[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF PENNSYLVANIA]

A Study of the Mixed Tischtschenko Reaction

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n-Butyraldehyde was used in the mixed Tischtschenko reactions with the following carbonyl compounds: benzaldehyde, furfural, *m*-nitrobenzaldehyde, chloral, cinnamaldehyde, acrolein and 1,3-dichloroacetone. Benzaldehyde and acetaldehyde were also studied. The mixed ester from the acid of the aldehyde which undergoes the simple Tischtschenko reaction most rapidly is formed in largest amounts. In general higher yields of the mixed ester were obtained by adding excess butyraldehyde slowly to a carbon tetrachloride solution containing the other aldehyde and the catalyst. The probable mechanism for the reaction is discussed.

Little work has been reported on the mixed Tischtschenko reaction. In general equimolecular amounts of different aldehydes were used. Nord[1] isolated furfuryl isobutyrate from furfural and isobutyraldehyde. He reported a fair yield of trichloroethanol from chloral and acetaldehyde; a 31% yield of benzyl isovalerate and 15% of isoamyl benzoate from benzaldehyde and isovaleraldehyde; a 25% yield of benzyl acetate, 29% of ethyl acetate and 8% of benzyl benzoate from benzaldehyde and acetaldehyde. Orloff[2] obtained a 15.3% yield of benzyl isobutyrate and 3.7% of isobutyl benzoate from benzaldehyde and isobutyraldehyde. From benzaldehyde and acetaldehyde, he obtained 39.4% of benzyl acetate and 1.6% of ethyl benzoate.

For the present study the following combinations were used in following the mixed Tischtschenko reaction: benzaldehyde and *n*-butyraldehyde, furfural and *n*-butyraldehyde, chloral and *n*-butyraldehyde, *m*-nitrobenzaldehyde and *n*-butyraldehyde, cinnamaldehyde and *n*-butyraldehyde, acrolein and *n*-butyraldehyde, *sym*-dichloroacetone and *n*-butyraldehyde, and benzaldehyde and acetaldehyde.

Since there is no hydrogen attached to the carbonyl group of ketones, it is apparent that ketones cannot undergo the Tischtschenko reaction. This does not exclude the possibility, however, of reducing active ketones with aldehydes. 1,3-Dichloroacetone gave a mixed Tischtschenko reaction with *n*-butyraldehyde. Acetone, cyclohexanone and dibenzyl ketone gave negative results.

Experimental

Purification of *n*-Butyraldehyde.—The aldehyde was shaken with anhydrous calcium sulfate for 10 minutes. This process was repeated until a 5-ml. sample when mixed with 2.5 ml. of carbon tetrachloride containing 0.5 g. of aluminum isopropoxide produced no precipitate and caused the solution to boil within 2 minutes. The butyraldehyde was then slowly fractionally distilled. An azeotrope of aldehyde and water came over at 68°. When the temperature reached 74°, the distillate was tested at intervals until a 5-ml. sample when mixed with 2.5 ml. of carbon tetrachloride containing 0.5 g. of aluminum isopropoxide remained clear and caused the solution to boil within 30 seconds.

Effect of Temperature on the Simple Tischtschenko Reaction.—*n*-Butyraldehyde (50 ml.) was mixed with 5 ml. of carbon tetrachloride containing 2.5 g. of aluminum isopropoxide. The temperature rose rapidly and the solution boiled. After the reaction was over, the solution was washed with dilute hydrochloric acid and then with water. After drying over anhydrous magnesium sulfate, fractional distillation[3] gave a 60% yield of *n*-butyl *n*-butyrate, b.p. 166°.

The same reaction, when carried out with cooling to keep the temperature below 20°, gave a 94% yield of *n*-butyl *n*-butyrate. It had been noted previously that higher temperatures favor aldol formation and lower temperatures favor the Tischtschenko reaction.[4]

When this reaction was carried out with aluminum *t*-butoxide, a 90% yield of butyl butyrate was obtained. The *t*-butoxide proved to be almost as efficient as the isopropoxide in this case.

Mixed Tischtschenko Reactions.—Aluminum isopropoxide was used throughout. **Procedure I.** The two aldehydes were mixed under nitrogen, cooled to 0° and a solution of aluminum isopropoxide in carbon tetrachloride added. For each mole of aldehyde, 0.025 mole of aluminum isopropoxide dissolved in 10 ml. of pure, dry carbon tetrachloride was used. In general freshly distilled aluminum isopropoxide (b.p. 114–122° at 2 mm.) was more reactive. Immediately after the addition of the isopropoxide, the flask was stoppered and swirled in an ice-bath to keep the temperature below 15°. The flask was kept in the ice-bath for 3 hours and then allowed to stand overnight at room temperature.

