BOWL-SHAPED [TRIS(2,6-DIPHENYLBENZYL)SILOXY]-DIMETHYLALUMINUM CATALYST FOR EFFECTING TISHCHENKO REACTION

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Abstract — High-speed Tishchenko reaction of various aldehydes can be realized by using a bowl-shaped [tris(2,6-diphenylbenzyl)siloxy]dimethylaluminum catalyst, which is readily prepared by treatment of tris(2,6-diphenylbenzyl)silanol with trimethylaluminum.

(Dedicated to Professor Yuichi Kanaoka on the occasion of his 75th birthday)

The Tishchenko reaction involves the dimerization of aldehydes giving the corresponding esters by an oxidation-reduction sequence under the influence of aluminum alkoxides as illustrated in Scheme 1.[1-4] Thus, aluminum alkoxide reacts with aldehyde to give a tetracoodinate intermediate [**A**], where an alkoxy moiety (RCH$_2$O-) shifts to carbonyl carbon of coordinated aldehyde to furnish an intermediate [**B**]. Further addition of another aldehyde to a trivalent aluminum in [**B**] affords a tetracoordinate intermediate [**C**], which undergoes a hydride transfer from the alkoxide to a carbonyl acceptor *via* a six-membered transition state (*i.e.*, Meerwein-Ponndorf-Verley type reduction)[5] to furnish an ester product in regeneration
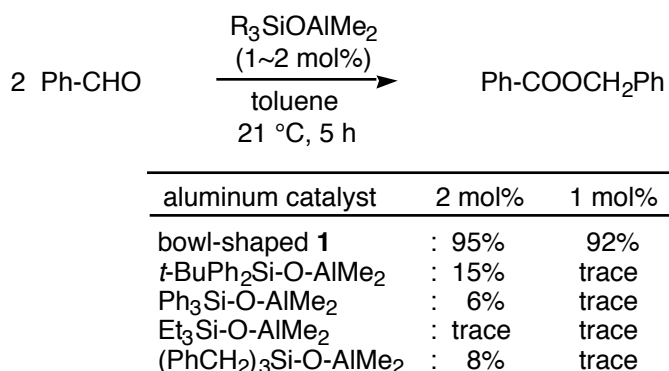
Scheme 1
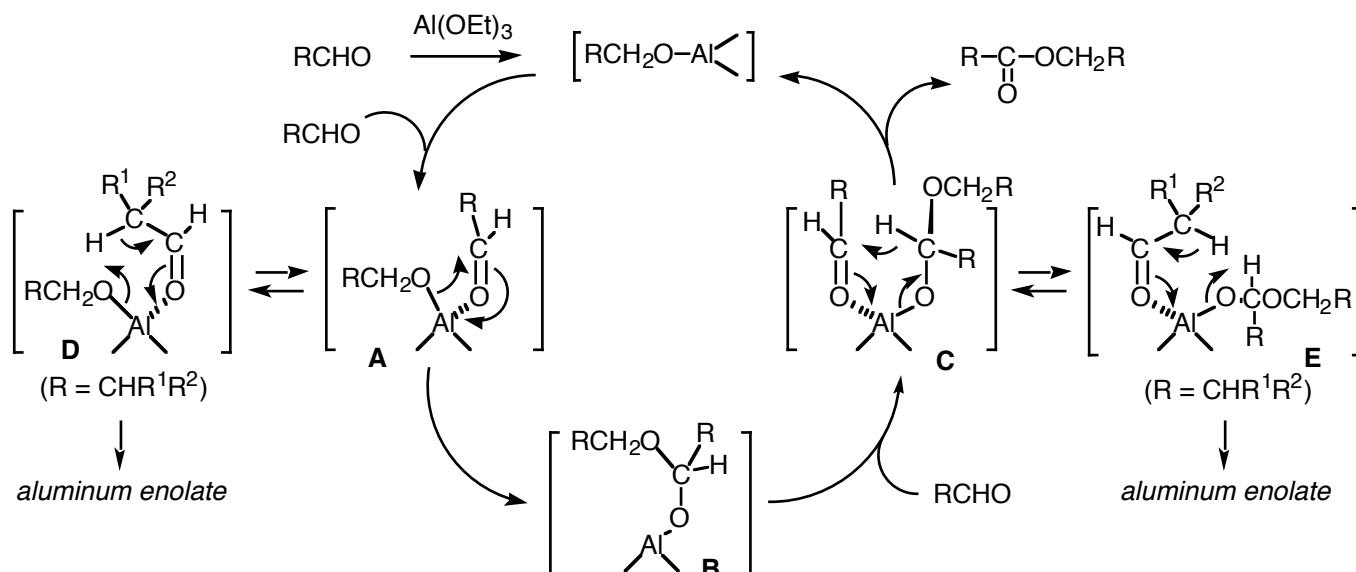
of aluminum alkoxide for further use in this catalytic cycle. However, there are several side-reactions in the Tishchenko reaction. For example, an alkoxy moiety might behave as a base in the case of aliphatic aldehyde (R = CHR^{1}R^2) having α-hydrogens by way of an intermediate [**D**] or [**E**] to give an aluminum enolate which easily reacts with an aldehyde acceptor to furnish aldols and their degradation products. In order to suppress such undesired aldol reactions, the intermediates [**A**] and [**C**] must be favorable compared to other intermediates [**D**] and [**E**], respectively. Accordingly, we are interested in the possibility of using a bowl-shaped [tris(2,6-diphenylbenzyl)siloxy]aluminum catalyst in order to accelerate the smooth alkoxy shift and hydride transfer in the bowl-shaped cavity as shown in [**F**] and [**G**].[6-8]
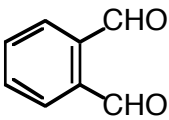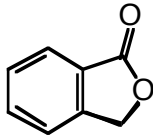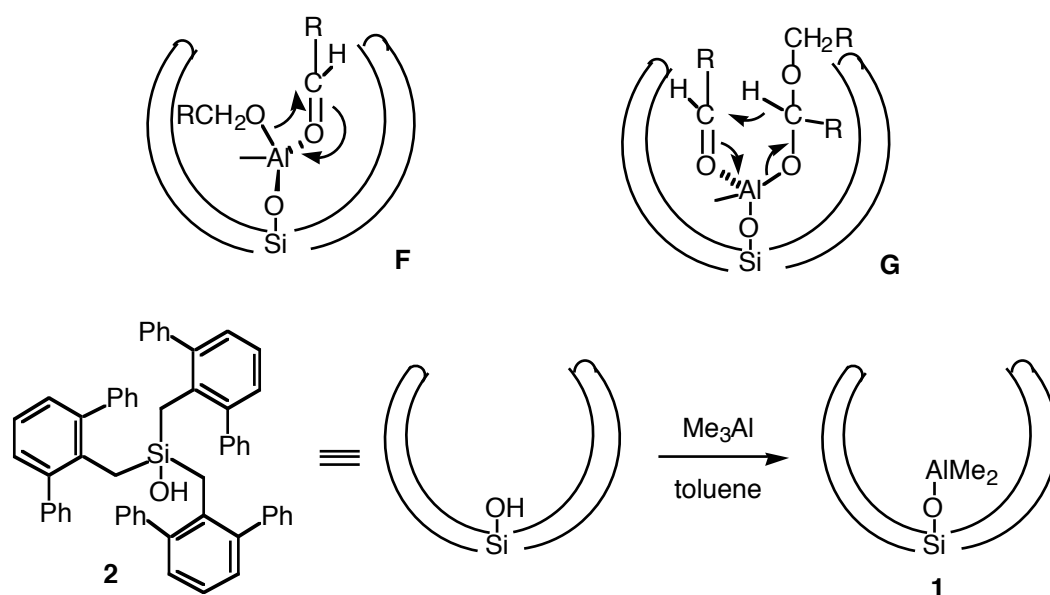

