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RECEIVED for review September 20, 1965
ACCEPTED December 6, 1965

# PREPARATION AND HYDROLYTIC STABILITY OF TRIALKYLACETIC ACID ESTERS

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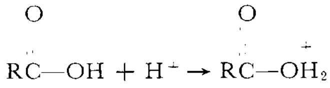
**Trialkylacetic acids (neo-acids) are difficult to esterify by conventional techniques. Laboratory experiments have shown that a standard method of esterification employing an acid catalyst and a water entrainer can be modified to produce esters of neo-acids in high yields. The rates of esterification can be adjusted over a fairly wide range by varying the type and concentration of catalyst and by the selection of an entrainer with a suitable boiling point. Once formed, neo-acid esters are about 20 times more resistant to acidic hydrolysis and from 170 to 1300 times more resistant to basic hydrolysis than unhindered acid esters of approximately equivalent molecular weight.**

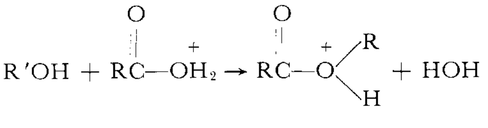
THE DIFFICULTY associated with the preparation of esters of trialkylacetic acids has been described (*2*, *3*, *8*). The enhanced hydrolytic stability of these esters once prepared has also been well documented (*7*, *8*). The acids discussed in this paper contain only methyl groups or mixtures of methyl and higher alkyl groups on the alpha carbon atom.

The difficulty in preparation and the enhanced hydrolytic stability of these trialkylacetic acid esters may, in theory, be attributed to either a steric or an ionization effect. As reported by Newman (*8*), the rate of esterification decreases sharply as the degree of acid chain branching increases. Since the ionization constants of organic carboxylic acids of the type reported are essentially equivalent—e.g., $1.76 \times 10^{-5}$ for acetic acid and $1.77 \times 10^{-5}$ for diethylacetic acid—this decrease in reaction rate is more closely relatable to steric effects than to those associated with ionization.

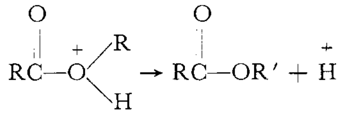
Several mechanisms have been employed to describe the acid-catalyzed esterification of organic acids. The one that appears operable for the trialkylacetic acids and is by far the most common is the acyl-oxy process. As given by Equations 1 to 3, an acid such as trimethylacetic acid is protonated to form a conjugated oxonium ion. This species then undergoes an exchange-type reaction with alcohol. The nucleophilic attack is oriented toward the positive end of the carbonyl dipole. Finally a proton is lost to form the ester.



$$\mathrm{R}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{—OH} + \mathrm{H}^{+} \rightarrow \mathrm{R}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{—}\overset{+}{\mathrm{O}}\mathrm{H}_2 \qquad (1)$$



$$\mathrm{R'OH} + \mathrm{R}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{—}\overset{+}{\mathrm{O}}\mathrm{H}_2 \rightarrow \mathrm{R}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{—}\overset{+}{\mathrm{O}}\begin{smallmatrix}\mathrm{R} \\ \mathrm{H}\end{smallmatrix} + \mathrm{HOH} \qquad (2)$$



$$\mathrm{R}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{—}\overset{+}{\mathrm{O}}\begin{smallmatrix}\mathrm{R} \\ \mathrm{H}\end{smallmatrix} \rightarrow \mathrm{R}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{—OR'} + \overset{+}{\mathrm{H}} \qquad (3)$$

The bulky nature of the alkyl group, owing to the $\alpha$-carbon branching, has a profound inhibiting effect on the formation of the bimolecular complex shown in Equation 2 (*8*). Hence the rate of the over-all reaction is markedly decreased. Steric hindrance also affects the rate of hydrolysis of the ester group in a similar way.

Carboxylic acids have been esterified by many techniques, the most commercially attractive being the Fischer method of esterification which uses an acid catalyst and an entrainer to remove, azeotropically, the formed water. Sterically hindered carboxylic acids have long been known not to be appreciably esterified by this technique. Hence, certain modified procedures were developed to prepare esters of hindered acids in high yields (*5*, *6*, *9*).