The reaction mixture was washed three times with 4 *N* hydrochloric acid and twice with water. After drying over anhydrous magnesium sulfate, the mixture was fractionally distilled. Each fraction was weighed and its density and refractive index determined. In some cases the unused aldehyde was determined by the bisulfite method.[5]

Procedure II.—This method was similar to I except for the following changes. The slower reacting aldehyde was added to the isopropoxide solution with stirring and cooling. The *n*-butyraldehyde was then added slowly, keeping the temperature below 15°.

The yields of the various esters usually could not be determined by fractional distillation alone. The mixed esters had boiling points which did not vary more than 5–10° at atmospheric pressure or 1–3° at reduced pressures. In these cases, the fraction containing the mixed esters was treated as follows: A 10-ml. sample was added to 36 ml. of ethylene glycol containing 0.5 ml. of water and 6 g. of potassium hydroxide. The mixture was heated until it became homogeneous and then was slowly distilled until no more butyl alcohol distilled over. The amount of butyl alcohol obtained was a measure of the amount of the butyl ester present. The accuracy of the method was confirmed by carrying out this procedure on mixtures of the two esters of known composition. In every case good results were obtained.

Reaction of Benzaldehyde and *n*-Butyraldehyde.—Similar results were obtained from both procedures I and II. In both cases the procedures were followed to the point where the reaction mixture was washed with water. At this point the solution was extracted with 10% sodium bisulfite to remove unreacted benzaldehyde. The ester mixture was dried over calcium chloride and fractionally distilled.

Example.—Benzaldehyde (28.9 g.), 49.4 g. of *n*-butyraldehyde, 4.5 g. of aluminum isopropoxide and 30 ml. of carbon tetrachloride were used. The molar ratio of benzal-

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[1] F. F. Nord, *Biochem. Z.*, **106**, 275 (1920); *Beitrage Physiologie*, **2**, 301 (1924); German Patent 434,728 (1926).

[2] N. A. Orloff, *Bull. soc. chim.*, **35**, 360 (1924).

[3] Most of the distillations reported in this paper were carried out in the Todd distillation apparatus, *Ind. Eng. Chem.*, *Anal. Ed.*, **17**, 175 (1945).

[4] W. C. Child and H. Adkins, THIS JOURNAL, **45**, 3013 (1923); **47**, 789 (1925).

[5] A. E. Parkinson and E. C. Wagner, *Ind. Eng. Chem.*, *Anal. Ed.*, **6**, 433 (1934).

dehyde to *n*-butyraldehyde was 1:2.5. The following yields were obtained: *n*-butyl *n*-butyrate 33.5 g. (b.p. 166°, 84° (41 mm.)), benzyl *n*-butyrate 34 g. (b.p. 240°, 124–126° (14 mm.)), *n*-butyl benzoate 2.2 g. The butyl benzoate was in the fraction distilling at 124–126° (14 mm.). It was determined by measuring the amount of *n*-butyl alcohol formed by saponification. The yields of benzyl *n*-butyrate and *n*-butyl benzoate, based on the benzaldehyde, were 70% and 4.5%, respectively. The molar ratio of *n*-butyl *n*-butyrate to benzyl *n*-butyrate was 1:0.82.

When benzaldehyde and *n*-butyraldehyde were used in the ratio of 1:1, the molar ratio of *n*-butyl *n*-butyrate to benzyl *n*-butyrate changed to 1:1.47 and appreciable amounts of benzyl benzoate were formed. For example, where 51.5 g. of benzaldehyde and 34.7 g. of butyraldehyde were used, 24 g. of benzyl benzoate were formed. The benzyl benzoate, left in the residue after the fractional distillation, was saponified and the benzyl alcohol separated by fractional distillation.

