# Thallium(III) Chloride Tetrahydrate as a Lewis Acid Catalyst for Aromatic Alkylation and Acylation[1]

Sakae Uemura, Kazuhiro Sohma, and Masaya Okano
*Institute for Chemical Research, Kyoto University, Uji, Kyoto*

(Received July 12, 1971)

From a study of aromatic alkylation and acylation using $TlCl_3 \cdot 4H_2O$ catalyst, it was revealed that this metal chloride was a milder Lewis acid catalyst than $AlCl_3$ and $FeCl_3$ and was similar in activity to $ZnCl_2$. Although the yields of the products were generally low, the characteristics of this catalyst were observed in the formation of $\beta,\beta'$-dimethylstyrene and benzoylacetone upon the respective methallylation and acetylation of benzene and in the fact that the hydrated chloride was more effective than the anhydrous one. In a sharp contrast to aromatic bromination, $Tl(OAc)_3$ showed little activity in these reactions.

Although many metal halides have been studied as Lewis acid catalysts for aromatic alkylation and acylation, Tl(III) salts seem to have received little attention so far[2]; only one report on the benzylation, benzoylation, and acetylation of benzene using the anhydrous $TlCl_3$ catalyst has been found in the literature.[3] Recently, Taylor and McKillop showed that the acetylation of anisole could be catalyzed by $Tl(OAc)_3$.[4] On the other hand, the use of Tl(III) salts, such as $Tl(OAc)_3$ and $TlBr_3 \cdot 4H_2O$, has been reported to be very effective in aromatic bromination[5,6], and their role has been considerably clarified.[6]

Our study of the Tl(III) salt-catalyzed aromatic alkylation and acylation has been started in the hope of finding some specific use for the catalyst in these reactions, as in the case of the Tl(III) salt-catalyzed aromatic bromination. Unfortunately, no distinctive feature was found from a synthetic point of view. Considering the yields of the products of butylation, allylation, haloalkylation, and acylation, however, it is clear that the activity of $TlCl_3 \cdot 4H_2O$ is qualitatively comparable to that of $ZnCl_2$ and inferior to that of $FeCl_3$ or $AlCl_3$. Here, it seems to be characteristic that the hydrated Tl(III) salt shows a moderate activity, in contrast to the fact that other active metal halide catalysts are used mostly in the anhydrous state. This report will deal with these observations.

## Results and Discussion

The reactions were generally carried out by adding the alkylating or acylating agents to aromatic compounds (in excess as solvents) containing $TlCl_3 \cdot 4H_2O$ at various temperatures and by stirring the resulting mixtures for appropriate periods. Although an $AlCl_3$- or $FeCl_3$-catalyzed Friedel-Crafts alkylation and acylation generally proceeds at a low temperature, it was necessary to heat the reaction mixture in most of these $TlCl_3 \cdot 4H_2O$ catalyzed reactions. Some typical results are summarized in Table 1.

*Butylation and Benzylation.* It has been reported[7] that, in the presence of $AlCl_3$, *n*- and *t*-butyl chlorides reacted with benzene at 0°C to give *s*- and *t*-butylbenzenes in 50 and 60% yields respectively, and that the reaction of *t*-butyl chloride with benzene gave an 80% yeild of *t*-butylbenzene at 25°C in the presence of the $FeCl_3$ catalyst. In the presence of the $TlCl_3 \cdot 4H_2O$ catalyst, the *s*- and *t*-butyl halides reacted with aromatic compounds to give *s*- and *t*-butylated compounds (I) respectively in 22—39% yields at 60—76°C. The lower the reaction temperature was, the lower the yields of I became. *n*-Butyl chloride or bromide afforded only a small amount of *s*-butylbenzene (*ca.* a 2% yield at 76°C for 10 hr) without any trace of *n*-butylbenzene which was expected to be formed by the attack of the strongly polarized but undissociated alkyl halide molecule. *t*-Butyl alcohol could not be used as an alkylating agent at 70°C because of its rapid oxidation by $TlCl_3 \cdot 4H_2O$; this is in sharp contrast to the reactions with other acidic catalysts (*e.g.*, $H_2SO_4$, HF, $AlCl_3$, $FeCl_3$, and $BF_3$), in which *t*-butylbenzene was obtained in high yields from benzene.[7] In the benzylation of toluene with benzyl bromide or acetate, $TlBr_3 \cdot 4H_2O$ showed an activity similar to that of $TlCl_3 \cdot 4H_2O$ as a Lewis acid catalyst. Although $Tl(OAc)_3$ was a very effective catalyst in aromatic bromination, the *s*-butylation of benzene using this catalyst was almost entirely unsuccessful because of the conversion of $Tl(OAc)_3$ to inactive $Tl_2O_3$.

