A New Method for the Preparation of Aluminum and Titanium Tris(2,6-diphenylphenoxide) Reagents and Their Application in Organic Synthesis

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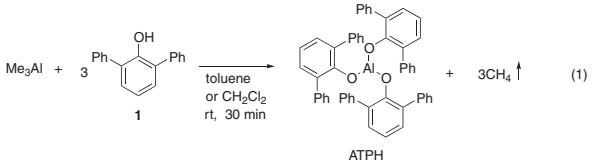
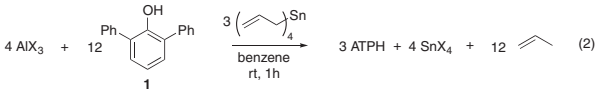
A new method for the preparation of aluminum and titanium trisphenoxides was realized using tetraallyltin or α-pinene as a proton-trapping agent. Thus obtained chlorotitanium reagent was converted to the corresponding cation-type reagent, which proved to be an effective catalyst for epoxide rearrangements.

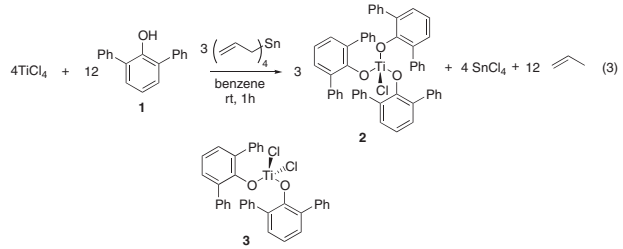
Over the last decade, extraordinary organic transformations have been realized using aluminum tris(2,6-diphenylphenoxide) (ATPH).[1] The preparation of ATPH was routinely carried out by treatment of Me_3Al with 2,6-diphenylphenol at room temperature (Eq 1). Although Me_3Al is a convenient reagent being reactive to phenols, it is extremely pyrophoric[2] and thus does not satisfy a demand for a large-scale preparation with easy handling. We report here a safer and more practical approach to this critical reagent by the combined use of $AlBr_3$ and tetraallyltin reagents (Eq 2). This obviates the need to remove side products such as alkali metal salts, which are inevitably generated during usual procedures,[3] by cumbersome decantation or other Schlenk techniques. These practical advantages further extend to the synthesis of a Ti-trisphenoxide reagent.





Treatment of 2,6-diphenylphenol (12 equiv.) with $AlBr_3$ (4 equiv.) in benzene at room temperature was followed by addition of tetraallyltin (3 equiv.) The mixture was stirred at room temperature for 1 h, and the solvent was evaporated in vacuo (0.05 mmHg, 40 °C) for 3 h with concomitant removal of the resulting $SnBr_4$ (bp 202 °C) and propene. The residual yellow solid was identified as pure ATPH by comparison with the authentic ^{1}H NMR data obtained by treatment of Me_3Al with the phenol.[4] Monitoring the reaction by ^{1}H NMR (benzene-d_6) showed that the peaks corresponding to tetraallyltin had disappeared in a region ranging from 5.0 to 6.5 ppm. Internal standard[5] peaks indicated the quantitative formation of ATPH. The use of $AlCl_3$ also resulted in the formation of ATPH but was contaminated with unidentified side products bearing phenoxide components.[6] In both cases, no free phenol remained, as ascertained by ^{1}H NMR analysis.

This procedure was also applicable to the preparation of Ti-trisphenoxide **2**.[7] A similar reaction proceeded smoothly using $TiCl_4$ at room temperature to give the corresponding trisphenoxide product **2** in quantitative yield (with respect to the internal standard, Eq 3), the structure of which was rigorously established by ^{1}H NMR and elemental analysis as well as by X-ray single crystal[8] analysis (Figure 1). This is in clear contrast to the results that afforded the bisphenoxide Ti-reagent **3** by treatment of the phenol with $TiCl_4$ upon benzene reflux and by sweeping out HCl under a flow of N_2.[3f] The crystal analysis revealed that **2** has a structure apparently distinct from, though slightly similar to, that of ATPH; three phenyl rings form a partial cavity, one of the rings being relatively exposed. The remaining two phenyl rings have a face-to-face orientation to form a sandwich structure involving the chloro group (Figure 1b).



