Report No. 1

on

CONTRACT NO. Nonr-495(04)
NR 055 298

Shalom Sarel and Melvin S. Newman
October 1, 1953

THE OHIO STATE UNIVERSITY
RESEARCH FOUNDATION

RF Project 497

Report No. 1

TECHNICAL

REPORT

by

THE OHIO STATE UNIVERSITY
RESEARCH FOUNDATION

Columbus 10, Ohio

To OFFICE OF NAVAL RESEARCH
Contract No. Nonr-495(04)
NR 055 298

On STERIC FACTORS IN ORGANIC CHEMISTRY

Submitted by Shalom Sarel and Melvin S. Newman
Department of Chemistry

Date October 1, 1953

SUMMARY

The synthesis of a number of acids, alcohols derived by reduction, and the acetates of these alcohols is described. Physical properties and yields are tabulated.

The rates of alkaline hydrolysis of these acetates at 20° and 30° in aqueous dioxane have been measured and calculations of rate constants and thermodynamic properties have been made.

ALKALINE HYDROLYSIS OF ACETATES OF HIGHLY BRANCHED ALCOHOLS

INTRODUCTION

The over-all objective of the work herein reported is to accumulate quantitative data on the saponification of a large number of primary, secondary, and tertiary acetates. These data will be used in a study of steric effects of various alkyl groups in alkaline hydrolysis. It is hoped that eventually these data will be useful in predicting the alkyl ester to be used in many different reactions where bifunctional compounds, one function of which is the ester function, are involved.

EXPERIMENTAL

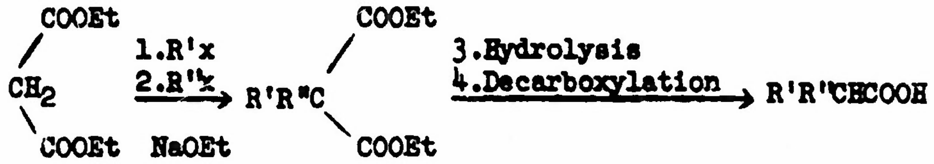
A. SYNTHESIS OF ACIDS

Five different methods were used for the preparation of the carboxylic acids or their esters. These methods are outlined below.

1. Carboxylation of the Grignard reagent:

$$R - x \xrightarrow{Mg} R - Mg\,x \xrightarrow[H_2O]{CO_2} RCOOH$$

2. **Alkykation of Malonic or Cyanoacetic Esters:**

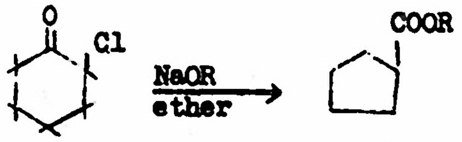


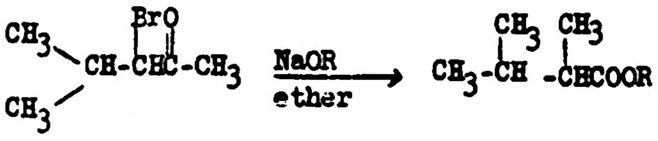
3. **Alkylation of Nitriles (Ziegler Method):**

$C_2H_5CH_2CH$ or $CH_3CN \xrightarrow[\text{ether, NaNH}_2]{\text{excess } C_2H_5Br} (C_2H_5)_3\ CCN \xrightarrow[\text{2.HNO}_2]{\text{1.Hydrolysis, 75\% } H_2SO_4}$

$(C_2H_5)_3CCOOH$

4. **Alkaline Rearrangement of α-Haloketones (Favorski Reaction):**





$(CH_3)_2CH\text{-}CHBr\text{-}CO\text{-}CH_3 \xrightarrow[\text{ether}]{\text{NaOR}} CH_3\text{-}CH(CH_3)\text{-}CH(CH_3)COOR$

5.

B. REDUCTION OF ACIDS AND ESTERS

The use of $LiAlH_4$ as a reducing reagent for converting carboxylic acids and esters into the corresponding primary alcohols has been found highly satisfactory.

C. FORMATION OF ACETATES

The primary alcohols were easily acetylated either by (1) acetyl chloride or (2) acetic anhydride in presence of dry pyridine, affording very good yields, depending on effectiveness of isolation methods of the product used. The data are summarized in Table I. The physical properties are listed in Table II.

