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PART I
THE REACTIONS OF CHLORODIFLUOROMETHANE AND
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$t$-BUTOXIDE IN $t$-BUTYL ALCOHOL

PART II
THE KINETICS OF DEUTERIUM EXCHANGE OF
SUBSTITUTED METHYL ACETATES

A DISSERTATION

Presented in Partial Fulfillment of the Requirements for
the Degree Doctor of Philosophy in the Graduate School
of The Ohio State University

By

Philip David Dalsin, B.A., M.S.

The Ohio State University
1970

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Adviser
Department of Chemistry
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PART I
INTRODUCTION

The formation of dihalomethylenes in the reactions of haloforms with base was first demonstrated by Hine.¹


He found that the basic hydrolysis of chloroform is more rapid than can be explained by an $S_N^2$ reaction mechanism and yet the reaction is kinetically second-order. This, plus the fact that the base-catalyzed deuterium exchange of chloroform is rapid compared to its hydrolysis,² led Hine to postulate the following mechanism.

\[
\begin{align*}
\text{CHCl}_3 + \text{-OH} & \xrightarrow{\text{fast}} \text{-CCl}_3 + \text{H}_2\text{O} \\
\text{-CCl}_3 & \xrightarrow{\text{slow}} \text{Cl}^- + \text{CCl}_2 \\
\text{CCl}_2 & \xrightarrow{\text{-OH fast}} \text{CO} + \text{HCO}_2^- 
\end{align*}
\]

Further investigations, by Hine and his coworkers,
of the reactions of potassium isopropoxide with chlorodifluoromethane, chloroform, and bromoform showed that


alkoxyhalomethylenes are also reaction intermediates. It has been suggested that, in the case of alkoxyfluoromethylenes, the intermediate undergoes further reaction with alkoxy ion to form dialkoxymethylenes which then react with solvent to give the observed trialkyl orthoformates.


Since the dialkoxymethylene is not the first methylene formed in the reaction its existence is difficult to prove.

\[
\begin{align*}
\text{HCX}_3 + \text{RO}^- & \rightleftharpoons \text{CX}_3 + \text{ROH} \\
\text{CX}_3 & \xrightarrow{\text{slow}} \text{CX}_2 + X^- \\
\text{CX}_2 + \text{RO}^- & \rightarrow \text{ROCX} + X^- \\
\text{ROCX} + \text{RO}^- & \rightarrow (\text{RO})_2\text{C} \\
(\text{RO})_2\text{C} & \xrightarrow{\text{ROH}} (\text{RO})_3\text{CH}
\end{align*}
\]
More recently, dimethoxymethylene has been postulated to be an intermediate in the thermal decomposition of certain norbornadienone ketals.\(^6,7\)


The presence of two fluorine atoms in a haloform results in a change of mechanism in its reaction with base.\(^8\)


Carbanion formation and the loss of a halide ion become concerted processes. This is supported by the observed absence of hydrogen-deuterium exchange in the basic hydrolysis of deuteriobromodifluoromethane. The presence of only one fluorine atom in the haloform is, evidently, insufficient to prevent carbanion formation, so its reaction with base proceeds via a carbanion formation followed by loss of halide ion.\(^9\)

The reaction of chlorodifluoromethane with secondary and tertiary alkoxides in alcohol solution has been reported by Cleaver\(^{10}\) to give varying amounts of cis and trans-1,2-

dialkoxy-1,2-difluoroethylenes and, in the case where secondary alkoxides are used, trialkyl orthoformates.

\[
\text{CHClF}_2 + ROK \rightarrow \text{ROCF}=\text{CFOR}
\]

The t-butyl compound was obtained in a 24% yield. The isopropyl compound was obtained in a smaller but unstated yield. When sodium ethoxide was used, the only reported reaction product was triethyl orthoformate.

The reaction of chlorodifluoromethane with potassium isopropoxide in isopropyl alcohol was initially reported to give triisopropyl orthoformate and difluoromethyl isopropyl ether.\(^3\) In view of the fact that alkyl difluoromethyl ethers had also been found in the reactions of bromodifluoromethane\(^{11}\) and difluoriodomethane\(^{12}\) with


ethanolic potassium hydroxide, and with sodium methoxide,\textsuperscript{13}


it seemed that they might also be formed in the reaction of chlorodifluoromethane with potassium \textit{t}-butoxide.

If the 1,2-dialkoxy-1,2-difluoroethylenes observed by Cleaver\textsuperscript{10} result from the dimerization of an intermediate alkoxyfluoromethylene,\textsuperscript{5} then they should also be formed from dichlorofluoromethane, whose reaction with secondary and tertiary alkoxide salts is believed to involve the formation of intermediate alkoxyfluoromethylene\textsuperscript{s}.\textsuperscript{4}

Since tertiary alkoxides appear to give higher yields of dialkoxydifluoroethylenes from chlorodifluoromethane than secondary alkoxides,\textsuperscript{10} the possibility of isolating such a product in the reaction of dichlorofluoromethane may be greater with potassium \textit{t}-butoxide than if a secondary alkoxide is used.

Preliminary work by Schreck\textsuperscript{14} showed that the 1,2-

\textsuperscript{(14)} J. O. Schreck, unpublished work.

di-\textit{t}-butoxy-1,2-difluoroethylenes are formed in the reaction of chlorodifluoromethane with potassium \textit{t}-butoxide and that
t-butyl difluoromethyl ether is also formed. He observed that, in certain runs, the t-butyl ester of di-t-butoxyacetic acid was also formed. This ester seemed to be formed during the work-up of the reaction mixture.

Since tetramethoxymethylene has been isolated in thermal decomposition of 7,7-dimethoxybicyclo[2.2.1]heptadiene derivatives and the reaction is believed to proceed via an intermediate dimethoxymethylene, it was thought that the t-butyl ester of di-t-butoxyacetic acid, obtained in the reaction of dichlorofluoromethane with potassium t-butoxide, might arise from tetra-t-butoxyethylene.

The following work was undertaken to determine how t-butyl di-t-butoxyacetate is formed, to isolate and/or identify its possible precursor(s), and to determine whether this ester is also formed in the reaction of chlorodifluoromethane with potassium t-butoxide.
RESULTS

The reaction of dichlorofluoromethane with potassium t-butoxide in t-butyl alcohol results in the formation of cis and trans-1,2-di-t-butoxy-1,2-difluoroethylene, as reported by Cleaver, as well as a compound whose nmr and ir spectra, molecular weight, and elemental analysis are consonant with the structure of tri-t-butyl orthoformate. The isolated yield of the isomeric tetrasubstituted

\[ t-\text{BuOK} + \text{HCFCl}_2 \rightarrow t-\text{BuOF}=\text{CFOBu-t} + (t-\text{BuO})_3\text{CH} \]  

ethylenes ranged from 30 to 44% based on added haloform. The yield of tri-t-butyl orthoformate is about 4%. Determination of yields in one run by gas chromatography indicated that yields of substituted ethylenes and tri-t-butyl orthoformate are 81% and 5%, respectively.

Chlorodifluoromethane reacts with potassium t-butoxide in t-butyl alcohol to give cis and trans-1,2-di-t-butoxy-1,2-difluoroethylene, tri-t-butyl orthoformate, and t-butyl

\[ \text{HCF}_2\text{Cl} + t-\text{BuOK} \xrightarrow{t-\text{BuOH}} t-\text{BuOF}=\text{CFOBu-t} + (t-\text{BuO})_3\text{CH} + t-\text{BuOCHF}_2 \]  

(2)
difluoromethyl ether. The isolated yields of cis and trans-1,2-di-t-butoxy-1,2-difluoroethylene, tri-t-butyl orthoformate, and t-butyl difluoromethyl ether, based on added haloform, are 21%, 3%, and 20-30%, respectively.

The products given in equations 1 and 2 vary depending on the procedure used in the reaction work-up. The products given above are observed when t-butyl alcohol is distilled from the reaction mixture under reduced pressure, taking care to maintain the temperature below 30°. Pentane is then added to precipitate the excess potassium t-butoxide. After filtration, several potassium hydroxide pellets are added to insure basicity and the mixture is distilled at reduced pressure.

Different products are observed when t-butyl alcohol is distilled from the reaction mixture at atmospheric pressure, water is added to dissolve the salts formed during the reaction, ether is added, and the dried organic layer is vacuum distilled. Under these conditions, no tri-t-butyl orthoformate is detectable. Additional products, t-butyl di-t-butoxyacetate and isobutylene, are formed. Subsequent experiments showed that the ester and olefin arise from the further reaction of cis and trans-1,2-di-t-butoxy-1,2-difluoroethylene with t-butyl alcohol in the absence of base. A sample of the isomeric olefin was
refluxed with t-butyl alcohol. The mixture became increasingly acid with time. After an hour, t-butyl di-t-butoxyacetate was detectable by glc and ir analysis. From the ir spectrum of the mixture, it appears that di-t-butoxyacetic acid is also formed, although attempts to isolate it were unsuccessful. In another experiment, 48% aqueous HF was added to a solution of the isomeric ethylenes in t-butyl alcohol. A vigorous reaction ensued, accompanied by the evolution of isobutylene. The formation of t-butyl di-t-butoxyacetate was evident from ir and glc analysis.

The previously unreported tri-t-butyl orthoformate was characterized by its ir, nmr, and mass spectra, molecular weight, and elemental analysis. The nmr spectrum showed two singlets at 1.26 ppm and 5.65 ppm relative to TMS with an intensity ratio of 26.5:1. Inasmuch as the methine proton of triethyl orthoformate absorbs at 4.96 ppm, the

structural assignment of tri-\textit{t}-butyl orthoformate seemed uncertain. The possibility that increasing substitution in orthoesters results in a downfield shift of the methine proton absorption was determined by obtaining the nmr spectra of trimethyl and triisopropyl orthoformates. The methine proton of trimethyl orthoformate absorbs at 4.85 ppm. Since neither the nmr spectrum nor a sample of triisopropyl orthoformate was available, the compound was prepared following the procedure of Hine, Ketley, and Tanabe. The nmr spectrum showed a methine proton absorption at 5.20 ppm. It appears that increasing branching in the alkyl groups of orthoesters results in a downfield shift of the methine proton absorption. It appears likely that this phenomenon is a result of a steric rather than a polar effect since the difference in chemical shifts is increasingly greater between trimethyl and triethyl (0.11 ppm), triethyl and triisopropyl (0.25 ppm), and triisopropyl and tri-\textit{t}-butyl orthoformates (0.45 ppm).

The structure of tri-\textit{t}-butyl orthoformate is consistent with other analytical data. The ir spectrum shows two broad C-O absorptions at 1070 cm$^{-1}$ and 1028 cm$^{-1}$ which

\begin{flushright}
\end{flushright}
are similar to those reported for triethylorthoformate.\textsuperscript{18}

\begin{center}
\end{center}

The molecular weight, determined by vapor pressure osmometry, is within 3\% of the calculated value. The results of the mass spectrographic analysis of tri-\textsuperscript{t}-butyl orthoformate are given in Table 1.

\begin{table}[h]
\centering
\caption{Mass Spectrographic Analysis of Tri-\textsuperscript{t}-butyl Orthoformate}
\begin{tabular}{lcc}
\hline
M/e & Intensity\textsuperscript{b} & M/e & Intensity\textsuperscript{b} \\
\hline
39 & 5.9 & 113 & 1 \\
41 & 15.7 & 137 & 1.6 \\
42 & 5.5 & 145 & 2.9 \\
43 & 7.5 & 159 & 2.5 \\
57 & 100 & 175 & 0.58 \\
58 & 5.5 & 217 & 0.08 \\
89 & 4.4 & 231 & 0.16 \\
103 & 20 & & \\
\hline
\end{tabular}
\end{table}

\textsuperscript{a} Includes all peaks where I > 1 from M/e 39 – 100, all peaks where I > .1 from M/e 101 – 200, and all peaks I > .01 M/e = 201 – 300.

\textsuperscript{b} Intensities are relative to the most intense peak = 100.
The M-1 peak at M/e 231 is also observed in the mass spectrum of tri-\textit{n}-butyl orthoformate as are the M-1 peaks of other orthoesters.\textsuperscript{19} The structures of other fragments


will be discussed later.

Difficulty was experienced in obtaining a correct elemental analysis for tri-\textit{t}-butyl orthoformate. Hydrolysis is evidently so rapid that the compound reacts with atmospheric moisture to a significant extent. In one analytical run, the percent carbon dropped as much as 1\% between successive analyses of the same sample, even when the sample was stored in a desiccator between runs. The best analytical results were obtained when freshly distilled tri-\textit{t}-butyl orthoformate was transferred to several glass ampoules under a nitrogen atmosphere in a dry box. Each of these ampoules was then analyzed and duplicate analyses were obtained. The analytical results are given in Table 2.
TABLE 2. Results of Combustion Analysis of Tri-t-butyl Orthoformate

<table>
<thead>
<tr>
<th></th>
<th>Carbon</th>
<th>Hydrogen</th>
<th>Carbon</th>
<th>Hydrogen</th>
<th>Carbon</th>
<th>Hydrogen</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>67.40%</td>
<td>11.76%</td>
<td>66.23%</td>
<td>11.53%</td>
<td>65.84%</td>
<td>11.76%</td>
</tr>
<tr>
<td></td>
<td>67.49%</td>
<td>12.21%</td>
<td>67.77%</td>
<td>12.08%</td>
<td>67.20%</td>
<td>12.11%</td>
</tr>
</tbody>
</table>

^a Results when one ampoule was sampled 3 times.

^b Each run sampled from a different ampoule.  

^c Calculated value.

The yield of tri-t-butyl orthoformate, relative to the tetrasubstituted ethylenes, decreases with increasing concentration of potassium t-butoxide. This is shown in Table 3. These values were obtained by glc analysis of the crude reaction mixtures before work-up. The percentage of tri-t-butyl orthoformate may be higher than those given in

TABLE 3. Product Composition with Varying Potassium t-Butoxide Concentration

<table>
<thead>
<tr>
<th>t-BuO⁻</th>
<th>% Ethylene</th>
<th>(t-BuO)₃CH</th>
</tr>
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<tbody>
<tr>
<td>0.01</td>
<td>44.9</td>
<td>55.1</td>
</tr>
<tr>
<td>0.10</td>
<td>56.1</td>
<td>43.9</td>
</tr>
<tr>
<td>0.72</td>
<td>88.2</td>
<td>11.8</td>
</tr>
</tbody>
</table>

^a The haloform was HCl₂F.
Table 3 because the orthoester suffers some decomposition under the glc conditions employed. However, the extent of decomposition should be the same if the glc conditions remain constant so that the trend of increasing orthoester concentration with decreasing concentration of potassium t-butoxide is clear.

The mass spectra of the other products of the reaction of chlorodifluoromethane and dichlorofluoromethane with potassium t-butoxide were determined. The mass spectral data for t-butyl di-t-butoxyacetate and 1,2-di-t-butoxy-1,2-difluoroethylene are given in Tables 4 and 5, respectively. The structure of some of the fragments observed in the mass spectra of these compounds will be discussed later.
TABLE 4. Mass Spectral Data for \( t \)-Butyl Di-\( t \)-butoxyacetate

<table>
<thead>
<tr>
<th>M/e</th>
<th>Intensity</th>
<th>M/e</th>
<th>Intensity</th>
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<tr>
<td>15</td>
<td>21.1</td>
<td>115</td>
<td>1.3</td>
</tr>
<tr>
<td>29</td>
<td>11.1</td>
<td>131</td>
<td>1.8</td>
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<td>41</td>
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<td>57</td>
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<td>113</td>
<td>2.0</td>
<td>245</td>
<td>0.005</td>
</tr>
</tbody>
</table>

\(^a\) Includes all peaks I > 10 at M/e 0→100; I > .1 at M/e 101→200 and I > .001 at M/e 201→300. \(^b\) Intensities are relative to the most intense peak = 100.

TABLE 5. Mass Spectral Data for 1,2-Di-\( t \)-Butoxy-1,2-Difluoroethylene

<table>
<thead>
<tr>
<th>M/e</th>
<th>Intensity</th>
<th>M/e</th>
<th>Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>29</td>
<td>15.2</td>
<td>119</td>
<td>1.2</td>
</tr>
<tr>
<td>39</td>
<td>15.2</td>
<td>137</td>
<td>7.5</td>
</tr>
<tr>
<td>41</td>
<td>54.5</td>
<td>152</td>
<td>0.9</td>
</tr>
<tr>
<td>56</td>
<td>21.6</td>
<td>159</td>
<td>1.7</td>
</tr>
<tr>
<td>57</td>
<td>100</td>
<td>175</td>
<td>0.41</td>
</tr>
<tr>
<td>61</td>
<td>16.7</td>
<td>193</td>
<td>0.16</td>
</tr>
<tr>
<td>103</td>
<td>10.1</td>
<td>210</td>
<td>0.08</td>
</tr>
<tr>
<td>104</td>
<td>1.0</td>
<td>210</td>
<td>0.08</td>
</tr>
</tbody>
</table>

\(^a\) Includes all peaks I > 10 at M/e 12→100; I > .5 at M/e 101→174 and I > .01 at M/e 201→300. \(^b\) Intensities are relative to the most intense peak = 100.
DISCUSSION

The formation of the products observed in the reaction of chlorodifluoromethane with potassium t-butoxide can be explained by a mechanism involving various substituted methylene intermediates.

\[
\text{HCF}_2\text{Cl} + \text{t-BuO}^- \xrightarrow{k_1} \text{CF}_2 \\
\xrightarrow{k_2} \text{t-BuOCHF}_2 \\
\text{FC-OBu-t} \xrightarrow{k_5} \text{dimer} \\
\xrightarrow{k_7 (\text{t-BuO}^-)} (\text{t-BuO})_2\text{C} \\
\text{t-BuOH} \xrightarrow{k_8} (\text{t-BuO})_2\text{CH} \\
\text{HC(OBu-t)}_3 \xrightarrow{k_8} \text{t-BuOH} \\
\rightarrow (\text{t-BuO})_2\text{CH} \\
\]

The formation of an alkoxyfluoromethylene \((k_3)\) was postulated in the formation of triisopropyl orthoformate from chlorodifluoromethane and potassium isopropoxide.\(^4\) The dimerization of t-butoxyfluoromethylene \((k_3)\) to give \textit{cis} and \textit{trans}-1,2-di-t-butoxy-1,2-difluoroethylene is the most direct mechanism that can be written to account for ethylene.
formation. Although dimerizations are not common reactions of methylene intermediates, they have been postulated in the formation of tetramethoxyethylene from dimethoxymethylene. The formation of tri-\text{-}t\text{-}butyl orthoformate may involve an intermediate di-\text{-}t\text{-}butoxymethylene (\(k_7\)) which then reacts in one or more steps to give the orthoester. It is also likely, however, that the t\text{-}butoxyfluoromethylene can react with \(t\text{-}\)butyl alcohol, in one or more steps, to form di-\(t\text{-}\)butoxyfluoromethane (\(k_6\)) which, being a halo-methyl ether, can solvolyze to di-\(t\text{-}\)butoxy carbonium ion (\(k_8\)). The carbonium ion can then combine with \(t\text{-}\)butyl alcohol to form the observed orthoester. The solvolytic reactivity of halomethyl ethers has been investigated by Ballinger and coworkers. They found, for example, that


chlorodimethyl ether is at least 10\(^{13}\) times more reactive than \(n\text{-}\)propyl chloride.

Borch\(^{21}\) and Olofson and his coworkers\(^{22}\) have


recently been successful in isolating the fluoroborate salts of dialkoxy carbonium ions, which indicates that they have considerable stability. The decomposition of \( t \)-butyl difluoromethyl ether to give \( t \)-butoxyfluoromethylenene \( (k_4) \) has not been investigated. Schreck isolated the ether by distillation from a basic solution of \( t \)-butyl alcohol, potassium hydroxide and the ether so it seems likely that the ether does not undergo further reaction under basic conditions. Hine and Tanabe\(^3 \) have also shown that difluoromethyl isopropyl ether is unreactive toward potassium isopropoxide in isopropyl alcohol.

