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ALKOXIDE TRANSFER FROM ALUMINIUM ALKOXIDE TO ALDEHYDE IN THE TISHCHENKO REACTION[1]

Y. OGATA and A. KAWASAKI
Department of Applied Chemistry, Faculty of Engineering, Nagoya University,
Chikusa-ku, Nagoya, Japan

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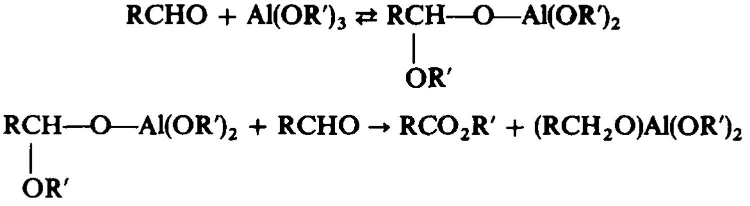
Abstract—Tishchenko reaction of benzaldehyde with various aluminium alkoxides has been studied kinetically in benzene at 20°. The aluminium t-butoxide catalysed reaction shows a long induction period and gives benzyl benzoate (75–90%) together with a small amount of t-butyl benzoate and benzyl alcohol. The initial rate of reaction is decreased in the order: aluminium benzyl oxide > di-t-butoxyaluminium benzyloxide [a reaction mixture of PhCHO–Al(O-t-Bu)$_3$] > aluminium isopropoxide > aluminium t-butoxide. The aluminium benzyloxide catalysed reaction is second-order in benzaldehyde. These results support a mechanism involving an alkoxide transfer from catalyst to aldehyde. A t-butoxide transfer to benzaldehyde is much slower than the benzyloxide transfer because of a large steric interaction between bulky t-butoxide and benzene ring. On the contrary, hydride transfer is rate-determining with aluminium benzyloxide. Electron-withdrawing substituents of aldehyde promote the Tishchenko reaction. Crossed Tishchenko reaction is discussed in terms of the alkoxide transfer and the hydride transfer.

LIN and Day have postulated for the Tishchenko reaction a mechanism where aluminium alkoxide acts as an acid catalyst alone, i.e. a carbonyl C atom activated by the catalyst attacks on the O atom of another aldehyde molecule.[2] However, aluminium alkoxide has been shown to act as an alkoxide transfer agent to aldehyde as well as a Lewis acid.[3–5] Therefore, the formation of esters containing an alkoxide group from aluminium alkoxide catalysts is not a side-reaction but a main reaction at early stages.

$$CH_3CHO \xrightarrow{Al(O\text{-}i\text{-}Pr)_3} CH_3CO_2\text{-}i\text{-}Pr + CH_3CO_2CH_2CH_3$$

The present report provides further evidence for the alkoxide transfer from the catalyst to aldehyde in the Tishchenko reaction of benzaldehyde.



$$RCHO + Al(OR')_3 \rightleftarrows \underset{\displaystyle OR'}{\underset{|}{RCH}}{-}O{-}Al(OR')_2$$

$$\underset{\displaystyle OR'}{\underset{|}{RCH}}{-}O{-}Al(OR')_2 + RCHO \rightarrow RCO_2R' + (RCH_2O)Al(OR')_2$$

RESULTS AND DISCUSSION

The reaction product of benzaldehyde with aluminium benzyloxide is benzyl benzoate and benzyl alcohol. The yield of benzyl benzoate was above 85% and that of benzyl alcohol was below 5%. The benzyl alcohol is formed by hydrolysis of the catalyst aluminium benzyloxide. The aluminium t-butoxide catalysed reaction gave a mixture of benzyl benzoate (75–90%), t-butyl benzoate (ca. 1%) and benzyl alcohol (ca. 0·5%). The data are shown in Fig. 1. Small amounts of t-butyl benzoate and benzyl alcohol are formed at early stages of the reaction with aluminium t-butoxide.

