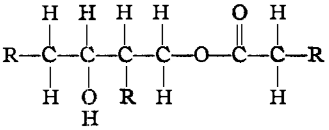
[CONTRIBUTION NO. 50 FROM THE DEPARTMENT OF ORGANIC CHEMISTRY, FORDHAM UNIVERSITY]

Essential Steps in the Catalytic Condensation of Carbonyl Compounds. III. The Action of Metallic Alkoxides[1]

BY FRANK J. VILLANI AND F. F. NORD[2,3]

A modification of the Cannizzaro reaction was discovered by Claisen,[4] who found that benzaldehyde was converted into benzyl benzoate in the presence of sodium alkoxides. Tischtschenko and co-workers[5] extended these findings by showing that both aliphatic and aromatic aldehydes were condensed in this way in the presence of aluminum alkoxides.

Later Kulpinski and Nord[6] investigated the functioning of magnesium aluminum coördination complexes of the general formula $Mg[Al(OR)_4]_2$ as catalysts for the condensation of aldehydes. They showed that in the presence of these agents aldehydes of general formula, RCH_2CHO, would condense not only to simple esters, $RCH_2COOCH_2CH_2R$, as with the aluminum alkoxides, but also to trimeric glycol esters of general formula



$$R-\overset{H}{\underset{H}{C}}-\overset{H}{\underset{OH}{C}}-\overset{H}{\underset{R}{C}}-\overset{H}{\underset{H}{C}}-O-\overset{O}{\overset{\|}{C}}-\overset{H}{\underset{H}{C}}-R$$

In the present study an investigation of the relative catalytic activity with respect to the various types of condensation has been carried out for a number of metallic alkoxides. In addition the catalytic condensing action of aluminum ethoxide and magnesium aluminum ethoxide with respect to a number of different types of aldehydes has been determined to discover the structural factors affecting the formation of the different types of condensation products.

Experimental

Preparation of Catalysts.[6]—The appropriate metal or metals were placed in a liter round-bottom flask, equipped with efficient reflux condenser and a calcium chloride tube, and treated with an excess of absolute ethanol, adding—for all but the sodium ethoxide—a small crystal of iodine and a few grains of mercuric chloride to facilitate the reaction. After the initial reaction had subsided, the mixture was heated on a water-bath for several hours. Excess solvent was then removed by evacuating the flask, first with a water pump and finally with an oil pump.

The crude aluminum ethoxide and magnesium aluminum ethoxide were then purified by distillation, the former boiling at 187–190° (7 mm.) and the latter at 235–237° (1 mm.). The crude sodium magnesium ethoxide was recrystallized from anhydrous bromobenzene. The other ethoxides could not be distilled and were used in the crude state.

Procedure.—A weighed quantity of the aldehyde being tested was placed in an Erlenmeyer flask and a weight of catalyst equal to 5% of the weight of aldehyde was added. The flask was stoppered quickly and placed in an ice-bath for several hours. Finally the mixture was permitted to stand for twenty-four to forty-eight hours at room temperature. In general the reaction mixture, which was usually pale yellow at this point, was fractionally distilled under vacuum without further treatment. The various fractions were then washed with 10% sodium carbonate, extracted with ether, dried over anhydrous sodium sulfate and redistilled. Frequently similar fractions from condensations with different catalysts were combined before the final redistillation.

Some of the condensations required variations of this procedure. In the condensations involving benzaldehyde the reaction mixture, after standing, was treated with excess 10% hydrochloric acid and warmed on a steam-bath for twenty minutes. It was then subjected to ether extraction, dried and distilled. A similar procedure was followed with the mixtures resulting from the crossed condensations with chloral and acetaldehyde and with benzaldehyde and acetaldehyde. In the case of acetophenone the reaction mixture was heated under reflux for five hours after the reactants were mixed and then was subjected to the usual distillation procedure.

The addition of the catalyst to phenylacetaldehyde and to the mixture of chloral and acetaldehyde led within a short time to the formation of precipitates, which were identified as a polymer of phenylacetaldehyde in the first instance and of chloral in the second.

Identification of Products.—The simple esters were saponified by refluxing them with alcoholic alkali and then the acid and alcohol formed were characterized by conversion to known solid derivatives. The glycol esters were similarly saponified and the physical properties of the glycol and acid were determined for comparison with values where known. Analyses and determination of physical constants were carried out for those substances previously unreported.