The object of the present investigation was to determine if the Fischer method of esterification could be modified to permit a convenient and rapid esterification of sterically hindered trialkylacetic acids and to determine the rate of hydrolysis of the hindered esters once formed under acidic and basic conditions. In this study, the trialkylacetic acids that were esterified include neo-pentanoic, neo-heptanoic, neo-decanoic, and neo-tridecanoic acids. They are called "neo" because of their quaternary carbon atom and neo-pentane–type structure.

## Results

**Esterification.** Data relating to the esterification of neo-pentanoic acid are given in Table I. Neo-pentanoic acid can

### Table I. Esterification of Neo-pentanoic Acid

| *Ester* | *Moles of Reagent* | | *Catalyst, Wt. %* | *Entrainer* | *Maximum Temperature, ° C.* | *Reaction Time, Hr.* | *Conversion, %* | *Boiling Point, ° C.* |
|---|---|---|---|---|---|---|---|---|
| | *Alcohol* | *Acid* | | | | | | |
| Methyl neo-pentanoate | 2.0 | 1.0 | 1.3 pTSA | Xylene[a] | 88.0 | 6.5 | 89.7 | 104 |
| Ethyl neo-pentanoate | 1.1 | 1.0 | 0.45 pTSA | Heptane | 80.0 | 10.5 | 67.8 | 120 |
| | 1.2 | 1.0 | 0.75 $H_2SO_4$ | Heptane | 87.0 | 3.0 | 45.4 | ... |
| | 2.0 | 1.0 | 1.0 $H_2SO_4$ | Heptane[a] | 86.0 | 3.2 | 99.8 | ... |
| | 2.0 | 1.0 | 1.4 $H_2SO_4$ | Heptane[a] | 94.0 | 3.5 | 100.0 | ... |
| | 2.0 | 1.0 | 2.8 $H_2SO_4$ | ...[b] | 86.0 | 6.0 | 85.0 | ... |
| *n*-Propyl neo-pentanoate | 2.0 | 1.0 | 1.0 pTSA | Benzene[a] | 105.0 | 2.0 | 96.6 | 140 |
| *n*-Butyl neo-pentanoate | 1.2 | 1.0 | 0.36 pTSA | Toluene | 126.0 | 6.0 | 99.5 | 164 |
| *n*-Amyl neo-pentanoate | 1.2 | 1.0 | 1.0 pTSA | Heptane | 134.0 | 2.0 | 95.8 | 180 |
| Hexyl neo-pentanoate | 1.2 | 1.0 | 0.22 pTSA | Toluene | 140.0 | 4.0 | 99.0 | 200 |
| Benayl neo-pentanoate | 1.2 | 1.0 | 0.50 pTSA | Heptane | 135.0 | 4.0 | 95.3 | 285 |

[a] *Molecular sieve, Type 3A, used to remove water.* [b] *Reaction allowed to come to equilibrium as measured by titration to phenolphthalein end point, water not removed.*

### Table II. Esterification of Neo-heptanoic Acid

| *Ester* | *Moles of Reagent* | | *Catalyst, Wt. %* | *Entrainer* | *Maximum Temp., ° C.* | *Reaction Time, Hrs.* | *Conversion, %* | *Boiling Point, ° C.* |
|---|---|---|---|---|---|---|---|---|
| | *Alcohol* | *Acid* | | | | | | |
| Methyl neo-heptanoate | 1.0 | 1.0 | 1.0 pTSA | ...[a] | 88 | 6.5 | 57.5 | 146 |
| Ethyl neo-heptanoate | 2.0 | 1.0 | 1.0 $H_2SO_4$ | Heptane[b] | 90 | 5.5 | 84.2 | 160 |
| *n*-Propyl neo-heptanoate | 2.0 | 1.0 | 1.0 pTSA | Heptane[b] | 108 | 5.0 | 89.0 | 181 |
| *n*-Butyl neo-heptanoate | 1.3 | 1.0 | 1.0 pTSA | Heptane | 150 | 3.0 | 98.5 | 242 |

[a] *Water not removed from reaction; reaction terminated before equilibrium reached as measured by titration.* [b] *Molecular sieve, Type 3A, used to remove water.*