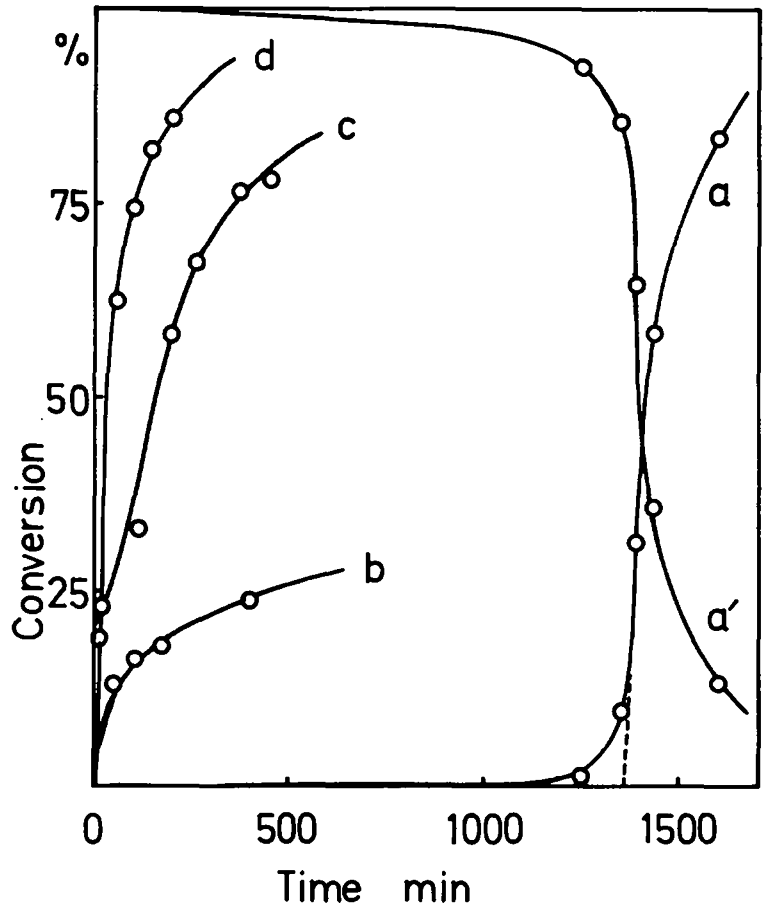
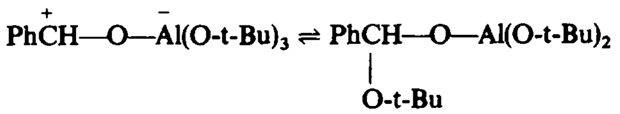


FIG. 1 Conversion of benzaldehyde to benzyl benzoate with various catalysts in benzene at 25°.

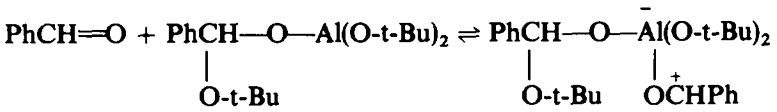
a: Benzaldehyde 3·27M; $Al(O\text{-}t\text{-}Bu)_3$ 0·136M. a′: Consumption of benzaldehyde corresponding to a. b: Benzaldehyde 3·27M; $Al(O\text{-}i\text{-}Pr)_3$ 0·136M. c: Benzaldehyde 2·86M: reaction mixture of (a) after 80% conversion corresponding to $(t\text{-}BuO)_2Al(OCH_2Ph)$ 0·034M. d: Benzaldehyde 1·40M; $Al(OCH_2Ph)_3$ 0·017M.

These facts together with a long induction period (ca. 15–20 hr) for the formation of benzyl benzoate supports the mechanism involving the alkoxide transfer for the Tishchenko reaction of acetaldehyde,[3] i.e.

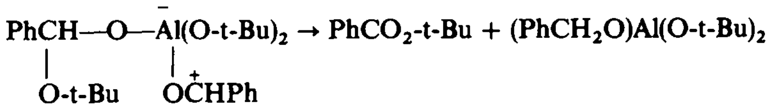
$$PhCH{=}O + Al(O\text{-}t\text{-}Bu)_3 \rightleftharpoons Ph\overset{+}{C}H{-}O{-}\overset{-}{Al}(O\text{-}t\text{-}Bu)_3 \qquad (1)$$



$$\overset{+}{\text{PhCH}}\text{—O—}\overset{-}{\text{Al}}\text{(O-t-Bu)}_3 \rightleftharpoons \underset{\text{O-t-Bu}}{\text{PhCH}}\text{—O—Al(O-t-Bu)}_2 \tag{2}$$



$$\text{PhCH=O} + \underset{\text{O-t-Bu}}{\text{PhCH}}\text{—O—Al(O-t-Bu)}_2 \rightleftharpoons \underset{\text{O-t-Bu}}{\text{PhCH}}\text{—O—}\underset{\text{O}\overset{+}{\text{C}}\text{HPh}}{\overset{-}{\text{Al}}}\text{(O-t-Bu)}_2 \tag{3}$$



