(V) chloride-benzyltriethyl-

ammonium chloride – SbCl_5 -TEBA complex, which has many advantages, such as ready access, minimal toxicity, reusability, insensitivity to atmosphere and moisture, rapid acylation with high yield, and ease of operation. It catalyzes Friedel–Crafts acylation reactions smoothly as shown in Scheme 1.

The acylation of anisole with acetyl chloride using the complex of SbCl_5 and TEBA as catalyst was investigated as an initial model reaction (Table 1).

It can be seen from Table 1 that three catalysts all have catalytic activity for the acylation of anisole, but the activity of the complex $\text{BnNEt}_3(\text{SbCl}_5)_2\text{Cl}$ is the best of all. Nitromethane was found to be a suitable solvent for this catalytic system. These acetylation reactions were also sensitive to the type of catalysts and anionic ligands, that have been proved to be critical for high yields in



Scheme 1.

Table 1. Reaction conditions for the acetylation of anisole.^[a]

Entry	Catalyst [5% mol]	T [°C] ^[b]	Time [min]	Yield [%] ^[c]
1	$\text{BnNEt}_3\text{AlCl}_4$	rt	120	< 10
2	$\text{BnNEt}_3\text{SbCl}_6$	rt	120	17
3	$\text{BnNEt}_3\text{SbCl}_6$	120	20	25
4	$\text{BnNEt}_3(\text{SbCl}_5)_2\text{Cl}$	rt	120	38
5	$\text{BnNEt}_3(\text{SbCl}_5)_2\text{Cl}$	40	60	57
6	$\text{BnNEt}_3(\text{SbCl}_5)_2\text{Cl}$	80	30	64
7	$\text{BnNEt}_3(\text{SbCl}_5)_2\text{Cl}$	120	20	96

^[a] All reactions were carried out in nitromethane with the substrates ratio: anisole/ MeCOCl /catalyst = 2/1/0.05.

^[b] Oil bath temperature.

^[c] Isolated yield.

the catalytic Friedel–Crafts process.^[10] A series of parallel reactions showed that $\text{AlCl}_3/\text{TEBA}$ and $\text{SbCl}_5/\text{TEBA}$ (1:1) were less effective (entries 1–3), while $\text{SbCl}_5/\text{TEBA}$ (2:1) was effective. Studies were also carried out by using 5 mol % of the 2:1 complex with different reaction periods and temperatures (entries 4–7), and 4-methoxyacetophenone was obtained in 96% yield when the reaction was carried out at 120 °C for 20 minutes (entry 7). One of the most important features of this catalyst is that the complex can be recycled. After reuse for more than seven times, the catalyst is still active (Figure 3). An additional feature of the $\text{BnNEt}_3(\text{SbCl}_5)_2\text{Cl}$ catalyst is that the complex is inert to water and oxygen and easy to handle in the atmosphere without changing the catalytic activity of antimony chloride.

The structure of $\text{BnNEt}_3\text{SbCl}_6$ was determined by an X-ray single-crystal analysis (Figure 1)^[11]; the catalyst $\text{BnNEt}_3(\text{SbCl}_5)_2\text{Cl}$ is a pale yellow powder. We have not confirmed its accurate structure due to the lack of a suitable single crystal, but it is probably a stable complex as indicated by its elemental analysis, ^1H NMR spectra and its fixed melting point, as shown in Figure 2.

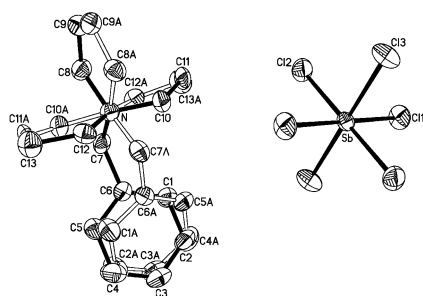


Figure 1. X-ray crystal structure of $\text{BnNEt}_3\text{SbCl}_6$.

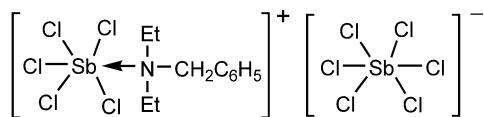


Figure 2. Proposed structure of $\text{BnNEt}_3(\text{SbCl}_5)_2\text{Cl}$.