A similar mechanism can be written for the reaction of dichlorofluoromethane and potassium \( t \)-butoxide. A major

\[
\begin{align*}
\text{\( t \)-OBu} + \text{Cl}_2\text{FCH} & \xrightarrow{k_1} \text{CFCl}_2 \xrightarrow{k_2} :\text{CFCl} + \text{Cl}^- \\
\text{t-BuOH} \xrightarrow{k_3} \text{t-BuOC}^+\text{-Cl} & \xrightarrow{k_6} \text{t-BuO}^- \xrightarrow{k_9} \text{t-BuOC}^+\text{-O}^- \\
\text{t-BuO} \xrightarrow{k_4} \text{t-BuOCF} & \xrightarrow{k_7} \text{t-BuO}^- \xrightarrow{k_8} \text{ ortho ester} \\
\end{align*}
\]
difference in the two mechanisms is, that in the case of dichlorofluoromethane, the first step is a reversible carbanion formation.\(^{23}\)

The observation that the yield of orthoester relative to dimer decreases with increasing base concentration in the reaction of \( \text{HCCl}_2\text{F} \) can be explained by this mechanism. As the concentration of \( \text{t-BuO}^- \) is increased, the ratio \( k_8/k_9(\text{t-BuO}^-) \) decreases and since \( k_8 \) leads only to orthoester, whereas \( k_9 \) leads to both orthoester and dimer, the amount of dimer should increase at the expense of orthoester when the base concentration is increased.

Perhaps tri-\( \text{t-Bu} \) orthoformate was not previously reported as a product of the reaction of dichlorofluoromethane with potassium \( \text{t-BuO}^- \) because water was used in the work-up of the reaction. Tri-\( \text{t-Bu} \) orthoformate undergoes rapid hydrolysis to give \( \text{t-Bu} \) alcohol and \( \text{t-Bu} \) formate under both acidic and basic conditions.

\[
\text{HC(OBu-t)}_3 \xrightarrow{\text{H}_2\text{O}} \text{HC} = \text{O} + \text{OBu-t} + \text{t-BuOH}
\]

The \( \text{t-Bu} \) formate may have been missed by Cleaver because the \( \text{t-Bu} \) alcohol fraction was not analyzed. Moreover,
it was found that t-butyl alcohol and t-butyl formate have identical retention times on at least one glc column (Carbowax 20 M). This might also be the reason that t-butyl formate was not reported as a product.

The formation of t-butyl di-t-butoxyacetate from cis and trans-1,2-di-t-butoxy-1,2-difluoroethylene can be rationalized as a protonation of the ethylene, followed by loss of isobutylene. The acid fluoride that is formed can react with t-butyl alcohol to give a t-butoxyfluoroacetate which is a type of halomethyl ether and hence could solvolyze to give the observed product.

An analysis of the mass spectra of the products in the reactions of dichlorofluoromethane and chlorodifluoro-methane with potassium t-butoxide in t-butyl alcohol leads
to fragmentation schemes that seem plausible in light of
the structures of the products and known fragmentation pathways of their structural types.\(^{21,24}\)

---


---

Many of the characteristic peaks observed in the mass spectrum of tri-\(t\)-butyl orthoformate can be rationalized by fragmentation schemes such as the following:

\[
\text{t-BuOCHOH}^+ \xrightarrow{-\text{HC}O_2\text{H}} \text{t-Bu}^+ \\
\text{m/e 103} \downarrow \quad \text{m/e 57} \\
\text{-C}_4\text{H}_8
\]

\[
\text{(t-BuO)_2CH}^+ \xrightarrow{-\text{t-BuO}^*} \text{(t-BuO)_2COH}^+ \\
\text{m/e 159} \downarrow \quad \text{m/e 175} \\
\text{-t-BuO}^* \\
\text{-C}_4\text{H}_8
\]

\[
[(\text{t-BuO})_3\text{CH}]^+ \xrightarrow{-\text{H}^*} (\text{t-BuO})_3\text{C}^+ \\
\text{-Me}^* \downarrow \quad \text{m/e 231} \\
\text{(t-BuO)_2CHOCHMe_2}
\]

\[
\text{Me}_2\text{CH}^+ \\
\text{m/e 43}
\]
No parent or M-1 peak is observed in the mass spectrum of \( \text{t-butyldi-t-butoxyacetate} \), however, many of the lines in the spectrum can be rationalized from data on other esters and t-butoxy compounds. \(^{25}\) The following scheme accounts for most of the characteristic peaks.

\[
\begin{align*}
\text{Me}_2\text{COBu-t}^+ & \quad \xrightarrow{-\text{C}_4\text{H}_8} \quad \text{Me}_2\text{CO}^+ \\
m/e 115 & \quad \text{m/e 59}
\end{align*}
\]

\[
\text{OBu-t}^+ \quad \text{Me}_2\text{COCHCO}_2\text{H}^+ \\
m/e 189
\]

\[\xrightarrow{-\text{C}_4\text{H}_8} \]

\[
\text{OBu-t}^+ \quad \text{Me}_2\text{COCHCO}_2\text{Bu-t}^+ \\
m/e 245
\]

\[\xrightarrow{-\text{Me}^*} \]

\[
[(\text{t-BuO})_2\text{CHCO}_2\text{Bu-t}]^+ \quad \xrightarrow{-\text{C}_4\text{H}_8} \quad (\text{t-BuO})_2\text{CHCO}_2\text{H}^+ \\
m/e 204
\]

\[\xrightarrow{-\text{t-BuOC}^*} \]

\[
(\text{t-BuO})_2\text{CH}^+ \\
m/e 159
\]

\[\xrightarrow{-\text{t-BuOCHO}} \quad \text{t-Bu}^+ \\
m/e 57
\]
Similar fragmentations and rearrangements can be written for 1,2-di-t-butoxy-1,2-difluoroethylene. Possible structures of some of the observed mass units are given in Table 6.

**TABLE 6.** Possible Structures of Some of the Fragments Observed in the Mass Spectrum of 1,2-Di-t-butoxy-1,2-Difluoroethylene

<table>
<thead>
<tr>
<th>Structure</th>
<th>M/e</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{H} = \text{C}=\text{O}$</td>
<td>29</td>
</tr>
<tr>
<td>$\text{CH}_2=\text{CHCH}_2^+$, $\text{H} = \text{C}=\text{C}=\text{O}$</td>
<td>41</td>
</tr>
<tr>
<td>$\text{Me}_2\text{C}=\text{CH}_2$</td>
<td>56</td>
</tr>
<tr>
<td>$\text{Me}_3\text{C}^+$</td>
<td>57</td>
</tr>
<tr>
<td>$\text{t-BuO} = \text{C}=\text{F}$</td>
<td>104</td>
</tr>
<tr>
<td>$\text{Me}_2\text{CHO} = \text{C}=\text{C}-\text{F}$ or $\text{Me}_2\text{COCHC}-\text{F}$</td>
<td>137</td>
</tr>
<tr>
<td>$\text{t-BuO} = \text{CH}=\text{C}=\text{F}$</td>
<td>152</td>
</tr>
<tr>
<td>$\text{CH}_3 = \text{C}=\text{O}=\text{C}=\text{C}$</td>
<td>193</td>
</tr>
</tbody>
</table>

The lines observed at m/e 103, 159, and 175 may arise from impurities (probably $(\text{t-BuO})_3\text{CH}$).
EXPERIMENTAL

Reagents

Chlorodifluoromethane and dichlorofluoromethane, from Matheson Company were used without further purification. t-Butyl alcohol, from Baker Chemical Company was purified by the addition of potassium and distillation with a 5-foot, vacuum-jacketed column packed with glass helices. Potassium, from Baker Chemical Company, and pentane and hexane, from Matheson, Coleman and Bell, were all used without further purification.

Instrumentation

Gas-liquid chromatography

Two gas-liquid chromatographs were used. An F and M Model 720 was used to obtain analytical data. An Aerograph Autoprep Model 700-A was used in an unsuccessful attempt to isolate reaction products. With both instruments the carrier gas used was helium. A 6-foot, stainless steel column packed with 10% Carbowax 20 M and 2% KOH on Chromosorb W was used in all analytical work except in cases where
$t$-butyl formate and $t$-butyl alcohol were both components of a mixture. In those cases a similar column that was packed with 10% diisodecyl phthalate on Chromosorb W was used. The temperature was usually about 100°, however, both the temperature and flow rate were changed to maximize peak separation and minimize tailing when necessary.

**Nuclear magnetic resonance spectrometer**

Varian Nuclear Magnetic Resonance Spectrometers, Models A-60 and A-60-A were used. Chemical shifts were determined using tetramethylsilane as an internal standard.

**Infrared instrument**

A Perkin-Elmer Grating Spectrophotometer, Model 337 was used. The sample cells were sodium chloride plates.

**Mass spectrograph**

An AEI, Model MS-9 double-focusing mass spectrometer was used. The ionizing energy was maintained at 70 eV with the inlet system heated to 200°. The intensities of mass peaks are reported relative to the largest peak in the spectrum (the base peak) which is taken as 100.

**Indices of refraction**

Indices of refraction were determined with a Bausch and Lomb, Abbe'-3L Refractometer.
Molecular weight

The molecular weight of tri-\( t \)-butyl orthoformate was determined using a Mechrolab Vapor Pressure Osmometer, Model 301A. The solvent was spectral grade chloroform.

Boiling points

All boiling points given are uncorrected.

Reaction of dichlorofluoromethane and potassium \( t \)-butoxide in \( t \)-butyl alcohol

In a typical run, dichlorofluoromethane gas (180 g, 1.75 moles) was added above the surface of 3800 ml of 1.18 M potassium \( t \)-butoxide in \( t \)-butyl alcohol in a 3-neck, 5-liter flask, which was fitted with a thermometer, Dry Ice condenser, gas collection apparatus, and magnetic stirrer. The amount of gaseous haloform added was determined by weighing the cylinder prior to and after the addition was completed. The addition took place over a ten-hour period with the rate adjusted so that temperature did not rise above 30°. The reaction mixture was 0.06 M in base when the addition was discontinued. The effluent gases (1 liter), collected through the condenser were retained for further analysis. The volume of the reaction mixture was reduced to 500 ml by vacuum distillation (25–30°, ~25 mm Hg). Pentane (500 ml) was added and the
light brown mixture was filtered through a sintered glass funnel. A few potassium hydroxide pellets were added to the light yellow mother liquor to insure basicity. The volume was reduced to about 125 ml under vacuum. The remaining yellow oil was vacuum distilled using a platinum spinning band column. The first four fractions (54.4 g, bp 24-26° at 0.15 mm Hg, 30%) contained more than 95% cis and trans-1,2-di-t-butoxy-1,2-difluoroethylenes.

The distillation was continued. Four additional fractions were collected. The final fraction (1.3 g, bp 54° at 0.8 mm) was a white crystalline substance (mp 26-27°, n\textsuperscript{26} \text{D} 1.41062). Glc analysis, on a six-foot Carbowax 20 M column, indicated the presence of only one component. The total yield of tri-t-butyl orthoformate was 12.3 g (3%). Earlier attempts to obtain a duplicate analysis on material obtained in previous runs were unsuccessful. When one ampoule of tri-t-butyl orthoformate was sampled three times the following analytical results were obtained: C, 67.40, 66.23, 65.84; H, 11.76, 11.53, 11.76. When the compound was sampled from individual ampoules sealed under nitrogen a duplicate analysis was obtained.

**Anal. Calcd. for C\textsubscript{13}H\textsubscript{28}O\textsubscript{3}:** C, 67.20; H, 12.11.

**Found:** C, 67.49; 67.77; H, 12.21; 12.08.

The ir spectrum had bands of decreasing intensities at 1057 (broad), 2980, 1028, 1192, 1345, 1236, 2940, 1123, 1455, and 896 cm\(^{-1}\). The nmr spectrum showed two singlets at 1.26 ppm and 5.65 ppm with relative intensities of 26.5:1. All the above data is compatible with structure of the previously unreported compound tri-t-butyl orthoformate.

The ir spectrum of the effluent gases was identical to that of dichlorofluoromethane.

The yield of isolated compounds, based on haloform, was 30% *cis* and *trans*-1,2-di-t-butoxy-1,2-difluoroethylene and 3% tri-t-butyl orthoformate. The yields, determined by glc analysis prior to work-up, were: *di*-t-butoxydifluoroethylene 81%, and *tri*-t-butyl orthoformate 5%. In other runs the yield of isolated substituted ethylenes was as high as 44%.

**Reaction of chlorodifluoromethane and potassium t-butoxide in t-buty alcohol**

Chlorodifluoromethane (200 g, 2.31 moles) was added to 3800 ml of 0.97 M potassium t-butoxide in t-buty alcohol following the procedure previously described for
dichlorofluoromethane. The reaction mixture was 0.11 M in base when the addition of haloform was stopped. Distillation with a spinning band column after work-up gave 51.8 g of a mixture of t-butyl alcohol (1%) and cis and trans-1,2-di-t-butoxy-1,2-difluoroethylenes (bp 28-44° at 0.82-1.6 mm Hg). The distillation was stopped and the pot residue (15.5 g, mp 26-27°) was recrystallized from pentane to give white needle crystals (mp 26-27°). The physical constants and analytical data for this compound were identical with those of the compound characterized as tri-t-buty l orthoformate obtained in the reaction of dichlorofluoromethane with potassium t-butoxide. The yield of cis and trans-di-t-butoxydifluoroethylenes was 22%. The yield of tri-t-buty l orthoformate was 3%.

The effect of base concentration in the reaction of t-butoxide with dichlorofluoromethane

The procedure employed was the same as the one previously described for dichlorofluoromethane. Three experiments were performed at initial potassium t-butoxide concentrations of 0.01, 0.10, and 0.72 M. After stripping off the t-butyl alcohol under reduced pressure the remaining oils were analyzed by gas-liquid chromatography on a six-foot, Carbowax 20 M column at 100°. It was found that
the amount of t-buty1 orthoformate relative to the tetra-
substituted ethylenes decreases with increasing base
concentration. Complete results are given in Table 3.

Reactions of tri-t-buty1 orthoformate

1. Hydrolysis

A sample of recrystallized tri-t-buty1 orthoformate
(1 g, mp 24-26°) was stored in the refrigerator over a
couple of potassium hydroxide pellets. After two days the
orthoester was no longer crystalline. The nmr showed the
presence of t-buty1 alcohol and t-buty1 formate as well
as tri-t-buty1 orthoformate (mainly). The presence of
t-buty1 formate was confirmed by comparison with an authen-
tic sample which was prepared by the method of Naff and
Rapp.26

(26) B. Naff and K. E. Rapp, J. Org. Chem., 19,
1317 (1957).

Evidently the flask had not been tightly stoppered
and moisture had condensed in the flask. A few drops of
water were added to the sample. After 24 hr, nmr and ir
analysis indicated that the amounts of t-buty1 alcohol and
t-buty1 formate had increased at the expense of the ortho-
ester.
2. **Thermal decomposition**

Tri-$t$-butyl orthoformate (0.087 g, 4 mmoles) in a 5-ml pear-shaped flask fitted with a reflux condenser and drying tube was heated in an oil bath at 95° for five hours. The weight of the sample decreased by 0.013 g. Glc analysis on a Carbowax 20 M column indicated that the compound suffered little decomposition. Small amounts (less than 10%) of $t$-butyl alcohol and $t$-butyl formate were formed. No $t$-butyl di-$t$-butoxyacetate was detectable.

3. **Reaction with hydrofluoric acid**

Hydrofluoric acid (5 drops, 48% aqueous) was added to $t$-butyl orthoformate (0.66 g, 30 mmoles) in a 5-ml pear-shaped flask which was fitted with a condenser and drying tube. After a vigorous initial reaction, two layers separated: a lower, cloudy aqueous layer and a clear organic layer. After 30 min, the mixture was transferred to a separatory funnel, ether (10 ml) was added and the layers were separated. The organic layer was washed with water (5 ml, 3 times), dried over magnesium sulfate, and the ether was removed. The ir spectrum of the remaining liquid showed a strong carbonyl absorption at 1720 cm$^{-1}$. Glc analyses on Carbowax 20 M and diisodecyl phthalate columns indicated the presence of $t$-butyl alcohol and $t$-butyl
formate in a ratio of about 4:1. No higher boiling components could be detected.

Preparation of t-butyl formate

Aluminum t-butoxide (Alpha Inorganics, 32.5 g, 0.13 mole) was added to n-butyl formate (K and K Labs, 100 g, 1.2 moles) in a 250-ml, one-neck flask which was fitted with a 10-inch Vigreux column, condenser, and receiver. The mixture was magnetically stirred for two hours and then slowly distilled. The first fraction (20 g) contained 75% t-butyl formate, 10% t-butyl alcohol, and 15% n-butyl formate as determined by glc analysis on a six-foot 10% diisodecyl phthalate column. The second fraction (60 g) contained more than 90% n-butyl formate. Further purification of the first fraction was not undertaken because only glc and nmr data were required for comparison with the data from products of hydrolysis of tri-t-butyl orthoformate.

The nmr spectrum showed singlets at δ 7.98 ppm and δ 1.50 ppm (t-butyl formate) and singlets at δ 3.48 ppm and δ 1.22 ppm (t-butyl alcohol).
The reaction of 1,2-di-t-butoxy 1,2-difluoroethylene and t-butyl alcohol

1,2-Di-t-butoxy-1,2-difluoroethylene (13 g, 0.06 mole) was diluted to 100 ml with t-butyl alcohol in a 250-ml flask, which was fitted with a condenser, gas collection apparatus, and heating mantle. The solution was refluxed for one hour. Ir and glc analyses indicated that no detectable amount of t-butyl di-t-butoxyacetate had been formed. The solution was slightly acidic (pH 4-6). After refluxing for another hour, the mixture became more strongly acidic (pH ~2) and analysis indicated that a small amount of ester had been formed. The amount of ester increased on standing at room temperature overnight.

The solution was made basic with aqueous sodium carbonate, ether (20 ml) was added, and the layers were separated. Comparison of the glc retention times and ir spectrum of the organic layer with those of an authentic sample confirmed that t-butyl di-t-butoxyacetate is formed in the reaction of cis and trans-1,2-di-t-butoxy-1,2-difluoroethylenes with t-butyl alcohol at reflux.

From the ir spectrum it appeared that di-t-butoxyacetic acid was also formed although attempts to isolate and purify it were unsuccessful.
Preparation of t-butyl
di-t-butoxyacetate

Dichlorofluoromethane (18 g, 0.17 mole) was added to 600 ml of 0.99 M potassium t-butoxide in t-butyl alcohol in the manner previously described for dichlorofluoromethane. The reaction mixture was 0.28 M in base when the addition was discontinued. The Dry Ice condenser was replaced with a Claisen head and the volume was reduced to about 100 ml by heating. Water (200 ml) was added to dissolve the precipitated salts. The solution was extracted with ether (30 ml, twice). The extract was dried over sodium carbonate, filtered, and the ether was removed under reduced pressure. The remaining dark yellow liquid was vacuum distilled. Four fractions were collected. When the temperature reached 70° (2 mm Hg), the distillation was stopped. The pot residue was distilled with a short-path distillation head. A clear liquid (2.1 g), bp 54-58° at 0.7 mm Hg, was collected. This fraction (mp 55-56°), which solidified within a few minutes, had ir and nmr spectra identical to those of t-butyl di-t-butoxyacetate obtained by Schreck.15

Triisopropyl orthoformate

Following the procedure of Hine, Ketley, and Tanabe,4 dichlorofluoromethane (46 g, 0.34 mole) was added to 765 ml of 1.3 M potassium isopropoxide in isopropyl
alcohol. The reaction mixture was cooled during the addition and the temperature was maintained below 40°C. After the addition was completed, the solution was no longer basic. The reaction mixture was stirred at room temperature for one hr and then filtered. The resulting colorless solution was fractionated at atmospheric pressure. The distillation gave 49 g (0.26 mole, 76%) of triisopropyl orthoformate, bp 168-171°C. The nmr (CCl₄) gave the following lines  δ 5.20 ppm [s, 1, CH(0 Pr-i)₃], δ 3.95 ppm [septet, 3, CH(OCH(CH₃)₂)₃], δ 1.13 [d, 18, CH(OCH(CH₃)₂)₃]. Gas-liquid chromatography of the crude reaction mixture and all distillation fractions did not indicate the presence of 1,2-difluoro-1,2-diisopropoxyethylene reported by Cleaver to be a product of this reaction. If this compound is formed in the reaction, it comprises much less than 1% of the reaction products.
PART II
INTRODUCTION

The anomalous effects of fluorine substituents have long been recognized in the chemistry of fluorinated organic compounds. These effects have been observed in the physical properties and reactivity of these compounds. In Table 1 the bond lengths of the fluoromethanes are presented.\(^1\) It is noteworthy that the C-F bond length decreases with increasing fluorine substitution. Pauling\(^2\)


<table>
<thead>
<tr>
<th>Compound</th>
<th>C-F Bond (Å)</th>
<th>C-H Bond (Å)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH(_3)F</td>
<td>1.391; 1.385</td>
<td>1.109</td>
</tr>
<tr>
<td>CH(_2)F(_2)</td>
<td>1.358</td>
<td>1.092</td>
</tr>
<tr>
<td>CHF(_3)</td>
<td>1.332; 1.326</td>
<td>1.098</td>
</tr>
<tr>
<td>CF(_4)</td>
<td>1.323</td>
<td>(1.093)(^a)</td>
</tr>
</tbody>
</table>

\(^a\) For CH\(_4\)
has suggested that this observation could be explained in terms of double-bond-no-bond resonance structures such as I. Increasing fluorine substitution in methane would lead to more canonical structures such as I and hence to the observed shorter C-F bond lengths. This explanation has until recently, enjoyed wide acceptance in the chemical literature.