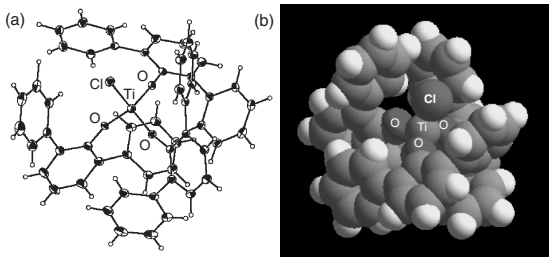
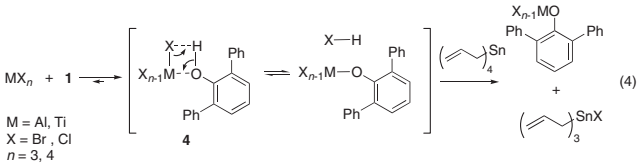


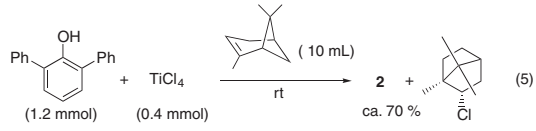
Figure 1. The X-ray single crystal structure of **2**. The (a) ORTEP and (b) CPK models.

Based on these results, a plausible mechanism for the reaction could be proposed (Eq 4). We also confirmed that no reaction occurred between the phenol and tetraallyltin alone even at 40 °C for 3 h. Thus the complexation-decomplexation equilibrium shifted to the right side and activated the release of HX from coordination complex **4** (Eq 4). Although it was reported that allyltributyltin was protonated by a mixture of binaphthol and $TiCl_2(O\textit{i}\text{-}Pr)_2$ affording propene and tributyltin chloride,[9] in general, monodentate ligands including **1** are less effective in forming such a metastable complex. It is also reasonable to suggest a mechanism corroborating a pathway involving the direct trap of HX from **4**. Undoubtedly the acidity of the hydroxy group of **4** is strengthened; otherwise the formation of metal phenoxides would not proceed.[10] Whichever mechanism is preferred,

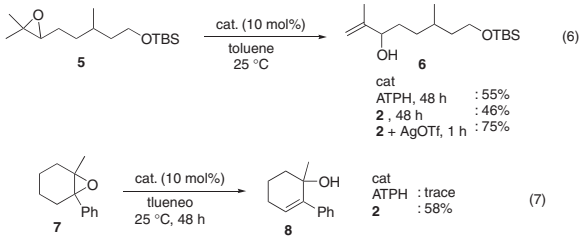
either of the reaction sequences is repeated in situ to give ATPH and Ti-trisphenoxide **2**.



In place of tetraallyltin, α-pinene as a proton scavenger was also capable of the synthesis of **2** (Eq 5). Although the yield was moderate (ca. 70%), pure trisphenoxide **2** was obtained through the Wagner–Meerwein–Whitmore rearrangement of α-pinene, followed by recrystallization.



Although the titanium reagent **2** showed relatively modest catalytic activity, it was used as a cation-type catalyst superior to the neutral catalyst ATPH (Eq 6). For example, treatment of a 10 mol% of **2** with AgOTf, followed by addition of **5** gave **6** in 75% yield within 1 h, compared with ATPH that afforded 55% yield after a prolonged reaction time (48 h). Tetra-substituted epoxide **7** was also compatible with similar conditions to give allylic alcohol **8** (Eq 7).



In summary, we achieved an alternative route to ATPH and the chlorotitanium trisphenoxide **2** by use of metal halide salts and tetraallyltin or α-pinene. Since organotin products are not generated, this method has an environmentally more benign nature. The reaction proceeded effectively with metals bearing strong coordination capability. Application of this method to phenols having a bidentate coordination site that would be expected to form more stable metal complexes[9,10] is now in progress in our laboratory.

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References and Notes

1 For review of ATPH, see: a) S. Saito and H. Yamamoto, *Chem. Commun.*, **1997**, 2585. Recent application of ATPH, see: b) S. Saito, S. Yamazaki, and H. Yamamoto, *Angew. Chem., Int. Ed.*, **40**, 3613 (2001). c) S. Saito, M. Shiozawa, T. Nagahara, M. Nakadai, and H. Yamamoto, *J. Am. Chem. Soc.*, **122**, 7847 (2000). d) S. Saito, T. Sone, M. Murase, and H. Yamamoto, *J. Am. Chem. Soc.*, **122**, 10216 (2000). e) S. Saito, M. Shiozawa, and H. Yamamoto, *Angew. Chem., Int. Ed.*, **38**, 1769 (1999).

2 "Encyclopedia of Reagents for Organic Synthesis," ed. by L. A. Paquette, John Wiley & Sons, Chichester (1995), Vol. 7, p 5186.