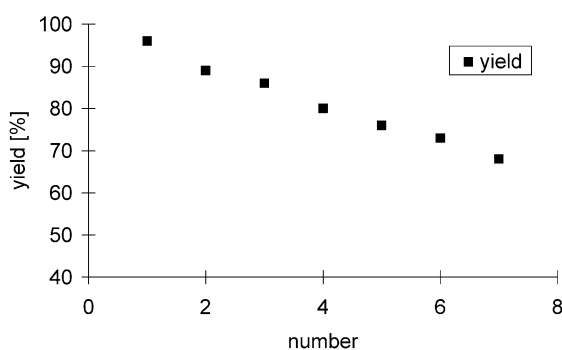


Figure 3. The relationship of catalytic recycle and reaction yield for the acylation of anisole in boiling nitromethane.

The activity of recovered catalyst was also examined. It is found that its catalytic activity decreases gradually: the yield in the acylation of anisole decreased from 96 to 68% after seven runs (Figure 3).

Examples of the Friedel–Crafts acylation reaction with acetyl chloride catalyzed by the complex of $\text{SbCl}_5/\text{TEBA}$ (2:1) are shown in Table 2. This catalyst is not a good choice for the acetylation of benzene and gives merely 37% isolated yield (entry 1), but it is highly effective for acylating anisole and other electron-rich derivatives, such as toluene, xylene, and mesitylene (entries 2–11). The catalyst affords the corresponding aromatic ketones in high yield. Under the optimized reaction conditions, this method could be carried out by using other different acylation agents (Table 3), the reactions were also extended to the use of a sulfonyl chloride (Table 4); in comparison with acetyl chloride these reactions take a longer period of time, but the yields are satisfactory.

In summary, this paper reports that the $\text{BnNEt}_3(\text{SbCl}_5)_2\text{Cl}$ complex is an efficient catalyst for Friedel–Crafts reactions with satisfactory yields. $\text{BnNEt}_3(\text{SbCl}_5)_2\text{Cl}$ can be reused and its activity could be maintained; this indicates the potential usefulness of this class of catalysts for future studies and their applications in the fields of organic synthesis, industrial production, and green chemistry.

Experimental Section

Synthesis of the $\text{BnNEt}_3(\text{SbCl}_5)_2\text{Cl}$ Complex

To a solution of benzyltriethylammonium chloride (2.28 g, 10 mmol) and dry dichloromethane (10 mL) was slowly added antimony(V) chloride (9 g, 30 mmol) at 0 °C in a conical flask under a nitrogen atmosphere. At the end of this exothermic reaction, filtration gave a pure pale yellow powder, which was washed with dry dichloromethane and diethyl ether (three times), and dried under vacuum to give the desired complex; yield: 6 g (72%); mp 206–208 °C; ^1H NMR (300 MHz, $\text{DMSO}-d_6$): δ = 1.3 (t, 9H, J = 6.6 Hz), 3.15 (q, 6H, J = 6.6 Hz), 4.47 (s, 1H), 7.52 (s, 5H); anal. calcd. for $\text{C}_{13}\text{H}_{22}\text{Cl}_{11}\text{NSb}_2$ (825.82): C 18.91, H 2.69, N 1.70; found: C 18.84, H 2.82, N 1.62.

Typical Procedure for the Acylation of Anisole (Table 2, entry 7)

The $\text{SbCl}_5/\text{TEBA}$ (2:1) catalyst (0.15 mmol, 5 mol %) was added to a mixture of anisole (6 mmol) and acetyl chloride (3 mmol) in nitromethane (2.5 mL). The mixture was stirred for 20 minutes at 120 °C (oil bath temperature). After cooling, the mixture was extracted with petroleum ether (60–90 °C, 5 × 10 mL), the complex catalyst remained in the nitromethane, which could be reused in the next reaction directly or could be recovered by removal of nitromethane under reduced pressure. The yield of recovered catalyst is above 98%. The petroleum ether layer was washed with water and dried over MgSO_4 .

Table 2. SbCl₅/TEBA-catalyzed acetylation reactions.^[a]

Entry	ArH	Acylation agent ^[b]	Time [min]	Yield [%] ^[c]
1	PhH	AcCl	120	37
2	PhMe	AcCl	60	82 ^d
3	<i>o</i> -Xylene	AcCl	30	90
4	<i>m</i> -Xylene	AcCl	30	88
5	<i>p</i> -Xylene	AcCl	30	89
6	Mesitylene	AcCl	20	89
7	PhOMe	AcCl	20	96
8	PhOEt	AcCl	20	95
9	Phenyl ether	AcCl	30	67
10	1,3-Dimethoxybenzene	AcCl	20	91
11	1,4-Dimethoxybenzene	AcCl	20	92

^[a] All reactions were carried out in boiling nitromethane until complete conversion of the substrate (as checked by TLC).