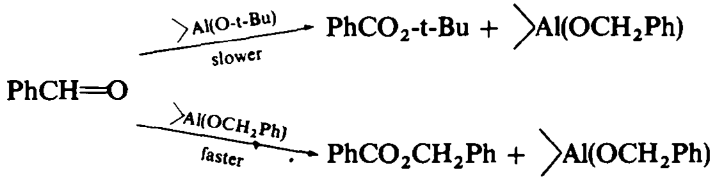
$$\underset{\text{O-t-Bu}}{\text{PhCH}}\text{—O—}\underset{\text{O}\overset{+}{\text{C}}\text{HPh}}{\overset{-}{\text{Al}}}\text{(O-t-Bu)}_2 \rightarrow \text{PhCO}_2\text{-t-Bu} + \text{(PhCH}_2\text{O)Al(O-t-Bu)}_2 \tag{4}$$

Since the Meerwein–Ponndorf–Verley reduction cannot occur with aluminium t-butoxide alone, the benzyl alcohol must be formed by the Tishchenko reaction, i.e. by the hydrolysis of di-t-butoxyaluminium benzyloxide with a trace of water in the system (Eq. 5) or by the exchange of benzyloxide with a trace of t-butyl alcohol in the system (Eq. 6).

$$\text{(t-BuO)}_2\text{Al(OCH}_2\text{Ph)} + \text{H}_2\text{O} \rightarrow \text{(t-BuO)}_2\text{AlOH} + \text{PhCH}_2\text{OH} \tag{5}$$

$$\text{(t-BuO)}_2\text{Al(OCH}_2\text{Ph)} + \text{t-BuOH} \rightarrow \text{(t-BuO)}_3\text{Al} + \text{PhCH}_2\text{OH} \tag{6}$$

The t-butoxide transfer from catalyst to aldehyde gives t-butyl benzoate (Eqs 1–4), whereas the benzyloxide transfer gives benzyl benzoate, i.e.



$$\text{PhCH=O} \xrightarrow[\text{slower}]{>\text{Al(O-t-Bu)}} \text{PhCO}_2\text{-t-Bu} + >\text{Al(OCH}_2\text{Ph)} \tag{7}$$

$$\text{PhCH=O} \xrightarrow[\text{faster}]{>\text{Al(OCH}_2\text{Ph)}} \text{PhCO}_2\text{CH}_2\text{Ph} + >\text{Al(OCH}_2\text{Ph)} \tag{8}$$

The observed long induction period with aluminium t-butoxide is also explicable by this mechanism. The transfer of bulky t-butoxide to coordinated benzaldehyde (Eq. 7) may be slow because of a large steric interaction between t-butoxide and benzene ring. Since most of the aluminium alkoxides are t-butoxide at an early stage, the transfer of t-butoxide ion gives t-butyl benzoate alone (Eqs. 1–4 and 7). But as the reaction proceeds aluminium benzyloxide, $>\text{Al(OCH}_2\text{Ph)}$, should accumulate (Eq. 4) and the transfer of benzyloxide ion (Eq. 8), which is much faster than that of bulky t-butoxide ion, gives benzyl benzoate. It is well known that the esterification of benzoic acid with t-butyl alcohol is sterically hindered. Therefore, the induction period with aluminium t-butoxide is the time for the accumulation of an appropriate amount of aluminium benzyloxide. The steric interferance between the Ph group and t-butoxide can be shown by the Stewart model, and it is also supported by the easy formation of benzoate (or benzyloxide ion transfer to benzaldehyde) in the sodium benzyloxide catalysed Tishchenko reaction of benzaldehyde and by no formation of it in the sodium t-butoxide catalysed reaction in 10 hr (started by t-butoxide ion transfer to benzaldehyde).

When a reaction mixture of benzaldehyde–aluminium t-butoxide after 80% conversion of aldehyde was used instead of aluminium t-butoxide, no induction period was observed and the reaction was fast. This fact suggests that the reaction mixture contains aluminium benzyloxide ($\rangle Al(OCH_2Ph)$) according to Eq. 4. In support of this assumption, the reaction was much faster and no induction period was observed with the aluminium tribenzyloxide catalyst, $Al(OCH_2Ph)_3$ (Eq. 8). Even with less bulky aluminium isopropoxide the reaction was faster than with aluminium t-butoxide and it had no induction period.

The initial rate decreases in the following order (Fig. 1):

$$Al(OCH_2Ph)_3 > \rangle Al(OCH_2Ph) > Al(O\text{-}i\text{-}Pr)_3 > Al(O\text{-}t\text{-}Bu)_3$$

The results agree with the expectation from the steric hindrance for an attack of alkoxide ion on the aldehyde molecule. The transfer of alkoxide ion (Eq. 2) is rate-determining at least with t-butoxide, but the rate-determining step for the benzyloxide catalysed reaction may be hydride transfer, since the reaction is second-order in benzaldehyde in the presence of a small amount of benzoic acid as shown in Table 1. This is in contrast with the Tishchenko reaction of acetaldehyde with aluminium isopropoxide,[3] in which alkoxide transfer is rate-determining.