Holtz\(^3\) has pointed out that it is not clear that

\[
\begin{align*}
\text{F} & \quad \text{F}^- \\
\text{F-C-F} & \leftrightarrow \text{F=C-F} & \leftrightarrow \text{etc.}
\end{align*}
\]

structures such as I would necessarily lead to shorter C-F bond lengths. He has suggested that the bond lengths can be rationalized from a consideration of an electrostatic model of the fluoromethanes in which the high electronegativity of fluorine induces a small negative charge on fluorine and an equal positive charge on carbon. The result of this charge induction would be a net electrostatic attraction leading to shorter C-F bond lengths.

Bent\textsuperscript{4} has rationalized the observed bond lengths by a consideration of changes in hybridization due to the large electronegativity of fluorine. Peters\textsuperscript{5} has pointed out that arguments from electrostatic models and bond hybridization are closely related and indeed may be indistinguishable.

Fluorine double-bond-no-bond resonance or fluorine hyperconjugation has also been invoked to rationalize the effect of fluorine substituents in reaction chemistry. Andreades\textsuperscript{6} has studied the rates of hydrogen isotope exchange of several polyfluorinated alkanes. The results are presented in Table 2. The nine powers of ten rate enhancement of tris(trifluoromethyl)methane over fluoromethane cannot be explained in terms of an inductive effect. Using the normal attenuation factor for inductive effect, (the effect decreases by about one third for every atom

\begin{itemize}
\end{itemize}
TABLE 2. Rates of Hydrogen Isotope Exchange of Polyfluorinated Alkanes

<table>
<thead>
<tr>
<th>Compound</th>
<th>Relative rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>CF₃H</td>
<td>1</td>
</tr>
<tr>
<td>CF₃(CF₂)₅CF₂H</td>
<td>6</td>
</tr>
<tr>
<td>(CF₃)₂CFH</td>
<td>2 x 10⁵</td>
</tr>
<tr>
<td>(CF₃)₃CH</td>
<td>10⁹</td>
</tr>
</tbody>
</table>

Further the substituent is removed from the reaction center, the reactivity of fluoroform and tris(trifluoromethyl)methane should be nearly equivalent. That is, nine β fluorines should have about the same inductive effect as three α fluorines. The results were rationalized in terms of structures such as III. Thus, increasing the number of trifluoromethyl groups will result in more canonical forms like III stabilizing the carbanion and hence leading to enhanced rates.

Andreades suggested that the validity of fluorine hyperconjugation could be tested by studying molecules where fluorine hyperconjugation would be prohibited by

\[ \overset{-}{C} \overset{\text{F}}{\text{C}} \overset{\text{F}}{\text{C}} \longleftrightarrow \overset{\text{F}}{\text{C}} = \overset{\text{F}}{\text{C}} \]

III
the molecular geometry. Such an approach has been used to demonstrate the planarity of carbonium ions. Bridgehead atoms in strained bicyclic systems cannot be \(sp^2\) hybridized and therefore a carbanion at a bridgehead atom would be much less stabilized by structures such as III than a carbanion that could acquire a planar configuration.

Streitwieser and Holtz\(^7\) have investigated the rates of hydrogen isotope exchange of \(1\) \(H\)-undecafluorobicyclo[2.2.1]heptane and tris(trifluoromethyl)methane. The carbanions IV and V are intermediates in the base-catalyzed exchange reactions in question. Carbanion IV has \(6\) \(\alpha\) and \(5\) \(\gamma\) fluorines and V has \(9\) \(\alpha\) fluorines. Qualitatively, the stabilization of the carbanions by inductive effects should be similar. In carbanion IV, stabilization by fluorine hyperconjugation is prohibited or at least minimized since such hyperconjugation would require a
double bond at the bridgehead of a strained bicyclic system and hence would be a violation of the familiar Bredt's rule. In the tris(trifluoromethyl)carbanion V

there is the possibility of three hyperconjugative structures that could stabilize the carbanion. Hence, if fluorine hyperconjugation is important, the rate of hydrogen isotope exchange of tris(trifluoromethyl)methane should be several orders of magnitude greater than that of 1 H-undecafluorobicyclo(2.2.1)heptane. The rate of exchange of the bicyclic compound was found to be twice that of tris(trifluoromethyl)methane. The authors concluded that the stabilization of alkyl anions by fluorine substituents is due entirely to inductive effects.

As further evidence that stabilization of alkyl anions by fluorine is exclusively inductive, Holtz has correlated the pK \textsubscript{a}'s of 14 substituted alkanes (derived from their base catalyzed exchange rates) with $\sigma^*$. The acidity of the compounds (including several polyfluorinated ones) varied by more than 30 powers of ten. A good correlation was obtained with the largest deviation from a straight line being 1.2 pK units.

Inductive effects alone, however, are not sufficient
to explain the observed reactivity of α-fluorinated alkyl anions. If this were true, then, as was pointed out earlier, fluoroform and tris(trifluoromethyl)methane should have similar reactivity. Recall that the reactivity of tris(trifluoromethyl)methane is nine orders of magnitude greater than that of fluoroform. Holtz has explained these results in terms of a deactivating effect of α-fluorine substituents. This deactivation is the result of π-π lone-pair repulsion which is the electrostatic effect resulting from the presence of four nonbonding electrons in adjacent π-orbitals. The low F-F bond strength in F₂ has been attributed to lone-pair repulsion.


The importance of the effect can be seen from the work of Adolf and Kamlet. The apparent equilibrium pKₐ's of a number of substituted nitromethanes were determined and are presented in Table 3.
TABLE 3. Apparent Equilibrium $pK_a$'s of Substituted Nitromethanes

<table>
<thead>
<tr>
<th>Compound</th>
<th>$X = \text{Cl}$</th>
<th>$H$</th>
<th>$F$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$X\text{C}_2\text{H} = \text{Cl}$</td>
<td>5.99</td>
<td>7.20</td>
<td>10.14</td>
</tr>
<tr>
<td>$X\text{C}_2\text{H} = \text{NO}_2$</td>
<td>3.80</td>
<td>3.5</td>
<td>7.70</td>
</tr>
<tr>
<td>$X\text{C}_2\text{H} = \text{CONH}_2$</td>
<td>3.50</td>
<td>5.18</td>
<td>5.89</td>
</tr>
<tr>
<td>$X\text{C}_2\text{H} = \text{CO}_2\text{C}_2\text{H}_5$</td>
<td>4.16</td>
<td>5.75</td>
<td>6.28</td>
</tr>
</tbody>
</table>

The acid weakening effect of $\alpha$-fluorine substituents is dramatically illustrated. Note that the replacement of hydrogen by highly electronegative fluorine results in a decrease in the acidity of all the compounds studied. Evidently this effect is of such importance that it outweighs the electron-withdrawing effect which would be expected to result from the high electronegativity of fluorine. It should also be noted that replacement of hydrogen by chlorine, whose large $p$ orbitals would be expected to cause less repulsion, results in smaller $pK_a$'s in all but one case. The acid weakening effect does, however,
seem to be important here also, because the increase in acidity is smaller than would be predicted from the normal inductive effect of chlorine.

There are several other examples of the anomalous effect of α-fluorine substituents. Streitwieser and Mares\textsuperscript{12} observed that 9-fluorofluorene is less reactive than fluorine itself towards sodium methoxide catalyzed hydrogen isotope exchange. Jullien and Thoi-Lai\textsuperscript{13} have observed a similar effect in the base catalyzed deuteration of substituted ketones. Kumler, Kun, and Shoolery\textsuperscript{14} found that diethyl oxaloacetate is 79% enolized in the pure liquid form and diethyl fluorooxaloacetate gave no detectable amounts of enol.

Hine, Mahone, and Liotta\textsuperscript{15} have observed the

\begin{itemize}
  \item \textsuperscript{12} A. Streitwieser, Jr. and F. Mares, \textit{J. Amer. Chem. Soc.}, 90, 2444 (1968).
  \item \textsuperscript{13} J. Jullien and N. Thoi-Lai, \textit{Bull. Soc. Chim.} (France), 4669 (1968).
  \item \textsuperscript{14} W. D. Kumler, E. Kun, and J. N. Shoolery, \textit{J. Org. Chem.}, 27, 1165 (1962).
  \item \textsuperscript{15} H. M. Hine, J. Mahone, and H. J. Liotta.
\end{itemize}
deactivating effect of α-fluorine substituents on the rates of deuterium exchange of substituted methyl acetates. In order to determine what the expected rates would be if only inductive effects were important, the rates of exchange of several alkyl substituted methyl acetates were determined.

\[
\text{NaOMe} \xrightarrow{\text{XYZCO}_2\text{CH}_3 + \text{CH}_3\text{OD}} \rightarrow \text{XYCDCO}_2\text{CH}_3 + \text{CH}_3\text{OH}
\]

It was found that the rates of exchange of the alkyl substituted acetates were well correlated with \( \sigma^* \) indicating that only inductive effects were contributing to the rates. The reaction constant \( \rho^* \) was 1.79 which is reasonable since electron-withdrawing substituents should stabilize the intermediate carbanion and therefore enhance the rates. The rates of exchange of the fluoro and difluoroacetates were 5 and 12 powers ten, respectively, less reactive than predicted by the Taft correlation. Interestingly, the rates of exchange of methyl methoxyacetate and methyl dimethoxyacetate were also several orders of magnitude smaller than predicted from the Taft plot. The deactivating effects of α-fluorine and oxygen substituents were rationalized in terms of an electronegativity effect. From a consideration
of bond energies using the Pauling equation\textsuperscript{16} and the

\begin{align}
\log\left(\frac{k_{YZ}}{k_{HH}}\right) &= \rho^*(\sigma_{-Y} + \sigma_{-Z} - 2\sigma_{-H}) + \rho^E(x_Y + x_Z - 2x_{HH})
\end{align}

was derived, where $k_{YZ}$ and $k_{HH}$ are the rate constants for exchange for the YZ substituted compound and methyl acetate, $x_Y$, $x_Z$, and $x_{HH}$ are the electronegativities of Y, Z and hydrogen and $\rho^*$ and $\sigma^*$ are the Taft reaction and substituent constants. A plot of $\log\left(\frac{k_{YZ}}{k_{HH}}\right) - \rho^*
\left(\sigma_{-Y} + \sigma_{-Z} - 2\sigma_{-H}\right)$ vs. $(x_Y + x_Z - 2x_{H})$ for the monosubstituted acetates gave a straight line, however the methyl dimethoxy and difluoroacetates gave negative deviations from the line.

The following work was undertaken to determine:

a) whether the electronegativity argument presented above is a good approximation of the effects of $\sigma$-fluorine and oxygen substituents, b) whether deviations from the electronegativity correlation are due to steric effects, and c) whether $\sigma$-nitrogen atoms are effective in retarding the rates of exchange of substituted esters.

EXPERIMENTAL

Chemicals

**Methyl isobutyrate**

Isobutyric acid (Aldrich Chemical Co.) was esterified either by the Fischer method or by the addition of ethereal diazomethane. The crude ester was distilled through a 20-cm column packed with glass helicies, bp 92-93°. Glc analysis (6 ft. DEGS column, 100°) showed the compound to be greater than 99.8% methyl isobutyrate.

**Methyl 2-ethylbutyrate**

2-Ethylbutyric acid (Aldrich Chemical Co.) was esterified by the addition of excess ethereal diazomethane. The crude ester was distilled with a platinum spinning band column and the fraction boiling at 135-136° was collected. Analysis by glc (6 ft. DEGS column, 120°) showed the fraction to be 99.9% methyl 2-ethylbutyrate.

**Methyl dimethoxyacetate**

Methyl dimethoxyacetate (Distillation Products Industries) was distilled through a 12-inch column that was packed with glass helicies. The material used in
the kinetic runs had bp 163-164° and was 99.6% pure by glc analysis (6 ft, DEGS column, 135°).

**Sodium dimethoxyacetate**

Methyl dimethoxyacetate (4.5 g, 0.034 mole) was refluxed with aqueous sodium hydroxide (17 ml, 2 N) for three hours. The solution was cooled, extracted with ether, and evaporated to dryness to obtain sodium dimethoxyacetate (4.7 g, 0.033 mole). The salt was purified by recrystallization from isopropyl alcohol. The purity of the sodium salt was determined by nmr spectrometry. A weighed amount of the sodium salt was dissolved in deuterium oxide. t-Butyl alcohol (25 µl) was added as reference. From the ratio of the integrated intensities of (CH₃)₃OH and (CH₃O)₂CHCO₂Na the purity (99.7%) could be calculated.

**Methyl cyclopentanecarboxylate**

Cyclopentanecarboxylic acid (Aldrich Chemical Co.) was esterified with excess diazomethane. The crude ester was distilled under reduced pressure and the fraction that had bp 93-94° (60 mm) was collected. Analysis by glc (6 ft, DEGS column, 120°) indicated that the fraction was 99.9% methyl cyclopentanecarboxylate.
Furoic acid

Silver nitrate (150 g, 0.89 mole) was dissolved in water (300 ml) in a one-liter, three-neck flask. Sodium hydroxide (70 g, 1.75 mole) in 300 ml of water was added with rapid stirring. A brown precipitate (Ag₂O) was formed during the addition. Furfural (70 g, 1.75 mole) was added dropwise over a period of four hours with rapid stirring. The solution was stirred at ambient temperature for an additional hour. The solution was vacuum filtered to remove the elemental silver and excess silver oxide. The precipitate was washed with hot water. The filtrate was cooled and acidified to congo red with hydrochloric acid. The white precipitate that resulted was filtered and recrystallized from hot water to give furoic acid (27 g, 0.24 mole), mp 124-125°, lit. 131-134°.


Methyl tetrahydrofuran-2-carboxylate

Furoic acid (27 g, 0.24 mole) was esterified by the addition of excess ethereal diazomethane. The ether was removed under reduced pressure and the crude methyl furoate was dissolved in cyclohexane (300 ml). Palladium
on carbon (1 g) was added to the solution. The solution was hydrogenated at ambient temperature and an initial pressure of hydrogen of 50 psi. The theoretical amount of hydrogen was absorbed in 12 hours. The catalyst was removed by filtration and the cyclohexane evaporated under reduced pressure. Analysis by glc (6 ft, 10% Apiezon L column, 150°) indicated that the hydrogenation was complete. The crude ester was distilled with a platinum spinning band column. The fraction of bp 51-52° (40 mm) was collected and analysis by glc (6 ft, 10% Apiezon L column, 100°) indicated that the fraction was 99.9% methyl tetrahydrofuran-2-carboxylate.

Tetrahydrofuran-2-carboxylic acid

Methyl tetrahydrofuran-2-carboxylate (2.5 g, 0.019 mole) was refluxed with aqueous sodium hydroxide (9.5 ml, 2 N for 12 hours. The solution was cooled, extracted with ether (5 ml) and acidified with hydrochloric acid (6 N) to pH 2. The solution was extracted with ether (2 times, 5 ml). The extract was dried over molecular sieve 5A (Linde), filtered, and the ether evaporated. The resulting acid was 99.5% pure by glc analysis (6 ft, Apiezon L column, 160°).
**N-Methylpyrrole-2-carboxylic acid**

Silver nitrate (22.1 g, 0.13 mole) was dissolved in distilled water (100 ml) in a 250-ml, three-neck flask that was fitted with a condenser, dropping funnel, and mechanical stirrer. Sodium hydroxide (10 g) was dissolved in 100 ml of water and the solution was poured slowly into the flask. N-Methylpyrrole-2-carboxaldehyde (Aldrich Chemical Co., 12.5 g, 0.12 mole) was added dropwise over a period of one hour. The solution was refluxed for five hours and allowed to cool to ambient temperature. The silver-silver oxide precipitate was removed by vacuum filtration and washed with hot water. The water white filtrate was acidified with 1 N hydrochloric acid to pH 3. During acidification the reaction mixture darkened. At pH 3 the solution was black. The solution was extracted with ether (2 times, 500 ml). The extract was dried over magnesium sulfate, filtered, and the ether was removed under reduced pressure. The resulting black solid was dissolved in 50% chloroform—50% hexane, activated charcoal was added and the solution was refluxed. Filtration, evaporation, and three recrystallizations from the same solvent gave nearly white needle crystals (8.7 g, 0.07 mole, 53%), mp 138-140°, lit. 135°.

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Methyl N-methylpyrrolidine-2-carboxylate

N-Methylpyrrole-2-carboxylic acid (7.5 g, 0.06 mole) was dissolved in 100 ml of ether and esterified with excess diazomethane. After drying and removal of the ether, the crude ester was distilled with a short-path column, bp 70-80° (10 mm). The distillate (6 g) was dissolved in glacial acetic acid (25 ml), rhodium on alumina (0.85 g) was added, and the solution was hydrogenated at 50 psi and ambient temperature. After the absorption of hydrogen ceased, the catalyst was removed by filtration and the solvent was removed by evaporation under reduced pressure. The remaining liquid was made basic with 3 N sodium methoxide in methanol. The methanol was evaporated and ether (50 ml) was added. The resulting precipitate (sodium acetate) was removed by filtration and the ether was removed from the filtrate. It was necessary to repeat this procedure twice to convert the ammonium salt to the amine. Sodium methoxide (1 g) was added to the remaining oil. The mixture was distilled with a short-path column and a water-white oil (2.4 g, 0.017 mole, 29%) was obtained, bp 76-77° (21 mm). Analysis by glc (6 ft, 10% silicon gum rubber column, 140°) indicated that the ester contained acetic acid (3%). The ester was purified by preparative glc
(6 ft, 10% SE 30 column, 110°). Analysis of the fraction collected (2.2 g) indicated it was 99.9% pure, \( n^D_{20} 1.4435 \), lit. \( n^D_{20} 1.4468 \), nmr spectrum #1.

The ir spectrum had bands of decreasing intensity at 1740, 1198, 1161, 2955, 2790, 1055, and 1425 cm\(^{-1}\).

2-[β-Chloroethyl]-1,3-dioxolane \(^{19} \)

______


Hydrochloric acid (150 g, 2.3 moles) was bubbled into ethylene glycol (350 g) in a 500-ml three-neck flask. The flask was weighed at intervals until the desired amount of acid had been added. The solution was cooled to 0° and acrolein (225 g, 4.0 moles) was added dropwise with mechanical stirring. The rate of addition was adjusted to maintain the temperature between 0 and 5°. When the addition was complete, the cooling bath was removed and the reaction mixture was allowed to come to ambient temperature over a period of one hour. The solution was poured into cold water (1 liter) shaken and the layers separated. The lower organic layer was washed twice with cold water (1 liter). Ether (500 ml) was added to the resulting light yellow oil and the solution was dried over Drierite. After evaporation of the ether, the
oil was distilled under reduced pressure. The main frac-
tion (bp 68-69° (10 mm), 204 g, 1.52 moles, 38%) was 98%
2-[β-chloroethyl]-1,3-dioxolane as determined by glc
analysis (6 ft, DEGS column, 150°), nmr (CCl₄): δ 4.98 ppm
[t, 1], δ 3.87 ppm [m, 4], δ 3.58 ppm [t, 2], δ 2.05
[sextet, 2].

2-Vinyl-1,3-dioxolane

(20) V. Faass and H. Hilgert, Ber., 87, 1343 (1954).