First, we examined the catalytic activity of bowl-shaped [tris(2,6-diphenylbenzyl)siloxy]-dimethylaluminum catalyst (**1**) in the Tishchenko reaction of benzaldehyde. The requisite bowl-shaped aluminum catalyst (**1**) can be prepared by treatment of tris(2,6-diphenylbenzyl)silanol (**2**) in toluene at 21 °C for 15 min. Treatment of benzaldehyde with 2 mol% of *in situ* generated aluminum catalyst (**1**) in toluene at 21 °C for 5 h resulted in formation of the corresponding Tishchenko product, benzyl benzoate in 95% isolated yield after purification by flash chromatography. In contrast, bulky *t*-BuPh$_2$Si-OH derived aluminum reagent gave benzyl benzoate in 15% yield under similar reaction conditions. Ph$_3$Si-O-AlMe$_2$ and Et$_3$Si-O-AlMe$_2$ exhibited only low reactivity (6% and <1% yields, respectively). In addition, (PhCH$_2$)$_3$Si-OH derived aluminum reagent afforded low chemical yield (8%), suggesting the importance of the bowl-shaped framework to accelerate the desired rearrangement. Even a large difference of reactivity was observable by using each 1 mol% of bowl-shaped (**1**) compared to other R$_3$Si-O-AlMe$_2$ catalysts. Notably, the dimerization of benzaldehyde with the standard aluminum catalyst (Al(OPr^i)$_3$; 2 mol%) under otherwise similar reaction conditions gave only 11% of the ester, indicating the remarkable catalytic activity of the bowl-shaped aluminum catalyst (**1**).

