Aluminum Tris(2,6-diphenylphenoxide)-ArCOCl Complex for Nucleophilic Dearomatic Functionalization

Susumu Saito, Toshihiko Sone, Masaaki Murase, and Hisashi Yamamoto*

Graduate School of Engineering, Nagoya University
CREST, Japan Science and Technology Corporation (JST)
Chikusa, Nagoya 464-8603, Japan

Received April 25, 2000

Recently, we demonstrated the nucleophilic dearomatization of benzaldehyde (PhCHO) complexed with aluminum tris(2,6-diphenylphenoxide) (ATPH) (Figure 1),[1] which proceeded smoothly with a variety of nucleophiles.[2] Unfortunately, however, conjugate addition to the ATPH-PhCHO complex did not proceed effectively with smaller nucleophiles (Scheme 1). For example, MeLi and the lithium enolates of methyl acetate undergo 1,2-addition predominantly. The lithium enolates of several ketones, methyl propionate, *tert*-butyl acetate, PhLi, and vinyl- and allyllithiums give equal amounts of 1,2- and 1,6-adducts. In sharp contrast, treatment of a toluene solution of ATPH (1.1 equiv) with benzoyl chloride (PhCOCl; 1.0 equiv) at −78 °C, followed by addition of MeLi (3.0 equiv)[3] and workup with concentrated HCl gives 1,6- and 1,4-adducts **1a** and **1b** in a ratio of 2.6:1 in 99% isolated yield (Scheme 1).

Nucleophiles that add in a 1,6-manner to ATPH-PhCOCl include Grignard reagents (*i*-PrMgBr and *t*-BuMgCl), which are ineffective for the conjugate addition to the ATPH-PhCHO complex. Figure 2 shows that enhanced regioselectivities (1,6- vs 1,2-addition) are achieved with the ATPH-PhCOCl complex. Addition products can be isolated as acids or esters by altering workup conditions. In each of these cases, 1,2-adduct could not be detected by ^{1}H NMR analysis.

Insight regarding the change in product distribution in the two types of complexes may be derived from a comparison of their X-ray crystal structures. The X-ray crystal structure of ATPH-PhCHO, Figure 3a,[4] shows one face of the extended π-system to be relatively exposed, at least in the region distal to the carbonyl group. On the other hand, the X-ray crystal structure of ATPH-PhCOCl,[4] Figure 3b, revealed that two of the phenyl rings (black) of ATPH and the flat PhCOCl form a sandwich structure, rendering the C═O highly congested. The C═O of ATPH-PhCOCl has a single bond-like character. The Al−*O*═*C* bond of 1.235(4) Å is longer than that of Al−*O*═*C*HPh (1.14(1) Å).[5] This is consistent with the FT-IR measurement of the ATPH-PhCOCl and ATPH-PhCHO complexes in solution (CD_2Cl_2, −40 °C). The frequency of the carbonyl of ATPH-PhCOCl is shifted to a lower frequency as a result of enhanced conjugation relative to that of the free substrates by 42 cm^{-1}.[6] The ATPH-PhCHO complex, on the other hand, exhibits no detectable shift. In fact, the π-deficiency of PhCOCl is significantly enhanced by complex-

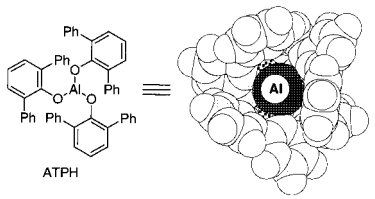


Figure 1. Molecular structure of ATPH.