2-[β-Chloroethyl]-1,3-dioxolane (150 g, 1.1 mole)
was added to powdered potassium hydroxide (350 g) in a
500-ml, three-neck flask that was fitted with a stopper,
thermometer, and Claisen distillation head. The reaction
mixture was heated slowly with an oil bath until most of
the liquid had distilled (bp 115-120°). The resulting
crude olefin (105 g) was redistilled with a platinum
spinning band column. The fraction of bp 110-112° was
collected (81 g, 0.81 mole, 73%), nmr spectrum #2.

Sodium 1,3-dioxolane-2-carboxylate

2-Vinyl-1,3-dioxolane (8.5 g, 0.085 mole) was dis-
solved in 100 ml of methanol. The solution was cooled
to -15° and excess ozone was bubbled into the solution.
The crude ozonide-methanol mixture was added to a slurry
of 5% aqueous sodium hydroxide (150 ml) and silver oxide
(42 g, 0.18 mole) with rapid stirring. After stirring for an hour, the silver-silver oxide precipitate was removed by filtration. The filtrate was extracted with ether (100 ml). Carbon dioxide was bubbled into the aqueous layer to convert the sodium hydroxide to sodium bicarbonate. The mixture was evaporated to dryness (20 mm Hg, 70°). The white solid material (26.5 g) that was obtained was dissolved in hot methanol and filtered. The filtrate was evaporated to dryness. A white crystalline compound (10.5 g) resulted. The nmr spectra (D₂O) indicated the presence of sodium formate and sodium 1,3-dioxolane-2-carboxylate, nmr:

(21) Chemical shifts are relative to (CH₃)₃COH.

(D₂O) 2.78 ppm [S, 4, O(CH₂)₂OCHCO₂Na], 3.88 ppm [S, 1, O(CH₂)₂OCHCO₂Na], 6 7.20 ppm [S, HCO₂Na].

Methyl 1,3-dioxolane-2-carboxylate

An equimolar mixture of sodium formate and sodium 1,3-dioxolane-2-carboxylate (7.5 g) was dissolved in 20 ml of water. Sufficient sulfuric acid (18 N) was added drop-wise to the cooled solution (0°) to reach pH 2. The solution was quickly extracted with ether (twice, 200 ml). Ethereal diazomethane was added to the extracts until the yellow color persisted for one hour. The solution was dried over anhydrous magnesium sulfate, filtered and the ether was
removed under reduced pressure. The remaining oil (4.5 g, 0.034 mole) was 97% methyl 1,3-dioxolane-2-carboxylate as determined by glc analysis (6 ft, DEGS column, 130°). The ester was distilled under reduced pressure with a short-path column and three fractions were collected. The center cut was 99.4% one component (bp 87-88° (24 mm), 3.1 g, 0.023 mole), nmr spectrum #3.

Anal. Calcd. for C_{5}H_{8}O_{4}: C, 45.42; H, 6.10.
Found: C, 45.10; H, 6.00.

The ir spectrum had bands of decreasing intensity at 1740, 1130, 1222, 940, 1035, 2955, 1292, 1420, and 2900 cm⁻¹.

**Preparation of sodium 1,3-dioxolane-2-carboxylate for the determination of the pKₐ**

It was necessary to prepare a pure sample of sodium 1,3-dioxolane-2-carboxylate in order to determine its pKₐ. Methyl 1,3-dioxolane-2-carboxylate (2.5 g, 0.018 mole) was added to aqueous sodium hydroxide (9 ml, 2 N) in a 25-ml flask. The mixture was refluxed under a stream of nitrogen for 12 hours. The reaction mixture was evaporated to dryness under reduced pressure. The resulting white salt was re-crystallized from ethanol and its purity determined by the method previously described for sodium dimethoxyacetate.
Diazomethane

The diazomethane employed in the previously described esterifications was a solution of undetermined concentration of the gas in ether. Ethereal diazomethane was prepared by mixing 200 ml of 50% aqueous potassium hydroxide and 150 ml of ether in a 500-ml distilling flask which was fitted with rubber stoppers and a condenser. The reaction mixture was cooled to 0° with an ice-water bath and N,N'-dimethyl-N,N'-dinitrosoterephthalamide (Aldrich Chemical Co., 26 g) was added. The solution was allowed to come to room temperature and was then slowly heated on a steam bath. The ether layer became bright yellow and heating was continued until most of the ether had been distilled and the remainder was colorless. The distillate was used directly in the previously described esterifications.

Methanol-0-d²²


Dimethyl Carbonate (Aldrich Chemical Co., 500 g, 5.5 moles) was purified by distillation with a two-meter silvered, vacuum-jacketed column packed with tantalum helices. The fraction boiling at 88-90° was collected.
Dimethyl carbonate (486.5 g, 5.42 moles) was added to 18 N deuterated sulfuric acid (10 ml) in a one-liter flask equipped with a magnetic stirrer and two condensers in tandem. Deuterium oxide (110 g, 5.5 moles) was added. The mixture was refluxed under a stream of dry nitrogen for eight days. The condensers were replaced by a Claisen distilling head. The mixture was distilled and the fraction of bp 55-70° was collected. The fraction (450 ml) was redistilled with the two-meter column described above. Methanol-0-d, bp 65-66°, was collected under nitrogen (298 g, 9.30 mole, 86%) and stored over molecular sieve 3A (Linde).

Instrumentation

Glc

An F and M Model 720 gas-liquid chromatograph was employed. The carrier gas was helium. All columns were six feet, stainless steel with Chromosorb W as the packing material.

Nuclear magnetic resonance spectrophotometer

Varian Nuclear Magnetic Resonance Spectrometers, Models A-60 and A-60-A were used. Chemical shifts were determined using tetramethyldisilane as the internal standard except where stated otherwise.
Infrared spectrophotometers

A Perkin Elmer Grating Spectrophotometer, Model 337 was used. Qualitative work was done employing sodium chloride plates. For quantitative spectroscopy, fixed path-length cells (.05 mm, IR Trans II cells, Perkin Elmer Corp.) were used. The cells were flushed with two ml each of methanol, chloroform, and n-pentane, dried with a stream of nitrogen and stored in a desiccator between determinations.

Boiling points

All boiling points given are uncorrected.

Titration equipment

Automatic titrations were carried out using a combination of a Radiometer

Model 26 pH meter

Model 11 titrator

Model ABU1b auto-burette equipped with 2.5 ml syringe

Model SBR2C titrigraph recorder

TTA3 titration assembly

K401 reference electrode.

All equipment was operated as directed in the Radiometer manuals.
Constant temperature baths

For kinetic runs carried out at 60° an American Instrument Company constant temperature bath, Model 4-1588, filled with Mobil Extra Hecla Super Cylinder Mineral Oil was used. The temperature was maintained at 60.0±0.5°. For kinetic runs at 35°, a Sargent Heater and Circulator for Thermostatic Baths connected to a Sargent Thermonitor unit was used. The heater and circulator were submersed in a 10-gallon glass bath filled with water. The temperature was maintained at 35.0±0.1°.

Preparation of kinetic solutions

1. Kinetics at 35°—kinetic solutions were prepared by adding 5 ml of sodium methoxide-methanol-0-d solution (usually 0.4 to 0.8 M) to a 15-ml centrifuge tube fitted with a serum cap. Sufficient ester to make the final solution between 0.4 - 0.8 M was weighed in a calibrated syringe, the volume noted, and the ester syringed into the centrifuge tube which had been cooled to 0°. All transfers were done under a stream of nitrogen. The centrifuge tube was then shaken and submersed in a constant temperature bath. Aliquots were taken at intervals with a syringe. Final concentrations were calculated and the base concentration was checked by titration.
2. **Kinetics at 60°.**—Solutions were prepared by syringing 1-ml aliquots each of 0.8 to 1.3 N ester in methanol-0-\textsubscript{d} and sodium methoxide in methanol-0-\textsubscript{d} of concentration in the same range into 2-ml ampoules. The ampoules were sealed, shaken, and submersed in the constant temperature bath. Final concentrations of ester and base were calculated and the base concentration was checked by titration.

**Preparation of sodium methoxide-methanol-0-\textsubscript{d} solutions**

Sodium was cut under n-pentane and weighed. In a dry box (nitrogen) the sodium was placed in a dry 100-ml bottle fitted with a septum cap. A small amount of methanol-0-\textsubscript{d} was injected and the bottle was vented with a hypodermic needle. After the sodium metal acquired a highly lustrous surface, the liquid was removed with a syringe and the required amount of methanol-0-\textsubscript{d} was added. The concentration of sodium methoxide was determined by titration with standard hydrochloric acid using the Radiometer Automatic Titrator.

**Determination of sodium methoxide concentrations of kinetic solutions**

The sodium methoxide concentration of any given kinetic solution was determined by removing a one-ml aliquot with a calibrated syringe and quickly adding it to sufficient excess 0.1 N hydrochloric acid so that the final solution was about 0.05 N in hydrochloric acid.
The samples were stored in the freezing compartment of a refrigerator until they were titrated with standard sodium hydroxide with the Radiometer Automatic Titrator.

**Determination of pK$_a$'s**

The pK$_a$ of tetrahydrofuroic acid was determined by potentiometric titration of a sample of the acid with aqueous sodium hydroxide. From the equation

$$pK_a = pH + \log([A]/[HA])$$

The pK$_a$ can be determined by following the pH during the course of the titration. At the point of half neutralization the pK$_a$ very nearly equals the pH for acids of pKa greater than about 3. With stronger acids, the concentrations of A$^-$ and HA are significantly affected by the dissociation of HA. In these cases

$$pK_a = pH + \log\left(\frac{[HA]-y}{[A]+y}\right)$$

Equation (1) should be true for all points during a titration. As a check on the accuracy of a given determination, the pK$_a$ was calculated using Equation (1) at 25, 50, and 75% equivalence. In all cases agreement within 0.02 pK units was obtained.
The pk_a's of dimethoxyacetic acid and 1,3-dioxolane-2-carboxylic acid were not determined by direct titration of the acids. Both compounds are acetals and hence undergo acid catalyzed hydrolysis. In order to avoid this complication the sodium salts were prepared and rapidly titrated with standard aqueous hydrochloric acid.

The pk_a's of the three compounds mentioned above were determined by titrating 10 ml of a 0.02 M solution of the acid or sodium salt with 0.1 N sodium hydroxide or hydrochloric acid. The titrations were carried out in thermostatted constant temperature vessels at 35°. The titrations were performed with the Radiometer Automatic Titrator. The pH meter was standardized with buffer solutions at pH 4.01 and 9.18 prior to the titrations. The initial pH of the solutions to be titrated was recorded. The axis of the chart paper on the titrator is a function of pH and the ordinate a function of volume of titrant. The pk_a's determined in this way are given in Table 4.

TABLE 4. The pk_a's of Acids at 35°

<table>
<thead>
<tr>
<th>Acid</th>
<th>pk_a</th>
<th>Ionic strength^a</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Tetrahydrofuroic acid</td>
<td>3.72±0.03</td>
<td>0.009</td>
</tr>
<tr>
<td>Dimethoxyacetic acid</td>
<td>2.88±0.03</td>
<td>0.0174</td>
</tr>
<tr>
<td>1,3-Dioxolane-2-carboxylic acid</td>
<td>2.92±0.03</td>
<td>0.0189</td>
</tr>
</tbody>
</table>

^a At half neutralization
RESULTS AND DISCUSSION

The kinetics of the methoxide ion catalyzed deuterium exchange of the α-hydrogen atoms of methyl isobutyrate, methyl 2-ethylbutyrate, methyl cyclopentane-carboxylate, methyl tetrahydrofuran-2-carboxylate, methyl 1,3-dioxolane-2-carboxylate, methyl N-methylpyrrolidine-2-carboxylate, and methyl dimethoxyacetate in methanol-0-d solution were investigated.

Synthesis

The esters investigated in this work were either articles of commerce or prepared from the commercially available acids with the exceptions of methyl tetrahydrofuran-2-carboxylate, methyl N-methylpyrrolidine-2-carboxylate, and methyl 1,3-dioxolane-2-carboxylate.

Methyl tetrahydrofuran-2-carboxylate was easily prepared from furfural employing standard procedures of organic chemistry which are given in the Experimental Section.

Methyl N-methylpyrrolidine-2-carboxylate is the methyl ester of the naturally occurring amino acid,
hygic acid, which has been synthesized by Sorm and Smrt.23


Likhosherstov, Lebedova, and Skoldinov24 have synthesized the methyl ester starting with 2,5-dichloropentanoic acid. In the present work the ester was prepared from commercially available N-methylpyrrole-2-carboxaldehyde via the following reaction sequence:

![Reaction Diagram]

The procedure of Signaigo and Adkins25 was used in the


hydrogenation reaction. The conversion of the ammonium acetate, which results from the hydrogenation, to the free amine was not a facile process. Treatment of the salt with sodium methoxide in methanol followed by distillation did not give free amine. Analysis by glc indicated the presence of acetic acid. Because of this impurity, early kinetic runs on this compound gave erratic kinetic results. The compound was purified by preparative gas chromatography and consistent kinetic results were obtained in later runs.

Several approaches were taken in order to find a successful synthetic procedure for the preparation of methyl 1,3-dioxolane-2-carboxylate. The acid-catalyzed acetal formation with methyl glyoxalate and ethylene glycol failed to give the desired product. Using either mineral acids or p-toluenesulfonic, either the reactants were recovered unchanged or intractable materials of high molecular weight, probably resulting from polymerization or trans-esterification, were obtained. The compound was successfully synthesized by first forming the cyclic acetal linkage and then in subsequent steps, forming the ester group. The procedure of Faass and Hilgert was used to prepare 2-vinyl-1,3-dioxolane. The reaction sequence is given on page 69.
Attempts to oxidize VI with a stoichiometric amount of potassium permanganate to the dioxolane carboxylate salt gave mainly potassium oxalate. Acidification, extraction into ether, and esterification with diazomethane gave less than 15% of the desired ester. Oxidative cleavage of VI by the Lemieux periodate-permanganate procedure was unsuccessful. Failure to separate the carboxylate salt from sodium periodate led to the formation of iodine during the acidification of the salt. Successful oxidation was achieved by treatment of VI with excess ozone followed by silver oxide oxidation of the crude ozonide to give sodium 1,3-dioxolane-2-carboxylate.

The methyl ester was obtained by careful acidification of the sodium salt, extraction into ether, and esterification with diazomethane.
Treatment of kinetic data

The base-catalyzed deuterium exchange of the alpha protons of esters in methanol-0-d follows simple pseudo first-order kinetics since base is not consumed during the reaction. The reaction proceeds with an increase in the concentration of protiomethanol which is followed by measuring the increase in the absorbance of the 3360 cm⁻¹ band in the infrared spectrum. The absorbance, A, is governed at time zero by the initial isotopic purity of the methanol-0-d solvent and at infinite time by the equilibrium concentration of exchangeable protium.

Using the equation for first-order kinetics,

$$\ln \frac{A_\infty - A_0}{A_\infty - A_t} = k_a t$$

where

- $A_\infty$ = absorbance of infinite time
- $A_0$ = the initial absorbance
- $A_t$ = absorbance at time $t$,

a plot of the ln function versus time should give a straight line passing through the origin with a slope of $k_a$.

The apparent second-order rate constant, $k$, for the sodium methoxide catalyzed exchange can then be calculated from

$$k = k_a / [\text{NaOCH}_3]$$
because sodium methoxide is not consumed during the reaction. The value of \( A_\infty \) was a calculated value assuming random distribution of all exchangeable protium and deuterium atoms. The equilibrium concentrations of protiomethanol is given by:

\[
\left[ \text{CH}_3\text{OH} \right]_\infty = \left[ \text{CH}_3\text{OH} \right]_0 + [\text{Ester}] \text{ (fraction of } \alpha\text{-hydrogens exchanged)}
\]

or

\[
\left[ \text{CH}_3\text{OH} \right]_\infty = \left[ \text{CH}_3\text{OH} \right]_0 + [\text{Ester}] \times \frac{[D]}{[H]+[D]}
\]

where \([H]\) and \([D]\) are the total molar concentrations of exchangeable protium and deuterium atoms. \([D]\) can be approximated as the molarity of methanol, protio and deutero, or very nearly 24 for dilute solutions. Substitution into the equation gives:

\[
\left[ \text{CH}_3\text{OH} \right]_\infty = \left[ \text{CH}_3\text{OH} \right]_0 + [\text{Ester}] \frac{24}{24 + [\text{ester}] + [\text{CH}_3\text{OH}]}_0
\]

The calculated absorbance at infinite time was verified experimentally by determining the absorbances of kinetic solutions of methyl 2-ethylbutyrate, methyl cyclopentane-carboxylate, methyl tetrahydrofuran-2-carboxylate, and methyl N-methylpyrrolidine-2-carboxylate after ten or more half-lives at 60°. In all cases the experimental and calculated values were in agreement within 3%.
A computer program was written to calculate the least squares second-order rate constant, the standard deviation, and the extinction coefficient. The program and its description are given in the Appendix.

The reactions of the compounds studied showed good pseudo first-order kinetic behavior beyond the first half-life. A plot of $\log[(A_\infty - A_0)/(A_\infty - A_t)]$ vs time for the kinetics of exchange of methyl tetrahydrofuran carboxylate at $60^\circ$ is shown in Figure 1.

The base concentration was followed acidimetrically throughout the reaction. In some kinetic runs there was an initial rapid decrease in methoxide concentration which leveled off and then remained constant during the remainder of the kinetic run. This was attributed to the presence of hydroxide ion due to traces of water present. The ester undergoes rapid hydrolysis until the hydroxide is consumed. A first-order kinetic plot of data of this type gives falling rates, however, assuming that the ester is hydrolyzed rapidly compared to its rate of exchange, a correction can be made. The ester concentration is decreased by exactly the amount of base that is consumed. Using the corrected value for the ester concentration, good pseudo first-order kinetic behavior was observed with standard deviations in the same range as those obtained in kinetic
Figure 1.—Plot of \( \log \left( \frac{A_{\omega} - A_{\infty}}{A_{t} - A_{\infty}} \right) \) vs time for methyl tetrahydrofuran-2-carboxylate at 60°.
runs where an initial rapid decrease in base concentration was not observed. More data on the changing base concentration are given in Table 13 of the Appendix.

Quantitative infrared spectrometry

The method used to determine the molar concentration of methanol in methanol-0-d was that of Duke. Methanol in methanol-0-d has a strong polymeric-associated OH stretching band at 3360 cm\(^{-1}\), which can be used to determine the concentration of methanol directly. The absorbance of this band is determined in the following manner. The spectrophotometer is set at 3900 cm\(^{-1}\) and scanned to 3000 cm\(^{-1}\). Prior to the absorption band a minimum absorption region is encountered that is a very nearly transparent region. The absorbance of the band is taken as the difference between this minimum and the maximum absorbance value. The band is broad so that the maximum absorbance is well defined and quite reproducible.

Owing to the solubility of sodium chloride in methanol, fixed path length cells constructed of sodium chloride plates were not used. A micro cell constructed

\(\text{(27) R. B. Duke, Ph.D. dissertation, Georgia Institute of Technology, 1967.}\)
with plates of IR Trans II material (Perkin Elmer Corp.) was used.

The optical path length or cell thickness was determined by two methods.

1. The absorbance of the $1960 \text{ cm}^{-1}$ band of spectrograde benzene was measured. A straight line was drawn tangent to the spectral curve on both sides of the absorbance maximum. The absorbance value was defined as the difference between the maximum value and that of the base line defined by the straight line. The cell thickness is then given by the equation:

$$l(\text{cm}) = 0.0100 \times \text{Absorbance}$$

2. The Interference Fringe Method.\(^{28}\) Cell spacing is given by the formula:

$$l = \frac{n}{2(\nu_1 - \nu_2)}$$

where

- $l =$ optical path length (cm)
- $n =$ number of fringes
- $\nu_1$ and $\nu_2 =$ frequencies between which fringes are counted.

The two methods gave 0.049 mm and 0.050 mm, respectively.

The extinction coefficient of methanol in methanol-0-d was determined by measuring the absorbance of several solutions of varying methanol concentration. The solutions were prepared by weighing various amounts of methanol into 2-ml volumetric flasks and diluting to the mark with methanol-0-d. The results are given in Table 5.