^[b] ArH/RCOCl/catalyst = 2/1/0.05 except for entries 2 and 3 (3/1/0.1).

^[c] Isolated yield.

^[d] *ortho/para* = 1/4.

Table 3. SbCl₅/TEBA-catalyzed acylation reactions.^[a]

Entry	ArH	Acylation agent ^[b]	Time [min]	Yield [%] ^[c]
1	PhOEt	PhCOCl	150	83
2	<i>o</i> -Xylene	PhCOCl	150	75
3	<i>p</i> -Xylene	PhCOCl	150	75
4	<i>o</i> -Xylene	ClCH ₂ COCl	150	73
5	<i>p</i> -Xylene	ClCH ₂ COCl	150	75
6	PhMe	<i>o</i> -ClC ₆ H ₄ COCl	150	77
7	<i>p</i> -Xylene	<i>o</i> -ClC ₆ H ₄ COCl	120	81
8	PhOEt	<i>m</i> -O ₂ NC ₆ H ₄ COCl	120	81
9	PhMe	<i>m</i> -O ₂ NC ₆ H ₄ COCl	180	77
10	<i>p</i> -Xylene	<i>m</i> -O ₂ NC ₆ H ₄ COCl	120	75

^[a] All reactions were carried out in boiling nitromethane until complete conversion of the substrate (as checked by TLC).

^[b] ArH/RCOCl/catalyst = 2/1/0.05.

^[c] Isolated yield.

Table 4. SbCl₅/TEBA-catalyzed tosylation reactions.^[a]

Entry	ArH	Acylation agent ^[b]	Time [min]	Yield [%] ^[c]
1	<i>o</i> -Xylene	TsCl	60	81
2	<i>m</i> -Xylene	TsCl	60	86
3	<i>p</i> -Xylene	TsCl	60	75
4	PhOEt	PhSO ₂ Cl	150	80
5	PhMe	PhSO ₂ Cl	120	78
6	<i>p</i> -Xylene	PhSO ₂ Cl	180	76

^[a] All reactions were carried out in boiling nitromethane until complete conversion of the substrate (as checked by TLC).

^[b] ArH/RCOCl/catalyst = 2/1/0.05.

^[c] Isolated yield.

After removal of the solvent under reduced pressure, the crude product was purified by column chromatograph (petroleum ether/ethyl acetate, 8:1) on silica gel to afford 4-methoxyacetophenone; yield: 96%; ¹H NMR (300 MHz, CDCl₃): δ = 2.53 (s, 3H), 3.85 (s, 3H), 6.90 (d, 2H, *J* = 11 Hz), 7.91 (d, 2H, *J* = 11 Hz); EIMS: *m/z* = 150 (M⁺), 135, 107, 77, 43.

Typical Procedure for Catalyst Recycling in the Acylation of Anisole

When the reaction was complete, the reaction mixture was extracted with petroleum ether several times; the catalyst remained in the nitromethane phase and was reused for the next reaction directly. In each run, the procedure above was followed for the reaction. The reused catalyst system gave 68% reaction yield after recycling seven times (Figure 3).

Acknowledgements

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- [11] Crystal data for $\text{BnNEt}_3\text{SbCl}_6$: $\text{C}_{13}\text{H}_{22}\text{Cl}_6\text{NSb}$, mp 192–194 °C; $M_R = 526.77$, monoclinic, space group C2/c , $a = 9.230(1)$, $b = 14.281(2)$, $c = 15.958(2)$ Å; $\alpha = 90^\circ$, $\beta = 97.010(9)^\circ$, $\gamma = 90^\circ$, $V = 2087.7(4)$ Å³. $T = 296(2)$ K, $Z = 4$, $D_{\text{calcd.}} = 1.676$ Mg/M³, $\mu = 2.083$ mm⁻¹, $\lambda = 0.71073$ E, $F(000)$ 1040, Crystal size $0.54 \times 0.40 \times 0.20$ mm³, 2525 independent reflections [$R(\text{int}) = 0.0120$], Reflections collected 2885: Refinement method, full-matrix least-squares on F^2 : Goodness-of-fit on F^2 0.930: Final R indices [$I > 2\sigma(I)$] $R_1 = 0.0348$, $wR_2 = 0.0818$, R indices (all data) $R_1 = 0.0600$, $wR_2 = 0.0875$. Extinction coefficient 0.00021(16), Largest diff. peak and hole 0.468 and -0.477 e. Å⁻³. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-235619. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: int. code +44(1223)336-033; E-mail: deposit@ccdc.cam.ac.uk].