Reaction of Furfural and *n*-Butyraldehyde.—Procedure II gave higher yields of furfuryl *n*-butyrate than procedure I. Example: furfural (86.6 g.), 66 g. of *n*-butyraldehyde, 7.5 g. of aluminum isopropoxide and 15 ml. of carbon tetrachloride were used. The furfural was purified by distillation in a nitrogen atmosphere. The fraction boiling at 161.5–162.5° was used. The addition of the isopropoxide to the furfural produced a white precipitate which did not disappear until two-thirds of the butyraldehyde was added; time of addition of the butyraldehyde, 8 hr. The following yields were obtained: *n*-butyl *n*-butyrate 35.4 g., furfuryl *n*-butyrate 52.3 g. (b.p. 129–129.5° (52 mm.), d^{24}_{4} 1.0480, n^{20}_{D} 1.4586), *n*-butyl furoate 1.1 g. (b.p. 118–120° at (25 mm.)). Forty-two grams of furfuraldehyde was recovered. In this particular experiment the molar ratio of furfural to butyraldehyde was 1:1. The use of larger amounts of butyraldehyde had little influence on the yields of furfuryl butyrate.

Reaction of Chloral and *n*-Butyraldehyde.—Chloral distilled from phosphorus pentoxide was used. Procedure I was followed for these experiments. Example: chloral (60.4 g.), 88.8 g. of *n*-butyraldehyde, 8.4 g. of aluminum isopropoxide and 16.8 ml. of carbon tetrachloride were used. Fractional distillation of the products gave a fraction boiling at 87.5–88° at 47 mm. which contained 73.2% by volume of *n*-butyl *n*-butyrate and 26.8% of trichloroethanol. The latter was removed by extraction with sodium hydroxide solution and reprecipitated as an oil by neutralization with hydrochloric acid. Its 2,4-dinitrobenzoate melted at 140–141°. The trichloroethyl *n*-butyrate fraction (115–130° (47 mm.)) was refractionated and the ester collected at 119.8–120° (48 mm.).

Anal. Calcd. for $C_6H_9O_2Cl_3$: C, 32.83; H, 4.13. Found: C, 32.86; H, 4.07.

The following yields were obtained: *n*-butyl *n*-butyrate 56 g., trichloroethanol 12 g. (19.8%), trichloroethyl *n*-butyrate 40.2 g. (44.7%). The molar ratio of chloral to butyraldehyde in this experiment was 1:3. The use of only one mole of butyraldehyde reduced the yield of butyl butyrate to 14 g. and the trichloroethanol to 5.7 g. The yield of the mixed ester was not changed significantly.

Reaction of *m*-Nitrobenzaldehyde and *n*-Butyraldehyde.—A mixture of 30 g. of *m*-nitrobenzaldehyde and 42 g. of *n*-butyraldehyde was added over a period of 20 minutes to a cold solution of 4 g. of aluminum isopropoxide in 8 ml. of carbon tetrachloride. Otherwise the experiment followed procedure I. The following yields were obtained: *n*-butyl *n*-butyrate 29.4 g., *m*-nitrobenzyl *n*-butyrate 30.3 g. (68%), *n*-butyl *m*-nitrobenzoate 4.5 g. (10%). The two mixed esters were in the fraction boiling at 171–173° (4 mm.). This fraction was analyzed by determining the amount of *n*-butyl alcohol formed by saponification. The molar ratio of *n*-butyl *n*-butyrate to *m*-nitrobenzyl *n*-butyrate was 1:0.67.

Reaction of Cinnamaldehyde and *n*-Butyraldehyde.—The cinnamaldehyde was purified by fractional distillation, b.p. 132–133° (15 mm.). Procedure II was followed. Example: cinnamaldehyde (52.3 g.) was added to a solution of 10.6 g. of aluminum isopropoxide in 21 ml. of carbon tetrachloride. A white precipitate formed which gradually dissolved as the butyraldehyde was added. The latter (119 g.) was added in 5-ml. portions at half-hour intervals. The following yields were obtained: *n*-butyl *n*-butyrate 82.5 g., cinnamyl *n*-butyrate 47.7 g. (59%), b.p. 136° (3 mm.). No *n*-butyl cinnamate was found. The molar ratio of *n*-buty-*n*-butyrate to cinnamyl *n*-butyrate was 1:0.41.

Reaction of Acrolein and *n*-Butyraldehyde.—The acrolein was freshly distilled before each experiment. Procedure II gave the best yield of allyl *n*-butyrate, the only mixed ester obtained. A voluminous white precipitate formed when the acrolein (20.2 g.) was added to a solution of 11 g. of aluminum isopropoxide in 22 ml. of carbon tetrachloride. The precipitate disappeared as the *n*-butyraldehyde (130 g.) was slowly added over a period of 9 hours. The molar ratio of acrolein to butyraldehyde was 1:5. A small amount of phenyl-β-naphthylamine (0.05 g.) was added to inhibit polymerization. The following yields were obtained: *n*-butyl *n*-butyrate 54 g., allyl *n*-butyrate 13.3 g. (28.8%), b.p. 147°, d^{25}_{4} 0.894, n^{24}_{D} 1.4126.