Unsaturated aldehydes obtained as a result of aldol-type condensations were identified by means of their 2,4-dinitrophenylhydrazones.

Results and Discussion

The studies on the functioning of various alkoxides were conducted with three aldehydes—butyraldehyde, octaldehyde and α-ethylbutyraldehyde. The yields of simple ester and glycol ester obtained for each of these compounds with each of the metallic ethoxides are shown in Table I. It is seen that with the α-CH_2 aldehydes, butyraldehyde and octaldehyde, both the simple and complex calcium and magnesium ethoxides, which are moderately basic, catalyzed the trimeric condensation of the aldehydes to glycol esters. On the other hand, the aluminum ethoxide, which is the least basic of the catalysts studied, catalyzed only the formation of simple esters by way of the Tischtschenko reaction, and the highly basic sodium ethoxide produced only aldol-type condensations with these aldehydes, to yield the α,β-

---

(1) For paper II in this series, see Villani and Nord, THIS JOURNAL, **68**, 1674 (1946).

(2) Abstracted from a portion of the thesis by Frank J. Villani submitted to the Graduate Faculty of Fordham University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(3) Presented in part before the Division of Organic Chemistry, American Chemical Society, Atlantic City, N. J., April, 1946.

(4) Claisen, *Ber.*, **20**, 646 (1887).

(5) Tischtschenko, *Chem. Zentr.*, **77**, I, 1309, 1554, 1556 (1906).

(6) Kulpinski and Nord, *J. Org. Chem.*, **8**, 256 (1943).

unsaturated aldehydes when subsequently distilled.

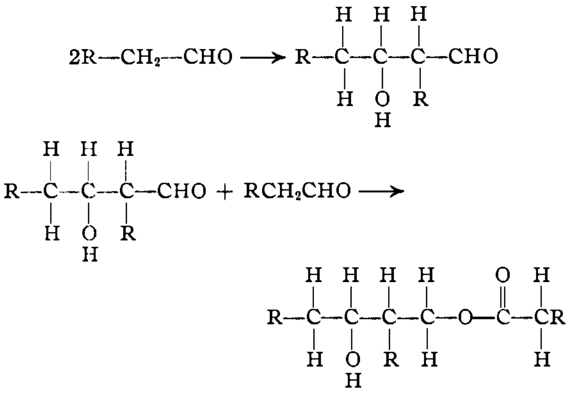
TABLE I

CONDENSATION OF α-CH_2 ALDEHYDES WITH METALLIC ETHOXIDE CATALYSTS

Catalyst	Yield of ester, % Butyraldehyde Simple[a]	 Butyraldehyde Glycol[b]	 Octaldehyde Simple[c]	 Octaldehyde Glycol[d]	 α-Ethyl butyraldehyde Simple[e]	 α-Ethyl butyraldehyde Glycol[f]
$Al(OC_2H_5)_3$	81.6	0	69.1	0	70	0
$Mg[Al(OC_2H_5)_4]_2$	26.4	44.4	19.6	42.5	54	6
$Ca[Al(OC_2H_5)_4]_2$	14.6	22.9	12.0	20.5	..	..
$Na_2Mg(OC_2H_5)_4$	3.1	41.1	..	..	..	..
$Mg(OC_2H_5)_2$	7.1	32.1	3.2	28.0	..	..
$Ca(OC_2H_5)_2$	6.8	50.3	13.1	40.4	51	4.3
$NaOC_2H_5$	0[g]	0	0[h]	0	..	34.3

[a] Butyl butyrate. [b] Monobutyrate of 2-ethyl-1,3-hexanediol. [c] Octyl octylate. [d] Monoöctylate of 2-hexyl-1,3-decanediol. [e] α-Ethylbutyl α-ethylbutyrate. [f] Mono-α-ethylbutyrate of 2,2,4-triethyl-1,3-hexanediol. [g] A yield of 88.5% of dehydrated aldol, α-ethyl-β-propylacrolein, was obtained. [h] A yield of 79.1% of dehydrated aldol, α-hexyl-β-heptylacrolein, was obtained.