*Allylation and Haloalkylation.* It has been reported[8,9] that the reaction of allyl halide and aromatic compounds gives 1-aryl-2-halopropane or 1,2-diarylpropane in the presence of mild Lews acid catalysts, such as $ZnCl_2$, or with strong catalysts, such as $AlCl_3$, respectively, and that both of the products are derived from allylated compounds. Although $TlCl_3 \cdot 4H_2O$ has been shown by the aromatic butylation described above to be a milder Lewis acid catalyst than $AlCl_3$ or $FeCl_3$, it is not known to what kind of metal salts the activity

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[1] Presented at the 24th Annual Meeting of the Chemical Society of Japan, Osaka, April, 1971.

[2] "Friedel-Crafts and Related Reactions," ed. by G. A. Olah, Intersceience, New York (1965), Vol. I, p. 255—256.

[3] L. I. Kashtanov, *J. Gen. Chem.* (*U.S.S.R.*), **2**, 515 (1932); *Chem. Abstr.*, **27**, 975 (1933).

[4] E. C. Taylor and A. McKillop, *Accounts Chem. Res.*, **3**, 338 (1970).

[5] A. McKillop, D. Bromley, and E. C. Taylor, *Tetrahedron Lett.*, **1969**, 1623.

[6] S. Uemura, K. Sohma, M. Okano, and K. Ichikawa, This Bulletin, **44**, 2490 (1971).

[7] C. C. Price, "Organic Reactions," John Wiley and Sons, New York (1946), Vol. III, Chap. 1. p. 30—33.

[8] Ref. 2, Vol. II, p. 359—360.

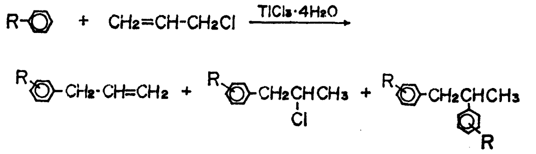
[9] C. D. Nenitzescu and D. A. Isacescu, *Chem. Ber.*, **66**, 1100 (1933).

TABLE 1

| $C_6H_5R$ R (1mol) | Alkylating or acylating agents (100 mmol) | $TlCl_3\cdot4H_2O$ (mmol) | React. temp. (°C) | React. time (hr) | Products (yield, %)[a] I | II | III | IV | V | VI |
|---|---|---|---|---|---|---|---|---|---|---|
| H | *s*-BuCl[b] | 25 | 76 | 4 | 23 | | | | | |
| H | *t*-BuBr | 10 | 76 | 0.3 | 39[c] | | | | | |
| H | $C_6H_5CH_2OAc$ | 25 | 80 | 5 | 50[d] | | | | | |
| $CH_3$ | $C_6H_5CH_2Br$ | 25[e] | 70 | 1 | 90[f] | | | | | |
| H | $CH_2$=CH-$CH_2Cl$ | 10 | 57 | 0.3 | | 4 | 5 | trace | | |
| H | $CH_2$=CH-$CH_2Cl$ | 25 | 70 | 4 | | 0 | 37 | trace | | |
| $CH_3$ | $CH_2$=CH-$CH_2Cl$ | 10 | 57 | 0.3 | | 7[g] | 22[h] | 0 | | |
| $CH_3$ | $CH_2$=CH-$CH_2Cl$ | 10 | 65 | 4 | | 0 | 52[h] | 31[i] | | |
| Cl | $CH_2$=CH-$CH_2Cl$ | 10 | 65 | 2 | | 0 | 18[j] | trace | | |
| H | $CH_3COCl$ | 25 | 56 | 5 | | | | | 3 | 6 |
| $CH_3$ | $CH_3COCl$ | 25 | 56 | 5 | | | | | 19 | 3 |
| $CH_3$ | $CH_3COCl$ | 25 | 25 | 0.3 | | | | | 23 | 0 |
| $CH_3$ | $CH_3COCl$ | 25[k] | 25 | 0.3 | | | | | 12 | 0 |

a) Based on alkylating of acylating agents.
b) 50 mmol.
c) The 12% yield of di-*p*-*t*-butylbenzene (mp 77—79° C; lit.[17] 76°C) was obtained.
d) Diphenylethane.
e) $TlBr_3\cdot4H_2O$.
f) Phenyltolylmethane, *o*/*p*=1.38.[6]
g) The *o*/*p* ratio was not determined.
h) *o*/*p*=0.15 (determined by NMR).
i) 1,1-Ditolypropane/1,2-isomer=3 (NMR).
j) *o*/*p*=1.21 (glc).
k) Anhydrous $TlCl_3$.