Anal. Calcd. for $C_7H_{12}O_2$: C, 65.60; H, 9.43. Found: C, 65.38; H, 9.42.

The molar ratio of *n*-butyl *n*-butyrate to allyl *n*-butyrate was 1:0.28. Equally good results were obtained when the acrolein and butyraldehyde were used in the ratio of 1:3 instead of the 1:5 ratio used above.

Reaction of 1,3-Dichloroacetone and *n*-Butyraldehyde.—Dichloroacetone (33 g.) and 18.8 g. of butyraldehyde in 35 ml. of carbon tetrachloride were added to a solution of 6 g. of aluminum isopropoxide in 12 ml. of carbon tetrachloride. The temperature was kept at 24° for 1.5 hours, to prevent the crystallization of the ketone. The temperature was then lowered to 16° and 56.4 g. (69 ml.) of butyraldehyde added in 5-ml. portions at 45-minute intervals. The ratio of ketone to aldehyde was 1:4. After standing overnight, the mixture was washed with dilute hydrochloric acid, water and finally with 5% sodium bisulfite. The solution was dried over anhydrous magnesium sulfate and fractionally distilled. The following yields were obtained: *n*-butyl *n*-butyrate 46.4 g., dichloroisopropyl *n*-butyrate 12.3 g. (23.8%), b.p. 110° at 15 mm., 1,3-dichloropropanol-2, 6.3 g. or 18.8%, b.p. 92° at 48 mm.

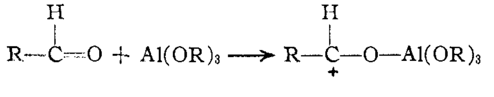
Reaction of Benzaldehyde and Acetaldehyde.—The acetaldehyde was distilled through a column of dry calcium chloride just before using, b.p. 20–21°. The benzaldehyde was distilled in an atmosphere of nitrogen, b.p. 179–180°. Procedure I was followed to the water-washing step and the mixture extracted several times with 5% sodium bisulfite solution. After drying, the solution was fractionally distilled. Example: acetaldehyde (28.5 g.) and 32 g. of benzaldehyde (molar ratio 2:1) were treated with 3 g. of aluminum isopropoxide in 25 ml. of dry ether. The following yields were obtained: ethyl acetate 16.3 g., benzyl acetate 27.7 g. (56.8%), ethyl benzoate 0.5 g. (1.1%). Eleven grams of benzaldehyde was recovered. The molar ratio of ethyl acetate to benzyl acetate was 1:0.92. The use of smaller amounts of acetaldehyde gave lower yields of benzyl acetate.

Discussion

It can be seen that the mixed ester derived from the acid of the aldehyde which undergoes the simple Tischtschenko reaction most rapidly is formed in largest amounts. The fact that one mixed ester greatly predominates over the other serves to eliminate the possibility of any significant ester exchange between two simple esters.

The yields of mixed esters can be increased by keeping the concentration of the faster reacting aldehyde low at all times. However, it was noted that when the slower reacting aldehyde was an α,β-unsaturated aldehyde, if the faster reacting aldehyde is added too slowly polymerization of the unsaturated aldehyde may become a predominant reaction.

It is believed that the first step in the Tischtschenko reaction is the coördination of the aluminum atom of the alkoxide with the oxygen of the carbonyl group.



$$R-\overset{\displaystyle H}{\overset{|}{C}}=O + Al(OR)_3 \longrightarrow R-\underset{+}{\overset{\displaystyle H}{\overset{|}{C}}}-O-Al(OR)_3$$

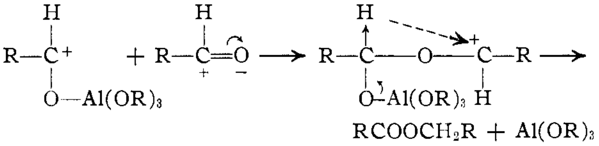
TABLE I

MOLAR RATIO OF MIXED ESTERS

Relative rates of aldehydes in simple Tischtschenko reaction[a]		Relative yields	
n-C_3H_7CHO	C_6H_5CHO	Benzyl butyrate	Butyl benzoate
1	0.07	1	0.07
n-C_3H_7CHO	$C_6H_5CH{=}CHCHO$	Cinnamyl butyrate	Butyl cinnamate
1	Very slow	1	0
n-C_3H_7CHO	Furfural	Furfuryl butyrate	Butyl furoate
1	0.02	1	0.02
n-C_3H_7CHO	Cl_3CCHO	Trichloroethyl butyrate	Butyl trichloroacetate
1	Slow	1	0.07
n-C_3H_7CHO	m-$O_2NC_6H_4CHO$	Nitrobenzyl butyrate	Butyl nitrobenzoate
1	0.30	1	0.15
CH_3CHO	C_6H_5CHO	Benzyl acetate	Ethyl benzoate
1	0.05	1	0.02

[a] Values from Child and Adkins, ref 2.