### Table III. Esterification of Neo-decanoic and Neo-tridecanoic Acids with Hexyl Alcohol

(Molar ratio of alcohol/acid = 1.2)

| *Ester* | *Catalyst, Wt. %* | *Entrainer* | *Maximum Temp., ° C.* | *Reaction Time, Hrs.* | *Conversion, %* | *Boiling Point, ° C./mm. Hg* |
|---|---|---|---|---|---|---|
| Hexyl neo-decanoate | 11.6 IR120H Amberlite | Heptane | 128 | 4.5 | 34.0[a] | 136/12 |
| | 2.0 $H_2SO_4$ | Heptane | 124 | 7.5 | 77.5 | ... |
| | 2.0 $H_2SO_4$ | Xylene | 169 | 3.5 | 99.7 | ... |
| | 2.0 $H_2SO_4$ | ... | 172 | 6.3 | 94.4 | ... |
| | 2.0 $H_3PO_4$<br>0.46 $H_2SO_4$ | Xylene | 164 | 5.3 | 85.7 | ... |
| | 5.0 $H_2SO_4$ | Xylene | 175 | 0.5 | 100.0 | ... |
| | 7.0 pTSA | Xylene | 171 | 7.5 | 99.9 | ... |
| Hexyl neo-tridecanoate | 2.0 $H_2SO_4$ | Xylene | 175 | 3.3 | 100.0 | 130/3 |

[a] *Olefin formation observed.*

be esterified readily by modifying the Fischer method. The rate of esterification can be adjusted over a fairly wide range by varying the type and concentration of acid catalyst and by the selection of an entrainer with a suitably high boiling point. High conversion in relatively short reaction times are obtainable when neo-pentanoic acid is esterified using either sulfuric acid or *p*-toluenesulfonic acid as catalyst, at concentrations of 0.3 to 1 wt. % of the total charge. Relatively low boiling entrainers such as *n*-pentane can be used for the esterification of neo-pentanoic acid.

Because of the ternary azeotrope that forms when neo-pentanoic acid is esterified with the lower molecular weight alcohols such as methanol, ethanol, or *n*-propanol, a modification in the Fischer method of esterification is needed. This involves using a molecular sieve in addition to an entrainer to remove the water of esterification. The reaction mixture is refluxed through a Soxhlet extractor which contains the molecular sieve, having a 15 wt. % capacity for water. A greater than theoretical amount of alcohol is employed because of holdup by the sieve.

Ethyl neo-pentanoate (Table I) was prepared using sulfuric acid as catalyst and allowing the system to come to equilibrium by not removing the water of esterification. In this reaction, the equilibrium lies far to the right, and up to an 85% conversion to ester is obtained in 6 hours. The conversion to ester was measured by titration of residual acid as a function of time using phenolphthalein as indicator.

Table II describes the esterification of neo-heptanoic acid. The Fischer method of esterification can also be applied to this hindered acid. Catalyst levels of up to 1.0 wt. % of either sulfuric acid or the relatively mild *p*-toluenesulfonic acid can be employed for the esterification of neo-heptanoic acid to high conversion levels. For example, after 3 hours of reaction a 98.5% conversion to ester is obtained when 1.0 wt. % *p*-toluenesulfonic acid is used as a catalyst. A molecular sieve technique with neo-heptanoic acid, as with neo-pentanoic acid, also results in high conversions to ester in a minimum amount of time. However, as with neo-pentanoic acid, an excess of alcohol is necessary because of alcohol adsorption by the sieve.

For the esterification of neo-decanoic and neo-tridecanoic acids, more vigorous conditions are required. As shown in Table III, the higher boiling entrainer xylene is preferred, and a higher catalyst concentration such as 2 wt. % $H_2SO_4$ is required. A very rapid esterification of neo-decanoic acid

(Table III, item 7) occurred when 5 wt. % $H_2SO_4$ was used as the catalyst. With these higher molecular weight acids, a higher boiling entrainer such as xylene is required to allow higher reaction temperatures to accelerate the reaction rates. The effect of temperature can be observed from Table III. Although run for less than half as long, the elevated reaction temperature (169° *vs.* 124° C.) allowed a significantly higher conversion to ester.

With these higher molecular weight neo-acids, the need for higher temperatures and catalyst concentrations to permit ease of reaction, may be explained in terms of increased energy of activation to esterification because of greater steric hindrance. These acids are composed of isomers containing dimethyl alkyl and methyl dialkyl groups on the alpha carbon atom. Hence, the amount of steric hindrance as caused by bulkiness of alkyl groups is markedly increased when compared with neo-pentanoic which has only methyl groups on the alpha carbon atom.