The secondary and tertiary alcohols were acetylated by acetyl chloride and magnesium metal in dry ether as follows: (See Table III).

$$2R'R''R'''C\text{-}OH + 2CH_3COCl + Mg \longrightarrow R'R''R'''C\text{-}OCOCH_3 + MgCl_2 + H_2$$

D. RATES OF SAPONIFICATION

The rate of hydrolysis of the acetates with 0.01 N sodium hydroxide, using water or 70% aqueous dioxane as solvents, was followed titrimetrically at 20°C and 30°C. The rate constants are given in Table IV. The thermodynamic data in Table IV were calculated using the equations listed below.

E. CALCULATION OF ARRHENIUS PARAMETERS

(1) $\Delta E^{*} = 2.303 \times R \times \frac{T_1 \cdot T_2}{T_2 - T_1} \cdot \log \frac{k_2}{k_1}$ (Energy of activation)

(2) $\log PZ = \log k + \frac{\Delta E^{*}}{2.303 \cdot RT} = B$

(3) $\Delta S^{*} = 2.303 \times R \left(B - \log \frac{RT}{Nh}\right)$ (entropy of activation for all degrees of freedom)

which are derived from the transition state theory of reaction velocity:

$$k = \frac{RT}{Nh} \cdot e^{-\Delta S^{*}/R} \cdot e^{-\Delta E^{*}/RT}$$

or

$$\log k = \log \frac{RT}{Nh} + \frac{\Delta S^{*}}{2.303\ R} - \frac{\Delta E^{*}}{2.303\ RT}$$

where R/N and h are the Boltzman and Planck constants, respectively, and ΔS* is the entropy of activation for all degrees of freedom.

Equation (2) is used for calculating B(= log PZ) at each temperature; average B is used in equation (3). In equation (3) the average temperature is used as T = 298.

F. INFRARED SPECTRA

Spectra were recorded between 5000 and 625 cm^{-1} with a Baird Infrared Recording Spectrophotometer, Model B. All liquids were measured in a sandwich-type sodium chloride cell. See data in Table II.

DISCUSSION OF RESULTS

As stated before, one of the prime purposes of this study is to obtain a quantitative measure of steric hindrance towards the alkaline hydrolysis of alkyl acetates. In order to rule out polar effects as much as possible, comparisons of relative rates will be made only within the members of the same class of esters. That is, the rates of primary alkyl esters will form one class, the rates of secondary esters another, and the rates of tertiary esters still another. It is hoped that a knowledge of the magnitude of the steric factors involved will prove useful in determining that ester of an acid to be used in certain reactions involving bifunctional compounds one function of which is the ester function.

There are certain cases described in the literature in which the use of t-butyl esters is preferable to that of ethyl esters. However, the preparation of t-butyl esters is often quite tedious. It would be helpful to know what primary and secondary alcohols might be expected to show the same degree of hindrance. The completion of our work on the alkaline saponification of primary alkyl acetates allows this to be done, as will be shown below.

The rates for alkaline hydrolysis of methyl, ethyl, isopropyl, and t-butyl acetates are 7.84, 4.57, 1.26, and 0.081 respectively, using the same units as those indicated in Table IV. Thus we see that compounds 3 and 9 saponify slightly more slowly than t-butylacetate even though primary alkyl groups are involved. All of the other primary alcohol esters listed in Table IV saponify more slowly than methyl and ethyl acetate and hence one has a nice selection of primary alkyl groups having larger steric requirements than ethyl. It remains for much future work to show how valuable this information may prove to be in the selection of the proper ester groups in various cases.

