

## Friedel-Crafts Acylation Reactions Using Catalytic $\text{SbCl}_5$ -TEBA Complex as an Efficient Catalyst

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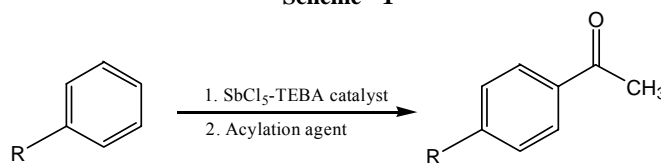
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**Abstract:**  $\text{SbCl}_5$ -TEBA ( $\text{PhCH}_2\text{NEt}_3\text{Cl}$ ) complex catalyzes the Friedel-Crafts acylation reactions efficiently.

**Keywords:** Friedel-Crafts acylation reactions,  $\text{SbCl}_5$ -TEBA ( $\text{PhCH}_2\text{NEt}_3\text{Cl}$ ) complex catalyst.

The Friedel-Crafts acylation reaction is a useful procedure for the formation of carbon-carbon bonds onto aryl systems, and has been accepted as one of the common transformations in organic synthesis as well as in industry<sup>1</sup>. The basic operation for the Friedel-Crafts acylation and related reactions requires the addition of a Lewis acid such as metal chloride<sup>2</sup> ( $\text{AlCl}_3$ ,  $\text{SbCl}_5$ ,  $\text{BF}_3$ ,  $\text{FeCl}_3$ ,  $\text{BiCl}_3$ ,  $\text{TiCl}_4$  and  $\text{SnCl}_4$ ) as catalyst, which is often strongly oxophilic. Additionally, some other systems containing triflic acid<sup>3</sup> and lithium perchlorate<sup>4</sup> have been reported for such reactions<sup>5</sup>. Various acylation conditions by using transition metal catalysts ( $\text{In}$ ,<sup>6</sup>  $\text{Hf}$ ,<sup>3a, 5c, 7</sup>  $\text{Ag}$ <sup>8</sup> and  $\text{Ga}$ <sup>9</sup>) have been reported recently. But those catalysts are generally expensive and require long reaction time to complete transformation, although the yield of product is good. Since the Friedel-Crafts acylation has unlimited potential for generating novel aryl compounds, the alternative catalysts for this type of reactions are desirable, which can be served for specific goals in terms of reaction time, yield, substrate scope, catalyst turnover, and operation practicality. Here we report a readily available, minimally toxic, and reusable  $\text{SbCl}_5$ -TEBA complex for catalyzing Friedel-Crafts and related reactions (**Scheme 1**).

**Scheme 1**



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**Table 1** Reaction conditions for anisole acetylation<sup>a</sup>

| Entry | Catalyst                                                | T   | Time | Yield <sup>b</sup> |
|-------|---------------------------------------------------------|-----|------|--------------------|
| 1     | BnNEt <sub>3</sub> AlCl <sub>4</sub>                    | rt  | 120  | <10                |
| 2     | BnNEt <sub>3</sub> SbCl <sub>6</sub>                    | rt  | 120  | 17                 |
| 3     | BnNEt <sub>3</sub> SbCl <sub>6</sub>                    | 120 | 20   | 25                 |
| 4     | BnNEt <sub>3</sub> (SbCl <sub>5</sub> ) <sub>2</sub> Cl | rt  | 120  | 38                 |
| 5     | BnNEt <sub>3</sub> (SbCl <sub>5</sub> ) <sub>2</sub> Cl | 40  | 60   | 57                 |
| 6     | BnNEt <sub>3</sub> (SbCl <sub>5</sub> ) <sub>2</sub> Cl | 80  | 30   | 64                 |
| 7     | BnNEt <sub>3</sub> (SbCl <sub>5</sub> ) <sub>2</sub> Cl | 120 | 20   | 96                 |

a. All reactions were carried out in nitromethane with the substrates ratio (mole ratio): Anisole/MeCOCl/ Catalyst=2/1/0.05. b. Isolated yield.