**Hydrolytic Stability.** The neo-acid esters, on the basis of the bulky groups on the alpha carbon atom, would be expected to hydrolyze at a very slow rate. That is, the effect which hinders esterification would also hinder hydrolytic cleavage. The neo-acid esters are considerably more stable to hydrolysis than the unhindered acid esters. On a roughly equivalent molecular weight basis, the neo-acid esters evaluated are from 170 to 1300 times more resistant to basic hydrolysis than their unhindered acid ester counterparts. These base hydrolyses follow normal second order kinetics (1c) as expressed by the following rate equation:

$$k_2 = \frac{2.3}{t(B - E)} \log \frac{E(B - X)}{B(E - X)}$$

where $k_2$ = second order rate constant, $t$ = time, $B$ = concentration of base at $t = 0$, $E$ = concentration of ester at $t = 0$, $X$ = amount of ester reacted at time $t$.

From plots of hydrolysis data shown in Figure 1, rate constants and relative rates were calculated (Table IV).

Acid catalyzed hydrolyses, as expected, proceed considerably slower than base catalyzed hydrolyses because the hydroxide ion is a better nucleophile than water. Under conditions of acid hydrolysis the trialkylacetic acids were hydrolyzed less than one-twentieth as fast as the unhindered esters. These acids hydrolyze in the presence of excess water exhibited pseudo-first-order kinetics (*2*) according to the expression:

$$k_1 = 2.3/t \log (E/E - X)$$

where $k_1$ = first order rate constant.

Rate constants and relative rates shown in Table V were determined from plots of the data shown in Figure 2. Hydrolysis of all the esters under neutral conditions proceeded at an immeasurably slow rate at 50° C.

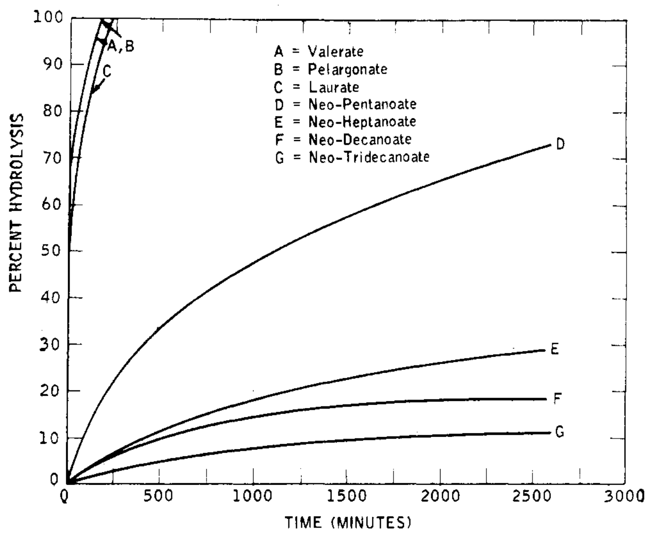
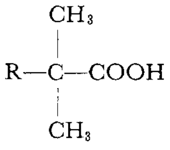


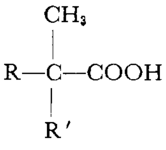
**Figure 1. Base hydrolysis of hexyl esters**

**Composition Analysis.** In the preparation of a neo-acid, an olefin reacts with carbon monoxide in the presence of an acid catalyst to form an acylonium complex. The complex is then hydrolyzed to a highly branched carboxylic acid. For the general case, four different structural-type acids can be produced:



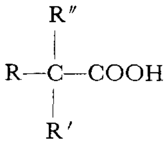
$$\begin{array}{c} \mathrm{CH_3} \\ | \\ \mathrm{R{-}C{-}COOH} \\ | \\ \mathrm{CH_3} \end{array}$$

I



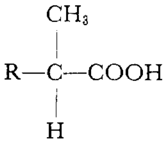
$$\begin{array}{c} \mathrm{CH_3} \\ | \\ \mathrm{R{-}C{-}COOH} \\ | \\ \mathrm{R'} \end{array}$$