of $TlCl_3\cdot4H_2O$ is comparable. If $TlCl_3\cdot4H_2O$ is a milder catalyst than $ZnCl_2$, we could expect the allylated aromatic compounds to be isolated using this catalyst. In this connection, several aromatic compounds were treated at 55—70°C for 0.3—4 hr with allyl chloride or bromide in the presence of this catalyst. 1-Aryl-2-halopropanes (III) were generally isolated as the main products, along with small or trace amounts of monoallylated compounds (II) and diarylpropanes (IV) (Eq. 1).



(II)　(III)　(IV)

This means that the catalytic activity of $TlCl_3\cdot4H_2O$ is qualitatively similar to that of $ZnCl_2$ and milder than that of $AlCl_3$ in aromatic allylation. The formation of II was observed only under milder conditions (a short reaction time or a low reaction temperature), though the yields were very poor. The yields of III, which was probably formed by the hydrochlorination of II, decreased in the following order of aromatics, as would be expected; toluene>benzene>halobenzenes. The allylation of halobenzenes with this catalyst at 65—70°C for 1.5—2 hr gave only 9—18% yields of III, while with the $FeCl_3$ catalyst somewhat higher yields (24—53%) were recorded, even at lower reaction temperatures (−21—−16°C).[10] Compound IV was probably produced by aromatic alkylation with III. An isomer of IV, 1,1-diarylpropane, was also formed, and the amount of which was larger than that of IV. The presence of such an isomer indicates that the hydrogen transfer has occurred in the intermediary cation ($ArCH_2\overset{+}{C}HCH_3$) derived from III on prolonged heating, as in the case of the *n*-butylation of benzene described above. The use of a solvent led to a significant decrease in the reaction rate; *e.g.*, with benzene and allyl chloride, no reaction occurred at 50°C after 4 hr in carbon disulfide, and only 6% of the III was obtained at 65°C after 4 hr in chloroform. Allyl bromide reacted more easily with benzene than allyl chloride, but a mixture of 2-bromo- and 2-chloro-1-phenylpropanes (in 4: 1 ratio) was obtained in a 43% yield, together with diphenylpropanes (14% yield), when the reaction was at 55°C for 0.3 hr. The allylation with allyl alcohol, which was easily achieved by other Lewis acid catalysts, was unsuccessful when we used $TlCl_3\cdot4H_2O$, which has a strong oxidizing property. The reaction with *trans*-crotyl chloride showed a behavior similar to that of the reaction with allyl chloride. With methallyl chloride, however, $\beta,\beta'$-dimethylstyrene was obtained in a 9% yield without any trace of such compounds as III and IV when the reaction was at 75°C for 5 hr. This compound, which is probably formed by the isomerization of the methallylated compound, has not been reported to be formed by a Friedel-Crafts reaction using any Lewis acid catalyst; rather its formation seems to be one of the characteristics of the $TlCl_3\cdot4H_2O$ catalyst.

The attacking species in this reaction seem to be rather reactive, because the $k_T/k_B$ ratio in the formation of II and III by the competitive reaction of toluene and

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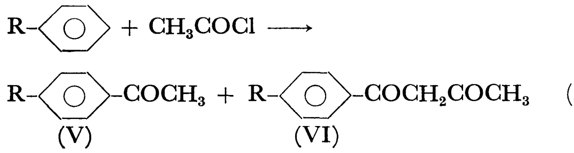
[10] T. M. Patrick, Jr., E. T. McBee, and H. B. Hass, *J. Amer. Chem. Soc.*, **68**, 1009 (1946).

benzene with allyl chloride (at 50°C for 0.3 hr) is revealed to be 2.6; this value is comparable with the value (3.2) obtained in the $AlCl_3$-catalyzed benzylation in nitromethane.[11] Further, it is interesting to note that the favorable attack at the *p*-position of toluene by allylic species (the *o*/*p* ratio is 0.15 in III) contrasts strikingly with that at the *o*-position by benzylic species (where the *o*/*p* ratio is 1.38), as is shown in Table 1.