The complex of antimony chloride (SbCl<sub>5</sub>) and triethylbenzyl ammonium chloride (TEBA) was initially investigated for the model studies of acetyl chloride with anisole (**Table 1**). The reaction of SbCl<sub>5</sub> (3 mol) with TEBA (1 mol) in dichloromethane at 0°C gave pale yellow crystalline complex with a 2/1 ratio of SbCl<sub>5</sub>/TEBA. This complex was used as a catalyst for the Friedel-Crafts reaction of anisole. In this reaction nitromethane was found to be the best solvent<sup>10</sup>. A series of parallel reactions showed that AlCl<sub>3</sub>/TEBA and SbCl<sub>5</sub>/TEBA (1:1) were less effective (entries 1-3), but SbCl<sub>5</sub>/TEBA (2:1) was effective (entries 4-7). Studies were also carried out by using 5 mol % of the 2:1 complex with different reaction periods and temperature (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). The SbCl<sub>5</sub>/TEBA catalyst is inert to water and oxygen, and can be handled easily in air atmosphere.

**Table 2** SbCl<sub>5</sub>/TEBA-catalyzed arene acylation with different reagents<sup>a</sup>

| Entry | ArH                  | Acylation <sup>b</sup> | Time (min) | Yield <sup>c</sup> (%) |
|-------|----------------------|------------------------|------------|------------------------|
| 1     | PhH                  | AcCl                   | 120        | 37                     |
| 2     | PhMe                 | AcCl                   | 60         | 82 <sup>d</sup>        |
| 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                     |
| 12    | PhOMe                | Ac <sub>2</sub> O      | 60         | 81                     |
| 13    | <i>o</i> -Xylene     | TsCl                   | 60         | 81                     |
| 14    | <i>m</i> -Xylene     | TsCl                   | 60         | 86                     |
| 15    | <i>p</i> -Xylene     | TsCl                   | 60         | 75                     |

All the reactions were carried out in boiling nitromethane. b. ArH/RCOCl/Catalyst (mole ratio)=2/1/0.05 except for entries 2 and 3 (3/1/0.1). c. Isolated yield. d. Ortho/para=1/4.

Examples of the Friedel-Crafts acylation reaction<sup>11, 12</sup> catalyzed by the complex of SbCl<sub>5</sub>/TEBA (2:1) are shown in **Table 2**. This catalyst is not a good choice for benzene acetylation. It only gave 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). This catalyst also can promote the coupling reaction of acid anhydride (entry 12). In comparison with acyl chloride, reactions with anhydride take a longer time. Under the optimized reaction conditions, this method can also be extended to the reaction with sulfonic acid chloride (entries 13-15).

In summary, this paper reported the efficient, commercially available catalyst of antimony chloride-TEBA complex for the Friedel-Crafts reactions with satisfactory yield. The complex of SbCl<sub>5</sub>/TEBA (2:1) can be reused, after three times recycles it was almost without deactivation. This implies the potential usefulness of this class in the field of organic synthesis.

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- To a solution of TEBA (2.28 g, 0.1 mol) and dry dichloromethane (10 mL) was slowly added antimony chloride (9 g, 0.3 mol) at 0°C in a conical flask under nitrogen atmosphere. At the end of this exothermic reaction, filtration gave a pure pale yellow crystal, which was washed

with dry dichloromethane and diethyl ether (three times), and dried in vacuum to give the desired complex (6 g).  $^1\text{H NMR}$  (300 MHz,  $\text{DMSO-}d_6$ ,  $\delta$ ppm): 1.3 (t, 9 H,  $J = 6.6$  Hz), 3.15 (q, 6 H,  $J = 6.6$  Hz), 4.47 (s, 1 H), 7.52 (s, 5 H). mp 206-208°C. Yield = 72%.

12. Typical procedure for the acylation of anisole (entry 7):  $\text{SbCl}_5/\text{TEBA}$  (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, chloroform (5 mL) and water (5 mL) were added to the red-brown crude mixture. The catalyst was filtrated and recovered. The aqueous layer was extracted with chloroform, which was dried over  $\text{MgSO}_4$ . After removal of the solvent under reduce pressure, the crude product was purified by column chromatograph (petroleum ether/ether acetate=8:1) on silica get to afford 4-methoxyactophenone (96%).  $^1\text{H NMR}$  (300 MHz,  $\text{CDCl}_3$ ,  $\delta$ ppm): 2.53 (s, 3 H), 3.85 (s, 3 H), 6.90 (d, 2 H,  $J = 11$  Hz), 7.91 (d, 2 H,  $J = 11$  Hz). EIMS  $m/z$ : 150 ( $\text{M}^+$ ), 135, 107, 77 and 43.

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