II



$$\begin{array}{c} \mathrm{R''} \\ | \\ \mathrm{R{-}C{-}COOH} \\ | \\ \mathrm{R'} \end{array}$$

III



$$\begin{array}{c} \mathrm{CH_3} \\ | \\ \mathrm{R{-}C{-}COOH} \\ | \\ \mathrm{H} \end{array}$$

IV

Of particular significance in the structure of neo-acids is the trialkyl substituents on the carbon atom alpha to the carboxyl group. Nuclear magnetic resonance spectroscopy (NMR Varian A-60) was used to define the type of substitution at the carbon atom alpha to the carboxyl group (Table VI). In all cases, NMR reveals no hydrogens on the alpha carbon atoms of the acids. This indicates that all acids present have the trialkylacetic acid configuration. Neo-pentanoic acid is exclusively trimethylacetic acid. Over 90% of neo-heptanoic acid is $\alpha,\alpha$-dimethylpentanoic acid, and the remainder is 2-ethyl-2-methylbutanoic acid. The higher molecular weight neo-acids contain larger amounts of methyl alkyl substitution, where the alkyl group can represent either ethyl or higher homologs. The increased bulkiness of the alkyl

**Table IV. Rate Constants for Base Hydrolysis of Hexyl Esters at 50° C.**

| *Ester* | $k_2$ *(Liter/Mole/Sec.)* × $10^5$ | *Relative Rate*[a] |
|---|---|---|
| Neo-pentanoate | 55.1 | 32 |
| Neo-heptanoate | 8.9 | 5.2 |
| Neo-decanoate | 3.2 | 1.9 |
| Neo-tridecanoate | 1.7 | 1.0 |
| Valerate | 9260 | 5400 |
| Pelargonate | 2960 | 1700 |
| Laurate | 2285 | 1300 |

[a] *Neo-tridecanoate rate arbitrarily set at 1.00.*

**Table V. Rate Constants for Acid Hydrolysis of Hexyl Esters at 50° C.**

| *Ester* | $k_1$ *(sec.$^{-1}$)* × $10^7$ | *Relative Rate*[a] |
|---|---|---|
| Neo-pentanoate | 5.2 | 1.8 |
| Neo-heptanoate | 1.5 | 0.5 |
| Neo-decanoate | 3.8 | 1.3 |
| Neo-tridecanoate | 2.8 | 1.0 |
| Valerate | 103 | 36 |
| Pelargonate | 76 | 26 |
| Laurate | 61 | 21 |

[a] *Neo-tridecanoate rate arbitrarily set at 1.00.*

**Table VI. Composition Analysis of Trialkylacetic Acids**[a]

| Sample | Av. No. of Carbon Atoms Per Molecule[b] | Dimethyl | Geminal Substitution of Alpha Carbon Atom, % Methyl-Alkyl | Methyl-Hydrogen | Dialkyl |
|---|---|---|---|---|---|
| Neo-pentanoic acid | 5 | >99+ | <1.0 | . . . | . . . |
| Neo-heptanoic acid | 7 | 93 | 7.0 | . . . | . . . |
| Neo-decanoic acid | 10 | 64.5 | 33.5 | . . . | 2.0 |
| Neo-tridecanoic acid | 13 | 63.0 | 26.0 | . . . | 11.0 |

[a] *Determined by NMR analysis.* [b] *Determined by mass spectrometry molecular weight distribution analysis.*

groups explains why neo-decanoic and neo-tridecanoic acids require more vigorous conditions for esterification but once esterified, are difficult to hydrolyze. Under the conditions of this study, the data are in agreement with previous assignments relative to ease of esterification and hydrolysis of trisubstituted acetic acids and esters:

$CH_3$, H, H > H, $CH_3$, $CH_3$ > $CH_3$, $CH_3$, $CH_3$ >

$CH_3$, $CH_3$, alkyl > alkyl, $CH_3$, alkyl > alkyl, alkyl, alkyl

### Experimental

The neo-acids and hexyl alcohol used in this study are commercial products supplied by the Enjay Chemical Co.