TABLE 1. SECOND-ORDER RATE CONSTANTS FOR THE TISHCHENKO REACTION OF BENZALDEHYDE WITH $Al(O\text{-}t\text{-}Bu)_3$–$Al(OCH_2Ph)_3$ IN BENZENE AT 20° $[Al(O\text{-}t\text{-}Bu)_3] = 0{\cdot}029M$; $[Al(OCH_2Ph)_3] = 0{\cdot}029M$; $[PhCO_2H] = 0{\cdot}059M$[a]

PhCHO (M)	1·40	1·035	0·690	0·345	0·345
10^4k_2 ($M^{-1}sec^{-1}$)	7·2	5·8	5·7	6·3	6·2

[a] Benzoic acid was added so that the effect of a trace of benzoic acid in benzaldehyde was negligible.

Substituent effect. Crossed Tishchenko reaction of an equimolar mixture of benzaldehyde and *p*-chlorobenzaldehyde (each 9·79 mmoles) with aluminium isopropoxide was carried out at 20°. The products were analysed by GLC at ca. 50% conversion, the data being shown in Table 2.

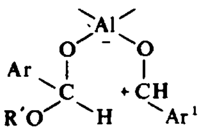
TABLE 2. CROSSED TISHCHENKO REACTION OF EACH 9·79 MMOLES OF PhCHO AND $p\text{-}ClC_6H_4CHO$ WITH $Al(O\text{-}i\text{-}Pr)_3$

Esters	$PhCO_2CH_2Ph$	$ClC_6H_4CO_2CH_2Ph$	$PhCO_2CH_2C_6H_4Cl$	$C_6H_4CO_2CH_2C_6H_4Cl$
mmoles	1·05	0·87	1·40	1·31

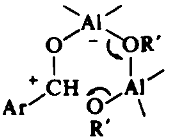
Aldehyde	Aldehyde reacted (mmoles)	Acid component in esters (mmoles)	Alcohol component in esters (mmoles)
PhCHO	4·37	2·45	1·92
p-ClC_6H_4CHO	4·89	2·18	2·71

p-Chlorobenzaldehyde reacts rather faster than benzaldehyde. As apparent from the structure of crossed esters, benzaldehyde tends to be an acid component of the resulting esters, while p-chlorobenzaldehyde to be an alcohol component. This tendency agrees with Lin and Day's observations,[2] i.e. aldenydes having electron-releasing substituents tend to be an acid component of the resulting esters, while aldehydes having electron-withdrawing substituents tend to be an alcohol component. Similar results were obtained with aluminium t-butoxide.

These facts together with the observed second-order kinetics with respect to benzaldehyde (Table 1) suggest that the hydride transfer (Eq. 4) is rate-determining except with aluminium t-butoxide. The activated complex (I) for the hydride transfer may be similar to that[6] of Meerwein–Ponndorf reduction:


(I).

Aldehydes having electron-releasing groups (in Ar of I) may be a better hydride donor, while aldehydes having electron-withdrawing groups (in Ar′ of I) may be a better hydride accepter. Therefore, the former, e.g. benzaldehyde in the present case, tends to be an acid component of the resulting ester and the latter, e.g. p-chlorobenzaldehyde, tends to be an alcohol component. If the alkoxide transfer (Eq. 2) were rate-determining or product-determining (II), the acid component of the resulting esters, derived from p-chlorobenzaldehyde, would be higher than that from benzaldehyde because of the more positive nature of the carbonyl carbon of II.


(II)

The nucleophilicity of p-chlorobenzyloxide ion, in which the reaction centre (oxide anion) is at β-position to p-chlorophenyl group, may be almost similar to that of benzyloxide ion, and then the alcohol component of the resulting ester from p-chlorobenzaldehyde should be higher than that from benzaldehyde, since the concentration of p-chlorobenzyloxide may be higher than that of benzyloxide as expected from the following equilibrium.[7, 8]

$$\mathrm{PhCHO} + \rangle\mathrm{Al(OCH_2C_6H_4Cl}\text{-}p) \rightleftharpoons p\text{-}\mathrm{ClC_6H_4CHO} + \rangle\mathrm{Al(OCH_2Ph)} \tag{9}$$