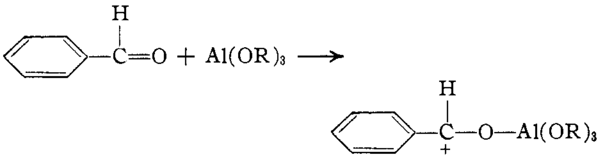
This coördination makes the carbonyl carbon atom sufficiently positive to initiate the next step.



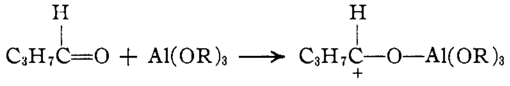
$$\mathrm{R{-}\overset{H}{\underset{O-Al(OR)_3}{C^+}} + R{-}\overset{H}{\underset{+\ \ -}{C{=}O}} \longrightarrow R{-}\overset{H}{\underset{O-Al(OR)_3}{C}}{-}O{-}\overset{+}{\underset{H}{C}}{-}R \longrightarrow RCOOCH_2R + Al(OR)_3}$$

The loss of a hydride ion (oxidation) and its acceptance (reduction) by another aldehyde molecule are the important features of the Tischtschenko reaction.

The mixed Tischtschenko mechanism is more complex. In the case of benzaldehyde and n-butyraldehyde, for example, either aldehyde could coördinate with the alkoxide.



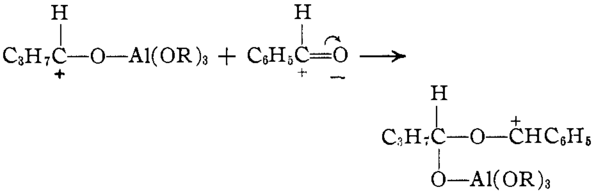
I



$$\mathrm{C_3H_7\overset{H}{C}{=}O + Al(OR)_3 \longrightarrow C_3H_7\overset{H}{\underset{+}{C}}{-}O{-}Al(OR)_3}$$

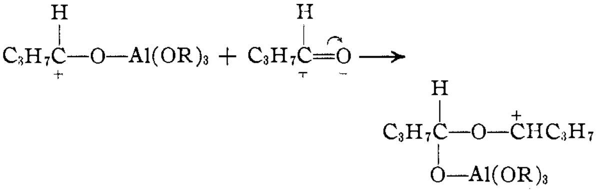
II

Carbonium ion II is undoubtedly more active than I and of the four possible combinations the following appear to be most probable.



$$\mathrm{C_3H_7\overset{H}{\underset{+}{C}}{-}O{-}Al(OR)_3 + C_6H_5\overset{H}{\underset{+\ -}{C{=}O}} \longrightarrow C_3H_7\overset{H}{\underset{O-Al(OR)_3}{C}}{-}O{-}\overset{+}{C}HC_6H_5}$$

III

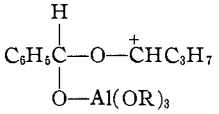


$$\mathrm{C_3H_7\overset{H}{\underset{+}{C}}{-}O{-}Al(OR)_3 + C_3H_7\overset{H}{\underset{+\ -}{C{=}O}} \longrightarrow C_3H_7\overset{H}{\underset{O-Al(OR)_3}{C}}{-}O{-}\overset{+}{C}HC_3H_7}$$

IV

The relative amounts of III and IV would depend to a considerable extent on the rate of addition of the butyraldehyde.

One might expect hydride ion transfer to take place most readily in the carbonium ion.



$$\mathrm{C_6H_5\overset{H}{\underset{O-Al(OR)_3}{C}}{-}O{-}\overset{+}{C}HC_3H_7}$$

V

However, very little n-butyl benzoate was formed. Until more data are available, it is not possible to say with certainty whether the formation of III, IV and V or the transfer of hydride ion is the rate-determining step.

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