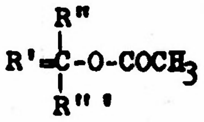
TABLE I. ACETATES OF PRIMARY ALCOHOLS OF FORMULA $R''-\underset{R'''}{\overset{R'}{C}}-CH_2OCOCH_3$

No.	Alcohol	R'	R"	R"	Acid yield	Ref.	Alco-hol yield	Ace-tate
1.	Isobutyl	CH_3	CH_3	H	-		-	-
2.	Neopentyl	CH_3	CH_3	CH_3			91%	80%
3.	2,2-Dimethylbutyl	CH_3	CH_3	C_2H_5	40%	A-1	90%	92%
4.	2,2-Diethylbutyl	C_2H_5	C_2H_5	C_2H_5	60%	A-3	65%	93%
5.	2-Methylbutyl	CH_3	C_2H_5	H				77%
6.	2-Ethylbutyl	C_2H_5	C_2H_5	H				70%
7.	3-Methyl-2-ethylbutyl	C_2H_5	$(CH_3)_2CH$	H	78.5%	A-2	83%	90%
8.	3,3-Dimethyl-2-ethylbutyl	C_2H_5	$(CH_3)_3C$	H			96%	97%
9.	2-2-Diisopropylethyl	$(CH_3)_2CH$	$(CH_3)_2CH$	H	50%	A-2	67%	75%
10.	2,3-Dimethylbutyl	$(CH_3)_2CH$	CH_3	H	60%	A-2 A-4	90%	92%
11.	Cyclopropanemethyl	Cyclopropane		H	94.8%	A-5	70%	88.9%
12.	Cyclobutanemethyl	Cyclobutane ring		H	-	-	80%	92%
13.	Cyclopentanemethyl	Cyclopentane ring		H	65%	A-4	80%	90%
14.	Cyclohexanemethyl	Cyclohexane ring		H	-	-	-	77%
15.	2-Ethylhexyl-1	C_2H_5	$n-C_4H_9$	H	-	-	-	93%

TABLE II. PHYSICAL PROPERTIES AND C-O ABSORPTION BAND IN THE INFRARED SPECTRA OF ACETATES OF PRIMARY ALCOHOLS

No.	Compound Acetate of	B.P. °C	Pressure in mm.	n_D^{25}	C-O Absorption cm^{-1}	C-O Absorption μ
1	2-Methylpropanol	117	741	1.3885	1046	9.56
2	2,2-Dimethylpropanol	127-127.5	741	1.3927	1031 (1050)	9.67 (9.55)
3.	2,2-Dimethylbutanol	152-153	740	1.4188	1038	9.64
4.	2,2-Diethylbutanol	103-104	40	1.4269	1034 (1055)	9.69 (9.50)
5.	2-Methylbutanol	138-139	741	1.4004	1042	9.58
6.	2-Ethylbutanol	160	740	1.4090	1038-1041	9.62-9.65
7.	3-Methyl-2-ethylbutanol	88-89	30	1.4156	1036	9.66
8.	3,3-Dimethyl-2-ethylbutanol	100	40	1.4220	1038	9.65
9.	2,3-Dimethylbutanol	147	740	1.4068	1038	9.65
10.	Cyclopropanemethanol	133.5	740	1.4156	1034	9.67
11.	Cyclobutanemethanol	150	741	1.4245	1033	9.70
12.	Cyclopentanemethanol	172.5	741	1.4340	1038	9.65
13.	Cyclohexanemethanol	108	40	1.4421	1040	9.63
14.	2,2-Diisopropylethanol	185-186	740	1.4214	1045	9.62
15.	2-Ethylhexanol-1	140	40	1.4182	1041	9.62

TABLE III. ACETATES OF SECONDARY AND TERTIARY ALCOHOLS



$$R'-\overset{R''}{\underset{R'''}{C}}-O-COCH_3$$

No.	Compound	R'	R''	R'''	Car-binol yield	Ace-tate yield	Ref.
16.	Triethyl carbinyl	C_2H_5	C_2H_5	C_2H_5	75%*	70%	Spassow
17.	Di-isopropyl carbinyl	$(CH_3)_2CH$	H	$(CH_3)_2CH$		90%	Spassow
18.	tert. Butyl methyl carbinyl	$(CH_3)_3C$	H	CH_3	87%**	63%	AcCl+Py

*Prepared by Grignard method
**Reduction of ketone with LiAlH

Rates of saponification of above acetates in 70% aqueous dioxane were too slow at 20°C, so that the error in the measurement is too great. Further studies on these compounds will be made.