**Esterification.** PREPARATION OF HEXYL NEO-TRIDECANOATE. To a 1-liter, three-necked reaction flask fitted with a stirrer, a thermometer, and a reflux condenser joined to a Dean-Stark water separator are added 214.0 grams (1.0 mole) of neo-tridecanoic acid, 122.0 grams (1.2 moles) of hexyl alcohol, and 100 grams of xylene. While the mixture is stirred, 8.7 grams of concentrated $H_2SO_4$ are added, and the reaction mixture is brought to reflux. After 170 minutes at reflux, the reaction is 96% complete (as determined by titration of residual acid), and after 200 minutes it is 100% complete. The mixture is cooled to 100° C. and washed with water (1 × 100 ml.), 5% sodium hydroxide solution (2 × 100 ml.), and again with water, until the water washes are neutral. The washed reaction mixture is stripped at atmospheric pressure to remove xylene, hexanol, and water, and then distilled under vacuum to obtain the desired ester. A total of 249 grams (83.5% of theoretical yield) of hexyl neo-tridecanoate, boiling at 130° C. and 3 mm. Hg pressure, is collected. The product has a color of 50 (Pt-Co).

**Hydrolysis.** HYDROLYSIS WITH BASE. The hydrolyzing solution consists of 0.1$N$ NaOH in 10% aqueous ethylene glycol monoethyl ether. Flasks are kept at 50° C., and aliquots are removed at various times for titration to determine the extent of hydrolysis. A plot of these data appears in Figure 1. Rate constants were determined by the normal, second-order kinetic plot (Table IV).

**Table VII. Base Catalyzed Hydrolysis of Hexyl Neo-decanoate**

($B$ = 29.7 meq./liter, $E$ = 19.5 mmole/liter, 50° C.)

| *Time, Sec.* | $X$ | $k_2$ (*Liter Mole*$^{-1}$ *Sec.*$^{-1}$) × $10^5$ |
|---|---|---|
| 5,040 | 1.05 | 3.8 |
| 7,020 | 1.12 | 2.9 |
| 9,000 | 1.20 | 2.4 |
| 70,000 | 1.80 | 4.2 |
| 154,800 | 2.55 | 2.8 |

**Table VIII. Acid Catalyzed Hydrolysis of Hexyl Neo-decanoate**

($E$ = 19.5 mmole/liter, 50° C.)

| *Time, Sec.* | $X$ | $k_1$ (*Sec.*$^{-1}$) × $10^7$ |
|---|---|---|
| 151,000 | 1.2 | 3.6 |
| 202,500 | 1.4 | 3.8 |
| 237,600 | 1.7 | 3.8 |
| 324,000 | 2.5 | 4.1 |

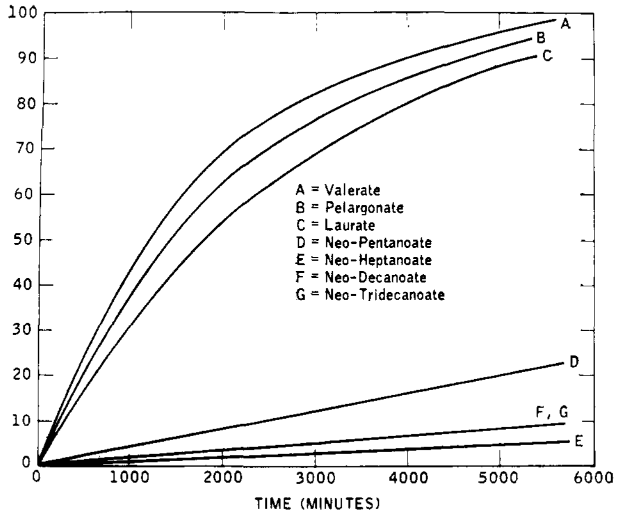


Figure 2. Acid hydrolysis of hexyl esters

Table VII illustrates the data obtained for the hydrolysis of hexyl neo-decanoate.

HYDROLYSIS WITH ACID. The hydrolyzing solution consists of 0.1$N$ HCl in 10% aqueous acetone. Flasks are kept at 50° C. and aliquots are removed as before to determine the extent of hydrolysis as shown in Figure 2. The rate constants as determined from a standard, first-order plot are shown in Table V.

Table VIII illustrates the data obtained for the hydrolysis of hexyl neo-decanoate.

### Acknowledgment

The authors thank the Enjay Chemical Laboratories and the Enjay Chemical Co. for permission to publish this paper.

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RECEIVED for review August 4, 1965
ACCEPTED January 6, 1966