**TABLE 5.** The Change in Absorbance at 3360 cm\(^{-1}\) with Changing Methanol Concentration

<table>
<thead>
<tr>
<th>[MeOH] added</th>
<th>[MeOH] corrected</th>
<th>Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>0.0</td>
<td>0.227</td>
</tr>
<tr>
<td>0.194</td>
<td>0.191</td>
<td>0.330</td>
</tr>
<tr>
<td>0.405</td>
<td>0.398</td>
<td>0.430</td>
</tr>
<tr>
<td>0.415</td>
<td>0.408</td>
<td>0.445</td>
</tr>
<tr>
<td>0.725</td>
<td>0.713</td>
<td>0.581</td>
</tr>
<tr>
<td>0.781</td>
<td>0.768</td>
<td>0.635</td>
</tr>
<tr>
<td>1.210</td>
<td>1.167</td>
<td>0.875</td>
</tr>
</tbody>
</table>

The methanol concentrations were corrected for the residual protio methanol in the methanol-0-d solvent. The correction was made in the following way:

\[
\text{Volume of } \text{MeOH}_{\text{add}} = \frac{\text{weight of } \text{MeOH}_{\text{add}}}{\text{density of } \text{MeOH}}
\]
The volume of solvent (MeOD) is given by:

\[ V_{\text{sol}} = 2.00 \text{ ml} - \text{Volume of MeOH}_{\text{add}} \]

The concentration of MeOH in the solvent can be calculated from:

\[ [\text{MeOH}]_{\text{solv}} = \frac{A}{\epsilon l} \]

where

\[ A = \text{absorbance of solvent at 3360 cm}^{-1} \]
\[ \epsilon = \text{extinction coefficient of MeOH in MeOD} \]
\[ l = \text{optical path length (cm)} \]

The weight of MeOH in the solvent is calculated from:

\[ \text{Wt of MeOH}_{\text{solv}} = V_{\text{sol}} \times [\text{MeOH}]_{\text{solv}} \times \text{Mol wt MeOH} \]

The corrected \([\text{MeOH}]\) is then given by:

\[ [\text{MeOH}]_{\text{corr}} = 500 \frac{\text{wt of MeOH}_{\text{add}} + \text{wt of MeOH}_{\text{solv}}}{\text{mol wt of MeOH}} - [\text{MeOH}]_{\text{solv}} \]

A plot of absorbance vs methanol concentration is given in Figure 2. The least squares slope is 0.544 from which the extinction coefficient, \(\epsilon\), can be calculated.

\[ \epsilon = \frac{\text{slope/path length (cm)}}{} = 108.8 \text{ M}^{-1} \text{cm}^{-1} \]

The extinction coefficient was checked by determining the methanol concentration of the methanol-methanol-0-d
Figure 2.—Beer's law plot for MeOH in MeOD at 3360 cm⁻¹
solutions by nmr spectrometry. With the spectrometer at
50 cps sweep width the absorbances of the $^{13}$C-H satellite
peak of CH$_3$OD(H) and CH$_3$OH were measured. The relative
areas of peaks were determined with a planimeter. The
percent protio methanol is given by the formula:

$$\% \text{ protiomethanol} = \frac{\text{area of OH peak} \times 1.1}{\text{area of } ^{13}\text{C-H peak} \times 2/3}$$

The infrared absorbance at 3360 cm$^{-1}$ of the same solution
is measured and assuming that methanol-0-d does not absorb
at 3360 cm$^{-1}$, the extinction coefficient can then be cal-
culated from the following equation:

$$\varepsilon = \frac{AM}{Hld}$$

where

- $A$ = absorbance at 3360 cm$^{-1}$
- $M$ = mol wt of methanol
- $H$ = fraction methanol determined by nmr
- $l$ = path length
- $d$ = density of methanol (g/l)

The results of this determination of the extinction
coefficient are given in Table 6.
TABLE 6. Determination of $\epsilon$ by Nmr Spectroscopy

<table>
<thead>
<tr>
<th>Absorbance</th>
<th>Relative areas</th>
<th>calc</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{13}C-H$</td>
<td>0-H</td>
<td></td>
</tr>
<tr>
<td>.210</td>
<td>35</td>
<td>37</td>
</tr>
<tr>
<td>.630</td>
<td>38</td>
<td>113</td>
</tr>
</tbody>
</table>

The effects of sodium methoxide and ester concentrations on the extinction coefficient were determined. Addition of the esters (0.6 M) to methanol-methanol-0-d solutions left the extinction coefficient unchanged. Sodium methoxide, however, is effective in decreasing the extinction coefficient of methanol in methanol-0-d solutions. The magnitude of the effect was determined by measuring the absorbances of solutions that were prepared by weighing various amounts of methanol in 2-ml volumetric flasks and diluting to the mark with 0.602 M sodium methoxide in methanol-0-d. The results are given in Table 7.

TABLE 7. The Absorbance of Methanol in 0.6021 M NaOMe-Methanol-0-d at 3360 cm$^{-1}$

<table>
<thead>
<tr>
<th>Added methanol concentration</th>
<th>Corrected methanol concentration</th>
<th>absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0</td>
<td>0.0</td>
<td>.182</td>
</tr>
<tr>
<td>0.375</td>
<td>0.370</td>
<td>.392</td>
</tr>
<tr>
<td>0.580</td>
<td>0.572</td>
<td>.490</td>
</tr>
<tr>
<td>0.760</td>
<td>0.749</td>
<td>.630</td>
</tr>
<tr>
<td>1.000</td>
<td>0.986</td>
<td>.680</td>
</tr>
</tbody>
</table>
A plot of absorbance vs methanol concentrations is given in Figure 3. The slope calculated by the method of least squares gave:

$$\varepsilon = 105.2 \text{ M}^{-1}\text{cm}^{-1}$$

Assuming that the extinction coefficient is a linear function of the sodium methoxide concentration, the extinction coefficient can be calculated from the equation:

$$\varepsilon = 108.8 - 5.98(\text{NaOMe})$$

The molar concentration of protiomethanol in sodium methoxide-methanol-$d$ solutions can then be calculated from:

$$[\text{CH}_3\text{OH}] = A_{ob}/\varepsilon_1$$

The extinction coefficient of methanol in methanol-$d$ was reported by Duke to be $137.3 \text{ M}^{-1}\text{cm}^{-1}$. It is to be noted that the value obtained in this work is significantly different. Similarly, Duke found that the extinction coefficient was decreased by 13.6 times the methoxide concentration compared to 5.98 obtained in this work. These differences may be due to the fact that the infrared instrument used by Duke was equipped with a sodium chloride prism whereas the instrument employed in the present work has a grating monochromator which gives better
Figure 3.—Beer's law plot for MeOH in 0.6021 M MeONa-MeOD solution at 3360 cm$^{-1}$.
resolution. Duke also used sodium chloride cells which gradually dissolved in methanol. This introduces uncertainty in the optical path length. It is felt that the value of the extinction coefficient determined in the present work is reliable because a) there is agreement between $\varepsilon$ determined by Beer's law plot and the nmr method discussed previously, b) the kinetic data give good first-order kinetic behavior, and c) the calculated absorbance at infinite time was in agreement with the experimental value for several kinetic runs.

**Kinetic results**

The rate constants for methoxide ion catalyzed deuterium exchange of the methyl esters investigated are presented in Table 8. The rates were measured at 35° and 60°. For those compounds where duplicate kinetic runs were made, the rate constants varied by less than ten percent. The precision of the rate constants was determined by comparing the standard deviation with the root mean square value of $\ln[(A_\infty - A_0)/(A_\infty - A_t)]$ for all of the kinetic points of a given run. In all but three runs the standard deviation was less than five percent of the RMS value. For the three exceptions; methyl cyclopentane-carboxylate at 60°, methyl isobutyrate at 35°, and methyl
### TABLE 8. The Apparent Second-order Rate Constants for Methoxide Catalyzed Deuterium Exchange of Methyl Esters

<table>
<thead>
<tr>
<th>Compound</th>
<th>$60^\circ$ kx10$^4$ M$^{-1}$sec</th>
<th>$35^\circ$ kx10$^5$ M$^{-1}$sec</th>
</tr>
</thead>
<tbody>
<tr>
<td>$(\text{CH}_3)_2\text{CHCO}_2\text{Me}$</td>
<td>0.991</td>
<td>0.978</td>
</tr>
<tr>
<td></td>
<td>1.07</td>
<td>1.01</td>
</tr>
<tr>
<td>$(\text{CH}_3\text{CH}_2)_2\text{CHCO}_2\text{Me}$</td>
<td>0.232</td>
<td>0.197</td>
</tr>
<tr>
<td></td>
<td>4.53</td>
<td>2.50</td>
</tr>
<tr>
<td>$(\text{CH}_3\text{O})_2\text{CHCO}_2\text{Me}$</td>
<td>1.58</td>
<td>1.01</td>
</tr>
<tr>
<td></td>
<td>1.15</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6.88</td>
<td>6.73</td>
</tr>
<tr>
<td></td>
<td>0.555</td>
<td>0.547</td>
</tr>
<tr>
<td></td>
<td>0.517</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.38</td>
<td>2.07</td>
</tr>
<tr>
<td></td>
<td>1.36</td>
<td></td>
</tr>
</tbody>
</table>
tetrahydrofuran-2-carboxylate at 35°, duplicate runs were made and the average values of the rate constants are used in the discussion.

The concentrations of ester and sodium methoxide were usually between 0.4 and 0.8 molar. Although it may have been preferable to use lower concentrations to preserve the methanolic character of the solvent, molar concentrations in the range used (from 0.4 to 0.8 M) were required for accurate kinetic measurements. Inasmuch as all the kinetic runs were made at roughly the same concentrations, solvent effects should tend to cancel.

Mahone has considered the consequences of isotope effects on the second-order rate constants for deuterium exchange of substituted methyl acetates. It was shown that with deuterium isotope effects of less than ten, the rate constants calculated from the first-order rate law,

\[ k_t = \ln \left( \frac{A_\infty - A_o}{A_o - A_t} \right) \]  

are constant within the experimental error of the infrared analytical technique. Inasmuch as the isotope effects

should be about the same for all the compounds studied, equation (2) will give relative rate constants. The apparent second-order rate constants obtained are the rate constants for hydrogen deuterium exchange. These will be equal to the second-order rate constants for carbanion formation only if $k_H/k_D$ equals one.

It might be suggested that the reactions of some of the esters, especially those with strongly electron-withdrawing substituents, are complicated by the transformation of significant fractions of the ester to complexes in which methanol or methoxide ion has added to the carbonyl groups. Bender\textsuperscript{30} has shown that sodium methoxide adds to ethyl trifluoroacetate and fluoroacetate in n-butyl ether. However, in methanol solutions no evidence for complex formation can be found. No addition of methanol or ethanol was observed in pure alcoholic solvents or in diethyl ether. Therefore, it seems unlikely that any of the esters under investigation exist as complexes to any appreciable extent under the conditions employed.

Discussion of kinetic results

A Taft correlation of the kinetic results was attempted by plotting log k vs $\sigma^*$ for the exchange reaction at 35°C.

\[ YZCH_2CHO + OMe \xrightarrow{k} YZCCO_2Me + MeOH \]

For many of the substituents $\sigma^*$ was not directly available. The useful but fallible rule\(^{31}\) that $\sigma^*_X$ equals

\[ \sigma^*_X = 2.8 \sigma^*_{CH_2X} \]

was used to calculate the $\sigma^*$ constants. For the cyclic compounds for which $\sigma^*$ has not been determined, it was calculated assuming that inductive effects of substituents removed farther than two atoms from the reaction center were insignificant. Hence, $\sigma^*$ for the dioxolane ester and its acyclic analog are the same. The validity of this assumption is supported by the fact that the pK\(_a\)'s of dimethoxyacetic acid and 1,3-dioxolane-2-carboxylic acid differ by only 0.04 units. The substituent constant for methyl N-methylpyrrolidine-2-carboxylate was taken as the sum of \[ 2.8^2 \sigma^*_{CH_2CH_2N(CH_3)_2} \] and $\sigma^*_{CH_2CH_3}$.


Figure 4—Taft plot of $\sigma_X^* + \sigma_Y^*$ vs log k for the esters $XYCHCO_2CH_3$ at 35°.
Included in the Taft plot shown in Figure 4 are the data of Hine, Mahone, and Liotta.\textsuperscript{15} The line of slope 1.79 is the best line through the points for compounds where \( Y \) is hydrogen and \( Z \) is either hydrogen or an alkyl group. If the substituent interactions are due solely to inductive effects the rates should fall on this line. When \( Y \) and \( Z \) are both ethyl or methyl groups negative deviations from the line of 0.74 and 0.25 log units are observed. It appears that steric factors affect the rate of exchange; however, in view of the much greater negative deviations of compounds where oxygen, nitrogen, or fluorine are adjacent to the carbanion site, steric effects alone are insufficient to rationalize the deactivating effects of these substituents. Further, if steric effects were a major cause of deactivation, the exchange rate of methyl 1,3-dioxolane-2-carboxylate should be significantly larger than that of methyl dimethoxyacetate. As can be seen from Table 8, the dioxolane ester is actually slower to exchange than its open chain analog.

Hine, Mahone, and Liotta\textsuperscript{15} have considered a dual mechanism for substituent interactions to explain the deactivating effects of a oxygen and fluorine substituents on the rates of carbanion formation. Substituent effects were divided into interactions due to inductive effects
and electronegativity effects. This resulted in the equation:

$$\log \left( \frac{k_{YZ}}{k_{HH}} \right) = \rho^*\left( \sigma_Y^{*+} + \sigma_Z^{*+} - 2\sigma_H^{*+} \right) + \rho^E(X_Y + X_Z - 2X_H)$$

where the subscripts Y and Z connote the substituents Y and Z, the k's are the second-order rate constants for deuterium exchange, and the X's are the electronegativity of the subscripted substituents. As was mentioned earlier, a correlation was obtained for monosubstituted methyl acetates by plotting $\log \left( \frac{k_{YZ}}{k_{HH}} \right) - \rho^*\left( \sigma_Y^{*+} + \sigma_Z^{*+} - 2\sigma_H^{*+} \right)$ vs $(X_Y + X_Z - 2X_H)$, however, negative deviations were found for methyl dimethoxyacetate and difluoroacetate. If these deviations are due to steric effects a similar treatment of the present data for the cyclic esters, where steric effects have been minimized, should give a better correlation. A combined plot of $\log \left( \frac{k_{YZ}}{k_{HH}} \right) - \rho^*\left( \sigma_Y^{*+} + \sigma_Z^{*+} - 2\sigma_H^{*+} \right)$ vs $(X_Y + X_Z - 2X_H)$ for the present data and that of Hine, Mahone, and Liotta is shown in Figure 5. It is important to note that the cyclic compounds containing oxygen as a substituents give larger deviations from the correlation than their acyclic analogs. Apparently this dual mechanism treatment of substituent effects is insufficient to explain the deactivating effects of a fluorine and oxygen substituents.
Figure 5—Plot of equation (2).
A plot of the pKₐ's of the acids corresponding to the esters studied together with those of several other substituted acetic acids vs σ* for the substituents is shown in Figure 6. A table of the values is given in the Appendix. The acids containing oxygen and fluorine substituents are seen to correlate as well as those containing other substituents which indicates that these substituents display normal inductive effects when further removed from the reaction center.

Although the electronegativity correlation has the advantage that it gives a quantitative treatment, the present data seem better rationalized by a consideration of lone pair repulsion which arises from two or more pairs of nonbonding electrons on adjacent atoms.

Bartlett and Woods\textsuperscript{33} have shown that carbanions

\begin{flushright}
\end{flushright}

adjacent to carbonyl groups are sp\textsuperscript{2} hybridized. The authors found that the bicyclic ketone VII is much less acidic than the cyclohexandione VIII. The electron pair of the bridgehead anion of the bicyclic system would be held in an sp\textsuperscript{3} orbital whose angular disposition makes
Figure 6.— A plot of the pKa of substituted acetic acids in water at $35^\circ$ vs $\Sigma \sigma^*$. 
overlap with the π orbital of the carbonyl group minimal. The carbanions resulting from the deprotonation of substituted methyl acetates therefore should be delocalized over a planar three-atom π system with the substituents lying in the plane of the π system. If X and/or Y have nonbonding occupied orbitals the resultant destabilization will be the greatest when the overlap of the filled nonbonding orbital(s) of the substituent with the conjugated π system is maximized. Since the overlap energy is a function of the square of cosine of the dihedral angle between the orbitals in question, the destabilization energy is

maximized when the dihedral angle is \(0^\circ\) and minimized when it is \(90^\circ\).

The rate of exchange of methyl difluoroacetate gives the largest deviation from the Taft correlation. This is reasonable in terms of the lone-pair repulsion argument because fluorine has more nonbonding electron pairs than the other substituents investigated. If these electrons are cylindrically symmetric about the fluorine nucleus there are no conformational changes that will result in less orbital overlap. If the three unshared pairs of electrons on fluorine are in three \(sp^3\) orbitals, it can be shown that all conformers resulting from rotation about the C-F bond give the same destabilization energy. The following is a projection of the fluorine substituted carbanion.

\[ \begin{align*}
&d \\
&b \\
&\theta \\
&a \\
&\ \ \\
&c \\
&\ \\
&e
\end{align*} \]
Line de represents the axis of the p orbital of the \( sp^2 \)
hybridized carbanion and lines a, b, and c are the axes 
of the three filled, nonbonding, \( sp^3 \) orbitals of fluorine.
Assuming that the energy of repulsion between two pairs 
of nonbonding electrons on adjacent atoms is a function of 
the cosine\(^2\) of the dihedral angle between the interacting 
orbitals, the destabilization energy, \( f \), can be written:

\[
f \propto \cos^2 ad + \cos^2 bd + \cos^2 ce
\]

If \( \theta \) is defined as the angle between orbital a 
and the axis of the carbanion, the angles can be defined 
in terms of \( \theta \). Thus

\[
f \propto \cos^2 (90^\circ - \theta) + \cos^2 (30^\circ + \theta) + \cos^2 (30^\circ - \theta)
\]
or

\[
f \propto \sin^2 \theta + (\cos 30^\circ \cos \theta - \sin 30^\circ \sin \theta)^2
\]
\[
+ (\cos 30^\circ \cos \theta + \sin 30^\circ \sin \theta)^2
\]
or

\[
f \propto \sin^2 \theta + (\frac{3}{2} \cos \theta - \frac{1}{2} \sin \theta)^2
\]
\[
+ (\frac{3}{2} \cos \theta + \frac{1}{2} \sin \theta)^2
\]
or

\[
f \propto \sin^2 \theta + \frac{3}{2} \cos^2 \theta + \frac{1}{2} \sin^2 \theta
\]
or

\[
f \propto \frac{3}{2} (\sin^2 \theta + \cos^2 \theta) = \frac{3}{2}
\]
Therefore the destabilization energy for fluorocarbanions is proportional to a constant and independent of "rotations" about the C-F bond.

The destabilization of carbanions by lone-pair repulsion increases with decreasing C-X bond distance. The bond length, $r_{CX}$, is given by the equation:\(^\text{(35)}\)

$$r_{CX} = r_C + r_X - 0.09 |X_C + X_X|.$$ 


where $r$ is the covalent bond radius of the subscripted atom and $X$ is its electronegativity. Fluorine, with the smallest covalent radius and largest electronegativity of the substituents in question, should have the smallest covalent bond distance, which will lead to a greater destabilization energy.

A semi-quantitative estimate of lone-pair repulsion in the dioxolane and dimethoxyacetate esters can be made. Assuming that the preferred conformations of the carbanions in question are those that have the least amount of overlap between orbitals containing nonbonding electrons, the destabilization energy resulting from this overlap can be
estimated. The two lowest energy conformers of the methyl dimethoxyacetate carbanion are shown below.

\[
\begin{align*}
\text{Me} & \quad \text{MeO} \quad \text{CO}_2\text{Me} \\
60^\circ & \quad 60^\circ 
\end{align*}
\]

The destabilization energy, \( f \), due to overlap of filled nonbonding orbitals is given by

\[
f \propto 2(\cos^2 60^\circ + \cos^2 60) \]

\[
f \propto 1.0
\]

Similarly, the conformation of the planar dioxolane carbanion is shown below.

\[
\begin{align*}
\text{O} & \quad \text{CO}_2\text{Me} \\
30^\circ & \quad 30^\circ 
\end{align*}
\]

The destabilization energy is given by:

\[
f \propto 2 \cos^2 30^\circ
\]
For each oxygen atom. The total destabilization energy is

\[ f \propto 4 \cos^2 30^\circ \]

or

\[ f \propto 3.0 \]

The hybridization of the oxygen atoms is assumed to be \( sp^3 \) because the C-O-C bond angle in simple ethers is nearly tetrahedral \((110^\circ)\) and \( sp^2 \) hybridization of the oxygen atoms of the dioxolane ester would require average angles of \(100^\circ\) for the C-C-O bonds in the ring.