It is believed that the formation of the glycol esters from aldehydes with two α-hydrogens can be explained as a two-step reaction involving first the formation of an aldol and secondly a crossed Cannizzaro reaction of the aldol with aldehyde to produce the trimeric glycol ester. This reaction scheme is indicated by the equations



$$2R{-}CH_2{-}CHO \longrightarrow R{-}\underset{H}{\overset{H}{C}}{-}\underset{\underset{H}{O}}{\overset{H}{C}}{-}\underset{R}{\overset{H}{C}}{-}CHO$$

$$R{-}\underset{H}{\overset{H}{C}}{-}\underset{\underset{H}{O}}{\overset{H}{C}}{-}\underset{R}{\overset{H}{C}}{-}CHO + RCH_2CHO \longrightarrow R{-}\underset{H}{\overset{H}{C}}{-}\underset{\underset{H}{O}}{\overset{H}{C}}{-}\underset{R}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}O{-}\overset{\overset{O}{\|}}{C}{-}\underset{H}{\overset{H}{C}}R$$

That some aldol is produced under conditions leading to the formation of glycol esters is shown by the condensation of phenylacetaldehyde in the presence of magnesium aluminum ethoxide, which gave 20% of glycol ester and 48% of α-phenyl-β-tolylacrolein.

Such a mechanism indicates that the reagents catalyzing glycol ester formation are bifunctional in nature.[7] Additional evidence for this view is the fact that the formation of simple esters invariably occurs along with glycol ester formation.

The proposed mechanism is further substantiated by the observation that the yield of glycol ester is increased at low temperatures, a condition which favors the accumulation of the supposed aldol intermediate. This is illustrated by experiments with butyraldehyde and calcium ethoxide. The addition of calcium ethoxide to butyraldehyde results in a rather vigorous exothermic reaction. When the reactants were mixed at room temperature without cooling, a yield of 24% of simple ester and 39% of glycol ester was obtained, but when the aldehyde was cooled in an ice–salt-bath before the calcium ethoxide was added, then only 7% of simple ester, but 50% of glycol ester, resulted.

Markedly different results were obtained with α-substituted aldehydes, as is illustrated by the experiments with α-ethyl butyraldehyde. Several decades ago the isolation of glycol esters from this type of aldehyde, using strongly basic inorganic catalysts or sodium ethoxide, was reported.[8] In the present experiments it was found that the magnesium coördination catalysts produced mainly simple esters with only a small fraction of the glycol ester. Even the basicity of calcium ethoxide was apparently insufficient to bring about the primary aldolization required for glycol ester formation.

Studies of the catalytic effects of aluminum ethoxide and of magnesium aluminum ethoxide on a variety of aldehydes, shown in Table II, indicate that other aldehydes than aliphatic ones having the α-CH_2 grouping do not give appreciable amounts of glycol ester with the magnesium alumi-

TABLE II

ACTION OF ALUMINUM ETHOXIDE AND MAGNESIUM ALUMINUM ETHOXIDE ON VARIOUS ALDEHYDES

Aldehyde	Yield of ester, % Catalyst, $Al(OC_2H_5)_3$ Simple[a]	 Catalyst, $Al(OC_2H_5)_3$ Glycol[b]	 Catalyst, $Mg[Al(OC_2H_5)_4]_2$ Simple[a]	 Catalyst, $Mg[Al(OC_2H_5)_4]_2$ Glycol[b]
Citronellal	75.2	..	32.8	46.3
Hydrocinnamic aldehyde	66.2	0	69.0	0
Benzaldehyde	..	..	57.0[c]	0
Chloral	26[c]	0	[d]	0
Phenylacetaldehyde	32.0	0	[e]	20
Chloral and acetaldehyde	..	..	..	22.5, 5.5[g]
Benzaldehyde and acetaldehyde	..	..	7.8[h]	37[i]
Acetophenone	10[j]	0	11[j]	0

[a] Formula is $RCOOCH_2R$, if aldehyde is RCHO. [b] Formula is $RCH_2CHOHCHRCH_2OOCCH_2R$, where aldehyde is RCH_2CHO. [c] Additional alcohol and acid components of the ester were isolated in these cases. [d] No ester was obtained, but 42% of trichloroethanol and 20% of trichloroacetic acid were isolated. [e] Dehydrated aldol, α-phenyl-β-tolylacrolein, was isolated in 48% yield. [f] A mixture of ethyl acetate, trichloroethyl acetate, ethyl trichloroacetate, trichloroethyl trichloroacetate and trichloroethanol was obtained. [g] Yield of 22% was monoacetate of 1,3-butanediol; 9.3% was monoacetate of 4,4,4-trichloro-1,3-butanediol. [h] Benzyl acetate. [i] Monoacetate of 1,3-butanediol; 6.1% (4 g.) of cinnamyl acetate was also obtained. [j] Identified as "dypnone."