The mixed Tishchenko reaction of benzaldehyde (9·82 mmoles) and p-anisaldehyde (8·26 mmoles) with aluminium t-butoxide gave benzyl benzoate (3·44 mmoles), benzyl p-methoxybenzoate (2·02 mmoles), and a trace of p-methoxybenzyl benzoate, but *p*-anisaldehyde alone with aluminium t-butoxide did not give the Tishchenko esters.

$$\mathrm{PhCHO} + p\text{-}\mathrm{CH_3OC_6H_4CHO} \rightarrow \mathrm{PhCO_2CH_2Ph} + p\text{-}\mathrm{CH_3OC_6H_4CO_2CH_2Ph} + \mathrm{PhCO_2CH_2C_6H_4OCH_3}\text{-}p\ (\text{trace}) \qquad (10)$$

These facts suggest that an attack of bulky t-butoxide group on *p*-anisaldehyde of weak electrophilicity is difficult because of the steric hindrance and hence Tishchenko esters cannot be formed from *p*-anisaldehyde alone. On the contrary, the attack of t-butoxide group on benzaldehyde having stronger electrophilicity occurs, even if slowly, to form t-butyl benzoate and di-t-butoxyaluminium benzyloxide, and hence an attack of the resulting less bulky benzyloxide group on the carbonyl carbon can give benzyl benzoate and *p*-methoxybenzoate. Since the concentration of the resulting benzyloxide may be much higher than that of *p*-methoxybenzyloxide, benzyl ester may be a major product. The fact that the amount of benzoate formed is more than that of *p*-methoxybenzoate indicates that the products in a mixed reaction may be controlled in part by alkoxide transfer (alkoxide uptake) as well as by hydride transfer (hydride donation).

EXPERIMENTAL

Materials. Commercial benzaldehyde was rectified in vacuum under N_2 atmosphere, b.p. 78° (26 mm). No ppt was formed by the addition of a soln of aluminium t-butoxide to benzaldehyde. *p*-Anisaldehyde was purified analogously, b.p. 159° (44 mm). *p*-Chlorobenzaldehyde was recrystallized from EtOH, m.p. 46·5–47·5°. Aluminium isopropoxide,[9] b.p. 123–129° (3·5 mm), t-butoxide,[10] and benzyloxide[11] were prepared according to the cited references, except for the extraction of t-butoxide with dry ether instead of centrifuge and its recrystallization from benzene. The alkoxides were used as a benzene soln (0·4M). Benzene was purified by the ordinary method and dried over Na, b.p. 80·5°. Sodium benzyloxide and t-butoxide were prepared by the reaction of the corresponding dry alcohol with Na, and used as a benzene soln. Authentic esters were prepared from the corresponding acid chlorides and alcohols in the presence of pyridine except for *p*-chlorobenzyl *p*-chlorobenzoate, which was prepared by the Tischchenko reaction of *p*-chlorobenzaldehyde with aluminium t-butoxide; m.p. 72–72·5°, from EtOH. They are confirmed by GLC and IR. Bps were as follows: *p*-chlorobenzyl benzoate, 199–204° (22 mm); benzyl *p*-chlorobenzoate, 168–174° (9 mm); benzyl benzoate, 194–196° (25 mm); *p*-methoxybenzyl benzoate, 181·5–182·5° (4 mm); benzyl *p*-methoxybenzoate, 188–190° (6 mm); t-butyl benzoate, 111–114° (21 mm).

A typical run for the rate measurements. Benzaldehyde (2·1 g, 0·0198 moles) and 1,2-diphenylethane (0·100 g) as an internal standard for GLC are dissolved in benzene (10·0 ml) in a silicone gum-stoppered test tube filled with N_2 gas. A benzene soln of aluminium t-butoxide (0·4M, 1·0 ml) was added to this soln at 20°, then the reaction was started. Aliquots were taken out at appropriate intervals of time by a syringe (ca. 50 µl) and analysed directly by GLC (Yanagimoto GCG model 220) on a column of 5 mm × 1 m packed with PEG 6000 (30%) or Silicone DC 550 (30%) on Celite 545 (80–100 mesh) with a H_2 flow of 105 ml/min at 220°.

The procedure was as follows for the mixture of catalysts. The reaction was started by addition of a benzene soln of aluminium benzyloxide (0·4M, 1·0 ml) to a benzene (10·0 ml) soln of benzaldehyde (2·1 g), 1,2-diphenylethane (0·100 g), benzoic acid (0·100 g) and aluminium t-butoxide (0·4M, 1·0 ml) which had been kept at 20° for 1 hr.

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