As can be seen from the Taft plot (Figure 4), the log \( k \)'s for methyl dimethoxyacetate and the dioxolane ester are 7.08 and 7.42 log units respectively, less reactive than expected from their substituent effects. These deviations from the Taft plot should be corrected for steric effects. Methyl 2-ethylbutyrate is 0.74 log units slower to exchange than expected on the basis of inductive effects. If it is assumed that this is a steric effect and that the steric effect in methyl dimethoxyacetate is about the same, then 6.34 \((7.08 - 0.74)\) log units of the deactivating effect in methyl dimethoxyacetate is unaccounted for. Similarly, since log \( k \) for methyl cyclopentanecarboxylate is 0.36 units larger than expected
on the basis of the Taft plot and if this rate-acceleration
is due to a ring size effect, then the rate of exchange
of the dioxolane ester should be accelerated by an equiva-
ient amount. This leaves 7.78 (7.42 + 0.36) log units of
unexplained deactivation for the dioxolane ester.

Assuming that the 6.34 log units of rate-decelera-
tion of methyl dimethoxyacetate is due to lone-pair repulson
and also that the conformers of the ester previously il-
lustrated are representative of the intermediate carbanions
then, from previous calculations, the planar conformer of
the dioxolane ester would be three times as deactivated as
the dimethoxy ester (4 cos^2 30° vs 4 cos^2 60°). On this
basis, the dioxolane ester should be 19.0 log units
deactivated compared to the 7.78 log units observed. One
explanation of this discrepancy may be that these estima-
tions are based on a planar configuration for the dioxolane
ester, whereas cyclopentane and tetrahydrofuran are known
36
to have nonplanar conformations. The conformers that

(36) E. L. Eliel, N. L. Allinger, S. J. Angyal,
and G. A. Morrison, "Conformational Analysis," Inter-

were used in the calculations are those that gave the
maximum amount of lone-pair repulsion for the cyclic ester
and the minimum amount for the acyclic ester. If lone-pair
repulsion is the determining factor in the deceleration of the rates of exchange of these esters, the effect is quite large and therefore the driving force to attain the conformation of minimum overlap will be large. Hence the conformers given for methyl dimethoxyacetate are reasonable. This is not the case, however, for the dioxolane ester. Here, increasing the nonplanarity of the ring results in a decrease in the destabilization of the carbanion due to lone-pair repulsion. Pitzer and Donath have determined the structures of the lowest energy conformers of cyclopentane and five-membered rings containing one hetero atom by calculation. The dihedral angles of substituents attached to adjacent atoms for cyclopentane, tetrahydrofuran, and methylcyclopentane are given in Table 9. Assuming that the dioxolane carbanion has the conformation of tetrahydrofuran, the destabilization energy due to lone-pair repulsion is given by:

\[ f \propto 2[\cos^2(30^\circ - 15.15^\circ) + \cos^2(30^\circ + 15.15^\circ)] \]

or

\[ f \propto 2.85 \]

### TABLE 9. The Torsional Angles in Five-Membered Rings

<table>
<thead>
<tr>
<th>Angle</th>
<th>Cyclopentane</th>
<th>Tetrahydrofuran&lt;sup&gt;a&lt;/sup&gt; or methylcyclopentene&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\theta_{12} = \theta_{51}$</td>
<td>46.1°</td>
<td>15.15°</td>
</tr>
<tr>
<td>$\theta_{23} = \theta_{45}$</td>
<td>28.6</td>
<td>39.45</td>
</tr>
<tr>
<td>$\theta_{34}$</td>
<td>0.0</td>
<td>48.10</td>
</tr>
</tbody>
</table>

<sup>a</sup> The oxygen atom is atom 1.

<sup>b</sup> The sp<sup>2</sup> hybridized carbon atom is atom 1.

From these calculations log k for the dioxolane ester exchange reaction should be 16.8 units less than expected on the basis of the Taft plot compared to the 7.78 log units observed. Assuming that the dioxolane has the conformation of cyclopentane with the sp<sup>2</sup> carbon at atom one leads to a negative deviation from the Taft plot of 11.6 log units which is still more than 4 log units greater than the observed value. The discrepancy between the observed and calculated values for destabilization of carbanions due to lone-pair repulsion may arise from the following facts: a) the angular dependence of lone-pair repulsion may not be a function of the cosine<sup>2</sup>, b) the detailed conformations of the intermediate carbanions...
are not known (a large deactivating effect due to lone-pair repulsion could force the conformation of the dioxolane carbanion further from planarity than cyclopentane),
c) the mechanism of deactivation of F, O, and N substituted carbanions include effects in addition to or other than lone-pair repulsion.

The destabilization of carbanions derived from methyl dimethoxyacetate and the dioxolane ester (but not the difference between them) could be due to a clustering effect


A molecule in which two oxygen atoms are attached to the same $sp^3$ hybridized carbon atom is stabilized relative to one in which the two oxygen atoms are attached to different $sp^3$ hybridized carbon atoms. This type of stabilization is probably not nearly as large in compounds where the carbon atoms bearing the oxygen substituents are $sp^2$ hybridized. Therefore, there may be a net destabilization of a molecule having two oxygen atoms attached to the same carbon atom when the carbon atom undergoes a change in the hybridization from $sp^3$ to $sp^2$. If this clustering effect is a source of destabilization then the destabilization of carbanions having only one α oxygen atom should be
relatively small since the difference in stability of compounds having oxygen attached to \( sp^3 \) or \( sp^2 \) hybridized carbon appears to be small.\(^{38}\) It is, therefore, instructive to examine the kinetic data for the deuterium exchange for methyl tetrahydrofuran-2-carboxylate and the racemization of methyl 2-methoxypropionate. Cowdrey, Hughes and Ingold\(^{39}\) have determined the rate of sodium methoxide catalyzed racemization of optically active methyl 2-methoxypropionate in methanol at 25°. Assuming that the temperature coefficient of the rate is the same for the tetrahydrofuran and propionate esters and that rates of exchange, carbanion formation, and racemization are equivalent, the data can be extrapolated to 35°. The rate constant obtained by this extrapolation is a minimum value since the rate of racemization was determined in protiomethanol and the rates of exchange were determined in methanol-0-d. Hine, Duke, and Glod have observed\(^{40}\)


reactions of methylene halides with alkali metal alkoxide in alcohol solution with \( k_{ROH}/k_{ROD} \) between 1.34 and 1.90. The kinetic data for methyl tetrahydrofuran-2-carboxylate and methyl 2-methoxypropionate are included in the Taft plot in Figure 4. The esters are 2.60 and 2.69 log units respectively less reactive than would be expected on the basis of inductive substituent effects. The corrections for steric and ring size effects that were made in the comparison of the rates of exchange of the dimethoxyacetate and dioxolane esters can be applied. Methyl tetrahydrofuran-2-carboxylate is then 2.96 (2.60 + 0.36) log units less reactive and methyl 2-methoxypropionate is 1.95 (2.69 - 0.74) log units less reactive than expected on the basis of inductive effects. It therefore seems likely that the clustering effect cannot account, at least completely, for the destabilizing effects of oxygen substituents on the rate of formation of carbanions.

As can be seen from Figure 4, methyl N-methylpyrrolidine-2-carboxylate is 2.35 log units less reactive than expected on the basis of inductive effects, which indicates that nitrogen atoms are probably also effective in retarding the rate of carbanion formation. However, the magnitude of the effects is uncertain. The rate can be corrected for a ring size effect; this leads to a larger
deviation from the Taft plot \((2.35 + 0.36 \text{ log units})\). There are, however, no data available that allow a steric correction to be made for the methyl group attached to the nitrogen atom. This correction would tend to make the deviation from the Taft plot smaller. There is the added complication that the species that is undergoing deuterium exchange may be the protonated amine:

\[
\begin{align*}
\text{N} & \quad \text{CO}_2\text{Me} \quad \text{H} \\
\text{CH}_3 & \\
\end{align*}
\quad \overset{\text{H}}{\leftrightarrow} \quad 
\begin{align*}
\text{+} & \quad \text{N} \quad \text{CO}_2\text{Me} \quad \text{H} \\
\text{CH}_3 & \\
\end{align*}
\]

Although the concentration of the protonated amine should be very small in such a strongly basic medium \((0.4 \text{ M NaOMe})\), its rate of exchange should be much greater than that for the unprotonated amine. If the exchange is taking place via the protonated amine then increasing the sodium methoxide concentration should lead to a decrease in the concentration of the protonated amine and hence to a decreased calculated second-order rate constant for exchange.

Approximate kinetic data at higher sodium methoxide
concentrations (0.65 M) seem to indicate that there is a slight increase in the second-order rate constant and therefore the exchange via the protonated species seems unlikely.

In an attempt to understand conformational effects in these reactions better, the kinetics of exchange of the esters were studied at 60°. These results are included in Table 8. From these data it is possible to calculate the Arrhenius activation energy for the equation:

\[
\frac{k_1}{k_2} = e^{-\frac{(E_a/R)(1/T_1 - 1/T_2)}{}}
\]


The activation parameters can then be calculated from the relationships:

\[
\Delta H^\pm = E_a - RT
\]

and

\[
k_T = (kT/h)e^{\frac{\Delta S^\pm}{R}}e^{-\frac{\Delta H^\pm}{RT}}
\]

The activation parameters are presented in Table 10. From a consideration of solvation effects, it might be expected that the entropy of activation, \(\Delta S^\pm\), should be
TABLE 10. Activation Parameters for the H-D Exchange of Methyl Esters

<table>
<thead>
<tr>
<th>Compound</th>
<th>( \text{Ea (kcal/mole)} )</th>
<th>( \Delta H^\ddagger_{35^\circ} )</th>
<th>( \Delta S^\ddagger_{35^\circ} )</th>
</tr>
</thead>
<tbody>
<tr>
<td>((\text{CH}_3)_2\text{CHCO}_2\text{Me})</td>
<td>19.1</td>
<td>18.5</td>
<td>-19.7</td>
</tr>
<tr>
<td>((\text{CH}_3\text{CH}_2)_2\text{CHCO}_2\text{Me})</td>
<td>20.1</td>
<td>19.5</td>
<td>-21.4</td>
</tr>
<tr>
<td>(\text{CO}_2\text{Me})</td>
<td>23.6</td>
<td>23.0</td>
<td>-5.0</td>
</tr>
<tr>
<td>((\text{CH}_3\text{O})_2\text{CHCO}_2\text{Me})</td>
<td>21.9</td>
<td>21.3</td>
<td>-12.3</td>
</tr>
<tr>
<td>(\text{CO}_2\text{Me})</td>
<td>19.0</td>
<td>18.4</td>
<td>-18.0</td>
</tr>
<tr>
<td>(\text{CO}_2\text{Me})</td>
<td>19.2</td>
<td>18.6</td>
<td>-22.4</td>
</tr>
<tr>
<td>(\text{CO}_2\text{Me})</td>
<td>15.4</td>
<td>14.8</td>
<td>-32.0</td>
</tr>
</tbody>
</table>

positive since in the ground state a full negative charge is localized on the oxygen atom of methoxide ion whereas, in the transition state, the negative charge is delocalized over the three atom \( \pi \) system and therefore solvent ordering should be less in the transition state than the ground state. On the other hand, in the ground state there are two particles, methoxide ion and ester, that become associated in the transition state. The expected result is
negative entropies of activation. If steric hindrance is important in the deprotonation reaction there will be some conformers of the esters that are more reactive to deprotonation than others. This would also lead to negative entropies of activation. Further, since rotation is constrained in the cyclic compounds, the entropies of activation should be less negative in these esters than the acyclic analogs. As can be seen from the data in Table 10, no one of the effects mentioned above seems to be dominant and no clear trends in the activation entropies are obvious. The entropies of activation of all the esters are negative. The entropy of activation of methyl cyclopentanecarboxylate is less negative than its acyclic analog by 15 eu. Conversely, the entropy of activation of the dioxolane ester is more negative than its acyclic analog by two eu.

Although the determination of the activation parameters of the exchange reaction does not lead to further elucidation of conformational effects in lone pair repulsion, there is evidence in the literature that suggests its importance. An effect similar to the deactivating effect of the α nitrogen substituent in the deuterium exchange of methyl N-methylpyrrolidine-2-carboxylate has been observed by Zoltewicz and his coworkers. The rates
methoxide ion catalyzed deuterium exchange of the various positions of pyridine were measured. It was found that the relative rates of exchange in positions 2,6;3,5;4 were 1.0:9.3:12. Contrary to the prediction based on inductive effects alone, nitrogen does not facilitate the formation of carbanions at adjacent positions to the degree that it facilitates anion formation at more removed centers. Similarly, recent extended Hückel calculations show that carbanions adjacent to nitrogen in pyridine are destabilized relative to carbanions in other positions. The conclusion of these calculations is supported by the fact that the treatment of a 3-halopyridine with a strong base leads only to 3- and 4-substituted pyridines. No 2-substituted pyridine is observed in these reactions.
Fessenden and Schuler\textsuperscript{45} have deduced from the esr spectra of methyl, difluoromethyl and trifluoromethyl radicals that these radicals become increasingly nonplanar with increasing fluorine substitution. Further calculations\textsuperscript{46} led to the assignment of the following structures:

\begin{center}
\begin{tikzpicture}
  \node at (0,0) {H};
  \node at (0.5,0) {C};
  \node at (1,0) {H};
  \node at (1.5,0) {F};
  \node at (2,0) {C};
  \node at (2.5,0) {H};
  \node at (3,0) {F};
  \node at (3.5,0) {F};
  \node at (4,0) {F};
  \node at (3.5,0.5) {\textbullet};
  \node at (3.5,-0.5) {\textbullet};
  \node at (3.5,1) {\textbullet};
  \node at (3.5,-1) {\textbullet};
  \draw (0,0) -- (0.5,0);
  \draw (0.5,0) -- (1,0);
  \draw (1,0) -- (1.5,0);
  \draw (1.5,0) -- (2,0);
  \draw (2,0) -- (2.5,0);
  \draw (2.5,0) -- (3,0);
  \draw (3,0) -- (3.5,0);
  \draw (3.5,0) -- (3.5,0.5);
  \draw (3.5,0.5) -- (3.5,1);
  \draw (3.5,0.5) -- (3.5,-0.5);
  \draw (3.5,0.5) -- (3.5,-1);
  \draw (3.5,0) -- (3.5,0.5);
  \draw (3.5,-0.5) -- (3.5,-1);
  \draw (3.5,1) -- (3.5,0.5);
  \draw (3.5,-0.5) -- (3.5,0);
  \draw (3.5,1) -- (3.5,0);
\end{tikzpicture}
\end{center}

\begin{center}
\begin{tikzpicture}
  \node at (0,0) {H};
  \node at (0.5,0) {O};
  \node at (1,0) {H};
  \node at (1.5,0) {O};
  \node at (2,0) {O};
  \node at (2.5,0) {O};
  \node at (3,0) {H};
  \node at (3.5,0) {\textbullet};
  \node at (3.5,0.5) {\textbullet};
  \node at (3.5,-0.5) {\textbullet};
  \draw (0,0) -- (0.5,0);
  \draw (0.5,0) -- (1,0);
  \draw (1,0) -- (1.5,0);
  \draw (1.5,0) -- (2,0);
  \draw (2,0) -- (2.5,0);
  \draw (2.5,0) -- (3,0);
  \draw (3,0) -- (3.5,0);
  \draw (3.5,0) -- (3.5,0.5);
  \draw (3.5,0.5) -- (3.5,0);
  \draw (3.5,0.5) -- (3.5,-0.5);
  \draw (3.5,-0.5) -- (3.5,0);
\end{tikzpicture}
\end{center}

\begin{center}
\begin{tikzpicture}
  \node at (0,0) {H};
  \node at (0.5,0) {O};
  \node at (1,0) {H};
  \node at (1.5,0) {O};
  \node at (2,0) {O};
  \node at (2.5,0) {O};
  \node at (3,0) {H};
  \node at (3.5,0) {\textbullet};
  \node at (3.5,0.5) {\textbullet};
  \node at (3.5,-0.5) {\textbullet};
  \draw (0,0) -- (0.5,0);
  \draw (0.5,0) -- (1,0);
  \draw (1,0) -- (1.5,0);
  \draw (1.5,0) -- (2,0);
  \draw (2,0) -- (2.5,0);
  \draw (2.5,0) -- (3,0);
  \draw (3,0) -- (3.5,0);
  \draw (3.5,0) -- (3.5,0.5);
  \draw (3.5,0.5) -- (3.5,0);
  \draw (3.5,0.5) -- (3.5,-0.5);
  \draw (3.5,-0.5) -- (3.5,0);
\end{tikzpicture}
\end{center}

Similarly, Dobbs, Gilbert, and Norman\textsuperscript{47} have investigated the esr spectra of radicals IX, X, and XI.

\begin{center}
\begin{tikzpicture}
  \node at (0,0) {H};
  \node at (0.5,0) {H};
  \node at (1,0) {H};
  \node at (1.5,0) {H};
  \node at (2,0) {H};
  \node at (2.5,0) {H};
  \node at (3,0) {H};
  \node at (3.5,0) {\textbullet};
  \node at (3.5,0.5) {\textbullet};
  \node at (3.5,-0.5) {\textbullet};
  \draw (0,0) -- (0.5,0);
  \draw (0.5,0) -- (1,0);
  \draw (1,0) -- (1.5,0);
  \draw (1.5,0) -- (2,0);
  \draw (2,0) -- (2.5,0);
  \draw (2.5,0) -- (3,0);
  \draw (3,0) -- (3.5,0);
  \draw (3.5,0) -- (3.5,0.5);
  \draw (3.5,0.5) -- (3.5,0);
  \draw (3.5,0.5) -- (3.5,-0.5);
  \draw (3.5,-0.5) -- (3.5,0);
\end{tikzpicture}
\end{center}

\begin{center}
\begin{tikzpicture}
  \node at (0,0) {H};
  \node at (0.5,0) {O};
  \node at (1,0) {O};
  \node at (1.5,0) {O};
  \node at (2,0) {O};
  \node at (2.5,0) {O};
  \node at (3,0) {H};
  \node at (3.5,0) {\textbullet};
  \node at (3.5,0.5) {\textbullet};
  \node at (3.5,-0.5) {\textbullet};
  \draw (0,0) -- (0.5,0);
  \draw (0.5,0) -- (1,0);
  \draw (1,0) -- (1.5,0);
  \draw (1.5,0) -- (2,0);
  \draw (2,0) -- (2.5,0);
  \draw (2.5,0) -- (3,0);
  \draw (3,0) -- (3.5,0);
  \draw (3.5,0) -- (3.5,0.5);
  \draw (3.5,0.5) -- (3.5,0);
  \draw (3.5,0.5) -- (3.5,-0.5);
  \draw (3.5,-0.5) -- (3.5,0);
\end{tikzpicture}
\end{center}

\begin{center}
\begin{tikzpicture}
  \node at (0,0) {H};
  \node at (0.5,0) {O};
  \node at (1,0) {O};
  \node at (1.5,0) {O};
  \node at (2,0) {O};
  \node at (2.5,0) {O};
  \node at (3,0) {H};
  \node at (3.5,0) {\textbullet};
  \node at (3.5,0.5) {\textbullet};
  \node at (3.5,-0.5) {\textbullet};
  \draw (0,0) -- (0.5,0);
  \draw (0.5,0) -- (1,0);
  \draw (1,0) -- (1.5,0);
  \draw (1.5,0) -- (2,0);
  \draw (2,0) -- (2.5,0);
  \draw (2.5,0) -- (3,0);
  \draw (3,0) -- (3.5,0);
  \draw (3.5,0) -- (3.5,0.5);
  \draw (3.5,0.5) -- (3.5,0);
  \draw (3.5,0.5) -- (3.5,-0.5);
  \draw (3.5,-0.5) -- (3.5,0);
\end{tikzpicture}
\end{center}


From the hyperfine $^{13}\text{C}$ splittings they have calculated that IX is planar and XI is nearly tetrahedral with X between the two. These results can be rationalized in terms of lone-pair electron repulsion. If the radicals are $sp^2$ hybridized and thus planar, they will be destabilized by nonbonding electrons on adjacent atoms. It appears then that when oxygen or fluorine atoms are adjacent to the radical site, a pyramidal structure is of lower energy. Contrary to the lone pair electron repulsion argument, Pauling\textsuperscript{48} has stated that the electronegativity difference of the atoms of the radical is the major factor in determining the configuration. From calculations he predicts that the structure of $^{\cdot}\text{CX}_3$ will be planar if the electronegativity of X is 0.2 units less than that of carbon. This would lead to the observed result that methyl radicals are planar. These calculations, however, also predict that the bond angles in trifluoromethyl radicals should be $92^\circ$ whereas the observed angle is $111^\circ$. This discrepancy was rationalized in terms of the double-bond-no-bond resonance structure XII. Since the angle

\begin{flushright}
\text{(48) L. Pauling, \textit{J. Chem. Phys.}, 51, 2767 (1969).}
\end{flushright}
between a double bond and a single bond is usually about 15° larger than the angle between two single bonds, it was reasoned that structures like XII could account for the difference between the calculated and observed bond angles. In view of recent research, however, the concept of fluorine double-bond resonance seems untenable. Pauling has proposed a means of verifying his electronegativity argument. The structures of 'SiH₃, 'SnH₃, and 'GeH₃ are predicted to be pyramidal on the basis of the electronegativity argument since the electronegativities of the three central atoms are less than that of hydrogen. On the basis of the lone-pair repulsion argument, these radicals should have the same structure as 'CH₃. Conversely, the structures of 'SiX₃, 'GeX₃, and 'SnX₃ should be more pyramidal than 'CX₃ from the electronegativity argument. From lone-pair repulsion, these radicals would be more planar than 'CX₃ because of the increased bond lengths in 'SiX₃, 'GeX₃, and 'SnX₃.