3 Alkali metal (Li, Na, K) phenoxides are frequently used to react with other metal (Ti, Zr, Hf, Ln, etc.) halide salts to give metal trisphenoxides. See for Sm: a) K. Katagiri, M. Kameoka, M. Nishiura, and T. Imamoto, *Chem. Lett.*, **2002**, 426. For various Ln: b) D. M. Barnhart, D. L. Clark, J. C. Gorden, J. C. Huffman, R. L. Vincent, J. G. Watkin, and B. D. Zwick, *Inorg. Chem.*, **33**, 3487 (1994). For Ti, Zr, Hf: c) S. L. Latesky, J. Keddington, A. K. McMullen, I. P. Rothwell, and J. C. Huffman, *Inorg. Chem.*, **24**, 995 (1985). d) L. Chamberlain, J. C. Huffman, J. Keddington, and I. P. Rothwell, *J. Chem. Soc., Chem. Commun.*, **1982**, 805. For $TiMe_4$: e) R. W. Chesnut, L. D. Durfee, P. E. Fanwick, and I. P. Rothwell, *Polyhedron*, **6**, 2019 (1987). f) M. G. Thorn, Z. C. Etheridge, P. E. Fanwick, and I. P. Rothwell, *J. Organomet. Chem.*, **591**, 148 (1999).

4 For the X-ray single crystal structures of various ATPH–carbonyl complexes, see Refs. 1d, 1e and: S. Saito, T. Nagahara, M. Shiozawa, M. Nakadai, and H. Yamamoto, *J. Am. Chem. Soc.*, **125**, 6200 (2003).

5 Trioctylmethylsilane (purchased from Shinetsu) was purified by column chromatography and used.

6 Unidentified tin phenoxides ($R_nSn(OAr)_{4-n}$) might be formed.

7 Ti-complex **2** is the new compound. Typical procedure: To a solution of **1** (295 mg, 1.2 mmol) in dry benzene (4.0 mL) was added $TiCl_4$ (44 µL, 0.4 mmol), followed by tetraallyltin (72 µL, 0.3 mmol), both being purified by distillation prior to use, at room temperature under argon. The resulting dark red solution was stirred for 1 h. The solvents and other volatile side products ($SnCl_4$: bp 114 °C (770 mmHg)) were evaporated in vacuo (0.03 mmHg) at 40 °C to give **2** in dark red crops (325 mg, 99%). Anal. Calcd for $C_{54}H_{39}O_3ClTi$: C, 79.17, H, 4.80%; Found: C, 79.08, H, 4.82%. The single crystals suitable for the X-ray crystal analysis were grown from hexane–benzene at room temperature for **1** to **2** days. A crystal was transferred to a glass capillary tube using a dry-box for the diffraction experiments.

8 The X-ray single crystal structure data of **2**: $a = 10.2910$ (2), $b = 21.0260$ (3), $c = 20.191$ (4) Å, $\beta = 104.177$ (3)°, monoclinic, $P21/c$, $Z = 4$, μ(Mo) = 0.437 mm^{-1}, $R = 0.050$, $R_w = 0.051$, GOF = 1.836, 4989 unique reflections with $I > 3.0\sigma(I)$. Crystallographic data (excluding structure factors) for the X-ray crystal structure analysis reported in this paper have been deposited with the Cambridge Crystallographic Data Centre (CCDC) as supplementary publication no. CCDC-184707. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambrdge CB2 1EZ, UK (fax: +44-1223-336-033, e-mail: deposit@ccdc.cam.ac.uk).

9 a) S. Casolari, D. D'Addario, and E. Tagliavini, *Org. Lett.*, **1**, 1061 (1999). The TiF_4-binaphthol-allyltrimethylsilane system to produce binaphthol-TiF_2 complex was also reported. See: b) R. O. Duthaler and A. Hafner, *Angew. Chem. Int. Ed.*, **36**, 43 (1997). c) D. R. Gauthier, Jr. and E. M. Carreira, *Angew. Chem. Int. Ed.*, **35**, 2363 (1996).

10 In cases where $ZrCl_4\cdot(THF)_2$ and $HfCl_4\cdot(THF)_2$ were reacted with **1**, no reaction or unknown product mixtures[6] were observed, respectively. This is probably due to the lack of sufficient Lewis acidity and/or of steric requirement requisite for the formation of stable trisphenoxides, which led to undesired disproportion reactions. Monitoring the reaction by ^{1}H NMR analysis (300 MHz, THF-d_8) showed a set of peaks corresponding to the free phenol. This implies that the metastable formation of the coordination complex (such as 4) should be a critical step to initiate the reaction. Similar to titanium complexes (Ref. 9), a bidentate complexation with zirconium was achieved by treatment of tributylallyltin with binaphthol and $ZrCl_4\cdot(THF)_2$. See: S. Casolari, P. G. Cozzi, P. Orioli, E. Tagliavini, and A. Umani-Ronchi, *Chem. Commun.*, **1997**, 2123.

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