*Acylation.* Although Kashtanov has obtained a 12% yield of acetophenone from the acetylation of benzene using anhydrous $TlCl_3$,[3] a recent description of Taylor and McKillop of the selective para acetylation of anisole by the $Tl(OAc)_3$ catalyst[4] encouraged us to reinvestigate the acylation using $TlCl_3\cdot4H_2O$. In the presence of $TlCl_3\cdot4H_2O$, the reactions of acetyl or propionyl chloride with benzene, toluene, and anisole were examined; the *para*-monoacylated compounds (V) were isolated as the main products, although the yields were low. It seems that the low yield is not be accounted for by the hydrolysis of acyl chloride with the water of the hydrated catalyst, because the reaction with anhydrous $TlCl_3$ gave a smaller amount of the product. In a contrast to Kashtanov's report, the acetylation of benzene and toluene at 56°C gave benzoylacetone and *p*-methylbenzoylacetone (VI) respectively, together with V (Eq. 2). When acetophenone was heated with $TlCl_3\cdot4H_2O$ at 56°C for 5 hr, α-methylchalcone, the Claisen condensation product of acetophenone, was obtained in a 10% yield, as in the $AlCl_3$-catalyzed reaction[12] (in this case, an 11.5% yield was reported); however, the presence of excess (*e.g.*, 5 equiv.) acetyl chloride changed the product to benzoylacetone (9% yield) under the same reaction conditions. Although it has been reported that the methyl group of acetophenone was acetylated with acetic anhydride using the $FeCl_3$ or $ZnCl_2$ catalyst to give benzoylacetone,[12] there have been no reports about acetylation with acetyl chloride. This $TlCl_3\cdot4H_2O$-catalyzed acetylation of acetophenone and this formation of VI seem to be characteristic of this catalyst. Acetic anhydride could not be used as the acetylating agent of aromatic compounds with the $TlCl_3\cdot4H_2O$ catalyst.



(2)

Recently, Taylor and McKillop reported,[4] without any detailed description of the experimental conditions, that, in the $CCl_4$ solvent, anisole was acetylated by acetyl chloride to give *p*-acetylanisole in an 80% yield when the $Tl(OAc)_3$ catalyst was used. When a similar reaction was carried out with anisole as the solvent and with the $TlCl_3\cdot4H_2O$ catalyst, only a 28% yield of the acetylated product was obtained at 25°C after 0.3 hr. For comparison, the reaction of anisole (0.1 mol) and acetyl chloride (0.05 mol) using the $Tl(OAc)_3$ (0.05 mol) catalyst was carried out in $CCl_4$ (80 m*l*) at 20°C for 3 hr, but only a 15% yield of *p*-acetylanisole was thus obtained. The reason for the discrepancy with Taylor's result is obscure.

## Experimental

*Materials.* All the organic starting materials were used after distillation. The $TlCl_3\cdot4H_2O$ (mp 35—37°C, lit.[13] 37°C; the purity (as determined by iodometry) was more than 96%) and $TlBr_3\cdot4H_2O$ (mp 40—42°C, lit.[13] 40°C; purity, 97%) catalysts were of commercial origin. The Tl $(OAc)_3$ was prepared by heating $Tl_2O_3$ in aceitc acid.[14] Anhydrous $TlCl_3$,[15] which is very hygroscopic, was prepared by dissolving $TlCl_3\cdot4H_2O$ into thionyl chloride at room temperature, evaporating the hydrogen chloride, sulfur dioxide, and excess thionyl chloride to dryness on a water bath, and drying under a vacuum for 6 hr (purity, 96.6%). The *n*-, *s*-, and *t*-butylbenzenes, allylbenzene, diphenylmethane, acetophenone, *p*-methylacetophenone, and benzoylacetone were commercial products and were used as the authentic samples for glc analysis. The 1-phenyl-2-chloropropane and 1,2-diphenylpropane were prepared from a benzene-allyl chloride-$FeCl_3$ system at −10—−20°C for 1 hr; the yields were 41% and 14% (1,2-isomer/1,1-isomer=1.5 by NMR) respectivey. The 1-halophenyl-2-chloropropanes were prepared by the reported method[10] using the corresponding halobenzene, allyl chloride, and $FeCl_3$ catalyst.

*Experimental Procedure.* The reaction of benzene with allyl chloride in the presence of $TlCl_3\cdot4H_2O$ is shown below as a typical example. Allyl chloride (15.2 g, 0.2 mol) was stirred into a suspension of molten $TlCl_3\cdot4H_2O$ (9.6 g, 0.025 mol) and benzene (78 g, 1 mol) at 60°C. The color of the reaction mixture changed from pale yellow to orange and finally to deep purple, while the reaction temperature rose to 70°C. After 4 hr, the black precipitates were filtered off, and the filtrate was washed with water and a saturated aqueous $NaHCO_3$ solution and dried over $Na_2SO_4$. Glc analysis showed that it consisted of almost pure III, 1-phenyl-2-chloropropane (37% yield), and trace amounts of II and IV. III was isolated in a pure state by vacuum distillation; bp 90—93°C/19 mmHg, 9.9 g (64.2 mmol). NMR $\tau$ 8.52 (d. $J$=6.5 Hz, 3H), 6.99 (m. 2H), 5.79 (m. 1H), 2.76 (m. 5H).