The structure of hydrazine is germane to the present discussion. Although early reports assigned a completely
eclipsed structure for hydrazine, recent microwave measurements\(^{50}\) and calculations\(^{51}\) have both led to the assignment of the lowest energy conformer as the structure in which the dihedral angle between the two lone pairs of electrons is 90° and the highest energy conformer is the one in which the dihedral angle is 0°; that is, when the two filled \(\text{sp}^3\) orbitals are best situated for overlap. Similarly, there is evidence of the preferred orthogonality of lone pairs in compounds with O-O,\(^{52}\) N-S,\(^{53}\) and N-P\(^{54}\) bonds. Lehn and Anderson\(^{55}\) have observed that the energy
barrier for nitrogen inversion is larger in compound XIII than XIV, which may be due to lone-pair repulsion because XIII cannot undergo ring inversion which could minimize overlap of the orbitals of the nonbonding electron pairs on the nitrogen atoms. The recent separation and isolation of the cis and trans methyl N-chloroaziridines also indicates that nonbonding pairs of electrons on adjacent atoms are effective in retarding the rates of nitrogen inversion.

Further evidence of the $\pi$ inductive effect of unshared electron pairs has been obtained by Hammons.


The electronic spectra of the lithium salts of substituted fluorenes were studied. Bathochromic shifts in the spectrum are the usual result for electron-withdrawing substituents, however, hypsochromic shifts were observed for methoxy, fluoro, and dimethylamino substituents. The author attributes this apparent anomaly to the electron repelling effect of the unshared pairs of electrons of these substituents. 9-Lithio-9-methoxyfluorene gave a spectral shift about equivalent to that observed for 9-lithio-9-methylfluorene, however in the 1,2,3, or 4 position, the methoxy substituent gave a spectral shift four times that of the methyl substituent in the same position. This decrease in the $\pi$ inductive effect of the unshared pairs in the 9 position was attributed to a conformational effect. The hydrogens at C-1 and C-8 force

\[ \text{OMe} \]

the 9-methoxy group out of the plane and the interaction between the $\pi$ electron system and the unshared pairs on oxygen is decreased. This conformational effect is not unlike that observed in the present work in the comparison
of the rates of exchange of methyl 1,3-dioxolane-2-carboxylate and methyl dimethoxyacetate.

The present data together with the evidence presented above seem to indicate that a source of destabilization of \( sp^2 \) hybridized carbanions by adjacent oxygen, fluorine, and nitrogen substituents is lone-pair repulsion. Streitwieser\(^{12}\) has suggested that these substituents stabilize \( sp^3 \) hybridized carbanions and destabilize \( sp^2 \) hybridized carbanions. In light of the experiments on substituent effects on rates of nitrogen inversion\(^ {55,56}\) this may not necessarily be the case. It is possible that \( sp^3 \) hybridized carbanions are also destabilized by these substituents but to a lesser degree than \( sp^2 \) hybridized carbanions. Further experiments on \( sp^3 \) hybridized carbanions are necessary in order to determine the effect of lone-pair repulsion on these anions.
Definition of Computer Program Symbols

NN = Number of kinetic runs

T = time

AT = absorbance at time T

AO = initial absorbance

M = sodium methoxide concentration

EST = ester concentration

N = number of kinetic points in a given run

E = extinction coefficient

CO = initial protio methanol concentration

CI = protiomethanol concentration at infinite time

AI = absorbance at infinite time

K = pseudo first-order rate constant

KSEC = second-order rate constant

KZ = second-order rate constant
C  CALCULATION OF RATE CONSTANTS FOR H-D EXCHANGE OF ESTERS IN MEOD

DO 200 KK=1,NN
NN=17
DIMENSION AT(10),T(10), Y(10),U(100),X(100),K(100),TITLE(20)
REAL M,K,KSEC
READ(5,3)(TITLE(I),I=1,20)
3  FORMAT(20A4)
READ (5,1) AU,M,EST,N
1  FORMAT (3F10.0,113)
READ (5,2) ( AT(I),T(I), I=1,N)
2  FORMAT(F10.3,F10.0)
E= 108.8-(5.98*M)
CO= AU/(E*.005)
CI= CO*(EST*24)/(24+CO+EST)
AI = CI+E*.005
T(I)=0
Y(I)= 0
K(I)=0
DO 4 I=2,N
Y(I) = ALOG((AI-AO)/(AI-AT(I)))
K(I) = Y(I)/T(I)
4  X(I)=T(I)
SUMY=0.0
SUMX=0.0
SUMXX=0.0
SUMXY=0.0
DO 20 I=1,N
SUMX= SUMX + X(I)
SUMY=SUMY + Y(I)
SUMXX = SUMXX +X(I)**2
20 SUMXY=SUMXY +X(I)*Y(I)
CONTINUE
S= FLOAT(N)
DENOM= S *SUMXX - SUMXX**2

Computer program for the calculation of rate constants from kinetic data
AIN = (SUMY*SUMXX-SUMX*SUMXY)/DENOM

33 SLOP = (S*SUMXY - SUMX*SUMY)/DENOM
SUMU = 0.0
DO 22 I = 2, N
   U(I) = (Y(I) - (X(I)*SLOP + AIN))**2
22 SUMU = SUMU + U(I)
CONTINUE
STD = SQRT(SUMU/(S-1.))
KSEC = SLOP/M
WRITE (6, 101) (TITLE(I), I = 1, 20)
101 FORMAT (1H1 ///// 3X, 20A4)
WRITE (6, 102) SLOP, KSEC, AIN, STD
WRITE (6, 103)
WRITE (6, 104) (AT(I), Y(I), K(I), T(I), I = 1, N)
104 FORMAT (F9.3, 5X, F14.6, 6X, E16.4, F16.0)
WRITE (6, 105) A1
105 FORMAT (F9.3, 53X, 'INF' //)
WRITE (6, 106) M, EST, E
106 FORMAT (3X, 'BASE CONC.=', F6.4, 4X, 'ESTER CONC.=', F6.4, 4X, 'EXT. COE 2FF.=', F6.1)
200 CONTINUE
STOP
END
TABLE 11. Summary of Data for Figure 5

<table>
<thead>
<tr>
<th>Compound</th>
<th>( X_Y^+X_Z^+2X_H^- )</th>
<th>( \log k/k_{HH} )</th>
<th>( \rho^<em>(\sigma^</em>_X^+\sigma^<em>_Y^+-2\sigma^</em>_H^-) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>((\text{CH}_3\text{)}_2\text{CHCO}_2\text{CH}_3)</td>
<td>.8</td>
<td>-1.07</td>
<td>-1.79</td>
</tr>
<tr>
<td>((\text{CH}_3\text{CH}_2)_2\text{CHCO}_2\text{CH}_3)</td>
<td>.8</td>
<td>-2.76</td>
<td>-1.07</td>
</tr>
</tbody>
</table>
| \[
\begin{array}{c}
\text{N} \\
\text{CH}_3
\end{array}
\] \(\text{CO}_2\text{CH}_3\) | 1.3 | -1.75 | 0.49 |
| \[
\begin{array}{c}
\text{O} \\
\text{CO}_2\text{CH}_3
\end{array}
\] | 1.8 | -1.23 | 1.28 |
| \[
\begin{array}{c}
\text{O} \\
\text{CO}_2\text{CH}_3
\end{array}
\] | 2.8 | -2.35 | 4.46 |
| \[
\begin{array}{c}
\text{MeO} \\
\text{CHCO}_2\text{CH}_3
\end{array}
\] | 2.8 | -2.05 | 4.62 |
<table>
<thead>
<tr>
<th>Compound</th>
<th>Temp.</th>
<th>pKₐ (^{a})</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH(_3)CO(_2)H</td>
<td>35°</td>
<td>4.76(^{b})</td>
</tr>
<tr>
<td>CH(_3)CH(_2)CO(_2)H</td>
<td>35</td>
<td>4.88(^{b})</td>
</tr>
<tr>
<td>(CH(_3))(_2)CHCO(_2)H</td>
<td>30</td>
<td>4.88(^{b})</td>
</tr>
<tr>
<td>CH(_3)CH(_2)CH(_2)CO(_2)H</td>
<td>35</td>
<td>4.84(^{b})</td>
</tr>
<tr>
<td></td>
<td>25</td>
<td>4.97(^{b})</td>
</tr>
<tr>
<td>FCH(_2)CO(_2)H</td>
<td>35</td>
<td>2.62(^{b})</td>
</tr>
<tr>
<td>F(_2)CHCO(_2)H</td>
<td>25</td>
<td>1.24(^{c})</td>
</tr>
<tr>
<td>CH(_3)OCH(_2)CO(_2)H</td>
<td>25</td>
<td>3.53(^{c})</td>
</tr>
<tr>
<td>(CH(_3))(_2)CHCO(_2)H</td>
<td>35</td>
<td>2.88</td>
</tr>
<tr>
<td></td>
<td>35</td>
<td>3.72</td>
</tr>
<tr>
<td></td>
<td>35</td>
<td>2.92</td>
</tr>
</tbody>
</table>

\(^{a}\) At zero ionic strength.


TABLE 13. Sodium Methoxide Concentrations in Kinetic Runs

<table>
<thead>
<tr>
<th>Compound</th>
<th>$[\text{MeONa}]^a$</th>
<th>$[\text{MeONa}]^b$</th>
<th>$[\text{MeONa}]^a$</th>
<th>$[\text{MeONa}]^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$(\text{CH}_3)_2\text{CHCO}_2\text{Me}$</td>
<td>0.49</td>
<td>0.47</td>
<td>0.60</td>
<td>0.55</td>
</tr>
<tr>
<td>$(\text{CH}_3\text{CH}_2)_2\text{CHCO}_2\text{Me}$</td>
<td>0.60</td>
<td>0.60</td>
<td>0.55</td>
<td>0.55</td>
</tr>
<tr>
<td>$\begin{array}{c} \begin{array}{c} \text{CO}_2\text{Me} \end{array} \ \end{array}$</td>
<td>0.50</td>
<td>0.45</td>
<td>0.60</td>
<td>0.58</td>
</tr>
<tr>
<td>$(\text{CH}_3\text{O})_2\text{CHCO}_2\text{Me}$</td>
<td>0.60</td>
<td>0.52</td>
<td>0.58</td>
<td>0.41</td>
</tr>
<tr>
<td>$\begin{array}{c} \begin{array}{c} \text{CO}_2\text{Me} \end{array} \ \end{array}$</td>
<td>0.54</td>
<td>0.44</td>
<td>0.60</td>
<td>0.47</td>
</tr>
<tr>
<td>$\begin{array}{c} \begin{array}{c} \text{CO}_2\text{Me} \ \end{array} \ \end{array}$</td>
<td>0.62</td>
<td>0.62</td>
<td>0.60</td>
<td>0.56</td>
</tr>
<tr>
<td>$\begin{array}{c} \begin{array}{c} \text{Me} \ \end{array} \ \end{array}$</td>
<td>0.60</td>
<td>0.45</td>
<td>0.60</td>
<td>0.40</td>
</tr>
</tbody>
</table>

$^a$ Concentration calculated from the amount of NaOMe added.

$^b$ Concentration of NaOMe determined titrimetrically.

$^c$ Approximate concentration.
TABLE 14. Data for the Taft Plot in Figure 4

<table>
<thead>
<tr>
<th>Compound</th>
<th>-log k</th>
<th>$\Sigma \sigma^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$(CH_3)_2CHCO_2Me$</td>
<td>5.01</td>
<td>0.0</td>
</tr>
<tr>
<td>$(CH_3CH_2)_2CHCO_2Me$</td>
<td>5.70</td>
<td>-0.20</td>
</tr>
<tr>
<td>$\text{[structure]}CO_2Me$</td>
<td>4.60</td>
<td>-0.20</td>
</tr>
<tr>
<td>$(CH_3O)_2CHCO_2Me$</td>
<td>4.97</td>
<td>3.58</td>
</tr>
<tr>
<td>$CH_3(CH_3O)CHCO_2Me$</td>
<td>4.48$^a$</td>
<td>1.79</td>
</tr>
<tr>
<td>$\text{[structure]}CO_2Me$</td>
<td>4.17</td>
<td>1.69</td>
</tr>
<tr>
<td>$\text{[structure]}CO_2Me$</td>
<td>5.28</td>
<td>3.58</td>
</tr>
<tr>
<td>$\text{[structure]}CO_2Me$</td>
<td>4.68</td>
<td>1.27</td>
</tr>
</tbody>
</table>

$^a$ Ref. 39 extrapolated to 35°.
Nmr Spectrum #1. Methyl N-methylpyrrole-2-carboxylate, sweep width 500 cps.
Nmr Spectrum #2. 2-Vinyl-1,3-dioxolane, a) 500 cps sweep width, b) 100 cps sweep width, 280 cps sweep offset.
Nmr Spectrum #3. Methyl 1,3-dioxolane-2-carboxylate, sweep width 500 cps.
METHYL 2-ETHYL BUTYRATE AT 60 RUN 1

LEAST SQRS. $k = 0.13791E-04 \text{ SEC}^{-1}$  $k_2 = 0.23210E-04 \text{M}^{-1} \text{S}^{-1}$
INTERCEPT 0.36811E-01  STD. DEV. = 0.24031E-01

<table>
<thead>
<tr>
<th>ABSORBANCE</th>
<th>$\ln\left(\frac{(A_1 - A_t)}{(A_i / A_0)}\right)$</th>
<th>RATE $k$ SEC$^{-1}$</th>
<th>TIME SEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.181</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>0.207</td>
<td>0.075045</td>
<td>0.2421E-04</td>
<td>3100.</td>
</tr>
<tr>
<td>0.300</td>
<td>0.401826</td>
<td>0.1740E-04</td>
<td>23100.</td>
</tr>
<tr>
<td>0.408</td>
<td>0.997551</td>
<td>0.1458E-04</td>
<td>68400.</td>
</tr>
<tr>
<td>0.430</td>
<td>1.178934</td>
<td>0.1420E-04</td>
<td>83000.</td>
</tr>
<tr>
<td>0.454</td>
<td>1.423501</td>
<td>0.1396E-04</td>
<td>102000.</td>
</tr>
<tr>
<td>0.541</td>
<td>INF</td>
<td>0.0</td>
<td>INF</td>
</tr>
</tbody>
</table>
METHYL ISOBUTYRATE AT 60, RUN 2

LEAST SQRS. K = 0.58874E-04 SEC-1  K2 = 0.99114E-04 M-1 S-1
INTERCEPT 0.10617E-01  STD. DEV. = 0.13891E-01

<table>
<thead>
<tr>
<th>ABSORBANCE</th>
<th>LN((AI-AT)/(AI/A0))</th>
<th>RATE K SEC-1</th>
<th>TIME SEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.171</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>0.251</td>
<td>0.256317</td>
<td>0.6408E-04</td>
<td>4000.0</td>
</tr>
<tr>
<td>0.266</td>
<td>0.312656</td>
<td>0.5984E-04</td>
<td>5275.0</td>
</tr>
<tr>
<td>0.312</td>
<td>0.508342</td>
<td>0.6378E-04</td>
<td>7970.0</td>
</tr>
<tr>
<td>0.329</td>
<td>0.591593</td>
<td>0.5916E-04</td>
<td>10000.0</td>
</tr>
<tr>
<td>0.349</td>
<td>0.699329</td>
<td>0.5828E-04</td>
<td>12000.0</td>
</tr>
<tr>
<td>0.371</td>
<td>0.833007</td>
<td>0.5950E-04</td>
<td>14000.0</td>
</tr>
<tr>
<td>0.389</td>
<td>0.957460</td>
<td>0.5984E-04</td>
<td>16000.0</td>
</tr>
<tr>
<td>0.525</td>
<td>INF</td>
<td></td>
<td>INF</td>
</tr>
</tbody>
</table>

BASE CONC. = 0.5940  ESTER CONC. = 0.7011  EXT. COEFF. = 105.2
**METHYL ISOBUTYRATE AT 60°C, RUN 3**

LEAST SQRS. K $0.63869 \times 10^{-4}$ SEC$^{-1}$  K2 = $0.10770 \times 10^{-3}$ M$^{-1}$ S$^{-1}$

INTERCEPT $0.47234 \times 10^{-3}$  STD. DEV. = $0.19549 \times 10^{-1}$

<table>
<thead>
<tr>
<th>ABSORBANCE</th>
<th>LN((AI-AT)/(AI/A0))</th>
<th>RATE K SEC$^{-1}$</th>
<th>TIME SEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.172</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>0.242</td>
<td>0.227626</td>
<td>0.6006E-04</td>
<td>3790.0</td>
</tr>
<tr>
<td>0.281</td>
<td>0.381262</td>
<td>0.6501E-04</td>
<td>5865.0</td>
</tr>
<tr>
<td>0.314</td>
<td>0.532685</td>
<td>0.6821E-04</td>
<td>7810.0</td>
</tr>
<tr>
<td>0.328</td>
<td>0.604967</td>
<td>0.6156E-04</td>
<td>9820.0</td>
</tr>
<tr>
<td>0.360</td>
<td>0.791319</td>
<td>0.6382E-04</td>
<td>12400.0</td>
</tr>
<tr>
<td>0.516</td>
<td>INF</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BASE CONC. = 0.5930  ESTER CONC. = 0.6808  EXT. COEFF. = 105.3
The Change in [NaOMe] During the Kinetics of Exchange of Methyl 2-Ethylbutyrate at 60°, Run 1

[NaOMe] calculated = 0.602

<table>
<thead>
<tr>
<th>Time, sec</th>
<th>Absorbance</th>
<th>[NaOMe]</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.181</td>
<td>0.600</td>
</tr>
<tr>
<td>3,100</td>
<td>0.207</td>
<td>0.605</td>
</tr>
<tr>
<td>23,100</td>
<td>0.300</td>
<td>0.595</td>
</tr>
<tr>
<td>68,400</td>
<td>0.408</td>
<td>0.594</td>
</tr>
<tr>
<td>83,000</td>
<td>0.430</td>
<td>0.594</td>
</tr>
<tr>
<td>102,000</td>
<td>0.454</td>
<td>0.593</td>
</tr>
<tr>
<td>171,600</td>
<td>0.460</td>
<td>0.589</td>
</tr>
</tbody>
</table>
**METHYL CYCLOPENTANE CARBOXYLATE AT 60, RUN 1**