---

(7) Kulpinski and Nord, *Nature*, **151**, 363 (1943).

(8) Fossek, *Monatsh.*, **2**, 614 (1881); Brauchbar and Kohn, *ibid.*, **19**, 16 (1898); Franke and Kohn, *ibid.*, **19**, 354 (1898).

TABLE III

NEW COMPOUNDS ISOLATED FROM CONDENSATIONS OF ALDEHYDES

Compound	Starting aldehyde	Yield, %	B. p. °C.	Mm.	n_{25}	d_{25}	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
Monoöctylate of 2-hexyl-1,3-decanediol	Octylaldehyde[a]		207–209	1	1.4530[b]	0.8344	75.00	75.09	12.50	12.83
Citronellyl citronellate	Citronellal	75.2	186–188	10	1.4732[c]	0.8574	...	...	...	...
Monophenylacetate of 2,4-diphenyl-1,3-butanediol	Phenyl acetaldehyde	20	240–245	2	....	....	...	...	...	...
Monoacetate of 4,4,4-trichloro-1,3-butanediol	Chloral and acetaldehyde	9.3	99–102	12	1.4689[e,f]	1.3327[f]	30.77	29.95	3.97	4.98
Monocitronellate of 5,9-dimethyl-2-(1,5-dimethyl-5-hexene)-9,10-decene-1,3-diol	Citronellal	46.3	273–276	13	1.4817[d]	0.8685	77.92	77.03	12.07	11.00

[a] See Table I. [b] Molar refraction: found 123.2; calcd. 124.4. [c] Molar refraction: found 98.67; calcd. 98.95. [d] Molar refraction: found 141.9; calcd. 142.4. [e] Molar refraction: found 48.78; calcd. 48.32. [f] 26°.

num ethoxide, and none is given in any instance with the aluminum ethoxide. Phenylacetaldehyde and α-ethylbutyraldehyde showed a slight tendency to form glycol esters under the influence of the complex catalyst, but hydrocinnamic aldehyde and the others tested gave none. However, the results of the crossed condensations of chloral and acetaldehyde and of benzaldehyde and acetaldehyde show that chloral and benzaldehyde—and presumably other aldehydes without the α-CH_2 grouping—may enter into certain phases of the formation of a mixed glycol trimer. This is further evidence for the two-step, bifunctional character of the catalysts which promote the glycol ester synthesis.

That a higher basicity may be required for glycol ester formation with some of these other aldehydes is indicated by the fact that sodium ethoxide is effective in producing this type of condensation with α-ethylbutyraldehyde.

The properties of compounds not previously reported which have been obtained as a result of these experiments are shown in Table III.

Acknowledgment.—A number of compounds used in this study were obtained through the courtesy of the Commercial Solvents Corporation, Givaudan–Delawanna, Inc., and the Carbide and Carbon Chemicals Corporation. The work also had the support of the Bache fund of the National Academy of Sciences.

Summary

1. Studies of the condensation of various aldehydes catalyzed by metallic alkoxides show that with α-CH_2 aldehydes the acidic ethoxide, $Al(OC_2H_5)_3$, produces simple esters by means of the Tischtschenko reaction, while mildly basic ethoxides, such as $Mg(OC_2H_5)_2$, $Ca(OC_2H_5)_2$, $Mg[Al(OC_2H_5)_4]_2$, and $Na_2Mg(OC_2H_5)_4$, lead to the formation of trimeric glycol esters in preference to the simple esters. The highly basic sodium ethoxide produces only aldol-type condensations with these aldehydes.

2. The formation of the glycol esters has been attributed to a bi-functional activity of the catalyst which results in an aldol-type condensation followed by a crossed ester condensation between the aldol-type compound and original aldehyde.

3. Experiments with aldehydes other than the aliphatic α-CH_2 group have shown that little or no glycol ester is produced with the mildly basic catalysts which were effective in the previous case. In the presence of the highly basic sodium ethoxide α-ethylbutyraldehyde showed considerable condensation to glycol ester.

NEW YORK 58, N. Y. RECEIVED JULY 24, 1946