TABLE IV. KINETICS OF ALKALINE HYDROLYSIS OF ACETATES OF PRIMARY ALCOHOLS

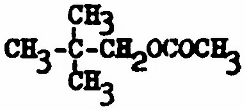
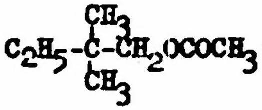
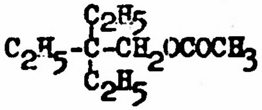
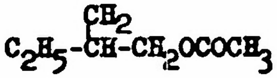
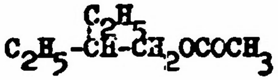
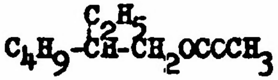
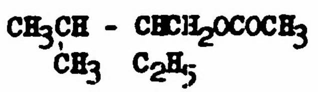
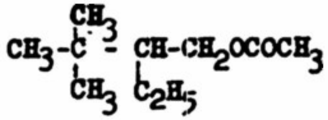
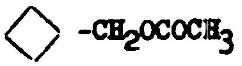
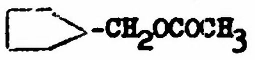
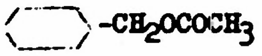
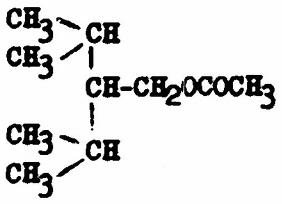
No.	Compound	k g.mole/ℓ . min^{-1} 20°C	30°C	ΔE* Cal./mole	log. PZ	ΔS* Cal./deg./mole
1	 $CH_3\text{-}\overset{CH_3}{\underset{CH_3}{C}}\text{-}CH_2OCOCH_3$	0.280	0.498	9925	7.3079 ± 0.130	+ 1.64
2	 $C_2H_5\text{-}\overset{CH_3}{\underset{CH_3}{C}}\text{-}CH_2OCOCH_3$	0.210	0.339	8258	6.0955 ± 0.111	- 3.91
3	 $C_2H_5\text{-}\overset{C_2H_5}{\underset{C_2H_5}{C}}\text{-}CH_2OCOCH_3$	0.050	0.108	13280	9.7773 ± 0.107	+12.94
4	 $C_2H_5\text{-}\overset{CH_2}{CH}\text{-}CH_2OCOCH_3$	0.470	0.777	8670	6.3766 ± 0.110	- 2.62
5	 $C_2H_5\text{-}\overset{C_2H_5}{CH}\text{-}CH_2OCOCH_3$	0.240	0.493	12420	9.1412 ± 0.163	+10.03
6	 $C_4H_9\text{-}\overset{C_2H_5}{CH}\text{-}CH_2OCCCH_3$	0.156	0.359	14300	10.4189 ± 0.311	+15.88
7	 $CH_3\underset{CH_3}{CH}\text{-}\underset{CH_3}{CH}\text{-}CH_2OCOCH_3$	0.350	0.718	12400	9.1063 ± 0.149	+ 9.87

Table IV (continued)

No.	Compound	k g. mole/ℓ. min^{-1} 20°C	30°C	ΔE* Cal./mole		ΔS* Cal./deg./mole
8	 $\underset{CH_3}{CH_3CH} - \underset{C_2H_5}{CH}CH_2OCOCH_3$	0.227	0.411	10240	7.5457 ± 0.135	+ 2.73
9	 $CH_3-\overset{CH_3}{\underset{CH_3}{C}}-\underset{C_2H_5}{CH}-CH_2OCOCH_3$	0.060	0.109	10700	7.9452 ± 0.137	+ 4.51
10	 $-CH_2OCOCH_3$	1.080	2.280	12900	9.6582 ± 0.004	+12.40
11	 $-CH_2OCOCH_3$	0.742	1.473	11820	8.7614 ± 0.068	+ 8.29
12	 $-CH_2OCOCH_3$	0.537	1.078	12020	8.8426 ± 0.141	+ 8.66
13	 $-CH_2OCOCH_3$	0.330	0.705	13100	9.6318 ± 0.170	+12.28
14	 $\underset{\underset{CH_3\ \ CH_3}{CH}}{\overset{\overset{CH_3\ \ CH_3}{CH}}{CH}}-CH_2OCOCH_3$	0.120^x				

^{x}This result is being checked

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