LEAST SQRS. $K = 0.20457 \times 10^{-3} \text{ SEC}^{-1}$  $K_2 = 0.45329 \times 10^{-3} \text{ M}^{-1} \text{ S}^{-1}$

INTERCEPT = $-0.9408 \times 10^{-2}$  STD. DEV. = $0.6730 \times 10^{-1}$

<table>
<thead>
<tr>
<th>ABSORBANCE</th>
<th>$\ln\left(\frac{(A_1-A_T)}{(A_1/A_0)}\right)$</th>
<th>RATE K SEC$^{-1}$</th>
<th>TIME SEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.133</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>0.156</td>
<td>0.063548</td>
<td>0.1059E-03</td>
<td>600.0</td>
</tr>
<tr>
<td>0.218</td>
<td>0.258183</td>
<td>0.1721E-03</td>
<td>1500.0</td>
</tr>
<tr>
<td>0.300</td>
<td>0.592509</td>
<td>0.2469E-03</td>
<td>2400.0</td>
</tr>
<tr>
<td>0.340</td>
<td>0.807756</td>
<td>0.1923E-03</td>
<td>4200.0</td>
</tr>
<tr>
<td>0.383</td>
<td>1.106405</td>
<td>0.2169E-03</td>
<td>5100.0</td>
</tr>
<tr>
<td>0.389</td>
<td>1.156188</td>
<td>0.1927E-03</td>
<td>6000.0</td>
</tr>
<tr>
<td>0.507</td>
<td>INF</td>
<td>INF</td>
<td>INF</td>
</tr>
</tbody>
</table>

BASE CONC. = 0.4513  ESTER CONC. = 0.7330  EXT. COEFF. = 106.1
The Change in $[\text{NaOMe}]$ During the Kinetics of Exchange of Methyl Cyclopentanecarboxylate at $60^\circ$, Run 1

$[\text{NaOMe}]$ calculated $= 0.496$

<table>
<thead>
<tr>
<th>Time, sec</th>
<th>Absorbance</th>
<th>$[\text{NaOMe}]$</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.133</td>
<td>0.451</td>
</tr>
<tr>
<td>600</td>
<td>0.156</td>
<td>0.451</td>
</tr>
<tr>
<td>30,000</td>
<td>0.502</td>
<td>0.471</td>
</tr>
</tbody>
</table>
METHYL DIMETHOXYACETATE AT 60°

LEAST SQRS. K 0.83236E-04 SEC-1  K2= 0.15861E-03M-1 S-1
INTERCEPT 0.19963E-01 STD. DEV.= 0.10383E-01

<table>
<thead>
<tr>
<th>ABSORBANCE</th>
<th>LN((AI-AT)/(AI/AD))</th>
<th>RATE K SEC-1</th>
<th>TIME SEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.202</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>0.272</td>
<td>0.271870</td>
<td>0.9710E-04</td>
<td>2800.</td>
</tr>
<tr>
<td>0.295</td>
<td>0.380180</td>
<td>0.8841E-04</td>
<td>4300.</td>
</tr>
<tr>
<td>0.318</td>
<td>0.501662</td>
<td>0.8649E-04</td>
<td>5800.</td>
</tr>
<tr>
<td>0.340</td>
<td>0.633543</td>
<td>0.8679E-04</td>
<td>7300.</td>
</tr>
<tr>
<td>0.360</td>
<td>0.770687</td>
<td>0.8563E-04</td>
<td>9000.</td>
</tr>
<tr>
<td>0.374</td>
<td>0.879271</td>
<td>0.9374E-04</td>
<td>10500.</td>
</tr>
<tr>
<td>0.496</td>
<td>INF</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

BASE CONC.=0.5248  ESTER CONC.=0.5789  EXT. CCEFF.= 105.7
METHYL TETRAHYDROFURANCARBOXYLATE AT 60, RUN 1

LEAST SQRS. K 0.30964E-03 SEC-1  \( K_2 = 0.68809E-03 M^{-1} S^{-1} \)
INTERCEPT 0.54664E-02 STD. DEV. = 0.33837E-01

<table>
<thead>
<tr>
<th>ABSORBANCE</th>
<th>( \ln((AI-A_T)/(AI/A_0)) )</th>
<th>RATE K SEC-1</th>
<th>TIME SEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.130</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>0.242</td>
<td>0.318953</td>
<td>0.3544E-03</td>
<td>900.0</td>
</tr>
<tr>
<td>0.287</td>
<td>0.482584</td>
<td>0.2839E-03</td>
<td>1700.0</td>
</tr>
<tr>
<td>0.360</td>
<td>0.822824</td>
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<tr>
<td>0.424</td>
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<td>0.3078E-03</td>
<td>4100.0</td>
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<tr>
<td>0.455</td>
<td>1.572382</td>
<td>0.3145E-03</td>
<td>5000.0</td>
</tr>
<tr>
<td>0.540</td>
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</table>

BASE CONC. = 0.4500  ESTER CONC. = 0.8069  EXT. COEFF. = 106.1
The Change in $[\text{NaOMe}]$ During the Kinetics of Exchange of Methyl Tetrahydrofuran-2-Carboxylate at 60°, Run 2

<table>
<thead>
<tr>
<th>Time, sec</th>
<th>Absorbance</th>
<th>$[\text{NaOMe}]$</th>
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<tbody>
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<td>0</td>
<td>0.130</td>
<td>0.443</td>
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<tr>
<td>900</td>
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<td>0.4318</td>
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<td>0.424</td>
<td>0.450</td>
</tr>
<tr>
<td>24,100</td>
<td>0.502</td>
<td>0.447</td>
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METHYL 1,3-DIOXOLANE-2-CARBOXYLATE AT 60, RUN 1

LEAST SQRS. K 0.34717E-04 SEC-1 K2 = 0.55547E-04 M-1 S-1
INTERCEPT 0.34673E-01 STD. DEV.= 0.37325E-01

<table>
<thead>
<tr>
<th>ABSORBANCE</th>
<th>LN((AI-AT)/(AI/A0))</th>
<th>RATE K SEC-1</th>
<th>TIME SEC</th>
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<tbody>
<tr>
<td>0.145</td>
<td>0.0</td>
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<td>0.259</td>
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<tr>
<td>0.302</td>
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<td>0.788423</td>
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<td>0.397</td>
<td>1.062840</td>
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<tr>
<td>0.530</td>
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METHYL N-METHYLPYRROLINE-2-CARBOXYLATE AT 60 RUN 3

LEAST SQRS, K 6.2531E-04 SEC-1  K2= 6.13594E-03M-1 S-1
INTERCEPT 6.15630E-01 STD. DEV.= 6.17193E-01

<table>
<thead>
<tr>
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<th>RATE K SEC-1</th>
<th>TIME SEC</th>
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<tbody>
<tr>
<td>0.253</td>
<td>0.0</td>
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<td>0.0</td>
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<tr>
<td>0.334</td>
<td>0.206714</td>
<td>6.6668E-04</td>
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<tr>
<td>0.426</td>
<td>0.508920</td>
<td>6.877E-04</td>
<td>7400.0</td>
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<tr>
<td>0.440</td>
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<td>10000.0</td>
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<tr>
<td>0.477</td>
<td>0.726575</td>
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<tr>
<td>0.494</td>
<td>0.811101</td>
<td>6.192E-04</td>
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<tr>
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BASE CONC.=0.4600  ESTER CONC.=0.8637  EXT. COEFF.= 106.0
METHYL-N-METHYL PYRROLINE-2-CARBOXYLATE AT 60, RUN 2

LEAST SQRS. K 0.61632E-04 SEC-1 K2= 0.13794E-03M-1 S-1
INTERCEPT 0.10267E-01 STD. DEV.= 0.19982E-01

<table>
<thead>
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<th>LN((AI-AT)/(AI/0))</th>
<th>RATE K SEC-1</th>
<th>TIME SEC</th>
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<tbody>
<tr>
<td>0.323</td>
<td>0.0</td>
<td>0.0</td>
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<tr>
<td>0.361</td>
<td>0.148685</td>
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<tr>
<td>0.367</td>
<td>0.174323</td>
<td>0.6226E-04</td>
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<td>0.400</td>
<td>0.328443</td>
<td>0.6440E-04</td>
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</tr>
<tr>
<td>0.426</td>
<td>0.469183</td>
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</tr>
<tr>
<td>0.441</td>
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<td>13430.0</td>
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<tr>
<td>0.598</td>
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</table>

BASE CONC. = 0.4468    ESTER CONC. = 0.5432    EXT. COEFF. = 106.1
**METHYL ISOBUTYRATE AT 35, RUN 1**

**LEAST SQRS. K** 0.53554E-05 SEC-1  
**K2** = 0.97797E-05 M-1 S-1  
**INTERCEPT** 0.55723E-03  
**STD. DEV.** = 0.14533E-01

<table>
<thead>
<tr>
<th>ABSORBANCE</th>
<th>LN((AI-AT)/(AI/DO))</th>
<th>RATE K SEC-1</th>
<th>TIME SEC</th>
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<tbody>
<tr>
<td>0.218</td>
<td>0.0</td>
<td>0.6378E-05</td>
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<tr>
<td>0.231</td>
<td>0.026891</td>
<td>0.6609E-05</td>
<td>10550.0</td>
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<tr>
<td>0.251</td>
<td>0.069728</td>
<td>0.4971E-05</td>
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<td>0.270</td>
<td>0.112193</td>
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<tr>
<td>0.286</td>
<td>0.149416</td>
<td>0.5841E-05</td>
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</tr>
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<td>0.708</td>
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</table>

**BASE CONC.** = 0.5476  
**ESTER CONC.** = 0.9826  
**EXT. COEFF.** = 105.5
**METHYL ISOBUTYRATE AT 35 RUN 2**

LEAST SQRS. K = 0.55397E-05 SEC-1  K2 = 0.10129E-04M-1 S-1
INTERCEPT = 0.29128E-02  STD. DEV. = 0.10151E-01

<table>
<thead>
<tr>
<th>ABSORBANCE</th>
<th>LN((AI-AT)/(AI/A0))</th>
<th>RATE K SEC-1</th>
<th>TIME SEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.192</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>0.268</td>
<td>0.314622</td>
<td>0.5848E-05</td>
<td>53800.</td>
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<tr>
<td>0.298</td>
<td>0.472388</td>
<td>0.5568F-05</td>
<td>84840.</td>
</tr>
<tr>
<td>0.304</td>
<td>0.507164</td>
<td>0.5431E-05</td>
<td>93390.</td>
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<tr>
<td>0.324</td>
<td>0.632682</td>
<td>0.5502E-05</td>
<td>115000.</td>
</tr>
<tr>
<td>0.342</td>
<td>0.760927</td>
<td>0.5636F-05</td>
<td>135000.</td>
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<tr>
<td>0.474</td>
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</table>

BASE CONC. = 0.5469  ESTER CONC. = 0.5540  EXT. COEFF. = 105.5
METHYL 2-ETHYLBUTYRATE AT 35

LEAST SQRS. K = 0.10963E-05 SEC-1  
K2 = 0.19747E-05 M-1 S-1

INTERCEPT = 0.51638F-02  
STD. DEV. = 0.26080E-01

<table>
<thead>
<tr>
<th>ABSORBANCE</th>
<th>LN((AI - AT) / (AI / AO))</th>
<th>RATE K SEC-1</th>
<th>TIME SEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.127</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>0.169</td>
<td>0.112630</td>
<td>0.1009E-05</td>
<td>111600</td>
</tr>
<tr>
<td>0.230</td>
<td>0.302763</td>
<td>0.1136E-05</td>
<td>266400</td>
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<tr>
<td>0.277</td>
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<td>422100</td>
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<tr>
<td>0.295</td>
<td>0.555261</td>
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</tr>
<tr>
<td>0.336</td>
<td>0.755152</td>
<td>0.1049E-05</td>
<td>720000</td>
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<tr>
<td>0.388</td>
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<tr>
<td>0.521</td>
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</table>

BASE CONC. = 0.5552  
ESTER CONC. = 0.7794  
EXT. COEFF. = 105.5
**METHYL CYCLOPENTANE CARBOXYLATE AT 35, RUN 1**

LEAST SQRs. $k = 0.14403E-04$ SEC$^{-1}$ $k_2 = 0.24949E-04$ M$^{-1}$ SEC$^{-1}$

INTERCEPT $0.17357E-01$ STD. DEV. $= 0.37789E-01$

<table>
<thead>
<tr>
<th>ABSORBANCE</th>
<th>LN((AI-AT)/(AI/AO))</th>
<th>RATE $k$ SEC$^{-1}$</th>
<th>TIME SEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.209</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>0.236</td>
<td>0.064508</td>
<td>0.1361E-04</td>
<td>4740.0</td>
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<tr>
<td>0.261</td>
<td>0.128192</td>
<td>0.1291E-04</td>
<td>9930.0</td>
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<tr>
<td>0.341</td>
<td>0.364445</td>
<td>0.1778E-04</td>
<td>20500.0</td>
</tr>
<tr>
<td>0.367</td>
<td>0.455038</td>
<td>0.1477E-04</td>
<td>30800.0</td>
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<tr>
<td>0.400</td>
<td>0.583272</td>
<td>0.1538E-04</td>
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</tr>
<tr>
<td>0.440</td>
<td>0.764604</td>
<td>0.1590E-04</td>
<td>48100.0</td>
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<tr>
<td>0.495</td>
<td>1.033937</td>
<td>0.1399E-04</td>
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<tr>
<td>0.641</td>
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</table>

BASE CONC. = 0.5773  ESTER CONC. = 0.8636  EXT. COEFF. = 105.3
METHYL DIMETHOXYACETATE AT 35

LEAST SQRS. $K = 0.41986E-05$ SEC$^{-1}$  
$K_2 = 0.10240E-04$ M$^{-1}$ SEC$^{-1}$

INTERCEPT $0.22222E-01$  
STD. DEV. $= 0.13159E-01$

<table>
<thead>
<tr>
<th>ABSORBANCE</th>
<th>$\ln((A_1 - A_T)/(A_1/A_0))$</th>
<th>RATE $K$ SEC$^{-1}$</th>
<th>TIME SEC</th>
</tr>
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<tbody>
<tr>
<td>0.200</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
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<tr>
<td>0.250</td>
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<td>0.318</td>
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<td>0.4875E-05</td>
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<td>0.334</td>
<td>0.409682</td>
<td>0.4377E-05</td>
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<td>0.402</td>
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<td>0.460</td>
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<td>0.599</td>
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<td>INF</td>
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</table>

BASE CONC.$= 0.4100$  
ESTER CONC.$= 0.7860$  
EXT. COEFF.$= 106.3$
The Change in [NaOMe] During the Kinetics of Exchange of Methyl Dimethoxyacetate at 35°

[NaOMe] calculated = 0.580

<table>
<thead>
<tr>
<th>Time, sec.</th>
<th>Absorbance</th>
<th>[NaOMe]</th>
</tr>
</thead>
<tbody>
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<td>25,200</td>
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<tr>
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<td>0.318</td>
<td>0.395</td>
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<td>162,000</td>
<td>0.402</td>
<td>0.407</td>
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<tr>
<td>248,400</td>
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<td>0.437</td>
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METHYL TETRAHYDROFURANCARBOXYLATE AT 35, RUN 1

LEAST SQRS. K = 0.31588E-04 SEC-1  K2 = 0.67309E-04M-1 S-1
INTERCEPT = 0.85334E-02 STD. DEV. = 0.45413E-01

<table>
<thead>
<tr>
<th>ABSORBANCE</th>
<th>LV((AI-AT)/(AI/A0))</th>
<th>RATE K SEC-1</th>
<th>TIME SEC</th>
</tr>
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<tbody>
<tr>
<td>0.226</td>
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<td>0.0</td>
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<tr>
<td>0.267</td>
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<td>0.2338E-04</td>
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<tr>
<td>0.283</td>
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<td>0.2461E-04</td>
<td>6075.5</td>
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<tr>
<td>0.347</td>
<td>0.349235</td>
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<tr>
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<td>0.2972E-04</td>
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<td>20500.6</td>
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<tr>
<td>0.450</td>
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<td>0.2887E-04</td>
<td>27325.6</td>
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<tr>
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BASE CONC. = 0.4693  ESTER CONC. = 0.8146  EXT. COEFF. = 106.0
**METHYL 1,3-DIOXOLANE-2-CARBOXYLATE AT 35°C, RUN 1**

**LEAST SQRS.**
- $k = 0.30825 \times 10^{-5} \text{ SEC}^{-1}$
- $k_2 = 0.54693 \times 10^{-5} \text{ M}^{-1} \text{ S}^{-1}$
- Intercept = $0.12503 \times 10^{-1}$
- Std. Dev. = $0.30756 \times 10^{-1}$

**ABSORBANCE** | $\ln\left(\frac{A_1 - A_t}{A_1/A_0}\right)$ | RATE $k$ SEC$^{-1}$ | TIME SEC
---|---|---|---
0.180 | 0.0 | 0.0 | 0.0
0.194 | 0.035949 | 0.2820E-05 | 12750
0.242 | 0.170049 | 0.2743E-05 | 62000
0.273 | 0.267311 | 0.2792E-05 | 95750
0.314 | 0.412457 | 0.2703E-05 | 152600
0.360 | 0.605130 | 0.3273E-05 | 184900
0.576 | INF | INF | INF

**BASE CONC.** = 0.5636  **ESTER CONC.** = 0.7875  **EXT. COEFF.** = 105.4
METHYL 1,3-DIOXOLANE-2-CARBOXYLATE AT 35, RUN 2

LEAST SQRS. K = 0.1878E-05 SEC^-1 \( K_2 = 0.51698E-05 \) M^-1 S^-1
INTERCEPT = -0.11943E-01
STD. DEV. = 0.14794E-01

<table>
<thead>
<tr>
<th>ABSORBANCE</th>
<th>LN(( (A_I - A_T) / (A_I / A_0) ))</th>
<th>RATE K SEC^-1</th>
<th>TIME SEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.232</td>
<td>0.0</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>0.238</td>
<td>0.014470</td>
<td>0.7459E-06</td>
<td>19400</td>
</tr>
<tr>
<td>0.281</td>
<td>0.124796</td>
<td>0.1760E-05</td>
<td>70900</td>
</tr>
<tr>
<td>0.334</td>
<td>0.280011</td>
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<td>160950</td>
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<tr>
<td>0.338</td>
<td>0.292764</td>
<td>0.1302E-05</td>
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<td>0.355</td>
<td>0.348857</td>
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<td>199150</td>
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<tr>
<td>0.384</td>
<td>0.452466</td>
<td>0.1849E-05</td>
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<tr>
<td>0.410</td>
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<td>0.1949E-05</td>
<td>285050</td>
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<tr>
<td>0.419</td>
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</tbody>
</table>

BASE CONC. = 0.3634 Est. ESTER CONC. = 0.8245 Ext. COEFF. = 106.6
METHYL N-METHYLPOYRROLINE-2-CARBOXYLATE AT 35 RUN 1

LEAST SQRS. \( K = 0.82868E-05 \) SEC\(^{-1} \) \( K_2 = 0.20707E-04 \) M\(^{-1}\) S\(^{-1} \)

INTERCEPT \( 0.29921E-02 \) STD. DEV. = \( 0.16520E-02 \)

<table>
<thead>
<tr>
<th>ABSORBANCE</th>
<th>( \ln \left( \frac{A_1 - A_T}{A_1/A_0} \right) )</th>
<th>RATE K SEC(^{-1} )</th>
<th>TIME SEC</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.259</td>
<td>( 0.0 )</td>
<td>( 0.0 )</td>
<td>0.0</td>
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<tr>
<td>0.309</td>
<td>( 0.164205 )</td>
<td>( 0.8620E-05 )</td>
<td>19050.</td>
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<td>0.413</td>
<td>( 0.628127 )</td>
<td>( 0.8342E-05 )</td>
<td>75300.</td>
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<td>0.425</td>
<td>( 0.698669 )</td>
<td>( 0.8322E-05 )</td>
<td>83950.</td>
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<td>0.438</td>
<td>( 0.781160 )</td>
<td>( 0.8310E-05 )</td>
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<td>0.453</td>
<td>( 0.885653 )</td>
<td>( 0.8308E-05 )</td>
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<tr>
<td>0.589</td>
<td>INF</td>
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<td>INF</td>
</tr>
</tbody>
</table>

BASE CONC. = 0.4002 FSTER CONC. = 0.6500 EXT. COEFF. = 106.4
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PART I


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