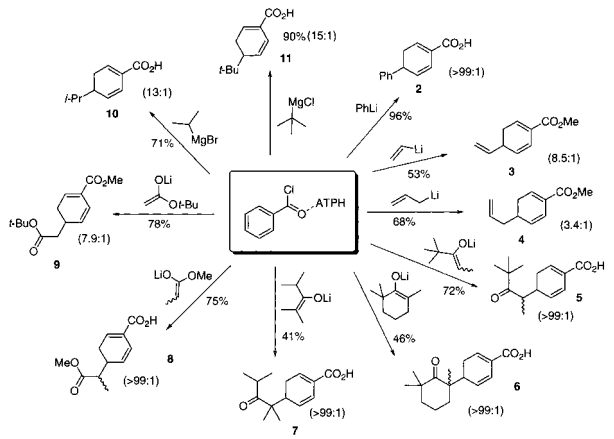


Figure 2. Conjugate addition of various nucleophiles using the ATPH-PhCOCl. The values in parentheses are ratios of 1,6- and 1,4-adducts, which were determined by ^{1}H NMR analysis. Combined yields of 1,6- and 1,4-adducts are indicated. Acids and esters are obtained with the following conditions: −78 °C to room temperature; acid, concentrated HCl; ester, Et_2O solution of HCl, followed by MeOH.

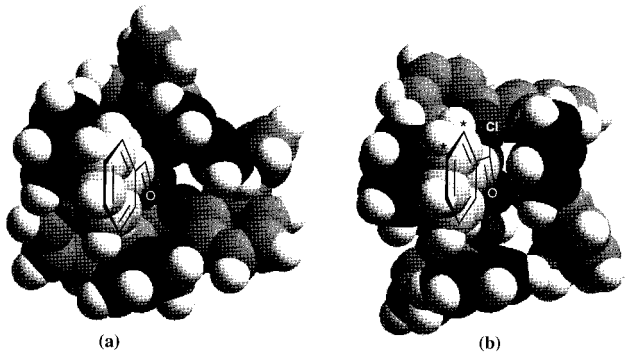
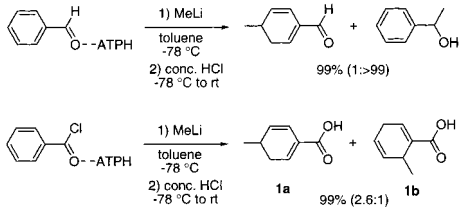


Figure 3. The X-ray crystal structures of (a) ATPH-PhCHO and (b) ATPH-PhCOCl.

Scheme 1



(1) (a) Saito, S.; Yamamoto, H. *Chem. Commun.* **1997**, 1585. (b) Yamamoto, H.; Saito, S. *Pure Appl. Chem.* **1999**, *71*, 235. (c) Saito, S.; Yamamoto, H. *Chem. Eur. J.* **1999**, *5*, 1959.

(2) For preliminary results concerning nucleophilic addition to aromatic rings using ATPH, see: (a) Maruoka, K.; Ito, M.; Yamamoto, H. *J. Am. Chem. Soc.* **1995**, *117*, 9091. (b) Saito, S.; Shimada, K.; Yamamoto, H. Marigorta, E. M.; Fleming, I. *Chem. Commun.* **1997**, 1299. (c) Saito, S.; Sone, T.; Yamamoto, H. *Synlett* **1999**, 81.

(3) The use of less nucleophile (1.1−2.5 equiv) gives the corresponding product in lower yield.

(4) The single-crystal structures of ATPH-PhCHO and ATPH-PhCOCl were established for the first time in this paper. See Supporting Information for details.

(5) The average bond length of C═O in free RCOCl is ca. 1.18 Å. The C═O of RCHO has a similar average length of ca. 1.22 Å. See also ref 1 in the Supporting Information.

(6) For benzoyl chlorides, an unequal intensity of doublet is usually seen in the C═O region. A second band is due to the Fermi resonance involving the stretch of the overtone of the Ph−C which interacts with the carbonyl stretch. IR frequency: PhCHO (1708 cm^{-1}); ATPH-PhCHO (1708 cm^{-1}); PhCOCl (1770 (C═O stretch) and 1728 ((due to the Fermi resonance) cm^{-1}); *ATPH-PhCOCl* (1728 cm^{-1}). See also ref 2 in the Supporting Information.