*Identification of the Products.* *Allyltoluene* (II, R=$CH_3$) was obtained as a mixture with 1-tolyl-2-chloropropane (III, R=$CH_3$) at bp 50—65°C/7 mmHg (the ratio of II/III=2). The NMR of a mixture of *o*- and *p*-isomers of III $\tau$ 7.68 (s. 3H), 6.25—6.05 (m. 2H), 5.30—4.75 (m. 2H), 4.30—3.90 (m. 1H), 3.0—2.75 (m. 5H).

*1-Tolyl-2-chloropropane* (III, R=$CH_3$) was obtained as a mixture of *o*- and *p*-isomers at bp 79—82°C/5 mmHg. Found: C, 71.39; H, 7.81%. Calcd for $C_{10}H_{13}Cl$: C, 71.21; H, 7.77%. NMR $\tau$ 8.53 (d. $J$=7.5 Hz, 3H, *o*-isomer), 8.50 (d. $J$=7.5 Hz, 3H, *p*-isomer).

*2-Bromo-1-phenylpropane*: Bp 85—89°C/5 mmHg. NMR $\tau$ 8.35 (d. $J$=6.4 Hz, 3H), 6.95—6.78 (m. 2H), 6.0—5.5 (m. 1H), 2.9—2.7 (m. 5H).

*Ditolylpropane* (IV, R=$CH_3$) was obtained as a mixture of 1,1- and 1,2-ditolylpropanes at bp 132—135°C/3 mmHg. Found: C, 89.70; H, 8.94%. Calcd for $C_{17}H_{20}$: C, 91.01; H, 8.99%. NMR $\tau$ 9.12 (t. $J$=8 Hz, 3H, 1,1-ditolylpro-

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[12] B. M. Perfetti and R. Levine, *ibid.*, **75**, 626 (1953).

[13] N. A. Lange, "Handbook of Chemictry," 10th ed., McGraw-Hill, New York (1961), p. 318.

[14] L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," John Wiley and Sons, New York (1967), p. 1150.

[15] V. H. Hecht, *Z. Anorg. Allg. Chem.*, **254**, 46 (1947).

pane), 8.78 (d. $J=8$ Hz, 3H, 1,2-isomer).

*β,β′-Dimethylstyrene*: Bp 85—86°C/25 mmHg. NMR $\tau$ 8.18—8.05 (m, 6H) 3.8—3.65 (m, 1H), 2.8—2.65 (m, 5H).

p-*Anisylacetophenone* (*V*, $R=CH_3O$): Bp 113—122°C/6 mmHg. NMR $\tau$ 7.48 (s, 3H), 6.17 (s, 3H), 3.1 (d, $J=9.5$ Hz, 2H), 2.05 (d, $J=9.5$ Hz, 2H).

*α-Methylchalcone*, $C_6H_5C(CH_3)=CHCOC_6H_5$: Bp 160—163°C/2 mmHg (lit.[16] bp 225°C/22 mmHg), IR (liq. film) 1670 (s, $\nu_{C=O}$), 1610 (s, $\nu_{C=C}$) cm$^{-1}$.

*Benzoylacetone*: Bp. 115°C/5 mmHg (lit.[12] bp 103—105°C/1.8 mmHg), mp 59°C (lit.[18] 60—61°C). Found: C, 74.03; H, 6.42%. Calcd for $C_{10}H_{10}O_2$: C, 74.05; H, 6.22%.

*Spectral Measurements.* The IR spectra were measured on Hitachi EPI-2 and EPS-3T spectrometers. The NMR spectra were determined on a Varian A-60 spectrometer, using TMS as the internal standard in $CDCl_3$. Glc analysis was carried out on Shimadzu 5APTF apparatus, using PEG 6000 (25%)-Chromosorb-W 3-m and Apz-L (30%)-Celite 3-m columns, and on a Hitachi F-6 apparatus, using Apz-L 1-m columns.

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16) I. Heilbron ed., "Dictionary of Organic Compounds," Maruzen, Tokyo (1965), p. 2153.

17) A. Baur, *Ber.*, **27**, 1608 (1894).

18) Ref. 13, p. 427.