$$2 \; Ph\text{-}CHO \xrightarrow[\substack{\text{toluene} \\ 21\,°C,\,5\,h}]{\substack{R_3SiOAlMe_2 \\ (1\sim2\ mol\%)}} Ph\text{-}COOCH_2Ph$$

aluminum catalyst	2 mol%	1 mol%
bowl-shaped **1**	: 95%	92%
t-BuPh$_2$Si-O-AlMe$_2$	: 15%	trace
Ph$_3$Si-O-AlMe$_2$	: 6%	trace
Et$_3$Si-O-AlMe$_2$	: trace	trace
(PhCH$_2$)$_3$Si-O-AlMe$_2$	: 8%	trace

As summarized in Table 1, selected aldehydes can be smoothly dimerized to the corresponding carboxylic esters, revealing the practicability of the present method. The potential of the bowl-shaped aluminum catalyst (**1**) was clearly demonstrated in the reaction of hexanal and hydrocinnamaldehyde, and the corresponding Tishchenko products were constantly obtained in high yields. Since the catalytic system is highly effective for the dimerization of aromatic aldehydes, 1 mol% of the catalyst is generally enough to attain a synthetically satisfactory level of reactivity and chemical yield. *o*-Phthalaldehyde was found to be rapidly converted to the 5-membered lactone almost quantitatively under relatively diluted conditions.

Table 1. High-Speed Tishchenko Reaction with Bowl-Shaped Aluminum Catalyst (**1**) [a]

entry	aldehyde	mol % of catalyst (**1**)	condition (°C, h)	product	% yield [b,c]
1	CH$_3$(CH$_2$)$_4$CHO	1	21, 0.5	CH$_3$(CH$_2$)$_4$CO$_2$(CH$_2$)$_5$CH$_3$	80
2	PhCH$_2$CH$_2$CHO	1	21, 2	PhCH$_2$CH$_2$CO$_2$(CH$_2$)$_3$Ph	80
3	PhCHO	1	21, 5	PhCO$_2$CH$_2$Ph	92
4		2	21, 5		95
5	(o-phthalaldehyde, 1,2-C$_6$H$_4$(CHO)$_2$)	1	21, 0.5	(1(3H)-isobenzofuranone)	99[d]

[a] The Tishchenko reaction of aldehydes was carried out in the presence of bowl-shaped aluminum catalyst (**1**) in freshly distilled toluene under the given reaction conditions. [b] Isolated yield. [c] Substrate concentration of the reaction: 10~20 M. [d] The reaction was performed in a concentration of 5 M because of low solubility of *o*-phthalaldehyde in toluene.

A typical experimental procedure is as follows (entry 3 in Table 1): [Tris(2,6-diphenylbenzyl)silanol (77.5 mg, 0.1 mmol) was placed in a dry two-neck flask with a stirring bar under Ar, and freshly distilled toluene (0.5 mL) was introduced. To this suspension was added a 1 M hexane solution of Me3Al (100

μL, 0.1 mmol) at 21 ℃ and the solution was stirred for 15 min.   Then, freshly distilled benzaldehyde (1.02 mL, 10 mmol) was added dropwise and the reaction mixture was stirred for 5 h at 21 ℃.   The reaction was quenched by the addition of 1 N HCl and the extractive workup was performed with ether. The ethereal extracts were washed with brine and dried over Na_2SO_4.   Evaporation of solvents and purification of the residual oil by column chromatography on silica gel (Et_2O/hexane = 1:40 as eluent) gave benzyl benzoate as colorless oil (976 mg, 4.6 mmol; 92%).

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