10.1021/ja0014382 CCC: $19.00
Published on Web 09/27/2000

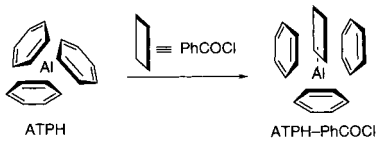
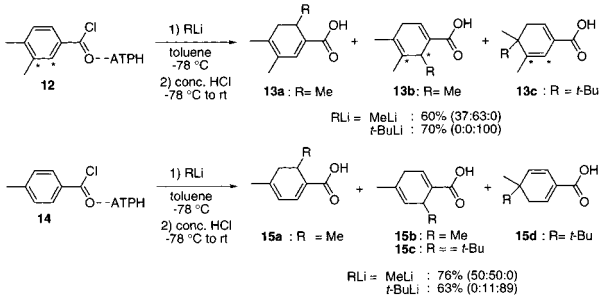


Figure 4. Schematic depiction of the induced conformational changes of ATPH as a "molecular tweezer" for effective inclusion of PhCOCl. The three benzene rings correspond to the darkened phenyls in Figure 3b.

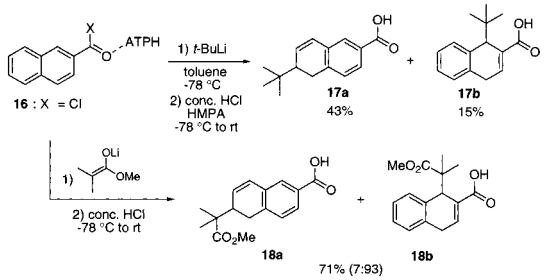
ation with ATPH. ^{13}C NMR measurements (75 MHz, CD_2Cl_2, −30 °C) show downfield shifts ($\Delta\delta$) for the carbonyl carbon from free to bound substrates of 9.49 ppm for ATPH-PhCHO and 18.0 ppm for ATPH-PhCOCl.[7] The π-stacking between two π-donors (ATPH phenyls) and one π-acceptor (complexed PhCOCl) involving the carbonyl carbon may act as a "molecular tweezer"[8] to stabilize the ATPH-PhCOCl complex (Figure 4). The interaction does not seem to be the primary binding force, but rather is induced upon intrinsic Lewis acid−base complexation.[9] This aspect was further demonstrated by a ^{13}C NMR (CD_2Cl_2, −78 °C to room temperature) competition experiment using a 1:1:1 mixture of ATPH, PhCHO, and PhCOCl. The analysis shows $K_{PhCOCl}/K_{PhCHO} = ([ATPH{\cdot}PhCOCl]/[ATPH{\cdot}PhCHO])([PhCHO]_{free}/[PhCOCl]_{free}) < 3.5 \times 10^{-3}$,[10] suggesting that PhCOCl forms complexes that are less stabilized than those of PhCHO by more than 14 kJ mol^{-1} (at 298 K). It should be emphasized that the relative destabilization, i.e., the higher reactivity of ATPH-PhCOCl, compared with ATPH-PhCHO, might be compensated for to some extent by the formation of the "molecular tweezer".

When *t*-BuLi was used for the *tert*-butylation of ATPH-PhCHO, the 1,6-adduct, but no 1,4-adduct, was produced.[2a] This could be ascribed to the distinctive structure of ATPH-PhCHO, which is not driven to π-sandwiching (Figure 3a). The two ortho positions of ATPH-PhCHO are sterically encumbered to an equal degree, while one of the two ortho positions (the asterisked ortho position: 1,4-addition site) of ATPH-PhCOCl is sterically deshielded due to the sandwich structure (Figure 3b). Alkyllithiums are prone to 1,4-addition with ATPH-PhCOCl in the order MeLi >BuLi > *s*-BuLi > *t*-BuLi,[11] although they show a general preference for 1,6-selectivity. Unexpectedly, we observed complete regiochemical reversal according to the size of RLi upon addition to acid chloride complexes **12** and **14**: 1,6-selectivity predominated with *t*-BuLi to give **13c** and **15d**, whereas MeLi underwent 1,4-addition exclusively to give **13a,b** and **15a,b** (Scheme 2).

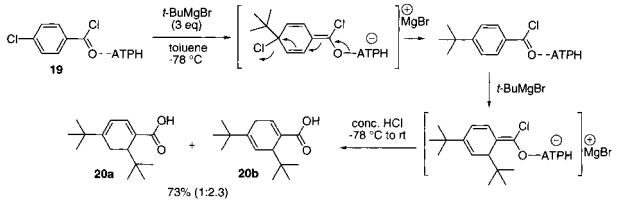
Scheme 2



Scheme 3



Scheme 4



As shown in Figure 3b, complex **12** should orient itself so that the *m*-methyl substituted carbon occupies the less-congested meta site which is marked with an asterisk. Attack at both ortho positions of **12** is unfavorable, and hence bulky *t*-BuLi suffers 1,6-addition to give **13c** exclusively (Scheme 2). This observation is in contrast to the formation of 1,6-adduct **15d** accompanied by a small amount of 1,4-adduct **15c**. The ratio of two different 1,4-adducts **13a,b** could be explained along similar lines (Scheme 2): the asterisked ortho position, which is less congested than the other ortho position, is selectively methylated.

The ATPH−β-naphthaldehyde complex (X = H, Scheme 3) did not undergo conjugate addition even with *t*-BuLi. However, the reaction proceeded smoothly with the use of acid chloride complex **16**. Of particular interest is the novel 1,8-selectivity to give **17a** (Scheme 3). In marked contrast, 1,4-addition predominated with the lithium enolate of 2-methylpropionate to give **18b** in 66% yield (Scheme 3).

Another striking advantage of the present method can be seen in the reaction of 4-chlorobenzoic acid chloride **19** with *t*-BuMgBr (3equiv) (Scheme 4). This facilitates a tandem 1,6-addition−chloride elimination−rearomatization−1,4-addition sequence, i.e., in situ double conjugate addition, to give **20a** and **20b** in 73% yield.

Supporting Information Available: Experimental procedures and analytical and spectral data for all new compounds (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA0014382

(7) ^{13}C NMR (75 MHz, CD_2Cl_2, −30 °C) chemical shifts: PhCHO (191.9 ppm); ATPH-PhCHO (201.4 ppm); PhCOCl (168.0 ppm); and *ATPH-PhCOCl (185.0 ppm)*. We can exclude the species [PhC≡O$^+$][ATPH·Cl$^-$] to account for this significant downfield shift, since a single crystal of ATPH-PhCOCl was grown in CH_2Cl_2-hexane at −20 °C to give the structure shown in Figure 3b.

(8) The two phenyl rings of ATPH which form the π-sandwich are separated by ca. 7.0 Å. This value is identical to the distance in "*molecular tweezers*" which can include aromatic guests by interactions between two π-donors and one π-acceptor, see: Zimmerman, S. C.; VanZyl, C. M.; Hamilton, G. S. *J. Am. Chem. Soc*. **1989**, *111*, 1373. See also ref 3 in the Supporting Information.

(9) Zimmerman (ref 8) pointed out that cooperative π-stacking with an electron donor−acceptor component can contribute to complex stability if hydrophobic forces or hydrogen bonding is present. In our case, the Lewis acid−base coordination may substitute for these forces and bonding.

(10) Although we encountered an experimental limit for measuring K_{PhCOCl}/K_{PhCHO}, the preferred order of binding to ATPH is $PhCO_2Me$ > PhCOCl, and the relative binding constant of $PhCO_2Me$ and PhCHO is $K_{PhCOOMe}/K_{PhCHO} = 3.5 \times 10^{-3}$. In these competition experiments using ATPH, we always observed a set of two chemical shifts, each corresponding to free and bound substrates, due to slow exchange at the NMR time scale.

(11) Exposure of ATPH-PhCOCl to these nucleophiles gives 1,6- and 1,4-product ratios of 2.6:1 (MeLi), 4.5:1 (*n*-BuLi), 14:1 (*s*-BuLi), and 39:1 (*t*-BuLi). A similar regiochemical trend was obtained previously using the ATPH−α-naphthaldehyde complex (see ref 2a).